AWARD NUMBER: W81XWH-16-C-0188

TITLE: Tesamorelin Therapy to Enhance Axonal Regeneration, Minimize Muscle Atrophy and Improve Functional Outcomes Following Peripheral Nerve Injury and Repair

PRINCIPAL INVESTIGATOR: Jaimie T. Shores, MD

CONTRACTING ORGANIZATION: Johns Hopkins University
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REPORT DATE: October 2018

TYPE OF REPORT: Annual

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

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October 2018	Annual	30 Sep 2017 - 29 Sep 2018

4. TITLE AND SUBTITLE

Tesamorelin Therapy to Enhance Axonal Regeneration, Minimize Muscle Atrophy and Improve Functional Outcomes Following Peripheral Nerve Injury and Repair

5a. CONTRACT NUMBER
W81XWH-16-C-0188

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
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8. PERFORMING ORGANIZATION REPORT NUMBER

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

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

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

We have hired and trained all necessary staff. We have received HRPO approval. We obtained IRB approval and continued review approval from JHU IRB and also IRB waivers from our primary recruitment sites (Union Memorial Hospital and University of Maryland Medical Center/Shock Trauma.

The placebo purchase agreement and material transfer agreement have been agreed on and signed by JHU and Theratechnologies responsible officials.

We have enrolled and screened our first patient to the trial.

15. SUBJECT TERMS
IRB, FDA IND exemption, HRPO, study set-up phase, patient recruitment

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	9	19b. TELEPHONE NUMBER *(include area code)*

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1. **INTRODUCTION**:

This study is a randomized, double-blinded, placebo-controlled clinical trial with the primary aim of assessing the efficacy of tesamorelin for peripheral nerve injuries. Patients with ulnar nerve lacerations at the wrist, repaired in a primary fashion, will be eligible for enrolment. Subject recruitment will take place primarily at Johns Hopkins Hospital, Union Memorial Hospital (Curtis National Hand Center), University of Maryland Medical Center/Shock Trauma, and Walter Reed National Military Medical Center. Subject follow up and outcome measurements will take place at Johns Hopkin Hospital. We plan to enroll 36 subjects over 4 years. At the end of the study, if tesamorelin is found to be efficacious, limited off-label use may be justified. Theratechnologies will then pursue a larger Phase 3 clinical trial aimed at achieving FDA-approval for tesamorelin to become the first drug indicated for treatment of peripheral nerve injuries.

2. KEYWORDS:

Tesamorelin, peripheral nerve injury, peripheral nerve regeneration, Phase 2 clinical trial, motor recovery, sensory recovery.

3. **ACCOMPLISHMENTS:**

- **What were the major goals of the project?**

Below is a table listing the goals of the study as listed in the statement of work for Year 2, including the timeline as initially anticipated. We had initially anticipated beginning patient recruitment in Year 1, however, initiation of patient recruitment was been delayed by the need for more time than anticipated for study set-up, which included contract agreement between JHU and Theratechnologies and HRPO approval. Because of this delay, patient recruitment began in the second half of Year 2 with enrollment of our first participant.

	Timeline	**Completed**
Major Task 1: Study Set Up	Months	Percentage (%)
Coordinate with Theratechnologies for material transfer agreements	1-3	100%
Complete Investigational New Drug (IND) application to the U.S. Food and Drug Administration	1-3	100%
Refine eligibility criteria, exclusion criteria, screening protocol	1-3	100%
Finalize consent form & human subjects protocol	1-3	100%
Finalize assessment measurements	1-4	100%

Coordinate with Sites for IRB** protocol submission	1-3	100%
Coordinate with Sites for UMH (Means) and UMMC (Pensy) IRB** review	1-6	100%
Coordinate with Sites for WR IRB** review (ORP/HRPO)	1-6	100%
Submit amendments, adverse events and protocol deviations as needed	As needed	NA
Coordinate with Sites for annual IRB report for continuing review	Annually	100%
Coordinate with Sites for UMH (Means) and UMMC (Pensy) IRB** review	1-6	100%
Coordinate with Sites for WR IRB** review (ORP/HRPO)	1-6	100%
Milestone Achieved: FDA IND approval	3	100%
*Milestone Achieved: Local IRB** approval at JHH, CNHC, UMMC/ST*	3, 4	100% (waived at CNHC and UMMC/STC)
*Milestone Achieved: HRPO*** approval for all protocols and local IRB**	6	100%
Major Task 2: Coordinate Study Staff for Clinical Trials		
Coordinate for space allocation for new staff	1-3	100%
Milestone Achieved: Study space allocated	2-3	100%
Coordinate with Sites for job descriptions design	1-4	100%
Advertise and interview for project related staff	1-4	100%
Train/orient newly hired staff	4-6	100%
Milestone Achieved: Research staff hired/trained	3-6	100%
Major Task 3: Randomized Controlled Trial		
Active participant recruitment efforts	4-36	100%
Milestone Achieved: 1st participant consented, screened and enrolled	6-9	100%
Participants randomized to study drug or placebo groups	6-36	0%
Participant follow-up visits from assessments	6-46	0%
Milestone Achieved: 18 participants consented, screened and enrolled	20-24	0%
Milestone Achieved: 36 participants consented, screened and enrolled	32-36	0%
Milestone Achieved: Final patient completed final follow-up visit	46-48	0%

- **What was accomplished under these goals**

  The primary goal for Year 2 was to complete study set up and being participant recruitment and enrollment. All of the aims pertaining to study set-up major task 1 and 2 have been achieved (see above table). Unanticipated hurdles and delays were encountered for all aspects of the study set-up, including negotiating a material transfer agreement with Theratechnologies, identifying and hiring qualified study personnel and obtaining IRB and HRPO approval. Patient enrollment was delayed by the need for more time than expected for study set-up, however, once we cleared all of hurdles pertaining to study set up, we were able to begin patient enrollment in August 2018.

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

  Our Clinical Coordinator, Ala Elhelali, has gained tremendous insights by familiarizing herself with the trial protocol and helping with patient recruitment and enrollment. She has attended courses run by the Sidney Kimmel Cancer Center at JHH to further advance her skills and expertise with running a clinical trial. In addition, she has also attended training courses and workshops for clinical study coordinators and research nurses run by the Institute for Clinical and Translational Research (ICTR) at JHU and CITI.

- **How were the results disseminated to communities of interest?**

  There are no results to report during this reporting period. The results of this study will remain blinded until the end of the study.

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

  During the next reporting period, we plan to continue actively recruit and enroll additional participants to the trial.

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**

  There were no significant changes in approach other than some changes to personnel, which are detailed below under 'changes that had a significant impact on expenditures'.

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

  We experienced a number of unexpected delays in study set up which subsequently have delayed the initiation of subject enrollment.

  - Our study coordinator and research technician positions applied from abroad and are not U.S. citizens and as such, the amount of time needed for them to come to Baltimore and commence work on the study was longer than expected. This issue has been resolved, as the research technician began work in early October 2017 and the clinical coordinator began work in early December 2017.
  - The IRB and HRPO approval process took longer than expected, but have now been completed.
  - The process of negotiating a material transfer agreement between Theratechnologies and JHU was also more time intensive and difficult than expected which delayed subsequent stages of the study set up. We now have a fully executed material transfer agreement.
  - Patient recruitment and enrollment was delayed by the delays described above in study set-up. However, this stage has now commenced.

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

  A detailed request for budget adjustments including rationale will be submitted.

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

  The study protocol was updated to include video recording and photography of participants wound and clinical functional assessments. Furthermore, the informed consent form was also updated to reflect these changes, which also included consent for video recording and photography of the participants wound and clinical functional exam. Both documents were submitted to IRB 2 on January 31, 2018 and approved on February 15, 2018.

  The study coordinator contact details in the study recruitment flyer and submitted and approved by the IRB.

  A continued review report has been submitted to the Johns Hopkins University IRB. The IRB continuing review approval is attached under Appendices.

- **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**

  Nothing to Report

- **Journal publications.**

  Nothing to Report

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

  Nothing to Report

- **Other 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*
Project Role:	*PI*
Nearest person month worked:	*2*
Contribution to Project:	*Dr. Shores has worked on all aspects of study set up and patient recruitment and enrollment*

Name:	*Sami Tuffaha*
Project Role:	*Co-Investigator*
Nearest person month worked:	*1*
Contribution to Project:	*Dr. Tuffaha has worked on all aspects of study set up and patient recruitment and enrollment*

Name:	*W.P. Andrew Lee*
Project Role:	*Co-Investigator*
Nearest person month worked:	*1*
Contribution to Project:	*Dr. Lee has worked on all aspects of study set up*

Name:	*Shivani Ahlawat*
Project Role:	*Co-Investigator*
Nearest person month worked:	*1*
Contribution to Project:	*She will be responsible for ensuring appropriate MRI data management according to protocol and will also work with Dr. Shores and the biostatistician in analysis of data.*

Name:	*Roberto Salvatori*
Project Role:	*Co-Investigator*
Nearest person month worked:	*1*
Contribution to Project:	*Dr. Salvatori will have an integral role in the study, particularly with regards to dosing and safety monitoring guidelines. He help with the PI to interpret safety data and implement necessary changes.*

Name:	*Todd Brown*
Project Role:	*Medical Monitor*
Nearest person month worked:	*1*
Contribution to Project:	*Dr. Brown will work as our medical monitor. He will ensure our study is conducted safely and he will perform site visits.*

Name:	*Ala Elhelali*
Project Role:	*Clinical Study Coordinator*
Nearest person month worked:	*11*
Contribution to Project:	*Dr. Elhelali has worked on all aspects of study set up and patient recruitment and enrollment*

Name:	*Chia Na Min*
Project Role:	*Sr. Research Technician*
Nearest person month worked:	*6*
Contribution to Project:	*Ms Min has worked on the regulatory paperwork*

- **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: Theratechnologies

  Location of Organization: *Quebec, Canada*

  Partner's contribution to the project: Material support (future). This company will provide the study drug and placebo, as previously described. During this reporting period, we were able to secure a material transfer agreement with Theratechnologies for this arrangement.

  Organization Name: Union Memorial Hospital

  Location of Organization: *Baltimore, MD*

  Partner's contribution to the project: Collaboration in research, study set-up

  Organization Name: University of Maryland/Shock Trauma

  Location of Organization: *Baltimore, MD*

  Partner's contribution to the project: Collaboration in research, study set-up

  Organization Name: Walter Reed NMMC

  Location of Organization: *Bethesda, MD*

  Partner's contribution to the project: Collaboration in research, study set-up

8. SPECIAL REPORTING REQUIREMENTS

QUAD CHARTS: An updated quad chart is attached to this report under Appendices.

9. APPENDICES:

Office of Human Subjects Research
Institutional Review Boards

1620 McElderry Street, Reed Hall, Suite B-130
Baltimore, Maryland 21205-1911
410-955-3008

410-955-4367 Fax e-mail:
jhmeirb@jhmi.edu

Date: October 23, 2018

CONTINUING REVIEW APPROVAL

Review Type:	Convened
Principal Investigator:	Jaimie Shores
Number:	IRB00110936 / CR00022918
Title:	Tesamorelin Therapy to Enhance Axonal Regeneration, Minimize Muscle Atrophy, and Improve Functional Outcomes following Peripheral Nerve Injury
Committee Chair:	B Douglas Smith
IRB Committee:	IRB-2

Date of approval: October 18, 2018

Date of Expiration: October 17, 2019

The JHM IRB approved the above-referenced Continuing Review.

The study remains open for enrollment. The PI included a CRMS summary.

Please remember to submit the DSMB report via a change in research application when the report is available.

If this study is a clinical trial and data collection is complete for the perspecified primary outcome, Section 801 of the Food and Drug Administration Amendments Act requires reporting of summary results information at http://www.clinicaltrials.gov. Reporting must be done within 12 months of completing data collection for the prespecified primary outcome, regardless of sponsor or funding source. Failure to comply with this law may result in civil penalties. For more information on results reporting go to http://www.clinicaltrials.gov. If the study is registered with Clinicaltrials.gov and is closed to recruitment and enrollment, the record must be updated within 30 days to reflect the study's enrollment status. See http://clinicaltrials.gov/ct2/manage-recs/how-edit for more information. Questions can be directed to register@clinicaltrials.gov.

Date of Approval and Expiration Date: The approval and expiration date for this research are listed above. If the approval lapses, the research must stop and you must submit a request to the IRB to determine whether it is in the best interests of individual participants to continue with protocol-related procedures.

Changes in Research: All proposed changes to the research must be submitted using a Change in Research application. The changes must be approved by the JHM IRB prior to implementation, with the following exception: changes made to eliminate apparent immediate hazards to participants may be made immediately, and promptly reported to the JHM IRB.

Continuing Review: Continuing Review Applications should be submitted at least 6 weeks prior to the study expiration date. Failure to allow sufficient time for review may result in a lapse of approval. If the Continuing Review Application is not submitted prior to the expiration date, your study will be terminated and a New Application must be submitted to reinitiate the research.

Unanticipated Problems: All unanticipated problems must be submitted using a Protocol Event Report.

If this research has a commercial sponsor, the research may not start until the sponsor and JHU have signed a contract.

The Johns Hopkins Institutions operate under multiple Federal-Wide Assurances: The Johns Hopkins University School of Medicine - FWA00005752, Johns Hopkins Health System and Johns Hopkins Hospital - FWA00006087