

Cysteamine in the Therapeutic Pipeline

Raptor Pharmaceuticals Corporation has received orphan drug status from the FDA for its compound cysteamine as a potential treatment for Huntington's Disease. Phase II clinical trials are being planned for later in 2008.

In December 2007, Raptor Pharmaceuticals Corp. acquired the worldwide rights to DR (delayed release) cysteamine, a proprietary enterically coated formulation of cysteamine bitartrate, a cystine depleting agent. Their formulation delays release of the drug from the stomach to the small intestine which they believe will reduce unpleasant side effects such as nausea and vomiting.

Cysteamine has been approved by the FDA and EMEA (European Medicines Agency) for treating nephropathic cystinosis, a rare lysosomal storage disease which, if left untreated, can lead to kidney failure and death. Raptor is working with the Cystinosis Research Foundation on that disorder but has been interested in researching other possible uses for the drug.

Pre-clinical indications of efficacy in HD

Previous research has suggested cysteamine as a potential therapy for Huntington's Disease. Ted Daley, president of Raptor's clinical products division, stated, "The FDA's decision to grant cysteamine orphan drug designation in Huntington's Disease complements our efforts to develop additional indications for cysteamine. We will be building off of the existing preclinical data that shows cysteamine's safety and potential efficacy to treat HD. We look forward to initiating a Phase II clinical study in HD patients in 2008."

Interest in this line of research dates back to 2002 when cystamine was tried in the R6/2 model. Tissue transglutaminase activity is known to be elevated in Huntington's Disease and it was hypothesized that it contributed to pathology through the facilitation of the formation of the HD protein aggregates. Cystamine is a transglutaminase inhibitor. Robert Ferrante and colleagues administered cystamine to the HD mice with the results that survival time was increased and body weight and motor performance were improved.

Cysteamine is the reduced form of cystamine and since it is FDA approved for cystinosis, researchers were interested in testing it in Huntington's Disease. A Phase I study was conducted in 2005 by Dr. David Dubinsky and Carolyn Gray who concluded that a dose of 20 mg/kg per day of cysteamine was tolerable in people with Huntington's disease.

In 2006, research by Frédéric Saudou, Sandrine Humbert, and colleagues clarified the mechanism by which cystamine and cysteamine are beneficial. They found that both compounds are neuroprotective in HD mice by increasing brain derived neurotrophic factor (BDNF) release from the cells in the brain. These compounds increase BDNF through two mechanisms. One is through an increase in the level of the heat shock DnaJ-

containing protein 1b (HSJ1b), which is known to be lowered in HD patients. The other is through the inhibition of tissue transglutaminase.

Another Raptor project holds promise for HD patients

Raptor is also working on a new method of delivering drugs to the brain that otherwise would not be able to cross the blood brain barrier. Only certain small molecules can get across the protective barrier which is a serious limitation in the development of treatments for neurological diseases. Success in this endeavor would likely benefit the Huntington's Disease community by opening up new possibilities for treatment. For example, this might be a way to get BDNF (brain derived neurotrophic factor) to the brain to protect it.

On August 1, 2006, Raptor signed an agreement to collaborate with Dr. William Mobley, Professor of Neurology and Neurological Sciences at the Stanford School of Medicine and Director, Neuroscience Institute at Stanford commencing August 1, 2006. Dr. Mobley's lab will study the utility of the Company's proprietary Receptor-Associated Protein ("RAP") vectors, collectively referred to as NeuroTrans™, as potential transporters of intravenously administered therapeutics across the blood-brain barrier.

"We appreciate Raptor's support of research into this important therapeutic area" stated Dr. Mobley in 2006. "The ability to deliver potential therapeutic compounds across the blood-brain barrier would be an exciting medical advance in our treatment of neurodegenerative diseases. We look forward to testing Raptor's approach to the delivery of therapeutic proteins, such as Nerve Growth Factor or NGF, to the brain."

View a video which explains the new technology here:

http://www.raptorpharma.com/programs_neurotrans.html

References

Raptor Press Releases

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