# Orchard Therapeutics Announces Multiple Presentations from across its Late-stage Neurometabolic Portfolio at SSIEM 2024

August 28, 2024

LONDON and BOSTON, Aug. 28, 2024 (GLOBE NEWSWIRE) -- Orchard Therapeutics, recently acquired by Kyowa Kirin with the goal of accelerating the delivery of new gene therapies to patients around the globe, today announced nine presentations from across its late-stage neurometabolic hematopoietic stem cell (HSC) gene therapy portfolio will be featured at the Society for the Study of Inborn Errors of Metabolism (SSIEM) 2024 Annual Symposium taking place September 3-6 in Porto, Portugal.

Featured data include several accepted abstracts and an oral presentation detailing neurological, skeletal, and other clinical outcomes from a proof-of-concept (PoC) study of investigational OTL-203 in the Hurler subtype of mucopolysaccharidosis type I (MPS-IH). In addition, an encore presentation highlighting the safety and efficacy of atidarsagene autotemcel, formerly OTL-200, which is marketed as Libmeldy® in Europe and was recently approved as Lenmeldy™ in the United States for the treatment of early-onset metachromatic leukodystrophy (MLD).

The company will also host a sponsored symposium on Thursday, September 5, from 12:30 to 1:30 p.m., local time titled “New horizons for metachromatic leukodystrophy with the advent of newborn screening,” featuring expert speakers with deep experience across the diagnostic journey and continuum of care who will discuss the evidence and efforts to support widespread newborn screening for this devastating neurometabolic disease.

Details of the oral presentations are as follows (all times in WEST):

- Title: Newborn Screening (NBS) for Metachromatic Leukodystrophy: A Prospective Study
  Date/Time: Wednesday, September 4 at 9:30 a.m.
  Presenter: Lucia Laugwitz

- Title: Interim analysis on neurological outcomes in Hurler syndrome patients treated with autologous ex-vivo haematopoietic stem cell gene therapy
  Date/Time: Thursday, September 5 at 11:30 a.m.
  Presenter: Giulia Consiglieri

Details of the poster presentations are as follows (all times in WEST):

- Title: Atidarsagene autotemcel (autologous hematopoietic stem cell gene therapy) preserves cognition, language, and speech and slows brain demyelination and atrophy in early-onset metachromatic leukodystrophy
  Date/Time: Wednesday, September 4 and Thursday, September 5 from 12:15 to 2:15 p.m.
  Presenter: Francesca Fumagalli
  #PO-190

- Title: Lentiviral hematopoietic stem cell gene therapy for late juvenile metachromatic leukodystrophy
  Date/Time: Wednesday, September 4 and Thursday, September 5 from 12:15 to 2:15 p.m.
  Presenter: Francesca Fumagalli
  #PO-198

- Title: Quantitative Sulfatides as diagnostic tool and disease biomarker for Metachromatic Leukodystrophy
  Date/Time: Wednesday, September 4 and Thursday, September 5 from 12:15 to 2:15 p.m.
  Presenter: Francesca Fumagalli
  #PO-232

- Title: Facilitating successful cross-border treatment of patients with rare disease via the S2 pathway for ATMPs
  Date/Time: Wednesday, September 4 and Thursday, September 5 from 12:15 to 2:15 p.m.
  Presenter: Cecilia Marinova
  #PO-199

- Title: Non-neurological, non-skeletal outcomes after autologous hematopoietic stem cell gene therapy in Hurler patients: retrospective comparison with allogeneic hematopoietic stem cell transplantation
  Date/Time: Wednesday, September 4 and Thursday, September 5 from 12:15 to 2:15 p.m.
  Presenter: Giulia Consiglieri
  #PO-191

- Title: Hematopoietic Stem Cell Gene Therapy for Hurler Syndrome: interim skeletal outcome and skeletal cross-correction mechanisms
  Date/Time: Wednesday, September 4 and Thursday, September 5 from 12:15 to 2:15 p.m.
  Presenter: Giulia Consiglieri
  #PO-189

- Title: Design of a randomized phase 3 clinical trial (HURCULES) evaluating the safety and efficacy of OTL-203 in patients with MPS-IH versus standard of care with allogeneic hematopoietic stem cell transplantation
  Date/Time: Wednesday, September 4 from 6:15 to 8:15 p.m. (poster walk)
  Presenter: Giulia Consiglieri
  #EP-042

**About Lenmeldy / Libmeldy**
Lenmeldy™ (atidarsagene autotemcel), formerly known as OTL-200, is the only approved therapy in the U.S. for the treatment of children with pre-symptomatic late infantile (PSLI), pre-symptomatic early juvenile (PSEJ) or early-symptomatic early juvenile (ESEJ) metachromatic leukodystrophy (MLD).

For additional details about Lenmeldy, please refer to the full Prescribing Information.

In Europe, Lenmeldy is known as Libmeldy®, where it has been approved by the European Commission (EC), UK Medicines and Healthcare products Regulatory Agency (MHRA), and Swiss Agency for Therapeutic Products (Swissmedic). For more information about Libmeldy, please see the Summary of Product Characteristics (SmPC) available on the EMA website.

The program was originated by and developed in partnership with the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) in Milan, Italy.

**INDICATION**

LENMELDY™ (atidarsagene autotemcel) is an autologous hematopoietic stem cell-based gene therapy indicated for the treatment of children with pre-symptomatic late infantile (PSLI), pre-symptomatic early juvenile (PSEJ), or early symptomatic early juvenile (ESEJ) metachromatic leukodystrophy (MLD).

**IMPORTANT SAFETY INFORMATION**

***WARNINGS AND PRECAUTIONS***

**Thrombosis and Thromboembolic Events:**
Treatment with LENMELDY may increase the risk of thrombosis and thromboembolic events. A child with PSEJ MLD died after experiencing a left hemisphere cerebral infarction secondary to a thrombotic event in a large blood vessel approximately 1 year after treatment with LENMELDY. Evaluate the risk factors for thrombosis prior to and after LENMELDY infusion according to best clinical practice.

**Encephalitis:**
Treatment with LENMELDY may increase the risk of encephalitis. A child with ESEJ developed a serious event of encephalitis after treatment with LENMELDY. The etiology of this event is unclear but attribution to LENMELDY cannot be ruled out. Treatment with LENMELDY may trigger a relapsing-remitting pattern of disease progression. No other events related to encephalitis have been reported during the clinical development of LENMELDY. Monitor children for signs or symptoms of encephalitis after LENMELDY treatment.

**Serious Infection:**
In the period between start of conditioning and within 1 year after LENMELDY treatment, severe Grade 3 infections occurred in 39% of all children (21% bacterial, 5% viral, 5% bacterial and viral or bacterial and fungal, and 8% unspecified). Grade 3 febrile neutropenia developed within 1 month after LENMELDY infusion in 82% of children. In the event of febrile neutropenia, monitor for signs and symptoms of infection and manage with broad-spectrum antibiotics, fluids, and other supportive care as medically indicated. Monitor children for signs and symptoms of infection after myeloablative conditioning and LENMELDY infusion and treat appropriately. Administer prophylactic antimicrobials according to best clinical practice.

**Veno-Occlusive Disease:**
Three children (8%) treated in clinical trials of LENMELDY developed veno-occlusive disease (VOD) with one Grade 4 SAE and two Grade 3 AEs. None of these three events met Hy's Law criteria. Monitor children for signs and symptoms of VOD including liver function tests in all children during the first month after LENMELDY infusion. Consider prophylaxis for VOD with anti-thrombotic agents based on risk factors for VOD and best clinical practice.

**Delayed Platelet Engraftment (DPE):**
DPE has been observed with LENMELDY treatment. Bleeding risk is increased prior to platelet engraftment and may continue after engraftment in children with prolonged thrombocytopenia. In clinical trials of LENMELDY, 4 (10%) children had delayed platelet engraftment after day 60 (range day 67-109), with 3 children requiring platelet transfusions until engraftment occurred. Patients should be informed of the risk of bleeding until platelet recovery has been achieved. Monitor patients for thrombocytopenia and bleeding until platelet engraftment and recovery are achieved.

**Neutrophil Engraftment Failure:**
There is a potential risk of neutrophil engraftment failure after treatment with LENMELDY. Monitor neutrophil counts until engraftment has been achieved. If neutrophil engraftment failure occurs in a child treated with LENMELDY, provide rescue treatment with the unmanipulated back-up collection of $CD34^+$ cells.

**Insertional Oncogenesis:**
There is a potential risk of LVV-mediated insertional oncogenesis after treatment with LENMELDY. Children treated with LENMELDY may develop hematologic malignancies and should be monitored life-long. Monitor for hematologic malignancies with a complete blood count (with differential)

annually and integration site analysis as warranted for at least 15 years after treatment with LENMELDY. In the event that a malignancy occurs, contact Orchard Therapeutics at 1-888-878-0185 for reporting and to obtain instructions on collection of samples for testing.

**Hypersensitivity Reactions:**
The dimethyl sulfoxide (DMSO) in LENMELDY may cause hypersensitivity reactions, including anaphylaxis which is potentially life-threatening and requires immediate intervention. Hypersensitivity including anaphylaxis can occur in children with and without prior exposure to DSMO. Monitor for hypersensitivity reactions during infusion and after infusion.

**Anti-Retroviral Use:**
Children should not take prophylactic HIV anti-retroviral medications for at least one month prior to mobilization, or for the expected duration of time needed for the elimination of the medications. Anti-retroviral medications may interfere with the manufacturing of LENMELDY. If a child requires antiretrovirals for HIV prophylaxis, initiation of LENMELDY treatment should be delayed until confirmation of a negative test for HIV.

**Interference With Serology Testing:**
Due to the likelihood of a false-positive test for HIV, children who have received LENMELDY should not be screened for HIV infection using a PCR-based assay.

***USE IN SPECIFIC POPULATIONS***

Females and Males of Reproductive Potential

Pregnancy Testing
As a precautionary measure, a negative serum pregnancy test must be confirmed prior to the start of mobilization, and reconfirmed prior to conditioning procedures, and before administration of LENMELDY in females of childbearing potential.

Contraception
Consult the Prescribing Information of the mobilization and conditioning agents for information on the need for effective contraception. Males capable of fathering a child and females of childbearing age should use an effective method of contraception from start of mobilization through at least 6 months after administration of LENMELDY.

Infertility
There are no data on the effects of LENMELDY on fertility.

Data are available on the risk of infertility with myeloablative conditioning. In clinical trials of LENMELDY, seven children (50% of females) developed ovarian failure. Advise children of the option to cryopreserve semen or ova before treatment, if appropriate.

For additional safety information, please see the full Prescribing Information.

**About OTL-203**
OTL-203 is an investigational hematopoietic stem cell gene therapy being developed for the treatment of Hurler subtype of mucopolysaccharidosis type I (MPS-IH). It uses a modified virus to insert a functional copy of the human IDUA gene into a patient's cells. 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 hematopoietic stem cell transplant (HSCT) is currently ongoing. 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, Orchard is advancing 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 and deliver novel medicines and treatments 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 with high unmet medical needs, such as bone & mineral, intractable hematological diseases/hemato oncology, and rare diseases. A shared commitment to our values, to sustainable growth, and to making people smile unites us across the globe. You can learn more about the business of Kyowa Kirin at www.kyowakirin.com.

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