Orchard Therapeutics Announces Acceptance of Biologics License Application for OTL-200 in MLD and Receives Priority Review

September 18, 2023

PDUFA date set for March 18, 2024

OTL-200 would be the first and only treatment in the U.S. for early-onset MLD

Previously published data demonstrated administration of one-time gene therapy enables sustained preservation of motor function and cognitive development

BOSTON and LONDON, Sept. 18, 2023 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today announced the U.S. Food and Drug Administration (FDA) has accepted the filing of its Biologics License Application (BLA) for OTL-200 in metachromatic leukodystrophy (MLD) under Priority Review. The agency has set a Prescription Drug User Fee Act (PDUFA) goal date of March 18, 2024.

"Today is another significant step forward for patients and families in the U.S. impacted by this devastating and cruel disease who for too long have dealt with the unimaginable burden of going through the diagnostic odyssey, being told there were no treatments beyond supportive care, and then having to watch their child slip away," said Bobby Gaspar, M.D., Ph.D., co-founder and chief executive officer of Orchard Therapeutics. "We look forward to collaborating with the FDA throughout the review and evaluation of our application. Due to the nature of the disease and the urgency to treat children affected by MLD, we are working diligently in parallel to prepare for a potential launch in 2024 and ensure OTL-200 will be available to patients in the U.S. as quickly as possible."

Dr. Gaspar continued, "Reflecting on the tremendous progress we've collectively made in the eight months since our Type B clinical meeting with the FDA, I want to take a moment to express my sincere gratitude to the Orchard team, as well as our clinical collaborators, external partners, and the MLD community, who contributed to the achievement of this milestone. While there is still work to be done, it is because of your efforts that we are making our shared vision of ending the devastation caused by severe genetic diseases a reality for MLD."

OTL-200 previously received both Rare Pediatric Disease (RPD) and Regenerative Medicine Advanced Therapy (RMAT) designations from the FDA and is approved as Libmeldy® (atidarsagene autotemcel) by the European Commission (EC) and UK Medicines and Healthcare products Regulatory Agency (MHRA).

Summary of OTL-200 Clinical Development Program
The BLA for OTL-200 is based on data from 39 pediatric patients with early-onset MLD, enrolled in two prospective non-randomized clinical studies (n=30) or treated under expanded access frameworks (n=9), who were administered OTL-200 and compared with natural history data from 49 untreated patients. All treated patients were administered OTL-200 and subsequently monitored at Ospedale San Raffaele in Milan, Italy. In clinical trials, treatment with OTL-200 resulted in preservation of motor function and cognitive development in most patients compared to disease natural history with up to 12 years of follow-up (median 6.76 years).

With more than a cumulative 250 patient-years of follow-up, treatment with OTL-200 was generally well-tolerated, with no treatment-related serious adverse events or deaths. Most adverse events were associated with busulfan conditioning or background disease.

The full clinical results comprising the BLA dataset were recently presented at the Society for the Study of Inborn Errors of Metabolism (SSIEM) Annual Symposium 2023 in Jerusalem.

About MLD
MLD is a rare and life-threatening inherited disease of the body's metabolic system estimated to occur in approximately one in every 100,000 live births based on existing literature. MLD is caused by a mutation in the *arylsulfatase-A* (*ARSA*) gene that results in the accumulation of sulfatides in the brain and other areas of the body, including the liver, gallbladder, kidneys, and/or spleen. Over time, the nervous system is damaged, leading to neurological problems such as motor, behavioral and cognitive regression, severe spasticity and seizures. Patients with MLD gradually lose the ability to move, talk, swallow, eat and see. In its late infantile form, mortality at five years from onset is estimated at 50 percent and 44 percent at 10 years for juvenile patients.[i]

About Libmeldy / OTL-200
Libmeldy (atidarsagene autotemcel), also known as OTL-200, has been approved by the European Commission for the treatment of metachromatic leukodystrophy (MLD) in patients characterized by biallelic mutations in the ARSA gene leading to a reduction of the ARSA enzymatic activity in children with i) late infantile or early juvenile forms, without clinical manifestations of the disease, or ii) the early juvenile form, with early clinical manifestations of the disease, who still have the ability to walk independently and before the onset of cognitive decline. Libmeldy is the first therapy approved for eligible patients with early-onset MLD.

The most common adverse reaction attributed to treatment with Libmeldy was the occurrence of anti-ARSA antibodies. In addition to the risks associated with the gene therapy, treatment with Libmeldy is preceded by other medical interventions, namely bone marrow harvest or peripheral blood mobilization and apheresis, followed by myeloablative conditioning, which carry their own risks. During the clinical studies of Libmeldy, the safety profiles of these interventions were consistent with their known safety and tolerability.

For more information about Libmeldy, please see the Summary of Product Characteristics (SmPC) available on the EMA website.

Libmeldy is approved in the European Union, UK, Iceland, Liechtenstein and Norway. OTL-200 is an investigational therapy in the U.S.

Libmeldy was developed in partnership with the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) in Milan, Italy.

About Orchard Therapeutics
At Orchard Therapeutics, our vision is to end the devastation caused by genetic and other severe diseases. We aim to do this by discovering, developing and commercializing new treatments that tap into the curative potential of hematopoietic stem cell (HSC) gene therapy. In this approach, a patient's own blood stem cells are genetically modified outside of the body and then reinserted, with the goal of correcting the underlying cause of disease in a single treatment.

In 2018, the company acquired GSK's rare disease gene therapy portfolio, which originated from a pioneering collaboration between GSK and the San Raffaele Telethon Institute for Gene Therapy in Milan, Italy. Today, Orchard is advancing a pipeline spanning pre-clinical, clinical and commercial stage HSC gene therapies designed to address serious diseases where the burden is immense for patients, families and society 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, and follow us on X (Twitter) and LinkedIn.

Availability of Other Information About Orchard
Investors and others should note that Orchard communicates with its investors and the public using the company website (www.orchard-tx.com), the investor relations website (ir.orchard-tx.com), and on social media (Twitter and LinkedIn), including but not limited to investor presentations and investor fact sheets, U.S. Securities and Exchange Commission filings, press releases, public conference calls and webcasts. The information that Orchard posts on these channels and websites could be deemed to be material information. As a result, Orchard encourages investors, the media, and others interested in Orchard to review the information that is posted on these channels, including the investor relations website, on a regular basis. This list of channels may be updated from time to time on Orchard's investor relations website and may include additional social media channels. The contents of Orchard's website or these channels, or any other website that may be accessed from its website or these channels, shall not be deemed incorporated by reference in any filing under the Securities Act of 1933.

Forward-looking Statements
This press release contains forward-looking statements, which are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements. 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, these risks and uncertainties include, without limitation, the risk that prior results, including signals of safety and efficacy, will not be replicated or will not continue in ongoing or future studies and the risk that long-term adverse safety findings may be discovered. 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 most recent annual or quarterly report filed with the U.S. Securities and Exchange Commission (SEC), 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.

[i] *Mahmood et al. Metachromatic Leukodystrophy: A Case of Triplets with the Late Infantile Variant and a Systematic Review of the Literature. Journal of Child Neurology 2010, DOI:* http://doi.org/10.1177/0883073809341669

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