What is a Clinical Trial?

A clinical trial, also called a clinical research study, tests an investigational medicine or treatment in a population of volunteers. All new drug products go through the clinical study process, so participants play a very important role in advancing medicine for present and future generations.

About the juMPStart Clinical Trial

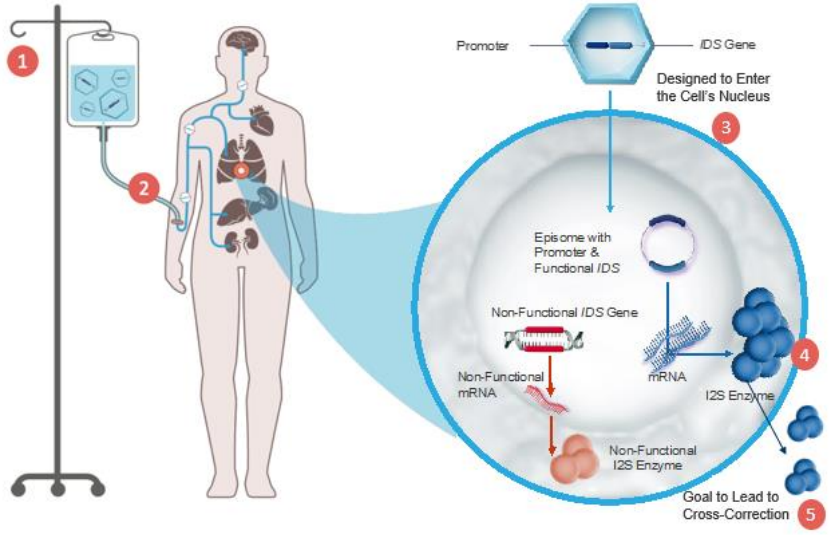
Homology Medicines is conducting a clinical trial, which is currently recruiting patients, to evaluate the safety and effectiveness of its one-time *in vivo* investigational gene therapy HMI-203 in adults with mucopolysaccharidosis type II (MPS II), or Hunter syndrome.

What is Hunter syndrome? MPS II, or Hunter syndrome, is a rare, X-linked lysosomal storage disorder caused by mutations in the iduronate-2-sulfatase (*IDS*) gene, which is responsible for producing the I2S enzyme that breaks down large sugar molecules, or cellular waste, called glycosaminoglycans (GAGs). Severe Hunter syndrome results in toxic lysosomal accumulation of GAGs that causes progressive debilitation and decline in intellectual function. 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.

What is HMI-203? HMI-203 is designed to use one of Homology's human hematopoietic stem cell-derived adeno-associated virus vectors (AAVHSCs) to deliver functional copies of the *IDS* gene to multiple organs where there are missing or mutated copies of the gene. HMI-203 is intended to enable the production of the I2S enzyme that is responsible for breaking down GAGs, which accumulate and cause progressive debilitation and shortened life expectancy in people with Hunter syndrome.

Step 1: A patient could receive a one-time intravenous (I.V.) administration of HMI-203.

Step 2: HMI-203 could reach organs throughout the body (peripheral organs) and the nervous system (by crossing the blood-brain and blood-nerve barriers) where I2S protein is required to eliminate the build-up of GAGs.



Step 3: HMI-203 could enter the cells, where it would deliver the functional gene and promoter, which would help "activate" the gene.

Step 4: HMI-203 could result in I2S protein expression and systematic reduction in GAGs.

Step 5: Goal to lead to cross-correction.

This approach is under investigation as a potential treatment for adult patients with Hunter syndrome.

What is the juMPStart Clinical Trial?

The Phase 1 juMPStart trial is an open-label, dose-escalation study designed to evaluate three doses of HMI-203. The trial is expected to enroll male patients ages 18-30 years old who have been diagnosed with Hunter syndrome and are currently receiving enzyme replacement therapy (ERT). In addition to safety endpoints, the trial plans to measure plasma I2S activity, urinary GAG levels and other peripheral disease manifestations.

What Does Participation in the juMPStart Trial Involve?

Screening Period: The trial will include a screening to ensure participants meet the eligibility criteria to enroll in the study.

***Study Period*:** Following a one-time I.V. dose of HMI-203, participants will be observed periodically for 52 weeks.

***Follow-Up Period*:** Participants will be seen less frequently for another four years.

HOMOLOGY Medicines, Inc.

Where Can I Learn More? Information about the juMPStart clinical trial is available at: www.clinicaltrials.gov (search for "HMI-203"), mpsjumpstart.com and/or by speaking with your physician.