Orchard Therapeutics Presents Clinical Proof-of-Concept Data for OTL-102 for the Treatment of X-CGD

February 25, 2019

Six Patients Continue to Show Sustained Levels of Functioning Neutrophils After 12 Months and No Longer Receive Treatment with CGD-related Prophylactic Antibiotics

Regulatory Discussions on Registrational Trial Design Planned for 2019

BOSTON and LONDON, Feb. 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, yesterday presented additional clinical proof-of-concept data evaluating OTL-102, an *ex vivo*, autologous, hematopoietic stem cell based gene therapy for the treatment of X-linked chronic granulomatous disease (X-CGD) during an oral presentation at the 2019 Transplantation and Cellular Therapy Meetings of ASBMT and CIBMTR in Houston, TX. The proof-of-concept data was first presented during the Presidential Symposium at the American Society of Hematology (ASH) Annual Meeting & Exposition in December 2018.

X-CGD is a rare, life-threatening, inherited immunodeficiency disorder caused by a genetic mutation that results in the inability of neutrophils to effectively kill bacterial and fungal infections. Patients with X-CGD are prone to recurrent severe infections and complications, leading to frequent hospitalizations, significant morbidity and early mortality.

“This proof-of-concept data set for OTL-102 demonstrates efficacy across multiple markers of clinical benefit in 6 of 7 evaluable patients treated for X-CGD at twelve months,” said Dr. Kohn, professor of Microbiology, Immunology & Molecular Genetics at the University of California, Los Angeles. “Of note, patients have shown sustained levels of functioning neutrophils associated with clinical benefit, freedom from infections and resolution of chronic inflammation. We look forward to continuing the development of this potentially transformative gene therapy for patients with X-CGD.”

Andrea Spezzi, M.D., chief medical officer of Orchard commented, “These data demonstrate that autologous, hematopoietic stem cell gene therapy can be used to correct X-CGD and OTL-102 has the potential to be a transformative new treatment option for these patients. In order to advance this potential therapy for the treatment of X-CGD as rapidly as possible, we are in the process of designing a registrational trial and intend to seek regulatory input this year on the clinical development path forward.”

The safety and efficacy of OTL-102, which utilizes a self-inactivating lentiviral vector (G1XCGD), was assessed in seven evaluable patients (aged 2-27 years) with X-CGD. As previously reported, two additional patients died within three months of treatment from complications deemed by the investigator to be related to pre-existing comorbidities due to advanced disease progression and unrelated to OTL-102.

Efficacy Data

- Six of seven eligible patients showed greater than 10% (ranging from 16%-46%) functioning, oxidase-positive neutrophils in circulation at 12 months, which is the minimum threshold of oxidase-positive neutrophils necessary to demonstrate potential clinical benefit
- The same six patients demonstrated stable vector copy number in neutrophils over 12 months, which correlates to the engraftment of long-term repopulating hematopoietic stem cells
- As of the last follow-up, those six patients were no longer receiving CGD-related prophylactic antibiotic treatment

Safety Data

- There were no gene therapy infusion-related adverse events and typical conditioning-related events included transient neutropenia, thrombocytopenia, mucositis
- One serious adverse event of immune reconstitution inflammatory syndrome fully resolved with steroids

About X-CGD and OTL-102
X-linked chronic granulomatous disease (X-CGD) is a rare, life-threatening, inherited disease of the immune system caused by mutations in the cytochrome B-245 beta chain (CYBB) gene. Because of the underlying genetic defect in the CYBB gene, the neutrophils of patients with X-CGD are unable to kill bacteria and fungi, leading to repeated chronic infections. The main clinical manifestations of X-CGD are pyoderma; pneumonia; colitis; lymphadenitis; brain, lung and liver abscesses; and osteomyelitis. Patients with X-CGD typically start to develop infections in the first decade of life and mortality has been estimated at approximately 40% by the age of 35 years.[1] The incidence of X-CGD is currently estimated to be between 2.6 in 1 million and 10 in 1 million male live births. OTL-102 is an autologous, *ex vivo,* hematopoietic stem cell gene therapy being studied for the treatment of X-CGD. The studies are supported by multiple institutions including the California Institute of Regenerative Medicine, the Gene Therapy Resource Program from the National Heart, Lung, and Blood Institute, the National Institute of Allergy and Infectious Diseases Intramural Program, the Wellcome Trust and the National Institute for Health Research Biomedical Research Centres at Great Ormond Street Hospital for Children NHS Foundation Trust, University College London Hospitals NHS Foundation Trust and University College London. Preclinical and clinical development of OTL-102 had originally been initiated by Genethon (Evry, France) before being licensed to Orchard.

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, 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 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 (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.

[1]van den Berg et. al, PLoS One.2009;4(4):e5234

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Source: Orchard Therapeutics Limited