Orchard Therapeutics Announces Presentation of Data from Neurometabolic Portfolio at Upcoming Society for the Study of Inborn Errors of Metabolism (SSIEM) 2019 Annual Symposium

August 27, 2019

Mucopolysaccharidosis Type I and Metachromatic Leukodystrophy Abstracts Accepted for Oral Presentations

BOSTON and LONDON, Aug. 27, 2019 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a leading commercial-stage biopharmaceutical company dedicated to transforming the lives of patients with serious and life-threatening rare diseases through innovative gene therapies, today announced the presentation of clinical data at the upcoming Society for the Study of Inborn Errors of Metabolism (SSIEM) symposium in Rotterdam, the Netherlands, September 3-6, 2019. The oral presentations will highlight data from the company's neurometabolic portfolio, including investigational candidates OTL-203 for mucopolysaccharidosis type I (MPS-I) and OTL-200 for metachromatic leukodystrophy (MLD). The studies for these programs are being conducted at the San Raffaele-Telethon Institute for Gene Therapy in Milan, Italy.

The presentations are listed below and the full preliminary program is available online via the SSIEM website: https://ssiem2019.org/preliminary-program/

Oral presentation details for OTL-203 and OTL-200:

Title: *O-021 | Hematopoietic stem cell gene therapy for Mucopolysaccharidosis type I, Hurler variant (MPS-IH)*
Presenter: ME Bernardo, San Raffaele Scientific Institute, Milan, Italy
Session: Parallel Session 1A: Gene therapy
Date: Wednesday, September 4, 2019
Time: 9:15-9:30 a.m. CEST
Location: Grote Zaal

Title: *O-016 | Lentiviral (LV) hematopoietic stem cell gene therapy (HSC-GT) for metachromatic leukodystrophy (MLD) provides sustained clinical benefit*
Presenter: V Calbi, IRCCS San Raffaele Scientific Institute, Milan, Italy
Session: Parallel Session 1A: Gene therapy
Date: Wednesday, September 4, 2019
Time: 9:30-9:45 a.m. CEST
Location: Grote Zaal

About MPS-I and OTL-203
Mucopolysaccharidosis type I (MPS-I) is a rare inherited neurometabolic disease caused by a deficiency of the IDUA (alpha-L-iduronidase) lysosomal enzyme required to break down glycosaminoglycans (also known as GAGs or mucopolysaccharides). The accumulation of GAGs across multiple organ systems results in the symptoms of MPS-I including neurocognitive impairment, skeletal deformity, loss of vision and hearing, hydrocephalus, and cardiovascular and pulmonary complications. MPS-I occurs at an overall estimated frequency of one in every 100,000 live births.[1] There are three subtypes of MPS-I; approximately 60 percent of MPS-I patients have the severe Hurler subtype and, when untreated, these patients rarely live past the age of 10.[Id] Treatment options for MPS-I include hematopoietic stem cell transplant and chronic enzyme replacement therapy, both of which have significant limitations. Though early intervention with enzyme replacement therapy has been shown to delay or prevent some clinical features of the condition, it has only limited efficacy on neurological symptoms. OTL-203 is an *ex vivo,* autologous, hematopoietic stem cell-based gene therapy being studied for the treatment of MPS-I. Orchard was granted an exclusive worldwide license to intellectual property rights to research, develop, manufacture and commercialize the gene therapy program for the treatment of MPS-I developed by the San Raffaele-Telethon Institute for Gene Therapy in Milan, Italy.

About MLD and OTL-200
Metachromatic leukodystrophy (MLD) is a rare and life-threatening inherited disease of the body's metabolic system occurring in approximately one in every 100,000 live births. MLD is caused by a mutation in the arylsulfatase-A (ARSA) gene that results in the accumulation of sulfatides in the brain and other areas of the body, including the liver, the gall bladder, kidneys, and/or spleen. Over time, the nervous system is damaged and patients with MLD will experience neurological problems such as motor, behavioral and cognitive regression, severe spasticity and seizures, finding it more and more difficult to move, talk, swallow, eat and see. Currently, there are no effective treatments for MLD. In its late infantile form, mortality at 5 years from onset is estimated at 50% and 44% at 10 years for juvenile patients.[2] OTL-200 is an *ex vivo*, autologous, hematopoietic stem cell-based gene therapy being studied for the treatment of MLD. OTL-200 was acquired from GSK in April 2018 and originated from a pioneering collaboration between GSK and the Hospital San Raffaele and the Telethon Foundation, acting through their joint San Raffaele-Telethon Institute for Gene Therapy in Milan, initiated in 2010.

About Orchard
Orchard Therapeutics is a fully integrated commercial-stage biopharmaceutical company dedicated to transforming the lives of patients with serious and life-threatening rare diseases through innovative gene therapies.

Orchard's portfolio of *ex vivo*, autologous, hematopoietic stem cell (HSC) based gene therapies includes Strimvelis®, a gammaretroviral vector-based gene therapy and the first such treatment approved by the European Medicines Agency for severe combined immune deficiency due to adenosine deaminase deficiency (ADA-SCID). Additional programs for neurometabolic disorders, primary immune deficiencies and hemoglobinopathies are all based on lentiviral vector-based gene modification of autologous HSCs and include three advanced registrational studies for metachromatic

leukodystrophy (MLD), ADA-SCID and Wiskott-Aldrich syndrome (WAS), clinical programs for X-linked chronic granulomatous disease (X-CGD), transfusion-dependent beta-thalassemia (TDT) and mucopolysaccharidosis type I (MPS-I), as well as an extensive preclinical pipeline. Strimvelis, as well as the programs in MLD, WAS and TDT were acquired by Orchard from GSK in April 2018 and originated from a pioneering collaboration between GSK and the San Raffaele Telethon Institute for Gene Therapy in Milan, Italy initiated in 2010.

Orchard currently has offices in the U.K. and the U.S., including London, San Francisco and Boston.

Forward-Looking Statements
This press release contains certain forward-looking statements which are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements may be identified by words such as “anticipates,” “believes,” “expects,” “intends,” “projects,” and “future” or similar expressions that are intended to identify forward-looking statements. Forward-looking statements include express or implied statements relating to, among other things, Orchard’s programs, including the therapeutic potential of its product candidates, including OTL-203 and OTL-200. These statements are neither promises nor guarantees and are subject to a variety of risks and uncertainties, many of which are beyond Orchard’s control, which could cause actual results to differ materially from those contemplated in these forward-looking statements. In particular, the risks and uncertainties include, without limitation: the risk that any one or more of Orchard’s product candidates, including OTL-203 and OTL-200, will not be successfully developed or commercialized, the risk of cessation or delay of any of Orchard’s ongoing or planned clinical trials, the risk that prior results, such as signals of safety, activity or durability of effect, observed from preclinical studies or clinical trials will not be replicated or will not continue in ongoing or future studies or trials involving Orchard’s product candidates, and the risk of delays in Orchard’s ability to commercialize its product candidates, if approved. Given these uncertainties, the reader is advised not to place any undue reliance on such forward-looking statements.

Other risks and uncertainties faced by Orchard include those identified under the heading “Risk Factors” in Orchard’s annual report on Form 20-F for the year ended December 31, 2018 as filed with the U.S. Securities and Exchange Commission (SEC) on March 22, 2019, as well as subsequent filings and reports filed with the SEC. The forward-looking statements contained in this press release reflect Orchard’s views as of the date hereof, and Orchard does not assume and specifically disclaims any obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required by law.

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[1]Beck et al. The Natural History of MPS I: Global Perspectives from the MPS I Registry. Genetics in Medicine 2014, *16*(10), 759

[2]Mahmood et al. Metachromatic Leukodystrophy: A Case of Triplets with the Late Infantile Variant and a Systematic Review of the Literature. Journal of Child Neurology 2010, DOI: http://doi.org/10.1177/0883073809341669

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