



Orchard Therapeutics Announces First Patient Dosed with Cryopreserved Formulation of OTL-103 Gene Therapy for the Treatment of Wiskott-Aldrich Syndrome

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Program on Track for MAA and BLA Regulatory Submissions in 2021

Recent Lancet Hematology Publication Describes Encouraging Safety and Efficacy Data from Interim Analysis of OTL-103 Fresh Formulation Registrational Trial

BOSTON and LONDON, April 25, 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 the first patient with Wiskott-Aldrich Syndrome (WAS) has been dosed in a open label study designed to evaluate engraftment of the cryopreserved formulation of OTL-103, its *ex vivo* autologous hematopoietic stem cell (HSC) gene therapy.

"We are excited to have reached this milestone with the infusion of cryopreserved gene-modified stem cells in a patient with Wiskott-Aldrich Syndrome, a life-threatening immune disorder for which there is no available therapy outside of allogeneic stem cell transplantation, which carries a significant risk of morbidity and mortality," said Mark Rothera, president and chief executive officer of Orchard. "We believe transitioning this program to a cryopreserved formulation is an essential step for the eventual commercialization of OTL-103, enabling patients to access treatment, if approved, on a global scale. As one of our lead programs, we are focused on advancing OTL-103 to regulatory filings in the U.S. and Europe in 2021."

While the registrational trial for OTL-103 for WAS used a fresh cell formulation, Orchard plans to commercialize this and other HSC gene therapies, if approved, using a cryopreserved formulation. In total, nearly 40 patients have been treated with a cryopreserved product across the company's portfolio. The WAS cryopreserved formulation trial will enroll up to six patients, with the number of patients with successful engraftment measured at six months as the primary endpoint. This patient data will be used to supplement the company's *in vitro* CMC comparability work between the fresh and cryopreserved formulation. Please refer to www.clinicaltrials.gov (NCT03837483) for additional clinical trial information.

Fresh Formulation Interim Results Recently Published in *Lancet Hematology*

An interim analysis (data cutoff April 2016) of the ongoing fresh formulation registrational trial of OTL-103 published this month in *Lancet Hematology* shows that gene therapy is an effective and safe treatment option for patients with severe WAS. The publication describes a significant reduction in the frequency of severe infections in patients treated with OTL-103 with follow-up ranging from 0.5 – 5.6 years. Moderate and severe bleeding episodes were also greatly reduced, with patients experiencing no severe bleeding events following gene therapy. The company intends to release the full registration trial data set, including the primary endpoint data with all patients at three years post-treatment with gene therapy later this year.

"Patients with WAS suffer from severe bleeding episodes, such as intracranial bleeds or severe gut bleeds, which can be fatal. Without treatment, the median survival for WAS patients is 14 years of age," said Alessandro Aiuti, professor of Pediatrics at the Vita-Salute San Raffaele University, and vice director of the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget) at Milan's San Raffaele Hospital. "To date, the only treatment available has been a bone marrow transplantation, which is not an option for everyone and carries its own risks. The interim results of the clinical study suggest that gene therapy may be an alternative."

"We are encouraged by recently published data demonstrating that the fresh formulation of OTL-103 can reduce the frequency and severity of both infections and severe bleeding episodes in WAS patients," said Andrea Spezzi, MBBS, FFPM, chief medical officer at Orchard. "The initiation of the cryo study is an important step to ensuring patients around the world with Wiskott-Aldrich Syndrome can have access to this potential treatment as soon as possible."

About WAS and OTL-103

WAS is a life-threatening inherited immune disorder characterized by autoimmunity and abnormal platelet function and 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 for the treatment of WAS that Orchard acquired from GSK in April 2018. The global incidence of WAS is estimated to be about 100-260 births per year, with a global prevalence of 2,900-4,700 patients.

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 autologous, *ex vivo*, hematopoietic stem cell 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 (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-103. 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-103, 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.

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