Orchard Therapeutics Announces Multiple Data Presentations and Publications

October 23, 2024

Ten presentations at ESGCT 2024 detail the therapeutic potential and applicability of the company's platform in rare neurometabolic diseases and beyond

Nature manuscript highlights clinical results supporting long-term durability and safety profile of genetically corrected hematopoietic stem and progenitor cells

Research letter detailing results from the world's first prospective, population-based newborn study for metachromatic leukodystrophy recently published in the New England Journal of Medicine

LONDON and BOSTON, Oct. 23, 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 multiple data presentations and publications highlighting the transformative potential of HSC gene therapy and newborn screening.

Ten presentations (three oral and seven posters) from across its hematopoietic stem cell (HSC) gene therapy portfolio will be featured at the European Society of Gene and Cell Therapy (ESGCT) 31st Annual Congress taking place October 22-25, 2024, in Rome, Italy.

Featured data include several accepted abstracts and encore presentations detailing clinical, biochemical and other functional outcomes from across the company's commercial- and clinical-stage neurometabolic portfolio in metachromatic leukodystrophy (MLD), the Hurler subtype of mucopolysaccharidosis type I (MPS-IH), and mucopolysaccharidosis type IIIA (MPS-IIIA), also known as Sanfilippo syndrome type A.

Pertaining to earlier-stage pipeline programs, company researchers will also highlight the potential of the platform beyond rare neurometabolic conditions, including:

- An oral presentation of preclinical proof-of-concept data showing the therapeutic potential of OTL-104 for NOD2-deficient Crohn's disease, a severe and treatment-refractory form of the condition;
- A poster presentation outlining the potential of HSC gene therapy as a mechanism to deliver therapeutic antibodies across the blood-brain-barrier and into the central nervous system; and
- Another poster presentation detailing the feasibility of utilizing HSC gene therapy to provide stable and targeted immunotherapy for autoimmune disorders through the ability of HSCs to differentiate into T regulatory (Treg) cells engineered to express chimeric antigen receptors (CAR). This approach combines the durability of HSC gene therapy with the suppressive activity of autoantigen-specific CAR-Treg cells.

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

- Title: Stem cell gene therapy for Childhood Dementias – a Sanfilippo story
  Date/Time: Wednesday, October 23 at 9:00 a.m.
  Presenter: Brian Bigger
  #INV20

- Title: Haematopoietic stem cell gene therapy as a treatment for NOD2-deficient severe Crohn's Disease
  Date/Time: Thursday, October 24 at 10:45 a.m.
  Presenter: Piv Sagoo
  #OR064

- Title: Lentiviral haematopoietic stem cell gene therapy (atidarsagene autotemcel) for late juvenile Metachromatic leukodystrophy (MLD)
  Date/Time: Friday, October 25 at 12:00 p.m.
  Presenter: Valeria Calbi
  #OR099

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

- Title: Lentiviral ex vivo autologous HSC gene therapy as a tool to deliver therapeutic antibodies beyond the blood brain barrier
  Date/Time: Tuesday, October 22 from 7:30 to 9:00 p.m.
  Presenter: Chiara Recchi
  #P0309

- Title: HSC-derived CAR-Treg gene therapy: a novel approach for the treatment of multiple sclerosis
  Date/Time: Tuesday, October 22 from 7:30 to 9:00 p.m.
  Presenter: Lily Du
  #P0293

- Title: Biological properties and clonality of engineered hematopoietic stem/progenitor cells persisting long-term after gene therapy
  Date/Time: Wednesday, October 23 from 1:30 to 3:00 p.m.
  Presenter: Pamela Quaranta
  #P0412

- 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, October 24 from 6:00 to 7:30 p.m.
  Presenter: Valeria Calbi
  #P0880

- Title: Unveiling myeloid-mediated enzymatic correction of ARSA-deficient neural cells in hematopoietic stem cell gene therapy for Metachromatic Leukodystrophy
  Date/Time: Thursday, October 24 from 6:00 to 7:30 p.m.
  Presenter: Vasco Meneghini
  #P0898

- Title: Hematopoietic Stem Cell Gene Therapy for Hurler Syndrome (OTL-203): interim skeletal, neurological and systemic outcomes
  Date/Time: Thursday, October 24 from 6:00 to 7:30 p.m.
  Presenter: Valeria Calbi
  #P0886

- Title: Hematopoietic stem cell-based gene therapy in Mucopolysaccharidosis type I Hurler (OTL-203): focus on skeletal damage and cross-correction mechanisms
  Date/Time: Thursday, October 24 from 6:00 to 7:30 p.m.
  Presenter: Ludovica Santi
  #P1016

Nature manuscript elucidates sustained long-term reconstitution and lineage commitment of genetically corrected HSPCs

In a paper published online today in Nature, titled “Long-term lineage commitment is modulated by the underlying disease in hematopoietic stem cell gene therapy patients,” researchers from the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget) detail clinical results elucidating the long-term reconstitution, lineage commitment and the incidence of somatic mutations of genetically corrected hematopoietic stem and progenitor cells (HSPCs).

In the study, researchers examined and compared hematopoietic reconstitution in 53 patients treated with Orchard’s current and former HSC gene therapy programs for three genetic diseases, including MLD (n=29), Wiskott-Aldrich syndrome (WAS; n=15), and β-thalassemia (β-Thal; n=9) with up to 8 years of follow-up (median 4 years), using vector integration sites as a surrogate of clonal identity.

Based on the analysis, all patients had a polyclonal repertoire consistent with other lentiviral-based HSC gene therapy studies and previously reported clinical results. Importantly, no somatic mutations known to drive clonal hematopoiesis or myeloid cancer were found in any patient from the MLD cohort and no increase of somatic mutations was observed over time. Program-specific differences in the clonal complexity of the various lineages and the incidence of somatic mutations suggest an impact of the underlying disease biology on hematopoietic reconstitution.

These findings add to the compendium of evidence supporting the long-term durability and safety profile of Orchard’s HSC gene therapy portfolio.

Results from the world’s first prospective, population-based NBS study for MLD published in NEJM

A research letter detailing results from the world’s first prospective, population-based newborn screening (NBS) study for MLD was published in the September 18, 2024, issue of the *New England Journal of Medicine* (*NEJM*).

The aim of the study, which was conducted in Hannover, Germany, was to evaluate the technical feasibility of MLD NBS and to develop and implement

a comprehensive care pathway to provide prompt confirmatory diagnostics, clinical assessment, subtype prediction, clinical follow-up, and treatment. Dried blood spot samples from the first 109,259 newborns were tested in a three tier, high-throughput screen based on increased sulfatide levels, reduced ARSA enzyme activity and ARSA gene sequencing.

Three newborns were identified as screen positive and were confirmed to have MLD and referred for pre-symptomatic treatment. The screening algorithm and comprehensive clinical care pathway represents a novel diagnostic and treatment paradigm for MLD, with the potential to significantly alter clinical practice by reducing morbidity and mortality in children with MLD by enabling pre-symptomatic treatment.

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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