



Orchard Therapeutics Announces FDA Clearance of IND Application for OTL-200 for Metachromatic Leukodystrophy (MLD)

November 19, 2020

BOSTON and LONDON, Nov. 19, 2020 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today announced that the U.S. Food and Drug Administration (FDA) has cleared the company's Investigational New Drug (IND) application for OTL-200, an autologous, hematopoietic stem cell, lentiviral vector-based gene therapy in development for the treatment of metachromatic leukodystrophy (MLD). The company also has applied for Regenerative Medicine Advanced Therapy (RMAT) designation for OTL-200 to help facilitate additional dialogue with the FDA on this important therapy.

"MLD is a devastating and rapidly progressing disease, especially in its most severe form where it causes young children to lose skills they once had, such as the ability to walk, talk and engage with the world around them. Sadly, most of these children will pass away by the age of five, and their families are left with no real options other than palliative care," said Bobby Gaspar, M.D., Ph.D., chief executive officer, Orchard Therapeutics. "We are committed to bringing OTL-200 forward as a potential treatment for children with this fatal neurodegenerative condition. The FDA's allowance of the IND associated with OTL-200 to move forward represents an important milestone on our journey, especially given our recent receipt of a positive CHMP opinion from the European Medicines Agency recommending full marketing authorization for the therapy."

As part of the IND filing, Orchard provided to the FDA data on 39 patients, including 9 patients from the U.S., who have received OTL-200 as part of clinical studies and compassionate use programs conducted at the San Raffaele-Telethon Institute for Gene Therapy in Milan, Italy. The company has post-treatment follow-up data of up to eight years in the earliest treated patients in these programs.

"Based on the extensive clinical data gathered to date, we believe that OTL-200 offers tremendous potential to transform the lives of many young patients with MLD," Gaspar continued. "The IND provides an opportunity for open dialogue with the FDA, allowing us to share the comprehensive data set that we have already collected in the clinical development program and to determine a path to file a Biologics License Application for regulatory approval of OTL-200 in the U.S."

About MLD and OTL-200

Metachromatic leukodystrophy (MLD) is a rare and life-threatening inherited disease of the body's metabolic system occurring in approximately one in every 100,000 live births in the U.S. 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. Currently, there are no approved treatments for MLD. In its late infantile form, mortality at 5 years from onset is estimated at 50% and 44% at 10 years for juvenile patients.¹ OTL-200 (autologous CD34+ cell enriched population that contains hematopoietic stem and progenitor cells (HSPC) transduced *ex vivo* using a lentiviral vector encoding the human *arylsulfatase-A (ARSA)* gene) is an investigational therapy being studied for the treatment of MLD in certain patients. OTL-200 was acquired from GSK in April 2018 and originated from a pioneering collaboration between GSK and the Hospital San Raffaele and Fondazione Telethon, acting through their joint San Raffaele-Telethon Institute for Gene Therapy in Milan, initiated in 2010.

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. In 2018, Orchard 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. Orchard now has one of the deepest and most advanced gene therapy product candidate pipelines in the industry spanning multiple therapeutic areas 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, and follow us on [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 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, Orchard's business strategy and goals, including its plans and expectations for the regulatory approval and commercialization of OTL-200 (known as Libmeldy™ in the European Union (EU)) in the U.S. and EU, and the therapeutic potential of OTL-200, including the potential implications of clinical data for eligible patients. 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 Orchard's marketing authorization application submitted for Libmeldy in the EU may not be approved by the European Commission when expected, or at all; the risk that prior results, such as signals of safety, activity or durability of effect, observed from clinical trials of OTL-200 will not continue or be repeated in Orchard's ongoing or planned clinical trials of OTL-200, will be insufficient to support regulatory submissions or marketing approval in the U.S. and EU or that long-term adverse safety findings may be discovered; the inability or risk of delays in Orchard's ability to commercialize OTL-200, if approved, including the risk that Orchard may not secure adequate pricing or reimbursement to support continued development or commercialization of OTL-200; and the severity of the impact of the COVID-19 pandemic on Orchard's business, including on clinical development of OTL-200 and other product candidates, its supply chain and commercial programs. 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 quarterly report on Form 10-Q for the quarter ended September 30, 2020, as 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.

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¹ 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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Source: Orchard Therapeutics (Europe) Limited