UNITED STATES SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER PURSUANT TO RULE 13a-16 OR 15d-16 UNDER THE SECURITIES EXCHANGE ACT OF 1934

For the month of April 2019

Commission File Number: 001-38722

ORCHARD THERAPEUTICS PLC

(Translation of registrant's name into English)

108 Cannon Street
London EC4N 6EU
United Kingdom
(Address of principal executive offices)

| ndicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F. Form 20-F 🗵 Form 40-F 🗆 | |
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| ndicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): \Box | |
| ndicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): \Box | |
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| rporated herein by referen | herapeutics plc (the "Company") nce. | <i>51</i> | , 10 | |
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EXHIBITS

| Exhibit | Description |
|---------|------------------------------------|
| 99.1 | Press Release Dated April 15, 2019 |

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ORCHARD THERAPEUTICS PLC

Date: April 15, 2019 By: /s/ Frank E. Thomas

Frank E. Thomas Chief Financial Officer

Orchard Therapeutics Announces Presentation of Clinical Proof-of-Concept for OTL-300 for the Treatment of Transfusion-Dependent Beta-Thalassemia at the 22nd American Society of Gene & Cell Therapy Annual Meeting

Data Supports Achievement of Proof-of-Concept Milestone for OTL-300

BOSTON and LONDON, April 15, 2019 - 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 achievement of clinical proof-of-concept based on data from the trial of its *ex vivo*, autologous, hematopoietic stem cell (HSC) gene therapy, OTL-300, for the treatment of transfusion-dependent beta-thalassemia (TDT). The data will be published online today in an abstract via the American Society of Gene & Cell Therapy (ASGCT) website, and the full data set will be featured in an oral presentation at the 22nd ASGCT Annual Meeting to be held on April 29 – May 2, 2019 in Washington, D.C. Specifically, the presentation will report the updated safety and efficacy results of OTL-300 in nine transfusion-dependent severe phenotype TDT patients (six pediatric, three adult), including $\beta 0/\beta 0$ genotype, with minimum one year post-treatment follow up, as well as details on engraftment of gene-modified cells and vector integration site analyses.

The primary endpoint of transfusion reduction was achieved after one year of follow-up in eight out of nine TDT patients treated with OTL-300. All nine patients met the safety endpoints with no adverse events related to the therapy.

"We are pleased OTL-300 has shown clinical benefit in severe transfusion-dependent beta-thalassemia and has the potential to be a part of a new wave of treatment options for these patients," said Andrea Spezzi, MBBS, FFPM, chief medical officer at Orchard. "We believe these data support proof-of-concept and the further development of this therapeutic approach. This marks the fifth program from Orchard's dedicated gene therapy portfolio to achieve clinical proof-of-concept and further supports our belief that a single administration of gene-modified autologous hematopoietic stem cells can lead to durable engraftment and potential disease correction."

The proof-of-concept study utilized a lentiviral vector containing the human beta-globin gene (GLOBE) and an adapted conditioning regimen. The study also included pediatric patients and patients with a spectrum of TDT genotypes, including the most severe genotype, $\beta 0/\beta 0$, and patients with notably high pre-treatment transfusion requirements.

Two additional abstracts from Orchard's clinical and preclinical pipeline were also accepted for presentation at ASGCT. All three accepted abstracts will be published online on the ASGCT website later today.

Presentation details for OTL-300:

Title: Gene Therapy for the Treatment of Adult and Pediatric Patients Affected by Transfusion Dependent Beta-Thalassemia **Presenter:** Giuliana Ferrari, San Raffaele-Telethon Institute for Gene Therapy (SR-TIGET) and University Vita-Salute San

Raffaele, Milan, Italy

Session: Clinical Gene Therapies for Blood Diseases

Date: Monday. April 29, 2019 **Time:** 10:30 - 10:45 a.m. ET

Location: Washington Hilton, Jefferson room

Abstract number: 49

About Beta-Thalassemia

Beta-thalassemia is a genetic blood disorder caused by a mutation in the beta-globin gene, a fundamental protein required for red blood cells to work correctly. Over 300 mutations in the beta-globin gene are known, which give rise to many different forms of beta-thalassemia, with variable severity. The most damaging mutations cause the almost complete absence of the protein in a patient's blood, causing them to rely on frequent blood transfusions to survive or a bone marrow transplant from a compatible donor. 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, 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 (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 forwardlooking 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 ofdelays 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 201-F.

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