
**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 March 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 March 27, 2019, Orchard Therapeutics plc (the "Company") issued the following press release, a copy of which is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

EXHIBITS

Exhibit	Description
99.1	Press Release Dated March 27, 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: March 27, 2019

By: /s/ Frank E. Thomas

Frank E. Thomas

Chief Financial Officer

Orchard Therapeutics Presents New Registrational Data Demonstrating Sustained Clinical Benefit of OTL-200 for the Treatment of MLD

Compared to Natural History, Late Infantile Patients Demonstrated Gross Motor Function Scores Higher by 65 and 72 Percentage Points at 2- and 3-Years Post Gene Therapy; Early Juvenile Patients Demonstrated Scores Higher by 40 Percentage Points at Both Time Points

No Effective Treatments Currently Available for MLD Patients, MAA Submission in Europe Planned for 2020

BOSTON and LONDON, March 27, 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, presented the full registrational dataset from a 20 patient trial evaluating the efficacy and safety of OTL-200, an *ex vivo* autologous hematopoietic stem cell-based (HSC) gene therapy for the treatment of metachromatic leukodystrophy (MLD). The data, which included updated results on the two-year primary endpoints, in addition to new follow-up data at three years, were featured yesterday in an oral presentation at the 45th Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT).

Dr. Valeria Calbi, a hematologist at San Raffaele Scientific Institute and San Raffaele-Telethon Institute for Gene Therapy and an investigator of the study said, “MLD is a devastating and rapidly progressing disease with no available treatments. In its most severe forms, patients will not survive beyond their first few years of life. It is highly encouraging that the outcomes of this registrational trial exceeded the primary efficacy endpoint for motor function in the most severe forms of the disease, while also demonstrating high levels of sustained and stable engraftment of gene corrected cells and reconstitution of enzymatic activity. Together these data show transformational potential for MLD patients, with near normal motor and cognitive development observed in the majority of treated children.”

“Providing effective therapies for metabolic diseases that affect the central nervous system has been an ongoing challenge in the field of gene therapy and beyond. We are thrilled that these data further confirm the potential of Orchard’s HSC approach to treat MLD and other neurometabolic diseases,” said Andrea Spezzi, MBBS, FFPM, chief medical officer of Orchard. “Moving forward, our focus is to bring the OTL-200 program to regulatory filings as quickly as possible, while broadly leveraging this technology across our neurometabolic franchise, with a second CNS program, OTL-201 in MPS-IIIa, preparing to enter the clinic.”

As of March 2018, twenty early-onset MLD patients (9 late infantile and 11 early juvenile) from the registrational study completed at least 3 years of follow-up (ranging from 3.0 to 7.5 years in 18 out of 20 patients) to assess the efficacy and safety of OTL-200 following gene therapy. As previously reported, two patients who were symptomatic at the time of treatment died due to rapid disease progression unrelated to treatment with gene therapy. A long-term follow-up phase is ongoing until all patients complete at least 8 years of follow-up post-treatment. Results from patients treated with OTL-200 were compared with those from an age-matched natural history cohort of 31 untreated early-onset MLD patients.

Efficacy Data

For the co-primary endpoints evaluated at two years and then at three years after gene therapy, OTL-200 has shown the following:

- A reconstitution of ARSA activity in the hematopoietic system was observed in all treated patients, with values within or above the normal reference range by 3 months post-treatment and remaining stable throughout the duration of the follow-up period.
- A clinically meaningful treatment difference in gross motor function (as measured by GMFM total score) – well above the pre-specified 10 percentage point threshold established in the trial – was observed between OTL-200 treated patients and untreated, age-matched participants in the natural history study.
 - Late infantile patients treated with gene therapy demonstrated GMFM total scores of 72.5% and 73.9% at two- and three-years post-treatment, respectively. In contrast, the untreated age-matched natural history cohort had GMFM total scores of 7.4% and 2.4% at two- and three-years post-diagnosis, respectively.
 - This resulted in treatment differences of 65.1 percentage points ($p < 0.001$) and 71.5 percentage points ($p < 0.001$) at two- and three-years of follow-up, respectively.
 - Early juvenile patients treated with gene therapy demonstrated GMFM total scores of 76.5% and 71.7% at two- and three-years post-treatment, respectively. In contrast, the untreated age-matched natural history cohort had GMFM total scores of 36.6% and 31.3% at two- and three-years post-diagnosis, respectively.
 - This resulted in treatment differences of 39.8 percentage points ($p = 0.026$) and 40.5 percentage points ($p = 0.020$) at two- and three-years of follow-up, respectively.

The co-primary endpoints were supported by the following data:

- Stable engraftment of gene-corrected cells was observed in treated patients from one-month post-treatment, with persistent and stable vector copy number in CD34+ bone marrow cells and peripheral blood mononuclear cells (PBMCs) throughout the follow-up period.
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- At an age when patients in the untreated natural history cohort showed severe cognitive impairment, cognitive performance scores were maintained within normal range for most treated patients, independent of their symptomatic status at the time of treatment.
- Changes observed on brain MRIs of patients treated with OTL-200 suggest that OTL-200 may prevent, stabilize or markedly delay the progressive atrophy and demyelination (damage to the protective covering of the myelin sheath that surrounds nerve fibers) typically observed with MLD. A greater effect was observed in early-onset MLD patients treated prior to the presentation of overt symptoms.

Safety Data

- Treatment with OTL-200 was well-tolerated and had a positive benefit-risk profile, with no adverse events or deaths related to treatment and no signs of genotoxicity.
- To date, no cases of malignancy or adverse events indicative of oncogenic transformation have been reported. There was no evidence of abnormal clonal proliferation as assessed by clinical and laboratory examination.

Next Steps for OTL-200

The company intends to complete the necessary development work and prepare a marketing authorization application, or MAA, for submission in Europe in 2020. Work is also underway to prepare a biologics licensing application, or BLA, for submission in the U.S.

About MLD and OTL-200

Metachromatic leukodystrophy (MLD) is a rare and life-threatening inherited metabolic disease occurring in approximately one in every 100,000 live births. MLD is caused by a mutation in the arylsulfataseA gene (ARSA) gene that results in the accumulation of sulfatides in the central and peripheral nervous system and other areas of the body, including the liver, the gall bladder, kidneys, and/or spleen. Over time, the nervous system is damaged and patients with MLD will experience neurological problems such as motor, behavioral and cognitive regression, severe spasticity and seizures finding it more and more difficult to move, talk, swallow, eat and see. Currently, there are no effective treatments for MLD. In its late infantile form, mortality at 5 years from onset is estimated at 50% and in juvenile patients, mortality at 10 years is 44%. OTL-200 is an *ex vivo*, autologous, hematopoietic stem cell-based gene therapy developed for the treatment of MLD that Orchard acquired from GSK in April 2018. OTL-200 originated from a pioneering collaboration between GSK and the San Raffaele Hospital and the Telethon Foundation, acting through their joint San Raffaele-Telethon Institute for Gene Therapy in Milan, initiated in 2010.

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. Strimvelis, as well as the programs in MLD, WAS and TDBT 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, planned marketing and licensing application submissions and next steps for Orchard's programs, including the therapeutic potential of its product candidates, including OTL-200. 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-200, 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.

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