Orchard Therapeutics Announces FDA Regenerative Medicine Advanced Therapy (RMAT) Designation Granted for OTL-103 for the Treatment of Wiskott-Aldrich Syndrome

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Three-Year Registrational Data Set to be Presented by Year End 2019

Regulatory Submissions Planned in the U.S. and Europe for 2021

BOSTON and LONDON, July 29, 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 that it has received Regenerative Medicine Advanced Therapy (RMAT) designation from the U.S. Food and Drug Administration (FDA) for OTL-103, Orchard's *ex vivo* autologous hematopoietic stem cell (HSC)-based gene therapy for the treatment of Wiskott-Aldrich Syndrome (WAS) developed at the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) in Milan, Italy. An investigational drug or therapy is eligible for RMAT designation if it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or therapy has the potential to address unmet medical needs for such disease or condition.

"Securing RMAT designation for OTL-103 is an important step in expediting the product development and review of our planned biologics license application and recognizes the unmet need for children and young adults afflicted with Wiskott-Aldrich Syndrome," said Anne Dupraz-Poiseau, Ph.D., chief regulatory officer at Orchard. "We remain on track to file for regulatory approval of our WAS gene therapy program in the U.S. and Europe in 2021 in the hope of bringing this potentially curative therapy to patients as soon as possible."

Established under the 21st Century Cures Act, RMAT designation is a dedicated program designed to expedite the drug development and review processes for promising pipeline products, including gene therapies. Similar to Breakthrough Therapy designation, RMAT designation provides the benefits of intensive FDA guidance on efficient drug development, including the ability for early interactions with FDA senior management to discuss surrogate or intermediate endpoints, potential ways to support accelerated approval and satisfy post-approval requirements, potential priority review of the biologics license application (BLA) and other opportunities to expedite development and review.

"This is good news for the WAS community both in the U.S. and worldwide, since it could speed patients' access to a potentially life-saving treatment for this serious condition," said Alessandro Aiuti, professor of Pediatrics at the Vita-Salute San Raffaele University and vice director of SR-Tiget.

Data from an interim analysis of a registrational trial in patients with severe WAS published by Ferrua et al. in May 2019 in *The Lancet Haematology* describes recovery of the immunological and platelet abnormalities associated with WAS, with a consequent significant reduction in the major complications of the disease. Following treatment with OTL-103 gene therapy, patients with follow-up ranging from 0.5 to 5.6 years showed a decrease in the frequency of severe infections. In addition, severe bleeding episodes were eliminated and moderate bleeding episodes were greatly reduced. Orchard intends to present the full registrational trial data set, including the primary endpoint data, with all patients at three years post-treatment with gene therapy, later this year.

About Wiskott-Aldrich Syndrome and OTL-103
Wiskott-Aldrich Syndrome (WAS) is a life-threatening inherited immune disorder characterized by autoimmunity, eczema, abnormal platelet number and function. WAS manifests with recurrent, severe infections and severe bleeding episodes, which are the leading causes of death in this disease. Without treatment, the median survival for WAS patients is 14 years of age and treatment with stem cell transplant carries significant risk of mortality and morbidities. OTL-103 is an *ex vivo,* autologous, hematopoietic stem cell-based gene therapy developed at the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) in Milan for the treatment of WAS that Orchard acquired from GSK in April 2018. The global incidence of WAS is estimated to be about 100-300 births per year, with a global prevalence of 3,000-5,000 patients in markets that typically reimburse for rare and orphan therapies.

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 about Orchard's strategy, future plans and prospects, 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, Orchard's expectations regarding the timing of regulatory submissions for approval of its product candidates, including OTL-103 for the treatment of Wiskott-Aldrich Syndrome, the timing of interactions with regulators and regulatory submissions related to ongoing and new clinical trials for its product candidates, the timing of announcement of clinical data for its product candidates, including OTL-103, and the likelihood that such data will be positive and support further clinical development and regulatory approval of these product candidates, and the likelihood of approval of such product candidates by the applicable regulatory authorities. 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 delay of any of Orchard's regulatory submissions, the failure to obtain marketing approval from the applicable regulatory authorities for any of Orchard's product candidates, the receipt of restricted marketing approvals, or 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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