Orchard Therapeutics Announces Multiple Presentations at ASGCT 2024

May 7, 2024

Eight presentations showcase the broad applicability of HSC gene therapy to address rare neurometabolic diseases and beyond

TOKYO, LONDON and BOSTON, May 07, 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 four oral and four poster presentations from across its hematopoietic stem cell (HSC) gene therapy platform will be featured at the 27th Annual Meeting of the American Society of Gene and Cell Therapy (ASGCT) taking place May 7-11, 2024, in Baltimore.

Featured data include several accepted abstracts and an Oral Presidential Symposium supporting the safety and efficacy of atidarsagene autotemcel (formerly OTL-200 which was recently approved as Lenmeldy™ in the U.S. and is marketed as Libmeldy® in Europe), as well as three presentations 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, Orchard Therapeutics will give an invited oral presentation highlighting the potential of OTL-104, a pre-clinical HSC gene therapy developed by its in-house research team, to address a severe and treatment refractory form of Crohn's disease.

"Our presentations at ASGCT add to the compendium of evidence supporting the transformative impact and broad applicability of our approach," said Leslie Meltzer, Ph.D., chief medical officer of Orchard Therapeutics. "In particular, the Presidential Symposium highlighting the long-term follow-up data in MLD and the invited oral presentation spotlighting our early pre-clinical pipeline continue to demonstrate the scientific interest generated by our platform and underscore our commitment to leveraging insights gleaned from our late-stage portfolio to inform the development strategy and indication prioritization of our earlier-stage programs."

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

- Title: Hematopoietic Stem Cell Gene Therapy for Hurler Syndrome: Interim Skeletal Outcome and Skeletal Cross-correction Mechanisms
  Date/Time: Tuesday, May 7 at 1:30 p.m.
  Presenter: Maria Ester Bernardo

- Title: Atidarsagene autotemcel (Hematopoietic Stem Cell Gene Therapy) Preserves Cognitive and Motor Development in Metachromatic Leukodystrophy with up to 12 Years Follow-up (Oral Presidential Symposium)
  Date/Time: Wednesday, May 8 at 11:15 a.m.
  Presenter: Alessandro Aiuti

- Title: Restoring Macrophage Immune Functions by Transplantation of Gene-modified HSCs: a Therapeutic Approach to NOD2 Crohn's Disease (Invited Oral Presentation)
  Date/Time: Thursday, May 9 at 9:18 a.m.
  Presenter: Pervinder Sagoo

- Title: Somatic Mutation Tracking in Hematopoietic Stem Cell Gene Therapy Reveals Absence of Clonal Hematopoiesis
  Date/Time: Saturday, May 11 at 11:45 a.m.
  Presenter: Francesco Gazzo

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

- Title: Development of an *Ex Vivo* Hematopoietic Stem Cell Gene Therapy for Frontotemporal Dementia (FTD)
  Date/Time: Thursday, May 9 from noon to 1:30 p.m. and from 5:30 to 7:00 p.m.
  Presenter: Yuri Ciervo
  Poster #1136

- Title: Lentiviral Hematopoietic Stem Cell Gene Therapy for Late Juvenile Metachromatic leukodystrophy
  Date/Time: Friday, May 10 from noon to 1:30 p.m. and from 5:30 to 7:00 p.m.
  Presenter: Valeria Calbi
  Poster #1905

- 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: Friday, May 10 from noon to 1:30 p.m. and from 5:30 to 7:00 p.m.
  Presenter: Maria Ester Bernardo

Poster #1904

- Title: Interim Analysis on Neurological Outcomes in Hurler Syndrome Patients Treated with Autologous Ex Vivo Hematopoietic Stem Cell Gene Therapy
  Date/Time: Friday, May 10 from noon to 1:30 p.m. and from 5:30 to 7:00 p.m.
  Presenter: Maria Ester Bernardo
  Poster #1903

Early skeletal outcomes from OTL-203 PoC study in MPS-IH published in Science Translational Medicine

In addition to the data presented at ASGCT, Orchard's collaborators at the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) in Milan, Italy, recently published a detailed analysis of early skeletal measures in eight children with MPS-IH treated with OTL-203 in the PoC study which continue to show improved clinical, functional, and radiological outcomes with a median follow-up of 3.78 years.

The manuscript, titled, "Early skeletal outcomes after hematopoietic stem and progenitor cell gene therapy for Hurler syndrome," was published in the May 1, 2024 issue of *Science Translational Medicine*.

About Lenmeldy
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 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 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 www.kyowakirin.com.

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