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Poster Presentation
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HMI-203: Investigational Gene Therapy for Mucopolysaccharidosis Type II (MPS II), or Hunter Syndrome

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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 CNS) toxic lysosomal accumulation of glycosaminoglycans (GAGs), large polysaccharides made of repeating disaccharide units responsible for providing structure and hydration to the cell¹. The disease results in skeletal dysplasia, joint stiffness, hepatosplenomegaly and airway obstruction and in severe cases, neurocognitive deficits². 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.

We report preclinical gene therapy data where a single intravenous (I.V.) dose of an investigational gene therapy construct (AAVHSC-HMI-203) delivering human *IDS* (hIDS) in the MPS II murine model^{3,4} resulted in systemic and CNS transduction and *IDS* expression. Significant levels of functionally active hI2S protein were observed in serum within a week post-administration and were found to be stable out to 28 weeks (last time point evaluated). The robust hIDS tissue expression significantly reduced murine GAG and LAMP-1 levels in the brain, liver, heart, spleen, lung and kidney tissue when compared to vehicle-treated MPS II mice.

Furthermore, *in vivo* circulating functional hI2S protein demonstrated the ability to cross-correct *in vitro*. Sustained levels of hI2S demonstrated amelioration of phenotypic symptoms associated with joints and digits in the MPS II mouse model following administration. Based on these nonclinical 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.

1. Wraith et. al, 2008 2. Scarpa M., 2018 3. Muenzer J. et. al, 2002 4. Garcia et. al. 2007