

**AWARD NUMBER:** W81XWH-18-2-0059

**TITLE:** A Phase 1 Randomized, Placebo-Controlled, Single Ascending Dose Study to Examine the Safety, Tolerability, and Pharmacokinetics of cP12 in Healthy Adults

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**CONTRACTING ORGANIZATION:** NeoMatrix Therapeutics, Inc., Stony Brook, NY

**REPORT DATE:** January 2023

**TYPE OF REPORT:** Final

**PREPARED FOR:** U.S. Army Medical Research and Development Command  
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| 14. ABSTRACT<br>The overall objective of this proposal is to assess the safety and tolerability of single ascending intravenous doses of cP12 in healthy subjects. This is a randomized double-blind, placebo-controlled single ascending dose study to evaluate the safety, tolerability, and pharmacokinetic profile of cP12 in healthy male and female subjects. Each subject is randomized to receive either a single dose of cP12 or placebo. Initial IRB, FDA and HRPO approval was given to recruit and screen subjects for 4 Cohorts (n=32) plus an option Cohort 5 (n=8) to be given a dose equal to, or less than, the dose given to Cohort 4. Cohorts 1-4 have been completed and no SAE's were noted. We submitted Amendment 4 to give a higher dose in Cohort 5 to the IRB and received approval (Amendments 1-3 were minor and did not need approvals). We then submitted Amendment 4 to the FDA and have received no comments after two months. Amendment 4 was submitted to HRPO December 30, 2019 and received approval on January 7, 2020. We plan to conduct Cohort 5 in February 2020. |                             |                              |                                                |                                          |                                            |
| 15. SUBJECT TERMS<br>None listed.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                             |                              |                                                |                                          |                                            |
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## 1. INTRODUCTION:

The overall objective of this proposal is to assess the safety and tolerability of single ascending intravenous (IV) doses of cP12 in healthy subjects. This was a randomized double-blind, placebo-controlled single ascending dose (SAD) study to evaluate the safety, tolerability, and PK profile of cP12 in healthy male and female subjects. Each subject was randomized to receive either a single dose of cP12 or placebo.

(see Attachment 1 for Phase 1 Clinical Trial Protocol and Attachment 2 for Informed Consent)

## 2. KEYWORDS:

Phase 1 Clinical Trial, safety, tolerability, pharmacokinetics, peptide, burn, intravenous therapy, Chemistry Manufacturing and Controls (CMC), Investigational New Drug (IND), Adverse Reactions (AEs)

## 3. ACCOMPLISHMENTS:

What were the major goals of the project?

**Specific Aim 1: Develop and validate bioanalytic assay for cP12 assay in human plasma and urine (months 1-24) UPDATE Status of all tasks below as needed.**

**Major Task 1: Development and Validation of cP12 Assay in Human Plasma. Months 1-6.**

Task 1.1: Set-up of HPLC/MS/MS Human Plasma Assay. Months 1-3. 100%

- STATUS: COMPLETED, MONTH 0. 100%

Task 1.2: Write Validation protocol. Months 1-3. 100%

- STATUS: COMPLETED, MONTH 1. 100%

Task 1.3: Validation of Human Plasma Assay. Months 4-6. 100%

- STATUS: COMPLETED, MONTH 3. 100%

Task 1.4: One-month frozen sample stability at -70°C and -20°C. Months 4-6.

- STATUS: COMPLETED, MONTH 3. 100%

Task 1.5: Audited Validation Report. Months 4-6.

- STATUS: COMPLETED, MONTH 6. 100%

Task 1.6: Extended Human Plasma Stability to 6 months.

- STATUS: COMPLETED, MONTH 10. 100%

Task 1.7: Extended Human Plasma Stability Report.

- STATUS: COMPLETED, MONTH 11. 100%

**Milestone Achieved: Development & Validation of cP12 Assay in Human Plasma. Month 6.**

- STATUS: COMPLETED, MONTH 6.

**Major Task 2: Development and Validation of cP12 Assay in Human Urine. Months 1-6.**

Task 2.1: Set-up of HPLC/MS/MS Human Urine Assay. Months 1-3.

- STATUS: COMPLETED, MONTH 0. 100%

Task 2.2: Write Validation protocol. Months 1-3.

- STATUS: COMPLETED, MONTH 1. 100%

Task 2.3: Validation of Human Urine Assay. Months 4-6.

- STATUS: COMPLETED, MONTH 2. 100%

Task 2.4: One-month frozen sample stability at -70°C and -20°C. Months 4-6.

- STATUS: COMPLETED, MONTH 5. 100%

Task 2.5: Audited Validation Report. Months 4-6.

- STATUS: COMPLETED, MONTH 5. 100%

Task 2.6: Extended Human Urine Stability to 6 months.

- STATUS: COMPLETED, MONTH 10. 100%

Task 2.7: Extended Human Urine Stability Report.

- STATUS: COMPLETED, MONTH 11. 100%

**Milestone Achieved: Development & Validation of cP12 Assay in Human Urine. Month 5**

- STATUS: COMPLETED, MONTH 5.

**~~Major Task 3: Development and Validation of cP12 Assay in Dosing Solutions.~~**

- STATUS: Deleted as not required.

**Major Task 4: Pharmacokinetic cP12 assays of Human Plasma samples and Human Urine samples. Months 13-31**

Task 4.1: Analysis of human plasma and urine samples. Months 13-24.

- STATUS: Complete: Plasma and urine analysis for Cohorts 1-5 have been analyzed.

Task 4.2: If appropriate reanalysis will be performed. Months 14-24.

- STATUS: Complete.

Task 4.3: Incurred Sample Reproducibility. Months 13-24.

- STATUS: Complete.

Task 4.4: Sample storage. Months 13-30.

- STATUS: Complete.

Task 4.5: Sample disposal. Months 31.

- STATUS: No sample disposal.

Task 4.6: If appropriate Expedited analysis will be performed. Months 13-24.

- STATUS: Complete.

**Milestone Achieved: Analyses of all samples completed and results relayed to Celerion. Month 24**

- STATUS: Complete. Data were locked by Celerion on April 2, 2020

## **Specific Aim 2: IRB and HRPO submission and approval (months 1-9)**

### **Major Task 5: IRB Approval.**

Task 5.1: Submit Protocol, Informed consent form and Investigator Brochure to IRB. Month 1.

- STATUS: COMPLETED, MONTH 0.

Task 5.2: Respond to IRB comments. Month 2.

- STATUS: COMPLETED, MONTH 0.

### **Milestone Achieved: IRB approval. Month 3.**

- STATUS: COMPLETED, MONTH 0.
- Approval of Protocol Amendment 1 (minor) – 10 July 2018
- Approval of Protocol Amendment 2 (minor) – 25 February 2019
- Approval for Continuing Review – 9 July 2019
- Approval of Protocol Amendment 3 (minor) – 12 July 2019
- Approval of Protocol Amendment 4 (major) – 29 October 2019

### **Major Task 6: HRPO Approval.**

Task 6.1: Submit Protocol, Informed consent form & Investigator Brochure to HRPO. Month 3.

- STATUS: COMPLETED, MONTH 1.

Task 6.2: Respond to HRPO comments. Months 3-6.

- STATUS: COMPLETED, MONTH 4.

-

### **Milestone Achieved: HRPO approval. Month 6**

- STATUS: COMPLETED, MONTH 5.
- HRPO notified of IRB approval of Continuing Review July 9, 2019- Renewal approval, Expiration July 5, 2020
- STATUS: USAMRMC HRPO renewal approval: Not needed as study is complete.
- Protocol Amendment 4 submitted and approval received January 7, 2020.

### **Major Task 7: Obtain FDA approval of any required changes.**

Task 7.1: Submit Amended Protocol, Informed Consent Form and Investigator Brochure to FDA. Month 6-7.

- STATUS: FDA submission, April 3, 2019. Month 7.
- FDA submission of Protocol Amendment 4 – Nov 13 – Dec 13 2019.

Task 7.2: Respond to FDA comments. Month 8.

- STATUS: No comments

### **Milestone Achieved: FDA approval. Month 9**

- STATUS: Complete.

**Specific Aim 3: Study design for first-in-human study to assess safety in humans of IV delivered cP12 (months 10-18)**

**Major Task 8: Recruit and Screen Subjects.**

Task 8.1: Subject Recruitment (N=40). Months 10-18

- STATUS: Complete.

Task 8.2: Subject Screening. Months 10-18

- STATUS: Complete.

**Milestone Achieved: All subjects needed for study recruited and screened. Month 16**

- STATUS: Completed.

**Major Task 9: Conduct Clinical Trial of lowest (0.003mg/kg) cP12 dose.**

Task 9.1: Test lowest cP12 dose (0.003mg/kg) in sentinel pair (one drug, one placebo). Month 10.

- STATUS: Dosing Complete.

Task 9.2: If appropriate. test 0.003mg/kg cP12 dose in six additional subjects (5 receiving cP12 dose, 1 receiving placebo). Month 10.

- STATUS: Infusion Complete, Safety data reviewed by Safety Review Committee. No concerns.

**Milestone Achieved: 0.003mg/kg cP12 dose safe in 6 test subjects compared to 2 placebo controls. Month 10**

- STATUS: Dosing completed on July 9, 2019.
- Safety Review Committee Meeting occurred on 19 July 2019. Dose escalation approved.

**Major Task 10: Conduct Clinical Trial of presumptive optimal cP12 dose**

Task 10.1: Test presumptive optimal cP12 dose (0.01mg/kg) in sentinel pair (one drug, one placebo). Month 11

- STATUS: Dosing Complete, Month 10.

Task 10.2: If appropriate. test 0.01 mg/kg cP12 dose in six additional subjects (5 receiving cP12 dose, 1 receiving placebo). Months 11-12

- STATUS: Infusion Complete, Safety data reviewed by Safety Review Committee. No concerns.

**Milestone Achieved: 0.01mg/kg cP12 dose safe in 6 test subjects compared to 2 placebo controls. Month 13**

- STATUS: Dosing completed on July 26, 2019
- Safety Review Committee Meeting occurred on August 7, 2019. Dose escalation approved.

**Major Task 11: Conduct Clinical Trial of 0.02mg/kg cP12 dose**

Task 11.1: Test next cP12 dose (0.02mg/kg) in sentinel pair (one drug, one placebo). Month 17

- STATUS: Dosing Complete, Month 11.

Task 11.2: If appropriate test 0.02 mg/kg cP12 dose in six additional subjects (5 receiving cP12 dose, 1 receiving placebo). Month 19

- STATUS: Dosing Completed August 13, 2019, Month 11.

***Milestone Achieved: 0.02mg/kg cP12 dose safe in 6 test subjects compared to 2 placebo controls. Month 19.***

- STATUS: Safety Review Committee Meeting occurred on August 21, 2019. Dose escalation approved.

**Major Task 12: Conduct Clinical Trial of 0.04mg/kg cP12 dose**

Task 12.1: Test highest dose cP12 dose (0.04mg/kg) in sentinel pair (one drug, one placebo).

Month 20

- STATUS: Dosing Complete, Month 11.

Task 12.2: If appropriate. test 0.04 mg/kg cP12 dose in six additional subjects (5 receiving cP12 dose, 1 receiving placebo). Month 22

- STATUS: Dosing Completed August 30, 2019, Month 11.

***Milestone Achieved: 0.04mg/kg cP12 dose safe in 6 test subjects compared to 2 placebo controls. Month 22***

- STATUS: Safety Review Committee Meeting occurred on September 11, 2019. Dose escalation approved for Cohort 5.

**Major Task 13: Conduct Clinical Trial of Optional Cohort**

Task 13.1: Test additional/repeat cP12 dose in sentinel pair (one drug, one placebo). Month 23

- STATUS: Dosing complete.

Task 13.2: If appropriate, test additional/repeat cP12 dose in six additional subjects. (5 receiving cP12 dose, 1 receiving placebo). Month 25

Note: Protocol Amendment 4; Cohort 5 to be tested with 0.08mg/kg cP12 in 6 test subjects compared to 2 placebo Controls. IRB approval received, FDA submission (Nov 13- Dec 13, 2019) no comments received, HRPO submission December 30, 2019, HRPO approval January 7, 2020.

- STATUS: Dosing completed February 2020, Month 14.

***Milestone Achieved: Additional/repeat cP12 dose safe in 6 test subjects compared to 2 placebo controls. Month 25***

- STATUS: Dosing completed on February 21, 2020. Month 14.

**Major Task 14: Biometrics of all data collected from Clinical Trial**

Task 14.1: PK Analysis. Month 13-26.

- STATUS: Clinical Study Report completed July 2020.

Task 14.2: Statistical Data Analysis and Summarization. Month 27-30.

- STATUS: Completed

Task 14.3: Celerion formatted Clinical Study Report. Month 31-32

- STATUS: Completed

***Milestone to Achieve: Biometrics completed of all collected data from Clinical Trial. Month 32.***

- STATUS: Completed July 2020



**Specific Aim 4: Submit clinical study report to FDA (months 10-30)**

**Major Task 15: Data capture, verification and disposition**

Task 15.1: Data capture. Months 10-25.

- STATUS: Complete: Database lock on April 2, 2020

Task 15.2: Data verification. Month 10-26.

- STATUS: Complete: Database lock on April 2, 2020

Task 15.3: Data disposition. Month 27-30.

Complete: Database lock on April 2, 2020

**Milestone Achieved: Data capture, verification and disposition completed. Month 30.**

- STATUS: Complete: Database lock on April 2, 2020

**Major Task 16: Report formatted for FDA submission to the IND**

Task 16.1: Report formatted for FDA submission. Months 30-32.

- STATUS: Clinical Study Report published July 2020

Task 16.2: Clinical Study Report submitted to the IND. Month 32.

- STATUS: Complete September 19, 2020 (Month 24)

**Milestone Achieved: Clinical Study Report submitted to FDA IND - Month 32.**

- STATUS: Clinical Study Report submitted to FDA IND - Month 24

**(see Attachment 3 for Clinical Study Report)**

**Specific Aim 5: Request Fast Track & Develop Phase 2a clinical trial protocol (months 1-12)**

**Major Task 17: Fast Track Designation (FTD)**

Task 17.1: Request and prepare Briefing Package for FDA meeting regarding Fast Track Designation. Month 1.

- STATUS: Fast Track application sent to FDA 5 March 2019 (Month 5)

Task 17.2: Respond to FDA comments.

- STATUS: Response not needed: received FTD, May 11, 2019 (Month 7.5)

**Milestone Achieved: Fast Track Designation received. Month 3.**

- STATUS: Month 7.5, complete

**(see Attachment 4 for Fast Track Designation)**

**Major Task 18: Develop Phase 2a Clinical Trial Protocol**

Task 18.1: Prepare Briefing Package for FDA meeting regarding Phase 2a Clinical Trial Design. ~~Month 3. This subtask should have been Month 30-32 as it could not have been done until the Clinical Study Report (Major Task 16) was complete (Month 24).~~ Therefore, the initial Phase 2a protocol was submitted to the FDA with the Briefing Package requesting an End of Phase 1 meeting (EOP1) on May 7, 2021.

- STATUS: Completed Month 31

~~Task 18.2: Respond to FDA comments. Month 3-6~~ Response occurs after the EOP1 meeting, which includes the Phase 2a guidance meeting. (See Task 18.3 below).

- STATUS: not performed as redundant with Task 18.4.

Task 18.3: ~~Type C~~ Phase 2a Guidance Meeting schedule and attended. This meeting is actually part of the EOP1 meeting.

FDA meeting minutes were received on August 12, 2021. The FDA advised that a small Phase 2a safety study in outpatients with 5% or less Total Body Surface Area (TBSA) burns be completed and approved prior to a Phase 2 study in hospitalized patients with 5-20% TBSA burns as we had proposed as the initial "Phase 2a" CT protocol.

During the EOP1 meeting the FDA continued to articulate the need of a small Phase 2a Safety Study with 5-15 subjects with 5% Total Body Surface Area burns of which some percentage is Partial Thickness Burns. A follow-on inpatient Phase 2b Study for Safety and Efficacy, as we previously planned for the Phase 2a CT, would be performed after the outpatient Phase 2a CT.

- STATUS: NMT had its End of Phase 1 (EOP1) meeting with the FDA on June 28<sup>th</sup> 2021. Completed Month 33.

(see Attachment 5 for FDA EOP1 meeting minutes)

Task 18.4: Respond to FDA comments from Phase 2a Guidance Meeting. ~~Month 9-12~~. This subtask completion target was changed to Month 36. However, such a study as the FDA recommended has never been done in outpatient; therefore, it took over a year to design and write this novel protocol. Therefore, NMT requested and received a one year NCE.

- STATUS: The new novel Phase 2a CT protocol was completed and submitted to the IND on September 26, 2022. Completed Month 48

***Milestone to Achieve: Phase 2a Clinical Trial Design Amended and writing of full Phase 2a protocol to proceed. ~~Month 12~~. Month 48***

(see Attachment 6 for new Phase 2a CT protocol)

**Major Task 19. This is a new task. It was noted that prior to a Phase 2a Clinical Trial, a rat micronucleus study is required by I.C.H. and FDA.**

Task 19.1: Draft protocol and submit to ACURO for review and approval.

- STATUS: ACURO approval received 11 June 2021, Month 33

Task 19.2: Complete Study and analysis (1 month) and obtain draft report (12-15 weeks). Month 35-36.

- STATUS: Study was completed (7/28/21). A draft report was received 9/20/21 for NMT review. The final report completed Month 36.

***Milestone to Achieve: Rat micronucleus study, data analysis and final report completed. ~~Month 35-36~~. Month 36.***

(see Attachment 7 for rat micronucleus study report)

**What was accomplished under these goals?**

***Key Findings or Accomplishments:***

**Major Task 18: Develop Phase 2a Clinical Trial Protocol**

Task 18.1: Prepare Briefing Package for FDA meeting regarding Phase 2a Clinical Trial Design. ~~Month 3.~~ **This subtask should have been Month 30-32 as it could not have been done until the Clinical Study Report (Major Task 16) was complete (Month 24).** Therefore, the initial Phase 2a protocol was submitted to the FDA with the Briefing Package requesting an End of Phase 1 meeting (EOP1) on May 7, 2021.

- STATUS: Completed Month 31

~~Task 18.2: Respond to FDA comments. Month 3-6~~ Response occurs after the EOP1 meeting, which includes the Phase 2a guidance meeting. (See Task 18.3 below).

- STATUS: not performed as redundant with Task 18.4.

Task 18.3: ~~Type C~~ Phase 2a Guidance Meeting schedule and attended. This meeting is actually part of the EOP1 meeting.

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During the EOP1 meeting the FDA continued to articulate the need of a small Phase 2a Safety Study with 5-15 subjects with 5% Total Body Surface Area burns of which some percentage is Partial Thickness Burns. A follow-on inpatient Phase 2b Study for Safety and Efficacy, as we previously planned for the Phase 2a CT, would be performed after the outpatient Phase 2a CT.

- STATUS: NMT had its End of Phase 1 (EOP1) meeting with the FDA on June 28<sup>th</sup> 2021. Completed Month 33.

Task 18.4: Respond to FDA comments from Phase 2a Guidance Meeting. ~~Month 9-12.~~ This subtask completion target was changed to Month 36. However, such a study as the FDA recommended has never been done in outpatient; therefore, it took over a year to design and write this novel protocol. Therefore, NMT requested and received a one year NCE.

- STATUS: Completion expected to be October – December 2021. Therefore, a No Cost Extension was requested, and the approval forwarded to NMT on September 7<sup>th</sup> 2021.

- STATUS: The new novel Phase 2a CT protocol was completed and submitted to the IND on September 26, 2022. This novel protocol was delayed for an entire year due to its uniqueness. Completed Month 48

**Major Task 19. This is a new task. It was noted that prior to a Phase 2a Clinical Trial, a rat micronucleus study is required by I.C.H. and FDA.**

Task 19.1: Draft protocol and submit to ACURO for review and approval.

- STATUS: ACURO approval received 11 June 2021, Month 33

Task 19.2: Complete Study and analysis (1 month) and obtain draft report (12-15 weeks). Month 35-36.

- STATUS: Study was completed (7/28/21). A draft report was received 9/20/21 for NMT review. The final report completed Month 36.

***Milestone to Achieve: Rat micronucleus study, data analysis and final report completed. Month 35-36. Month 36. (This Major Task section is revised for clarity)***

## What opportunities for training and professional development has the project provided?

Richard Clark, MD, Principal Investigator and President of NMT, gained immense professional development in Phase 1 CT management, data collection and analysis, and reporting. Furthermore, he gained further development through creating an entirely new type of outpatient Phase 2a CT for systemic therapy of severe burns.

Consultants, including James Streisand, MD, Clinical Trial Consultant, Caron Shake, PhD, Executive Assistant to the President and Government Liaison, Susan Szambelan, Director of Clinical Operations, and Linda Burke, Clinical Studies writer, all gained professional development through the development of entirely new type of outpatient Phase 2a CT for systemic therapy of severe burns.

## How were the results disseminated to communities of interest?

Abstracts were submitted to the Military Health System Research Symposium (MHSRS) for the August 2020 and 2021 meetings (both meetings were cancelled due to COVID-19). The 2020 was selected for a podium presentation and the 2021 abstracts were selected for poster presentations.

2020: A novel bioactive peptide, cP12, for intravenous (IV) treatment of burns, produces pharmacokinetic (PK) concentrations in a Phase 1 Clinical Trial that correlate with cP12 concentrations causing microvascular vasodilation. **(see Attachment 8)**

2021: Fibronectin-derived peptide P12 mitigates burn conversion, speeds healing and reduces scarring through its ability to dilate the microvasculature, decrease microvascular occlusion, and increase angiogenesis. **(see Attachment 9)**

2021: cP12 plasma levels in Phase 1 Clinical Trial correlates with cP12 concentrations that induce microvascular vasodilation and mitigate burn conversion in animal models. **(see Attachment 10)**

Abstract and Poster Presentation at the Wound Healing Society on April 8, 2022

2022: Tunability of P12, a multi-functional, fibronectin-derived peptide for mechanistically defined wound therapy. **(see Attachment 11)**

Abstract and Poster Presentation at the MHSRS on September 14, 2022

2022: Fibronectin (FN)-derived peptide P12 promotes *in vitro* and *in vivo* angiogenesis. **(see Attachment 12)**

#### 4. IMPACT:

1. NMT discovered that the optimal dose of cP12 (0.01mg/kg) that accelerated wound closure in a porcine burn model did not have any adverse effects in normal healthy adult volunteers. In addition, NMT found that 0.01mg/kg gave a blood concentration of 100pM to 10nM during and within an hour after infusion. This is a dose that dilates the microvascular in a hamster cheek pouch model; and therefore suggests that IV cP12 at this dose may dilate the periburn microvasculature and thereby mitigate ischemia.
2. The FDA advised NMT that a small Phase 2a safety study in **outpatients** with 5% or less Total Body Surface Area (TBSA) burns be completed and approved prior to a Phase 2 study in hospitalized patients with 5-20% TBSA burns as we had proposed as the initial “Phase 2a” CT protocol. This guidance resulted in the NMT team developing an entirely new type of Phase 2a CT, in which patients with small burns would be treated in the Emergency facility with cP12 intravenous therapy and then followed as an outpatient.
3. A Proposal for this Phase 2a CT entitled, “A Phase 2a, Open-label, Outpatient/Inpatient Study of the Safety, Tolerability, and Pharmacokinetics of a Single Dose of cP12 in Otherwise Healthy Adults with Up to and Including 5% Total Body Surface Area (TBSA) Thermal Burns” was submitted to the MTEC pursuant to Request for Project Proposal MTEC-22-07-NavyMultiTopic Award-057. The proposal was approved for funding; however, sufficient funding has not available to date.

#### **What was the impact on the development of the principal discipline(s) of the project?**

The blood level analysis at the dose that gave optimal efficacy in the preclinical porcine burn model, gave us blood levels in humans that were similar to the blood levels in swine at that dose. Now we know that the blood concentrations presumably needed for optimal efficacy in humans is the same as in swine, being 100pM to 10nM.

Adverse events of itching or transient hives occurred in several subjects of the 5<sup>th</sup> Cohort receiving 0.08mg/kg cP12 during or shortly after the 30 min intravenous infusing while subjects in the 4<sup>th</sup> Cohort receiving 0.04mg/kg had little reaction (no hives, but transient warmth of the skin or transient itching). No adverse events were observed in the 2<sup>nd</sup> or 3<sup>rd</sup> Cohorts receiving 0.01 and 0.02mg/kg, the dose in a porcine burn model that speeds wound closure. At present we are planning to use doses no higher than 0.03mg/kg in our Phase 2a Clinical Trial (CT).

A novel Proposal for Phase 2a CT in patients with small burns that are treated in an emergency facility but followed up as outpatients was created. Clearly this is pertinent to prolonged field care (PFC).

A proposal entitled, “A Phase 2a, Open-label, Outpatient/Inpatient Study of the Safety, Tolerability, and Pharmacokinetics of a Single Dose of cP12 in Otherwise Healthy Adults with Up to and Including 5% Total Body Surface Area (TBSA) Thermal Burns” was submitted to the MTEC pursuant to Request for Project Proposal MTEC-22-07-NavyMultiTopic Award-057. The proposal was approved for funding but sufficient funding has not available to date.

### What was the impact on other disciplines?

Nothing to Report

### What was the impact on technology transfer?

1. NMT discovered that the optimal dose of cP12 (0.01mg/kg) that accelerated wound closure in a porcine burn model did not have any adverse effects in normal healthy adult volunteers. In addition, NMT found that 0.01mg/kg gave a blood concentration of 100pM to 10nM during and within an hour after infusion. This is a dose that dilates the microvascular in a hamster cheek pouch model; and therefore, suggests that IV cP12 at this dose may dilate the peri-burn microvasculature and thereby mitigate ischemia.
2. The FDA advised NMT that a small Phase 2a safety study in **outpatients** with 5% or less Total Body Surface Area (TBSA) burns be completed and approved prior to a Phase 2 study in hospitalized patients with 5-20% TBSA burns as we had proposed as the initial “Phase 2a” CT protocol. This guidance resulted in the NMT team developing an entirely new type of Phase 2a CT, in which patients with small burns would be treated in the Emergency facility with cP12 intravenous therapy and then followed as an outpatient.
3. A Proposal for this Phase 2a CT entitled, “A Phase 2a, Open-label, Outpatient/Inpatient Study of the Safety, Tolerability, and Pharmacokinetics of a Single Dose of cP12 in Otherwise Healthy Adults with Up to and Including 5% Total Body Surface Area (TBSA) Thermal Burns” was submitted to the MTEC pursuant to Request for Project Proposal MTEC-22-07-NavyMultiTopic Award-057. The proposal was approved for funding; however, sufficient funding has not available to date.

### What was the impact on society beyond science and technology?

The FDA advised NMT that a small Phase 2a safety study in **outpatients** with 5% or less Total Body Surface Area (TBSA) burns be completed and approved prior to a Phase 2 study in hospitalized patients with 5-20% TBSA burns as we had proposed as the initial “Phase 2a” CT protocol. This guidance resulted in the NMT team developing an entirely new type of Phase 2a CT, in which patients with small burns would be treated in the Emergency facility with cP12 intravenous therapy and then followed as an outpatient.

## **5. CHANGES/PROBLEMS:**

1. Major Task 19. This was a new task. It was noted that prior to a Phase 2a Clinical Trial, a rat micronucleus study is required by I.C.H. and FDA.
2. FDA guidance to design a novel Phase 2a CT for patients with small (<5% TBSA) burns initially treated in an emergency facility and then follow-up as outpatients. This replaced NMT initial Phase 2a CT for burn inpatients and resulted in the need for a one-year NCE.

### **Actual or anticipated problems or delays and actions or plans to resolve them**

1. Major Task 19. This was a new task. It was noted that prior to a Phase 2a Clinical Trial, a rat micronucleus study is required by I.C.H. and FDA.
2. FDA guidance to design a novel Phase 2a CT for patients with small (<5% TBSA) burns initially treated in an emergency facility and then follow-up as outpatients. This replaced NMT initial Phase 2a CT for burn inpatients and resulted in the need for a one-year NCE.

### **Changes that had a significant impact on expenditures**

1. Major Task 19. This was a new task. It was noted that prior to a Phase 2a Clinical Trial, a rat micronucleus study is required by I.C.H. and FDA.
2. FDA guidance to design a novel Phase 2a CT for patients with small (<5% TBSA) burns initially treated in an emergency facility and then follow-up as outpatients. This replaced NMT initial Phase 2a CT for burn inpatients and resulted in the need for a one-year NCE.

### **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

No unexpected outcomes occurred in the Phase 2 Clinical Trial

**Significant changes in use or care of human subjects**

FDA guidance to design a novel Phase 2a CT for patients with small (<5% TBSA) burns initially treated in an emergency facility and then follow-up as outpatients. This replaced NMT initial Phase 2a CT for burn inpatients and resulted in the need for a one-year NCE.

**Significant changes in use or care of vertebrate animals**

Nothing to Report

**Significant changes in use of biohazards and/or select agents**

Nothing to Report

**6. PRODUCTS:**

**Publications, conference papers, and presentations**

**Journal publications.**

Nothing to Report

**Books or other non-periodical, one-time publications.**

Nothing to Report

**Other publications, conference papers and presentations.**



Abstracts were submitted to the Military Health System Research Symposium (MHSRS) for the August 2020 and 2021 meetings (both meetings were cancelled due to COVID-19). The 2020 was selected for a podium presentation and the 2021 abstracts were selected for poster presentations.

2020: A novel bioactive peptide, cP12, for intravenous (IV) treatment of burns, produces pharmacokinetic (PK) concentrations in a Phase 1 Clinical Trial that correlate with cP12 concentrations causing microvascular vasodilation. **(see Attachment 8)**

2021: Fibronectin-derived peptide P12 mitigates burn conversion, speeds healing and reduces scarring through its ability to dilate the microvasculature, decrease microvascular occlusion, and increase angiogenesis. **(see Attachment 9)**

2021: cP12 plasma levels in Phase 1 Clinical Trial correlates with cP12 concentrations that induce microvascular vasodilation and mitigate burn conversion in animal models. **(see Attachment 10)**

Abstract and Poster Presentation at the Wound Healing Society on April 8, 2022

2022: Tunability of p12, a multi-functional, fibronectin-derived peptide for mechanistically defined wound therapy. **(see Attachment 11)**

Abstract and Poster Presentation at the MHSRS on September 14, 2022

2022: Fibronectin (FN)-derived peptide P12 promotes *in vitro* and *in vivo* angiogenesis. **(see Attachment 12)**

#### Website(s) or other Internet site(s)

www.neomatrixtx.com

#### Technologies or techniques

Nothing to report

#### Inventions, patent applications, and/or licenses

Nothing to report

## Other Products

|                                                                           |
|---------------------------------------------------------------------------|
| Data/databases for cP12 SAD tolerability in humans and cP12 PK in humans. |
|---------------------------------------------------------------------------|

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

**What individuals have worked on the project?**

**Name:** Richard A. Clark, MD

**Project Role:** Principal Investigator of Contract, President & Chief Scientific Officer of NMT

**Research Identifier:** ORCID 0000-0003-3828-710X

**Nearest person month worked:** 3

**Contribution to Project:** Assisted in design and development of all Clinical Trials, watched over the cP12 Phase 1 Clinical Trial including data analysis and writing to the Study Report.

**Funding Support:** NMT from this contract.

**Name:** Danielle Armas, MD

**Project Role:** Principal Investigator at Celerion for Phase 1 Clinical Trial.

**Research Identifier:** Arizona Medical License #37416

**Nearest person month worked:** 2 Remuneration through Celerion, NMT's Clinical Research Organization for this study.

**Contribution to Project:** Dr. Armas was responsible for overseeing the recruitment, consent form explanation and signature, physical exam, monitoring, drug delivery, observation of any adverse events, and collection of all clinical results.

**Funding Support:** NMT from this contract.

**Name: James Streisand, MD**

**Project Role: Clinical Trial Consultant.**

**Research Identifier: ORCID 0000-0002-7212-3339**

**Nearest person month worked: 1**

**Contribution to Project:** Dr. Streisand provided guidance for the Phase 2a CT protocol development.

**Funding Support:** NMT from this contract.

**Name: Jzaneen Lalani, JD**

**Project Role:** NMT Acting Chief Operating Officer.

**Contribution to Project:** Ms. Lalani oversees administrative and operational functions of NeoMatrix.

**Research Identifier: N/A**

**Nearest person month worked: 2**

**Funding Support:** NMT from this contract.

**Name: Dr. Caron Shake, PhD, CDR US Navy (Retired Research Physiologist)**

**Project Role:** Executive Assistant to Dr. Clark, Government Liaison, and Director of Contracting.

**Contribution to Project:** Dr. Shake will be the overall Program Director with responsibility for conducting final reviews of all invoices, reports, and milestones achievements. Dr. Shake will be responsible for addressing any contract issues with the Government.

**Research Identifier: N/A**

**Nearest person month worked: 4**

**Funding Support:** NMT from this contract.

**Name: Marjorie Lundgren, MBA**

**Project Role:** Treasurer

**Contribution to Project:** Ms. Lundgren oversees the general financial management of the contract including contract budgets, individual subcontractors and consultants. Ms. Lundgren was also responsible for reconciling bank statements and managing cash flow in conjunction with NMT's CPA and bookkeeper, Mary Ann Demmitt.

**Research Identifier: N/A**

**Nearest person month worked: 4**

**Funding Support:** NMT from this contract.

**Name: Mary Ann Demmitt, CPA**

**Project Role:** CPA and bookkeeper

**Contribution to Project:** Ms. Demmitt is a New York State Certified Public Accountant with over 35 years of experience. She provided tax return preparation and/or accounting services for NMT.

**Research Identifier: N/A**

**Nearest person month worked: 1**

**Funding Support:** NMT from this contract.

**Name: Susan Szambelan,**

**Project Role:** Director of Clinical Operations.

**Contribution to Project:** Ms. Szambelan assisted with creation of the cP12 Phase 1 protocol, qualified Celerion as our clinical site, oversaw study logistics and development of study manuals, and assist Dr. Armas in monitoring the clinical study.

**Research Identifier:** N/A

**Nearest person month worked:** 3

**Funding Support:** NMT from this contract.

**Name:** Roslin Heflin, Ph.D.

**Head of Regulatory Service at B&H.**

**Contribution to Project:** Dr. Haflin advised NMT and oversaw implementation of all FDA regulatory requirements for the cP12 Clinical Trial. She also play a major part in monitoring data collection and organization.

**Research Identifier:** Remuneration through B&H, NMT's regulatory agent.

**Nearest person month worked:** 3

**Funding Support:** NMT from this contract.

**Name:** Melinda Burke, B.S. in Veterinary Technology

**Project Role:** Grant Writer with over 45+ years of experience.

**Contribution to Project:** Wrote the novel cP12 Phase 2a with the assistance of Drs. Clark and Streisand and with Susan Szambelan.

**Research Identifier:** N/A

**Nearest person month worked:** 2

**Funding Support:** NMT from this contract.

**Name:** Debbi Kotlovker, B.S., M.S.,

**Project Role:** Consulting Statistician.

**Contribution to Project:** Ms. Kotlovker performed statistical analyses and interpreted data for NMT.

**Research Identifier:** N/A

**Nearest person month worked:** 1

**Funding Support:** NMT from this contract.

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Nothing to Report

**What other organizations were involved as partners?**

Nothing to Report

**8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:**

**QUAD CHARTS:**

**9. APPENDICES:**

# A Phase 1 Randomized, Placebo-Controlled, Single Ascending Dose Study to Examine the Safety, Tolerability, and Pharmacokinetics of cP12 in Healthy Adults

MB170008

W81XWH-18-20059

PI: Richard A. Clark, MD

Org: NeoMatrix Therapeutics, Inc.

Award Amount: \$2,194,516

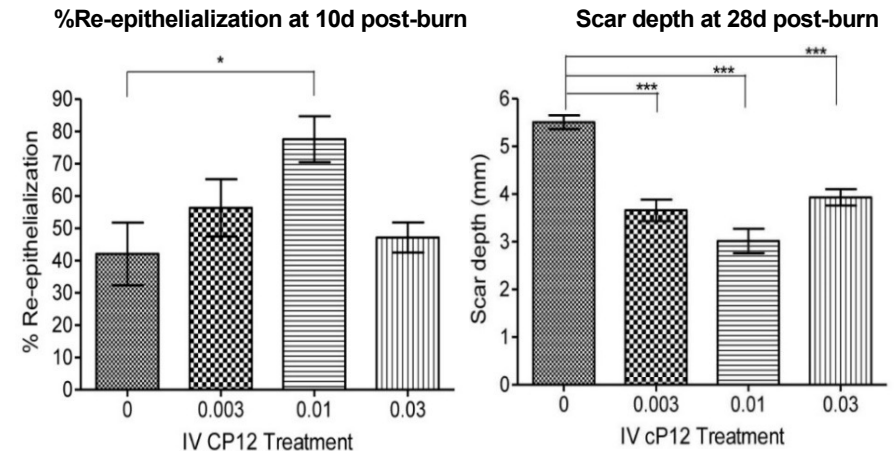


## Study/Product Aims

- Aim 1: cP12 assay development, validation for Clinical Trial PK
- Aim 2: IRB and HRPO submission and approval of Phase 1 CT
- Aim 3: Completion of Phase 1 CT
- Aim 4: Submission of Phase 1 CT report to the FDA Phase 2a protocol with FDA input
- Aim 5: Request Fast Track Designation from the FDA and develop Phase 2a CT protocol with FDA input

## Approach

This is a randomized double-blind, placebo-controlled single ascending dose (SAD) study to evaluate the safety, tolerability, and PK profile of cP12 in healthy male and female subjects. Each subject will be randomized to receive either a single dose of cP12 or placebo. Each dose cohort will include 6 subjects dosed with cP12 and 2 subjects dosed with placebo. Cohorts will be studied sequentially starting with the lowest cP12 dose to dose 2-fold higher than presumed optimal dose. All subjects will be monitored by vital signs and EKG for events that are considered severe and/or serious. Blood and urine will be collected for pharmacokinetics as well as for chemistries and blood elements.



Swine infused with an optimal dose of cP12, beginning 4h after deep-dermal burn injury, demonstrate a remarkable enhancement of 10d re-epithelialization and reduction of 28d scarring. \*P<0.01, \*\*\*P<0.0001 (n=7)

**Accomplishments:** Cohorts 1-4 have been completed without any SAEs. Submitted Amendment #4 to give higher dose to Cohort 5 received HRPO approval 01/07/2020. Amendment approved and Cohort 5 study completed.

## Timeline and Cost

| Activities                                                                                               | CY | 18 | 19           | 20            | 21            | 22            |
|----------------------------------------------------------------------------------------------------------|----|----|--------------|---------------|---------------|---------------|
| cP12 Assay development, validation, and use for pharmacokinetics in CT                                   |    |    |              |               |               |               |
| IRB and HRPO approval of CT and recruitment of 40 healthy adults                                         |    |    |              |               |               |               |
| Initiation to completion of Phase 1 CT                                                                   |    |    |              |               |               |               |
| Compilation, writing & submission of Phase 1 CT report to FDA, and feedback                              |    |    |              |               |               |               |
| Rewrite Phase 2a CT to align with FDA request for new Phase 2a CT and submission of Phase 2a CT proposal |    |    |              |               |               |               |
| <b>Estimated Budget (\$2,195K)</b>                                                                       |    |    | <b>\$64K</b> | <b>\$1.3M</b> | <b>\$248K</b> | <b>\$583K</b> |

Updated 01/20/2023

## Goals/Milestones

### CY18 Goal

- ☒ cP12 plasma and urine assay development and validation

### CY19 Goals

- ☒ Protocol approval obtained from IRB, HRPO, and FDA
- ☒ Initiation of Phase 1 CT

### CY20 Goal

- ☒ Completion of Phase 1 CT and submission of report to FDA

### CY21 Goal

- ☒ Completion of Phase 2a CT protocol and meeting with FDA (6/28/21)

### CY22 Goal

- ☒ Completion of Phase 2a CT protocol rewrite and proposal submission

## Comments/Challenges/Issues/Concerns

- Timelines change: FDA written comments on Phase 2a CT resulted in a rewrite of the Phase 2aCT that was sent as a proposal to the FDA
- Spending deviation: N/A

## Budget Expenditure to Date

Projected Expenditure: **\$2,194,516**

Actual Expenditures: **\$2,194,516**

## ATTACHMENT 1

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## CLINICAL TRIAL PROTOCOL

|                                          |                                                                                                                                                           |
|------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Protocol Number</b>                   | <b>NMT-16-01</b>                                                                                                                                          |
| <b>Title</b>                             | A Phase 1 Randomized, Placebo-Controlled, Single Ascending Dose Study to Examine the Safety, Tolerability, and Pharmacokinetics of cP12 in Healthy Adults |
| <b>Investigational Medicinal Product</b> | cP12                                                                                                                                                      |
| <b>Indication</b>                        | Burn therapy                                                                                                                                              |
| <b>Sponsor</b>                           | NeoMatrix Therapeutics, Inc.<br>25 Health Sciences Dr., Suite 124<br>Stony Brook, NY 11790<br>Phone: 631-241-4964<br>Email: richard.clarknmf@yahoo.com    |
| <b>Principal Investigator</b>            | Danielle Armas, MD                                                                                                                                        |
| <b>Amendment:</b>                        | 2                                                                                                                                                         |
| <b>Version:</b>                          | 3                                                                                                                                                         |
| <b>Date</b>                              | <b>15 February 2019</b>                                                                                                                                   |
| <b>Replaces:</b>                         |                                                                                                                                                           |
| <b>Amendment 1 V2</b>                    | <b>3 June 2018</b>                                                                                                                                        |
| <b>Original V1</b>                       | <b>24 August 2017</b>                                                                                                                                     |

### Confidentiality Statement

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This document contains information that is proprietary to the Sponsor, NeoMatrix Therapeutics, Inc. This information is being provided to you solely for the purpose of evaluating and/or conducting a clinical trial for the Sponsor. You may disclose the contents of this document only to study personnel under your supervision, the Institutional Review Board, the United States Food and Drug Administration, or duly authorized representatives of regulatory agencies for this purpose under the condition that they maintain confidentiality. The contents of this document may not be used in any other clinical trial, disclosed to any other person or entity, and/or published without the prior written permission of



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the Sponsor. The foregoing shall not apply to disclosure required by any regulations; however, you will give prompt notice to the Sponsor of any such disclosure.

---

## 1. SIGNATURES

### 1.1. Sponsor Signatures

**Protocol Number:** NMT-16-01  
**Sponsor:** Neomatrix Therapeutics, Inc.  
**Sponsor Contacts:** Richard Clark, MD  
President  
Neomatrix Therapeutics, Inc.  
25 Health Sciences Dr., Suite 124  
Stony Brook, NY 11790  
Phone: 631-241-4964  
Email: Richard.clarknmf@yahoo.com

02/16/2019

(Signature)

(Date)

**Susan Szambelan**  
Clinical Operations Consultant

**Neomatrix Therapeutics, Inc.**  
25 Health Sciences Dr., Suite 124  
Stony Brook, NY 11790  
Phone: 508-404-3454  
Email: susan.szambelan@gmail.com

DocuSigned by:  
*Susan Szambelan*  
45781E95956B45F...

2/15/2019

(Signature)

(Date)

---

## 1.2. Investigator Signature

I confirm that I have read and that I understand this protocol, the Investigator's Brochure, and other product information provided by the Sponsor. I agree to conduct this study in accordance with the requirements of this protocol and also protect the rights, safety, privacy, and well-being of study subjects in accordance with the following:

- The ethical principles that have their origin in the Declaration of Helsinki.<sup>1</sup>
- International Council on Harmonization Guidance for Industry, Good Clinical Practice E6.<sup>2</sup>
- All applicable laws and regulations, including, without limitation, data privacy laws and regulations.
- The requirement to obtain written and dated approval by the Institutional Review Board (IRB) for the study protocol and amendments, written informed consents, consent form updates, recruitment materials and any other written information to be provided to the subject.
- Regulatory requirements for reporting serious adverse events as defined in this protocol.
- To permit direct monitoring by the Sponsor and its representatives and inspection by regulatory authority(ies).
- To provide adequate resourcing of qualified staff and facilities for the duration of the study to conduct it properly, ethically and safely.
- Terms outlined in the Clinical Study Site Agreement.

**Investigator:**

\_\_\_\_\_  
(Signature)

\_\_\_\_\_  
(Date)

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## 2. SYNOPSIS

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Study Title:</b><br>A Phase 1 Randomized, Placebo-Controlled, Single Ascending Dose Study to Examine the Safety, Tolerability, and Pharmacokinetics of cP12 in Healthy Adults                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <b>Sponsor:</b><br>NeoMatrix Therapeutics, Inc.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Investigational Medicinal Product:</b><br>cP12 for Injection                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Name of Active Ingredient:</b><br>cP12                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <b>Protocol Number:</b><br>NMT-16-01                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <b>Study Phase:</b><br>Phase 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| <b>Primary Objective:</b><br>To assess the safety and tolerability of single ascending intravenous (IV) doses of cP12 in healthy subjects.<br><br><b>Secondary Objective:</b><br>To investigate the pharmacokinetic (PK) profile of cP12 after single ascending IV doses in healthy subjects.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <b>Study Design:</b><br>This is a randomized double-blind, placebo-controlled single ascending dose (SAD) study to evaluate the safety, tolerability, and PK profile of cP12 in healthy male and female subjects. Each subject will be randomized to receive either a single dose of cP12 or placebo. Each dose cohort will include 6 subjects dosed with cP12 and 2 subjects dosed with placebo. As this is a first-in-human study, the first two subjects in each cohort will be dosed as sentinel subjects (one with cP12 and one with placebo) and monitored for acute events that are considered severe and/or serious. If no serious or severe events occur in the acute post-dose period (24 hours postdose), the remaining 6 subjects in the cohort will be dosed. If acute serious or severe events are noted, the remainder of the cohort will not be treated until complete safety data through Day 8 for the sentinel subjects are reviewed and it is determined safe to proceed. Cohorts will be studied sequentially starting with the lowest cP12 dose. One additional cohort may be enrolled in order to complete the study objectives after review of the safety data by the Safety Review Committee (SRC). Subjects will receive a single, approximately 30-minute IV infusion of cP12 or placebo at their assigned dose level. |

| <b>Table S-1: Planned Dose Levels</b> |              |                           |                           |                |              |
|---------------------------------------|--------------|---------------------------|---------------------------|----------------|--------------|
| <b>Cohorts/Dose Levels</b>            |              |                           | <b>Number of Subjects</b> |                |              |
| <b>Cohort</b>                         | <b>Group</b> | <b>Dose Level (mg/kg)</b> | <b>cP12</b>               | <b>Placebo</b> | <b>Total</b> |
| 1                                     | Sentinel     | 0.003                     | 1                         | 1              | 2            |
|                                       |              |                           | 5                         | 1              | 6            |
| 2                                     | Sentinel     | 0.01                      | 1                         | 1              | 2            |
|                                       |              |                           | 5                         | 1              | 6            |
| 3                                     | Sentinel     | 0.02                      | 1                         | 1              | 2            |
|                                       |              |                           | 5                         | 1              | 6            |
| 4                                     | Sentinel     | 0.04                      | 1                         | 1              | 2            |
|                                       |              |                           | 5                         | 1              | 6            |
| 5<br>(optional)                       | Sentinel     | ≤ 0.04                    | 1                         | 1              | 2            |
|                                       |              |                           | 5                         | 1              | 6            |
| <b>Total</b>                          |              |                           | 30                        | 10             | 40           |

Subjects will be confined to the research facility from Day -1 prior to study drug administration through completion of Day 3 safety assessments.

Subjects will be required to fast overnight (for at least 8 hours) prior to dosing on the morning of Day 1.

Blood samples for serum chemistries and hematology, urinalysis, vital signs, and ECGs will be obtained at several time points during the study for safety evaluation. Blood samples for cP12 plasma pharmacokinetic analysis will be collected at predose, and 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6, 12, and 24 hours (Day 2) postdose from the start of infusion.

A urine PK sample will be obtained within 2 hours predose and from 0 to 2 hours, 2 hours to 4 hours, 4 hours to 6 hours.

#### **Dose Escalation:**

Prior to dose escalation to the next higher dose level, the Investigator, Sponsor, and Independent Medical Monitor (IMM) will determine if escalation is warranted by reviewing the following blinded data from the previous lower dose cohorts:

- All AEs including serious AEs (SAEs)
- Clinical safety laboratory data
- Clinical signs and symptoms including vital signs and physical examination findings
- Safety ECG findings
- Available pharmacokinetic data

If 2 of 6 subjects receiving active study drug experience moderate or severe adverse effects in the same body system, consideration will be given to halting dose escalation. Any serious, potentially drug-related adverse event will halt dose escalation. Subsequent cohorts may receive the same or lower doses to better characterize the safety and tolerability of cP12.

#### **Planned Number of Subjects:**

A maximum of 32 subjects are planned for Cohorts 1 through 4. An optional 5<sup>th</sup> cohort may be added for a maximum of 40 evaluable subjects. Subjects may be replaced at the discretion of the Sponsor and Principal Investigator.

**Subject Inclusion/Exclusion Criteria:**

The criteria below will be assessed at the screening visit (to occur within 30 days prior to administration of study drug on Day 1). Continued subject eligibility will be verified on Day -1 upon admittance to the research facility.

**Inclusion Criteria**

A subject may be included in the study only if all of the following inclusion criteria are met:

1. Healthy male or female between the ages of 18 and 65 years, inclusive, at the time of screening.
2. Body mass index between 18 kg/m<sup>2</sup> and 32 kg/m<sup>2</sup>(inclusive) and body weight of  $\geq 50$  kg
3. Female subjects must be of non-child-bearing potential. Subject must have undergone one of the following sterilization procedures at least 6 months prior to the first dose/ dosing:
  - hysteroscopic sterilization;
  - bilateral tubal ligation or bilateral salpingectomy;
  - hysterectomy;
  - bilateral oophorectomy;
  - or be postmenopausal with amenorrhea for at least 1 year prior to the first dose/ dosing and FSH serum levels consistent with postmenopausal status.
4. All females must have a negative pregnancy test on Day -1 regardless of childbearing potential.
5. Male subjects with female partners (including postmenopausal women) must agree to use highly effective contraceptive measures from the Screening visit until one month after taking the dose of study medication. Highly effective contraception includes vasectomy, abstaining from intercourse, double-barrier method (e.g. male using a condom and female using a diaphragm or cervical cap), or barrier plus hormonal contraception (e.g. male using a condom and female using a hormonal contraception). Males must be willing to inform female partners of their participation in the study and must agree to use adequate contraceptive methods.
6. Continuous non-smoker who has not used nicotine containing products for at least 3 months prior to the first dose/dosing and throughout the study;
7. Able to understand the study procedures, voluntarily consent to participate in this study, and provide written informed consent prior to start of any study-specific procedures;
8. Willing and able to remain in the study unit for the entire duration of the confinement period (4 days and 3 nights) and return for 1 outpatient visit.

**Exclusion Criteria**

Subjects who meet any of the following criteria will be excluded from the study:

1. Clinically significant laboratory abnormality or other clinical findings indicative to the Investigator of a clinically significant exclusionary disease (including but not limited to renal, hepatic, gastrointestinal, cardiovascular, neurological disease);
2. Significant history or current evidence of chronic infectious disease, system disorder or organ dysfunction;
3. A history of allergy or hypersensitivity to the study drugs;
4. Positive results for hepatitis B surface antigen (HBsAg), hepatitis C antibody, or human immunodeficiency virus (HIV) antibody;
5. Positive result for alcohol at screening or upon admission to the research facility;
6. Positive result for substances of abuse at screening or upon admission to the research facility;

7. A recent history of alcoholism (< 2 years) or of moderate alcohol use (greater than an average of 3 alcoholic drinks per day or a total of 21 alcoholic drinks per week). One drink is defined as 1 bottle (12 oz) beer, 1 glass (4 oz) wine or 1 oz liquor;
8. Has any history of dependency or treatment for substance abuse in the past year (other than alcohol);
9. An electrocardiogram (ECG) abnormality deemed by the Investigator to be clinically significant;
10. The donation of blood (1 pint or more) within 56 days or plasma within 7 days of receiving study drug until after the end-of study visit;
11. History of difficulty with phlebotomy;
12. Use of any prescription drug therapy (with the exception of birth control pills), dietary or herbal supplements, or megavitamin supplements within 14 days or 5 half-lives (whichever is longer) prior to receiving study drug; restriction applies until after the end-of-study visit;
13. Use of over-the-counter (OTC) medications within 7 days or 5 half-lives (whichever is longer) prior to receiving study drug; restriction applies until after the end-of-study visit with exceptions noted in Section 10.5;
14. Consumption of alcohol within 48 hours prior to admission to the research facility until after the end-of-study visit;
15. Any condition which in the opinion of Investigator would interfere with the participant's ability to provide informed consent, comply with study instructions, possibly confound interpretation of study results, or endanger the participant if he or she took part in the trial.
16. Use of an investigational drug or product within 30 days prior to receiving study drug.

**Test Product, Dose, and Mode of Administration:**

Each subject will receive a single IV dose of cP12 or placebo administered over approximately 30 minutes. The planned dose levels for this study are 0.003, 0.01, 0.02 and 0.04 mg/kg. Dose levels beyond the starting dose may be modified so that the dose levels are less than planned or may be repeated after review of the data after each cohort. Dose escalation may also be terminated.

**Duration of Treatment:**

The total duration of the study is approximately 6 months. The duration for each subject's participation will be approximately 38 days, including a maximum of a 30-day screening period and a treatment and observation period of approximately 8 days.

**Statistical Plan and Methods:**

Pharmacokinetics:

The pharmacokinetic profile of cP12 will be calculated for the PK parameters shown below using non-compartmental methods as implemented in Phoenix WinNonLin (v6.3) using the actual sampling times for each subject. Pharmacokinetic parameters will be determined using all available data. Dose-corrected parameters will also be calculated for dose proportionality assessments. A Statistical Analysis Plan will be developed that will dictate the required statistical and pharmacokinetic analyses to be performed for the study.

**Pharmacokinetic Parameters**

|                        |                                                                                                                                                                              |
|------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| C <sub>max</sub>       | The maximum drug concentration in plasma determined directly from individual concentration-time data                                                                         |
| T <sub>max</sub>       | The observed time to reach maximum concentration                                                                                                                             |
| AUC <sub>last</sub>    | The area under the plasma concentration-time curve from time zero to the time of the last measureable concentration calculated using the linear-up/log-down trapezoidal rule |
| AUC <sub>inf</sub>     | The area under the plasma concentration-time curve from time zero extrapolated to infinity, calculated using the linear-up/log-down trapezoidal rule                         |
| %AUC <sub>extrap</sub> | The percent of AUC <sub>inf</sub> resulting from extrapolation (AUC <sub>inf</sub> -AUC <sub>last</sub> )/AUC <sub>inf</sub> *100                                            |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                         |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| $\lambda_z$                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | The terminal elimination rate constant, estimated by linear regression through the terminal phase of the log concentration-time profile |
| $t_{1/2}$                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | The terminal elimination half-life, calculated as: $t_{1/2} = \ln(2)/\lambda_z$                                                         |
| CL                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Systemic clearance, calculated as $\text{Dose}/\text{AUC}_{\text{inf}}$                                                                 |
| $V_z$                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Volume of distribution calculated as $\text{Dose}/(\lambda_z \times \text{AUC}_{\text{inf}})$                                           |
| Plasma concentrations and PK parameters will be summarized using descriptive statistics and graphical displays for each cohort after dosing on Day 1 (single dose). Individual subject and mean plasma cP12 concentrations will be plotted vs. time on linear and semi-logarithmic axes.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                         |
| <p><b>Safety:</b></p> <p>Adverse events (AEs), physical exams, vital signs, ECG readings, and clinical laboratory values will be assessed through the end-of-study (follow-up) visit (Day 8 <math>\pm</math> 1 day). Clinically significant AEs that occur during the study will be followed until resolution or until stabilized. Treatment emergent AEs (TEAEs occurring after the initial dose of cP12 or placebo) will be summarized based on the frequency of AEs and their severity for all dosed subjects. All AEs will be coded using MedDRA (version 20.0) and summarized by cohort, using preferred term and primary system organ class. Overall safety and tolerability will be assessed by clinical review of all safety parameters, including AEs, laboratory values, vital signs, physical exams and ECG data.</p> <p>Summary statistics including, number (n), mean, standard deviation (SD), median, and range (minimum, maximum) will be tabulated for the observed values and the change (or percent change) from baseline for all continuous parameters for vital signs, ECG, and laboratory tests.</p> <p><b>Determination of Sample Size:</b></p> <p>This is a first-in-human (FIH) study aimed at evaluating the safety, tolerability, and pharmacokinetic profile of cP12 in healthy adults after a single dose. The pharmacokinetic data from this study will be used to estimate sample size for future studies.</p> |                                                                                                                                         |



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## 5. LIST OF ABBREVIATIONS

|                                           |                                                                                                         |
|-------------------------------------------|---------------------------------------------------------------------------------------------------------|
| AE(s)                                     | Adverse event(s)                                                                                        |
| AHDF                                      | Adult human dermal fibroblasts                                                                          |
| AUC <sub>inf</sub>                        | Area under the concentration-time curve from time zero to infinity                                      |
| AUC <sub>0-T</sub> or AUC <sub>last</sub> | Area under the concentration-time curve from time zero to the time of the last measurable concentration |
| BMI                                       | Body mass index                                                                                         |
| CFR                                       | Code of Federal Regulations                                                                             |
| CL                                        | Systemic clearance                                                                                      |
| C <sub>max</sub>                          | Maximum drug concentration                                                                              |
| CRF                                       | Case report form                                                                                        |
| DoD                                       | Department of Defense                                                                                   |
| ECG                                       | Electrocardiogram                                                                                       |
| EDTA                                      | Ethylenediaminetetraacetic acid                                                                         |
| FN                                        | Fibronectin                                                                                             |
| FDA                                       | Food and Drug Administration                                                                            |
| FIH                                       | First-In-Human                                                                                          |
| FSH                                       | Follicle stimulating hormone                                                                            |
| GCP                                       | Good Clinical Practice                                                                                  |
| HbsAg                                     | Hepatitis B surface antigen                                                                             |
| HCV                                       | Hepatitis C virus                                                                                       |
| HED                                       | Human equivalent dose                                                                                   |
| HIV                                       | Human immunodeficiency virus                                                                            |
| ICH                                       | International Council on Harmonization                                                                  |
| IND                                       | Investigational New Drug                                                                                |
| IRB                                       | Institutional Review Board                                                                              |
| IV                                        | Intravenous                                                                                             |
| $\lambda_z$                               | apparent terminal elimination rate constant                                                             |
| MAD                                       | Multiple ascending dose                                                                                 |
| MED                                       | Minimum effective dose                                                                                  |
| MedDRA                                    | Medical Dictionary for Regulatory Activities                                                            |
| N, n                                      | Number                                                                                                  |
| NOAEL                                     | No observed adverse effect level                                                                        |

---

|           |                                                  |
|-----------|--------------------------------------------------|
| PBS       | Phosphate buffered saline                        |
| PDGF-BB   | Platelet-derived growth factor-BB                |
| PK        | Pharmacokinetic                                  |
| SAD       | Single ascending dose                            |
| SAE       | Serious adverse event                            |
| SD        | Standard deviation                               |
| SRC       | Safety Review Committee                          |
| TK        | Toxicokinetic                                    |
| $t_{1/2}$ | Apparent terminal elimination half life          |
| TEAE      | Treatment emergent adverse event                 |
| $T_{max}$ | Time to maximum concentration                    |
| $V_z$     | Volume of distribution during the terminal phase |

---

## 6. INTRODUCTION

### 6.1. Background

According to the American Burn Association, burn injuries claim the lives of at least 3,000 United States civilians, and send another 500,000 to seek medical attention each year, of which 40,000 cases require hospitalization. The resulting estimated annual expenditure is more than \$2 billion direct costs and much greater indirect costs.<sup>3, 4</sup> Of burn patients admitted to hospitals, 10% have burns that exceed 30% of the total body surface area.<sup>4</sup>

In addition, burns represent 5 to 20% of all combat related injuries;<sup>5, 6, 7, 8, 9</sup> twenty percent of which are considered severe or involve more than 20% of total body surface area.<sup>10</sup> These burns result in significant morbidity and mortality, as well as long-term complications including functional impairment and aesthetic disfigurement. Burns are dynamic injuries characterized by progressive extension of the size and severity (depth) of the burn over the course of several days.<sup>11</sup>

Current burn therapies focus on preventing infection and optimizing wound healing. Topical antimicrobial agents reduce bacterial contamination, subsequent burn wound infection, and the incidence of sepsis; a variety of synthetic and biological dressings have been developed to optimize the wound-healing environment, resulting in more rapid healing and reduced pain; and early excision of deep burns followed by grafting with autologous, allogeneic or xenogeneic skin or with skin substitutes has been shown to improve outcomes. However, no current treatments have been shown to limit or prevent burn injury progression and it is not known whether such treatments would mitigate scarring.

Fibronectin (FN) has been shown to play a vital role in wound healing and is deficient in burn patients' wounds and blood. cP12 is a novel FN derived, 14-mer peptide (P12) from the first FN type III repeat that promotes mesenchymal cell growth, proliferation and migration *in vitro* and acts synergistically with a variety of growth factors including platelet-derived growth factor-BB (PDGF-BB).<sup>12, 13</sup> Furthermore, P12 protects adult human dermal fibroblasts (AHDF) from cell death induced by oxidative and cytokine stress *in vitro*<sup>12</sup> and speeds healing and reduces scarring in a vertical burn progression model in pigs.<sup>14, 15</sup> The Sponsor is pursuing development of cP12 for injection for treatment to limit burn injury progression, shorten healing time, and reduce scarring of acute, deep burns in hospitalized patients.

### 6.2. Description and Composition of the Drug Product (cP12)

The drug product is a sterile lyophilized peptide. The composition of the drug product is provided in Table 1. The drug product is reconstituted with sterile 0.9% sodium chloride injection to form a concentrated solution of cP12. The concentrated solution is further diluted in 0.9% sodium chloride injection to form a solution for infusion.

**Table 1: Composition of cP12 for Injection**

| Ingredient              | Function      | Quantity per vial  |
|-------------------------|---------------|--------------------|
| cP12                    | Active        | 10 mg <sup>a</sup> |
| Sodium Hydroxide NF     | pH Adjustment | as needed          |
| Glacial Acetic Acid USP | pH Adjustment | as needed          |

<sup>a</sup> Calculated as free peptide; cP12 is provided as acetate salt

### 6.3. Summary of Nonclinical Information

To support this single-dose, Phase 1 clinical trial in humans, the Sponsor performed a series of nonclinical studies including single-dose toxicity, safety pharmacology and genetic toxicity. The pivotal studies (discussed below) were GLP-compliant and the *in vivo* studies involved the clinical route of administration, intravenous (IV) dosing.

#### 6.3.1. Efficacy Studies

A series of 16 efficacy studies have been performed in which cP12 was administered intravenously in a validated pig model of vertical burn progression in which partial-thickness burns were produced which progress or convert to full-thickness injuries resulting in significant scarring and wound contraction.<sup>14</sup> In all studies, cP12 was administered via a 30 minute infusion. This occurred between 1 and 24 hours post-burn. Samples of the burn site were collected post-dose and were evaluated microscopically for depth of injury (24 hours), re-epithelialization (Days 10 to 17), wound closure (Days 14 to 17), and depth of scarring (Day 28).

Following a 30-minute IV infusion of cP12, a positive effect on burn healing at doses ranging from 0.003 to 0.1 mg/kg (1, 2 and 4 hours post burn) was demonstrated. Improvements included increased Day 10 and 14 re-epithelialization, enhanced wound closure on Day 14, and reduced scar depth on Day 28. When cP12 was administered 8 to 24 hours post burn, no improvement in healing was noted. These data provide a time frame for the activity of cP12 as well as efficacious doses.

cP12's effect on erythrocyte aggregation and occlusion of blood vessels post burn was evaluated. This occlusion occurs quickly following the burn (i.e., within 24 hours), involves no or minimal or fibrinogen/fibrin, and inhibits healing secondary to tissue ischemia and necrosis. In the vertical burn progression model, cP12 administered 1 hour post burn was shown to significantly decrease erythrocyte occlusion in blood vessels by at least 50% which resulted in enhanced healing (increased re-epithelialization on Day 10) and reduced scarring (Day 28) at all doses tested (0.003 to 0.03 mg/kg). Treatments administered at 2 and 4 hours post burn produced a lesser effect on BV occlusion, but scar depth was still significantly decreased.

Collectively, the cP12 animal efficacy data indicate that this drug has a positive effect on both burn progression and burn healing. Importantly, cP12's role in decreasing erythrocyte aggregation, an early event in burn injury progression, is believed to explain its efficacious effect on long-term healing since cP12 infusions are effective at 1 to 4 hours post burn, a time when burn injury progression is occurring but healing has not commenced.



---

### 6.3.2. Safety Pharmacology Studies

Safety pharmacology studies assessing the central nervous system, respiratory system and cardiovascular system have been conducted.

In a central nervous system study, male Sprague-Dawley rats (n = 8/group) received a single 3-minute IV slow bolus dose of 0 (PBS), 0.2, 0.5 and 2 mg/kg and a functional observational battery was performed predose as well as at 5 minutes and 2 and 24 hours postdose.

There were no adverse effects at 0.2 mg/kg. Changes at 0.5 and 2 mg/kg were transient, being limited to the 5 minute time point only. These included: myoclonic jerks, prostration in the home cage and in the arena, impaired gait, flaccid body tone and slightly drooping right and left eyelids at 0.5 and 2 mg/kg; minimal response to tactile reflex at 2 mg/kg; and a decrease in body temperature at 2 mg/kg. The changes generally followed a dose-response in terms of the incidence and severity and were reversible with no biologically significant alterations noted at 2 hours postdose.

A respiratory safety pharmacology study was conducted in male Sprague-Dawley rats (n = 6/group). Animals received a single 3-minute IV slow bolus dose of 0 (PBS), 0.2, 0.5 and 2 mg/kg and respiratory assessments were performed using a “head out” plethysmograph. Ventilation parameters (tidal volume, respiratory rate and derived minute volume) were measured for a 30-minute period predose, continuously from immediately postdose (within 2 minutes following the end of dosing) to 2 hours postdose and for a 30 minute period at 24 hours postdose.

No effects on any respiratory parameter were noted at any dose.

The effects of cP12 on cardiovascular function were assessed *in vitro* and *in vivo*.

In an *in vitro* hERG assay, cP12 concentrations of 30 and 100  $\mu$ M produced 6 and 9.7% inhibition, respectively. In comparison, the control material produced 1.3% inhibition. A higher concentration, 300  $\mu$ M, could not be tested due to a disruption caused by cP12 in forming the seal between the electrode and the cell membrane, which is necessary for performing the patch clamp recordings.

A cardiovascular study was conducted in four male telemetrized beagle dogs. cP12 was administered via a 30-minute infusion at doses of 0 (PBS), 0.05, 0.1 and 0.25 mg/kg to the dogs using a Latin square design with a 7-day washout between doses. Electrocardiograms were collected continuously beginning prior to dosing and continuing through 24 hours.

At 0.1 and 0.25 mg/kg, red skin and swelling of the pinna, gums, muzzle, and/or periorbital area were noted. These clinical signs were present on the day of dose administration only. No effects on heart rate or blood pressure were observed at 0.05 or 0.1 mg/kg and no effect on ECG interval duration and body temperature was observed at any dose. There was a trend towards slightly decreased systolic blood pressure and increased heart rate in the first hour following dosing at 0.25 mg/kg. However, the effects noted were highly variable and predominantly occurred in two animals which, when coupled with the overall low magnitude and transient nature of the change, suggest that they were non-adverse. It was concluded that there were no effects on ECG waveform, calculated parameters or body temperature at any dose.

---

### 6.3.3. Toxicology Studies

An expanded single-dose toxicity study was conducted in Sprague-Dawley rats ( $n = 20/\text{sex}/\text{group}$ ) in which cP12 was administered via a slow bolus (3-minute) IV injection at doses of 0 (phosphate buffered saline), 1, 2.5, and 7.5 mg/kg. On Day 2, 10/sex/group were sacrificed and on Day 15 the remaining 10/sex/group were sacrificed. A comprehensive toxicological assessment was performed along with an assessment of toxicokinetics (using satellite animals).

No adverse effects on body weight, food consumption, ophthalmology, clinical pathology, gross pathology or organ weights were observed.

cP12 produced reversible, minor, transient and non-adverse dose-related clinical observations. These signs resolved within 2 hours postdose and consisted of decreased activity, blue or red skin discoloration of the extremities, and soft swelling of the paws and/or pinna which occurred at an increased incidence in males and females at 1 mg/kg and above. Additional signs in the high-dose animals included abnormal gait, dark eyeballs, decreased muscle tone, prostration, irregular respiratory rate, incoordination and/or weakness.

Microscopic findings included minimal to moderate mononuclear cell infiltration with myofiber degeneration/necrosis in the heart at  $\geq 1$  mg/kg (moderate changes only occurred at the high-dose), minimal to mild centrilobular single cell necrosis of hepatocytes at 7.5 mg/kg, and minimal to mild perivascular inflammation with or without hemorrhage at the injection site at  $\geq 1$  mg/kg. Heart and injection site changes were also noted in the control animals. In addition, heart and liver changes were considered adverse at 7.5 mg/kg only. After a 14 day recovery period, changes in the heart, liver and injection site were no longer present or were seen with a similar incidence and severity when compared to control animals, indicating full recovery.

Time of maximum concentration ( $T_{\text{max}}$ ) occurred 5 minutes postdose in both sexes followed by a rapid decline to levels below the quantitation limit (10 ng/mL) by 60 minutes. Maximum drug concentration ( $C_{\text{max}}$ ) and area under the curve from time 0 to the time of the last measureable concentration ( $\text{AUC}_{0-\text{T}}$ ) increased as a function of dose. The increase was slightly greater than dose proportional for males and slightly less than dose proportional for females. In males, the  $C_{\text{max}}$  and  $\text{AUC}_{0-\text{T}}$  values were slightly higher than in females for the 2.5 and the 7.5 mg/kg doses and were approximately 25% lower than in females for the 1 mg/kg dose. The terminal half-life values of cP12 could not be determined for any of the doses since there were not enough data in the post-distribution phase to allow the parameter to be calculated.

Based on adverse heart and liver findings at 7.5 mg/kg, the NOAEL was considered to be 2.5 mg/kg (associated with Day 1  $\text{AUC}_{0-\text{T}}$  values of 4830 ng·min/mL and 3120 ng·min/mL in males and females, respectively).

In beagle dogs ( $n = 6/\text{sex}/\text{group}$ ), cP12 was administered as a single, 30-minute IV infusion at doses of 0 (phosphate buffered saline), 0.1, 0.25, and 0.75 mg/kg. On Day 2, 3/sex/group were sacrificed and on Day 15 the remaining 3/sex/group were sacrificed. A comprehensive toxicological assessment was performed along with an assessment of toxicokinetics.

There were no adverse test article-related effects on body weight, food consumption, ophthalmology, electrocardiography, clinical pathology, gross pathology, organ weights or histopathology.

The main finding involved transient clinical signs, none of which lasted beyond the postdose cage side observation period (0 to 2 hours post-start of infusion). At 0.75 mg/kg, these signs included slight to moderate soft swelling of the cranium, mouth, muzzle, periorbital area and/or pinna generally seen in combination with red skin at the gums, mouth, muzzle, periorbital area and/or pinna. On occasion, additional clinical signs were recorded such as decreased activity, red eyeballs, salivation, weakness, and excessive scratching. The severity and promptness of the reaction noted for four high-dose animals (3 males and 1 female) required the intra-muscular administration of diphenhydramine. Less severe urticarial reactions (soft swelling or red skin of the gums, mouth and/or pinna) were also noted in a few animals at 0.25 mg/kg. Isolated reports of salivation were noted at 0.1 and 0.25 mg/kg.

$T_{max}$  occurred towards the end of the infusion in both sexes followed by a rapid decline of the plasma concentrations to levels below the limit of quantitation (10 ng/mL) at 80 minutes post-initiation of infusion.  $C_{max}$  and  $AUC_{0-T}$  increased as a function of cP12 dose in both sexes. The increases were dose proportional from 0.1 to 0.25 mg/kg and greater than dose proportional from 0.25 to 0.75 mg/kg. In addition, these kinetic values in males were slightly higher than in females for the 0.75 mg/kg dose and were approximately equivalent in both genders for the 0.1 and 0.25 mg/kg doses.

Based on these results, the NOAEL was considered to be 0.75 mg/kg. However, given the severity of the clinical signs at 0.75 mg/kg and the requirement for diphenhydramine treatment, 0.25 mg/kg is considered a more appropriate NOAEL (associated with Day 1  $AUC_{0-T}$  values of 5,330 ng•min/mL and 5,460 ng•min/mL in males and females, respectively).

#### **6.3.4. cP12 Genotoxicity Studies**

In an Ames assay, *S. typhimurium* strains TA98, TA100, TA1537 and TA1537 and *E. coli* strain WPuvrA pKM101 were incubated with cP12 at doses ranging from 16 to 5000 µg/plate with and without metabolic activation using a treat and plate method.

Toxicity was observed at 1600 and/or 5000 µg/plate. No increase in revertant colonies occurred at any dose either with or without metabolic activation. cP12 was not mutagenic in this assay.

In an *in vitro* chromosomal aberration assay, Chinese hamster ovary cells were incubated with cP12 concentrations ranging from 3.39 to 500 µg/mL for 3 hours with and without metabolic activation and for 20 hours without metabolic activation.

No statistically significant increase in aberrant cells was observed at any concentration with or without metabolic activation. cP12 was determined to be negative for the induction of chromosomal aberrations in Chinese hamster ovary cells.

#### **6.4. Rationale for Starting First-In-Human Clinical Dose**

The planned dose levels for this study are 0.003, 0.01, 0.02 and 0.04 mg/kg.

The doses will not exceed 0.04 mg/kg. This is based on the FDA guideline on application of a safety factor of 10 to the human equivalent dose (HED) calculated from the NOAEL doses from the expanded single-dose toxicity studies in rats and dogs.

The NOAEL dose was 2.5 mg/kg in rats and 0.25 mg/kg in dogs. The HED was calculated using the conversion factors provided in FDA's 2005 Guidance for Industry, Estimating the Maximum Safe Starting Dose in Initial Clinical Trials for Therapeutics in Adult Healthy Volunteers.<sup>16</sup> The resulting HEDs were 0.40 mg/kg (from the rat NOAEL) and 0.14 mg/kg (from the dog adjusted NOAEL) indicating that dogs are more sensitive to cP12 than rats. Applying a safety factor of 10 to the dog HED resulted in an initial starting dose in humans of 0.014 mg/kg.

Pharmacodynamic data obtained using the pig vertical burn progression model indicates some degree of efficacy at a dose of 0.003 mg/kg. Therefore, administration of cP12 in the initial clinical trial is planned to initiate at this dose (0.003 mg/kg), with subsequent incremental increases in the dose according to standard industry practices.

## **7. STUDY OBJECTIVES AND ENDPOINTS**

### **7.1. Study Objectives**

Primary Objective: To assess the safety and tolerability of single ascending intravenous (IV) doses of cP12 in healthy subjects.

Secondary Objective: To investigate the pharmacokinetic (PK) profile of cP12 after single ascending IV doses in healthy subjects.

### **7.2. Study Endpoints**

#### **7.2.1. Safety and Tolerability**

- Adverse event (AE) reporting
- Vital signs
- Clinical laboratory values (hematology, chemistry, and urinalysis)
- QTc interval and other ECG parameters

#### **7.2.2. Pharmacokinetic**

- Plasma cP12 concentrations and PK parameters following a single dose of cP12 (Day 1).

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## **8. INVESTIGATIONAL PLAN**

### **8.1. Overall Study Design**

This is a randomized double-blind, placebo-controlled single ascending dose (SAD) study to evaluate the safety, tolerability, and PK profile of cP12 in healthy male and female subjects. Each subject will be randomized to receive either a single dose of cP12 or placebo. Each dose cohort will include 6 subjects dosed with cP12 and 2 subjects dosed with placebo. As this is a First-In-Human (FIH) study, the first two subjects in each cohort will be dosed as sentinel subjects (one with cP12 and one with placebo) and monitored for acute events that are considered severe and/or serious. If no serious or severe events occur in the acute postdose period (24 hours postdose), the remaining 6 subjects in the cohort will be dosed. If acute serious or severe events are noted, the remainder of the cohort will not be treated until complete safety data through Day 8 for the sentinel subjects are reviewed and it is determined safe to proceed. Cohorts will be studied sequentially starting with the lowest cP12 dose. One additional cohort may be enrolled in order to complete the study objectives after review of the blinded safety data by the Safety Review Committee (SRC). Subjects will receive a single, approximately 30-minute IV infusion of cP12 or placebo at their assigned dose level.

**Table 2: Planned Dose Levels**

| Cohorts/Dose Levels |          |                    | Number of Subjects |           |           |
|---------------------|----------|--------------------|--------------------|-----------|-----------|
| Cohort              | Group    | Dose Level (mg/kg) | cP12               | Placebo   | Total     |
| 1                   | Sentinel | 0.003              | 1                  | 1         | 2         |
|                     |          |                    | 5                  | 1         | 6         |
| 2                   | Sentinel | 0.01               | 1                  | 1         | 2         |
|                     |          |                    | 5                  | 1         | 6         |
| 3                   | Sentinel | 0.02               | 1                  | 1         | 2         |
|                     |          |                    | 5                  | 1         | 6         |
| 4                   | Sentinel | 0.04               | 1                  | 1         | 2         |
|                     |          |                    | 5                  | 1         | 6         |
| 5<br>(optional)     | Sentinel | ≤ 0.04             | 1                  | 1         | 2         |
|                     |          |                    | 5                  | 1         | 6         |
| <b>Total</b>        |          |                    | <b>30</b>          | <b>10</b> | <b>40</b> |

Subjects will be confined to the research facility from Day -1 (the day before study drug administration) through completion of the Day 3 safety assessment.

Blood samples for serum chemistries and hematology, urinalysis, and ECGs will be obtained at several time points during the study for safety evaluation. Blood samples for cP12 plasma PK analysis will be collected at predose, and 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6, 12, and 24 (Day 2) hours postdose from the start of infusion.

During the infusion period, blood samples should be drawn from the arm contralateral to the arm receiving the infusion. Once the infusion is completed, both arms may be used for blood sampling.

A urine PK sample will be obtained within 2 hours predose and from 0 to 2 hours, 2 hours to 4 hours, 4 hours to 6 hours to be stored for future analysis.

## 8.2. Sentinel Dosing

For each cohort, a sentinel dosing plan will be employed at each dose level. The first 2 subjects will be randomized and dosed as sentinels (N=2, 1:1 cP12:placebo). If severe and/or serious adverse events (AEs) are experienced by the sentinel subjects in the acute period following dosing (24 hours postdose), the remaining 6 subjects of the cohort will not be dosed until a full review of all safety data from the sentinel subjects is completed. The acute safety data will be evaluated by the Investigator in collaboration with the Sponsor. If the acute safety data of the sentinel group indicate that the dose was safe and well-tolerated, the remaining subjects of that cohort may be randomized (N=6, 5:1 cP12:placebo) and treated the day following the dosing of the sentinel subjects.

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### **8.3. Dose Escalation/Stopping Criteria**

The Safety Review Committee (SRC) is responsible for reviewing data between cohorts and will determine if escalation is warranted. The SRC consists of the Investigator, Sponsor, and Independent Research Monitor. Dr. William Riddle, the Independent Research Monitor, in collaboration with the Principal Investigator, will oversee the safety of the research and will report applicable events to the IRB, regulatory authorities and DoD. The Independent Research Monitor will review unanticipated problems involving risk to the subjects and will have the authority to stop a research protocol in process, remove individual human subjects from the study and take whatever steps are necessary to protect the safety and well-being of the participants.

Prior to dose escalation to the next higher dose, the SRC will review the following blinded data from the previous lower dose cohorts:

- All AEs and serious AEs (SAEs)
- Clinical safety laboratory data
- Clinical signs and symptoms including vital signs and physical exam findings
- Safety ECG findings
- Available PK data

If 2 of 6 subjects receiving active study drug experience moderate or severe adverse effects in the same body system, consideration will be given to halting dose escalation. Any serious, potentially drug-related adverse event will halt dose escalation. Subsequent cohorts may receive the same or lower doses to better characterize the safety and tolerability of cP12.

The goal is to characterize the safety, tolerability, and PK over the dose range described in [Table 2](#). However, actual dose levels may be adjusted as the emerging safety, tolerability, and PK data permit, and subsequent cohorts may receive the same or lower doses.

If, in the opinion of the study physician, Independent Research Monitor or Sponsor, any drug related adverse event is potentially life threatening or irreversible in nature, escalation to the next higher dose group will NOT be undertaken and the study will be stopped.

### **8.4. Study Duration**

One study site will be used for this study. The maximum duration of the study for each subject from screening to study exit will be approximately 38 days.

## **9. SELECTION AND WITHDRAWAL OF SUBJECTS**

### **9.1. Study Population**

Individuals are eligible for the study if they meet all of the inclusion and none of the exclusion criteria. The criteria below will be assessed at the screening visit that should occur 1-30 days prior to administration of study drug on Day 1. Continued subject eligibility will be verified on Day -1 upon admittance to the research facility.

### **9.2. Subject Inclusion Criteria**

A subject may be included in the study only if all of the following inclusion criteria are met:

- 
1. Healthy male or female between the ages of 18 and 65 years, inclusive, at the time of Screening;
  2. Body mass index between 18 kg/m<sup>2</sup> and 32 kg/m<sup>2</sup>(inclusive) and body weight of  $\geq 50$  kg;
  3. Female subjects must be of non-child-bearing potential. Subject must have undergone one of the following sterilization procedures at least 6 months prior to the first dose/ dosing:
    - hysteroscopic sterilization;
    - bilateral tubal ligation or bilateral salpingectomy;
    - hysterectomy;
    - bilateral oophorectomy;
    - or be postmenopausal with amenorrhea for at least 1 year prior to the first dose/ dosing and FSH serum levels consistent with postmenopausal status;
  4. All females must have a negative pregnancy test on Day -1 regardless of childbearing potential;
  5. Male subjects with female partners (including postmenopausal women) must agree to use highly effective contraceptive measures from the Screening visit until one month after taking the dose of study medication. Highly effective contraception includes documented vasectomy, abstaining from intercourse, double-barrier method (e.g. male using a condom and female using a diaphragm or cervical cap), or barrier plus hormonal contraception (e.g. male using a condom and female using a hormonal contraception). Males must be willing to inform female partners of their participation in the study and must agree to use adequate contraceptive methods;
  6. Continuous non-smoker who has not used nicotine containing products for at least 3 months prior to the first dose/dosing and throughout the study;
  7. Able to understand the study procedures, voluntarily consent to participate in this study, and provide written informed consent prior to start of any study-specific procedures;
  8. Willing and able to remain in the study unit for the entire duration of the confinement period (4 days and 3 nights) and return for 1 outpatient visit.

### **9.3. Subject Exclusion Criteria**

Subjects who meet any of the following criteria will be excluded from the study:

1. Clinically significant laboratory abnormality or other clinical findings indicative to the Investigator of a clinically significant exclusionary disease (including but not limited to renal, hepatic, gastrointestinal, cardiovascular, neurological disease);
2. Significant history or current evidence of chronic infectious disease, system disorder or organ dysfunction;
3. A history of allergy or hypersensitivity to the study drugs;
4. Positive results for hepatitis B surface antigen (HBsAg), hepatitis C antibody, or human immunodeficiency virus (HIV) antibody;



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5. Positive result for alcohol at screening or upon admission to the research facility;
  6. Positive result for substances of abuse at screening or upon admission to the research facility;
  7. A recent history of alcoholism (< 2 years) or of moderate alcohol use (greater than an average of 3 alcoholic drinks per day or a total of 21 alcoholic drinks per week). One drink is defined as 1 bottle (12 oz) beer, 1 glass (4 oz) wine or 1 oz liquor;
  8. Has any history of dependency or treatment for substance abuse in the past year (other than alcohol);
  9. An electrocardiogram (ECG) abnormality deemed by the Investigator to be clinically significant;
  10. The donation of blood (1 pint or more) within 56 days or plasma within 7 days of receiving study drug until after the end-of study visit;
  11. History of difficulty with phlebotomy;
  12. Use of any prescription drug therapy (with the exception of birth control pills), dietary or herbal supplements, or megavitamin supplements within 14 days or 5 half-lives (whichever is longer) prior to receiving study drug; restriction applies until after the end-of-study visit;
  13. Use of over-the-counter (OTC) medications within 7 days or 5 half-lives (whichever is longer) prior to receiving study drug; restriction applies until after the end-of-study visit;
  14. Consumption of alcohol within 48 hours prior to admission to the research facility until after the end-of-study visit;
  15. Any condition which in the opinion of Investigator would interfere with the participant's ability to provide informed consent, comply with study instructions, possibly confound interpretation of study results, or endanger the participant if he or she took part in the trial;
  16. Use of an investigational drug or product within 30 days prior to receiving study drug.

#### **9.4. Enrollment of Subjects**

An informed consent form must be signed and dated by each subject before any study-specific tests are performed. Each subject is assigned an identification number at Screening. This number will be used to identify the subject throughout the study and should appear on all study-related documentation. Subjects who fail to meet all inclusion criteria or present with an exclusion criterion may be rescreened as deemed appropriate by the investigator.

Subjects will be randomly selected for participation from among all those subjects found to be eligible among those screened. Additional subjects will also be selected to serve as alternates in the event that a selected subject is unable to participate due to becoming ineligible, illness, etc.

There will be up to 4 dose levels evaluated in this study. For each dose level, 6 subjects will be randomized to active study drug (cP12) and 2 subjects to placebo. A maximum of 32 subjects will participate in this study. An optional 5<sup>th</sup> cohort may be added for a maximum of 40 subjects to participate in the study.

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## 9.5. Subject Withdrawal

All subjects have the right to withdraw from this study at any time. In addition, it is the right of the Investigator to remove subjects from the study as a result of adverse reactions, a protocol violation, or non-compliance. The study may also be terminated by the Sponsor.

Should a subject withdraw after administration of study drug, or should the Investigator decide to withdraw the subject, all efforts will be made to complete and report the protocol-stipulated observations up to the time of withdrawal. End-of-study/Early Termination procedures will be completed at the time of the subject's withdrawal and an explanation provided as to why the subject is withdrawing or being withdrawn from the study.

The Investigator must document the primary reason for discontinuation of a study subject on the appropriate CRF. If the reason for withdrawal is a clinical AE, monitoring will continue until the AE resolves or the Investigator assesses the AE as chronic or stabilized.

## 9.6. Replacement of Subjects

Subjects who do not receive study drug or placebo may be replaced. Subject who withdraw or are withdrawn due to an AE will not be replaced. Subjects who drop out after receiving study drug for reasons other than AEs may be replaced at the discretion of the Sponsor in consultation with the investigator.

# 10. TREATMENT OF SUBJECTS

## 10.1. Investigational Product

Vials of lyophilized cP12 peptide will be provided in a 10 mg vial and reconstituted and diluted in 0.9% sodium chloride injection for the appropriate IV dose. Placebo will be 0.9% sodium chloride. **The CP12 peptide will be provided by the sponsor and the placebo will be commercially sourced by the clinical site.** Both active and placebo doses will be prepared in the research facility pharmacy in accordance with the randomization schedule by the site pharmacist or designee.

cP12 should be stored refrigerated at 2-8° C in a secure area with access limited to authorized study personnel.

Detailed instructions for preparation, use, storage, and disposal of this solution will be provided by the Sponsor in the Pharmacy Manual prior to the start of the study.

### 10.1.1. Investigational Product Accountability

The unblinded pharmacy staff is responsible for keeping accurate records of the clinical supplies received from the Sponsor and the study drug administered to each subject. The unblinded study monitor will review study drug records periodically during the conduct of the study. At the end of the study, all partial and empty containers must be returned to the Sponsor or they must be destroyed at the clinical study sites according to standard operating procedure (SOP). Records of destruction of study drug at the study site must include study drug identifying information and quantities.

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## **10.2. Blinding**

This is a randomized, double-blind study. An unblinded pharmacist or designee will be required at the Clinical Site to comply with the study's randomization and blinding requirements. The unblinded pharmacy staff will be responsible for all drug accountability issues throughout the study including, preparing, labeling, and dispensing study drug according to the randomization code provided, yet remain independent of all subject assessments.

The unblinded pharmacy staff will be trained on the requirements of the study. Specific topics covered in the training will include the randomization procedure, drug preparation and dispensing procedures, and drug accountability guidelines.

Randomization codes will be provided to the unblinded pharmacist. Confirmation of receipt of the randomization code will be required by the Sponsor. The unblinded pharmacy staff will be responsible for maintaining the blind, consistent with protocol design, throughout the study.

The subjects, Investigator, study personnel involved with subject assessments, and the Sponsor (with the exception of the unblinded CRA) will remain blinded to the actual treatment assignments of the subjects (cP12 or placebo) during the treatment period of each cohort of subjects. The Investigator will be ultimately responsible for ensuring that the integrity of the blind is maintained throughout the treatment period of each cohort. The Investigator will be required to notify the Sponsor in the event of any breaking of the blind for any reason other than safety and PK evaluations performed at the end of each cohort to determine whether escalation to the next dosing level is warranted.

If an emergency unblinding is required, the investigator will have immediate access to the sealed randomization codes. When possible, such emergencies should be discussed with the Sponsor prior to disclosure of the treatment. If the treatment assignment is revealed, record the reason and justification for breaking the blind, the date and time in which the blind was broken, the identity of the person breaking the blind and any others unblinded. Do not record information that would lead to further unblinding in the case report form or source documentation.

Under some circumstances, the investigator, Sponsor and independent medical monitor may require review of unblinded data. Prior to unblinding the data, the reviewers should consider the consequences on study continuation or dose level changes.

## **10.3. Assignment of Subjects to Treatment Groups**

A randomization schedule for the allocation of placebo or cP12 will be generated by the study statistician prior to the start of the study. After reconfirming eligibility, subjects will be considered randomized at the time of administration of study drug or placebo. If a randomized subject withdraws/is withdrawn from the study, the randomization code cannot be reused. The randomization list will provide replacement numbers.

If a subject who does not meet eligibility criteria receives study drug prior to the error being identified, the subject should complete all study assessments. The investigator will notify the Sponsor of the error and a joint decision will be made as to whether the subject should be replaced. If applicable, the IRB should be notified.

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#### **10.4. Selection and Timing of Dose for Each Subject**

Subjects will be fasted from all food and drink (except for water) for a period of 8 hours prior to study drug (or placebo) administration. Study drug or placebo will be infused over a period of approximately 30 minutes, and subjects will continue fasting for 4 hours after the start of the infusion. Study drug infusion will occur in the morning of Day 1.

#### **10.5. Prior and Concomitant Medications**

1. Subjects must not take any OTC medication from 7 days or 5 half-lives (whichever is longer) prior to receiving study drug; restriction applies through the End of Study Visit.
2. Subjects must not take any prescription medication (with the exception of birth control pills), dietary or herbal supplements, or megavitamin supplements from 14 days or 5 half-lives (whichever is longer) prior to receiving study drug; restriction applies through the End of Study Visit.
3. Investigational drugs must be discontinued within 30 days prior to receiving study drug on Day 1.

Over the counter acetaminophen or ibuprofen may be taken during the confinement period and through the End of study visit in amounts no greater than as directed on the label. In the event any concomitant medication is prescribed during the study (e.g., treatment of an adverse event) the name of the medication taken during the study should be recorded with indication, daily dose, and start and stop dates of administration.

#### **10.6. Study Restrictions**

The following restrictions must be adhered to throughout the study or the subject may be excluded or withdrawn from the study.

1. Subjects must not donate blood or plasma from 8 weeks or 7 days, respectively, prior to study drug administration until the End of Study visit.
2. Subjects must not engage in strenuous exercise from 48 hours prior to admission to the research facility until the End of Study visit.
3. Subjects must fast from all food and drink (except water) for at least 8 hours prior to clinical laboratory blood sampling and dosing. Fasting and fluid restrictions may be made shorter at the discretion of the SRC.
4. Subjects should receive meals served at scheduled times during confinement. On non-dosing days, meals will be served at normal times after study assessments have been completed.
5. From Screening through the End of Study visit, subjects should refrain from grapefruit or grapefruit juice, Seville oranges and quinine (tonic water).
6. Subjects must not consume alcohol within 48 hours prior to admission to the research facility until after the End of Study visit.

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## **11. STUDY PROCEDURES AND ASSESSMENTS**

Procedures to be performed during this study are detailed in Section 17.1 Schedule of Assessments and instructions provided in the Study Operations Manual.

When several assessments are to be conducted at the same timepoint, the preferred order of assessments is vital signs, safety 12-lead ECGs, Cardiodynamic ECGs, and blood draws including PK sampling.

Unscheduled or additional safety assessments may be performed, if necessary, in the opinion of the investigator. Any nonscheduled procedures required for urgent evaluation of safety concerns take precedence over all routine scheduled procedures.

### **11.1. Informed Consent**

Informed consent must be obtained prior to the subject entering into the study and before any protocol-directed procedures are performed.

A unique subject identification number (Screen Number) will be assigned to each subject and will be used throughout the study. Each subject will also be assigned a randomization number within 24 hours of dosing on Day 1.

### **11.2. Physical Examination**

The full physical examination will include:

- General appearance
- Skin
- Eyes, ears, nose, and throat (EENT)
- Head/neck
- Musculoskeletal examination
- Respiratory examination
- Cardiovascular assessment including rhythm and presence of cardiac abnormalities
- Abdominal examination
- Neurologic examination to record the presence of abnormalities in mental status, motor, and sensory function, and
- Any additional assessments necessary to establish baseline status or evaluate symptoms or adverse experiences

The brief physical examination will include:

- General appearance
- Skin
- Respiratory examination
- Cardiovascular assessment including rhythm and presence of cardiac abnormalities

- Abdominal examination

Significant findings prior to the start of dosing (baseline, i.e., Screening and Day -1) will be recorded on the Medical History page of the CRF (or electronic CRF). Only changes from baseline physical examination findings that meet the definition of a treatment-emergent AE (TEAE) will be recorded as an AE.

### **11.3. Height, Weight, Body Mass Index**

Body weight and height are to be measured at Screening, and body weight will be repeated on Day -1 and at the End of Study visit. Subjects will be required to wear indoor clothing and remove their shoes prior to the measurements. Body Mass Index (BMI) will be calculated and recorded at the Screening visit.

### **11.4. Vital Signs**

Vital signs (respiration rate, temperature, blood pressure and pulse) will be measured at screening, on Day 1 at predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6 and 12 hours postdose, on Day 2 (24 hours postdose), Day 3 (48 hours postdose), and at the End of Study/Early Termination visit (Day 8 ±1 day).

Vital signs will be collected prior to blood collection whenever possible. Subject will be in a supine position and obtained after resting for at least 5 minutes.

For purposes of qualifying any given subject for study participation, out-of-range vital signs may be repeated once. Additional vital signs measurements may be performed as deemed medically necessary by research facility personnel.

### **ECG Monitoring**

For study conduct, ECGs will be classified as either 12-lead Safety ECGs which will be collected for real time safety review or 12-lead Cardiodynamic ECGs which will be extracted from the Holter recordings for future analysis. ECGs will be performed as outlined in the Schedule of Assessments ([Section 17.1](#)).

A subject will be withdrawn from the study by the PI or designee if, in their medical judgment, ECG findings are present which make continued study participation not in the subject's best interest.

### **11.5. Electrocardiograms (12-lead Safety ECG)**

On-study safety ECGs are planned as single 12-lead ECGs using Bluetooth transmission from the Holter monitor and interpreted on-site by the PI or designee.

Single 12-lead ECGs will be performed as outlined in the Schedule of Assessments ([Section 17.1](#)) and should be obtained after the subject has been resting comfortably in a supine position for approximately 5 minutes.

The Investigator may perform additional ECGs for safety at other times if deemed necessary.

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### **11.6. Holter Monitoring (12-lead Cardiodynamic ECGs)**

Holter monitors will be used to collect continuous 12-lead ECG data on Day 1 for the purpose of collecting cardiodynamic ECGs as outlined in the Schedule of Assessments ([Section 17.1](#)). Recording will be started and stopped at logistically optimal times to ensure that all scheduled time points are collected. Triplicate 10-second, 12-lead ECG recordings will be extracted from the Holter monitor data within a 5-minute time window.

Timing and recording technique for ECGs will be standardized for all subjects. Subjects will be required to lie quietly in a supine position with minimal movement and minimal exposure to noise and other environmental stimuli for at least 10 minutes prior to and 5 minutes during the ECG extraction window to allow for quality ECG extraction. If targeted ECG time points are artifactual and/or of poor quality, analyzable 10-second ECGs will be extracted as close as possible to the targeted time points.

Holter ECG observation timepoints for all cohorts following Cohort 1 may be changed by the SRC.

### **11.7. Laboratory Assessments**

[Table 3](#) provides a list of the clinical laboratory tests that will be performed according to the collection schedule provided in [Section 17.1](#). All blood samples for hematology and chemistries will be collected following at least an 8 hour fast, and will be collected in accordance with acceptable laboratory procedures.

**Table 3: Clinical Laboratory Tests**

| <u><b>Routine Chemistry</b></u>           | <u><b>Hematology</b></u>                       |
|-------------------------------------------|------------------------------------------------|
| Albumin                                   | Hemoglobin                                     |
| Alkaline Phosphatase                      | Hematocrit                                     |
| Alanine aminotransferase (ALT)            | Platelets                                      |
| Aspartate aminotransferase (AST)          | Red blood cell count (RBC)                     |
| Blood urea nitrogen (BUN)                 | White blood cell count (WBC) with differential |
| Calcium                                   |                                                |
| Chloride                                  | <u><b>Urinalysis</b></u>                       |
| Creatinine                                | Bilirubin                                      |
| Glucose                                   | Blood                                          |
| Lactate dehydrogenase (LDH)               | Glucose                                        |
| Potassium                                 | Ketones                                        |
| Sodium                                    | Leukocyte esterase                             |
| Total Bilirubin                           | Nitrite                                        |
| Uric Acid                                 | pH                                             |
|                                           | Protein                                        |
| <u><b>Other</b></u>                       | Specific gravity                               |
| Drug/cotinine/alcohol screen <sup>a</sup> | Microscopic exam <sup>b</sup>                  |
| HbsAg, HCV, HIV <sup>c</sup>              | Urobilinogen                                   |
| FSH <sup>d</sup>                          |                                                |
| Pregnancy <sup>e</sup>                    |                                                |
| Troponin                                  |                                                |
| CRP                                       |                                                |
| Total CK                                  |                                                |
| CK-MB if elevated CK                      |                                                |
| GGT                                       |                                                |

<sup>a</sup> Based on standard testing at the clinical research unit (performed at Screening and upon admission to the research facility).

<sup>b</sup> If protein, urine occult blood, nitrite, or leukocyte esterase values are out of range, the microscopic examination will be reported.  
Micro panel – RBC, WBC, casts, bacteria

<sup>c</sup> Screen only; hepatitis B surface antigen (HBsAg), hepatitis C (HCV) antibody, and human immunodeficiency virus (HIV) antibody

<sup>d</sup> Screen only, and only in females declaring post-menopausal status.

<sup>e</sup> Serum pregnancy on all females at screening visit, and a urine pregnancy upon admission to the research facility and at the End of Study visit (Day 8 ±1 day).



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The Investigator is responsible for reviewing laboratory results for clinical significance. The Investigator and the Sponsor will maintain a copy of the laboratory accreditation and the reference ranges for each laboratory used.

#### **11.7.1. Management of Abnormal Clinical Laboratory Tests**

It is the responsibility of the Investigator or designee to review the results of all lab tests as they become available and to document their review by signing and dating the lab report. For each lab test outside of the laboratory normal range, the Investigator must ascertain if this is a clinically significant change from baseline for the individual subject. This determination does not necessarily need to be made the first time an abnormal lab is observed. The Investigator may repeat the lab test or request additional tests to verify the results of the original lab test.

All clinically significant laboratory abnormalities occurring during the study that were not present at baseline should be followed and evaluated with additional tests if necessary until diagnosis of the underlying cause or adverse event resolution.

#### **11.8. Additional Safety Measures**

Subjects will be closely monitored during each confinement period in the research facility.

Subjects will be instructed to inform the study physician and/or research personnel of any AEs that occur at any time during the study.

Procedures will be completed as specified in this protocol unless contraindicated due to a reported AE.

#### **11.9. Pharmacokinetic Assessment**

##### **11.9.1. Plasma Pharmacokinetic Samples**

Blood samples for cP12 concentrations will be drawn on Day 1 at predose, and 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6, 12 and 24 hours (Day 2) postdose from the start of the infusion. The predose blood sample will be collected within 60 minutes prior to dosing. Special care must be taken to ensure that PK samples are collected on time; a window of  $\pm 10\%$  is permitted for all time points.

Based on the safety review after each cohort, the Safety Review Committee may add no more than 2 plasma PK samples without a protocol amendment.

##### **11.9.2. Urine Pharmacokinetic Samples**

A urine PK sample will be obtained within 2 hours predose and from 0 to 2 hours, 2 hours to 4 hours, 4 hours to 6 hours.

##### **11.9.3. Processing and Shipment of Pharmacokinetic Samples**

The procedures regarding plasma and urine sample collection and storage will be detailed in a separate lab manual.

Plasma and urine samples will be transferred to MicroConstants, the analytical laboratory, at specified time points during the clinical conduct of the study.

#### 11.9.4. Analytical Method

Plasma samples will be analyzed for cP12 using a validated assay. The samples from all evaluable subjects will be analyzed. Urine samples may be stored for possible future assay at MicroConstants, San Diego CA.

#### 11.9.5. Plasma Pharmacokinetic Parameters

The following PK parameters will be calculated following administration of a single IV dose of cP12 on Day 1. Actual sampling times and non-compartmental methods as implemented in Phoenix WinNonlin will be used for the analysis. Dose-corrected parameters ( $AUC_{inf}$ ,  $AUC_{last}$ , and  $C_{max}$ ) will be calculated for dose proportionality assessments.

| Single Dose PK Parameter | Definition                                                                               | Calculation Method                                                                                                                         |
|--------------------------|------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| $C_{max}$                | maximum drug concentration                                                               | observed                                                                                                                                   |
| $T_{max}$                | time of maximum drug concentration                                                       | observed                                                                                                                                   |
| $AUC_{last}$             | area under the concentration time curve from time zero to last measureable concentration | linear/logarithmic trapezoidal method                                                                                                      |
| $AUC_{inf}$              | area under the concentration time curve extrapolated to infinity                         | linear/logarithmic trapezoidal method                                                                                                      |
| % $AUC_{extrap}$         | The percent of $AUC_{inf}$ resulting from extrapolation                                  | $(AUC_{inf} - AUC_{last}) / AUC_{inf} * 100$                                                                                               |
| $\lambda_z$              | apparent terminal elimination rate constant                                              | the negative of the slope from linear regression of the natural logarithm concentration-time curve during the terminal phase (if possible) |
| $t_{1/2}$                | apparent terminal half-life                                                              | $\ln(2) / \lambda_z$                                                                                                                       |
| CL                       | systemic clearance                                                                       | dose/ $AUC_{inf}$                                                                                                                          |
| $V_z$                    | volume of distribution during the terminal phase                                         | dose/ $(\lambda_z \times AUC_{inf})$                                                                                                       |

#### 11.10. Total Blood Volume: Safety Laboratory and PK Samples

A total of up to 50 mL will be collected from each subject for screening, treatment phase, and end-of-study clinical laboratory evaluations. The total volume of blood collected will not exceed 50 mL, unless unplanned collection(s) are required for safety laboratory tests by the Investigator or designee.

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## **12. EVALUATION AND REPORTING OF ADVERSE EVENTS**

### **12.1. Adverse Events**

Subjects will be monitored for any adverse events from the beginning of confinement until the end-of-study visit. The Investigator or a medically qualified designee will review each event. The Investigator or a Sub-Investigator will assess its relationship to the study drug. Each sign or symptom will be graded for severity, and the date and time of onset, cessation and resolution will be recorded. Treatment of any adverse reactions will be evaluated and managed by a physician, either at the study site or at a nearby hospital emergency room, as appropriate. All non-serious AEs will be reported on a regular basis or as specified by the Sponsor.

### **12.2. Definitions**

#### **12.2.1. Adverse Event**

An adverse event (AE) is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product, including control, and which does not necessarily have a causal relationship with treatment.

An AE can be:

- Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.
- Any new disease or exacerbation of an existing disease.
- Any deterioration in non-protocol-required measurements of laboratory value or other clinical test (e.g., ECG or x-ray) that results in symptoms, a change in treatment, or discontinuation from study drug.

Treatment emergent AEs (TEAEs) are defined as AEs that begin or worsen after the start of cP12 dosing.

#### **12.2.2. Reporting Adverse Events**

All AEs occurring during the course of the study (starting from the start of dosing through study completion) will be collected on the AE CRF. Any AE occurring prior to receiving study drug should be recorded on the Medical History CRF. For each AE, the following information will be recorded:

- Description of the event (e.g., headache)
- Date of onset
- Date of resolution (or that the event is continuing)
- Action taken as a result of the event
- Seriousness of the event
- Severity of the event
- Outcome of the event
- Investigator's assessment of relationship to study drug

A cluster of signs and symptoms that results from a single cause should be reported as a single AE (e.g., fever, elevated WBC, cough, abnormal chest x-ray, etc., can all be reported as “pneumonia.”)

The Investigator will carefully evaluate the comments of the subject and the response to treatment in order that he may judge the true nature and severity of the AE. The question of the relationship of AEs to study drug administration should be determined by the Investigator or study physician after thorough consideration of all facts that are available.

### **12.3. Assessment of AEs**

The Investigator is responsible for assessing the intensity (severity), duration, severity, seriousness, and causal relationship to the study drug of each AE.

#### **12.3.1. Grading Intensity**

The severity of the AE will be characterized as “mild, moderate or severe” according to the following definitions:

- **Mild:** Events are usually transient and do not interfere with the subject’s daily activities.
- **Moderate:** Events introduce a low level of inconvenience or concern to the subject and may interfere with daily activities.
- **Severe:** Events interrupt the subject’s usual daily activity. Incapacitating with inability to do usual activities or significantly affects clinical status, and warrants intervention and/or close follow-up.

It should be noted that a severe AE need not be serious and that a serious adverse event (SAE) need not, by definition, be severe.

#### **12.3.2. Relationship to Study Treatment (Causality)**

The degree of “relatedness” of the AE to the study drug may be described using the following scale:

- **Not Related:** No temporal association and other etiologies are likely the cause.
- **Possible:** Temporal association, but other etiologies are likely the cause. However, involvement of the study drug cannot be excluded.
- **Probable:** Temporal association, other etiologies are possible but unlikely. The event may resolve if the study drug is discontinued.
- **Definite:** Established temporal association with administration of the study drug with no other more probable cause. The event should resolve when the study drug is discontinued and recur on re-challenge.

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### **12.3.3. Monitoring and Follow-up**

Subjects who experience AEs will be monitored with relevant clinical assessments and laboratory tests, as determined by the Investigator. In accordance with Good Clinical Practice, all AEs must be followed to satisfactory resolution or stabilization of the event(s), or, if a chronic condition, until fully characterized. All follow-up results are to be reported to the Sponsor. Any actions taken and follow-up results must be recorded either on the appropriate page of the CRF or in a follow-up letter to the Sponsor, as well as in the subject's source documentation. Follow-up laboratory results should be filed with the subject's source documentation.

For all AEs that require the subject to be discontinued from the study, relevant clinical assessments and laboratory tests must be repeated at appropriate intervals until final resolution or stabilization of the event(s).

Subjects who have non-serious AEs that are ongoing at study completion or study withdrawal must be followed until AEs are stabilized, until resolution of the AEs or for 30 days after the last dose of study drug, whichever comes first. Subjects who have an ongoing SAE at study completion or study withdrawal must be followed until the event resolves or the event or sequela stabilizes.

### **12.3.4. Definition of Serious Adverse Event**

An SAE is defined by federal regulation as any AE occurring at any dose that results in any of the following outcomes:

- results in death;
- is life-threatening;
- requires in-patient hospitalization or prolongation of existing hospitalization;
- results in persistent or significant disability/incapacity; or
- is a congenital anomaly/birth defect.

Important medical events that may not result in death, be life threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

### **12.3.5. Reporting Serious Adverse Events**

The Investigator or designee will notify the Sponsor contact within 24 hours after the SAE detection, observation, or report of occurrence (regardless of the relationship to study treatment) by telephone or email.

The report should contain available information including: description of the event and any sequelae, including the Investigator determined relationship to study drug to enable the Sponsor to file a report that satisfies regulatory reporting requirements. In addition to the initial 24 hour report, a completed, separate Serious Adverse Event Report Form must be completed and sent to the Sponsor via fax or email within 48 hours of becoming aware of the event.

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All SAEs should be recorded on the CRF and source documents. Criteria for documenting the relationship to study drug and severity will be the same as those previously described.

SAEs that occur at any time after the inclusion of the subject in the study (defined as the time when the subject signs the informed consent) up to 30 days after the subject completed or discontinued the study must be reported. The subject is considered to have completed the study after the completion of the last visit or contact (e.g., phone contact with the Investigator or designee)

All serious event reporting will adhere to 21 CFR 312.32 (7- and 15-day alerts) for IND drugs. The clinical research site will be responsible for reporting SAEs to the Institutional Review Board (IRB) per FDA regulations. The Sponsor will be responsible for reporting and processing any SAEs to the FDA or other applicable regulatory agency.

#### **12.4. Reports of Pregnancy**

Pregnancies will not be documented or reported as AEs unless directed to do so by the Sponsor. However, if at any time the pregnancy falls under the scope and definition of an SAE, it will then be reported as such.

### **13. STUDY PROCEDURES AND ASSESSMENTS BY VISIT**

#### **13.1. Schedule of Assessments**

The Schedule of Assessments in [Section 17.1](#) shows the schedule of planned study procedures. Every effort should be made to adhere to this procedure schedule.

Unscheduled or repeat assessments may be performed, if necessary, in the opinion of the investigator.

#### **13.2. Screening (Day -30 to Day -1)**

The informed consent document will be discussed with each potential participant, and each individual will sign and date an informed consent document for the study prior to any study-specific procedures being performed.

Each potential study participant will have the following assessments by the Investigator or designee within 30 days prior to the first dose of study medication:

- Evaluate inclusion and exclusion criteria.
- Obtain demographic data including, sex, age, race, ethnicity, body weight (kg), height (cm), BMI (kg/m<sup>2</sup>) and smoking habits.
- Obtain vital signs (respiration rate, temperature, blood pressure and pulse).
- Draw blood samples for HbsAg, HIV antibody, HCV antibody.
- Obtain medical history and current medication use.
- Collect urine for safety urinalysis.
- Complete drug, cotinine, and alcohol testing.
- Draw blood samples for serum chemistry and hematology (following a minimum 8-hour fast).

- 
- Complete the serum pregnancy test (all females) and FSH (in female subjects declaring postmenopausal status).
  - Conduct full physical examination.
  - Perform a single safety ECG.

Only medically healthy subjects with clinically acceptable laboratory profiles and ECGs will be enrolled in the study.

A positive test result for pregnancy, HIV, hepatitis B, hepatitis C, or drug screen will end the screening process.

### **13.3. Admission to the Research Facility (Day -1)**

Subjects will be admitted to the research center on Day -1. The following assessments will be performed:

- All subjects will be asked to affirm that the exclusion criteria and restrictions have not been violated since the screening visit. The subjects' responses will be documented.
- Update medical history, including medication use.
- Assess adverse events.
- Complete drug, cotinine, and alcohol test.
- Collect urine for safety urinalysis.
- Draw blood samples for serum chemistry and hematology (following a minimum 8-hour fast).
- Perform brief physical examination.
- Perform a single safety ECG
- Obtain body weight (kg).
- Complete urine pregnancy test (all females).
- Instruct subjects to fast overnight for at least 8 hours prior to morning dosing.

### **13.4. Day 1**

- Collect predose urine PK sample (within 2 hours of dosing).
- Collect predose plasma PK sample (within 60 minutes of dosing).
- Obtain predose cardiodynamic ECGs (in triplicate). Baseline measurements will be obtained in triplicate at 3 different timepoints before dosing separated by approximately 15-30 minutes.
- Initiate Holter monitoring (Recording will be started and stopped at logistically optimal times to ensure that all scheduled time points are collected.)
- Obtain respiration rate, temperature, blood pressure, and pulse at predose (within 60 minutes of dosing), 0.25, 0.5, 0.75, 1, 1.5, 2, 4 and 12 hours post dose from the start of the infusion.
- Obtain cardiodynamic ECGs (in triplicate) at 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6 and 12 hours post dose from the start of the infusion.

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- **Administer a single IV infusion of the assigned treatment (cP12 or placebo) over approximately 30 minutes. Subject to remain in supine position for 120 minutes post start of infusion.**
  - Draw blood for cP12 PK samples at 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6 and 12 hours post dose from the start of the infusion.
  - Draw blood for troponin, CRP, Total CK, GGT at 4 and 12 hours postdose.
  - Collect a single safety ECG at 1 and 6 hours postdose.
  - A urine PK sample will be obtained within 2 hours predose and from 0 to 2 hours, 2 hours to 4 hours, 4 hours to 6 hours to be stored for future analysis.
  - Assess AEs.
  - Record concomitant medication use.
  - Subject is allowed to eat 4 hours post start of infusion.

### **13.5. Day 2**

- Obtain respiration rate, temperature, blood pressure, and pulse.
- Draw blood samples for serum chemistry and hematology, including troponin, CRP, Total CK, GGT
- Draw blood for cP12 PK sample.
- Perform a safety ECG.
- Obtain cardiodynamic ECGs (in triplicate) at 24 hours post dose from the start of the infusion.
- Assess AEs.
- Record concomitant medication use.
- Subject should fast at least 8 hours prior to Day 3 safety lab assessments.

### **13.6. Day 3**

- Obtain respiration rate, temperature, blood pressure, and pulse.
- Perform a single safety ECG.
- Collect urine for safety urinalysis.
- Draw blood samples for serum chemistry and hematology, including troponin, CRP, Total CK, GGT.
- Draw blood for cP12 PK sample.
- Assess AEs.
- Record concomitant medication use.
- Discharge subjects from the research facility with instructions for returning to the research facility for the end-of study visit on Day 8.

### **13.7. End-of-Study Visit (Day 8 ± 1 day) or Early Termination**

- Perform brief physical examination.



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- Obtain respiration rate, temperature, blood pressure, and pulse.
  - Record body weight.
  - Perform a single safety ECG.
  - Draw blood samples for serum chemistry and hematology, including troponin, CRP, Total CK, GGT.
  - Collect urine for safety urinalysis.
  - Complete urine pregnancy test (all females).
  - Assess AEs.
  - Record concomitant medication use.

## **14. PLANNED STATISTICAL METHODS**

### **14.1. Sample Size**

This is the first study aimed at evaluating the safety, tolerability, and PK profile of cP12 in healthy subjects after administration of a single IV dose of study drug. The PK data from this study will be used to estimate sample size for future studies.

### **14.2. Demographics**

Summary statistics [number (n), mean, standard deviation (SD), minimum, median, and maximum] will be tabulated for the observed values for all continuous demographic parameters. Frequencies and percentages will be tabulated for categorical data.

### **14.3. Pharmacokinetic Analysis**

Plasma concentrations and PK parameters will be summarized using descriptive statistics and graphical displays for each cohort following dosing on Day 1 (single dose). Individual subject and mean plasma cP12 concentrations versus time will be plotted on linear and semi-logarithmic axes.

Dose proportionality of PK exposure parameters ( $C_{\max}$  and AUC parameters) across dose levels will be determined using dose-adjusted  $C_{\max}$  and AUC, calculated for each subject by dividing AUC and  $C_{\max}$  by dose. Analysis of variance appropriate for a dose-ascending design will be performed on the dose-adjusted parameters to assess dose proportionality. Dose level will be the main effect variable. Given the small sample size in each cohort, statistical power may be low. For this reason, regression analysis may be performed using a simple linear regression and/or by using a power model.

Details of the PK and associated statistical analyses will be included in a Pharmacokinetic Analysis Plan and a Statistical Analysis Plan, respectively.

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#### **14.4. Safety Analysis**

Safety analysis will be based on all subjects enrolled who receive at least one dose of the study drug. Treatment emergent AEs will be summarized based on the frequency of AEs and their severity for all dosed subjects. All AEs will be coded using MedDRA and summarized by cohort using preferred term and primary system organ class. Overall safety and tolerability will be assessed by clinical review of all safety parameters including adverse experiences, laboratory values, and vital signs, and ECG data. General clinical and laboratory adverse events will be presented in frequency tables. Summary statistics (n, mean, SD, median, and range (minimum, maximum)) will be tabulated for the observed values and the change (or percent change) from baseline for all continuous parameters for vital signs, ECG, and laboratory tests.

### **15. ETHICS AND DATA HANDLING**

#### **15.1. Institutional Review Board (IRB)**

Before initiation of the study, the Investigator must obtain approval or favorable opinion of the research protocol, informed consent form, and any advertisement for subject recruitment from an IRB complying with the provisions specified in the Code of Federal Regulations (CFR) 21 CFR Part 56 and applicable pertinent state and federal requirements of each participating location including International Council on Harmonization (ICH) and Good Clinical Practice (GCP) guidelines.

Institutional Review Boards must be constituted according to the applicable laws. It is the responsibility of each investigational site to submit the protocol, Investigators' Brochure, subject informed consent, subject recruitment materials (if applicable), and other documentation as required by the IRB to their IRB for review and approval. A copy of the written approval must be provided to the Sponsor.

Sites must adhere to all requirements stipulated by their respective IRB. This includes notification to the IRB regarding: protocol amendments, updates to the subject informed consent, recruitment materials intended for viewing by subjects, Investigational New Drug (IND) Safety Reports, serious and unexpected AEs, protocol deviations, reports and updates regarding the ongoing review of the trial at intervals specified by the respective IRB, and submission of final summaries to the IRB.

The Investigator must promptly inform his/her IRB of all SAEs or other safety information reported from the research facility or the Sponsor.

#### **15.2. Ethical Conduct of Study**

The Investigator agrees, when signing the protocol, to adhere to the instructions and procedures that are described in the protocol and to conduct the study in accordance with the CFRs (21 CFR Parts 11, 50, 54, 56, 312, 314, and 320), which originate from the ethical principles laid down in the current revision of the Declaration of Helsinki, GCPs, and the policies and procedures as outlined by the ethical requirements for IRB review and informed consent form.

The Investigator agrees to allow monitoring and auditing of all essential clinical study documents by the Sponsor or its authorized representatives and inspection by the FDA or other appropriate regulatory authorities. Monitoring and auditing visits by the Sponsor will be scheduled with the appropriate staff at mutually agreeable times periodically throughout the study.

The Investigator will ensure proper implementation and conduct of the trial, including those study-related duties that are delegated to other appropriately qualified individuals. The Investigator will ensure that study staff cooperates with monitoring and audits and will demonstrate due diligence in recruiting and screening study subjects.

For this study and all studies conducted under an IND, the Investigator must sign and return a completed Form FDA 1572, "Statement of Investigator," to the Sponsor.

### **15.3. Study Monitoring and Auditing**

During study conduct, the Sponsor or its agent will conduct periodic monitoring visits to ensure that the protocol and GCP are being followed. The monitor will review source documents to confirm that the data recorded on CRFs is accurate. The Investigator/institution will allow Sponsor monitors or designees, DoD representatives and appropriate regulatory authorities direct access to source documents to perform this verification.

The study site may also be subject to Quality Assurance audits performed by the Sponsor or companies working with or on behalf of the Sponsor, and/or review by the independent review board (IRB), and/or to inspection by appropriate regulatory authorities.

It is important that the Investigator and their relevant personnel are available during the monitoring visits and possible audits or inspections and that sufficient time is devoted to the process.

### **15.4. Case Report Forms and Study Records**

All subjects who screen for the study will be recorded on a screening log and reason for all screen failures will be documented. CRFs are required and should be completed for each subject who has received study drug. The completed original CRFs are the sole property of the Sponsor and should not be made available in any form to third parties, except for authorized representatives of the Sponsor or appropriate regulatory authorities, without written permission from the Sponsor. CRFs may be electronic or paper-based.

The Investigator has ultimate responsibility for the accuracy, authenticity, and timely collection and reporting of all clinical, safety, and laboratory data entered on the CRFs and any other data collection forms. The CRFs must be signed by the Investigator (for electronic CRFs, they can be signed electronically) to attest that the data contained on the CRFs is true. Any corrections to entries made in the CRFs and source documents must be dated, initialed and explained (if necessary) and should not obscure the original entry.

### **15.5. Protocol Amendments and Deviations**

Changes to the research covered by this protocol must be implemented by formal protocol amendment. Amendments to the protocol may be initiated by the Sponsor or at the request of the Investigator. In either case, a formal amendment cannot be initiated until the Sponsor has approved it, the Investigator has signed it, and it has been reviewed and has received approval or favorable opinion by the IRB.

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Emergency deviations or modifications may be initiated without the Sponsor or IRB/IEC approval or favorable opinion, but only in cases where the change is necessary to eliminate an immediate apparent hazard to subjects. Emergency deviations or modifications must be reported to the Sponsor and to the IRB within 3 business days of the occurrence.

#### **15.6. Access to Source Documentation**

The Sponsor (or the Sponsor's authorized representative) must have access to inspect all documents and records that are to be maintained by the Investigator, including, but not limited to, medical records (office, clinic, or hospital) for the subjects in this trial. These regulations also allow the Sponsor's records to be inspected by authorized representatives of the DoD, FDA or other regulatory authorities. The names and identities of all research subjects will be kept in strict confidence and will not appear on CRFs or other records that are provided to or retained by the Sponsor (or the Sponsor's authorized representative). The names and identities of the subjects need not be divulged; however, the records must never the less be inspected. The informed consent form must include appropriate statements explaining these requirements.

#### **15.7. Retention of Data**

To enable evaluations and/or audits from regulatory authorities or the Sponsor, the Investigator agrees to keep records, including the identity of all participating subjects (sufficient information to link records, e.g., CRFs and hospital records), all original signed Informed Consent Forms, copies of all CRFs, SAE forms, source documents, detailed records of drug disposition, and adequate documentation of relevant correspondence (e.g., letters, meeting minutes, telephone calls reports). The records should be retained by the Investigator according to the International Council on Harmonization (ICH) and local regulations.

If the Investigator becomes unable for any reason to continue to retain study records for the required period (e.g., retirement, relocation), the Sponsor should be prospectively notified. The study records must be transferred to a designee acceptable to the Sponsor, such as another Investigator, another institution, or to a third party storage facility. The Investigator must obtain Sponsor's written permission before disposing of any records, even if retention requirements have been met.

#### **15.8. Publication and Disclosure Policy**

It is understood by the Investigator that the information and data included in this protocol may be disclosed to and used by the Investigator's staff and associates as may be necessary to conduct this clinical study.

The information derived from this clinical study will be used by the Sponsor (or designee) and, therefore, may be disclosed by the Sponsor (or designee) as required to other clinical investigators, to the FDA, and to other government agencies. In order to allow for the use of the information derived from this clinical study, it is understood by the Investigator that there is an obligation to provide the Sponsor with complete test results and all data from this clinical study.

Manuscript(s) and abstract(s) may only be prepared through cooperation between the Sponsor (or designee) and the study Investigator(s). The Investigator agrees not to publish or publicly present any results of the study without prior written consent of the Sponsor.

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## 17. APPENDICES

### 17.1. Schedule of Assessments

| Study Period                                                              | Screen    | Admit | Treatment and Observation |   |      |     |      |   |     |   |   |   |    |    |    | EOS/ET |              |
|---------------------------------------------------------------------------|-----------|-------|---------------------------|---|------|-----|------|---|-----|---|---|---|----|----|----|--------|--------------|
| Day                                                                       | -30 to -2 | -1    | 1                         |   |      |     |      |   |     |   |   |   |    |    | 2  | 3      | Day 8±1 day) |
| Hour                                                                      |           |       | Pre-dose                  | 0 | 0.25 | 0.5 | 0.75 | 1 | 1.5 | 2 | 4 | 6 | 12 | 24 | 48 |        |              |
| Informed consent                                                          | X         |       |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |              |
| Medical history                                                           | X         | X     |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |              |
| Demographics                                                              | X         |       |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |              |
| Physical Examination <sup>1</sup>                                         | X         |       |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |              |
| Brief Physical Examination <sup>2</sup>                                   |           | X     |                           |   |      |     |      |   |     |   |   |   |    |    |    | X      |              |
| Vital signs <sup>3</sup>                                                  | X         |       | X                         |   | X    | X   | X    | X | X   | X | X | X | X  | X  | X  | X      |              |
| Height and Weight <sup>4</sup>                                            | X         | X     |                           |   |      |     |      |   |     |   |   |   |    |    |    | X      |              |
| 12-lead Safety ECG (single) <sup>5</sup>                                  | X         | X     |                           |   |      |     |      | X |     |   |   | X |    | X  | X  | X      |              |
| 12-lead Cardiodynamic ECG (triplicate) via Holter Monitoring <sup>6</sup> |           |       | X                         |   | X    | X   | X    | X | X   | X | X | X | X  | X  |    |        |              |
| Serology (HBsAg, HCV, HIV)                                                | X         |       |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |              |
| Serum chemistry and hematology (fasted) <sup>7</sup>                      | X         | X     |                           |   |      |     |      |   |     |   |   |   |    |    | X  | X      |              |
| Troponin, CRP, Total CK, GGT <sup>7</sup>                                 | X         | X     |                           |   |      |     |      |   |     |   | X |   | X  | X  | X  | X      |              |
| Urinalysis                                                                | X         | X     |                           |   |      |     |      |   |     |   |   |   |    |    | X  | X      |              |
| FSH (postmenopausal females)                                              | X         |       |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |              |
| Drug, cotinine and alcohol screen <sup>8</sup>                            | X         | X     |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |              |

| Study Period                  | Screen    | Admit | Treatment and Observation |   |      |     |      |   |     |   |   |   |    |    |    | EOS/ET |              |
|-------------------------------|-----------|-------|---------------------------|---|------|-----|------|---|-----|---|---|---|----|----|----|--------|--------------|
| Day                           | -30 to -2 | -1    | 1                         |   |      |     |      |   |     |   |   |   |    |    | 2  | 3      | Day 8±1 day) |
| Hour                          |           |       | Pre-dose                  | 0 | 0.25 | 0.5 | 0.75 | 1 | 1.5 | 2 | 4 | 6 | 12 | 24 | 48 |        |              |
| Pregnancy test (females)      | X         | X     |                           |   |      |     |      |   |     |   |   |   |    |    |    | X      |              |
| IV infusion (cP12 or placebo) |           |       |                           | X | X    | X   |      |   |     |   |   |   |    |    |    |        |              |
| Plasma PK <sup>9</sup>        |           |       | X                         |   | X    | X   | X    | X | X   | X | X | X | X  | X  |    |        |              |
| Urine PK <sup>10</sup>        |           |       | X                         | X | X    | X   | X    | X | X   | X | X | X |    |    |    |        |              |
| Adverse events                | X         | X     | X                         | X | X    | X   | X    | X | X   | X | X | X | X  | X  | X  | X      |              |
| Concomitant medications       | X         | X     | X                         | X | X    | X   | X    | X | X   | X | X | X | X  | X  | X  | X      |              |

ECG = electrocardiogram, FSH = follicle-stimulating hormone, IV = intravenous, PK = pharmacokinetic.

Note: When several assessments are to be conducted at the same timepoint, the preferred order of assessments is ECG, vital signs and blood draws.

- <sup>1</sup> Full physical examination (PE) includes general appearance, skin, EENT, Head/neck, musculoskeletal, respiratory, cardiovascular (including rhythm and presence of cardiac abnormalities), Abdominal examination, neurologic examination to record the presence of abnormalities in mental status, motor, and sensory function, and any additional assessments necessary to establish baseline status or evaluate symptoms or adverse experiences. Significant findings prior to dosing will be recorded on the Medical History page of the CRF. Only changes from baseline that meet the definition of a TEAE will be recorded as an AE.
- <sup>2</sup> Brief PE includes general appearance, skin, respiratory, cardiovascular (including rhythm and presence of cardiac abnormalities), abdominal examination. Significant findings prior to dosing will be recorded on the Medical History page of the CRF. Only changes from baseline that meet the definition of a TEAE will be recorded as an AE.
- <sup>3</sup> Vital signs will include respiration rate, temperature, blood pressure and pulse.
- <sup>4</sup> Height is collected only at Screening. Weight is collected at Screening, Day -1, and the EOS/ET visit.
- <sup>5</sup> A single ECG is obtained after the subject has been in a supine position for approximately 5 minutes.
- <sup>6</sup> Cardiodynamic ECGs will be collected in triplicate. Baseline measurements will be obtained in triplicate at 3 different timepoints before dosing separated by approximately 15-30 minutes. Postdose collection timepoints will be based off the start of the infusion. Triplicate ECGs are collected within a 5 minute window after subject has been in a supine position for approximately 10 minutes. For the 0.25, 0.5, 0.75 and 1 hour timepoints it will not be feasible for subjects to be completely undisturbed for the full 10 minute duration. For these timepoints every effort should be made to minimize external stimuli and maximize the time subjects are undisturbed. Holter monitoring will be used to collect continuous 12-lead ECG data for the purpose of collecting cardiodynamic ECGs. Recording will be started and stopped at logistically optimal times to ensure that all scheduled time points are collected. Collection will begin on D1 and end on D2.
- <sup>7</sup> Subjects should be fasted for at least 8 hours prior to collection. Safety labs may be added at the discretion of the investigator. If Total CK is elevated, CK-MB may be collected.
- <sup>8</sup> Drug and alcohol screen will be based on standard testing at the clinical research unit.
- <sup>9</sup> Timing of serum PK sampling is from the start of the infusion. It is important that PK sampling occurs as close as possible to the scheduled time (± 10%). Unscheduled or additional PK samples may be collected if appropriate in the opinion of the investigator and/or sponsor.
- <sup>10</sup> A urine PK sample will be obtained within 2 hours predose and from 0 to 2 hours, 2 hours to 4 hours, 4 hours to 6 hours.

## ATTACHMENT 2



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## Informed Consent Form

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## INFORMED CONSENT FORM

**Sponsor:** NeoMatrix Therapeutics, Inc.

**Study Title:** A Phase 1 Randomized, Placebo-Controlled, Single Ascending Dose Study to Examine the Safety, Tolerability, and Pharmacokinetics of cP12 in Healthy Adults

**Study Doctor:** Danielle Armas, M.D.

**Telephone:** (602) 437-0097 (Normal Business Hours)  
(602) 757-6087 (24-hour Nurse's Line)

**Address:** Celerion  
2420 W. Baseline Rd  
Tempe, AZ 85283

You have been offered this consent form in English and Spanish, and have chosen this format as your preferred language. (please check one box)

Please confirm that this is correct: ☐ Yes ☐ No

**It is important that you give a true and complete medical history. You must be honest about your past and present usage of medications. Giving information that is not true could be very harmful to your health. If you give false information, you may be dismissed from the study.**

You are being asked to take part in a research study sponsored by NeoMatrix Therapeutics, Inc. The Department of Defense is providing funds to NeoMatrix to conduct this study. You should read this form before you decide if you want to take part in the study. This form will tell you about the study. The Study Doctor or study staff can explain words or information that you do not understand. Ask the study staff as many questions as needed for you to decide if you want to take part in the study. Research studies are voluntary and include only those who wish to take part. If you decide to take part in this study, you must sign your name at the end of the form and date it. You cannot take part in this study until you sign and date this form.

### 1. PURPOSE OF THE STUDY

The study drug, cP12, is experimental. That means the United States Food and Drug Administration (FDA) has not approved it for sale or use. cP12 is being studied to treat burns.

This is the first study in which cP12 will be given to humans.

The purposes of this study are to:

- Learn about the safety of cP12.
- Learn how subjects tolerate cP12.

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- Find out how much cP12 is in the blood and urine of healthy subjects after single intravenous (IV) dose of the study drug. Intravenous means the drug will be given through your vein.

## 2. NUMBER OF SUBJECTS AND LENGTH OF STUDY

This study will enroll up to 40 subjects. Your participation in the study will last about 9 days plus up to 30 days for screening. There is 1 confinement period where you will stay in the clinic the entire time. The confinement period will last about 4 days. There is 1 return visit to the clinic about 7 days after you receive the study drug.

## 3. SCREENING VISIT

The following procedures will be done during this visit(s) to help the Study Doctor determine if you qualify for this study. This is called the screening visit. Screening may consist of 1 or more visits and involves the following procedures.

- Read, sign, and date the Informed Consent Form.
- Provide your medical history including all medications, vitamins, herbal products or supplements you are taking.
- Provide information such as your name, age, date of birth, sex, race, ethnicity, address, social security number or tax identification number, and phone number.
- An ECG - electrocardiogram (a test that measures and records the electrical activity of your heart) will be done.
- A physical examination will be done.
- Height and weight will be measured.
- Vital Signs (blood pressure, pulse rate, respiratory rate, and body temperature, obtained by mouth) will be done.
- Blood and urine samples will be collected. Your blood and urine sample will be used for routine laboratory tests. Your urine sample will be tested for drugs of abuse and alcohol and cotinine (nicotine exposure). If you are female, your blood will be used for a pregnancy test.
- Your blood will also be used to test for HIV and hepatitis B and C. If your results are positive, the laws require that your name and positive result be reported to the local health department. Your HIV and hepatitis B and C results must be negative to be in the study. If you are not selected to be in the study, for any reason, it is possible that we will not complete this testing on your blood. You can call the study staff to find out if your blood was tested for HIV and hepatitis B and C and the test results, if applicable.

## 4. SUBJECT RESPONSIBILITIES

You must:

- Follow all clinic rules and instructions of the study staff.
- Follow the study restrictions.
- Report any side effects.
- Give true and complete answers to any questions.
- Comply with the terms of the Informed Consent Form.

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## 5. GENERAL CLINIC RULES AND STUDY RESTRICTIONS

Meals and snacks will be served at scheduled times during your stay in the study clinic. You can eat only the food and drink provided to you. You can eat only at the times food is provided. You may be awakened during the night for scheduled events such as vital signs or blood draws.

Some drugs, foods, drinks, or activities can increase or decrease the effect of the study drug. This can be a risk to your health or lead to false study results. Some of the restrictions and requirements for this study are listed below.

- You must be a continuous non-smoker who has not used nicotine containing products for at least 3 months prior to the dosing and throughout the study.
- You must not donate blood (1 pint or more) within 56 days of receiving the study drug until after the end-of study visit.
- You must not donate plasma within 7 days of receiving the study drug until after the end-of study visit.
- You must not use any prescription drug therapy, dietary or herbal supplements, or megavitamin supplements within 14 days prior to receiving the study drug and until after the end-of-study visit.
- You must not use over-the-counter (OTC) drugs within 7 days prior to receiving the study drug and until after the end-of-study visit.
- You must not use an investigational drug or product within 30 days prior to receiving the study drug.
- You must refrain from strenuous exercise from 48 hours prior to check in to the research clinic until the end of study visit.
- You must not consume foods or beverages that contain grapefruit or grapefruit juice, Seville oranges and quinine (tonic water) from screening through the end of study visit.
- You must not consume foods or beverages that contain alcohol within 48 hours prior to check in to the research clinic until after the end of study visit.

## 6. STUDY DRUG DOSING

You will be enrolled into a study dose level group. In each study dose level group, you will be randomly assigned (by chance like flipping a coin) to take cP12 or placebo. Out of 8 subjects, 6 will receive cP12 and 2 will receive placebo. A placebo is a liquid that looks like cP12 but contains no study drug. The use of a placebo helps to make sure that any side effects during the study are judged fairly. Neither you nor the study staff will know who is taking cP12 and who is taking placebo. If necessary for safety reasons, the Study Doctor can find out which study treatment you were assigned to.

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The Study Doctor and the Sponsor will review the safety data of each dose level. The next dose level will not be dosed until the safety data has been reviewed. The Sponsor and/or the Study Doctor can stop the study at any time.

- Study Dose Level 1: 0.003 mg/kg cP12 or placebo
- Study Dose Level 2: 0.01 mg/kg cP12 or placebo
- Study Dose Level 3: 0.02 mg/kg cP12 or placebo
- Study Dose Level 4: 0.04 mg/kg cP12 or placebo

\*Study Dose Level 5: less than or equal to 0.04 mg/kg cP12 or placebo

\*The Sponsor will review data from the first 4 dose levels. One additional group of 8 subjects may be enrolled into the study and dose at less than or equal to 0.04 mg/kg cP12 or placebo.

You will receive the study drug directly into your vein. This will happen over a period of 30 minutes. An IV will be inserted into a vein in your hand or arm. The IV will be flushed or cleaned out with a small amount of saline (salt water) before and after it is used. You may have discomfort or pain when the IV is inserted. There is a risk of infection, bleeding, or bruising at the IV site.

You will have to lie down for 2 hours after the start of the infusion.

You will fast (nothing to eat or drink, except water) over night for at least 8 hours prior to dosing. You will fast for at least 4 hours after dosing.

### ***Risks of cP12:***

**This is the first time cP12 will be given to humans. There is a risk of death in first in human studies such as this study.**

In other first in human studies some unexpected serious, life-threatening side effects have occurred following the administration of new experimental treatments. It is unknown whether some unexpected serious, life threatening side effects could occur with cP12. You will be monitored closely for them and treated if they occur.

cP12 has been studied in laboratory animals, but not in humans. When cP12 was administered to healthy animals (dogs and rats), the animals tolerated the study treatment with side effects only at very high doses. In animal studies using high doses of cP12, which were much larger than the doses we plan to give to you in this study, an allergic-like response occurred (for example, red and swollen skin, gums, mouth, eyes). There was also some incoordination, decreased activity, and respiratory changes at the highest dose tested. The changes were transient (short term) and resolved rapidly. Only at an extremely high dose in dogs was Benadryl required to help resolve the effects.

Even though lower doses of cP12 were well tolerated when administered to animals, it is possible that cP12 may cause side effects that were not seen in animals. You will be monitored for all side effects for the duration of the study.

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This study will use a conservative approach in the study dosing. Each cohort of eight subjects will be sub-divided into two dosing groups. In the first dosing group, one subject will receive cP12 and one subject will receive placebo. Based on the review of safety results through the first 24 hours, the remaining 6 subjects will be dosed. An interval of approximately three weeks will separate the cohorts. This will allow for a thorough review of safety data before starting the next higher dose cohort. Guidelines known as Stopping Rules will be used to prevent giving subjects too high of a dose.

There is always a chance that an unexpected or serious side effect or allergic reaction may happen. This can happen to people who take this or any other drug. Some symptoms of allergic reactions are:

- Rash
- Wheezing and difficulty breathing
- Dizziness and fainting
- Swelling around the mouth, throat or eyes
- A fast pulse
- Sweating

Please seek treatment immediately and tell the Study Doctor and study staff if you have any of these symptoms.

## **7. PROCEDURES AND POSSIBLE RISKS OR DISCOMFORTS**

Procedures will be done during the study at assigned times. The procedures will be done to monitor your health, assess the safety of the study drug, and to see how the study drug is broken down in your body. You will be given a schedule of all study procedures.

### **A. BLOOD COLLECTIONS**

A needle will be used to take blood samples from a vein in your arm about 15 times during the study. About 1/3 cup of blood will be taken. Two cups is the amount you would give if you were donating blood. Additional samples may need to be taken.

You may have discomfort or pain when your blood is collected. You may feel faint or pass out. There is a risk of infection, bleeding, or bruising at the puncture site. You may develop a small scar at the puncture site where multiple blood samples are taken.

If the study staff has a difficult time obtaining your blood from the individual needle sticks you may be dropped from the study. On rare occasions, if blood cannot be obtained per the usual needle stick, we may place an IV (intravenous; in a vein) catheter (a small hollow tube) in a vein in your arm to obtain the blood. Blood is then withdrawn from a port on the IV at scheduled time points. The tube will be flushed or cleaned out with a small amount of saline (salt water) before and after it is used. You may have discomfort or pain when the IV is inserted. There is a risk of infection, bleeding and/or bruising at the insertion site.

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## **B. URINE COLLECTION**

Urine samples will be collected during the study to see how much of the study drug is in the urine at the various collection time points. From just before dosing until 6 hours after you take the study drug all of your urine will be collected. During this time the restroom doors will be locked. You will contact the study staff each time you need to use the restroom. The study staff will provide you with a container and unlock the door for you. Urine collection is very important. You must follow the instructions of the study staff during this time.

## **C. VITAL SIGNS**

Your vital signs will be measured at multiple times during the study. These include blood pressure, pulse rate, respiration rate, and body temperature (obtained by mouth).

## **D. ECG**

ECGs (electrocardiograms) will be done. An ECG traces the electrical activity of the heart. You may have mild irritation, slight redness, or itching at the sites on your skin where the recording patches are placed. If male, it may be necessary to shave the area on your chest for placement of ECG tabs directly on skin.

## **E. WEIGHT**

Your weight will be taken.

## **F. PHYSICAL EXAM**

A physical examination will be done.

## **G. HOLTER MONITOR**

You will wear a Holter monitor from before dosing until 24 hours after dosing. A Holter monitor is a device that will record the electrical activity of your heart. The device is worn on a strap at your waist or over your shoulder. Small pads will be attached to your chest. The pads are connected to the device with wires. You will not be allowed to shower or take a bath while the Holter monitor is in place. You will also be asked to lie still for short periods of time when data is being collected.

## **H. FASTING RESTRICTION**

You will be asked to fast at certain times during this study. This may cause discomfort.

## **I. PHOTOGRAPH**

If you develop a skin condition (reaction or rash) while being in this study, your skin condition may be photographed as soon as it is noticed and several other times until it is gone.

**If the skin condition is on your face, all reasonable attempts will be made to disguise your facial features to hide your identity. It is possible that your face may be recognizable.**

Your image may be sent electronically to the sponsor. The photographs or electronic images will be labeled with your study number and not your name. People working at Celerion, the Sponsor, the FDA, and IRB will have access to your photographs if they have a valid reason for seeing them. Valid reasons include but are not limited to, monitoring or auditing the study, to assess the skin condition or to determine the cause

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of the skin condition. When the study is over, your photograph or electronic image will be stored with the study files indefinitely. Your picture will not be used for teaching purposes and will not be published in any medical journal. You may be asked to have additional tests to assess the skin condition. The Study Doctor will discuss this with you before any other tests are done.

## **8. STUDY RE-CHECKS AND BLOOD EXPOSURE PROCEDURE**

You may be asked to return to the clinic after the study is complete to follow up on abnormal laboratory tests. The study staff may also call you to follow up on any unresolved adverse events. It is important for your safety that you comply with study staff requests to return and/or respond to any telephone calls. You may not be able to do future studies if we are unable to ensure that all your abnormal results have returned to acceptable levels and all of your adverse events have resolved.

If a study staff member sustains an exposure to your blood, tissue or body fluids by needle stick, cut or splash to mucosa or damaged skin, your name, address, telephone and date of birth will be given to the private doctor who is treating the study staff member. You may be contacted in order to collect your blood or to ask your permission to use an existing blood sample to test for HIV and hepatitis B and C. If your blood is tested, you will receive a copy of the results.

This is to enable the study staff member to receive appropriate counseling, monitoring and treatment if necessary. If your blood tests positive the results will need to be reported to the local health authorities.

## **9. UNKNOWN RISKS**

There is always a chance that an unexpected or serious side effect may happen. This can happen to people who take this or any other drug. You must report any new symptoms/signs of illness to the study nurses any time after you have signed and dated this Informed Consent Form.

## **10. POSSIBLE RISKS TO AN UNBORN BABY OR CHILD WHO IS BREASTFEEDING**

The risks of using cP12 during pregnancy are not known. It is possible that this study drug may cause harm to an unborn baby. This includes death, congenital malformations or other unforeseen health problems for the baby.

### Female

If you are able to become pregnant, you are not eligible to take part in this study.

### Male

You and your female partner (including postmenopausal women) must agree to use highly effective birth control measures from the Screening visit until one month after taking the dose of study drug. Highly effective birth control includes documented vasectomy, abstaining from intercourse (not having sex), double-barrier method (for example, male using a condom and female using a diaphragm or cervical cap), or barrier plus hormonal birth control (for example, male using a condom and female using a

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hormonal birth control). You must be willing to inform your female partners of your participation in the study and must agree to use adequate birth control methods.

### **11. SIGNIFICANT NEW SAFETY FINDINGS DURING THE STUDY**

You will be told of any significant new safety findings that Celerion is made aware of by the Sponsor that might influence your willingness to continue your participation in this study.

### **12. POSSIBLE BENEFITS FROM THE STUDY**

You will not receive any health benefits from being in this study. The tests provided may help you learn about your general health. They may also help you discover an unknown medical condition. This study may help doctors and scientists learn things about the study drug that will help others.

### **13. TAKING PART IN THE STUDY OF YOUR OWN FREE WILL**

You are being asked to take part in this study because you are healthy. You will not be taking the study drug to treat any disease or condition. The only other option is not to take part in this study.

You will take part in the study by your own choice and your own free will. No one can force you to be in the study. If you enter the study, no one can force you to stay in the study. If you choose not to be in the study or if you leave the study early, there will be no penalty or loss of benefits. **If you leave or are removed from the study for any reason your stipend will be prorated to the amount of the study that you complete.** You will not lose any rights that you are entitled to as a research subject.

### **14. COST AND PAYMENT FOR TAKING PART IN THE STUDY**

There are no costs to you for being in the study. The study drug and study procedures are provided to you at no charge.

Celerion will pay you by check shortly after completion of the study. The amount you will be paid will depend on how much of the study you complete. You will earn \$920 if you complete the confinement period (your stay in the clinic). You will earn \$200 for the study return visit you complete. You will earn a completion bonus (\$280) if you complete the entire study. You will be paid a total of \$1,400 for completing the entire study.

If you leave the study early, you will receive a pro-rated amount based on the study days you completed. If you complete an unscheduled study return visit you will be paid \$150 for travel and time.

To ensure that the study doses the required number of subjects, extra subjects are recruited. These extra subjects are called alternates. If you are randomly chosen to be an alternate you will be told after you check in to the clinic. As an alternate you will be asked to complete study procedures up to the time of dosing. In the event that an on-study subject is unable to dose, you may be chosen to take that subject's place on the study. If you are not needed, you will be released from the clinic after dosing. If you complete all the alternate requirements, you will receive an alternate stipend check for

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\$300 within approximately 1 week after being released from the clinic. If you are an alternate or a study subject who is released prior to the initial dosing you will receive a prorated portion of the alternate stipend based on the amount of the study that you complete.

You understand the following:

- No deductions will be withheld from your stipend check for tax purposes. You are responsible for reporting any payment on your state and federal tax returns. At the end of each year, Celerion will notify the IRS of all stipends you have received throughout the year.
- Being in this study does not make you an employee of the Sponsor, Celerion, or the FDA.
- You will not receive the full payment for the study if you leave before it is complete or are removed from the study for any reason. **This includes leaving the study due to an adverse event.**

## **15. COMPENSATION FOR AN INJURY DIRECTLY RELATED TO YOUR PARTICIPATION IN THIS STUDY**

There is a chance that you could become ill or injured while being in this study. Celerion will help you make arrangements if your illness or injury requires care outside of Celerion (hospital, medical specialist). Unless other arrangements have been made by Celerion, all billing will be under your name. The cost of this care will be billed to you or your insurer in the ordinary manner. If you do not have insurance, the cost of the care will be billed to you directly.

The Study Doctor and Sponsor will decide if an injury or illness is directly related to the performance of the protocol (study plan) or use of the study drug. If your injury or illness is directly related to the performance of the protocol or use of the study drug, the Sponsor and/or Celerion will reimburse you for your reasonable out-of-pocket medical costs (not covered by insurance) to treat a study-related illness or injury.

To pay these medical expenses, the Sponsor will need to know some information about you like your name, date of birth, and social security number or Medicare Beneficiary Identifier (MBI). This is because the Sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

You will need to sign a “release of information” form. This form will allow Celerion to obtain your medical records related to the illness or injury. These records will help the Study Doctor determine the cause of the illness or injury. They may also help the Sponsor learn more about the safety of the study drug.

Any injury or illness that is not directly related to the performance of the protocol or use of the study drug will be your responsibility to pay and to follow up with private doctor or clinic. This includes any injury or illness that would have occurred even if you had not participated in the clinical trial.

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In no way does signing and dating this consent form waive your legal rights nor does it relieve the Study Doctor, Sponsor or involved institutions from their legal and professional responsibilities.

## **16. REASONS YOU CAN BE REMOVED FROM THE STUDY**

**You can be removed from the study at any time and for any reason without your consent.** Some of the reasons you can be removed are listed below.

- You do not follow the instructions, rules, and restrictions given by the study staff.
- You do not continue to meet the requirements for the study.
- The Study Doctor decides it is best for your health.
- The Sponsor stops the study or asks that you be removed from the study.
- You become pregnant.

## **17. LEAVING THE STUDY BEFORE IT IS COMPLETED**

Leaving the study before it is complete may be harmful to your health. If you choose to leave the study, you must notify the study staff. It is very important that you agree to have the following procedures completed. The procedures will be done for your safety and well-being.

- Physical examination
- ECG
- Weight
- Vital Signs
- Provide blood and urine samples
- Record any side effects you may have or medications you have taken.

All data that has been collected from you will be used for its original intention. If you leave the study early or you are removed from the study, all samples collected from you before you leave will be used and analyzed as described in this consent.

## **18. CONFIDENTIALITY, DATA PROTECTION, AND PRIVACY**

Information collected about you and your participation in this study, including all medical and health information as outlined below, will be kept confidential according to privacy laws in this country. The information in both paper and electronic format that Celerion will collect about you will include study records that may contain your name and other personally identifiable information (PII) such as your date of birth. PII is information that directly identifies you, and will also include special information such as your racial or ethnic origin, physical or mental health, sexual life, or genetic data and/or biometric data for the purpose of uniquely identifying you. These records (including any photographs) containing your PII will be kept for a minimum of either two years following the approval of the study drug, or two years after the Sponsor discontinues its research on the study drug, and may be kept for as long as the Sponsor is developing or commercializing the study drug, which may be indefinitely. Your study results will be coded with numbers and/or initials wherever possible. Celerion will keep a list that links your name to your study results. This list will be kept confidential, however it may be provided to the sponsor and third parties listed below. Celerion may share your PII among Celerion

|                      |                                             |  |
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affiliates who are located in other countries around the world. All Celerion affiliates will comply with the terms of this ICF and all Celerion policies and applicable laws and regulations at all times with respect to your PII.

The study results, including your PII, may be disclosed to, audited by, and/or monitored by the people listed below. This is to analyze the study data for the purposes of development and/or commercialization of the study drug, and also to make sure the study was done correctly. In order for this to take place, some third parties will have direct access to your PII, and may copy some of the original records that contain your PII. This includes the laboratory report linking your name to your HIV and/or hepatitis test results. Your original records maintained by Celerion and accessed by the people listed below may contain your PII. PII may be disclosed to the third parties listed below as necessary with respect to any investigation, complaint, or claim, including with respect to any investigation by a governmental authority. These third parties include:

- Regulatory authorities, such as the FDA, MHRA (Medicines and Healthcare products Regulatory Agency), EMA (European Medicines Agency) or Health Canada
- The Sponsor and third parties working with the sponsor, including the Department of Defense
- Celerion and third parties working with Celerion
- The Institutional Review Board (IRB is a group of people who review research studies to protect the rights and welfare of research subjects.)

All of the parties listed above will maintain, use, disclose, transfer and access your PII confidentially and in accordance with applicable law or regulation.

Under certain circumstances, some tests results will be reported to health and regulatory authorities. This is done when required by law or regulation. If a medical emergency happens, your study results, including your PII, may be given to emergency medical staff not employed by Celerion or the Sponsor.

In addition to the purposes outlined above, Celerion or the Sponsor may utilize your study results, including your PII, for publication purposes, such as presenting on the study results at a conference, publishing in a medical book or journal, writing a white paper about the study, or used for teaching purposes. In the event of any such publication, your PII will be anonymized prior to disclosure to third parties. Neither your name nor other identifiers will be used in any publication or teaching material. Further, Celerion may use your PII to make automated decisions, such as whether or not you are eligible to participate in any other study at Celerion.

You may withdraw your consent from Celerion's collection, use, processing, disclosure, and onward transfer of your PII at any time. If you withdraw your consent, Celerion will not collect any further PII about you, and you may be removed from the study. If you required that your PII be erased, the PII already gathered will still be kept in the study database where required under regulations applicable to clinical trial study files, however all other PII will be erased from our databases. Any PII that cannot be erased will be used as described in this Informed Consent Form. In accordance with applicable law, you may request (in writing) to see or have a copy of the study data collected about you.

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You have the right to request a correction to any PII about you that is not correct. You may not be able to see some data until after the study is over.

By signing and dating this form, you are allowing the collection, processing, use, disclosure, and onward transfer of your PII as described in this consent.

If you have any questions or concerns about Celerion's collection of your PII or the information outlined in this ICF, you may contact the Celerion Privacy Officer by electronic message at [privacy@celerion.com](mailto:privacy@celerion.com); or by mail at 621 Rose Street, Lincoln, NE 68502. In addition, you have the right to lodge a complaint with any applicable governmental authority if you believe we have not complied with the requirements of applicable law with regard to your PII.

## 19. WHOM TO CONTACT ABOUT THE STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject and/or concerns or complaints regarding this research study, contact:

- By mail: Study Subject Adviser  
Advarra  
6940 Columbia Gateway Drive, Suite 110  
Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: [adviser@advarra.com](mailto:adviser@advarra.com)

Please reference the following number when contacting the Study Subject Adviser: Pro00028517.

**See Next Page**

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|----------------------|---------------------------------------------|--|

## 20. YOUR CONSENT

Your signature below verifies that:

- You have had adequate time to read this written Informed Consent Form.
- A study staff member has explained this form to you.
- You have had the chance to ask questions about the study.
- All of your questions have been answered.
- You understand the information in this Informed Consent Form.
- You agree to follow the restrictions of the study.
- You agree to take part in the study and give your consent for study procedures.
- You are aware that nothing contained in this Informed Consent Form waives any of your legal rights as a research subject, nor does it release the Study Doctor, the Sponsor, Celerion, or its agents from any liability for negligence.

Would you like Celerion to inform your healthcare provider of your participation in this study? Check one: Yes ☐ No ☐

Name of healthcare provider: \_\_\_\_\_

Address of healthcare provider: \_\_\_\_\_

Subject Name (Print): \_\_\_\_\_

Subject Signature: \_\_\_\_\_ Date: \_\_\_\_\_

## 21. FOR CELERION STUDY STAFF

I have discussed this study with the above subject. This person had an opportunity to ask questions. The Subject signed and dated in my presence.

Signature: \_\_\_\_\_  
(Study Staff Member explaining study and ICF) Date \_\_\_\_\_ Time \_\_\_\_\_

## 22. ACKNOWLEDGEMENT

You have been given a signed and dated copy of this document. Initials \_\_\_\_\_

|                      |                                             |  |
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## ATTACHMENT 3

**PHASE I CLINICAL STUDY REPORT:**

---

**A Phase 1 Randomized, Placebo-Controlled, Single Ascending Dose Study to Examine  
the Safety, Tolerability, and Pharmacokinetics of cP12 in Healthy Adults**

---

**Protocol No. NMT-16-01  
Celerion Project No. CA21478**

**Final Report Date: 01 July 2020**

**Active Drug: cP12; IND Number: 112487  
Indication studied: Burn therapy**

**First subject enrolled: 19 June 2019  
Last subject completed: 27 March 2020**

**NeoMatrix Therapeutics Inc.  
25 Health Sciences Drive, Suite 124  
Stony Brook, New York 11790, USA  
Telephone: (631) 241-4964**

**Principal Investigator:**

**Danielle Armas, MD  
Celerion  
2420 West Baseline Road  
Tempe, Arizona 85283, USA  
danielle.armas@celerion.com  
Telephone: (602) 437-0097**

*This study was conducted in compliance with the International Council for Harmonisation Harmonized  
Tripartite Guideline regarding Good Clinical Practice.*

*Nothing herein is to be disclosed in any way without the prior written permission of the study Sponsor.*



## **2. SYNOPSIS**

Click here for detailed [SYNOPSIS](#).

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#### 4. LIST OF ABBREVIATIONS

Pharmacokinetic (PK) parameter abbreviations and definitions may be found in [Section 9.5.3](#).

|           |                                    |
|-----------|------------------------------------|
| AE        | Adverse event                      |
| AHDF      | Adult human dermal fibroblasts     |
| BLQ       | Below the limit of quantitation    |
| BMI       | Body mass index                    |
| CFR       | Code of Federal Regulations        |
| CI        | Confidence interval                |
| CK        | Creatine phosphokinase             |
| cm        | Centimeter                         |
| CRF       | Case report form                   |
| CRU       | Clinical research unit             |
| CS        | Clinically significant             |
| CSR       | Clinical study report              |
| CV        | Coefficient of variation           |
| DoD       | Department of Defense              |
| ECG       | Electrocardiogram                  |
| EOI       | End of infusion                    |
| EOS       | End-of-Study                       |
| ET        | Early Termination                  |
| EU        | European Union                     |
| FDA       | Food and Drug Administration       |
| FIH       | First-In-Human                     |
| FN        | Fibronectin                        |
| FSH       | Follicle stimulating hormone       |
| GCP       | Good Clinical Practice             |
| Geom CV   | Geometric coefficient of variation |
| Geom Mean | Geometric mean                     |



|                     |                                                             |
|---------------------|-------------------------------------------------------------|
| HBsAg               | Hepatitis B surface antigen                                 |
| HED                 | Human equivalent dose                                       |
| HIPAA               | Health Insurance Portability and Accountability Act of 1996 |
| HIV                 | Human immunodeficiency virus                                |
| IB                  | Investigator's Brochure                                     |
| ICF                 | Informed Consent Form                                       |
| ICH                 | International Council for Harmonisation                     |
| IRB                 | Institutional Review Board                                  |
| IV                  | Intravenous                                                 |
| kg                  | Kilogram                                                    |
| kg/m <sup>2</sup>   | Kilogram per meter square                                   |
| LDH                 | Lactate dehydrogenase                                       |
| LLOQ                | Lower limit of quantitation                                 |
| ln                  | Natural log                                                 |
| Mean                | Arithmetic mean                                             |
| MedDRA <sup>®</sup> | Medical Dictionary for Regulatory Activities                |
| mg                  | Milligram                                                   |
| mL                  | Milliliter                                                  |
| n                   | Sample size; number of observations                         |
| NOAEL               | No observed adverse effect level                            |
| OTC                 | Over-the-counter                                            |
| oz                  | Ounces                                                      |
| PE                  | Physical examination                                        |
| PI                  | Principal Investigator                                      |
| PK                  | Pharmacokinetic                                             |
| PDGF-BB             | Platelet-derived growth factor-BB                           |
| QA                  | Quality Assurance                                           |
| QC                  | Quality Control                                             |
| QTcF                | Corrected QTc interval using Fridericia's correction        |
| SAD                 | Single ascending dose                                       |

|      |                                  |
|------|----------------------------------|
| SAE  | Serious adverse event            |
| SAP  | Statistical analysis plan        |
| SD   | Standard deviation               |
| SEM  | Standard error of the mean       |
| SOC  | System Organ Class               |
| SOP  | Standard operating procedure     |
| SRC  | Safety Review Committee          |
| TEAE | Treatment-emergent adverse event |
| ULOQ | Upper limit of quantitation      |
| US   | United States                    |
| USA  | United States of America         |
| WHO  | World Health Organization        |

## **5. ETHICS**

### **5.1 Institutional Review Board**

All pertinent study documents were reviewed by the Advarra Institutional Review Board (IRB) prior to study initiation. The Advarra IRB is organized and operates in compliance with Food and Drug Administration (FDA) regulations as described in the Code of Federal Regulations (CFR) 21 Parts 50 and 56, Department of Health and Human Services regulations as described in 45 CFR 46, guidelines resulting from the International Council for Harmonisation (ICH) E6 Good Clinical Practice (GCP). In addition, the IRB operates in compliance with the portions of the Health Insurance Portability and Accountability Act of 1996 (HIPAA Privacy Rule) that apply to research, as described in 45 CFR Parts 160 and 164. The Advarra IRB has been awarded Full Accreditation from the Association for the Accreditation of Human Research Protection Programs, Inc<sup>®</sup>.

A copy of the protocol and amendments are included in [Appendix 16.1.1](#), and IRB information is included in [Appendix 16.1.3](#).

### **5.2 Ethical Conduct of the Study**

Celerion attests that the clinical portion of this study was performed in compliance with Celerion Standard Operating Procedures (SOPs). The SOPs are written based on the principles and requirements of GCP as defined by the regulatory agencies standards and guidance listed in the Celerion Global Quality Manual. These SOPs are also in accordance with the ethical requirements referred to in the European Union (EU) directive 2001/20/EC and the ethical principles set forth in the Declaration of Helsinki.

### **5.3 Subject Information and Consent**

Prior to initiation of any study-specific procedures, subjects received a copy of the Informed Consent Form (ICF) that summarized, in non-technical terms, the purpose of the study, the procedures to be carried out, and the potential hazards. The Principal Investigator (PI) or her representative explained the nature of the study to the subjects, in non-technical terms, and answered all questions regarding the study. Subjects reviewed, signed, and dated the ICF. Subjects received a copy of the fully signed ICF. A sample ICF is located in [Appendix 16.1.3](#).

## **6. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE**

This study was performed under the direction of the PI:

Danielle Armas, MD  
Celerion  
2420 West Baseline Road  
Tempe, Arizona 85283, USA  
danielle.armas@celerion.com  
Telephone: (602) 437-0097

Clinical laboratory tests required by this protocol were performed by the following certified clinical laboratory facility:

Celerion  
2420 West Baseline Road  
Tempe, Arizona 85283, USA  
Telephone: (602) 437-0097

Sample analysis for cP12 in plasma and urine was performed at MicroConstants, under the direction of:

Sheen Legaspi and Gregory Reynolds  
MicroConstants, Inc.  
9050 Camino Santa Fe  
San Diego, California 92121, USA  
Telephone: (858) 652-4600

PK, safety, and statistical analyses were performed and a report was prepared at Celerion, Data Management and Biometrics department, under the direction of:

Anthea Cromie, PhD  
Senior Director, Clinical Pharmacology Sciences  
Data Management and Biometrics  
Celerion  
22-24 Lisburn Road  
Belfast, Northern Ireland BT9 6AD  
Telephone: + 44 (0) 28 90 554040  
Email: anthea.cromie@celerion.com

Curriculum vitae of the PI is included in [Appendix 16.1.4](#).

The signature pages for the PI and Data Management and Biometrics Senior Director from Celerion and NeoMatrix Therapeutics, Inc. are located in [Appendix 16.1.5](#).

## 7. INTRODUCTION

### 7.1 Background

According to the American Burn Association, burn injuries claim the lives of at least 3,000 United States civilians, and send another 500,000 to seek medical attention each year, of which 40,000 cases require hospitalization. The resulting estimated annual expenditure is more than \$2 billion direct costs and much greater indirect costs ([America Burn Association, 2016](#); [Sierra Zúñiga et al., 2016](#)). Of burn patients admitted to hospitals, 10% have burns that exceed 30% of the total body surface area.

In addition, burns represent 5 to 20% of all combat related injuries ([Cancio et al., 2005](#); [Chan et al., 2015](#); [Kauvar et al., 2006a, 2006b](#); [Thomas et al., 2003](#)), twenty percent of which are considered severe or involve more than 20% of total body surface area ([Chung et al., 2006](#)). These burns result in significant morbidity and mortality, as well as long-term complications including functional impairment and aesthetic disfigurement. Burns are dynamic injuries characterized by progressive extension of the size and severity (depth) of the burn over the course of several days ([Lanier et al., 2011](#)).

Current burn therapies focus on preventing infection and optimizing wound healing. Topical antimicrobial agents reduce bacterial contamination, subsequent burn wound infection, and the incidence of sepsis. A variety of synthetic and biological dressings have been developed to optimize the wound-healing environment, resulting in more rapid healing and reduced pain; and early excision of deep burns followed by grafting with autologous, allogeneic or xenogeneic skin or with skin substitutes has been shown to improve outcomes. However, no current treatments have been shown to limit or prevent burn injury progression and it is not known whether such treatments would mitigate scarring.

Fibronectin (FN) has been shown to play a vital role in wound healing and is deficient in burn patients' wounds and blood. cP12 is a novel FN derived, 14-mer peptide (P12) from the first FN type III repeat that promotes mesenchymal cell growth, proliferation and migration in vitro and acts synergistically with a variety of growth factors including platelet-derived growth factor-BB (PDGF-BB) ([Lin et al., 2014](#); [Zhu et al., 2014](#)). Furthermore, P12 protects adult human dermal fibroblasts (AHDF) from cell death induced by oxidative and cytokine stress in vitro ([Lin et al., 2014](#)) and speeds healing and reduces scarring in a vertical burn progression model in pigs ([Asif et al., 2016](#); [Singer et al., 2011](#)). The intravenous efficacy of cP12 is largely due to its ability to reduce microvascular occlusion by red blood cell aggregates ([Asif et al., 2016](#)) presumably through microvasculature dilation ([Frame et al., 2017](#)) without any effects on the central cardiovascular system ([Asif et al., 2016](#)).

The Sponsor is pursuing development of cP12 for injection for treatment to limit burn injury progression, shorten healing time, and reduce scarring of acute, deep burns in hospitalized patients.

### 7.2 Rationale for Starting First-In-Human Clinical Dose and Planned Dose Levels

The planned dose levels for this study were 0.003, 0.01, 0.02, 0.04, and 0.08 mg/kg.

The doses in the first 4 cohorts did not exceed 0.04 mg/kg. This was based on the data generated from the pivotal toxicology studies which identified the dog as the most sensitive species. As specified in the FDA guideline for establishing safe initial clinical doses, a safety factor of 10 was applied to the human equivalent dose (HED) calculated from the no observed adverse effect level (NOAEL) dose in the most sensitive species (dogs). In addition, when considering the findings from the dog expanded acute toxicology study, it was concluded that dosing in humans up to 0.04 mg/kg would be safe.

The NOAEL dose was 2.5 mg/kg in rats and 0.25 mg/kg in dogs. The HED was calculated using the conversion factors provided in FDA's 2005 Guidance for Industry, Estimating the Maximum Safe Starting Dose in Initial Clinical Trials for Therapeutics in Adult Healthy Volunteers ([US FDA and CDER, 2005](#)). The resulting HEDs were 0.40 mg/kg (from the rat NOAEL) and 0.14 mg/kg (from the dog adjusted NOAEL) indicating that dogs are more sensitive to cP12 than rats. Applying a safety factor of 10 to the dog HED resulted in an initial starting dose in humans of 0.014 mg/kg.

Pharmacodynamic data obtained using the pig vertical burn progression model indicated some degree of efficacy at a dose of 0.003 mg/kg. Therefore, administration of cP12 in the initial clinical trial was planned to initiate at this dose (0.003 mg/kg), with subsequent incremental increases in the dose according to standard industry practices.

As of 14 October 2019, 4 cohorts had completed the study and no safety concerns were observed upon review by the Safety Review Committee (SRC). Therefore, Cohort 5 was conducted and the dose was increased to 0.08 mg/kg.

The higher dose in Cohort 5 helped inform dosing decisions for the planned Phase 2a clinical study in burn patients. In the Phase 2a study, the dose will likely advance to at least 0.03 mg/kg; therefore, it was important to increase the margin of safety through the inclusion of a higher dose (0.08 mg/kg) cohort in healthy subjects.

Additional information may be found in the protocol ([Appendix 16.1.1](#)) and the Investigator Brochure ([IB, 2017](#)).

## **8. STUDY OBJECTIVES AND ENDPOINTS**

### **8.1 Study Objectives**

Primary Objective: To assess the safety and tolerability of single ascending intravenous (IV) doses of cP12 in healthy subjects.

Secondary Objective: To investigate the PK profile of cP12 after single ascending IV doses in healthy subjects.

## **8.2 Study Endpoints**

### **8.2.1 Safety and Tolerability**

- Adverse event (AE) reporting
- Vital signs
- Clinical laboratory values (hematology, chemistry, and urinalysis)
- QTc interval and other electrocardiogram (ECG) parameters

### **8.2.2 Pharmacokinetic**

- Plasma cP12 concentrations and PK parameters following a single dose of cP12 (Day 1).

## **9. INVESTIGATIONAL PLAN**

### **9.1 Overall Study Design and Plan**

This was a randomized double-blind, placebo-controlled single ascending dose (SAD) study to evaluate the safety, tolerability, and PK profile of cP12 in healthy male and female subjects. Each subject was randomized to receive either a single dose of cP12 or placebo. Each dose cohort included 6 subjects dosed with cP12 and 2 subjects dosed with placebo. As this was a First-In-Human (FIH) study, the first two subjects in each cohort were dosed as sentinel subjects (one with cP12 and one with placebo) and monitored for acute events that were considered severe and/or serious. If no serious or severe events occurred in the acute postdose period (24 hours postdose), the remaining 6 subjects in the cohort were dosed. If acute serious or severe events were noted, the remainder of the cohort was not treated until complete safety data through Day 8 for the sentinel subjects were reviewed and were determined safe to proceed. Cohorts were studied sequentially starting with the lowest cP12 dose. The cohort was enrolled in order to complete the study objectives after review of the blinded safety data by the SRC. Subjects received a single, approximately 30-minute IV infusion of cP12 or placebo at their assigned dose level.

Subjects were confined to the research facility from Day -1 (the day before study drug administration) through completion of the Day 3 safety assessments.

Blood samples for serum chemistry and hematology, urinalysis, and ECGs were obtained at several time points during the study for safety evaluation. Blood samples for cP12 plasma PK analysis were collected at predose, and 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6, 12, and 24 (Day 2) hours postdose from the start of infusion. During the infusion period, blood samples were drawn from the arm contralateral to the arm receiving the infusion. Once the infusion was completed, both arms may have been used for blood sampling.

A urine PK sample was obtained within 2 hours predose and from 0 to 2 hours, 2 hours to 4 hours, and 4 hours to 6 hours postdose. However, whilst urine samples were analyzed the results were not required to be reported within this CSR.

## 9.2 Discussion of Study Design and Choice of Control Groups

This study was designed to meet the objectives outlined in [Section 8](#).

## 9.3 Selection of Study Population

Individuals were eligible for the study if they met all of the inclusion and none of the exclusion criteria. The criteria below were assessed at the screening visit that occurred 1 – 30 days prior to administration of study drug on Day 1. Continued subject eligibility was verified on Day -1 upon admittance to the research facility.

### 9.3.1 Inclusion Criteria

A subject was included in the study only if all of the following inclusion criteria were met:

1. Healthy male or female between the ages of 18 and 65 years, inclusive, at the time of Screening;
2. Body mass index (BMI) between 18 kg/m<sup>2</sup> and 32 kg/m<sup>2</sup> (inclusive) and body weight of  $\geq 50$  kg;
3. Female subjects were of non-childbearing potential. Subject had undergone one of the following sterilization procedures at least 6 months prior to the first dose/dosing:
  - hysteroscopic sterilization;
  - bilateral tubal ligation or bilateral salpingectomy;
  - hysterectomy;
  - bilateral oophorectomy;or been postmenopausal with amenorrhea for at least 1 year prior to the first dose/dosing and follicle stimulating hormone (FSH) serum levels consistent with postmenopausal status;
4. All females had a negative pregnancy test on Day -1 regardless of childbearing potential;
5. Male subjects with female partners (including postmenopausal women) agreed to use highly effective contraceptive measures from the screening visit until one month after taking the dose of study medication. Highly effective contraception included documented vasectomy, abstaining from intercourse, double-barrier method (e.g., male using a condom and female using a diaphragm or cervical cap), or barrier plus hormonal contraception (e.g., male using a condom and female using a hormonal contraception). Males were willing to inform female partners of their participation in the study and agreed to use adequate contraceptive methods;
6. Continuous non-smoker who had not used nicotine containing products for at least 3 months prior to the first dose/dosing and throughout the study;
7. Able to understand the study procedures, voluntarily consented to participate in this study, and provided written informed consent prior to start of any study-specific procedures;



8. Willing and able to remain in the study unit for the entire duration of the confinement period (4 days and 3 nights) and return for 1 outpatient visit.

### **9.3.2 Exclusion Criteria**

Subjects who met any of the following criteria were excluded from the study:

1. Clinically significant laboratory abnormality or other clinical findings indicative to the Investigator of a clinically significant exclusionary disease (included but not limited to renal, hepatic, gastrointestinal, cardiovascular, neurological disease);
2. Significant history or current evidence of chronic infectious disease, system disorder or organ dysfunction;
3. A history of allergy or hypersensitivity to drugs;
4. Positive results for hepatitis B surface antigen (HBsAg), hepatitis C antibody, or human immunodeficiency virus (HIV) antibody;
5. Positive result for alcohol at screening or upon admission to the research facility;
6. Positive result for substances of abuse at screening or upon admission to the research facility;
7. A recent history of alcoholism (< 2 years) or of moderate alcohol use (greater than an average of 3 alcoholic drinks per day or a total of 21 alcoholic drinks per week). One drink was defined as 1 bottle (12 oz) beer, 1 glass (4 oz) wine or 1 oz liquor;
8. Had any history of dependency or treatment for substance abuse in the past year (other than alcohol);
9. An ECG abnormality deemed by the Investigator to be clinically significant;
10. The donation of blood (1 pint or more) within 56 days or plasma within 7 days of receiving study drug until after the End-of-Study visit;
11. History of difficulty with phlebotomy;
12. Use of any prescription drug therapy, dietary or herbal supplements, or megavitamin supplements within 14 days or 5 half-lives (whichever was longer) prior to receiving study drug; restriction applied until after the End-of-Study (EOS) visit;
13. Use of over-the-counter (OTC) medications within 7 days or 5 half-lives (whichever was longer) prior to receiving study drug; restriction applied until after the EOS visit;
14. Consumption of alcohol within 48 hours prior to admission to the research facility until after the EOS visit;
15. Any condition which in the opinion of the Investigator would have interfered with the participant's ability to provide informed consent, comply with study instructions, possibly confound interpretation of study results, or endanger the participant if he or she took part in the trial;

16. Use of an investigational drug or product within 30 days prior to receiving study drug.

### 9.3.3 Removal of Subjects From Assessment

All subjects had the right to withdraw from this study at any time. In addition, it was the right of the Investigator to remove subjects from the study as a result of adverse reactions, a protocol violation, or non-compliance. The study may have also been terminated by the Sponsor.

Had a subject withdrawn after administration of study drug, or had the Investigator decided to withdraw the subject, all efforts were made to complete and report the protocol-stipulated observations up to the time of withdrawal. EOS/Early Termination (ET) procedures were completed at the time of the subject's withdrawal and an explanation was provided as to why the subject was withdrawing or being withdrawn from the study.

The Investigator documented the primary reason for discontinuation of a study subject on the appropriate case report form (CRF). If the reason for withdrawal was a clinical AE, monitoring continued until the AE was resolved or the Investigator assessed the AE as chronic or stabilized.

Subjects who did not receive study drug or placebo may have been replaced. Subjects who withdrew or were withdrawn due to an AE were not replaced. Subjects who dropped out after receiving study drug for reasons other than AEs may have been replaced at the discretion of the Sponsor in consultation with the Investigator. However, there were no subject dropouts in this study.

## 9.4 Treatments

### 9.4.1 Treatments Administered

Vials of lyophilized cP12 peptide were provided (10 mg in a 5 mL vial) and reconstituted and diluted in 0.9% sodium chloride injection for the appropriate IV dose. Placebo was 0.9% sodium chloride. The cP12 peptide was provided by the sponsor and the placebo was commercially sourced by the clinical site. Both active and placebo doses were prepared in the research facility pharmacy in accordance with the randomization schedule by the site pharmacist or designee.

The treatments descriptions were as follows:

| Treatment   | Short Description | Long Description                                                                  |
|-------------|-------------------|-----------------------------------------------------------------------------------|
| Placebo     | Placebo           | a single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes       |
| Treatment A | 0.003 mg/kg cP12  | a single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1) |

| <b>Treatment</b> | <b>Short Description</b> | <b>Long Description</b>                                                          |
|------------------|--------------------------|----------------------------------------------------------------------------------|
| Treatment B      | 0.01 mg/kg cP12          | a single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2) |
| Treatment C      | 0.02 mg/kg cP12          | a single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3) |
| Treatment D      | 0.04 mg/kg cP12          | a single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4) |
| Treatment E      | 0.08 mg/kg cP12          | a single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5) |

#### **9.4.2 Identity of Investigational Products**

The following study drugs were administered during the course of the study.

Placebo for cP12

0.9% Sodium Chloride Injection, USP 1000 mL

Manufactured by: Hospira, Inc.

Lot No.: 01-022-JT

Expiration date: 01 January 2021

Received from: McKesson

cP12 Peptide Injection 10 mg/vial

Manufactured by: The University of Iowa Pharmaceuticals

Lot No.: 078I0915

Expiration date: The Certificate of Testing was supplied but the expiration date was not provided.

Received from: University of Iowa Pharmaceuticals

The same batch and/or lot number were used during the entire course of the study.

Upon receipt at Celerion (Tempe, Arizona), the study drug was transferred to the pharmacy. All drug products were kept in a locked pharmacy storage room which had access limited to authorized associates. Both the temperature and humidity were continually monitored.

#### **9.4.3 Method of Assigning Subjects to Treatment Groups**

A randomization schedule for the allocation of placebo or cP12 was generated by the Celerion statistician prior to the start of the study. After reconfirming eligibility, subjects were considered randomized at the time of administration of study drug or placebo. If a randomized subject withdrew/was withdrawn from the study, the randomization code was not reused. The randomization list provided replacement numbers.

If a subject who did not meet eligibility criteria received study drug prior to the error being identified, the subject should have completed all study assessments. The Investigator would

have notified the Sponsor of the error and a joint decision would have been made as to whether the subject should have been replaced. If applicable, the IRB was notified.

The randomization schedule is presented in [Appendix 16.1.7](#).

#### **9.4.4 Selection of Doses in the Study**

Refer to [Section 7.1](#).

#### **9.4.5 Selection and Timing of Dose for Each Subject**

Subjects fasted from all food and drink (except for water) for a period of 8 hours prior to study drug (or placebo) administration. Study drug or placebo was infused over a period of approximately 30 minutes, and subjects continued fasting for 4 hours after the start of the infusion. Study drug infusion occurred in the morning of Day 1.

A listing of scheduled and actual drug administration times is presented in [Appendix 16.2.5.4.2](#).

#### **9.4.6 Blinding**

This was a randomized, double-blind study. An unblinded pharmacist or designee was required at the Clinical Site to comply with the study's randomization and blinding requirements. The unblinded pharmacy staff was responsible for all drug accountability issues throughout the study including, preparing, labeling, and dispensing study drug according to the randomization code provided, yet remained independent of all subject assessments.

The unblinded pharmacy staff was trained on the requirements of the study. Specific topics covered in the training included the randomization procedure, drug preparation and dispensing procedures, and drug accountability guidelines.

Randomization codes were provided to the unblinded pharmacist. Confirmation of receipt of the randomization code was provided by the pharmacist. The unblinded pharmacy staff was responsible for maintaining the blind, consistent with protocol design, throughout the study.

The subjects, Investigator, study personnel involved with subject assessments, and the Sponsor remained blinded to the actual treatment assignments of the subjects (cP12 or placebo) during the treatment period of each cohort of subjects. The Investigator was ultimately responsible for ensuring that the integrity of the blind was maintained throughout the treatment period of each cohort. The Investigator was required to notify the Sponsor in the event of any breaking of the blind for any reason other than safety and PK evaluations performed at the end of each cohort to determine whether escalation to the next dosing level was warranted.

If an emergency unblinding was required, the Investigator would have immediate access to the sealed randomization codes. When possible, such emergencies were discussed with the Sponsor prior to disclosure of the treatment. If the treatment assignment was revealed, the

reason and justification for breaking the blind was recorded, the date and time in which the blind was broken, the identity of the person breaking the blind and any others unblinded. Information that would lead to further unblinding in the CRF or source documentation were not recorded.

Under some circumstances, the Investigator, Sponsor and Independent Medical Monitor may have required review of unblinded data. However, no unblinding was needed on this study.

#### **9.4.7 Sentinel Dosing**

For each cohort, a sentinel dosing plan was employed at each dose level. The first 2 subjects were randomized and dosed as sentinels (N=2, 1:1 cP12:placebo). If severe and/or serious AEs (SAEs) were experienced by the sentinel subjects in the acute period following dosing (24 hours postdose), the remaining 6 subjects of the cohort were not dosed until a full review of all safety data from the sentinel subjects was completed. The acute safety data were evaluated by the Investigator in collaboration with the Sponsor. If the acute safety data of the sentinel group indicated that the dose was safe and well tolerated, the remaining subjects of that cohort were randomized (N=6, 5:1 cP12:placebo) and treated the day following the dosing of the sentinel subjects.

#### **9.4.8 Dose Escalation/Stopping Criteria**

The SRC was responsible for reviewing data between cohorts and determined if escalation was warranted. The SRC consisted of the Investigator, Sponsor, and Independent Research Monitor. Dr. William Riddle acted as the Independent Research Monitor for Cohorts 1 to 4, and was subsequently replaced by Dr. Gil Price for Cohort 5. The Independent Research Monitor(s), in collaboration with the PI, oversaw the safety of the research and reported applicable events to the IRB, regulatory authorities, and Department of Defense (DoD). The Independent Research Monitor reviewed unanticipated problems involving risk to the subjects and had the authority to stop a research protocol in process, remove individual human subjects from the study, and take whatever steps necessary to protect the safety and well-being of the participants.

Prior to dose escalation to the next higher dose, the SRC reviewed the following blinded data from the previous lower dose cohorts:

- All AEs and SAEs
- Clinical safety laboratory data
- Clinical signs and symptoms including vital signs and physical examination findings
- Safety ECG findings
- Available PK data

If 2 of 6 subjects receiving active study drug experienced moderate or severe adverse effects in the same body system, consideration was given to halting dose escalation. Any serious, potentially drug-related AE halted dose escalation. Subsequent cohorts may have received the same or lower doses to better characterize the safety and tolerability of cP12.

The goal was to characterize the safety, tolerability, and PK over the dose range described in [Section 9.4.1](#). However, actual dose levels may have been adjusted as the emerging safety, tolerability, and PK data permit, and subsequent cohorts may have received the same or lower doses.

If, in the opinion of the study physician, Independent Research Monitor, or Sponsor, any drug-related AE was potentially life threatening or irreversible in nature, escalation to the next higher dose group was NOT undertaken and the study was stopped.

#### **9.4.9 Prior and Concomitant Therapy**

##### **9.4.9.1 Concomitant Medications**

1. Subjects did not take any OTC medication from 7 days or 5 half-lives (whichever was longer) prior to receiving study drug; restriction applied through the EOS visit.
2. Subjects did not take any prescription medication, dietary or herbal supplements, or megavitamin supplements from 14 days or 5 half-lives (whichever was longer) prior to receiving study drug; restrictions applied through the EOS Visit.
3. Investigational drugs were discontinued within 30 days prior to receiving study drug on Day 1.

OTC acetaminophen or ibuprofen may have been taken during the confinement period and through the EOS visit in amounts no greater than as directed on the label. In the event any concomitant medication was prescribed during the study (e.g., treatment of an AE), the name of the medication taken during the study was recorded with indication, daily dose, and start and stop dates of administration.

A complete listing of all prior and concomitant medications can be found in [Appendix 16.2.5.8](#).

##### **9.4.9.2 Other Restrictions**

The following restrictions were adhered to throughout the study or the subject may have been excluded or withdrawn from the study.

1. Subjects did not donate blood or plasma from 8 weeks or 7 days, respectively, prior to study drug administration until the End-of-Study visit.
2. Subjects did not engage in strenuous exercise from 48 hours prior to admission to the research facility until the EOS visit.
3. Subjects fasted from all food and drink (except water) for at least 8 hours prior to clinical laboratory blood sampling and dosing. Fasting and fluid restrictions may have been made shorter at the discretion of the SRC.
4. Subjects received meals served at scheduled times during confinement. On non-dosing days, meals were served at normal times after study assessments were completed.
5. From Screening through the EOS visit, subjects refrained from grapefruit or grapefruit juice, Seville oranges and quinine (tonic water).

6. Subjects did not consume alcohol within 48 hours prior to admission to the research facility until after the EOS visit.

#### **9.4.10 Treatment Compliance**

Clinic personnel at Celerion ensured dosing compliance by closely monitoring the subjects as they were being dosed, as appropriate for the method of dosing. Drug administration was noted in [Appendix 16.2.5.4.2](#).

Treatment compliance was ensured by dosing subjects in a closed clinical setting and by monitoring subjects frequently during the course of each drug administration.

### **9.5 Pharmacokinetic and Safety Variables**

#### **9.5.1 Pharmacokinetic and Safety Measurements Assessed and Flow Chart**

The study design and schedule of assessments conducted during this trial were summarized in the following schematic ([Table 9–1](#)), and were described in detail in the sections that follow.

**Table 9–1 Study Events Flow Chart**

| Study Period                                                              | Screen    | Admit | Treatment and Observation |   |      |     |      |   |     |   |   |   |    |    |    | EOS/ET |               |
|---------------------------------------------------------------------------|-----------|-------|---------------------------|---|------|-----|------|---|-----|---|---|---|----|----|----|--------|---------------|
| Day                                                                       | -30 to -2 | -1    | 1                         |   |      |     |      |   |     |   |   |   |    |    | 2  | 3      | Day 8 ± 1 day |
| Hour                                                                      |           |       | Predose                   | 0 | 0.25 | 0.5 | 0.75 | 1 | 1.5 | 2 | 4 | 6 | 12 | 24 | 48 |        |               |
| Informed consent                                                          | X         |       |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |               |
| Medical history                                                           | X         | X     |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |               |
| Demographics                                                              | X         |       |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |               |
| Physical Examination <sup>1</sup>                                         | X         |       |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |               |
| Brief Physical Examination <sup>2</sup>                                   |           | X     |                           |   |      |     |      |   |     |   |   |   |    |    |    | X      |               |
| Inspection of infusion site <sup>11</sup>                                 |           |       | X                         |   | X    |     |      |   |     |   |   |   |    |    |    |        |               |
| Vital signs <sup>3</sup>                                                  | X         |       | X                         |   | X    | X   | X    | X | X   | X | X | X | X  | X  | X  | X      |               |
| Height and Weight <sup>4</sup>                                            | X         | X     |                           |   |      |     |      |   |     |   |   |   |    |    |    | X      |               |
| 12-lead Safety ECG (single) <sup>5</sup>                                  | X         | X     |                           |   |      |     |      | X |     |   |   | X |    | X  | X  | X      |               |
| 12-lead Cardiodynamic ECG (triplicate) via Holter Monitoring <sup>6</sup> |           |       | X                         |   | X    | X   | X    | X | X   | X | X | X | X  | X  |    |        |               |
| Serology (HBsAg, HCV, HIV)                                                | X         |       |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |               |
| Serum chemistry and hematology (fasted) <sup>7</sup>                      | X         | X     |                           |   |      |     |      |   |     |   |   |   |    |    | X  | X      |               |
| Troponin, CRP, Total CK, GGT <sup>7</sup>                                 | X         | X     |                           |   |      |     |      |   |     |   | X |   | X  | X  | X  | X      |               |
| Urinalysis                                                                | X         | X     |                           |   |      |     |      |   |     |   |   |   |    |    | X  | X      |               |
| FSH (postmenopausal females)                                              | X         |       |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |               |



| Study Period                                   | Screen    | Admit | Treatment and Observation |   |      |     |      |   |     |   |   |   |    |    |    | EOS/ET |               |
|------------------------------------------------|-----------|-------|---------------------------|---|------|-----|------|---|-----|---|---|---|----|----|----|--------|---------------|
| Day                                            | -30 to -2 | -1    | 1                         |   |      |     |      |   |     |   |   |   |    |    | 2  | 3      | Day 8 ± 1 day |
| Hour                                           |           |       | Predose                   | 0 | 0.25 | 0.5 | 0.75 | 1 | 1.5 | 2 | 4 | 6 | 12 | 24 | 48 |        |               |
| Drug, cotinine and alcohol screen <sup>8</sup> | X         | X     |                           |   |      |     |      |   |     |   |   |   |    |    |    |        |               |
| Pregnancy test (females)                       | X         | X     |                           |   |      |     |      |   |     |   |   |   |    |    |    | X      |               |
| IV infusion (cP12 or placebo)                  |           |       |                           | X | X    | X   |      |   |     |   |   |   |    |    |    |        |               |
| Plasma PK <sup>9</sup>                         |           |       | X                         |   | X    | X   | X    | X | X   | X | X | X | X  | X  |    |        |               |
| Urine PK <sup>10</sup>                         |           |       | X                         | X | X    | X   | X    | X | X   | X | X | X |    |    |    |        |               |
| Adverse events                                 | X         | X     | X                         | X | X    | X   | X    | X | X   | X | X | X | X  | X  | X  | X      |               |
| Concomitant medications                        | X         | X     | X                         | X | X    | X   | X    | X | X   | X | X | X | X  | X  | X  | X      |               |

ECG = electrocardiogram, FSH = follicle-stimulating hormone, IV = intravenous, PK = pharmacokinetic.

Note: When several assessments were to be conducted at the same time point, the preferred order of assessments was ECG, vital signs and blood draws.

- 1 Full physical examination (PE) included general appearance, skin, EENT, Head/neck, musculoskeletal, respiratory, cardiovascular (including rhythm and presence of cardiac abnormalities), abdominal examination, neurologic examination to record the presence of abnormalities in mental status, motor, and sensory function, and any additional assessments necessary to establish baseline status or evaluate symptoms or adverse experiences. Significant findings prior to dosing were recorded on the Medical History page of the CRF. Only changes from baseline that met the definition of a treatment-emergent adverse event (TEAE) were recorded as an AE.
- 2 Brief PE included general appearance, skin, respiratory, cardiovascular (including rhythm and presence of cardiac abnormalities), abdominal examination. Significant findings prior to dosing were recorded on the Medical History page of the CRF. Only changes from baseline that met the definition of a TEAE were recorded as an AE.
- 3 Vital signs included respiration rate, temperature, blood pressure and pulse.
- 4 Height was collected only at Screening. Weight was collected at Screening, Day -1, and the EOS/ET visit.
- 5 A single ECG was obtained after the subject had been in a supine position for approximately 5 minutes.
- 6 Cardiodynamic ECGs were collected in triplicate. Baseline measurements were obtained in triplicate at 3 different time points before dosing separated by approximately 15 - 30 minutes. Postdose collection time points were based off the start of the infusion. Triplicate ECGs were collected within a 5 minute window after subject had been in a supine position for approximately 10 minutes. For the 0.25, 0.5, 0.75, and 1 hour time points it was not feasible for subjects to be completely undisturbed for the full 10 minute duration. For these time points every effort was made to minimize external stimuli and maximize the time subjects were undisturbed. Holter monitoring was used to collect continuous 12-lead ECG data for the purpose of collecting

cardiodynamic ECGs. Recording was started and stopped at logistically optimal times to ensure that all scheduled time points were collected. Collection began on Day 1 and ended on Day 2.

- 7 Subjects fasted for at least 8 hours prior to collection. Safety labs may have been added at the discretion of the Investigator. If Total CK was elevated, CK-MB may have been collected.
- 8 Drug and alcohol screen were based on standard testing at the clinical research unit (CRU).
- 9 Timing of serum PK sampling was from the start of the infusion. It was important that PK sampling occurred as close as possible to the scheduled time ( $\pm 10\%$ ). Unscheduled or additional PK samples may have been collected if appropriate in the opinion of the Investigator and/or Sponsor.
- 10 A urine PK sample was obtained within 2 hours predose and from 0 to 2 hours, 2 hours to 4 hours, 4 hours to 6 hours.
- 11 Site staff assessed the infusion site at predose and at 2 minutes, 5 minutes and 15 minutes after the initiation of the infusion. Any infusion site reactions were recorded as AEs.

### 9.5.2 Appropriateness of Measurements

The safety assessments conducted in this study are standard and were judged appropriate by the PI.

The selection and timing of blood samples for PK analysis were judged appropriate for characterizing the PK profiles, given the treatment and dose administered.

### 9.5.3 Primary Pharmacokinetic Parameters

The appropriate noncompartmental PK parameters were calculated from the plasma cP12 concentration-time data using Phoenix<sup>®</sup> WinNonlin<sup>®</sup> Version 7.0. Actual sample times and infusion times were used in the calculations of the PK parameters. The calculation of the actual time for cP12 was in respect to the start of infusion time on Day 1. All PK parameters included in the protocol are listed in Table 9–2 below, and are defined as appropriate for study design.

**Table 9–2 Noncompartmental Pharmacokinetic Parameters Calculated**

| Parameter             | Label Used in the Tables and Figures* | Definition                                                                                                           | Method of Determination                                                                                                                                        |
|-----------------------|---------------------------------------|----------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| AUC <sub>0-last</sub> | AUC0-last                             | Area under the concentration-time curve from time 0 to the time of the last observed/measured non-zero concentration | Calculated using the Linear up/log down Trapezoidal rule                                                                                                       |
| AUC <sub>0-inf</sub>  | AUC0-inf                              | Area under the concentration-time curve from time 0 extrapolated to infinity                                         | $AUC_{0-inf} = AUC_{0-last} + (C_{last}/K_{el})$<br>where $C_{last}$ is the last observed/measured concentration                                               |
| C <sub>max</sub>      | Cmax                                  | The maximum observed concentration                                                                                   | Taken directly from bioanalytical data                                                                                                                         |
| T <sub>max</sub>      | Tmax                                  | The time to reach C <sub>max</sub>                                                                                   | Taken from clinical database as the difference in the time of start of infusion and the time of the blood draw which is associated with the C <sub>max</sub> . |
| λ <sub>z</sub>        | Kel                                   | Apparent elimination rate constant                                                                                   | Estimated by linear regression of the log-transformed plasma concentrations during the terminal log-linear decline phase                                       |
| t <sub>½</sub>        | t1/2                                  | Apparent half-life                                                                                                   | Calculated as $0.693/K_{el}$                                                                                                                                   |
| CL                    | CL                                    | Systemic plasma clearance                                                                                            | Calculated as $Dose/(AUC_{0-inf})$                                                                                                                             |
| V <sub>z</sub>        | Vz                                    | Volume of distribution during the terminal elimination phase                                                         | Calculated as $Dose/(AUC_{0-inf} \times K_{el})$                                                                                                               |

| Parameter                | Label Used in the Tables and Figures* | Definition                               | Method of Determination                   |
|--------------------------|---------------------------------------|------------------------------------------|-------------------------------------------|
| DN AUC <sub>0-last</sub> | DN AUC0-last                          | Dose-normalized AUC <sub>0-last</sub> ** | Calculated as AUC <sub>0-last</sub> /Dose |
| DN AUC <sub>0-inf</sub>  | DN AUC0-inf                           | Dose-normalized AUC <sub>0-inf</sub> **  | Calculated as AUC <sub>0-inf</sub> /Dose  |
| DN C <sub>max</sub>      | DN Cmax                               | Dose-normalized C <sub>max</sub> **      | Calculated as C <sub>max</sub> /Dose      |

\*In the text of the clinical study report (CSR), subscripts are used in parameter names, as appropriate.

\*\*Dose-normalized refers to the dose-adjusted and dose-corrected terms used throughout the protocol.

For the calculation of the PK parameters, plasma concentrations below the limit of quantitation (BLQ) prior to the first quantifiable concentration were set to 0 and plasma concentrations BLQ after the first quantifiable concentration were treated as missing. The K<sub>el</sub> was determined using linear regressions composed of at least 3 data points. The K<sub>el</sub> was not assigned if 1) the terminal elimination phase was not apparent, 2) if T<sub>max</sub> was one of the 3 last data points, or 3) if the R<sup>2</sup> value was less than 0.75. In cases where the K<sub>el</sub> interval was not assigned, the values of t<sub>1/2</sub>, AUC<sub>0-inf</sub>, CL, and V<sub>z</sub> were considered not calculable and were not reported. Wherever the resulting t<sub>1/2</sub> was more than half as long as the sampling interval, the K<sub>el</sub> values and associated parameters (t<sub>1/2</sub>, AUC<sub>0-inf</sub>, CL, and V<sub>z</sub>) may not have been presented as judged appropriate and in accordance with Celerion SOPs.

The drug product is a sterile lyophilized peptide containing 10 mg of cP12. The subject weight on Day -1 was used to calculate the actual dose as follows:

$$\text{Actual dose (mg)} = \text{nominal dose (mg/kg)} \times \text{weight (kg)}$$

Dose-dependent PK parameters (CL, V<sub>z</sub>, DN AUC<sub>0-last</sub>, DN AUC<sub>0-inf</sub>, and DN C<sub>max</sub>) were calculated using the actual dose.

#### 9.5.4 Drug Concentration Measurements

Blood samples for plasma cP12 PK determination were drawn at predose (within 60 minutes of dosing) and at 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6, 12, and 24 hours postdose. Hour 0 was the start of infusion.

A urine PK sample was obtained within 2 hours predose and from 0 to 2 hours, 2 hours to 4 hours, and 4 hours to 6 hours postdose.

All concentration data were included in the calculation of the individual PK parameters, the individual concentration-time plots (based on actual sample times), and in the mean concentration-time plots (based on nominal sample times). However, if there were any significant deviations from nominal sample times, some concentration data may have been excluded from mean concentration-time plots and/or additional concentration-time plots of

the mean data may have been provided. All deviations and excluded data were provided and discussed in the CSR.

#### **9.5.5 Analytical Procedures**

Plasma and urine samples were transferred to the analytical laboratory MicroConstants (San Diego, California), at specified time points during the clinical conduct of the study. Plasma samples were analyzed for cP12 using a validated assay. The analytical range (lower limit of quantitation [LLOQ] – upper limit of quantitation [ULOQ]) for cP12 was 0.200 – 200 ng/mL (the LLOQ was adjusted to be 0.400 ng/mL via dilution for one sample only [Subject 039, 24 hours]). The samples from all evaluable subjects were analyzed. Placebo samples were not analyzed. Urine samples were analyzed for cP12 using a validated assay, however, urine sample results are not reported in this CSR.

#### **9.6 Data Quality Assurance**

Data were handled and processed according to Celerion SOPs, which are written based on the principles of GCP. Training sessions are conducted on a regular basis for site personnel.

Documentation of clinical laboratory reference ranges is included in [Appendix 16.1.10.1](#).

All clinical data underwent a 100% quality control (QC) check prior to database lock. When the database was declared to be complete and accurate, access to the database was restricted.

CRFs were printed directly from the database. Each CRF was reviewed and signed by the PI. A sample CRF is presented in [Appendix 16.1.2](#).

Various phases of the study were audited by the Quality Assurance (QA) department of Celerion, with a final issuance of a QA audit certificate with the final report. The QA audit certificate is presented in [Appendix 16.1.8](#).

Final bioanalytical data were received from MicroConstants (San Diego, California) in Microsoft Excel format.

The Study Monitor, Susan Szambelan, visited Celerion on 04 June 2019 for a study initiation visit, and on 08 and 29 July 2019, and 16 and 17 September 2019 to monitor the study. Due to the COVID-19 pandemic and the subsequent travel restrictions, remote monitoring was performed on Cohort 5 data and the study close-out visit.

#### **9.7 Statistical Methods Planned in the Protocol and Determination of Sample Size**

##### **9.7.1 Statistical and Analytical Plans**

Full details of the statistical analyses performed on the study data can be found in the final statistical analysis plan (SAP), presented in [Appendix 16.1.9.1](#).

### **9.7.1.1 Analysis Populations**

#### **Safety Population**

The safety population included all subjects who received at least one dose of study drug (active or placebo).

#### **Pharmacokinetic Population**

The PK population included data from all subjects who received at least one dose of active study drug (cP12) and completed at least one PK blood draw resulting in at least one quantifiable plasma concentration. All available data were included in the concentration and PK parameter tables to the extent possible. Data for each subject were included in the summary statistics and statistical comparisons of PK parameters with the following exception: data from subjects who significantly violated a protocol inclusion or exclusion criteria, deviated significantly from the protocol, or had unavailable or incomplete data which may have influenced the PK analysis were to be excluded from the PK analysis population. However, no subject met criteria for exclusion.

### **9.7.1.2 Data Summarization and Presentation**

All cP12 PK concentrations and/or PK parameters descriptive statistics were generated using SAS®.

The plasma concentrations of cP12 were listed and summarized by treatment (dose level) and time point for all subjects in the PK Analysis Population. Plasma concentrations of cP12 were presented with the same level of precision as received from the bioanalytical laboratory. Summary statistics, including sample size (n), arithmetic mean (Mean), standard deviation (SD), coefficient of variation (CV%), standard error of the mean (SEM), minimum, median, and maximum were calculated for all nominal concentration time points. Excluded subjects were included in the concentration listings, but were excluded from the summary statistics and noted as such in the tables. All BLQ values were presented as “BLQ” in the concentration listings and footnoted accordingly.

Mean and individual concentration-time profiles were presented on linear and semi-log scales. Linear mean plots were presented with and without SD.

Plasma cP12 PK parameters were listed and summarized by treatment (dose level) for all subjects in the PK Analysis Population. Pharmacokinetic parameters were reported to at least 3 significant figures for individual parameters, with the exception of  $T_{max}$  and  $t_{1/2}$ , which were presented with 2 decimal places. Summary statistics (n, arithmetic mean, SD, CV%, SEM, minimum, median, maximum, geometric mean [Geom Mean], and geometric CV% [Geom CV%]) were calculated for plasma cP12 PK parameters. Excluded subjects were listed in the PK parameter tables, but were excluded from the summary statistics and noted as such in the tables.

The level of precision for each concentration and PK parameter statistic was presented as follows: minimum/maximum in same precision as in bioanalytical data and/or parameter output, mean/Geom Mean/median in one more level of precision than minimum/maximum,

SD/SEM in one more level of precision than mean/median, n was presented as an integer and CV%/Geom CV% were presented to the nearest tenth.

#### 9.7.1.3 Statistical Analysis of PK Parameters

Dose proportionality was evaluated using a regression approach. A linear relationship between the natural log (ln)-transformed  $C_{max}$ ,  $AUC_{0-last}$ , and  $AUC_{0-inf}$  and the ln-transformed actual dose was fitted by using the following regression model:

$$\text{Ln}(Y) = \beta_0 + \beta \text{ Ln Dose} + \varepsilon \quad (1)$$

where Y represents the PK parameter. This approach is usually referred to as a power model because after exponentiation:

$$Y = \alpha (\text{Dose})^\beta \quad (2)$$

where  $\alpha$  only depends on  $\beta_0$  and error. Dose proportionality required that  $\beta = 1$  for dose-dependent parameters.

The linear relationship between the ln-transformed PK parameters (i.e.,  $AUC_{0-last}$ ,  $AUC_{0-inf}$ , and  $C_{max}$ ) and the ln-transformed actual dose was tested by including the cubic  $[\ln(\text{dose})]^3$  (Step 1) and quadratic  $[\ln(\text{dose})]^2$  (Step 2) terms in Model (1). A 5% level of significance was used in sequential testing of the cubic and quadratic effects. The linear relationship was concluded if the quadratic and cubic terms were not statistically significant. In the third step, Model (1) was used to calculate the 95% confidence intervals (CIs) for the slopes of the ln-transformed PK parameters versus ln(dose).

Dose proportionality could not be rejected if a statistical linear relationship was demonstrated and if the 95% CI for the slope included the value of 1 for the PK parameters (i.e.,  $AUC_{0-last}$ ,  $AUC_{0-inf}$ , and  $C_{max}$ ).

The relationship between ln-transformed PK parameter values versus ln-transformed actual dose was also displayed graphically.

#### 9.7.1.4 Safety

All CRF data were listed by subject and chronologically by assessment time points. This included rechecks, unscheduled assessments, and early termination.

Applicable continuous variables were summarized using n, arithmetic mean, SD, minimum, median, and maximum. Data from subjects who received the placebo treatment were pooled across cohorts.

Where individual data points were missing, the data were summarized based on reduced denominators.

### **Subject Discontinuation**

Subjects were summarized by number of subjects enrolled, completed, and discontinued the study with discontinuation reasons by treatment (pooled placebo and individual dose levels) and active treatment overall (all dose levels pooled).

### **Demographics**

Descriptive statistics were calculated for continuous variables (age, weight, height, and BMI) by treatment (pooled placebo and individual dose levels) and active treatment overall (all dose levels pooled). Age was derived from date of birth to date of first dosing.

Frequency counts were provided for categorical variables (race, ethnicity, and sex) for each treatment (pooled placebo and individual dose levels) and active treatment overall (all dose levels pooled).

### **Adverse Events**

All AEs occurring during this clinical trial were coded using the Medical Dictionary for Regulatory Activities (MedDRA<sup>®</sup>), Version 22.0.

All AEs captured in the database were listed in by-subject data listings including verbatim term, coded term, treatment, severity, relationship to study drug, and action; however, only treatment-emergent adverse events (TEAEs) were summarized.

A TEAE was defined as an AE that had onset after study drug administration.

TEAEs were tabulated by System Organ Class (SOC) and Preferred Term. Summary tables included the number of subjects reporting the AE and as a percent of the number of subjects dosed by treatment (pooled placebo and individual dose levels) and active treatment overall (all dose levels pooled). The number of AEs was tabulated in a similar manner. Tables which tabulated the number of TEAEs by severity and relationship to study drug were also included.

SAEs, if present, were also listed. Applicable narratives were included in the CSR.

### **Clinical Laboratory Tests (Serum Chemistry, Hematology, Urinalysis)**

Out-of-normal range flags were recorded as follows: high (H) and low (L) for numerical results and did-not-match (\*) for categorical results. If a value failed the reference range, it was automatically compared to a computer clinically significant (CS) range. If the value fell within the computer CS range, it was noted as “N” for not clinically significant. If the value failed (i.e., fell outside of the CS range) the computer CS range, it was flagged with a “Y” which prompted the PI to determine how the out-of-range value should be followed using 4 PI flags: “N”, not clinically significant, “R”, requesting a recheck, “^”, checking at the next scheduled visit, or “Y”, clinically significant. To distinguish the PI flag from the computer CS range flags, the PI flags of “N” and “Y” were presented as “-“ and “+”, respectively, in the data listing. Additionally, the PI provided a fourth flag when the third flag indicated “R”



or “^”. This fourth flag was intended to capture final CS (+)/NCS (-) when the third flag did not document significance.

Out-of-range values and corresponding recheck results were listed. Results that were indicated as CS by the PI were listed by subject in a table. This table also listed the results at all other time points for the laboratory test and subject with at least one value deemed as CS by the PI.

For all numeric laboratory values, descriptive statistics were presented for each laboratory test by assessment time point, treatment (pooled placebo and individual dose levels), and active treatment overall (all dose levels pooled). Change from baseline was summarized in a similar manner. Baseline was defined as the result closest and prior to dose which may have included unscheduled or recheck results. This typically was the result collected on Day -1. Postdose unscheduled events or rechecks were not included in summaries. Similarly, early termination results were not included in summaries.

For each laboratory test, a shift table was developed to compare the frequency of the results at baseline (above normal, normal, or below normal) with the respective postdose results. For urinalysis tests, the categories were normal and outside normal.

### **Vital Signs**

Descriptive statistics were presented for each vital sign parameter by assessment time point, treatment (pooled placebo and individual dose levels), and active treatment overall (all dose levels pooled). Change from baseline was summarized in a similar manner. Baseline was defined as the result closest and prior to dose which may have included unscheduled or recheck results. This typically was the result collected prior to dosing on Day 1. Postdose unscheduled events or rechecks were not included in summaries. Similarly, early termination results were not included in summaries.

### **Electrocardiogram**

Descriptive statistics were presented for all safety ECG parameters by assessment time point, treatment (pooled placebo and individual dose levels), and active treatment overall (all dose levels pooled). Change from baseline was summarized in a similar manner. Baseline was defined as the result closest and prior to dose which may have included unscheduled or recheck results. This was typically the result collected on Day -1. Postdose unscheduled events or rechecks were not included in summaries. Similarly, early termination results were not included in summaries. QTcF values that were > 450 msec and increased from baseline > 30 msec were flagged in the data listing.

Twelve (12)-lead ECGs were extracted from continuous (Holter) recordings on Day 1. Holter monitoring times as found in the CRF were listed. Note that Celerion did not receive or analyze cardiodynamic ECG data.

### **Concomitant Medications**

All concomitant medications recorded during the study were coded with the World Health Organization (WHO) Dictionary Version 01 March 2019 and listed.

### **Physical Examination**

Full and abbreviated physical examinations were performed as summarized in [Table 9–1](#). Abnormal findings were reported as medical history or AEs. All data found in the CRF were listed.

### **9.7.2 Determination of Sample Size**

This was the first study aimed at evaluating the safety, tolerability, and PK profile of cP12 in healthy subjects after administration of a single IV dose of study drug. The PK data from this study were used to estimate sample size for future studies.

### **9.8 Changes in the Conduct of the Study or Planned Analyses**

As per protocol, PK parameters were to be calculated using Phoenix<sup>®</sup> WinNonlin<sup>®</sup> Version 6.3. Celerion currently uses a higher version of Phoenix<sup>®</sup> WinNonlin<sup>®</sup>. Therefore, PK parameters were calculated using Phoenix<sup>®</sup> WinNonlin<sup>®</sup> Version 7.0.

PK parameters  $C_{max}$  and AUC were to be dose-normalized prior to dose proportionality analysis. The power model analysis was selected to assess dose proportionality and in the selected model PK parameters were not dose-normalized. All other analyses described in the SAP are aligned with those analyses described in the protocol.

The dose proportionality analysis outlined in this report differs from how the analysis was described in the SAP, whereby Step 3, for calculating the 95% CIs for the slopes, was performed for all PK parameters and was not dependent on a linear relationship being established in Steps 1 and 2.

## **10. STUDY SUBJECTS**

### **10.1 Disposition of Subjects**

A total of 40 subjects entered the study and were randomized to treatment. Thirty (30) subjects received active dose (cP12) and 10 subjects received placebo. All 40 subjects completed the study. A summary of subject disposition can be found in [Table 14.1.1](#) and [Table 10–1](#). A complete listing of subject discontinuation can be found in [Appendix 16.2.1](#).

**Table 10–1      Subject Disposition Summary**

| Category                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Pooled<br>Placebo | Treatment |   |   |   |   |         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|-----------|---|---|---|---|---------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                   | A         | B | C | D | E | Overall |
| Enrolled                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 10                | 6         | 6 | 6 | 6 | 6 | 30      |
| Completed                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 10                | 6         | 6 | 6 | 6 | 6 | 30      |
| Discontinued From Study                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 0                 | 0         | 0 | 0 | 0 | 0 | 0       |
| Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)<br>Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)<br>Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)<br>Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)<br>Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)<br><br>Source: <a href="#">Table 14.1.1</a><br>Program: /CA21478/sas_prg/stsas/intext/t_disp.sas 01JUN2020 10:43 |                   |           |   |   |   |   |         |

## **10.2 Protocol Deviations**

Deviations included documentation errors, procedural errors, samples late to the centrifuge, and samples late to the freezers. Actual blood draw times were used in the PK analyses, hence, the collection time deviations observed in this study were not considered to impact the robustness of the PK analysis.

All protocol deviations are listed in [Appendix 16.2.2](#). All protocol deviations were minor and none of these deviations were determined to have affected the results/conclusions of the study.

## **11. PHARMACOKINETIC EVALUATION**

### **11.1 Data Sets Analyzed**

All 30 subjects who were enrolled and randomized to be administered cP12 completed the study, and were included in the PK analysis.

### **11.2 Demographic and Other Baseline Characteristics**

Demographic descriptions of the subjects are summarized in [Table 14.1.2](#) and [Table 11–1](#). Individual demographic information is presented in [Appendix 16.2.4.1](#).

**Table 11–1 Demographic Summary by Treatment**

|                         |                                  |                | Treatment |          |          |          |          |           |
|-------------------------|----------------------------------|----------------|-----------|----------|----------|----------|----------|-----------|
| Trait                   |                                  | Pooled Placebo | A         | B        | C        | D        | E        | Overall   |
| Sex                     | Female                           | 2 (20%)        | 0 (0%)    | 2 (33%)  | 1 (17%)  | 1 (17%)  | 1 (17%)  | 5 (17%)   |
|                         | Male                             | 8 (80%)        | 6 (100%)  | 4 (67%)  | 5 (83%)  | 5 (83%)  | 5 (83%)  | 25 (83%)  |
| Race                    | American Indian or Alaska Native | 1 (10%)        | 0 (0%)    | 0 (0%)   | 0 (0%)   | 0 (0%)   | 0 (0%)   | 0 (0%)    |
|                         | Black or African American        | 1 (10%)        | 0 (0%)    | 0 (0%)   | 0 (0%)   | 0 (0%)   | 0 (0%)   | 0 (0%)    |
|                         | White                            | 8 (80%)        | 6 (100%)  | 6 (100%) | 6 (100%) | 6 (100%) | 6 (100%) | 30 (100%) |
| Ethnicity               | Hispanic or Latino               | 5 (50%)        | 2 (33%)   | 5 (83%)  | 5 (83%)  | 5 (83%)  | 1 (17%)  | 18 (60%)  |
|                         | Not Hispanic or Latino           | 5 (50%)        | 4 (67%)   | 1 (17%)  | 1 (17%)  | 1 (17%)  | 5 (83%)  | 12 (40%)  |
| Age* (yrs)              | n                                | 10             | 6         | 6        | 6        | 6        | 6        | 30        |
|                         | Mean                             | 41.5           | 48.2      | 44.8     | 46.2     | 38.8     | 51.7     | 45.9      |
|                         | SD                               | 12.72          | 12.59     | 11.29    | 10.59    | 13.96    | 10.29    | 11.79     |
|                         | Minimum                          | 26             | 33        | 28       | 34       | 20       | 35       | 20        |
|                         | Median                           | 41.0           | 48.0      | 46.0     | 42.5     | 37.5     | 55.5     | 43.5      |
|                         | Maximum                          | 59             | 62        | 58       | 62       | 57       | 60       | 62        |
| Weight (kg)             | n                                | 10             | 6         | 6        | 6        | 6        | 6        | 30        |
|                         | Mean                             | 87.46          | 89.63     | 77.48    | 75.00    | 85.08    | 86.25    | 82.69     |
|                         | SD                               | 16.165         | 8.046     | 10.494   | 15.229   | 14.971   | 7.720    | 12.275    |
|                         | Minimum                          | 64.9           | 78.7      | 60.6     | 60.2     | 70.1     | 71.7     | 60.2      |
|                         | Median                           | 89.10          | 91.05     | 80.20    | 71.60    | 84.10    | 87.30    | 86.05     |
|                         | Maximum                          | 110.1          | 98.2      | 88.5     | 96.9     | 108.5    | 94.8     | 108.5     |
| Height (cm)             | n                                | 10             | 6         | 6        | 6        | 6        | 6        | 30        |
|                         | Mean                             | 174.8          | 180.8     | 165.3    | 170.0    | 175.7    | 174.0    | 173.2     |
|                         | SD                               | 13.40          | 4.02      | 9.93     | 7.97     | 9.33     | 6.07     | 8.97      |
|                         | Minimum                          | 155            | 175       | 153      | 155      | 167      | 168      | 153       |
|                         | Median                           | 176.0          | 181.0     | 165.5    | 172.5    | 172.5    | 172.0    | 174.0     |
|                         | Maximum                          | 194            | 186       | 177      | 176      | 192      | 184      | 192       |
| Body Mass Index (kg/m²) | n                                | 10             | 6         | 6        | 6        | 6        | 6        | 30        |
|                         | Mean                             | 28.467         | 27.465    | 28.253   | 25.940   | 27.395   | 28.572   | 27.525    |
|                         | SD                               | 2.4824         | 2.7679    | 2.3970   | 4.5425   | 2.6845   | 2.6717   | 3.0336    |
|                         | Minimum                          | 22.48          | 22.81     | 25.18    | 19.63    | 23.58    | 24.89    | 19.63     |
|                         | Median                           | 29.000         | 27.535    | 28.450   | 24.690   | 27.765   | 29.365   | 28.080    |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |         |                | Treatment |       |       |       |       |         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|----------------|-----------|-------|-------|-------|-------|---------|
| Trait                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         | Pooled Placebo | A         | B     | C     | D     | E     | Overall |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Maximum | 31.60          | 30.69     | 31.66 | 31.91 | 30.66 | 31.86 | 31.91   |
| <p>* Age is calculated from the date of first dosing.</p> <p>Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)</p> <p>Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)</p> <p>Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)</p> <p>Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)</p> <p>Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)</p> <p>Source: <a href="#">Table 14.1.2</a></p> <p>Program: /CA21478/sas_prg/stmts/intext/t_dem.sas 01JUN2020 10:43</p> |         |                |           |       |       |       |       |         |

All subjects satisfied all inclusion and none of the exclusion criteria, with brief verification at check-in. Individual subjects' information related to check-in and inclusion/exclusion criteria is presented in [Appendices 16.2.5.1.1 through 16.2.5.3.2](#).

Information obtained at screening may be found in the following locations:

|                                   |                                                            |
|-----------------------------------|------------------------------------------------------------|
| Physical Examinations             | <a href="#">Appendix 16.2.4.2</a>                          |
| Medical and Surgical History      | <a href="#">Appendix 16.2.4.3</a>                          |
| Substance Use                     | <a href="#">Appendix 16.2.4.4</a>                          |
| Prior and Concomitant Medications | <a href="#">Appendix 16.2.5.8</a>                          |
| Clinical Laboratory Information   | <a href="#">Appendices 16.2.8.1.1.1 through 16.2.8.1.6</a> |
| Vital Signs                       | <a href="#">Appendix 16.2.8.2</a>                          |
| 12-Lead Electrocardiograms        | <a href="#">Appendix 16.2.8.3</a>                          |

The PI considered all screening abnormalities to be clinically insignificant and approved the subjects for study participation.

### 11.3 Measurements of Treatment Compliance

The test compound described in [Appendix 16.2.5.4.1](#) was administered at the time points listed in [Appendix 16.2.5.4.2](#) under the supervision of clinic personnel.

### 11.4 Pharmacokinetic Results and Tabulations of Individual Subject Data

#### 11.4.1 Analysis of Pharmacokinetics

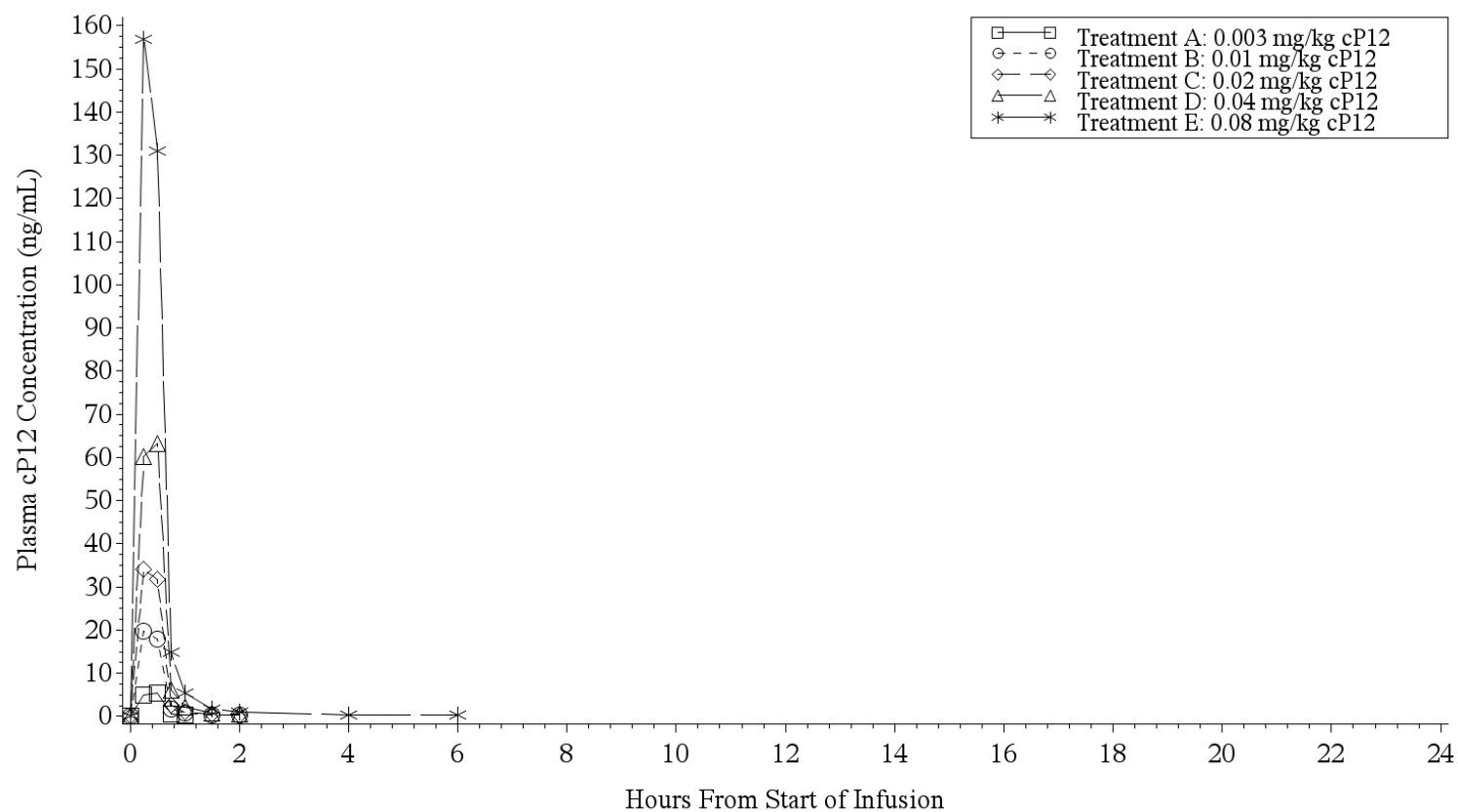
##### 11.4.1.1 Plasma Concentrations of cP12

The locations of individual and mean estimates of plasma cP12 concentrations are tabulated below:

|                                                      |                                                       |
|------------------------------------------------------|-------------------------------------------------------|
| Plasma Concentrations of cP12                        | <a href="#">Tables 14.2.1.1 through 14.2.1.5</a>      |
| Mean cP12 Concentrations – Linear and Semi-Log Scale | <a href="#">Figures 14.2.2.1.1 through 14.2.2.3.2</a> |
| Individual Figures of cP12                           | <a href="#">Appendix 16.2.6.1</a>                     |

Mean cP12 concentration-time profiles following single IV infusions of 0.003, 0.01, 0.02, 0.04, or 0.08 mg/kg cP12 over approximately 30 minutes on the linear scale are presented in [Figure 11–1](#) (up to 24 hours post start of infusion) and [Figure 11–2](#) (0-8 hours only).

**Figure 11–1      Arithmetic Mean Plasma cP12 Concentration-Time Profiles Following Single IV Infusions Over Approximately 30 Minutes**

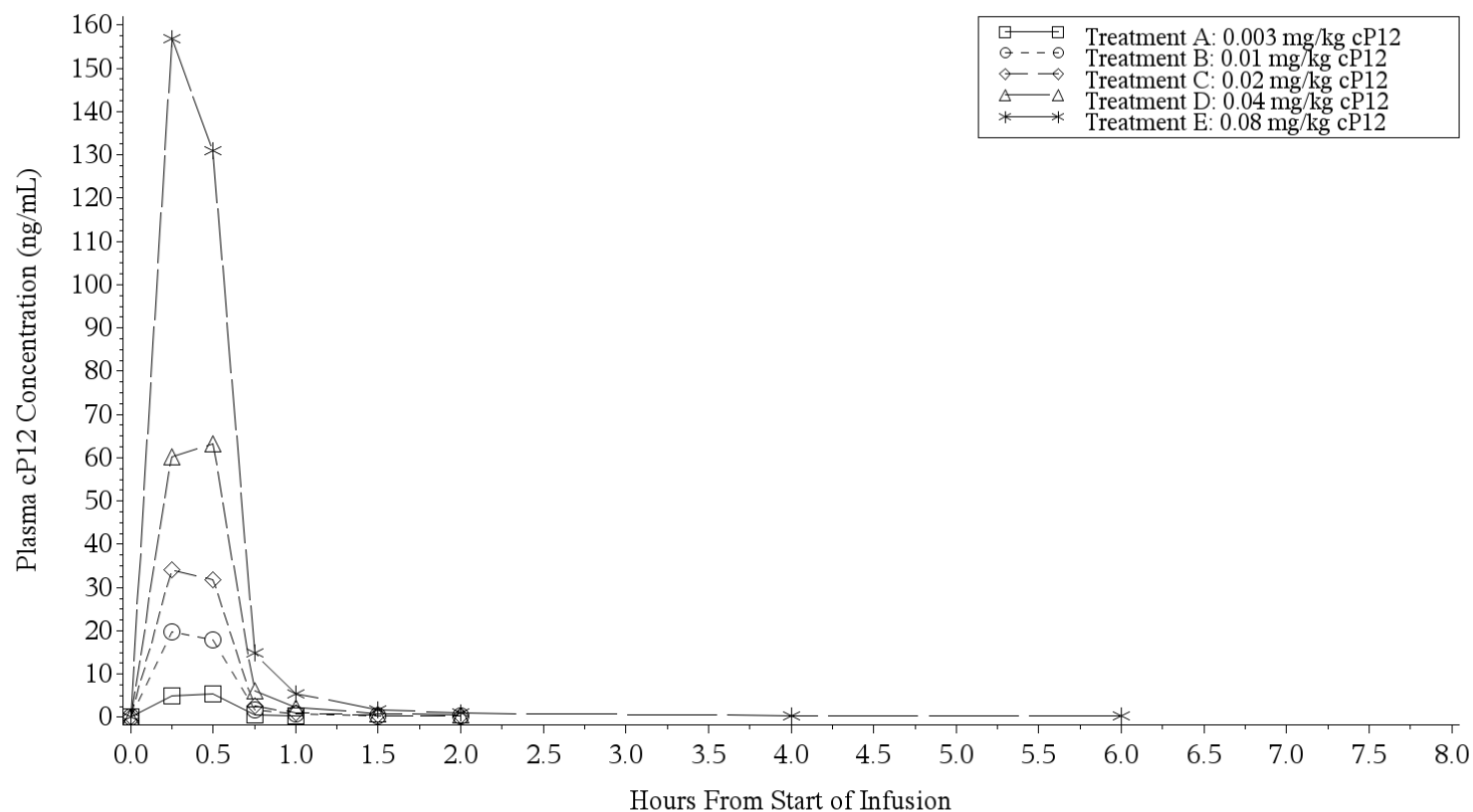


Program: /CA21478/sas\_prg/pksas/adam\_intext\_meangraph.sas 29MAY2020 10:46

Source: [Figure 14.2.2.1.1](#)



**Figure 11–2 Arithmetic Mean Plasma cP12 Concentration-Time Profiles Following Single IV Infusions Over Approximately 30 Minutes (up to 8 Hours Post Start of Infusion)**



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Source: [Figure 14.2.2.1.2](#)

Plasma concentrations were measurable up to 1 hour in at least one subject at 0.003 mg/kg, up to 2 hours at 0.01, 0.02, and 0.04 mg/kg, and up to 6 hours postdose at the highest dose of 0.08 mg/kg. Mean cP12 plasma concentrations increased with increasing dose, across the studied doses of cP12.

Following single ascending doses, arithmetic mean concentrations increased in a dose-dependent fashion and maintained a similar profile shape. Mean concentrations peaked at, or the preceding sample to, the end of infusion (0.5 hour postdose). Overall, across the evaluated doses, cP12 PK profiles showed a multi-phasic decline in plasma concentrations.

#### 11.4.1.2 Pharmacokinetic Parameters of cP12

The locations of individual and mean estimates of cP12 PK parameters are tabulated below. Statistical outputs are presented in [Appendix 16.1.9.2](#).

|                                                        |                                                   |
|--------------------------------------------------------|---------------------------------------------------|
| PK Parameters of cP12                                  | <a href="#">Tables 14.2.1.6 through 14.2.1.10</a> |
| Intervals used for cP12 $K_{el}$ Values                | <a href="#">Table 14.2.1.11</a>                   |
| Dose Proportionality Analysis of PK Parameters of cP12 | <a href="#">Table 14.2.1.12</a>                   |
| PK Parameters of cP12 Versus Dose Figures              | <a href="#">Figures 14.2.2.4 through 14.2.2.6</a> |

The summary of cP12 PK parameters is presented in [Table 11–2](#).

**Table 11–2 Summary of cP12 Pharmacokinetics Following Single IV Infusions Over Approximately 30 Minutes**

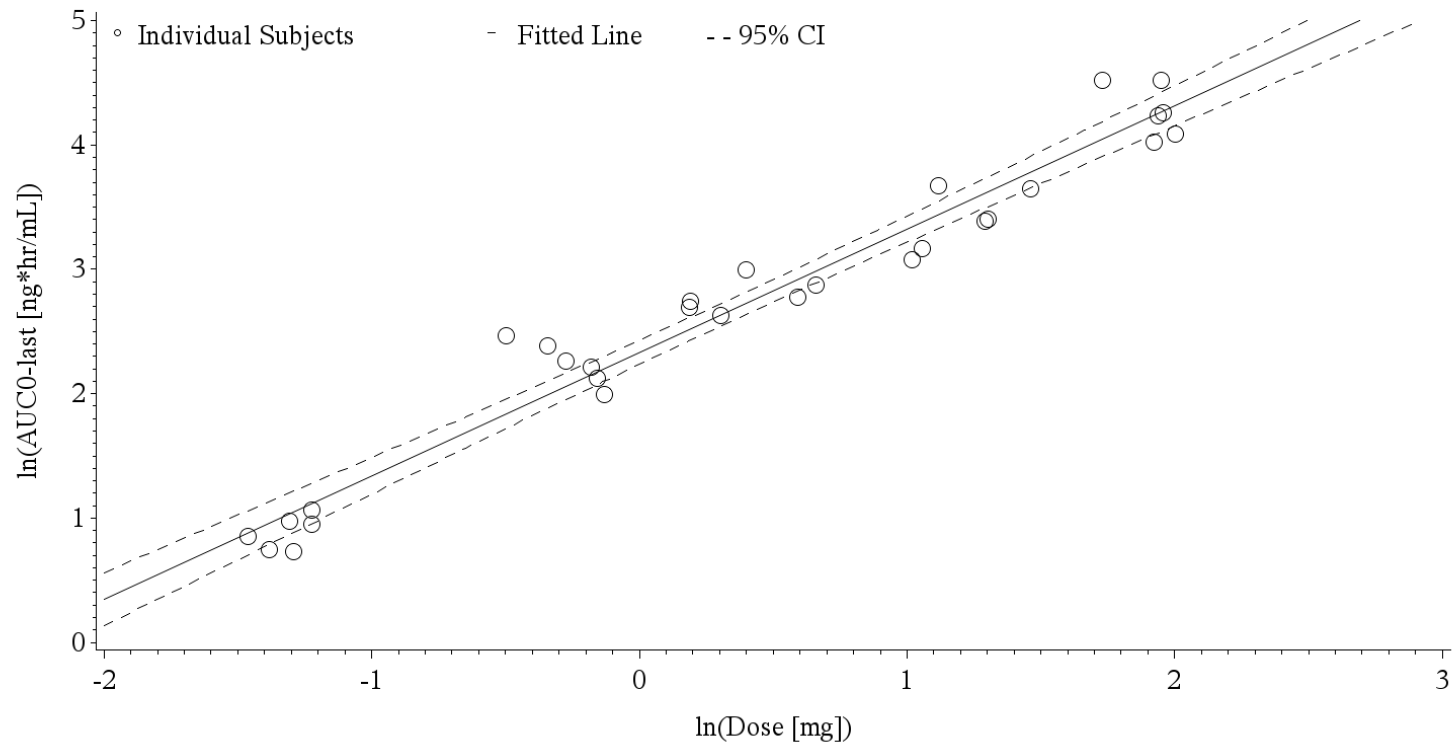
| Pharmacokinetic Parameters                                                                                                                                                                                                                                                                                                                                                                                         | 0.003 mg/kg                    | 0.01 mg/kg                     | 0.02 mg/kg                     | 0.04 mg/kg                     | 0.08 mg/kg                     |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|
| AUC <sub>0-last</sub> (ng*hr/mL)                                                                                                                                                                                                                                                                                                                                                                                   | 2.425 (13.3)<br>[n=6]          | 9.397 (17.2)<br>[n=6]          | 16.22 (13.2)<br>[n=6]          | 29.69 (24.5)<br>[n=6]          | 71.70 (21.1)<br>[n=6]          |
| AUC <sub>0-inf</sub> (ng*hr/mL)                                                                                                                                                                                                                                                                                                                                                                                    | 2.953 [n=1]                    | 9.530 (17.3)<br>[n=6]          | 16.37 (13.3)<br>[n=6]          | 28.33 (22.6)<br>[n=5]          | 72.30 (20.8)<br>[n=6]          |
| C <sub>max</sub> (ng/mL)                                                                                                                                                                                                                                                                                                                                                                                           | 5.511 (5.6)<br>[n=6]           | 19.64 (17.4)<br>[n=6]          | 35.66 (15.5)<br>[n=6]          | 65.28 (30.9)<br>[n=6]          | 154.0 (26.7)<br>[n=6]          |
| T <sub>max</sub> (hr)                                                                                                                                                                                                                                                                                                                                                                                              | 0.5045 (0.251,<br>0.512) [n=6] | 0.2545 (0.249,<br>0.506) [n=6] | 0.2510 (0.250,<br>0.501) [n=6] | 0.3935 (0.249,<br>0.526) [n=6] | 0.2620 (0.250,<br>0.504) [n=6] |
| K <sub>el</sub> (1/hr)                                                                                                                                                                                                                                                                                                                                                                                             | 5.614 [n=1]                    | 2.733 ± 1.8069<br>[n=6]        | 2.732 ± 2.5521<br>[n=6]        | 1.714 ± 0.37727<br>[n=5]       | 0.4945 ± 0.12323<br>[n=6]      |
| t <sub>½</sub> (hr)                                                                                                                                                                                                                                                                                                                                                                                                | 0.1235 [n=1]                   | 0.3159 ± 0.12571<br>[n=6]      | 0.3727 ± 0.16368<br>[n=6]      | 0.4198 ± 0.088493<br>[n=5]     | 1.480 ± 0.38753<br>[n=6]       |
| CL (L/hr)                                                                                                                                                                                                                                                                                                                                                                                                          | 99.77 [n=1]                    | 83.76 ± 24.374<br>[n=6]        | 91.31 ± 16.584<br>[n=6]        | 120.4 ± 5.3503<br>[n=5]        | 96.79 ± 24.310<br>[n=6]        |
| V <sub>z</sub> (L)                                                                                                                                                                                                                                                                                                                                                                                                 | 17.77 [n=1]                    | 35.04 ± 10.282<br>[n=6]        | 47.63 ± 20.830<br>[n=6]        | 72.75 ± 14.876<br>[n=5]        | 206.0 ± 67.369<br>[n=6]        |
| DN AUC <sub>0-last</sub><br>(ng*hr/mL/mg)                                                                                                                                                                                                                                                                                                                                                                          | 9.038 (11.4)<br>[n=6]          | 12.22 (31.2)<br>[n=6]          | 11.00 (18.1)<br>[n=6]          | 8.872 (18.7)<br>[n=6]          | 10.55 (28.0)<br>[n=6]          |
| DN AUC <sub>0-inf</sub><br>(ng*hr/mL/mg)                                                                                                                                                                                                                                                                                                                                                                           | 10.02 [n=1]                    | 12.40 (31.3)<br>[n=6]          | 11.10 (18.3)<br>[n=6]          | 8.313 (4.5)<br>[n=5]           | 10.64 (27.7)<br>[n=6]          |
| DN C <sub>max</sub> (ng/mL/mg)                                                                                                                                                                                                                                                                                                                                                                                     | 20.54 (7.0)<br>[n=6]           | 25.55 (30.7)<br>[n=6]          | 24.18 (14.2)<br>[n=6]          | 19.51 (20.3)<br>[n=6]          | 22.66 (33.6)<br>[n=6]          |
| AUCs and C <sub>max</sub> are presented as geometric mean and geometric CV%. Where n=1, no geometric CV% value is presented<br>T <sub>max</sub> are presented as median (minimum, maximum)<br>Other parameters are presented as arithmetic mean ± SD. Where n=1, no SD value is presented.<br>Source: Tables 14.2.1.6 through 14.2.1.10<br>Program: /CA21478/sas_prg/pksas/adam_intext_pkparam.sas 08JUN2020 12:10 |                                |                                |                                |                                |                                |

Following single IV infusions of cP12 for 30 minutes, overall exposure, as measured by geometric mean AUC<sub>0-last</sub> and AUC<sub>0-inf</sub>, appeared to increase in a dose-proportional manner by approximately 29.6- and 24.5-times for a 26.7-times increase from the lowest (0.003 mg/kg) to highest (0.08 mg/kg) dose. Peak cP12 exposure, as measured by geometric mean C<sub>max</sub>, also appeared to increase dose-proportionally by approximately 27.9-fold for a 26.7-times increase in dose between 0.003 mg/kg and 0.08 mg/kg. Dose-normalized AUC<sub>0-last</sub>, AUC<sub>0-inf</sub>, and C<sub>max</sub> were generally comparable across the evaluated dose range, suggesting dose proportionality for exposure parameters. Median T<sub>max</sub> was 0.5045 hours at the lowest dose of 0.003 mg/kg and was slightly later than those observed at higher doses of 0.01, 0.02, 0.04, or 0.08 mg/kg, which occurred between 0.2510 and 0.3935 hours. Mean t<sub>½</sub> ranged between 0.1235 and 1.480 hours, and increased as dose increased. Consistent with the apparent proportional increases in exposure with ascending doses, mean CL was similar at 0.003, 0.01, 0.02, and 0.08 mg/kg (83.76 L/hr to 99.77 L/hr), although a slightly higher value of 120.4 L/hr was observed at 0.04 mg/kg. Mean V<sub>z</sub> increased with increasing dose ranging from 17.77 L to 206 L, which is a reflection of the increase in t<sub>½</sub> due to cP12 being measurable for a longer period as dose increases, thus likely beginning to capture the true terminal phase at the highest dose. However, if considering volume of distribution at steady

state (based on  $V_{ss} = \text{mean dose}/C_{\max}$ ), estimates are generally similar across the dose range (~39 to 52 L).

Mean plasma cP12  $AUC_{0-\text{last}}$ ,  $AUC_{0-\text{inf}}$ , and  $C_{\max}$  versus actual dose profiles following single IV infusions of 0.003, 0.01, 0.02, 0.04, or 0.08 mg/kg cP12 over approximately 30 minutes on the semi-log scale are presented in [Figure 11–3](#), [Figure 11–4](#), and [Figure 11–5](#).

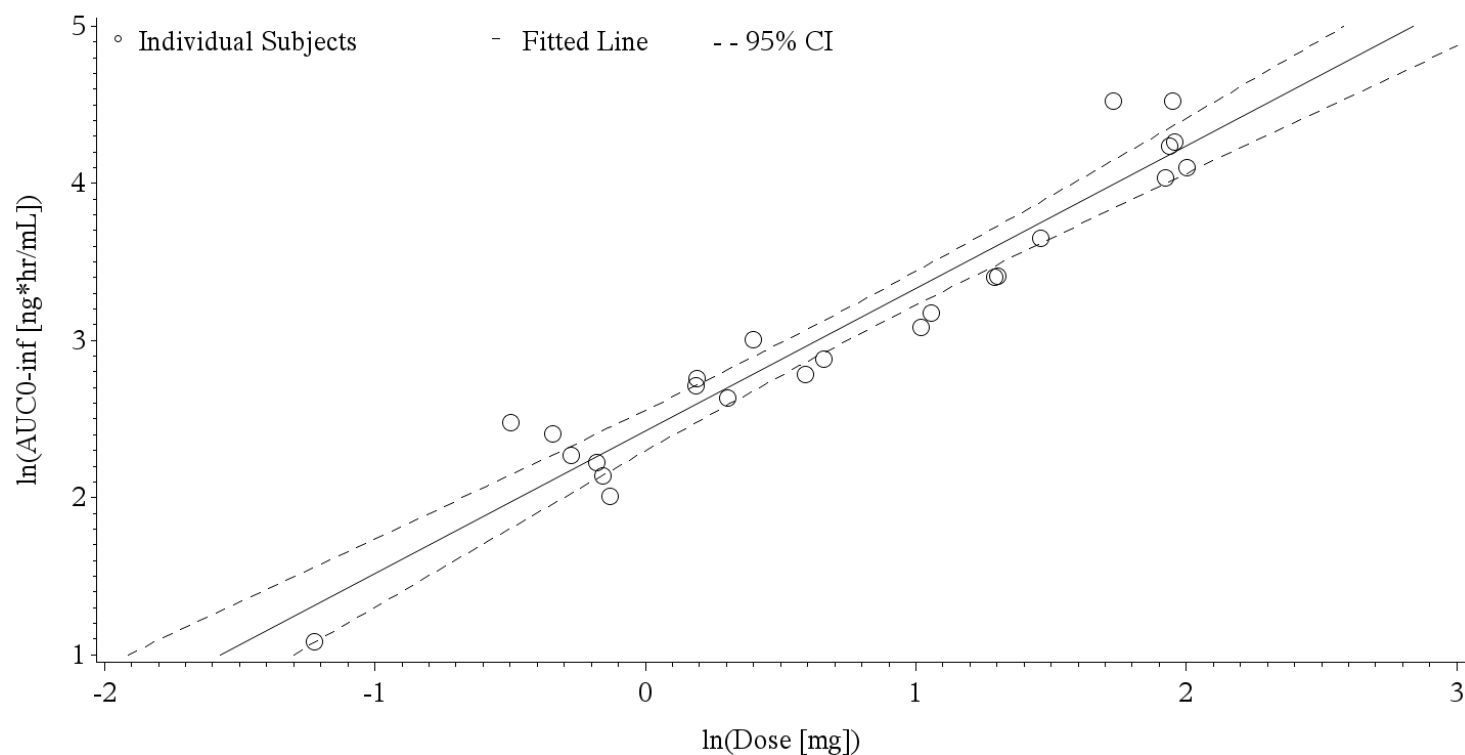
**Figure 11–3      Plasma cP12 AUC0-last Versus Dose Following Single IV Infusions Over Approximately 30 Minutes**



$\ln(\text{AUC0-last}) = \text{Intercept} + \text{Slope} * \ln(\text{Dose})$   
Slope = 0.9917 (95% CI: 0.9109 - 1.0724); Intercept = 2.3315 (95% CI: 2.2348 - 2.4282)  
95% Confidence Interval (CI) is based on mean predicted values. P-value (Slope) = <.0001;  $R^2 = 0.9576$   
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Source: [Figure 14.2.2.4](#)

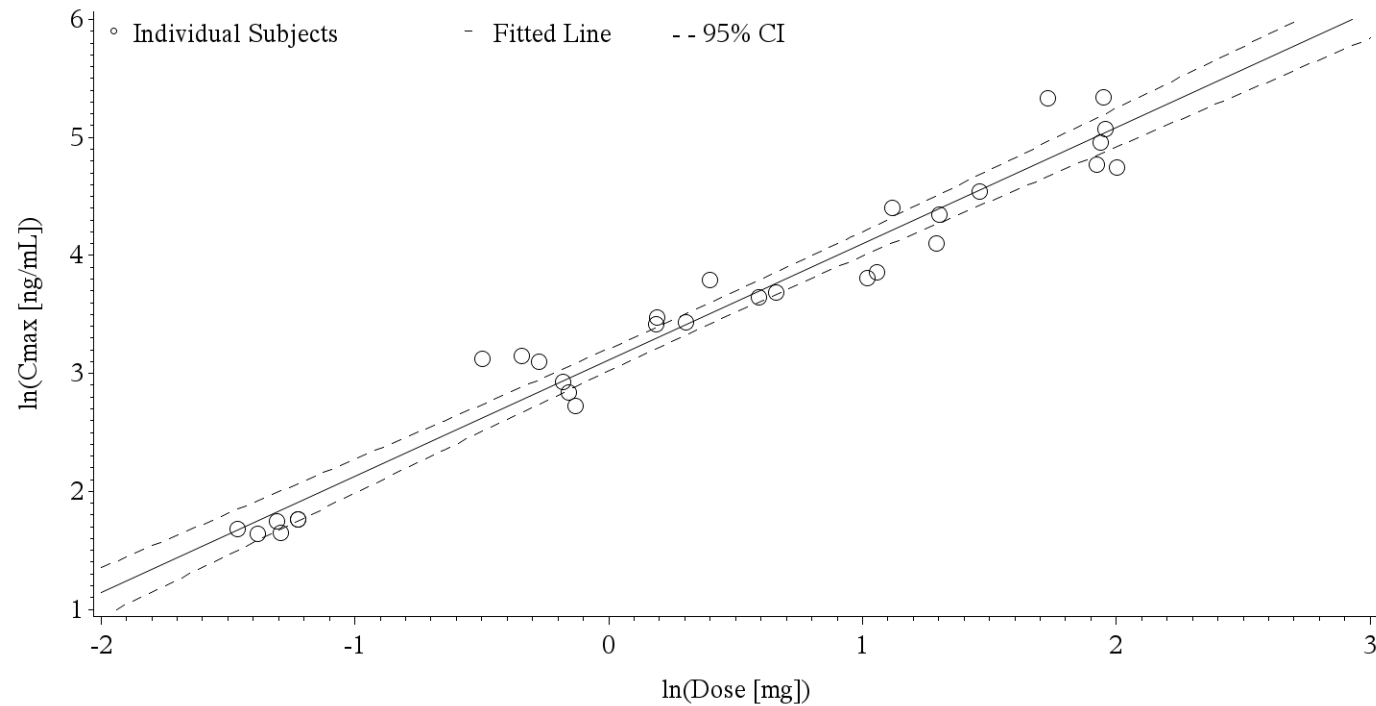
**Figure 11–4 Plasma cP12 AUC0-inf Versus Dose Following Single IV Infusions Over Approximately 30 Minutes**



$\ln(\text{AUC0-inf}) = \text{Intercept} + \text{Slope} * \ln(\text{Dose})$   
Slope = 0.9067 (95% CI: 0.7960 - 1.0174); Intercept = 2.4262 (95% CI: 2.2967 - 2.5557)  
95% Confidence Interval (CI) is based on mean predicted values. P-value (Slope) = <.0001;  $R^2 = 0.9292$   
Program: /CA21478/sas\_prg/pksas/adam\_intext\_scatterreg.sas 29MAY2020 10:48

Source: [Figure 14.2.2.5](#)

**Figure 11–5      Plasma cP12 Cmax Versus Dose Following Single IV Infusions Over Approximately 30 Minutes**



$\ln(\text{Cmax}) = \text{Intercept} + \text{Slope} * \ln(\text{Dose})$   
Slope = 0.9848 (95% CI: 0.9059 - 1.0638); Intercept = 3.1138 (95% CI: 3.0193 - 3.2084)  
95% Confidence Interval (CI) is based on mean predicted values. P-value (Slope) = <.0001;  $R^2 = 0.9589$   
Program: /CA21478/sas\_prg/pksas/adam\_intext\_scatterreg.sas 29MAY2020 10:48

Source: [Figure 14.2.2.6](#)

The dose-proportionality analysis of cP12 PK parameters are summarized in [Table 11–3](#).

**Table 11–3 Dose Proportionality Analysis of Plasma cP12 Pharmacokinetic Parameters Following Single IV Infusions Over Approximately 30 Minutes**

| Pharmacokinetic Parameters                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Estimate of Slope (b) | Standard Error | 95% Confidence Interval for Slope |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|----------------|-----------------------------------|
| AUC <sub>0-last</sub> (ng*hr/mL)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0.9917                | 0.0394         | 0.9109 - 1.0724                   |
| AUC <sub>0-inf</sub> (ng*hr/mL)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 0.9067                | 0.0534         | 0.7960 - 1.0174                   |
| C <sub>max</sub> (ng/mL)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 0.9848                | 0.0385         | 0.9059 - 1.0638                   |
| <p>Note: Actual dose was used in the dose proportionality analysis, where Actual dose (mg) = nominal dose (mg/kg) x weight (kg).<br/>Parameters were ln-transformed prior to analysis.<br/>The following statistical model using PROC MIXED of SAS was used to test dose proportionality: Parameter = a * Dose<sup>b</sup> which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)]<br/>Dose proportionality is not rejected if the 95% CI for the estimate of slope (b) contains 1.<br/>There was a statistically significant cubic effect for the models on AUC<sub>0-last</sub> and AUC<sub>0-inf</sub>. Therefore a statistical linear relationship could not be established for these pharmacokinetic parameters.<br/>Source: <a href="#">Table 14.2.1.12</a><br/>Program: /CA21478/sas_prg/pksas/adam_intext_dosemixed.sas 08JUN2020 12:13</p> |                       |                |                                   |

For AUC<sub>0-last</sub> and AUC<sub>0-inf</sub>, the 95% CI for the estimate of slope (b) contained 1. However, dose proportionality was rejected since a statistical linear relationship could not be established due to a statistically significant cubic effect for the models on AUC<sub>0-last</sub> and AUC<sub>0-inf</sub>. However, there was insufficient evidence to reject dose proportionality for C<sub>max</sub> as a statistical linear relationship was demonstrated and the 95% CI around the slope estimate included the value of 1.

#### 11.4.2 Statistical/Analytical Issues

The statistical analyses described in the protocol ([Appendix 16.1.1](#)), SAP ([Appendix 16.1.9.1](#)), and [Section 9.7](#) were performed and all statistical outputs are presented in [Appendix 16.1.9.2](#).

Several sampling time deviations occurred during the clinical conduct of this study. These are listed in [Appendix 16.2.2](#). Actual sampling times relative to dosing time were used for calculation of PK parameters; hence, collection time deviations were not considered to impact the robustness of the PK analysis.

##### 11.4.2.1 Adjustments for Covariates

Not applicable.

##### 11.4.2.2 Handling of Dropouts or Missing Data

There was insufficient sample quantity to be able to quantify cP12 in Subject 027 at 0.25 and 12-hour post start of infusion blood draws, and the samples were set to missing for PK analysis.



The  $K_{el}$ , and therefore subsequent  $K_{el}$ -dependent parameters ( $t_{1/2}$ ,  $AUC_{0-inf}$ ,  $CL$ , and  $V_z$ ), was not calculated for subjects listed in [Table 11–4](#).

**Table 11–4      Subjects for Whom a  $K_{el}$  Interval was Not Assigned**

| Subject                                                              | Treatment: Dose |
|----------------------------------------------------------------------|-----------------|
| 002                                                                  | A: 0.003 mg/kg  |
| 003                                                                  | A: 0.003 mg/kg  |
| 005                                                                  | A: 0.003 mg/kg  |
| 006                                                                  | A: 0.003 mg/kg  |
| 007                                                                  | A: 0.003 mg/kg  |
| 029                                                                  | D: 0.04 mg/kg   |
| Source: <a href="#">Tables 14.2.1.6</a> and <a href="#">14.2.1.9</a> |                 |

No imputations were made for missing blood draws or missing PK parameters and values were summarized using a reduced denominator.

#### **11.4.2.3 Interim Analyses and Data Monitoring**

Celerion did not perform interim analyses on this study.

#### **11.4.2.4 Multicenter Studies**

This was a single-center study.

#### **11.4.2.5 Use of a “Pharmacokinetic Subset” of Subjects**

Not applicable.

#### **11.4.2.6 Examination of Subgroups**

Not applicable.

#### **11.4.3 Tabulation of Individual Response Data**

Individual concentration and PK data can be found in [Section 14.2.1](#).

#### **11.4.4 Drug Dose, Drug Concentration, and Relationships to Response**

Not applicable.

#### **11.4.5 Drug-Drug and Drug-Disease Interactions**

Not applicable.

#### **11.4.6 By-Subject Displays**

The individual PK profiles (linear and semi-log plots) are presented in [Appendix 16.2.6.1](#).

#### 11.4.7 Pharmacokinetic Conclusions

- Across a dose range of 0.003 mg/kg to 0.08 mg/kg, cP12 total and peak exposure increased in a dose-dependent manner across the evaluated dose range. Dose proportionality was not rejected for  $C_{max}$ , but was rejected for  $AUC_{0-last}$  and  $AUC_{0-inf}$ , since a statistical linear relationship could not be established for AUCs.

### 12. SAFETY EVALUATION

#### 12.1 Extent of Exposure

All 40 subjects who entered the study completed the study per protocol and were included in the safety analysis. All subjects received a single ascending dose of cP12 or matching placebo as a 30-minute IV infusion as shown in [Section 9.4.1](#).

#### 12.2 Adverse Events

##### 12.2.1 Brief Summary of Adverse Events

There were no deaths, SAEs, or subject discontinuations due to AEs in this study. Overall, a total of 10 (33%) subjects experienced 31 AEs in this study, including 6 (100%) subjects in the highest dose level (0.08 mg/kg cP12) and 2 (33%) subjects each following 0.003 mg/kg and 0.04 mg/kg cP12 reporting events. No subjects following 0.01 mg/kg cP12, 0.02 mg/kg cP12, or placebo experienced AEs. One (1) subject experienced an increased creatine phosphokinase (CK) AE and is discussed in [Section 12.4.2.3](#).

The most frequent AEs by SOC were ‘skin and subcutaneous tissue disorder’ events, with 12 events experienced by 6 (20%) subjects; all in the higher dose level cohorts (0.04 and 0.08 mg/kg cP12). The majority of these events were considered treatment-related by the PI. Overall, the most common AEs were pruritus, feeling hot, and flushing, each experienced by 4 (13%) subjects at the higher doses levels, and headache also experienced by 4 (13%) subjects.

Of the 31 AEs, 23 were mild in severity and 8 were moderate. The PI considered the majority of AEs (22) to be probably related to study drug, 4 possibly related, and 5 not related.

AEs by subject incidence and treatment are presented in [Table 12-1](#).

**Table 12–1 Adverse Event Frequency by Treatment - Number of Subjects Reporting the Event (% of Subjects Dosed)**

| Adverse Event*                                              | Pooled Placebo | Treatment |          |          |          |          |           |
|-------------------------------------------------------------|----------------|-----------|----------|----------|----------|----------|-----------|
|                                                             |                | A         | B        | C        | D        | E        | Overall   |
| Number of Subjects Dosed                                    | 10 (100%)      | 6 (100%)  | 6 (100%) | 6 (100%) | 6 (100%) | 6 (100%) | 30 (100%) |
| Number of Subjects With TEAEs                               | 0 (0%)         | 2 (33%)   | 0 (0%)   | 0 (0%)   | 2 (33%)  | 6 (100%) | 10 (33%)  |
| Number of Subjects Without TEAEs                            | 10 (100%)      | 4 (67%)   | 6 (100%) | 6 (100%) | 4 (67%)  | 0 (0%)   | 20 (67%)  |
| <b>General disorders and administration site conditions</b> | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 1 (17%)  | 3 (50%)  | 4 (13%)   |
| Feeling hot                                                 | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 1 (17%)  | 3 (50%)  | 4 (13%)   |
| <b>Injury, poisoning and procedural complications</b>       | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 1 (17%)  | 0 (0%)   | 1 (3%)    |
| Scratch                                                     | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 1 (17%)  | 0 (0%)   | 1 (3%)    |
| <b>Investigations</b>                                       | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 0 (0%)   | 1 (17%)  | 1 (3%)    |
| Blood creatine phosphokinase increased                      | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 0 (0%)   | 1 (17%)  | 1 (3%)    |
| <b>Nervous system disorders</b>                             | 0 (0%)         | 2 (33%)   | 0 (0%)   | 0 (0%)   | 1 (17%)  | 2 (33%)  | 5 (17%)   |
| Headache                                                    | 0 (0%)         | 2 (33%)   | 0 (0%)   | 0 (0%)   | 0 (0%)   | 2 (33%)  | 4 (13%)   |
| Paraesthesia                                                | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 1 (17%)  | 1 (17%)  | 2 (7%)    |
| <b>Psychiatric disorders</b>                                | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 0 (0%)   | 1 (17%)  | 1 (3%)    |
| Restlessness                                                | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 0 (0%)   | 1 (17%)  | 1 (3%)    |
| <b>Skin and subcutaneous tissue disorders</b>               | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 2 (33%)  | 4 (67%)  | 6 (20%)   |
| Erythema                                                    | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 0 (0%)   | 1 (17%)  | 1 (3%)    |
| Generalised erythema                                        | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 0 (0%)   | 1 (17%)  | 1 (3%)    |
| Pruritus                                                    | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 2 (33%)  | 2 (33%)  | 4 (13%)   |
| Pruritus generalised                                        | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 0 (0%)   | 1 (17%)  | 1 (3%)    |
| Rash maculo-papular                                         | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 1 (17%)  | 0 (0%)   | 1 (3%)    |
| Urticaria                                                   | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 0 (0%)   | 2 (33%)  | 2 (7%)    |
| <b>Vascular disorders</b>                                   | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 0 (0%)   | 4 (67%)  | 4 (13%)   |
| Flushing                                                    | 0 (0%)         | 0 (0%)    | 0 (0%)   | 0 (0%)   | 0 (0%)   | 4 (67%)  | 4 (13%)   |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                | Treatment |   |   |   |   |         |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|-----------|---|---|---|---|---------|
| Adverse Event*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Pooled Placebo | A         | B | C | D | E | Overall |
| <p>* Adverse events are classified according to MedDRA Version 22.0. TEAEs = Treatment-emergent adverse events</p> <p>Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)</p> <p>Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)</p> <p>Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)</p> <p>Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)</p> <p>Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)</p> <p>Source: <a href="#">Table 14.3.1.1</a></p> <p>Program: /CA21478/sas_prg/stmts/intext/t_ae.sas 01JUN2020 10:43</p> |                |           |   |   |   |   |         |

### 12.2.2 Display of Adverse Events

The locations of AE summary tables and listings are presented below:

|                                                                                                                              |                                                        |
|------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| Treatment-Emergent Adverse Event Frequency by Treatment - Number of Subjects Reporting the Event (% of Subjects Dosed)       | <a href="#">Table 14.3.1.1</a>                         |
| Treatment-Emergent Adverse Event Frequency by Treatment- Number of Adverse Events (% of Total Adverse Events)                | <a href="#">Table 14.3.1.2</a>                         |
| Treatment-Emergent Adverse Event Frequency by Treatment, Severity, and Relationship to Study Drug - Number of Adverse Events | <a href="#">Table 14.3.1.3</a>                         |
| Serious Adverse Events (none reported)                                                                                       | <a href="#">Table 14.3.2.1</a>                         |
| Individual Adverse Event Listings                                                                                            | <a href="#">Appendices 16.2.7.1.1 through 16.2.7.3</a> |

### 12.2.3 Analysis of Adverse Events

Pruritus was experienced 5 times by 4 (13%) subjects, with 2 subjects following 0.04 mg/kg cP12 and 2 subjects following 0.08 mg/kg cP12. Four (4) events were mild in severity and 1 was moderate. Onset for 4 of the pruritus events ranged from 5 minutes to approximately 1 day after the initiation of the IV infusion and resolution was within 1 hour. Onset and resolution for the remaining event was approximately 6 days and 1.8 days, respectively. Additionally, 1 (3%) subject following 0.08 mg/kg cP12 experienced moderate generalized pruritus that began 9 minutes after the initiation of the IV infusion and resolved in 37 minutes. With the exception of the pruritus event that occurred 6 days after dosing and was considered not related, the PI considered these events to be probably/possibly related to study drug.

Mild feeling hot was experienced 5 times by 4 (13%) subjects, with 1 subject following 0.04 mg/kg cP12 and 3 subjects following 0.08 mg/kg cP12. All feeling hot events occurred within 12 minutes after the initiation of the IV infusion and were resolved within approximately 1 hour. The PI considered the feeling hot events to be probably related to study drug.

Mild flushing was experienced 5 times by 4 (13%) subjects, all following 0.08 mg/kg cP12. All flushing events occurred within 18 minutes after the initiation of the IV infusion and were resolved within 2 hours. The PI considered the flushing events to be probably related to study drug. Of note, 2 of these subjects also concurrently experienced feeling hot events.

Headache was experienced 4 times by 4 (13%) subjects, with 2 subjects following 0.003 mg/kg cP12 and 2 subjects following 0.08 mg/kg cP12. Two (2) events were mild in severity and 2 were moderate. Onset of the headache events ranged from 10 minutes to 12.3 hours after the initiation of the IV infusion, and all were resolved within approximately 17.5 hours. Two (2) subjects received acetaminophen and 2 subjects received ice bags for

headache resolution. The PI considered the headache events to be probably/possibly related to study drug.

Additional treatment-related ‘skin and subcutaneous disorder’ events all occurred in subjects in the highest dose cohort (0.08 mg/kg cP12) and included moderate urticaria in 2 subjects, and mild erythema and moderate generalized erythema in 1 subject each. These events all occurred within 16 minutes after the initiation of the IV infusion and resolved within 1.7 hours. Both subjects with urticaria received oral diphenhydramine for AE resolution. Maculopapular rash was experienced in 1 subject approximately 6 days after dosing and was considered not related to study drug.

All remaining AEs were reported by 2 or fewer ( $\leq 7\%$ ) subjects each. The PI considered 2 paresthesia events (0.04 mg/kg cP12 and 0.08 mg/kg cP12) to be probably related to study drug and the remaining events not related. With the exception of elevated CK in 1 subject, all AEs resolved by the end of the study. Concomitant medications and non-drug therapies administered for AE resolution are presented in [Appendices 16.2.5.8](#) and [16.2.7.2](#), respectively.

#### **12.2.4 Listing of Adverse Events by Subject**

[Appendix 16.2.7.1.1](#) lists AEs by individual subject number, cohort/treatment, treatment-emergent status, AE verbatim and preferred terms, time from last dose, date and time of onset/resolution, and total AE duration. [Appendix 16.2.7.1.2](#) lists AEs by individual subject number, cohort/treatment, AE verbatim term, date and time of onset, AE frequency, severity, seriousness, outcome, relationship to study drug, and action taken. [Appendix 16.2.7.2](#) lists AE non-drug therapy. [Appendix 16.2.7.3](#) lists AE preferred term classification.

### **12.3 Deaths, Other Serious Adverse Events, and Other Significant Adverse Events**

There were no deaths, SAEs, or other significant AEs in this study.

## **12.4 Clinical Laboratory Evaluation**

### **12.4.1 Listing of Individual Laboratory Measurements by Subject and Each Abnormal Laboratory Value**

The locations of clinical laboratory results are presented in the table below.

|                                                                            |                                                                      |
|----------------------------------------------------------------------------|----------------------------------------------------------------------|
| Serum Chemistry Out-of-Range Values and Recheck Results                    | <a href="#">Tables 14.3.4.1.1</a> through <a href="#">14.3.4.1.4</a> |
| Hematology Out-of-Range Values and Recheck Results                         | <a href="#">Tables 14.3.4.2.1</a> through <a href="#">14.3.4.2.4</a> |
| Urinalysis Out-of-Range Values and Recheck Results                         | <a href="#">Tables 14.3.4.3.1</a> through <a href="#">14.3.4.3.4</a> |
| Clinically Significant Laboratory Values and Corresponding Recheck Results | <a href="#">Table 14.3.4.4</a>                                       |

|                                                  |                                                              |
|--------------------------------------------------|--------------------------------------------------------------|
| Serum Chemistry Summary and Change from Baseline | <a href="#">Tables 14.3.5.1 and 14.3.5.2</a>                 |
| Serum Chemistry Shift from Baseline              | <a href="#">Table 14.3.5.3</a>                               |
| Hematology Summary and Change from Baseline      | <a href="#">Tables 14.3.5.4 and 14.3.5.5</a>                 |
| Hematology Shift from Baseline                   | <a href="#">Table 14.3.5.6</a>                               |
| Urinalysis Summary and Change from Baseline      | <a href="#">Tables 14.3.5.7 and 14.3.5.8</a>                 |
| Urinalysis Shift from Baseline                   | <a href="#">Table 14.3.5.9</a>                               |
| Individual Clinical Laboratory Results           | <a href="#">Appendices 16.2.8.1.1.1 through 16.2.8.1.5.6</a> |
| Comments on Clinical Laboratory Results          | <a href="#">Appendix 16.2.8.1.6</a>                          |

## **12.4.2 Evaluation of Each Laboratory Parameter**

### **12.4.2.1 Laboratory Values Over Time**

Mean serum CK exceeded reference range (34 - 329 IU/L) at the Day 8 EOS visit for Treatment C (0.02 mg/kg cP12), with a value of 409.0 IU/L. This can be attributed to the elevated individual value of 1964 IU/L that was considered not clinically significant by the PI.

All remaining mean serum chemistry, hematology, and urinalysis parameters remained within reference ranges at the postdose time points.

### **12.4.2.2 Individual Subject Changes**

There were no clinically notable shifts from normal at baseline to abnormal postdose for the serum chemistry, hematology, or urinalysis parameters in this study.

### **12.4.2.3 Individual Clinically Significant Abnormalities**

One (1) subject experienced a laboratory AE in this study.

Subject 033 (a 60-year-old White male; Cohort 5 [0.08 mg/kg cP12]) experienced the mild laboratory AE of increased blood CK upon returning to the clinic for the EOS visit on Day 8 (7 days after receiving study drug infusion). At the time of the event, the subject's CK value was 986 IU/L (male reference range 44 - 329 IU/L; 3.0 x upper limit normal [ULN]). The subject was advised to stay hydrated, avoid strenuous exercise, and report any muscle soreness/pain. The CK values decreased slightly, but remained elevated (608 to 834 IU/L) over the next several weeks, with no known etiology. Serum lactate dehydrogenase (LDH) (reference range: 125 - 248 IU/L) and aldolase (reference range 0 - 8.1 IU/L) were obtained with the last CK recheck, 25 days after AE onset, and were both within normal range at 193 IU/L and 6.4 IU/L, respectively. The subject stated he has had elevated CK values since he was young; however, this was not reported in the medical history at screening. The subject was advised to follow up with a primary care physician. The AE remained unresolved at the end of the study and the PI considered it not related to study treatment (source data on file with Celerion).

## **12.5 Vital Signs, Physical Findings, and Other Observations Related to Safety**

### **12.5.1 Vital signs**

Vital sign summary statistics (blood pressure, pulse rate, respiration rate, and oral temperature) and change from baseline are presented in [Tables 14.3.5.10](#) and [14.3.5.11](#), respectively. Vital signs are listed by individual subject in [Appendix 16.2.8.2](#).

Mean vital signs remained within normal limits at all study time points, with generally small changes from baseline for all treatments. There were no individual clinically significant vital sign findings in this study.

### **12.5.2 Electrocardiograms**

Twelve (12)-lead ECG summary statistics (heart rate, PR, QRS, QT, and QTcF) and change from baseline are presented in [Tables 14.3.5.12](#) and [14.3.5.13](#), respectively. ECGs are listed by individual subject in [Appendix 16.2.8.3](#). Individual holter monitoring times are presented in [Appendix 16.2.8.4](#).

Mean ECG parameters remained within normal limits at all assessed time points and changes from baseline were small for all treatments. There were no ECG-related AEs in this study and the PI considered all individual ECG abnormalities to be not clinically significant.

### **12.5.3 Physical Examinations**

Physical examinations were performed as presented in [Appendix 16.2.4.2](#).

## **12.6 Safety Conclusions**

Single ascending IV doses of cP12 appeared to be generally safe and well tolerated by the healthy male and female subjects in this study. Frequent events including feeling hot, flushing, and pruritus were experienced by subjects in the higher dose level cohorts. Most of these events occurred within minutes of the start of the study drug infusion, resolved without treatment, and were considered drug-related by the PI. There were no notable findings in the safety assessments for vital signs, ECGs, clinical laboratory, or physical examinations.



### 13. DISCUSSION AND OVERALL CONCLUSIONS

#### 13.1 Discussion

Fibronectin has been shown to play a vital role in wound healing and is deficient in burn patients' wounds and blood. cP12 is a novel FN derived, 14-mer peptide (P12) from the first FN type III repeat and is being developed for injection for treatment to limit burn injury progression, shorten healing time, and reduce scarring of acute, deep burns in hospitalized patients.

The primary objective of this study was to assess the safety and tolerability of single ascending IV doses of cP12 in healthy subjects. The secondary objective was to investigate the PK profile of cP12 after single ascending IV doses in healthy subjects.

There were no deaths, SAEs, or subject discontinuations due to AEs in this study. Overall, AEs were experienced by 33% of subjects, with the majority of events occurring in the higher dose level cohorts. The majority of AEs were mild in severity and considered probably related to study drug by the PI. 'Skin and subcutaneous tissue disorder' events were the most frequent AEs by SOC, experienced by 50% of subjects in the higher dose level cohorts, and frequent AEs included feeling hot, flushing, and pruritus also experienced by subjects in the higher dose level cohorts. Most of these events occurred within minutes of the start of the study drug infusion, resolved without treatment, and were considered drug-related by the PI. There were no notable findings in the safety assessments for vital signs, ECGs, clinical laboratory, or physical examinations.

Following single IV infusions of 0.003, 0.01, 0.02, 0.04, or 0.08 mg/kg cP12 over approximately 30 minutes, exposure to cP12 increased in a dose-proportional manner across the evaluated dose range. The  $AUC_{0-last}$ ,  $AUC_{0-inf}$ , and  $C_{max}$  increased by approximately 29.6-, 24.5-, and 27.9-times, respectively, for a 26.7-times increase in dose from the lowest (0.003 mg/kg) to the highest (0.08 mg/kg) dose. Peak cP12 concentrations were expected to be observed at the end of infusion (0.5 hours). This was true for the lowest dose (0.003 mg/kg) where median  $T_{max} = 0.5045$  hours. However, for 2 of 6 subjects at 0.003 mg/kg, and the majority of subjects across the higher dose levels (17 of 24 subjects on active treatment), peak cP12 levels were observed at the preceding sample (0.25 hours). The scheduled 0.5-hour draw was taken immediately before (3 subjects on active treatment), after (26 subjects on active treatment), or at the same time as the end of infusion (1 subject on active treatment) in all cases without significant deviations. The apparent rapid distribution half-life of cP12 may partly explain this finding. Clearance estimates of cP12 were similar across the evaluated dose range ( $CL = 83.76$  L/hr to  $120.4$  L/hr) consistent with the apparent proportional increase in exposure with dose. cP12 was measurable for increasingly longer periods as dose increased, thus the true terminal phase was likely captured at higher doses reflected in the increase in  $t_{1/2}$  (0.1235 and 1.480 hours), and corresponding increase in volume of distribution ( $V_z = 17.77$  L to 206 L) with ascending doses. However, if considering estimation of volume of distribution at steady state (based on  $V_{ss} = \text{mean dose}/C_{max}$ ), this suggests  $V_{ss}$  would generally be similar across the dose range (~39 to 52 L).

The draw was taken shortly after the end of infusion (EOI) which explains this. Preferably, the draw should be taken right before the EOI in these studies. We likely have underestimated the  $C_{\max}$ .

A dose-proportional relationship between exposure and actual dose was inferred based on increases in geometric mean  $AUC_{0-\text{last}}$ ,  $AUC_{0-\text{inf}}$ , and  $C_{\max}$  across the evaluated dose range. For  $AUC_{0-\text{last}}$  and  $AUC_{0-\text{inf}}$ , the 95% CI for the estimate of slope (b) contained 1; however, dose proportionality was rejected due to a statistically significant cubic effect for the models on  $AUC_{0-\text{last}}$  and  $AUC_{0-\text{inf}}$ . Truncated PK profiles due to assay LOQ limitations at the lower dose levels and the emergence of a terminal phase at the highest dose level may partially explain this outcome. Dose proportionality was not rejected for  $C_{\max}$  as the criteria of a statistical linear relationship was demonstrated and the 95% CI around the slope estimate included the value of 1.

### 13.2 Conclusions

- Single ascending IV doses of cP12 appeared to be generally safe and well tolerated by the healthy male and female subjects in this study.
- Across a dose range of 0.003 mg/kg to 0.08 mg/kg, cP12 total and peak exposure increased in a dose-dependent manner across the evaluated dose range. Dose proportionality was concluded for  $C_{\max}$ , but was rejected for  $AUC_{0-\text{last}}$  and  $AUC_{0-\text{inf}}$ , since a statistical linear relationship could not be established for AUCs.

## **14. TABLES, FIGURES AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT**

### **14.1 Demographic Data Summary Tables**

|              |                                            |
|--------------|--------------------------------------------|
| Table 14.1.1 | Summary of Disposition (Safety Population) |
| Table 14.1.2 | Demographic Summary (Safety Population)    |

Table 14.1.1 Summary of Disposition (Safety Population)

| Category                | Pooled<br>Placebo | Treatment |   |   |   |   | Overall |
|-------------------------|-------------------|-----------|---|---|---|---|---------|
|                         |                   | A         | B | C | D | E |         |
| Enrolled                | 10                | 6         | 6 | 6 | 6 | 6 | 30      |
| Completed               | 10                | 6         | 6 | 6 | 6 | 6 | 30      |
| Discontinued from Study | 0                 | 0         | 0 | 0 | 0 | 0 | 0       |

Note: Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.1.2 Demographic Summary (Safety Population)

| Trait       |                                  | Pooled<br>Placebo | Treatment |          |          |          |          | Overall   |
|-------------|----------------------------------|-------------------|-----------|----------|----------|----------|----------|-----------|
|             |                                  |                   | A         | B        | C        | D        | E        |           |
| Sex         | Female                           | 2 ( 20%)          | 0 ( 0%)   | 2 ( 33%) | 1 ( 17%) | 1 ( 17%) | 1 ( 17%) | 5 ( 17%)  |
|             | Male                             | 8 ( 80%)          | 6 (100%)  | 4 ( 67%) | 5 ( 83%) | 5 ( 83%) | 5 ( 83%) | 25 ( 83%) |
| Race        | American Indian or Alaska Native | 1 ( 10%)          | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)   |
|             | Black or African American        | 1 ( 10%)          | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)   |
|             | White                            | 8 ( 80%)          | 6 (100%)  | 6 (100%) | 6 (100%) | 6 (100%) | 6 (100%) | 30 (100%) |
| Ethnicity   | Hispanic or Latino               | 5 ( 50%)          | 2 ( 33%)  | 5 ( 83%) | 5 ( 83%) | 5 ( 83%) | 1 ( 17%) | 18 ( 60%) |
|             | Not Hispanic or Latino           | 5 ( 50%)          | 4 ( 67%)  | 1 ( 17%) | 1 ( 17%) | 1 ( 17%) | 5 ( 83%) | 12 ( 40%) |
| Age* (yrs)  | n                                | 10                | 6         | 6        | 6        | 6        | 6        | 30        |
|             | Mean                             | 41.5              | 48.2      | 44.8     | 46.2     | 38.8     | 51.7     | 45.9      |
|             | SD                               | 12.72             | 12.59     | 11.29    | 10.59    | 13.96    | 10.29    | 11.79     |
|             | Minimum                          | 26                | 33        | 28       | 34       | 20       | 35       | 20        |
|             | Median                           | 41.0              | 48.0      | 46.0     | 42.5     | 37.5     | 55.5     | 43.5      |
|             | Maximum                          | 59                | 62        | 58       | 62       | 57       | 60       | 62        |
| Weight (kg) | n                                | 10                | 6         | 6        | 6        | 6        | 6        | 30        |
|             | Mean                             | 87.46             | 89.63     | 77.48    | 75.00    | 85.08    | 86.25    | 82.69     |
|             | SD                               | 16.165            | 8.046     | 10.494   | 15.229   | 14.971   | 7.720    | 12.275    |
|             | Minimum                          | 64.9              | 78.7      | 60.6     | 60.2     | 70.1     | 71.7     | 60.2      |
|             | Median                           | 89.10             | 91.05     | 80.20    | 71.60    | 84.10    | 87.30    | 86.05     |
|             | Maximum                          | 110.1             | 98.2      | 88.5     | 96.9     | 108.5    | 94.8     | 108.5     |

Note: \* Age is calculated from the date of first dosing.  
 Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
 Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
 Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
 Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
 Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.1.2 Demographic Summary (Safety Population)

| Trait                                |         | Pooled<br>Placebo | Treatment |        |        |        |        | Overall |
|--------------------------------------|---------|-------------------|-----------|--------|--------|--------|--------|---------|
|                                      |         |                   | A         | B      | C      | D      | E      |         |
| Height (cm)                          | n       | 10                | 6         | 6      | 6      | 6      | 6      | 30      |
|                                      | Mean    | 174.8             | 180.8     | 165.3  | 170.0  | 175.7  | 174.0  | 173.2   |
|                                      | SD      | 13.40             | 4.02      | 9.93   | 7.97   | 9.33   | 6.07   | 8.97    |
|                                      | Minimum | 155               | 175       | 153    | 155    | 167    | 168    | 153     |
|                                      | Median  | 176.0             | 181.0     | 165.5  | 172.5  | 172.5  | 172.0  | 174.0   |
|                                      | Maximum | 194               | 186       | 177    | 176    | 192    | 184    | 192     |
| Body Mass Index (kg/m <sup>2</sup> ) | n       | 10                | 6         | 6      | 6      | 6      | 6      | 30      |
|                                      | Mean    | 28.467            | 27.465    | 28.253 | 25.940 | 27.395 | 28.572 | 27.525  |
|                                      | SD      | 2.4824            | 2.7679    | 2.3970 | 4.5425 | 2.6845 | 2.6717 | 3.0336  |
|                                      | Minimum | 22.48             | 22.81     | 25.18  | 19.63  | 23.58  | 24.89  | 19.63   |
|                                      | Median  | 29.000            | 27.535    | 28.450 | 24.690 | 27.765 | 29.365 | 28.080  |
|                                      | Maximum | 31.60             | 30.69     | 31.66  | 31.91  | 30.66  | 31.86  | 31.91   |

Note: \* Age is calculated from the date of first dosing.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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## 14.2 Pharmacokinetic Data Summary Tables and Figures

### 14.2.1 Plasma cP12 Tables

|                 |                                                                                                                                                                 |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Table 14.2.1.1  | Plasma cP12 Concentrations (ng/mL) Following a Single IV Infusion of 0.003 mg/kg cP12 Over Approximately 30 Minutes (Cohort 1) (Pharmacokinetic Population)     |
| Table 14.2.1.2  | Plasma cP12 Concentrations (ng/mL) Following a Single IV Infusion of 0.01 mg/kg cP12 Over Approximately 30 Minutes (Cohort 2) (Pharmacokinetic Population)      |
| Table 14.2.1.3  | Plasma cP12 Concentrations (ng/mL) Following a Single IV Infusion of 0.02 mg/kg cP12 Over Approximately 30 Minutes (Cohort 3) (Pharmacokinetic Population)      |
| Table 14.2.1.4  | Plasma cP12 Concentrations (ng/mL) Following a Single IV Infusion of 0.04 mg/kg cP12 Over Approximately 30 Minutes (Cohort 4) (Pharmacokinetic Population)      |
| Table 14.2.1.5  | Plasma cP12 Concentrations (ng/mL) Following a Single IV Infusion of 0.08 mg/kg cP12 Over Approximately 30 Minutes (Cohort 5) (Pharmacokinetic Population)      |
| Table 14.2.1.6  | Plasma cP12 Pharmacokinetic Parameters Following a Single IV Infusion of 0.003 mg/kg cP12 Over Approximately 30 Minutes (Cohort 1) (Pharmacokinetic Population) |
| Table 14.2.1.7  | Plasma cP12 Pharmacokinetic Parameters Following a Single IV Infusion of 0.01 mg/kg cP12 Over Approximately 30 Minutes (Cohort 2) (Pharmacokinetic Population)  |
| Table 14.2.1.8  | Plasma cP12 Pharmacokinetic Parameters Following a Single IV Infusion of 0.02 mg/kg cP12 Over Approximately 30 Minutes (Cohort 3) (Pharmacokinetic Population)  |
| Table 14.2.1.9  | Plasma cP12 Pharmacokinetic Parameters Following a Single IV Infusion of 0.04 mg/kg cP12 Over Approximately 30 Minutes (Cohort 4) (Pharmacokinetic Population)  |
| Table 14.2.1.10 | Plasma cP12 Pharmacokinetic Parameters Following a Single IV Infusion of 0.08 mg/kg cP12 Over Approximately 30 Minutes (Cohort 5) (Pharmacokinetic Population)  |
| Table 14.2.1.11 | Intervals (Hours) Used for Determination of Plasma cP12 Kel Values (Pharmacokinetic Population)                                                                 |
| Table 14.2.1.12 | Dose Proportionality Analysis of Plasma cP12 Pharmacokinetic Parameters (Pharmacokinetic Population)                                                            |

Table 14.2.1.1 Plasma cP12 Concentrations (ng/mL) Following  
a Single IV Infusion of 0.003 mg/kg cP12 Over Approximately 30 Minutes (Cohort 1) (Pharmacokinetic Population)

| Subject<br>Number | Sample Times (hr) |         |          |          |        |     |     |     |     |     |     |
|-------------------|-------------------|---------|----------|----------|--------|-----|-----|-----|-----|-----|-----|
|                   | Predose           | 0.25    | 0.5      | 0.75     | 1      | 1.5 | 2   | 4   | 6   | 12  | 24  |
| 002               | BLQ               | 3.83    | 5.16     | 0.392    | BLQ    | BLQ | BLQ | BLQ | BLQ | BLQ | BLQ |
| 003               | BLQ               | 4.45    | 5.36     | 0.511    | BLQ    | BLQ | BLQ | BLQ | BLQ | BLQ | BLQ |
| 005               | BLQ               | 5.81    | 5.10     | 0.453    | BLQ    | BLQ | BLQ | BLQ | BLQ | BLQ | BLQ |
| 006               | BLQ               | 3.81    | 5.21     | 0.383    | BLQ    | BLQ | BLQ | BLQ | BLQ | BLQ | BLQ |
| 007               | BLQ               | 5.40    | 5.74     | 0.405    | BLQ    | BLQ | BLQ | BLQ | BLQ | BLQ | BLQ |
| 008               | BLQ               | 5.83    | 5.34     | 0.750    | 0.327  | BLQ | BLQ | BLQ | BLQ | BLQ | BLQ |
| n                 | 6                 | 6       | 6        | 6        | 1      | .   | .   | .   | .   | .   | .   |
| Mean              | 0.00              | 4.855   | 5.318    | 0.4823   | 0.3270 | .   | .   | .   | .   | .   | .   |
| SD                | 0.00              | 0.94513 | 0.22999  | 0.13952  | .      | .   | .   | .   | .   | .   | .   |
| CV%               | .                 | 19.5    | 4.3      | 28.9     | .      | .   | .   | .   | .   | .   | .   |
| SEM               | 0.00              | 0.38585 | 0.093894 | 0.056961 | .      | .   | .   | .   | .   | .   | .   |
| Minimum           | 0.00              | 3.81    | 5.10     | 0.383    | 0.327  | .   | .   | .   | .   | .   | .   |
| Median            | 0.00              | 4.925   | 5.275    | 0.4290   | 0.3270 | .   | .   | .   | .   | .   | .   |
| Maximum           | 0.00              | 5.83    | 5.74     | 0.750    | 0.327  | .   | .   | .   | .   | .   | .   |

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 0.00 before the first quantifiable concentration and as missing elsewhere.  
. = Value missing or not reportable.



Table 14.2.1.2 Plasma cP12 Concentrations (ng/mL) Following  
a Single IV Infusion of 0.01 mg/kg cP12 Over Approximately 30 Minutes (Cohort 2) (Pharmacokinetic Population)

| Subject<br>Number | Sample Times (hr) |        |        |         |          |          |        |     |     |     |     |
|-------------------|-------------------|--------|--------|---------|----------|----------|--------|-----|-----|-----|-----|
|                   | Predose           | 0.25   | 0.5    | 0.75    | 1        | 1.5      | 2      | 4   | 6   | 12  | 24  |
| 009               | BLQ               | 15.3   | 15.1   | 1.40    | 0.586    | BLQ      | BLQ    | BLQ | BLQ | BLQ | BLQ |
| 011               | BLQ               | 17.1   | 16.4   | 1.29    | 0.542    | 0.271    | BLQ    | BLQ | BLQ | BLQ | BLQ |
| 012               | BLQ               | 17.9   | 18.7   | 1.49    | 0.781    | 0.273    | BLQ    | BLQ | BLQ | BLQ | BLQ |
| 014               | BLQ               | 23.2   | 20.2   | 1.67    | 0.860    | 0.335    | BLQ    | BLQ | BLQ | BLQ | BLQ |
| 015               | BLQ               | 22.8   | 21.2   | 2.35    | 1.07     | 0.442    | 0.271  | BLQ | BLQ | BLQ | BLQ |
| 016               | BLQ               | 22.2   | 15.6   | 1.52    | 0.659    | 0.263    | BLQ    | BLQ | BLQ | BLQ | BLQ |
| n                 | 6                 | 6      | 6      | 6       | 6        | 5        | 1      | .   | .   | .   | .   |
| Mean              | 0.00              | 19.75  | 17.87  | 1.620   | 0.7497   | 0.3168   | 0.2710 | .   | .   | .   | .   |
| SD                | 0.00              | 3.3898 | 2.5375 | 0.37937 | 0.19693  | 0.075691 | .      | .   | .   | .   | .   |
| CV%               | .                 | 17.2   | 14.2   | 23.4    | 26.3     | 23.9     | .      | .   | .   | .   | .   |
| SEM               | 0.00              | 1.3839 | 1.0359 | 0.15488 | 0.080395 | 0.033850 | .      | .   | .   | .   | .   |
| Minimum           | 0.00              | 15.3   | 15.1   | 1.29    | 0.542    | 0.263    | 0.271  | .   | .   | .   | .   |
| Median            | 0.00              | 20.05  | 17.55  | 1.505   | 0.7200   | 0.2730   | 0.2710 | .   | .   | .   | .   |
| Maximum           | 0.00              | 23.2   | 21.2   | 2.35    | 1.07     | 0.442    | 0.271  | .   | .   | .   | .   |

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 0.00 before the first quantifiable concentration and as missing elsewhere.  
. = Value missing or not reportable.

Table 14.2.1.3 Plasma cP12 Concentrations (ng/mL) Following  
a Single IV Infusion of 0.02 mg/kg cP12 Over Approximately 30 Minutes (Cohort 3) (Pharmacokinetic Population)

| Subject<br>Number | Sample Times (hr) |        |        |         |         |          |          |     |     |     |     |
|-------------------|-------------------|--------|--------|---------|---------|----------|----------|-----|-----|-----|-----|
|                   | Predose           | 0.25   | 0.5    | 0.75    | 1       | 1.5      | 2        | 4   | 6   | 12  | 24  |
| 017               | BLQ               | 44.2   | 35.3   | 3.07    | 1.40    | 0.687    | 0.327    | BLQ | BLQ | BLQ | BLQ |
| 020               | BLQ               | 30.4   | 25.1   | 3.32    | 1.31    | 0.527    | 0.300    | BLQ | BLQ | BLQ | BLQ |
| 021               | BLQ               | 29.5   | 32.3   | 3.02    | 1.32    | 0.497    | 0.280    | BLQ | BLQ | BLQ | BLQ |
| 022               | BLQ               | 31.0   | 27.3   | 1.74    | 0.540   | BLQ      | BLQ      | BLQ | BLQ | BLQ | BLQ |
| 023               | BLQ               | 29.5   | 38.2   | 2.34    | 0.947   | 0.303    | BLQ      | BLQ | BLQ | BLQ | BLQ |
| 024               | BLQ               | 40.0   | 32.1   | 2.45    | 0.901   | 0.321    | 0.221    | BLQ | BLQ | BLQ | BLQ |
| n                 | 6                 | 6      | 6      | 6       | 6       | 5        | 4        | .   | .   | .   | .   |
| Mean              | 0.00              | 34.10  | 31.72  | 2.657   | 1.070   | 0.4670   | 0.2820   | .   | .   | .   | .   |
| SD                | 0.00              | 6.3630 | 4.8713 | 0.58756 | 0.33274 | 0.15899  | 0.044996 | .   | .   | .   | .   |
| CV%               | .                 | 18.7   | 15.4   | 22.1    | 31.1    | 34.0     | 16.0     | .   | .   | .   | .   |
| SEM               | 0.00              | 2.5977 | 1.9887 | 0.23987 | 0.13584 | 0.071103 | 0.022498 | .   | .   | .   | .   |
| Minimum           | 0.00              | 29.5   | 25.1   | 1.74    | 0.540   | 0.303    | 0.221    | .   | .   | .   | .   |
| Median            | 0.00              | 30.70  | 32.20  | 2.735   | 1.129   | 0.4970   | 0.2900   | .   | .   | .   | .   |
| Maximum           | 0.00              | 44.2   | 38.2   | 3.32    | 1.40    | 0.687    | 0.327    | .   | .   | .   | .   |

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 0.00 before the first quantifiable concentration and as missing elsewhere.  
. = Value missing or not reportable.

Table 14.2.1.4 Plasma cP12 Concentrations (ng/mL) Following  
a Single IV Infusion of 0.04 mg/kg cP12 Over Approximately 30 Minutes (Cohort 4) (Pharmacokinetic Population)

| Subject<br>Number | Sample Times (hr) |        |        |         |         |         |          |     |     |     |     |
|-------------------|-------------------|--------|--------|---------|---------|---------|----------|-----|-----|-----|-----|
|                   | Predose           | 0.25   | 0.5    | 0.75    | 1       | 1.5     | 2        | 4   | 6   | 12  | 24  |
| 026               | BLQ               | 46.1   | 47.5   | 4.56    | 1.60    | 0.573   | 0.353    | BLQ | BLQ | BLQ | BLQ |
| 027               | BLQ               | QNS    | 77.2   | 8.74    | 3.39    | 0.751   | 0.540    | BLQ | BLQ | QNS | BLQ |
| 028               | BLQ               | 67.3   | 94.1   | 5.45    | 1.86    | 0.749   | 0.384    | BLQ | BLQ | BLQ | BLQ |
| 029               | BLQ               | 81.9   | 67.4   | 8.03    | 3.04    | 1.34    | 0.775    | BLQ | BLQ | BLQ | BLQ |
| 031               | BLQ               | 45.2   | 38.1   | 4.76    | 1.82    | 0.662   | 0.268    | BLQ | BLQ | BLQ | BLQ |
| 032               | BLQ               | 60.6   | 54.4   | 5.11    | 1.97    | 0.999   | 0.540    | BLQ | BLQ | BLQ | BLQ |
| n                 | 6                 | 5      | 6      | 6       | 6       | 6       | 6        | .   | .   | .   | .   |
| Mean              | 0.00              | 60.22  | 63.12  | 6.108   | 2.280   | 0.8457  | 0.4767   | .   | .   | .   | .   |
| SD                | 0.00              | 15.373 | 20.603 | 1.8035  | 0.74246 | 0.28081 | 0.18135  | .   | .   | .   | .   |
| CV%               | .                 | 25.5   | 32.6   | 29.5    | 32.6    | 33.2    | 38.0     | .   | .   | .   | .   |
| SEM               | 0.00              | 6.8748 | 8.4110 | 0.73629 | 0.30311 | 0.11464 | 0.074038 | .   | .   | .   | .   |
| Minimum           | 0.00              | 45.2   | 38.1   | 4.56    | 1.60    | 0.573   | 0.268    | .   | .   | .   | .   |
| Median            | 0.00              | 60.60  | 60.90  | 5.280   | 1.915   | 0.7500  | 0.4620   | .   | .   | .   | .   |
| Maximum           | 0.00              | 81.9   | 94.1   | 8.74    | 3.39    | 1.34    | 0.775    | .   | .   | .   | .   |

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 0.00 before the first quantifiable concentration and as missing elsewhere.

QNS = Sample quantity not sufficient for analysis.

. = Value missing or not reportable.

Table 14.2.1.5 Plasma cP12 Concentrations (ng/mL) Following  
a Single IV Infusion of 0.08 mg/kg cP12 Over Approximately 30 Minutes (Cohort 5) (Pharmacokinetic Population)

| Subject<br>Number | Sample Times (hr) |        |        |        |         |         |         |          |          |     |      |
|-------------------|-------------------|--------|--------|--------|---------|---------|---------|----------|----------|-----|------|
|                   | Predose           | 0.25   | 0.5    | 0.75   | 1       | 1.5     | 2       | 4        | 6        | 12  | 24   |
| 033               | BLQ               | 105    | 115    | 19.5   | 7.26    | 2.77    | 1.83    | 0.660    | 0.342    | BLQ | BLQ  |
| 035               | BLQ               | 209    | 164    | 19.2   | 6.84    | 2.43    | 0.855   | 0.474    | 0.229    | BLQ | BLQ  |
| 036               | BLQ               | 160    | 129    | 9.94   | 3.70    | 1.12    | 0.668   | 0.200    | BLQ      | BLQ | BLQ  |
| 037               | BLQ               | 142    | 120    | 14.0   | 5.56    | 1.67    | 1.17    | 0.419    | 0.236    | BLQ | BLQ  |
| 038               | BLQ               | 118    | 84.4   | 14.6   | 5.73    | 1.58    | 0.781   | 0.359    | BLQ      | BLQ | BLQ  |
| 039               | BLQ               | 207    | 173    | 11.9   | 3.42    | 1.11    | 0.645   | 0.235    | BLQ      | BLQ | BLQ* |
| n                 | 6                 | 6      | 6      | 6      | 6       | 6       | 6       | 6        | 3        | .   | .    |
| Mean              | 0.00              | 156.8  | 130.9  | 14.86  | 5.418   | 1.780   | 0.9915  | 0.3912   | 0.2690   | .   | .    |
| SD                | 0.00              | 43.961 | 32.880 | 3.8507 | 1.5796  | 0.68399 | 0.45224 | 0.16845  | 0.063317 | .   | .    |
| CV%               | .                 | 28.0   | 25.1   | 25.9   | 29.2    | 38.4    | 45.6    | 43.1     | 23.5     | .   | .    |
| SEM               | 0.00              | 17.947 | 13.423 | 1.5721 | 0.64488 | 0.27924 | 0.18463 | 0.068769 | 0.036556 | .   | .    |
| Minimum           | 0.00              | 105    | 84.4   | 9.94   | 3.42    | 1.11    | 0.645   | 0.200    | 0.229    | .   | .    |
| Median            | 0.00              | 151.0  | 124.5  | 14.30  | 5.645   | 1.625   | 0.8180  | 0.3890   | 0.2360   | .   | .    |
| Maximum           | 0.00              | 209    | 173    | 19.5   | 7.26    | 2.77    | 1.83    | 0.660    | 0.342    | .   | .    |

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 0.00 before the first quantifiable concentration and as missing elsewhere.

\* = For this sample the limit of quantitation was 0.400 ng/mL due to dilution.

. = Value missing or not reportable.

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Table 14.2.1.6 Plasma cP12 Pharmacokinetic Parameters Following  
a Single IV Infusion of 0.003 mg/kg cP12 Over Approximately 30 Minutes (Cohort 1) (Pharmacokinetic Population)

| Subject<br>Number | Parameters              |                        |                 |              |               |                          |              |           |                               |                              |                       |
|-------------------|-------------------------|------------------------|-----------------|--------------|---------------|--------------------------|--------------|-----------|-------------------------------|------------------------------|-----------------------|
|                   | AUC0-last<br>(ng*hr/mL) | AUC0-inf<br>(ng*hr/mL) | Cmax<br>(ng/mL) | Tmax<br>(hr) | Kel<br>(1/hr) | t <sub>1/2</sub><br>(hr) | CL<br>(L/hr) | Vz<br>(L) | DN AUC0-last<br>(ng*hr/mL/mg) | DN AUC0-inf<br>(ng*hr/mL/mg) | DN Cmax<br>(ng/mL/mg) |
| 002               | 2.12                    | .                      | 5.16            | 0.512        | .             | .                        | .            | .         | 8.45                          | .                            | 20.6                  |
| 003               | 2.35                    | .                      | 5.36            | 0.507        | .             | .                        | .            | .         | 10.1                          | .                            | 23.1                  |
| 005               | 2.58                    | .                      | 5.81            | 0.253        | .             | .                        | .            | .         | 8.79                          | .                            | 19.8                  |
| 006               | 2.07                    | .                      | 5.21            | 0.502        | .             | .                        | .            | .         | 7.54                          | .                            | 19.0                  |
| 007               | 2.64                    | .                      | 5.74            | 0.510        | .             | .                        | .            | .         | 9.78                          | .                            | 21.2                  |
| 008               | 2.89                    | 2.95                   | 5.83            | 0.251        | 5.61          | 0.123                    | 99.8         | 17.8      | 9.83                          | 10.0                         | 19.8                  |
| n                 | 6                       | 1                      | 6               | 6            | 1             | 1                        | 1            | 1         | 6                             | 1                            | 6                     |
| Mean              | 2.443                   | 2.953                  | 5.518           | 0.4225       | 5.614         | 0.1235                   | 99.77        | 17.77     | 9.086                         | 10.02                        | 20.58                 |
| SD                | 0.32172                 | .                      | 0.30980         | 0.13211      | .             | .                        | .            | .         | 1.0005                        | .                            | 1.4780                |
| CV%               | 13.2                    | .                      | 5.6             | 31.3         | .             | .                        | .            | .         | 11.0                          | .                            | 7.2                   |
| SEM               | 0.13134                 | .                      | 0.12648         | 0.053935     | .             | .                        | .            | .         | 0.40846                       | .                            | 0.60338               |
| Minimum           | 2.07                    | 2.95                   | 5.16            | 0.251        | 5.61          | 0.123                    | 99.8         | 17.8      | 7.54                          | 10.0                         | 19.0                  |
| Median            | 2.466                   | 2.953                  | 5.550           | 0.5045       | 5.614         | 0.1235                   | 99.77        | 17.77     | 9.284                         | 10.02                        | 20.19                 |
| Maximum           | 2.89                    | 2.95                   | 5.83            | 0.512        | 5.61          | 0.123                    | 99.8         | 17.8      | 10.1                          | 10.0                         | 23.1                  |
| Geom Mean         | 2.425                   | 2.953                  | 5.511           | 0.4020       | 5.614         | 0.1235                   | 99.77        | 17.77     | 9.038                         | 10.02                        | 20.54                 |
| Geom CV%          | 13.3                    | .                      | 5.6             | 37.4         | .             | .                        | .            | .         | 11.4                          | .                            | 7.0                   |

Note: Dose-dependent parameters (CL, Vz, DN AUC0-last, DN AUC0-inf, and DN Cmax) were calculated using actual dose, where  
Actual dose (mg) = nominal dose (mg/kg) x weight (kg).  
. = Value missing or not reportable.

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Table 14.2.1.7 Plasma cP12 Pharmacokinetic Parameters Following  
a Single IV Infusion of 0.01 mg/kg cP12 Over Approximately 30 Minutes (Cohort 2) (Pharmacokinetic Population)

| Subject<br>Number | Parameters              |                        |                 |              |               |                          |              |           |                               |                              |                       |
|-------------------|-------------------------|------------------------|-----------------|--------------|---------------|--------------------------|--------------|-----------|-------------------------------|------------------------------|-----------------------|
|                   | AUC0-last<br>(ng*hr/mL) | AUC0-inf<br>(ng*hr/mL) | Cmax<br>(ng/mL) | Tmax<br>(hr) | Kel<br>(1/hr) | t <sub>1/2</sub><br>(hr) | CL<br>(L/hr) | Vz<br>(L) | DN AUC0-last<br>(ng*hr/mL/mg) | DN AUC0-inf<br>(ng*hr/mL/mg) | DN Cmax<br>(ng/mL/mg) |
| 009               | 7.37                    | 7.46                   | 15.3            | 0.253        | 6.36          | 0.109                    | 118          | 18.5      | 8.38                          | 8.49                         | 17.4                  |
| 011               | 8.37                    | 8.50                   | 17.1            | 0.251        | 2.05          | 0.339                    | 101          | 49.2      | 9.79                          | 9.94                         | 20.0                  |
| 012               | 9.13                    | 9.25                   | 18.7            | 0.506        | 2.24          | 0.309                    | 90.4         | 40.4      | 10.9                          | 11.1                         | 22.4                  |
| 014               | 10.9                    | 11.0                   | 23.2            | 0.259        | 2.12          | 0.326                    | 64.2         | 30.2      | 15.4                          | 15.6                         | 32.7                  |
| 015               | 11.7                    | 11.9                   | 22.8            | 0.249        | 1.37          | 0.504                    | 51.0         | 37.1      | 19.3                          | 19.6                         | 37.4                  |
| 016               | 9.58                    | 9.69                   | 22.2            | 0.256        | 2.25          | 0.308                    | 78.5         | 34.9      | 12.6                          | 12.7                         | 29.2                  |
| n                 | 6                       | 6                      | 6               | 6            | 6             | 6                        | 6            | 6         | 6                             | 6                            | 6                     |
| Mean              | 9.510                   | 9.646                  | 19.88           | 0.2957       | 2.733         | 0.3159                   | 83.76        | 35.04     | 12.72                         | 12.90                        | 26.52                 |
| SD                | 1.6065                  | 1.6400                 | 3.3175          | 0.10310      | 1.8069        | 0.12571                  | 24.374       | 10.282    | 4.0140                        | 4.0897                       | 7.8425                |
| CV%               | 16.9                    | 17.0                   | 16.7            | 34.9         | 66.1          | 39.8                     | 29.1         | 29.3      | 31.6                          | 31.7                         | 29.6                  |
| SEM               | 0.65587                 | 0.66952                | 1.3544          | 0.042092     | 0.73766       | 0.051320                 | 9.9508       | 4.1975    | 1.6387                        | 1.6696                       | 3.2017                |
| Minimum           | 7.37                    | 7.46                   | 15.3            | 0.249        | 1.37          | 0.109                    | 51.0         | 18.5      | 8.38                          | 8.49                         | 17.4                  |
| Median            | 9.350                   | 9.469                  | 20.45           | 0.2545       | 2.182         | 0.3179                   | 84.46        | 35.99     | 11.75                         | 11.90                        | 25.77                 |
| Maximum           | 11.7                    | 11.9                   | 23.2            | 0.506        | 6.36          | 0.504                    | 118          | 49.2      | 19.3                          | 19.6                         | 37.4                  |
| Geom Mean         | 9.397                   | 9.530                  | 19.64           | 0.2845       | 2.401         | 0.2886                   | 80.67        | 33.59     | 12.22                         | 12.40                        | 25.55                 |
| Geom CV%          | 17.2                    | 17.3                   | 17.4            | 28.8         | 54.7          | 54.7                     | 31.3         | 34.3      | 31.2                          | 31.3                         | 30.7                  |

Note: Dose-dependent parameters (CL, Vz, DN AUC0-last, DN AUC0-inf, and DN Cmax) were calculated using actual dose, where  
Actual dose (mg) = nominal dose (mg/kg) x weight (kg).

Table 14.2.1.8 Plasma cP12 Pharmacokinetic Parameters Following  
a Single IV Infusion of 0.02 mg/kg cP12 Over Approximately 30 Minutes (Cohort 3) (Pharmacokinetic Population)

| Subject<br>Number | Parameters              |                        |                 |              |               |                          |              |           |                               |                              |                       |
|-------------------|-------------------------|------------------------|-----------------|--------------|---------------|--------------------------|--------------|-----------|-------------------------------|------------------------------|-----------------------|
|                   | AUC0-last<br>(ng*hr/mL) | AUC0-inf<br>(ng*hr/mL) | Cmax<br>(ng/mL) | Tmax<br>(hr) | Kel<br>(1/hr) | t <sub>1/2</sub><br>(hr) | CL<br>(L/hr) | Vz<br>(L) | DN AUC0-last<br>(ng*hr/mL/mg) | DN AUC0-inf<br>(ng*hr/mL/mg) | DN Cmax<br>(ng/mL/mg) |
| 017               | 20.0                    | 20.2                   | 44.2            | 0.251        | 1.46          | 0.476                    | 73.6         | 50.6      | 13.4                          | 13.6                         | 29.7                  |
| 020               | 14.8                    | 15.0                   | 30.4            | 0.250        | 1.47          | 0.473                    | 80.2         | 54.7      | 12.3                          | 12.5                         | 25.2                  |
| 021               | 15.6                    | 15.7                   | 32.3            | 0.495        | 1.54          | 0.450                    | 76.8         | 49.8      | 12.9                          | 13.0                         | 26.7                  |
| 022               | 13.9                    | 13.9                   | 31.0            | 0.250        | 7.85          | 0.0883                   | 97.5         | 12.4      | 10.2                          | 10.3                         | 22.8                  |
| 023               | 16.1                    | 16.2                   | 38.2            | 0.501        | 2.67          | 0.260                    | 111          | 41.8      | 8.91                          | 8.97                         | 21.2                  |
| 024               | 17.7                    | 17.9                   | 40.0            | 0.251        | 1.42          | 0.490                    | 108          | 76.5      | 9.16                          | 9.24                         | 20.7                  |
| n                 | 6                       | 6                      | 6               | 6            | 6             | 6                        | 6            | 6         | 6                             | 6                            | 6                     |
| Mean              | 16.34                   | 16.50                  | 36.02           | 0.3330       | 2.732         | 0.3727                   | 91.31        | 47.63     | 11.14                         | 11.26                        | 24.38                 |
| SD                | 2.2070                  | 2.2422                 | 5.6237          | 0.12782      | 2.5521        | 0.16368                  | 16.584       | 20.830    | 1.9661                        | 2.0121                       | 3.4918                |
| CV%               | 13.5                    | 13.6                   | 15.6            | 38.4         | 93.4          | 43.9                     | 18.2         | 43.7      | 17.6                          | 17.9                         | 14.3                  |
| SEM               | 0.90100                 | 0.91537                | 2.2959          | 0.052184     | 1.0419        | 0.066821                 | 6.7703       | 8.5038    | 0.80265                       | 0.82143                      | 1.4255                |
| Minimum           | 13.9                    | 13.9                   | 30.4            | 0.250        | 1.42          | 0.0883                   | 73.6         | 12.4      | 8.91                          | 8.97                         | 20.7                  |
| Median            | 15.83                   | 15.98                  | 35.25           | 0.2510       | 1.504         | 0.4612                   | 88.86        | 50.20     | 11.25                         | 11.36                        | 24.04                 |
| Maximum           | 20.0                    | 20.2                   | 44.2            | 0.501        | 7.85          | 0.490                    | 111          | 76.5      | 13.4                          | 13.6                         | 29.7                  |
| Geom Mean         | 16.22                   | 16.37                  | 35.66           | 0.3150       | 2.145         | 0.3231                   | 90.06        | 41.98     | 11.00                         | 11.10                        | 24.18                 |
| Geom CV%          | 13.2                    | 13.3                   | 15.5            | 36.6         | 76.6          | 76.6                     | 18.3         | 69.6      | 18.1                          | 18.3                         | 14.2                  |

Note: Dose-dependent parameters (CL, Vz, DN AUC0-last, DN AUC0-inf, and DN Cmax) were calculated using actual dose, where  
Actual dose (mg) = nominal dose (mg/kg) x weight (kg).

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Table 14.2.1.9 Plasma cP12 Pharmacokinetic Parameters Following  
a Single IV Infusion of 0.04 mg/kg cP12 Over Approximately 30 Minutes (Cohort 4) (Pharmacokinetic Population)

| Subject<br>Number | Parameters              |                        |                 |              |               |                          |              |           |                               |                              |                       |
|-------------------|-------------------------|------------------------|-----------------|--------------|---------------|--------------------------|--------------|-----------|-------------------------------|------------------------------|-----------------------|
|                   | AUC0-last<br>(ng*hr/mL) | AUC0-inf<br>(ng*hr/mL) | Cmax<br>(ng/mL) | Tmax<br>(hr) | Kel<br>(1/hr) | t <sub>1/2</sub><br>(hr) | CL<br>(L/hr) | Vz<br>(L) | DN AUC0-last<br>(ng*hr/mL/mg) | DN AUC0-inf<br>(ng*hr/mL/mg) | DN Cmax<br>(ng/mL/mg) |
| 026               | 23.7                    | 24.0                   | 47.5            | 0.508        | 1.52          | 0.455                    | 120          | 78.8      | 8.25                          | 8.33                         | 16.5                  |
| 027               | 30.0                    | 30.3                   | 77.2            | 0.526        | 2.26          | 0.307                    | 121          | 53.8      | 8.17                          | 8.24                         | 21.0                  |
| 028               | 38.3                    | 38.5                   | 94.1            | 0.504        | 1.58          | 0.439                    | 112          | 71.0      | 8.86                          | 8.92                         | 21.8                  |
| 029               | 39.2                    | .                      | 81.9            | 0.283        | .             | .                        | .            | .         | 12.8                          | .                            | 26.8                  |
| 031               | 21.7                    | 21.8                   | 45.2            | 0.249        | 1.92          | 0.362                    | 127          | 66.3      | 7.82                          | 7.87                         | 16.3                  |
| 032               | 29.5                    | 30.0                   | 60.6            | 0.249        | 1.29          | 0.537                    | 121          | 93.8      | 8.13                          | 8.25                         | 16.7                  |
| n                 | 6                       | 5                      | 6               | 6            | 5             | 5                        | 5            | 5         | 6                             | 5                            | 6                     |
| Mean              | 30.42                   | 28.90                  | 67.75           | 0.3865       | 1.714         | 0.4198                   | 120.4        | 72.75     | 9.012                         | 8.320                        | 19.85                 |
| SD                | 7.2359                  | 6.5236                 | 19.766          | 0.13896      | 0.37727       | 0.088493                 | 5.3503       | 14.876    | 1.9061                        | 0.37781                      | 4.1726                |
| CV%               | 23.8                    | 22.6                   | 29.2            | 36.0         | 22.0          | 21.1                     | 4.4          | 20.4      | 21.1                          | 4.5                          | 21.0                  |
| SEM               | 2.9540                  | 2.9174                 | 8.0696          | 0.056731     | 0.16872       | 0.039575                 | 2.3927       | 6.6530    | 0.77815                       | 0.16896                      | 1.7034                |
| Minimum           | 21.7                    | 21.8                   | 45.2            | 0.249        | 1.29          | 0.307                    | 112          | 53.8      | 7.82                          | 7.87                         | 16.3                  |
| Median            | 29.79                   | 29.96                  | 68.90           | 0.3935       | 1.579         | 0.4390                   | 121.2        | 71.04     | 8.210                         | 8.250                        | 18.84                 |
| Maximum           | 39.2                    | 38.5                   | 94.1            | 0.526        | 2.26          | 0.537                    | 127          | 93.8      | 12.8                          | 8.92                         | 26.8                  |
| Geom Mean         | 29.69                   | 28.33                  | 65.28           | 0.3650       | 1.682         | 0.4122                   | 120.3        | 71.53     | 8.872                         | 8.313                        | 19.51                 |
| Geom CV%          | 24.5                    | 22.6                   | 30.9            | 38.9         | 21.9          | 21.9                     | 4.5          | 20.9      | 18.7                          | 4.5                          | 20.3                  |

Note: Dose-dependent parameters (CL, Vz, DN AUC0-last, DN AUC0-inf, and DN Cmax) were calculated using actual dose, where  
Actual dose (mg) = nominal dose (mg/kg) x weight (kg).  
. = Value missing or not reportable.

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Table 14.2.1.10 Plasma cP12 Pharmacokinetic Parameters Following  
a Single IV Infusion of 0.08 mg/kg cP12 Over Approximately 30 Minutes (Cohort 5) (Pharmacokinetic Population)

| Subject<br>Number | Parameters              |                        |                 |              |               |                          |              |           |                               |                              |                       |
|-------------------|-------------------------|------------------------|-----------------|--------------|---------------|--------------------------|--------------|-----------|-------------------------------|------------------------------|-----------------------|
|                   | AUC0-last<br>(ng*hr/mL) | AUC0-inf<br>(ng*hr/mL) | Cmax<br>(ng/mL) | Tmax<br>(hr) | Kel<br>(1/hr) | t <sub>1/2</sub><br>(hr) | CL<br>(L/hr) | Vz<br>(L) | DN AUC0-last<br>(ng*hr/mL/mg) | DN AUC0-inf<br>(ng*hr/mL/mg) | DN Cmax<br>(ng/mL/mg) |
| 033               | 59.7                    | 60.5                   | 115             | 0.504        | 0.419         | 1.65                     | 122          | 292       | 8.05                          | 8.16                         | 15.5                  |
| 035               | 91.4                    | 92.1                   | 209             | 0.328        | 0.329         | 2.11                     | 76.2         | 232       | 13.0                          | 13.1                         | 29.8                  |
| 036               | 70.8                    | 71.1                   | 160             | 0.263        | 0.664         | 1.04                     | 99.5         | 150       | 10.0                          | 10.0                         | 22.6                  |
| 037               | 68.8                    | 69.3                   | 142             | 0.261        | 0.432         | 1.60                     | 100          | 232       | 9.89                          | 9.97                         | 20.4                  |
| 038               | 55.8                    | 56.5                   | 118             | 0.250        | 0.535         | 1.29                     | 121          | 226       | 8.17                          | 8.27                         | 17.3                  |
| 039               | 91.8                    | 92.2                   | 207             | 0.252        | 0.587         | 1.18                     | 61.2         | 104       | 16.3                          | 16.3                         | 36.7                  |
| n                 | 6                       | 6                      | 6               | 6            | 6             | 6                        | 6            | 6         | 6                             | 6                            | 6                     |
| Mean              | 73.03                   | 73.60                  | 158.5           | 0.3097       | 0.4945        | 1.480                    | 96.79        | 206.0     | 10.90                         | 10.98                        | 23.72                 |
| SD                | 15.419                  | 15.353                 | 41.736          | 0.099532     | 0.12323       | 0.38753                  | 24.310       | 67.369    | 3.1851                        | 3.1784                       | 8.0718                |
| CV%               | 21.1                    | 20.9                   | 26.3            | 32.1         | 24.9          | 26.2                     | 25.1         | 32.7      | 29.2                          | 28.9                         | 34.0                  |
| SEM               | 6.2948                  | 6.2678                 | 17.039          | 0.040634     | 0.050308      | 0.15821                  | 9.9244       | 27.503    | 1.3003                        | 1.2976                       | 3.2953                |
| Minimum           | 55.8                    | 56.5                   | 115             | 0.250        | 0.329         | 1.04                     | 61.2         | 104       | 8.05                          | 8.16                         | 15.5                  |
| Median            | 69.75                   | 70.18                  | 151.0           | 0.2620       | 0.4839        | 1.449                    | 99.92        | 228.7     | 9.947                         | 10.01                        | 21.53                 |
| Maximum           | 91.8                    | 92.2                   | 209             | 0.504        | 0.664         | 2.11                     | 122          | 292       | 16.3                          | 16.3                         | 36.7                  |
| Geom Mean         | 71.70                   | 72.30                  | 154.0           | 0.2990       | 0.4814        | 1.440                    | 94.01        | 195.3     | 10.55                         | 10.64                        | 22.66                 |
| Geom CV%          | 21.1                    | 20.8                   | 26.7            | 28.0         | 26.1          | 26.1                     | 27.7         | 39.0      | 28.0                          | 27.7                         | 33.6                  |

Note: Dose-dependent parameters (CL, Vz, DN AUC0-last, DN AUC0-inf, and DN Cmax) were calculated using actual dose, where  
Actual dose (mg) = nominal dose (mg/kg) x weight (kg).

Table 14.2.1.11 Intervals (Hours) Used for Determination of Plasma cP12 Kel Values (Pharmacokinetic Population)

| Subject Number | Dose Level  | Interval  | R <sup>2</sup> | n |
|----------------|-------------|-----------|----------------|---|
| 002            | 0.003 mg/kg | . - .     | .              | 0 |
| 003            | 0.003 mg/kg | . - .     | .              | 0 |
| 005            | 0.003 mg/kg | . - .     | .              | 0 |
| 006            | 0.003 mg/kg | . - .     | .              | 0 |
| 007            | 0.003 mg/kg | . - .     | .              | 0 |
| 008            | 0.003 mg/kg | 0.5 - 1.0 | 0.939          | 3 |
| 009            | 0.01 mg/kg  | 0.5 - 1.0 | 0.927          | 3 |
| 011            | 0.01 mg/kg  | 0.8 - 1.5 | 0.951          | 3 |
| 012            | 0.01 mg/kg  | 0.8 - 1.5 | 0.997          | 3 |
| 014            | 0.01 mg/kg  | 0.8 - 1.5 | 0.992          | 3 |
| 015            | 0.01 mg/kg  | 1.0 - 2.0 | 0.973          | 3 |
| 016            | 0.01 mg/kg  | 0.8 - 1.5 | 0.973          | 3 |
| 017            | 0.02 mg/kg  | 1.0 - 2.0 | 1.000          | 3 |
| 020            | 0.02 mg/kg  | 1.0 - 2.0 | 0.983          | 3 |
| 021            | 0.02 mg/kg  | 1.0 - 2.0 | 0.979          | 3 |
| 022            | 0.02 mg/kg  | 0.5 - 1.0 | 0.953          | 3 |
| 023            | 0.02 mg/kg  | 0.8 - 1.5 | 0.982          | 3 |
| 024            | 0.02 mg/kg  | 1.0 - 2.0 | 0.928          | 3 |
| 026            | 0.04 mg/kg  | 1.0 - 2.0 | 0.958          | 3 |
| 027            | 0.04 mg/kg  | 0.8 - 2.0 | 0.935          | 4 |
| 028            | 0.04 mg/kg  | 1.0 - 2.0 | 0.994          | 3 |
| 029            | 0.04 mg/kg  | . - .     | .              | 0 |
| 031            | 0.04 mg/kg  | 1.0 - 2.0 | 0.999          | 3 |
| 032            | 0.04 mg/kg  | 1.0 - 2.0 | 1.000          | 3 |
| 033            | 0.08 mg/kg  | 2.0 - 6.0 | 0.984          | 3 |
| 035            | 0.08 mg/kg  | 2.0 - 6.0 | 0.996          | 3 |
| 036            | 0.08 mg/kg  | 1.5 - 4.0 | 0.988          | 3 |
| 037            | 0.08 mg/kg  | 1.5 - 6.0 | 0.975          | 4 |
| 038            | 0.08 mg/kg  | 1.5 - 4.0 | 0.909          | 3 |
| 039            | 0.08 mg/kg  | 1.5 - 4.0 | 0.974          | 3 |

R<sup>2</sup> = Coefficient of determination  
n = Number of points used in Kel calculation  
. = Kel value not reportable.

Table 14.2.1.12 Dose Proportionality Analysis of Plasma cP12 Pharmacokinetic Parameters (Pharmacokinetic Population)

| Pharmacokinetic Parameters | Estimate of Slope (b) | Standard Error | 95% Confidence Interval for Slope |
|----------------------------|-----------------------|----------------|-----------------------------------|
| AUC0-last (ng*hr/mL)       | 0.9917                | 0.0394         | 0.9109 - 1.0724                   |
| AUC0-inf (ng*hr/mL)        | 0.9067                | 0.0534         | 0.7960 - 1.0174                   |
| Cmax (ng/mL)               | 0.9848                | 0.0385         | 0.9059 - 1.0638                   |

Note: Actual dose was used in the dose proportionality analysis, where Actual dose (mg) = nominal dose (mg/kg) x weight (kg).

Parameters were ln-transformed prior to analysis.

The following statistical model using PROC MIXED of SAS was used to test dose proportionality:

Parameter =  $a * \text{Dose}^b$  which was equivalent to  $\ln(\text{Parameter}) = \ln(a) + b[\ln(\text{Dose})]$

Dose proportionality is not rejected if the 95% CI for the estimate of slope (b) contains 1.

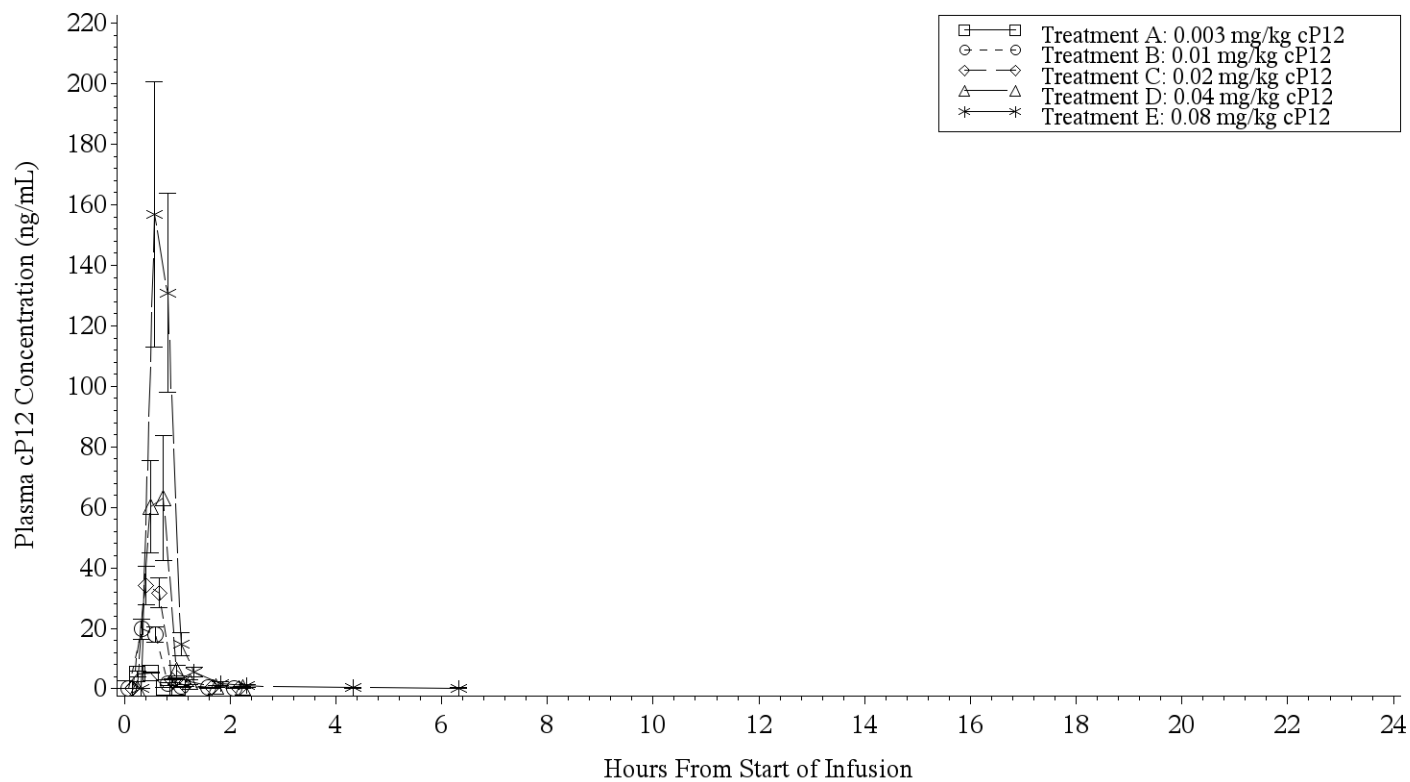
There was a statistically significant cubic effect for the models on AUC0-last and AUC0-inf. Therefore a statistical linear relationship could not be established for these pharmacokinetic parameters.

## 14.2.2 Plasma cP12 Figures

- Figure 14.2.2.1.1 Mean (SD) Plasma cP12 Concentration Versus Time Profiles Following Single IV Infusions Over Approximately 30 Minutes (Linear Scale) (Pharmacokinetic Population)
- Figure 14.2.2.1.2 Mean (SD) Plasma cP12 Concentration Versus Time Profiles Following Single IV Infusions Over Approximately 30 Minutes (up to 8 Hours Post Start of Infusion) (Linear Scale) (Pharmacokinetic Population)
- Figure 14.2.2.2.1 Mean Plasma cP12 Concentration Versus Time Profiles Following Single IV Infusions Over Approximately 30 Minutes (Linear Scale) (Pharmacokinetic Population)
- Figure 14.2.2.2.2 Mean Plasma cP12 Concentration Versus Time Profiles Following Single IV Infusions Over Approximately 30 Minutes (up to 8 Hours Post Start of Infusion) (Linear Scale) (Pharmacokinetic Population)
- Figure 14.2.2.3.1 Mean Plasma cP12 Concentration Versus Time Profiles Following Single IV Infusions Over Approximately 30 Minutes (Semi-Log Scale) (Pharmacokinetic Population)
- Figure 14.2.2.3.2 Mean Plasma cP12 Concentration Versus Time Profiles Following Single IV Infusions Over Approximately 30 Minutes (up to 8 Hours Post Start of Infusion) (Semi-Log Scale) (Pharmacokinetic Population)
- Figure 14.2.2.4 Plasma cP12 AUC<sub>0-last</sub> Versus Dose Following Single IV Infusions Over Approximately 30 Minutes (Pharmacokinetic Population)
- Figure 14.2.2.5 Plasma cP12 AUC<sub>0-inf</sub> Versus Dose Following Single IV Infusions Over Approximately 30 Minutes (Pharmacokinetic Population)
- Figure 14.2.2.6 Plasma cP12 C<sub>max</sub> Versus Dose Following Single IV Infusions Over Approximately 30 Minutes (Pharmacokinetic Population)

Figure 14.2.2.1.1

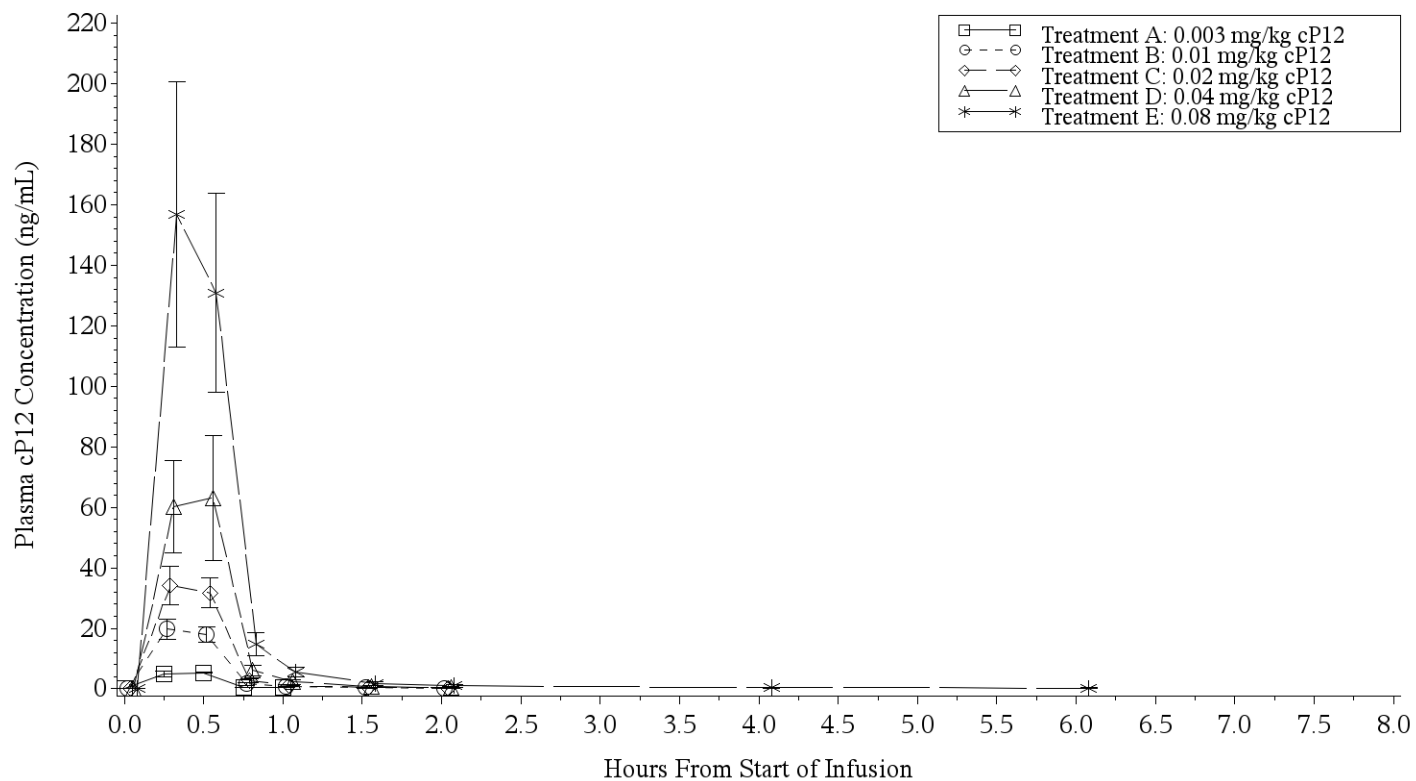
Mean (SD) Plasma cP12 Concentration Versus Time Profiles Following Single IV Infusions Over Approximately 30 Minutes  
(Linear Scale) (Pharmacokinetic Population)



Treatments B, C, D, and E are shifted to the right for ease of reading  
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Figure 14.2.2.1.2

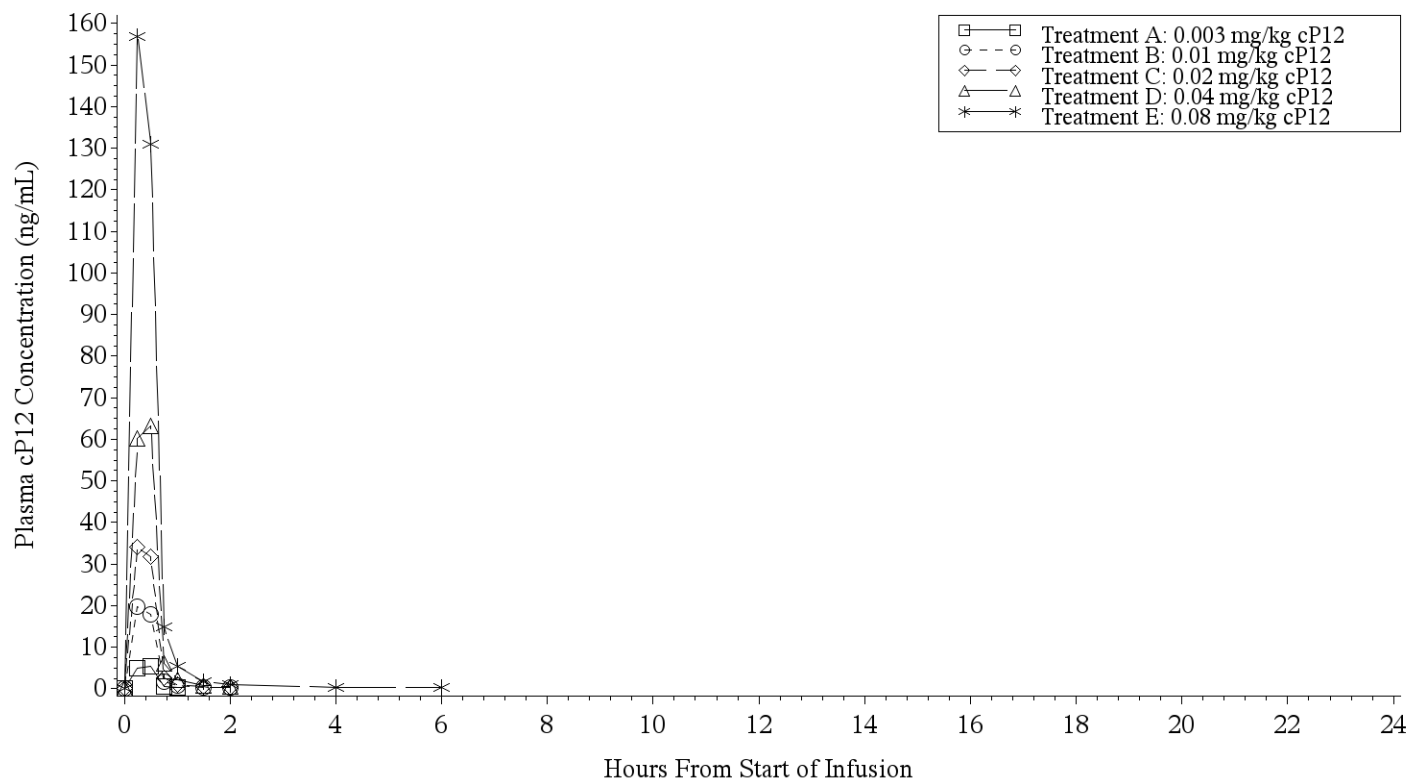
Mean (SD) Plasma cP12 Concentration Versus Time Profiles Following Single IV Infusions Over Approximately 30 Minutes  
(up to 8 Hours Post Start of Infusion) (Linear Scale) (Pharmacokinetic Population)



Treatments B, C, D, and E are shifted to the right for ease of reading  
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Figure 14.2.2.2.1

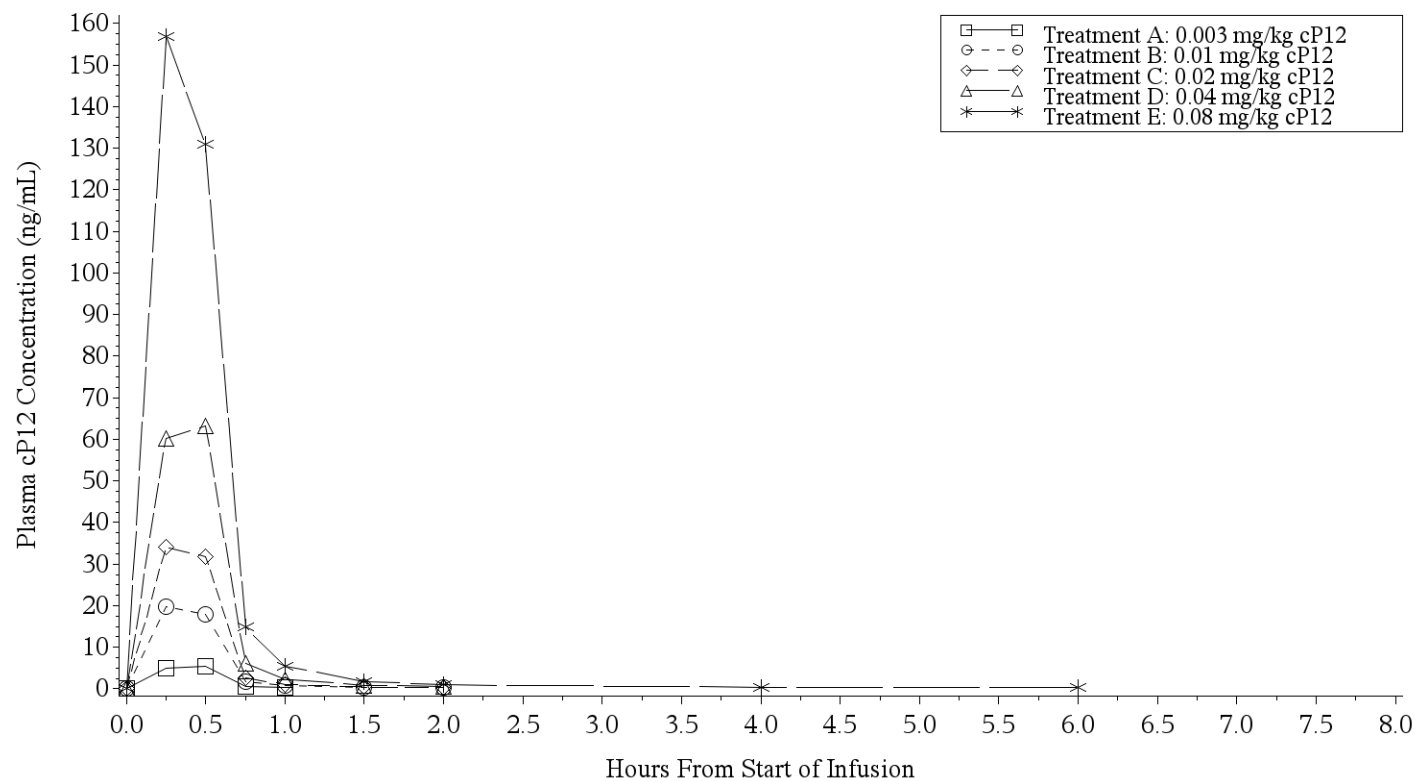
Mean Plasma cP12 Concentration Versus Time Profiles Following Single IV Infusions Over Approximately 30 Minutes  
(Linear Scale) (Pharmacokinetic Population)



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Figure 14.2.2.2.2

Mean Plasma cP12 Concentration Versus Time Profiles Following Single IV Infusions Over Approximately 30 Minutes  
(up to 8 Hours Post Start of Infusion) (Linear Scale) (Pharmacokinetic Population)

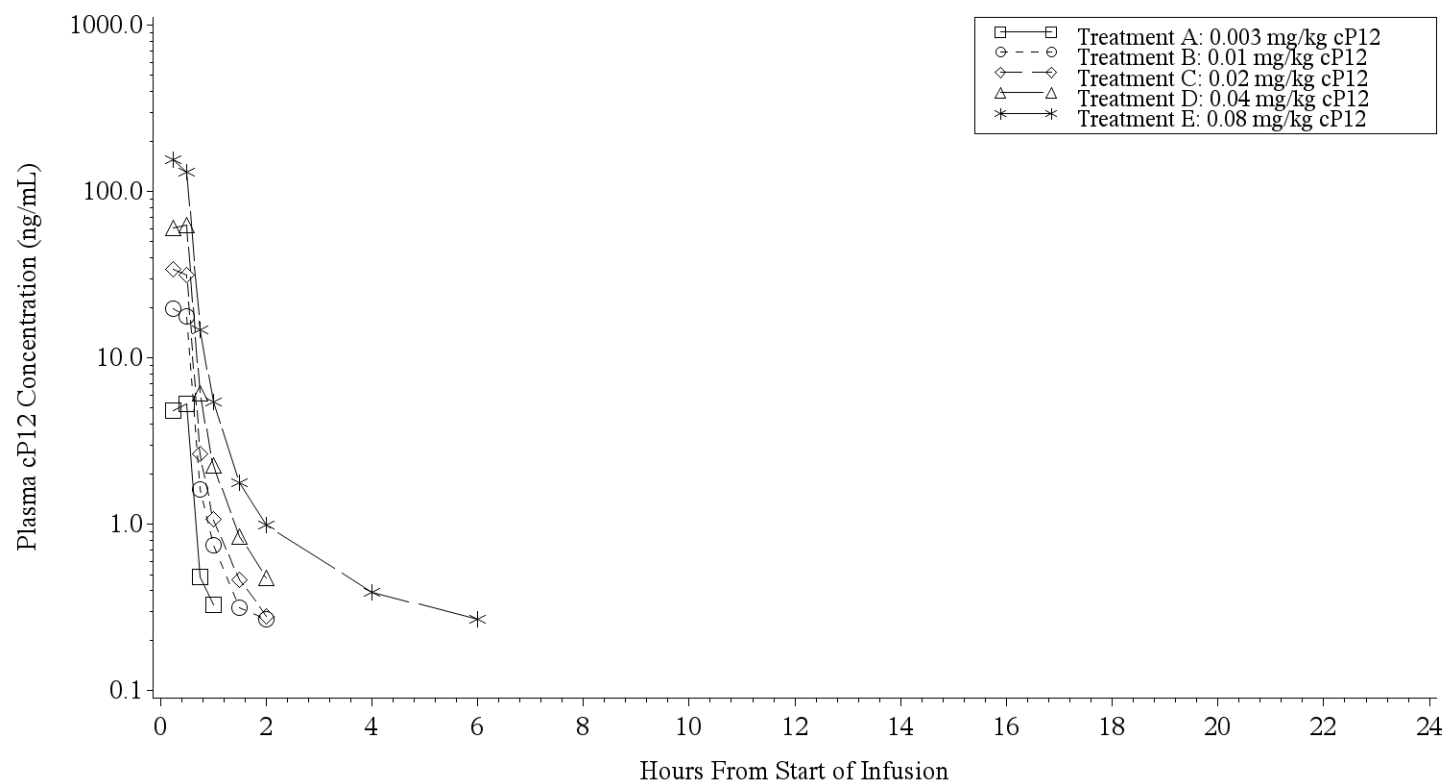


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Figure 14.2.2.3.1

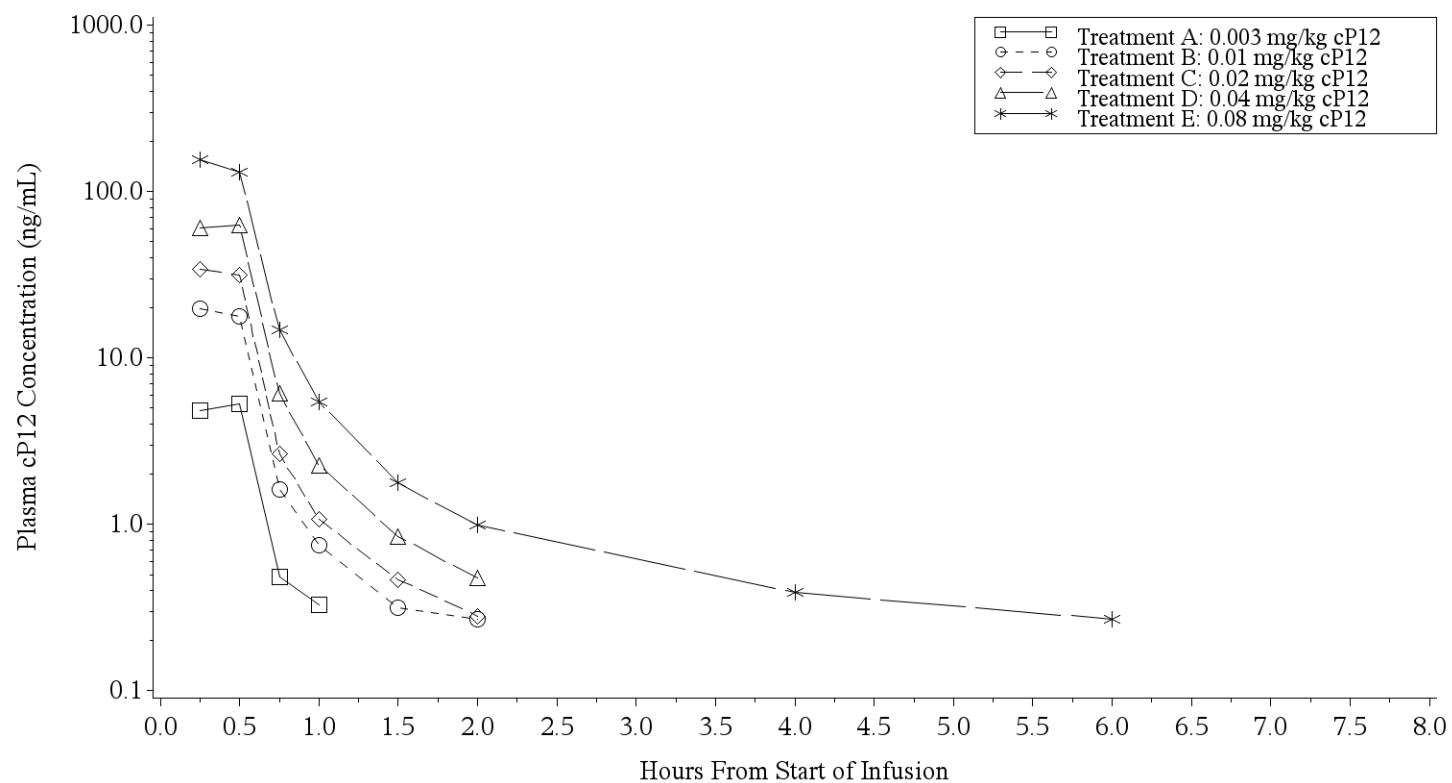
Mean Plasma cP12 Concentration Versus Time Profiles Following Single IV Infusions Over Approximately 30 Minutes  
(Semi-Log Scale) (Pharmacokinetic Population)



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Figure 14.2.2.3.2

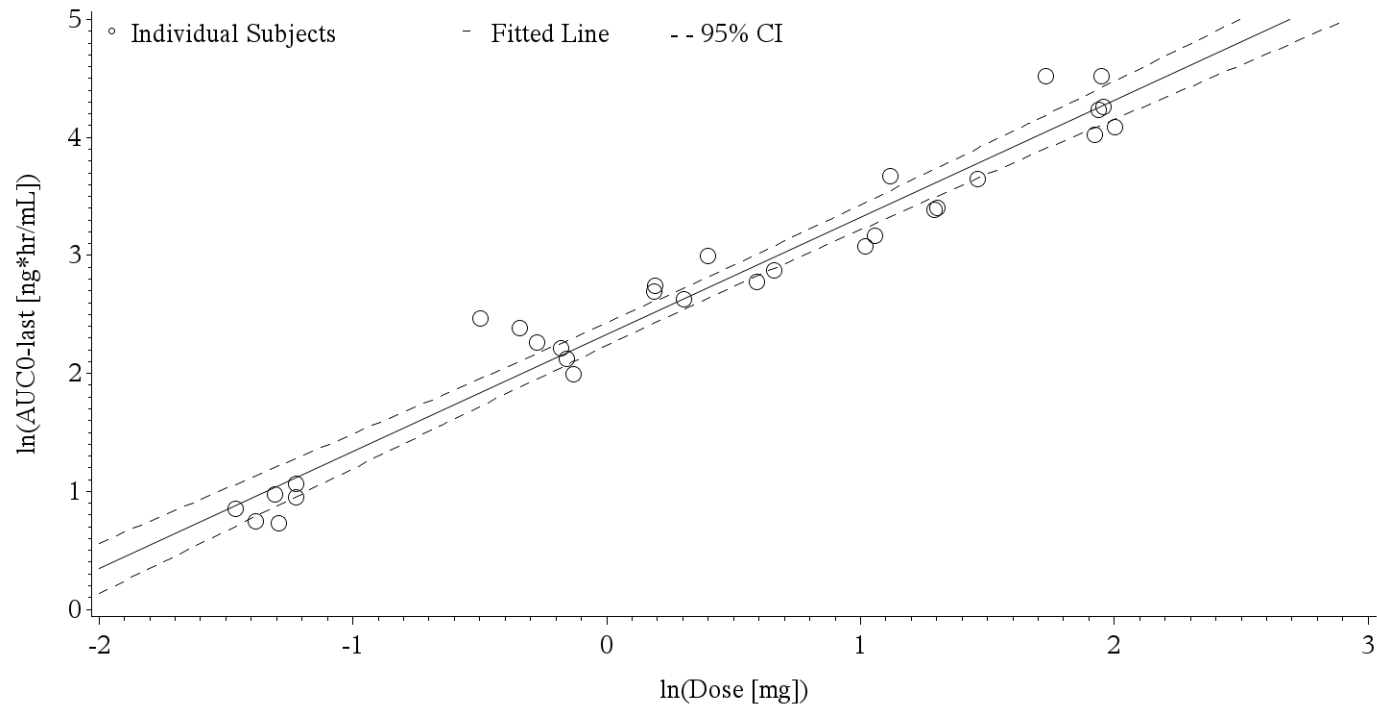
Mean Plasma cP12 Concentration Versus Time Profiles Following Single IV Infusions Over Approximately 30 Minutes  
(up to 8 Hours Post Start of Infusion) (Semi-Log Scale) (Pharmacokinetic Population)



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Figure 14.2.2.4

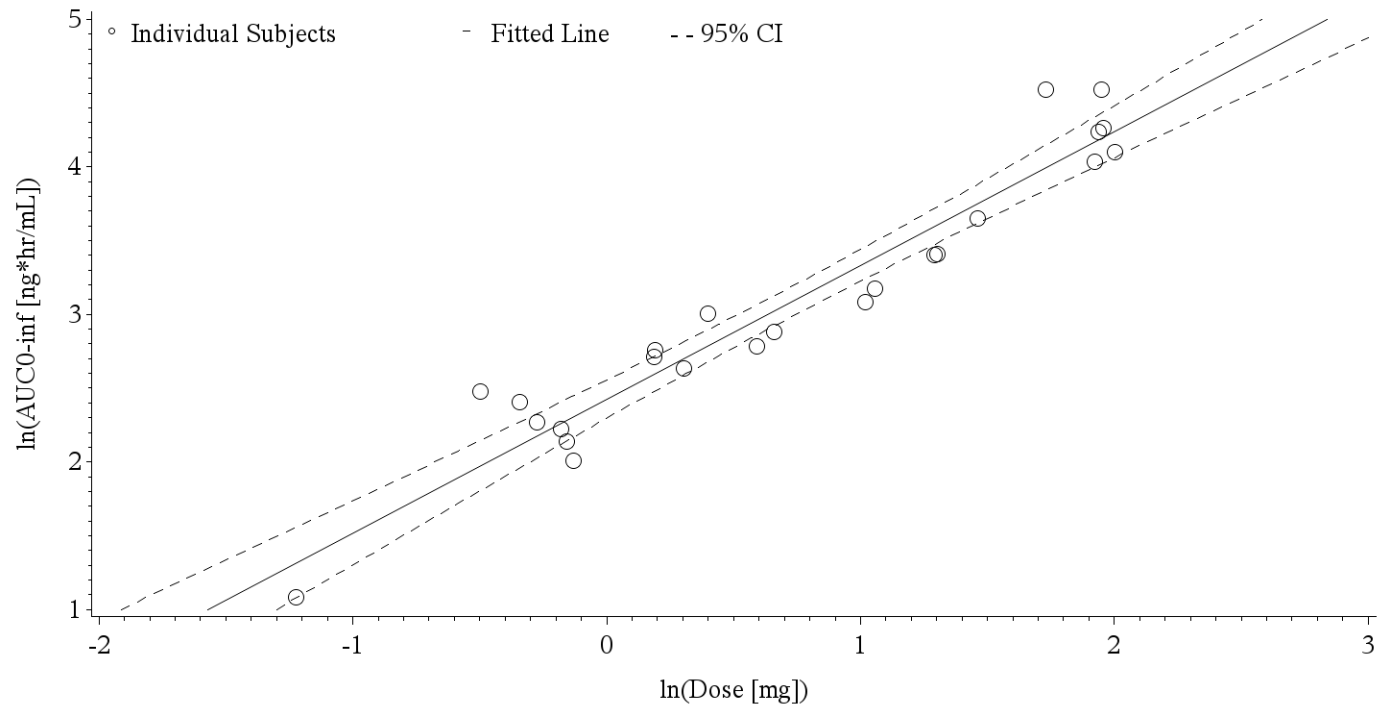
Plasma cP12 AUC0-last Versus Dose Following Single IV Infusions Over Approximately 30 Minutes (Pharmacokinetic Population)



$\ln(\text{AUC0-last}) = \text{Intercept} + \text{Slope} * \ln(\text{Dose})$   
Slope = 0.9917 (95% CI: 0.9109 - 1.0724); Intercept = 2.3315 (95% CI: 2.2348 - 2.4282)  
95% Confidence Interval (CI) is based on mean predicted values. P-value (Slope) = <.0001;  $R^2 = 0.9576$   
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Figure 14.2.2.5

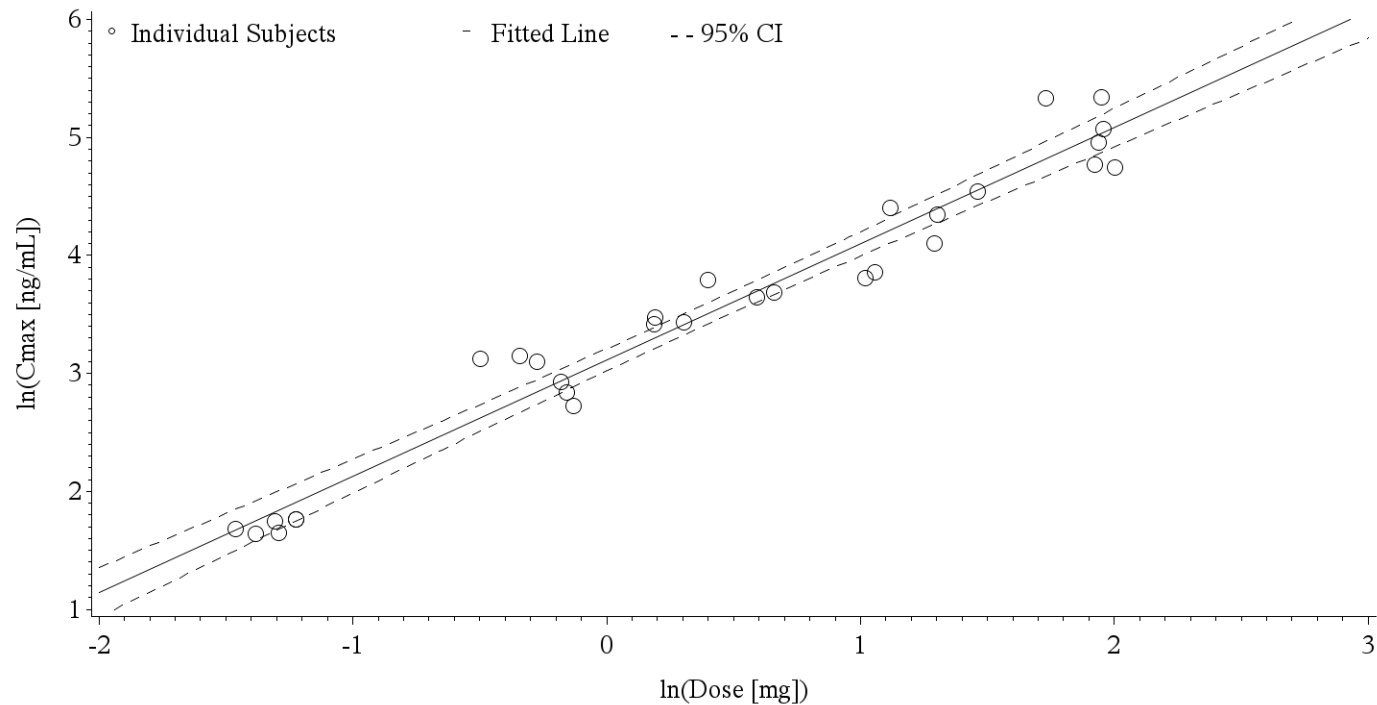
Plasma cP12 AUC0-inf Versus Dose Following Single IV Infusions Over Approximately 30 Minutes (Pharmacokinetic Population)



$\ln(\text{AUC0-inf}) = \text{Intercept} + \text{Slope} * \ln(\text{Dose})$   
Slope = 0.9067 (95% CI: 0.7960 - 1.0174); Intercept = 2.4262 (95% CI: 2.2967 - 2.5557)  
95% Confidence Interval (CI) is based on mean predicted values. P-value (Slope) = <.0001;  $R^2 = 0.9292$   
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Figure 14.2.2.6

Plasma cP12 Cmax Versus Dose Following Single IV Infusions Over Approximately 30 Minutes (Pharmacokinetic Population)



$\ln(C_{\max}) = \text{Intercept} + \text{Slope} * \ln(\text{Dose})$   
Slope = 0.9848 (95% CI: 0.9059 - 1.0638); Intercept = 3.1138 (95% CI: 3.0193 - 3.2084)  
95% Confidence Interval (CI) is based on mean predicted values. P-value (Slope) = <.0001;  $R^2 = 0.9589$   
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### **14.3 Safety Data Summary Tables**

#### **14.3.1 Displays of Adverse Events**

|                |                                                                                                                                                  |
|----------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| Table 14.3.1.1 | Treatment-Emergent Adverse Event Frequency by Treatment – Number of Subjects Reporting the Event (% of Subjects Dosed) (Safety Population)       |
| Table 14.3.1.2 | Treatment-Emergent Adverse Event Frequency by Treatment – Number of Adverse Events (% of Total Adverse Events) (Safety Population)               |
| Table 14.3.1.3 | Treatment-Emergent Adverse Event Frequency by Treatment, Severity, and Relationship to Study Drug – Number of Adverse Events (Safety Population) |

Table 14.3.1.1 Treatment-Emergent Adverse Event Frequency by Treatment -  
Number of Subjects Reporting the Event (% of Subjects Dosed) (Safety Population)

| Adverse Event*                                       | Pooled<br>Placebo | Treatment |          |          |          |          | Overall   |
|------------------------------------------------------|-------------------|-----------|----------|----------|----------|----------|-----------|
|                                                      |                   | A         | B        | C        | D        | E        |           |
| Number of Subjects Dosed                             | 10 (100%)         | 6 (100%)  | 6 (100%) | 6 (100%) | 6 (100%) | 6 (100%) | 30 (100%) |
| Number of Subjects With TEAEs^                       | 0 ( 0%)           | 2 ( 33%)  | 0 ( 0%)  | 0 ( 0%)  | 2 ( 33%) | 6 (100%) | 10 ( 33%) |
| Number of Subjects Without TEAEs^                    | 10 (100%)         | 4 ( 67%)  | 6 (100%) | 6 (100%) | 4 ( 67%) | 0 ( 0%)  | 20 ( 67%) |
| General disorders and administration site conditions | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 3 ( 50%) | 4 ( 13%)  |
| Feeling hot                                          | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 3 ( 50%) | 4 ( 13%)  |
| Injury, poisoning and procedural complications       | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 0 ( 0%)  | 1 ( 3%)   |
| Scratch                                              | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 0 ( 0%)  | 1 ( 3%)   |
| Investigations                                       | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 1 ( 3%)   |
| Blood creatine phosphokinase increased               | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 1 ( 3%)   |
| Nervous system disorders                             | 0 ( 0%)           | 2 ( 33%)  | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 2 ( 33%) | 5 ( 17%)  |
| Headache                                             | 0 ( 0%)           | 2 ( 33%)  | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 2 ( 33%) | 4 ( 13%)  |
| Paraesthesia                                         | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 1 ( 17%) | 2 ( 7%)   |
| Psychiatric disorders                                | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 1 ( 3%)   |
| Restlessness                                         | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 1 ( 3%)   |
| Skin and subcutaneous tissue disorders               | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 2 ( 33%) | 4 ( 67%) | 6 ( 20%)  |
| Erythema                                             | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 1 ( 3%)   |
| Generalised erythema                                 | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 1 ( 3%)   |
| Pruritus                                             | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 2 ( 33%) | 2 ( 33%) | 4 ( 13%)  |
| Pruritus generalised                                 | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 1 ( 3%)   |
| Rash maculo-papular                                  | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 1 ( 17%) | 0 ( 0%)  | 1 ( 3%)   |
| Urticaria                                            | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 2 ( 33%) | 2 ( 7%)   |
| Vascular disorders                                   | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 4 ( 67%) | 4 ( 13%)  |
| Flushing                                             | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%)  | 0 ( 0%)  | 0 ( 0%)  | 4 ( 67%) | 4 ( 13%)  |

Note: \* Adverse events are classified according to MedDRA Version 22.0. ^ = Treatment-emergent adverse events  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.1.2 Treatment-Emergent Adverse Event Frequency by Treatment -  
Number of Adverse Events (% of Total Adverse Events) (Safety Population)

| Adverse Event*                                       | Pooled<br>Placebo | Treatment |         |         |          |           | Overall   |
|------------------------------------------------------|-------------------|-----------|---------|---------|----------|-----------|-----------|
|                                                      |                   | A         | B       | C       | D        | E         |           |
| Number of TEAEs^                                     | 0 ( 0%)           | 2 (100%)  | 0 ( 0%) | 0 ( 0%) | 7 (100%) | 22 (100%) | 31 (100%) |
| General disorders and administration site conditions | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 1 ( 14%) | 4 ( 18%)  | 5 ( 16%)  |
| Feeling hot                                          | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 1 ( 14%) | 4 ( 18%)  | 5 ( 16%)  |
| Injury, poisoning and procedural complications       | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 1 ( 14%) | 0 ( 0%)   | 1 ( 3%)   |
| Scratch                                              | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 1 ( 14%) | 0 ( 0%)   | 1 ( 3%)   |
| Investigations                                       | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 0 ( 0%)  | 1 ( 5%)   | 1 ( 3%)   |
| Blood creatine phosphokinase increased               | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 0 ( 0%)  | 1 ( 5%)   | 1 ( 3%)   |
| Nervous system disorders                             | 0 ( 0%)           | 2 (100%)  | 0 ( 0%) | 0 ( 0%) | 1 ( 14%) | 3 ( 14%)  | 6 ( 19%)  |
| Headache                                             | 0 ( 0%)           | 2 (100%)  | 0 ( 0%) | 0 ( 0%) | 0 ( 0%)  | 2 ( 9%)   | 4 ( 13%)  |
| Paraesthesia                                         | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 1 ( 14%) | 1 ( 5%)   | 2 ( 6%)   |
| Psychiatric disorders                                | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 0 ( 0%)  | 1 ( 5%)   | 1 ( 3%)   |
| Restlessness                                         | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 0 ( 0%)  | 1 ( 5%)   | 1 ( 3%)   |
| Skin and subcutaneous tissue disorders               | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 4 ( 57%) | 8 ( 36%)  | 12 ( 39%) |
| Erythema                                             | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 0 ( 0%)  | 1 ( 5%)   | 1 ( 3%)   |
| Generalised erythema                                 | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 0 ( 0%)  | 1 ( 5%)   | 1 ( 3%)   |
| Pruritus                                             | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 3 ( 43%) | 2 ( 9%)   | 5 ( 16%)  |
| Pruritus generalised                                 | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 0 ( 0%)  | 1 ( 5%)   | 1 ( 3%)   |
| Rash maculo-papular                                  | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 1 ( 14%) | 0 ( 0%)   | 1 ( 3%)   |
| Urticaria                                            | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 0 ( 0%)  | 3 ( 14%)  | 3 ( 10%)  |
| Vascular disorders                                   | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 0 ( 0%)  | 5 ( 23%)  | 5 ( 16%)  |
| Flushing                                             | 0 ( 0%)           | 0 ( 0%)   | 0 ( 0%) | 0 ( 0%) | 0 ( 0%)  | 5 ( 23%)  | 5 ( 16%)  |

Note: \* Adverse events are classified according to MedDRA Version 22.0. ^ = Treatment-emergent adverse events  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.1.3 Treatment-Emergent Adverse Event Frequency by Treatment, Severity, and Relationship to Study Drug -  
Number of Adverse Events (Safety Population)

| Adverse Event*                         | Treatment                | Number of<br>Subjects<br>with<br>TEAEs^ | Number<br>of<br>TEAEs^ | Severity |          |        | Relationship to Study Drug |          |          |          |
|----------------------------------------|--------------------------|-----------------------------------------|------------------------|----------|----------|--------|----------------------------|----------|----------|----------|
|                                        |                          |                                         |                        | Mild     | Moderate | Severe | Not Related                | Possible | Probable | Definite |
| Blood creatine phosphokinase increased | E                        | 1                                       | 1                      | 1        | 0        | 0      | 1                          | 0        | 0        | 0        |
| Erythema                               | E                        | 1                                       | 1                      | 1        | 0        | 0      | 0                          | 0        | 1        | 0        |
| Feeling hot                            | D                        | 1                                       | 1                      | 1        | 0        | 0      | 0                          | 0        | 1        | 0        |
|                                        | E                        | 3                                       | 4                      | 4        | 0        | 0      | 0                          | 0        | 4        | 0        |
| Flushing                               | E                        | 4                                       | 5                      | 5        | 0        | 0      | 0                          | 0        | 5        | 0        |
| Generalised erythema                   | E                        | 1                                       | 1                      | 0        | 1        | 0      | 0                          | 0        | 1        | 0        |
| Headache                               | A                        | 2                                       | 2                      | 1        | 1        | 0      | 0                          | 2        | 0        | 0        |
|                                        | E                        | 2                                       | 2                      | 1        | 1        | 0      | 0                          | 0        | 2        | 0        |
| Paraesthesia                           | D                        | 1                                       | 1                      | 1        | 0        | 0      | 0                          | 0        | 1        | 0        |
|                                        | E                        | 1                                       | 1                      | 1        | 0        | 0      | 0                          | 0        | 1        | 0        |
| Pruritus                               | D                        | 2                                       | 3                      | 3        | 0        | 0      | 1                          | 2        | 0        | 0        |
|                                        | E                        | 2                                       | 2                      | 1        | 1        | 0      | 0                          | 0        | 2        | 0        |
| Pruritus generalised                   | E                        | 1                                       | 1                      | 0        | 1        | 0      | 0                          | 0        | 1        | 0        |
| Rash maculo-papular                    | D                        | 1                                       | 1                      | 1        | 0        | 0      | 1                          | 0        | 0        | 0        |
| Restlessness                           | E                        | 1                                       | 1                      | 1        | 0        | 0      | 1                          | 0        | 0        | 0        |
| Scratch                                | D                        | 1                                       | 1                      | 1        | 0        | 0      | 1                          | 0        | 0        | 0        |
| Urticaria                              | E                        | 2                                       | 3                      | 0        | 3        | 0      | 0                          | 0        | 3        | 0        |
|                                        |                          |                                         |                        |          |          |        |                            |          |          |          |
|                                        | Pooled Placebo           | 0                                       | 0                      | 0        | 0        | 0      | 0                          | 0        | 0        | 0        |
|                                        | A                        | 2                                       | 2                      | 1        | 1        | 0      | 0                          | 2        | 0        | 0        |
|                                        | B                        | 0                                       | 0                      | 0        | 0        | 0      | 0                          | 0        | 0        | 0        |
|                                        | C                        | 0                                       | 0                      | 0        | 0        | 0      | 0                          | 0        | 0        | 0        |
|                                        | D                        | 2                                       | 7                      | 7        | 0        | 0      | 3                          | 2        | 2        | 0        |
|                                        | E                        | 6                                       | 22                     | 15       | 7        | 0      | 2                          | 0        | 20       | 0        |
|                                        | Active Treatment Overall | 10                                      | 31                     | 23       | 8        | 0      | 5                          | 4        | 22       | 0        |

Note: \* Adverse events are classified according to MedDRA Version 22.0. ^ = Treatment-emergent adverse events  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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### **14.3.2 Listings of Deaths, Other Serious and Significant Adverse Events**

#### **Table 14.3.2.1      Serious Adverse Events (Safety Population)**

Table 14.3.2.1 Serious Adverse Events (Safety Population)

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No serious adverse events were reported.

**14.3.3 Narratives of Deaths, Other Serious and Certain Other Significant Adverse Events**

Not applicable.

#### **14.3.4 Abnormal Laboratory Value Listing (Each Subject)**

|                  |                                                                                           |
|------------------|-------------------------------------------------------------------------------------------|
| Table 14.3.4.1.1 | Out-of-Range Values and Recheck Results - Serum Chemistry (I of IV) (Safety Population)   |
| Table 14.3.4.1.2 | Out-of-Range Values and Recheck Results - Serum Chemistry (II of IV) (Safety Population)  |
| Table 14.3.4.1.3 | Out-of-Range Values and Recheck Results - Serum Chemistry (III of IV) (Safety Population) |
| Table 14.3.4.1.4 | Out-of-Range Values and Recheck Results - Serum Chemistry (IV of IV) (Safety Population)  |
| Table 14.3.4.2.1 | Out-of-Range Values and Recheck Results - Hematology (I of IV) (Safety Population)        |
| Table 14.3.4.2.2 | Out-of-Range Values and Recheck Results - Hematology (II of IV) (Safety Population)       |
| Table 14.3.4.2.3 | Out-of-Range Values and Recheck Results - Hematology (III of IV) (Safety Population)      |
| Table 14.3.4.2.4 | Out-of-Range Values and Recheck Results - Hematology (IV of IV) (Safety Population)       |
| Table 14.3.4.3.1 | Out-of-Range Values and Recheck Results - Urinalysis (I of IV) (Safety Population)        |
| Table 14.3.4.3.2 | Out-of-Range Values and Recheck Results - Urinalysis (II of IV) (Safety Population)       |
| Table 14.3.4.3.3 | Out-of-Range Values and Recheck Results - Urinalysis (III of IV) (Safety Population)      |
| Table 14.3.4.3.4 | Out-of-Range Values and Recheck Results - Urinalysis (IV of IV) (Safety Population)       |
| Table 14.3.4.4   | Clinically Significant Values and Recheck Results (Safety Population)                     |

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Table 14.3.4.1.1 Out-of-Range Values and Recheck Results - Serum Chemistry (I of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Calcium<br>8.5-10.2<br>(mg/dL) | Chloride<br>97-105<br>(mEq/L) | Potassium<br>3.7-5.2<br>(mEq/L) | Albumin<br>4-5.1<br>(g/dL) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|----------|--------------------------------|-------------------------------|---------------------------------|----------------------------|
| 002               | 1      | A              | 40/M         | 1               | 3   | 48.00  | 10JUL2019 | 9:38:48  | 10.3 HN                        |                               |                                 |                            |
| 003               | 1      | A              | 60/M         | 1               | -1  | -20.00 | 08JUL2019 | 14:08:48 |                                | 106 HN                        |                                 |                            |
|                   |        |                |              |                 | 2   | 24.00  | 10JUL2019 | 9:45:20  |                                | 108 HN                        |                                 |                            |
| 004               | 1      | P              | 48/M         | Screen<br>1     |     |        | 21JUN2019 | 7:52:04  |                                | 107 HN                        |                                 |                            |
|                   |        |                |              |                 | -1  | -20.00 | 08JUL2019 | 13:46:40 |                                | 107 HN                        |                                 |                            |
|                   |        |                |              |                 | 2   | 24.00  | 10JUL2019 | 9:56:33  |                                | 109 HN                        |                                 |                            |
|                   |        |                |              |                 | 3   | 48.00  | 11JUL2019 | 9:48:33  |                                | 106 HN                        |                                 |                            |
| 006               | 1      | A              | 33/M         | 1               | 2   | 24.00  | 10JUL2019 | 10:18:20 | 10.3 HN                        |                               |                                 |                            |
|                   |        |                |              |                 | 3   | 48.00  | 11JUL2019 | 10:10:52 | 10.4 HN                        |                               |                                 |                            |
| 010               | 2      | P              | 53/M         | Screen<br>1     |     |        | 08JUL2019 | 8:20:21  |                                |                               |                                 | 3.9 LN                     |
|                   |        |                |              |                 | 8   | 168.00 | 01AUG2019 | 9:32:51  |                                | 96 LN                         |                                 |                            |
| 012               | 2      | B              | 54/M         | 1               | -1  | -20.00 | 25JUL2019 | 13:45:01 |                                | 107 HN                        |                                 |                            |
|                   |        |                |              |                 | 2   | 24.00  | 27JUL2019 | 9:56:28  |                                | 106 HN                        |                                 |                            |
|                   |        |                |              |                 | 8   | 168.00 | 02AUG2019 | 9:56:01  |                                | 107 HN                        |                                 |                            |
| 016               | 2      | B              | 37/M         | Screen<br>1     |     |        | 10JUL2019 | 8:30:29  |                                | 96 LN                         |                                 |                            |
|                   |        |                |              |                 | 3   | 48.00  | 28JUL2019 | 10:40:22 |                                |                               | 5.4 HN                          |                            |
|                   |        |                |              |                 | 8   | 168.00 | 02AUG2019 | 10:04:20 |                                |                               | 5.3 HN                          |                            |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male  
H = Above Reference Range, L = Below Reference Range  
Computer: N = Not Clinically Significant, Y = Clinically Significant  
PI Interpretation: - = Not Clinically Significant, ^ = Will be Retested at a Later Event  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)  
Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.1.1 Out-of-Range Values and Recheck Results - Serum Chemistry (I of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Calcium<br>8.5-10.2<br>(mg/dL) | Chloride<br>97-105<br>(mEq/L) | Potassium<br>3.7-5.2<br>(mEq/L) | Albumin<br>4-5.1<br>(g/dL) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|----------|--------------------------------|-------------------------------|---------------------------------|----------------------------|
| 017               | 3      | C              | 62/M         | 1               | -1  | -20.00 | 11AUG2019 | 13:28:26 |                                | 96 LN                         |                                 |                            |
|                   |        |                |              |                 | 2   | 24.00  | 13AUG2019 | 9:30:26  |                                |                               | 5.9 HY^-                        |                            |
|                   |        |                |              |                 | 3   | 48.00  | 14AUG2019 | 9:30:11  |                                |                               | 5.5 HN                          |                            |
|                   |        |                |              |                 | 8   | 168.00 | 19AUG2019 | 9:30:02  |                                |                               | 5.4 HN                          |                            |
| 018               | 3      | P              | 57/F         | 1               | 2   | 24.00  | 13AUG2019 | 9:41:41  |                                | 106 HN                        |                                 |                            |
| 020               | 3      | C              | 56/M         | Screen<br>1     |     |        | 02AUG2019 | 8:06:38  |                                | 96 LN                         |                                 |                            |
|                   |        |                |              |                 | -1  | -20.00 | 12AUG2019 | 13:46:22 |                                | 95 LN                         |                                 |                            |
|                   |        |                |              |                 | 2   | 24.00  | 14AUG2019 | 9:56:26  |                                | 96 LN                         |                                 |                            |
|                   |        |                |              |                 | 3   | 48.00  | 15AUG2019 | 9:56:15  | 10.5 HN                        | 95 LN                         |                                 |                            |
|                   |        |                |              |                 | 8   | 168.00 | 20AUG2019 | 9:50:13  |                                | 95 LN                         |                                 |                            |
| 021               | 3      | C              | 43/F         | 1               | 8   | 168.00 | 20AUG2019 | 9:59:17  | 10.4 HN                        |                               |                                 |                            |
| 022               | 3      | C              | 34/M         | Screen          |     |        | 02AUG2019 | 8:08:58  |                                | 106 HN                        |                                 |                            |
| 027               | 4      | D              | 30/M         | 1               | -1  | -20.00 | 29AUG2019 | 13:51:18 |                                | 91 LN                         |                                 |                            |
|                   |        |                |              |                 | 3   | 48.00  | 01SEP2019 | 9:49:31  |                                |                               | 5.5 HN                          |                            |
| 033               | 5      | E              | 60/M         | 1               | -1  | -20.00 | 19FEB2020 | 13:18:32 |                                | 92 LN                         |                                 |                            |
|                   |        |                |              |                 | 8   | 168.00 | 27FEB2020 | 9:15:02  |                                | 96 LN                         |                                 |                            |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male  
H = Above Reference Range, L = Below Reference Range  
Computer: N = Not Clinically Significant, Y = Clinically Significant  
PI Interpretation: - = Not Clinically Significant, ^ = Will be Retested at a Later Event  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)  
Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.1.1 Out-of-Range Values and Recheck Results - Serum Chemistry (I of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Calcium<br>8.5-10.2<br>(mg/dL) | Chloride<br>97-105<br>(mEq/L) | Potassium<br>3.7-5.2<br>(mEq/L) | Albumin<br>4-5.1<br>(g/dL) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|----------|--------------------------------|-------------------------------|---------------------------------|----------------------------|
| 034               | 5      | P              | 59/M         | 1               | -1  | -20.00 | 19FEB2020 | 13:20:12 |                                |                               |                                 | 3.9 LN                     |
|                   |        |                |              |                 | 2   | 24.00  | 21FEB2020 | 9:28:08  |                                |                               |                                 | 3.8 LN                     |
|                   |        |                |              |                 | 3   | 48.00  | 22FEB2020 | 9:19:52  |                                | 106 HN                        |                                 |                            |
| 036               | 5      | E              | 52/F         | Screen          |     |        | 07FEB2020 | 9:27:02  |                                | 95 LN                         |                                 |                            |
| 037               | 5      | E              | 60/M         | Screen          |     |        | 10FEB2020 | 10:54:34 |                                | 96 LN                         |                                 |                            |
|                   |        |                |              | 1               | -1  | -20.00 | 20FEB2020 | 13:54:11 |                                | 95 LN                         |                                 |                            |
|                   |        |                |              |                 | 2   | 24.00  | 22FEB2020 | 10:07:55 |                                | 108 HN                        |                                 | 3.8 LN                     |
| 038               | 5      | E              | 59/M         | 1               | -1  | -20.00 | 20FEB2020 | 13:55:56 |                                | 96 LN                         |                                 |                            |
| 040               | 5      | P              | 48/F         | Screen          |     |        | 10FEB2020 | 10:52:28 |                                | 96 LN                         |                                 |                            |
|                   |        |                |              | 1               | -1  | -20.00 | 20FEB2020 | 14:02:33 |                                | 91 LN                         |                                 |                            |
|                   |        |                |              |                 | 3   | 48.00  | 23FEB2020 | 10:40:02 |                                |                               |                                 | 5.3 HN                     |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male  
H = Above Reference Range, L = Below Reference Range  
Computer: N = Not Clinically Significant, Y = Clinically Significant  
PI Interpretation: - = Not Clinically Significant, ^ = Will be Retested at a Later Event  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)  
Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.1.2 Out-of-Range Values and Recheck Results - Serum Chemistry (II of IV) (Safety Population)

| Subject<br>Number | Treat-<br>ment Cohort | Age#/<br>Sex | Study<br>Period | Day     | Hour | Date      | Time      | Creatinine<br>F: 0.44-0.93<br>M: 0.67-1.22<br>(mg/dL) | Glucose<br>75-108<br>(mg/dL) | Alkaline<br>Phosphatase<br>F: 41-129<br>M: 47-132<br>(IU/L) | Alanine<br>Amino-<br>transferase<br>10-60<br>(IU/L) |
|-------------------|-----------------------|--------------|-----------------|---------|------|-----------|-----------|-------------------------------------------------------|------------------------------|-------------------------------------------------------------|-----------------------------------------------------|
| 004               | 1                     | P            | 48/M            | Screen  |      | 21JUN2019 | 7:52:04   |                                                       | 115 HNR                      |                                                             |                                                     |
|                   |                       |              |                 | Recheck |      | 28JUN2019 | 13:21:22  |                                                       | 101                          |                                                             |                                                     |
|                   |                       |              |                 | 1       | 8    | 168.00    | 16JUL2019 | 9:49:56                                               | 111 HNR-                     |                                                             |                                                     |
|                   |                       |              |                 | Recheck | 8    | 05AUG2019 | 8:25:41   |                                                       | 123 HN                       |                                                             |                                                     |
| 005               | 1                     | A            | 56/M            | 1       | -1   | -20.00    | 08JUL2019 | 13:59:51                                              |                              |                                                             | 9 LN                                                |
|                   |                       |              |                 |         | 2    | 24.00     | 10JUL2019 | 10:07:44                                              |                              |                                                             | 8 LN                                                |
|                   |                       |              |                 |         | 8    | 168.00    | 16JUL2019 | 9:56:27                                               | 118 HNR-                     |                                                             |                                                     |
|                   |                       |              |                 | Recheck | 8    | 18JUL2019 | 10:24:21  |                                                       | 93                           |                                                             |                                                     |
| 006               | 1                     | A            | 33/M            | 1       | 2    | 24.00     | 10JUL2019 | 10:18:20                                              | 1.26 HN                      |                                                             |                                                     |
| 011               | 2                     | B            | 58/M            | 1       | 8    | 168.00    | 02AUG2019 | 9:54:26                                               |                              | 109 HN                                                      |                                                     |
| 013               | 2                     | P            | 34/M            | Screen  |      | 16JUL2019 | 11:02:34  | 1.29 HN                                               |                              |                                                             |                                                     |
|                   |                       |              |                 | 1       | 2    | 24.00     | 27JUL2019 | 10:07:14                                              | 1.40 HN^-                    |                                                             |                                                     |
|                   |                       |              |                 |         | 3    | 48.00     | 28JUL2019 | 10:07:01                                              | 1.24 HN                      |                                                             |                                                     |
|                   |                       |              |                 |         | 8    | 168.00    | 02AUG2019 | 9:57:27                                               | 1.24 HN                      |                                                             |                                                     |
| 018               | 3                     | P            | 57/F            | 1       | 8    | 168.00    | 19AUG2019 | 9:31:29                                               |                              | 109 HN                                                      |                                                     |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant

PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.1.2 Out-of-Range Values and Recheck Results - Serum Chemistry (II of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period   | Day           | Hour                | Date                                | Time                           | Creatinine<br>F: 0.44-0.93<br>M: 0.67-1.22<br>(mg/dL) | Glucose<br>75-108<br>(mg/dL) | Alkaline<br>Phosphatase<br>F: 41-129<br>M: 47-132<br>(IU/L) | Alanine<br>Amino-<br>transferase<br>10-60<br>(IU/L) |
|-------------------|--------|----------------|--------------|-------------------|---------------|---------------------|-------------------------------------|--------------------------------|-------------------------------------------------------|------------------------------|-------------------------------------------------------------|-----------------------------------------------------|
| 020               | 3      | C              | 56/M         | 1                 | 2             | 24.00               | 14AUG2019                           | 9:56:26                        |                                                       |                              | 42 LN                                                       |                                                     |
|                   |        |                |              |                   | 3             | 48.00               | 15AUG2019                           | 9:56:15                        |                                                       |                              | 45 LN                                                       |                                                     |
|                   |        |                |              |                   | 8             | 168.00              | 20AUG2019                           | 9:50:13                        |                                                       |                              | 44 LN                                                       |                                                     |
| 027               | 4      | D              | 30/M         | 1                 | 3             | 48.00               | 01SEP2019                           | 9:49:31                        |                                                       |                              |                                                             | 61 HN                                               |
| 030               | 4      | P              | 30/M         | Screen<br>1       | -1            | -20.00              | 20AUG2019<br>29AUG2019              | 8:25:06<br>13:54:41            |                                                       |                              |                                                             | 9 LN<br>9 LN                                        |
| 032               | 4      | D              | 51/M         | 1                 | 8             | 168.00              | 06SEP2019                           | 9:56:55                        |                                                       | 109 HN                       |                                                             |                                                     |
| 033               | 5      | E              | 60/M         | 1<br>Recheck<br>1 | -1<br>-1<br>3 | -20.00<br><br>48.00 | 19FEB2020<br>20FEB2020<br>22FEB2020 | 13:18:32<br>2:13:41<br>9:16:15 | 1.32 HNR-<br>1.16<br>1.30 HN                          |                              |                                                             |                                                     |
|                   |        |                |              |                   | 8             | 168.00              | 27FEB2020                           | 9:15:02                        | 1.24 HN                                               | 70 LN                        |                                                             |                                                     |
| 037               | 5      | E              | 60/M         | Screen<br>Recheck |               |                     | 10FEB2020<br>14FEB2020              | 10:54:34<br>10:32:18           |                                                       | 114 HNR<br>104               |                                                             |                                                     |
| 038               | 5      | E              | 59/M         | Screen<br>Recheck |               |                     | 07FEB2020<br>14FEB2020              | 9:17:14<br>10:29:43            |                                                       | 113 HNR<br>104               |                                                             |                                                     |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant

PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.1.2 Out-of-Range Values and Recheck Results - Serum Chemistry (II of IV) (Safety Population)

| Subject<br>Number | Treat-<br>ment<br>Cohort | Age#/<br>Sex | Study<br>Period | Day | Hour | Date   | Time               | Creatinine<br>F: 0.44-0.93<br>M: 0.67-1.22<br>(mg/dL) | Glucose<br>75-108<br>(mg/dL) | Alkaline<br>Phosphatase<br>F: 41-129<br>M: 47-132<br>(IU/L) | Alanine<br>Amino-<br>transferase<br>10-60<br>(IU/L) |
|-------------------|--------------------------|--------------|-----------------|-----|------|--------|--------------------|-------------------------------------------------------|------------------------------|-------------------------------------------------------------|-----------------------------------------------------|
| 038               | 5                        | E            | 59/M            | 1   | 8    | 168.00 | 28FEB2020 9:57:42  |                                                       | 113 HN                       |                                                             |                                                     |
| 040               | 5                        | P            | 48/F            | 1   | 3    | 48.00  | 23FEB2020 10:40:02 |                                                       | 110 HN                       |                                                             |                                                     |
|                   |                          |              |                 |     | 8    | 168.00 | 28FEB2020 10:01:25 |                                                       | 118 HN                       |                                                             |                                                     |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant

PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.1.3 Out-of-Range Values and Recheck Results - Serum Chemistry (III of IV) (Safety Population)

| Subject<br>Number | Treat-<br>ment<br>Cohort | Age#/<br>Sex | Study<br>Period | Day    | Hour | Date   | Time               | Aspartate<br>Amino-<br>transferase<br>14-47<br>(IU/L) | GGT<br>6-74<br>(IU/L) | Creatine<br>Kinase<br>F: 34-200<br>M: 44-329<br>(IU/L) | Lactate<br>Dehydrogenase<br>125-248<br>(IU/L) |
|-------------------|--------------------------|--------------|-----------------|--------|------|--------|--------------------|-------------------------------------------------------|-----------------------|--------------------------------------------------------|-----------------------------------------------|
| 002               | 1                        | A            | 40/M            | 1      | 3    | 48.00  | 10JUL2019 9:38:48  |                                                       | 78 HN                 |                                                        |                                               |
| 006               | 1                        | A            | 33/M            | 1      | 2    | 24.00  | 10JUL2019 10:18:20 |                                                       |                       |                                                        | 124 LN                                        |
|                   |                          |              |                 |        | 8    | 168.00 | 16JUL2019 9:57:35  |                                                       |                       |                                                        | 124 LN                                        |
| 008               | 1                        | A            | 62/M            | Screen |      |        | 22JUN2019 10:15:39 | 13 LN                                                 |                       |                                                        |                                               |
| 009               | 2                        | B            | 28/M            | Screen |      |        | 12JUL2019 12:07:11 | 13 LN                                                 |                       |                                                        |                                               |
|                   |                          |              |                 | 1      | -1   | -20.00 | 24JUL2019 13:30:02 | 13 LN                                                 |                       |                                                        |                                               |
|                   |                          |              |                 |        | 2    | 24.00  | 26JUL2019 9:30:18  | 10 LN                                                 |                       |                                                        |                                               |
|                   |                          |              |                 |        | 3    | 48.00  | 27JUL2019 9:31:52  | 12 LN                                                 |                       |                                                        |                                               |
|                   |                          |              |                 |        | 8    | 168.00 | 01AUG2019 9:30:10  | 12 LN                                                 |                       |                                                        |                                               |
| 016               | 2                        | B            | 37/M            | 1      | 2    | 24.00  | 27JUL2019 10:40:23 |                                                       |                       |                                                        | 120 LN                                        |
| 020               | 3                        | C            | 56/M            | 1      | 2    | 24.00  | 14AUG2019 9:56:26  | 13 LN                                                 |                       |                                                        |                                               |
| 021               | 3                        | C            | 43/F            | Screen |      |        | 02AUG2019 8:26:10  | 11 LN                                                 |                       |                                                        |                                               |
|                   |                          |              |                 | 1      | -1   | -20.00 | 12AUG2019 13:53:50 | 11 LN                                                 |                       |                                                        |                                               |
|                   |                          |              |                 |        | 2    | 24.00  | 14AUG2019 10:07:19 | 10 LN                                                 |                       |                                                        |                                               |
|                   |                          |              |                 |        | 3    | 48.00  | 15AUG2019 10:07:13 | 11 LN                                                 |                       |                                                        |                                               |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant, Y = Clinically Significant

PI Interpretation: + = Clinically Significant, - = Not Clinically Significant, R = To be Rechecked

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.1.3 Out-of-Range Values and Recheck Results - Serum Chemistry (III of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Aspartate<br>Amino-<br>transferase<br>14-47<br>(IU/L) | GGT<br>6-74<br>(IU/L) | Creatine<br>Kinase<br>F: 34-200<br>M: 44-329<br>(IU/L) | Lactate<br>Dehydrogenase<br>125-248<br>(IU/L) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|----------|-------------------------------------------------------|-----------------------|--------------------------------------------------------|-----------------------------------------------|
| 021               | 3      | C              | 43/F         | 1               | 8   | 168.00 | 20AUG2019 | 9:59:17  | 12 LN                                                 |                       |                                                        |                                               |
| 022               | 3      | C              | 34/M         | 1               | 2   | 24.00  | 14AUG2019 | 10:18:24 | 13 LN                                                 |                       |                                                        |                                               |
| 024               | 3      | C              | 40/M         | Screen          |     |        | 31JUL2019 | 8:13:10  | 83 HNR                                                |                       | 1609 HYR                                               |                                               |
|                   |        |                |              | Recheck         |     |        | 06AUG2019 | 13:20:56 | 30                                                    |                       | 170                                                    |                                               |
|                   |        |                |              | 1               | 8   | 168.00 | 20AUG2019 | 10:05:40 | 89 HNR-                                               |                       | 1964 HYR-                                              |                                               |
|                   |        |                |              | Recheck         | 8   |        | 23AUG2019 | 9:01:42  | 42                                                    |                       | 345 HN                                                 |                                               |
| 025               | 4      | P              | 30/M         | 1               | 2   | 24.00  | 30AUG2019 | 9:52:51  |                                                       |                       |                                                        | 115 LN                                        |
|                   |        |                |              |                 | 3   | 48.00  | 31AUG2019 | 9:47:12  |                                                       |                       |                                                        | 124 LN                                        |
|                   |        |                |              |                 | 9   | 192.00 | 06SEP2019 | 9:31:22  |                                                       |                       |                                                        | 119 LN                                        |
| 026               | 4      | D              | 43/M         | 1               | 9   | 192.00 | 06SEP2019 | 9:30:09  |                                                       |                       | 345 HN                                                 |                                               |
| 030               | 4      | P              | 30/M         | 1               | -1  | -20.00 | 29AUG2019 | 13:54:41 | 13 LN                                                 |                       |                                                        |                                               |
| 033               | 5      | E              | 60/M         | 1               | -1  | -20.00 | 19FEB2020 | 13:18:32 |                                                       |                       | 368 HN                                                 |                                               |
|                   |        |                |              |                 | 8   | 168.00 | 27FEB2020 | 9:15:02  |                                                       |                       | 986 HYR+                                               |                                               |
|                   |        |                |              | Recheck         | 8   |        | 03MAR2020 | 10:32:44 |                                                       |                       | 608 HYR+                                               |                                               |
|                   |        |                |              |                 | 8   |        | 10MAR2020 | 9:54:59  |                                                       |                       | 709 HYR+                                               |                                               |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant, Y = Clinically Significant

PI Interpretation: + = Clinically Significant, - = Not Clinically Significant, R = To be Rechecked

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.1.3 Out-of-Range Values and Recheck Results - Serum Chemistry (III of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Aspartate<br>Amino-<br>transferase<br>14-47<br>(IU/L) | GGT<br>6-74<br>(IU/L) | Creatine<br>Kinase<br>F: 34-200<br>M: 44-329<br>(IU/L) | Lactate<br>Dehydrogenase<br>125-248<br>(IU/L) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|----------|-------------------------------------------------------|-----------------------|--------------------------------------------------------|-----------------------------------------------|
| 033               | 5      | E              | 60/M         | Recheck         | 8   |        | 16MAR2020 | 9:58:27  |                                                       |                       | 834 HYR+                                               |                                               |
|                   |        |                |              |                 | 8   |        | 23MAR2020 | 9:44:59  |                                                       |                       | 624 HY+                                                | 193                                           |
| 038               | 5      | E              | 59/M         | 1               | 2   | 24.00  | 22FEB2020 | 10:18:25 | 12 LN                                                 |                       | 40 LN                                                  |                                               |
|                   |        |                |              |                 | 3   | 48.00  | 23FEB2020 | 10:18:00 | 13 LN                                                 |                       | 40 LN                                                  |                                               |
| 039               | 5      | E              | 44/M         | 1               | -1  | -20.00 | 20FEB2020 | 13:58:32 |                                                       |                       | 348 HN-                                                |                                               |
| 040               | 5      | P              | 48/F         | 1               | 2   | 24.00  | 22FEB2020 | 10:40:28 | 11 LN                                                 |                       |                                                        | 118 LN                                        |
|                   |        |                |              |                 | 3   | 48.00  | 23FEB2020 | 10:40:02 |                                                       |                       |                                                        | 120 LN                                        |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant, Y = Clinically Significant

PI Interpretation: + = Clinically Significant, - = Not Clinically Significant, R = To be Rechecked

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.1.4 Out-of-Range Values and Recheck Results - Serum Chemistry (IV of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date                   | Time                | Urea<br>Nitrogen<br>F: 6-20<br>M: 7-21<br>(mg/dL) | Sodium<br>134-145<br>(mEq/L) | Bilirubin<br>0.2-1.6<br>(mg/dL) | CK MB<br>Fraction<br>M: 0-4.8<br>(ug/L) | Urate<br>F: 2.3-6.6<br>M: 3.7-7.7<br>(mg/dL) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|------------------------|---------------------|---------------------------------------------------|------------------------------|---------------------------------|-----------------------------------------|----------------------------------------------|
| 002               | 1      | A              | 40/M         | 1               | 2   | 24.00  | 09JUL2019              | 9:41:31             | 22 HN                                             |                              |                                 |                                         |                                              |
|                   |        |                |              |                 | 3   | 48.00  | 10JUL2019              | 9:38:48             | 25 HN                                             |                              |                                 |                                         |                                              |
| 003               | 1      | A              | 60/M         | 1               | 2   | 24.00  | 10JUL2019              | 9:45:20             |                                                   | 146 HN                       |                                 |                                         |                                              |
| 004               | 1      | P              | 48/M         | 1               | 2   | 24.00  | 10JUL2019              | 9:56:33             |                                                   | 146 HN                       |                                 |                                         |                                              |
| 005               | 1      | A              | 56/M         | 1               | -1  | -20.00 | 08JUL2019              | 13:59:51            |                                                   |                              |                                 |                                         | 8.6 HN                                       |
| 007               | 1      | A              | 38/M         | 1<br>Recheck    | -1  | -20.00 | 08JUL2019<br>09JUL2019 | 13:55:52<br>4:14:27 |                                                   |                              | 2.3 HNR-<br>1.6                 |                                         |                                              |
| 016               | 2      | B              | 37/M         | 1               | -1  | -20.00 | 25JUL2019              | 13:48:10            | 24 HN                                             |                              |                                 |                                         |                                              |
|                   |        |                |              |                 | 2   | 24.00  | 27JUL2019              | 10:40:23            |                                                   |                              |                                 |                                         | 3.6 LN                                       |
|                   |        |                |              |                 | 3   | 48.00  | 28JUL2019              | 10:40:22            |                                                   |                              |                                 |                                         | 3.2 LN                                       |
| 018               | 3      | P              | 57/F         | Screen<br>1     |     |        | 26JUL2019              | 9:40:31             |                                                   |                              |                                 |                                         | 1.9 LN                                       |
|                   |        |                |              |                 | 2   | 24.00  | 13AUG2019              | 9:41:41             |                                                   |                              |                                 |                                         | 1.8 LN                                       |
|                   |        |                |              |                 | 3   | 48.00  | 14AUG2019              | 9:51:08             |                                                   |                              |                                 |                                         | 1.7 LN                                       |
|                   |        |                |              |                 | 8   | 168.00 | 19AUG2019              | 9:31:29             |                                                   |                              |                                 |                                         | 1.9 LN                                       |
| 024               | 3      | C              | 40/M         | Screen          |     |        | 31JUL2019              | 8:13:10             |                                                   |                              |                                 | 16.75 H R                               |                                              |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant

PI Interpretation: - = Not Clinically Significant, R = To be Rechecked

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.1.4 Out-of-Range Values and Recheck Results - Serum Chemistry (IV of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Urea<br>Nitrogen<br>F: 6-20<br>M: 7-21<br>(mg/dL) | Sodium<br>134-145<br>(mEq/L) | Bilirubin<br>0.2-1.6<br>(mg/dL) | CK MB<br>Fraction<br>M: 0-4.8<br>(ug/L) | Urate<br>F: 2.3-6.6<br>M: 3.7-7.7<br>(mg/dL) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|----------|---------------------------------------------------|------------------------------|---------------------------------|-----------------------------------------|----------------------------------------------|
| 024               | 3      | C              | 40/M         | Recheck         |     |        | 06AUG2019 | 13:20:56 |                                                   |                              |                                 | 2.75                                    |                                              |
| 025               | 4      | P              | 30/M         | 1               | 3   | 48.00  | 31AUG2019 | 9:47:12  |                                                   |                              | 1.7 HN                          |                                         |                                              |
| 027               | 4      | D              | 30/M         | Screen<br>1     |     |        | 20AUG2019 | 8:33:54  |                                                   |                              |                                 |                                         | 9.1 HN                                       |
|                   |        |                |              |                 | -1  | -20.00 | 29AUG2019 | 13:51:18 | 6 LN                                              | 133 LN                       |                                 |                                         | 9.1 HN                                       |
|                   |        |                |              |                 | 2   | 24.00  | 31AUG2019 | 9:45:30  |                                                   |                              |                                 |                                         | 10.2 HN                                      |
|                   |        |                |              |                 | 3   | 48.00  | 01SEP2019 | 9:49:31  |                                                   |                              |                                 |                                         | 9.7 HN                                       |
|                   |        |                |              |                 | 8   | 168.00 | 06SEP2019 | 9:49:08  |                                                   |                              |                                 |                                         | 11.1 HN                                      |
| 028               | 4      | D              | 20/M         | Screen<br>1     |     |        | 20AUG2019 | 8:36:24  |                                                   |                              |                                 |                                         | 2.4 LN                                       |
|                   |        |                |              |                 | -1  | -20.00 | 29AUG2019 | 13:52:51 |                                                   |                              |                                 |                                         | 2.0 LN                                       |
|                   |        |                |              |                 | 2   | 24.00  | 31AUG2019 | 9:56:18  |                                                   |                              |                                 |                                         | 2.0 LN                                       |
|                   |        |                |              |                 | 3   | 48.00  | 01SEP2019 | 9:51:21  |                                                   |                              |                                 |                                         | 2.0 LN                                       |
|                   |        |                |              |                 | 8   | 168.00 | 06SEP2019 | 10:35:10 |                                                   |                              |                                 |                                         | 1.8 LN                                       |
| 033               | 5      | E              | 60/M         | Screen<br>1     |     |        | 06FEB2020 | 10:28:31 |                                                   |                              |                                 |                                         | 3.1 LN                                       |
|                   |        |                |              |                 | -1  | -20.00 | 19FEB2020 | 13:18:32 |                                                   |                              |                                 |                                         | 3.0 LN                                       |
|                   |        |                |              |                 | 3   | 48.00  | 22FEB2020 | 9:16:15  |                                                   |                              |                                 |                                         | 3.6 LN                                       |
|                   |        |                |              |                 | 8   | 168.00 | 27FEB2020 | 9:15:02  | 26 HN                                             |                              |                                 |                                         |                                              |
| 034               | 5      | P              | 59/M         | Screen          |     |        | 06FEB2020 | 8:46:26  | 23 HN                                             |                              |                                 |                                         |                                              |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant

PI Interpretation: - = Not Clinically Significant, R = To be Rechecked

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.1.4 Out-of-Range Values and Recheck Results - Serum Chemistry (IV of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/ Sex | Study<br>Period | Day | Hour   | Date      | Time     | Urea<br>Nitrogen<br>F: 6-20<br>M: 7-21<br>(mg/dL) | Sodium<br>134-145<br>(mEq/L) | Bilirubin<br>0.2-1.6<br>(mg/dL) | CK MB<br>Fraction<br>M: 0-4.8<br>(ug/L) | Urate<br>F: 2.3-6.6<br>M: 3.7-7.7<br>(mg/dL) |
|-------------------|--------|----------------|-----------|-----------------|-----|--------|-----------|----------|---------------------------------------------------|------------------------------|---------------------------------|-----------------------------------------|----------------------------------------------|
| 034               | 5      | P              | 59/M      | 1               | 3   | 48.00  | 22FEB2020 | 9:19:52  | 22 HN                                             |                              |                                 |                                         |                                              |
|                   |        |                |           |                 | 8   | 168.00 | 27FEB2020 | 9:19:50  |                                                   |                              |                                 |                                         | 8.0 HN                                       |
| 037               | 5      | E              | 60/M      | 1               | -1  | -20.00 | 20FEB2020 | 13:54:11 |                                                   | 133 IN                       |                                 |                                         |                                              |
|                   |        |                |           |                 | 3   | 48.00  | 23FEB2020 | 10:07:02 |                                                   | 146 HN                       |                                 |                                         |                                              |
| 038               | 5      | E              | 59/M      | 1               | -1  | -20.00 | 20FEB2020 | 13:55:56 |                                                   |                              | 1.7 HN                          |                                         |                                              |
| 040               | 5      | P              | 48/F      | 1               | -1  | -20.00 | 20FEB2020 | 14:02:33 |                                                   | 131 LNR-                     |                                 |                                         |                                              |
|                   |        |                | Recheck   |                 | -1  |        | 21FEB2020 | 3:57:27  |                                                   | 142                          |                                 |                                         |                                              |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant

PI Interpretation: - = Not Clinically Significant, R = To be Rechecked

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.2.1 Out-of-Range Values and Recheck Results - Hematology (I of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Hemoglobin<br>F: 12.1-15.4<br>M: 13.6-17.4<br>(g/dL) | Hematocrit<br>F: 35-45.4<br>M: 39.7-51.1<br>(%) | Platelet<br>Count<br>162-399<br>(thou/uL) | Red Blood<br>Cell Count<br>F: 3.7-5<br>M: 4.3-5.85<br>(mil/uL) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|----------|------------------------------------------------------|-------------------------------------------------|-------------------------------------------|----------------------------------------------------------------|
| 001               | 1      | P              | 30/M         | Screen<br>1     | -1  | -20.00 | 07JUL2019 | 13:33:34 |                                                      |                                                 | 159 LN                                    |                                                                |
|                   |        |                |              |                 | 2   | 24.00  | 09JUL2019 | 9:31:17  |                                                      |                                                 | 160 LN                                    |                                                                |
|                   |        |                |              |                 |     |        |           |          |                                                      |                                                 | 157 LN                                    |                                                                |
| 002               | 1      | A              | 40/M         | 1               | -1  | -20.00 | 07JUL2019 | 13:35:26 | 13.4 LN                                              |                                                 |                                           |                                                                |
|                   |        |                |              |                 | 8   | 168.00 | 15JUL2019 | 9:35:47  | 13.0 LN                                              | 39.5 LN                                         |                                           |                                                                |
| 006               | 1      | A              | 33/M         | 1               | 3   | 48.00  | 11JUL2019 | 10:11:12 |                                                      |                                                 |                                           | 5.93 HN                                                        |
| 008               | 1      | A              | 62/M         | 1               | 8   | 168.00 | 16JUL2019 | 10:06:09 | 13.5 LN                                              |                                                 |                                           |                                                                |
| 010               | 2      | P              | 53/M         | Screen          |     |        | 08JUL2019 | 8:20:36  | 13.3 LN                                              |                                                 |                                           |                                                                |
| 011               | 2      | B              | 58/M         | 1               | 8   | 168.00 | 02AUG2019 | 9:54:52  |                                                      |                                                 | 155 LN                                    |                                                                |
| 013               | 2      | P              | 34/M         | 1               | 2   | 24.00  | 27JUL2019 | 10:07:31 | 17.9 HN                                              |                                                 |                                           |                                                                |
| 014               | 2      | B              | 42/F         | Screen<br>1     | -1  | -20.00 | 10JUL2019 | 8:30:44  | 11.7 LN                                              |                                                 |                                           |                                                                |
|                   |        |                |              |                 |     |        | 25JUL2019 | 13:46:48 | 11.6 LN                                              | 34.8 LN                                         |                                           |                                                                |
|                   |        |                |              |                 | 8   | 168.00 | 02AUG2019 | 9:59:12  | 10.9 LN                                              | 32.8 LN                                         |                                           | 3.57 LN                                                        |
| 015               | 2      | B              | 50/F         | Screen          |     |        | 08JUL2019 | 8:42:47  |                                                      |                                                 |                                           | 5.14 HN                                                        |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.2.1 Out-of-Range Values and Recheck Results - Hematology (I of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date                   | Time               | Hemoglobin<br>F: 12.1-15.4<br>M: 13.6-17.4<br>(g/dL) | Hematocrit<br>F: 35-45.4<br>M: 39.7-51.1<br>(%) | Platelet<br>Count<br>162-399<br>(thou/uL) | Red Blood<br>Cell Count<br>F: 3.7-5<br>M: 4.3-5.85<br>(mil/uL) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|------------------------|--------------------|------------------------------------------------------|-------------------------------------------------|-------------------------------------------|----------------------------------------------------------------|
| 020               | 3      | C              | 56/M         | 1               | 8   | 168.00 | 20AUG2019              | 9:50:33            | 13.2 LN                                              |                                                 |                                           | 4.15 LN                                                        |
| 026               | 4      | D              | 43/M         | 1               | -1  | -20.00 | 28AUG2019              | 13:38:00           | 13.5 LN                                              |                                                 |                                           |                                                                |
| 030               | 4      | P              | 30/M         | Screen<br>1     |     |        | 20AUG2019<br>06SEP2019 | 8:25:25<br>9:52:44 | 13.2 LN<br>13.5 LN                                   | 39.5 LN                                         |                                           |                                                                |
| 032               | 4      | D              | 51/M         | 1               | 8   | 168.00 | 06SEP2019              | 9:57:12            | 13.3 LN                                              |                                                 |                                           |                                                                |
| 033               | 5      | E              | 60/M         | 1               | 8   | 168.00 | 27FEB2020              | 9:15:40            | 13.1 LN                                              |                                                 |                                           |                                                                |
| 034               | 5      | P              | 59/M         | 1               | 2   | 24.00  | 21FEB2020              | 9:28:24            |                                                      |                                                 | 152 LN                                    |                                                                |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.2.2 Out-of-Range Values and Recheck Results - Hematology (II of IV) (Safety Population)

| Subject<br>Number | Treat-<br>ment Cohort | Age#/<br>Sex | Study<br>Period | Day         | Hour | Date   | Time                                     | White Blood<br>Cell Count<br>3.9-10.7<br>(thou/uL) | Basophils<br>0-0.7<br>(%) | Absolute<br>Basophils<br>0-0.1<br>(thou/uL) | Eosinophils<br>0.2-9<br>(%) |
|-------------------|-----------------------|--------------|-----------------|-------------|------|--------|------------------------------------------|----------------------------------------------------|---------------------------|---------------------------------------------|-----------------------------|
| 001               | 1                     | P            | 30/M            | Screen<br>1 | 3    | 48.00  | 19JUN2019 7:37:03<br>10JUL2019 9:30:23   |                                                    | 1.0 HN<br>1.2 HN          |                                             |                             |
| 005               | 1                     | A            | 56/M            | Screen<br>1 | 3    | 48.00  | 21JUN2019 7:59:02<br>11JUL2019 10:09:44  |                                                    | 0.8 HN<br>0.8 HN          |                                             |                             |
| 009               | 2                     | B            | 28/M            | Screen<br>1 | -1   | -20.00 | 12JUL2019 12:07:30<br>24JUL2019 13:30:17 |                                                    |                           |                                             | 13.6 HN<br>14.3 HN          |
|                   |                       |              |                 |             | 2    | 24.00  | 26JUL2019 9:30:36                        |                                                    |                           |                                             | 16.9 HN                     |
|                   |                       |              |                 |             | 3    | 48.00  | 27JUL2019 9:32:10                        |                                                    |                           |                                             | 16.4 HN                     |
|                   |                       |              |                 |             | 8    | 168.00 | 01AUG2019 9:30:28                        |                                                    |                           |                                             | 19.8 HN                     |
| 011               | 2                     | B            | 58/M            | 1           | -1   | -20.00 | 25JUL2019 13:45:20<br>27JUL2019 9:48:28  |                                                    | 0.9 HN<br>0.9 HN          |                                             |                             |
|                   |                       |              |                 |             | 3    | 48.00  | 28JUL2019 9:48:57                        |                                                    | 1.0 HN                    |                                             |                             |
| 019               | 3                     | P            | 26/M            | 1           | -1   | -20.00 | 12AUG2019 13:45:25                       |                                                    | 0.8 HN                    |                                             |                             |
| 020               | 3                     | C            | 56/M            | Screen<br>1 | 2    | 24.00  | 02AUG2019 8:07:04<br>14AUG2019 9:56:48   |                                                    | 0.9 HN<br>0.9 HN          |                                             |                             |
|                   |                       |              |                 |             | 3    | 48.00  | 15AUG2019 9:56:47                        | 3.5 LN                                             | 0.8 HN                    |                                             |                             |
|                   |                       |              |                 |             | 8    | 168.00 | 20AUG2019 9:50:33                        | 3.8 LN                                             | 0.8 HN                    |                                             |                             |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male  
H = Above Reference Range, L = Below Reference Range  
Computer: N = Not Clinically Significant, Y = Clinically Significant  
PI Interpretation: - = Not Clinically Significant, ^ = Will be Retested at a Later Event  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)  
Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.2.2 Out-of-Range Values and Recheck Results - Hematology (II of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period        | Day | Hour   | Date                                | Time                            | White Blood<br>Cell Count<br>3.9-10.7<br>(thou/uL) | Basophils<br>0-0.7<br>(%) | Absolute<br>Basophils<br>0-0.1<br>(thou/uL) | Eosinophils<br>0.2-9<br>(%) |
|-------------------|--------|----------------|--------------|------------------------|-----|--------|-------------------------------------|---------------------------------|----------------------------------------------------|---------------------------|---------------------------------------------|-----------------------------|
| 026               | 4      | D              | 43/M         | Screen<br>1            | 3   | 48.00  | 22AUG2019<br>31AUG2019              | 10:07:00<br>9:35:01             |                                                    | 0.9 HN<br>0.8 HN          |                                             |                             |
| 027               | 4      | D              | 30/M         | Screen<br>1            | 2   | 24.00  | 20AUG2019<br>31AUG2019              | 8:34:10<br>9:45:47              |                                                    | 0.9 HN<br>1.1 HN          |                                             |                             |
|                   |        |                |              |                        | 8   | 168.00 | 06SEP2019                           | 9:49:24                         |                                                    | 1.1 HN                    |                                             |                             |
| 030               | 4      | P              | 30/M         | Screen<br>Recheck<br>1 | -1  | -20.00 | 20AUG2019<br>23AUG2019<br>29AUG2019 | 8:25:25<br>15:24:10<br>13:54:52 | 3.3 LN<br>5.2                                      |                           | 0.4                                         | 1.9                         |
|                   |        |                |              |                        | 2   | 24.00  | 31AUG2019                           | 10:19:41                        | 2.9 LY^-                                           |                           |                                             |                             |
|                   |        |                |              |                        | 3   | 48.00  | 01SEP2019                           | 10:21:16                        | 3.2 LN                                             |                           |                                             |                             |
|                   |        |                |              | Recheck<br>1           | 3   |        | 01SEP2019                           | 18:22:00                        | 5.1                                                | 0.4                       | 0.0                                         | 2.1                         |
|                   |        |                |              |                        | 8   | 168.00 | 06SEP2019                           | 9:52:44                         | 3.5 LN                                             |                           |                                             |                             |
| 034               | 5      | P              | 59/M         | 1                      | 2   | 24.00  | 21FEB2020                           | 9:28:24                         | 3.7 LN                                             |                           |                                             |                             |
| 036               | 5      | E              | 52/F         | Screen<br>1            | 2   | 24.00  | 07FEB2020<br>22FEB2020              | 9:27:11<br>9:57:09              |                                                    | 0.8 HN<br>0.8 HN          |                                             |                             |
| 037               | 5      | E              | 60/M         | 1                      | 2   | 24.00  | 22FEB2020                           | 10:08:18                        |                                                    | 1.0 HN                    |                                             | 12.2 HN                     |
|                   |        |                |              |                        | 8   | 168.00 | 28FEB2020                           | 9:55:52                         |                                                    | 1.1 HN                    |                                             | 10.6 HN                     |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male  
H = Above Reference Range, L = Below Reference Range  
Computer: N = Not Clinically Significant, Y = Clinically Significant  
PI Interpretation: - = Not Clinically Significant, ^ = Will be Retested at a Later Event  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)  
Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.2.3 Out-of-Range Values and Recheck Results - Hematology (III of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Absolute<br>Eosinophils<br>0-0.8<br>(thou/uL) | Lymphocytes<br>14-43<br>(%) | Absolute<br>Lymphocytes<br>1-3<br>(thou/uL) | Monocytes<br>3.9-11.5<br>(%) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|----------|-----------------------------------------------|-----------------------------|---------------------------------------------|------------------------------|
| 002               | 1      | A              | 40/M         | Screen<br>1     |     |        | 19JUN2019 | 7:28:20  |                                               |                             |                                             | 12.4 HN                      |
|                   |        |                |              |                 | -1  | -20.00 | 07JUL2019 | 13:35:26 |                                               |                             |                                             | 12.1 HN                      |
|                   |        |                |              |                 | 2   | 24.00  | 09JUL2019 | 9:41:47  |                                               |                             |                                             | 13.2 HN                      |
|                   |        |                |              |                 | 8   | 168.00 | 15JUL2019 | 9:35:47  |                                               |                             |                                             | 12.3 HN                      |
| 003               | 1      | A              | 60/M         | Screen          |     |        | 21JUN2019 | 8:14:18  |                                               |                             |                                             | 12.8 HN                      |
| 006               | 1      | A              | 33/M         | Screen<br>1     |     |        | 22JUN2019 | 10:20:01 |                                               | 52.1 HN                     |                                             |                              |
|                   |        |                |              |                 | -1  | -20.00 | 08JUL2019 | 13:52:03 |                                               | 50.8 HN                     |                                             |                              |
|                   |        |                |              |                 | 2   | 24.00  | 10JUL2019 | 10:18:48 |                                               | 52.6 HN                     | 3.1 HN                                      |                              |
|                   |        |                |              |                 | 3   | 48.00  | 11JUL2019 | 10:11:12 |                                               | 52.9 HN                     |                                             |                              |
|                   |        |                |              |                 | 8   | 168.00 | 16JUL2019 | 9:57:52  |                                               | 52.1 HN                     |                                             |                              |
| 008               | 1      | A              | 62/M         | 1               | -1  | -20.00 | 08JUL2019 | 14:03:38 |                                               |                             | 3.1 HN                                      |                              |
| 009               | 2      | B              | 28/M         | Screen<br>1     |     |        | 12JUL2019 | 12:07:30 | 0.9 HN                                        |                             |                                             |                              |
|                   |        |                |              |                 | 2   | 24.00  | 26JUL2019 | 9:30:36  | 0.9 HN                                        |                             |                                             |                              |
|                   |        |                |              |                 | 3   | 48.00  | 27JUL2019 | 9:32:10  | 1.0 HN                                        |                             |                                             |                              |
|                   |        |                |              |                 | 8   | 168.00 | 01AUG2019 | 9:30:28  | 1.4 HN                                        |                             |                                             |                              |
| 010               | 2      | P              | 53/M         | 1               | 3   | 48.00  | 27JUL2019 | 9:41:44  |                                               |                             | 3.3 HN                                      |                              |
| 013               | 2      | P              | 34/M         | 1               | 8   | 168.00 | 02AUG2019 | 9:57:44  |                                               |                             |                                             | 14.2 HN                      |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.2.3 Out-of-Range Values and Recheck Results - Hematology (III of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day         | Hour                     | Date                                | Time                          | Absolute<br>Eosinophils<br>0-0.8<br>(thou/uL) | Lymphocytes<br>14-43<br>(%)   | Absolute<br>Lymphocytes<br>1-3<br>(thou/uL) | Monocytes<br>3.9-11.5<br>(%) |
|-------------------|--------|----------------|--------------|-----------------|-------------|--------------------------|-------------------------------------|-------------------------------|-----------------------------------------------|-------------------------------|---------------------------------------------|------------------------------|
| 015               | 2      | B              | 50/F         | Screen<br>1     | 2           | 24.00                    | 08JUL2019<br>27JUL2019              | 8:42:47<br>10:53:13           |                                               | 43.7 HN<br>45.3 HN            |                                             |                              |
| 016               | 2      | B              | 37/M         | Screen<br>1     | 8           | 168.00                   | 10JUL2019<br>02AUG2019              | 8:30:45<br>10:04:42           |                                               | 52.8 HN                       | 3.3 HN                                      |                              |
| 018               | 3      | P              | 57/F         | 1               | 2<br>3<br>8 | 24.00<br>48.00<br>168.00 | 13AUG2019<br>14AUG2019<br>19AUG2019 | 9:42:01<br>9:51:30<br>9:31:43 |                                               | 43.1 HN<br>44.9 HN<br>45.6 HN |                                             |                              |
| 019               | 3      | P              | 26/M         | Screen<br>1     | 8           | 168.00                   | 31JUL2019<br>20AUG2019              | 8:26:53<br>9:48:56            |                                               | 44.3 HN<br>48.8 HN            |                                             | 12.8 HN                      |
| 020               | 3      | C              | 56/M         | Screen<br>1     | 2<br>3      | 24.00<br>48.00           | 02AUG2019<br>14AUG2019<br>15AUG2019 | 8:07:04<br>9:56:48<br>9:56:47 |                                               |                               | 0.9 LN<br>0.8 LN                            | 11.7 HN                      |
| 024               | 3      | C              | 40/M         | Screen          |             |                          | 31JUL2019                           | 8:14:05                       |                                               | 47.4 HN                       |                                             |                              |
| 027               | 4      | D              | 30/M         | 1               | 8           | 168.00                   | 06SEP2019                           | 9:49:24                       |                                               |                               | 0.9 LN                                      |                              |
| 028               | 4      | D              | 20/M         | Screen          |             |                          | 20AUG2019                           | 8:36:39                       |                                               | 44.6 HN                       |                                             |                              |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.2.3 Out-of-Range Values and Recheck Results - Hematology (III of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time      | Absolute<br>Eosinophils<br>0-0.8<br>(thou/uL) | Lymphocytes<br>14-43<br>(%) | Absolute<br>Lymphocytes<br>1-3<br>(thou/uL) | Monocytes<br>3.9-11.5<br>(%) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|-----------|-----------------------------------------------|-----------------------------|---------------------------------------------|------------------------------|
| 029               | 4      | D              | 57/F         | 1               |     | 8      | 168.00    | 06SEP2019 | 9:50:59                                       |                             |                                             | 11.7 HN                      |
| 030               | 4      | P              | 30/M         | Screen          |     |        |           | 20AUG2019 | 8:25:25                                       |                             |                                             |                              |
|                   |        |                |              | Recheck         |     |        |           | 23AUG2019 | 15:24:10                                      | 0.1                         |                                             | 10.8                         |
|                   |        |                |              | 1               | -1  | -20.00 | 29AUG2019 | 13:54:52  |                                               |                             | 2.1                                         |                              |
|                   |        |                |              |                 | 2   | 24.00  | 31AUG2019 | 10:19:41  |                                               |                             |                                             |                              |
|                   |        |                |              |                 | 3   | 48.00  | 01SEP2019 | 10:21:16  |                                               |                             |                                             |                              |
|                   |        |                |              | Recheck         |     |        |           | 01SEP2019 | 18:22:00                                      | 0.1                         | 2.6                                         | 8.8                          |
|                   |        |                |              | 1               | 8   | 168.00 | 06SEP2019 | 9:52:44   |                                               |                             |                                             | 13.7 HN                      |
| 032               | 4      | D              | 51/M         | Screen          |     |        |           | 20AUG2019 | 8:03:22                                       |                             | 3.2 HN                                      |                              |
|                   |        |                |              | 1               | -1  | -20.00 | 29AUG2019 | 13:58:39  |                                               |                             | 3.4 HN                                      |                              |
| 033               | 5      | E              | 60/M         | Screen          |     |        |           | 06FEB2020 | 10:28:47                                      |                             |                                             | 12.8 HN                      |
|                   |        |                |              | 1               | -1  | -20.00 | 19FEB2020 | 13:18:52  |                                               |                             |                                             | 13.4 HN                      |
|                   |        |                |              |                 | 2   | 24.00  | 21FEB2020 | 9:15:56   |                                               |                             |                                             | 12.4 HN                      |
|                   |        |                |              |                 | 8   | 168.00 | 27FEB2020 | 9:15:40   |                                               |                             |                                             | 13.1 HN                      |
| 034               | 5      | P              | 59/M         | 1               | -1  | -20.00 | 19FEB2020 | 13:20:34  |                                               |                             | 0.9 LN                                      | 11.9 HN                      |
|                   |        |                |              |                 | 2   | 24.00  | 21FEB2020 | 9:28:24   |                                               |                             | 0.9 LN                                      | 13.4 HN                      |
|                   |        |                |              |                 | 3   | 48.00  | 22FEB2020 | 9:20:15   |                                               |                             |                                             | 13.1 HN                      |
|                   |        |                |              |                 | 8   | 168.00 | 27FEB2020 | 9:20:19   |                                               |                             |                                             | 11.7 HN                      |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.2.3 Out-of-Range Values and Recheck Results - Hematology (III of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Absolute<br>Eosinophils<br>0-0.8<br>(thou/uL) | Lymphocytes<br>14-43<br>(%) | Absolute<br>Lymphocytes<br>1-3<br>(thou/uL) | Monocytes<br>3.9-11.5<br>(%) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|----------|-----------------------------------------------|-----------------------------|---------------------------------------------|------------------------------|
| 035               | 5      | E              | 35/M         | Screen<br>1     |     |        | 12FEB2020 | 10:24:02 |                                               |                             |                                             | 14.2 HN                      |
|                   |        |                |              |                 | 2   | 24.00  | 22FEB2020 | 9:51:09  |                                               |                             |                                             | 11.6 HN                      |
|                   |        |                |              |                 | 3   | 48.00  | 23FEB2020 | 9:45:35  |                                               |                             |                                             | 13.1 HN                      |
|                   |        |                |              |                 | 8   | 168.00 | 28FEB2020 | 9:50:03  |                                               |                             |                                             | 15.1 HN                      |
| 037               | 5      | E              | 60/M         | 1               | -1  | -20.00 | 20FEB2020 | 13:54:25 |                                               |                             | 0.9 LN                                      |                              |
| 038               | 5      | E              | 59/M         | 1               | -1  | -20.00 | 20FEB2020 | 13:56:12 |                                               | 11.4 LN                     |                                             |                              |
| 039               | 5      | E              | 44/M         | Screen          |     |        | 12FEB2020 | 10:29:53 |                                               |                             |                                             | 11.6 HN                      |
| 040               | 5      | P              | 48/F         | 1               | 8   | 168.00 | 28FEB2020 | 10:01:45 |                                               |                             |                                             | 3.5 LN                       |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

H = Above Reference Range, L = Below Reference Range

Computer: N = Not Clinically Significant

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.2.4 Out-of-Range Values and Recheck Results - Hematology (IV of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Absolute<br>Monocytes<br>0.2-0.8<br>(thou/uL) | Neutrophils<br>42-80<br>(%) | Absolute<br>Neutrophils<br>1.9-7.9<br>(thou/uL) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|----------|-----------------------------------------------|-----------------------------|-------------------------------------------------|
| 002               | 1      | A              | 40/M         | Screen          |     |        | 19JUN2019 | 7:28:20  | 0.9 HN                                        |                             |                                                 |
| 006               | 1      | A              | 33/M         | Screen          |     |        | 22JUN2019 | 10:20:01 |                                               | 35.6 LN                     |                                                 |
|                   |        |                |              | 1               | -1  | -20.00 | 08JUL2019 | 13:52:03 |                                               | 36.6 LN                     |                                                 |
|                   |        |                |              |                 | 2   | 24.00  | 10JUL2019 | 10:18:48 |                                               | 34.8 LN                     |                                                 |
|                   |        |                |              |                 | 3   | 48.00  | 11JUL2019 | 10:11:12 |                                               | 35.7 LN                     |                                                 |
|                   |        |                |              |                 | 8   | 168.00 | 16JUL2019 | 9:57:52  |                                               | 34.2 LN                     | 1.8 LN                                          |
| 016               | 2      | B              | 37/M         | 1               | 8   | 168.00 | 02AUG2019 | 10:04:42 |                                               | 37.3 LN                     |                                                 |
| 019               | 3      | P              | 26/M         | Screen          |     |        | 31JUL2019 | 8:26:53  |                                               | 39.8 LN                     | 1.8 LN                                          |
|                   |        |                |              | 1               | 8   | 168.00 | 20AUG2019 | 9:48:56  |                                               | 38.9 LN                     |                                                 |
| 024               | 3      | C              | 40/M         | Screen          |     |        | 31JUL2019 | 8:14:05  |                                               | 38.3 LN                     | 1.8 LN                                          |
| 030               | 4      | P              | 30/M         | Screen          |     |        | 20AUG2019 | 8:25:25  |                                               | 34.9 LN                     | 1.2 LYR                                         |
|                   |        |                |              | Recheck         |     |        | 23AUG2019 | 15:24:10 | 0.6                                           | 47.5                        | 2.5                                             |
|                   |        |                |              | 1               | -1  | -20.00 | 29AUG2019 | 13:54:52 |                                               | 41.1 LN                     | 1.5 LN                                          |
|                   |        |                |              |                 | 2   | 24.00  | 31AUG2019 | 10:19:41 |                                               |                             | 1.2 LY^-                                        |
|                   |        |                |              |                 | 3   | 48.00  | 01SEP2019 | 10:21:16 |                                               |                             | 1.4 LYR-                                        |
|                   |        |                |              | Recheck         | 3   |        | 01SEP2019 | 18:22:00 | 0.5                                           | 37.5 LN                     | 1.9                                             |
|                   |        |                |              | 1               | 8   | 168.00 | 06SEP2019 | 9:52:44  |                                               | 31.7 LN                     | 1.1 LYR-                                        |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male  
H = Above Reference Range, L = Below Reference Range  
Computer: N = Not Clinically Significant, Y = Clinically Significant  
PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)  
Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.2.4 Out-of-Range Values and Recheck Results - Hematology (IV of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Absolute<br>Monocytes<br>0.2-0.8<br>(thou/uL) | Neutrophils<br>42-80<br>(%) | Absolute<br>Neutrophils<br>1.9-7.9<br>(thou/uL) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|----------|-----------------------------------------------|-----------------------------|-------------------------------------------------|
| 038               | 5      | E              | 59/M         | 1               | -1  | -20.00 | 20FEB2020 | 13:56:12 |                                               | 82.3 HN                     |                                                 |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male  
H = Above Reference Range, L = Below Reference Range  
Computer: N = Not Clinically Significant, Y = Clinically Significant  
PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)  
Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.3.1 Out-of-Range Values and Recheck Results - Urinalysis (I of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Occult<br>Blood<br>F: NEG, TRACE<br>M: NEGATIVE | pH, Urine<br>5-8 | Specific<br>Gravity<br>1.005-1.03 | Leukocyte<br>Esterase<br>NEGATIVE |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|----------|-------------------------------------------------|------------------|-----------------------------------|-----------------------------------|
| 002               | 1      | A              | 40/M         | 1               | -1  | -21.00 | 07JUL2019 | 12:37:27 |                                                 |                  | 1.004 LN                          |                                   |
| 006               | 1      | A              | 33/M         | Screen<br>1     |     |        | 22JUN2019 | 10:04:00 |                                                 |                  | 1.002 LN                          |                                   |
|                   |        |                |              |                 | -1  | -21.00 | 08JUL2019 | 13:13:32 |                                                 |                  | 1.002 LN                          |                                   |
| 009               | 2      | B              | 28/M         | 1               | 3   | 47.00  | 27JUL2019 | 8:30:08  |                                                 |                  |                                   | 1+ *N                             |
| 010               | 2      | P              | 53/M         | Screen          |     |        | 08JUL2019 | 7:50:20  |                                                 |                  | 1.003 LN                          |                                   |
| 011               | 2      | B              | 58/M         | 1               | -1  | -21.00 | 25JUL2019 | 13:08:16 |                                                 |                  | 1.004 LN                          |                                   |
| 012               | 2      | B              | 54/M         | 1               | -1  | -21.00 | 25JUL2019 | 13:11:11 |                                                 |                  |                                   | 1+ *NR-                           |
|                   |        |                |              | Recheck         | -1  |        | 26JUL2019 | 5:12:07  | NEGATIVE                                        | 5.0              | 1.024                             | NEGATIVE                          |
|                   |        |                |              | 1               | 3   | 47.00  | 28JUL2019 | 9:04:02  |                                                 |                  |                                   | 1+ *N                             |
| 013               | 2      | P              | 34/M         | Screen<br>1     |     |        | 16JUL2019 | 10:43:52 |                                                 |                  | 1.004 LN                          |                                   |
|                   |        |                |              |                 | -1  | -21.00 | 25JUL2019 | 13:13:44 |                                                 |                  | 1.003 LN                          |                                   |
|                   |        |                |              |                 | 3   | 47.00  | 28JUL2019 | 8:54:50  |                                                 |                  |                                   | 1+ *N                             |
|                   |        |                |              |                 | 8   | 167.50 | 02AUG2019 | 9:24:29  |                                                 |                  | 1.003 LN                          |                                   |
| 014               | 2      | B              | 42/F         | Screen<br>1     |     |        | 10JUL2019 | 8:15:12  | 2+ *Y-                                          |                  |                                   |                                   |
|                   |        |                |              |                 | 3   | 47.00  | 28JUL2019 | 8:48:56  | 1+ *N                                           |                  |                                   |                                   |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male  
 \* = No Match to Reference Range, H = Above Reference Range, L = Below Reference Range  
 Computer: N = Not Clinically Significant, Y = Clinically Significant  
 PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event  
 Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
 Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
 Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
 Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
 Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)  
 Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.3.1 Out-of-Range Values and Recheck Results - Urinalysis (I of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period   | Day | Hour   | Date      | Time     | Occult<br>Blood<br>F: NEG, TRACE<br>M: NEGATIVE | pH, Urine<br>5-8 | Specific<br>Gravity<br>1.005-1.03 | Leukocyte<br>Esterase<br>NEGATIVE |
|-------------------|--------|----------------|--------------|-------------------|-----|--------|-----------|----------|-------------------------------------------------|------------------|-----------------------------------|-----------------------------------|
| 014               | 2      | B              | 42/F         | 1                 | 8   | 167.50 | 02AUG2019 | 9:24:14  | 2+ *Y-                                          |                  |                                   |                                   |
| 015               | 2      | B              | 50/F         | Screen<br>1       |     |        | 08JUL2019 | 8:12:07  | 1+ *N                                           |                  |                                   |                                   |
|                   |        |                |              |                   | -1  | -21.00 | 25JUL2019 | 13:07:01 | 3+ *Y-                                          |                  |                                   |                                   |
|                   |        |                |              |                   | 3   | 47.00  | 28JUL2019 | 8:54:35  | 4+ *Y^                                          |                  |                                   |                                   |
|                   |        |                |              |                   | 8   | 167.50 | 02AUG2019 | 9:23:54  | 3+ *YR-                                         |                  |                                   |                                   |
|                   |        |                |              | Recheck           | 8   |        | 06AUG2019 | 10:41:00 | 1+ *N                                           | 5.0              | 1.006                             | NEGATIVE                          |
| 017               | 3      | C              | 62/M         | 1                 | -1  | -21.00 | 11AUG2019 | 12:56:55 |                                                 |                  | 1.003                             | LN                                |
| 018               | 3      | P              | 57/F         | Screen<br>1       |     |        | 26JUL2019 | 9:22:52  |                                                 |                  | 1.002                             | LN                                |
|                   |        |                |              | Recheck           | 8   | 167.50 | 19AUG2019 | 9:08:16  |                                                 |                  |                                   | 1+ *NR-                           |
|                   |        |                |              |                   | 8   |        | 22AUG2019 | 8:18:55  | NEGATIVE                                        | 6.5              | 1.019                             | NEGATIVE                          |
| 019               | 3      | P              | 26/M         | 1                 | 3   | 47.00  | 15AUG2019 | 8:37:47  |                                                 |                  | 1.004                             | LN                                |
| 020               | 3      | C              | 56/M         | Screen<br>1       |     |        | 02AUG2019 | 7:54:09  |                                                 |                  | 1.003                             | LN                                |
|                   |        |                |              |                   | -1  | -21.00 | 12AUG2019 | 13:01:34 |                                                 |                  | 1.002                             | LN                                |
|                   |        |                |              |                   | 8   | 167.50 | 20AUG2019 | 9:23:12  |                                                 |                  | 1.002                             | LN                                |
| 021               | 3      | C              | 43/F         | Screen<br>Recheck |     |        | 02AUG2019 | 8:12:31  | 3+ *YR                                          |                  |                                   | 1+ *NR                            |
|                   |        |                |              |                   |     |        | 06AUG2019 | 13:19:21 | TRACE                                           | 7.0              | 1.003                             | LN<br>NEGATIVE                    |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male  
 \* = No Match to Reference Range, H = Above Reference Range, L = Below Reference Range  
 Computer: N = Not Clinically Significant, Y = Clinically Significant  
 PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event  
 Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
 Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
 Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
 Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
 Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)  
 Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.3.1 Out-of-Range Values and Recheck Results - Urinalysis (I of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period        | Day | Hour   | Date                                | Time                            | Occult<br>Blood<br>F: NEG, TRACE<br>M: NEGATIVE | pH, Urine<br>5-8 | Specific<br>Gravity<br>1.005-1.03 | Leukocyte<br>Esterase<br>NEGATIVE |
|-------------------|--------|----------------|--------------|------------------------|-----|--------|-------------------------------------|---------------------------------|-------------------------------------------------|------------------|-----------------------------------|-----------------------------------|
| 021               | 3      | C              | 43/F         | 1                      | 8   | 167.50 | 20AUG2019                           | 9:35:51                         |                                                 |                  | 1.003 LN                          |                                   |
| 023               | 3      | C              | 42/M         | 1                      | -1  | -21.00 | 12AUG2019                           | 12:58:25                        |                                                 |                  | 1.002 LN                          |                                   |
| 024               | 3      | C              | 40/M         | 1                      | -1  | -21.00 | 12AUG2019                           | 13:09:27                        |                                                 |                  | 1.003 LN                          |                                   |
| 025               | 4      | P              | 30/M         | Screen                 |     |        | 12AUG2019                           | 9:31:03                         |                                                 |                  | 1.002 LN                          |                                   |
| 026               | 4      | D              | 43/M         | Screen<br>1            | -1  | -21.00 | 22AUG2019<br>28AUG2019              | 9:54:33<br>12:45:08             |                                                 |                  | 1.003 LN<br>1.002 LN              |                                   |
| 027               | 4      | D              | 30/M         | Screen<br>1            | -1  | -21.00 | 20AUG2019<br>29AUG2019              | 8:18:17<br>13:11:36             |                                                 |                  | 1.003 LN<br>1.002 LN              |                                   |
|                   |        |                |              | Recheck                | 8   | 167.50 | 06SEP2019<br>10SEP2019              | 9:29:11<br>12:42:57             | 2+ *YR-<br>TRACE *N                             | 6.5              | 1.007                             | NEGATIVE                          |
| 029               | 4      | D              | 57/F         | 1                      | -1  | -21.00 | 29AUG2019                           | 13:02:57                        |                                                 |                  | 1.004 LN                          |                                   |
|                   |        |                |              |                        | 8   | 167.50 | 06SEP2019                           | 9:20:27                         |                                                 |                  | 1.003 LN                          |                                   |
| 030               | 4      | P              | 30/M         | Screen<br>Recheck<br>1 | -1  | -21.00 | 20AUG2019<br>23AUG2019<br>29AUG2019 | 8:13:24<br>15:21:33<br>13:28:54 |                                                 |                  | 1.036 HYR<br>1.028<br>1.032 HN    |                                   |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male  
 \* = No Match to Reference Range, H = Above Reference Range, L = Below Reference Range  
 Computer: N = Not Clinically Significant, Y = Clinically Significant  
 PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event  
 Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
 Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
 Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
 Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
 Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)  
 Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.3.1 Out-of-Range Values and Recheck Results - Urinalysis (I of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time      | Occult<br>Blood<br>F: NEG, TRACE<br>M: NEGATIVE | pH, Urine<br>5-8 | Specific<br>Gravity<br>1.005-1.03 | Leukocyte<br>Esterase<br>NEGATIVE |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|-----------|-------------------------------------------------|------------------|-----------------------------------|-----------------------------------|
| 032               | 4      | D              | 51/M         | 1               |     | 8      | 167.50    | 06SEP2019 | 9:20:57                                         |                  | 1.003                             | LN                                |
| 033               | 5      | E              | 60/M         | 1               |     | 8      | 167.50    | 27FEB2020 | 8:51:20                                         |                  | 1.002                             | LN                                |
| 034               | 5      | P              | 59/M         | Screen<br>1     |     |        |           | 06FEB2020 | 8:35:21                                         |                  | 1.003                             | LN                                |
|                   |        |                |              |                 | -1  | -21.00 | 19FEB2020 | 12:24:38  |                                                 |                  | 1.002                             | LN                                |
| 037               | 5      | E              | 60/M         | Screen<br>1     |     |        |           | 10FEB2020 | 10:33:40                                        |                  | 1.002                             | LN                                |
|                   |        |                |              |                 | -1  | -21.00 | 20FEB2020 | 13:00:07  |                                                 |                  | 1.002                             | LN                                |
|                   |        |                |              | Recheck         | 3   |        | 26FEB2020 | 13:29:33  | NEGATIVE                                        | 5.0              | 1.011                             | NEGATIVE                          |
|                   |        |                |              |                 | 8   |        | 05MAR2020 | 14:22:50  | NEGATIVE                                        | 5.0              | 1.005                             | NEGATIVE                          |
| 038               | 5      | E              | 59/M         | 1               |     | -1     | -21.00    | 20FEB2020 | 12:56:36                                        |                  | 1.004                             | LN                                |
| 039               | 5      | E              | 44/M         | 1               |     | -1     | -21.00    | 20FEB2020 | 13:21:12                                        |                  | 1.003                             | LN                                |
|                   |        |                |              |                 | 3   | 47.00  | 23FEB2020 | 8:06:22   |                                                 |                  | 1.003                             | LN                                |
|                   |        |                |              |                 | 8   | 167.50 | 28FEB2020 | 9:23:10   |                                                 |                  | 1.003                             | LN                                |
| 040               | 5      | P              | 48/F         | Screen<br>1     |     |        |           | 10FEB2020 | 10:33:16                                        |                  | 1.003                             | LN                                |
|                   |        |                |              |                 | -1  | -21.00 | 20FEB2020 | 13:00:48  |                                                 |                  | 1.002                             | LN                                |
|                   |        |                |              |                 | 3   | 47.00  | 23FEB2020 | 8:31:15   |                                                 |                  | 1.002                             | LN                                |
|                   |        |                |              |                 | 8   | 167.50 | 28FEB2020 | 9:24:21   |                                                 |                  | 1.003                             | LN                                |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male  
 \* = No Match to Reference Range, H = Above Reference Range, L = Below Reference Range  
 Computer: N = Not Clinically Significant, Y = Clinically Significant  
 PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event  
 Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
 Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
 Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
 Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
 Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)  
 Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.3.2 Out-of-Range Values and Recheck Results - Urinalysis (II of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Nitrite<br>NEGATIVE | Bilirubin<br>NEGATIVE | Glucose<br>NEGATIVE | RBC<br>F: 0-7<br>M: 0-3<br>(/HPF) |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|-----------|----------|---------------------|-----------------------|---------------------|-----------------------------------|
| 012               | 2      | B              | 54/M         | Recheck         | -1  |        | 26JUL2019 | 5:12:07  | NEGATIVE            | NEGATIVE              | NEGATIVE            |                                   |
| 015               | 2      | B              | 50/F         | 1               | 3   | 47.00  | 28JUL2019 | 8:54:35  |                     |                       |                     | 25-30 HY^-                        |
|                   |        |                |              |                 | 8   | 167.50 | 02AUG2019 | 9:23:54  |                     |                       |                     | 8-10 HN                           |
|                   |        |                |              | Recheck         | 8   |        | 06AUG2019 | 10:41:00 | NEGATIVE            | NEGATIVE              | NEGATIVE            | 4-5                               |
| 018               | 3      | P              | 57/F         | Recheck         | 8   |        | 22AUG2019 | 8:18:55  | NEGATIVE            | NEGATIVE              | NEGATIVE            |                                   |
| 021               | 3      | C              | 43/F         | Recheck         |     |        | 06AUG2019 | 13:19:21 | NEGATIVE            | NEGATIVE              | NEGATIVE            |                                   |
| 027               | 4      | D              | 30/M         | 1               | 8   | 167.50 | 06SEP2019 | 9:29:11  |                     |                       |                     | 4-5 HNR-                          |
|                   |        |                |              | Recheck         | 8   |        | 10SEP2019 | 12:42:57 | NEGATIVE            | NEGATIVE              | NEGATIVE            | 1-2                               |
| 037               | 5      | E              | 60/M         | 1               | 3   | 47.00  | 23FEB2020 | 7:49:26  | POSITIVE *YR-       |                       |                     |                                   |
|                   |        |                |              | Recheck         | 3   |        | 26FEB2020 | 13:29:33 | NEGATIVE            | NEGATIVE              | NEGATIVE            |                                   |
|                   |        |                |              | 1               | 8   | 167.50 | 28FEB2020 | 9:47:17  | POSITIVE *YR-       |                       |                     |                                   |
|                   |        |                |              | Recheck         | 8   |        | 05MAR2020 | 14:22:50 | NEGATIVE            | NEGATIVE              | NEGATIVE            |                                   |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

\* = No Match to Reference Range, H = Above Reference Range

Computer: N = Not Clinically Significant, Y = Clinically Significant

PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.3.3 Out-of-Range Values and Recheck Results - Urinalysis (III of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date                   | Time               | WBC<br>0-7<br>(/HPF) | Protein<br>NEG, TRACE | Ketones<br>NEG, TRACE | Urobilinogen<br>NEGATIVE |
|-------------------|--------|----------------|--------------|-----------------|-----|--------|------------------------|--------------------|----------------------|-----------------------|-----------------------|--------------------------|
| 012               | 2      | B              | 54/M         | Recheck         | -1  |        | 26JUL2019              | 5:12:07            |                      | NEGATIVE              | NEGATIVE              | NEGATIVE                 |
| 015               | 2      | B              | 50/F         | Recheck         | 8   |        | 06AUG2019              | 10:41:00           | 0-1                  | NEGATIVE              | NEGATIVE              | NEGATIVE                 |
| 018               | 3      | P              | 57/F         | 1<br>Recheck    | 8   | 167.50 | 19AUG2019<br>22AUG2019 | 9:08:16<br>8:18:55 | 11-15 HNR-           | NEGATIVE              | NEGATIVE              | NEGATIVE                 |
| 021               | 3      | C              | 43/F         | Recheck         |     |        | 06AUG2019              | 13:19:21           |                      | NEGATIVE              | NEGATIVE              | NEGATIVE                 |
| 027               | 4      | D              | 30/M         | Recheck         | 8   |        | 10SEP2019              | 12:42:57           | 0-1                  | NEGATIVE              | NEGATIVE              | NEGATIVE                 |
| 030               | 4      | P              | 30/M         | Screen          |     |        | 20AUG2019              | 8:13:24            |                      |                       | 1+ *N                 | 4 MG/DL *N               |
| 031               | 4      | D              | 32/M         | 1               | -1  | -21.00 | 29AUG2019              | 15:03:18           |                      |                       |                       | 4 MG/DL *N               |
| 035               | 5      | E              | 35/M         | 1               | 3   | 47.00  | 23FEB2020              | 7:53:33            |                      |                       | 2+ *N                 |                          |
|                   |        |                |              |                 | 8   | 167.50 | 28FEB2020              | 9:23:30            |                      |                       | 2+ *N                 |                          |
| 037               | 5      | E              | 60/M         | 1<br>Recheck    | 3   | 47.00  | 23FEB2020              | 7:49:26            | 11-15 HYR-           |                       |                       |                          |
|                   |        |                |              |                 | 3   |        | 26FEB2020              | 13:29:33           |                      | NEGATIVE              | NEGATIVE              | NEGATIVE                 |
|                   |        |                |              |                 | 8   |        | 05MAR2020              | 14:22:50           |                      | NEGATIVE              | NEGATIVE              | NEGATIVE                 |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

\* = No Match to Reference Range, H = Above Reference Range

Computer: N = Not Clinically Significant, Y = Clinically Significant

PI Interpretation: - = Not Clinically Significant, R = To be Rechecked

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.3.4 Out-of-Range Values and Recheck Results - Urinalysis (IV of IV) (Safety Population)

| Subject<br>Number | Cohort | Treat-<br>ment | Age#/Sex | Study<br>Period | Day | Hour   | Date      | Time     | Bacteria<br>F: NEG, TRACE<br>M: NEGATIVE | Casts<br>0-1<br>(/LPF) |
|-------------------|--------|----------------|----------|-----------------|-----|--------|-----------|----------|------------------------------------------|------------------------|
| 015               | 2      | B              | 50/F     | Recheck         | 8   |        | 06AUG2019 | 10:41:00 | NEGATIVE                                 | 0                      |
| 027               | 4      | D              | 30/M     | Recheck         | 8   |        | 10SEP2019 | 12:42:57 | NEGATIVE                                 | 0                      |
| 037               | 5      | E              | 60/M     | 1               | 3   | 47.00  | 23FEB2020 | 7:49:26  | 4+ *YR-                                  |                        |
|                   |        |                |          |                 | 8   | 167.50 | 28FEB2020 | 9:47:17  | 3+ *YR-                                  |                        |

Note: # Age is calculated from the date of first dosing. F = Female, M = Male

\* = No Match to Reference Range

Computer: Y = Clinically Significant

PI Interpretation: - = Not Clinically Significant, R = To be Rechecked

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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Table 14.3.4.4 Clinically Significant Values and Recheck Results (Safety Population)

| Subject<br>Number | Cohort | Treatment | Age#/<br>Sex | Study<br>Period | Day | Hour   | Date      | Time     | Department | Test            | Result   | Reference Range | Unit |
|-------------------|--------|-----------|--------------|-----------------|-----|--------|-----------|----------|------------|-----------------|----------|-----------------|------|
| 033               | 5      | E         | 60/M         | Screen          |     |        | 06FEB2020 | 10:28:31 | Chemistry  | Creatine Kinase | 256      | 44-329          | IU/L |
|                   |        |           |              | 1               | -1  | -20.00 | 19FEB2020 | 13:18:32 | Chemistry  | Creatine Kinase | 368 HN   | 44-329          | IU/L |
|                   |        |           |              |                 | 1   | 4.00   | 20FEB2020 | 13:15:35 | Chemistry  | Creatine Kinase | 281      | 44-329          | IU/L |
|                   |        |           |              |                 |     | 12.00  | 20FEB2020 | 21:17:34 | Chemistry  | Creatine Kinase | 237      | 44-329          | IU/L |
|                   |        |           |              |                 | 2   | 24.00  | 21FEB2020 | 9:15:39  | Chemistry  | Creatine Kinase | 208      | 44-329          | IU/L |
|                   |        |           |              |                 | 3   | 48.00  | 22FEB2020 | 9:16:15  | Chemistry  | Creatine Kinase | 200      | 44-329          | IU/L |
|                   |        |           |              |                 | 8   | 168.00 | 27FEB2020 | 9:15:02  | Chemistry  | Creatine Kinase | 986 HYR+ | 44-329          | IU/L |
|                   |        |           |              | Recheck         | 8   |        | 03MAR2020 | 10:32:44 | Chemistry  | Creatine Kinase | 608 HYR+ | 44-329          | IU/L |
|                   |        |           |              |                 |     |        | 10MAR2020 | 9:54:59  | Chemistry  | Creatine Kinase | 709 HYR+ | 44-329          | IU/L |
|                   |        |           |              |                 |     |        | 16MAR2020 | 9:58:27  | Chemistry  | Creatine Kinase | 834 HYR+ | 44-329          | IU/L |
|                   |        |           |              |                 |     |        | 23MAR2020 | 9:44:59  | Chemistry  | Creatine Kinase | 624 HY+  | 44-329          | IU/L |

Note: # Age is calculated from the date of first dosing. M = Male  
H = Above Reference Range  
Computer: Y = Clinically Significant, N = Not Clinically Significant  
PI Interpretation: + = Clinically Significant, R = To be Rechecked  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)  
Treatment P: A single IV infusion of placebo (Cohorts 1-5) over approximately 30 minutes

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#### **14.3.5 Displays of Other Laboratory, Vital Signs, Electrocardiogram, Physical Examination, and Other Safety Data**

|                 |                                                                                |
|-----------------|--------------------------------------------------------------------------------|
| Table 14.3.5.1  | Clinical Laboratory Summary - Serum Chemistry (Safety Population)              |
| Table 14.3.5.2  | Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population) |
| Table 14.3.5.3  | Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)  |
| Table 14.3.5.4  | Clinical Laboratory Summary - Hematology (Safety Population)                   |
| Table 14.3.5.5  | Clinical Laboratory Change From Baseline - Hematology (Safety Population)      |
| Table 14.3.5.6  | Clinical Laboratory Shift From Baseline - Hematology (Safety Population)       |
| Table 14.3.5.7  | Clinical Laboratory Summary - Urinalysis (Safety Population)                   |
| Table 14.3.5.8  | Clinical Laboratory Change From Baseline - Urinalysis (Safety Population)      |
| Table 14.3.5.9  | Clinical Laboratory Shift From Baseline - Urinalysis (Safety Population)       |
| Table 14.3.5.10 | Vital Sign Summary (Safety Population)                                         |
| Table 14.3.5.11 | Vital Sign Change From Baseline (Safety Population)                            |
| Table 14.3.5.12 | 12-Lead Electrocardiogram Summary (Safety Population)                          |
| Table 14.3.5.13 | 12-Lead Electrocardiogram Change From Baseline (Safety Population)             |

Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Calcium (mg/dL)         | 8.5-10.2        | Screen     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 9.62           | 9.78      | 9.50  | 9.53  | 9.68  | 9.65  | 9.63    |
|                         |                 |            | SD        | 0.305          | 0.248     | 0.400 | 0.301 | 0.313 | 0.176 | 0.295   |
|                         |                 |            | Minimum   | 9.1            | 9.5       | 8.8   | 9.2   | 9.2   | 9.5   | 8.8     |
|                         |                 |            | Median    | 9.60           | 9.75      | 9.55  | 9.45  | 9.80  | 9.60  | 9.60    |
|                         |                 |            | Maximum   | 10.0           | 10.1      | 10.0  | 9.9   | 10.0  | 10.0  | 10.1    |
|                         |                 | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 9.54           | 9.72      | 9.35  | 9.70  | 9.68  | 9.52  | 9.59    |
|                         |                 |            | SD        | 0.403          | 0.279     | 0.274 | 0.456 | 0.349 | 0.313 | 0.347   |
|                         |                 |            | Minimum   | 9.0            | 9.2       | 8.9   | 9.1   | 9.0   | 9.0   | 8.9     |
|                         |                 |            | Median    | 9.50           | 9.75      | 9.40  | 9.70  | 9.80  | 9.55  | 9.70    |
|                         |                 |            | Maximum   | 10.2           | 10.0      | 9.7   | 10.2  | 9.9   | 9.8   | 10.2    |
|                         |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 9.67           | 9.73      | 9.53  | 9.68  | 9.75  | 9.48  | 9.64    |
|                         |                 |            | SD        | 0.337          | 0.372     | 0.344 | 0.098 | 0.339 | 0.214 | 0.293   |
|                         |                 |            | Minimum   | 9.3            | 9.3       | 8.9   | 9.6   | 9.1   | 9.2   | 8.9     |
|                         |                 |            | Median    | 9.75           | 9.75      | 9.65  | 9.65  | 9.85  | 9.50  | 9.65    |
|                         |                 |            | Maximum   | 10.1           | 10.3      | 9.8   | 9.8   | 10.0  | 9.8   | 10.3    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Calcium (mg/dL)         | 8.5-10.2        | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 9.69           | 9.90      | 9.67  | 9.88  | 9.77  | 9.55  | 9.75    |
|                         |                 |              | SD        | 0.328          | 0.447     | 0.356 | 0.313 | 0.216 | 0.226 | 0.329   |
|                         |                 |              | Minimum   | 9.3            | 9.2       | 9.2   | 9.7   | 9.5   | 9.4   | 9.2     |
|                         |                 |              | Median    | 9.70           | 9.95      | 9.65  | 9.75  | 9.75  | 9.50  | 9.70    |
|                         |                 |              | Maximum   | 10.1           | 10.4      | 10.2  | 10.5  | 10.1  | 10.0  | 10.5    |
|                         |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 9.43           | 9.45      | 9.47  | 9.77  | 9.52  | 9.52  | 9.54    |
|                         |                 |              | SD        | 0.377          | 0.383     | 0.344 | 0.388 | 0.337 | 0.354 | 0.356   |
|                         |                 |              | Minimum   | 8.8            | 9.0       | 9.0   | 9.3   | 8.9   | 9.2   | 8.9     |
|                         |                 |              | Median    | 9.40           | 9.40      | 9.45  | 9.70  | 9.60  | 9.45  | 9.55    |
|                         |                 |              | Maximum   | 10.0           | 10.1      | 9.9   | 10.4  | 9.8   | 10.1  | 10.4    |
| Chloride (mEq/L)        | 97-105          | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 101.5          | 100.8     | 100.5 | 100.3 | 99.5  | 97.5  | 99.7    |
|                         |                 |              | SD        | 3.17           | 1.83      | 3.15  | 3.27  | 1.64  | 2.07  | 2.61    |
|                         |                 |              | Minimum   | 96             | 99        | 96    | 96    | 97    | 95    | 95      |
|                         |                 |              | Median    | 101.5          | 100.0     | 100.0 | 100.0 | 99.5  | 97.5  | 100.0   |
|                         |                 |              | Maximum   | 107            | 104       | 105   | 106   | 102   | 101   | 106     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Chloride (mEq/L)        | 97-105          | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 99.4           | 102.0     | 102.3 | 98.8  | 97.3  | 96.3^ | 99.4    |
|                         |                 |            | SD        | 4.09           | 2.37      | 2.66  | 2.99  | 3.33  | 2.66  | 3.60    |
|                         |                 |            | Minimum   | 91             | 99        | 99    | 95    | 91    | 92    | 91      |
|                         |                 |            | Median    | 99.0           | 101.5     | 102.0 | 99.0  | 98.0  | 96.5  | 99.5    |
|                         |                 |            | Maximum   | 107            | 106       | 107   | 102   | 100   | 99    | 107     |
|                         |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 102.2          | 104.2     | 102.2 | 100.3 | 101.0 | 102.7 | 102.1   |
|                         |                 |            | SD        | 3.71           | 2.14      | 2.56  | 2.50  | 2.19  | 3.08  | 2.70    |
|                         |                 |            | Minimum   | 98             | 102       | 99    | 96    | 99    | 99    | 96      |
|                         |                 |            | Median    | 102.0          | 103.5     | 102.0 | 101.0 | 101.0 | 102.0 | 102.0   |
|                         |                 |            | Maximum   | 109            | 108       | 106   | 103   | 103   | 108   | 108     |
|                         |                 | Day 3      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 101.7          | 102.0     | 100.7 | 98.8  | 100.5 | 100.8 | 100.6   |
|                         |                 |            | SD        | 2.91           | 2.45      | 2.07  | 2.32  | 2.59  | 2.48  | 2.45    |
|                         |                 |            | Minimum   | 98             | 98        | 97    | 95    | 97    | 98    | 95      |
|                         |                 |            | Median    | 101.5          | 102.0     | 101.0 | 99.0  | 100.0 | 100.5 | 101.0   |
|                         |                 |            | Maximum   | 106            | 105       | 103   | 101   | 104   | 105   | 105     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Chloride (mEq/L)        | 97-105          | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 101.1          | 101.7     | 103.0 | 98.7  | 101.0 | 99.2  | 100.7   |
|                         |                 |              | SD        | 2.60           | 0.82      | 2.61  | 2.42  | 2.00  | 1.83  | 2.49    |
|                         |                 |              | Minimum   | 96             | 101       | 99    | 95    | 99    | 96    | 95      |
|                         |                 |              | Median    | 101.0          | 101.5     | 103.0 | 99.0  | 101.0 | 100.0 | 101.0   |
|                         |                 |              | Maximum   | 105            | 103       | 107   | 101   | 104   | 101   | 107     |
| Potassium (mEq/L)       | 3.7-5.2         | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 4.26           | 4.42      | 4.20  | 4.57  | 4.40  | 4.37  | 4.39    |
|                         |                 |              | SD        | 0.171          | 0.133     | 0.245 | 0.497 | 0.341 | 0.186 | 0.310   |
|                         |                 |              | Minimum   | 4.0            | 4.3       | 3.9   | 3.8   | 3.8   | 4.1   | 3.8     |
|                         |                 |              | Median    | 4.25           | 4.40      | 4.20  | 4.70  | 4.45  | 4.40  | 4.40    |
|                         |                 |              | Maximum   | 4.5            | 4.6       | 4.6   | 5.1   | 4.8   | 4.6   | 5.1     |
|                         |                 | Baseline     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 4.15           | 4.38      | 4.05  | 4.32  | 4.25  | 4.25  | 4.25    |
|                         |                 |              | SD        | 0.251          | 0.147     | 0.187 | 0.504 | 0.333 | 0.197 | 0.304   |
|                         |                 |              | Minimum   | 3.8            | 4.1       | 3.8   | 3.7   | 3.8   | 4.0   | 3.7     |
|                         |                 |              | Median    | 4.25           | 4.40      | 4.05  | 4.35  | 4.25  | 4.35  | 4.30    |
|                         |                 |              | Maximum   | 4.5            | 4.5       | 4.3   | 5.0   | 4.6   | 4.4   | 5.0     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Potassium (mEq/L)       | 3.7-5.2         | Day 2        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 4.50           | 4.63      | 4.55  | 4.73  | 4.72  | 4.57  | 4.64    |
|                         |                 |              | SD        | 0.226          | 0.186     | 0.373 | 0.609 | 0.117 | 0.242 | 0.335   |
|                         |                 |              | Minimum   | 4.2            | 4.3       | 4.3   | 4.1   | 4.6   | 4.2   | 4.1     |
|                         |                 |              | Median    | 4.40           | 4.65      | 4.35  | 4.60  | 4.70  | 4.60  | 4.60    |
|                         |                 |              | Maximum   | 4.8            | 4.8       | 5.2   | 5.9   | 4.9   | 4.8   | 5.9     |
|                         |                 | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 4.33           | 4.60      | 4.42  | 4.70  | 4.78  | 4.33  | 4.57    |
|                         |                 |              | SD        | 0.157          | 0.253     | 0.588 | 0.434 | 0.449 | 0.163 | 0.415   |
|                         |                 |              | Minimum   | 4.1            | 4.4       | 3.8   | 4.3   | 4.1   | 4.1   | 3.8     |
|                         |                 |              | Median    | 4.35           | 4.50      | 4.40  | 4.60  | 4.75  | 4.35  | 4.50    |
|                         |                 |              | Maximum   | 4.6            | 5.1       | 5.4   | 5.5   | 5.5   | 4.5   | 5.5     |
|                         |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 4.25           | 4.28      | 4.30  | 4.57  | 4.35  | 4.20  | 4.34    |
|                         |                 |              | SD        | 0.190          | 0.172     | 0.537 | 0.547 | 0.176 | 0.335 | 0.383   |
|                         |                 |              | Minimum   | 3.9            | 4.0       | 3.8   | 3.7   | 4.1   | 3.7   | 3.7     |
|                         |                 |              | Median    | 4.30           | 4.30      | 4.15  | 4.60  | 4.40  | 4.25  | 4.30    |
|                         |                 |              | Maximum   | 4.6            | 4.5       | 5.3   | 5.4   | 4.6   | 4.7   | 5.4     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Albumin (g/dL)          | 4-5.1           | Screen     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 4.47           | 4.58      | 4.57  | 4.42  | 4.73  | 4.58  | 4.58    |
|                         |                 |            | SD        | 0.330          | 0.319     | 0.225 | 0.248 | 0.082 | 0.172 | 0.231   |
|                         |                 |            | Minimum   | 3.9            | 4.2       | 4.3   | 4.1   | 4.6   | 4.3   | 4.1     |
|                         |                 |            | Median    | 4.50           | 4.65      | 4.60  | 4.45  | 4.75  | 4.60  | 4.60    |
|                         |                 |            | Maximum   | 5.0            | 4.9       | 4.8   | 4.8   | 4.8   | 4.8   | 4.9     |
|                         |                 | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 4.49           | 4.53      | 4.47  | 4.68  | 4.78  | 4.47  | 4.59    |
|                         |                 |            | SD        | 0.296          | 0.175     | 0.242 | 0.376 | 0.117 | 0.266 | 0.266   |
|                         |                 |            | Minimum   | 3.9            | 4.3       | 4.2   | 4.2   | 4.6   | 4.2   | 4.2     |
|                         |                 |            | Median    | 4.45           | 4.55      | 4.40  | 4.65  | 4.80  | 4.45  | 4.60    |
|                         |                 |            | Maximum   | 5.0            | 4.8       | 4.8   | 5.1   | 4.9   | 4.9   | 5.1     |
|                         |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 4.33           | 4.45      | 4.37  | 4.50  | 4.57  | 4.28  | 4.43    |
|                         |                 |            | SD        | 0.236          | 0.295     | 0.327 | 0.126 | 0.103 | 0.343 | 0.262   |
|                         |                 |            | Minimum   | 3.8            | 4.0       | 4.0   | 4.3   | 4.4   | 3.8   | 3.8     |
|                         |                 |            | Median    | 4.40           | 4.55      | 4.40  | 4.55  | 4.60  | 4.25  | 4.50    |
|                         |                 |            | Maximum   | 4.6            | 4.8       | 4.8   | 4.6   | 4.7   | 4.8   | 4.8     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

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Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |        |        |        |        | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|--------|--------|--------|--------|---------|
|                         |                 |              |           |                | A         | B      | C      | D      | E      |         |
| Albumin (g/dL)          | 4-5.1           | Day 3        | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                         |                 |              | Mean      | 4.59           | 4.57      | 4.67   | 4.70   | 4.68   | 4.53   | 4.63    |
|                         |                 |              | SD        | 0.328          | 0.339     | 0.288  | 0.253  | 0.232  | 0.288  | 0.271   |
|                         |                 |              | Minimum   | 4.0            | 4.0       | 4.3    | 4.4    | 4.4    | 4.2    | 4.0     |
|                         |                 |              | Median    | 4.60           | 4.65      | 4.65   | 4.65   | 4.65   | 4.50   | 4.60    |
|                         |                 |              | Maximum   | 5.3            | 5.0       | 5.1    | 5.0    | 5.0    | 5.0    | 5.1     |
|                         |                 | End of Study | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                         |                 |              | Mean      | 4.45           | 4.53      | 4.40   | 4.63   | 4.63   | 4.57   | 4.55    |
|                         |                 |              | SD        | 0.310          | 0.333     | 0.310  | 0.207  | 0.234  | 0.163  | 0.254   |
|                         |                 |              | Minimum   | 4.0            | 4.1       | 4.1    | 4.4    | 4.3    | 4.4    | 4.1     |
|                         |                 |              | Median    | 4.45           | 4.60      | 4.35   | 4.65   | 4.65   | 4.55   | 4.60    |
|                         |                 |              | Maximum   | 5.0            | 5.0       | 4.8    | 4.9    | 4.9    | 4.8    | 5.0     |
| Creatinine (mg/dL)      | 0.44-1.22 #     | Screen       | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                         |                 |              | Mean      | 0.945          | 1.010     | 0.782  | 0.907  | 0.907  | 0.942  | 0.909   |
|                         |                 |              | SD        | 0.2056         | 0.1193    | 0.2227 | 0.1199 | 0.1770 | 0.1638 | 0.1709  |
|                         |                 |              | Minimum   | 0.58           | 0.89      | 0.52   | 0.80   | 0.60   | 0.66   | 0.52    |
|                         |                 |              | Median    | 0.970          | 0.955     | 0.815  | 0.870  | 0.935  | 0.960  | 0.935   |
|                         |                 |              | Maximum   | 1.29           | 1.18      | 1.08   | 1.11   | 1.10   | 1.15   | 1.18    |

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Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

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Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |        |        |        |        | Overall |
|-------------------------|-----------------|------------|-----------|----------------|-----------|--------|--------|--------|--------|---------|
|                         |                 |            |           |                | A         | B      | C      | D      | E      |         |
| Creatinine (mg/dL)      | 0.44-1.22       | # Baseline | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                         |                 |            | Mean      | 0.937          | 0.993     | 0.805  | 0.903  | 0.942  | 1.010  | 0.931   |
|                         |                 |            | SD        | 0.2049         | 0.1111    | 0.2231 | 0.1347 | 0.1699 | 0.1744 | 0.1721  |
|                         |                 |            | Minimum   | 0.54           | 0.87      | 0.52   | 0.77   | 0.63   | 0.72   | 0.52    |
|                         |                 |            | Median    | 0.985          | 0.975     | 0.820  | 0.895  | 0.965  | 1.040  | 0.950   |
|                         |                 |            | Maximum   | 1.20           | 1.13      | 1.14   | 1.06   | 1.14   | 1.16   | 1.16    |
|                         |                 | Day 2      | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                         |                 |            | Mean      | 0.974          | 1.038     | 0.787  | 0.852  | 0.933  | 0.993  | 0.921   |
|                         |                 |            | SD        | 0.2413         | 0.1430    | 0.2347 | 0.1372 | 0.1968 | 0.1637 | 0.1904  |
|                         |                 |            | Minimum   | 0.60           | 0.87      | 0.51   | 0.69   | 0.63   | 0.70   | 0.51    |
|                         |                 |            | Median    | 1.010          | 1.005     | 0.820  | 0.840  | 0.995  | 1.010  | 0.975   |
|                         |                 |            | Maximum   | 1.40           | 1.26      | 1.05   | 1.02   | 1.16   | 1.18   | 1.26    |
|                         |                 | Day 3      | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                         |                 |            | Mean      | 0.930          | 1.033     | 0.770  | 0.813  | 0.913  | 0.987  | 0.903   |
|                         |                 |            | SD        | 0.2238         | 0.1353    | 0.2104 | 0.1337 | 0.1802 | 0.2112 | 0.1936  |
|                         |                 |            | Minimum   | 0.55           | 0.86      | 0.52   | 0.69   | 0.61   | 0.67   | 0.52    |
|                         |                 |            | Median    | 0.955          | 1.045     | 0.810  | 0.770  | 0.980  | 1.000  | 0.935   |
|                         |                 |            | Maximum   | 1.24           | 1.20      | 1.00   | 1.04   | 1.10   | 1.30   | 1.30    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

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Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point     | Statistic | Pooled Placebo | Treatment |        |        |        |        | Overall |
|-------------------------|-----------------|----------------|-----------|----------------|-----------|--------|--------|--------|--------|---------|
|                         |                 |                |           |                | A         | B      | C      | D      | E      |         |
| Creatinine (mg/dL)      | 0.44-1.22       | # End of Study | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                         |                 |                | Mean      | 0.913          | 1.005     | 0.845  | 0.862  | 0.908  | 1.028  | 0.930   |
|                         |                 |                | SD        | 0.2195         | 0.1719    | 0.2696 | 0.0913 | 0.1629 | 0.1844 | 0.1877  |
|                         |                 |                | Minimum   | 0.51           | 0.69      | 0.52   | 0.77   | 0.63   | 0.72   | 0.52    |
|                         |                 |                | Median    | 0.965          | 1.050     | 0.880  | 0.830  | 0.915  | 1.090  | 0.955   |
|                         |                 |                | Maximum   | 1.24           | 1.16      | 1.16   | 0.99   | 1.10   | 1.24   | 1.24    |
| Glucose (mg/dL)         | 75-108          | Screen         | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                         |                 |                | Mean      | 95.6           | 93.8      | 92.8   | 96.8   | 96.3   | 99.8   | 95.9    |
|                         |                 |                | SD        | 7.35           | 4.02      | 6.18   | 6.74   | 4.59   | 6.85   | 5.93    |
|                         |                 |                | Minimum   | 84             | 91        | 86     | 91     | 90     | 91     | 86      |
|                         |                 |                | Median    | 94.5           | 92.0      | 93.0   | 94.0   | 96.0   | 104.0  | 94.0    |
|                         |                 |                | Maximum   | 106            | 101       | 103    | 108    | 103    | 105    | 108     |
|                         |                 | Baseline       | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                         |                 |                | Mean      | 95.8           | 89.7      | 94.2   | 96.5   | 90.8   | 97.0   | 93.6    |
|                         |                 |                | SD        | 4.26           | 4.13      | 3.19   | 3.39   | 1.94   | 5.18   | 4.57    |
|                         |                 |                | Minimum   | 88             | 83        | 90     | 91     | 89     | 89     | 83      |
|                         |                 |                | Median    | 96.0           | 90.0      | 94.5   | 97.0   | 90.5   | 97.0   | 93.5    |
|                         |                 |                | Maximum   | 103            | 94        | 97     | 101    | 94     | 104    | 104     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |      |       |       |       | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|------|-------|-------|-------|---------|
|                         |                 |              |           |                | A         | B    | C     | D     | E     |         |
| Glucose (mg/dL)         | 75-108          | Day 2        | n         | 10             | 6         | 6    | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 98.1           | 96.0      | 94.7 | 96.3  | 97.3  | 96.3  | 96.1    |
|                         |                 |              | SD        | 5.20           | 2.37      | 6.25 | 5.57  | 5.24  | 5.72  | 4.92    |
|                         |                 |              | Minimum   | 90             | 93        | 88   | 90    | 90    | 89    | 88      |
|                         |                 |              | Median    | 98.0           | 96.0      | 92.5 | 96.5  | 97.5  | 96.5  | 96.5    |
|                         |                 |              | Maximum   | 105            | 99        | 106  | 105   | 103   | 104   | 106     |
|                         |                 | Day 3        | n         | 10             | 6         | 6    | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 97.8           | 94.3      | 93.7 | 97.8  | 96.8  | 94.8  | 95.5    |
|                         |                 |              | SD        | 6.88           | 4.80      | 6.86 | 5.67  | 4.71  | 7.65  | 5.84    |
|                         |                 |              | Minimum   | 88             | 87        | 85   | 93    | 92    | 85    | 85      |
|                         |                 |              | Median    | 97.0           | 95.5      | 93.5 | 95.0  | 95.5  | 95.5  | 95.0    |
|                         |                 |              | Maximum   | 110            | 99        | 105  | 106   | 104   | 103   | 106     |
|                         |                 | End of Study | n         | 10             | 6         | 6    | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 103.7          | 100.8     | 98.5 | 103.8 | 102.3 | 93.5  | 99.8    |
|                         |                 |              | SD        | 6.95           | 9.66      | 6.63 | 3.76  | 5.35  | 14.60 | 9.01    |
|                         |                 |              | Minimum   | 95             | 89        | 91   | 98    | 93    | 70    | 70      |
|                         |                 |              | Median    | 101.5          | 99.5      | 97.0 | 104.5 | 103.0 | 92.5  | 102.0   |
|                         |                 |              | Maximum   | 118            | 118       | 109  | 107   | 109   | 113   | 118     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units)     | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-----------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                             |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Alkaline Phosphatase (IU/L) | 41-132 #        | Screen     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                             |                 |            | Mean      | 79.7           | 79.8      | 80.5  | 75.5  | 85.0  | 73.0  | 78.8    |
|                             |                 |            | SD        | 12.05          | 20.10     | 10.95 | 19.04 | 21.03 | 11.76 | 16.46   |
|                             |                 |            | Minimum   | 58             | 57        | 66    | 48    | 60    | 58    | 48      |
|                             |                 |            | Median    | 82.0           | 81.5      | 78.5  | 75.5  | 84.5  | 73.5  | 77.0    |
|                             |                 |            | Maximum   | 92             | 109       | 94    | 105   | 112   | 88    | 112     |
|                             |                 | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                             |                 |            | Mean      | 74.5           | 79.8      | 73.8  | 72.0  | 85.8  | 75.3  | 77.4    |
|                             |                 |            | SD        | 10.76          | 20.45     | 10.32 | 20.91 | 20.82 | 11.71 | 17.02   |
|                             |                 |            | Minimum   | 55             | 58        | 64    | 48    | 59    | 56    | 48      |
|                             |                 |            | Median    | 76.0           | 83.0      | 71.0  | 70.0  | 85.5  | 78.0  | 75.0    |
|                             |                 |            | Maximum   | 91             | 113       | 92    | 108   | 110   | 88    | 113     |
|                             |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                             |                 |            | Mean      | 68.9           | 82.0      | 74.3  | 67.7  | 83.8  | 71.2  | 75.8    |
|                             |                 |            | SD        | 10.45          | 15.01     | 9.69  | 19.43 | 17.90 | 13.08 | 15.64   |
|                             |                 |            | Minimum   | 53             | 64        | 64    | 42    | 61    | 55    | 42      |
|                             |                 |            | Median    | 70.0           | 85.5      | 72.5  | 64.5  | 82.5  | 67.5  | 72.5    |
|                             |                 |            | Maximum   | 86             | 102       | 91    | 101   | 108   | 91    | 108     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units)         | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|---------------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                                 |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Alkaline Phosphatase (IU/L)     | 41-132 #        | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                 |                 |              | Mean      | 71.8           | 80.8      | 81.8  | 69.5  | 84.7  | 72.0  | 77.8    |
|                                 |                 |              | SD        | 13.21          | 13.91     | 11.25 | 19.42 | 14.29 | 11.56 | 14.65   |
|                                 |                 |              | Minimum   | 51             | 61        | 66    | 45    | 65    | 53    | 45      |
|                                 |                 |              | Median    | 72.5           | 81.5      | 83.0  | 69.0  | 83.5  | 71.0  | 76.5    |
|                                 |                 |              | Maximum   | 91             | 100       | 98    | 103   | 101   | 86    | 103     |
|                                 |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                 |                 |              | Mean      | 74.8           | 80.2      | 81.3  | 71.2  | 83.7  | 75.0  | 78.3    |
|                                 |                 |              | SD        | 13.22          | 16.19     | 11.99 | 21.42 | 19.76 | 18.32 | 17.19   |
|                                 |                 |              | Minimum   | 50             | 58        | 69    | 44    | 61    | 50    | 44      |
|                                 |                 |              | Median    | 77.5           | 80.0      | 80.0  | 69.5  | 85.0  | 81.5  | 78.5    |
|                                 |                 |              | Maximum   | 91             | 106       | 103   | 108   | 108   | 95    | 108     |
| Alanine Aminotransferase (IU/L) | 10-60           | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                 |                 |              | Mean      | 23.0           | 22.5      | 22.7  | 22.8  | 23.0  | 24.2  | 23.0    |
|                                 |                 |              | SD        | 10.85          | 11.90     | 14.95 | 12.42 | 11.49 | 5.74  | 10.88   |
|                                 |                 |              | Minimum   | 9              | 12        | 11    | 10    | 12    | 17    | 10      |
|                                 |                 |              | Median    | 22.5           | 17.5      | 18.5  | 21.0  | 18.5  | 24.0  | 19.0    |
|                                 |                 |              | Maximum   | 38             | 42        | 51    | 39    | 43    | 32    | 51      |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units)         | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |      | Overall |
|---------------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|------|---------|
|                                 |                 |            |           |                | A         | B     | C     | D     | E    |         |
| Alanine Aminotransferase (IU/L) | 10-60           | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6    | 30      |
|                                 |                 |            | Mean      | 22.3           | 19.7      | 20.5  | 19.7  | 24.8  | 22.8 | 21.5    |
|                                 |                 |            | SD        | 11.06          | 10.61     | 13.31 | 12.06 | 15.38 | 5.34 | 11.18   |
|                                 |                 |            | Minimum   | 9              | 9         | 10    | 10    | 13    | 13   | 9       |
|                                 |                 |            | Median    | 17.5           | 17.5      | 16.5  | 14.0  | 19.0  | 24.0 | 20.5    |
|                                 |                 |            | Maximum   | 46             | 37        | 45    | 41    | 55    | 29   | 55      |
|                                 |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6    | 30      |
|                                 |                 |            | Mean      | 19.8           | 21.5      | 18.8  | 19.0  | 24.0  | 20.7 | 20.8    |
|                                 |                 |            | SD        | 9.90           | 14.60     | 12.32 | 13.27 | 18.30 | 6.98 | 12.77   |
|                                 |                 |            | Minimum   | 11             | 8         | 10    | 10    | 12    | 12   | 8       |
|                                 |                 |            | Median    | 17.0           | 15.5      | 15.0  | 11.5  | 16.0  | 20.0 | 17.0    |
|                                 |                 |            | Maximum   | 43             | 44        | 42    | 41    | 60    | 33   | 60      |
|                                 |                 | Day 3      | n         | 10             | 6         | 6     | 6     | 6     | 6    | 30      |
|                                 |                 |            | Mean      | 21.3           | 24.7      | 19.5  | 20.5  | 25.3  | 22.2 | 22.4    |
|                                 |                 |            | SD        | 12.70          | 18.67     | 11.98 | 15.16 | 18.81 | 8.52 | 14.26   |
|                                 |                 |            | Minimum   | 11             | 10        | 10    | 10    | 12    | 14   | 10      |
|                                 |                 |            | Median    | 18.0           | 15.5      | 15.5  | 12.0  | 17.5  | 20.5 | 17.5    |
|                                 |                 |            | Maximum   | 53             | 56        | 41    | 45    | 61    | 38   | 61      |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units)           | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |      | Overall |
|-----------------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|------|---------|
|                                   |                 |              |           |                | A         | B     | C     | D     | E    |         |
| Alanine Aminotransferase (IU/L)   | 10-60           | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6    | 30      |
|                                   |                 |              | Mean      | 20.2           | 21.8      | 20.7  | 23.7  | 20.3  | 22.2 | 21.7    |
|                                   |                 |              | SD        | 10.10          | 15.22     | 12.79 | 18.75 | 9.52  | 6.01 | 12.33   |
|                                   |                 |              | Minimum   | 10             | 11        | 10    | 10    | 12    | 15   | 10      |
|                                   |                 |              | Median    | 17.0           | 15.0      | 16.5  | 13.5  | 16.5  | 23.5 | 16.0    |
|                                   |                 |              | Maximum   | 41             | 51        | 45    | 52    | 38    | 29   | 52      |
| Aspartate Aminotransferase (IU/L) | 14-47           | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6    | 30      |
|                                   |                 |              | Mean      | 21.2           | 19.8      | 21.5  | 22.3  | 20.7  | 21.0 | 21.1    |
|                                   |                 |              | SD        | 7.69           | 4.40      | 7.29  | 7.34  | 3.33  | 6.10 | 5.55    |
|                                   |                 |              | Minimum   | 15             | 13        | 13    | 11    | 17    | 15   | 11      |
|                                   |                 |              | Median    | 20.0           | 19.0      | 21.0  | 24.5  | 20.0  | 19.5 | 20.0    |
|                                   |                 |              | Maximum   | 41             | 26        | 33    | 30    | 26    | 32   | 33      |
|                                   |                 | Baseline     | n         | 10             | 6         | 6     | 6     | 6     | 6    | 30      |
|                                   |                 |              | Mean      | 21.8           | 20.3      | 20.2  | 21.0  | 24.3  | 21.8 | 21.5    |
|                                   |                 |              | SD        | 6.11           | 4.27      | 6.43  | 6.84  | 11.27 | 5.15 | 6.87    |
|                                   |                 |              | Minimum   | 13             | 14        | 13    | 11    | 17    | 15   | 11      |
|                                   |                 |              | Median    | 21.5           | 21.0      | 18.5  | 22.0  | 21.0  | 22.5 | 21.0    |
|                                   |                 |              | Maximum   | 35             | 26        | 31    | 29    | 47    | 29   | 47      |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units)           | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |      |       |       |      | Overall |
|-----------------------------------|-----------------|--------------|-----------|----------------|-----------|------|-------|-------|------|---------|
|                                   |                 |              |           |                | A         | B    | C     | D     | E    |         |
| Aspartate Aminotransferase (IU/L) | 14-47           | Day 2        | n         | 10             | 6         | 6    | 6     | 6     | 6    | 30      |
|                                   |                 |              | Mean      | 17.7           | 20.5      | 17.7 | 18.0  | 21.3  | 18.0 | 19.1    |
|                                   |                 |              | SD        | 6.24           | 8.38      | 6.44 | 6.87  | 9.33  | 4.69 | 6.97    |
|                                   |                 |              | Minimum   | 11             | 14        | 10   | 10    | 15    | 12   | 10      |
|                                   |                 |              | Median    | 16.0           | 19.0      | 16.0 | 17.0  | 18.5  | 18.5 | 18.5    |
|                                   |                 |              | Maximum   | 32             | 37        | 29   | 26    | 40    | 24   | 40      |
|                                   |                 | Day 3        | n         | 10             | 6         | 6    | 6     | 6     | 6    | 30      |
|                                   |                 |              | Mean      | 19.3           | 21.7      | 18.8 | 19.8  | 22.7  | 19.0 | 20.4    |
|                                   |                 |              | SD        | 6.65           | 9.46      | 5.98 | 7.83  | 10.03 | 5.93 | 7.61    |
|                                   |                 |              | Minimum   | 14             | 14        | 12   | 11    | 15    | 13   | 11      |
|                                   |                 |              | Median    | 17.0           | 20.0      | 17.5 | 18.0  | 19.5  | 18.5 | 18.5    |
|                                   |                 |              | Maximum   | 33             | 40        | 29   | 30    | 42    | 28   | 42      |
|                                   |                 | End of Study | n         | 10             | 6         | 6    | 6     | 6     | 6    | 30      |
|                                   |                 |              | Mean      | 20.1           | 19.8      | 20.3 | 31.5  | 19.3  | 22.3 | 22.7    |
|                                   |                 |              | SD        | 7.94           | 4.71      | 7.06 | 28.99 | 3.44  | 7.71 | 13.81   |
|                                   |                 |              | Minimum   | 15             | 14        | 12   | 12    | 14    | 14   | 12      |
|                                   |                 |              | Median    | 17.5           | 21.5      | 19.0 | 20.5  | 19.0  | 21.0 | 20.0    |
|                                   |                 |              | Maximum   | 41             | 25        | 33   | 89    | 23    | 32   | 89      |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point    | Statistic | Pooled Placebo | Treatment |      |      |       |      | Overall |
|-------------------------|-----------------|---------------|-----------|----------------|-----------|------|------|-------|------|---------|
|                         |                 |               |           |                | A         | B    | C    | D     | E    |         |
| GGT (IU/L)              | 6-74            | Screen        | n         | 10             | 6         | 6    | 6    | 6     | 6    | 30      |
|                         |                 |               | Mean      | 20.5           | 26.7      | 16.8 | 18.3 | 26.3  | 16.7 | 21.0    |
|                         |                 |               | SD        | 11.60          | 17.14     | 6.85 | 7.34 | 14.80 | 3.88 | 11.40   |
|                         |                 |               | Minimum   | 8              | 14        | 9    | 9    | 7     | 10   | 7       |
|                         |                 |               | Median    | 17.0           | 17.0      | 16.0 | 19.0 | 23.5  | 18.5 | 18.5    |
|                         |                 |               | Maximum   | 39             | 52        | 27   | 27   | 47    | 20   | 52      |
|                         |                 | Baseline      | n         | 10             | 6         | 6    | 6    | 6     | 6    | 30      |
|                         |                 |               | Mean      | 18.5           | 28.2      | 14.8 | 17.5 | 27.3  | 15.3 | 20.6    |
|                         |                 |               | SD        | 7.79           | 18.23     | 5.64 | 6.95 | 14.73 | 4.23 | 12.14   |
|                         |                 |               | Minimum   | 8              | 11        | 8    | 8    | 9     | 9    | 8       |
|                         |                 |               | Median    | 18.5           | 21.0      | 13.5 | 19.0 | 23.5  | 17.5 | 18.5    |
|                         |                 |               | Maximum   | 29             | 54        | 22   | 27   | 50    | 19   | 54      |
|                         |                 | Day 1, Hour 4 | n         | 10             | 6         | 6    | 6    | 6     | 6    | 30      |
|                         |                 |               | Mean      | 17.3           | 28.0      | 14.5 | 16.3 | 25.2  | 14.5 | 19.7    |
|                         |                 |               | SD        | 7.47           | 20.39     | 4.55 | 7.09 | 14.08 | 3.67 | 12.42   |
|                         |                 |               | Minimum   | 7              | 11        | 9    | 7    | 9     | 9    | 7       |
|                         |                 |               | Median    | 17.5           | 18.0      | 13.0 | 17.5 | 21.5  | 16.0 | 17.0    |
|                         |                 |               | Maximum   | 28             | 62        | 20   | 27   | 48    | 18   | 62      |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point     | Statistic | Pooled Placebo | Treatment |      |      |       |      | Overall |
|-------------------------|-----------------|----------------|-----------|----------------|-----------|------|------|-------|------|---------|
|                         |                 |                |           |                | A         | B    | C    | D     | E    |         |
| GGT (IU/L)              | 6-74            | Day 1, Hour 12 | n         | 10             | 6         | 6    | 6    | 6     | 6    | 30      |
|                         |                 |                | Mean      | 16.4           | 27.3      | 13.8 | 16.0 | 23.8  | 14.0 | 19.0    |
|                         |                 |                | SD        | 7.09           | 21.01     | 4.58 | 7.04 | 14.16 | 3.85 | 12.54   |
|                         |                 |                | Minimum   | 7              | 10        | 9    | 7    | 7     | 9    | 7       |
|                         |                 |                | Median    | 16.0           | 17.5      | 12.0 | 16.5 | 20.5  | 15.0 | 16.0    |
|                         |                 |                | Maximum   | 28             | 64        | 20   | 27   | 48    | 19   | 64      |
|                         |                 | Day 2          | n         | 10             | 6         | 6    | 6    | 6     | 6    | 30      |
|                         |                 |                | Mean      | 17.3           | 29.5      | 14.2 | 17.7 | 24.5  | 14.5 | 20.1    |
|                         |                 |                | SD        | 7.60           | 22.14     | 4.88 | 7.53 | 13.28 | 3.56 | 12.97   |
|                         |                 |                | Minimum   | 8              | 12        | 8    | 9    | 8     | 9    | 8       |
|                         |                 |                | Median    | 16.5           | 19.5      | 12.5 | 17.5 | 21.5  | 16.5 | 17.0    |
|                         |                 |                | Maximum   | 31             | 68        | 21   | 30   | 46    | 17   | 68      |
|                         |                 | Day 3          | n         | 10             | 6         | 6    | 6    | 6     | 6    | 30      |
|                         |                 |                | Mean      | 17.8           | 31.5      | 15.7 | 19.0 | 25.5  | 14.8 | 21.3    |
|                         |                 |                | SD        | 8.02           | 25.97     | 5.72 | 8.49 | 13.14 | 3.43 | 14.41   |
|                         |                 |                | Minimum   | 8              | 11        | 9    | 9    | 8     | 10   | 8       |
|                         |                 |                | Median    | 17.5           | 20.0      | 14.0 | 19.0 | 23.5  | 16.5 | 18.0    |
|                         |                 |                | Maximum   | 34             | 78        | 24   | 32   | 46    | 18   | 78      |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |        | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|--------|---------|
|                         |                 |              |           |                | A         | B     | C     | D     | E      |         |
| GGT (IU/L)              | 6-74            | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6      | 30      |
|                         |                 |              | Mean      | 18.0           | 26.7      | 14.3  | 18.3  | 24.7  | 13.7   | 19.5    |
|                         |                 |              | SD        | 8.52           | 16.88     | 5.47  | 8.80  | 14.72 | 3.20   | 11.65   |
|                         |                 |              | Minimum   | 8              | 11        | 9     | 8     | 8     | 9      | 8       |
|                         |                 |              | Median    | 15.5           | 18.5      | 12.5  | 18.5  | 19.5  | 14.5   | 16.5    |
|                         |                 |              | Maximum   | 35             | 51        | 22    | 29    | 47    | 17     | 51      |
| Creatine Kinase (IU/L)  | 34-329 #        | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6      | 30      |
|                         |                 |              | Mean      | 127.1          | 121.8     | 97.3  | 147.8 | 116.0 | 131.8  | 123.0   |
|                         |                 |              | SD        | 49.23          | 42.54     | 27.04 | 82.63 | 37.18 | 71.28  | 54.95   |
|                         |                 |              | Minimum   | 69             | 84        | 50    | 73    | 62    | 64     | 50      |
|                         |                 |              | Median    | 112.5          | 110.5     | 106.0 | 131.5 | 126.5 | 112.5  | 112.0   |
|                         |                 |              | Maximum   | 193            | 205       | 120   | 298   | 153   | 256    | 298     |
|                         |                 | Baseline     | n         | 10             | 6         | 6     | 6     | 6     | 6      | 30      |
|                         |                 |              | Mean      | 115.2          | 122.8     | 107.0 | 130.3 | 129.2 | 206.2  | 139.1   |
|                         |                 |              | SD        | 59.98          | 38.62     | 39.69 | 59.38 | 51.58 | 129.04 | 75.51   |
|                         |                 |              | Minimum   | 63             | 72        | 54    | 83    | 53    | 65     | 53      |
|                         |                 |              | Median    | 93.0           | 122.0     | 123.5 | 116.0 | 133.5 | 189.0  | 125.5   |
|                         |                 |              | Maximum   | 241            | 169       | 145   | 246   | 203   | 368    | 368     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point     | Statistic | Pooled Placebo | Treatment |       |       |       |        | Overall |
|-------------------------|-----------------|----------------|-----------|----------------|-----------|-------|-------|-------|--------|---------|
|                         |                 |                |           |                | A         | B     | C     | D     | E      |         |
| Creatine Kinase (IU/L)  | 34-329 #        | Day 1, Hour 4  | n         | 10             | 6         | 6     | 6     | 6     | 6      | 30      |
|                         |                 |                | Mean      | 95.3           | 91.2      | 82.7  | 94.5  | 99.8  | 158.3  | 105.3   |
|                         |                 |                | SD        | 35.10          | 32.10     | 30.66 | 27.06 | 33.09 | 107.42 | 58.34   |
|                         |                 |                | Minimum   | 56             | 56        | 42    | 59    | 47    | 49     | 42      |
|                         |                 |                | Median    | 86.5           | 92.5      | 85.0  | 95.5  | 104.5 | 135.5  | 98.5    |
|                         |                 |                | Maximum   | 169            | 141       | 126   | 132   | 137   | 292    | 292     |
|                         |                 | Day 1, Hour 12 | n         | 10             | 6         | 6     | 6     | 6     | 6      | 30      |
|                         |                 |                | Mean      | 87.2           | 83.8      | 77.7  | 92.0  | 95.5  | 139.5  | 97.7    |
|                         |                 |                | SD        | 28.65          | 28.63     | 26.21 | 24.35 | 31.80 | 89.86  | 49.20   |
|                         |                 |                | Minimum   | 57             | 52        | 39    | 58    | 46    | 47     | 39      |
|                         |                 |                | Median    | 80.0           | 83.5      | 81.5  | 102.5 | 97.0  | 120.0  | 91.0    |
|                         |                 |                | Maximum   | 140            | 130       | 105   | 115   | 133   | 255    | 255     |
|                         |                 | Day 2          | n         | 10             | 6         | 6     | 6     | 6     | 6      | 30      |
|                         |                 |                | Mean      | 75.5           | 77.2      | 67.5  | 82.2  | 91.7  | 118.3  | 87.4    |
|                         |                 |                | SD        | 19.26          | 28.34     | 21.27 | 20.41 | 37.22 | 75.35  | 42.63   |
|                         |                 |                | Minimum   | 55             | 48        | 35    | 52    | 46    | 40     | 35      |
|                         |                 |                | Median    | 70.5           | 77.5      | 69.0  | 91.5  | 90.5  | 98.5   | 82.0    |
|                         |                 |                | Maximum   | 106            | 126       | 89    | 100   | 150   | 210    | 210     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units)      | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |        |        |        | Overall |
|------------------------------|-----------------|--------------|-----------|----------------|-----------|-------|--------|--------|--------|---------|
|                              |                 |              |           |                | A         | B     | C      | D      | E      |         |
| Creatine Kinase (IU/L)       | 34-329 #        | Day 3        | n         | 10             | 6         | 6     | 6      | 6      | 6      | 30      |
|                              |                 |              | Mean      | 75.3           | 73.0      | 68.3  | 86.0   | 85.5   | 114.8  | 85.5    |
|                              |                 |              | SD        | 18.57          | 26.23     | 19.58 | 23.78  | 36.21  | 69.50  | 40.16   |
|                              |                 |              | Minimum   | 53             | 44        | 36    | 53     | 40     | 40     | 36      |
|                              |                 |              | Median    | 72.0           | 75.5      | 71.0  | 96.0   | 81.5   | 94.5   | 78.0    |
|                              |                 |              | Maximum   | 112            | 116       | 89    | 112    | 147    | 200    | 200     |
|                              |                 | End of Study | n         | 10             | 6         | 6     | 6      | 6      | 6      | 30      |
|                              |                 |              | Mean      | 122.3          | 108.3     | 100.8 | 409.0* | 144.8  | 266.0  | 205.8   |
|                              |                 |              | SD        | 62.77          | 25.11     | 37.27 | 762.12 | 101.62 | 358.38 | 372.45  |
|                              |                 |              | Minimum   | 62             | 73        | 45    | 68     | 53     | 48     | 45      |
|                              |                 |              | Median    | 100.5          | 114.5     | 107.5 | 102.5  | 120.0  | 115.0  | 114.5   |
|                              |                 |              | Maximum   | 215            | 142       | 137   | 1964   | 345    | 986    | 1964    |
| Lactate Dehydrogenase (IU/L) | 125-248         | Screen       | n         | 10             | 6         | 6     | 6      | 6      | 6      | 30      |
|                              |                 |              | Mean      | 166.2          | 159.5     | 157.3 | 170.5  | 172.3  | 168.3  | 165.6   |
|                              |                 |              | SD        | 27.81          | 18.79     | 20.10 | 14.60  | 18.10  | 24.15  | 19.03   |
|                              |                 |              | Minimum   | 130            | 134       | 134   | 153    | 142    | 137    | 134     |
|                              |                 |              | Median    | 162.5          | 156.5     | 153.0 | 166.0  | 174.0  | 171.5  | 166.0   |
|                              |                 |              | Maximum   | 209            | 181       | 185   | 194    | 196    | 194    | 196     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units)      | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|------------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                              |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Lactate Dehydrogenase (IU/L) | 125-248         | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |            | Mean      | 165.8          | 166.5     | 156.5 | 162.5 | 177.3 | 174.7 | 167.5   |
|                              |                 |            | SD        | 30.13          | 19.10     | 15.33 | 7.92  | 30.64 | 22.68 | 20.64   |
|                              |                 |            | Minimum   | 125            | 131       | 145   | 153   | 144   | 149   | 131     |
|                              |                 |            | Median    | 163.0          | 170.0     | 152.5 | 160.0 | 171.0 | 178.0 | 165.0   |
|                              |                 |            | Maximum   | 212            | 187       | 185   | 173   | 231   | 201   | 231     |
|                              |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |            | Mean      | 149.4          | 150.7     | 142.5 | 142.3 | 155.7 | 148.0 | 147.8   |
|                              |                 |            | SD        | 22.99          | 14.00     | 28.99 | 6.86  | 20.16 | 15.07 | 17.96   |
|                              |                 |            | Minimum   | 115            | 124       | 120   | 134   | 137   | 127   | 120     |
|                              |                 |            | Median    | 148.0          | 155.0     | 130.5 | 143.0 | 149.5 | 155.0 | 147.5   |
|                              |                 |            | Maximum   | 187            | 162       | 198   | 152   | 194   | 163   | 198     |
|                              |                 | Day 3      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |            | Mean      | 156.6          | 158.0     | 151.0 | 153.7 | 161.3 | 156.7 | 156.1   |
|                              |                 |            | SD        | 26.18          | 15.17     | 20.77 | 8.71  | 29.17 | 18.33 | 18.57   |
|                              |                 |            | Minimum   | 120            | 133       | 125   | 144   | 139   | 128   | 125     |
|                              |                 |            | Median    | 155.0          | 160.0     | 145.0 | 152.0 | 153.5 | 162.5 | 155.0   |
|                              |                 |            | Maximum   | 207            | 173       | 182   | 167   | 218   | 178   | 218     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units)      | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|------------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                              |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Lactate Dehydrogenase (IU/L) | 125-248         | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |              | Mean      | 163.0          | 164.3     | 155.8 | 167.5 | 169.3 | 163.5 | 164.1   |
|                              |                 |              | SD        | 28.13          | 25.02     | 17.47 | 19.73 | 22.92 | 26.79 | 21.55   |
|                              |                 |              | Minimum   | 119            | 124       | 142   | 150   | 140   | 128   | 124     |
|                              |                 |              | Median    | 156.0          | 162.0     | 147.0 | 163.0 | 170.0 | 167.0 | 162.0   |
|                              |                 |              | Maximum   | 205            | 201       | 182   | 204   | 203   | 199   | 204     |
| C Reactive Protein (mg/L)    | 0-15            | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |              | Mean      | 2.21           | 1.45      | 3.08  | 1.47  | 1.32  | 0.88  | 1.64    |
|                              |                 |              | SD        | 1.806          | 0.873     | 2.715 | 1.145 | 0.776 | 0.605 | 1.543   |
|                              |                 |              | Minimum   | 0.4            | 0.9       | 0.7   | 0.5   | 0.4   | 0.5   | 0.4     |
|                              |                 |              | Median    | 1.85           | 1.15      | 2.05  | 1.10  | 1.20  | 0.65  | 1.05    |
|                              |                 |              | Maximum   | 5.8            | 3.2       | 6.6   | 3.5   | 2.5   | 2.1   | 6.6     |
|                              |                 | Baseline     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |              | Mean      | 1.07           | 1.15      | 3.00  | 1.03  | 1.20  | 1.60  | 1.60    |
|                              |                 |              | SD        | 0.663          | 0.547     | 2.382 | 0.459 | 0.888 | 1.647 | 1.489   |
|                              |                 |              | Minimum   | 0.5            | 0.6       | 0.5   | 0.5   | 0.3   | 0.5   | 0.3     |
|                              |                 |              | Median    | 0.75           | 1.05      | 2.85  | 0.90  | 0.85  | 0.85  | 1.00    |
|                              |                 |              | Maximum   | 2.5            | 2.1       | 6.3   | 1.8   | 2.8   | 4.7   | 6.3     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units)   | Reference Range | Time Point     | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|---------------------------|-----------------|----------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                           |                 |                |           |                | A         | B     | C     | D     | E     |         |
| C Reactive Protein (mg/L) | 0-15            | Day 1, Hour 4  | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                           |                 |                | Mean      | 1.07           | 1.02      | 2.82  | 1.00  | 1.35  | 1.57  | 1.55    |
|                           |                 |                | SD        | 0.770          | 0.343     | 2.407 | 0.576 | 1.097 | 1.801 | 1.518   |
|                           |                 |                | Minimum   | 0.5            | 0.6       | 0.8   | 0.5   | 0.4   | 0.5   | 0.4     |
|                           |                 |                | Median    | 0.75           | 0.95      | 2.10  | 0.80  | 0.80  | 0.95  | 0.95    |
|                           |                 |                | Maximum   | 2.6            | 1.5       | 6.8   | 2.0   | 2.8   | 5.2   | 6.8     |
|                           |                 | Day 1, Hour 12 | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                           |                 |                | Mean      | 1.11           | 1.03      | 2.70  | 1.07  | 1.48  | 1.53  | 1.56    |
|                           |                 |                | SD        | 0.775          | 0.367     | 2.285 | 0.622 | 1.278 | 1.772 | 1.480   |
|                           |                 |                | Minimum   | 0.4            | 0.6       | 0.8   | 0.5   | 0.3   | 0.5   | 0.3     |
|                           |                 |                | Median    | 0.80           | 1.00      | 2.00  | 0.85  | 0.85  | 0.95  | 1.00    |
|                           |                 |                | Maximum   | 2.5            | 1.5       | 6.6   | 2.1   | 3.3   | 5.1   | 6.6     |
|                           |                 | Day 2          | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                           |                 |                | Mean      | 1.09           | 1.07      | 2.58  | 1.03  | 1.48  | 1.32  | 1.50    |
|                           |                 |                | SD        | 0.719          | 0.413     | 2.267 | 0.596 | 1.240 | 1.338 | 1.373   |
|                           |                 |                | Minimum   | 0.4            | 0.6       | 0.8   | 0.4   | 0.3   | 0.5   | 0.3     |
|                           |                 |                | Median    | 0.80           | 1.05      | 1.80  | 0.85  | 0.90  | 0.90  | 1.00    |
|                           |                 |                | Maximum   | 2.5            | 1.7       | 6.5   | 1.9   | 3.1   | 4.0   | 6.5     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units)   | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|---------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                           |                 |              |           |                | A         | B     | C     | D     | E     |         |
| C Reactive Protein (mg/L) | 0-15            | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                           |                 |              | Mean      | 0.95           | 0.92      | 2.80  | 0.92  | 1.25  | 0.83  | 1.34    |
|                           |                 |              | SD        | 0.593          | 0.426     | 2.910 | 0.402 | 0.997 | 0.501 | 1.518   |
|                           |                 |              | Minimum   | 0.3            | 0.5       | 0.6   | 0.4   | 0.4   | 0.4   | 0.4     |
|                           |                 |              | Median    | 0.70           | 0.85      | 2.05  | 0.90  | 0.80  | 0.75  | 0.80    |
|                           |                 |              | Maximum   | 2.2            | 1.7       | 8.2   | 1.5   | 2.7   | 1.8   | 8.2     |
|                           |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                           |                 |              | Mean      | 1.22           | 1.95      | 2.87  | 1.17  | 2.15  | 0.82  | 1.79    |
|                           |                 |              | SD        | 0.818          | 2.036     | 2.710 | 0.356 | 2.497 | 0.286 | 1.908   |
|                           |                 |              | Minimum   | 0.4            | 0.7       | 0.6   | 0.8   | 0.4   | 0.5   | 0.4     |
|                           |                 |              | Median    | 0.95           | 0.95      | 1.75  | 1.05  | 1.30  | 0.80  | 0.90    |
|                           |                 |              | Maximum   | 3.0            | 5.9       | 6.8   | 1.7   | 7.1   | 1.3   | 7.1     |
| Troponin I (ug/L)         | 0-0.3           | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                           |                 |              | Mean      | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                           |                 |              | SD        | 0.000          | 0.000     | 0.000 | 0.000 | 0.000 | 0.000 | 0.000   |
|                           |                 |              | Minimum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |
|                           |                 |              | Median    | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                           |                 |              | Maximum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

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Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point     | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|----------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |                |           |                | A         | B     | C     | D     | E     |         |
| Troponin I (ug/L)       | 0-0.3           | Baseline       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |                | Mean      | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                         |                 |                | SD        | 0.000          | 0.000     | 0.000 | 0.000 | 0.000 | 0.000 | 0.000   |
|                         |                 |                | Minimum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |
|                         |                 |                | Median    | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                         |                 |                | Maximum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |
|                         |                 | Day 1, Hour 4  | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |                | Mean      | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                         |                 |                | SD        | 0.000          | 0.000     | 0.000 | 0.000 | 0.000 | 0.000 | 0.000   |
|                         |                 |                | Minimum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |
|                         |                 |                | Median    | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                         |                 |                | Maximum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |
|                         |                 | Day 1, Hour 12 | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |                | Mean      | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                         |                 |                | SD        | 0.000          | 0.000     | 0.000 | 0.000 | 0.000 | 0.000 | 0.000   |
|                         |                 |                | Minimum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |
|                         |                 |                | Median    | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                         |                 |                | Maximum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Troponin I (ug/L)       | 0-0.3           | Day 2        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                         |                 |              | SD        | 0.000          | 0.000     | 0.000 | 0.000 | 0.000 | 0.000 | 0.000   |
|                         |                 |              | Minimum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |
|                         |                 |              | Median    | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                         |                 |              | Maximum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |
|                         |                 | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                         |                 |              | SD        | 0.000          | 0.000     | 0.000 | 0.000 | 0.000 | 0.000 | 0.000   |
|                         |                 |              | Minimum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |
|                         |                 |              | Median    | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                         |                 |              | Maximum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |
|                         |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                         |                 |              | SD        | 0.000          | 0.000     | 0.000 | 0.000 | 0.000 | 0.000 | 0.000   |
|                         |                 |              | Minimum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |
|                         |                 |              | Median    | 0.30           | 0.30      | 0.30  | 0.30  | 0.30  | 0.30  | 0.30    |
|                         |                 |              | Maximum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.3   | 0.3     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |      |      |      |      | Overall |
|-------------------------|-----------------|------------|-----------|----------------|-----------|------|------|------|------|---------|
|                         |                 |            |           |                | A         | B    | C    | D    | E    |         |
| Urea Nitrogen (mg/dL)   | 6-21 #          | Screen     | n         | 10             | 6         | 6    | 6    | 6    | 6    | 30      |
|                         |                 |            | Mean      | 13.6           | 12.7      | 13.2 | 12.3 | 12.8 | 13.3 | 12.9    |
|                         |                 |            | SD        | 4.38           | 4.13      | 3.43 | 1.63 | 3.49 | 3.20 | 3.07    |
|                         |                 |            | Minimum   | 9              | 8         | 11   | 10   | 9    | 8    | 8       |
|                         |                 |            | Median    | 12.0           | 12.5      | 12.0 | 12.5 | 12.0 | 13.5 | 12.5    |
|                         |                 |            | Maximum   | 23             | 19        | 20   | 14   | 19   | 17   | 20      |
|                         |                 | Baseline   | n         | 10             | 6         | 6    | 6    | 6    | 6    | 30      |
|                         |                 |            | Mean      | 11.9           | 12.2      | 13.2 | 11.3 | 12.3 | 13.3 | 12.5    |
|                         |                 |            | SD        | 2.77           | 2.86      | 5.74 | 2.73 | 4.50 | 3.39 | 3.79    |
|                         |                 |            | Minimum   | 9              | 7         | 8    | 8    | 6    | 7    | 6       |
|                         |                 |            | Median    | 12.0           | 13.0      | 11.5 | 11.0 | 11.5 | 14.0 | 13.0    |
|                         |                 |            | Maximum   | 17             | 15        | 24   | 15   | 18   | 17   | 24      |
|                         |                 | Day 2      | n         | 10             | 6         | 6    | 6    | 6    | 6    | 30      |
|                         |                 |            | Mean      | 14.8           | 15.5      | 13.7 | 12.7 | 13.3 | 16.8 | 14.4    |
|                         |                 |            | SD        | 2.94           | 3.89      | 2.66 | 1.21 | 3.14 | 2.40 | 3.04    |
|                         |                 |            | Minimum   | 11             | 12        | 12   | 11   | 10   | 13   | 10      |
|                         |                 |            | Median    | 14.5           | 14.5      | 13.0 | 12.5 | 13.0 | 17.0 | 13.0    |
|                         |                 |            | Maximum   | 21             | 22        | 19   | 14   | 19   | 20   | 22      |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Urea Nitrogen (mg/dL)   | 6-21 #          | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 14.9           | 15.5      | 13.2  | 12.5  | 13.8  | 16.7  | 14.3    |
|                         |                 |              | SD        | 3.41           | 4.76      | 2.56  | 0.84  | 3.06  | 3.01  | 3.28    |
|                         |                 |              | Minimum   | 11             | 12        | 11    | 12    | 10    | 13    | 10      |
|                         |                 |              | Median    | 14.0           | 14.0      | 13.0  | 12.0  | 13.5  | 16.5  | 13.0    |
|                         |                 |              | Maximum   | 22             | 25        | 18    | 14    | 19    | 21    | 25      |
|                         |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 12.7           | 11.7      | 13.0  | 10.2  | 11.8  | 17.5  | 12.8    |
|                         |                 |              | SD        | 2.91           | 2.88      | 3.46  | 0.75  | 3.97  | 5.47  | 4.24    |
|                         |                 |              | Minimum   | 8              | 8         | 10    | 9     | 7     | 12    | 7       |
|                         |                 |              | Median    | 12.5           | 11.0      | 12.5  | 10.0  | 10.5  | 16.5  | 11.0    |
|                         |                 |              | Maximum   | 18             | 15        | 19    | 11    | 18    | 26    | 26      |
| Sodium (mEq/L)          | 134-145         | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 141.0          | 139.7     | 139.7 | 140.7 | 139.5 | 138.5 | 139.6   |
|                         |                 |              | SD        | 2.21           | 2.42      | 2.94  | 2.34  | 1.52  | 1.05  | 2.13    |
|                         |                 |              | Minimum   | 137            | 137       | 135   | 138   | 137   | 137   | 135     |
|                         |                 |              | Median    | 141.0          | 139.5     | 140.0 | 141.0 | 139.5 | 138.5 | 139.0   |
|                         |                 |              | Maximum   | 144            | 144       | 143   | 144   | 141   | 140   | 144     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Sodium (mEq/L)          | 134-145         | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 139.6          | 141.2     | 140.2 | 139.3 | 137.8 | 137.5 | 139.2   |
|                         |                 |            | SD        | 1.78           | 1.94      | 1.83  | 2.66  | 2.40  | 2.88  | 2.62    |
|                         |                 |            | Minimum   | 137            | 138       | 138   | 137   | 133   | 133   | 133     |
|                         |                 |            | Median    | 139.0          | 141.0     | 140.0 | 139.0 | 139.0 | 137.5 | 139.0   |
|                         |                 |            | Maximum   | 142            | 144       | 143   | 144   | 139   | 141   | 144     |
|                         |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 140.6          | 143.3     | 139.5 | 140.2 | 140.7 | 140.8 | 140.9   |
|                         |                 |            | SD        | 2.67           | 1.51      | 1.64  | 1.60  | 1.51  | 2.48  | 2.12    |
|                         |                 |            | Minimum   | 138            | 142       | 137   | 138   | 139   | 138   | 137     |
|                         |                 |            | Median    | 140.0          | 143.0     | 139.5 | 140.0 | 141.0 | 140.5 | 141.0   |
|                         |                 |            | Maximum   | 146            | 146       | 142   | 142   | 143   | 145   | 146     |
|                         |                 | Day 3      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 141.7          | 142.3     | 141.3 | 140.0 | 140.2 | 141.3 | 141.0   |
|                         |                 |            | SD        | 1.89           | 1.63      | 0.82  | 2.10  | 1.83  | 2.94  | 2.04    |
|                         |                 |            | Minimum   | 139            | 140       | 140   | 137   | 137   | 138   | 137     |
|                         |                 |            | Median    | 141.5          | 142.5     | 141.5 | 140.5 | 141.0 | 141.0 | 141.0   |
|                         |                 |            | Maximum   | 145            | 144       | 142   | 142   | 142   | 146   | 146     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Sodium (mEq/L)          | 134-145         | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 140.2          | 141.2     | 141.5 | 139.0 | 139.7 | 139.0 | 140.1   |
|                         |                 |              | SD        | 1.87           | 1.17      | 1.52  | 1.90  | 1.03  | 1.67  | 1.76    |
|                         |                 |              | Minimum   | 138            | 139       | 139   | 136   | 138   | 136   | 136     |
|                         |                 |              | Median    | 140.0          | 141.5     | 141.5 | 139.0 | 140.0 | 140.0 | 140.0   |
|                         |                 |              | Maximum   | 143            | 142       | 143   | 142   | 141   | 140   | 143     |
| Bilirubin (mg/dL)       | 0.2-1.6         | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 0.70           | 0.87      | 0.70  | 0.50  | 0.50  | 0.68  | 0.65    |
|                         |                 |              | SD        | 0.249          | 0.472     | 0.352 | 0.155 | 0.089 | 0.293 | 0.316   |
|                         |                 |              | Minimum   | 0.2            | 0.2       | 0.3   | 0.3   | 0.4   | 0.3   | 0.2     |
|                         |                 |              | Median    | 0.70           | 0.80      | 0.65  | 0.50  | 0.50  | 0.70  | 0.60    |
|                         |                 |              | Maximum   | 1.0            | 1.4       | 1.1   | 0.7   | 0.6   | 1.0   | 1.4     |
|                         |                 | Baseline     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 0.73           | 0.83      | 0.82  | 0.58  | 0.68  | 0.73  | 0.73    |
|                         |                 |              | SD        | 0.279          | 0.423     | 0.417 | 0.117 | 0.306 | 0.516 | 0.366   |
|                         |                 |              | Minimum   | 0.4            | 0.4       | 0.3   | 0.4   | 0.4   | 0.3   | 0.3     |
|                         |                 |              | Median    | 0.70           | 0.80      | 0.85  | 0.60  | 0.55  | 0.55  | 0.60    |
|                         |                 |              | Maximum   | 1.3            | 1.6       | 1.4   | 0.7   | 1.2   | 1.7   | 1.7     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Bilirubin (mg/dL)       | 0.2-1.6         | Day 2        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 0.78           | 0.83      | 0.70  | 0.50  | 0.53  | 0.63  | 0.64    |
|                         |                 |              | SD        | 0.355          | 0.423     | 0.210 | 0.141 | 0.225 | 0.242 | 0.275   |
|                         |                 |              | Minimum   | 0.3            | 0.5       | 0.4   | 0.3   | 0.3   | 0.4   | 0.3     |
|                         |                 |              | Median    | 0.70           | 0.70      | 0.70  | 0.50  | 0.45  | 0.60  | 0.60    |
|                         |                 |              | Maximum   | 1.4            | 1.6       | 1.0   | 0.7   | 0.9   | 1.0   | 1.6     |
|                         |                 | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 0.78           | 0.80      | 0.67  | 0.50  | 0.52  | 0.62  | 0.62    |
|                         |                 |              | SD        | 0.410          | 0.400     | 0.197 | 0.126 | 0.214 | 0.223 | 0.257   |
|                         |                 |              | Minimum   | 0.3            | 0.5       | 0.4   | 0.3   | 0.2   | 0.3   | 0.2     |
|                         |                 |              | Median    | 0.65           | 0.65      | 0.70  | 0.55  | 0.50  | 0.60  | 0.55    |
|                         |                 |              | Maximum   | 1.7            | 1.5       | 0.9   | 0.6   | 0.8   | 0.9   | 1.5     |
|                         |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 0.67           | 0.70      | 0.67  | 0.43  | 0.50  | 0.50  | 0.56    |
|                         |                 |              | SD        | 0.368          | 0.363     | 0.216 | 0.151 | 0.228 | 0.303 | 0.266   |
|                         |                 |              | Minimum   | 0.2            | 0.2       | 0.4   | 0.3   | 0.3   | 0.3   | 0.2     |
|                         |                 |              | Median    | 0.60           | 0.85      | 0.65  | 0.40  | 0.45  | 0.40  | 0.50    |
|                         |                 |              | Maximum   | 1.4            | 1.1       | 1.0   | 0.7   | 0.9   | 1.1   | 1.1     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

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Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Urate (mg/dL)           | 2.3-7.7 #       | Screen     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 5.42           | 5.73      | 5.22  | 5.22  | 5.77  | 4.75  | 5.34    |
|                         |                 |            | SD        | 1.555          | 0.952     | 1.601 | 0.999 | 2.257 | 0.896 | 1.391   |
|                         |                 |            | Minimum   | 1.9            | 4.8       | 3.3   | 3.6   | 2.4   | 3.1   | 2.4     |
|                         |                 |            | Median    | 5.65           | 5.55      | 5.10  | 5.45  | 6.00  | 4.80  | 5.40    |
|                         |                 |            | Maximum   | 7.7            | 7.5       | 7.6   | 6.2   | 9.1   | 5.6   | 9.1     |
|                         |                 | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 5.16           | 5.75      | 5.15  | 5.10  | 5.62  | 5.43  | 5.41    |
|                         |                 |            | SD        | 1.343          | 1.457     | 1.623 | 1.092 | 2.421 | 1.578 | 1.591   |
|                         |                 |            | Minimum   | 2.3            | 4.8       | 3.0   | 3.4   | 2.0   | 3.0   | 2.0     |
|                         |                 |            | Median    | 5.50           | 5.15      | 5.10  | 5.30  | 5.95  | 5.40  | 5.35    |
|                         |                 |            | Maximum   | 6.7            | 8.6       | 7.6   | 6.6   | 9.1   | 7.5   | 9.1     |
|                         |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 5.27           | 5.47      | 4.77  | 5.18  | 5.47  | 5.72  | 5.32    |
|                         |                 |            | SD        | 1.564          | 0.942     | 1.244 | 1.272 | 2.727 | 1.162 | 1.524   |
|                         |                 |            | Minimum   | 1.8            | 4.3       | 3.4   | 3.0   | 2.0   | 4.0   | 2.0     |
|                         |                 |            | Median    | 5.75           | 5.30      | 4.75  | 5.25  | 5.25  | 5.65  | 5.25    |
|                         |                 |            | Maximum   | 7.3            | 6.7       | 6.6   | 6.6   | 10.2  | 7.3   | 10.2    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Urate (mg/dL)           | 2.3-7.7 #       | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 5.08           | 5.42      | 4.50  | 5.07  | 5.27  | 5.15  | 5.08    |
|                         |                 |              | SD        | 1.568          | 0.922     | 1.210 | 1.140 | 2.583 | 1.071 | 1.439   |
|                         |                 |              | Minimum   | 1.7            | 4.2       | 3.2   | 3.1   | 2.0   | 3.6   | 2.0     |
|                         |                 |              | Median    | 5.30           | 5.35      | 4.60  | 5.10  | 4.90  | 5.10  | 5.05    |
|                         |                 |              | Maximum   | 7.5            | 6.8       | 6.1   | 6.4   | 9.7   | 6.6   | 9.7     |
|                         |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 5.63           | 5.77      | 5.37  | 5.15  | 6.32  | 5.83  | 5.69    |
|                         |                 |              | SD        | 1.663          | 0.933     | 1.428 | 1.054 | 3.107 | 0.819 | 1.625   |
|                         |                 |              | Minimum   | 1.9            | 4.8       | 3.5   | 3.3   | 1.8   | 4.8   | 1.8     |
|                         |                 |              | Median    | 6.00           | 5.60      | 5.25  | 5.30  | 6.45  | 5.90  | 5.75    |
|                         |                 |              | Maximum   | 8.0            | 7.2       | 7.7   | 6.3   | 11.1  | 6.7   | 11.1    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.

\* Above Reference Range, ^ Below Reference Range

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E     |         |
| Calcium (mg/dL)         | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.13              | 0.02      | 0.18  | -0.02 | 0.07  | -0.03 | 0.04    |
|                         |              | SD        | 0.337             | 0.449     | 0.183 | 0.407 | 0.186 | 0.250 | 0.304   |
|                         |              | Minimum   | -0.5              | -0.5      | 0.0   | -0.5  | -0.2  | -0.5  | -0.5    |
|                         |              | Median    | 0.10              | 0.00      | 0.15  | 0.00  | 0.10  | 0.05  | 0.10    |
|                         |              | Maximum   | 0.8               | 0.7       | 0.4   | 0.5   | 0.3   | 0.2   | 0.7     |
|                         | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.15              | 0.18      | 0.32  | 0.18  | 0.08  | 0.03  | 0.16    |
|                         |              | SD        | 0.331             | 0.542     | 0.147 | 0.440 | 0.417 | 0.288 | 0.377   |
|                         |              | Minimum   | -0.4              | -0.5      | 0.2   | -0.4  | -0.4  | -0.3  | -0.5    |
|                         |              | Median    | 0.10              | 0.10      | 0.25  | 0.30  | 0.05  | 0.00  | 0.20    |
|                         |              | Maximum   | 0.8               | 1.1       | 0.5   | 0.7   | 0.7   | 0.5   | 1.1     |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | -0.11             | -0.27     | 0.12  | 0.07  | -0.17 | 0.00  | -0.05   |
|                         |              | SD        | 0.233             | 0.388     | 0.117 | 0.592 | 0.163 | 0.346 | 0.368   |
|                         |              | Minimum   | -0.5              | -0.9      | 0.0   | -0.7  | -0.5  | -0.5  | -0.9    |
|                         |              | Median    | -0.10             | -0.20     | 0.10  | 0.10  | -0.10 | 0.05  | -0.05   |
|                         |              | Maximum   | 0.3               | 0.1       | 0.3   | 1.0   | -0.1  | 0.3   | 1.0     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                         |              |           |                   | A         | B    | C    | D    | E    |         |
| Chloride (mEq/L)        | Day 2        | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                         |              | Mean      | 2.8               | 2.2       | -0.2 | 1.5  | 3.7  | 6.3  | 2.7     |
|                         |              | SD        | 4.32              | 1.47      | 1.60 | 1.76 | 3.08 | 4.37 | 3.35    |
|                         |              | Minimum   | -1                | 1         | -3   | 0    | -1   | 2    | -3      |
|                         |              | Median    | 1.5               | 2.0       | 0.5  | 1.0  | 4.0  | 5.5  | 2.0     |
|                         |              | Maximum   | 13                | 5         | 1    | 5    | 8    | 13   | 13      |
|                         | Day 3        | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                         |              | Mean      | 2.3               | 0.0       | -1.7 | 0.0  | 3.2  | 4.5  | 1.2     |
|                         |              | SD        | 4.47              | 2.97      | 1.37 | 2.61 | 2.86 | 3.94 | 3.53    |
|                         |              | Minimum   | -1                | -4        | -4   | -2   | 0    | 0    | -4      |
|                         |              | Median    | 1.0               | -0.5      | -1.5 | -0.5 | 3.5  | 4.0  | 0.0     |
|                         |              | Maximum   | 12                | 5         | 0    | 5    | 6    | 10   | 10      |
|                         | End of Study | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                         |              | Mean      | 1.7               | -0.3      | 0.7  | -0.2 | 3.7  | 2.8  | 1.3     |
|                         |              | SD        | 3.43              | 2.80      | 2.25 | 1.94 | 2.66 | 2.32 | 2.78    |
|                         |              | Minimum   | -3                | -5        | -3   | -3   | 0    | -1   | -5      |
|                         |              | Median    | 1.0               | 0.5       | 0.5  | -0.5 | 4.0  | 4.0  | 1.0     |
|                         |              | Maximum   | 9                 | 3         | 3    | 2    | 8    | 5    | 8       |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E     |         |
| Potassium (mEq/L)       | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.35              | 0.25      | 0.50  | 0.42  | 0.47  | 0.32  | 0.39    |
|                         |              | SD        | 0.422             | 0.207     | 0.358 | 0.504 | 0.350 | 0.133 | 0.326   |
|                         |              | Minimum   | -0.3              | -0.1      | 0.2   | -0.3  | 0.0   | 0.1   | -0.3    |
|                         |              | Median    | 0.30              | 0.25      | 0.35  | 0.35  | 0.40  | 0.40  | 0.35    |
|                         |              | Maximum   | 0.9               | 0.5       | 1.0   | 1.2   | 1.0   | 0.4   | 1.2     |
|                         | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.18              | 0.22      | 0.37  | 0.38  | 0.53  | 0.08  | 0.32    |
|                         |              | SD        | 0.305             | 0.248     | 0.497 | 0.560 | 0.501 | 0.286 | 0.435   |
|                         |              | Minimum   | -0.3              | -0.1      | -0.1  | -0.5  | 0.0   | -0.3  | -0.5    |
|                         |              | Median    | 0.20              | 0.15      | 0.25  | 0.60  | 0.45  | 0.05  | 0.20    |
|                         |              | Maximum   | 0.7               | 0.6       | 1.1   | 0.9   | 1.1   | 0.5   | 1.1     |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.10              | -0.10     | 0.25  | 0.25  | 0.10  | -0.05 | 0.09    |
|                         |              | SD        | 0.294             | 0.237     | 0.451 | 0.476 | 0.447 | 0.274 | 0.392   |
|                         |              | Minimum   | -0.4              | -0.4      | -0.1  | -0.4  | -0.4  | -0.4  | -0.4    |
|                         |              | Median    | 0.05              | -0.15     | 0.05  | 0.15  | 0.10  | -0.05 | 0.00    |
|                         |              | Maximum   | 0.5               | 0.3       | 1.0   | 0.9   | 0.6   | 0.3   | 1.0     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E     |         |
| Albumin (g/dL)          | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | -0.16             | -0.08     | -0.10 | -0.18 | -0.22 | -0.18 | -0.15   |
|                         |              | SD        | 0.207             | 0.223     | 0.126 | 0.299 | 0.098 | 0.183 | 0.193   |
|                         |              | Minimum   | -0.6              | -0.4      | -0.3  | -0.5  | -0.3  | -0.4  | -0.5    |
|                         |              | Median    | -0.15             | 0.00      | -0.05 | -0.20 | -0.25 | -0.20 | -0.10   |
|                         |              | Maximum   | 0.2               | 0.2       | 0.0   | 0.2   | -0.1  | 0.1   | 0.2     |
|                         | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.10              | 0.03      | 0.20  | 0.02  | -0.10 | 0.07  | 0.04    |
|                         |              | SD        | 0.294             | 0.367     | 0.167 | 0.382 | 0.210 | 0.197 | 0.278   |
|                         |              | Minimum   | -0.4              | -0.4      | 0.0   | -0.5  | -0.4  | -0.2  | -0.5    |
|                         |              | Median    | 0.10              | -0.05     | 0.25  | -0.10 | -0.05 | 0.05  | 0.00    |
|                         |              | Maximum   | 0.7               | 0.7       | 0.4   | 0.6   | 0.1   | 0.4   | 0.7     |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | -0.04             | 0.00      | -0.07 | -0.05 | -0.15 | 0.10  | -0.03   |
|                         |              | SD        | 0.267             | 0.179     | 0.082 | 0.288 | 0.176 | 0.200 | 0.201   |
|                         |              | Minimum   | -0.4              | -0.3      | -0.2  | -0.5  | -0.4  | -0.2  | -0.5    |
|                         |              | Median    | 0.00              | 0.05      | -0.05 | -0.05 | -0.10 | 0.20  | 0.00    |
|                         |              | Maximum   | 0.4               | 0.2       | 0.0   | 0.3   | 0.0   | 0.3   | 0.3     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |        |        |        |        | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|--------|--------|--------|--------|---------|
|                         |              |           |                   | A         | B      | C      | D      | E      |         |
| Creatinine (mg/dL)      | Day 2        | n         | 10                | 6         | 6      | 6      | 6      | 6      | 30      |
|                         |              | Mean      | 0.037             | 0.045     | -0.018 | -0.052 | -0.008 | -0.017 | -0.010  |
|                         |              | SD        | 0.0762            | 0.0761    | 0.0765 | 0.0564 | 0.0763 | 0.0650 | 0.0728  |
|                         |              | Minimum   | -0.04             | -0.02     | -0.11  | -0.14  | -0.16  | -0.12  | -0.16   |
|                         |              | Median    | 0.020             | 0.015     | -0.010 | -0.045 | 0.015  | 0.000  | 0.000   |
|                         |              | Maximum   | 0.21              | 0.15      | 0.10   | 0.03   | 0.05   | 0.06   | 0.15    |
|                         | Day 3        | n         | 10                | 6         | 6      | 6      | 6      | 6      | 30      |
|                         |              | Mean      | -0.007            | 0.040     | -0.035 | -0.090 | -0.028 | -0.023 | -0.027  |
|                         |              | SD        | 0.0733            | 0.1176    | 0.0997 | 0.0607 | 0.0682 | 0.0900 | 0.0933  |
|                         |              | Minimum   | -0.12             | -0.10     | -0.19  | -0.19  | -0.14  | -0.10  | -0.19   |
|                         |              | Median    | 0.005             | 0.020     | -0.020 | -0.070 | -0.030 | -0.060 | -0.030  |
|                         |              | Maximum   | 0.13              | 0.25      | 0.11   | -0.02  | 0.07   | 0.14   | 0.25    |
|                         | End of Study | n         | 10                | 6         | 6      | 6      | 6      | 6      | 30      |
|                         |              | Mean      | -0.024            | 0.012     | 0.040  | -0.042 | -0.033 | 0.018  | -0.001  |
|                         |              | SD        | 0.0458            | 0.1085    | 0.0820 | 0.0719 | 0.0520 | 0.0828 | 0.0821  |
|                         |              | Minimum   | -0.10             | -0.20     | -0.06  | -0.15  | -0.09  | -0.08  | -0.20   |
|                         |              | Median    | -0.030            | 0.050     | 0.020  | -0.045 | -0.040 | -0.005 | 0.000   |
|                         |              | Maximum   | 0.05              | 0.09      | 0.18   | 0.06   | 0.05   | 0.15   | 0.18    |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |      |      |      |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|------|------|------|-------|---------|
|                         |              |           |                   | A         | B    | C    | D    | E     |         |
| Glucose (mg/dL)         | Day 2        | n         | 10                | 6         | 6    | 6    | 6    | 6     | 30      |
|                         |              | Mean      | 2.3               | 6.3       | 0.5  | -0.2 | 6.5  | -0.7  | 2.5     |
|                         |              | SD        | 6.53              | 4.37      | 4.81 | 4.36 | 4.32 | 7.66  | 5.88    |
|                         |              | Minimum   | -9                | 1         | -4   | -7   | 1    | -10   | -10     |
|                         |              | Median    | 1.0               | 5.5       | 0.0  | 0.5  | 5.5  | -1.5  | 2.5     |
|                         |              | Maximum   | 14                | 12        | 9    | 4    | 12   | 9     | 12      |
|                         | Day 3        | n         | 10                | 6         | 6    | 6    | 6    | 6     | 30      |
|                         |              | Mean      | 2.0               | 4.7       | -0.5 | 1.3  | 6.0  | -2.2  | 1.9     |
|                         |              | SD        | 7.42              | 3.72      | 5.09 | 5.61 | 4.20 | 7.11  | 5.81    |
|                         |              | Minimum   | -8                | -1        | -7   | -4   | 2    | -14   | -14     |
|                         |              | Median    | 1.0               | 4.5       | -1.5 | 0.5  | 4.5  | -1.5  | 2.5     |
|                         |              | Maximum   | 12                | 10        | 8    | 11   | 13   | 8     | 13      |
|                         | End of Study | n         | 10                | 6         | 6    | 6    | 6    | 6     | 30      |
|                         |              | Mean      | 7.9               | 11.2      | 4.3  | 7.3  | 11.5 | -3.5  | 6.2     |
|                         |              | SD        | 9.19              | 8.08      | 7.71 | 4.37 | 4.85 | 14.38 | 9.79    |
|                         |              | Minimum   | -8                | 1         | -2   | 0    | 4    | -25   | -25     |
|                         |              | Median    | 5.5               | 11.5      | 2.0  | 7.5  | 12.5 | -3.5  | 6.0     |
|                         |              | Maximum   | 21                | 24        | 19   | 12   | 17   | 18    | 24      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)     | Time Point   | Statistic | Pooled<br>Placebo | Treatment |      |      |      |       | Overall |
|-----------------------------|--------------|-----------|-------------------|-----------|------|------|------|-------|---------|
|                             |              |           |                   | A         | B    | C    | D    | E     |         |
| Alkaline Phosphatase (IU/L) | Day 2        | n         | 10                | 6         | 6    | 6    | 6    | 6     | 30      |
|                             |              | Mean      | -5.6              | 2.2       | 0.5  | -4.3 | -2.0 | -4.2  | -1.6    |
|                             |              | SD        | 5.78              | 7.08      | 2.43 | 6.28 | 5.18 | 5.85  | 5.81    |
|                             |              | Minimum   | -15               | -11       | -2   | -13  | -12  | -14   | -14     |
|                             |              | Median    | -3.5              | 6.0       | -0.5 | -6.0 | -1.0 | -3.0  | -1.0    |
|                             |              | Maximum   | 1                 | 7         | 4    | 4    | 2    | 3     | 7       |
|                             | Day 3        | n         | 10                | 6         | 6    | 6    | 6    | 6     | 30      |
|                             |              | Mean      | -2.7              | 1.0       | 8.0  | -2.5 | -1.2 | -3.3  | 0.4     |
|                             |              | SD        | 7.47              | 9.12      | 4.05 | 5.65 | 8.33 | 4.93  | 7.48    |
|                             |              | Minimum   | -15               | -13       | 2    | -8   | -14  | -9    | -14     |
|                             |              | Median    | 0.0               | 2.0       | 8.0  | -4.0 | 2.5  | -4.5  | 1.5     |
|                             |              | Maximum   | 9                 | 13        | 14   | 7    | 6    | 3     | 14      |
|                             | End of Study | n         | 10                | 6         | 6    | 6    | 6    | 6     | 30      |
|                             |              | Mean      | 0.3               | 0.3       | 7.5  | -0.8 | -2.2 | -0.3  | 0.9     |
|                             |              | SD        | 6.43              | 6.83      | 4.85 | 7.55 | 3.25 | 12.68 | 7.96    |
|                             |              | Minimum   | -5                | -7        | 1    | -12  | -6   | -21   | -21     |
|                             |              | Median    | -2.0              | -1.5      | 8.0  | -1.0 | -1.5 | 0.0   | 0.0     |
|                             |              | Maximum   | 17                | 12        | 14   | 11   | 2    | 15    | 15      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)            | Time Point   | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|------------------------------------|--------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                                    |              |           |                   | A         | B    | C    | D    | E    |         |
| Alanine Aminotransferase<br>(IU/L) | Day 2        | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                    |              | Mean      | -2.5              | 1.8       | -1.7 | -0.7 | -0.8 | -2.2 | -0.7    |
|                                    |              | SD        | 7.17              | 7.99      | 1.21 | 2.16 | 3.13 | 3.43 | 4.21    |
|                                    |              | Minimum   | -18               | -3        | -3   | -3   | -3   | -5   | -5      |
|                                    |              | Median    | -2.0              | -1.0      | -1.5 | -1.0 | -2.0 | -3.0 | -1.5    |
|                                    |              | Maximum   | 10                | 18        | 0    | 3    | 5    | 4    | 18      |
|                                    | Day 3        | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                    |              | Mean      | -1.0              | 5.0       | -1.0 | 0.8  | 0.5  | -0.7 | 0.9     |
|                                    |              | SD        | 9.14              | 12.43     | 1.67 | 3.82 | 4.23 | 5.57 | 6.54    |
|                                    |              | Minimum   | -16               | -3        | -4   | -2   | -5   | -7   | -7      |
|                                    |              | Median    | -2.0              | 1.5       | -1.0 | -1.0 | -0.5 | -1.0 | -1.0    |
|                                    |              | Maximum   | 20                | 30        | 1    | 7    | 6    | 9    | 30      |
|                                    | End of Study | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                    |              | Mean      | -2.1              | 2.2       | 0.2  | 4.0  | -4.5 | -0.7 | 0.2     |
|                                    |              | SD        | 2.18              | 6.79      | 2.14 | 7.64 | 6.53 | 4.72 | 6.21    |
|                                    |              | Minimum   | -5                | -5        | -2   | -3   | -17  | -10  | -17     |
|                                    |              | Median    | -3.0              | 1.0       | -0.5 | 0.5  | -2.5 | 0.5  | 0.0     |
|                                    |              | Maximum   | 2                 | 14        | 4    | 16   | 2    | 3    | 16      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)              | Time Point   | Statistic | Pooled<br>Placebo | Treatment |      |       |      |      | Overall |
|--------------------------------------|--------------|-----------|-------------------|-----------|------|-------|------|------|---------|
|                                      |              |           |                   | A         | B    | C     | D    | E    |         |
| Aspartate Aminotransferase<br>(IU/L) | Day 2        | n         | 10                | 6         | 6    | 6     | 6    | 6    | 30      |
|                                      |              | Mean      | -4.1              | 0.2       | -2.5 | -3.0  | -3.0 | -3.8 | -2.4    |
|                                      |              | SD        | 4.61              | 5.46      | 1.05 | 2.61  | 2.19 | 1.94 | 3.15    |
|                                      |              | Minimum   | -15               | -4        | -4   | -6    | -7   | -6   | -7      |
|                                      |              | Median    | -3.0              | -2.0      | -2.5 | -3.5  | -2.0 | -4.5 | -2.0    |
|                                      |              | Maximum   | 1                 | 11        | -1   | 1     | -1   | -1   | 11      |
|                                      | Day 3        | n         | 10                | 6         | 6    | 6     | 6    | 6    | 30      |
|                                      |              | Mean      | -2.5              | 1.3       | -1.3 | -1.2  | -1.7 | -2.8 | -1.1    |
|                                      |              | SD        | 4.38              | 6.50      | 1.37 | 3.06  | 2.73 | 2.93 | 3.73    |
|                                      |              | Minimum   | -9                | -4        | -3   | -5    | -5   | -8   | -8      |
|                                      |              | Median    | -2.0              | 0.0       | -1.5 | -1.0  | -2.0 | -2.0 | -1.0    |
|                                      |              | Maximum   | 6                 | 14        | 1    | 3     | 3    | 0    | 14      |
|                                      | End of Study | n         | 10                | 6         | 6    | 6     | 6    | 6    | 30      |
|                                      |              | Mean      | -1.7              | -0.5      | 0.2  | 10.5  | -5.0 | 0.5  | 1.1     |
|                                      |              | SD        | 3.59              | 2.74      | 1.72 | 26.35 | 9.51 | 5.47 | 13.00   |
|                                      |              | Minimum   | -7                | -3        | -2   | -5    | -24  | -8   | -24     |
|                                      |              | Median    | -2.5              | -1.0      | 0.0  | 1.0   | -2.5 | 0.5  | 0.0     |
|                                      |              | Maximum   | 6                 | 4         | 2    | 64    | 2    | 9    | 64      |

Note: Baseline is the last predose measurement.  
 Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
 Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
 Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
 Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
 Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point     | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|-------------------------|----------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                         |                |           |                   | A         | B    | C    | D    | E    |         |
| GGT (IU/L)              | Day 1, Hour 4  | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                         |                | Mean      | -1.2              | -0.2      | -0.3 | -1.2 | -2.2 | -0.8 | -0.9    |
|                         |                | SD        | 0.79              | 4.49      | 1.21 | 0.75 | 1.47 | 1.17 | 2.23    |
|                         |                | Minimum   | -2                | -4        | -2   | -2   | -4   | -3   | -4      |
|                         |                | Median    | -1.0              | -1.0      | -0.5 | -1.0 | -2.5 | -0.5 | -1.0    |
|                         |                | Maximum   | 0                 | 8         | 1    | 0    | 0    | 0    | 8       |
|                         | Day 1, Hour 12 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                         |                | Mean      | -2.1              | -0.8      | -1.0 | -1.5 | -3.5 | -1.3 | -1.6    |
|                         |                | SD        | 1.66              | 5.85      | 1.26 | 1.05 | 2.35 | 1.51 | 2.94    |
|                         |                | Minimum   | -5                | -7        | -2   | -3   | -8   | -4   | -8      |
|                         |                | Median    | -1.5              | -2.0      | -1.5 | -1.5 | -2.5 | -1.0 | -2.0    |
|                         |                | Maximum   | 0                 | 10        | 1    | 0    | -2   | 0    | 10      |
|                         | Day 2          | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                         |                | Mean      | -1.2              | 1.3       | -0.7 | 0.2  | -2.8 | -0.8 | -0.6    |
|                         |                | SD        | 1.99              | 6.50      | 1.21 | 1.72 | 1.83 | 0.98 | 3.28    |
|                         |                | Minimum   | -4                | -4        | -2   | -2   | -6   | -2   | -6      |
|                         |                | Median    | -1.5              | 0.0       | -0.5 | 0.0  | -2.0 | -0.5 | -1.0    |
|                         |                | Maximum   | 2                 | 14        | 1    | 3    | -1   | 0    | 14      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point    | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|---------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |               |           |                   | A         | B     | C     | D     | E     |         |
| GGT (IU/L)              | Day 3         | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |               | Mean      | -0.7              | 3.3       | 0.8   | 1.5   | -1.8  | -0.5  | 0.7     |
|                         |               | SD        | 2.98              | 10.17     | 0.98  | 2.07  | 2.14  | 1.05  | 4.79    |
|                         |               | Minimum   | -4                | -2        | 0     | 0     | -5    | -2    | -5      |
|                         |               | Median    | -1.0              | 0.0       | 0.5   | 0.5   | -1.0  | -0.5  | 0.0     |
|                         |               | Maximum   | 5                 | 24        | 2     | 5     | 0     | 1     | 24      |
|                         | End of Study  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |               | Mean      | -0.5              | -1.5      | -0.5  | 0.8   | -2.7  | -1.7  | -1.1    |
|                         |               | SD        | 2.84              | 2.07      | 0.84  | 2.86  | 1.51  | 1.97  | 2.19    |
|                         |               | Minimum   | -5                | -3        | -1    | -2    | -5    | -5    | -5      |
|                         |               | Median    | -1.0              | -2.5      | -1.0  | 0.0   | -3.0  | -1.0  | -1.0    |
|                         |               | Maximum   | 6                 | 2         | 1     | 6     | -1    | 0     | 6       |
| Creatine Kinase (IU/L)  | Day 1, Hour 4 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |               | Mean      | -19.9             | -31.7     | -24.3 | -35.8 | -29.3 | -47.8 | -33.8   |
|                         |               | SD        | 28.27             | 13.57     | 14.83 | 38.43 | 20.29 | 30.99 | 25.02   |
|                         |               | Minimum   | -72               | -49       | -44   | -114  | -66   | -87   | -114    |
|                         |               | Median    | -9.0              | -33.0     | -25.0 | -21.5 | -27.5 | -41.5 | -26.5   |
|                         |               | Maximum   | 7                 | -16       | -5    | -17   | -6    | -16   | -5      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point     | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|----------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |                |           |                   | A         | B     | C     | D     | E     |         |
| Creatine Kinase (IU/L)  | Day 1, Hour 12 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                | Mean      | -28.0             | -39.0     | -29.3 | -38.3 | -33.7 | -66.7 | -41.4   |
|                         |                | SD        | 35.55             | 18.77     | 16.11 | 45.72 | 33.48 | 46.58 | 34.80   |
|                         |                | Minimum   | -101              | -65       | -43   | -131  | -99   | -131  | -131    |
|                         |                | Median    | -14.0             | -42.5     | -36.5 | -23.0 | -25.5 | -67.5 | -31.5   |
|                         |                | Maximum   | -2                | -15       | -4    | -13   | -7    | -18   | -4      |
|                         | Day 2          | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                | Mean      | -39.7             | -45.7     | -39.5 | -48.2 | -37.5 | -87.8 | -51.7   |
|                         |                | SD        | 44.31             | 19.82     | 21.55 | 49.71 | 37.41 | 57.99 | 41.80   |
|                         |                | Minimum   | -135              | -71       | -56   | -149  | -103  | -160  | -160    |
|                         |                | Median    | -22.5             | -46.5     | -50.5 | -30.5 | -37.5 | -90.5 | -41.5   |
|                         |                | Maximum   | -6                | -21       | -6    | -17   | 4     | -23   | 4       |
|                         | Day 3          | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                | Mean      | -39.9             | -49.8     | -38.7 | -44.3 | -43.7 | -91.3 | -53.6   |
|                         |                | SD        | 49.54             | 20.86     | 23.51 | 50.85 | 39.83 | 65.05 | 44.73   |
|                         |                | Minimum   | -153              | -74       | -61   | -147  | -111  | -168  | -168    |
|                         |                | Median    | -20.5             | -53.5     | -47.0 | -29.0 | -40.0 | -94.5 | -47.0   |
|                         |                | Maximum   | -9                | -25       | -2    | -12   | 1     | -14   | 1       |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)      | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |        |       |        | Overall |
|------------------------------|--------------|-----------|-------------------|-----------|-------|--------|-------|--------|---------|
|                              |              |           |                   | A         | B     | C      | D     | E      |         |
| Creatine Kinase (IU/L)       | End of Study | n         | 10                | 6         | 6     | 6      | 6     | 6      | 30      |
|                              |              | Mean      | 7.1               | -14.5     | -6.2  | 278.7  | 15.7  | 59.8   | 66.7    |
|                              |              | SD        | 62.08             | 32.78     | 12.54 | 763.03 | 64.05 | 289.13 | 357.80  |
|                              |              | Minimum   | -113              | -68       | -24   | -113   | -36   | -216   | -216    |
|                              |              | Median    | -2.0              | -12.5     | -8.5  | -13.0  | 0.0   | 0.0    | -8.5    |
|                              |              | Maximum   | 113               | 22        | 13    | 1834   | 142   | 618    | 1834    |
| Lactate Dehydrogenase (IU/L) | Day 2        | n         | 10                | 6         | 6     | 6      | 6     | 6      | 30      |
|                              |              | Mean      | -16.4             | -15.8     | -14.0 | -20.2  | -21.7 | -26.7  | -19.7   |
|                              |              | SD        | 10.36             | 8.95      | 15.21 | 10.30  | 15.62 | 11.34  | 12.53   |
|                              |              | Minimum   | -34               | -30       | -28   | -37    | -43   | -38    | -43     |
|                              |              | Median    | -16.5             | -13.0     | -17.0 | -18.5  | -18.0 | -28.5  | -19.0   |
|                              |              | Maximum   | 0                 | -7        | 13    | -6     | -7    | -10    | 13      |
|                              | Day 3        | n         | 10                | 6         | 6     | 6      | 6     | 6      | 30      |
|                              |              | Mean      | -9.2              | -8.5      | -5.5  | -8.8   | -16.0 | -18.0  | -11.4   |
|                              |              | SD        | 10.08             | 12.08     | 11.69 | 12.56  | 12.71 | 8.99   | 11.89   |
|                              |              | Minimum   | -30               | -27       | -22   | -29    | -38   | -25    | -38     |
|                              |              | Median    | -7.5              | -7.0      | -4.0  | -8.5   | -14.5 | -22.5  | -12.0   |
|                              |              | Maximum   | 6                 | 3         | 11    | 9      | -3    | -6     | 11      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)      | Time Point     | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|------------------------------|----------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                              |                |           |                   | A         | B     | C     | D     | E     |         |
| Lactate Dehydrogenase (IU/L) | End of Study   | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                | Mean      | -2.8              | -2.2      | -0.7  | 5.0   | -8.0  | -11.2 | -3.4    |
|                              |                | SD        | 12.34             | 10.78     | 9.37  | 26.35 | 14.79 | 15.72 | 16.39   |
|                              |                | Minimum   | -14               | -15       | -12   | -21   | -28   | -30   | -30     |
|                              |                | Median    | -7.5              | -5.0      | -2.5  | 3.0   | -9.5  | -15.0 | -4.5    |
|                              |                | Maximum   | 18                | 14        | 16    | 51    | 17    | 9     | 51      |
| C Reactive Protein (mg/L)    | Day 1, Hour 4  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                | Mean      | 0.00              | -0.13     | -0.18 | -0.03 | 0.15  | -0.03 | -0.05   |
|                              |                | SD        | 0.267             | 0.250     | 0.685 | 0.151 | 0.485 | 0.505 | 0.440   |
|                              |                | Minimum   | -0.5              | -0.6      | -1.4  | -0.2  | -0.2  | -1.0  | -1.4    |
|                              |                | Median    | 0.00              | -0.05     | -0.10 | 0.00  | 0.05  | 0.10  | 0.00    |
|                              |                | Maximum   | 0.6               | 0.1       | 0.5   | 0.2   | 1.1   | 0.5   | 1.1     |
|                              | Day 1, Hour 12 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                | Mean      | 0.04              | -0.12     | -0.30 | 0.03  | 0.28  | -0.07 | -0.03   |
|                              |                | SD        | 0.350             | 0.286     | 0.802 | 0.186 | 0.708 | 0.480 | 0.544   |
|                              |                | Minimum   | -0.6              | -0.6      | -1.7  | -0.2  | -0.2  | -1.0  | -1.7    |
|                              |                | Median    | 0.05              | 0.00      | -0.25 | 0.00  | 0.05  | 0.05  | 0.00    |
|                              |                | Maximum   | 0.8               | 0.2       | 0.6   | 0.3   | 1.7   | 0.4   | 1.7     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)   | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|---------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                           |              |           |                   | A         | B     | C     | D     | E     |         |
| C Reactive Protein (mg/L) | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                           |              | Mean      | 0.02              | -0.08     | -0.42 | 0.00  | 0.28  | -0.28 | -0.10   |
|                           |              | SD        | 0.319             | 0.407     | 0.880 | 0.179 | 0.585 | 0.542 | 0.581   |
|                           |              | Minimum   | -0.7              | -0.8      | -2.0  | -0.2  | -0.2  | -1.2  | -2.0    |
|                           |              | Median    | 0.05              | 0.05      | -0.30 | -0.05 | 0.15  | 0.00  | 0.00    |
|                           |              | Maximum   | 0.5               | 0.3       | 0.5   | 0.3   | 1.4   | 0.1   | 1.4     |
|                           | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                           |              | Mean      | -0.12             | -0.23     | -0.20 | -0.12 | 0.05  | -0.77 | -0.25   |
|                           |              | SD        | 0.282             | 0.528     | 1.207 | 0.271 | 0.383 | 1.174 | 0.808   |
|                           |              | Minimum   | -0.7              | -1.2      | -1.4  | -0.6  | -0.4  | -2.9  | -2.9    |
|                           |              | Median    | 0.00              | -0.10     | -0.50 | -0.05 | 0.00  | -0.15 | -0.10   |
|                           |              | Maximum   | 0.3               | 0.3       | 1.9   | 0.2   | 0.7   | 0.0   | 1.9     |
|                           | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                           |              | Mean      | 0.15              | 0.80      | -0.13 | 0.13  | 0.95  | -0.78 | 0.19    |
|                           |              | SD        | 0.251             | 2.336     | 1.141 | 0.513 | 2.294 | 1.668 | 1.736   |
|                           |              | Minimum   | -0.2              | -1.3      | -2.0  | -0.8  | -0.8  | -3.8  | -3.8    |
|                           |              | Median    | 0.20              | 0.05      | 0.10  | 0.25  | 0.10  | 0.05  | 0.10    |
|                           |              | Maximum   | 0.5               | 5.3       | 1.3   | 0.6   | 5.5   | 0.4   | 5.5     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point     | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|----------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |                |           |                   | A         | B     | C     | D     | E     |         |
| Troponin I (ug/L)       | Day 1, Hour 4  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                | Mean      | 0.00              | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                         |                | SD        | 0.000             | 0.000     | 0.000 | 0.000 | 0.000 | 0.000 | 0.000   |
|                         |                | Minimum   | 0.0               | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                         |                | Median    | 0.00              | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                         |                | Maximum   | 0.0               | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                         | Day 1, Hour 12 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                | Mean      | 0.00              | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                         |                | SD        | 0.000             | 0.000     | 0.000 | 0.000 | 0.000 | 0.000 | 0.000   |
|                         |                | Minimum   | 0.0               | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                         |                | Median    | 0.00              | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                         |                | Maximum   | 0.0               | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                         | Day 2          | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                | Mean      | 0.00              | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                         |                | SD        | 0.000             | 0.000     | 0.000 | 0.000 | 0.000 | 0.000 | 0.000   |
|                         |                | Minimum   | 0.0               | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                         |                | Median    | 0.00              | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                         |                | Maximum   | 0.0               | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E     |         |
| Troponin I (ug/L)       | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.00              | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                         |              | SD        | 0.000             | 0.000     | 0.000 | 0.000 | 0.000 | 0.000 | 0.000   |
|                         |              | Minimum   | 0.0               | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                         |              | Median    | 0.00              | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                         |              | Maximum   | 0.0               | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.00              | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                         |              | SD        | 0.000             | 0.000     | 0.000 | 0.000 | 0.000 | 0.000 | 0.000   |
|                         |              | Minimum   | 0.0               | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                         |              | Median    | 0.00              | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                         |              | Maximum   | 0.0               | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
| Urea Nitrogen (mg/dL)   | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 2.9               | 3.3       | 0.5   | 1.3   | 1.0   | 3.5   | 1.9     |
|                         |              | SD        | 1.85              | 3.01      | 3.39  | 3.14  | 2.61  | 4.18  | 3.32    |
|                         |              | Minimum   | 0                 | -1        | -5    | -3    | -3    | -1    | -5      |
|                         |              | Median    | 3.5               | 3.0       | 1.0   | 2.5   | 1.0   | 2.5   | 2.0     |
|                         |              | Maximum   | 5                 | 8         | 5     | 5     | 5     | 11    | 11      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                         |              |           |                   | A         | B    | C    | D    | E    |         |
| Urea Nitrogen (mg/dL)   | Day 3        | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                         |              | Mean      | 3.0               | 3.3       | 0.0  | 1.2  | 1.5  | 3.3  | 1.9     |
|                         |              | SD        | 1.83              | 4.23      | 3.58 | 2.93 | 2.74 | 4.76 | 3.70    |
|                         |              | Minimum   | -1                | 0         | -6   | -3   | -2   | -1   | -6      |
|                         |              | Median    | 3.0               | 2.0       | 0.5  | 2.5  | 1.0  | 3.0  | 1.0     |
|                         |              | Maximum   | 5                 | 11        | 5    | 4    | 6    | 12   | 12      |
|                         | End of Study | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                         |              | Mean      | 0.8               | -0.5      | -0.2 | -1.2 | -0.5 | 4.2  | 0.4     |
|                         |              | SD        | 1.99              | 2.35      | 3.43 | 3.25 | 2.51 | 7.73 | 4.48    |
|                         |              | Minimum   | -2                | -3        | -5   | -6   | -3   | -1   | -6      |
|                         |              | Median    | 1.0               | -0.5      | 0.0  | -0.5 | -1.0 | 1.0  | 0.0     |
|                         |              | Maximum   | 5                 | 3         | 4    | 2    | 4    | 19   | 19      |
| Sodium (mEq/L)          | Day 2        | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                         |              | Mean      | 1.0               | 2.2       | -0.7 | 0.8  | 2.8  | 3.3  | 1.7     |
|                         |              | SD        | 2.11              | 1.94      | 1.51 | 2.48 | 2.86 | 4.37 | 3.00    |
|                         |              | Minimum   | -2                | 1         | -2   | -4   | 0    | 0    | -4      |
|                         |              | Median    | 1.0               | 1.5       | -1.0 | 1.5  | 2.0  | 2.0  | 1.5     |
|                         |              | Maximum   | 4                 | 6         | 2    | 3    | 8    | 12   | 12      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E     |         |
| Sodium (mEq/L)          | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 2.1               | 1.2       | 1.2   | 0.7   | 2.3   | 3.8   | 1.8     |
|                         |              | SD        | 1.79              | 2.56      | 1.72  | 2.42  | 1.03  | 4.79  | 2.85    |
|                         |              | Minimum   | 0                 | -1        | -1    | -2    | 1     | -1    | -2      |
|                         |              | Median    | 2.0               | 0.0       | 1.0   | 0.5   | 2.0   | 2.5   | 1.5     |
|                         |              | Maximum   | 6                 | 6         | 4     | 5     | 4     | 13    | 13      |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.6               | 0.0       | 1.3   | -0.3  | 1.8   | 1.5   | 0.9     |
|                         |              | SD        | 2.27              | 2.19      | 1.21  | 1.51  | 1.72  | 2.88  | 2.05    |
|                         |              | Minimum   | -3                | -2        | 0     | -2    | 0     | -1    | -2      |
|                         |              | Median    | 0.5               | 0.0       | 1.5   | -1.0  | 1.5   | 0.5   | 0.5     |
|                         |              | Maximum   | 4                 | 4         | 3     | 2     | 5     | 7     | 7       |
| Bilirubin (mg/dL)       | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.05              | 0.00      | -0.12 | -0.08 | -0.15 | -0.10 | -0.09   |
|                         |              | SD        | 0.212             | 0.167     | 0.319 | 0.147 | 0.217 | 0.316 | 0.232   |
|                         |              | Minimum   | -0.2              | -0.3      | -0.6  | -0.3  | -0.5  | -0.7  | -0.7    |
|                         |              | Median    | 0.00              | 0.00      | -0.10 | -0.05 | -0.10 | -0.05 | 0.00    |
|                         |              | Maximum   | 0.5               | 0.2       | 0.3   | 0.1   | 0.1   | 0.2   | 0.3     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E     |         |
| Bilirubin (mg/dL)       | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.05              | -0.03     | -0.15 | -0.08 | -0.17 | -0.12 | -0.11   |
|                         |              | SD        | 0.303             | 0.151     | 0.281 | 0.172 | 0.207 | 0.366 | 0.235   |
|                         |              | Minimum   | -0.4              | -0.3      | -0.6  | -0.3  | -0.4  | -0.8  | -0.8    |
|                         |              | Median    | 0.00              | 0.00      | -0.10 | -0.10 | -0.15 | 0.00  | -0.10   |
|                         |              | Maximum   | 0.6               | 0.1       | 0.2   | 0.2   | 0.1   | 0.2   | 0.2     |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | -0.06             | -0.13     | -0.15 | -0.15 | -0.18 | -0.23 | -0.17   |
|                         |              | SD        | 0.190             | 0.327     | 0.327 | 0.187 | 0.194 | 0.242 | 0.247   |
|                         |              | Minimum   | -0.3              | -0.5      | -0.6  | -0.4  | -0.5  | -0.6  | -0.6    |
|                         |              | Median    | -0.10             | -0.10     | -0.05 | -0.15 | -0.15 | -0.20 | -0.10   |
|                         |              | Maximum   | 0.3               | 0.3       | 0.2   | 0.1   | 0.0   | 0.0   | 0.3     |
| Urate (mg/dL)           | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.11              | -0.28     | -0.38 | 0.08  | -0.15 | 0.28  | -0.09   |
|                         |              | SD        | 0.314             | 1.085     | 0.454 | 0.627 | 0.873 | 0.422 | 0.728   |
|                         |              | Minimum   | -0.5              | -1.9      | -1.0  | -0.8  | -1.6  | -0.2  | -1.9    |
|                         |              | Median    | 0.05              | -0.35     | -0.45 | 0.10  | -0.05 | 0.25  | -0.10   |
|                         |              | Maximum   | 0.6               | 1.5       | 0.4   | 0.9   | 1.1   | 1.0   | 1.5     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.2 Clinical Laboratory Change From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E     |         |
| Urate (mg/dL)           | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | -0.08             | -0.33     | -0.65 | -0.03 | -0.35 | -0.28 | -0.33   |
|                         |              | SD        | 0.476             | 1.432     | 0.568 | 0.476 | 0.794 | 0.553 | 0.806   |
|                         |              | Minimum   | -0.6              | -2.6      | -1.5  | -0.7  | -1.8  | -0.9  | -2.6    |
|                         |              | Median    | -0.20             | -0.30     | -0.65 | -0.10 | -0.25 | -0.40 | -0.30   |
|                         |              | Maximum   | 0.8               | 1.9       | 0.2   | 0.6   | 0.6   | 0.6   | 1.9     |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.47              | 0.02      | 0.22  | 0.05  | 0.70  | 0.40  | 0.28    |
|                         |              | SD        | 0.672             | 0.783     | 0.293 | 0.437 | 1.121 | 1.126 | 0.809   |
|                         |              | Minimum   | -0.4              | -1.4      | -0.2  | -0.5  | -0.6  | -1.4  | -1.4    |
|                         |              | Median    | 0.50              | 0.10      | 0.15  | 0.05  | 0.45  | 0.45  | 0.20    |
|                         |              | Maximum   | 1.3               | 1.0       | 0.6   | 0.7   | 2.1   | 2.0   | 2.1     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Calcium (mg/dL)         | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         | A              | Day 2        | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 4  | 2 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | B              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | C              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         | D              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Calcium (mg/dL)         | E              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | Overall*       | Day 2        | 0          | 0 | 0 | 0          | 29 | 1 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 27 | 3 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 29 | 1 | 0          | 0 | 0 |
| Chloride (mEq/L)        | Pooled Placebo | Day 2        | 0          | 1 | 0 | 0          | 7  | 1 | 0          | 0 | 1 |
|                         |                | Day 3        | 0          | 1 | 0 | 0          | 7  | 1 | 0          | 0 | 1 |
|                         |                | End of Study | 0          | 1 | 0 | 1          | 7  | 0 | 0          | 1 | 0 |
|                         | A              | Day 2        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 1 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                         | B              | Day 2        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 1 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 1 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Chloride (mEq/L)        | C              | Day 2        | 1          | 1 | 0 | 0          | 4  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 1          | 1 | 0 | 0          | 4  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 1          | 1 | 0 | 0          | 4  | 0 | 0          | 0 | 0 |
|                         | D              | Day 2        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         | E              | Day 2        | 0          | 2 | 1 | 0          | 3  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 3 | 0 | 0          | 3  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 1          | 2 | 0 | 0          | 3  | 0 | 0          | 0 | 0 |
|                         | Overall*       | Day 2        | 1          | 4 | 1 | 0          | 22 | 0 | 0          | 0 | 2 |
|                         |                | Day 3        | 1          | 5 | 0 | 0          | 22 | 0 | 0          | 2 | 0 |
|                         |                | End of Study | 2          | 4 | 0 | 0          | 22 | 0 | 0          | 1 | 1 |
| Potassium (mEq/L)       | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                |              |            |   |   |            |    |   |            |   |   |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment | Time Point   | Baseline L |   |   | Baseline N |   |   | Baseline H |   |   |
|-------------------------|-----------|--------------|------------|---|---|------------|---|---|------------|---|---|
|                         |           |              | Postdose   |   |   | Postdose   |   |   | Postdose   |   |   |
|                         |           |              | L          | N | H | L          | N | H | L          | N | H |
| Potassium (mEq/L)       | A         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         | B         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         | C         | Day 2        | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         | D         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         | E         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Potassium (mEq/L)       | Overall*       | Day 2        | 0          | 0 | 0 | 0          | 29 | 1 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 27 | 3 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 28 | 2 | 0          | 0 | 0 |
| Albumin (g/dL)          | Pooled Placebo | Day 2        | 1          | 0 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 1 | 0 | 0          | 8  | 1 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 1 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                         | A              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | B              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | C              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Albumin (g/dL)          | D              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | E              | Day 2        | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | Overall*       | Day 2        | 0          | 0 | 0 | 1          | 29 | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
| Creatinine (mg/dL)      | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 9  | 1 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 9  | 1 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 9  | 1 | 0          | 0 | 0 |
|                         | A              | Day 2        | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|-----------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |           |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |           |              | L          | N | H | L          | N  | H | L          | N | H |
| Creatinine (mg/dL)      | B         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | C         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | D         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | E         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         | Overall*  | Day 2        | 0          | 0 | 0 | 0          | 29 | 1 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 29 | 1 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 29 | 1 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Glucose (mg/dL)         | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 9  | 1 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 7  | 3 | 0          | 0 | 0 |
|                         | A              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         | B              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         | C              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | D              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)     | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-----------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                             |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                             |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Glucose (mg/dL)             | E              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                             |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                             |                | End of Study | 0          | 0 | 0 | 1          | 4  | 1 | 0          | 0 | 0 |
|                             | Overall*       | Day 2        | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                             |                | Day 3        | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                             |                | End of Study | 0          | 0 | 0 | 1          | 25 | 4 | 0          | 0 | 0 |
| Alkaline Phosphatase (IU/L) | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                             |                | Day 3        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                             |                | End of Study | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                             | A              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                             |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                             |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                             | B              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                             |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                             |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)         | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|---------------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                                 |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                                 |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Alkaline Phosphatase (IU/L)     | C              | Day 2        | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                                 | D              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 | E              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 | Overall*       | Day 2        | 0          | 0 | 0 | 1          | 29 | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 1          | 29 | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 1          | 29 | 0 | 0          | 0 | 0 |
| Alanine Aminotransferase (IU/L) | Pooled Placebo | Day 2        | 0          | 1 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 1 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 1 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)         | Treatment | Time Point   | Baseline L |   |   | Baseline N |   |   | Baseline H |   |   |
|---------------------------------|-----------|--------------|------------|---|---|------------|---|---|------------|---|---|
|                                 |           |              | Postdose   |   |   | Postdose   |   |   | Postdose   |   |   |
|                                 |           |              | L          | N | H | L          | N | H | L          | N | H |
| Alanine Aminotransferase (IU/L) | A         | Day 2        | 1          | 0 | 0 | 0          | 5 | 0 | 0          | 0 | 0 |
|                                 |           | Day 3        | 0          | 1 | 0 | 0          | 5 | 0 | 0          | 0 | 0 |
|                                 |           | End of Study | 0          | 1 | 0 | 0          | 5 | 0 | 0          | 0 | 0 |
|                                 | B         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 | C         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 | D         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | Day 3        | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                                 |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 | E         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)           | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-----------------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                                   |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                                   |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Alanine Aminotransferase (IU/L)   | Overall*       | Day 2        | 1          | 0 | 0 | 0          | 29 | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 0          | 1 | 0 | 0          | 28 | 1 | 0          | 0 | 0 |
|                                   |                | End of Study | 0          | 1 | 0 | 0          | 29 | 0 | 0          | 0 | 0 |
| Aspartate Aminotransferase (IU/L) | Pooled Placebo | Day 2        | 0          | 1 | 0 | 1          | 8  | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 0          | 1 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                                   |                | End of Study | 0          | 1 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                                   | A              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   | B              | Day 2        | 1          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 1          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                                   |                | End of Study | 1          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                                   | C              | Day 2        | 1          | 0 | 0 | 2          | 3  | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 1          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                                   |                | End of Study | 1          | 0 | 0 | 0          | 4  | 1 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)           | Treatment      | Time Point     | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-----------------------------------|----------------|----------------|------------|---|---|------------|----|---|------------|---|---|
|                                   |                |                | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                                   |                |                | L          | N | H | L          | N  | H | L          | N | H |
| Aspartate Aminotransferase (IU/L) | D              | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   | E              | Day 2          | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                                   |                | Day 3          | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                                   |                | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   | Overall*       | Day 2          | 2          | 0 | 0 | 3          | 25 | 0 | 0          | 0 | 0 |
|                                   |                | Day 3          | 2          | 0 | 0 | 1          | 27 | 0 | 0          | 0 | 0 |
|                                   |                | End of Study   | 2          | 0 | 0 | 0          | 27 | 1 | 0          | 0 | 0 |
| GGT (IU/L)                        | Pooled Placebo | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                                   |                | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                                   |                | Day 2          | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                                   |                | Day 3          | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                                   |                | End of Study   | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                                   | A              | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment | Time Point     | Baseline L |   |   | Baseline N |   |   | Baseline H |   |   |
|-------------------------|-----------|----------------|------------|---|---|------------|---|---|------------|---|---|
|                         |           |                | Postdose   |   |   | Postdose   |   |   | Postdose   |   |   |
|                         |           |                | L          | N | H | L          | N | H | L          | N | H |
| GGT (IU/L)              | A         | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 2          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 3          | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         |           | End of Study   | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         | B         | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 2          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 3          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | End of Study   | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         | C         | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 2          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 3          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | End of Study   | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         | D         | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point     | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|----------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |                | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |                | L          | N | H | L          | N  | H | L          | N | H |
| GGT (IU/L)              | D              | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | E              | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | Overall*       | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                         |                | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                         |                | Day 2          | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                         |                | Day 3          | 0          | 0 | 0 | 0          | 29 | 1 | 0          | 0 | 0 |
|                         |                | End of Study   | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
| Creatine Kinase (IU/L)  | Pooled Placebo | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point     | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|----------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |                | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |                | L          | N | H | L          | N  | H | L          | N | H |
| Creatine Kinase (IU/L)  | Pooled Placebo | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | Day 2          | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | Day 3          | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | End of Study   | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         | A              | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | B              | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | C              | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment | Time Point     | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|-----------|----------------|------------|---|---|------------|----|---|------------|---|---|
|                         |           |                | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |           |                | L          | N | H | L          | N  | H | L          | N | H |
| Creatine Kinase (IU/L)  | C         | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | End of Study   | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         | D         | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | End of Study   | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         | E         | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 4  | 0 | 0          | 2 | 0 |
|                         |           | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 4  | 0 | 0          | 2 | 0 |
|                         |           | Day 2          | 0          | 0 | 0 | 1          | 3  | 0 | 0          | 2 | 0 |
|                         |           | Day 3          | 0          | 0 | 0 | 1          | 3  | 0 | 0          | 2 | 0 |
|                         |           | End of Study   | 0          | 0 | 0 | 0          | 4  | 0 | 0          | 1 | 1 |
|                         | Overall*  | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 28 | 0 | 0          | 2 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)      | Treatment      | Time Point     | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|------------------------------|----------------|----------------|------------|---|---|------------|----|---|------------|---|---|
|                              |                |                | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                              |                |                | L          | N | H | L          | N  | H | L          | N | H |
| Creatine Kinase (IU/L)       | Overall*       | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 28 | 0 | 0          | 2 | 0 |
|                              |                | Day 2          | 0          | 0 | 0 | 1          | 27 | 0 | 0          | 2 | 0 |
|                              |                | Day 3          | 0          | 0 | 0 | 1          | 27 | 0 | 0          | 2 | 0 |
|                              |                | End of Study   | 0          | 0 | 0 | 0          | 26 | 2 | 0          | 1 | 1 |
| Lactate Dehydrogenase (IU/L) | Pooled Placebo | Day 2          | 0          | 0 | 0 | 2          | 8  | 0 | 0          | 0 | 0 |
|                              |                | Day 3          | 0          | 0 | 0 | 2          | 8  | 0 | 0          | 0 | 0 |
|                              |                | End of Study   | 0          | 0 | 0 | 1          | 9  | 0 | 0          | 0 | 0 |
|                              | A              | Day 2          | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                              |                | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              |                | End of Study   | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                              | B              | Day 2          | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                              |                | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              |                | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              | C              | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              |                | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)      | Treatment      | Time Point     | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|------------------------------|----------------|----------------|------------|---|---|------------|----|---|------------|---|---|
|                              |                |                | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                              |                |                | L          | N | H | L          | N  | H | L          | N | H |
| Lactate Dehydrogenase (IU/L) | C              | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              | D              | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              |                | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              |                | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              | E              | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              |                | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              |                | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              | Overall*       | Day 2          | 0          | 0 | 0 | 2          | 28 | 0 | 0          | 0 | 0 |
|                              |                | Day 3          | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                              |                | End of Study   | 0          | 0 | 0 | 1          | 29 | 0 | 0          | 0 | 0 |
| C Reactive Protein (mg/L)    | Pooled Placebo | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                              |                | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                              |                | Day 2          | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                              |                | Day 3          | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                              |                | End of Study   | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                              |                |                |            |   |   |            |    |   |            |   |   |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)   | Treatment | Time Point     | Baseline L |   |   | Baseline N |   |   | Baseline H |   |   |
|---------------------------|-----------|----------------|------------|---|---|------------|---|---|------------|---|---|
|                           |           |                | Postdose   |   |   | Postdose   |   |   | Postdose   |   |   |
|                           |           |                | L          | N | H | L          | N | H | L          | N | H |
| C Reactive Protein (mg/L) | A         | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           |           | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           |           | Day 2          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           |           | Day 3          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           |           | End of Study   | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           | B         | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           |           | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           |           | Day 2          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           |           | Day 3          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           |           | End of Study   | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           | C         | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           |           | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           |           | Day 2          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           |           | Day 3          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                           |           | End of Study   | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units)   | Treatment | Time Point     | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|---------------------------|-----------|----------------|------------|---|---|------------|----|---|------------|---|---|
|                           |           |                | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                           |           |                | L          | N | H | L          | N  | H | L          | N | H |
| C Reactive Protein (mg/L) | D         | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                           |           | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                           |           | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                           |           | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                           |           | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                           | E         | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                           |           | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                           |           | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                           |           | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                           |           | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                           | Overall*  | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                           |           | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                           |           | Day 2          | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                           |           | Day 3          | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                           |           | End of Study   | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point     | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|----------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |                | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |                | L          | N | H | L          | N  | H | L          | N | H |
| Troponin I (ug/L)       | Pooled Placebo | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | Day 2          | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | Day 3          | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | End of Study   | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         | A              | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | B              | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment | Time Point     | Baseline L |   |   | Baseline N |   |   | Baseline H |   |   |
|-------------------------|-----------|----------------|------------|---|---|------------|---|---|------------|---|---|
|                         |           |                | Postdose   |   |   | Postdose   |   |   | Postdose   |   |   |
|                         |           |                | L          | N | H | L          | N | H | L          | N | H |
| Troponin I (ug/L)       | C         | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 2          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 3          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | End of Study   | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         | D         | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 2          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 3          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | End of Study   | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         | E         | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 2          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 3          | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | End of Study   | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point     | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|----------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |                | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |                | L          | N | H | L          | N  | H | L          | N | H |
| Troponin I (ug/L)       | Overall*       | Day 1, Hour 4  | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                         |                | Day 1, Hour 12 | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                         |                | Day 2          | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                         |                | Day 3          | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                         |                | End of Study   | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
| Urea Nitrogen (mg/dL)   | Pooled Placebo | Day 2          | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | Day 3          | 0          | 0 | 0 | 0          | 9  | 1 | 0          | 0 | 0 |
|                         |                | End of Study   | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         | A              | Day 2          | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         |                | Day 3          | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         |                | End of Study   | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | B              | Day 2          | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                         |                | Day 3          | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                         |                | End of Study   | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                         | C              | Day 2          | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Urea Nitrogen (mg/dL)   | C              | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | D              | Day 2        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         | E              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         | Overall*       | Day 2        | 0          | 1 | 0 | 0          | 27 | 1 | 0          | 1 | 0 |
|                         |                | Day 3        | 0          | 1 | 0 | 0          | 27 | 1 | 0          | 1 | 0 |
|                         |                | End of Study | 0          | 1 | 0 | 0          | 27 | 1 | 0          | 1 | 0 |
| Sodium (mEq/L)          | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 9  | 1 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         | A              | Day 2        | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         |                |              |            |   |   |            |    |   |            |   |   |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|-----------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |           |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |           |              | L          | N | H | L          | N  | H | L          | N | H |
| Sodium (mEq/L)          | A         | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | B         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | C         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | D         | Day 2        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         | E         | Day 2        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 1 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         | Overall*  | Day 2        | 0          | 2 | 0 | 0          | 27 | 1 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Sodium (mEq/L)          | Overall*       | Day 3        | 0          | 1 | 1 | 0          | 28 | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 2 | 0 | 0          | 28 | 0 | 0          | 0 | 0 |
| Bilirubin (mg/dL)       | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 9  | 1 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         | A              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | B              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | C              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | D              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Bilirubin (mg/dL)       | D              | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | E              | Day 2        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                         | Overall*       | Day 2        | 0          | 0 | 0 | 0          | 29 | 0 | 0          | 1 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 29 | 0 | 0          | 1 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 29 | 0 | 0          | 1 | 0 |
| Urate (mg/dL)           | Pooled Placebo | Day 2        | 0          | 0 | 0 | 1          | 9  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 1          | 9  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 1          | 8  | 1 | 0          | 0 | 0 |
|                         | A              | Day 2        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                         | B              | Day 2        | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                         |                |              |            |   |   |            |    |   |            |   |   |
|                         |                |              |            |   |   |            |    |   |            |   |   |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

| Laboratory Test (units) | Treatment | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|-----------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |           |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |           |              | L          | N | H | L          | N  | H | L          | N | H |
| Urate (mg/dL)           | B         | Day 3        | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | C         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | D         | Day 2        | 1          | 0 | 0 | 0          | 4  | 0 | 0          | 0 | 1 |
|                         |           | Day 3        | 1          | 0 | 0 | 0          | 4  | 0 | 0          | 0 | 1 |
|                         |           | End of Study | 1          | 0 | 0 | 0          | 4  | 0 | 0          | 0 | 1 |
|                         | E         | Day 2        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 1          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         | Overall*  | Day 2        | 1          | 1 | 0 | 1          | 25 | 0 | 0          | 1 | 1 |
|                         |           | Day 3        | 2          | 0 | 0 | 1          | 25 | 0 | 0          | 1 | 1 |
|                         |           | End of Study | 1          | 1 | 0 | 0          | 26 | 0 | 0          | 1 | 1 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Hemoglobin (g/dL)       | 12.1-17.4       | # Screen   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 14.69          | 14.53     | 14.32 | 14.97 | 14.90 | 14.63 | 14.67   |
|                         |                 |            | SD        | 1.294          | 0.755     | 1.443 | 1.194 | 0.986 | 0.677 | 1.005   |
|                         |                 |            | Minimum   | 12.8           | 13.6      | 11.7  | 13.1  | 13.4  | 13.6  | 11.7    |
|                         |                 |            | Median    | 14.95          | 14.70     | 14.50 | 14.85 | 15.00 | 14.80 | 14.65   |
|                         |                 |            | Maximum   | 16.4           | 15.2      | 15.7  | 16.6  | 15.8  | 15.4  | 16.6    |
|                         |                 | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 14.64          | 14.48     | 13.93 | 14.88 | 14.65 | 14.42 | 14.47   |
|                         |                 |            | SD        | 1.246          | 0.655     | 1.375 | 1.227 | 1.328 | 0.760 | 1.080   |
|                         |                 |            | Minimum   | 12.7           | 13.4      | 11.6  | 12.7  | 13.0  | 13.5  | 11.6    |
|                         |                 |            | Median    | 14.85          | 14.45     | 14.20 | 15.05 | 14.65 | 14.30 | 14.50   |
|                         |                 |            | Maximum   | 16.7           | 15.3      | 15.2  | 16.1  | 16.4  | 15.8  | 16.4    |
|                         |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 15.10          | 15.17     | 14.48 | 15.08 | 15.33 | 14.42 | 14.90   |
|                         |                 |            | SD        | 1.486          | 0.501     | 1.422 | 1.194 | 1.157 | 0.799 | 1.060   |
|                         |                 |            | Minimum   | 12.8           | 14.3      | 12.1  | 13.1  | 13.6  | 13.8  | 12.1    |
|                         |                 |            | Median    | 15.25          | 15.30     | 14.90 | 15.75 | 15.55 | 14.10 | 15.00   |
|                         |                 |            | Maximum   | 17.9           | 15.7      | 16.1  | 15.9  | 16.5  | 15.8  | 16.5    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Hemoglobin (g/dL)       | 12.1-17.4 #     | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 15.24          | 15.58     | 14.87 | 15.25 | 15.53 | 14.62 | 15.17   |
|                         |                 |              | SD        | 1.229          | 0.549     | 1.560 | 1.263 | 1.419 | 0.512 | 1.134   |
|                         |                 |              | Minimum   | 13.1           | 15.0      | 12.2  | 12.9  | 12.8  | 13.9  | 12.2    |
|                         |                 |              | Median    | 15.55          | 15.45     | 15.20 | 15.90 | 16.15 | 14.65 | 15.30   |
|                         |                 |              | Maximum   | 17.0           | 16.3      | 16.7  | 16.1  | 16.6  | 15.3  | 16.7    |
|                         |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 14.38          | 14.10     | 13.65 | 14.70 | 14.23 | 14.55 | 14.25   |
|                         |                 |              | SD        | 1.073          | 0.716     | 1.595 | 1.319 | 1.120 | 0.969 | 1.160   |
|                         |                 |              | Minimum   | 12.8           | 13.0      | 10.9  | 13.0  | 12.8  | 13.1  | 10.9    |
|                         |                 |              | Median    | 14.40          | 14.35     | 13.95 | 15.10 | 14.15 | 14.65 | 14.45   |
|                         |                 |              | Maximum   | 15.9           | 14.8      | 15.3  | 16.2  | 15.5  | 16.0  | 16.2    |
| Hematocrit (%)          | 35-51.1 #       | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 43.89          | 43.62     | 42.83 | 44.25 | 44.08 | 43.87 | 43.73   |
|                         |                 |              | SD        | 2.985          | 2.098     | 3.898 | 2.542 | 2.051 | 1.148 | 2.387   |
|                         |                 |              | Minimum   | 40.0           | 40.8      | 35.2  | 39.9  | 41.5  | 41.8  | 35.2    |
|                         |                 |              | Median    | 44.55          | 43.55     | 44.55 | 44.65 | 43.70 | 44.35 | 44.25   |
|                         |                 |              | Maximum   | 48.7           | 46.2      | 45.5  | 47.5  | 47.4  | 44.8  | 47.5    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Hematocrit (%)          | 35-51.1 #       | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 43.28          | 43.20     | 41.47 | 43.50 | 42.97 | 44.08 | 43.04   |
|                         |                 |            | SD        | 2.939          | 1.524     | 3.566 | 2.565 | 2.717 | 1.813 | 2.521   |
|                         |                 |            | Minimum   | 39.1           | 41.5      | 34.8  | 38.9  | 39.8  | 41.5  | 34.8    |
|                         |                 |            | Median    | 43.80          | 42.80     | 42.20 | 43.75 | 43.30 | 43.70 | 43.35   |
|                         |                 |            | Maximum   | 47.0           | 45.2      | 44.3  | 46.7  | 45.7  | 46.4  | 46.7    |
|                         |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 44.66          | 44.83     | 42.93 | 44.02 | 45.23 | 44.27 | 44.26   |
|                         |                 |            | SD        | 3.390          | 1.544     | 3.817 | 2.381 | 2.301 | 1.280 | 2.395   |
|                         |                 |            | Minimum   | 39.1           | 42.4      | 35.7  | 40.2  | 42.0  | 42.6  | 35.7    |
|                         |                 |            | Median    | 45.20          | 44.95     | 44.50 | 45.05 | 45.30 | 43.95 | 44.65   |
|                         |                 |            | Maximum   | 50.2           | 46.9      | 46.3  | 46.1  | 48.2  | 46.1  | 48.2    |
|                         |                 | Day 3      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 45.22          | 45.88     | 44.70 | 44.87 | 45.73 | 45.58 | 45.35   |
|                         |                 |            | SD        | 2.646          | 2.057     | 4.265 | 2.868 | 3.110 | 1.264 | 2.732   |
|                         |                 |            | Minimum   | 40.3           | 42.9      | 36.7  | 39.3  | 40.2  | 43.2  | 36.7    |
|                         |                 |            | Median    | 45.95          | 46.00     | 46.15 | 45.80 | 46.05 | 45.95 | 45.95   |
|                         |                 |            | Maximum   | 47.8           | 49.1      | 49.1  | 46.9  | 49.6  | 46.7  | 49.6    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)  | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|--------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                          |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Hematocrit (%)           | 35-51.1 #       | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                          |                 |              | Mean      | 42.67          | 41.92     | 40.83 | 43.32 | 42.07 | 44.52 | 42.53   |
|                          |                 |              | SD        | 2.598          | 1.594     | 4.246 | 2.771 | 2.458 | 2.102 | 2.887   |
|                          |                 |              | Minimum   | 39.5           | 39.5      | 32.8  | 39.8  | 39.8  | 41.3  | 32.8    |
|                          |                 |              | Median    | 42.80          | 42.35     | 42.35 | 44.05 | 41.20 | 45.30 | 42.80   |
|                          |                 |              | Maximum   | 45.9           | 43.8      | 44.2  | 46.5  | 46.3  | 47.0  | 47.0    |
| Platelet Count (thou/uL) | 162-399         | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                          |                 |              | Mean      | 205.8          | 242.5     | 238.5 | 222.3 | 245.2 | 227.3 | 235.2   |
|                          |                 |              | SD        | 29.96          | 18.21     | 52.63 | 50.82 | 26.07 | 52.35 | 40.63   |
|                          |                 |              | Minimum   | 159            | 224       | 174   | 181   | 197   | 192   | 174     |
|                          |                 |              | Median    | 209.5          | 236.0     | 229.5 | 200.5 | 258.0 | 205.5 | 231.5   |
|                          |                 |              | Maximum   | 267            | 268       | 318   | 311   | 263   | 329   | 329     |
|                          |                 | Baseline     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                          |                 |              | Mean      | 204.9          | 232.5     | 219.2 | 221.8 | 240.7 | 244.8 | 231.8   |
|                          |                 |              | SD        | 27.29          | 33.20     | 42.06 | 44.34 | 32.96 | 46.67 | 38.76   |
|                          |                 |              | Minimum   | 160            | 199       | 163   | 174   | 182   | 202   | 163     |
|                          |                 |              | Median    | 205.5          | 230.5     | 217.5 | 207.0 | 248.5 | 227.5 | 226.5   |
|                          |                 |              | Maximum   | 252            | 275       | 281   | 301   | 268   | 325   | 325     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)  | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|--------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                          |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Platelet Count (thou/uL) | 162-399         | Day 2        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                          |                 |              | Mean      | 196.3          | 214.7     | 229.0 | 213.8 | 244.8 | 238.5 | 228.2   |
|                          |                 |              | SD        | 27.22          | 17.70     | 37.38 | 48.47 | 29.65 | 49.91 | 37.96   |
|                          |                 |              | Minimum   | 152            | 195       | 170   | 174   | 190   | 189   | 170     |
|                          |                 |              | Median    | 200.5          | 209.0     | 228.5 | 198.0 | 252.5 | 227.0 | 228.5   |
|                          |                 |              | Maximum   | 225            | 237       | 276   | 301   | 269   | 328   | 328     |
|                          |                 | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                          |                 |              | Mean      | 205.6          | 233.0     | 248.5 | 219.3 | 248.3 | 246.8 | 239.2   |
|                          |                 |              | SD        | 24.75          | 13.11     | 41.49 | 42.31 | 32.28 | 53.27 | 37.96   |
|                          |                 |              | Minimum   | 163            | 219       | 183   | 174   | 186   | 198   | 174     |
|                          |                 |              | Median    | 210.5          | 228.0     | 258.0 | 208.0 | 258.5 | 233.5 | 241.0   |
|                          |                 |              | Maximum   | 245            | 255       | 289   | 287   | 272   | 348   | 348     |
|                          |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                          |                 |              | Mean      | 199.9          | 221.0     | 224.3 | 219.2 | 227.8 | 252.7 | 229.0   |
|                          |                 |              | SD        | 22.48          | 10.55     | 45.35 | 42.05 | 28.05 | 65.59 | 41.35   |
|                          |                 |              | Minimum   | 171            | 208       | 155   | 176   | 181   | 194   | 155     |
|                          |                 |              | Median    | 200.0          | 221.5     | 231.0 | 218.0 | 230.5 | 238.5 | 230.5   |
|                          |                 |              | Maximum   | 244            | 232       | 277   | 285   | 266   | 378   | 378     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)       | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |        |        |        |        | Overall |
|-------------------------------|-----------------|------------|-----------|----------------|-----------|--------|--------|--------|--------|---------|
|                               |                 |            |           |                | A         | B      | C      | D      | E      |         |
| Red Blood Cell Count (mil/uL) | 3.7-5.85 #      | Screen     | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                               |                 |            | Mean      | 4.859          | 4.933     | 4.900  | 4.738  | 4.732  | 4.675  | 4.796   |
|                               |                 |            | SD        | 0.4161         | 0.4455    | 0.5905 | 0.3954 | 0.2631 | 0.1781 | 0.3865  |
|                               |                 |            | Minimum   | 4.32           | 4.57      | 3.80   | 4.06   | 4.28   | 4.33   | 3.80    |
|                               |                 |            | Median    | 4.915          | 4.725     | 5.140  | 4.785  | 4.760  | 4.735  | 4.765   |
|                               |                 |            | Maximum   | 5.59           | 5.65      | 5.37   | 5.22   | 5.03   | 4.80   | 5.65    |
|                               |                 | Baseline   | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                               |                 |            | Mean      | 4.817          | 4.908     | 4.763  | 4.687  | 4.657  | 4.620  | 4.727   |
|                               |                 |            | SD        | 0.4071         | 0.3252    | 0.5566 | 0.4368 | 0.3133 | 0.2918 | 0.3833  |
|                               |                 |            | Minimum   | 4.18           | 4.53      | 3.78   | 3.93   | 4.19   | 4.21   | 3.78    |
|                               |                 |            | Median    | 4.915          | 4.815     | 4.870  | 4.805  | 4.785  | 4.570  | 4.765   |
|                               |                 |            | Maximum   | 5.42           | 5.37      | 5.36   | 5.22   | 4.96   | 4.99   | 5.37    |
|                               |                 | Day 2      | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                               |                 |            | Mean      | 4.959          | 5.093     | 4.888  | 4.740  | 4.860  | 4.623  | 4.841   |
|                               |                 |            | SD        | 0.4353         | 0.3900    | 0.5375 | 0.4261 | 0.2833 | 0.2174 | 0.3936  |
|                               |                 |            | Minimum   | 4.18           | 4.58      | 3.89   | 4.06   | 4.36   | 4.33   | 3.89    |
|                               |                 |            | Median    | 4.990          | 5.040     | 4.960  | 4.920  | 4.985  | 4.660  | 4.885   |
|                               |                 |            | Maximum   | 5.52           | 5.68      | 5.39   | 5.14   | 5.10   | 4.85   | 5.68    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)          | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |        |        |        |        | Overall |
|----------------------------------|-----------------|--------------|-----------|----------------|-----------|--------|--------|--------|--------|---------|
|                                  |                 |              |           |                | A         | B      | C      | D      | E      |         |
| Red Blood Cell Count (mil/uL)    | 3.7-5.85 #      | Day 3        | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                                  |                 |              | Mean      | 5.014          | 5.193     | 5.063  | 4.812  | 4.922  | 4.742  | 4.946   |
|                                  |                 |              | SD        | 0.3853         | 0.4558    | 0.6035 | 0.4629 | 0.4078 | 0.1998 | 0.4462  |
|                                  |                 |              | Minimum   | 4.30           | 4.61      | 3.94   | 3.96   | 4.19   | 4.40   | 3.94    |
|                                  |                 |              | Median    | 5.040          | 5.185     | 5.145  | 5.035  | 4.945  | 4.795  | 4.970   |
|                                  |                 |              | Maximum   | 5.62           | 5.93      | 5.62   | 5.12   | 5.34   | 4.98   | 5.93    |
|                                  |                 | End of Study | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                                  |                 |              | Mean      | 4.730          | 4.735     | 4.663  | 4.643  | 4.537  | 4.678  | 4.651   |
|                                  |                 |              | SD        | 0.3581         | 0.4055    | 0.5935 | 0.4421 | 0.2706 | 0.2158 | 0.3844  |
|                                  |                 |              | Minimum   | 4.25           | 4.32      | 3.57   | 4.01   | 4.13   | 4.38   | 3.57    |
|                                  |                 |              | Median    | 4.750          | 4.595     | 4.770  | 4.870  | 4.505  | 4.670  | 4.635   |
|                                  |                 |              | Maximum   | 5.35           | 5.42      | 5.20   | 5.02   | 4.94   | 4.99   | 5.42    |
| White Blood Cell Count (thou/uL) | 3.9-10.7        | Screen       | n         | 10             | 6         | 6      | 6      | 6      | 6      | 30      |
|                                  |                 |              | Mean      | 5.78           | 6.07      | 6.80   | 6.43   | 5.72   | 5.20   | 6.04    |
|                                  |                 |              | SD        | 1.140          | 0.758     | 0.853  | 1.544  | 1.094  | 0.456  | 1.094   |
|                                  |                 |              | Minimum   | 4.6            | 4.7       | 5.9    | 4.6    | 4.9    | 4.4    | 4.4     |
|                                  |                 |              | Median    | 5.45           | 6.30      | 6.50   | 6.65   | 5.35   | 5.30   | 5.85    |
|                                  |                 |              | Maximum   | 8.2            | 6.9       | 7.9    | 8.5    | 7.9    | 5.7    | 8.5     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)          | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|----------------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                                  |                 |            |           |                | A         | B     | C     | D     | E     |         |
| White Blood Cell Count (thou/uL) | 3.9-10.7        | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                  |                 |            | Mean      | 5.61           | 6.50      | 6.08  | 6.63  | 6.00  | 6.48  | 6.34    |
|                                  |                 |            | SD        | 1.365          | 1.122     | 1.130 | 1.807 | 1.535 | 1.775 | 1.419   |
|                                  |                 |            | Minimum   | 3.7            | 5.3       | 4.6   | 4.0   | 4.6   | 4.8   | 4.0     |
|                                  |                 |            | Median    | 5.65           | 6.35      | 6.05  | 7.25  | 5.60  | 6.05  | 5.90    |
|                                  |                 |            | Maximum   | 7.4            | 8.3       | 7.3   | 8.3   | 9.0   | 9.3   | 9.3     |
|                                  |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                  |                 |            | Mean      | 5.08           | 5.88      | 5.85  | 5.55  | 5.43  | 4.72  | 5.49    |
|                                  |                 |            | SD        | 1.283          | 1.074     | 0.761 | 1.286 | 1.374 | 0.611 | 1.076   |
|                                  |                 |            | Minimum   | 2.9            | 4.4       | 5.2   | 3.5   | 4.1   | 4.0   | 3.5     |
|                                  |                 |            | Median    | 4.95           | 5.95      | 5.55  | 6.20  | 5.15  | 4.65  | 5.35    |
|                                  |                 |            | Maximum   | 6.7            | 7.6       | 7.1   | 6.6   | 7.9   | 5.5   | 7.9     |
|                                  |                 | Day 3      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                  |                 |            | Mean      | 5.59           | 6.00      | 7.05  | 5.88  | 5.78  | 5.18  | 5.98    |
|                                  |                 |            | SD        | 1.293          | 0.908     | 1.703 | 1.363 | 1.192 | 0.500 | 1.276   |
|                                  |                 |            | Minimum   | 3.2            | 4.5       | 5.2   | 3.9   | 4.2   | 4.7   | 3.9     |
|                                  |                 |            | Median    | 5.75           | 6.20      | 6.75  | 6.00  | 5.95  | 5.00  | 5.85    |
|                                  |                 |            | Maximum   | 8.0            | 7.0       | 9.4   | 7.5   | 7.5   | 5.9   | 9.4     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)          | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|----------------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                                  |                 |              |           |                | A         | B     | C     | D     | E     |         |
| White Blood Cell Count (thou/uL) | 3.9-10.7        | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                  |                 |              | Mean      | 5.15           | 6.70      | 5.93  | 5.93  | 5.53  | 5.38  | 5.90    |
|                                  |                 |              | SD        | 1.032          | 1.055     | 0.845 | 1.465 | 1.484 | 0.806 | 1.180   |
|                                  |                 |              | Minimum   | 3.5            | 5.2       | 5.0   | 3.8   | 4.6   | 4.6   | 3.8     |
|                                  |                 |              | Median    | 5.05           | 6.50      | 5.85  | 6.30  | 4.90  | 5.25  | 5.90    |
|                                  |                 |              | Maximum   | 6.9            | 8.0       | 6.9   | 7.7   | 8.4   | 6.6   | 8.4     |
| Basophils (%)                    | 0-0.7           | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                  |                 |              | Mean      | 0.44           | 0.47      | 0.40  | 0.53  | 0.55  | 0.52  | 0.49    |
|                                  |                 |              | SD        | 0.255          | 0.197     | 0.167 | 0.258 | 0.274 | 0.232 | 0.220   |
|                                  |                 |              | Minimum   | 0.1            | 0.2       | 0.3   | 0.2   | 0.3   | 0.2   | 0.2     |
|                                  |                 |              | Median    | 0.40           | 0.45      | 0.30  | 0.55  | 0.40  | 0.55  | 0.45    |
|                                  |                 |              | Maximum   | 1.0            | 0.8       | 0.7   | 0.9   | 0.9   | 0.8   | 0.9     |
|                                  |                 | Baseline     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                  |                 |              | Mean      | 0.38           | 0.33      | 0.43  | 0.40  | 0.43  | 0.40  | 0.40    |
|                                  |                 |              | SD        | 0.244          | 0.082     | 0.234 | 0.237 | 0.242 | 0.141 | 0.188   |
|                                  |                 |              | Minimum   | 0.0            | 0.2       | 0.3   | 0.1   | 0.1   | 0.2   | 0.1     |
|                                  |                 |              | Median    | 0.40           | 0.35      | 0.35  | 0.40  | 0.50  | 0.40  | 0.40    |
|                                  |                 |              | Maximum   | 0.8            | 0.4       | 0.9   | 0.7   | 0.7   | 0.6   | 0.9     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Basophils (%)           | 0-0.7           | Day 2        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 0.40           | 0.33      | 0.47  | 0.42  | 0.55  | 0.53  | 0.46    |
|                         |                 |              | SD        | 0.163          | 0.225     | 0.242 | 0.279 | 0.308 | 0.308 | 0.267   |
|                         |                 |              | Minimum   | 0.1            | 0.1       | 0.3   | 0.2   | 0.3   | 0.2   | 0.1     |
|                         |                 |              | Median    | 0.40           | 0.25      | 0.35  | 0.35  | 0.45  | 0.45  | 0.40    |
|                         |                 |              | Maximum   | 0.6            | 0.7       | 0.9   | 0.9   | 1.1   | 1.0   | 1.1     |
|                         |                 | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 0.44           | 0.37      | 0.38  | 0.40  | 0.45  | 0.43  | 0.41    |
|                         |                 |              | SD        | 0.303          | 0.225     | 0.343 | 0.261 | 0.288 | 0.163 | 0.246   |
|                         |                 |              | Minimum   | 0.2            | 0.2       | 0.1   | 0.1   | 0.1   | 0.2   | 0.1     |
|                         |                 |              | Median    | 0.35           | 0.30      | 0.30  | 0.35  | 0.45  | 0.45  | 0.35    |
|                         |                 |              | Maximum   | 1.2            | 0.8       | 1.0   | 0.8   | 0.8   | 0.6   | 1.0     |
|                         |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 0.41           | 0.48      | 0.37  | 0.50  | 0.50  | 0.57  | 0.48    |
|                         |                 |              | SD        | 0.228          | 0.117     | 0.137 | 0.237 | 0.363 | 0.294 | 0.239   |
|                         |                 |              | Minimum   | 0.0            | 0.4       | 0.2   | 0.2   | 0.1   | 0.3   | 0.1     |
|                         |                 |              | Median    | 0.45           | 0.45      | 0.35  | 0.50  | 0.45  | 0.45  | 0.40    |
|                         |                 |              | Maximum   | 0.7            | 0.7       | 0.6   | 0.8   | 1.1   | 1.1   | 1.1     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)      | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|------------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                              |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Absolute Basophils (thou/uL) | 0-0.1           | Screen     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |            | Mean      | 0.01           | 0.02      | 0.00  | 0.00  | 0.03  | 0.00  | 0.01    |
|                              |                 |            | SD        | 0.032          | 0.041     | 0.000 | 0.000 | 0.052 | 0.000 | 0.031   |
|                              |                 |            | Minimum   | 0.0            | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                              |                 |            | Median    | 0.00           | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                              |                 |            | Maximum   | 0.1            | 0.1       | 0.0   | 0.0   | 0.1   | 0.0   | 0.1     |
|                              |                 | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |            | Mean      | 0.00           | 0.00      | 0.02  | 0.00  | 0.00  | 0.00  | 0.00    |
|                              |                 |            | SD        | 0.000          | 0.000     | 0.041 | 0.000 | 0.000 | 0.000 | 0.018   |
|                              |                 |            | Minimum   | 0.0            | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                              |                 |            | Median    | 0.00           | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                              |                 |            | Maximum   | 0.0            | 0.0       | 0.1   | 0.0   | 0.0   | 0.0   | 0.1     |
|                              |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |            | Mean      | 0.00           | 0.00      | 0.02  | 0.00  | 0.02  | 0.00  | 0.01    |
|                              |                 |            | SD        | 0.000          | 0.000     | 0.041 | 0.000 | 0.041 | 0.000 | 0.025   |
|                              |                 |            | Minimum   | 0.0            | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                              |                 |            | Median    | 0.00           | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                              |                 |            | Maximum   | 0.0            | 0.0       | 0.1   | 0.0   | 0.1   | 0.0   | 0.1     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)      | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|------------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                              |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Absolute Basophils (thou/uL) | 0-0.1           | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |              | Mean      | 0.01           | 0.02      | 0.02  | 0.00  | 0.02  | 0.00  | 0.01    |
|                              |                 |              | SD        | 0.032          | 0.041     | 0.041 | 0.000 | 0.041 | 0.000 | 0.031   |
|                              |                 |              | Minimum   | 0.0            | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                              |                 |              | Median    | 0.00           | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                              |                 |              | Maximum   | 0.1            | 0.1       | 0.1   | 0.0   | 0.1   | 0.0   | 0.1     |
|                              |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |              | Mean      | 0.00           | 0.02      | 0.00  | 0.00  | 0.02  | 0.02  | 0.01    |
|                              |                 |              | SD        | 0.000          | 0.041     | 0.000 | 0.000 | 0.041 | 0.041 | 0.031   |
|                              |                 |              | Minimum   | 0.0            | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                              |                 |              | Median    | 0.00           | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                              |                 |              | Maximum   | 0.0            | 0.1       | 0.0   | 0.0   | 0.1   | 0.1   | 0.1     |
| Eosinophils (%)              | 0.2-9           | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |              | Mean      | 2.27           | 3.53      | 4.68  | 2.60  | 4.00  | 2.60  | 3.48    |
|                              |                 |              | SD        | 1.141          | 1.790     | 4.581 | 1.867 | 2.143 | 1.532 | 2.578   |
|                              |                 |              | Minimum   | 0.9            | 1.3       | 0.6   | 0.9   | 1.0   | 1.0   | 0.6     |
|                              |                 |              | Median    | 2.05           | 3.60      | 3.70  | 2.00  | 4.80  | 2.45  | 3.10    |
|                              |                 |              | Maximum   | 4.2            | 6.6       | 13.6  | 6.0   | 6.6   | 5.3   | 13.6    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Eosinophils (%)         | 0.2-9           | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 2.01           | 3.03      | 4.35  | 2.27  | 3.20  | 1.90  | 2.95    |
|                         |                 |            | SD        | 1.193          | 2.284     | 5.078 | 1.812 | 1.997 | 1.251 | 2.759   |
|                         |                 |            | Minimum   | 0.4            | 0.3       | 0.5   | 0.7   | 0.4   | 0.2   | 0.2     |
|                         |                 |            | Median    | 1.65           | 2.80      | 2.55  | 2.00  | 3.55  | 1.75  | 2.30    |
|                         |                 |            | Maximum   | 4.1            | 7.2       | 14.3  | 5.6   | 5.6   | 4.1   | 14.3    |
|                         |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 2.35           | 3.63      | 5.17  | 2.42  | 3.43  | 4.20  | 3.77    |
|                         |                 |            | SD        | 1.028          | 1.813     | 5.971 | 1.636 | 1.997 | 4.033 | 3.393   |
|                         |                 |            | Minimum   | 1.2            | 0.8       | 0.8   | 1.1   | 0.8   | 1.2   | 0.8     |
|                         |                 |            | Median    | 2.10           | 3.60      | 2.80  | 1.75  | 3.55  | 2.55  | 3.10    |
|                         |                 |            | Maximum   | 4.0            | 6.4       | 16.9  | 5.3   | 5.9   | 12.2  | 16.9    |
|                         |                 | Day 3      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 2.03           | 3.63      | 4.78  | 2.28  | 3.13  | 3.33  | 3.43    |
|                         |                 |            | SD        | 0.806          | 1.861     | 5.883 | 1.478 | 1.836 | 2.396 | 3.032   |
|                         |                 |            | Minimum   | 1.3            | 1.1       | 0.7   | 1.3   | 0.7   | 0.9   | 0.7     |
|                         |                 |            | Median    | 1.55           | 3.55      | 2.30  | 1.80  | 3.35  | 2.45  | 2.45    |
|                         |                 |            | Maximum   | 3.3            | 6.5       | 16.4  | 5.2   | 5.1   | 7.3   | 16.4    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)              | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                                      |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Eosinophils (%)                      | 0.2-9           | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                      |                 |              | Mean      | 2.44           | 4.00      | 5.42  | 2.63  | 3.05  | 3.85  | 3.79    |
|                                      |                 |              | SD        | 0.988          | 2.705     | 7.226 | 1.726 | 1.491 | 3.445 | 3.762   |
|                                      |                 |              | Minimum   | 1.0            | 0.8       | 0.5   | 0.9   | 0.6   | 0.6   | 0.5     |
|                                      |                 |              | Median    | 2.50           | 3.00      | 2.40  | 2.40  | 2.95  | 3.00  | 2.85    |
|                                      |                 |              | Maximum   | 4.3            | 8.1       | 19.8  | 5.4   | 4.8   | 10.6  | 19.8    |
| Absolute Eosinophils (thou/uL) 0-0.8 |                 | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                      |                 |              | Mean      | 0.14           | 0.22      | 0.33  | 0.18  | 0.23  | 0.15  | 0.22    |
|                                      |                 |              | SD        | 0.070          | 0.098     | 0.301 | 0.160 | 0.121 | 0.084 | 0.172   |
|                                      |                 |              | Minimum   | 0.1            | 0.1       | 0.0   | 0.1   | 0.1   | 0.1   | 0.0     |
|                                      |                 |              | Median    | 0.10           | 0.20      | 0.30  | 0.10  | 0.25  | 0.10  | 0.20    |
|                                      |                 |              | Maximum   | 0.3            | 0.4       | 0.9   | 0.5   | 0.4   | 0.3   | 0.9     |
|                                      |                 | Baseline     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                      |                 |              | Mean      | 0.13           | 0.18      | 0.25  | 0.15  | 0.17  | 0.10  | 0.17    |
|                                      |                 |              | SD        | 0.082          | 0.147     | 0.243 | 0.122 | 0.103 | 0.063 | 0.147   |
|                                      |                 |              | Minimum   | 0.0            | 0.0       | 0.0   | 0.1   | 0.0   | 0.0   | 0.0     |
|                                      |                 |              | Median    | 0.10           | 0.15      | 0.20  | 0.10  | 0.20  | 0.10  | 0.10    |
|                                      |                 |              | Maximum   | 0.3            | 0.4       | 0.7   | 0.4   | 0.3   | 0.2   | 0.7     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)        | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                                |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Absolute Eosinophils (thou/uL) | 0-0.8           | Day 2        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |              | Mean      | 0.14           | 0.23      | 0.30  | 0.13  | 0.18  | 0.18  | 0.21    |
|                                |                 |              | SD        | 0.070          | 0.103     | 0.303 | 0.082 | 0.075 | 0.160 | 0.166   |
|                                |                 |              | Minimum   | 0.1            | 0.1       | 0.1   | 0.1   | 0.1   | 0.1   | 0.1     |
|                                |                 |              | Median    | 0.10           | 0.20      | 0.20  | 0.10  | 0.20  | 0.10  | 0.20    |
|                                |                 |              | Maximum   | 0.3            | 0.4       | 0.9   | 0.3   | 0.3   | 0.5   | 0.9     |
|                                |                 | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |              | Mean      | 0.12           | 0.23      | 0.32  | 0.15  | 0.18  | 0.18  | 0.21    |
|                                |                 |              | SD        | 0.079          | 0.103     | 0.343 | 0.122 | 0.075 | 0.133 | 0.180   |
|                                |                 |              | Minimum   | 0.0            | 0.1       | 0.1   | 0.1   | 0.1   | 0.1   | 0.1     |
|                                |                 |              | Median    | 0.10           | 0.20      | 0.20  | 0.10  | 0.20  | 0.10  | 0.20    |
|                                |                 |              | Maximum   | 0.3            | 0.4       | 1.0   | 0.4   | 0.3   | 0.4   | 1.0     |
|                                |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |              | Mean      | 0.12           | 0.27      | 0.35  | 0.15  | 0.15  | 0.20  | 0.22    |
|                                |                 |              | SD        | 0.042          | 0.151     | 0.524 | 0.122 | 0.084 | 0.167 | 0.257   |
|                                |                 |              | Minimum   | 0.1            | 0.1       | 0.0   | 0.1   | 0.1   | 0.0   | 0.0     |
|                                |                 |              | Median    | 0.10           | 0.20      | 0.15  | 0.10  | 0.10  | 0.20  | 0.15    |
|                                |                 |              | Maximum   | 0.2            | 0.5       | 1.4   | 0.4   | 0.3   | 0.5   | 1.4     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Lymphocytes (%)         | 14-43           | Screen     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 33.28          | 35.25     | 36.85 | 29.90 | 36.57 | 28.75 | 33.46   |
|                         |                 |            | SD        | 7.526          | 8.870     | 7.228 | 9.483 | 5.764 | 6.427 | 7.948   |
|                         |                 |            | Minimum   | 22.5           | 28.4      | 25.3  | 19.7  | 29.8  | 20.2  | 19.7    |
|                         |                 |            | Median    | 32.55          | 32.75     | 39.15 | 27.95 | 36.05 | 32.25 | 32.40   |
|                         |                 |            | Maximum   | 44.3           | 52.1      | 43.7  | 47.4  | 44.6  | 33.8  | 52.1    |
|                         |                 | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 32.50          | 34.30     | 34.28 | 30.13 | 33.55 | 22.77 | 31.01   |
|                         |                 |            | SD        | 8.166          | 9.702     | 5.954 | 7.271 | 5.255 | 8.406 | 8.271   |
|                         |                 |            | Minimum   | 19.5           | 25.4      | 26.4  | 19.5  | 23.3  | 11.4  | 11.4    |
|                         |                 |            | Median    | 32.90          | 32.85     | 35.70 | 29.10 | 34.40 | 21.45 | 32.05   |
|                         |                 |            | Maximum   | 44.8           | 50.8      | 41.8  | 40.1  | 38.0  | 34.5  | 50.8    |
|                         |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 35.61          | 34.07     | 34.12 | 29.92 | 32.93 | 31.65 | 32.54   |
|                         |                 |            | SD        | 8.486          | 9.167     | 6.465 | 6.459 | 5.102 | 7.081 | 6.681   |
|                         |                 |            | Minimum   | 21.5           | 28.8      | 27.9  | 23.6  | 28.5  | 20.6  | 20.6    |
|                         |                 |            | Median    | 37.55          | 30.45     | 32.95 | 29.00 | 31.50 | 32.35 | 31.05   |
|                         |                 |            | Maximum   | 47.0           | 52.6      | 45.3  | 37.1  | 42.0  | 40.6  | 52.6    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)            | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |        |       |       |       | Overall |
|------------------------------------|-----------------|--------------|-----------|----------------|-----------|--------|-------|-------|-------|---------|
|                                    |                 |              |           |                | A         | B      | C     | D     | E     |         |
| Lymphocytes (%)                    | 14-43           | Day 3        | n         | 10             | 6         | 6      | 6     | 6     | 6     | 30      |
|                                    |                 |              | Mean      | 35.32          | 35.08     | 33.80  | 31.60 | 32.20 | 31.13 | 32.76   |
|                                    |                 |              | SD        | 7.863          | 9.451     | 4.853  | 5.169 | 5.615 | 6.139 | 6.183   |
|                                    |                 |              | Minimum   | 23.9           | 26.8      | 26.9   | 24.9  | 25.9  | 22.9  | 22.9    |
|                                    |                 |              | Median    | 36.25          | 32.35     | 33.55  | 30.75 | 31.00 | 31.60 | 32.25   |
|                                    |                 |              | Maximum   | 45.6           | 52.9      | 39.8   | 38.4  | 42.3  | 38.4  | 52.9    |
|                                    |                 | End of Study | n         | 10             | 6         | 6      | 6     | 6     | 6     | 30      |
|                                    |                 |              | Mean      | 37.25          | 34.00     | 35.85  | 31.10 | 33.00 | 29.68 | 32.73   |
|                                    |                 |              | SD        | 9.595          | 11.292    | 11.449 | 5.802 | 7.475 | 5.224 | 8.340   |
|                                    |                 |              | Minimum   | 25.1           | 16.5      | 20.1   | 25.4  | 19.5  | 22.4  | 16.5    |
|                                    |                 |              | Median    | 36.55          | 33.60     | 36.70  | 30.10 | 34.50 | 30.40 | 33.00   |
|                                    |                 |              | Maximum   | 52.6           | 52.1      | 52.8   | 42.1  | 42.1  | 35.2  | 52.8    |
| Absolute Lymphocytes (thou/uL) 1-3 |                 | Screen       | n         | 10             | 6         | 6      | 6     | 6     | 6     | 30      |
|                                    |                 |              | Mean      | 1.91           | 2.12      | 2.55   | 1.90  | 2.12  | 1.48  | 2.03    |
|                                    |                 |              | SD        | 0.463          | 0.556     | 0.666  | 0.603 | 0.611 | 0.279 | 0.628   |
|                                    |                 |              | Minimum   | 1.3            | 1.3       | 1.5    | 0.9   | 1.5   | 1.1   | 0.9     |
|                                    |                 |              | Median    | 1.85           | 2.10      | 2.80   | 1.95  | 2.00  | 1.55  | 1.95    |
|                                    |                 |              | Maximum   | 3.0            | 3.0       | 3.3    | 2.7   | 3.2   | 1.8   | 3.3     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)        | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                                |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Absolute Lymphocytes (thou/uL) | 1-3             | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |            | Mean      | 1.82           | 2.23      | 2.12  | 1.95  | 2.05  | 1.38  | 1.95    |
|                                |                 |            | SD        | 0.583          | 0.742     | 0.608 | 0.497 | 0.750 | 0.349 | 0.640   |
|                                |                 |            | Minimum   | 0.9            | 1.4       | 1.3   | 1.2   | 1.1   | 0.9   | 0.9     |
|                                |                 |            | Median    | 1.80           | 2.20      | 2.40  | 2.05  | 1.95  | 1.40  | 1.90    |
|                                |                 |            | Maximum   | 3.0            | 3.1       | 2.7   | 2.6   | 3.4   | 1.8   | 3.4     |
|                                |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |            | Mean      | 1.76           | 2.00      | 2.00  | 1.67  | 1.78  | 1.50  | 1.79    |
|                                |                 |            | SD        | 0.472          | 0.632     | 0.420 | 0.550 | 0.534 | 0.374 | 0.514   |
|                                |                 |            | Minimum   | 0.9            | 1.3       | 1.5   | 0.8   | 1.3   | 1.0   | 0.8     |
|                                |                 |            | Median    | 1.85           | 1.95      | 2.00  | 1.60  | 1.70  | 1.50  | 1.70    |
|                                |                 |            | Maximum   | 2.6            | 3.1       | 2.6   | 2.4   | 2.8   | 2.0   | 3.1     |
|                                |                 | Day 3      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |            | Mean      | 1.96           | 2.10      | 2.40  | 1.88  | 1.85  | 1.60  | 1.97    |
|                                |                 |            | SD        | 0.585          | 0.580     | 0.672 | 0.549 | 0.404 | 0.363 | 0.560   |
|                                |                 |            | Minimum   | 1.1            | 1.4       | 1.4   | 1.0   | 1.2   | 1.2   | 1.0     |
|                                |                 |            | Median    | 1.90           | 2.05      | 2.55  | 1.90  | 1.85  | 1.55  | 1.90    |
|                                |                 |            | Maximum   | 3.3            | 2.9       | 3.0   | 2.5   | 2.4   | 2.2   | 3.0     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)        | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                                |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Absolute Lymphocytes (thou/uL) | 1-3             | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |              | Mean      | 1.89           | 2.18      | 2.10  | 1.82  | 1.83  | 1.60  | 1.91    |
|                                |                 |              | SD        | 0.461          | 0.504     | 0.559 | 0.382 | 0.677 | 0.297 | 0.513   |
|                                |                 |              | Minimum   | 1.1            | 1.3       | 1.4   | 1.2   | 0.9   | 1.2   | 0.9     |
|                                |                 |              | Median    | 1.80           | 2.25      | 2.35  | 1.80  | 1.80  | 1.55  | 1.80    |
|                                |                 |              | Maximum   | 2.5            | 2.7       | 2.7   | 2.4   | 3.0   | 2.1   | 3.0     |
| Monocytes (%)                  | 3.9-11.5        | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |              | Mean      | 9.20           | 9.42      | 8.02  | 8.08  | 7.92  | 9.88  | 8.66    |
|                                |                 |              | SD        | 2.408          | 2.768     | 0.595 | 1.359 | 0.823 | 3.435 | 2.133   |
|                                |                 |              | Minimum   | 3.9            | 5.5       | 7.5   | 6.4   | 6.8   | 5.9   | 5.5     |
|                                |                 |              | Median    | 9.35           | 8.90      | 7.75  | 8.05  | 8.20  | 9.80  | 8.20    |
|                                |                 |              | Maximum   | 12.8           | 12.8      | 9.1   | 10.3  | 8.8   | 14.2  | 14.2    |
|                                |                 | Baseline     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |              | Mean      | 8.12           | 7.70      | 6.52  | 7.05  | 7.45  | 8.38  | 7.42    |
|                                |                 |              | SD        | 2.248          | 2.527     | 0.842 | 1.291 | 1.300 | 3.027 | 1.946   |
|                                |                 |              | Minimum   | 5.3            | 5.1       | 5.7   | 5.6   | 6.1   | 5.5   | 5.1     |
|                                |                 |              | Median    | 7.60           | 7.05      | 6.45  | 6.90  | 6.95  | 7.60  | 6.80    |
|                                |                 |              | Maximum   | 11.9           | 12.1      | 8.0   | 8.7   | 9.6   | 13.4  | 13.4    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Monocytes (%)           | 3.9-11.5        | Day 2        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 8.41           | 8.43      | 7.78  | 7.42  | 7.97  | 9.08  | 8.14    |
|                         |                 |              | SD        | 2.722          | 2.945     | 1.444 | 1.798 | 1.846 | 2.915 | 2.193   |
|                         |                 |              | Minimum   | 5.2            | 5.0       | 5.8   | 5.7   | 5.1   | 5.6   | 5.0     |
|                         |                 |              | Median    | 8.05           | 8.15      | 7.85  | 7.20  | 7.90  | 9.40  | 8.00    |
|                         |                 |              | Maximum   | 13.4           | 13.2      | 9.8   | 10.5  | 10.4  | 12.4  | 13.2    |
|                         |                 | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 8.13           | 7.62      | 7.60  | 7.57  | 7.60  | 9.05  | 7.89    |
|                         |                 |              | SD        | 2.708          | 2.354     | 1.128 | 2.221 | 1.823 | 2.458 | 1.998   |
|                         |                 |              | Minimum   | 4.0            | 4.7       | 6.1   | 5.6   | 4.4   | 6.4   | 4.4     |
|                         |                 |              | Median    | 8.30           | 7.50      | 8.00  | 7.10  | 7.75  | 8.65  | 7.75    |
|                         |                 |              | Maximum   | 13.1           | 11.4      | 8.7   | 11.7  | 9.6   | 13.1  | 13.1    |
|                         |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |              | Mean      | 8.91           | 8.28      | 7.00  | 8.08  | 8.58  | 10.18 | 8.43    |
|                         |                 |              | SD        | 3.511          | 2.385     | 0.687 | 1.770 | 2.402 | 3.437 | 2.393   |
|                         |                 |              | Minimum   | 3.5            | 5.2       | 6.1   | 5.4   | 5.3   | 5.6   | 5.2     |
|                         |                 |              | Median    | 8.50           | 8.20      | 7.00  | 8.10  | 9.20  | 9.65  | 7.85    |
|                         |                 |              | Maximum   | 14.2           | 12.3      | 7.7   | 10.6  | 11.7  | 15.1  | 15.1    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)      | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|------------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                              |                 |            |           |                | A         | B     | C     | D     | E     |         |
| Absolute Monocytes (thou/uL) | 0.2-0.8         | Screen     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |            | Mean      | 0.53           | 0.58      | 0.57  | 0.53  | 0.45  | 0.52  | 0.53    |
|                              |                 |            | SD        | 0.149          | 0.194     | 0.082 | 0.103 | 0.084 | 0.147 | 0.129   |
|                              |                 |            | Minimum   | 0.2            | 0.3       | 0.5   | 0.4   | 0.4   | 0.3   | 0.3     |
|                              |                 |            | Median    | 0.50           | 0.60      | 0.55  | 0.50  | 0.40  | 0.55  | 0.50    |
|                              |                 |            | Maximum   | 0.8            | 0.9       | 0.7   | 0.7   | 0.6   | 0.7   | 0.9     |
|                              |                 | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |            | Mean      | 0.44           | 0.52      | 0.40  | 0.47  | 0.45  | 0.53  | 0.47    |
|                              |                 |            | SD        | 0.070          | 0.194     | 0.063 | 0.121 | 0.105 | 0.121 | 0.128   |
|                              |                 |            | Minimum   | 0.3            | 0.3       | 0.3   | 0.3   | 0.3   | 0.4   | 0.3     |
|                              |                 |            | Median    | 0.45           | 0.45      | 0.40  | 0.45  | 0.45  | 0.55  | 0.40    |
|                              |                 |            | Maximum   | 0.5            | 0.8       | 0.5   | 0.6   | 0.6   | 0.7   | 0.8     |
|                              |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |                 |            | Mean      | 0.42           | 0.50      | 0.45  | 0.42  | 0.43  | 0.45  | 0.45    |
|                              |                 |            | SD        | 0.123          | 0.141     | 0.084 | 0.041 | 0.121 | 0.152 | 0.111   |
|                              |                 |            | Minimum   | 0.2            | 0.3       | 0.3   | 0.4   | 0.3   | 0.3   | 0.3     |
|                              |                 |            | Median    | 0.45           | 0.50      | 0.50  | 0.40  | 0.45  | 0.45  | 0.45    |
|                              |                 |            | Maximum   | 0.6            | 0.7       | 0.5   | 0.5   | 0.6   | 0.7   | 0.7     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)      | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |        |       |       | Overall |
|------------------------------|-----------------|--------------|-----------|----------------|-----------|-------|--------|-------|-------|---------|
|                              |                 |              |           |                | A         | B     | C      | D     | E     |         |
| Absolute Monocytes (thou/uL) | 0.2-0.8         | Day 3        | n         | 10             | 6         | 6     | 6      | 6     | 6     | 30      |
|                              |                 |              | Mean      | 0.43           | 0.47      | 0.55  | 0.45   | 0.43  | 0.47  | 0.47    |
|                              |                 |              | SD        | 0.149          | 0.151     | 0.105 | 0.105  | 0.121 | 0.121 | 0.120   |
|                              |                 |              | Minimum   | 0.2            | 0.3       | 0.4   | 0.3    | 0.3   | 0.3   | 0.3     |
|                              |                 |              | Median    | 0.45           | 0.40      | 0.55  | 0.45   | 0.45  | 0.45  | 0.50    |
|                              |                 |              | Maximum   | 0.6            | 0.7       | 0.7   | 0.6    | 0.6   | 0.6   | 0.7     |
|                              |                 | End of Study | n         | 10             | 6         | 6     | 6      | 6     | 6     | 30      |
|                              |                 |              | Mean      | 0.44           | 0.58      | 0.43  | 0.47   | 0.47  | 0.55  | 0.50    |
|                              |                 |              | SD        | 0.143          | 0.183     | 0.052 | 0.121  | 0.103 | 0.197 | 0.144   |
|                              |                 |              | Minimum   | 0.2            | 0.3       | 0.4   | 0.3    | 0.3   | 0.4   | 0.3     |
|                              |                 |              | Median    | 0.50           | 0.60      | 0.40  | 0.45   | 0.50  | 0.45  | 0.50    |
|                              |                 |              | Maximum   | 0.6            | 0.8       | 0.5   | 0.6    | 0.6   | 0.8   | 0.8     |
| Neutrophils (%)              | 42-80           | Screen       | n         | 10             | 6         | 6     | 6      | 6     | 6     | 30      |
|                              |                 |              | Mean      | 54.81          | 51.33     | 50.05 | 58.88  | 50.97 | 58.25 | 53.90   |
|                              |                 |              | SD        | 8.712          | 8.075     | 6.522 | 11.124 | 5.704 | 9.831 | 8.800   |
|                              |                 |              | Minimum   | 39.8           | 35.6      | 44.0  | 38.3   | 42.1  | 48.0  | 35.6    |
|                              |                 |              | Median    | 57.35          | 54.45     | 48.65 | 63.75  | 51.15 | 56.75 | 53.85   |
|                              |                 |              | Maximum   | 66.0           | 58.2      | 62.0  | 68.4   | 59.2  | 69.9  | 69.9    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |        | Overall |
|-------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|--------|---------|
|                         |                 |            |           |                | A         | B     | C     | D     | E      |         |
| Neutrophils (%)         | 42-80           | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6      | 30      |
|                         |                 |            | Mean      | 56.99          | 54.63     | 54.42 | 60.15 | 55.37 | 66.55  | 58.22   |
|                         |                 |            | SD        | 8.998          | 10.292    | 4.963 | 9.308 | 4.744 | 12.312 | 9.483   |
|                         |                 |            | Minimum   | 41.1           | 36.6      | 49.1  | 49.4  | 51.0  | 47.4   | 36.6    |
|                         |                 |            | Median    | 58.20          | 57.20     | 53.85 | 61.25 | 54.85 | 69.50  | 56.45   |
|                         |                 |            | Maximum   | 66.6           | 65.5      | 61.8  | 72.5  | 64.3  | 82.3   | 82.3    |
|                         |                 | Day 2      | n         | 10             | 6         | 6     | 6     | 6     | 6      | 30      |
|                         |                 |            | Mean      | 53.23          | 53.53     | 52.47 | 59.83 | 55.12 | 54.53  | 55.10   |
|                         |                 |            | SD        | 9.102          | 9.446     | 7.202 | 7.028 | 5.330 | 9.962  | 7.842   |
|                         |                 |            | Minimum   | 42.1           | 34.8      | 42.8  | 51.1  | 45.8  | 46.8   | 34.8    |
|                         |                 |            | Median    | 50.25          | 56.70     | 55.15 | 60.55 | 56.75 | 49.60  | 56.05   |
|                         |                 |            | Maximum   | 69.9           | 60.3      | 60.5  | 69.4  | 60.3  | 71.9   | 71.9    |
|                         |                 | Day 3      | n         | 10             | 6         | 6     | 6     | 6     | 6      | 30      |
|                         |                 |            | Mean      | 54.08          | 53.30     | 53.43 | 58.15 | 56.62 | 56.05  | 55.51   |
|                         |                 |            | SD        | 8.015          | 9.457     | 6.445 | 4.053 | 6.632 | 7.523  | 6.813   |
|                         |                 |            | Minimum   | 43.2           | 35.7      | 42.2  | 53.5  | 45.0  | 46.2   | 35.7    |
|                         |                 |            | Median    | 54.45          | 57.10     | 53.90 | 58.40 | 59.20 | 55.45  | 56.55   |
|                         |                 |            | Maximum   | 66.5           | 61.5      | 60.8  | 63.5  | 63.4  | 68.5   | 68.5    |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)        | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                                |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Neutrophils (%)                | 42-80           | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |              | Mean      | 50.99          | 53.23     | 51.37 | 57.68 | 54.87 | 55.72 | 54.57   |
|                                |                 |              | SD        | 10.615         | 12.027    | 7.626 | 7.459 | 7.138 | 8.064 | 8.327   |
|                                |                 |              | Minimum   | 31.7           | 34.2      | 37.3  | 45.3  | 45.3  | 48.7  | 34.2    |
|                                |                 |              | Median    | 53.75          | 53.35     | 52.35 | 59.60 | 54.65 | 53.00 | 53.95   |
|                                |                 |              | Maximum   | 63.9           | 71.7      | 59.3  | 64.1  | 66.6  | 71.1  | 71.7    |
| Absolute Neutrophils (thou/uL) | 1.9-7.9         | Screen       | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |              | Mean      | 3.20           | 3.13      | 3.40  | 3.83  | 2.90  | 3.05  | 3.26    |
|                                |                 |              | SD        | 0.975          | 0.671     | 0.529 | 1.154 | 0.555 | 0.718 | 0.780   |
|                                |                 |              | Minimum   | 1.8            | 2.1       | 2.8   | 1.8   | 2.2   | 2.1   | 1.8     |
|                                |                 |              | Median    | 3.10           | 3.30      | 3.50  | 4.25  | 2.85  | 2.95  | 3.20    |
|                                |                 |              | Maximum   | 5.4            | 3.8       | 4.1   | 4.9   | 3.9   | 4.0   | 4.9     |
|                                |                 | Baseline     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |              | Mean      | 3.23           | 3.55      | 3.35  | 4.08  | 3.32  | 4.47  | 3.75    |
|                                |                 |              | SD        | 0.991          | 0.848     | 0.758 | 1.554 | 0.828 | 1.889 | 1.258   |
|                                |                 |              | Minimum   | 1.5            | 2.2       | 2.3   | 2.4   | 2.9   | 2.3   | 2.2     |
|                                |                 |              | Median    | 3.10           | 3.55      | 3.40  | 4.10  | 3.00  | 4.35  | 3.40    |
|                                |                 |              | Maximum   | 4.6            | 4.6       | 4.3   | 6.0   | 5.0   | 7.6   | 7.6     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.4 Clinical Laboratory Summary - Hematology (Safety Population)

| Laboratory Test (units)        | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------|-----------------|--------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                                |                 |              |           |                | A         | B     | C     | D     | E     |         |
| Absolute Neutrophils (thou/uL) | 1.9-7.9         | Day 2        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |              | Mean      | 2.77           | 3.17      | 3.10  | 3.35  | 3.02  | 2.58  | 3.04    |
|                                |                 |              | SD        | 1.050          | 0.887     | 0.732 | 0.948 | 0.895 | 0.682 | 0.818   |
|                                |                 |              | Minimum   | 1.2            | 2.0       | 2.2   | 2.2   | 1.9   | 2.0   | 1.9     |
|                                |                 |              | Median    | 2.60           | 3.20      | 3.00  | 3.55  | 2.85  | 2.35  | 2.95    |
|                                |                 |              | Maximum   | 4.6            | 4.4       | 4.3   | 4.6   | 4.5   | 3.6   | 4.6     |
|                                |                 | Day 3        | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |              | Mean      | 3.04           | 3.20      | 3.80  | 3.38  | 3.32  | 2.92  | 3.32    |
|                                |                 |              | SD        | 0.897          | 0.782     | 1.190 | 0.752 | 0.928 | 0.564 | 0.858   |
|                                |                 |              | Minimum   | 1.4            | 2.0       | 2.5   | 2.3   | 1.9   | 2.4   | 1.9     |
|                                |                 |              | Median    | 3.15           | 3.45      | 3.50  | 3.70  | 3.30  | 2.70  | 3.30    |
|                                |                 |              | Maximum   | 4.3            | 4.0       | 5.7   | 4.0   | 4.5   | 4.0   | 5.7     |
|                                |                 | End of Study | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 |              | Mean      | 2.68           | 3.65      | 3.07  | 3.47  | 3.03  | 3.03  | 3.25    |
|                                |                 |              | SD        | 0.921          | 1.237     | 0.712 | 1.111 | 0.954 | 0.876 | 0.961   |
|                                |                 |              | Minimum   | 1.1            | 1.8       | 1.9   | 2.0   | 2.1   | 2.3   | 1.8     |
|                                |                 |              | Median    | 2.70           | 3.60      | 3.05  | 4.00  | 2.95  | 2.75  | 3.10    |
|                                |                 |              | Maximum   | 4.4            | 5.6       | 3.9   | 4.4   | 4.8   | 4.7   | 5.6     |

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.  
Baseline is the last predose measurement.  
Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E     |         |
| Hemoglobin (g/dL)       | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.46              | 0.68      | 0.55  | 0.20  | 0.68  | 0.00  | 0.42    |
|                         |              | SD        | 0.731             | 0.861     | 0.464 | 0.502 | 0.331 | 0.424 | 0.581   |
|                         |              | Minimum   | -0.5              | -0.4      | 0.1   | -0.4  | 0.1   | -0.6  | -0.6    |
|                         |              | Median    | 0.40              | 0.85      | 0.40  | 0.15  | 0.75  | 0.00  | 0.45    |
|                         |              | Maximum   | 1.7               | 1.9       | 1.3   | 0.8   | 1.0   | 0.6   | 1.9     |
|                         | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.60              | 1.10      | 0.93  | 0.37  | 0.88  | 0.20  | 0.70    |
|                         |              | SD        | 0.598             | 1.122     | 0.497 | 0.528 | 0.979 | 0.482 | 0.799   |
|                         |              | Minimum   | 0.2               | -0.2      | 0.4   | -0.3  | -0.2  | -0.5  | -0.5    |
|                         |              | Median    | 0.35              | 0.75      | 0.75  | 0.20  | 0.90  | 0.40  | 0.50    |
|                         |              | Maximum   | 2.2               | 2.9       | 1.6   | 1.1   | 2.1   | 0.7   | 2.9     |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | -0.26             | -0.38     | -0.28 | -0.18 | -0.42 | 0.13  | -0.23   |
|                         |              | SD        | 0.347             | 0.417     | 0.306 | 0.868 | 0.691 | 0.763 | 0.632   |
|                         |              | Minimum   | -0.8              | -1.0      | -0.7  | -1.3  | -1.3  | -1.4  | -1.4    |
|                         |              | Median    | -0.20             | -0.40     | -0.30 | 0.30  | -0.50 | 0.45  | -0.20   |
|                         |              | Maximum   | 0.4               | 0.3       | 0.1   | 0.5   | 0.4   | 0.6   | 0.6     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E     |         |
| Hematocrit (%)          | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 1.38              | 1.63      | 1.47  | 0.52  | 2.27  | 0.18  | 1.21    |
|                         |              | SD        | 1.866             | 1.981     | 1.189 | 1.535 | 0.991 | 1.477 | 1.572   |
|                         |              | Minimum   | -0.8              | -0.8      | 0.4   | -1.3  | 1.0   | -2.2  | -2.2    |
|                         |              | Median    | 1.00              | 2.10      | 0.95  | 0.65  | 2.15  | 0.30  | 1.20    |
|                         |              | Maximum   | 4.2               | 4.2       | 3.6   | 2.6   | 3.7   | 2.0   | 4.2     |
|                         | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 1.94              | 2.68      | 3.23  | 1.37  | 2.77  | 1.50  | 2.31    |
|                         |              | SD        | 1.703             | 3.009     | 1.400 | 1.588 | 2.499 | 1.515 | 2.092   |
|                         |              | Minimum   | -0.3              | -0.1      | 1.9   | -0.9  | 0.0   | -0.6  | -0.9    |
|                         |              | Median    | 1.65              | 2.10      | 2.85  | 1.20  | 2.40  | 1.90  | 2.00    |
|                         |              | Maximum   | 5.9               | 7.6       | 5.0   | 3.4   | 5.5   | 3.4   | 7.6     |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | -0.61             | -1.28     | -0.63 | -0.18 | -0.90 | 0.43  | -0.51   |
|                         |              | SD        | 0.986             | 1.157     | 0.882 | 2.305 | 2.006 | 2.541 | 1.858   |
|                         |              | Minimum   | -1.9              | -2.4      | -2.0  | -3.2  | -4.0  | -4.6  | -4.6    |
|                         |              | Median    | -0.25             | -1.70     | -0.45 | 0.60  | -0.90 | 1.15  | -0.20   |
|                         |              | Maximum   | 0.6               | 0.7       | 0.2   | 1.9   | 1.7   | 2.2   | 2.2     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units)  | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                          |              |           |                   | A         | B     | C     | D     | E     |         |
| Platelet Count (thou/uL) | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                          |              | Mean      | -8.6              | -17.8     | 9.8   | -8.0  | 4.2   | -6.3  | -3.6    |
|                          |              | SD        | 16.26             | 24.29     | 17.22 | 11.05 | 8.38  | 10.31 | 17.37   |
|                          |              | Minimum   | -28               | -55       | -21   | -29   | -11   | -20   | -55     |
|                          |              | Median    | -6.0              | -11.0     | 11.0  | -5.0  | 7.0   | -8.0  | 0.5     |
|                          |              | Maximum   | 20                | 7         | 28    | 1     | 13    | 8     | 28      |
|                          | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                          |              | Mean      | 0.7               | 0.5       | 29.3  | -2.5  | 7.7   | 2.0   | 7.4     |
|                          |              | SD        | 13.16             | 24.01     | 14.62 | 9.93  | 16.94 | 14.46 | 19.35   |
|                          |              | Minimum   | -27               | -29       | 5     | -14   | -12   | -21   | -29     |
|                          |              | Median    | 4.5               | 0.0       | 34.0  | -1.5  | 7.0   | 3.0   | 6.0     |
|                          |              | Maximum   | 15                | 27        | 42    | 9     | 36    | 23    | 42      |
|                          | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                          |              | Mean      | -5.0              | -11.5     | 5.2   | -2.7  | -12.8 | 7.8   | -2.8    |
|                          |              | SD        | 18.68             | 23.13     | 17.99 | 16.65 | 16.99 | 32.10 | 22.28   |
|                          |              | Minimum   | -53               | -43       | -19   | -25   | -36   | -40   | -43     |
|                          |              | Median    | -4.5              | -9.0      | 3.5   | -1.0  | -7.0  | 8.0   | -1.0    |
|                          |              | Maximum   | 13                | 12        | 29    | 23    | 5     | 53    | 53      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units)       | Time Point   | Statistic | Pooled<br>Placebo | Treatment |        |        |        |        | Overall |
|-------------------------------|--------------|-----------|-------------------|-----------|--------|--------|--------|--------|---------|
|                               |              |           |                   | A         | B      | C      | D      | E      |         |
| Red Blood Cell Count (mil/uL) | Day 2        | n         | 10                | 6         | 6      | 6      | 6      | 6      | 30      |
|                               |              | Mean      | 0.142             | 0.185     | 0.125  | 0.053  | 0.203  | 0.003  | 0.114   |
|                               |              | SD        | 0.1970            | 0.2381    | 0.1274 | 0.1469 | 0.1199 | 0.1282 | 0.1662  |
|                               |              | Minimum   | -0.07             | -0.12     | 0.03   | -0.12  | 0.05   | -0.17  | -0.17   |
|                               |              | Median    | 0.105             | 0.235     | 0.080  | 0.060  | 0.210  | -0.020 | 0.115   |
|                               |              | Maximum   | 0.49              | 0.49      | 0.36   | 0.26   | 0.34   | 0.18   | 0.49    |
|                               | Day 3        | n         | 10                | 6         | 6      | 6      | 6      | 6      | 30      |
|                               |              | Mean      | 0.197             | 0.285     | 0.300  | 0.125  | 0.265  | 0.122  | 0.219   |
|                               |              | SD        | 0.2024            | 0.3640    | 0.1519 | 0.1608 | 0.2793 | 0.1326 | 0.2329  |
|                               |              | Minimum   | -0.02             | -0.09     | 0.16   | -0.10  | -0.03  | -0.08  | -0.10   |
|                               |              | Median    | 0.170             | 0.210     | 0.245  | 0.105  | 0.250  | 0.185  | 0.185   |
|                               |              | Maximum   | 0.69              | 0.84      | 0.50   | 0.35   | 0.62   | 0.24   | 0.84    |
|                               | End of Study | n         | 10                | 6         | 6      | 6      | 6      | 6      | 30      |
|                               |              | Mean      | -0.087            | -0.173    | -0.100 | -0.043 | -0.120 | 0.058  | -0.076  |
|                               |              | SD        | 0.1040            | 0.1408    | 0.0844 | 0.2456 | 0.2211 | 0.2506 | 0.2018  |
|                               |              | Minimum   | -0.25             | -0.36     | -0.21  | -0.35  | -0.43  | -0.44  | -0.44   |
|                               |              | Median    | -0.075            | -0.215    | -0.100 | 0.045  | -0.135 | 0.150  | -0.055  |
|                               |              | Maximum   | 0.07              | 0.05      | 0.00   | 0.18   | 0.15   | 0.24   | 0.24    |

Note: Baseline is the last predose measurement.  
 Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)  
 Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)  
 Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)  
 Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)  
 Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units)             | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                                     |              |           |                   | A         | B     | C     | D     | E     |         |
| White Blood Cell Count<br>(thou/uL) | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                     |              | Mean      | -0.53             | -0.62     | -0.23 | -1.08 | -0.57 | -1.77 | -0.85   |
|                                     |              | SD        | 0.812             | 0.331     | 0.771 | 0.778 | 0.565 | 1.727 | 1.042   |
|                                     |              | Minimum   | -1.9              | -1.0      | -1.4  | -2.3  | -1.2  | -4.4  | -4.4    |
|                                     |              | Median    | -0.70             | -0.65     | -0.05 | -0.75 | -0.60 | -1.75 | -0.70   |
|                                     |              | Maximum   | 0.7               | -0.1      | 0.6   | -0.4  | 0.3   | 0.7   | 0.7     |
|                                     | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                     |              | Mean      | -0.02             | -0.50     | 0.97  | -0.75 | -0.22 | -1.30 | -0.36   |
|                                     |              | SD        | 0.809             | 0.544     | 1.025 | 1.009 | 0.884 | 1.601 | 1.254   |
|                                     |              | Minimum   | -1.2              | -1.3      | -0.1  | -1.9  | -1.5  | -3.4  | -3.4    |
|                                     |              | Median    | 0.10              | -0.50     | 0.80  | -0.65 | 0.15  | -1.25 | -0.15   |
|                                     |              | Maximum   | 1.1               | 0.3       | 2.7   | 0.4   | 0.8   | 0.9   | 2.7     |
|                                     | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                     |              | Mean      | -0.46             | 0.20      | -0.15 | -0.70 | -0.47 | -1.10 | -0.44   |
|                                     |              | SD        | 1.005             | 1.213     | 1.377 | 0.967 | 0.378 | 1.514 | 1.170   |
|                                     |              | Minimum   | -2.3              | -0.7      | -1.7  | -2.1  | -1.0  | -2.7  | -2.7    |
|                                     |              | Median    | -0.60             | -0.35     | -0.30 | -0.55 | -0.50 | -1.30 | -0.40   |
|                                     |              | Maximum   | 1.0               | 2.5       | 2.3   | 0.6   | 0.0   | 1.2   | 2.5     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E     |         |
| Basophils (%)           | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.02              | 0.00      | 0.03  | 0.02  | 0.12  | 0.13  | 0.06    |
|                         |              | SD        | 0.230             | 0.179     | 0.082 | 0.117 | 0.232 | 0.294 | 0.190   |
|                         |              | Minimum   | -0.4              | -0.2      | 0.0   | -0.1  | -0.1  | -0.2  | -0.2    |
|                         |              | Median    | 0.00              | -0.05     | 0.00  | 0.00  | 0.10  | 0.10  | 0.00    |
|                         |              | Maximum   | 0.3               | 0.3       | 0.2   | 0.2   | 0.5   | 0.6   | 0.6     |
|                         | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.06              | 0.03      | -0.05 | 0.00  | 0.02  | 0.03  | 0.01    |
|                         |              | SD        | 0.341             | 0.225     | 0.138 | 0.237 | 0.117 | 0.216 | 0.182   |
|                         |              | Minimum   | -0.6              | -0.2      | -0.2  | -0.4  | -0.2  | -0.3  | -0.4    |
|                         |              | Median    | 0.15              | -0.05     | -0.05 | 0.05  | 0.05  | 0.05  | 0.00    |
|                         |              | Maximum   | 0.6               | 0.4       | 0.1   | 0.3   | 0.1   | 0.3   | 0.4     |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.03              | 0.15      | -0.07 | 0.10  | 0.07  | 0.17  | 0.08    |
|                         |              | SD        | 0.258             | 0.105     | 0.151 | 0.063 | 0.266 | 0.320 | 0.209   |
|                         |              | Minimum   | -0.3              | 0.0       | -0.3  | 0.0   | -0.2  | -0.1  | -0.3    |
|                         |              | Median    | -0.05             | 0.15      | 0.00  | 0.10  | 0.05  | 0.05  | 0.10    |
|                         |              | Maximum   | 0.5               | 0.3       | 0.1   | 0.2   | 0.5   | 0.7   | 0.7     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units)      | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|------------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                              |              |           |                   | A         | B     | C     | D     | E     |         |
| Absolute Basophils (thou/uL) | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |              | Mean      | 0.00              | 0.00      | 0.00  | 0.00  | 0.02  | 0.00  | 0.00    |
|                              |              | SD        | 0.000             | 0.000     | 0.000 | 0.000 | 0.041 | 0.000 | 0.018   |
|                              |              | Minimum   | 0.0               | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                              |              | Median    | 0.00              | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                              |              | Maximum   | 0.0               | 0.0       | 0.0   | 0.0   | 0.1   | 0.0   | 0.1     |
|                              | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |              | Mean      | 0.01              | 0.02      | 0.00  | 0.00  | 0.02  | 0.00  | 0.01    |
|                              |              | SD        | 0.032             | 0.041     | 0.000 | 0.000 | 0.041 | 0.000 | 0.025   |
|                              |              | Minimum   | 0.0               | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                              |              | Median    | 0.00              | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                              |              | Maximum   | 0.1               | 0.1       | 0.0   | 0.0   | 0.1   | 0.0   | 0.1     |
|                              | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |              | Mean      | 0.00              | 0.02      | -0.02 | 0.00  | 0.02  | 0.02  | 0.01    |
|                              |              | SD        | 0.000             | 0.041     | 0.041 | 0.000 | 0.041 | 0.041 | 0.037   |
|                              |              | Minimum   | 0.0               | 0.0       | -0.1  | 0.0   | 0.0   | 0.0   | -0.1    |
|                              |              | Median    | 0.00              | 0.00      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                              |              | Maximum   | 0.0               | 0.1       | 0.0   | 0.0   | 0.1   | 0.1   | 0.1     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E     |         |
| Eosinophils (%)         | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.34              | 0.60      | 0.82  | 0.15  | 0.23  | 2.30  | 0.82    |
|                         |              | SD        | 0.647             | 0.829     | 1.127 | 0.704 | 0.665 | 3.981 | 1.964   |
|                         |              | Minimum   | -0.6              | -0.8      | -0.8  | -0.7  | -1.0  | 0.1   | -1.0    |
|                         |              | Median    | 0.20              | 0.55      | 0.75  | 0.10  | 0.35  | 0.85  | 0.55    |
|                         |              | Maximum   | 1.7               | 1.7       | 2.6   | 0.9   | 1.0   | 10.4  | 10.4    |
|                         | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.02              | 0.60      | 0.43  | 0.02  | -0.07 | 1.43  | 0.48    |
|                         |              | SD        | 0.872             | 0.912     | 0.937 | 0.595 | 0.814 | 2.016 | 1.212   |
|                         |              | Minimum   | -1.1              | -0.7      | -0.8  | -0.6  | -1.4  | 0.1   | -1.4    |
|                         |              | Median    | 0.05              | 0.70      | 0.30  | -0.20 | 0.10  | 0.75  | 0.30    |
|                         |              | Maximum   | 1.4               | 1.9       | 2.1   | 0.9   | 1.0   | 5.5   | 5.5     |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.43              | 0.97      | 1.07  | 0.37  | -0.15 | 1.95  | 0.84    |
|                         |              | SD        | 0.955             | 1.186     | 2.202 | 0.728 | 1.031 | 3.489 | 1.993   |
|                         |              | Minimum   | -1.3              | 0.1       | -0.3  | -0.6  | -1.8  | -1.2  | -1.8    |
|                         |              | Median    | 0.45              | 0.65      | 0.25  | 0.30  | 0.10  | 1.15  | 0.35    |
|                         |              | Maximum   | 1.5               | 3.3       | 5.5   | 1.2   | 1.2   | 8.8   | 8.8     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units)        | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                                |              |           |                   | A         | B     | C     | D     | E     |         |
| Absolute Eosinophils (thou/uL) | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |              | Mean      | 0.01              | 0.05      | 0.05  | -0.02 | 0.02  | 0.08  | 0.04    |
|                                |              | SD        | 0.057             | 0.055     | 0.084 | 0.041 | 0.041 | 0.160 | 0.089   |
|                                |              | Minimum   | -0.1              | 0.0       | 0.0   | -0.1  | 0.0   | 0.0   | -0.1    |
|                                |              | Median    | 0.00              | 0.05      | 0.00  | 0.00  | 0.00  | 0.00  | 0.00    |
|                                |              | Maximum   | 0.1               | 0.1       | 0.2   | 0.0   | 0.1   | 0.4   | 0.4     |
|                                | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |              | Mean      | -0.01             | 0.05      | 0.07  | 0.00  | 0.02  | 0.08  | 0.04    |
|                                |              | SD        | 0.057             | 0.055     | 0.121 | 0.000 | 0.041 | 0.117 | 0.082   |
|                                |              | Minimum   | -0.1              | 0.0       | 0.0   | 0.0   | 0.0   | 0.0   | 0.0     |
|                                |              | Median    | 0.00              | 0.05      | 0.00  | 0.00  | 0.00  | 0.05  | 0.00    |
|                                |              | Maximum   | 0.1               | 0.1       | 0.3   | 0.0   | 0.1   | 0.3   | 0.3     |
|                                | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |              | Mean      | -0.01             | 0.08      | 0.10  | 0.00  | -0.02 | 0.10  | 0.05    |
|                                |              | SD        | 0.057             | 0.075     | 0.297 | 0.000 | 0.075 | 0.155 | 0.155   |
|                                |              | Minimum   | -0.1              | 0.0       | -0.1  | 0.0   | -0.1  | 0.0   | -0.1    |
|                                |              | Median    | 0.00              | 0.10      | 0.00  | 0.00  | 0.00  | 0.05  | 0.00    |
|                                |              | Maximum   | 0.1               | 0.2       | 0.7   | 0.0   | 0.1   | 0.4   | 0.7     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E     |         |
| Lymphocytes (%)         | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 3.11              | -0.23     | -0.17 | -0.22 | -0.62 | 8.88  | 1.53    |
|                         |              | SD        | 5.815             | 5.030     | 5.939 | 5.220 | 5.666 | 6.730 | 6.519   |
|                         |              | Minimum   | -4.3              | -8.1      | -8.3  | -5.6  | -5.7  | 1.7   | -8.3    |
|                         |              | Median    | 1.90              | 1.65      | 1.60  | -1.20 | -2.55 | 7.80  | 1.70    |
|                         |              | Maximum   | 13.9              | 4.7       | 8.1   | 6.2   | 7.6   | 21.2  | 21.2    |
|                         | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 2.82              | 0.78      | -0.48 | 1.47  | -1.35 | 8.37  | 1.76    |
|                         |              | SD        | 4.673             | 2.263     | 4.877 | 6.455 | 5.855 | 5.468 | 5.960   |
|                         |              | Minimum   | -2.4              | -3.1      | -7.3  | -4.1  | -7.6  | 2.5   | -7.6    |
|                         |              | Median    | 1.30              | 1.75      | -1.00 | -1.30 | -2.55 | 7.40  | 1.75    |
|                         |              | Maximum   | 10.6              | 2.9       | 5.6   | 9.8   | 7.9   | 17.5  | 17.5    |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 4.75              | -0.30     | 1.57  | 0.97  | -0.55 | 6.92  | 1.72    |
|                         |              | SD        | 3.939             | 7.597     | 6.998 | 3.790 | 4.251 | 6.305 | 6.202   |
|                         |              | Minimum   | -0.9              | -12.0     | -8.1  | -5.1  | -3.8  | -0.7  | -12.0   |
|                         |              | Median    | 5.15              | -0.30     | 1.50  | 1.95  | -2.35 | 7.55  | 1.10    |
|                         |              | Maximum   | 9.9               | 7.9       | 11.0  | 5.9   | 7.7   | 15.8  | 15.8    |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units)        | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                                |              |           |                   | A         | B     | C     | D     | E     |         |
| Absolute Lymphocytes (thou/uL) | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |              | Mean      | -0.06             | -0.23     | -0.12 | -0.28 | -0.27 | 0.12  | -0.16   |
|                                |              | SD        | 0.337             | 0.398     | 0.279 | 0.194 | 0.288 | 0.286 | 0.314   |
|                                |              | Minimum   | -0.4              | -0.9      | -0.4  | -0.6  | -0.6  | -0.2  | -0.9    |
|                                |              | Median    | -0.10             | -0.10     | -0.15 | -0.25 | -0.30 | 0.10  | -0.15   |
|                                |              | Maximum   | 0.5               | 0.1       | 0.3   | -0.1  | 0.2   | 0.5   | 0.5     |
|                                | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |              | Mean      | 0.14              | -0.13     | 0.28  | -0.07 | -0.20 | 0.22  | 0.02    |
|                                |              | SD        | 0.284             | 0.242     | 0.279 | 0.344 | 0.415 | 0.279 | 0.355   |
|                                |              | Minimum   | -0.4              | -0.5      | -0.1  | -0.6  | -1.0  | -0.2  | -1.0    |
|                                |              | Median    | 0.20              | -0.10     | 0.35  | -0.10 | -0.10 | 0.25  | 0.00    |
|                                |              | Maximum   | 0.6               | 0.2       | 0.6   | 0.3   | 0.1   | 0.5   | 0.6     |
|                                | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |              | Mean      | 0.07              | -0.05     | -0.02 | -0.13 | -0.22 | 0.22  | -0.04   |
|                                |              | SD        | 0.419             | 0.442     | 0.248 | 0.242 | 0.172 | 0.214 | 0.299   |
|                                |              | Minimum   | -0.5              | -0.5      | -0.3  | -0.4  | -0.4  | -0.1  | -0.5    |
|                                |              | Median    | 0.15              | -0.25     | -0.05 | -0.10 | -0.25 | 0.30  | -0.10   |
|                                |              | Maximum   | 0.9               | 0.6       | 0.4   | 0.2   | 0.1   | 0.4   | 0.6     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E     |         |
| Monocytes (%)           | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.29              | 0.73      | 1.27  | 0.37  | 0.52  | 0.70  | 0.72    |
|                         |              | SD        | 1.777             | 1.421     | 1.166 | 1.296 | 1.089 | 1.787 | 1.313   |
|                         |              | Minimum   | -3.1              | -0.9      | -0.9  | -1.9  | -1.7  | -1.0  | -1.9    |
|                         |              | Median    | 0.55              | 1.00      | 1.60  | 0.60  | 1.00  | 0.15  | 1.00    |
|                         |              | Maximum   | 3.2               | 2.9       | 2.5   | 1.8   | 1.0   | 4.0   | 4.0     |
|                         | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.01              | -0.08     | 1.08  | 0.52  | 0.15  | 0.67  | 0.47    |
|                         |              | SD        | 1.449             | 0.637     | 1.227 | 1.439 | 1.596 | 2.803 | 1.628   |
|                         |              | Minimum   | -2.4              | -0.7      | -0.6  | -1.1  | -2.4  | -3.6  | -3.6    |
|                         |              | Median    | -0.10             | -0.30     | 0.80  | 0.35  | 0.50  | 1.75  | 0.50    |
|                         |              | Maximum   | 2.7               | 1.1       | 2.5   | 3.0   | 1.9   | 3.3   | 3.3     |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |              | Mean      | 0.79              | 0.58      | 0.48  | 1.03  | 1.13  | 1.80  | 1.01    |
|                         |              | SD        | 2.454             | 0.618     | 1.366 | 1.381 | 1.603 | 1.964 | 1.432   |
|                         |              | Minimum   | -1.9              | -0.1      | -1.9  | -1.2  | -1.5  | -0.3  | -1.9    |
|                         |              | Median    | 0.50              | 0.50      | 0.90  | 1.85  | 1.60  | 1.95  | 1.05    |
|                         |              | Maximum   | 6.6               | 1.5       | 2.0   | 2.0   | 2.8   | 4.8   | 4.8     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units)      | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|------------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                              |              |           |                   | A         | B     | C     | D     | E     |         |
| Absolute Monocytes (thou/uL) | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |              | Mean      | -0.02             | -0.02     | 0.05  | -0.05 | -0.02 | -0.08 | -0.02   |
|                              |              | SD        | 0.114             | 0.117     | 0.105 | 0.105 | 0.075 | 0.147 | 0.114   |
|                              |              | Minimum   | -0.2              | -0.2      | -0.1  | -0.2  | -0.1  | -0.3  | -0.3    |
|                              |              | Median    | 0.00              | 0.00      | 0.05  | -0.05 | 0.00  | -0.05 | 0.00    |
|                              |              | Maximum   | 0.2               | 0.1       | 0.2   | 0.1   | 0.1   | 0.1   | 0.2     |
|                              | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |              | Mean      | -0.01             | -0.05     | 0.15  | -0.02 | -0.02 | -0.07 | 0.00    |
|                              |              | SD        | 0.129             | 0.084     | 0.105 | 0.075 | 0.098 | 0.163 | 0.129   |
|                              |              | Minimum   | -0.2              | -0.2      | 0.0   | -0.1  | -0.1  | -0.3  | -0.3    |
|                              |              | Median    | 0.00              | 0.00      | 0.15  | 0.00  | -0.05 | -0.05 | 0.00    |
|                              |              | Maximum   | 0.2               | 0.0       | 0.3   | 0.1   | 0.1   | 0.1   | 0.3     |
|                              | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                              |              | Mean      | 0.00              | 0.07      | 0.03  | 0.00  | 0.02  | 0.02  | 0.03    |
|                              |              | SD        | 0.156             | 0.137     | 0.082 | 0.110 | 0.117 | 0.172 | 0.120   |
|                              |              | Minimum   | -0.3              | -0.1      | -0.1  | -0.2  | -0.1  | -0.2  | -0.2    |
|                              |              | Median    | 0.05              | 0.05      | 0.05  | 0.00  | 0.00  | 0.00  | 0.00    |
|                              |              | Maximum   | 0.2               | 0.3       | 0.1   | 0.1   | 0.2   | 0.3   | 0.3     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |        | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|--------|---------|
|                         |              |           |                   | A         | B     | C     | D     | E      |         |
| Neutrophils (%)         | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6      | 30      |
|                         |              | Mean      | -3.76             | -1.10     | -1.95 | -0.32 | -0.25 | -12.02 | -3.13   |
|                         |              | SD        | 6.883             | 5.728     | 7.158 | 5.654 | 6.880 | 9.397  | 8.014   |
|                         |              | Minimum   | -15.5             | -6.2      | -10.4 | -7.7  | -9.5  | -24.9  | -24.9   |
|                         |              | Median    | -3.70             | -3.30     | -4.30 | 1.95  | 1.10  | -9.05  | -4.25   |
|                         |              | Maximum   | 5.3               | 8.4       | 7.5   | 6.0   | 8.5   | -0.6   | 8.5     |
|                         | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6      | 30      |
|                         |              | Mean      | -2.91             | -1.33     | -0.98 | -2.00 | 1.25  | -10.50 | -2.71   |
|                         |              | SD        | 5.478             | 2.709     | 5.903 | 7.104 | 7.714 | 6.085  | 7.038   |
|                         |              | Minimum   | -10.7             | -4.9      | -6.9  | -11.5 | -10.3 | -16.5  | -16.5   |
|                         |              | Median    | -2.55             | -0.70     | -1.90 | 0.65  | 3.15  | -11.80 | -1.05   |
|                         |              | Maximum   | 3.0               | 2.5       | 7.8   | 4.7   | 11.6  | -1.2   | 11.6    |
|                         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6      | 30      |
|                         |              | Mean      | -6.00             | -1.40     | -3.05 | -2.47 | -0.50 | -10.83 | -3.65   |
|                         |              | SD        | 4.127             | 7.318     | 6.348 | 5.256 | 5.349 | 7.925  | 7.131   |
|                         |              | Minimum   | -10.9             | -10.0     | -12.3 | -9.0  | -10.0 | -19.2  | -19.2   |
|                         |              | Median    | -7.90             | -1.00     | -3.30 | -3.55 | 2.10  | -11.35 | -3.20   |
|                         |              | Maximum   | 1.1               | 10.4      | 4.5   | 6.4   | 3.9   | 1.3    | 10.4    |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.5 Clinical Laboratory Change From Baseline - Hematology (Safety Population)

| Laboratory Test (units)        | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                                |              |           |                   | A         | B     | C     | D     | E     |         |
| Absolute Neutrophils (thou/uL) | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |              | Mean      | -0.46             | -0.38     | -0.25 | -0.73 | -0.30 | -1.88 | -0.71   |
|                                |              | SD        | 0.765             | 0.397     | 0.782 | 0.914 | 0.529 | 1.476 | 1.042   |
|                                |              | Minimum   | -2.1              | -0.9      | -1.4  | -2.1  | -1.0  | -4.0  | -4.0    |
|                                |              | Median    | -0.30             | -0.35     | -0.20 | -0.20 | -0.35 | -1.90 | -0.40   |
|                                |              | Maximum   | 0.6               | 0.2       | 0.8   | -0.1  | 0.6   | 0.3   | 0.8     |
|                                | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |              | Mean      | -0.19             | -0.35     | 0.45  | -0.70 | 0.00  | -1.55 | -0.43   |
|                                |              | SD        | 0.597             | 0.362     | 0.942 | 1.035 | 0.756 | 1.411 | 1.130   |
|                                |              | Minimum   | -1.4              | -0.7      | -0.4  | -2.0  | -1.0  | -3.6  | -3.6    |
|                                |              | Median    | -0.05             | -0.40     | 0.30  | -0.65 | 0.00  | -1.65 | -0.25   |
|                                |              | Maximum   | 0.5               | 0.1       | 2.2   | 0.5   | 1.2   | 0.4   | 2.2     |
|                                | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |              | Mean      | -0.55             | 0.10      | -0.28 | -0.62 | -0.28 | -1.43 | -0.50   |
|                                |              | SD        | 0.615             | 1.164     | 1.042 | 0.904 | 0.412 | 1.346 | 1.086   |
|                                |              | Minimum   | -1.5              | -0.9      | -1.5  | -1.6  | -0.8  | -2.9  | -2.9    |
|                                |              | Median    | -0.45             | -0.20     | -0.55 | -0.50 | -0.10 | -1.65 | -0.40   |
|                                |              | Maximum   | 0.4               | 2.4       | 1.4   | 0.8   | 0.1   | 0.6   | 2.4     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Hemoglobin (g/dL)       | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 9  | 1 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 1          | 9  | 0 | 0          | 0 | 0 |
|                         | A              | Day 2        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 1          | 0 | 0 | 1          | 4  | 0 | 0          | 0 | 0 |
|                         | B              | Day 2        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 1          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         | C              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                         | D              | Day 2        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 1 | 0 | 1          | 4  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Hemoglobin (g/dL)       | E              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                         | Overall*       | Day 2        | 0          | 3 | 0 | 0          | 27 | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 3 | 0 | 0          | 27 | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 2          | 1 | 0 | 4          | 23 | 0 | 0          | 0 | 0 |
| Hematocrit (%)          | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 1          | 9  | 0 | 0          | 0 | 0 |
|                         | A              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                         | B              | Day 2        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |                | End of Study | 1          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)  | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|--------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                          |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                          |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Hematocrit (%)           | C              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                          |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                          |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                          | D              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                          |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                          |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                          | E              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                          |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                          |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                          | Overall*       | Day 2        | 0          | 1 | 0 | 0          | 29 | 0 | 0          | 0 | 0 |
|                          |                | Day 3        | 0          | 1 | 0 | 0          | 29 | 0 | 0          | 0 | 0 |
|                          |                | End of Study | 1          | 0 | 0 | 1          | 28 | 0 | 0          | 0 | 0 |
| Platelet Count (thou/uL) | Pooled Placebo | Day 2        | 1          | 0 | 0 | 1          | 8  | 0 | 0          | 0 | 0 |
|                          |                | Day 3        | 0          | 1 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                          |                | End of Study | 0          | 1 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                          |                |              |            |   |   |            |    |   |            |   |   |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)  | Treatment | Time Point   | Baseline L |   |   | Baseline N |   |   | Baseline H |   |   |
|--------------------------|-----------|--------------|------------|---|---|------------|---|---|------------|---|---|
|                          |           |              | Postdose   |   |   | Postdose   |   |   | Postdose   |   |   |
|                          |           |              | L          | N | H | L          | N | H | L          | N | H |
| Platelet Count (thou/uL) | A         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                          |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                          |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                          | B         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                          |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                          |           | End of Study | 0          | 0 | 0 | 1          | 5 | 0 | 0          | 0 | 0 |
|                          | C         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                          |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                          |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                          | D         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                          |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                          |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                          | E         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                          |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                          |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)       | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                               |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                               |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Platelet Count (thou/uL)      | Overall*       | Day 2        | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                               |                | Day 3        | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                               |                | End of Study | 0          | 0 | 0 | 1          | 29 | 0 | 0          | 0 | 0 |
| Red Blood Cell Count (mil/uL) | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                               |                | Day 3        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                               |                | End of Study | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                               | A              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                               |                | Day 3        | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                               |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                               | B              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                               |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                               |                | End of Study | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                               | C              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                               |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                               |                | End of Study | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)             | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                                     |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                                     |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Red Blood Cell Count<br>(mil/uL)    | D              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     | E              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     | Overall*       | Day 2        | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                                     |                | Day 3        | 0          | 0 | 0 | 0          | 29 | 1 | 0          | 0 | 0 |
|                                     |                | End of Study | 0          | 0 | 0 | 2          | 28 | 0 | 0          | 0 | 0 |
| White Blood Cell Count<br>(thou/uL) | Pooled Placebo | Day 2        | 1          | 0 | 0 | 1          | 8  | 0 | 0          | 0 | 0 |
|                                     |                | Day 3        | 1          | 0 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                                     |                | End of Study | 1          | 0 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                                     | A              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)             | Treatment | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------------------|-----------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                                     |           |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                                     |           |              | L          | N | H | L          | N  | H | L          | N | H |
| White Blood Cell Count<br>(thou/uL) | B         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     | C         | Day 2        | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                                     |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     |           | End of Study | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                                     | D         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     | E         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                     | Overall*  | Day 2        | 0          | 0 | 0 | 1          | 29 | 0 | 0          | 0 | 0 |
|                                     |           | Day 3        | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                                     |           | End of Study | 0          | 0 | 0 | 1          | 29 | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline L |   |   | Baseline N |   |   | Baseline H |   |   |
|-------------------------|----------------|--------------|------------|---|---|------------|---|---|------------|---|---|
|                         |                |              | Postdose   |   |   | Postdose   |   |   | Postdose   |   |   |
|                         |                |              | L          | N | H | L          | N | H | L          | N | H |
| Basophils (%)           | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 9 | 0 | 0          | 1 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 8 | 1 | 0          | 1 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 9 | 0 | 0          | 1 | 0 |
|                         | A              | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         | B              | Day 2        | 0          | 0 | 0 | 0          | 5 | 0 | 0          | 0 | 1 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 5 | 0 | 0          | 0 | 1 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 5 | 0 | 0          | 1 | 0 |
|                         | C              | Day 2        | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         | D              | Day 2        | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         |                | Day 3        | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         |                | End of Study | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)         | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|---------------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                                 |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                                 |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Basophils (%)                   | E              | Day 2        | 0          | 0 | 0 | 0          | 4  | 2 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                                 | Overall*       | Day 2        | 0          | 0 | 0 | 0          | 25 | 4 | 0          | 0 | 1 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 26 | 3 | 0          | 0 | 1 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 26 | 3 | 0          | 1 | 0 |
| Absolute Basophils<br>(thou/uL) | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                                 | A              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 | B              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)         | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|---------------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                                 |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                                 |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Absolute Basophils<br>(thou/uL) | C              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 | D              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 | E              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 | Overall*       | Day 2        | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
| Eosinophils (%)                 | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units) | Treatment | Time Point   | Baseline L |   |   | Baseline N |   |   | Baseline H |   |   |
|-------------------------|-----------|--------------|------------|---|---|------------|---|---|------------|---|---|
|                         |           |              | Postdose   |   |   | Postdose   |   |   | Postdose   |   |   |
|                         |           |              | L          | N | H | L          | N | H | L          | N | H |
| Eosinophils (%)         | A         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         | B         | Day 2        | 0          | 0 | 0 | 0          | 5 | 0 | 0          | 0 | 1 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 5 | 0 | 0          | 0 | 1 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 5 | 0 | 0          | 0 | 1 |
|                         | C         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         | D         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         | E         | Day 2        | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 5 | 1 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)        | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|--------------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                                |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                                |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Eosinophils (%)                | Overall*       | Day 2        | 0          | 0 | 0 | 0          | 28 | 1 | 0          | 0 | 1 |
|                                |                | Day 3        | 0          | 0 | 0 | 0          | 29 | 0 | 0          | 0 | 1 |
|                                |                | End of Study | 0          | 0 | 0 | 0          | 28 | 1 | 0          | 0 | 1 |
| Absolute Eosinophils (thou/uL) | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                                |                | Day 3        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                                |                | End of Study | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                                | A              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                | B              | Day 2        | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                                |                | Day 3        | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                                |                | End of Study | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                                | C              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)           | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-----------------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                                   |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                                   |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Absolute Eosinophils<br>(thou/uL) | D              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   | E              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   | Overall*       | Day 2        | 0          | 0 | 0 | 0          | 29 | 1 | 0          | 0 | 0 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 29 | 1 | 0          | 0 | 0 |
|                                   |                | End of Study | 0          | 0 | 0 | 0          | 29 | 1 | 0          | 0 | 0 |
| Lymphocytes (%)                   | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 8  | 1 | 0          | 0 | 1 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 8  | 1 | 0          | 0 | 1 |
|                                   |                | End of Study | 0          | 0 | 0 | 0          | 7  | 2 | 0          | 0 | 1 |
|                                   | A              | Day 2        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 1 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 1 |
|                                   |                | End of Study | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 1 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units) | Treatment | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-------------------------|-----------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                         |           |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                         |           |              | L          | N | H | L          | N  | H | L          | N | H |
| Lymphocytes (%)         | B         | Day 2        | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                         | C         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | D         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                         | E         | Day 2        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |           | Day 3        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         |           | End of Study | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                         | Overall*  | Day 2        | 0          | 1 | 0 | 0          | 27 | 1 | 0          | 0 | 1 |
|                         |           | Day 3        | 0          | 1 | 0 | 0          | 28 | 0 | 0          | 0 | 1 |
|                         |           | End of Study | 0          | 1 | 0 | 0          | 27 | 1 | 0          | 0 | 1 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)           | Treatment      | Time Point   | Baseline L |   |   | Baseline N |   |   | Baseline H |   |   |
|-----------------------------------|----------------|--------------|------------|---|---|------------|---|---|------------|---|---|
|                                   |                |              | Postdose   |   |   | Postdose   |   |   | Postdose   |   |   |
|                                   |                |              | L          | N | H | L          | N | H | L          | N | H |
| Absolute Lymphocytes<br>(thou/uL) | Pooled Placebo | Day 2        | 1          | 0 | 0 | 0          | 9 | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 0          | 1 | 0 | 0          | 8 | 1 | 0          | 0 | 0 |
|                                   |                | End of Study | 0          | 1 | 0 | 0          | 9 | 0 | 0          | 0 | 0 |
|                                   | A              | Day 2        | 0          | 0 | 0 | 0          | 4 | 1 | 0          | 1 | 0 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 5 | 0 | 0          | 1 | 0 |
|                                   |                | End of Study | 0          | 0 | 0 | 0          | 5 | 0 | 0          | 1 | 0 |
|                                   | B              | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                   |                | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                   | C              | Day 2        | 0          | 0 | 0 | 1          | 5 | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                   |                | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                   | D              | Day 2        | 0          | 0 | 0 | 0          | 5 | 0 | 0          | 1 | 0 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 5 | 0 | 0          | 1 | 0 |
|                                   |                | End of Study | 0          | 0 | 0 | 1          | 4 | 0 | 0          | 1 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)           | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-----------------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                                   |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                                   |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Absolute Lymphocytes<br>(thou/uL) | E              | Day 2        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                                   |                | End of Study | 0          | 1 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                                   | Overall*       | Day 2        | 0          | 1 | 0 | 1          | 25 | 1 | 0          | 2 | 0 |
|                                   |                | Day 3        | 0          | 1 | 0 | 0          | 27 | 0 | 0          | 2 | 0 |
|                                   |                | End of Study | 0          | 1 | 0 | 1          | 26 | 0 | 0          | 2 | 0 |
| Monocytes (%)                     | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 9  | 0 | 0          | 0 | 1 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 9  | 0 | 0          | 0 | 1 |
|                                   |                | End of Study | 0          | 0 | 0 | 1          | 6  | 2 | 0          | 0 | 1 |
|                                   | A              | Day 2        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 1 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                                   |                | End of Study | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 1 |
|                                   | B              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)      | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|------------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                              |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                              |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Monocytes (%)                | C              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              |                | Day 3        | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                              |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              | D              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                              |                | End of Study | 0          | 0 | 0 | 0          | 5  | 1 | 0          | 0 | 0 |
|                              | E              | Day 2        | 0          | 0 | 0 | 0          | 4  | 1 | 0          | 0 | 1 |
|                              |                | Day 3        | 0          | 0 | 0 | 0          | 4  | 1 | 0          | 1 | 0 |
|                              |                | End of Study | 0          | 0 | 0 | 0          | 4  | 1 | 0          | 0 | 1 |
|                              | Overall*       | Day 2        | 0          | 0 | 0 | 0          | 27 | 1 | 0          | 0 | 2 |
|                              |                | Day 3        | 0          | 0 | 0 | 0          | 26 | 2 | 0          | 2 | 0 |
|                              |                | End of Study | 0          | 0 | 0 | 0          | 26 | 2 | 0          | 0 | 2 |
| Absolute Monocytes (thou/uL) | Pooled Placebo | Day 2        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                              |                | Day 3        | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |
|                              |                | End of Study | 0          | 0 | 0 | 0          | 10 | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)         | Treatment | Time Point   | Baseline L |   |   | Baseline N |   |   | Baseline H |   |   |
|---------------------------------|-----------|--------------|------------|---|---|------------|---|---|------------|---|---|
|                                 |           |              | Postdose   |   |   | Postdose   |   |   | Postdose   |   |   |
|                                 |           |              | L          | N | H | L          | N | H | L          | N | H |
| Absolute Monocytes<br>(thou/uL) | A         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 | B         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 | C         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 | D         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 | E         | Day 2        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | Day 3        | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |
|                                 |           | End of Study | 0          | 0 | 0 | 0          | 6 | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)         | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|---------------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                                 |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                                 |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Absolute Monocytes<br>(thou/uL) | Overall*       | Day 2        | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
| Neutrophils (%)                 | Pooled Placebo | Day 2        | 0          | 1 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 1 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 1          | 0 | 0 | 1          | 8  | 0 | 0          | 0 | 0 |
|                                 | A              | Day 2        | 1          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 1          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 1          | 0 | 0 | 0          | 5  | 0 | 0          | 0 | 0 |
|                                 | B              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |
|                                 | C              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                 |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)           | Treatment      | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-----------------------------------|----------------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                                   |                |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                                   |                |              | L          | N | H | L          | N  | H | L          | N | H |
| Neutrophils (%)                   | D              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   | E              | Day 2        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                                   |                | End of Study | 0          | 0 | 0 | 0          | 5  | 0 | 0          | 1 | 0 |
|                                   | Overall*       | Day 2        | 1          | 0 | 0 | 0          | 28 | 0 | 0          | 1 | 0 |
|                                   |                | Day 3        | 1          | 0 | 0 | 0          | 28 | 0 | 0          | 1 | 0 |
|                                   |                | End of Study | 1          | 0 | 0 | 1          | 27 | 0 | 0          | 1 | 0 |
| Absolute Neutrophils<br>(thou/uL) | Pooled Placebo | Day 2        | 1          | 0 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 1          | 0 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                                   |                | End of Study | 1          | 0 | 0 | 0          | 9  | 0 | 0          | 0 | 0 |
|                                   | A              | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |                | End of Study | 0          | 0 | 0 | 1          | 5  | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.6 Clinical Laboratory Shift From Baseline - Hematology (Safety Population)

| Laboratory Test (units)           | Treatment | Time Point   | Baseline L |   |   | Baseline N |    |   | Baseline H |   |   |
|-----------------------------------|-----------|--------------|------------|---|---|------------|----|---|------------|---|---|
|                                   |           |              | Postdose   |   |   | Postdose   |    |   | Postdose   |   |   |
|                                   |           |              | L          | N | H | L          | N  | H | L          | N | H |
| Absolute Neutrophils<br>(thou/uL) | B         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   | C         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   | D         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   | E         | Day 2        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |           | Day 3        | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   |           | End of Study | 0          | 0 | 0 | 0          | 6  | 0 | 0          | 0 | 0 |
|                                   | Overall*  | Day 2        | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                                   |           | Day 3        | 0          | 0 | 0 | 0          | 30 | 0 | 0          | 0 | 0 |
|                                   |           | End of Study | 0          | 0 | 0 | 1          | 29 | 0 | 0          | 0 | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, L = Below Reference Range, H = Above Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.7 Clinical Laboratory Summary - Urinalysis (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point | Statistic | Pooled Placebo | Treatment |       |       |       |       | Overall |
|-------------------------|-----------------|------------|-----------|----------------|-----------|-------|-------|-------|-------|---------|
|                         |                 |            |           |                | A         | B     | C     | D     | E     |         |
| pH, Urine               | 5-8             | Screen     | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 5.75           | 5.92      | 5.25  | 6.08  | 6.42  | 6.08  | 5.95    |
|                         |                 |            | SD        | 0.979          | 0.801     | 0.612 | 1.281 | 0.736 | 0.861 | 0.913   |
|                         |                 |            | Minimum   | 5.0            | 5.0       | 5.0   | 5.0   | 5.0   | 5.0   | 5.0     |
|                         |                 |            | Median    | 5.00           | 6.00      | 5.00  | 5.75  | 6.50  | 6.50  | 6.25    |
|                         |                 |            | Maximum   | 7.0            | 7.0       | 6.5   | 8.0   | 7.0   | 7.0   | 8.0     |
|                         |                 | Baseline   | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 5.65           | 5.67      | 5.25  | 6.00  | 5.83  | 5.58  | 5.67    |
|                         |                 |            | SD        | 0.883          | 1.033     | 0.612 | 1.225 | 0.931 | 0.917 | 0.932   |
|                         |                 |            | Minimum   | 5.0            | 5.0       | 5.0   | 5.0   | 5.0   | 5.0   | 5.0     |
|                         |                 |            | Median    | 5.00           | 5.00      | 5.00  | 5.75  | 5.75  | 5.00  | 5.00    |
|                         |                 |            | Maximum   | 7.0            | 7.0       | 6.5   | 8.0   | 7.0   | 7.0   | 8.0     |
|                         |                 | Day 3      | n         | 10             | 6         | 6     | 6     | 6     | 6     | 30      |
|                         |                 |            | Mean      | 5.55           | 5.17      | 5.25  | 5.83  | 5.75  | 5.58  | 5.52    |
|                         |                 |            | SD        | 0.725          | 0.408     | 0.612 | 0.931 | 0.880 | 0.917 | 0.771   |
|                         |                 |            | Minimum   | 5.0            | 5.0       | 5.0   | 5.0   | 5.0   | 5.0   | 5.0     |
|                         |                 |            | Median    | 5.00           | 5.00      | 5.00  | 5.75  | 5.50  | 5.00  | 5.00    |
|                         |                 |            | Maximum   | 6.5            | 6.0       | 6.5   | 7.0   | 7.0   | 7.0   | 7.0     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.7 Clinical Laboratory Summary - Urinalysis (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |         |         |         |         | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|---------|---------|---------|---------|---------|
|                         |                 |              |           |                | A         | B       | C       | D       | E       |         |
| pH, Urine               | 5-8             | End of Study | n         | 10             | 6         | 6       | 6       | 6       | 6       | 30      |
|                         |                 |              | Mean      | 6.35           | 6.08      | 5.42    | 6.17    | 5.92    | 5.83    | 5.88    |
|                         |                 |              | SD        | 1.029          | 1.281     | 0.665   | 0.931   | 1.021   | 0.931   | 0.953   |
|                         |                 |              | Minimum   | 5.0            | 5.0       | 5.0     | 5.0     | 5.0     | 5.0     | 5.0     |
|                         |                 |              | Median    | 6.50           | 5.75      | 5.00    | 6.50    | 5.75    | 5.75    | 5.50    |
|                         |                 |              | Maximum   | 8.0            | 8.0       | 6.5     | 7.0     | 7.0     | 7.0     | 8.0     |
| Specific Gravity        | 1.005-1.03      | Screen       | n         | 10             | 6         | 6       | 6       | 6       | 6       | 30      |
|                         |                 |              | Mean      | 1.0093         | 1.0133    | 1.0165  | 1.0090  | 1.0113  | 1.0075  | 1.0115  |
|                         |                 |              | SD        | 0.01024        | 0.00807   | 0.00855 | 0.00822 | 0.01104 | 0.00442 | 0.00839 |
|                         |                 |              | Minimum   | 1.002          | 1.002     | 1.006   | 1.003   | 1.003   | 1.002   | 1.002   |
|                         |                 |              | Median    | 1.0035         | 1.0165    | 1.0160  | 1.0055  | 1.0055  | 1.0065  | 1.0090  |
|                         |                 |              | Maximum   | 1.028          | 1.023     | 1.026   | 1.024   | 1.026   | 1.014   | 1.026   |
|                         |                 | Baseline     | n         | 10             | 6         | 6       | 6       | 6       | 6       | 30      |
|                         |                 |              | Mean      | 1.0117         | 1.0147    | 1.0150  | 1.0065  | 1.0092  | 1.0087  | 1.0108  |
|                         |                 |              | SD        | 0.01006        | 0.00975   | 0.01110 | 0.00822 | 0.00935 | 0.00789 | 0.00933 |
|                         |                 |              | Minimum   | 1.002          | 1.002     | 1.004   | 1.002   | 1.002   | 1.002   | 1.002   |
|                         |                 |              | Median    | 1.0095         | 1.0165    | 1.0145  | 1.0030  | 1.0050  | 1.0050  | 1.0060  |
|                         |                 |              | Maximum   | 1.032          | 1.025     | 1.028   | 1.023   | 1.025   | 1.021   | 1.028   |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.7 Clinical Laboratory Summary - Urinalysis (Safety Population)

| Laboratory Test (units) | Reference Range | Time Point   | Statistic | Pooled Placebo | Treatment |         |         |         |         | Overall |
|-------------------------|-----------------|--------------|-----------|----------------|-----------|---------|---------|---------|---------|---------|
|                         |                 |              |           |                | A         | B       | C       | D       | E       |         |
| Specific Gravity        | 1.005-1.03      | Day 3        | n         | 10             | 6         | 6       | 6       | 6       | 6       | 30      |
|                         |                 |              | Mean      | 1.0137         | 1.0150    | 1.0212  | 1.0112  | 1.0147  | 1.0180  | 1.0160  |
|                         |                 |              | SD        | 0.00854        | 0.00395   | 0.00640 | 0.00655 | 0.00836 | 0.00894 | 0.00740 |
|                         |                 |              | Minimum   | 1.002          | 1.011     | 1.010   | 1.007   | 1.005   | 1.003   | 1.003   |
|                         |                 |              | Median    | 1.0140         | 1.0135    | 1.0220  | 1.0085  | 1.0155  | 1.0205  | 1.0155  |
|                         |                 |              | Maximum   | 1.027          | 1.022     | 1.030   | 1.024   | 1.023   | 1.029   | 1.030   |
|                         |                 | End of Study | n         | 10             | 6         | 6       | 6       | 6       | 6       | 30      |
|                         |                 |              | Mean      | 1.0142         | 1.0133    | 1.0218  | 1.0108  | 1.0107  | 1.0112  | 1.0136  |
|                         |                 |              | SD        | 0.00954        | 0.00683   | 0.00496 | 0.00898 | 0.00712 | 0.00954 | 0.00832 |
|                         |                 |              | Minimum   | 1.003          | 1.006     | 1.013   | 1.002   | 1.003   | 1.002   | 1.002   |
|                         |                 |              | Median    | 1.0130         | 1.0120    | 1.0225  | 1.0085  | 1.0115  | 1.0080  | 1.0125  |
|                         |                 |              | Maximum   | 1.028          | 1.022     | 1.028   | 1.022   | 1.022   | 1.024   | 1.028   |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.8 Clinical Laboratory Change From Baseline - Urinalysis (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |         |         |         |         | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|---------|---------|---------|---------|---------|
|                         |              |           |                   | A         | B       | C       | D       | E       |         |
| pH, Urine               | Day 3        | n         | 10                | 6         | 6       | 6       | 6       | 6       | 30      |
|                         |              | Mean      | -0.10             | -0.50     | 0.00    | -0.17   | -0.08   | 0.00    | -0.15   |
|                         |              | SD        | 1.197             | 0.837     | 0.000   | 1.602   | 1.281   | 0.000   | 0.939   |
|                         |              | Minimum   | -2.0              | -2.0      | 0.0     | -3.0    | -2.0    | 0.0     | -3.0    |
|                         |              | Median    | 0.00              | 0.00      | 0.00    | 0.00    | 0.00    | 0.00    | 0.00    |
|                         |              | Maximum   | 1.5               | 0.0       | 0.0     | 2.0     | 2.0     | 0.0     | 2.0     |
|                         | End of Study | n         | 10                | 6         | 6       | 6       | 6       | 6       | 30      |
|                         |              | Mean      | 0.70              | 0.42      | 0.17    | 0.17    | 0.08    | 0.25    | 0.22    |
|                         |              | SD        | 1.567             | 1.800     | 0.408   | 1.472   | 0.970   | 0.880   | 1.127   |
|                         |              | Minimum   | -2.0              | -2.0      | 0.0     | -1.5    | -1.5    | -0.5    | -2.0    |
|                         |              | Median    | 1.25              | 0.00      | 0.00    | 0.25    | 0.00    | 0.00    | 0.00    |
|                         |              | Maximum   | 3.0               | 3.0       | 1.0     | 2.0     | 1.5     | 2.0     | 3.0     |
| Specific Gravity        | Day 3        | n         | 10                | 6         | 6       | 6       | 6       | 6       | 30      |
|                         |              | Mean      | 0.0020            | 0.0003    | 0.0062  | 0.0047  | 0.0055  | 0.0093  | 0.0052  |
|                         |              | SD        | 0.01000           | 0.01111   | 0.00813 | 0.00308 | 0.00596 | 0.01088 | 0.00834 |
|                         |              | Minimum   | -0.014            | -0.012    | -0.002  | 0.001   | -0.002  | -0.008  | -0.012  |
|                         |              | Median    | 0.0015            | -0.0030   | 0.0040  | 0.0040  | 0.0045  | 0.0140  | 0.0040  |
|                         |              | Maximum   | 0.013             | 0.018     | 0.017   | 0.010   | 0.016   | 0.020   | 0.020   |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.8 Clinical Laboratory Change From Baseline - Urinalysis (Safety Population)

| Laboratory Test (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |         |         |         |         | Overall |
|-------------------------|--------------|-----------|-------------------|-----------|---------|---------|---------|---------|---------|
|                         |              |           |                   | A         | B       | C       | D       | E       |         |
| Specific Gravity        | End of Study | n         | 10                | 6         | 6       | 6       | 6       | 6       | 30      |
|                         |              | Mean      | 0.0025            | -0.0013   | 0.0068  | 0.0043  | 0.0015  | 0.0025  | 0.0028  |
|                         |              | SD        | 0.00737           | 0.01288   | 0.00924 | 0.00829 | 0.00669 | 0.00451 | 0.00861 |
|                         |              | Minimum   | -0.004            | -0.017    | -0.003  | -0.003  | -0.004  | -0.004  | -0.017  |
|                         |              | Median    | 0.0005            | -0.0035   | 0.0045  | 0.0010  | -0.0020 | 0.0020  | 0.0000  |
|                         |              | Maximum   | 0.017             | 0.018     | 0.019   | 0.019   | 0.011   | 0.008   | 0.019   |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.9 Clinical Laboratory Shift From Baseline - Urinalysis (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline N |   | Baseline O |   |
|-------------------------|----------------|--------------|------------|---|------------|---|
|                         |                |              | Postdose   |   | Postdose   |   |
|                         |                |              | N          | O | N          | O |
| Occult Blood            | Pooled Placebo | Day 3        | 10         | 0 | 0          | 0 |
|                         |                | End of Study | 10         | 0 | 0          | 0 |
|                         | A              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | B              | Day 3        | 4          | 1 | 0          | 1 |
|                         |                | End of Study | 4          | 1 | 0          | 1 |
|                         | C              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | D              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 5          | 1 | 0          | 0 |
|                         | E              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | Overall*       | Day 3        | 28         | 1 | 0          | 1 |
|                         |                | End of Study | 27         | 2 | 0          | 1 |
| pH, Urine               | Pooled Placebo | Day 3        | 10         | 0 | 0          | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, O = Outside Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.9 Clinical Laboratory Shift From Baseline - Urinalysis (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline N |   | Baseline O |   |
|-------------------------|----------------|--------------|------------|---|------------|---|
|                         |                |              | Postdose   |   | Postdose   |   |
|                         |                |              | N          | O | N          | O |
| pH, Urine               | Pooled Placebo | End of Study | 10         | 0 | 0          | 0 |
|                         | A              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | B              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | C              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | D              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | E              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | Overall*       | Day 3        | 30         | 0 | 0          | 0 |
|                         |                | End of Study | 30         | 0 | 0          | 0 |
| Specific Gravity        | Pooled Placebo | Day 3        | 5          | 1 | 3          | 1 |
|                         |                | End of Study | 6          | 0 | 2          | 2 |

Note: \* Represents active treatment overall

N = Within Reference Range, O = Outside Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.9 Clinical Laboratory Shift From Baseline - Urinalysis (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline N |   | Baseline O |   |
|-------------------------|----------------|--------------|------------|---|------------|---|
|                         |                |              | Postdose   |   | Postdose   |   |
|                         |                |              | N          | O | N          | O |
| Specific Gravity        | A              | Day 3        | 4          | 0 | 2          | 0 |
|                         |                | End of Study | 4          | 0 | 2          | 0 |
|                         | B              | Day 3        | 5          | 0 | 1          | 0 |
|                         |                | End of Study | 5          | 0 | 1          | 0 |
|                         | C              | Day 3        | 2          | 0 | 4          | 0 |
|                         |                | End of Study | 1          | 1 | 3          | 1 |
|                         | D              | Day 3        | 3          | 0 | 3          | 0 |
|                         |                | End of Study | 2          | 1 | 2          | 1 |
|                         | E              | Day 3        | 3          | 0 | 2          | 1 |
|                         |                | End of Study | 2          | 1 | 2          | 1 |
| Leukocyte Esterase      | Overall*       | Day 3        | 17         | 0 | 12         | 1 |
|                         |                | End of Study | 14         | 3 | 10         | 3 |
|                         | Pooled Placebo | Day 3        | 9          | 1 | 0          | 0 |
|                         |                | End of Study | 9          | 1 | 0          | 0 |
|                         | A              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                |              |            |   |            |   |
|                         |                |              |            |   |            |   |

Note: \* Represents active treatment overall

N = Within Reference Range, O = Outside Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.9 Clinical Laboratory Shift From Baseline - Urinalysis (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline N |   | Baseline O |   |
|-------------------------|----------------|--------------|------------|---|------------|---|
|                         |                |              | Postdose   |   | Postdose   |   |
|                         |                |              | N          | O | N          | O |
| Leukocyte Esterase      | A              | End of Study | 6          | 0 | 0          | 0 |
|                         | B              | Day 3        | 4          | 2 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | C              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | D              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | E              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | Overall*       | Day 3        | 28         | 2 | 0          | 0 |
|                         |                | End of Study | 30         | 0 | 0          | 0 |
| Nitrite                 | Pooled Placebo | Day 3        | 10         | 0 | 0          | 0 |
|                         |                | End of Study | 10         | 0 | 0          | 0 |
|                         | A              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, O = Outside Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.9 Clinical Laboratory Shift From Baseline - Urinalysis (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline N |   | Baseline O |   |
|-------------------------|----------------|--------------|------------|---|------------|---|
|                         |                |              | Postdose   |   | Postdose   |   |
|                         |                |              | N          | O | N          | O |
| Nitrite                 | B              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | C              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | D              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | E              | Day 3        | 5          | 1 | 0          | 0 |
|                         |                | End of Study | 5          | 1 | 0          | 0 |
|                         | Overall*       | Day 3        | 29         | 1 | 0          | 0 |
|                         |                | End of Study | 29         | 1 | 0          | 0 |
| Bilirubin               | Pooled Placebo | Day 3        | 10         | 0 | 0          | 0 |
|                         |                | End of Study | 10         | 0 | 0          | 0 |
|                         | A              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | B              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, O = Outside Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.9 Clinical Laboratory Shift From Baseline - Urinalysis (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline N |   | Baseline O |   |
|-------------------------|----------------|--------------|------------|---|------------|---|
|                         |                |              | Postdose   |   | Postdose   |   |
|                         |                |              | N          | O | N          | O |
| Bilirubin               | B              | End of Study | 6          | 0 | 0          | 0 |
|                         |                |              |            |   |            |   |
|                         | C              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | D              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | E              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | Overall*       | Day 3        | 30         | 0 | 0          | 0 |
|                         |                | End of Study | 30         | 0 | 0          | 0 |
| Glucose                 | Pooled Placebo | Day 3        | 10         | 0 | 0          | 0 |
|                         |                | End of Study | 10         | 0 | 0          | 0 |
|                         | A              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | B              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, O = Outside Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.9 Clinical Laboratory Shift From Baseline - Urinalysis (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline N |   | Baseline O |   |
|-------------------------|----------------|--------------|------------|---|------------|---|
|                         |                |              | Postdose   |   | Postdose   |   |
|                         |                |              | N          | O | N          | O |
| Glucose                 | C              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | D              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | E              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | Overall*       | Day 3        | 30         | 0 | 0          | 0 |
|                         |                | End of Study | 30         | 0 | 0          | 0 |
|                         | Pooled Placebo | Day 3        | 10         | 0 | 0          | 0 |
|                         |                | End of Study | 10         | 0 | 0          | 0 |
| Protein                 | A              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | B              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | C              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, O = Outside Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.9 Clinical Laboratory Shift From Baseline - Urinalysis (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline N |   | Baseline O |   |
|-------------------------|----------------|--------------|------------|---|------------|---|
|                         |                |              | Postdose   |   | Postdose   |   |
|                         |                |              | N          | O | N          | O |
| Protein                 | C              | End of Study | 6          | 0 | 0          | 0 |
|                         |                |              |            |   |            |   |
|                         | D              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | E              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | Overall*       | Day 3        | 30         | 0 | 0          | 0 |
|                         |                | End of Study | 30         | 0 | 0          | 0 |
| Ketones                 | Pooled Placebo | Day 3        | 10         | 0 | 0          | 0 |
|                         |                | End of Study | 10         | 0 | 0          | 0 |
|                         | A              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | B              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | C              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         |                |              |            |   |            |   |

Note: \* Represents active treatment overall

N = Within Reference Range, O = Outside Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.9 Clinical Laboratory Shift From Baseline - Urinalysis (Safety Population)

| Laboratory Test (units) | Treatment      | Time Point   | Baseline N |   | Baseline O |   |
|-------------------------|----------------|--------------|------------|---|------------|---|
|                         |                |              | Postdose   |   | Postdose   |   |
|                         |                |              | N          | O | N          | O |
| Ketones                 | D              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | E              | Day 3        | 5          | 1 | 0          | 0 |
|                         |                | End of Study | 5          | 1 | 0          | 0 |
|                         | Overall*       | Day 3        | 29         | 1 | 0          | 0 |
|                         |                | End of Study | 29         | 1 | 0          | 0 |
| Urobilinogen            | Pooled Placebo | Day 3        | 10         | 0 | 0          | 0 |
|                         |                | End of Study | 10         | 0 | 0          | 0 |
|                         | A              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | B              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | C              | Day 3        | 6          | 0 | 0          | 0 |
|                         |                | End of Study | 6          | 0 | 0          | 0 |
|                         | D              | Day 3        | 5          | 0 | 1          | 0 |
|                         |                | End of Study | 5          | 0 | 1          | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, O = Outside Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.9 Clinical Laboratory Shift From Baseline - Urinalysis (Safety Population)

| Laboratory Test (units) | Treatment | Time Point   | Baseline N |   | Baseline O |   |
|-------------------------|-----------|--------------|------------|---|------------|---|
|                         |           |              | Postdose   |   | Postdose   |   |
|                         |           |              | N          | O | N          | O |
| Urobilinogen            | D         | End of Study | 5          | 0 | 1          | 0 |
|                         | E         | Day 3        | 6          | 0 | 0          | 0 |
|                         |           | End of Study | 6          | 0 | 0          | 0 |
|                         | Overall*  | Day 3        | 29         | 0 | 1          | 0 |
|                         |           | End of Study | 29         | 0 | 1          | 0 |

Note: \* Represents active treatment overall

N = Within Reference Range, O = Outside Reference Range

Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units)             | Time Point       | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------|------------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                                |                  |           |                   | A         | B     | C     | D     | E     |         |
| Systolic Blood Pressure (mmHg) | Screen           | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                  | Mean      | 118.5             | 119.5     | 121.0 | 119.7 | 114.2 | 123.0 | 119.5   |
|                                |                  | SD        | 8.07              | 7.84      | 10.95 | 12.68 | 10.23 | 10.22 | 10.19   |
|                                |                  | Minimum   | 108               | 110       | 107   | 105   | 105   | 111   | 105     |
|                                |                  | Median    | 117.5             | 119.0     | 117.0 | 120.0 | 111.5 | 120.0 | 117.0   |
|                                |                  | Maximum   | 131               | 132       | 137   | 134   | 134   | 138   | 138     |
|                                | Baseline         | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                  | Mean      | 116.2             | 125.3     | 120.8 | 125.2 | 116.3 | 116.2 | 120.8   |
|                                |                  | SD        | 8.98              | 19.34     | 14.27 | 14.37 | 11.64 | 12.61 | 14.24   |
|                                |                  | Minimum   | 101               | 104       | 106   | 109   | 106   | 106   | 104     |
|                                |                  | Median    | 117.0             | 120.0     | 118.5 | 127.0 | 113.0 | 112.0 | 116.0   |
|                                |                  | Maximum   | 131               | 154       | 146   | 146   | 138   | 141   | 154     |
|                                | Day 1, Hour 0.25 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                  | Mean      | 113.5             | 120.7     | 117.0 | 122.8 | 114.2 | 114.8 | 117.9   |
|                                |                  | SD        | 8.90              | 15.21     | 13.04 | 12.48 | 9.58  | 8.33  | 11.64   |
|                                |                  | Minimum   | 99                | 104       | 100   | 106   | 105   | 105   | 100     |
|                                |                  | Median    | 118.0             | 114.5     | 118.0 | 121.5 | 111.0 | 113.5 | 114.5   |
|                                |                  | Maximum   | 123               | 145       | 131   | 143   | 128   | 127   | 145     |
|                                | Day 1, Hour 0.5  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                  | Mean      | 112.2             | 123.8     | 113.5 | 118.5 | 109.5 | 111.8 | 115.4   |
|                                |                  | SD        | 6.89              | 19.77     | 8.69  | 12.71 | 6.47  | 4.79  | 12.11   |
|                                |                  | Minimum   | 98                | 105       | 104   | 105   | 100   | 106   | 100     |
|                                |                  | Median    | 114.5             | 120.5     | 112.5 | 118.0 | 110.5 | 110.5 | 113.0   |
|                                |                  | Maximum   | 119               | 162       | 124   | 141   | 118   | 119   | 162     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units)             | Time Point       | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------|------------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                                |                  |           |                   | A         | B     | C     | D     | E     |         |
| Systolic Blood Pressure (mmHg) | Day 1, Hour 0.75 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                  | Mean      | 111.4             | 119.7     | 119.0 | 118.7 | 112.2 | 113.0 | 116.5   |
|                                |                  | SD        | 7.52              | 15.49     | 17.16 | 10.33 | 8.18  | 10.70 | 12.35   |
|                                |                  | Minimum   | 96                | 103       | 105   | 108   | 102   | 104   | 102     |
|                                |                  | Median    | 112.0             | 118.0     | 114.0 | 118.5 | 110.5 | 109.5 | 112.0   |
|                                |                  | Maximum   | 121               | 144       | 151   | 135   | 125   | 134   | 151     |
|                                | Day 1, Hour 1    | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                  | Mean      | 111.5             | 123.0     | 113.7 | 117.8 | 113.0 | 118.5 | 117.2   |
|                                |                  | SD        | 7.20              | 13.07     | 8.71  | 9.99  | 5.29  | 7.04  | 9.31    |
|                                |                  | Minimum   | 96                | 110       | 103   | 104   | 108   | 109   | 103     |
|                                |                  | Median    | 114.0             | 119.0     | 116.5 | 118.0 | 112.5 | 117.0 | 117.0   |
|                                |                  | Maximum   | 119               | 142       | 124   | 134   | 120   | 128   | 142     |
|                                | Day 1, Hour 1.5  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                  | Mean      | 111.9             | 117.5     | 114.3 | 120.7 | 115.2 | 120.8 | 117.7   |
|                                |                  | SD        | 7.03              | 10.13     | 8.50  | 16.98 | 8.75  | 13.78 | 11.55   |
|                                |                  | Minimum   | 100               | 107       | 104   | 100   | 102   | 105   | 100     |
|                                |                  | Median    | 111.0             | 114.5     | 115.0 | 119.0 | 116.5 | 120.5 | 117.5   |
|                                |                  | Maximum   | 123               | 134       | 124   | 151   | 125   | 145   | 151     |
|                                | Day 1, Hour 2    | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                  | Mean      | 113.4             | 122.5     | 116.7 | 120.8 | 114.5 | 108.0 | 116.5   |
|                                |                  | SD        | 10.50             | 8.83      | 14.64 | 15.74 | 10.27 | 5.80  | 12.01   |
|                                |                  | Minimum   | 90                | 113       | 98    | 102   | 97    | 99    | 97      |
|                                |                  | Median    | 115.5             | 120.5     | 116.5 | 119.0 | 115.5 | 108.5 | 115.5   |
|                                |                  | Maximum   | 126               | 134       | 136   | 149   | 129   | 116   | 149     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units)             | Time Point     | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------|----------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                                |                |           |                   | A         | B     | C     | D     | E     |         |
| Systolic Blood Pressure (mmHg) | Day 1, Hour 4  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                | Mean      | 111.8             | 122.2     | 114.0 | 118.5 | 114.2 | 112.8 | 116.3   |
|                                |                | SD        | 6.81              | 10.74     | 8.65  | 10.56 | 9.93  | 13.06 | 10.54   |
|                                |                | Minimum   | 98                | 108       | 100   | 106   | 98    | 99    | 98      |
|                                |                | Median    | 114.5             | 118.5     | 116.0 | 120.0 | 115.5 | 110.5 | 117.5   |
|                                |                | Maximum   | 120               | 136       | 122   | 135   | 128   | 137   | 137     |
|                                | Day 1, Hour 6  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                | Mean      | 110.2             | 117.7     | 111.5 | 113.7 | 111.0 | 110.2 | 112.8   |
|                                |                | SD        | 9.60              | 12.08     | 8.02  | 7.00  | 3.58  | 8.23  | 8.13    |
|                                |                | Minimum   | 99                | 104       | 102   | 103   | 105   | 100   | 100     |
|                                |                | Median    | 110.5             | 116.5     | 111.0 | 115.0 | 111.5 | 109.0 | 112.0   |
|                                |                | Maximum   | 125               | 138       | 122   | 123   | 116   | 122   | 138     |
|                                | Day 1, Hour 12 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                | Mean      | 109.4             | 116.8     | 114.3 | 114.0 | 114.3 | 106.7 | 113.2   |
|                                |                | SD        | 6.50              | 8.54      | 6.02  | 11.59 | 5.32  | 5.75  | 8.05    |
|                                |                | Minimum   | 100               | 102       | 108   | 99    | 107   | 98    | 98      |
|                                |                | Median    | 109.5             | 120.0     | 114.5 | 113.5 | 113.0 | 107.5 | 112.0   |
|                                |                | Maximum   | 120               | 125       | 121   | 129   | 121   | 115   | 129     |
|                                | Day 2          | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                | Mean      | 107.5             | 116.7     | 113.2 | 117.0 | 112.5 | 113.7 | 114.6   |
|                                |                | SD        | 6.84              | 13.46     | 5.85  | 10.08 | 4.55  | 11.22 | 9.14    |
|                                |                | Minimum   | 99                | 107       | 107   | 102   | 106   | 103   | 102     |
|                                |                | Median    | 106.5             | 111.5     | 112.0 | 118.5 | 112.0 | 109.0 | 112.0   |
|                                |                | Maximum   | 120               | 143       | 121   | 130   | 119   | 133   | 143     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units)              | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|---------------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                                 |              |           |                   | A         | B     | C     | D     | E     |         |
| Systolic Blood Pressure (mmHg)  | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                 |              | Mean      | 112.7             | 119.2     | 115.0 | 119.3 | 110.3 | 115.3 | 115.8   |
|                                 |              | SD        | 5.95              | 6.34      | 7.67  | 14.90 | 8.12  | 10.88 | 9.92    |
|                                 |              | Minimum   | 105               | 113       | 107   | 107   | 100   | 104   | 100     |
|                                 |              | Median    | 111.0             | 118.0     | 114.0 | 115.0 | 112.0 | 112.5 | 113.5   |
|                                 |              | Maximum   | 124               | 130       | 124   | 145   | 123   | 134   | 145     |
|                                 | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                 |              | Mean      | 117.2             | 129.8     | 117.8 | 126.2 | 120.8 | 114.3 | 121.8   |
|                                 |              | SD        | 10.13             | 13.91     | 10.44 | 12.34 | 8.50  | 9.71  | 11.80   |
|                                 |              | Minimum   | 104               | 118       | 102   | 110   | 107   | 103   | 102     |
|                                 |              | Median    | 115.0             | 123.0     | 119.0 | 132.0 | 122.0 | 116.0 | 120.5   |
|                                 |              | Maximum   | 139               | 149       | 129   | 138   | 131   | 129   | 149     |
| Diastolic Blood Pressure (mmHg) | Screen       | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                 |              | Mean      | 73.3              | 73.5      | 75.3  | 72.3  | 71.8  | 75.7  | 73.7    |
|                                 |              | SD        | 6.72              | 3.67      | 4.03  | 5.65  | 6.18  | 6.65  | 5.23    |
|                                 |              | Minimum   | 62                | 70        | 69    | 66    | 66    | 67    | 66      |
|                                 |              | Median    | 73.0              | 72.5      | 76.5  | 71.0  | 70.5  | 74.5  | 73.0    |
|                                 |              | Maximum   | 82                | 78        | 79    | 79    | 83    | 86    | 86      |
|                                 | Baseline     | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                 |              | Mean      | 73.2              | 76.5      | 72.5  | 76.7  | 69.3  | 71.5  | 73.3    |
|                                 |              | SD        | 6.16              | 9.52      | 4.14  | 8.07  | 3.98  | 4.93  | 6.73    |
|                                 |              | Minimum   | 64                | 65        | 69    | 70    | 65    | 67    | 65      |
|                                 |              | Median    | 73.0              | 74.0      | 71.0  | 73.5  | 69.0  | 70.5  | 71.0    |
|                                 |              | Maximum   | 84                | 89        | 79    | 91    | 76    | 80    | 91      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units)              | Time Point       | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|---------------------------------|------------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                                 |                  |           |                   | A         | B    | C    | D    | E    |         |
| Diastolic Blood Pressure (mmHg) | Day 1, Hour 0.25 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                  | Mean      | 71.0              | 76.3      | 73.2 | 75.7 | 69.3 | 74.2 | 73.7    |
|                                 |                  | SD        | 5.19              | 9.69      | 3.82 | 7.58 | 3.50 | 3.13 | 6.22    |
|                                 |                  | Minimum   | 60                | 65        | 69   | 67   | 66   | 68   | 65      |
|                                 |                  | Median    | 72.5              | 74.0      | 73.0 | 74.5 | 68.0 | 75.5 | 73.5    |
|                                 |                  | Maximum   | 76                | 93        | 79   | 89   | 75   | 76   | 93      |
|                                 | Day 1, Hour 0.5  | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                  | Mean      | 71.4              | 75.7      | 73.0 | 73.3 | 66.5 | 70.2 | 71.7    |
|                                 |                  | SD        | 3.41              | 8.64      | 5.22 | 7.06 | 5.47 | 4.58 | 6.72    |
|                                 |                  | Minimum   | 66                | 63        | 68   | 65   | 57   | 66   | 57      |
|                                 |                  | Median    | 72.5              | 76.0      | 71.0 | 73.0 | 67.5 | 69.5 | 71.0    |
|                                 |                  | Maximum   | 75                | 89        | 80   | 85   | 72   | 78   | 89      |
|                                 | Day 1, Hour 0.75 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                  | Mean      | 70.8              | 77.0      | 68.7 | 74.2 | 67.7 | 70.7 | 71.6    |
|                                 |                  | SD        | 4.64              | 10.06     | 8.19 | 5.04 | 3.67 | 6.92 | 7.52    |
|                                 |                  | Minimum   | 63                | 62        | 55   | 68   | 63   | 65   | 55      |
|                                 |                  | Median    | 72.0              | 78.5      | 69.5 | 73.5 | 69.5 | 68.0 | 70.0    |
|                                 |                  | Maximum   | 76                | 87        | 80   | 81   | 71   | 83   | 87      |
|                                 | Day 1, Hour 1    | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                  | Mean      | 70.8              | 74.2      | 72.7 | 72.5 | 68.7 | 72.7 | 72.1    |
|                                 |                  | SD        | 5.12              | 7.08      | 4.55 | 6.83 | 1.75 | 5.20 | 5.38    |
|                                 |                  | Minimum   | 61                | 66        | 67   | 64   | 66   | 64   | 64      |
|                                 |                  | Median    | 71.0              | 74.0      | 72.0 | 70.5 | 68.5 | 73.5 | 71.0    |
|                                 |                  | Maximum   | 76                | 83        | 78   | 83   | 71   | 80   | 83      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units)              | Time Point      | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|---------------------------------|-----------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                                 |                 |           |                   | A         | B    | C    | D    | E    |         |
| Diastolic Blood Pressure (mmHg) | Day 1, Hour 1.5 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                 | Mean      | 70.3              | 73.7      | 71.5 | 74.0 | 71.0 | 73.5 | 72.7    |
|                                 |                 | SD        | 5.01              | 5.61      | 2.66 | 8.60 | 5.22 | 6.98 | 5.84    |
|                                 |                 | Minimum   | 62                | 66        | 68   | 64   | 62   | 63   | 62      |
|                                 |                 | Median    | 71.0              | 74.0      | 72.0 | 72.5 | 72.0 | 74.0 | 73.0    |
|                                 |                 | Maximum   | 77                | 80        | 75   | 90   | 76   | 83   | 90      |
|                                 | Day 1, Hour 2   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                 | Mean      | 70.7              | 75.5      | 70.5 | 74.2 | 68.3 | 69.3 | 71.6    |
|                                 |                 | SD        | 7.89              | 7.66      | 5.43 | 8.66 | 6.15 | 4.63 | 6.81    |
|                                 |                 | Minimum   | 51                | 67        | 62   | 66   | 58   | 64   | 58      |
|                                 |                 | Median    | 73.0              | 74.0      | 71.0 | 71.5 | 70.0 | 69.0 | 71.5    |
|                                 |                 | Maximum   | 80                | 86        | 76   | 91   | 75   | 76   | 91      |
|                                 | Day 1, Hour 4   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                 | Mean      | 70.3              | 75.7      | 70.0 | 72.5 | 67.2 | 69.3 | 70.9    |
|                                 |                 | SD        | 4.42              | 6.59      | 2.97 | 7.18 | 6.85 | 7.23 | 6.62    |
|                                 |                 | Minimum   | 62                | 68        | 65   | 64   | 56   | 60   | 56      |
|                                 |                 | Median    | 70.0              | 75.0      | 71.0 | 72.5 | 68.5 | 69.0 | 70.0    |
|                                 |                 | Maximum   | 78                | 83        | 73   | 83   | 75   | 82   | 83      |
|                                 | Day 1, Hour 6   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                 | Mean      | 68.6              | 68.7      | 67.7 | 69.7 | 67.8 | 68.8 | 68.5    |
|                                 |                 | SD        | 4.81              | 5.24      | 6.77 | 4.50 | 2.93 | 6.43 | 5.03    |
|                                 |                 | Minimum   | 63                | 63        | 55   | 63   | 65   | 61   | 55      |
|                                 |                 | Median    | 70.0              | 68.0      | 70.0 | 69.0 | 66.5 | 68.5 | 69.0    |
|                                 |                 | Maximum   | 78                | 77        | 73   | 77   | 72   | 80   | 80      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units)              | Time Point     | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|---------------------------------|----------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                                 |                |           |                   | A         | B    | C    | D    | E    |         |
| Diastolic Blood Pressure (mmHg) | Day 1, Hour 12 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                | Mean      | 68.2              | 68.8      | 69.3 | 69.5 | 68.3 | 66.0 | 68.4    |
|                                 |                | SD        | 6.39              | 5.46      | 5.32 | 6.28 | 2.73 | 5.18 | 4.94    |
|                                 |                | Minimum   | 54                | 61        | 63   | 62   | 65   | 61   | 61      |
|                                 |                | Median    | 68.0              | 68.0      | 69.5 | 70.5 | 68.5 | 65.0 | 69.0    |
|                                 |                | Maximum   | 78                | 75        | 77   | 79   | 72   | 74   | 79      |
|                                 | Day 2          | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                | Mean      | 68.3              | 73.2      | 70.2 | 73.0 | 70.5 | 71.5 | 71.7    |
|                                 |                | SD        | 4.55              | 5.08      | 3.19 | 6.29 | 3.08 | 5.82 | 4.70    |
|                                 |                | Minimum   | 62                | 68        | 65   | 66   | 68   | 67   | 65      |
|                                 |                | Median    | 68.0              | 71.0      | 70.0 | 72.5 | 69.5 | 70.0 | 70.0    |
|                                 |                | Maximum   | 75                | 80        | 74   | 81   | 76   | 83   | 83      |
|                                 | Day 3          | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                | Mean      | 72.4              | 73.3      | 72.3 | 72.5 | 67.7 | 72.5 | 71.7    |
|                                 |                | SD        | 4.38              | 3.98      | 2.73 | 7.77 | 4.55 | 6.38 | 5.41    |
|                                 |                | Minimum   | 66                | 69        | 68   | 65   | 63   | 63   | 63      |
|                                 |                | Median    | 72.0              | 72.0      | 72.5 | 70.5 | 67.0 | 72.0 | 71.5    |
|                                 |                | Maximum   | 80                | 80        | 76   | 87   | 75   | 80   | 87      |
|                                 | End of Study   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                | Mean      | 72.9              | 81.8      | 72.8 | 78.7 | 72.5 | 74.3 | 76.0    |
|                                 |                | SD        | 6.61              | 6.43      | 5.42 | 7.06 | 5.13 | 6.12 | 6.74    |
|                                 |                | Minimum   | 62                | 72        | 63   | 70   | 65   | 68   | 63      |
|                                 |                | Median    | 73.5              | 80.5      | 73.5 | 79.5 | 74.0 | 74.0 | 76.0    |
|                                 |                | Maximum   | 83                | 89        | 79   | 87   | 78   | 84   | 89      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units) | Time Point       | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------|------------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                    |                  |           |                   | A         | B     | C     | D     | E     |         |
| Pulse Rate (bpm)   | Screen           | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 66.9              | 57.7      | 61.8  | 60.5  | 60.0  | 65.0  | 61.0    |
|                    |                  | SD        | 13.49             | 11.22     | 9.41  | 11.79 | 9.92  | 13.70 | 10.78   |
|                    |                  | Minimum   | 48                | 41        | 54    | 50    | 52    | 55    | 41      |
|                    |                  | Median    | 67.0              | 57.0      | 57.5  | 58.0  | 57.5  | 59.5  | 58.0    |
|                    |                  | Maximum   | 93                | 76        | 76    | 82    | 79    | 91    | 91      |
|                    | Baseline         | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 62.7              | 52.0      | 64.8  | 61.7  | 62.8  | 53.5  | 59.0    |
|                    |                  | SD        | 14.19             | 4.20      | 9.26  | 11.13 | 14.70 | 3.99  | 10.35   |
|                    |                  | Minimum   | 44                | 44        | 56    | 51    | 50    | 48    | 44      |
|                    |                  | Median    | 61.0              | 53.5      | 63.5  | 59.0  | 59.0  | 53.0  | 55.5    |
|                    |                  | Maximum   | 80                | 55        | 76    | 82    | 88    | 58    | 88      |
|                    | Day 1, Hour 0.25 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 62.9              | 52.3      | 63.7  | 53.5  | 58.7  | 58.0  | 57.2    |
|                    |                  | SD        | 10.95             | 7.53      | 10.33 | 7.94  | 11.43 | 5.76  | 9.18    |
|                    |                  | Minimum   | 43                | 41        | 55    | 47    | 50    | 50    | 41      |
|                    |                  | Median    | 67.0              | 52.5      | 60.0  | 51.0  | 56.0  | 58.5  | 55.0    |
|                    |                  | Maximum   | 76                | 64        | 83    | 69    | 80    | 64    | 83      |
|                    | Day 1, Hour 0.5  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 58.8              | 54.5      | 62.3  | 55.7  | 61.7  | 62.8  | 59.4    |
|                    |                  | SD        | 10.86             | 3.56      | 8.71  | 5.75  | 9.40  | 3.82  | 7.20    |
|                    |                  | Minimum   | 45                | 49        | 52    | 50    | 53    | 57    | 49      |
|                    |                  | Median    | 60.5              | 54.0      | 59.5  | 54.0  | 59.5  | 64.0  | 58.0    |
|                    |                  | Maximum   | 75                | 60        | 73    | 65    | 78    | 66    | 78      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units) | Time Point       | Statistic | Pooled<br>Placebo | Treatment |       |       |       |      | Overall |
|--------------------|------------------|-----------|-------------------|-----------|-------|-------|-------|------|---------|
|                    |                  |           |                   | A         | B     | C     | D     | E    |         |
| Pulse Rate (bpm)   | Day 1, Hour 0.75 | n         | 10                | 6         | 6     | 6     | 6     | 6    | 30      |
|                    |                  | Mean      | 61.8              | 56.8      | 64.2  | 53.8  | 64.7  | 64.0 | 60.7    |
|                    |                  | SD        | 13.12             | 7.73      | 8.82  | 6.40  | 8.12  | 6.42 | 8.37    |
|                    |                  | Minimum   | 46                | 48        | 54    | 45    | 54    | 56   | 45      |
|                    |                  | Median    | 60.0              | 55.5      | 63.5  | 53.0  | 66.0  | 64.0 | 59.5    |
|                    |                  | Maximum   | 88                | 67        | 74    | 65    | 75    | 71   | 75      |
|                    | Day 1, Hour 1    | n         | 10                | 6         | 6     | 6     | 6     | 6    | 30      |
|                    |                  | Mean      | 63.1              | 55.2      | 63.3  | 53.8  | 60.0  | 57.2 | 57.9    |
|                    |                  | SD        | 12.24             | 2.64      | 10.95 | 5.19  | 7.46  | 4.88 | 7.23    |
|                    |                  | Minimum   | 45                | 51        | 54    | 46    | 50    | 52   | 46      |
|                    |                  | Median    | 62.5              | 56.0      | 58.5  | 53.0  | 62.5  | 56.5 | 56.0    |
|                    |                  | Maximum   | 84                | 58        | 82    | 62    | 68    | 65   | 82      |
|                    | Day 1, Hour 1.5  | n         | 10                | 6         | 6     | 6     | 6     | 6    | 30      |
|                    |                  | Mean      | 58.9              | 54.2      | 64.3  | 59.2  | 62.3  | 58.2 | 59.6    |
|                    |                  | SD        | 11.39             | 5.74      | 8.02  | 13.53 | 13.17 | 6.01 | 9.86    |
|                    |                  | Minimum   | 44                | 43        | 54    | 47    | 52    | 48   | 43      |
|                    |                  | Median    | 59.0              | 56.0      | 64.5  | 57.0  | 57.0  | 59.0 | 58.0    |
|                    |                  | Maximum   | 76                | 59        | 77    | 84    | 85    | 66   | 85      |
|                    | Day 1, Hour 2    | n         | 10                | 6         | 6     | 6     | 6     | 6    | 30      |
|                    |                  | Mean      | 60.7              | 52.8      | 61.7  | 57.8  | 62.2  | 58.7 | 58.6    |
|                    |                  | SD        | 10.47             | 4.22      | 9.22  | 11.37 | 8.98  | 7.97 | 8.74    |
|                    |                  | Minimum   | 43                | 47        | 49    | 48    | 52    | 51   | 47      |
|                    |                  | Median    | 64.0              | 55.0      | 59.0  | 52.0  | 62.0  | 55.5 | 56.0    |
|                    |                  | Maximum   | 76                | 56        | 73    | 76    | 76    | 71   | 76      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units) | Time Point     | Statistic | Pooled<br>Placebo | Treatment |       |       |       |      | Overall |
|--------------------|----------------|-----------|-------------------|-----------|-------|-------|-------|------|---------|
|                    |                |           |                   | A         | B     | C     | D     | E    |         |
| Pulse Rate (bpm)   | Day 1, Hour 4  | n         | 10                | 6         | 6     | 6     | 6     | 6    | 30      |
|                    |                | Mean      | 61.5              | 53.3      | 61.5  | 59.8  | 62.2  | 56.2 | 58.6    |
|                    |                | SD        | 8.81              | 4.84      | 8.26  | 9.09  | 11.94 | 4.92 | 8.39    |
|                    |                | Minimum   | 52                | 45        | 51    | 52    | 50    | 49   | 45      |
|                    |                | Median    | 60.0              | 54.5      | 61.5  | 56.0  | 60.0  | 57.0 | 56.0    |
|                    |                | Maximum   | 82                | 59        | 74    | 73    | 79    | 62   | 79      |
|                    | Day 1, Hour 6  | n         | 10                | 6         | 6     | 6     | 6     | 6    | 30      |
|                    |                | Mean      | 74.3              | 63.2      | 72.7  | 62.3  | 65.5  | 66.0 | 65.9    |
|                    |                | SD        | 14.58             | 6.49      | 10.88 | 5.57  | 3.89  | 7.35 | 7.66    |
|                    |                | Minimum   | 56                | 52        | 60    | 55    | 61    | 52   | 52      |
|                    |                | Median    | 73.0              | 64.5      | 71.5  | 62.0  | 65.0  | 69.0 | 65.5    |
|                    |                | Maximum   | 103               | 69        | 90    | 71    | 70    | 72   | 90      |
|                    | Day 1, Hour 12 | n         | 10                | 6         | 6     | 6     | 6     | 6    | 30      |
|                    |                | Mean      | 64.4              | 62.2      | 69.3  | 59.3  | 62.0  | 66.0 | 63.8    |
|                    |                | SD        | 10.21             | 6.46      | 5.28  | 7.87  | 11.66 | 9.42 | 8.61    |
|                    |                | Minimum   | 47                | 55        | 62    | 49    | 50    | 51   | 49      |
|                    |                | Median    | 66.5              | 62.0      | 71.0  | 58.5  | 60.5  | 65.0 | 63.5    |
|                    |                | Maximum   | 79                | 72        | 74    | 71    | 81    | 76   | 81      |
|                    | Day 2          | n         | 10                | 6         | 6     | 6     | 6     | 6    | 30      |
|                    |                | Mean      | 59.9              | 56.0      | 59.2  | 62.8  | 62.3  | 57.8 | 59.6    |
|                    |                | SD        | 10.32             | 5.14      | 7.78  | 10.28 | 9.95  | 8.77 | 8.41    |
|                    |                | Minimum   | 44                | 49        | 52    | 54    | 55    | 50   | 49      |
|                    |                | Median    | 59.0              | 58.5      | 58.5  | 59.5  | 58.0  | 57.5 | 58.0    |
|                    |                | Maximum   | 79                | 61        | 73    | 80    | 81    | 74   | 81      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units)     | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|------------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                        |              |           |                   | A         | B     | C     | D     | E     |         |
| Pulse Rate (bpm)       | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                        |              | Mean      | 66.0              | 57.2      | 63.5  | 61.0  | 63.0  | 60.5  | 61.0    |
|                        |              | SD        | 11.79             | 2.23      | 9.48  | 10.16 | 7.48  | 5.89  | 7.42    |
|                        |              | Minimum   | 46                | 54        | 55    | 50    | 55    | 55    | 50      |
|                        |              | Median    | 67.5              | 57.0      | 60.5  | 57.0  | 62.0  | 60.0  | 59.0    |
|                        |              | Maximum   | 85                | 60        | 80    | 76    | 75    | 71    | 80      |
|                        | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                        |              | Mean      | 65.3              | 62.8      | 69.0  | 65.5  | 64.3  | 63.3  | 65.0    |
|                        |              | SD        | 13.29             | 8.66      | 13.70 | 8.87  | 15.92 | 11.17 | 11.36   |
|                        |              | Minimum   | 47                | 54        | 57    | 52    | 47    | 51    | 47      |
|                        |              | Median    | 66.0              | 59.5      | 63.5  | 68.0  | 57.5  | 62.0  | 60.5    |
|                        |              | Maximum   | 88                | 76        | 93    | 76    | 90    | 80    | 93      |
| Respiration Rate (bpm) | Screen       | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                        |              | Mean      | 15.2              | 13.3      | 15.3  | 15.7  | 16.7  | 16.0  | 15.4    |
|                        |              | SD        | 3.01              | 2.42      | 1.63  | 1.51  | 3.50  | 1.79  | 2.42    |
|                        |              | Minimum   | 10                | 10        | 12    | 14    | 14    | 14    | 10      |
|                        |              | Median    | 15.0              | 13.0      | 16.0  | 16.0  | 15.0  | 16.0  | 16.0    |
|                        |              | Maximum   | 20                | 16        | 16    | 18    | 22    | 18    | 22      |
|                        | Baseline     | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                        |              | Mean      | 13.8              | 14.0      | 12.7  | 13.0  | 13.7  | 15.3  | 13.7    |
|                        |              | SD        | 1.75              | 2.19      | 1.03  | 1.10  | 1.51  | 1.03  | 1.64    |
|                        |              | Minimum   | 12                | 12        | 12    | 12    | 12    | 14    | 12      |
|                        |              | Median    | 14.0              | 14.0      | 12.0  | 13.0  | 14.0  | 16.0  | 14.0    |
|                        |              | Maximum   | 16                | 16        | 14    | 14    | 16    | 16    | 16      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units)     | Time Point       | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|------------------------|------------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                        |                  |           |                   | A         | B    | C    | D    | E    |         |
| Respiration Rate (bpm) | Day 1, Hour 0.25 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                  | Mean      | 14.4              | 15.0      | 12.3 | 13.3 | 13.3 | 15.3 | 13.9    |
|                        |                  | SD        | 2.46              | 2.76      | 0.82 | 1.03 | 1.03 | 2.07 | 1.96    |
|                        |                  | Minimum   | 12                | 12        | 12   | 12   | 12   | 12   | 12      |
|                        |                  | Median    | 14.0              | 14.0      | 12.0 | 14.0 | 14.0 | 16.0 | 14.0    |
|                        |                  | Maximum   | 18                | 20        | 14   | 14   | 14   | 18   | 20      |
|                        | Day 1, Hour 0.5  | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                  | Mean      | 14.4              | 16.0      | 12.3 | 13.0 | 13.7 | 14.7 | 13.9    |
|                        |                  | SD        | 1.84              | 2.53      | 1.97 | 2.45 | 0.82 | 1.63 | 2.26    |
|                        |                  | Minimum   | 12                | 12        | 10   | 12   | 12   | 12   | 10      |
|                        |                  | Median    | 15.0              | 17.0      | 12.0 | 12.0 | 14.0 | 15.0 | 14.0    |
|                        |                  | Maximum   | 16                | 18        | 16   | 18   | 14   | 16   | 18      |
|                        | Day 1, Hour 0.75 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                  | Mean      | 15.2              | 15.0      | 13.0 | 13.3 | 13.7 | 14.7 | 13.9    |
|                        |                  | SD        | 2.15              | 2.10      | 1.10 | 2.42 | 0.82 | 1.63 | 1.78    |
|                        |                  | Minimum   | 12                | 12        | 12   | 12   | 12   | 12   | 12      |
|                        |                  | Median    | 16.0              | 15.0      | 13.0 | 12.0 | 14.0 | 15.0 | 14.0    |
|                        |                  | Maximum   | 18                | 18        | 14   | 18   | 14   | 16   | 18      |
|                        | Day 1, Hour 1    | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                  | Mean      | 13.2              | 11.7      | 12.0 | 11.7 | 12.3 | 14.3 | 12.4    |
|                        |                  | SD        | 2.70              | 1.97      | 0.00 | 2.94 | 1.51 | 0.82 | 1.92    |
|                        |                  | Minimum   | 8                 | 10        | 12   | 6    | 10   | 14   | 6       |
|                        |                  | Median    | 13.0              | 11.0      | 12.0 | 12.0 | 12.0 | 14.0 | 12.0    |
|                        |                  | Maximum   | 18                | 14        | 12   | 14   | 14   | 16   | 16      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units)     | Time Point      | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|------------------------|-----------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                        |                 |           |                   | A         | B    | C    | D    | E    |         |
| Respiration Rate (bpm) | Day 1, Hour 1.5 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                 | Mean      | 13.2              | 11.7      | 13.0 | 12.7 | 13.3 | 15.7 | 13.3    |
|                        |                 | SD        | 1.69              | 2.66      | 2.45 | 1.63 | 1.63 | 1.51 | 2.32    |
|                        |                 | Minimum   | 12                | 8         | 12   | 12   | 12   | 14   | 8       |
|                        |                 | Median    | 12.0              | 12.0      | 12.0 | 12.0 | 13.0 | 16.0 | 12.0    |
|                        |                 | Maximum   | 16                | 16        | 18   | 16   | 16   | 18   | 18      |
|                        | Day 1, Hour 2   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                 | Mean      | 14.4              | 14.3      | 12.0 | 12.7 | 16.7 | 15.7 | 14.3    |
|                        |                 | SD        | 2.27              | 1.51      | 0.00 | 1.03 | 2.42 | 2.34 | 2.39    |
|                        |                 | Minimum   | 12                | 12        | 12   | 12   | 14   | 12   | 12      |
|                        |                 | Median    | 15.0              | 14.0      | 12.0 | 12.0 | 17.0 | 16.0 | 14.0    |
|                        |                 | Maximum   | 18                | 16        | 12   | 14   | 20   | 18   | 20      |
|                        | Day 1, Hour 4   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                 | Mean      | 14.4              | 13.7      | 12.7 | 12.0 | 15.7 | 14.3 | 13.7    |
|                        |                 | SD        | 2.27              | 1.51      | 1.63 | 0.00 | 1.51 | 0.82 | 1.75    |
|                        |                 | Minimum   | 12                | 12        | 12   | 12   | 14   | 14   | 12      |
|                        |                 | Median    | 14.0              | 14.0      | 12.0 | 12.0 | 16.0 | 14.0 | 14.0    |
|                        |                 | Maximum   | 18                | 16        | 16   | 12   | 18   | 16   | 18      |
|                        | Day 1, Hour 6   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                 | Mean      | 13.0              | 13.0      | 13.0 | 12.3 | 12.0 | 15.0 | 13.1    |
|                        |                 | SD        | 1.41              | 1.67      | 1.67 | 2.66 | 0.00 | 2.10 | 2.02    |
|                        |                 | Minimum   | 12                | 12        | 10   | 10   | 12   | 12   | 10      |
|                        |                 | Median    | 12.0              | 12.0      | 14.0 | 12.0 | 12.0 | 15.0 | 12.0    |
|                        |                 | Maximum   | 16                | 16        | 14   | 16   | 12   | 18   | 18      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units)     | Time Point     | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|------------------------|----------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                        |                |           |                   | A         | B    | C    | D    | E    |         |
| Respiration Rate (bpm) | Day 1, Hour 12 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                | Mean      | 14.6              | 13.3      | 13.0 | 13.3 | 14.0 | 15.3 | 13.8    |
|                        |                | SD        | 1.65              | 1.63      | 2.10 | 2.42 | 1.26 | 1.03 | 1.85    |
|                        |                | Minimum   | 12                | 12        | 10   | 10   | 12   | 14   | 10      |
|                        |                | Median    | 14.0              | 13.0      | 13.0 | 13.0 | 14.0 | 16.0 | 14.0    |
|                        |                | Maximum   | 18                | 16        | 16   | 16   | 16   | 16   | 16      |
|                        | Day 2          | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                | Mean      | 13.4              | 14.0      | 16.3 | 14.0 | 13.0 | 12.3 | 13.9    |
|                        |                | SD        | 1.90              | 1.26      | 1.97 | 1.26 | 1.67 | 0.82 | 1.93    |
|                        |                | Minimum   | 10                | 12        | 14   | 12   | 12   | 12   | 12      |
|                        |                | Median    | 14.0              | 14.0      | 17.0 | 14.0 | 12.0 | 12.0 | 14.0    |
|                        |                | Maximum   | 16                | 16        | 18   | 16   | 16   | 14   | 18      |
|                        | Day 3          | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                | Mean      | 14.2              | 13.7      | 14.7 | 13.7 | 13.0 | 15.0 | 14.0    |
|                        |                | SD        | 2.20              | 1.51      | 3.72 | 0.82 | 2.45 | 1.10 | 2.17    |
|                        |                | Minimum   | 12                | 12        | 10   | 12   | 10   | 14   | 10      |
|                        |                | Median    | 14.0              | 14.0      | 16.0 | 14.0 | 12.0 | 15.0 | 14.0    |
|                        |                | Maximum   | 18                | 16        | 18   | 14   | 16   | 16   | 18      |
|                        | End of Study   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                | Mean      | 14.8              | 15.7      | 17.0 | 14.3 | 13.0 | 13.7 | 14.7    |
|                        |                | SD        | 1.69              | 1.51      | 2.10 | 1.51 | 1.67 | 1.51 | 2.13    |
|                        |                | Minimum   | 12                | 14        | 14   | 12   | 10   | 12   | 10      |
|                        |                | Median    | 14.0              | 16.0      | 17.0 | 14.0 | 14.0 | 14.0 | 14.0    |
|                        |                | Maximum   | 18                | 18        | 20   | 16   | 14   | 16   | 20      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units) | Time Point       | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------|------------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                    |                  |           |                   | A         | B     | C     | D     | E     |         |
| Temperature (°C)   | Screen           | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 36.50             | 36.63     | 36.57 | 36.67 | 36.65 | 36.65 | 36.63   |
|                    |                  | SD        | 0.163             | 0.234     | 0.163 | 0.266 | 0.164 | 0.251 | 0.207   |
|                    |                  | Minimum   | 36.3              | 36.4      | 36.4  | 36.4  | 36.4  | 36.4  | 36.4    |
|                    |                  | Median    | 36.50             | 36.60     | 36.55 | 36.65 | 36.65 | 36.60 | 36.60   |
|                    |                  | Maximum   | 36.8              | 37.0      | 36.8  | 37.1  | 36.9  | 37.0  | 37.1    |
|                    | Baseline         | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 36.53             | 36.62     | 36.65 | 36.42 | 36.62 | 36.55 | 36.57   |
|                    |                  | SD        | 0.164             | 0.183     | 0.243 | 0.147 | 0.160 | 0.176 | 0.191   |
|                    |                  | Minimum   | 36.3              | 36.4      | 36.4  | 36.3  | 36.3  | 36.4  | 36.3    |
|                    |                  | Median    | 36.55             | 36.60     | 36.60 | 36.40 | 36.70 | 36.50 | 36.60   |
|                    |                  | Maximum   | 36.8              | 36.9      | 37.1  | 36.7  | 36.7  | 36.8  | 37.1    |
|                    | Day 1, Hour 0.25 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 36.63             | 36.50     | 36.73 | 36.43 | 36.53 | 36.48 | 36.54   |
|                    |                  | SD        | 0.149             | 0.179     | 0.197 | 0.103 | 0.121 | 0.098 | 0.171   |
|                    |                  | Minimum   | 36.5              | 36.3      | 36.4  | 36.3  | 36.4  | 36.4  | 36.3    |
|                    |                  | Median    | 36.60             | 36.45     | 36.80 | 36.40 | 36.55 | 36.45 | 36.50   |
|                    |                  | Maximum   | 36.9              | 36.8      | 36.9  | 36.6  | 36.7  | 36.6  | 36.9    |
|                    | Day 1, Hour 0.5  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 36.58             | 36.47     | 36.62 | 36.43 | 36.57 | 36.47 | 36.51   |
|                    |                  | SD        | 0.193             | 0.121     | 0.194 | 0.151 | 0.137 | 0.137 | 0.156   |
|                    |                  | Minimum   | 36.2              | 36.3      | 36.3  | 36.2  | 36.4  | 36.3  | 36.2    |
|                    |                  | Median    | 36.60             | 36.45     | 36.65 | 36.40 | 36.55 | 36.45 | 36.50   |
|                    |                  | Maximum   | 36.9              | 36.6      | 36.8  | 36.6  | 36.8  | 36.7  | 36.8    |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units) | Time Point       | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------|------------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                    |                  |           |                   | A         | B     | C     | D     | E     |         |
| Temperature (°C)   | Day 1, Hour 0.75 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 36.58             | 36.52     | 36.70 | 36.48 | 36.50 | 36.47 | 36.53   |
|                    |                  | SD        | 0.181             | 0.194     | 0.335 | 0.172 | 0.141 | 0.163 | 0.215   |
|                    |                  | Minimum   | 36.3              | 36.3      | 36.2  | 36.2  | 36.3  | 36.3  | 36.2    |
|                    |                  | Median    | 36.60             | 36.45     | 36.75 | 36.50 | 36.50 | 36.45 | 36.50   |
|                    |                  | Maximum   | 36.8              | 36.8      | 37.2  | 36.7  | 36.7  | 36.7  | 37.2    |
|                    | Day 1, Hour 1    | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 36.70             | 36.58     | 36.83 | 36.57 | 36.60 | 36.58 | 36.63   |
|                    |                  | SD        | 0.176             | 0.160     | 0.186 | 0.103 | 0.167 | 0.271 | 0.201   |
|                    |                  | Minimum   | 36.4              | 36.4      | 36.5  | 36.4  | 36.4  | 36.3  | 36.3    |
|                    |                  | Median    | 36.65             | 36.60     | 36.85 | 36.60 | 36.65 | 36.55 | 36.60   |
|                    |                  | Maximum   | 37.0              | 36.8      | 37.0  | 36.7  | 36.8  | 36.9  | 37.0    |
|                    | Day 1, Hour 1.5  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 36.62             | 36.58     | 36.73 | 36.57 | 36.70 | 36.38 | 36.59   |
|                    |                  | SD        | 0.140             | 0.183     | 0.216 | 0.175 | 0.200 | 0.117 | 0.210   |
|                    |                  | Minimum   | 36.4              | 36.3      | 36.5  | 36.3  | 36.5  | 36.3  | 36.3    |
|                    |                  | Median    | 36.60             | 36.70     | 36.70 | 36.65 | 36.60 | 36.35 | 36.60   |
|                    |                  | Maximum   | 36.8              | 36.7      | 37.1  | 36.7  | 37.0  | 36.6  | 37.1    |
|                    | Day 1, Hour 2    | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 36.61             | 36.55     | 36.73 | 36.62 | 36.60 | 36.60 | 36.62   |
|                    |                  | SD        | 0.145             | 0.197     | 0.216 | 0.075 | 0.089 | 0.126 | 0.154   |
|                    |                  | Minimum   | 36.4              | 36.3      | 36.4  | 36.5  | 36.5  | 36.4  | 36.3    |
|                    |                  | Median    | 36.60             | 36.65     | 36.75 | 36.60 | 36.60 | 36.65 | 36.60   |
|                    |                  | Maximum   | 36.8              | 36.7      | 37.0  | 36.7  | 36.7  | 36.7  | 37.0    |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units) | Time Point     | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------|----------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                    |                |           |                   | A         | B     | C     | D     | E     |         |
| Temperature (°C)   | Day 1, Hour 4  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                | Mean      | 36.69             | 36.53     | 36.70 | 36.45 | 36.73 | 36.80 | 36.64   |
|                    |                | SD        | 0.218             | 0.163     | 0.276 | 0.187 | 0.234 | 0.310 | 0.260   |
|                    |                | Minimum   | 36.3              | 36.3      | 36.4  | 36.2  | 36.4  | 36.3  | 36.2    |
|                    |                | Median    | 36.70             | 36.55     | 36.70 | 36.45 | 36.75 | 36.90 | 36.65   |
|                    |                | Maximum   | 37.0              | 36.7      | 37.1  | 36.7  | 37.1  | 37.2  | 37.2    |
|                    | Day 1, Hour 6  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                | Mean      | 36.60             | 36.62     | 36.82 | 36.55 | 36.65 | 36.68 | 36.66   |
|                    |                | SD        | 0.163             | 0.172     | 0.075 | 0.084 | 0.176 | 0.214 | 0.169   |
|                    |                | Minimum   | 36.4              | 36.4      | 36.7  | 36.4  | 36.4  | 36.4  | 36.4    |
|                    |                | Median    | 36.60             | 36.60     | 36.80 | 36.60 | 36.60 | 36.70 | 36.60   |
|                    |                | Maximum   | 36.8              | 36.9      | 36.9  | 36.6  | 36.9  | 36.9  | 36.9    |
|                    | Day 1, Hour 12 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                | Mean      | 36.67             | 36.70     | 36.78 | 36.52 | 36.63 | 36.68 | 36.66   |
|                    |                | SD        | 0.106             | 0.063     | 0.223 | 0.133 | 0.225 | 0.172 | 0.185   |
|                    |                | Minimum   | 36.6              | 36.6      | 36.6  | 36.3  | 36.3  | 36.5  | 36.3    |
|                    |                | Median    | 36.60             | 36.70     | 36.75 | 36.60 | 36.60 | 36.65 | 36.60   |
|                    |                | Maximum   | 36.9              | 36.8      | 37.2  | 36.6  | 37.0  | 37.0  | 37.2    |
|                    | Day 2          | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                | Mean      | 36.60             | 36.50     | 36.78 | 36.57 | 36.57 | 36.70 | 36.62   |
|                    |                | SD        | 0.133             | 0.167     | 0.214 | 0.186 | 0.103 | 0.155 | 0.189   |
|                    |                | Minimum   | 36.4              | 36.3      | 36.5  | 36.3  | 36.4  | 36.6  | 36.3    |
|                    |                | Median    | 36.60             | 36.55     | 36.80 | 36.60 | 36.60 | 36.65 | 36.60   |
|                    |                | Maximum   | 36.8              | 36.7      | 37.1  | 36.8  | 36.7  | 37.0  | 37.1    |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.10 Vital Sign Summary (Safety Population)

| Vital Sign (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                    |              |           |                   | A         | B     | C     | D     | E     |         |
| Temperature (°C)   | Day 3        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |              | Mean      | 36.61             | 36.58     | 36.62 | 36.58 | 36.58 | 36.93 | 36.66   |
|                    |              | SD        | 0.185             | 0.147     | 0.075 | 0.147 | 0.194 | 0.103 | 0.190   |
|                    |              | Minimum   | 36.4              | 36.4      | 36.5  | 36.3  | 36.3  | 36.8  | 36.3    |
|                    |              | Median    | 36.60             | 36.65     | 36.60 | 36.60 | 36.65 | 36.90 | 36.70   |
|                    |              | Maximum   | 36.9              | 36.7      | 36.7  | 36.7  | 36.8  | 37.1  | 37.1    |
|                    | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |              | Mean      | 36.60             | 36.62     | 36.77 | 36.55 | 36.73 | 36.60 | 36.65   |
|                    |              | SD        | 0.176             | 0.075     | 0.186 | 0.243 | 0.175 | 0.190 | 0.189   |
|                    |              | Minimum   | 36.3              | 36.5      | 36.6  | 36.3  | 36.4  | 36.3  | 36.3    |
|                    |              | Median    | 36.65             | 36.60     | 36.75 | 36.55 | 36.80 | 36.60 | 36.70   |
|                    |              | Maximum   | 36.9              | 36.7      | 37.1  | 36.8  | 36.9  | 36.8  | 37.1    |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units)             | Time Point       | Statistic | Pooled<br>Placebo | Treatment |       |       |       |      | Overall |
|--------------------------------|------------------|-----------|-------------------|-----------|-------|-------|-------|------|---------|
|                                |                  |           |                   | A         | B     | C     | D     | E    |         |
| Systolic Blood Pressure (mmHg) | Day 1, Hour 0.25 | n         | 10                | 6         | 6     | 6     | 6     | 6    | 30      |
|                                |                  | Mean      | -2.7              | -4.7      | -3.8  | -2.3  | -2.2  | -1.3 | -2.9    |
|                                |                  | SD        | 5.23              | 13.97     | 11.16 | 6.12  | 7.88  | 8.98 | 9.37    |
|                                |                  | Minimum   | -12               | -30       | -15   | -12   | -13   | -14  | -30     |
|                                |                  | Median    | -2.0              | -1.5      | -5.5  | -3.0  | 0.0   | -0.5 | -2.0    |
|                                |                  | Maximum   | 5                 | 10        | 15    | 7     | 8     | 12   | 15      |
|                                | Day 1, Hour 0.5  | n         | 10                | 6         | 6     | 6     | 6     | 6    | 30      |
|                                |                  | Mean      | -4.0              | -1.5      | -7.3  | -6.7  | -6.8  | -4.3 | -5.3    |
|                                |                  | SD        | 3.56              | 10.21     | 11.93 | 5.13  | 10.01 | 9.07 | 9.13    |
|                                |                  | Minimum   | -12               | -21       | -22   | -16   | -20   | -22  | -22     |
|                                |                  | Median    | -3.5              | 1.5       | -5.0  | -5.5  | -2.0  | -2.0 | -2.5    |
|                                |                  | Maximum   | 1                 | 8         | 9     | -1    | 3     | 4    | 9       |
|                                | Day 1, Hour 0.75 | n         | 10                | 6         | 6     | 6     | 6     | 6    | 30      |
|                                |                  | Mean      | -4.8              | -5.7      | -1.8  | -6.5  | -4.2  | -3.2 | -4.3    |
|                                |                  | SD        | 8.63              | 11.94     | 8.68  | 5.01  | 5.64  | 4.40 | 7.32    |
|                                |                  | Minimum   | -24               | -24       | -17   | -11   | -13   | -9   | -24     |
|                                |                  | Median    | -2.5              | -5.5      | -2.0  | -8.0  | -3.5  | -3.0 | -3.0    |
|                                |                  | Maximum   | 6                 | 7         | 8     | 0     | 2     | 3    | 8       |
|                                | Day 1, Hour 1    | n         | 10                | 6         | 6     | 6     | 6     | 6    | 30      |
|                                |                  | Mean      | -4.7              | -2.3      | -7.2  | -7.3  | -3.3  | 2.3  | -3.6    |
|                                |                  | SD        | 8.35              | 13.56     | 11.99 | 8.04  | 9.00  | 9.37 | 10.48   |
|                                |                  | Minimum   | -24               | -23       | -22   | -13   | -21   | -13  | -23     |
|                                |                  | Median    | -4.5              | 0.5       | -3.5  | -11.0 | -1.0  | 2.5  | -2.0    |
|                                |                  | Maximum   | 5                 | 13        | 5     | 8     | 4     | 15   | 15      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units)             | Time Point      | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------|-----------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                                |                 |           |                   | A         | B     | C     | D     | E     |         |
| Systolic Blood Pressure (mmHg) | Day 1, Hour 1.5 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 | Mean      | -4.3              | -7.8      | -6.5  | -4.5  | -1.2  | 4.7   | -3.1    |
|                                |                 | SD        | 7.73              | 14.29     | 12.57 | 10.41 | 12.30 | 4.59  | 11.47   |
|                                |                 | Minimum   | -21               | -28       | -24   | -21   | -17   | -1    | -28     |
|                                |                 | Median    | -3.5              | -5.5      | 0.0   | -5.0  | 3.0   | 4.5   | 0.5     |
|                                |                 | Maximum   | 6                 | 10        | 5     | 8     | 11    | 12    | 12      |
|                                | Day 1, Hour 2   | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 | Mean      | -2.8              | -2.8      | -4.2  | -4.3  | -1.8  | -8.2  | -4.3    |
|                                |                 | SD        | 8.98              | 10.94     | 10.65 | 7.69  | 16.19 | 13.60 | 11.50   |
|                                |                 | Minimum   | -23               | -20       | -20   | -12   | -23   | -31   | -31     |
|                                |                 | Median    | 0.0               | 0.5       | -4.5  | -6.5  | 6.5   | -4.5  | -2.5    |
|                                |                 | Maximum   | 10                | 11        | 9     | 7     | 13    | 5     | 13      |
|                                | Day 1, Hour 4   | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 | Mean      | -4.4              | -3.2      | -6.8  | -6.7  | -2.2  | -3.3  | -4.4    |
|                                |                 | SD        | 8.82              | 14.33     | 11.62 | 5.16  | 16.61 | 3.01  | 10.78   |
|                                |                 | Minimum   | -27               | -24       | -25   | -14   | -21   | -7    | -25     |
|                                |                 | Median    | -2.5              | 2.5       | -3.5  | -5.5  | 1.0   | -3.5  | -3.0    |
|                                |                 | Maximum   | 5                 | 11        | 6     | -1    | 19    | 1     | 19      |
|                                | Day 1, Hour 6   | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                 | Mean      | -6.0              | -7.7      | -9.3  | -11.5 | -5.3  | -6.0  | -8.0    |
|                                |                 | SD        | 12.02             | 18.53     | 13.03 | 8.71  | 12.01 | 9.63  | 12.15   |
|                                |                 | Minimum   | -32               | -39       | -27   | -23   | -26   | -19   | -39     |
|                                |                 | Median    | -2.0              | -4.5      | -5.5  | -10.0 | -5.0  | -6.5  | -7.0    |
|                                |                 | Maximum   | 6                 | 14        | 3     | 0     | 7     | 7     | 14      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units)             | Time Point     | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------------------|----------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                                |                |           |                   | A         | B     | C     | D     | E     |         |
| Systolic Blood Pressure (mmHg) | Day 1, Hour 12 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                | Mean      | -6.8              | -8.5      | -6.5  | -11.2 | -2.0  | -9.5  | -7.5    |
|                                |                | SD        | 9.91              | 14.10     | 13.72 | 7.83  | 11.33 | 9.99  | 11.27   |
|                                |                | Minimum   | -31               | -32       | -28   | -24   | -18   | -26   | -32     |
|                                |                | Median    | -4.5              | -3.5      | -3.0  | -8.5  | -2.5  | -9.0  | -5.0    |
|                                |                | Maximum   | 6                 | 7         | 10    | -4    | 12    | 1     | 12      |
|                                | Day 2          | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                | Mean      | -8.7              | -8.7      | -7.7  | -8.2  | -3.8  | -2.5  | -6.2    |
|                                |                | SD        | 6.53              | 9.56      | 11.59 | 11.05 | 8.23  | 4.51  | 9.04    |
|                                |                | Minimum   | -21               | -25       | -27   | -24   | -19   | -8    | -27     |
|                                |                | Median    | -7.0              | -8.5      | -1.5  | -6.5  | -3.5  | -2.5  | -3.5    |
|                                |                | Maximum   | 0                 | 3         | 1     | 5     | 4     | 5     | 5       |
|                                | Day 3          | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                | Mean      | -3.5              | -6.2      | -5.8  | -5.8  | -6.0  | -0.8  | -4.9    |
|                                |                | SD        | 8.48              | 14.39     | 11.16 | 9.15  | 9.03  | 6.77  | 9.90    |
|                                |                | Minimum   | -15               | -24       | -22   | -23   | -19   | -7    | -24     |
|                                |                | Median    | -6.0              | -5.5      | 0.0   | -2.0  | -3.5  | -2.0  | -2.5    |
|                                |                | Maximum   | 11                | 10        | 4     | 2     | 3     | 11    | 11      |
|                                | End of Study   | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                                |                | Mean      | 1.0               | 4.5       | -3.0  | 1.0   | 4.5   | -1.8  | 1.0     |
|                                |                | SD        | 5.89              | 16.26     | 13.34 | 7.40  | 9.29  | 10.70 | 11.42   |
|                                |                | Minimum   | -7                | -23       | -23   | -12   | -7    | -12   | -23     |
|                                |                | Median    | -1.0              | 9.0       | 4.5   | 1.5   | 4.0   | -2.5  | 4.5     |
|                                |                | Maximum   | 8                 | 23        | 7     | 9     | 18    | 12    | 23      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units)              | Time Point       | Statistic | Pooled<br>Placebo | Treatment |       |      |      |      | Overall |
|---------------------------------|------------------|-----------|-------------------|-----------|-------|------|------|------|---------|
|                                 |                  |           |                   | A         | B     | C    | D    | E    |         |
| Diastolic Blood Pressure (mmHg) | Day 1, Hour 0.25 | n         | 10                | 6         | 6     | 6    | 6    | 6    | 30      |
|                                 |                  | Mean      | -2.2              | -0.2      | 0.7   | -1.0 | 0.0  | 2.7  | 0.4     |
|                                 |                  | SD        | 4.13              | 6.49      | 2.25  | 2.61 | 4.52 | 4.97 | 4.32    |
|                                 |                  | Minimum   | -8                | -12       | -1    | -4   | -7   | -6   | -12     |
|                                 |                  | Median    | -3.0              | 0.5       | 0.0   | -1.5 | 1.5  | 3.5  | 1.0     |
|                                 |                  | Maximum   | 6                 | 7         | 5     | 3    | 4    | 8    | 8       |
|                                 | Day 1, Hour 0.5  | n         | 10                | 6         | 6     | 6    | 6    | 6    | 30      |
|                                 |                  | Mean      | -1.8              | -0.8      | 0.5   | -3.3 | -2.8 | -1.3 | -1.6    |
|                                 |                  | SD        | 4.89              | 4.62      | 5.47  | 3.08 | 5.71 | 3.98 | 4.56    |
|                                 |                  | Minimum   | -10               | -8        | -7    | -6   | -13  | -8   | -13     |
|                                 |                  | Median    | -1.5              | -1.0      | 0.0   | -4.0 | -0.5 | -1.5 | -1.0    |
|                                 |                  | Maximum   | 8                 | 5         | 10    | 1    | 2    | 4    | 10      |
|                                 | Day 1, Hour 0.75 | n         | 10                | 6         | 6     | 6    | 6    | 6    | 30      |
|                                 |                  | Mean      | -2.4              | 0.5       | -3.8  | -2.5 | -1.7 | -0.8 | -1.7    |
|                                 |                  | SD        | 5.30              | 4.93      | 11.74 | 4.85 | 3.01 | 4.07 | 6.22    |
|                                 |                  | Minimum   | -11               | -5        | -24   | -12  | -6   | -8   | -24     |
|                                 |                  | Median    | -1.0              | -1.0      | 0.0   | -0.5 | -2.0 | -0.5 | -0.5    |
|                                 |                  | Maximum   | 5                 | 7         | 10    | 1    | 3    | 3    | 10      |
|                                 | Day 1, Hour 1    | n         | 10                | 6         | 6     | 6    | 6    | 6    | 30      |
|                                 |                  | Mean      | -2.4              | -2.3      | 0.2   | -4.2 | -0.7 | 1.2  | -1.2    |
|                                 |                  | SD        | 5.48              | 7.81      | 5.12  | 3.43 | 3.72 | 3.97 | 5.09    |
|                                 |                  | Minimum   | -9                | -11       | -9    | -8   | -7   | -3   | -11     |
|                                 |                  | Median    | -4.0              | -3.0      | 1.0   | -4.5 | -0.5 | 1.0  | -0.5    |
|                                 |                  | Maximum   | 9                 | 9         | 6     | 1    | 3    | 7    | 9       |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units)              | Time Point      | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|---------------------------------|-----------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                                 |                 |           |                   | A         | B    | C    | D    | E    |         |
| Diastolic Blood Pressure (mmHg) | Day 1, Hour 1.5 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                 | Mean      | -2.9              | -2.8      | -1.0 | -2.7 | 1.7  | 2.0  | -0.6    |
|                                 |                 | SD        | 6.06              | 7.65      | 4.47 | 4.84 | 5.32 | 3.74 | 5.41    |
|                                 |                 | Minimum   | -10               | -11       | -8   | -10  | -8   | -4   | -11     |
|                                 |                 | Median    | -3.0              | -4.5      | -0.5 | -1.0 | 4.0  | 3.5  | -0.5    |
|                                 |                 | Maximum   | 8                 | 7         | 4    | 3    | 6    | 6    | 7       |
|                                 | Day 1, Hour 2   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                 | Mean      | -2.5              | -1.0      | -2.0 | -2.5 | -1.0 | -2.2 | -1.7    |
|                                 |                 | SD        | 7.71              | 2.97      | 4.98 | 3.27 | 7.54 | 5.98 | 4.90    |
|                                 |                 | Minimum   | -19               | -6        | -8   | -7   | -12  | -12  | -12     |
|                                 |                 | Median    | -1.5              | -1.0      | -2.0 | -2.0 | 1.5  | -2.5 | -1.0    |
|                                 |                 | Maximum   | 7                 | 2         | 4    | 1    | 7    | 5    | 7       |
|                                 | Day 1, Hour 4   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                 | Mean      | -2.9              | -0.8      | -2.5 | -4.2 | -2.2 | -2.2 | -2.4    |
|                                 |                 | SD        | 4.25              | 6.68      | 4.59 | 4.02 | 7.47 | 3.54 | 5.20    |
|                                 |                 | Minimum   | -8                | -9        | -8   | -8   | -14  | -7   | -14     |
|                                 |                 | Median    | -2.5              | -1.0      | -2.5 | -5.0 | -2.0 | -1.0 | -2.0    |
|                                 |                 | Maximum   | 4                 | 9         | 3    | 2    | 7    | 2    | 9       |
|                                 | Day 1, Hour 6   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                 | Mean      | -4.6              | -7.8      | -4.8 | -7.0 | -1.5 | -2.7 | -4.8    |
|                                 |                 | SD        | 5.66              | 6.37      | 6.79 | 4.73 | 4.85 | 5.13 | 5.79    |
|                                 |                 | Minimum   | -14               | -18       | -15  | -14  | -6   | -13  | -18     |
|                                 |                 | Median    | -3.0              | -7.0      | -3.5 | -7.0 | -3.0 | -0.5 | -3.5    |
|                                 |                 | Maximum   | 3                 | -1        | 3    | -1   | 7    | 0    | 7       |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units)              | Time Point     | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|---------------------------------|----------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                                 |                |           |                   | A         | B    | C    | D    | E    |         |
| Diastolic Blood Pressure (mmHg) | Day 1, Hour 12 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                | Mean      | -5.0              | -7.7      | -3.2 | -7.2 | -1.0 | -5.5 | -4.9    |
|                                 |                | SD        | 5.29              | 4.50      | 5.04 | 3.66 | 3.52 | 4.04 | 4.65    |
|                                 |                | Minimum   | -10               | -14       | -12  | -12  | -5   | -13  | -14     |
|                                 |                | Median    | -6.0              | -6.5      | -1.5 | -8.0 | -1.0 | -5.0 | -4.5    |
|                                 |                | Maximum   | 5                 | -3        | 1    | -2   | 5    | -2   | 5       |
|                                 | Day 2          | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                | Mean      | -4.9              | -3.3      | -2.3 | -3.7 | 1.2  | 0.0  | -1.6    |
|                                 |                | SD        | 4.36              | 5.43      | 6.83 | 6.31 | 1.72 | 3.41 | 5.12    |
|                                 |                | Minimum   | -9                | -10       | -11  | -11  | -1   | -4   | -11     |
|                                 |                | Median    | -5.5              | -4.0      | -1.0 | -4.0 | 1.0  | 0.5  | 0.0     |
|                                 |                | Maximum   | 5                 | 5         | 5    | 4    | 3    | 4    | 5       |
|                                 | Day 3          | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                | Mean      | -0.8              | -3.2      | -0.2 | -4.2 | -1.7 | 1.0  | -1.6    |
|                                 |                | SD        | 6.97              | 6.18      | 4.79 | 3.19 | 3.83 | 6.87 | 5.16    |
|                                 |                | Minimum   | -11               | -13       | -8   | -9   | -6   | -11  | -13     |
|                                 |                | Median    | 1.0               | -2.5      | 0.5  | -3.0 | -1.5 | 1.0  | -1.5    |
|                                 |                | Maximum   | 11                | 4         | 5    | -1   | 3    | 9    | 9       |
|                                 | End of Study   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                                 |                | Mean      | -0.3              | 5.3       | 0.3  | 2.0  | 3.2  | 2.8  | 2.7     |
|                                 |                | SD        | 5.21              | 8.43      | 6.71 | 4.00 | 4.58 | 4.79 | 5.75    |
|                                 |                | Minimum   | -9                | -6        | -13  | -4   | -2   | -3   | -13     |
|                                 |                | Median    | -1.0              | 4.0       | 3.5  | 2.0  | 2.5  | 2.5  | 3.5     |
|                                 |                | Maximum   | 8                 | 15        | 4    | 6    | 10   | 11   | 15      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units) | Time Point       | Statistic | Pooled<br>Placebo | Treatment |      |       |       |      | Overall |
|--------------------|------------------|-----------|-------------------|-----------|------|-------|-------|------|---------|
|                    |                  |           |                   | A         | B    | C     | D     | E    |         |
| Pulse Rate (bpm)   | Day 1, Hour 0.25 | n         | 10                | 6         | 6    | 6     | 6     | 6    | 30      |
|                    |                  | Mean      | 0.2               | 0.3       | -1.2 | -8.2  | -4.2  | 4.5  | -1.7    |
|                    |                  | SD        | 6.20              | 4.63      | 6.65 | 5.34  | 4.02  | 5.39 | 6.54    |
|                    |                  | Minimum   | -8                | -3        | -9   | -13   | -9    | -1   | -13     |
|                    |                  | Median    | -1.5              | -1.5      | 0.0  | -10.5 | -4.0  | 4.0  | -1.0    |
|                    |                  | Maximum   | 10                | 9         | 9    | 0     | 0     | 12   | 12      |
|                    | Day 1, Hour 0.5  | n         | 10                | 6         | 6    | 6     | 6     | 6    | 30      |
|                    |                  | Mean      | -3.9              | 2.5       | -2.5 | -6.0  | -1.2  | 9.3  | 0.4     |
|                    |                  | SD        | 5.70              | 4.85      | 4.46 | 7.27  | 12.58 | 4.37 | 8.68    |
|                    |                  | Minimum   | -13               | -2        | -9   | -17   | -26   | 4    | -26     |
|                    |                  | Median    | -5.0              | 0.5       | -2.0 | -5.5  | 2.5   | 8.5  | 1.0     |
|                    |                  | Maximum   | 4                 | 10        | 3    | 3     | 9     | 15   | 15      |
|                    | Day 1, Hour 0.75 | n         | 10                | 6         | 6    | 6     | 6     | 6    | 30      |
|                    |                  | Mean      | -0.9              | 4.8       | -0.7 | -7.8  | 1.8   | 10.5 | 1.7     |
|                    |                  | SD        | 8.18              | 5.08      | 8.04 | 7.25  | 10.82 | 8.02 | 9.69    |
|                    |                  | Minimum   | -16               | -1        | -13  | -17   | -19   | -2   | -19     |
|                    |                  | Median    | 1.5               | 3.0       | -1.0 | -9.5  | 4.5   | 10.5 | 2.0     |
|                    |                  | Maximum   | 11                | 12        | 11   | 2     | 11    | 19   | 19      |
|                    | Day 1, Hour 1    | n         | 10                | 6         | 6    | 6     | 6     | 6    | 30      |
|                    |                  | Mean      | 0.4               | 3.2       | -1.5 | -7.8  | -2.8  | 3.7  | -1.1    |
|                    |                  | SD        | 7.40              | 5.19      | 6.47 | 7.78  | 13.12 | 5.43 | 8.69    |
|                    |                  | Minimum   | -15               | -2        | -13  | -20   | -23   | -6   | -23     |
|                    |                  | Median    | 1.5               | 3.0       | -0.5 | -8.5  | -3.0  | 5.5  | -0.5    |
|                    |                  | Maximum   | 8                 | 12        | 6    | 2     | 18    | 9    | 18      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units) | Time Point      | Statistic | Pooled<br>Placebo | Treatment |      |      |       |      | Overall |
|--------------------|-----------------|-----------|-------------------|-----------|------|------|-------|------|---------|
|                    |                 |           |                   | A         | B    | C    | D     | E    |         |
| Pulse Rate (bpm)   | Day 1, Hour 1.5 | n         | 10                | 6         | 6    | 6    | 6     | 6    | 30      |
|                    |                 | Mean      | -3.8              | 2.2       | -0.5 | -2.5 | -0.5  | 4.7  | 0.7     |
|                    |                 | SD        | 6.30              | 3.31      | 7.34 | 4.23 | 11.00 | 5.61 | 6.85    |
|                    |                 | Minimum   | -18               | -1        | -9   | -10  | -17   | -2   | -17     |
|                    |                 | Median    | -1.5              | 2.0       | -1.5 | -2.5 | 1.0   | 4.0  | 1.0     |
|                    |                 | Maximum   | 4                 | 8         | 12   | 2    | 16    | 12   | 16      |
|                    | Day 1, Hour 2   | n         | 10                | 6         | 6    | 6    | 6     | 6    | 30      |
|                    |                 | Mean      | -2.0              | 0.8       | -3.2 | -3.8 | -0.7  | 5.2  | -0.3    |
|                    |                 | SD        | 8.12              | 2.64      | 5.04 | 4.71 | 15.03 | 8.61 | 8.48    |
|                    |                 | Minimum   | -14               | -4        | -9   | -9   | -29   | -3   | -29     |
|                    |                 | Median    | -3.0              | 1.0       | -2.5 | -4.5 | 2.0   | 2.5  | 0.5     |
|                    |                 | Maximum   | 14                | 4         | 2    | 3    | 15    | 19   | 19      |
|                    | Day 1, Hour 4   | n         | 10                | 6         | 6    | 6    | 6     | 6    | 30      |
|                    |                 | Mean      | -1.2              | 1.3       | -3.3 | -1.8 | -0.7  | 2.7  | -0.4    |
|                    |                 | SD        | 10.82             | 2.25      | 7.37 | 6.71 | 4.46  | 4.63 | 5.47    |
|                    |                 | Minimum   | -20               | -1        | -10  | -9   | -9    | -2   | -10     |
|                    |                 | Median    | 1.5               | 0.5       | -4.0 | -3.0 | 1.0   | 0.5  | 0.0     |
|                    |                 | Maximum   | 12                | 5         | 10   | 8    | 3     | 9    | 10      |
|                    | Day 1, Hour 6   | n         | 10                | 6         | 6    | 6    | 6     | 6    | 30      |
|                    |                 | Mean      | 11.6              | 11.2      | 7.8  | 0.7  | 2.7   | 12.5 | 7.0     |
|                    |                 | SD        | 15.85             | 3.54      | 9.62 | 9.35 | 12.83 | 6.44 | 9.54    |
|                    |                 | Minimum   | -12               | 8         | -9   | -11  | -22   | 4    | -22     |
|                    |                 | Median    | 10.0              | 10.0      | 9.5  | 3.5  | 7.0   | 14.5 | 8.5     |
|                    |                 | Maximum   | 42                | 16        | 18   | 13   | 12    | 18   | 18      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units) | Time Point     | Statistic | Pooled<br>Placebo | Treatment |       |      |       |       | Overall |
|--------------------|----------------|-----------|-------------------|-----------|-------|------|-------|-------|---------|
|                    |                |           |                   | A         | B     | C    | D     | E     |         |
| Pulse Rate (bpm)   | Day 1, Hour 12 | n         | 10                | 6         | 6     | 6    | 6     | 6     | 30      |
|                    |                | Mean      | 1.7               | 10.2      | 4.5   | -2.3 | -0.8  | 12.5  | 4.8     |
|                    |                | SD        | 12.90             | 5.81      | 8.26  | 5.85 | 13.76 | 7.87  | 10.11   |
|                    |                | Minimum   | -13               | 1         | -5    | -11  | -27   | 3     | -27     |
|                    |                | Median    | 1.0               | 10.0      | 4.5   | -0.5 | 2.0   | 12.5  | 4.5     |
|                    |                | Maximum   | 32                | 19        | 18    | 3    | 12    | 24    | 24      |
|                    | Day 2          | n         | 10                | 6         | 6     | 6    | 6     | 6     | 30      |
|                    |                | Mean      | -2.8              | 4.0       | -5.7  | 1.2  | -0.5  | 4.3   | 0.7     |
|                    |                | SD        | 8.77              | 2.61      | 8.52  | 7.14 | 12.18 | 9.40  | 8.77    |
|                    |                | Minimum   | -18               | -1        | -17   | -7   | -22   | -2    | -22     |
|                    |                | Median    | -1.0              | 4.5       | -4.5  | 0.5  | 4.5   | 1.0   | 2.5     |
|                    |                | Maximum   | 8                 | 6         | 5     | 13   | 12    | 23    | 23      |
|                    | Day 3          | n         | 10                | 6         | 6     | 6    | 6     | 6     | 30      |
|                    |                | Mean      | 3.3               | 5.2       | -1.3  | -0.7 | 0.2   | 7.0   | 2.1     |
|                    |                | SD        | 9.18              | 2.93      | 6.86  | 6.25 | 10.74 | 7.18  | 7.54    |
|                    |                | Minimum   | -11               | 1         | -14   | -7   | -21   | -3    | -21     |
|                    |                | Median    | 4.5               | 5.0       | 0.0   | -1.0 | 5.0   | 6.5   | 4.5     |
|                    |                | Maximum   | 19                | 10        | 5     | 6    | 7     | 19    | 19      |
|                    | End of Study   | n         | 10                | 6         | 6     | 6    | 6     | 6     | 30      |
|                    |                | Mean      | 2.6               | 10.8      | 4.2   | 3.8  | 1.5   | 9.8   | 6.0     |
|                    |                | SD        | 10.06             | 7.28      | 10.30 | 9.50 | 11.93 | 11.72 | 10.24   |
|                    |                | Minimum   | -13               | 2         | -12   | -13  | -11   | -7    | -13     |
|                    |                | Median    | 2.5               | 9.0       | 3.5   | 5.0  | 0.0   | 7.5   | 6.0     |
|                    |                | Maximum   | 23                | 21        | 19    | 14   | 21    | 26    | 26      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units)     | Time Point       | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|------------------------|------------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                        |                  |           |                   | A         | B    | C    | D    | E    |         |
| Respiration Rate (bpm) | Day 1, Hour 0.25 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                  | Mean      | 0.6               | 1.0       | -0.3 | 0.3  | -0.3 | 0.0  | 0.1     |
|                        |                  | SD        | 1.90              | 2.10      | 0.82 | 1.51 | 1.51 | 2.53 | 1.74    |
|                        |                  | Minimum   | -2                | -2        | -2   | -2   | -2   | -4   | -4      |
|                        |                  | Median    | 0.0               | 1.0       | 0.0  | 0.0  | 0.0  | 1.0  | 0.0     |
|                        |                  | Maximum   | 4                 | 4         | 0    | 2    | 2    | 2    | 4       |
|                        | Day 1, Hour 0.5  | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                  | Mean      | 0.6               | 2.0       | -0.3 | 0.0  | 0.0  | -0.7 | 0.2     |
|                        |                  | SD        | 1.90              | 3.79      | 2.66 | 2.19 | 1.26 | 1.63 | 2.48    |
|                        |                  | Minimum   | -2                | -4        | -4   | -2   | -2   | -4   | -4      |
|                        |                  | Median    | 0.0               | 2.0       | 0.0  | 0.0  | 0.0  | 0.0  | 0.0     |
|                        |                  | Maximum   | 4                 | 6         | 4    | 4    | 2    | 0    | 6       |
|                        | Day 1, Hour 0.75 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                  | Mean      | 1.4               | 1.0       | 0.3  | 0.3  | 0.0  | -0.7 | 0.2     |
|                        |                  | SD        | 2.50              | 2.10      | 1.51 | 2.34 | 1.26 | 2.42 | 1.92    |
|                        |                  | Minimum   | -2                | -2        | -2   | -2   | -2   | -4   | -4      |
|                        |                  | Median    | 2.0               | 1.0       | 0.0  | 0.0  | 0.0  | -1.0 | 0.0     |
|                        |                  | Maximum   | 6                 | 4         | 2    | 4    | 2    | 2    | 4       |
|                        | Day 1, Hour 1    | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                  | Mean      | -0.6              | -2.3      | -0.7 | -1.3 | -1.3 | -1.0 | -1.3    |
|                        |                  | SD        | 3.13              | 3.20      | 1.03 | 3.72 | 1.63 | 1.10 | 2.31    |
|                        |                  | Minimum   | -4                | -6        | -2   | -8   | -4   | -2   | -8      |
|                        |                  | Median    | -2.0              | -2.0      | 0.0  | -1.0 | -1.0 | -1.0 | -1.0    |
|                        |                  | Maximum   | 6                 | 2         | 0    | 2    | 0    | 0    | 2       |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units)     | Time Point      | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|------------------------|-----------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                        |                 |           |                   | A         | B    | C    | D    | E    |         |
| Respiration Rate (bpm) | Day 1, Hour 1.5 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                 | Mean      | -0.6              | -2.3      | 0.3  | -0.3 | -0.3 | 0.3  | -0.5    |
|                        |                 | SD        | 1.65              | 4.46      | 2.94 | 1.51 | 2.34 | 1.97 | 2.81    |
|                        |                 | Minimum   | -4                | -8        | -2   | -2   | -4   | -2   | -8      |
|                        |                 | Median    | 0.0               | -2.0      | 0.0  | 0.0  | 0.0  | 0.0  | 0.0     |
|                        |                 | Maximum   | 2                 | 4         | 6    | 2    | 2    | 4    | 6       |
|                        | Day 1, Hour 2   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                 | Mean      | 0.6               | 0.3       | -0.7 | -0.3 | 3.0  | 0.3  | 0.5     |
|                        |                 | SD        | 2.32              | 1.51      | 1.03 | 1.51 | 3.29 | 2.66 | 2.40    |
|                        |                 | Minimum   | -4                | -2        | -2   | -2   | -2   | -4   | -4      |
|                        |                 | Median    | 0.0               | 0.0       | 0.0  | 0.0  | 4.0  | 0.0  | 0.0     |
|                        |                 | Maximum   | 4                 | 2         | 0    | 2    | 6    | 4    | 6       |
|                        | Day 1, Hour 4   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                 | Mean      | 0.6               | -0.3      | 0.0  | -1.0 | 2.0  | -1.0 | -0.1    |
|                        |                 | SD        | 1.90              | 3.44      | 2.19 | 1.10 | 2.19 | 1.10 | 2.32    |
|                        |                 | Minimum   | -2                | -4        | -2   | -2   | 0    | -2   | -4      |
|                        |                 | Median    | 0.0               | 0.0       | 0.0  | -1.0 | 2.0  | -1.0 | 0.0     |
|                        |                 | Maximum   | 4                 | 4         | 4    | 0    | 4    | 0    | 4       |
|                        | Day 1, Hour 6   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                 | Mean      | -0.8              | -1.0      | 0.3  | -0.7 | -1.7 | -0.3 | -0.7    |
|                        |                 | SD        | 1.69              | 3.03      | 1.51 | 2.42 | 1.51 | 2.94 | 2.31    |
|                        |                 | Minimum   | -4                | -4        | -2   | -4   | -4   | -4   | -4      |
|                        |                 | Median    | 0.0               | -1.0      | 0.0  | -1.0 | -2.0 | -1.0 | 0.0     |
|                        |                 | Maximum   | 2                 | 4         | 2    | 2    | 0    | 4    | 4       |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units)     | Time Point     | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|------------------------|----------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                        |                |           |                   | A         | B    | C    | D    | E    |         |
| Respiration Rate (bpm) | Day 1, Hour 12 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                | Mean      | 0.8               | -0.7      | 0.3  | 0.3  | 0.3  | 0.0  | 0.1     |
|                        |                | SD        | 2.35              | 3.27      | 1.51 | 2.94 | 1.51 | 1.79 | 2.20    |
|                        |                | Minimum   | -2                | -4        | -2   | -4   | -2   | -2   | -4      |
|                        |                | Median    | 0.0               | -1.0      | 0.0  | 1.0  | 0.0  | 0.0  | 0.0     |
|                        |                | Maximum   | 6                 | 4         | 2    | 4    | 2    | 2    | 4       |
|                        | Day 2          | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                | Mean      | -0.4              | 0.0       | 3.7  | 1.0  | -0.7 | -3.0 | 0.2     |
|                        |                | SD        | 2.95              | 2.53      | 2.66 | 2.10 | 2.73 | 1.10 | 3.08    |
|                        |                | Minimum   | -4                | -2        | 0    | -2   | -4   | -4   | -4      |
|                        |                | Median    | 0.0               | -1.0      | 4.0  | 1.0  | -1.0 | -3.0 | 0.0     |
|                        |                | Maximum   | 4                 | 4         | 6    | 4    | 4    | -2   | 6       |
|                        | Day 3          | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                | Mean      | 0.4               | -0.3      | 2.0  | 0.7  | -0.7 | -0.3 | 0.3     |
|                        |                | SD        | 1.58              | 2.94      | 4.20 | 1.63 | 3.72 | 1.51 | 2.96    |
|                        |                | Minimum   | -2                | -4        | -4   | -2   | -4   | -2   | -4      |
|                        |                | Median    | 0.0               | 1.0       | 3.0  | 1.0  | -2.0 | 0.0  | 0.0     |
|                        |                | Maximum   | 2                 | 2         | 6    | 2    | 4    | 2    | 6       |
|                        | End of Study   | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                        |                | Mean      | 1.0               | 1.7       | 4.3  | 1.3  | -0.7 | -1.7 | 1.0     |
|                        |                | SD        | 1.94              | 2.34      | 2.94 | 1.03 | 2.07 | 1.97 | 2.91    |
|                        |                | Minimum   | -4                | -2        | 0    | 0    | -4   | -4   | -4      |
|                        |                | Median    | 2.0               | 2.0       | 5.0  | 2.0  | 0.0  | -2.0 | 1.0     |
|                        |                | Maximum   | 2                 | 4         | 8    | 2    | 2    | 2    | 8       |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units) | Time Point       | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------|------------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                    |                  |           |                   | A         | B     | C     | D     | E     |         |
| Temperature (°C)   | Day 1, Hour 0.25 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 0.10              | -0.12     | 0.08  | 0.02  | -0.08 | -0.07 | -0.03   |
|                    |                  | SD        | 0.156             | 0.194     | 0.264 | 0.183 | 0.117 | 0.121 | 0.186   |
|                    |                  | Minimum   | -0.1              | -0.4      | -0.2  | -0.3  | -0.2  | -0.3  | -0.4    |
|                    |                  | Median    | 0.10              | -0.05     | 0.10  | 0.00  | -0.10 | 0.00  | 0.00    |
|                    |                  | Maximum   | 0.3               | 0.1       | 0.5   | 0.2   | 0.1   | 0.0   | 0.5     |
|                    | Day 1, Hour 0.5  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 0.05              | -0.15     | -0.03 | 0.02  | -0.05 | -0.08 | -0.06   |
|                    |                  | SD        | 0.222             | 0.176     | 0.151 | 0.279 | 0.164 | 0.248 | 0.203   |
|                    |                  | Minimum   | -0.4              | -0.3      | -0.3  | -0.5  | -0.2  | -0.4  | -0.5    |
|                    |                  | Median    | 0.10              | -0.20     | 0.00  | 0.05  | -0.10 | -0.15 | -0.05   |
|                    |                  | Maximum   | 0.3               | 0.1       | 0.1   | 0.3   | 0.2   | 0.3   | 0.3     |
|                    | Day 1, Hour 0.75 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 0.05              | -0.10     | 0.05  | 0.07  | -0.12 | -0.08 | -0.04   |
|                    |                  | SD        | 0.165             | 0.141     | 0.308 | 0.301 | 0.194 | 0.075 | 0.222   |
|                    |                  | Minimum   | -0.2              | -0.3      | -0.3  | -0.5  | -0.3  | -0.2  | -0.5    |
|                    |                  | Median    | 0.05              | -0.10     | 0.00  | 0.10  | -0.15 | -0.10 | -0.10   |
|                    |                  | Maximum   | 0.3               | 0.1       | 0.5   | 0.4   | 0.2   | 0.0   | 0.5     |
|                    | Day 1, Hour 1    | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                  | Mean      | 0.17              | -0.03     | 0.18  | 0.15  | -0.02 | 0.03  | 0.06    |
|                    |                  | SD        | 0.149             | 0.121     | 0.160 | 0.152 | 0.117 | 0.294 | 0.190   |
|                    |                  | Minimum   | -0.2              | -0.1      | -0.1  | -0.1  | -0.2  | -0.5  | -0.5    |
|                    |                  | Median    | 0.20              | -0.10     | 0.25  | 0.15  | 0.00  | 0.15  | 0.10    |
|                    |                  | Maximum   | 0.3               | 0.2       | 0.3   | 0.3   | 0.1   | 0.3   | 0.3     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units) | Time Point      | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------|-----------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                    |                 |           |                   | A         | B     | C     | D     | E     |         |
| Temperature (°C)   | Day 1, Hour 1.5 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                 | Mean      | 0.09              | -0.03     | 0.08  | 0.15  | 0.08  | -0.17 | 0.02    |
|                    |                 | SD        | 0.213             | 0.151     | 0.117 | 0.259 | 0.204 | 0.250 | 0.221   |
|                    |                 | Minimum   | -0.2              | -0.2      | -0.1  | -0.3  | -0.1  | -0.5  | -0.5    |
|                    |                 | Median    | 0.10              | 0.00      | 0.10  | 0.25  | 0.05  | -0.20 | 0.00    |
|                    |                 | Maximum   | 0.4               | 0.2       | 0.2   | 0.4   | 0.3   | 0.2   | 0.4     |
|                    | Day 1, Hour 2   | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                 | Mean      | 0.08              | -0.07     | 0.08  | 0.20  | -0.02 | 0.05  | 0.05    |
|                    |                 | SD        | 0.249             | 0.151     | 0.204 | 0.126 | 0.117 | 0.266 | 0.193   |
|                    |                 | Minimum   | -0.3              | -0.2      | -0.2  | 0.0   | -0.1  | -0.4  | -0.4    |
|                    |                 | Median    | 0.05              | -0.10     | 0.05  | 0.20  | -0.05 | 0.10  | 0.00    |
|                    |                 | Maximum   | 0.5               | 0.2       | 0.4   | 0.4   | 0.2   | 0.3   | 0.4     |
|                    | Day 1, Hour 4   | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                 | Mean      | 0.16              | -0.08     | 0.05  | 0.03  | 0.12  | 0.25  | 0.07    |
|                    |                 | SD        | 0.190             | 0.117     | 0.187 | 0.294 | 0.160 | 0.207 | 0.218   |
|                    |                 | Minimum   | -0.1              | -0.2      | -0.2  | -0.5  | -0.1  | -0.1  | -0.5    |
|                    |                 | Median    | 0.15              | -0.10     | 0.05  | 0.15  | 0.10  | 0.25  | 0.10    |
|                    |                 | Maximum   | 0.4               | 0.1       | 0.3   | 0.3   | 0.4   | 0.5   | 0.5     |
|                    | Day 1, Hour 6   | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                 | Mean      | 0.07              | 0.00      | 0.17  | 0.13  | 0.03  | 0.13  | 0.09    |
|                    |                 | SD        | 0.177             | 0.261     | 0.207 | 0.225 | 0.121 | 0.151 | 0.196   |
|                    |                 | Minimum   | -0.2              | -0.4      | -0.2  | -0.3  | -0.1  | 0.0   | -0.4    |
|                    |                 | Median    | 0.10              | 0.00      | 0.20  | 0.20  | 0.05  | 0.10  | 0.10    |
|                    |                 | Maximum   | 0.3               | 0.4       | 0.4   | 0.3   | 0.2   | 0.4   | 0.4     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.11 Vital Sign Change From Baseline (Safety Population)

| Vital Sign (units) | Time Point     | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|--------------------|----------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                    |                |           |                   | A         | B     | C     | D     | E     |         |
| Temperature (°C)   | Day 1, Hour 12 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                | Mean      | 0.14              | 0.08      | 0.13  | 0.10  | 0.02  | 0.13  | 0.09    |
|                    |                | SD        | 0.135             | 0.194     | 0.320 | 0.155 | 0.293 | 0.121 | 0.218   |
|                    |                | Minimum   | 0.0               | -0.2      | -0.4  | -0.1  | -0.4  | 0.0   | -0.4    |
|                    |                | Median    | 0.10              | 0.05      | 0.15  | 0.10  | -0.05 | 0.15  | 0.10    |
|                    |                | Maximum   | 0.4               | 0.3       | 0.5   | 0.3   | 0.4   | 0.3   | 0.5     |
|                    | Day 2          | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                | Mean      | 0.07              | -0.12     | 0.13  | 0.15  | -0.05 | 0.15  | 0.05    |
|                    |                | SD        | 0.195             | 0.172     | 0.175 | 0.152 | 0.197 | 0.122 | 0.193   |
|                    |                | Minimum   | -0.1              | -0.4      | 0.0   | 0.0   | -0.3  | 0.0   | -0.4    |
|                    |                | Median    | 0.05              | -0.10     | 0.05  | 0.15  | -0.10 | 0.20  | 0.00    |
|                    |                | Maximum   | 0.5               | 0.1       | 0.4   | 0.4   | 0.3   | 0.3   | 0.4     |
|                    | Day 3          | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                | Mean      | 0.08              | -0.03     | -0.03 | 0.17  | -0.03 | 0.38  | 0.09    |
|                    |                | SD        | 0.239             | 0.137     | 0.225 | 0.175 | 0.151 | 0.098 | 0.226   |
|                    |                | Minimum   | -0.1              | -0.2      | -0.4  | -0.1  | -0.3  | 0.3   | -0.4    |
|                    |                | Median    | -0.05             | -0.05     | 0.00  | 0.25  | 0.00  | 0.35  | 0.00    |
|                    |                | Maximum   | 0.6               | 0.2       | 0.3   | 0.3   | 0.1   | 0.5   | 0.5     |
|                    | End of Study   | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                    |                | Mean      | 0.07              | 0.00      | 0.12  | 0.13  | 0.12  | 0.05  | 0.08    |
|                    |                | SD        | 0.291             | 0.179     | 0.299 | 0.216 | 0.098 | 0.138 | 0.191   |
|                    |                | Minimum   | -0.3              | -0.3      | -0.4  | -0.1  | 0.0   | -0.1  | -0.4    |
|                    |                | Median    | 0.15              | 0.05      | 0.15  | 0.05  | 0.10  | 0.05  | 0.10    |
|                    |                | Maximum   | 0.6               | 0.2       | 0.4   | 0.4   | 0.3   | 0.2   | 0.4     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.12 12-Lead Electrocardiogram Summary (Safety Population)

| Measurement (units) | Time Point    | Statistic | Pooled<br>Placebo | Treatment |       |      |       |      | Overall |
|---------------------|---------------|-----------|-------------------|-----------|-------|------|-------|------|---------|
|                     |               |           |                   | A         | B     | C    | D     | E    |         |
| Heart Rate (bpm)    | Screen        | n         | 10                | 6         | 6     | 6    | 6     | 6    | 30      |
|                     |               | Mean      | 70.2              | 61.2      | 68.0  | 63.0 | 72.3  | 66.7 | 66.2    |
|                     |               | SD        | 10.97             | 7.19      | 11.40 | 7.64 | 13.28 | 7.55 | 9.87    |
|                     |               | Minimum   | 57                | 49        | 48    | 54   | 62    | 57   | 48      |
|                     |               | Median    | 69.0              | 61.5      | 68.5  | 64.0 | 66.5  | 66.0 | 66.0    |
|                     |               | Maximum   | 92                | 70        | 82    | 71   | 98    | 76   | 98      |
|                     | Baseline      | n         | 10                | 6         | 6     | 6    | 6     | 6    | 30      |
|                     |               | Mean      | 68.3              | 62.7      | 65.8  | 58.3 | 64.8  | 66.2 | 63.6    |
|                     |               | SD        | 10.66             | 10.15     | 5.95  | 5.68 | 13.85 | 9.43 | 9.30    |
|                     |               | Minimum   | 55                | 50        | 59    | 54   | 53    | 54   | 50      |
|                     |               | Median    | 66.0              | 61.5      | 64.5  | 56.5 | 59.5  | 69.0 | 60.5    |
|                     |               | Maximum   | 85                | 78        | 73    | 69   | 86    | 75   | 86      |
|                     | Day 1, Hour 1 | n         | 10                | 6         | 6     | 6    | 6     | 6    | 30      |
|                     |               | Mean      | 59.9              | 53.7      | 60.5  | 55.3 | 57.2  | 57.7 | 56.9    |
|                     |               | SD        | 9.28              | 4.27      | 7.09  | 5.89 | 4.54  | 4.68 | 5.53    |
|                     |               | Minimum   | 47                | 46        | 55    | 49   | 52    | 51   | 46      |
|                     |               | Median    | 61.0              | 55.0      | 57.0  | 55.0 | 56.0  | 59.0 | 56.0    |
|                     |               | Maximum   | 73                | 58        | 71    | 66   | 64    | 63   | 71      |
|                     | Day 1, Hour 6 | n         | 10                | 6         | 6     | 6    | 6     | 6    | 30      |
|                     |               | Mean      | 68.5              | 60.3      | 66.3  | 60.7 | 64.2  | 61.5 | 62.6    |
|                     |               | SD        | 11.76             | 5.99      | 6.12  | 4.68 | 5.04  | 6.72 | 5.83    |
|                     |               | Minimum   | 52                | 51        | 59    | 55   | 58    | 52   | 51      |
|                     |               | Median    | 67.0              | 61.5      | 66.5  | 60.5 | 64.0  | 61.5 | 63.0    |
|                     |               | Maximum   | 91                | 67        | 73    | 67   | 72    | 71   | 73      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.12 12-Lead Electrocardiogram Summary (Safety Population)

| Measurement (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|---------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                     |              |           |                   | A         | B     | C     | D     | E     |         |
| Heart Rate (bpm)    | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |              | Mean      | 60.2              | 55.2      | 59.5  | 56.5  | 59.2  | 56.8  | 57.4    |
|                     |              | SD        | 8.24              | 5.27      | 6.57  | 4.59  | 7.08  | 5.49  | 5.70    |
|                     |              | Minimum   | 43                | 47        | 51    | 51    | 53    | 51    | 47      |
|                     |              | Median    | 60.5              | 55.5      | 60.0  | 55.5  | 56.0  | 56.5  | 56.5    |
|                     |              | Maximum   | 71                | 62        | 67    | 64    | 69    | 66    | 69      |
|                     | Day 3        | n         | 9                 | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |              | Mean      | 65.3              | 58.0      | 62.2  | 59.7  | 60.0  | 57.8  | 59.5    |
|                     |              | SD        | 9.99              | 4.56      | 7.03  | 5.05  | 6.66  | 2.71  | 5.29    |
|                     |              | Minimum   | 48                | 51        | 55    | 53    | 55    | 54    | 51      |
|                     |              | Median    | 69.0              | 59.5      | 60.5  | 59.5  | 57.0  | 59.0  | 59.0    |
|                     |              | Maximum   | 75                | 63        | 75    | 67    | 71    | 61    | 75      |
|                     | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |              | Mean      | 62.1              | 61.0      | 65.0  | 62.3  | 63.3  | 65.5  | 63.4    |
|                     |              | SD        | 8.88              | 5.90      | 11.75 | 5.92  | 10.09 | 9.59  | 8.49    |
|                     |              | Minimum   | 50                | 54        | 58    | 53    | 56    | 51    | 51      |
|                     |              | Median    | 65.0              | 62.0      | 59.0  | 62.0  | 58.0  | 66.0  | 61.0    |
|                     |              | Maximum   | 72                | 70        | 88    | 70    | 82    | 77    | 88      |
| PR (msec)           | Screen       | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |              | Mean      | 163.6             | 167.7     | 158.3 | 159.7 | 155.7 | 168.0 | 161.9   |
|                     |              | SD        | 22.19             | 20.99     | 18.65 | 5.85  | 19.45 | 16.10 | 16.67   |
|                     |              | Minimum   | 138               | 142       | 134   | 152   | 136   | 140   | 134     |
|                     |              | Median    | 156.0             | 163.0     | 158.0 | 161.0 | 151.0 | 170.0 | 163.0   |
|                     |              | Maximum   | 198               | 200       | 182   | 166   | 188   | 190   | 200     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.12 12-Lead Electrocardiogram Summary (Safety Population)

| Measurement (units) | Time Point    | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|---------------------|---------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                     |               |           |                   | A         | B     | C     | D     | E     |         |
| PR (msec)           | Baseline      | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 168.5             | 166.7     | 159.7 | 161.7 | 156.3 | 166.0 | 162.1   |
|                     |               | SD        | 23.34             | 21.38     | 20.57 | 14.88 | 15.97 | 18.11 | 17.49   |
|                     |               | Minimum   | 136               | 148       | 132   | 144   | 142   | 134   | 132     |
|                     |               | Median    | 166.5             | 156.0     | 168.0 | 161.0 | 153.0 | 168.0 | 162.0   |
|                     |               | Maximum   | 206               | 194       | 182   | 184   | 184   | 188   | 194     |
|                     | Day 1, Hour 1 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 172.2             | 173.0     | 160.7 | 159.5 | 156.7 | 172.0 | 164.4   |
|                     |               | SD        | 26.79             | 22.47     | 24.52 | 12.96 | 17.04 | 17.47 | 19.23   |
|                     |               | Minimum   | 132               | 153       | 127   | 145   | 140   | 143   | 127     |
|                     |               | Median    | 168.5             | 163.0     | 173.5 | 157.0 | 154.0 | 174.0 | 164.0   |
|                     |               | Maximum   | 223               | 206       | 184   | 182   | 186   | 197   | 206     |
|                     | Day 1, Hour 6 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 171.2             | 163.7     | 154.7 | 157.5 | 154.7 | 167.2 | 159.5   |
|                     |               | SD        | 25.81             | 24.62     | 22.06 | 15.20 | 19.08 | 21.23 | 19.87   |
|                     |               | Minimum   | 134               | 134       | 121   | 146   | 135   | 131   | 121     |
|                     |               | Median    | 166.5             | 161.5     | 164.5 | 149.5 | 155.0 | 169.0 | 162.5   |
|                     |               | Maximum   | 217               | 195       | 173   | 178   | 184   | 196   | 196     |
|                     | Day 2         | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 173.0             | 165.7     | 163.8 | 160.7 | 155.5 | 171.0 | 163.3   |
|                     |               | SD        | 25.36             | 25.03     | 24.60 | 14.76 | 16.74 | 19.62 | 19.80   |
|                     |               | Minimum   | 139               | 141       | 131   | 144   | 139   | 140   | 131     |
|                     |               | Median    | 167.5             | 158.5     | 176.0 | 159.5 | 153.0 | 171.5 | 163.0   |
|                     |               | Maximum   | 217               | 203       | 185   | 185   | 183   | 201   | 203     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.12 12-Lead Electrocardiogram Summary (Safety Population)

| Measurement (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|---------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                     |              |           |                   | A         | B     | C     | D     | E     |         |
| PR (msec)           | Day 3        | n         | 9                 | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |              | Mean      | 177.1             | 173.0     | 164.0 | 160.7 | 158.7 | 168.3 | 164.9   |
|                     |              | SD        | 24.48             | 22.41     | 21.32 | 13.06 | 15.47 | 19.28 | 18.10   |
|                     |              | Minimum   | 150               | 148       | 132   | 144   | 144   | 144   | 132     |
|                     |              | Median    | 170.0             | 165.0     | 175.0 | 163.0 | 156.0 | 172.0 | 164.0   |
|                     |              | Maximum   | 214               | 208       | 182   | 180   | 186   | 194   | 208     |
|                     | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |              | Mean      | 170.7             | 173.7     | 160.3 | 159.7 | 159.7 | 172.3 | 165.1   |
|                     |              | SD        | 30.21             | 18.39     | 21.74 | 15.62 | 21.67 | 10.39 | 18.01   |
|                     |              | Minimum   | 136               | 158       | 130   | 142   | 140   | 154   | 130     |
|                     |              | Median    | 168.0             | 165.0     | 162.0 | 156.0 | 155.0 | 175.0 | 164.0   |
|                     |              | Maximum   | 216               | 200       | 186   | 188   | 198   | 184   | 200     |
| QRS (msec)          | Screen       | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |              | Mean      | 97.6              | 96.7      | 95.0  | 96.0  | 94.7  | 93.7  | 95.2    |
|                     |              | SD        | 13.46             | 11.64     | 10.02 | 8.10  | 9.35  | 10.46 | 9.33    |
|                     |              | Minimum   | 70                | 86        | 82    | 86    | 82    | 76    | 76      |
|                     |              | Median    | 101.0             | 94.0      | 98.0  | 96.0  | 97.0  | 96.0  | 96.0    |
|                     |              | Maximum   | 114               | 116       | 104   | 108   | 108   | 106   | 116     |
|                     | Baseline     | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |              | Mean      | 97.6              | 94.7      | 92.3  | 98.7  | 91.0  | 93.0  | 93.9    |
|                     |              | SD        | 13.56             | 5.47      | 14.17 | 7.87  | 9.53  | 11.30 | 9.76    |
|                     |              | Minimum   | 68                | 86        | 72    | 90    | 80    | 76    | 72      |
|                     |              | Median    | 102.0             | 97.0      | 97.0  | 97.0  | 91.0  | 93.0  | 96.0    |
|                     |              | Maximum   | 112               | 100       | 106   | 110   | 102   | 108   | 110     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.12 12-Lead Electrocardiogram Summary (Safety Population)

| Measurement (units) | Time Point    | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|---------------------|---------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                     |               |           |                   | A         | B     | C     | D     | E     |         |
| QRS (msec)          | Day 1, Hour 1 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 99.2              | 97.3      | 95.2  | 98.8  | 94.2  | 95.8  | 96.3    |
|                     |               | SD        | 11.45             | 6.77      | 10.34 | 8.95  | 12.19 | 10.98 | 9.45    |
|                     |               | Minimum   | 79                | 89        | 84    | 86    | 80    | 77    | 77      |
|                     |               | Median    | 101.5             | 96.0      | 94.5  | 100.0 | 92.5  | 97.5  | 96.5    |
|                     |               | Maximum   | 114               | 108       | 110   | 109   | 109   | 110   | 110     |
|                     | Day 1, Hour 6 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 101.0             | 97.5      | 95.2  | 100.8 | 89.7  | 89.8  | 94.6    |
|                     |               | SD        | 10.47             | 5.92      | 11.53 | 7.88  | 5.61  | 11.84 | 9.43    |
|                     |               | Minimum   | 79                | 90        | 80    | 90    | 83    | 76    | 76      |
|                     |               | Median    | 100.0             | 97.5      | 96.0  | 104.0 | 90.0  | 90.5  | 94.5    |
|                     |               | Maximum   | 117               | 104       | 110   | 109   | 97    | 106   | 110     |
|                     | Day 2         | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 98.5              | 94.7      | 95.0  | 100.3 | 92.8  | 92.3  | 95.0    |
|                     |               | SD        | 11.62             | 9.24      | 10.83 | 9.18  | 8.98  | 11.47 | 9.71    |
|                     |               | Minimum   | 79                | 78        | 84    | 86    | 83    | 74    | 74      |
|                     |               | Median    | 101.5             | 97.5      | 93.0  | 104.5 | 92.0  | 93.0  | 96.0    |
|                     |               | Maximum   | 114               | 104       | 110   | 109   | 106   | 108   | 110     |
|                     | Day 3         | n         | 9                 | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 97.6              | 96.7      | 91.3  | 97.0  | 92.3  | 94.7  | 94.4    |
|                     |               | SD        | 14.17             | 7.87      | 9.52  | 7.87  | 7.94  | 12.11 | 8.86    |
|                     |               | Minimum   | 74                | 88        | 76    | 88    | 82    | 76    | 76      |
|                     |               | Median    | 102.0             | 96.0      | 94.0  | 97.0  | 94.0  | 96.0  | 95.0    |
|                     |               | Maximum   | 114               | 110       | 100   | 106   | 102   | 108   | 110     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.12 12-Lead Electrocardiogram Summary (Safety Population)

| Measurement (units) | Time Point    | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|---------------------|---------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                     |               |           |                   | A         | B     | C     | D     | E     |         |
| QRS (msec)          | End of Study  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 97.7              | 97.7      | 93.3  | 97.0  | 93.0  | 95.0  | 95.2    |
|                     |               | SD        | 13.18             | 9.58      | 10.71 | 8.83  | 7.24  | 11.01 | 9.09    |
|                     |               | Minimum   | 74                | 86        | 78    | 86    | 84    | 78    | 78      |
|                     |               | Median    | 100.0             | 95.0      | 95.0  | 97.0  | 93.0  | 95.0  | 94.0    |
|                     |               | Maximum   | 110               | 112       | 104   | 108   | 102   | 106   | 112     |
| QT (msec)           | Screen        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 391.2             | 414.3     | 402.7 | 404.3 | 387.0 | 390.3 | 399.7   |
|                     |               | SD        | 22.26             | 25.31     | 32.73 | 22.11 | 27.71 | 21.96 | 26.40   |
|                     |               | Minimum   | 358               | 392       | 352   | 372   | 342   | 356   | 342     |
|                     |               | Median    | 388.0             | 405.0     | 401.0 | 407.0 | 388.0 | 395.0 | 397.0   |
|                     |               | Maximum   | 426               | 448       | 454   | 434   | 424   | 422   | 454     |
|                     | Baseline      | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 391.9             | 413.7     | 412.7 | 417.0 | 408.7 | 390.0 | 408.4   |
|                     |               | SD        | 21.43             | 20.57     | 20.62 | 19.46 | 27.76 | 23.19 | 23.06   |
|                     |               | Minimum   | 358               | 390       | 376   | 380   | 376   | 370   | 370     |
|                     |               | Median    | 392.0             | 411.0     | 416.0 | 424.0 | 406.0 | 383.0 | 413.0   |
|                     |               | Maximum   | 436               | 446       | 438   | 432   | 456   | 432   | 456     |
|                     | Day 1, Hour 1 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 412.4             | 434.2     | 422.0 | 422.8 | 420.3 | 425.2 | 424.9   |
|                     |               | SD        | 14.77             | 24.19     | 25.65 | 17.59 | 25.24 | 11.82 | 20.65   |
|                     |               | Minimum   | 390               | 413       | 372   | 392   | 386   | 409   | 372     |
|                     |               | Median    | 412.0             | 425.0     | 430.5 | 427.5 | 419.5 | 426.5 | 426.5   |
|                     |               | Maximum   | 445               | 475       | 443   | 438   | 460   | 438   | 475     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.12 12-Lead Electrocardiogram Summary (Safety Population)

| Measurement (units) | Time Point    | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|---------------------|---------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                     |               |           |                   | A         | B     | C     | D     | E     |         |
| QT (msec)           | Day 1, Hour 6 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 389.6             | 412.3     | 398.3 | 401.5 | 396.8 | 399.0 | 401.6   |
|                     |               | SD        | 24.52             | 23.57     | 19.69 | 10.54 | 19.13 | 18.38 | 18.31   |
|                     |               | Minimum   | 347               | 390       | 368   | 385   | 375   | 379   | 368     |
|                     |               | Median    | 394.5             | 404.5     | 400.5 | 404.0 | 390.0 | 395.5 | 402.0   |
|                     |               | Maximum   | 426               | 456       | 421   | 415   | 425   | 421   | 456     |
|                     | Day 2         | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 411.7             | 428.7     | 426.0 | 412.0 | 413.5 | 408.2 | 417.7   |
|                     |               | SD        | 14.98             | 23.01     | 24.03 | 17.36 | 18.58 | 16.39 | 20.42   |
|                     |               | Minimum   | 387               | 406       | 379   | 392   | 393   | 388   | 379     |
|                     |               | Median    | 415.0             | 423.0     | 431.5 | 412.5 | 410.5 | 406.5 | 413.5   |
|                     |               | Maximum   | 433               | 464       | 449   | 429   | 448   | 435   | 464     |
|                     | Day 3         | n         | 9                 | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 398.9             | 418.7     | 415.7 | 411.0 | 405.0 | 404.0 | 410.9   |
|                     |               | SD        | 13.20             | 24.09     | 16.71 | 19.67 | 20.89 | 17.84 | 19.47   |
|                     |               | Minimum   | 380               | 394       | 392   | 382   | 372   | 384   | 372     |
|                     |               | Median    | 398.0             | 417.0     | 415.0 | 413.0 | 404.0 | 399.0 | 410.0   |
|                     |               | Maximum   | 424               | 456       | 436   | 434   | 434   | 432   | 456     |
|                     | End of Study  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 407.9             | 418.0     | 416.3 | 401.3 | 414.3 | 392.0 | 408.4   |
|                     |               | SD        | 17.09             | 19.72     | 35.49 | 16.95 | 29.70 | 16.83 | 25.30   |
|                     |               | Minimum   | 388               | 400       | 344   | 374   | 384   | 376   | 344     |
|                     |               | Median    | 402.0             | 411.0     | 430.0 | 405.0 | 408.0 | 384.0 | 408.0   |
|                     |               | Maximum   | 434               | 454       | 434   | 424   | 460   | 418   | 460     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.12 12-Lead Electrocardiogram Summary (Safety Population)

| Measurement (units) | Time Point    | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|---------------------|---------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                     |               |           |                   | A         | B     | C     | D     | E     |         |
| QTcF (msec)         | Screen        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 410.2             | 416.0     | 417.2 | 409.5 | 409.7 | 403.0 | 411.1   |
|                     |               | SD        | 10.86             | 14.23     | 16.90 | 9.73  | 13.41 | 14.60 | 13.98   |
|                     |               | Minimum   | 396               | 402       | 391   | 393   | 390   | 385   | 385     |
|                     |               | Median    | 412.0             | 414.0     | 416.0 | 410.0 | 409.5 | 403.5 | 413.0   |
|                     |               | Maximum   | 424               | 442       | 444   | 419   | 429   | 424   | 444     |
|                     | Baseline      | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 407.6             | 418.0     | 425.0 | 412.3 | 416.5 | 401.5 | 414.7   |
|                     |               | SD        | 17.83             | 10.64     | 16.17 | 13.34 | 16.63 | 11.78 | 15.13   |
|                     |               | Minimum   | 384               | 406       | 401   | 398   | 396   | 389   | 389     |
|                     |               | Median    | 409.0             | 415.5     | 424.5 | 413.0 | 419.0 | 399.5 | 415.0   |
|                     |               | Maximum   | 438               | 434       | 448   | 430   | 438   | 417   | 448     |
|                     | Day 1, Hour 1 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 410.7             | 417.8     | 422.2 | 410.7 | 412.8 | 419.2 | 416.5   |
|                     |               | SD        | 15.58             | 15.84     | 18.90 | 6.71  | 19.14 | 7.57  | 14.28   |
|                     |               | Minimum   | 386               | 403       | 388   | 403   | 394   | 407   | 388     |
|                     |               | Median    | 412.5             | 412.5     | 427.0 | 410.0 | 410.5 | 420.5 | 415.5   |
|                     |               | Maximum   | 429               | 440       | 444   | 421   | 447   | 427   | 447     |
|                     | Day 1, Hour 6 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 404.9             | 412.3     | 411.3 | 402.7 | 405.2 | 401.3 | 406.6   |
|                     |               | SD        | 15.54             | 16.39     | 15.88 | 9.33  | 14.40 | 13.71 | 13.92   |
|                     |               | Minimum   | 383               | 393       | 384   | 390   | 392   | 383   | 383     |
|                     |               | Median    | 407.5             | 409.5     | 416.0 | 403.5 | 400.0 | 398.0 | 404.0   |
|                     |               | Maximum   | 426               | 432       | 426   | 412   | 426   | 421   | 432     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.12 12-Lead Electrocardiogram Summary (Safety Population)

| Measurement (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|---------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                     |              |           |                   | A         | B     | C     | D     | E     |         |
| QTcF (msec)         | Day 2        | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |              | Mean      | 411.0             | 416.2     | 423.8 | 403.3 | 410.7 | 400.3 | 410.9   |
|                     |              | SD        | 17.35             | 14.34     | 19.59 | 11.13 | 13.05 | 11.93 | 15.88   |
|                     |              | Minimum   | 372               | 394       | 393   | 385   | 395   | 388   | 385     |
|                     |              | Median    | 419.0             | 415.0     | 430.0 | 406.0 | 411.0 | 397.5 | 410.0   |
|                     |              | Maximum   | 425               | 435       | 446   | 414   | 430   | 423   | 446     |
|                     | Day 3        | n         | 9                 | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |              | Mean      | 408.9             | 413.2     | 420.0 | 409.3 | 404.2 | 399.0 | 409.1   |
|                     |              | SD        | 13.47             | 15.60     | 15.75 | 9.54  | 16.19 | 14.56 | 15.37   |
|                     |              | Minimum   | 382               | 396       | 400   | 396   | 387   | 385   | 385     |
|                     |              | Median    | 411.0             | 409.5     | 425.0 | 411.5 | 401.0 | 395.0 | 409.0   |
|                     |              | Maximum   | 425               | 432       | 435   | 421   | 432   | 417   | 435     |
|                     | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |              | Mean      | 411.2             | 419.8     | 425.0 | 405.7 | 420.0 | 402.2 | 414.5   |
|                     |              | SD        | 10.23             | 19.59     | 18.29 | 10.05 | 22.18 | 11.84 | 18.24   |
|                     |              | Minimum   | 393               | 392       | 391   | 394   | 397   | 386   | 386     |
|                     |              | Median    | 410.0             | 421.5     | 428.0 | 405.5 | 418.5 | 402.5 | 409.5   |
|                     |              | Maximum   | 427               | 441       | 446   | 423   | 455   | 416   | 455     |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.13 12-Lead Electrocardiogram Change From Baseline (Safety Population)

| Measurement (units) | Time Point    | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|---------------------|---------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                     |               |           |                   | A         | B    | C    | D    | E    |         |
| Heart Rate (bpm)    | Day 1, Hour 1 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                     |               | Mean      | -8.4              | -9.0      | -5.3 | -3.0 | -7.7 | -8.5 | -6.7    |
|                     |               | SD        | 4.53              | 8.85      | 2.66 | 1.41 | 9.58 | 5.86 | 6.48    |
|                     |               | Minimum   | -17               | -22       | -9   | -5   | -22  | -16  | -22     |
|                     |               | Median    | -8.5              | -5.5      | -4.5 | -3.0 | -4.0 | -8.0 | -4.0    |
|                     |               | Maximum   | -1                | -1        | -2   | -1   | 2    | -1   | 2       |
|                     | Day 1, Hour 6 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                     |               | Mean      | 0.2               | -2.3      | 0.5  | 2.3  | -0.7 | -4.7 | -1.0    |
|                     |               | SD        | 10.14             | 7.26      | 6.22 | 5.47 | 9.31 | 6.83 | 7.06    |
|                     |               | Minimum   | -20               | -13       | -5   | -3   | -14  | -15  | -15     |
|                     |               | Median    | 0.0               | 1.0       | 0.0  | 1.0  | 4.0  | -4.5 | 0.5     |
|                     |               | Maximum   | 18                | 4         | 12   | 10   | 7    | 3    | 12      |
|                     | Day 2         | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                     |               | Mean      | -8.1              | -7.5      | -6.3 | -1.8 | -5.7 | -9.3 | -6.1    |
|                     |               | SD        | 11.20             | 9.99      | 3.93 | 4.67 | 7.15 | 8.07 | 7.07    |
|                     |               | Minimum   | -24               | -22       | -12  | -10  | -17  | -23  | -23     |
|                     |               | Median    | -7.0              | -3.5      | -6.5 | -1.0 | -3.5 | -9.5 | -4.5    |
|                     |               | Maximum   | 10                | 2         | 0    | 4    | 1    | 1    | 4       |
|                     | Day 3         | n         | 9                 | 6         | 6    | 6    | 6    | 6    | 30      |
|                     |               | Mean      | -3.8              | -4.7      | -3.7 | 1.3  | -4.8 | -8.3 | -4.0    |
|                     |               | SD        | 6.91              | 10.54     | 3.93 | 2.66 | 8.18 | 7.20 | 7.32    |
|                     |               | Minimum   | -12               | -19       | -9   | -2   | -15  | -16  | -19     |
|                     |               | Median    | -5.0              | -1.0      | -3.0 | 1.5  | -4.5 | -9.0 | -2.0    |
|                     |               | Maximum   | 8                 | 8         | 2    | 4    | 6    | 0    | 8       |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.13 12-Lead Electrocardiogram Change From Baseline (Safety Population)

| Measurement (units) | Time Point    | Statistic | Pooled<br>Placebo | Treatment |      |      |      |      | Overall |
|---------------------|---------------|-----------|-------------------|-----------|------|------|------|------|---------|
|                     |               |           |                   | A         | B    | C    | D    | E    |         |
| Heart Rate (bpm)    | End of Study  | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                     |               | Mean      | -6.2              | -1.7      | -0.8 | 4.0  | -1.5 | -0.7 | -0.1    |
|                     |               | SD        | 7.45              | 5.72      | 8.04 | 6.54 | 8.55 | 5.43 | 6.81    |
|                     |               | Minimum   | -16               | -9        | -6   | -6   | -18  | -8   | -18     |
|                     |               | Median    | -9.0              | -0.5      | -3.5 | 5.0  | 1.0  | -1.0 | -1.0    |
|                     |               | Maximum   | 7                 | 5         | 15   | 11   | 5    | 5    | 15      |
| PR (msec)           | Day 1, Hour 1 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                     |               | Mean      | 3.7               | 6.3       | 1.0  | -2.2 | 0.3  | 6.0  | 2.3     |
|                     |               | SD        | 9.56              | 8.41      | 5.51 | 9.77 | 4.23 | 5.02 | 7.26    |
|                     |               | Minimum   | -9                | -3        | -9   | -21  | -6   | 1    | -21     |
|                     |               | Median    | 2.0               | 4.0       | 1.5  | 0.0  | 0.5  | 6.0  | 2.0     |
|                     |               | Maximum   | 17                | 20        | 6    | 7    | 6    | 13   | 20      |
|                     | Day 1, Hour 6 | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                     |               | Mean      | 2.7               | -3.0      | -5.0 | -4.2 | -1.7 | 1.2  | -2.5    |
|                     |               | SD        | 10.24             | 12.35     | 6.36 | 7.65 | 6.77 | 7.00 | 8.03    |
|                     |               | Minimum   | -12               | -18       | -15  | -14  | -11  | -8   | -18     |
|                     |               | Median    | 2.5               | -2.0      | -3.5 | -2.5 | 1.0  | 1.5  | -1.5    |
|                     |               | Maximum   | 26                | 15        | 1    | 4    | 6    | 8    | 15      |
|                     | Day 2         | n         | 10                | 6         | 6    | 6    | 6    | 6    | 30      |
|                     |               | Mean      | 4.5               | -1.0      | 4.2  | -1.0 | -0.8 | 5.0  | 1.3     |
|                     |               | SD        | 7.91              | 9.78      | 5.23 | 4.69 | 3.31 | 6.32 | 6.44    |
|                     |               | Minimum   | -6                | -15       | -2   | -8   | -7   | -1   | -15     |
|                     |               | Median    | 2.5               | 0.0       | 4.0  | 0.5  | -0.5 | 3.0  | 0.5     |
|                     |               | Maximum   | 16                | 9         | 11   | 5    | 2    | 13   | 13      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.13 12-Lead Electrocardiogram Change From Baseline (Safety Population)

| Measurement (units) | Time Point    | Statistic | Pooled<br>Placebo | Treatment |       |      |      |       | Overall |
|---------------------|---------------|-----------|-------------------|-----------|-------|------|------|-------|---------|
|                     |               |           |                   | A         | B     | C    | D    | E     |         |
| PR (msec)           | Day 3         | n         | 9                 | 6         | 6     | 6    | 6    | 6     | 30      |
|                     |               | Mean      | 5.0               | 6.3       | 4.3   | -1.0 | 2.3  | 2.3   | 2.9     |
|                     |               | SD        | 5.20              | 9.07      | 3.88  | 3.52 | 1.97 | 11.34 | 6.92    |
|                     |               | Minimum   | 0                 | -8        | 0     | -6   | 0    | -18   | -18     |
|                     |               | Median    | 4.0               | 11.0      | 5.0   | 0.0  | 2.0  | 5.0   | 2.0     |
|                     |               | Maximum   | 16                | 14        | 10    | 4    | 6    | 14    | 14      |
|                     | End of Study  | n         | 10                | 6         | 6     | 6    | 6    | 6     | 30      |
|                     |               | Mean      | 2.2               | 7.0       | 0.7   | -2.0 | 3.3  | 6.3   | 3.1     |
|                     |               | SD        | 8.51              | 4.86      | 11.50 | 7.59 | 6.53 | 7.94  | 8.18    |
|                     |               | Minimum   | -16               | 0         | -16   | -16  | -6   | -4    | -16     |
|                     |               | Median    | 1.0               | 7.0       | -1.0  | 0.0  | 2.0  | 6.0   | 3.0     |
|                     |               | Maximum   | 16                | 14        | 18    | 4    | 14   | 20    | 20      |
| QRS (msec)          | Day 1, Hour 1 | n         | 10                | 6         | 6     | 6    | 6    | 6     | 30      |
|                     |               | Mean      | 1.6               | 2.7       | 2.8   | 0.2  | 3.2  | 2.8   | 2.3     |
|                     |               | SD        | 6.29              | 5.54      | 6.11  | 3.92 | 7.03 | 7.36  | 5.79    |
|                     |               | Minimum   | -11               | -3        | -3    | -4   | -6   | -8    | -8      |
|                     |               | Median    | 2.0               | 0.5       | 1.5   | 0.0  | 3.5  | 1.5   | 1.0     |
|                     |               | Maximum   | 11                | 10        | 13    | 6    | 12   | 13    | 13      |
|                     | Day 1, Hour 6 | n         | 10                | 6         | 6     | 6    | 6    | 6     | 30      |
|                     |               | Mean      | 3.4               | 2.8       | 2.8   | 2.2  | -1.3 | -3.2  | 0.7     |
|                     |               | SD        | 8.44              | 2.86      | 5.38  | 6.18 | 4.89 | 4.92  | 5.25    |
|                     |               | Minimum   | -12               | 0         | -2    | -5   | -10  | -12   | -12     |
|                     |               | Median    | 5.5               | 2.5       | 1.0   | 0.0  | 0.0  | -2.0  | 0.0     |
|                     |               | Maximum   | 16                | 6         | 13    | 13   | 3    | 2     | 13      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.13 12-Lead Electrocardiogram Change From Baseline (Safety Population)

| Measurement (units) | Time Point    | Statistic | Pooled<br>Placebo | Treatment |      |       |      |       | Overall |
|---------------------|---------------|-----------|-------------------|-----------|------|-------|------|-------|---------|
|                     |               |           |                   | A         | B    | C     | D    | E     |         |
| QRS (msec)          | Day 2         | n         | 10                | 6         | 6    | 6     | 6    | 6     | 30      |
|                     |               | Mean      | 0.9               | 0.0       | 2.7  | 1.7   | 1.8  | -0.7  | 1.1     |
|                     |               | SD        | 6.77              | 4.52      | 6.53 | 5.01  | 4.17 | 3.33  | 4.66    |
|                     |               | Minimum   | -12               | -8        | -5   | -4    | -4   | -6    | -8      |
|                     |               | Median    | 0.0               | 0.5       | 2.5  | 0.0   | 2.0  | -0.5  | 0.5     |
|                     |               | Maximum   | 11                | 6         | 13   | 10    | 8    | 4     | 13      |
|                     | Day 3         | n         | 9                 | 6         | 6    | 6     | 6    | 6     | 30      |
|                     |               | Mean      | 0.0               | 2.0       | -1.0 | -1.7  | 1.3  | 1.7   | 0.5     |
|                     |               | SD        | 6.78              | 5.06      | 7.77 | 3.44  | 7.55 | 1.97  | 5.45    |
|                     |               | Minimum   | -14               | -2        | -12  | -6    | -4   | 0     | -12     |
|                     |               | Median    | 2.0               | 0.0       | -1.0 | -2.0  | -1.0 | 1.0   | 0.0     |
|                     |               | Maximum   | 6                 | 12        | 12   | 4     | 16   | 4     | 16      |
|                     | End of Study  | n         | 10                | 6         | 6    | 6     | 6    | 6     | 30      |
|                     |               | Mean      | 0.1               | 3.0       | 1.0  | -1.7  | 2.0  | 2.0   | 1.3     |
|                     |               | SD        | 5.51              | 6.54      | 7.97 | 4.27  | 9.47 | 9.12  | 7.34    |
|                     |               | Minimum   | -12               | -4        | -12  | -6    | -6   | -10   | -12     |
|                     |               | Median    | 1.5               | 2.0       | 2.0  | -2.0  | -1.0 | 2.0   | 0.0     |
|                     |               | Maximum   | 6                 | 14        | 12   | 4     | 20   | 18    | 20      |
| QT (msec)           | Day 1, Hour 1 | n         | 10                | 6         | 6    | 6     | 6    | 6     | 30      |
|                     |               | Mean      | 20.5              | 20.5      | 9.3  | 5.8   | 11.7 | 35.2  | 16.5    |
|                     |               | SD        | 10.66             | 24.22     | 7.79 | 14.19 | 6.35 | 16.96 | 17.81   |
|                     |               | Minimum   | 3                 | -8        | -4   | -11   | 4    | 6     | -11     |
|                     |               | Median    | 24.0              | 19.0      | 11.5 | 6.5   | 9.5  | 39.5  | 12.0    |
|                     |               | Maximum   | 32                | 52        | 18   | 25    | 22   | 55    | 55      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.13 12-Lead Electrocardiogram Change From Baseline (Safety Population)

| Measurement (units) | Time Point    | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|---------------------|---------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                     |               |           |                   | A         | B     | C     | D     | E     |         |
| QT (msec)           | Day 1, Hour 6 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | -2.3              | -1.3      | -14.3 | -15.5 | -11.8 | 9.0   | -6.8    |
|                     |               | SD        | 19.48             | 17.13     | 14.77 | 10.80 | 12.46 | 16.11 | 16.44   |
|                     |               | Minimum   | -42               | -19       | -37   | -27   | -31   | -12   | -37     |
|                     |               | Median    | -3.5              | -2.5      | -12.5 | -18.5 | -7.5  | 7.0   | -11.0   |
|                     |               | Maximum   | 25                | 22        | 7     | 5     | -1    | 37    | 37      |
|                     | Day 2         | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 19.8              | 15.0      | 13.3  | -5.0  | 4.8   | 18.2  | 9.3     |
|                     |               | SD        | 24.07             | 26.65     | 14.87 | 22.50 | 11.51 | 10.42 | 19.03   |
|                     |               | Minimum   | -7                | -15       | -7    | -34   | -8    | 3     | -34     |
|                     |               | Median    | 18.0              | 13.0      | 12.5  | 1.5   | 5.5   | 19.5  | 12.0    |
|                     |               | Maximum   | 58                | 47        | 35    | 18    | 17    | 32    | 47      |
|                     | Day 3         | n         | 9                 | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 7.2               | 5.0       | 3.0   | -6.0  | -3.7  | 14.0  | 2.5     |
|                     |               | SD        | 16.34             | 25.07     | 15.32 | 18.37 | 13.82 | 16.88 | 18.46   |
|                     |               | Minimum   | -12               | -24       | -20   | -28   | -22   | -4    | -28     |
|                     |               | Median    | 8.0               | 0.0       | 5.0   | -4.0  | -1.0  | 11.0  | 2.0     |
|                     |               | Maximum   | 27                | 36        | 18    | 14    | 12    | 34    | 36      |
|                     | End of Study  | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 16.0              | 4.3       | 3.7   | -15.7 | 5.7   | 2.0   | 0.0     |
|                     |               | SD        | 13.47             | 11.76     | 20.68 | 25.69 | 9.24  | 10.88 | 17.65   |
|                     |               | Minimum   | -8                | -12       | -32   | -56   | -4    | -14   | -56     |
|                     |               | Median    | 17.0              | 4.0       | 12.0  | -19.0 | 5.0   | 5.0   | 5.0     |
|                     |               | Maximum   | 32                | 18        | 22    | 12    | 22    | 12    | 22      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.13 12-Lead Electrocardiogram Change From Baseline (Safety Population)

| Measurement (units) | Time Point    | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|---------------------|---------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                     |               |           |                   | A         | B     | C     | D     | E     |         |
| QTcF (msec)         | Day 1, Hour 1 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 3.1               | -0.2      | -2.8  | -1.7  | -3.7  | 17.7  | 1.9     |
|                     |               | SD        | 10.55             | 9.89      | 10.34 | 12.47 | 14.79 | 11.83 | 13.78   |
|                     |               | Minimum   | -9                | -13       | -18   | -18   | -30   | 3     | -30     |
|                     |               | Median    | 0.0               | -1.0      | 0.5   | 3.0   | 2.5   | 18.5  | 3.0     |
|                     |               | Maximum   | 17                | 15        | 8     | 10    | 9     | 31    | 31      |
|                     | Day 1, Hour 6 | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | -2.7              | -5.7      | -13.7 | -9.7  | -11.3 | -0.2  | -8.1    |
|                     |               | SD        | 9.82              | 9.52      | 5.92  | 11.74 | 14.84 | 7.25  | 10.76   |
|                     |               | Minimum   | -18               | -13       | -22   | -24   | -26   | -6    | -26     |
|                     |               | Median    | -2.5              | -9.0      | -13.0 | -9.0  | -12.0 | -4.0  | -7.0    |
|                     |               | Maximum   | 15                | 12        | -4    | 5     | 12    | 11    | 12      |
|                     | Day 2         | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 3.4               | -1.8      | -1.2  | -9.0  | -5.8  | -1.2  | -3.8    |
|                     |               | SD        | 14.74             | 7.73      | 12.34 | 16.09 | 4.92  | 8.38  | 10.37   |
|                     |               | Minimum   | -14               | -12       | -19   | -34   | -12   | -17   | -34     |
|                     |               | Median    | 2.0               | 0.0       | -1.0  | -5.0  | -6.0  | 0.5   | -2.0    |
|                     |               | Maximum   | 31                | 8         | 12    | 6     | 2     | 6     | 12      |
|                     | Day 3         | n         | 9                 | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |               | Mean      | 0.0               | -4.8      | -5.0  | -3.0  | -12.3 | -2.5  | -5.5    |
|                     |               | SD        | 11.02             | 9.81      | 12.93 | 16.63 | 10.78 | 5.99  | 11.50   |
|                     |               | Minimum   | -14               | -15       | -25   | -19   | -31   | -14   | -31     |
|                     |               | Median    | 4.0               | -5.0      | -0.5  | -6.0  | -10.0 | 0.0   | -4.0    |
|                     |               | Maximum   | 15                | 12        | 10    | 23    | 0     | 2     | 23      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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Table 14.3.5.13 12-Lead Electrocardiogram Change From Baseline (Safety Population)

| Measurement (units) | Time Point   | Statistic | Pooled<br>Placebo | Treatment |       |       |       |       | Overall |
|---------------------|--------------|-----------|-------------------|-----------|-------|-------|-------|-------|---------|
|                     |              |           |                   | A         | B     | C     | D     | E     |         |
| QTcF (msec)         | End of Study | n         | 10                | 6         | 6     | 6     | 6     | 6     | 30      |
|                     |              | Mean      | 3.6               | 1.8       | 0.0   | -6.7  | 3.5   | 0.7   | -0.1    |
|                     |              | SD        | 12.36             | 11.72     | 13.07 | 16.35 | 18.26 | 10.60 | 13.73   |
|                     |              | Minimum   | -19               | -14       | -22   | -36   | -24   | -6    | -36     |
|                     |              | Median    | 6.0               | 0.5       | 6.5   | 0.5   | 2.0   | -3.0  | 0.5     |
|                     |              | Maximum   | 25                | 21        | 10    | 9     | 29    | 22    | 29      |

Note: Baseline is the last predose measurement.

Treatment A: A single IV infusion of 0.003 mg/kg cP12 over approximately 30 minutes (Cohort 1)

Treatment B: A single IV infusion of 0.01 mg/kg cP12 over approximately 30 minutes (Cohort 2)

Treatment C: A single IV infusion of 0.02 mg/kg cP12 over approximately 30 minutes (Cohort 3)

Treatment D: A single IV infusion of 0.04 mg/kg cP12 over approximately 30 minutes (Cohort 4)

Treatment E: A single IV infusion of 0.08 mg/kg cP12 over approximately 30 minutes (Cohort 5)

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## ATTACHMENT 4



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring, MD 20993

IND 112487

**GRANT FAST TRACK**

NeoMatrix Therapeutics, Inc.  
c/o B&H Consulting Services, Inc  
Rosalind Hafen, RAC  
50 Division Street, Suite 206  
Somerville, NJ 08876

Dear Ms. Hafen:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for cP12.

We also refer to your March 15, 2019, request for Fast Track designation. We have reviewed your request and concluded that it meets the criteria for the Fast Track designation. Therefore, we are designating as a Fast Track development program the investigation of cP12 as treatment to limit burn injury progression of acute, deep dermal burns in hospitalized patients. Please note that if the clinical development program you pursue does not continue to meet the criteria for Fast Track designation, the application will not be reviewed under the Fast Track program.

For further information regarding Fast Track Drug Development Programs, please refer to the FDA document "Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics"<sup>1</sup>. This document may be requested from the Office of Communications, Division of Drug Information at 301-796-3400 or 1-888-463-6332.

We remind you that under section 561A(f)(2) of the FD&C Act<sup>2</sup>, you are required to make your expanded access policy for cP12 publicly available within 15 days of the signature date of this letter. For further information regarding how to make your expanded access policy publicly available, you may visit our expanded access webpage on FDA.gov at <https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/ucm429687.htm#IndustryRole>.

<sup>1</sup> <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf>

<sup>2</sup> §360bbb-0



If you have any questions, contact Jennifer Harmon, Regulatory Project Manager, at 240-402-4880.

Sincerely,

*{See appended electronic signature page}*

Kendall A. Marcus, MD  
Director  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
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/s/  
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KENDALL A MARCUS  
05/06/2019 01:24:26 PM

## ATTACHMENT 5

IND 112487

## MEETING MINUTES

NeoMatrix Therapeutics, Inc.  
c/o B&H Consulting Services, Inc.  
Attention: Rosalind Hafen, MA, RAC  
Director, CMC and Regulatory Affairs  
50 Division Street, Suite 206  
Somerville, NJ 08876

Dear Ms. Hafen:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for cP12 injection (fibronectin-derived, cyclic 14-mer peptide).

We also refer to the teleconference between representatives of your firm and the FDA on June 28, 2021. The purpose of the meeting was to discuss your planned Phase 2a clinical study protocol.

A copy of the official minutes of the meeting/telecon is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Jennifer Harmon, Regulatory Project Manager at 240-402-4880.

Sincerely,

*{See appended electronic signature page}*

Shari Targum, MD, MPH, FACP, FACC  
Deputy Director  
Division of Dermatology and Dentistry  
Office of Immunology and Inflammation  
Office of New Drugs  
Center for Drug Evaluation and Research

Enclosure:

- Meeting Minutes



## MEMORANDUM OF MEETING MINUTES

**Meeting Type:** B  
**Meeting Category:** End of Phase 1

**Meeting Date and Time:** June 28, 2021 9:30 a.m. -10:00a.m. ET  
**Meeting Location:** Teleconference

**Application Number:** IND 112487

**Product Name:** cP12 injection (fibronectin-derived, cyclic 14-mer peptide)

**Proposed Indication:** To limit burn injury progression, to shorten healing time and reduce scarring of acute, deep second degree burns in hospitalized patients

**Sponsor Name:** NeoMatrix Therapeutics, Inc.  
**Regulatory Pathway:** 505(b)(1) of the Federal Food, Drug, and Cosmetic Act

**Meeting Chair:** Shari Targum  
**Meeting Recorder:** Jennifer Harmon

### FDA ATTENDEES

Gordana Diglisic, MD, Clinical Team Leader, DDD  
Kapil (Dev) Verma, MD, Clinical Reviewer, DDD  
Mohamed Alesh, PhD, Biometrics Team Leader, Division of Biometrics III  
Chinmay Shukla, PhD, Clinical Pharmacology Scientific Lead, Division of Inflammation and Immune Pharmacology (DIIP)  
Luke Oh, PhD, PhD, Clinical Pharmacology Reviewer, DIIP  
Barbara Hill, PhD, Pharmacology Supervisor, Division of Pharmacology Toxicology for Immunology and Inflammation (DPT – II)  
Jianying (Jerry) Wang, PhD, Pharmacology Reviewer, DPT – II  
Jennifer Harmon, PharmD, Regulatory Health Project Manager, Division of Regulatory Operations for Dermatology and Dentistry (DRO – DD)

### SPONSOR ATTENDEES

Richard A. Clark, MD, President  
Jzaneen Lalani, JD, Acting Chief Operating Officer  
Leopoldo “Lee” Cancio, MD, U.S. Army Institute of Surgical Research Burn Center Director  
James H. Holmes IV, MD, Professor of Surgery & Burn Center Chief, Wake Forest Hospital

Adam J. Singer, MD, Professor & Vice Chair for Research, Emergency Medicine  
Department, Stony Brook Medical Center  
Susan Szambelan, Clinical Operations Consultant for NeoMatrix Therapeutics  
Linda Fossati Wood, MedWrite, Inc., Clinical Consultant  
Caron Shake, PhD, CDR US Navy (RET.) Government Liaison, Director Contracting  
Rosalind Hafen, Regulatory Agent, B&H Consulting Services, Inc.  
Kristina Carroll, Regulatory Consultant, B&H Consulting Services, Inc.

## 1.0 BACKGROUND

The purpose of this meeting is to discuss the planned Phase 2a clinical study protocol for cP12 injection. FDA sent Preliminary Comments to NeoMatrix Therapeutics, Inc. on June 24, 2021.

### Coronavirus 19 (COVID-19) Clinical Trial Guidance

During the COVID-19 pandemic, ensuring the safety of trial participants is paramount. Sponsors should consider each circumstance, focus on the potential impact on the safety of trial participants, and modify study conduct accordingly. It is critical that trial participants are kept informed of changes to the study and monitoring plans that could impact them, and that the Agency is appropriately informed of these changes. Refer to the FDA guidance on *Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency*. We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

### Regulatory Correspondence History:

We have had the following meetings/teleconferences with you:

September 28, 2016 — Guidance Type C

August 17, 2011 — Pre-IND Type B

We have sent the following correspondences:

May 6, 2019 — Grant Fast Track

October 20, 2017 — Study May Proceed

September 21, 2011 — Advice

## 2.0 DISCUSSION

### Introductory Clinical Comments:

The Sponsor is developing cP12 (fibronectin-derived, cyclic 14-mer peptide) intravenous infusion, for the indication(s), “to limit burn injury progression, to shorten healing time (defined as the time until complete re-epithelization/wound closure) and reduce scarring of acute, deep second degree burns in hospitalized patients” via a

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505(b)(1) regulatory pathway. This application has been granted Fast Track and Orphan designation.

- A first-in-human (FIH) Phase 1 trial (NMT-16-01) has been completed, which was a randomized double-blind, placebo-controlled single ascending dose (placebo and five drug arms with dose ranges from 0.003 mg/kg – 0.08 mg/kg) trial to evaluate the safety, tolerability, and pharmacokinetics (PK) profile of cP12 in 40 healthy male and female subjects. Mean half-life ranged between 0.1235 and 1.480 hours and increased as dose increased. There were no deaths, serious adverse events, or subject discontinuations due to adverse events (AEs). The most common AEs were “pruritus, feeling hot, and flushing,” each experienced by 4 (13%) subjects at the higher dose levels, and headache also experienced by 4 (13%) subjects. One subject experienced increased serum creatinine kinase.
- Based on the clinical data from the Phase 1 trial conducted in healthy subjects and available nonclinical data, the Sponsor is planning a Phase 2a “proof-of-concept” trial (NMT-16-02), “A Phase 2a, Randomized, Double-Blind, Placebo-Controlled, Single Ascending Dose, Multicenter Study to Examine Safety, Tolerability, Efficacy, and Pharmacokinetics of cP12 in Otherwise Healthy Adults with 5% to 19% Total Body Surface Area Burns.” The plan is to enroll 48 subjects with “deep second-degree burns” in up to 8 sites in the United States. Subjects will be randomized to receive either cP12 or placebo (0.9% sodium chloride) within each cohort of 12 subjects: 10 subjects will receive cP12 and 2 subjects will receive placebo. Doses of cP12 will be 0.003 mg/kg for Cohort 1, 0.01 mg/kg for Cohort 2, or 0.03 mg/kg for Cohort 3. Trial drug will be administered over 30 minutes by IV infusion within 2 to 6 hours post burn. Cohorts will be studied sequentially starting with the lowest cP12 dose, and dose escalation will only occur after review by the Principal Investigator, Sponsor, Data Safety Monitoring Board and the Independent Medical Monitor. After an interim analysis of data from Cohorts 1 to 3, twelve subjects (10 to receive cP12 and 2 to receive placebo) will be enrolled in Cohort 4 at the optimal dose. Duration of participation in this clinical trial will be approximately 12 weeks for each subject.

**Trial objectives:**

- Primary objective: to assess the safety and tolerability of single ascending IV doses of cP12 in otherwise healthy adults with 5% to 19% TBSA burns.
- Secondary objectives: to evaluate cP12 efficacy via the proportion of subjects who achieve wound closure within 3 weeks post burn of a selected burn site based on visual assessment, and recorded via photography, and to evaluate the PK profile of cP12 after single ascending IV doses in otherwise healthy adults.

**Safety and Efficacy:**

- The proposed safety endpoints include analysis of TEAEs, AEs, laboratory values, vital signs, physical exams, and ECG data. Local dermal safety assessments are not specified in the proposed protocol.

- The proposed efficacy endpoints include PK parameters and “wound closure,” which are defined as “95% epithelialization, with a dressing that is needed only to protect the wound, not to heal the wound. Wound closure within 3 weeks post burn of a selected burn site based on visual assessment (with photographs), and confirmed 2 weeks thereafter, will be considered to have met the objective for closure.”
- The proposed exploratory endpoints include “assessing Forward Looking Infrared imaging (FLIR) as a predictor of depth of injury,” using transepidermal water loss (TEWL) to “ascertain whether decreased water loss is associated with a closed wound,” pain assessment using a visual assessment scale of 0-10, cytokine profile of IL-1 $\beta$ , IL-6, IL-8 levels, wound closure stability assessed for 2 weeks after closure, time to wound closure, ~~and depth of injury by histologic evaluation (4mm optional punch biopsy performed at 24 hours post burn).~~

## 2.1. Clinical/Biostatistics

### **Question 1:**

Does the Agency agree that the design of the Phase 2a study (NMT-16-02) is appropriate for assessment of safety, tolerability, efficacy, and pharmacokinetics of cP12 infusion in the proposed patient population?

### **FDA Response to Question 1:**

- You should clarify the indication you are seeking for your drug product. Per 21CFR 201.57(c), a drug can be indicated for the treatment, prevention, mitigation, cure or diagnosis of a recognized disease or condition, or for the relief of symptoms associated with a recognized disease or condition. We recommend that you adequately define the condition under treatment and targeted patient population before deciding on the efficacy endpoints, statistical analysis plan, and other features of trial design. In your meeting package, you discuss use of your product “to limit burn injury progression, to shorten healing time and reduce scarring of acute, deep second degree burns in hospitalized patients.” However, in the protocol synopsis it appears that your primary efficacy endpoint is focused on “wound closure within 3 weeks post deep second degree burns.”
  - o Clinically meaningful endpoints for wounds include improved wound healing such as incidence of complete wound closure.
  - o Regarding “reduction of scarring,” you should address whether you intend the product to (1) reduce the risk of pathologic scar formation (with specification of the type of pathologic scar, e.g.: hypertrophic scars, keloids, atrophic, etc.) or (2) reduce the severity of scarring. These are two distinct claims that would need to be independently assessed with appropriate scales.



It is important that you identify an appropriate trial population and reach agreement with Agency regarding measures and endpoints that meaningfully and reliably assess the treatment effect of your product.

- You should modify your protocol to include local dermal safety active assessments (for e.g.: erythema, edema, vesiculation) using separate acceptable scales.
- You propose a final assessment at Week 12. For this early Phase 2a “proof-of-concept” trial, which is primarily focused on pharmacokinetics and safety, this trial duration is acceptable. However, 12 weeks would be too soon to evaluate scarring outcomes, for which primary endpoint assessment is typically performed at 12 months.
- You plan to include subjects with “at least 1 deep second degree burn” and select a “target burn” for each subject for analyses. The location of the burns should be clearly documented, since burns on areas of thicker skin (e.g.: back) will likely heal faster than burns on areas of thinner skin (e.g.: ventral forearm). We agree with your exclusion of burns isolated to the face, ears, hands, feet, and genitalia. However, since your product is systemically administered, evaluation of all intra-subject burn wounds for safety and treatment effect should be performed.
- In your proposed protocol, all subjects should receive standard-of-care. The standard-of-care (SOC) for burn wounds should address specific elements of nutrition, pain control, rehabilitation, as well as any debridement surgically or chemically. All elements of the SOC should be reported in the case report forms. We refer you to the guidance for industry: *Chronic Cutaneous Ulcer and Burn Wounds - Developing Products for Treatment*. Your proposed plan that “The clinical site may use any dressing of its choosing with the exception of Silvadene, and may change the dressings as needed” is vague and should be clarified. Several professional groups have initiated development of care guidelines for burns. The Agency does not require adherence to any specific guidelines, the basic principle being that standard care regimens in wound-treatment product trials should optimize conditions for healing and be prospectively defined in the protocol. The rationale for the standard of care chosen should be included in the protocol, and the trial plan should be of sufficient detail for consistent and uniform application across trial centers. The value of trial site consistency in standard care regimens within a trial cannot be over emphasized because of the effects these procedures have on clinical outcome for burns and chronic wounds. Consistency in standard of care regimens is important for minimizing variability and allowing assessment of treatment effect. It may be reasonable to evaluate a single standard care regimen in early trials to minimize this variability.

### **Meeting Discussion:**

The Sponsor clarified that their standard of care dressings will include moist dressings. The Agency stated that the standard of care including dressings should be clearly

documented in the Case Report Forms (e.g.: because silver-containing dressings may impact safety and efficacy outcomes).

**Question 2:**

Does the Agency agree with the proposed inclusion criterion for TBSA thermal burns of 5% to 19% (inclusive) coupled with the proposed exclusion criteria to limit potential variability in the study?

**FDA Response to Question 2:**

- **No, we do not agree.** We reiterate guidance we gave you at the Type C Guidance Meeting on September 28, 2016, “Enrollment of subjects with a wide range of TBSA thermal burns (5 to 20%) may make it more difficult to demonstrate a treatment effect in the proof-of-concept study, because of the variability in the study population. Your product is systemically administered and could therefore potentially impact wounds beyond any ‘target’ lesion, including donor sites. **You have no clinical evidence supporting the safety and/or efficacy of your product in the treatment of burns.** Therefore, for initial study of the investigational product in affected individuals, we recommend that you limit enrollment to those with one thermal burn involving  $\leq$  5% BSA involvement and that subjects be otherwise healthy. We note that data from your proposed ascending single-dose study may provide some support for enrollment of subjects with TBSA burns larger than 5% BSA.”

We acknowledge your concern that “enrollment of subjects with  $\leq$  5% TBSA would severely limit eligible subjects, and therefore extend study enrollment or require a much larger number of investigational sites.” However, since your product is systemically administered and has not previously been studied in human subjects with burns, **we reiterate our initial recommendation for your Phase 2a “proof-of-concept” trial.**

**Meeting Discussion:**

The Sponsor clarified that they would like to include subjects with up to 19% TBSA non-target burns in their protocol, and that they would plan on including  $\leq$  5% target-burns. The Agency indicated that because this is the first study in subjects with burns and because the product is systemically administered, all burns including the non-target burns should be limited to  $\leq$  5% TBSA inclusion area prior to studying subjects with larger burn areas. **The Sponsor proposed a stepwise cohort approach in which they will plan to enroll 5-10 subjects in a first cohort for  $\leq$  5% TBSA burns, having an independent safety data monitoring board review this data, and then proceed. The Agency stated the Sponsor should submit their proposal in a protocol for review.**

- You should specify the method by which you will determine the extent of BSA involvement (e.g. rule of nines, Lund and Browder chart). You should state what percent BSA you will consider the palm to represent (0.5% or 1%) and whether this would or would not be inclusive of the fingers.

- Your inclusion criteria include subjects “able to be infused with the study drug within 2 to 6 hours post burn.” Since burns are dynamic injuries and may evolve in depth over the first several hours of injury, the time post-burn that subjects receive the drug should be clearly documented as this timing may affect your efficacy results.

**Question 3:**

Does the Agency agree with the proposed single dose of cP12?

**FDA Response to Question 3:**

You proposed three doses of 0.003 mg/kg, 0.01 mg/kg, and 0.03 mg/kg single IV infusion in the proposed Phase 2a trial. We acknowledge that your proposed doses were within the range of doses evaluated in Phase 1 trial. Your proposed doses and dose escalation/stopping criteria appear reasonable.

In addition, we reiterate previous guidance to you, that evaluation of immunogenicity after a rechallenge of CP12 at approximately one (1) month should be assessed during development.

**Question 4:**

Does the Agency agree that the Sponsor is correct in specifying the proposed burn depth as deep second degree?

**FDA Response to Question 4:**

- You state that the target burn used per subject be selected based on “visual assessment conducted prior to dosing with cP12. The selected burn must be deep second degree,” and you are excluding “full thickness burn.” You should specify which “visual assessment” criteria you are using to determine burn depth (e.g.: appearance of the tissue, capillary refill, pinprick bleeding, sensation). In addition, since burns are rarely uniform in depth, you should clearly document what percentage of the included second degree burn appears to be superficial second degree versus deep second degree.
- Since inter-rater variability may affect burn depth classification, you should clearly document which rater is assessing the burns, and we recommend that the raters receive formal training in clinical burn depth assessment.

**Question 5:**

Does the Agency agree that, if results from the porcine burn model support dosing up to 8 hours post-burn, the Phase 2a clinical protocol could be amended to reflect this expanded time to administration?

**FDA Response to Question 5:**

There is no objection to the proposed change of dosing regimen from a pharmacology/toxicology perspective.

We reiterate that an in vivo rat micronucleus study needs be completed and submitted to the IND for review prior to the initiation of your Phase 2 clinical trial.

**Question 6:**

Does the Agency agree that the Sponsor's definition of wound closure is appropriate?

**FDA Response to Question 6:**

- No, we do not agree. Your definition of wound closure as "95% epithelialization, with a dressing that is needed only to protect the wound, not to heal the wound" appears to be a definition of partial wound healing, and not complete wound closure. Complete wound closure is defined as skin re-epithelialization without drainage or dressing requirements confirmed at two consecutive trial visits 2 weeks apart, and "complete" implies 100% re-epithelialization.
- It appears that you plan to utilize digital photographs when performing wound closure efficacy assessments. Assessments of photographs as a substitute for in person clinical examination would not be acceptable for evaluation of primary endpoints.

**Question 7:**

Does the Agency agree that assessment of TEWL is useful as an exploratory endpoint as verification of wound closure?

**FDA Response to Question 7:**

- See response to Question 6 for definition of complete wound closure.
- The use of Transepidermal Water Loss (TEWL) is considered exploratory and the clinical utility of TEWL is unclear. In addition to TEWL, your proposed use of Forward Looking Infrared (FLIR) thermography is also considered exploratory. For future trials if you plan on using TEWL and FLIR as validation tools to support endpoints, submit supporting data for Agency review. Regarding your proposal for FLIR, we reiterate guidance we gave you at the Type C Guidance Meeting on September 28, 2016, "It is not clear that FLIR imaging has been validated in clinical trials for determination of burn depth. Additionally, it is not clear that FLIR devices are approved for the use that you propose. We would consider your proposed use of FLIR imaging to be exploratory."

**Additional Clinical Comments**

- You propose "an optional biopsy of the selected burn may be performed 24 hours post burn, if the subject consents." The utility of the timing of this biopsy ("24 hour post burn") and location of this biopsy ("at the center of a regular light and FLIR image of the target site") is unclear. The burn depth may evolve over the first several days of a burn, therefore the result of a biopsy at 24 hours may be different from one performed at a different time point, and the center of the burn may have a different depth of injury than other areas. We reiterate guidance we gave you at the Type C

Guidance Meeting on September 28, 2016, “A biopsy would provide confirmation of the depth of injury only at the biopsy site. The biopsy findings may not be representative of the depth of injury throughout the burn, as burns may not be of uniform depth throughout the area of injury.”

- Since **smoking status** may impact wound healing outcomes, you should clearly document subject smoking status.
- **Nutritional status** may impact wound healing outcomes, and you are planning to assess nutritional status with serum albumin levels. Albumin is a marker for long term nutritional status (half-life = 21 days), and **prealbumin is a better marker of immediate nutritional status** (half-life = 3 days). Therefore, you should consider adding serum prealbumin to your laboratory assessments.
- You are planning to **utilize a 0 - 10 numeric rating scale to assess subject pain, which is a patient reported outcome. For further information on development of Patient Reported Outcomes, see guidance for industry: *Patient-Reported Outcome Measures, Use in Medical Product Development to Support Labeling Claims.***
- Your current proposed cohort stopping criteria, “The occurrence of SAEs or safety concerns may lead to a temporary suspension of study activity or discontinuation of further treatments,” are vague and need to be specified [e.g.: if 2/3 of subjects in cohort meet discontinuation criteria ( e.g. AEs that are ≥Grade 3 per CTCAE v5.0 and ≥Grade 2 for the system organ classes of cardiac disorders and blood and lymphatic disorders)].
- During your development program you should assess the **cardiovascular safety** of your product in accordance with the guidance for industry: *E14 Clinical Evaluation of QT/QTc Interval prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs.*
- Regarding **contraception** requirements during the trial and after trial completion: Medically acceptable methods of contraception should be defined as highly effective methods of birth control, identified as those with failures rates less than 1% per year per ICH M3, section IX C. For an acceptable method of contraception, refer to the ICH M3 guidance document entitled, “Nonclinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals.” **The protocol should specify methods that meet the M3 standards.**

### **3.0 ADMINISTRATIVE COMMENTS**

#### **PREA REQUIREMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new

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indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Please be advised that under the Food and Drug Administration Safety and Innovation Act (FDASIA), you must submit an Initial Pediatric Study Plan (iPSP) within 60 days of an End-of-Phase-2 (EOP2) meeting. In the absence of an EOP2 meeting, refer to the draft guidance below. The iPSP must contain an outline of the pediatric study or studies that you plan to conduct (including, to the extent practicable study objectives and design, age groups, relevant endpoints, and statistical approach); any request for a deferral, partial waiver, or waiver, if applicable, along with any supporting documentation, and any previously negotiated pediatric plans with other regulatory authorities. The iPSP should be submitted in PDF and Word format. Failure to include an Agreed iPSP with a marketing application could result in a refuse to file action.

For additional guidance on the timing, content, and submission of the iPSP, including an iPSP Template, please refer to the draft guidance for industry *Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Pediatric Study Plans*.<sup>1</sup> In addition, you may contact the Division of Pediatric and Maternal Health at 301-796-2200 or email [Pedsdrugs@fda.hhs.gov](mailto:Pedsdrugs@fda.hhs.gov). For further guidance on pediatric product development, please refer to FDA.gov.<sup>2</sup>

## **DATA STANDARDS FOR STUDIES**

Under section 745A(a) of the FD&C Act, electronic submissions “shall be submitted in such electronic format as specified by [FDA].” FDA has determined that study data contained in electronic submissions (i.e., NDAs, BLAs, ANDAs and INDs) must be in a format that the Agency can process, review, and archive. Currently, the Agency can process, review, and archive electronic submissions of clinical and nonclinical study data that use the standards specified in the Data Standards Catalog.<sup>3</sup>

On December 17, 2014, FDA issued the guidance for industry *Providing Electronic Submissions in Electronic Format - Standardized Study Data*. This guidance describes the submission types, the standardized study data requirements, and when standardized study data are required. Further, it describes the availability of implementation support in the form of a technical specifications document, *Study Data Technical Conformance Guide*, as well as email access to the eData Team ([cdeleredata@fda.hhs.gov](mailto:cdeleredata@fda.hhs.gov)) for specific questions related to study data standards.

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<sup>1</sup> When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at

<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

<sup>2</sup> <https://www.fda.gov/drugs/development-resources/pediatric-and-maternal-health-product-development>

<sup>3</sup> <http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm>



Standardized study data are required in marketing application submissions for clinical and nonclinical studies that started after December 17, 2016. Standardized study data are required in commercial IND application submissions for clinical and nonclinical studies that started after December 17, 2017. CDER has produced a Study Data Standards Resources web page<sup>4</sup> that provides specifications for sponsors regarding implementation and submission of clinical and nonclinical study data in a standardized format. This web page will be updated regularly to reflect CDER's growing experience in order to meet the needs of its reviewers.

For commercial INDs and NDAs, Standard for Exchange of Nonclinical Data (SEND) datasets are required to be submitted along with nonclinical study reports for study types that are modeled in an FDA-supported SEND Implementation Guide version. The FDA Data Standards Catalog, which can be found on the Study Data Standards Resources web page noted above, lists the supported SEND Implementation Guide versions and associated implementation dates.

Although the submission of study data in conformance to the standards listed in the FDA Data Standards Catalog will not be required in studies that started on or before December 17, 2016, CDER strongly encourages IND sponsors to use the FDA supported data standards for the submission of IND applications and marketing applications. The implementation of data standards should occur as early as possible in the product development lifecycle, so that data standards are accounted for in the design, conduct, and analysis of clinical and nonclinical studies. For clinical and nonclinical studies, IND sponsors should include a plan (e.g., in the IND) describing the submission of standardized study data to FDA. This study data standardization plan (see the FDA Study Data Technical Conformance Guide) will assist FDA in identifying potential data standardization issues early in the development program.

If you have not previously submitted an eCTD submission or standardized study data, we encourage you to send us samples for validation following the instructions at FDA.gov. For general toxicology, supporting nonclinical toxicokinetic, and carcinogenicity studies, submit data in the Standards for the Exchange of Nonclinical Data (SEND) format. The validation of sample submissions tests conformance to FDA supported electronic submission and data standards; there is no scientific review of content.

The Agency encourages submission of sample data for review before submission of the marketing application. These datasets will be reviewed only for conformance to standards, structure, and format. They will not be reviewed as a part of an application review. These datasets should represent datasets used for the phase 3 trials. The FDA Study Data Technical Conformance Guide (Section 7.2 eCTD Sample Submission pg. 30) includes the link to the instructions for submitting eCTD and sample data to the Agency. The Agency strongly encourages Sponsors to submit standardized sample

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<sup>4</sup> <http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm>

data using the standards listed in the Data Standards Catalog referenced on the FDA Study Data Standards Resources web site. When submitting sample data sets, clearly identify them as such with **SAMPLE STANDARDIZED DATASETS** on the cover letter of your submission.

Additional information can be found at [FDA.gov](http://FDA.gov).<sup>5</sup>

## **LABORATORY TEST UNITS FOR CLINICAL TRIALS**

CDER strongly encourages IND sponsors to identify the laboratory test units that will be reported in clinical trials that support applications for investigational new drugs and product registration. Although Système International (SI) units may be the standard reporting mechanism globally, dual reporting of a reasonable subset of laboratory tests in U.S. conventional units and SI units might be necessary to minimize conversion needs during review. Identification of units to be used for laboratory tests in clinical trials and solicitation of input from the review divisions should occur as early as possible in the development process. For more information, please see the FDA website entitled Study Data Standards Resources<sup>6</sup> and the CDER/CBER Position on Use of SI Units for Lab Tests website.<sup>7</sup>

## **ABUSE POTENTIAL ASSESSMENT**

Drugs that affect the central nervous system, are chemically or pharmacologically similar to other drugs with known abuse potential, or produce psychoactive effects such as mood or cognitive changes (e.g., euphoria, hallucinations) need to be evaluated for their abuse potential and a proposal for scheduling will be required at the time of the NDA submission [21 CFR 314.50(d)(5)(vii)]. For information on the abuse potential evaluation and information required at the time of your NDA submission, see the guidance for industry *Assessment of Abuse Potential of Drugs*.<sup>8</sup>

## **PATIENT-FOCUSED ENDPOINTS**

An important component of patient-focused drug development is describing the patient's perspective of treatment benefit in labeling based on data from patient-focused outcome measures [e.g., patient-reported outcome (PRO) measures]. Therefore, early in product development, we encourage sponsors to consider incorporating well-defined and reliable patient-focused outcome measures as key efficacy endpoints in clinical trials, when appropriate, and to discuss those measures with the Agency in advance of confirmatory trials. For additional information, refer to FDA's guidance for industry

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<sup>5</sup> <https://www.fda.gov/industry/study-data-standards-resources/study-data-submission-cder-and-cber>

<sup>6</sup> <http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm>

<sup>7</sup> <https://www.fda.gov/media/109533/download>

<sup>8</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.



*Patient-Reported Outcome Measures: Use in Medical Product Development to Support Claims.*

## **NEW PROTOCOLS AND CHANGES TO PROTOCOLS**

To ensure that the Division is aware of your continued drug development plans and to facilitate successful interactions with the Division, including provision of advice and timely responses to your questions, we request that the cover letter for all new phase 2 or phase 3 protocol submissions to your IND or changes to these protocols include the following information:

- (1) Study phase
- (2) Statement of whether the study is intended to support marketing and/or labeling changes
- (3) Study objectives (e.g., dose finding)
- (4) Population
- (5) A brief description of the study design (e.g., placebo or active controlled)
- (6) Specific concerns for which you anticipate the Division will have comments
- (7) For changes to protocols only, also include the following information:
  - A brief summary of the substantive change(s) to the protocol (e.g., changes to endpoint measures, dose, and/or population)
  - Other significant changes
  - Proposed implementation date

We recommend you consider requesting a meeting to facilitate discussion of multiple and/or complex issues.

## **UNITED STATES PATIENT POPULATION**

FDA expects sponsors to enroll participants who are relevant to the planned use of the drug in the US population. Describe the steps you are taking to ensure that the clinical trial population will be relevant to the US patient population that will receive the drug. Include a discussion of participation of US vs. non-US sites and discuss whether the

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subjects likely to be enrolled will adequately represent the US patient population in terms of disease characteristics, sex, race/ethnicity, age, and standards of care. See 21 CFR 312.33(a)(2) and 21 CFR 314.50(d)(5)(v) and the guidance for industry *Collection of Race and Ethnicity Data in Clinical Trials* for more information.

We recommend you consider requesting a meeting to facilitate discussion of multiple and/or complex issues.

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**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
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/s/  
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SHARI L TARGUM  
08/12/2021 01:19:50 PM

## ATTACHMENT 5

# CLINICAL TRIAL PROTOCOL

|                                  |                                                                                                                                                                                    |
|----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Protocol Number</b>           | NMT-cP12-201                                                                                                                                                                       |
| <b>Title</b>                     | A Phase 2a, Open-label Study of the Safety and Tolerability of a Single Dose of cP12 in Otherwise Healthy Adults with Up to and Including 5% Total Body Surface Area Thermal Burns |
| <b>Investigational Product</b>   | cP12                                                                                                                                                                               |
| <b>Phase</b>                     | 2a                                                                                                                                                                                 |
| <b>Sponsor</b>                   | NeoMatrix Therapeutics, Inc.<br>25 Health Sciences Drive, Suite 124<br>Stony Brook, NY 11790<br>Phone: 631-241-4964<br>Email: raclark@neomatrixtx.com                              |
| <b>Version/Date of Protocol:</b> | 6 September 2022                                                                                                                                                                   |
| <b>Replaces:</b>                 | NA                                                                                                                                                                                 |

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## 1. SYNOPSIS

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| <b>Study Title:</b><br>A Phase 2a, Open-label Study of the Safety and Tolerability of a Single Dose of cP12 in Otherwise Healthy Adults with Up to and Including 5% Total Body Surface Area Thermal Burns                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <b>Sponsor:</b><br>NeoMatrix Therapeutics, Inc.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Investigational Medicinal Product:</b><br>cP12 for Injection                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Protocol Number:</b><br>NMT-cP12-201                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| <b>Study Phase:</b><br>Phase 2a                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Number of Sites:</b><br>Up to 3 clinical sites in the United States                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| <b>Primary Objective:</b> <ul style="list-style-type: none"><li>To assess the safety and tolerability of a single intravenous (IV) dose of cP12 infused over 30 minutes in otherwise healthy adults with up to and including 5% total body surface area (TBSA) thermal burns, and at least 1% deep partial-thickness burns.</li></ul> <b>Exploratory Objectives:</b> <ul style="list-style-type: none"><li>To evaluate pain using the subject rated visual numerical rating scale (0-10) assessment of pain at the target burn.</li></ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <b>Study Design:</b> <p>This is a Phase 2a, open-label, single-dose, 1- to 3-site study to evaluate the safety and tolerability of cP12 in 6 male and female subjects with thermal burns of up to and including 5% TBSA. TBSA of the subject's burns will be calculated using the Lund and Browder chart (<a href="#">Appendix 2.2</a>). Enrolled patients must have at least 1% TBSA deep partial-thickness burns. With the exception of the burns, subjects should be healthy and will be assessed to rule-out smoke inhalation and other injuries. Vital signs prior to dosing must be stable and an electrocardiogram (ECG) must not show clinically significant abnormalities.</p> <p>The target burn used in this study will be selected based on a burn classification description conducted prior to dosing with cP12. The selected burn must be deep partial-thickness (based on appearance of the tissue, refer to <a href="#">Appendix 2.3</a>), and must not be a circumferential burn.</p> <p>In the absence of burn-specific, validated, dermal assessment tools, NeoMatrix has developed scales to characterize the burn and surrounding tissues for this trial. Burn dermal assessments will include erythema, capillary refill, blisters, and edema/swelling. In this trial, the target burn and all other burns of each subject will be assessed (see <a href="#">Section 2.4</a>).</p> <p>Eligible subjects will receive a single administration of 0.01 mg/kg cP12. Study drug will be administered over approximately 30 minutes by IV infusion, and the infusion is to be initiated and completed within 2 to 12 hours after the burn has occurred. Subjects may receive study drug in the emergency department, burn unit, or other area in the hospital that is equipped with appropriate monitoring for IV infusions at intervals specified in the Schedule of Events and Assessments (location depends on the judgement of the surgeon based on the extent of the burn and overall medical condition of the subject). The general guidelines and principals of wound care for this study will be elucidated in the study manual.</p> <p>Vital signs, ECGs, blood samples for serum chemistries, serologies, hematology, troponin, C-reactive protein (CRP), total creatine kinase (CK), gamma-glutamyl transferase (GGT), prealbumin, and urine will be obtained at</p> |

screening and at several time points during the study for safety evaluation. Dermal assessments will be completed at specified times.

Subjects will remain at the clinical site for at least 6 hours post infusion for the purpose of safety monitoring and evaluation of other study assessments. Subsequent evaluations will be performed at the clinical site by the investigator.

Subjects will return to the clinical site 28 ( $\pm$ 2) days after dosing for an End-of-Study visit.

**Safety Review Committee:**

A Safety Review Committee (SRC) composed of the sponsor, medical monitor, and principal investigator will meet on an ad hoc basis to review any serious adverse events (SAEs) and any other unexpected safety findings that occur during the study.

**Stopping Rules:**

The sponsor retains the right to pause enrollment or terminate the study. The stopping criteria are as follows:

- If  $\geq 2$  subjects experience a Grade 3 (severe) or higher adverse event (AE) affecting the same organ system and considered by the investigator to be at least possibly study-drug related.
- Any SAEs related to study drug.

In the event of one of the above, further enrollment in the study will be paused. The sponsor will conduct due diligence including an assessment and recommendation from the SRC. The SRC will review all available data and make a recommendation for next steps. The sponsor will review the recommendation and inform the necessary groups across participating sites.

**Planned Number of Subjects:**

A total of 6 evaluable subjects is planned. Enrollment will continue until 6 subjects have completed all study visits.

**Subject Inclusion/Exclusion Criteria:**

Inclusion/exclusion criteria will be assessed prior to dosing.

**Inclusion Criteria**

A subject may be included in the study only if all of the following inclusion criteria are met:

1. Male or female between the ages of 18 and 65 years, inclusive.
2. Healthy subjects, with the exception of thermal burns, and without smoke inhalation or other injuries.
3. Body mass index between 18 kg/m<sup>2</sup> and 40 kg/m<sup>2</sup> (inclusive) and body weight of  $\geq 50$  kg.
4. TBSA thermal burns up to and including 5%, with at least 1% deep partial-thickness burn.
5. Female subjects that meet 1 of the following:
  - a. Woman of childbearing potential must have a negative serum pregnancy test predose and must agree to use acceptable method(s) of contraception combined with an acceptable method of contraception for her male partner(s) (as defined in Inclusion Criterion #6) after informed consent, throughout the study, and for a minimum of 30 days after the dose of study drug. Acceptable methods of contraception include hormonal contraception, hormonal or non-hormonal intrauterine device, bilateral tubal occlusion, complete abstinence, cervical cap with spermicide, vaginal sponge with spermicide, or male or female condom with or without spermicide.
  - b. Woman of non-child-bearing potential must either be postmenopausal with amenorrhea for at least 1 year prior to receiving study drug or have undergone 1 of the following sterilization procedures at least 6 months prior to receiving study drug:
    - i. hysteroscopic sterilization
    - ii. bilateral tubal ligation or bilateral salpingectomy
    - iii. hysterectomy
    - iv. bilateral oophorectomy

6. Male subjects who are sexually abstinent or surgically sterilized (vasectomy), or those who are sexually active with a female partner(s) and agree to use an acceptable method of contraception (such as condom with spermicide) combined with an acceptable method of contraception for their non-pregnant female partner(s) (as defined in Inclusion Criterion No. 5) after informed consent, throughout the study, and for a minimum of 30 days after the dose of study drug, and who do not intend to donate sperm in the period from screening until 12 weeks following administration of study drug.
7. Able to be infused with the study drug within 2 to 12 hours post burn.
8. Able to understand the study procedures, voluntarily consent to participate in this study, and provide written informed consent prior to start of any study-specific procedures.
9. Willing and able to remain at the clinical site for at least 6 hours post infusion, and to return to the clinical site 3 days ( $\pm 1$  day), 1 week ( $\pm 2$  days), and 4 weeks ( $\pm 2$  days) post burn.

#### **Exclusion Criteria**

Subjects who meet any of the following criteria will be excluded from the study:

1. Burns isolated to the head, face, and genitalia.
2. Smoke inhalation.
3. Active burn infection needing systemic antimicrobial treatment.
4. Full-thickness burn in the target burn.
5. Circumferential target burn.
6. Known history of radiation therapy at target burn area.
7. Clinically significant laboratory abnormality or other clinical findings indicative to the investigator of a clinically significant exclusionary disease (including but not limited to renal, hepatic, gastrointestinal, cardiovascular, neurological disease).
8. Significant history or current evidence of chronic infectious disease, system disorder, or organ dysfunction.
9. Has positive coronavirus disease-2019 (COVID-19) quantitative polymerase chain reaction (qPCR) test result at screening.
10. History of human immunodeficiency virus, hepatitis B or C.
11. At high risk for hypersensitivity to cP12 (refer to [Appendix 2.7](#)).
12. An ECG abnormality deemed by the investigator to be clinically significant.
13. Prior exposure to cP12.
14. Any condition which in the opinion of investigator would interfere with the subject's ability to provide informed consent, comply with study instructions, possibly confound interpretation of study results, or endanger the subject if he or she took part in the trial.
15. Use of an investigational drug or product within 30 days prior to receiving study drug.

#### **Test Product, Dose, and Mode of Administration:**

cP12 (fibronectin-derived, cyclic 14-mer peptide) for Injection

Each subject will receive a single IV dose of 0.01 mg/kg cP12 administered by infusion over approximately 30 minutes.

#### **Duration of Treatment:**

Duration of treatment for each subject is a single dose of cP12 initiated and completed within 2 to 12 hours post burn, over 30 minutes, by IV infusion. Duration of participation in this clinical trial for each subject will be approximately 4 weeks.



**Endpoints:**

**Safety**

- All AEs including SAEs
- Clinical safety laboratory data (serum chemistry, complete blood count [CBC], differential), troponin, CRP, CK, GGT, prealbumin, and urinalysis
- Vital signs and physical examination (PE) findings
- ECG findings
- Dermal assessment scores for erythema, capillary refill, blisters, and edema/swelling in the target and all other burns

**Exploratory**

- Pain assessment at the target burn

**Statistical Plan and Methods:**

No formal hypothesis testing is planned.

All subjects who receive any study drug will be included in the safety analysis set. Data will be summarized using descriptive statistics. Mean, median, standard deviation, etc. will be used for continuous data. Frequency counts will be summarized for categorical data. Time-dependent data will be summarized using Kaplan-Meier methods.

**Determination of Sample Size:**

This is a first-in-burn-patient study aimed at evaluating the safety and tolerability of cP12 after a single dose is infused over 30 minutes in 6 otherwise healthy adult subjects with up to and including 5% TBSA thermal burns. Sample size for this study was not determined using statistical considerations.

**Safety Endpoints:**

**AEs:** Treatment emergent AEs (TEAEs) occurring after dosing with cP12 will be summarized based on the frequency of the TEAEs, relationship to study drug, and severity for all dosed subjects. AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 24.0 or higher. Overall safety and tolerability will be assessed by clinical review of all safety parameters, including AEs, laboratory values, vital signs, PEs, and ECG data. AEs reported prior to study drug infusion will be recorded as medical history.

**Dermal Assessment Scores** specific for erythema, capillary refill, blisters, and edema/swelling will be scored at baseline and several times points post infusion.

**Exploratory Endpoint:**

**Pain Assessment** using a numeric rating scale of 0-10, where zero is no pain and 10 is worst pain imaginable (see [Section 2.6](#)). These assessments will be used for the target burn. The most critical time to assess pain is during cP12 infusion and 2 hours thereafter, as this time window encompassed detectable cP12 blood levels on pharmacokinetics analysis in the Phase 1 clinical trial.

## 2. APPENDICES

### 2.1. Schedule of Events and Assessments

| Study Period                             | Screen          | Clinical Site                              |                    |              |                |                  |                |                 |               | Post Dose  |               |                     |
|------------------------------------------|-----------------|--------------------------------------------|--------------------|--------------|----------------|------------------|----------------|-----------------|---------------|------------|---------------|---------------------|
|                                          |                 | Baseline<br>Within 30 Min<br>Prior to Dose | Dosing Minutes     |              | Post Dose      |                  |                |                 |               |            |               |                     |
|                                          |                 |                                            | 2, 5, 15<br>±2 min | 30<br>±2 min | 1 hr<br>±5 min | 1.5 hr<br>±5 min | 2 hr<br>±5 min | 4 hr<br>±30 min | 6 hr<br>±1 hr | 3<br>±1 dy | 1 wk<br>±2 dy | EOS/ET<br>4 wk±2 dy |
| Informed consent                         | X               |                                            |                    |              |                |                  |                |                 |               |            |               |                     |
| Medical history                          | X               |                                            |                    |              |                |                  |                |                 |               |            |               |                     |
| Demographics                             | X               |                                            |                    |              |                |                  |                |                 |               |            |               |                     |
| Full PE <sup>1</sup>                     | X               |                                            |                    |              |                |                  |                |                 |               |            |               | X                   |
| TBSA, select target burn                 | X               |                                            |                    |              |                |                  |                |                 |               |            |               |                     |
| Brief PE <sup>2</sup>                    |                 |                                            |                    |              |                |                  |                |                 |               | X          | X             |                     |
| Inspection infusion site <sup>3</sup>    |                 | X                                          | X                  | X            |                |                  |                |                 |               |            |               |                     |
| Vital signs <sup>4</sup>                 | X               |                                            | X                  | X            | X              | X                | X              | X               | X             | X          | X             | X                   |
| 12-lead safety ECG (single) <sup>5</sup> | X               |                                            |                    |              | X              |                  |                |                 | X             | X          | X             | X                   |
| Serum chemistry, CBC, diff               | X               |                                            |                    |              |                |                  |                |                 |               | X          |               | X                   |
| Troponin, CRP, total CK, prealbumin, GGT | X               |                                            |                    |              |                |                  |                |                 | X             | X          |               | X                   |
| COVID-19 qPCR test                       | X               |                                            |                    |              |                |                  |                |                 |               |            |               |                     |
| Urinalysis                               | X               |                                            |                    |              |                |                  |                |                 |               |            |               | X                   |
| Pregnancy test (females)                 | X <sup>6</sup>  |                                            |                    |              |                |                  |                |                 |               |            |               | X <sup>7</sup>      |
| Dermal assessments <sup>8</sup>          | X               | X                                          | X                  |              |                |                  | X              | X               | X             | X          | X             | X                   |
| Pain assessment                          |                 | X                                          | X                  | X            | X              |                  | X              | X               | X             | X          | X             | X                   |
| IV infusion (cP12)                       |                 |                                            | X <sup>9</sup>     |              |                |                  |                |                 |               |            |               |                     |
| PK sampling                              |                 | X                                          |                    | X            | X              |                  | X              |                 |               |            |               |                     |
| AE assessment                            | X <sup>10</sup> | X <sup>10</sup>                            | X                  | X            | X              | X                | X              | X               | X             | X          | X             | X                   |
| Concomitant medications                  | X               |                                            | X                  | X            | X              | X                | X              | X               | X             | X          | X             | X                   |

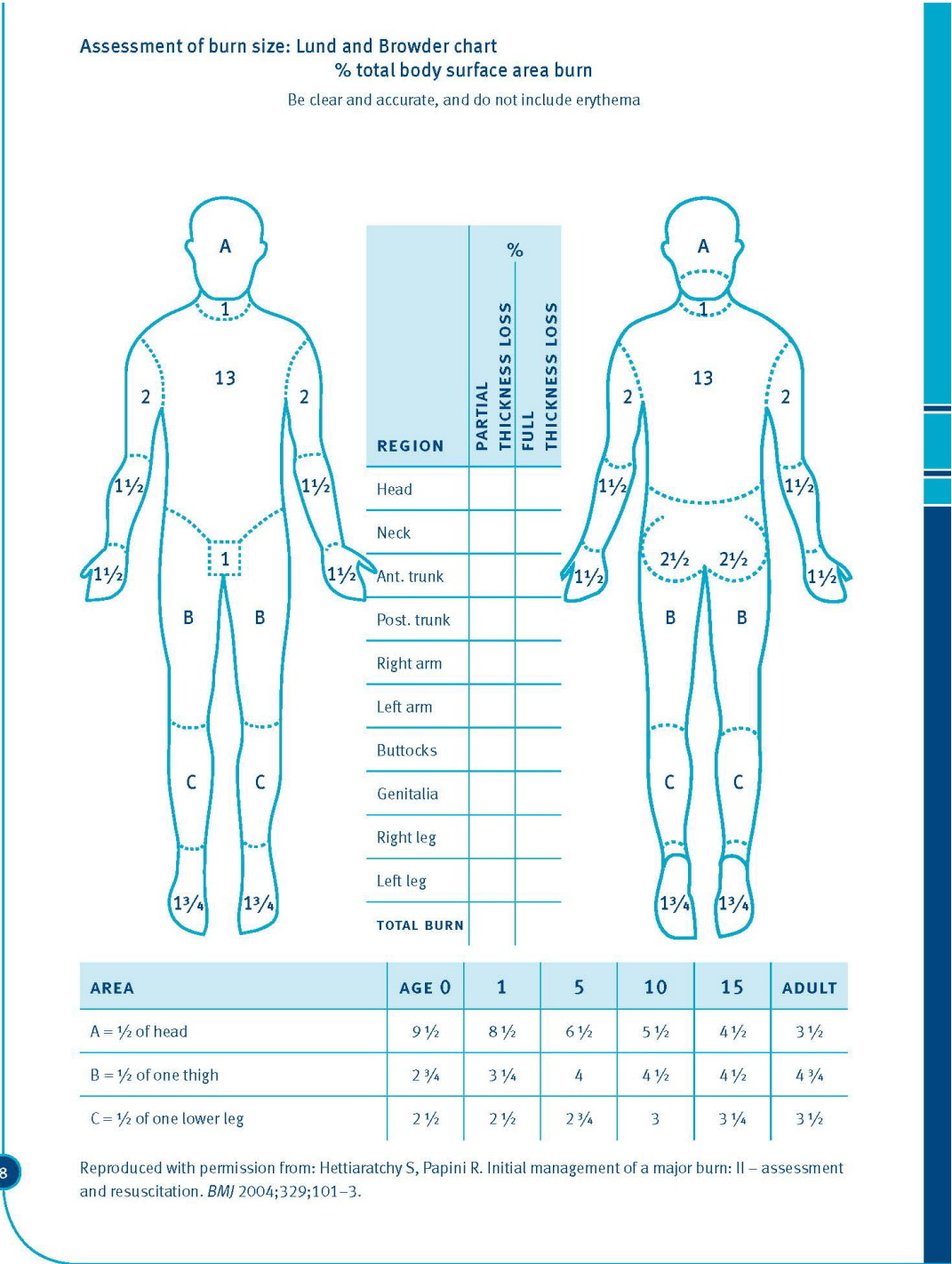
Abbreviations: AE=adverse event; CBC=complete blood count; CK=creatinine kinase; COVID=coronavirus disease 2019; CRP=C-reactive protein; diff=differential; dy=day; ECG=electrocardiogram, EOS=End of Study; ET=Early Termination; GGT=gamma-glutamyl transferase; hr=hour; IV=intravenous; qPCR= quantitative polymerase chain reaction; PE=physical examination; PK=pharmacokinetic; min=minute; TBSA= total body surface area; wk=week.

**Note:** When several assessments are to be conducted at the same time point, the preferred order of assessments is ECG, vital signs, and blood draws.

- <sup>1</sup> Full PE includes general appearance, skin, eyes, ears, nose, and throat, head/neck, musculoskeletal, respiratory, cardiovascular (including rhythm and presence of cardiac abnormalities), abdominal examination, neurologic examination to record the presence of abnormalities in mental status, motor, and sensory function, height, weight, and body mass index (BMI); and any additional assessments necessary to establish baseline status or evaluate symptoms or AEs. Significant findings prior to dosing will be recorded on the medical history page of the case report form (CRF).
- <sup>2</sup> Brief PE includes general appearance, skin, respiratory, cardiovascular (including rhythm and presence of cardiac abnormalities), abdominal examination. Significant findings prior to dosing will be recorded on the medical history page of the CRF. Only changes from baseline that meet the definition of a TEAE will be recorded as an AE.
- <sup>3</sup> Clinical site staff will assess the infusion site at predose and at 2 minutes, 5 minutes, and 15 minutes after the initiation of the infusion. Any infusion site reactions will be recorded as AEs.
- <sup>4</sup> Vital signs will include respiration rate, temperature, blood pressure, and pulse and are to be collected after the subject has been in the sitting or supine position for 5 minutes.
- <sup>5</sup> A single ECG is obtained after the subject has been in a supine position for approximately 5 minutes.
- <sup>6</sup> Serum pregnancy test.
- <sup>7</sup> Urine pregnancy test. Any positive urine pregnancy test result to be confirmed by serum pregnancy test.
- <sup>8</sup> Erythema, capillary refill, blisters, and edema/swelling will be scored.
- <sup>9</sup> Infusion of study drug must commence and be completed from 2 to 12 hours post burn.
- <sup>10</sup> AEs reported prior to study drug infusion are to be recorded as medical history.

2.2. Total Body Surface Area

TBSA of the subject’s burns will be calculated using the Lund and Browder chart. The subject’s entire palmar surface will be considered to be 1% TBSA.<sup>1</sup> Eligible subjects must have TBSA burns of up to and including 5%, and at least 1% TBSA deep partial-thickness burns (Figure 1).



### 2.3. Selection of Target Burn for Eligibility

Selection of the target burn, performed to determine inclusion in the study, will be based on a burn classification description ([Table 1](#)) conducted prior to dosing with cP12. Classification of burn depth will differentiate deep partial-thickness burns from superficial/epidermal, superficial partial-thickness, or full-thickness burns.<sup>2</sup>

The American Burn Association has published the classification and management of the burn wounds as described in [Table 1](#). Deep partial-thickness are the burns to be studied in this trial.

**Partial-thickness** — Partial-thickness burns involve the epidermis and portions of the dermis. They are characterized as either superficial or deep.

- Superficial partial-thickness – These burns characteristically form blisters within 24 hours between the epidermis and dermis. They are painful, red, and weeping and blanch with pressure. Burns that initially appear to be only superficial/epidermal in depth may be determined to be partial-thickness 12 to 24 hours later. These burns generally heal in 7 to 21 days; scarring is unusual, although pigment changes may occur. A layer of fibrinous exudates and necrotic debris may accumulate on the surface, which may predispose the burn wound to heavy bacterial colonization and delayed healing. These burns typically heal without functional impairment or hypertrophic scarring.
- Deep partial-thickness – These burns extend into the deeper dermis and are characteristically different from superficial partial-thickness burns. Deep burns damage hair follicles and glandular tissue. They are painful, always blister (easily unroofed), are wet or waxy dry, and have variable mottled colorization from patchy cheesy white to red. They blanch slowly, if at all, with pressure. If infection is prevented and wounds are allowed to heal spontaneously without grafting, they will heal in 2 to 9 weeks. These burns may cause hypertrophic scarring. If they involve a joint, joint dysfunction is expected even with aggressive physical therapy. A deep partial-thickness burn that fails to heal in 3 weeks is functionally and cosmetically similar to a full-thickness burn.

**Table 1. Classification of Burn Injury**

| Depth                                      | Appearance                                                                                                                                | Sensation                          | Healing Time                                  |
|--------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|-----------------------------------------------|
| Superficial (epidermal)                    | Dry, red<br>Blanches with pressure                                                                                                        | Painful                            | 3-6 days                                      |
| Superficial partial-thickness              | Blisters<br>Moist, red, weeping<br>Blanches with pressure                                                                                 | Painful to temperature, air, touch | 7-21 days                                     |
| Deep partial-thickness                     | Blisters (easily unroofed)<br>Wet or waxy dry<br>Variable color (patchy to cheesy white to red)<br>Blanches with pressure may be sluggish | Painful to pressure only           | >21 days, usually requires surgical treatment |
| Full-thickness                             | Waxy white to leathery gray to charred and black<br>Dry and inelastic<br>No blanching with pressure                                       | Deep pressure                      | Months, unless surgically treated             |
| Deeper injury (ie, 4 <sup>th</sup> degree) | Extends into fascia and/or muscle                                                                                                         | Deep pressure only                 | Rare, unless surgically treated               |

Adapted from:

- Mertens DM, Jenkins ME, Warden GD. Outpatient burn management. *Nurs Clin North Am*. 1997; 32:343-364.
- Peate WF. Outpatient management of burns. *Am Fam Physician*. 1992; 45:1321-1330.
- Clayton MC, Solem LD. No ice, no butter. Advice on management of burns for primary care physicians. *Postgrad Med*. 1995 May;97(5):151-5, 159-60, 165.

## 2.4. Dermal Assessments for All Burns

The sponsor has developed 4 scales specific to the local evaluation of acute burns including erythema, capillary refill, blistering and edema/swelling ([Table 2](#)) These evaluations will be done at baseline and at each time point as noted in the Schedule of Events and Assessments for the target burn site and all other burns.

**Table 2. Dermal Assessment Scales for Burns**

| Assessment                                                                                | Score | Description                                                                                       |
|-------------------------------------------------------------------------------------------|-------|---------------------------------------------------------------------------------------------------|
| Erythema assessed by visual examination                                                   | 0     | None                                                                                              |
|                                                                                           | 1     | Mild, faintly detectable, pink                                                                    |
|                                                                                           | 2     | Moderate, clearly distinguishable dull red                                                        |
|                                                                                           | 3     | Severe, deep dark or fiery bright red                                                             |
| Capillary refill by pressure and visual examination <sup>3</sup>                          | 1     | Fast, immediate capillary refill <3 seconds                                                       |
|                                                                                           | 2     | 3-10 seconds capillary refill                                                                     |
|                                                                                           | 3     | >10 seconds                                                                                       |
| Blisters by visual examination                                                            | 0     | None                                                                                              |
|                                                                                           | 1     | Bumpy skin                                                                                        |
|                                                                                           | 2     | Tiny blisters (<5 mm)                                                                             |
|                                                                                           | 3     | Raised areas containing fluid (≥5 mm) or denuded skin                                             |
| Edema/Swelling assessed by visual examination and palpation burn wound and peri-burn area | 0     | None                                                                                              |
|                                                                                           | 1     | Mild, barely perceptible elevation, little or no indentation after 5 seconds of pressure          |
|                                                                                           | 2     | Moderate, clearly perceptible elevation, mild to moderate indentation after 5 seconds of pressure |
|                                                                                           | 3     | Severe, prominent elevation, marked indentation after 5 seconds of pressure                       |

## 2.5. Record of Burn Assessments for Each Subject

All burns including the target burn for each subject will be assessed based on body areas as defined in [Figure 1](#) and using the Dermal Assessment scoring system in [Table 2](#) (erythema, capillary refill, blisters, and edema) and recorded in the case record form.

If there is more than 1 burn at a given body site, a drawing of each burn in that area will be labeled 1, 2, 3, etc. on that subject's [Figure 1](#). For example, 3 burns on the anterior trunk will be labeled 1, 2, and 3. One burn must be labeled as the target burn. Body sites without a burn will not be included in the form.

## 2.6. Pain Assessment/Site

Pain will be assessed using a numeric rating scale of 0 to 10, where zero is no pain and 10 is worst pain imaginable ([Figure 2](#)). This assessment will be used for only the target burn. Pain will be assessed per the Schedule of Events and Assessments.

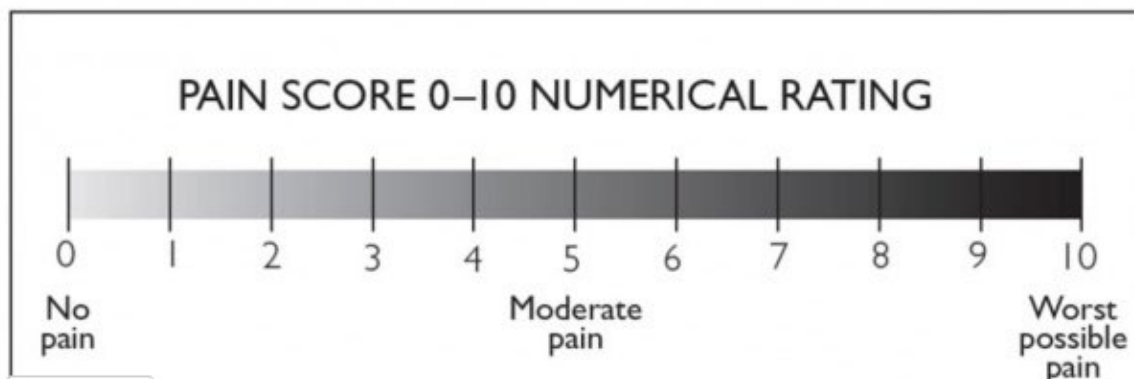


**Figure 2. Pain Score Numerical Rating**

### **2.7. At High Risk for Hypersensitivity to cP12**

Subjects are excluded if they have a history of:

1. Idiopathic hives for 6 weeks or longer (chronic urticaria).
2. Idiopathic anaphylaxis or systemic mastocytosis.
3. Allergic-like reaction to contrast agents for radiology imaging.
4. Allergic-like reactions to any of the following substances:
  - Morphine, codeine, tramadol, and meperidine
  - Antibiotics: ciprofloxacin (Cipro®), levofloxacin (Levaquin®), vancomycin, and amphotericin B
  - Tranexamic acid
  - Drugs for hereditary angioedema such as icatibant (Firazyr®)
  - Drugs used in surgery to block muscle movement (non-depolarizing muscle relaxants such as atracurium, mivacurium, tubocurarine, and rocuronium)
  - Vasoactive intestinal peptide nasal spray

### **2.8. Wound Dressings**

The clinical site may use any dressing of its choosing, with the exception of silver sulfadiazine (SSD, Silvadene®), and may change the dressings as needed. The wound must be maintained in a moist wound healing environment and protected from further damage.

### 3. REFERENCES

- <sup>1</sup> Hettiaratchy S, Papini R. Initial management of a major burn: II – assessment and resuscitation. *BMJ* 2004;329;101-103.
- <sup>2</sup> Johnson RM and Richard R. Partial-thickness burns: identification and management. *Adv Skin Wound Care*. 2003;16(4):178-187.
- <sup>3</sup> McGuire D, Gotlib A, King J. Capillary Refill Time. 2022 Apr 21. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan. PMID: 32491685.



## ATTACHMENT 7

## **FINAL REPORT**

### Study Title

*In Vivo* Mammalian Erythrocyte Micronucleus Assay in Rats

### Test Article

cP12

### Author

Marie E. McKeon, MPhil

### Study Completion Date

28 October 2021

### Testing Facility

BioReliance Corporation  
9630 Medical Center Drive  
Rockville, MD 20850

### BioReliance Study Number

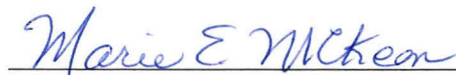
AG53LV.125M012ICH.BTL

### Sponsor

Neomatrix Therapeutics, Inc.  
25 Health Sciences Dr.  
Stony Brook, NY 11790

## 1. STATEMENT OF COMPLIANCE

Study No. AG53LV.125M012ICH.BTL was conducted in compliance with the following regulation: US FDA Good Laboratory Practice Regulations as published in 21 CFR Part 58. This regulation is compatible to non-US regulations, OECD Principles of Good Laboratory Practice (C(97)186/Final); Japanese Ministry of Health, Labor and Welfare Good Laboratory Practices (Ordinance Nos. 21 and 114, if applicable); Japanese Ministry of Agriculture, Forestry and Fisheries Good Laboratory Practices (No. 11 Nousan-6283); Japanese Ministry of Economy, Trade and Industry Good Laboratory Practices, and allows submission of the report under the Mutual Acceptance of Data (MAD) agreement with applicable OECD member countries.



Marie E. McKeon, MPhil  
Study Director



Date

## 2. QUALITY ASSURANCE STATEMENT



### Quality Assurance Statement

#### Study Information

**Number:** AG53LV.125M012ICH.BTL

#### Compliance

Procedures, documentation, equipment and other records were examined in order to assure this study was performed in accordance with the regulation(s) listed below and conducted according to the protocol and relevant Standard Operating Procedures. Verification of the study protocol was performed and documented by Quality Assurance.

US FDA Good Laboratory Practices 21CFR 58

#### Inspections

Quality Assurance performed the inspections(s) below for this study.

| Insp. Dates (From/To) |             | Phase Inspected           | To Study Director To Management |             |
|-----------------------|-------------|---------------------------|---------------------------------|-------------|
| 16-Apr-2021           | 16-Apr-2021 | Protocol Review           | 16-Apr-2021                     | 16-Apr-2021 |
| 06-Jul-2021           | 06-Jul-2021 | Body weight measurement   | 06-Jul-2021                     | 06-Jul-2021 |
| 08-Sep-2021           | 08-Sep-2021 | Protocol Amendment Review | 08-Sep-2021                     | 08-Sep-2021 |
| 08-Sep-2021           | 08-Sep-2021 | Protocol Amendment Review | 08-Sep-2021                     | 08-Sep-2021 |
| 08-Sep-2021           | 08-Sep-2021 | Protocol Amendment Review | 08-Sep-2021                     | 08-Sep-2021 |
| 08-Sep-2021           | 08-Sep-2021 | Protocol Amendment Review | 08-Sep-2021                     | 08-Sep-2021 |
| 09-Sep-2021           | 15-Sep-2021 | Data/Draft Report         | 15-Sep-2021                     | 15-Sep-2021 |
| 09-Sep-2021           | 15-Sep-2021 | Data - Formulation        | 15-Sep-2021                     | 15-Sep-2021 |
| 22-Oct-2021           | 25-Oct-2021 | Final Report              | 25-Oct-2021                     | 25-Oct-2021 |
| 22-Oct-2021           | 22-Oct-2021 | Protocol Amendment Review | 22-Oct-2021                     | 22-Oct-2021 |

The Final Report for this study describes the methods and procedures used in the study and the reported results accurately reflect the raw data of the study.

For a multisite study, test site QA Statements are located in the corresponding contributing scientist report.

#### E-signature

**Quality Assurance:** Jeannie Eberle

28-Oct-2021 11:50 am GMT

Reason for signature: QA Approval

Printed by: Jeannie Eberle

Printed on: 28-Oct-21

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#### 4. STUDY INFORMATION

##### Study Conduct

Sponsor: Neomatrix Therapeutics, Inc.  
25 Health Sciences Dr.  
Stony Brook, NY 11790

Sponsor's Authorized Representative: Richard Clark

Study Monitor: Colleen Johnson  
243 W. Virginia Ave.  
Hamilton, VA 20158

Testing Facility: BioReliance Corporation  
9630 Medical Center Drive  
Rockville, MD 20850

BioReliance Study No.: AG53LV.125M012ICH.BTL

##### Test Article

Identification: cP12

Lot No.: 2K15032

Purity: 77.1% peptide content and 98.8% purity (a correction factor of 1.31 was used for dose formulations)

Molecular Weight: 1763.1

Description: White powder

Storage Conditions: -10 to -30°C, protected from light with dessicant  
(dessicant was removed on same date as receipt)

Receipt Date: 22 December 2020

##### Study Dates

Study Initiation Date: 02 March 2021

Experimental Starting Date (First Day of Data Collection): 30 June 2021

Experimental Start Date (First Day of Dosing): 06 July 2021

Experimental Completion Date: 15 August 2021

Key Personnel

|                                                          |                                                                        |
|----------------------------------------------------------|------------------------------------------------------------------------|
| Study Directors:                                         | Marie E. McKeon, MPhil<br>Shannon Bruce, MFS (from 01 to 05 July 2021) |
| Test Facility Management:                                | David Bruning, BS, MBA<br>Study Management<br>Genetic Toxicology       |
| Laboratory Supervisor:                                   | Tiffany Blaylock, BS                                                   |
| Laboratory Supervisor (Dose<br>Formulation Preparation): | Ann Noland, BS, RLATG, CMAR                                            |
| Report Writer:                                           | Joan Huynh, BS                                                         |
| Principal Investigator (Dose<br>Formulation Analysis):   | Jason Conerty, Supervisor                                              |
| Test Site (Dose Formulation Analysis):                   | MicroConstants, Inc.<br>9050 Camino Santa Fe<br>San Diego, CA 92121    |

## 5. SUMMARY

The test article, cP12, was evaluated for its clastogenic activity and/or disruption of the mitotic apparatus by detecting micronuclei (Mn) in polychromatic erythrocytes (PCEs) in Sprague-Dawley rat bone marrow. Sterile phosphate buffered saline pH7.4 was used to prepare the formulations and as the vehicle control. Doses were administered once, via intravenous slow bolus at a dose volume of 1 mL/kg/day.

In the dose range-finding assay (DRF), the maximum dose levels tested were 1, 5 and 7.5 mg/kg/day in 3 animals/sex/dose level. In the absence of evidence of toxicity in either sex, the high dose for the definitive assay (15 mg/kg/day) was selected based upon sponsor-supplied data which estimated 15 mg/kg/day to be the maximum tolerated dose (MTD) based upon clinical observations in a previous study.

In the definitive assay, the dose levels tested were 0, 5, 7.5 and 15 mg/kg/day in males only. Doses were delivered by slow intravenous bolus injection on Day 1 followed by collection of femoral bone marrow on Day 2 and 3. Mortality, body weight and clinical observation data were collected. There was no mortality and only a small decrease in body weight gain on Day 2 in animals receiving 5 mg/kg/day and higher. Transient clinical signs noted primarily at 15 mg/kg/day included labored breathing, unresponsive/decreased activity, discharge, discoloration of the skin (ears, dose site), hypersalivation, swelling (ears, one or more legs) and crusty eye present through the first 5 minutes after dosing. Most animals were normal or noted with ruffled fur or crusty eye at 90 minutes post dose and were otherwise considered normal.

No significant differences in the %PCEs were observed indicating no bone marrow toxicity. No statistically significant increases in the incidence of MnPCEs in the cP12-treated groups were observed relative to the vehicle control group at either 24 or 48 hours post dose. The positive control induced a statistically significant increase in the incidence of MnPCEs. The number of MnPCEs in the vehicle control group did not exceed the historical control range. All valid assay criteria were met.

Under the conditions of the assay described in this report, a single intravenous injection of cP12 given to male Sprague-Dawley rats at doses up to and including 15 mg/kg/day was concluded to be negative for the induction of micronucleated polychromatic erythrocytes (MnPCE).



## 6. PURPOSE

The purpose of this study was to evaluate the test article for *in vivo* clastogenic activity and/or disruption of the mitotic apparatus by detecting micronuclei in polychromatic erythrocytes in rat bone marrow. This assay design is based on OECD Guideline 474 (OECD, 2016) and ISO/IEC 17025:2017 (ISO/IEC, 2017). This study is required prior to initiating Phase 2 clinical trials.

Historical control data are found in [Appendix I](#). A copy of the study protocol and amendments is found in [Appendix II](#).

The micronucleus assay is a short-term *in vivo* cytogenetic assay for detecting agents that induce chromosomal breakage or spindle malfunction. In this study, femoral bone marrow was microscopically evaluated for the presence of polychromatic erythrocytes (PCEs) containing micronuclei (MnPCEs). A clastogenic effect may be seen if micronuclei are formed during cell division as a result of chromosome breakage or malfunctioning of the mitotic spindle. In the case of chromosome breakage, acentric chromosome fragments may not be included in the nuclei of daughter cells forming single or multiple micronuclei in the cytoplasm. An aneugenic effect is seen if the test material interferes with the mitotic spindle apparatus; non-disjunction or lagging chromosome at anaphase may not be included in the nuclei of daughter cells forming single or multiple micronuclei in cytoplasm of the new cells. In this study, the incidence of micronucleated PCEs served as an indicator of test article genotoxicity.

## 7. CHARACTERIZATION AND PREPARATION OF TEST AND CONTROL ARTICLES

PolyPeptide (San Diego, CA) has determined the identity, strength, purity, and composition or other characteristics to define the test article. A copy of the Certificate of Analysis is included in [Appendix III](#). The Certificate of Analysis does not include a retest date or expiration date; however, revision history describes that up to 36 months of stability have been demonstrated and the most recent analysis of this lot of cP12 occurred in September 2020.

All unused test article was returned to the following individual at the address below prior to report finalization.

Fubao Lin  
25 Health Sciences Dr.  
Stony Brook, NY 11790  
Phone: 631-974-0844  
Email: fubao.lin@neomatrixtx.com

Residual of dose formulations were discarded after use.

The following reagent was used for formulations and as the vehicle control:

| Component                                | Supplier/Source | Lot/Batch Number | Expiration/Retest Date |
|------------------------------------------|-----------------|------------------|------------------------|
| Phosphate buffered saline pH7.4, sterile | Sigma           | RNBH7571         | 31 Jan 23              |

Scoring positive control slides (fixed and unstained), generated from BioReliance Study No. AG70PD.125M012.BTL were included to verify scoring. These slides were generated from male rats treated once with cyclophosphamide monohydrate (CP) at 40 mg/kg, and the bone marrow harvested 24 hours after treatment; dosing occurred on 08 April, 2021.

The vehicle control and positive control articles have been characterized as per the Certificates of Analysis on file with the testing facility. The stability of the vehicle control and positive control articles and their mixtures was demonstrated by acceptable results that met the criteria for a valid test.

### **Preparation of Test Article Dose Formulations**

Dosing formulations were adjusted to compensate for the peptide content and purity of the test article using a correction factor of 1.31.

Dose formulations were prepared on the day of use as follows:

In the Dose Range-Finding Assay:

Formulations were prepared individually in a biosafety cabinet/laminar flow hood, using a suitable sized sterile amber glass vial which was calibrated to the target batch size. Approximately 70% of the total volume of vehicle was added and contents were stirred magnetically for at least 14 minutes until uniform using a polytetrafluoroethylene (PTFE) stir bar. Additional vehicle was added to achieve the final target volume and then stirred magnetically again until uniform. Formulations were stored at room temperature until delivered to in-life for dosing.

In the Definitive Assay:

Formulations were prepared on the day of use in a biosafety cabinet/laminar flow hood using aseptic technique, and sterile polypropylene containers calibrated to the target batch size. A 20 mg/mL stock was prepared by adding approximately 70% of the total volume of vehicle into the container along with the appropriate amount of cP12 and the contents were vortex for two minutes. Additional vehicle was added to achieve the final target volume. The 20 mg/mL stock was used to prepare each dosing formulation by dilution. Specific amounts of vehicle and test article stock were added to a precalibrated sterile polypropylene container, and contents were vortexed for two minutes. The formulations were stored at room temperature until delivered to in-life for dosing and were dosed within 2 hours of formulation.

## Dose Formulation Collection and Analysis

Dose formulation samples were collected in 15 mL sterile polypropylene conical tubes sealed with polypropylene screw caps from the definitive assay as follows:

| Vehicle Sampling               |        |
|--------------------------------|--------|
| Number of Samples <sup>A</sup> | Volume |
| 2                              | 1 mL   |

<sup>A</sup>One sample was used for analysis and the other served as the backup

| Solution Sampling  |                                |        |
|--------------------|--------------------------------|--------|
| Dose Level         | Number of Samples <sup>C</sup> | Volume |
| Stock <sup>B</sup> | 2                              | 1 mL   |
| High Dose          | 2                              | 1 mL   |
| Mid Dose           | 2                              | 1 mL   |
| Low Dose           | 2                              | 1 mL   |

<sup>B</sup>Both samples of the stock were to be retained by BioReliance as backup (see Deviations)

<sup>C</sup>One sample was used for analysis and the other served as the backup

One set of samples for analysis was sent to the Principal Investigator on dry ice on the day of preparation. The backup aliquot(s) of each sample were stored at BioReliance at -10 to -30°C and were discarded upon acceptance of the analytical results by the Study Director. A copy of the analytical report is included in [Appendix IV](#).

The samples were shipped to:

Jason Conerty  
Supervisor, MicroConstants, Inc.  
9050 Camino Santa Fe  
San Diego, CA 92121  
P: 858-652-4614  
Fax: 858-652-4699  
JConerty@microconstants.com

The recipient was notified of the shipment.

Analysis of the samples was performed using validated analytical method MN13126.

## 8. MATERIALS AND METHODS

The assay was conducted according to established procedures ([Heddle, 1973](#); [Mavournin et al., 1990](#); [Hayashi et al., 1994](#); [OECD, 2016](#)).

Animals were treated (on Day 1 at  $t = 0$ ) with the test or control articles as described below.

The following procedures were used for both the dose range finder (DRF) and definitive (DEF) micronucleus assays as indicated below.

### Test System

Sprague-Dawley ((Hsd:SD) rats were received from Envigo RMS, Inc. (Frederick, MD) on 30 June 2021 (DRF) and 21 July 2021 (DEF).

The age at time of initiation, as well as the body weights and days of acclimation, of the rats assigned to the study groups at randomization are indicated below:

| Study | Sex    | Body Weight Range at Randomization (grams) | Age at Initiation (weeks) | Days of Acclimation |
|-------|--------|--------------------------------------------|---------------------------|---------------------|
| DRF   | Male   | 171.4 to 180.1                             | 6                         | 6                   |
|       | Female | 137.5 to 143.9                             |                           |                     |
| DEF   | Male   | 169.2 to 184.0                             | 6                         | 5                   |

### Justification for the Test System

This species has been routinely used as an animal model of choice for the mammalian bone marrow erythrocyte micronucleus assay. This strain is an outbred strain that maximizes genetic heterogeneity and therefore tends to eliminate strain-specific response to the test article.

### Animal Welfare Provisions

This study is not duplicative or unnecessary. The number of animals, procedures, and design used for this study, has been reviewed and were approved by the BioReliance Institutional Animal Care and Use Committee protocol number 491. Procedures involving animals performed at BioReliance follow the specifications recommended in the most current version of *The Guide for the Care and Use of Laboratory Animals* adopted by BioReliance ([National Academy Press, Washington, D.C., 2011](#)).

### Animal Receipt and Acclimation

Virus antibody-free (VAF) animals were acclimated as noted above and were judged to be healthy prior to utilization in the study.

## **Housing**

Animals were housed in a controlled environment at  $72 \pm 3^{\circ}\text{F}$  and  $50 \pm 20\%$  relative humidity with a 12-hour light/dark cycle. The light cycle was not interrupted for study-related activities. The animal rooms were supplied with at least 10 changes of fresh HEPA-filtered air per hour. Animals of the same sex were housed up to five per Micro-Barrier cage. Cages were placed on racks equipped with an automatic watering system and Micro-VENT full ventilation, HEPA filtered system.

## **Environmental Enrichment**

Animals were provided with Nylabones as environmental enrichment.

## **Bedding, Food and Water**

Heat treated hardwood chips were used for bedding to absorb liquids. A certified laboratory rodent chow (Envigo 2018C Teklad Global 18% Protein Rodent Diet) was provided *ad libitum*. The food was analyzed by the manufacturer for the concentrations of specified heavy metals, aflatoxin, chlorinated hydrocarbons, organophosphates and specified nutrients. Animals had free access to tap water, which met U.S. EPA drinking water standards [Washington Suburban Sanitary Commission (WSSC) Potomac Plant]. Drinking water was monitored at least annually for levels of specified microorganisms, pesticides, heavy metals, alkalinity and halogens. The results of bedding, food and water analyses are on file at BioReliance. There were no contaminants in the bedding, feed and water that were expected to interfere with the study.

## **Randomization and Identification**

Animals were assigned to groups using a randomization procedure within Provantis™. At the time of randomization, the weight variation per sex of animals did not exceed  $\pm 20\%$  of the mean weight. Following randomization, animals were identified by sequentially numbered ear tags. The cage card contained, at least, the animal number(s), sex, study number, treatment group number, dose level, test article ID and route of administration. Cage cards were color coded by treatment group. Raw data records and specimens were also identified by the unique animal number.

## **Body Weights and Animal Observation**

Body weights were recorded prior to the first dose for the purpose of dose volume calculations for all animals and once on the day of euthanasia. Animals were observed once daily for signs of illness and poor health during the acclimation period. Once dosing was initiated, animals were observed for signs of illness or poor health or for clinical signs of toxicity as indicated below.

| Procedure                               | Dose Range-Finder Animals                                                                                                                 | Micronucleus Assay Animals                                                                        |
|-----------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Moribundity and Mortality Check         | Twice daily, beginning on the first day of dose administration                                                                            |                                                                                                   |
| Detailed Hands-On Clinical Observations | Pre-dose on Day 1                                                                                                                         | On Day 1: Pre-dose, immediately post dose, and at 5, 30 and 90 minutes post dose for each animal. |
| Cage Side Observations                  | 5 minutes, 30 minutes, and 1.5 hours post-dose based upon the last animal dosed in each group, and at least once daily on non-dosing days | At least once daily on non-dosing days                                                            |

### Dose Administration

All dose formulations were administered at a volume 1 mg/kg/day by slow bolus intravenous injection into a tail vein. The dose levels were 1, 5, 7.5 mg/kg/day for the DRF and 5, 7.5 and 15 mg/kg/day for the DEF. The route of administration has been routinely used and is widely-accepted for use in the mammalian bone marrow erythrocyte micronucleus assay.

All the formulations vials for dosing for DRF were stirred prior to and during dosing and all the formulation vials for dosing for DEF were swirled gently prior to dosing.

### Dose Range-Finding Assay (DRF)

In the DRF assay, 3 animals/sex were exposed to 1, 5, 7.5 mg/kg/day of cP12. No mortality was observed. Cage side observation was limited to ruffled fur. Following the two-day observation period, all animals were euthanized by carbon dioxide inhalation, and discarded without further examination. Since no mortality or signs of toxicity were observed in the DRF study, only males were used for the micronucleus assay and the maximum dose of 15 mg/kg/day was selected.

### Definitive Micronucleus Assay

Animals were dosed with the test article or vehicle control and euthanized at the appropriate time.

Based upon the results of the DRF assays, the definitive assay design was as follows:

| Group | Treatment | Dose Level<br>(mg/kg/day) | Dose<br>Volume <sup>A</sup><br>(mL/kg/day) | Euthanasia<br>Time<br>(hrs after<br>treatment) <sup>B</sup> |    |
|-------|-----------|---------------------------|--------------------------------------------|-------------------------------------------------------------|----|
|       |           |                           |                                            | 24                                                          | 48 |
|       |           |                           |                                            | Number of<br>Male Animals                                   |    |
| 1     | Vehicle   | 0                         | 1                                          | 5                                                           | 5  |
| 2     | cP12      | 5                         | 1                                          | 5                                                           | 0  |
| 3     | cP12      | 7.5                       | 1                                          | 5                                                           | 0  |
| 4     | cP12      | 15                        | 1                                          | 5                                                           | 5  |

<sup>A</sup>Based upon individual body weight

<sup>B</sup>Range(s): 24-27 hours and 45-48 hours, respectively

### Bone Marrow Collection and Slide Preparation

Animals were euthanized by carbon dioxide inhalation at approximately 24 or 48 hours after the final dose administration. Immediately following euthanasia, the femurs were exposed, cut just above the knee, and the bone marrow was aspirated into a syringe containing fetal bovine serum. The bone marrow was transferred to a centrifuge tube containing 2 mL fetal bovine serum, the cells were pelleted by centrifugation, and the supernatant was drawn off leaving a small amount of fetal bovine serum with the pellet. Cells were re-suspended and a small drop of the bone marrow suspension was spread onto a clean glass slide. Four slides were prepared from each animal, air dried and fixed by dipping in methanol. One set of two slides (including five positive control slides) were stained with acridine orange for microscopic evaluation. The other set of slides and were kept as backup and were archived. Each slide was identified by the harvest date, study number, and animal number (or slide number for positive control slides). Slides were coded using a random number table by an individual not involved with the scoring process.

### Scoring

Bone marrow was evaluated by fluorescent microscopy. The staining procedure permitted the differentiation by color of polychromatic and normochromatic erythrocytes (bright orange PCEs and ghost-like, dark green NCEs, respectively).

The criteria for the identification of micronuclei are those of [Schmid \(1975\)](#). Micronuclei are brightly stained bodies that generally are round and that generally are between 1/20 and 1/5 the size of the PCE. Scoring was based upon the micronucleated cell, not the micronucleus; thus, occasional cells with more than one micronucleus were counted as one micronucleated PCE (MnPCE), not two (or more) micronuclei.

Four thousand (4000) PCEs/animal were scored for the presence of micronuclei (MnPCEs). In addition, at least 500 total erythrocytes (PCEs + NCEs) were scored per animal to determine the proportion of PCEs as an index of bone marrow cytotoxicity.

Stained slides were discarded prior to report finalization.

### **Statistical Analysis**

Statistical analysis was performed on the micronucleus frequency (%MnPCE) and %PCE using the animal as the unit. The mean and standard deviation of %MnPCE and %PCE were presented for each treatment group.

The use of parametric or non-parametric statistical methods in the evaluation of data was based on the variation between groups. The group variances for micronucleus frequency for the vehicle control and test article groups at the respective sampling time were compared using Levene's test (significance level of  $p \leq 0.05$ ). Since the variation between groups was found not to be significant in PCE; a parametric one-way ANOVA was performed followed by a Dunnett's post-hoc analysis to compare each dose group to the concurrent vehicle control.

A linear regression analysis was conducted to assess dose responsiveness in the test article treated groups ( $p \leq 0.01$  and  $R^2 \geq 70\%$ ).

A pair-wise comparison (Student's T-test;  $p \leq 0.05$ ) was used to compare the positive control group to the concurrent vehicle control group.

### **Criteria for Determination of a Valid Test**

The group mean frequency of MnPCEs for the vehicle control group should ideally be within the 95% control limits of the distribution of the historical vehicle control database. If the concurrent vehicle control data fall outside the 95% control limits, they may be acceptable as long as these data are not extreme outliers (indicative of experimental or human error).

The frequency of MnPCEs for the scoring positive controls must be significantly greater than the concurrent vehicle control ( $p \leq 0.05$ ) and should be compatible with those observed in the historical positive control data base.

Three doses were tested for at least one sampling time. Five animals/group were available for analysis.

The maximum dose evaluated for micronucleus induction must:

- a) be the MTD or MFD, or
- b) demonstrate cytotoxicity in the bone marrow (reduction in the PCE/NCE ratio of more than 50% but not less than 20% of the control value), or
- c) in the absence of cytotoxicity or MFD, a dose (limit dose) was used.



## Evaluation of Test Results

A test article was considered to have induced a positive response if:

- a) at least one of the test article doses exhibited a statistically significant increase when compared with the concurrent vehicle control ( $p \leq 0.05$ ), and
- b) when multiple doses were examined at a particular sampling time, the increase was dose-related ( $p \leq 0.01$  and  $R^2 \geq 70\%$ ), and
- c) results of the group mean in at least one group were outside the 95% control limit of the historical vehicle control data.

A test article was considered to have induced a clear vehicle response if none of the criteria for a positive response were met and there was evidence that the bone marrow was exposed to the test article.

## Electronic Data Collection Systems

The primary computer or electronic systems used for the collection of data or analysis included, but were not limited to, the following:

| System                                     | Purpose                                                               |
|--------------------------------------------|-----------------------------------------------------------------------|
| LIMS Labware System                        | Test Article Tracking                                                 |
| Provantis™ (Instem)                        | Captures in-life toxicology, animal randomization and management data |
| Excel (Microsoft Corporation)              | Calculations/Randomization                                            |
| Kaye Lab Watch Monitoring system (Kaye GE) | Environmental Monitoring                                              |
| BRIQS                                      | Deviation and audit reporting                                         |
| Provantis™ Tables and Stats (Instem)       | Generates in-life toxicology tables                                   |

## Records and Archives

All raw data, the original signed protocol, amendments, and the original signed final report will be archived by BioReliance at JK Records (Sterling, VA) as directed by the applicable SOP. A copy of the draft report, including Study Director and Sponsor comments, if applicable, will be archived electronically by BioReliance. Following the SOP retention period, the Sponsor will be contacted by BioReliance for disposition instructions or return of materials. Slides and/or specimens (as applicable) will be archived at EPL Archives and indexed as such in the BioReliance archive database.

BioReliance reserves the right to retain true copies (i.e. photocopies, scans, microfilm, or other accurate reproductions of the original records) for at least the minimum retention period specified by the relevant regulations.

The raw data, reports, and other documents generated at locations other than BioReliance will be archived by the Test Site.

## Deviations

The following deviations from the protocol or assay-method SOPs occurred during the conduct of this study.

Event #470403: On 26 Jul 2021, the technician recorded the five minute post dose detailed observations for animal 910 (Group 1, last animal in the group) at 1252. The animal was dosed at 1242, so the observation was recorded in Provantis 10 minutes post dose. Group 1 animals all appeared normal at five minutes post dose or had ruffled fur. The technician did observe the animal at five minutes and entered the observation into Provantis by hitting the enter button once. But that doesn't submit the entry entirely since the enter button needs to be hit a second time to write the entry and have it stamped in the system with the time and tech's initials. When the technician went to record the first animal in Group 2 at its five minute post dose time they realized they never submitted the entry for animal 910 so they checked the animal again and entered the observation correctly. Animal 910 appeared normal at 10 minutes.

This has no impact on the study since Group 1 is the control group which sets a baseline for comparison to the test article groups.

Event # 472556: On 09 August 2021 the study director was notified by the principal investigator for formulation analysis that a single sample of the 20 mg/mL stock prepared for the formulation on 26 July 2021 was received. Protocol Amendment 4 indicated that no samples of the 20 mg/mL stock were to be shipped but were to be retained by BioReliance. This deviates from the protocol.

This is a low impact event. The analytical lab noticed the discrepancy and contacted the study director. The sample is being retained by them under appropriate storage and will not be analyzed.

## 9. RESULTS AND DISCUSSION

### Dose Range Finding Assay

Clinical signs are presented in [Table 1](#) (Hands-On) and [Table 2](#) (Cage side and Mortality). Body weight data is presented in [Table 3](#).

No mortality or evidence of toxicity occurred at any dose level during the course of the dose range finding assay. Cage side observations were limited to ruffled fur in one control female and one mid-dose male. There was no effect on body weight or weight gain.

Since no mortality or evidence of toxicity was observed in the DRF, only males were used for the micronucleus assay and the high dose of 15 mg/kg was selected.

### Definitive Micronucleus Assay

Clinical signs are presented in [Table 4](#) (Hands-On) and [Table 5](#) (Cage side and Mortality). Body weight data are found in [Table 6](#).

No mortality occurred at any dose level during the course of the micronucleus assay. A small decrease in body weight gain that was not dose related occurred on Day 2 relative to the control group in animals receiving 5 mg/kg/day and higher. On Day 3, weight gain in the treated group was similar to the control. Cage side observations on Day 2 and 3 were limited to ruffled fur and a crusty eye.

Detailed hands-on observations were done on Day 1 to better determine any effects and their time course. The pre-dose observations were all normal except for a crusty eye in one animal in the 15 mg/kg/day group. The following post dose clinical signs were noted during hands on observations:

| Dose Level<br>(mg/kg/day) | Immediate Post<br>Dose                                                                                                                  | 5 Minutes<br>(Post-dose)                                                                                           | 30 Minutes<br>(Post-dose)         | 90 Minutes<br>(Post-dose)         |
|---------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|-----------------------------------|-----------------------------------|
| 0                         | ruffled fur                                                                                                                             | ruffled fur                                                                                                        | None                              | None                              |
| 5                         | ruffled fur                                                                                                                             | skin discoloration                                                                                                 | ruffled fur<br>skin discoloration | ruffled fur skin<br>discoloration |
| 7.5                       | ruffled fur                                                                                                                             | ruffled fur,<br>skin discoloration,<br>decreased motor<br>activity swelling                                        | ruffled fur<br>skin discoloration | skin discoloration                |
| 15                        | ruffled fur, labored<br>breathing,<br>discoloration,<br>swelling,<br>unresponsive, nasal<br>discharge,<br>hypersalivation<br>crusty eye | swelling,<br>discoloration<br>(skin), labored<br>breathing, nasal<br>discharge,<br>hypersalivation &<br>crusty eye | ruffled fur                       | Crusty Eye                        |

The instances of discoloration of the skin included the ears, nose, tail (dose site) or one or more limbs and were noted as white, purple or dark red depending upon the location. Swelling of the ears and/or one or more legs was also described. Most animals were normal or noted with ruffled fur or crusty eye at 90 minutes post dose and were otherwise considered normal.

Cage side observations performed on Day 2 and 3 (non dose days) was limited to ruffled fur in one rat at 15 mg/kg/day on Day 2.

### **Bone Marrow Analysis**

The incidence of MnPCEs per 20,000 PCEs scored (4000 PCEs/animal) and the proportion of polychromatic erythrocytes per total erythrocytes (%PCE) are summarized and presented for each treatment group by sacrifice time in [Table 7](#). Individual animal data are presented in [Table 8](#).

The scoring results and a statistical analysis of data of the assay indicated the following:

- No appreciable reductions in the %PCE value were observed in the test article groups compared to the vehicle control group, indicating the test article did not induce bone marrow cytotoxicity.
- Group variances for the mean of the micronucleus frequency in the vehicle control and test article groups were compared using Levene's test. The test indicated that there was no significant difference in the group variance ( $p > 0.05$ ); therefore, the parametric approach, ANOVA followed by Dunnett's post-hoc analysis, was used in the statistical analysis of data.
- No statistically significant increase in the incidence of MnPCEs was observed in the test article treated groups relative to the vehicle control groups (ANOVA followed by Dunnett's post-hoc analysis,  $p > 0.05$ ).
- The positive control, CP, induced an increase in the incidence of MnPCEs (Student's t-test,  $p < 0.05$ ).
- The number of MnPCEs in the vehicle control did not exceed the historical control range ([Appendix I](#)).

Since cP12 was dosed via the intravenous route, demonstration of bone marrow exposure is not required. Based upon these data, all criteria for a valid test were met as specified in the protocol.

The Common Technical Document (CTD) Summary Table is included in [Appendix V](#).

## Dose Formulation Analysis

The dose formulation reports is in [Appendix IV](#). Mean values for the analysis results ranged from 101 to 102% of theoretical. cP12 was not detected in the vehicle.

## 10. CONCLUSION

Under the conditions of the assay described in this report, cP12 given to male Sprague-Dawley rats by intravenous injection at doses up to and including 15 mg/kg/day was concluded to be negative for the induction of micronucleated polychromatic erythrocytes.

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## ATTACHMENT 8

## Attachment 8, 2020 MHSRS Abstract:

**A novel, bioactive peptide, cP12, for intravenous (IV) treatment of burns, produces pharmacokinetic (PK) concentrations in a Phase 1 Clinical Trial that correlate with cP12 concentrations causing microvascular vasodilation.**

Fubao Lin, PhD and Richard A. Clark, MD; NeoMatrix Therapeutics, Inc., Stony Brook, NY

Several years ago, we discovered a **14-residue, fibronectin-derived peptide (P12)** that at **10 to 30 $\mu$ M** binds PDGF-BB and enhances its bioactivity. Through this mechanism of action, P12 stimulates growth and survival of human dermal fibroblasts cultured under stress conditions, such as nutrient deprivation, reactive oxygen stress, and endoplasmic reticulum stress (*J Invest Dermatol* 134:1119-1127, 2014). P12 was then cyclized (cP12) to resist digestion by exopeptidases found in normal blood and tissue. When cP12 is administered intravenously at 0.01mg/kg, 1-4h post-burn, it limits burn injury progression, speeds healing, and reduces scarring in our porcine vertical injury progression burn model (*Wound Repair Regen* 24:501-513, 2016). In the same study, we demonstrated that aggregated red blood cells (RBCs) occlude the peri-burn microvasculature as early as 1h and increasingly for at least 48h post-burn. Importantly, the RBC occlusion decreases when cP12 is administered intravenously 1-4h post-burn at the same 0.01mg/kg dose that optimally speeds healing and reduces scarring. Concurrently, we found that **P12 at 100pM to 10nM** dilates the mucocutaneous microvasculature of the hamster cheek pouch through a  $\beta$ -adrenergic-dependent pathway (*Microcirculation*, 24:e12369, 2017). Therefore, P12/cP12 has two distinct mechanisms of action that work at entirely different concentrations: **1. PDGF-BB receptor signal biasing toward cell survival and growth *in vitro* at 10 to 30 $\mu$ M** (*J Invest Dermatol*, 134:921-929, 2014) and **2. microvascular vasodilation of the hamster cheek pouch through the  $\beta$ -adrenergic system when applied *ex vivo* at 100pM to 10nM** (*Microcirculation*, 24:e12369, 2017). From our porcine vertical injury progression burn model results, it appeared that IV administered cP12 might be working through a vasodilation mechanism (*Wound Repair Regen* 24:501-513, 2016). Although we attempted to perform PK analysis in the porcine burn model, a sufficiently sensitive test for determining porcine plasma levels around 10nM or below was not available. Due to the inadequate sensitivity of a cP12 assay, plasma levels with the optimal IV dose of 0.01mg/kg cP12 could not be obtained. Recently we completed a Phase 1 Clinical Trial of cP12 using IV doses of 0.003, 0.01, 0.02, and 0.04mg/kg. During this Clinical Trial, a clinical research organization (CRO) was able to routinely measure cP12 levels in human plasma in the range of 200pM and above. Human volunteers given 0.01mg/kg cP12 infusions attained plasma concentrations between 180pM to 11.2nM from 15 to 90min post-infusion. This is the same concentration range of P12 that stimulates microvascular dilation in the hamster cheek pouch and the likely plasma concentration range attained by an IV 0.01mg/kg cP12 dose in pigs that optimally reduces peri-burn microvascular RBC occlusion. Thus, we believe that the main mechanism of intravenously delivered cP12 for burn treatment is peri-burn microvascular dilation. At 0.01mg/kg IV dose of cP12, no central cardiovascular dilation as manifested by increased heart rate or decreased blood pressure occurs in either humans or animals. Thus, IV cP12 could be extremely useful in the setting of Prolonged Field Care and may be useful for other microvascular occlusive diseases while avoiding adverse effects on the central circulation.

### What do you expect the attendee to be able to do at the end of the session?

1. Understand how pharmacokinetics in a Phase 1 Clinical Trial can be important.
2. Describe how clinical pharmacokinetics can give important information on a drug product's mechanism of action.
3. Describe how clinical pharmacokinetics can be related to preclinical animal studies.

## ATTACHMENT 9



## Attachment 9, 2021 MHSRS Abstract:

### **Fibronectin-derived peptide P12 mitigates burn conversion, speeds healing and reduces scarring through its ability to dilate the microvasculature, decrease microvascular occlusion, and increase angiogenesis.**

Monica McTigue, PhD<sup>1</sup>, Marcia G. Tonnesen, MD,<sup>1,2</sup> and Richard A. Clark, MD<sup>1\*</sup>,

<sup>1</sup>Department of Biomedical Engineering and Dermatology, Stony Brook, NY, and <sup>2</sup>Dermatology Section, VAMC, Northport, NY

**Background:** When cyclized P12 (cP12) is administered intravenously (IV) at 0.01mg/kg, 1-4h post-burn, it limits burn injury progression, speeds healing, and reduces scarring in our porcine vertical injury progression burn model (*Wd Repair Regen* 24:501-513, 2016). In the same study, we demonstrated that aggregated red blood cells (RBCs) occlude the peri-burn microvasculature as early as 1h and increasingly for at least 48h post-burn, and that RBC occlusion is decreased when 0.01mg/kg cP12 is administered IV 1-4h post-burn. Concurrently, we found that P12 at 100pM to 10nM dilates the mucocutaneous microvasculature of the hamster cheek pouch through a  $\beta$ -adrenergic-dependent pathway (*Microcirculation*, 24:e12369, 2017). This is the same concentration range found in human plasma after 0.01mg/ml cP12 IV infusion during a Phase 1 clinical trial (180pM to 11.2nM), and in pig plasma (<100nM) after the IV 0.01mg/kg cP12 that optimally reduces peri-burn microvascular RBC occlusion.

**Methods:** For studies on angiogenesis we used two previously established methods:

1. An *in vitro* angiogenesis assay using human dermal microvascular endothelial cells (EC) cultured on collagen-coated microbeads that were dispersed in a human fibrin gel (XD Feng, MG Tonnesen, S Mousa, RA Clark *Int J Cell Biol*, 13:231-279, 2013).
2. An *in vivo* angiogenesis assay using nude mice and a commercially available assay kit containing angioreactors and matrix for implanting into the flanks of the mice. Although the kit also contained Matrigel<sup>TM</sup> as a hydrogel delivery system for potential angiogenesis factors, we found that human fibrin for delivery of peptides was far superior.

**Results:** P12 increased angiogenesis both *in vitro* and *in vivo*.

1. The *in vitro* angiogenesis assay demonstrated that 3 $\mu$ M P12 with vascular endothelial growth factor (VEGF) and Fibroblast Growth Factor-2 (FGF-2) at suboptimal doses (15 $\mu$ g/ml and 12.5  $\mu$ g/ml, respectively) doubled sprout angiogenesis from EC-covered beads compared to no P12 under the same conditions. Higher P12 concentrations showed a lesser effect.
2. The *in vivo* angiogenesis assay demonstrated that the addition of 10 or 30 $\mu$ M cP12 to a low dose of FGF-2 (50ng/ml) in fibrin gel increased angiogenesis 7-fold and 15-fold compared to no cP12 added to the same conditions. Similarly, 10 or 30 $\mu$ M cP12 addition to a low dose of VEGF (125ng/ml) in fibrin gel increased angiogenesis 80% and 130% compared to control.

**Conclusions:** We posit that IV cP12 abates burns by complimentary mechanisms, including dilation of peri-burn microvasculature, reduction of BV occlusion, and enhancement of angiogenesis. At an optimal dose of IV cP12 (0.01mg/kg), no central cardiovascular dilation, as manifested by increased heart rate or decreased blood pressure, occurs in either humans or animals. Thus, IV cP12 could be extremely beneficial in the setting of Prolonged Field Care, and may be useful for other microvascular occlusive diseases, while avoiding adverse effects on the central circulation.

### **Learning Objectives**

1. Understand how peptides can have a multitude of activities that work together to effect important biologic outcomes.
2. Learn how *in vitro* angiogenesis assays can give important clues about *in vivo* angiogenesis.
3. Acquire knowledge about a simple *in vivo* angiogenesis assay in small animals.

## ATTACHMENT 10

## **Attachment 10, 2021 MHSRS Abstract:**

### **cP12 plasma levels in Phase 1 Clinical Trial correlates with cP12 concentrations that induce microvascular vasodilation and mitigate burn conversion in animal models.**

Fubao Lin, PhD and Richard A. Clark, MD; NeoMatrix Therapeutics, Inc., Stony Brook, NY

**Background:** P12, a bioactive, 14-residue, fibronectin-derived peptide, binds PDGF-BB with a  $K_D = 200\text{nM}$ . P12 enhances growth and survival activity in adult human dermal fibroblasts (AHDF) cultured under stress conditions, e.g. nutrient deprivation, reactive oxygen stress, and endoplasmic reticulum stress (*J Invest Dermatol* 134:1119-1127, 2014). For *in vivo* studies, P12 was cyclized (cP12) to resist digestion by exopeptidases found in normal blood and tissue. When cP12 is administered intravenously (IV) at 0.01mg/kg, 1-4h post-burn, it limits burn injury progression, speeds healing, and reduces scarring in our porcine vertical injury progression burn model (*Wd Repair Regen* 24:501-513, 2016). In the same study, we found that aggregated red blood cells (RBCs) occlude the peri-burn microvasculature as early as 1h and increasingly for at least 48h post-burn. Furthermore, RBC occlusion decreases when cP12 is administered at the same dose that optimally speeds healing and reduces scarring. Concurrently, we discovered that P12 (100pM to 10nM) dilates the microvasculature of the hamster cheek pouch through a  $\beta$ -adrenergic-dependent pathway (*Microcirculation*, 24:e12369, 2017). Therefore, P12/cP12 has two distinct mechanisms of action that work at entirely different concentrations, i.e. 1) P12 induces PDGF-BB receptor signal biasing toward cell survival and growth *in vitro* at 10 to 30 $\mu\text{M}$  (*J Invest Dermatol*, 134:921-929, 2014) and 2) P12 induces microvascular vasodilation in the hamster cheek pouch when applied *ex vivo* at 100pM to 10nM (*Ibid*).

#### **Methods:**

1. AHDF cultures under nutrient deprivation (no serum) with 1nM PDGF-BB  $\pm$  P12 (*Ibid*).
2. Hamster cheek pouch intravital microscopy model for microvascular measurements (*Ibid*).
3. Yorkshire pig vertical injury progression burn model (*J Burn Care Res*, 6:638-646, 2011).
4. A Phase 1 Randomized, Placebo-Controlled, Single Ascending Dose Study to Examine Safety, Tolerability, and Pharmacokinetics of cP12 in Healthy Adults (FY17/18 MBRP Burn Program)

**Results:** From our porcine burn model results (*Wd Repair Regen* 24:501-513, 2016), it appeared that IV administered cP12 might be working through a vasodilation mechanism. Unfortunately, porcine plasma levels of cP12 could not be detected (assay sensitivity limit 100nM) when the optimal dose (0.01mg/kg) for mitigation of burn conversion was administered. With a more sensitive assay, cP12 could be detected in human plasma at picomolar concentrations. In fact, Phase 1 Clinical Trial volunteers given 0.01mg/kg cP12 infusions attained plasma levels between 180pM to 11.2nM from 15 to 90min post-infusion. This human plasma concentration range is similar to the P12 levels that stimulate microvascular dilation in the hamster cheek pouch (100pM to 10nM). Following optimal dosing of IV cP12 (0.01mg/kg) in pigs that reduces peri-burn microvascular occlusion and burn conversion, cP12 plasma levels were <100nM, a low nM or pM concentration consistent with plasma levels detected in humans given the same dose.

**Conclusion:** We posit that a main mechanism of IV cP12 in burns is peri-burn microvascular dilation. At 0.01mg/kg IV dose of cP12, no central cardiovascular dilation, as manifested by increased heart rate or decreased blood pressure, occurred in either humans or animals. Thus, IV cP12 could be extremely useful in the setting of Prolonged Field Care and may be useful for other microvascular occlusive diseases while avoiding adverse effects on the central circulation.

#### **What do you expect the attendee to be able to do at the end of the session?**

1. Understand how pharmacokinetics in a Phase 1 Clinical Trial can be important.
2. Describe how clinical pharmacokinetics can give important information on a drug product's mechanisms of action.
3. Describe how clinical pharmacokinetics can be related to preclinical animal studies.

## ATTACHMENT 11

Attachment 11, 2022 Wound Healing Society:

## TUNABILITY OF P12, A MULTI-FUNCTIONAL PEPTIDE FOR DEFINED WOUND THERAPY

Richard A. Clark, MD, Department of Dermatology and Biomedical Engineering, Stony Brook University

**BACKGROUND:** Effective wound healing requires a multitude of biologic processes. Key prerequisites include: adequate blood supply, robust granulation tissue ingrowth, increased re-epithelialization, and infection control.

**STUDY GOAL:** Identify the optimal routes of administration, doses, and delivery times for P12 that address the key prerequisites for effective wound healing.

**METHODS:** *In vitro* human dermal fibroblast and endothelial cell growth assays; *in vivo* small and large animal models to assess adequate blood supply, angiogenesis, granulation tissue formation, re-epithelialization, and rapid wound closure; and *in vitro* anti-bacterial assays.

**RESULTS:** Cyclized P12 (cP12), at optimal 0.01mg/kg iv dose in a porcine burn model, reduces microvascular occlusion by aggregated RBCs at 24h post-burn, increases re-epithelialization at 10d post burn (Asif et al. *WRR* 24:501-512,2016), and promotes wound closure at 14d post-burn (data submitted to an Investigation New Drug, IND, for cP12). Pharmacokinetics of cP12 porcine studies and a cP12 Phase 1 clinical trial showed that 0.01mg/kg cP12 iv gives blood concentrations of 100pM to 10nM over the first 2 hours of administration (data submitted to an IND for cP12). Importantly, P12 at 100pM-10nM dilates the mucocutaneous microvasculature of the hamster cheek pouch (Frame et al. *Microcirculation* 24:e12369,2017). Thus, 100pM to 10nM cP12 blood concentrations probably clear RBC aggregates from peri-burn microvasculature in our porcine burn model via microvascular dilation and thus promote burn wound healing. In contrast, P12 at 10–30microM promotes cultured fibroblast survival and growth by biasing platelet-derived growth factor-BB (PDGF-BB) activity toward cell survival/growth and away from apoptosis *in vitro* (Lin et al *JID* 134:1119-1127,2014; Zhu et al *JID* 134:921-929,2014), and stimulates fibroblast migration *in vitro* (Prasad et al *WRR* 27:634-649,2019). Furthermore, 10–30microM P12 also stimulates *in vitro* and *in vivo* human endothelial cell angiogenesis (see McTigue et al. 2022 WHS Abstract). Importantly, cP12 applied topically at 600microM promotes early healing in acute porcine wounds (likely 10-30microM concentration deep within the wound since the delivery vehicle is <1/10 volume of wound bed)(*WRR* 27:634-649,2019). Recently we found that cP12 is an anti-microbial peptide (AMP) as determined by sequence analysis and by bacterial growth inhibition (100nM-1microM) and bacterial killing (10microM or higher) of *P aeruginosa* and *S aureus*. Thus, 600microM P12 applied topically at the wound surface would be a strong anti-microbial.

**CONCLUSIONS:** The mechanisms of action of P12 are differentially concentration-dependent and therefore tunable by changing the route of administration, dose, and/or duration of delivery. Perhaps two routes of administration, e.g. cP12 iv and topically, might be synergistic.

## ATTACHMENT 12

## Attachment 12, 2022 MHSRS Abstract:

### FIBRONECTIN (FN)-DERIVED PEPTIDE P12 PROMOTES IN VITRO AND IN VIVO ANGIOGENESIS

Monica McTigue<sup>1</sup>, PhD, Marcia G. Tonnesen, MD<sup>1</sup>, and Richard A. Clark, MD<sup>1,2,3</sup>,

<sup>1</sup>Department of Dermatology and <sup>2</sup>Biomedical Engineering, Stony Brook University, Stony Brook, NY 11794, and <sup>3</sup>NeoMatrix Therapeutics, Inc., Stony Brook, NY 11790

**BACKGROUND:** Burns are one of the most devastating injuries known to mankind. In 2019 about 486,000 patients with burns in the United States (US) presented to emergency departments, of which 30,000 patients were admitted to one of the 128 burn centers in the US. Burns are dynamic injuries characterized by progressive extension of the depth of the tissue damage over the course of several days post-burn. Complications associated with burn injury are directly related to the depth of dermal destruction. Burn injury progression through the entire dermis is called burn conversion and has significant impact on both short-term consequences of increased infection, fluid imbalance, and skin grafts, and long-term consequences of increased scarring and scar contraction. Despite immense advances in understanding the healing processes at the cell and molecular level and how they can be undermined, *no cost effective, transformative therapy has reached the market for catastrophic burn conversion.*

Cyclized P12 (cP12), a 14-residue peptide from fibronectin (FN), mitigates burn conversion and speeds burn healing when an optimal 0.01mg/kg intravenous (IV) dose is infused within 6 hours post-burn in a porcine burn model. In fact, wound closure was 70% with treatment versus 20% control at 14 days post-burn. Data from these preclinical studies were submitted and accepted as an Investigational New Drug (IND) application for cP12 (funded by W81XWH-15-C-0043). In addition, cP12 has received both **Orphan Drug** and **Fast Track** designations from the FDA and completed a Phase 1 Clinical Trial in healthy adults (funded by W81XWH-18-2-0059). At present, the **cP12 for IV Injection** drug product is currently at TRL 6. Furthermore, NeoMatrix Therapeutics, Inc. (NMT), a spin-off company from Stony Brook University, is preparing a Phase 2a Clinical Trial following FDA guidance from minutes of an End of Phase 1 (EOP1) meeting.

Like many small bioactive peptides, cP12 has several mechanisms of action. Firstly, cP12 reduces microvascular occlusion by aggregated red blood cells (RBCs) at 24h post-burn, increases re-epithelialization at 10d post burn (*Wd Repair Regen* 24:501-512,2016), as well as promotes wound closure at 14d post-burn. Pharmacokinetics of cP12 porcine studies and a cP12 Phase 1 Clinical Trial showed that 0.01mg/kg cP12 IV gives blood concentrations of 100pM to 10nM over the first 2 hours of administration (data submitted to an IND for cP12). Importantly, P12 at 100pM-10nM dilates the mucocutaneous microvasculature of the hamster cheek pouch (*Microcirculation* 24:e12369, 2017). Thus, cP12 at blood concentrations of 100pM to 10nM probably clears RBC aggregates from the peri-burn microvasculature via microvascular dilation; and thereby, promotes burn wound healing in our porcine burn model. In contrast, P12 at 10–30microM promotes cultured human dermal fibroblast survival and growth by biasing platelet-derived growth factor-BB (PDGF-BB) activity toward cell survival/growth and away from cell apoptosis *in vitro* (*J Invest Dermatol* 134:1119-1127,2014; *Ibid* 134:921-929,2014), and stimulates fibroblast migration *in vitro* (*Wd Repair Regen* 27:634-649,2019).

**STUDY GOAL:** 1. To determine whether P12 promotes cultured human endothelial cells (HEC) growth and *in vitro* angiogenesis. 2. To determine whether P12 in an angio-reactor mouse model stimulates *in vivo* angiogenesis.

**METHOD:** For studies on angiogenesis we used three established methods:

1. XTT assay to determine HEC growth on collagen-coated plates.

2. An *in vitro* angiogenesis assay using HEC cultured on collagen-coated microbeads that were dispersed in a human fibrin gel (*Int J Cell Biol*, 13:231-279, 2013).
3. An *in vivo* angiogenesis assay using nude mice and a commercially available assay kit containing angioreactors and matrix for implanting into the flanks of the mice. Although the kit contained Matrigel™ as a hydrogel delivery system for potential angiogenesis factors, we found that human fibrin gel for delivery of peptides was superior.

RESULTS: P12 increased angiogenesis both *in vitro* and *in vivo*.

1. In endothelial cell defined medium with or without vascular endothelial cell growth factor (VEGF), P12 stimulated HEC growth in a dose response manner from 3-30uM without VEGF or with 1 or 50ng/ml VEGF. P12 stimulated optimal HEC growth when 10uM P12 was added to cultures containing 50ng/ml VEGF.
2. The *in vitro* angiogenesis assay demonstrated that 3uM P12 with VEGF and Fibroblast Growth Factor-2 (FGF-2) at suboptimal doses (15 ug/ml and 12.5 ug/ml, respectively) doubled sprout angiogenesis from HEC-covered beads compared to no P12 under the same conditions.
3. The *in vivo* angiogenesis assay demonstrated that the addition of 10 or 30uM cP12 to a low dose of FGF-2 (50ng/ml) in fibrin gel increased angiogenesis 7-fold and 15-fold compared to no cP12. Similarly, 10 or 30uM cP12 addition to a low dose of VEGF (125ng/ml) in fibrin gel increased angiogenesis 80% and 130% compared to control.

CONCLUSIONS: P12, a fibronectin-derived peptide, promotes HEC growth and stimulates angiogenesis by enhancing the effect of angiogenic growth factors *in vitro* and *in vivo*.

LEARNING OBJECTIVES: What do you expect the attendee to be able to do at the end of the session?

1. Describe the clinical benefit of the cP12 Drug Production for burn conversion, an unmet need in severe and/or extensive burns.
2. Describe the multiple mechanisms of action of cP12.
3. Discuss which mechanism of action is most likely to be important during the intravenous infusion of cP12 at its optimal dose. What different route of administration might be useful for the other mechanisms of action?