

## 18th Annual WORLDSymposium™ Meeting

### Poster Presentation

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#### **Patient and physician perspectives inform clinical trial design for a single intravenous dose of HMI-203, a gene therapy candidate for adults with mucopolysaccharidosis type II (MPS II), or Hunter syndrome**

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MPS II, a rare lysosomal storage disorder caused by mutations in the *IDS* gene, progresses as a multisystem disorder. Peripheral (non-neuronopathic) manifestations are debilitating in all patients, independent of neurological involvement. HMI-203 is an investigational AAVHSC vector-mediated gene therapy with preclinical data demonstrating broad tissue biodistribution, including the CNS. Ahead of its clinical trial in MPS II adults, Homology sought to more fully understand the specific disease burden experiences of patients and physicians to better inform study design.

We conducted both panel and 1:1 interviews with nine adults with MPS II and three caregivers, as well as six 1:1 physician interviews, collecting qualitative data to understand the most burdensome aspects of disease and perceptions about current and future therapies. Physicians were also asked about potential endpoints and an enzyme replacement therapy (ERT)-discontinuation regimen to follow any potential HMI-203 administration.

All patients queried receive weekly ERT, citing it as their most beneficial therapy but noted the expense, time, and inconvenience involved. Additionally, all patients have undergone multiple high-risk surgeries and other supportive care therapies. Patients wanted ERT to better address their daily symptoms, of which the most burdensome were reported as limited mobility (9), pain (8) and hearing loss (7). All patients desired a potential one-time gene therapy that could alleviate the burden of weekly ERT and provide at least equal therapeutic benefit. Physicians provided feedback that informed a proposed ERT-discontinuation regimen along with key endpoints following HMI-203 administration, including motor function tests, pulmonary and cardiovascular tests, and patient-reported pain scales.

Patients with MPS II currently require weekly ERT infusions with the added burden that many disease manifestations are incompletely resolved by ERT. Based on the input from MPS II patient and physician experiences, Homology aims with this study to incorporate patient-focused endpoints into its planned clinical trial of HMI-203, including the potential to safely discontinue ERT based on expert input.