CONTRACT NUMBER: W81XWH-22-F-0118

TITLE: Calcium and Vasopressin following Injury Early Resuscitation (CAVALIER)

PRINCIPAL INVESTIGATOR: Jason Sperry

CONTRACTING ORGANIZATION: University of Pittsburgh, Pittsburgh, PA

REPORT DATE: October 2023

TYPE OF REPORT: Annual

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

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Calcium and Vasopressin following Injury Early Resuscitation (CAVALIER)

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-22-F-0118

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Jason L. Sperry, Laura Vincent, Meghan Buck, Laurie Silfies, Natalie Rogers, Hannah Hayes

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

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

University of Pittsburgh
Pittsburgh, Pennsylvania 15213

8. PERFORMING ORGANIZATION REPORT NUMBER

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Task Order 0010 will be a 4-year (3-year enrollment) multi-center, prehospital and early in-hospital, double blind, randomized, interventional trial to examine safety and efficacy of prehospital calcium to patients at risk of hemorrhagic shock, early in-hospital vasopressin in patients at risk of hemorrhagic shock requiring blood transfusion and early operative procedures, or both compared to placebo in patients at risk of hemorrhagic shock.

15. SUBJECT TERMS
Prehospital calcium, in-hospital vasopressin, hemorrhagic shock

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRDC
Unclassified	Unclassified	Unclassified	Unclassified	14	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

Task Order 0010 will be a 4-year (3-year enrollment) multi-center, prehospital and early in-hospital, double blind, randomized, interventional trial to examine safety and efficacy of prehospital calcium to patients at risk of hemorrhagic shock, early in-hospital vasopressin in patients at risk of hemorrhagic shock requiring blood transfusion and early operative procedures, or both compared to placebo in patients at risk of hemorrhagic shock. Trial will utilize prehospital agencies at approximately twelve LITES Network sites and will enroll a total of 1,050 subjects.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Prehospital calcium, in-hospital vasopressin, hemorrhagic shock

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Multicenter, randomized, double-blind EFIC trial designed to determine the safety and efficacy of prehospital calcium, early in-hospital vasopressin, or both in patients at risk of hemorrhagic shock.

What was accomplished under these goals?
For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

- Notice of award for Task Order 0010 was received on 19-SEP-2022.
- Investigators and CCC/DCC continue meeting weekly to discuss study start-up and logistics.
- Conducted planning meeting with University of Pittsburgh's Investigational Drug Services (IDS) in NOV-2022.
  - IDS cost estimate was finalized/executed on 18-JUL-2023!
- Successful virtual In Progress Review (IPR) meeting held on 13-DEC-2022.
  - CCC/DCC worked on/finalized the PPT presentation in preparation for the DEC IPR meeting.
- Began drafting initial data variable list for eDCF (electronic Data Collection Forms) creation.
  - CCC/DCC meeting to continue refining data variable list for eDCF (electronic Data Collection Forms) creation.
- PM worked with finance personnel to develop the Scope of Work (SOW).
- LITES Finance team distributed sub-contracts to sites in MAY-2023.
- DCC launched CAVALIER web page in JUN-2023. https://www.litesnetwork.org/cavalier/
- PM and study team continued drafting Manual of Procedures.
- Study was registered on ClinicalTrials.gov and the NCT# was released (NCT05958342) on 21-JUL-2023.

IND/FDA

Initial Investigational New Drug (IND) Application was submitted to the FDA on 23-NOV-2022.

- CCC submitted response to FDA request for information 02-DEC and 19-DEC-2022.
- FDA hosted a teleconference with investigators and study staff to obtain clarification of targeted patient population, discuss EFIC criteria and to detail forthcoming Clinical Hold.
  - Full Clinical Hold letter received 23-DEC-2022.
  - Investigator and study team submitted the response to FDA Clinical Hold comments on 02-MAR-2023.
- FDA remove full clinical hold letter received 31-MAR-2023!

CCC finalized/submitted the response to FDA non-hold comments, revised Informed Consent templates and protocol v3 to the University of Pittsburgh office for IND & IDE Support (IIS) on 23-JUN-2023.

- IIS submitted these documents through the FDA's electronic submission Gateway and delivery confirmation was received on 26-JUN-2023.

University of Pittsburgh sIRB

Initial IRB application submitted 18-APR-2023. Committee Review date: 26-APR-2023 – Modifications Required to Secure Approval (memo received 08-MAY). Modifications included:

- Clarification of staff training (prehospital and in-hospital) for potential additional doses of calcium and/or vasopressin and persistent hypertension.
- Defining in-hospital procedure inclusion criteria as "major hemorrhage control" procedures.
- Wording changes to consent forms.
- Providing more specificity to required activities in community consultation and public disclosure plan.
- Response submitted and IRB approval granted on 18-MAY-2023.

Modification submitted to the sIRB on 24-MAY-2023

- Modification included: addition of study team and Pitt site CC/PD plan v2 (addition of media release; revisions to video script and survey for consistency and video production needs)
- Committee Review date: 30-MAY-2023 – approval was granted on 30-MAY.

Modification submitted to the sIRB on 09-JUN-2023.

- Modification included: Pitt site CC/PD plan v3 (revised to update language in the study survey to address survey flow following pre-release testing).
- Expedited (minor modification) – approval was granted on 14-JUN-2023.

Modification submitted to the sIRB on 14-JUL-2023.

- Modification includes: Spanish translations of CC/PD video script and survey, Pitt site CC/PD plan v4

(incl. Facebook page, QR code survey flyer, larger text brochure)
- Committee Review date: 24-JUL-2023. Approval was granted on 24-JUL-2023.

OHRO

Documents were submitted to OHRO for initial review. Confirmation of receipt was obtained on 06-JUN-2023.
- Additional information was sent to OHRO on 26-JUL-2023.
- Received confirmation that the submission for the 10 USC 980 waiver request is in progress.
- 25-SEP-2023 – the CAVALIER EFIC request has gone to Legal and AHRPO for review.

Site Selection

CCC worked to select participating sites.
- Feasibility survey distributed to all sites and responses collected throughout Q4 2022.
- The site selection process continued with the collection of site feasibility surveys and the CCC held initial calls with sites in Q1 2023.

Finalized site selection and participating sites were identified:
- Arizona, Denver, Hennepin County, Miami, Mississippi, New Mexico, Ohio State, Texas Tech, Tulane, UCSF, Pittsburgh
- Alternate sites identified: UT Houston, UT San Antonio, Arkansas, Boston, BAMC

Notification letters for study participation and alternate sites were distributed on 02-MAR-2023.

Participating Sites

CCC drafted study-related materials and Community Consultation and Public Disclosure toolkit.
- CCC distributed Community Consultation and Public Disclosure toolkit to enrolling sites in JUN-2023.

CCC submitted ECS-HSR Multicenter Application to University of Pittsburgh office for IND & IDE Support (IIS) on 26-JUL-2023.
- Notified of application approval on 10-AUG-2023.

CCC is working with vendors to supply goods and services needed for Community Consultation and Public Disclosure (CC/PD) campaigns.

PM drafting template materials for study execution and workflows.

CCC/DCC conducted the first All-Sites Call on 07-JUL-2023 and continued to hold monthly calls throughout the reporting period.
- Sites are working to draft their CC/PD plans for submission to the sIRB.

External site planning continues; via email and meetings with site research staff and prehospital agencies as-needed.

Site logistics and regulatory calls were conducted throughout this reporting period. See below for prehospital agency survey status, logistics, and regulatory calls held/scheduled.

	Logistics Call	**Regulatory Call**	**Top Five Prehospital Agencies (calcium phase)**
Arizona *PH/ In-Hosp*	06-APR-2023	08-MAY-2023	Received
Denver *PH/ In-Hosp*	12-APR-2023	15-MAY-2023	Received
Hennepin *PH/ In-Hosp*	24-MAY-2023	21-JUN-2023	Received
Miami *PH/ In-Hosp*	31-MAR-2023	09-MAY-2023	Received
Mississippi *PH/ In-Hosp*	10-MAY-2023	Via email	Received
New Mexico *PH/ In-Hosp*	18-APR-2023	16-MAY-2023	Received
Ohio State *PH/ In-Hosp*	19-APR-2023	08-JUN-2023	Received

Texas Tech *PH/ In-Hosp*	24-MAY-2023	21-JUN-2023	Received
Tulane *PH only*	05-MAY-2023	19-MAY-2023	Received
UCSF *In-Hosp*	26-MAY-2023	Via email	N/A
Pittsburgh *PH/ In-Hosp*	31-MAR-2023	N/A	Received
	IRB approval of community consultation and public disclosure plan was granted on 18-MAY-2023. ▪ Site demographics and catchment areas are the same for UPMC and AGH institutions. CC/PD efforts will be completed in tandem.		
	Site planning continues; collaboration with Dr. Martin-Gill and MACRO ongoing. ▪ CCC coordinated with vendors to prepare for community consultation and public disclosure efforts. ▪ Community consultation and public disclosure activities were initiated in AUG-2023 and are on-going.		
	The ECS-HSR initial Research Investigator Start-up Education (RISE) meeting was conducted on 25-AUG-2023. Report received – CCC is working to address comments.		
AGH *PH/ In-Hosp*	DoD COR and USAMRAA Contract Specialist approved the addition of Allegheny General Hospital as a twelfth enrolling site on 01-JUN-2023. ▪ PM worked with finance personnel to develop an adjusted Scope of Work (SOW) for AGH site that eliminates funds for CC/PD activities that we be conducted for overlapping catchment area by the Pittsburgh site.		
Emory *PH/ In-Hosp*	Considerations for site participation underway and feasibility call held in SEP-2023.		
Enrollment	Nothing to report as enrollment has not yet begun.		

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to report.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

- Prepare In-Progress Review (IPR) presentation for NOV-2023 meeting.
- Submit participating sites CC/PD plans for sIRB approval.
- Continue Pitt site CC/PD activities/efforts.
- Order additional supplies for Community Consultation and Public Disclosure as needed.
- Continue working with sites to execute contracts.
- Obtain fully executed reliance agreements.
- Continue drafting study-related materials.
- Continue drafting initial data variable list for eDCF (electronic Data Collection Forms) creation.

Travel Reporting:

- No travel was conducted during this reporting period.
  - Note: the training/conference subcode was used for an online Project Management course for Natalie Rogers.
- No travel is anticipated for the next quarter.

Cumulative to Billing Period: 30-SEP-2023	**Travel Funds Budgeted**	**Cumulative Actual Spent**	**Remaining Balance**
Upcoming Travel for Quarter: OCT-2023 to DEC-2023	**Traveler Name**	**Destination/ Purpose**	**Estimated Date of Travel**
	N/A	N/A	N/A

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to report.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report.

5. **CHANGES/PROBLEMS:** The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Staff addition:

- Natalie Rogers (promoted to Project Manager for TO10 in OCT-2022).
- Hannah Hayes (promoted to Assistant Project Manager for TO10 in AUG-2023).

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

- The study team met with the manufacturer of the proposed vasopressin product, Central Admixture Pharmacy Services (CAPS) a 503B compounding pharmacy, on 09-FEB-2023.
  - CAPS informed us on 16-FEB-2023 that another product will need to be selected for the study.
  - Study team is pivoting to a new product with the assistance of Pitt's Investigational Drug Service (IDS) and amended the hold response accordingly.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to report,

Significant changes in use or care of vertebrate animals

Not applicable to TO 0010

Significant changes in use of biohazards and/or select agents

Not applicable to TO 0010

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**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation);*

status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).

Nothing to report.

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to report.

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report.

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to report.

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report.

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:
  - *data or databases;*
  - *physical collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*

- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Example:

Name:	*Mary Smith*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*1234567*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support:	*The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Personnel Listing: see page 14

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to report.

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

Quad Chart: see page 14

9. APPENDICES: Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

Annual and final reports are submitted to: https://ers.amedd.army.mil/

AND
One Copy: Contract Specialist, Ronnie Sanford
Email: ronald.s.sanford2.civ@health.mil

One e-Copy: Science Officer, René Smith
Email: rene.k.smith.civ@health.mil

Personnel Listing (as of 30-SEP-2023)

W81XWH-16-D-0024 / W81XWH-22-F-0118			
Department	**Personnel Name**	**UPitt Role**	**T0 % Effort**
Surgery	Buck, Meghan L	Asst Proj Mgr	18.2%
Emergency Medicine	Guyette, Francis X III	Co-PI	2.9%
Emergency Medicine	Martin-Gill, Christian	Co-Investigator	20.6%
Surgery	Rogers, Natalie	Research Coordinator (CRC)	20.0%
Surgery	Rush, James	EMS Assistant Project Manager	53.9%
Surgery	Sperry, Jason L	PI	5.0%
Surgery	Vincent, Laura Everett	Program Administrator	2.5%
Emergency Medicine	Weiss, Leonard S	Co-Investigator	5.0%
Epidemiology (GSPH)	Wisniewski, Stephen R	Co-PI	5.0%
Emergency Medicine	Zikmund, Chase	Data Analyst	2.8%

YEAR 1 QUAD CHART

Linking Investigations in Trauma and Emergency Services – TO10

17052001-T10/W81XWH-16-D-0024, W81XWH-22-F-0118

Task Order 0010: **CA**lcium and **VA**sopressin following **I**njury **E**arly **R**esuscitation (CAVALIER) Trial

PI: Jason Sperry MD MPH **Org:** University of Pittsburgh **Award Amount: $11,999,380**

STUDY AIMS

To determine whether:

AIM#1A. Prehospital calcium as compared to a placebo results in lower 30-day mortality in patients at risk of hemorrhagic shock.

AIM#1B. Early in-hospital vasopressin as compared to placebo results in lower 30-day mortality in patients at risk of hemorrhagic shock.

AIM#2A. Prehospital calcium results in lower 6-hour and 24-hour mortality, lower blood and blood component transfusion requirements, lower rates of multiple organ dysfunction, lower rates of nosocomial infection, fewer deaths from hemorrhage and brain injury, improved hemostasis, and more ICU-free and hospital-free days.

AIM#2B. Early in-hospital vasopressin results in lower 6-hour and 24-hour mortality, lower blood and blood component transfusion requirements, lower rates of multiple organ dysfunction, lower rates of nosocomial infection, fewer deaths from hemorrhage and brain injury, improved hemostasis and fewer ICU free days and hospital length of stay.

AIM#3. Prehospital calcium and/or early in-hospital vasopressin results in differential or additive primary or secondary outcome effects.

APPROACH: multi-center, double blind, prehospital & in-hospital phase randomized trial

ACCOMPLISHMENTS

- ✓ Notice of award received in SEP-2022.
- ✓ FDA remove Full Clinical Hold letter received in MAR-2023.
- ✓ Initial sIRB application was approved MAY-2023.
- ✓ DCC launched CAVALIER web page in JUN-2023. https://www.litesnetwork.org/cavalier/
- ✓ Study was registered on ClinicalTrials.gov (NCT05958342).

Timeline and Cost

Activities CY	2022	2023	2024	2025	2026
Study Development & Startup					
IRB approval, Database creation, OHRO approval					
4-year (3-year enrollment), N=1050					
Data analysis and publication					
Estimated Budget	Current Total Paid: $248,136 Remaining Balance: $11,751,244 2% Utilized				

Updated: (University of Pittsburgh 13-OCT-2023)

Goals/Milestones

CY22 | CY23 Goal – Study Development & Startup
- ✓ Initial IND submission

CY23 Goals
- ✓ Obtain FDA/IND approval
- ✓ Finalize site selection
- ✓ Initial sIRB submission, sIRB approval

CY24 Goal
- ❑ Army Surgeon General EFIC waiver approval; OHRO approval
- ❑ Data base creation and CRF completion, data dictionary
- ❑ Site Initiation Visits
- ❑ Begin patient enrollment (N=1050), Continue patient enrollment

CY25 Goal
- ❑ Finish patient enrollment

CY26 Goal
- ❑ Data analysis and publication

Budget Expenditure compared to Actual thru 30-SEP-2023
- Actual Expenditure: $275,584.63
- Scheduled Expenditures: $2,079,341.81