

AWARD NUMBER: W81XWH-22-1-0257

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

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CONTRACTING ORGANIZATION: Johns Hopkins University, Baltimore, MD

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# REPORT DOCUMENTATION PAGE

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<b>6. AUTHOR(S)</b>  Sami Tuffaha, MD, Ala Elhelali, PhD, MSc  E-Mail: <a href="mailto:stuffah1@jhmi.edu">stuffah1@jhmi.edu</a> ; <a href="mailto:aelhela1@jhmi.edu">aelhela1@jhmi.edu</a>				<b>5d. PROJECT NUMBER</b>	
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<b>14. ABSTRACT</b>  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 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.					
<b>15. SUBJECT TERMS</b> Tesamorelin, clinical trial, peripheral nerve injury, PNI, ulnar nerve, IRB, FDA IND exemption, HRPO, study set-up phase, patient recruitment					
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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. Subjects 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 1 planning phase, including the timeline as initially anticipated.

	<b>Timeline</b>	<b>Completed</b>
	<b>Months</b>	<b>Yes/No</b>
Major Task 1: Prepare Regulatory Documents and Research Protocol		
Coordinate with Theratechnologies for material transfer Agreements	1-6	Yes

Coordinate with Sites for material transfer agreements (MTAs) or clinical trial agreements (CTAs) submission	1-3	Yes
Submission a Pre-Investigational New Drug (IND) meeting request to the U.S. Food and Drug Administration	1-3	Yes
Submission an Investigational New Drug (IND) application to the U.S. Food and Drug Administration	3-9	Yes
Refine eligibility criteria, exclusion criteria, screening protocol	3-9	Yes
Finalize consent form & human subjects protocol	3-9	Yes
Coordinate with Sites to initiate single IRB submission	3-12	Yes
Clinicaltrial.gov registration	1	Yes
Milestone Achieved: FDA IND approval	7-9	Yes
Milestone Achieved: IRB** approval at JHH	9-12	Yes
Milestone Achieved: HRPO *** approval for all protocols and local IRB approval	9-12	Yes

**What was accomplished under these goals?**

The primary goal for planning phase Year 1 was to set up the study. All of the aims pertaining to study set-up have been achieved (see above table). Of note, we anticipate beginning study enrollment in clinical trial phase Year 1 by the end of July 2023.

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, FDA IND clearance, and IRB clearance. However, we have now cleared all of hurdles pertaining to study set-up, other than HRPO approval, and we anticipate beginning subject enrollment in the next month.

**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 actively recruit and enroll participants into 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:**

*Nothing to Report*

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

We do not anticipate any problems or delays.

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

The delay in hiring our research coordinator, Aston King, and an additional co-investigator, Ala Elhelali, had an impact on the study's expenditure during the first year, resulting in lower than expected spending. Additionally, the FDA's decision to proceed with an IND exemption unintentionally led to reduced costs in the planning phase of year 1.

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

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

We have made modifications to our clinical trial design, including a change in the primary outcome measure and a reduction in the number of in-person visits. These adjustments were implemented to address the specific challenges associated with conducting a large-scale clinical trial for peripheral nerve injury.

To measure our primary outcome, we have decided to use three-point pinch testing instead of the traditional nerve conduction study. The three-point pinch testing method is a reliable and objective tool for assessing muscle function and nerve regeneration, ensuring accurate and valid results.

We reduced the number of in-person visits from 13 to 6, aiming to alleviate the travel burden on study participants. This reduction in visits will enhance convenience and improve overall participant experience during the trial.

**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.**

*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**

*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:	<i>Sami Tuffaha, M.D.</i>
Project Role:	<i>Principal Investigator</i>
Researcher Identifier (e.g. ORCID ID):	<a href="https://orcid.org/0000-0003-2921-0928">https://orcid.org/0000-0003-2921-0928</a>
Nearest person month worked:	2
Contribution to Project:	<i>Dr. Tuffaha</i> has worked on all aspects of study design, regulatory setup and study start up efforts. He will lead and oversee the rest of the study team in the execution of the study. Dr. Tuffaha will maintain open communication with all co- investigators, medical monitor and collaborators. He will schedule regular group meetings to give progress updates and provide a forum to trouble shoot problems. He will also maintain close communication with and oversight of the study coordinator.
Funding Support:	

Name:	Jaimie Shores, M.D.
Project Role:	Co-Investigator

Researcher Identifier (e.g. ORCID ID):	1234567
Nearest person month worked:	1
Contribution to Project:	<i>Dr. Shores</i> has worked on all aspects of study set up, and regulatory set up. <i>Dr. Shores</i> provided his input with regards to study design
Funding Support:	

Name:	<i>Roberto Salvatori, M.D.</i>
Project Role:	<i>Co-Investigator</i>
Researcher Identifier (e.g. ORCID ID):	<a href="https://orcid.org/0000-0001-6495-2244">https://orcid.org/0000-0001-6495-2244</a>
Nearest person month worked:	0
Contribution to Project:	<i>Dr. Salvatori</i> will have an integral role in the study, particularly with regards to dosing and safety monitoring guidelines. He will be present for all meeting with the Safety Monitor and the Principal Investigator to help interpret safety data and implement necessary changes.
Funding Support:	

Name:	<i>Shivani Ahlawat, M.D.</i>
Project Role:	<i>Co-Investigator</i>

Researcher Identifier (e.g. ORCID ID):	<a href="https://orcid.org/0000-0003-4437-5237">https://orcid.org/0000-0003-4437-5237</a>
Nearest person month worked:	0
Contribution to Project:	<i>Dr. Ahlawat</i> will be responsible for performing the MRI imaging on all study patients. She will work to ensure optimal implementation of standardized imaging protocols. She will also be responsible for ensuring appropriate MRI data management according to protocol and will also work with <i>Dr. Tuffaha</i> and the biostatistician in analysis of data.
Funding Support:	

Name:	<i>Ahmet Hoke, M.D., Ph.D.</i>
Project Role:	<i>Co-Investigator</i>
Researcher Identifier (e.g. ORCID ID):	<a href="https://orcid.org/0000-0003-1215-3373">https://orcid.org/0000-0003-1215-3373</a>
Nearest person month worked:	0
Contribution to Project:	<i>Dr. Hoke</i> will perform the electromyography (EMG) and oversee performance of the nerve conduction studies (NCS) on study patients. He helped design the protocols for these assessments. He will be intimately involved in troubleshooting any issues that arise and in data analysis and interpretation.
Funding Support:	

Name:	<i>Todd Brown, M.D.</i>
Project Role:	<i>Study Monitor</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	0
Contribution to Project:	<i>Dr. Brown will serve as the study medical monitor. He has ample biostatistical expertise to allow effective analysis of safety data. He has no stake in the outcome of this study and has no financial or fiduciary interests related to the study. He is in no way a member of the study team and will not receive compensation. He has no incentives, financial or otherwise, related to this study.</i>
Funding Support:	

Name:	<i>Ala Elhelali, Ph.D.</i>
Project Role:	<i>Co-Investigator</i>
Researcher Identifier (e.g. ORCID ID):	0000-0002-7147-3564
Nearest person month worked:	6

Contribution to Project:	<i>Dr. Elhelali</i> has worked on all aspects of study set up, study design and regulatory document preparation and submission. She will dedicate her protected research time to ensuring that all regulatory hurdles are cleared in a timely manner.
Funding Support:	

Name:	<i>Sheiza Baksh, Ph.D.</i>
Project Role:	Epidemiologist
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2
Contribution to Project:	<i>Dr. Baksh</i> has provided her statistical expertise with regards to the study design.
Funding Support:	

Name:	<i>Aston King, BS</i>
Project Role:	Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	3
Contribution to Project:	<i>Mr King</i> is responsible for ensuring patient coordination and administrative tasks, setting up meetings with the research team, preparing study documentation, setting up study database.
Funding Support:	

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

Dr. Elhelali was added as a co-investigator.

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

*Nothing to Report*

**8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:**

**QUAD CHARTS:**

**9. APPENDICES:**