Orchard Therapeutics Announces Regulatory and Clinical Updates for Lead Gene Therapy Programs

June 29, 2021

Expected clinical package for OTL-200 BLA for MLD using data from existing patients clarified with FDA

Guidance obtained on design of OTL-203 global registrational trial for MPS-IH

Enrollment goal met in OTL-201 POC trial for MPS-IIIA

Updates for OTL-103 MAA and BLA submission timelines for WAS

Company to host conference call today at 8:00 a.m. ET

BOSTON and LONDON, June 29, 2021 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today announced several program updates for the company's portfolio of approved and investigational hematopoietic stem cell (HSC) gene therapies. These updates follow recent regulatory interactions for multiple programs within the company's clinical-stage pipeline targeting metachromatic leukodystrophy (MLD), mucopolysaccharidosis type I Hurler syndrome (MPS-IH) and Wiskott-Aldrich syndrome (WAS).

OTL-200 and MLD Updates

U.S. Regulatory Guidance

Orchard recently held a productive meeting with the U.S. Food and Drug Administration (FDA) and has received written feedback concerning the clinical package expected to support a Biologics License Application (BLA) for OTL-200 in MLD. Based on the feedback from this meeting and previous interactions, the company is now preparing for a BLA filing for OTL-200 in pre-symptomatic, early-onset MLD in late 2022 or early 2023, using data from existing patients. This approach and timeline are subject to the successful completion of the remaining regulatory activities in advance of an expected pre-BLA meeting with FDA, including CMC interactions and demonstration of the natural history data as a representative comparator for the treated population.

Newborn Screening

In May 2021, the New York ScreenPlus pilot program, of which Orchard is an official sponsor, started newborn screening (NBS) for MLD. Data collected from this pilot could be used to support a nomination of MLD to the U.S. Recommended Uniform Screening Panel (RUSP), a list of recommended disorders for states to screen as part of their newborn screening programs. These pilot data will also contribute to the body of evidence for MLD universal NBS that will be generated by additional pilots in Germany and Italy.

"We're extremely pleased to have received further input from FDA on a potential path forward for OTL-200 in the pre-symptomatic, early onset MLD population and look forward to working with the agency to continue to advance this program," said Bobby Gaspar, M.D., Ph.D., chief executive officer of Orchard Therapeutics. "This milestone represents an important step forward in our ongoing journey to bring a treatment option to young patients in the U.S. diagnosed with MLD, a devastating and life-limiting neurodegenerative disease. In addition to our U.S. regulatory progress, we are also actively partnering with stakeholders to advance early screening and diagnostic initiatives to benefit patients globally."

Additional Regulatory and Clinical Updates

- OTL-203 for MPS-IH: Orchard recently received feedback on the design of a global registrational trial for OTL-203 following a parallel scientific advice meeting with FDA and the European Medicines Agency (EMA). The interaction offered guidance on the proposed clinical trial protocol from each of the regulatory agencies, including elements of the trial design, comparator arm and recommended endpoints. Orchard will be incorporating this feedback in a revised global clinical study protocol, with study initiation now expected to occur in 2022.
- OTL-201 for MPS-IIIA: The proof-of-concept (POC) trial for OTL-201 has met its recruitment goal with the enrollment of a fifth patient. Interim data from this study is expected to be presented at medical meetings in the second half of 2021 and 2022.
- OTL-103 for WAS: Taking into account remaining work on potency assay development and validation, Orchard is updating its guidance regarding the Marketing Authorization Application (MAA) and BLA submissions for the OTL-103 program in WAS. The company now expects the MAA submission timeline to shift from 2021 to 2022, subject to further dialogue with EMA. Orchard will provide updated guidance regarding the timing of a BLA submission, previously expected in 2022,

following further regulatory interactions with FDA.

“Taken together, these regulatory and clinical updates have helped to refine our product development and timing plans for key programs in our portfolio, shaping an informed execution plan in support of the company’s continued leadership in HSC gene therapy,” continued Gaspar. “As a leader in the gene therapy field with some of the most advanced datasets, we have appreciated the collaborative dialog with both regulatory bodies to support a successful filing and ultimate approval.”

Conference Call Information

Orchard will host a conference call today at 8:00 a.m. ET to discuss recent regulatory and clinical updates for its lead programs. The conference call will be broadcast live in listen-only mode under "News & Events" in the “Investors & Media” section of the company's website at www.orchard-tx.com, and a replay will be archived on the Orchard website following the presentation. To ask a question, please dial (866) 987-6504 (U.S. domestic) or +1 (602) 563-8620 (international) and refer to conference ID 2856986. Please dial in at least 10 minutes in advance to ensure a timely connection to the call.

About Libmeldy / OTL-200

Libmeldy™ (atidarsagene autotemcel), 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 EMA website.

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

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 severe 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 and product development strategy and goals, including its plans and expectations for the commercialization of Libmeldy (OTL-200), the therapeutic potential of Libmeldy (OTL-200) and Orchard’s product candidates, including the product candidates referred to in this release, and Orchard’s expectations with respect to regulatory submissions for these candidates, including OTL-200 and OTL-103, Orchard’s expectations regarding its ongoing preclinical and clinical trials, including the timing of enrollment for clinical trials and release of additional preclinical and clinical data, and the likelihood that data from clinical trials will be positive and support further clinical development and regulatory approval of Orchard's product candidates. 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 the product candidates referred to in this release will not continue or be repeated in our ongoing or planned clinical trials of such products, will be insufficient to support regulatory submissions or support or maintain marketing approval in the US or EU, or that long-term adverse safety findings may be discovered; the risk that any one or more of Orchard’s product candidates, including the product candidates referred to in this release, will not be approved, successfully developed or commercialized; the risk that FDA could ultimately

conclude that Orchard's proposed data package, natural history cohorts and/or other aspects of its planned regulatory submission for Libmeldy (OTL-200) are insufficient to support submission of a BLA, or approval of the BLA, and that the FDA could require that Orchard conduct additional clinical trials prior to any such submission or approval; the risk that the EMA or FDA could ultimately conclude that Orchard's proposed CMC data package, clinical data and/or other aspects of its planned regulatory submissions for OTL-103 are insufficient to support submission of a MAA or BLA, or approval of the MAA or BLA, and that the EMA or FDA could require that Orchard conduct additional clinical trials prior to any such submission or approval; 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 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; 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 its product candidates, if approved, or Libmeldy (OTL-200), including the risk that Orchard may not secure adequate pricing or reimbursement to support continued development or commercialization of Libmeldy (OTL-200); the risk that the market opportunity for Libmeldy (OTL-200), 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 March 31, 2021, 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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