



## **Orchard Therapeutics Announces FDA Granted Orphan Drug Designation for OTL-102 for the Treatment of X-linked Chronic Granulomatous Disease (X-CGD)**

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### **Early Clinical Data Support *ex vivo* Hematopoietic Stem Cell Gene Therapy as a Potentially Promising Treatment Option for X-CGD**

BOSTON and LONDON, Jan. 29, 2020 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today announced that it has received orphan drug designation from the U.S. Food and Drug Administration (FDA) for OTL-102, the company's *ex vivo* autologous hematopoietic stem cell (HSC) gene therapy being investigated for the treatment of X-linked chronic granulomatous disease (X-CGD). The FDA may grant orphan designation to drugs and biologics intended to treat a rare disease or condition affecting fewer than 200,000 persons in the U.S.

"We are pleased to have received this orphan drug designation from the FDA, which recognizes the potential of OTL-102 to address a rare population of patients with X-CGD, a life-threatening disease with a critical unmet need," said Anne Dupraz-Poiseau, Ph.D., chief regulatory officer at Orchard. "We are encouraged by the clinical data published to date and are eager to advance OTL-102 development as quickly as possible for patients with X-CGD."

Orphan designation qualifies a company for certain benefits, including financial incentives to support clinical development and the potential for seven years of market exclusivity in the U.S. upon regulatory approval.

Early academic clinical trial data for OTL-102 that was recently published in *Nature Medicine* demonstrates that *ex vivo* autologous HSC gene therapy may be a promising approach for the treatment of X-CGD. The letter, which was led by researchers at the University of California, Los Angeles (UCLA) — including Donald B. Kohn, M.D., one of the study's lead investigators and professor of microbiology, immunology and molecular genetics at UCLA — and Great Ormond Street Hospital (UK), provides an analysis of safety and efficacy outcomes in nine severely affected patients with X-CGD. At 12 months post-treatment, six of seven surviving patients, all of whom were adults or late adolescents, exceeded the minimum threshold hypothesized in published literature to demonstrate potential clinical benefit, defined as 10% functioning, oxidase-positive neutrophils in circulation and have discontinued preventive antibiotics.<sup>1</sup>

As previously reported, two pediatric patients died within three months of treatment from complications deemed by the investigators and independent data and safety monitoring board to be related to pre-existing comorbidities due to advanced disease progression and unrelated to OTL-102. Investigators are planning to enroll additional pediatric patients in 2020 to assess outcomes in this patient population. In addition, there is work underway to improve the efficiency of the drug product manufacturing process prior to initiating a registrational study.

"Patients with X-CGD experience significantly reduced quality and length of life, and currently must take daily medications that do not eliminate the risk of fatal infections," said Adrian Thrasher, Ph.D., M.D., one of the study's lead investigators and professor of pediatric immunology and Wellcome Trust Principal Research Fellow at UCL Great Ormond Street Institute of Child Health in London. "These data demonstrate that OTL-102 has the potential to become a transformative new treatment option for patients with X-CGD with the evaluation of longer follow up and more patients."

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

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 encoding the gp91phox subunit of phagocytic NADPH oxidase. Because of this genetic defect, phagocytes, or white blood cells, of X-CGD patients are unable to kill bacteria and fungi, leading to chronic, severe infections. The main clinical manifestations of X-CGD are pyoderma, a type of skin infection; pneumonia; colitis; lymphadenitis, an infection of the lymph nodes; brain, lung and liver abscesses; and osteomyelitis, an infection of the bone. Patients with X-CGD typically start to develop infections in the first decade of life, and an estimated 40 percent of patients die by the age of 35.<sup>2</sup> The incidence of X-CGD is currently estimated at between 1 in 100,000 and 1 in 400,000 male births.

#### **About OTL-102**

OTL-102 is an *ex vivo* autologous 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) and funded by an EU framework 7 funded consortium, NET4CGD, before being licensed to Orchard.

#### **About Orchard**

Orchard Therapeutics is a global gene therapy leader dedicated to transforming the lives of people affected by rare diseases through the development of innovative, potentially curative gene therapies. Our *ex vivo* autologous gene therapy approach harnesses the power of genetically-modified blood stem cells and seeks to correct the underlying cause of disease in a single administration. The company has one of the deepest gene therapy product candidate pipelines in the industry and is advancing seven clinical-stage programs across multiple therapeutic areas, including inherited neurometabolic disorders, primary immune deficiencies and blood disorders, where the disease burden on children, families and caregivers is immense and current treatment options are limited or do not exist.

Orchard has its global headquarters in London and U.S. headquarters in Boston. For more information, please visit [www.orchard-tx.com](http://www.orchard-tx.com), and follow us on [Twitter](#) and [LinkedIn](#).

### **Forward-Looking Statements**

This press release contains certain forward-looking statements about Orchard's strategy, future plans and prospects, 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," "plans," "intends," "projects," 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 therapeutic potential of Orchard's product candidates, including the product candidate or candidates referred to in this release, Orchard's expectations regarding the timing of regulatory submissions for approval of its product candidates, including the product candidate or candidates referred to in this release, the timing of interactions with regulators and regulatory submissions related to ongoing and new clinical trials for its product candidates, the timing of announcement of clinical data for its product candidates and the likelihood that such data will be positive and support further clinical development and regulatory approval of these product candidates, and the likelihood of approval of such product candidates by the applicable regulatory authorities. These statements are neither promises nor guarantees and 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 the product candidate or candidates referred to in this release, 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, the delay of any of Orchard's regulatory submissions, the failure to obtain marketing approval from the applicable regulatory authorities for any of Orchard's product candidates, the receipt of restricted marketing approvals, and the risk of delays in Orchard's ability to commercialize its product candidates, if approved. Given these uncertainties, the reader is advised not to place any undue reliance on such forward-looking statements.

Other risks and uncertainties faced by Orchard include those identified under the heading "Risk Factors" in Orchard's annual report on Form 20-F for the year ended December 31, 2018, as filed with the U.S. Securities and Exchange Commission (SEC) on March 22, 2019, as well as subsequent filings and reports filed with the SEC. The forward-looking statements contained in this press release reflect Orchard's views as of the date hereof, and Orchard does not assume and specifically disclaims any 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.

### **References**

<sup>1</sup>Kang et al. *Blood*. 2010;115(4):783-91

<sup>2</sup>van den Berg et al. *PLoS One*. 2009;4(4):e5234

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