Orchard Therapeutics Announces Last Patient Treated in Registrational Trial of OTL-203 for MPS-I Hurler Syndrome

July 7, 2025

Completion of enrollment achieved nearly one year ahead of schedule

Primary analysis anticipated two years post-treatment

TOKYO and LONDON and BOSTON, July 07, 2025 (GLOBE NEWSWIRE) -- Orchard Therapeutics, a Kyowa Kirin company, today announced the last patient has been treated in a registrational trial evaluating the efficacy and safety of OTL-203, an investigational hematopoietic stem cell (HSC) gene therapy, in patients with the Hurler subtype of mucopolysaccharidosis type I (MPS-IH). The trial (NCT06149403), referred to as HURCULES, compares treatment with OTL-203 to standard of care with allogeneic hematopoietic stem cell transplant (allo-HSCT).

MPS-I is a rare, inherited neurometabolic disease caused by a deficiency of the alpha-L-iduronidase (IDUA) lysosomal enzyme resulting in the accumulation of glycosaminoglycans (GAGs) in multiple organs, including the musculoskeletal and central nervous systems, as well as the heart, eyes, and ears. It is estimated to occur globally in 1 in 100,000 live births. Approximately 60 percent of children born with MPS-I have the most severe subtype, MPS-IH, also called Hurler syndrome, and rarely live past the age of 10 when untreated. Current treatment options for MPS-IH include allo-HSCT and enzyme replacement therapy (ERT), both of which have significant limitations.

“The completion of study enrollment nearly a year ahead of schedule underscores the urgent medical need that still exists in MPS-IH, and the hopefulness of physicians and patients to contribute to the development of new treatment options,” said Leslie Meltzer, Ph.D., chief medical officer of Orchard Therapeutics. “We’d like to thank the investigators, clinical trial sites, as well as study participants and their families for making the recruitment and enrollment phase of the trial a success. As we look ahead to the two-year primary analysis, we will continue to keep the MPS-IH community apprised of pertinent updates pertaining to OTL-203 and the HURCULES study.”

OTL-203 has received Fast Track and Rare Pediatric Disease (RPD) designations from the U.S. Food and Drug Administration (FDA), as well as priority medicines (PRIME) status from the European Medicines Agency (EMA). The program was originated by, and initially developed in partnership with, the San Raffaele Telethon Institute for Gene Therapy (SR-TIGET) in Milan, Italy.

In an earlier single-center proof-of-concept (PoC) study, eight patients diagnosed with MPS-IH were treated at Ospedale San Raffaele in Milan, Italy with investigational OTL-203 between July 2018 and December 2019. An oral presentation summarizing promising neurological, skeletal, and other clinical outcomes was presented at the 21st Annual WORLDSymposium™.

“Current treatments for MPS-IH are associated with significant morbidity and mortality leaving patients and families desperate for new options,” said Maria Ester Bernardo, M.D., Ph.D., clinical coordinator, pediatric clinical research unit at SR-TIGET and a HURCULES study investigator. “Previously reported results from an earlier proof-of-concept study in children showed robust metabolic correction, continued cognitive, motor, and physical development, as well as early improvements in skeletal, ocular and auditory health demonstrating that one-time treatment with OTL-203 has the potential to positively impact a broad range of clinical manifestations not fully addressed by the current standard of care.”

Dr. Bernardo added, “Coupled with the increased adoption of newborn screening for MPS-I in Europe and the U.S., we are working toward at a future where affected children may be able to avoid some of the most devastating consequences of this life-limiting disease.”

About the HURCULES Study
HURCULES—a study name that combines the target indication HURler syndrome and HerCULES, the classical mythological character—is a multi-center, randomized, active controlled clinical trial designed to evaluate the efficacy and safety of OTL-203 in patients with MPS-IH compared to standard of care with allogeneic HSCT. Patients with a confirmed diagnosis of MPS-IH who met the study inclusion criteria enrolled in the study across four clinical sites in the U.S. and Europe and were randomized 1:1 to receive either OTL-203 or allogeneic HSCT. The study is powered to demonstrate superiority of OTL-203 over allogeneic HSCT.

For more information, please visit www.clinicaltrials.gov (NCT06149403).

About MPS-I
Mucopolysaccharidosis type I (MPS-I) is a rare, inherited neurometabolic disease caused by a deficiency of the alpha-L-iduronidase (IDUA) lysosomal enzyme, which is required to break down sugar molecules called glycosaminoglycans (GAGs). The accumulation of GAGs across multiple organ systems results in multiple symptomatic manifestations of the disease including severe neurocognitive impairment, skeletal deformities, cardiovascular and pulmonary complications, impaired motor function, loss of hearing and corneal clouding. MPS-I occurs at an overall estimated frequency of one in every 100,000 live births. There are three subtypes of MPS-I. Approximately 60 percent of children born with MPS-I have the most

severe subtype, called Hurler syndrome (MPS-IH), and rarely live past the age of 10 when untreated.

Treatment options for MPS-I include allogeneic hematopoietic stem cell transplant (allo-HSCT) and enzyme replacement therapy (ERT), both of which have limitations, such as inadequate impact on some of the more severe manifestations of disease, as well as significant morbidity and mortality. At present, Newborn Screening for MPS-I has been established in multiple geographies, including the United States and Europe.

About OTL-203
OTL-203 is an investigational hematopoietic stem cell gene therapy being developed for the treatment of MPS-IH. It uses a modified virus to insert a functional copy of the human *IDUA* gene into a patient's cells. OTL-203 was originated by, and initially developed in partnership with, the San Raffaele Telethon Institute for Gene Therapy in Milan, Italy. OTL-203 has received Rare Pediatric Disease (RPD) and Fast Track designations from the U.S. FDA, as well as priority medicines (PRIME) status from the EMA.

About Orchard Therapeutics
Orchard Therapeutics, a Kyowa Kirin company, is a global gene therapy leader focused on ending the devastation caused by genetic and other severe diseases by discovering, developing, and commercializing new treatments that tap into the curative potential of hematopoietic stem cell (HSC) gene therapy. In this approach, a patient's own blood stem cells are genetically modified outside of the body and then reinserted, with the goal of correcting the underlying cause of disease with a single treatment.

Founded in 2015, Orchard's roots go back to some of the first research and clinical developments involving HSC gene therapy. Our team has played a central role in the evolution of this technology from a promising scientific idea to a potentially life-transforming reality. Today, as a vital part of Kyowa Kirin's global business, Orchard continuing to advance a pipeline of HSC gene therapies designed to address serious diseases where the burden is immense for patients, families and society and current treatment options are limited or do not exist.

For more information, please visit www.orchard-tx.com.

About Kyowa Kirin
Kyowa Kirin aims to discover novel medicines with life-changing value. As a Japan-based Global Specialty Pharmaceutical Company, we have invested in drug discovery and biotechnology innovation for more than 70 years and are currently working to engineer the next generation of antibodies and cell and gene therapies with the potential to help patients affected by a severe or rare disease. A shared commitment to our values, to sustainable growth, and to making people smile unites us across our four regions – Japan, Asia Pacific, North America, and EMEA/International. You can learn more about the business of Kyowa Kirin at: https://www.kyowakirin.com.

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