Orchard Therapeutics Presents Two-Year Follow-Up Data Versus Historical Control from Registrational Trial of OTL-101 for the Treatment of ADA-SCID

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100% Overall Survival and 100% Event Free Survival in Patients Treated with OTL-101 Compared to 88% OS and 56% EvFS with Historical HSCT Overall at 24 months

Biologics License Application Submission Planned for the U.S. in 2020

BOSTON and LONDON, Feb. 22, 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 will present two-year follow-up data in 20 patients from the registrational trial evaluating OTL-101, an autologous, *ex vivo,* hematopoietic stem cell gene therapy for the treatment of severe combined immune deficiency due to adenosine deaminase deficiency (ADA-SCID) during the President's Symposia at the 2019 Transplantation and Cellular Therapy Meetings of ASBMT and CIBMTR in Houston, TX.

ADA-SCID is a rare, life-threatening, inherited disease caused by mutations in the ADA gene. Deficiencies of the ADA enzyme leads to dysfunction of cells of the immune system, including B, T and natural killer cells. Patients with ADA-SCID are unable to fight off and frequently succumb to complications from bacterial, viral and fungal infections.

"With some patients in this trial approaching 5 years of follow-up, treatment with OTL-101 continues to be well-tolerated with higher rates of overall and event free survival for patients with ADA-SCID compared to a historical control group of patients receiving hematopoietic stem cell transplants," said Donald B. Kohn, M.D., professor of Microbiology, Immunology & Molecular Genetics at the University of California, Los Angeles and the principal investigator of the study. "We are very encouraged by the results and look forward to advancing this potentially transformative treatment option for patients with this serious and life-threatening condition."

Bobby Gaspar, M.D., Ph.D., chief scientific officer of Orchard commented, "These results demonstrate that by engrafting autologous, gene-modified, long-term repopulating hematopoietic stem cells, we are able to see durable recovery of the immune system. With 100% overall survival and 100% event free survival in this trial maintained at 24 months, we believe OTL-101 has the potential to enable patients with ADA-SCID to lead healthier lives with restored immunity to fight infections."

Andrea Spezzi, M.D., chief medical officer of Orchard continued, "For the remainder of 2019, we are focused on completing the clinical and manufacturing activities to enable a BLA filing in 2020, bringing us closer to our goal of providing patients with a new treatment option."

The reported data are the complete 24 month results from a trial evaluating the safety and efficacy of OTL-101. OTL-101 was administered post-busulfan conditioning in 20 pediatric patients, who lacked a medically eligible donor for bone marrow transplantation. Patients were followed for 24 months post treatment and compared with a historical control cohort of 26 patients with ADA-SCID who underwent hematopoietic stem cell transplant (HSCT), 12 from matched related donors (MRD) and 14 without a MRD. The median age at treatment for patients receiving OTL-101 was 9.0 months and 7.3 months for patients treated with HSCT.

Efficacy Data

• Treatment with OTL-101 resulted in 100% overall survival (OS) and 100% event free survival (EvFS) at 24 months

- For OS, there was a difference of 12% (95% CI: -5.6, 31.2, p = 0.121) between the patients treated with OTL-101 compared with HSCT overall
- For EvFS, there was a statistically significant difference of 44% (95% CI: 22.8, 65.2, p = 0.001) between the patients treated with OTL-101 compared with HSCT overall

• Genetically modified cells, as indicated by increasing and then sustained vector copy number in both peripheral blood mononuclear cells and granulocytes, were detectable in all patients treated with OTL-101 and were maintained through 24 months post-treatment. A similar pattern was observed in ADA enzyme activity.

• Evidence of immune reconstitution was observed in patients treated with OTL-101

- By 24 months post-treatment, 90% of patients receiving OTL-101 were able to stop immunoglobulin replacement therapy compared with 55% receiving HSCT overall

- Over 24 months, none of the patients treated with OTL-101 restarted enzyme replacement therapy (ERT) after stopping 30 days post-treatment per protocol, whereas three patients in the historical control group received long-term ERT after HSCT and seven required additional rescue HSCT

Safety Data

• Treatment with OTL-101 was well-tolerated and had a positive benefit-risk profile

• There were no deaths or reports of graft-versus-host disease (GvHD) in the patients treated with OTL-101

- In the historical HSCT control group, five acute and three chronic GvHD events were reported, including one death due to GvHD

• Nine out of the 20 patients who received OTL-101 experienced a total of 27 serious adverse events (SAEs)

- The most frequent SAEs were infections and gastrointestinal events
- One SAE of bacteremia was deemed related to treatment with OTL-101 and resolved with antibiotics
- Two cases of immune reconstitution inflammatory syndrome were deemed unrelated to OTL-101 and resolved with corticosteroids

About ADA-SCID and OTL-101
Severe combined immune deficiency due to adenosine deaminase deficiency (ADA-SCID) is a rare, life-threatening, inherited disease of the immune system caused by mutations in the ADA gene resulting in a lack of, or minimal, immune system development.[1-4] The first symptoms of ADA-SCID typically manifest during infancy with recurrent severe bacterial, viral and fungal infections and overall failure to thrive, and without treatment the condition can be fatal within the first two years of life. The incidence of ADA-SCID is currently estimated to be one in 500,000 live births in the United States and between one in 200,000 and one in 1 million in Europe.[3] Higher incidence rates are reported in geographies of higher consanguinity, such as Turkey and the Middle-East. OTL-101 is an autologous, *ex vivo,* hematopoietic stem cell gene therapy for the treatment of patients diagnosed with ADA-SCID being investigated in multiple clinical trials in the United States and Europe, including a registrational trial at the University of California, Los Angeles (UCLA). OTL-101 has received orphan drug designation from the U.S. Food and Drug Administration (FDA) and the EMA for the treatment of ADA-SCID, and Breakthrough Therapy Designation from the FDA. The studies are supported by multiple institutions including the National Institute of Allergy and Infectious Diseases (NIAID), the National Institutes of Health (NIH), the National Gene Vector Biorepository, the California Institute of Regenerative Medicine, Medical Research Council and the National Institute for Health Research Biomedical Research Centre at Great Ormond Street Hospital for Children NHS Foundation Trust and University College London.

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 the timing of regulatory submissions for approval of its product candidates, including OTL-101; Orchard's views with respect to the potential for OTL-101 for the treatment of ADA-SCID; its expectations regarding the reporting and outcome of data from its clinical trials, and the regulatory pathway for ADA-SCID. 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]Orphanet. SCID due to ADA deficiency [2]Whitmore KV, Gaspar HB. Front Immunol. 2016;7:314. [3]Kwan A, et al. JAMA. 2014;312:729-738. [4]Sauer AV, et al. Front Immunol. 2012;3:265.

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