



## **Donald B. Kohn, MD, Orchard Therapeutics Scientific Advisory Board Member, Presents Clinical Proof-of-Concept Data for OTL-102 Gene Therapy for the Treatment of Patients with X-CGD at the Presidential Symposium at the 2018 ASH Annual Meeting**

December 5, 2018

### **First demonstration of potential gene therapy treatment in this population leading to sustained levels of functioning neutrophils after 12 months**

BOSTON and LONDON, Dec. 05, 2018 (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 Scientific Advisory Board Member, Donald B. Kohn, MD, presented clinical proof-of-concept data from an ongoing academic clinical trial evaluating OTL-102 for the treatment of X-Linked Chronic Granulomatous Disease (X-CGD) during the Presidential Symposium at the 2018 American Society of Hematology (ASH) Annual Meeting & Exposition on December 4, 2018. X-CGD is a life-threatening inherited immunodeficiency disorder which is caused by a genetic mutation that results in the inability of neutrophils to effectively kill bacterial and fungal pathogens. This immune deficiency leads to repeated chronic and severe infections often requiring hospitalization and resulting in chronic sequelae leading to early mortality. Preclinical and clinical development of OTL-102 had originally been initiated by Genethon (Evry, France) before licensing to Orchard.

"These clinical proof-of-concept data demonstrate, for the first time, 12 months or more of restoration of immunity in X-CGD patients treated with *ex-vivo* autologous gene therapy," said Adrian Thrasher, professor of pediatric immunology and Wellcome Trust Principal Research Fellow at UCL Great Ormond Street Institute of Child Health in London. "In six of the seven evaluated patients, we are encouraged to see sustained levels of functioning neutrophils at greater than 10%, which prior publicly available data suggests is the level sufficient to see potential clinical benefit. This important milestone, together with improved clinical outcomes and an emerging safety profile with no signs of genotoxicity, suggest OTL-102 may provide a transformative treatment for X-CGD patients."

The clinical proof-of-concept data are from seven patients (ages 2-27) severely affected by X-CGD treated with OTL-102, an autologous *ex vivo* lentiviral gene therapy which utilizes a self-inactivating lentiviral vector (G1XCGD). Six of the seven evaluable patients showed persistence of 16-46% (mean 30.2%) functioning neutrophils 12 or more months after treatment, which prior publicly available data suggests is above the 10% minimum threshold necessary to show potential clinical benefit and restoration of both biochemical function and immunity. Two additional patients were treated but died within three months of treatment from complications deemed by the investigator to be related to pre-existing disease-associated comorbidities due to advanced disease progression. These results are the first demonstration that *ex vivo* autologous hematopoietic stem cell gene therapy has the potential to produce sustained corrected neutrophil function for 12 months or more in severely affected X-CGD patients.

The 12-month follow-up data for OTL-102 were previewed as part of a presentation given by Dr. Kohn during the Presidential Symposium at the ASH. Dr. Kohn is a distinguished professor of pediatric hematology/oncology; microbiology, immunology and molecular genetics; and molecular and medical pharmacology at the University of California Los Angeles.

Dr. Kohn commented, "X-CGD is a severe, life-threatening disease that leads to a significantly reduced quality and length of life in affected patients. Current treatment options, including prophylactic antibiotics, antifungals, and hematopoietic stem cell transplants all have significant associated risk and limitations. By providing the first-ever demonstration that autologous hematopoietic stem cell gene therapy has the potential to lead to sustained levels of functioning neutrophils and thereby a long-term clinical benefit, we are hopeful that OTL-102 may provide a new treatment option for X-CGD patients to improve the quality and length of their lives, escaping the chronic infections and inflammation associated with the disease."

In 2019, Orchard intends to meet with regulatory authorities to discuss the clinical development path forward for the OTL-102 program in patients with X-CGD.

#### **About X-CGD**

X-linked CGD is a rare and life-threatening primary immune deficiency resulting from a mutation in the CYBB gene. CYBB encodes for the gp91phox protein, a vital component of the NADPH oxidase complex that is required for generation of superoxide and the respiratory burst that is required for effective killing of ingested microorganisms. As a result, specific white blood cells, including predominantly neutrophils, are unable to effectively eradicate both bacteria and fungi. Patients suffering from this disease are susceptible to severe, chronic bacterial and fungal infections. In addition, X-CGD also causes inflammation, characterized by granuloma formation that may compromise vital organs, including the gastrointestinal tract and lungs. Repeated episodes of infection and inflammation severely reduce the life expectancy and quality of life of patients. Prophylactic antibacterial and antifungal medication does not prevent disease progression and the only current curative therapy, allogeneic hematopoietic stem cell transplant, can be associated with toxicities related to graft versus host disease and the chemotherapy conditioning required for engraftment of allogeneic cells.

#### **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* gene therapies includes Strimvelis, the first autologous *ex vivo* gene therapy approved by the European Medicines Agency for adenosine deaminase severe combined immunodeficiency (ADA-SCID). Additional programs for primary immune deficiencies, neurometabolic disorders and hemoglobinopathies include three advanced registrational studies for ADA-SCID, metachromatic leukodystrophy (MLD) and Wiskott-Aldrich syndrome (WAS), clinical programs for X-linked chronic granulomatous disease (X-CGD) and transfusion dependent beta-thalassemia (TDBT), as well as an extensive preclinical pipeline.

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, Orchard’s expectations regarding timing of discussions with regulatory authorities [in the U.S. and in Europe] and the timing of regulatory submissions for approval of its product candidates, including OTL-102; Orchard’s views with respect to the potential for OTL-102 for the treatment of X-CGD; its expectations regarding the reporting and outcome of data from its clinical trials, and the regulatory pathway for X-CGD,. 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 success, cost, and timing of Orchard’s product development activities and clinical trials, including that prior results, such as safety or durability of effect, observed from prior studies or clinical trials will be replicated or will continue in ongoing or future studies or trials involving Orchard’s product candidates, and Orchard’s ability to obtain and maintain regulatory approval for its product candidates. 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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