



## Orchard Therapeutics Announces Clinical Proof-of-Concept Data for Gene Therapy OTL-300 Demonstrating Efficacy in Transfusion-Dependent Beta-Thalassemia

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*Study Used the GLOBE Lentiviral Vector and Treated Adult and Pediatric Patients with Severe Phenotypes*

*At 12 Months Following Treatment, Eight of Nine Patients Had Reduced or Eliminated Need for Transfusions, with Four Pediatric Patients Achieving Transfusion Independence*

BOSTON and LONDON, April 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 the presentation of the full clinical proof-of-concept data from its trial of *ex vivo*, autologous, hematopoietic stem cell (HSC) gene therapy, OTL-300, for the treatment of transfusion-dependent beta-thalassemia (TDT). The data will be featured today in an oral presentation at the 22nd American Society of Gene & Cell Therapy (ASGCT) Annual Meeting in Washington, D.C.

The presentation will report the updated safety and efficacy results of OTL-300 in nine TDT patients (six pediatric and three adult), with severe phenotypes including  $\beta^+/\beta^+$ ,  $\beta^0/\beta^+$  and  $\beta^0/\beta^0$ , with a minimum of one year of follow-up post-treatment. All patients had high pre-treatment red blood cell transfusion requirements of  $\geq 200$  ml/kg/yr of packed red blood cells. The study utilized a lentiviral vector containing the human beta-globin gene (GLOBE) and a conditioning protocol with treosulfan and thiopeta. The data presented today and included in this release were analyzed as of April 2019.

"Patients with transfusion-dependent beta-thalassemia are not able to make enough hemoglobin to survive due to a mutation in the beta-globin gene which causes ineffective red blood cell production. Beta-thalassemia patients, especially those with severe phenotypes such as the  $\beta^0/\beta^0$  genotype, rely on frequent blood transfusions and iron chelation therapy to survive. They may be treated with a bone marrow transplant, however this carries significant risk and can lead to early mortality," said Dr. Giuliana Ferrari, head of the gene transfer into stem cell unit at San Raffaele Scientific Institute and San Raffaele-Telethon Institute for Gene Therapy. "Today's results demonstrate that HSC gene therapy with OTL-300 has the potential to provide clinical benefit and a new, life-changing treatment for patients burdened with this devastating condition."

"With each of our first five programs now demonstrating clinical proof of concept, these results in TDT further validate our belief that the process of modifying hematopoietic stem cells using a lentiviral vector to introduce normal copies of the affected gene to a patient, has the potential for durable disease correction across a spectrum of disorders," said Andrea Spezzi, MBBS, FFPM, chief medical officer of Orchard. "We look forward to furthering our discussions with key stakeholders to determine the registrational path forward to enable us to serve the large number of patients living with transfusion-dependent beta-thalassemia."

### Safety Data

- All nine patients met the safety endpoint of survival with follow-up ranging from 16 to 43 months (3.6 years). No adverse events related to the product were reported.
- Vector integration profiles had the expected polyclonal genomic distribution seen with other lentiviral vector mediated HSC gene therapy studies, and no evidence of abnormal proliferation or clonal dominance was observed.

### Efficacy Results

- The primary efficacy endpoint of transfusion reduction at 12 months following treatment was achieved in eight of nine TDT patients treated with OTL-300.
  - Of the six pediatric patients treated, four achieved transfusion independence and one showed a reduction in transfusion requirement.
  - All three adult patients had a reduction in their transfusion requirements.
  - As published previously in *Nature Medicine*, one pediatric patient did not have a reduced transfusion requirement compared to pre-treatment levels at 12 months, which was attributed to poor engraftment of the gene-modified cells.

### About Beta-Thalassemia

Beta-thalassemia is a genetic blood disorder caused by a mutation in the beta-globin gene which causes ineffective red blood cell production. Over 300 mutations in the beta-globin gene are known, which give rise to different forms of beta-thalassemia, with variable severity. The most damaging

mutations cause the almost complete absence of beta-globin resulting in no hemoglobin production. The treatment of these patients requires frequent red blood cell transfusions along with iron chelation therapy to survive or a bone marrow transplant from a compatible donor. The global incidence of TDT is estimated to be about 20,000 births per year, with a global prevalence of approximately 288,000 patients. OTL-300 is an *ex vivo*, autologous, hematopoietic stem cell-based gene therapy developed for the treatment of TDT that Orchard acquired from GSK in April 2018.

#### **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, the achievement of proof of concept for OTL-300 and the safety and efficacy of this investigational therapy, as well as statements concerning the therapeutic potential of its product candidates generally. 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-300, 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 including but not limited to the disclosures set forth under the heading "Risk Factors" in Part I, Item 3 of Orchard's most recent Annual Report on Form 20-F.

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