AWARD NUMBER: W81XWH-20-1-0825

TITLE: Polyethylene Glycol (PEG)-Mediated Fusion (PEG Fusion) Repair of Mixed Motor-Sensory Acute Peripheral Nerve Injuries (PNI) for Rapid and Immediate Improvement in Outcome

PRINCIPAL INVESTIGATOR: Jaimie Shores, M.D.

CONTRACTING ORGANIZATION:
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Polyethylene Glycol (PEG)-Mediated Fusion (PEG Fusion) Repair of Mixed Motor-Sensory Acute Peripheral Nerve Injuries (PNI) for Rapid and Immediate Improvement in Outcome

5a. CONTRACT NUMBER
W81XWH-20-1-0825

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Johns Hopkins University
Department of Plastic and Reconstructive Surgery
4940 Eastern Avenue, Suite A513

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

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13. SUPPLEMENTARY NOTES

14. ABSTRACT:

The overall objective of this study is to determine the safety of PEG fusion when used with primary repair or reconstruction in patients with an acute upper extremity peripheral nerve injury. PEG is safe and effective for extending the half-life of circulating pharmaceutical products, when used in conjunction with a topical hemostatic agent in surgical wounds, and when used as a colon cleanser for endoscopic surgical procedures. However, PEG fusion has not been rigorously tested as a safe reagent to promote nerve regeneration in humans. Therefore, the goal of this Phase 2a clinical trial is to establish safety data and to examine the effect of PEG fusion on clinical outcomes including recovery of sensory and motor function. The study will enroll 40 patients receiving autograft reconstruction within 24 hours of injury. Patients within each group will be randomized to either PEG mediated reconstruction (n=120); or conventional nerve reconstruction (n=20). Patients will be enrolled across 7 participating centers and followed for 2 years. Results will be externally validated using data collected in the DoD funded prospective NERVE study and will provide preliminary evidence to power a larger phase II efficacy trial.

15. SUBJECT TERMS

NONE LISTED

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRDC
Unclassified	Unclassified	Unclassified	Unclassified	15	**19b. TELEPHONE NUMBER** *(include area code)*

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1. **INTRODUCTION:**

The overall objective of this study is to determine the safety of PEG fusion when used with primary repair or reconstruction in patients with an acute upper extremity peripheral nerve injury. PEG is safe and effective for extending the half-life of circulating pharmaceutical products, when used in conjunction with a topical hemostatic agent in surgical wounds, and when used as a colon cleanser for endoscopic surgical procedures. However, PEG fusion has not been rigorously tested as a safe reagent to promote nerve regeneration in humans. Therefore, the goal of this Phase 2a clinical trial is to establish safety data and to examine the effect of PEG fusion on clinical outcomes including recovery of sensory and motor function. The study will enroll 40 patients receiving autograft reconstruction within 24 hours of injury. Patients within each group will be randomized to either PEG mediated reconstruction (n=120); or conventional nerve reconstruction (n=20). Patients will be enrolled across 7 participating centers and followed for 2 years. Results will be externally validated using data collected in the DoD funded prospective NERVE study and will provide preliminary evidence to power a larger phase II efficacy trial.

2. **KEYWORDS:** Polyethylene Glycol, upper extremity peripheral nerve injury, repair, reconstruction

3. **ACCOMPLISHMENTS:**

What were the major goals of the project?

Major Tasks 1: **Prepare Research Study Protocol and Prepare Regulatory Documents**

- Subtask 1: Finalize clinical protocol: Month 2 (100% complete)
- Subtask 2: Finalize case report forms (CFR) for data capture: Month 2 (75% complete)
- Subtask 3: Program and pilot test REDCap the web-based data collection system: Month 4 (0% complete)
- Subtask 4: Coordinate Sites for Clinical Trial Agreements (CTA) and Material Transfer Agreements (MTA) with Neuraptive Therapeutics, Inc.: Month 2 (90% complete)
- Subtask 5: Submit and obtain FDA IND application OR IDE application (this process has already begin in earnest prior to submission of this application, with IND application pending submission already, though FDA is considering allowing change to IDE application which has also already begun preparation pending this decision): Month 3 (100% complete)
- Subtask 6: Respond to FDA Inquiries/obtain approval: Month 9 (100% complete)
- Subtask 7: Obtain **Single Umbrella IRB** approval for the master protocol: Month 12 (100% complete)
- Subtask 8: USAMRMC Human Research Protections Office review and approval of umbrella IRB approved human use documents: Month 12 (0% complete)

Major Task 2: Train Study Personnel for Clinical Trials

- Subtask 1: Provide training for Research Coordinators on study procedures and data collection: Month 12 (0% complete)
- Subtask 2: Surgeon training: Surgeons performing PEG fusion will be required to undergo microsurgical laboratory training course on an animal model with successful completion a requirement for participation. This training will take place at JHU or SAMMC Animal Laboratory Facilities: Month 12 (0% complete)
- Subtask 3: Certify sites to begin screening and enrolling patients: Month 12 (0% complete)
- Subtask 4: Conduct study initiation calls with each site once screening and enrollment begins to address challenges and to monitor adherence to the protocol.: Month 12 (0% complete)

Major Task 3: Conduct Study (Participant Recruitment, Intervention, and Follow up)

- Subtask 1: enrollment of (n=40, 20 per group) autograft reconstruction patients randomized to PEG Fusion or non-PEG fusion repairs: Month 30 (0% complete)
- Subtask 2: Follow-up patients who have been randomized to treatment with or without PEG fusion in autograft reconstruction of segmental PNI at 30 days and then 3, 6, 9, 12, 18, and 24 months. (n=20 total, 10 per group): Month 54 (0% complete)
- Subtask 3: Generate and distribute monthly enrollment and follow-up reports to ensure that we will reach our target enrollment and to ensure complete follow-up and data quality. Provide ongoing training and support to address problems with enrollment and follow-up as they are identified: Month 54 (0% complete)

Major Task 4: Data Analysis and Report Writing (Investigators from all centers will participate, but will be headed by JHU/BSPH)

- Subtask 1: Prepare files for data analysis and begin preliminary analysis: Month 58 (0% complete)
- Subtask 2: Complete data analysis and prepare manuscripts for publication: Month 60 (0% complete)
- Subtask 3: Reporting and dissemination of findings (abstracts, presentation, publications, DOD): Month 60 (0% complete)

What was accomplished under these goals?

1) Major activities*: During the second year of the study, we executed additional agreements between Hopkins, participating sites, and Neurpative necessary for the conduct and oversight of the trial, we amended the scope of the study to focus on nerve injuries treated with operative reconstruction, we obtained sIRB and DoD HRPO approval for the master protocol, and scheduled in-person surgeon training at Hopkins.*

2) Specific objectives*: (a) Modified subcontracts with participating centers recognizing Neuraptive as regulatory sponsor for the trial; (b) fully executed a clinical trial agreement between Hopkins School of Medicine and Neuraptive for conduct of the study; (c) fully executed a service agreement between Hopkins School of Public Health and Neuraptive outlining roles and responsibilities for trial coordination and oversight; (d) received Johns Hopkins sIRB and DoD HRPO approval for the master protocol; (e) completed REDCap programming for patient randomization and data collection; (f) scheduled in-person surgeon training for November 16, 2022; (g) distributed study materials to sites on 8/29/22 to initiate local regulatory review and approval and hosted a training on the regulatory review process; (h) initiated clinical trial agreements between participating sites and Neuraptive*

3) Significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative): *None to report*

4) Other achievements*. None to report*

Describe the Regulatory Protocol and Activity Status

Describe the Protocol and Activity Status for sections a-c, as applicable, using the format described for each section. If there is nothing significant to report during this reporting period, state "Nothing to Report."

Human Use Regulatory Protocols

TOTAL PROTOCOLS: 7

PROTOCOL(S):

PROTOCOL (1 of 7 total): Johns Hopkins School of Medicine

Protocol [HRPO Assigned Number]:

Target required for clinical significance: 40 participants (20 treated with nerve repair; 20 treated with autograft reconstruction)

Target approved for clinical significance: N/A

Submitted to and Approved by:

- *Submitted to JHU sIRB: 5/22/2021*
- *Approved by JHU sIRB: 1/13/2022*
- *Submitted to DoD HRPO: 7/27/2022*
- *Approved by DoD HRPO: 8/18/2022*

Status:

(i) Number of subjects recruited/original planned target: N/A
Number of subjects screened/original planned target: N/A
Number of patients enrolled/original planned target: N/A
Number of patients completed/original planned target: N/A

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review:
None

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation:
None

PROTOCOL (2 of 7 total): Virginia Commonwealth University

Protocol [HRPO Assigned Number]:

Target required for clinical significance:

Target approved for clinical significance:

SUBMITTED TO AND APPROVED BY:

- *Submitted to local IRB* N/A
- *Approved by local IRB* N/A
- *Submitted to HRPO* N/A
- *Approved by HRPO N/A*
- *Certified by the Coordinating Center* N/A

STATUS:

(i) *Number of subjects recruited/original planned target: N/A*
Number of subjects screened/original planned target: N/A
Number of patients enrolled/original planned target: N/A
Number of patients completed/original planned target: N/A

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review:
None.

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation:
None.

PROTOCOL (3 of 7 total): Wellspan

Protocol [HRPO Assigned Number]:

Target required for clinical significance:

Target approved for clinical significance:

SUBMITTED TO AND APPROVED BY:

- *Submitted to local IRB* N/A
- *Approved by local IRB* N/A
- *Submitted to HRPO* N/A
- *Approved by HRPO* N/A
- *Certified by the Coordinating Center* N/A

STATUS:

(i) *Number of subjects recruited/original planned target: N/A*
Number of subjects screened/original planned target: N/A
Number of patients enrolled/original planned target: N/A
Number of patients completed/original planned target: N/A

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review:
None.

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation:
None.

PROTOCOL (4 of 7 total): University of Maryland Shock Trauma

Protocol [HRPO Assigned Number]:

Target required for clinical significance:

Target approved for clinical significance:

SUBMITTED TO AND APPROVED BY:

- *Submitted to local IRB 9/21/2022*
- *Approved by local IRB N/A*
- *Submitted to HRPO N/A*
- *Approved by HRPO N/A*

- *Certified by the Coordinating Center* N/A

STATUS:

(i) *Number of subjects recruited/original planned target: N/A*
Number of subjects screened/original planned target: N/A
Number of patients enrolled/original planned target: N/A
Number of patients completed/original planned target: N/A

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review:
None.

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation:
None.

PROTOCOL (5 of 7 total): **OrthoCarolina**

Protocol [HRPO Assigned Number]:
Target required for clinical significance: N/A

Target approved for clinical significance: N/A

SUBMITTED TO AND APPROVED BY:

- *Submitted to local IRB N/A*
- *Approved by local IRB N/A*
- *Submitted to HRPO N/A*
- *Approved by HRPO* N/A
- *Certified by the Coordinating Center N/A*

STATUS:

(i) *Number of subjects recruited/original planned target: N/A*
Number of subjects screened/original planned target: N/A
Number of patients enrolled/original planned target: N/A
Number of patients completed/original planned target: N/A

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review:
None.

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation:
None.

PROTOCOL (6 of 7 total): **San Antonio Military Medical Center**

Protocol [HRPO Assigned Number]:
Target required for clinical significance: N/A

Target approved for clinical significance: N/A

SUBMITTED TO AND APPROVED BY:

- *Submitted to local IRB N/A*

- *Approved by local IRB* N/A
- *Submitted to HRPO* N/A
- *Approved by HRPO* N/A
- *Certified by the Coordinating Center* N/A

STATUS:

(i) *Number of subjects recruited/original planned target: N/A*
Number of subjects screened/original planned target: N/A
Number of patients enrolled/original planned target: N/A
Number of patients completed/original planned target: N/A

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review:
None.

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation:
None.

PROTOCOL (7 of 7 total): Walter Reed National Military Medical Center
Protocol [HRPO Assigned Number]:
Target required for clinical significance:
Target approved for clinical significance:

SUBMITTED TO AND APPROVED BY:

- *Submitted to local IRB N/A*
- *Approved by local IRB N/A*
- *Submitted to HRPO N/A*
- *Approved by HRPO N/A*
- *Certified by the Coordinating Center N/A*

STATUS:

(i) *Number of subjects recruited/original planned target: N/A*
Number of subjects screened/original planned target: N/A
Number of patients enrolled/original planned target: N/A
Number of patients completed/original planned target: N/A

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review:
None.

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation:
None.

(b) Use of Human Cadavers for Research Development Test & Evaluation (RDT&E), Education or Training

TOTAL ACTIVITIES: *No RDT&E, education or training activities involving human cadavers will be performed to complete the Statement of Work (SOW)*

(c) Animal Use Regulatory Protocols
TOTAL PROTOCOL(S): 1

PROTOCOL(S):

Protocol (1 of 1):

Protocol [ACURO Assigned Number]: DM190618.e001

Target required for statistical significance: N/A -Animals used here are for training on a surgical protocol, and not necessarily for gathering quantitative data

Target approved for statistical significance: N/A

Submitted to and Approved by:

We obtained ACUC approval for changes to our animal protocol 11/15/2021, which was certified by ACURO on 12/07/2021.

Status:

To date, no swine have been used on this protocol. We anticipate training to commence in the coming months, dependent upon travel restrictions etc.

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

Nothing to report.

How were the results disseminated to communities of interest?

Nothing to report

What do you plan to do during the next reporting period to accomplish the goals?

During the next reporting period, we plan to complete surgeon training on November 16, 2022, initiate the study at Johns Hopkins, and on-board centers once they receive IRB approval.

4. **IMPACT:**

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

     Nothing to report.

   - **What was the impact on other disciplines?**

     Nothing to report.

- **What was the impact on technology transfer?**

  Nothing to report.

- **What was the impact on society beyond science and technology?**

  Nothing to report.

5. **CHANGES/PROBLEMS:**

   - **Changes in approach and reasons for change**

     Nothing to report.

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

     Nothing to report.

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

     Nothing to report.

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

     Nothing to report.

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

     Nothing to report.

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

     N/A

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

     N/A

6. **PRODUCTS:** *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

   - **Publications, conference papers, and presentations**
     Nothing to report.

- **Website(s) or other Internet site(s)**
  Nothing to report

- **Technologies or techniques**
  Nothing to report.

- **Inventions, patent applications, and/or licenses**
  Nothing to report.

- **Other Products**
  Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Jaimie Shores, M.D. Project Role: Principal Investigator Researcher Identifier (e.g. ORCID ID): N/A Nearest person month worked: 2.46 calendar months Contribution to Project: Dr. Shores is the primary investigator for this METRC clinical trial evaluating PEG fusion for PNI repair/reconstruction. As the PI of METRC and the site PI for JHU, he oversees the clinical trial with METRC personnel, performing as the JHU site local PI, as well as will be personally training all participating surgeons at clinical sites enrolling patients in PEG fusion based PNI repair in the JHU Animal facilities in the first year. He will recruit, enroll, and execute the trial intervention as well as follow his patients for the study duration.
Name: Lisa Reider, Ph.D. Project Role: METRC Coordinating Center Principal Investigator Researcher Identifier (e.g. ORCID ID): N/A Nearest person month worked: 1.1 calendar months Contribution to Project: Dr. Reider oversees all scientific and implementation aspects of the proposed study in her role as METRC Coordinating Center PI. In addition, she will collaborate with the study statistician and study PIs to conduct the data analysis.
Name: Sami Tuffaha, M.D. Project Role: Co-Investigator Researcher Identifier (e.g. ORCID ID): N/A Nearest person month worked: 0.2 calendar months Contribution to Project: Dr. Tuffaha runs an active peripheral nerve basic science research lab with multiple animal models and is already well published in basic science peripheral nerve research. He is the JHU clinical site Co-Investigator actively recruiting/enrolling, executing the study intervention, and following patients for this study at JHU.
Name: Rick Thompson, Ph.D. Project Role: Biostatistician Researcher Identifier (e.g. ORCID ID): N/A Nearest person month worked: 0.5 calendar months Contribution to Project: Dr. Thompson serves as the biostatistician for the study. He is responsible for producing DSMB reports, and design and overseeing the main study analysis.
Name: Manisha Kumar, MBA, MA Project Role: Finance Manager Researcher Identifier (e.g. ORCID ID): N/A Nearest person month worked: 1.1 calendar months (**Departed in May 2022**)

Contribution to Project:Ms. Kumar was responsible for establishing necessary contracts and agreements with all participating facilities and tracking and processing disbursement of all study payments to sites. She will also assist with preparing and submitting financial reports.

Name: Elizabeth Wysocki
Project Role: Study Manager
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 2.4 calendar months
Contribution to Project; Ms. Wysocki is responsible for the day to day management of the clinical study. She will be in routine contact with the clinical research coordinators at the study sites and assist them in meeting their goals for study recruitment, enrollment and data collection. She will field questions from the sites and triage questions as appropriate to members of the study team.

Name: Elias Weston-Farber
Project Role: Programmer
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 0.60 calendar months
Contribution to Project: Mr. Weston Farber works with the study team to create processes and programs when needed for data transfer and maintenance.

Name: Cameron L. Ghergherehchi, PhD
Project Role: Postdoctoral fellow
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 7.9 calendar months
Contribution to Project:Dr. Ghergherachi is an integral part of this project managing the animals day to day as well as helping execute the training operations with Dr. Shores in year 1. He will conduct all electrophysiologic testing during our training sessions with visiting surgeons as well as manage all animal related administrative activities. He will then participate in microsurgical review of reported cases with Dr. Shores and continue to provide continuous microsurgical training support as needed throughout the study. He will participate in data analysis and review of human research metrics and gain experience in clinical research execution during his post-doctoral time coordinating with Dr. Shores and METRC staff and sites while assisting in tabulation presentation, and authorship of data collected.

Name: Ala Elhelali, Ph.D.
Project Role: Research Coordinator
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 0.0
Contribution to Project: Dr. Elhelali will participate in study trainings and complete study certification paper work required by the METRC Coordinating Center. Upon IRB approval and certification, she will screen, enroll and follow patients according to the procedures outlined in the study protocol. Site research coordinators will enter data into REDCap and respond to monthly data quality queries from the METRC Coordinating Center.

Name: Richard Trevino, M.D.
Project Role: WellSpan Health Principal Investigator
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked
Contribution to Project: Dr. Trevino will be the clinical site PI for the clinical trial at WellSpan Health, in York, PA. He is an orthopedic hand surgeon trained in microsurgery who was the first to suggest to Dr. Bittner the use of microsutures to provide mechanical strength to PEG-fusion sites to repair simple transection PNIs in mammalian peripheral nerves. Together with Dr. Thayer, he has been the first to successfully repair ablation gap injuries in rats with PEG-fused autografts and allografts—as well as singly transected digital nerves and 2 mixed motor/sensory nerves in human case studies. Dr. Trevino is also the first to repair a more

proximal mixed nerve in a human case study. He has published 7 peer reviewed papers with Drs. Bittner and/or Ghergherehchi.

Name: COL Joseph F Alderete Jr, M.D., FAOA.
Project Role: SAMMC/RESTORE Principal Investigator,
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 0
Contribution to Project: Dr. Alderete, will serve as the submitting PI for ***Synergistic Validation of Polyethylene Glycol mediated fusion (PEG-fusion) autograft reconstruction in large animal model of Segmental Nerve Injury (SNI)*** at SAMMC/RESTORE***.*** He is the Chief of Orthopaedic Oncology and Surgical Director, Center for the Intrepid (CFI) at San Antonio Military Medical Center (SAMMC). He is the senior surgeon of the Limb Reconstruction Team at SAMMC, comprised of Hand and Upper Extremity, Vascular, Trauma, and Orthopaedic Oncology surgeons. He has had extensive surgical experience with combat Peripheral Nerve Injury since 2001, including 4 deployments into the combat theatre with Forward Surgical Teams and larger Combat Support Hospitals. As the senior surgeon for the SAMMC Limb Reconstruction Team he has performed and directed the surgical reconstruction and post-traumatic rehabilitation of the only 4 successful and functional Major (above wrist) Upper Extremity Replantation in the Department of Defense (DOD).

Name: Jonathan Isaacs, M.D.
Project Role: Virginia Commonwealth University Principal Investigator
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 0
Contribution to Project: Dr. Isaacs will serve as submitting PI for “Multimodal muscle recovery following acute and delayed nerve repair initiated through Virginia Commonwealth University. Dr. Isaacs is Professor and Chief of the Division of Hand Surgery and Vice Chairman of Research and Education in the Department of Orthopaedic Surgery within the Virginia Commonwealth University Health System. He has a vast experience in clinical nerve surgery and translational nerve research utilizing rodent and rabbit models. As co-inventor of Nerve Tape he is intimately familiar with this tool and well suited to lead the Nerve Tape optimization team.Much of his research career has focused on denervation atrophy and strategies to limit its development. As a current co-investigator on the METRC nerve study, he will easily transition to a co-investigator for the clinical application of PEG-fusion lead by Dr. Shores.

Name: Raymond Pensy, M.D.
Project Role: University of Maryland Shock Trauma Principal Investigator
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 0
Contribution to Project: Dr. Pensy will be responsible for implementing the protocol at University of Maryland Shock Trauma in a manner that will ensure recruitment goals are met. The site PI will provide clinical and scientific input on the development of the protocol, reviewing case report forms, and provide input on study progress.

Name: Glenn Gaston, M.D.
Project Role: OrthoCarolina Principal Investigator
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 0
Contribution to Project: Dr. Gaston will be responsible for implementing the protocol at OrthoCarolina in a manner that will ensure recruitment goals are met. The site PI will provide clinical and scientific input on the development of the protocol, reviewing case report forms, and provide input on study progress.

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?

Organization Name: Neuraptive Therapeutics, Inc.

Location of Organization: *(if foreign location list country)*

Partner's contribution to the project- Collaboration- Neuraptive is the regulatory sponsor for the study and is providing product for use in the trial.

8. **SPECIAL REPORTING REQUIREMENTS**
    - **COLLABORATIVE AWARDS:** *N/A*
    - **QUAD CHARTS:** *N/A*
9. **APPENDICES: *N/A***