Mucopolysaccharidosis type II (MPS II) is a rare X-linked lysosomal storage disorder affecting primarily males. The disease is caused by mutations in the iduronate 2-sulfatase (IDS) gene resulting in the loss of iduronate 2-sulfatase (I2S) enzyme activity and subsequent systemic accumulation of glycosaminoglycans (GAGs).

- Deafening skeletal dysplasia, hepatosplenomegaly and airway obstruction
- Neurogenic form of MPS II –progressive neurocognitive effects due to GAG accumulation in the central nervous system (CNS)
- Weekly ERT (idursulfase) administration does not cross the blood-brain barrier, therefore does not impact CNS disease manifestations
- Therapeutic burden due to the frequency and duration of infusions, limited ability to travel, repeated needle sticks and spasmic infusion-related reactions

Current standard of care does not address the full spectrum of clinical manifestations experienced by patients with MPS II. This leaves high unmet medical need for MPS II treatment that addresses both the peripheral and cognitive aspects.

HMI-203 has the potential to effectively treat the features of MPS II with a single dose delivered via peripheral infusion.

HMI-203 is a Gene Therapy delivered as a one-time I.V. administration

HMI-203 has been designed to deliver functional copies of the IDS gene and restore I2S enzyme function through both direct cell transduction and cross-correction.

HMI-203 Mechanism of Action

HMI-203 Significantly Reduced GAG-HS Levels in Cerebrospinal Fluid (CSF) and Lysosomal Burden was Similar to WT levels in CNS Tissues of the MPS II Mouse Model

HMI-203 Prevented Progression of Craniofacial and Hindlimb Abnormalities in MPS II Mouse Model Compared to Vehicle MPS II Mouse Model Controls

References


ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT05236324

Based on studies demonstrating efficacy of HMI-203 studies in the MPS II mouse model, the jumPSart Phase I gene therapy clinical trial (NCT05236324) has been initiated, and recruitment is ongoing in the United States and Canada.

Demonstration of positive safety and efficacy results in the adult population may allow for enrollment of younger and more severely affected participants in future studies.

Overview

HMI-203 is a Phase 1, open-label, dose-escalation study to evaluate the safety and efficacy of HMI-203 in ERT-Treated Adults with MPS II

Primary study endpoints include:
- Incidence and severity of treatment-emergent adverse events (TEAEs) and adverse events of special interest (AESI; hepatic assessments)
- Mean percent change from Baseline in urine GAG levels and I2S activity through Week 52 following HMI-203 administration

jumPSart Clinical Design

To decrease the potential for an immune response to HMI-203, jumPSart uses a prophylactic immunosuppressive regimen with a corticosteroid and the T-cell inhibitor, tacrolimus.