Orchard Therapeutics Announces OTL-200 Granted Regenerative Medicine Advanced Therapy (RMAT) Designation by FDA for the Treatment of Metachromatic Leukodystrophy (MLD)

January 14, 2021

Interactions with FDA anticipated by mid-2021 to determine the BLA filing strategy for OTL-200

BOSTON and LONDON, Jan. 14, 2021 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today announced that the U.S. Food and Drug Administration (FDA) has granted Regenerative Medicine Advanced Therapy (RMAT) designation to OTL-200, an investigational *ex vivo* autologous hematopoietic stem cell (HSC) gene therapy for the treatment of early-onset metachromatic leukodystrophy (MLD). In late 2020, the FDA cleared the company's Investigational New Drug (IND) application for OTL-200, and the therapy also recently was approved in the European Union (EU) under the brand name, Libmeldy™.

"Receipt of RMAT designation for OTL-200 underscores both the severe nature of MLD and the transformative potential of the therapy for young patients suffering from this devastating, fatal neurodegenerative condition," said Bobby Gaspar, M.D., Ph.D., chief executive officer, Orchard Therapeutics. "Alongside our open IND, RMAT designation provides an opportunity for enhanced interactions with the FDA to determine the optimal path to submit a Biologics License Application (BLA) for OTL-200 in the U.S."

Established under the 21st Century Cures Act, the RMAT designation program was created to expedite the development and review of regenerative medicine therapies intended to treat, modify, reverse or cure a serious condition. The FDA granted Orchard RMAT designation for OTL-200 based on data submitted 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 (SR-Tiget) in Milan, Italy. This data set includes post-treatment follow-up data of up to eight years in the earliest treated patients in these programs.

"We look forward to continued engagement with the FDA in the coming months to discuss the comprehensive data set we have already collected in the OTL-200 clinical development program and agree on the potential next steps on the regulatory path to approval for this innovative gene therapy," said Anne Dupraz, chief regulatory officer at Orchard.

About Libmeldy / OTL-200

Libmeldy (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), also known as OTL-200, has been approved by the European Commission for the treatment of MLD in eligible early-onset 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, 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 European Medicines Agency (EMA) website.

Libmeldy is not approved outside of 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

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. Forward-looking statements include express or implied statements relating to, among other things, Orchard's business strategy and goals, the therapeutic potential of Libmeldy (OTL-200), the likelihood that data from clinical trials will support further clinical development and regulatory approval of OTL-200, and the outcome of planned FDA interactions regarding the potential approval pathway for OTL-200. 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, such as signals of safety, activity or durability of effect, observed from clinical trials of Libmeldy will not continue or be repeated in our ongoing or planned clinical trials of OTL-200, will be insufficient to support regulatory submissions or marketing approval in the US or to maintain marketing approval in the EU, or that long-term adverse safety findings may be discovered; the risk that OTL-200 or any one or more of Orchard's product candidates will not be approved, successfully developed or commercialized; the risk of cessation or delay of any of Orchard's ongoing or planned clinical trials; the risk that Orchard may not successfully recruit or enroll a sufficient number of patients for its clinical trials; the delay of any of Orchard's regulatory submissions; the failure to obtain marketing approval from the applicable regulatory authorities for any of Orchard's product candidates or the receipt of restricted marketing approvals; the inability or risk of delays in Orchard's ability to commercialize OTL-200, if approved, or Libmeldy in the EU; the risk that the market opportunity for Libmeldy, or any of Orchard's product candidates, may be lower than estimated; and the severity of the impact of the COVID-19 pandemic on Orchard's business, including on clinical development, 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.

Contacts

Investors
Renee Leck
Director, Investor Relations
+1 862-242-0764
Renee.Leck@orchard-tx.com

Media
Christine Harrison
Vice President, Corporate Affairs
+1 202-415-0137
media@orchard-tx.com