A Study of Intrathecal Enzyme Replacement Therapy for Spinal Cord Compression in Mucopolysaccharidosis I (MIRC-001)

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Synopsis:

This is a pilot study of the effects of intrathecal enzyme replacement therapy with iaronidase (Aldurazyme, recombinant human α-L-iduronidase, EC 3.2.1.76) on spinal cord compression in mucopolysaccharidosis I. We are studying up to 10 subjects with the mild-moderate form of the disease who have developed spinal cord compression to determine the safety and efficacy of applying enzyme replacement therapy into the spinal fluid to treat their disease. As this is a pilot study, the principle outcome is safety.

In MPS I, substantial neurologic morbidity can be caused by spinal cord compression from GAG storage. GAG storage can also obstruct cerebrospinal fluid (CSF) reabsorption with resultant hydrocephalus and developmental decline or chronic headaches. Treatment of these problems often requires the implantation of a ventricular-peritoneal shunt to relieve CSF pressure and decompression of the cord using a cervical laminectomy with removal of thickened meninges. Intrathecal rhIDU may provide a non-surgical alternative to treat spinal cord compression in these patients. IT rhIDU can reduce GAG storage to near normal levels in 4 monthly doses in a canine model of MPS I.

The MIRC trial has been open since November 2005, under BB IND 12561. At Harbor/UCLA one subject has completed the trial and two other subjects were screened but not enrolled, due to failure to meet inclusion criteria. Non-study patient 01-03 is undergoing off-label IT iaronidase treatment administered by the lead PI. This patient (01-03), who began treatment in August 2006, is a minor. The local (Harbor/UCLA) IRB withdrew their initial approval of the inclusion of minors after the subject was screened. The FDA has been informed that the patient is receiving off-label treatment while not on study. An additional adult patient (BR-01) was treated in Brazil by another investigator prior to the initiation of the study but following our protocol (Muñoz Rojas et al., Manuscript in preparation). No other study sites or subjects are active at this time. No new safety concerns have been identified.