Orchard Therapeutics, Fondazione Telethon and Ospedale San Raffaele Announce Exclusive Worldwide License Agreement for the Treatment of MPS-I

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Encouraging Clinical Data Generated from Ongoing Proof-of-Concept Study Conducted by the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget); Enrollment Expected to Complete in the First Half of 2020

Leverages Orchard's Expertise in Treating Neurometabolic Diseases Using its Investigational Autologous Hematopoietic Stem Cell Gene Therapy

Builds Upon Orchard / SR-Tiget Partnership to Develop Novel Gene Therapy Candidates

Conference Call Scheduled for Today at 8:00 a.m. ET

BOSTON, LONDON and MILAN, Italy, May 28, 2019 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), Fondazione Telethon and Ospedale San Raffaele today announced that Orchard has been granted an exclusive worldwide license to intellectual property rights to research, develop, manufacture and commercialize the *ex vivo* autologous hematopoietic stem cell (HSC) gene therapy program for the treatment of Mucopolysaccharidosis Type I (MPS-I) developed by the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) in Milan, Italy. The clinical-stage program is currently enrolling patients in an ongoing proof-of-concept study. As of data presented by SR-Tiget at the American Society of Gene & Cell Therapy (ASGCT) annual meeting in April 2019, four patients have been enrolled in the trial with follow-up of up to nine months.

MPS-I is a progressive, debilitating and often life-threatening inherited lysosomal storage disorder. Patients often experience neurocognitive impairment, skeletal deformity, loss of vision and hearing, and cardiovascular and pulmonary complications, with the most severe form known as Hurler syndrome.

"We believe the use of *ex vivo* autologous hematopoietic stem cell gene therapy in MPS-I has the potential to fundamentally change the lives of patients born with this devastating and rapidly progressive condition," said Mark Rothera, president and chief executive officer of Orchard. "This program leverages our expertise in developing *ex vivo* autologous HSC gene therapy candidates for neurometabolic disorders. Given the transformative potential seen in our MLD program, we hope we will be able to correct multiple aspects of the condition, including central nervous system dysfunction."

The terms of the deal include an upfront payment in cash as well as contingent payments on the achievement of future development, regulatory and sales milestones, as well as royalty payments on net sales.

The MPS-I program has shown promising clinical data in an ongoing proof-of-concept study in patients with the severe Hurler subtype, who were treated with *ex vivo* autologous HSC gene therapy, referred to as OTL-203, using a cryopreserved formulation and a lentiviral vector.

- Preliminary data in four patients presented at last month's 22nd ASGCT annual meeting indicate treatment with gene therapy and the selected conditioning regime was well-tolerated in these patients.
- Engraftment and high alpha-L-iduronidase enzyme (IDUA) expression was seen in the first two patients with sufficient follow-up to assess these parameters.
- As of the data presented at ASGCT, four patients have been enrolled in the trial with up to nine months of follow up. The trial is expected to enroll up to eight patients by the first half of 2020, with preliminary findings after one year of follow-up.

"Developing safe and effective treatments for neurometabolic diseases has been a challenge that we believe *ex vivo* autologous HSC gene therapy has the potential to overcome," said Luigi Naldini, director of SR-Tiget and head of the Gene Transfer Technologies and New Gene Therapy Strategies Unit. "Preliminary data obtained to date from the ongoing clinical trial for MPS-I show signs of metabolic correction in patients with the most severe subtype of MPS-I, known as Hurler syndrome. We are pleased to continue our partnership with Orchard as we work together to develop potential *ex vivo* HSC gene therapies to treat MPS-I and other devastating rare diseases."

About the Orchard Therapeutics / San Raffaele Telethon Institute for Gene Therapy Partnership
Orchard and the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget) are two leaders in gene therapy dedicated to transforming the lives of patients with serious and life-threatening rare diseases and already collaborate as part of a research and development partnership. Current development programs under the partnership are metachromatic leukodystrophy (MLD), Wiskott-Aldrich syndrome (WAS) and transfusion-dependent beta-thalassemia (TDT).

SR-Tiget was created in 1995 through a joint venture between Ospedale San Raffaele, a highly specialized internationally renowned scientific, clinical and academic facility, and Fondazione Telethon, one of the main biomedical charities in Italy focused on rare genetic diseases. SR-Tiget is now an international point of reference for gene therapy research and cell transplantation for many genetic disorders.

About MPS-I
The mucopolysaccharidoses (MPS) are a group of inherited lysosomal storage disorders (LSD), of which MPS-I is one type. MPS-I is a rare inherited neurometabolic LSD caused by a deficiency of the alpha-L-iduronidase enzyme (IDUA) needed to break down complex carbohydrates. There are three subtypes of MPS-I with an overall estimated frequency of approximately one in every 100,000 live births. Approximately 60 percent of MPS-I patients have the severe Hurler subtype. MPS-I can cause neurocognitive impairment, skeletal deformity, loss of vision and hearing, hydrocephalus,

cardiovascular and pulmonary complications. Treatment options for MPS-I include bone marrow 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. Untreated, patients with the most severe form of MPS-I, Hurler syndrome, rarely live past the age of 10.

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) and transfusion-dependent beta-thalassemia (TDT), 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," "anticipates," 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, planned marketing and licensing application submissions and next steps for Orchard's programs, including the therapeutic potential of its product candidates, including OTL-203 for the treatment of MPS-I. These statements are neither promises nor guarantees, but 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, 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. Orchard undertakes no 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. For additional disclosure regarding these and other risks faced by Orchard, see the disclosure contained in Orchard's public filings with the Securities and Exchange Commission.

Orchard Contact:
Renee Leck, Director of Investor Relations
Orchard Therapeutics
+1 862-242-0764
Renee.Leck@orchard-tx.com

Fondazione Telethon press office
HAVAS PR Milan
Thomas Balanzoni
Ph. 02 85457047 – cell. 3463204520
e-mail: thomas.balanzoni@havaspr.com

IRCCS Ospedale San Raffaele
Press office
Gea Gardini – Marta Ammoni
Ph. 02 2643 6255/4466 - 334 6090384
e-mail: ufficio.stampa@hsr.it
web: www.hsr.it

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