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

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PUBLIC ABSTRACT

Background: This study will aim to address the topic area of Peripheral Neuropathy. Peripheral nerves can be thought of as the circuitry between the central nervous system (brain and spinal cord) and the rest of the body. Following injury to peripheral nerves, the ability to move the muscles and feel sensations from the skin supplied by those nerves is lost, resulting in paralysis and numbness. Fortunately, injured peripheral nerves can regenerate (regrow), but they do so at a very slow rate and they must often travel long distances to reach their targets. Unfortunately, during the process of nerve regeneration, the muscles that are no longer receiving input from those nerves experience permanent breakdown known as atrophy (muscle wasting). Because of this, after nerve regeneration is complete, patients often fail to regain full muscle function and sensation and remain permanently debilitated.

For many decades, researchers have been looking for therapeutic options to speed the process of nerve regeneration. Although a number of promising experimental agents have been identified in animal studies, none of these therapies have transitioned from the laboratory to clinical use. As a result, beyond some advancements in surgical technique, the way we manage peripheral nerve injures has not changed much over the past century.

Objective: Our goal is to introduce tesamorelin as the first therapy clinically indicated for treatment of peripheral nerve injuries.

Tesamorelin is a drug that causes the body to produce increased amounts of growth hormone. Many animal studies have shown that growth hormone, via its downstream factors, can speed peripheral nerve regeneration following injury and can directly act on muscle to prevent atrophy, thereby improving functional outcomes. There is also reason to believe tesamorelin may accelerate bone, tendon, and wound healing when those tissues are also injured. Importantly, because tesamorelin is already a Food and Drug Administration (FDA)-approved drug (for another use) with a known safety profile, it is well suited for clinical investigations.

To introduce tesamorelin as a therapy for peripheral nerve injuries, a multidisciplinary and multi-institutional team of military and civilian physician-scientists will test the efficacy of the drug in a clinical trial. Patients with upper extremity nerve injuries will receive either the drug or a placebo (inactive drug), and outcomes will be compared in a blinded fashion (to avoid bias, neither patients nor doctors will know which patients receive the active drug). A number of electrodiagnostic, imaging, and functional assessments (testing muscle function and sensation) will be performed at set time points, and

outcomes in the patients treated with tesamorelin will be compared to outcomes in patients treated with placebo.

Impact: If we find tesamorelin to be effective in speeding nerve regeneration, preventing muscle atrophy, and ultimately improving outcomes after peripheral nerve injuries, there will be the potential to help many patients, both civilian and military. Peripheral nerve injury is not uncommon among civilians, as peripheral nerves are present throughout the body and are frequently injured due to trauma. Situations in which this can occur include motor vehicle accidents, assaults, and sports injuries, to name a few. It is important to note that we are only including patients with a specific injury type (ulnar nerve cuts) to limit differences between study participants and allow us to produce meaningful data that can be compared statistically. However, if we find that tesamorelin is effective, the results will be applicable to many clinical scenarios, including large nerve defects and hand and face transplantation, to name a few. This study also has the potential to help many of our wounded Warriors who are returning from the battlefield with mangled limbs that often involve devastating peripheral nerve injuries. Even when we are able to reconstruct the blood vessels, bones, and soft tissues in their injured arms and legs, peripheral nerve injuries often prevent these soldiers from regaining function in their limbs and can lead to amputation. With this in mind, we seek to establish tesamorelin as the first treatment for peripheral nerve injuries that will allow injured Soldiers and civilians to regain meaningful muscle function and sensation. Such a breakthrough would have a huge impact in minimizing disability and improving quality of life for those affected.