Prevention and Treatment of TBI-Mediated Visual and Brain Damage Using a Novel Protective Compound

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PUBLIC ABSTRACT

Traumatic brain injury (TBI) and resulting damage and dysfunction to both cognitive and visual processes is among the leading injury of military personnel, with over 250,000 documented cases ranging from mild to severe. TBI is also highly prevalent among civilian populations and is the leading cause of death for individuals 1-44 years old. Nearly 2% of the American population (5.4 million individuals) suffers from consequences of TBI at some point in their lives. Not only does TBI create everyday challenges, it also puts individuals at greater risk to develop chronic and currently untreatable neurodegenerative diseases, such as Alzheimer's disease.

One issue confronting healthcare workers is lack of neuroprotective treatment options for patients with TBI. Current therapy consists primarily of physical and cognitive rehabilitation. While sometimes effective, these treatments fail to address the underlying cause of TBI-mediated impairments: neuronal damage and dysfunction. There is thus a critical need for neuroprotective pharmacologic treatments that can both prevent and rehabilitate visual and cognitive dysfunction after TBI.

The goal of this application is to use a rigorous preclinical rodent model to evaluate the efficacy of a newly developed neuroprotective compound in preventing damage and dysfunction in the brain and eye after blast-mediated TBI. We have excellent preliminary evidence that treatment soon after injury significantly protects neurons in the brain and retina. We propose to determine the optimal dose and treatment window of our neuroprotective compound for prevention of acute neuronal damage and dysfunction immediately after TBI. We will also determine whether our novel neuroprotective compound can be used to rehabilitate neuronal functioning in the brain and retina chronically after TBI.

Our study addresses two important aspects of TBI: cognitive dysfunction and visual dysfunction. Because we explore both of these parameters in the same animal, we will be able to draw meaningful relationships between retinal and cognitive outcomes. If visual system damage mirrors damage in the brain, retinal outcomes may be important for the identification and monitoring of individuals with TBI. This would advance medical care of these patients, as the objective retinal measures we employ are readily quantifiable in repeated noninvasive measures in the same study subject.

We believe that the compound we will test in this proposal, named (-)-P7C3-S243, will have a substantial positive clinical impact for TBI-affected Service Members, Veterans, and their families. We anticipate that our compound can be delivered to patients immediately post-injury to help prevent TBI-mediated neuronal damage. We also anticipate that our compound will facilitate rehabilitation from neuronal damage and dysfunction in the retina and brain. We have strong preliminary data that our compound is safe and effective, with no adverse outcomes following prolonged exposure in small animal models of neurodegenerative damage and diseases. We are currently...
completing a safety profile of our compound in non-human primates.

We are projecting that our compound will be ready for deployment for clinical studies to prevent acute TBI-mediated neuronal dysfunction in the next few years, as we are currently in discussions with pharmaceutical companies regarding drug development of our novel neuroprotective compound.