ASGCT 2021 Annual Meeting
Digital Presentation
May 11, 2021

Long-Term Expression of HMI-203: Investigational Gene Therapy Candidate for Mucopolysaccharidosis Type II (MPS II), or Hunter Syndrome

Smith L, Patel K, Gingras J, Tzianabos A, Schulman L, Zhivich V, Kivaa M, Faulkner D, Sengooba A, Behmoiras L, Seabrook T, Dollive S, Avila N, Zhao J, White Y, Newman J, Woodcock S, Smith S, Francone O and Seymour A

Homology Medicines, Inc.

Mucopolysaccharidosis Type II (MPS II), or Hunter syndrome, is a rare X-linked lysosomal storage disorder (LSD) caused by mutations in the iduronate-2-sulfatase (*IDS*) gene, resulting in loss of I2S enzyme activity leading to subsequent systemic (peripheral organs and central nervous system (CNS)) toxic lysosomal accumulation of glycosaminoglycans (GAGs), which are large polysaccharides made of repeating disaccharide units responsible for providing structure and hydration to the cell. The disease results in skeletal dysplasia, joint stiffness, hepatosplenomegaly and airway obstruction and in severe cases, neurocognitive deficits. Hunter syndrome occurs in approximately 1 in 100,000 to 1 in 170,000 males, and the severe form leads to life expectancy of 10 to 20 years. Herein, we report preclinical gene therapy data where a single intravenous (I.V.) dose of an investigational gene therapy candidate (HMI-203) delivering human *IDS* (hIDS) in the MPS II murine model resulted in significant levels of functionally active hI2S protein in the serum out to 44 weeks post-dose (study on-going). Circulating hI2S protein collected from the serum demonstrated cross-correction activity using an *in vitro* cross-correction assay. Robust *IDS* tissue expression from HMI-203 was demonstrated in the brain, liver, heart, spleen, lung and kidney when compared to age-matched vehicle-treated MPS II mice out to 24 weeks post-dose (last time point evaluated) demonstrating systemic and CNS transduction. Lastly, sustained levels of hI2S demonstrated amelioration of phenotypic symptoms associated with joint and digit deformities in the MPS II murine model starting at onset of the phenotype (between 20 and 28 weeks of age) and was maintained out to 45 weeks following administration. Based on this IND-enabling data, HMI-203 IND-enabling studies are ongoing to support the development of HMI-203 as a gene therapy for the treatment of MPS II.