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 February 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)

Indicate 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 ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): ☐

On February 22, 2019 and February 25, 2019, Orchard Therapeutics plc (the “Company”) issued press releases, copies of which are attached hereto as Exhibit 99.1 and Exhibit 99.2 and are incorporated herein by reference.

EXHIBITS

Exhibit	Description
99.1	Press Release Dated February 22, 2019
99.2	Press Release Dated February 25, 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: February 25, 2019

By: /s/ Frank E. Thomas
Frank E. Thomas
Chief Financial Officer

Exhibit 99.1

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

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 between 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.

Contacts

Corporate contact
Renee Leck
Orchard Therapeutics
+1 862-242-0764
renee.leck@orchard-tx.com

Media contact
Allison Blum, Ph.D.
LifeSci Public Relations
+1 646-627-8383
Allison@lifescipublicrelations.com

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

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.

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

Contacts

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Renee Leck
Orchard Therapeutics
+1 862-242-0764
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Allison@lifescipublicrelations.com