Orchard Therapeutics Announces Multiple Data Presentations and Receives 2025 New Treatment Award at the 21st Annual WORLDSymposium™

February 3, 2025

Featured data showcase the transformative potential of HSC gene therapy to enable cross-correction and restore enzymatic function in a variety of tissues and organs, including the CNS

TOKYO, LONDON and BOSTON, Feb. 03, 2025 (GLOBE NEWSWIRE) -- Orchard Therapeutics, a Kyowa Kirin company, today announced presentations from seven abstracts from across its hematopoietic stem cell (HSC) gene therapy portfolio will be featured at the 21st Annual WORLD*Symposium*™taking place February 3-7 in San Diego.

In totality, the presentations reinforce the transformative potential of HSC gene therapy to enable cross-correction and restore enzymatic function in a variety of tissues and organs, including the central nervous system (CNS), which may address some of the more life-limiting manifestations of various severe and complex multi-system disorders.

Featured data includes presentations detailing the long-term efficacy of atidarsagene autotemcel, formerly OTL-200, which was approved in March 2024 as Lenmeldy™ in the United States and is known as Libmeldy® in Europe for the treatment of early-onset metachromatic leukodystrophy (MLD). Other data highlights include a poster presentation underscoring the need, feasibility and cost-effectiveness of newborn screening for MLD, as well as an encore oral presentation summarizing neurological, skeletal, and other clinical outcomes from a proof-of-concept study of investigational OTL-203 in the Hurler subtype of mucopolysaccharidosis type I (MPS-IH).

In addition, researchers will present pre-clinical proof-of-concept data showing that HSC gene therapy has the potential to enable multisystemic cross-correction and reduce toxic glycogen accumulation in the heart, skeletal muscles and CNS in a murine model of Pompe disease. In the experiments, mice transplanted with genetically corrected HSCs exhibited robust engraftment and reduction of intra-organ glycogen accumulation to levels comparable to wild-type cohorts. This research was conducted under a previous collaboration with University College London (UCL) and Amicus Therapeutics.

Orchard Therapeutics to Receive WORLD*Symposium*™ New Treatment Award
The company also announced it is receiving a 2025 New Treatment Award for Lenmeldy™ (atidarsagene autotemcel) from WORLD*Symposium*™. The award, which will be presented on Friday, February 7 at 7:30 a.m. PST, recognizes important achievements in advancing new treatments for lysosomal storage diseases (LSDs) which have achieved major regulatory approval.

“We are truly humbled by this recognition which we share with our academic and clinical collaborators, as well as the broader MLD community,” said Leslie Meltzer, Ph.D., chief medical officer of Orchard Therapeutics. “Bringing new treatments which have the potential to end the devastation caused by severe genetic diseases is central to our shared mission. This award is the culmination of decades-long research and development activities carried out in partnership with the San Raffaele Telethon Institute for Gene Therapy in Milan, Italy, data from which underpinned the regulatory approvals in the U.S. and Europe. We’d also like to extend our sincere gratitude to the patients and families who participated in the clinical trials as well as the patient advocacy organizations—this achievement would not have been possible without your sacrifice, contributions and support.”

“Lenmeldy represents a significant step forward in the treatment of MLD, a cruel and ultimately fatal disease for which there were previously no effective treatment options,” said Professor Alessandro Aiuti, deputy director of the San Raffaele Telethon Institute for Gene Therapy in Milan and full professor of pediatrics at the Vita-Salute San Raffaele University of Milan. “We thank the organizers of WORLD *Symposium* and the awards committee for acknowledging this important treatment advance, and we would like to extend our appreciation to the Orchard Therapeutics team whose stewardship of the later-stage development and regulatory submissions enabled this therapy to be approved for eligible patients in the U.S. and Europe. We strongly believe our collaboration serves as a model for how non-profit research centers can partner with industry to advance new treatments for ultra-rare diseases.”

MLD is an ultra-rare, rapidly progressive, irreversible and ultimately fatal neurometabolic disease that affects approximately one in 100,000 live births. It is caused by a mutation in the gene responsible for encoding the enzyme arylsulfatase A (ARSA) leading to neurological damage and developmental regression. In the most severe form of MLD, babies develop normally but in late infancy start to rapidly lose the ability to walk, talk and interact with the world around them. These children eventually deteriorate into a vegetative state, which may require 24-hour intensive care, and the majority pass away within five years of symptom onset, creating an enormous emotional and financial burden on the family. Prior to Lenmeldy, there were no treatment options in the U.S. for early-onset MLD beyond supportive and end-of-life care.

Lenmeldy aims to correct the underlying genetic cause of MLD by inserting one or more functional copies of the human *ARSA* gene *ex vivo* (outside the body) into the genome of a patient’s own hematopoietic stem cells (HSCs) using a lentiviral vector. The genetically repaired cells are infused back

into the patient, where, once engrafted, they differentiate into multiple cell types, some of which migrate across the blood-brain barrier into the central nervous system and express the functional enzyme. Prior to treatment, patients must undergo high-dose chemotherapy, a process that removes cells from the bone marrow so they can be replaced with the modified cells in Lenmeldy. This approach has the potential to restore enzymatic function to stop or slow disease progression with a single treatment.

Overview of Data Presentations at the 21st Annual WORLD*Symposium* ™
Details of the oral presentations are as follows (all times in PST; * denotes corresponding poster):

- Title: Hematopoietic stem cell gene therapy for mucopolysaccharidosis type I-Hurler (OTL-203): Interim skeletal, neurological and systemic outcomes from a phase I/II study
  Date/Time: Thursday, February 6 at 11:00 a.m.
  Presenter: Maria Ester Bernardo

- 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: Thursday, February 6 at 11:12 a.m.
  Presenter: Valeria Calbi

- Title: Correction of glycogen accumulation in muscle, heart and CNS in a pre-clinical model of hematopoietic stem cell gene therapy for Pompe disease*
  Date/Time: Friday, February 7 at 1:20 p.m.
  Presenter: Slawomir Wantuch

- Title: Investigation of the treatment effect of atidarsagene autotemcel on age-matched treated vs. untreated sibling pairs with early-onset metachromatic leukodystrophy*
  Date/Time: Friday, February 7 at 2:00 p.m.
  Presenter: Karen Bean

Details of the poster presentations are as follows (all times in PST; * denotes corresponding oral presentation):

- Title: Validation of quality-of-life states in late-infantile and early-juvenile metachromatic leukodystrophy
  Date/Time: Wednesday, February 5 from 3:30 to 5:30 p.m.
  Presenter: Francis Pang
  #260

- Title: Exploring the net monetary benefit of implementing newborn screening for metachromatic leukodystrophy (MLD) in California
  Date/Time: Wednesday, February 5 from 3:30 to 5:30 p.m.
  Presenter: Karen Bean
  #24

- Title: Investigation of the treatment effect of atidarsagene autotemcel on age-matched treated vs. untreated sibling pairs with early-onset metachromatic leukodystrophy*
  Date/Time: Wednesday, February 5 from 3:30 to 5:30 p.m.
  Presenter: Karen Bean
  LB-06

- Title: Characterizing diagnostic delays in metachromatic leukodystrophy: A real-world data approach
  Date/Time: Thursday, February 6 from 3:30 to 5:30 p.m.
  Presenter: Laura Adang
  #3

- 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: Thursday, February 6 from 3:30 to 5:30 p.m.
  Presenter: Valeria Calbi
  #99

- Title: Correction of glycogen accumulation in muscle, heart and CNS in a pre-clinical model of hematopoietic stem cell gene therapy for Pompe disease*
  Date/Time: Thursday, February 6 from 3:30 to 5:30 p.m.
  Presenter: Slawomir Wantuch
  #351

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) and UK Medicines and Healthcare products Regulatory Agency (MHRA). 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 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.

Contact Benjamin Navon +1 857-248-9454 Benjamin.Navon@orchard-tx.com