NorLeu3-A(1-7) Stimulates Corneal Repair After Injury

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Objectives/Rationale: Traumatic corneal abrasions are caused by mechanical damage to, or loss of, the epithelial surface layer of the eye's cornea. The cornea's shape and location make it particularly susceptible to blunt or sharp trauma. When the corneal epithelium is breached and the sensory nerves are exposed, significant discomfort or pain can result. Defects in the barrier of the corneal epithelium are a gateway for outside organisms, leading to corneal ulcers and subsequent vision loss. Corneal-wound management typically includes pain relief and topical antibiotic administration and has historically included eye patching, although this practice is no longer recommended due to a lack of evidence for effectiveness and indications that it may even hinder healing.

This proposal aims to demonstrate that treatment of corneal abrasions with USB005, a preserved eye-drop formulation of NorLeu3-A(1-7), is safe and will enhance corneal healing. Tissue regeneration and anti-inflammatory activity of USB005 will reduce scar formation, preserve vision, and decrease distortion of visual acuity as well as the associated optical discomfort. In order to accomplish the objectives of this proposal, three specific aims must be met: (1) optimization of an easily transportable, room temperature stable, eye-drop formulation of USB005, (2) completion of a robust efficacy evaluation in a rabbit model of corneal abrasions, and (3) completion of a 28-day, repeat dosing toxicology study demonstrating safety and tolerability of USB005.

Impact: According to the American Academy of Ophthalmology, 2.5 million eye injuries occur in the United States every year, many of which can lead to permanent vision loss. Traumatic corneal abrasions, accounting for roughly 1% of all office visits to primary care physicians and 10% of all emergency department visits in the United States, are the most common form of ocular injuries. Currently, there is no Food and Drug Administration-approved drug to facilitate wound healing and tissue repair in the cornea. USB005 provides a unique opportunity to treat traumatic corneal abrasions through clear corneal healing and the reduction of associated pain. By accelerating the wound healing process and the restoration of visual acuity, USB005 will maximize function for return to duty or civilian life as well as reduce the initial and long-term costs associated with restorative and rehabilitative or acute care of ocular injuries. At the end of the proposed 16-month project, USB005 will be ready for investigation in human subjects. Upon completion of successful clinical trials, the product will be available as an over-the-counter treatment that facilitates complete healing of corneal abrasions while reducing post-injury complications such as blurred vision.

Military Benefit: Recent conflicts such as those in Iraq and Afghanistan have exposed US military personnel to combat injuries and environmental conditions that increase the risk of traumatic corneal abrasions. Such injuries significantly reduce visual function and cause severe pain due to inflammation, corneal vascularization, scar formation, and disordered stromal healing. In 2005, the Department of Defense found that 26% of ocular injuries suffered by active duty personnel were attributed to traumatic corneal abrasions and...
lacerations; with an incident rate of 5.89 per 1000 personnel, these were three times more common than the next leading ocular injury. According to a study done on the incidence and cost of vision dysfunction and blindness in the US military from 2000 through 2010, the cost per superficial eye injury was $344 and the annual cost to treat superficial eye injuries was $4,189,573. A novel, easily transported therapeutic intervention to preserve vision, decrease associated optical discomfort, and induce accelerated avascular healing would optimize the ocular health and performance of military personnel across the full spectrum of operations.