

Title: A Study of Intrathecal Enzyme Replacement for Cognitive Decline in Mucopolysaccharidosis I

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Synopsis:

This study is a 24-month open label, prospective, randomized trial in 16 MPS I patients age six years or older who have documented evidence of cognitive decline. The study will test the safety and efficacy of intrathecal recombinant human alpha-L iduronidase (rhIDU) to reduce or stabilize cognitive decline by assessing the subjects at baseline with neuropsychological, clinical, radiological, and biochemical evaluations and then monitoring the change in these parameters during a regimen of first monthly, then quarterly, intrathecal treatments with rhIDU. The clinical safety of the regimen will be assessed by monitoring of adverse events, cerebrospinal fluid (CSF) laboratory assessments, and clinical evaluations.

Subjects will be randomized to a treatment or a control group for 12 months, following which all subjects will receive 12 months of active treatment. During the first 12 months, the control group will receive similar study assessments but will be unblinded with no placebo administered. Subjects will have extensive baseline screening evaluations, after which subjects who were randomized to the treatment group will receive their first dose of intrathecal rhIDU. The enzyme will be administered via intrathecal injection at 1-3 month intervals throughout the 24-month study period. There will be a mid-study analysis after 12 months comparing changes in IQ and memory tests between controls and the treatment group. If pre-established criteria of improvement are met, the study will terminate at the 12 month point. If shown to be effective, intrathecal enzyme replacement therapy (ERT) would be the only treatment for cognitive decline in patients who do not qualify for and/or are unable to have hematopoietic stem cell transplantation.