Orchard Therapeutics Announces 2021 Corporate Priorities Supporting the Build-out of its Commercial Business in Hematopoietic Stem Cell (HSC) Gene Therapy and Expansion of its Clinical Applications

January 11, 2021

Preparations on Track for First Half 2021 Commercial Launch of Libmeldy™ (OTL-200), the First Approved Product for Metachromatic Leukodystrophy (MLD) in the EU

Filing Strategy for OTL-200 Biologics License Application (BLA) in MLD in the U.S. to be Communicated by Mid-2021 Following Additional Regulatory Interactions

Marketing Authorization Application (MAA) Filing for OTL-103 in Wiskott-Aldrich Syndrome (WAS) on Track for Year End 2021 in the EU; Followed by BLA Filing in 2022 in the U.S.

New Clinical Data for OTL-203 (for MPS-I) and OTL-201 (for MPS-IIIA) Accepted for Oral Presentation at February 2021 WORLD Symposium; Preclinical Data from Research Programs in Larger Indications Expected in 2021

$192M in Cash and Investments to Support Strategic Execution into the First Half of 2022

BOSTON and LONDON, Jan. 11, 2021 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today outlined the company's 2021 strategic priorities in advance of its attendance at the virtual 39 th Annual J.P. Morgan Healthcare Conference. These priorities support the company's plan of building a successful commercial business in HSC gene therapy and advancing its portfolio of investigational medicines for high-value, high-need indications.

"In a year that challenged how we live and work, I'm extremely proud of Orchard's achievements in 2020," said Bobby Gaspar, M.D., Ph.D., chief executive officer, Orchard Therapeutics. "Our accomplishments were a direct result of the drive and innovation that fuels our commitment to bring our potentially life-saving HSC therapies to patients, including Libmeldy, which is the first product approved for the treatment of eligible patients with early-onset MLD in the EU. With the HSC approach to gene therapy as our scientific foundation, we are focused on the capabilities that can deliver our therapies on a global commercial scale and support our ability to also treat larger indications over time. It has been a privilege to be a pioneer in changing the way medicine is practiced in these conditions, and we look forward to another year of continued execution and scientific progress."

2021 Corporate Priorities
Orchard has outlined the following key corporate objectives and expected milestones for 2021:

1. Build a successful commercial business in HSC gene therapy
   - OTL-200 for MLD:
     - Launch Libmeldy for the treatment of eligible patients with early-onset MLD in the EU in the first half of 2021.
     - By mid-2021, complete interactions with the U.S. Food and Drug Administration (FDA) to determine the path to a BLA filing for OTL-200. The company also expects to receive a decision regarding its regenerative medicine advanced therapy (RMAT) designation application for OTL-200 in the first quarter, which, if granted, has the potential to enhance regulatory interactions and open an expedited path to a BLA filing.
   - OTL-103 for WAS: File an MAA for OTL-103 in the EU by year-end 2021.
2. Continue to lead the development of gene therapies for neurodegenerative disorders by advancing two proof-of-concept (POC) programs in MPS-I and MPS-IIIA
   - OTL-203 for MPS-I: Initiate a registrational trial for OTL-203 by year-end 2021.
   - OTL-201 for MPS-IIIA: Complete enrollment in the five-patient POC trial for OTL-201.
   - POC trial data: Present clinical data from the OTL-203 and OTL-201 POC trials, including two abstracts that have been accepted for oral presentation at the WORLD Symposium in February 2021.
3. Investigate the potential of HSC gene therapy in larger indications
   - Announce new pre-clinical data from research programs in frontotemporal dementia with progranulin mutations (GRN-FTD) and Crohn's disease with mutations in the nucleotide-binding oligomerization domain-containing protein 2 (NOD2-CD) in the second half of 2021.

In preparation for a European launch, Orchard has put in place the commercial infrastructure to support Libmeldy as well as future product launches. The company is qualifying five treatment centers in the UK, Germany, Italy, France and the Netherlands with specialized expertise in transplant and disease area knowledge. In addition, the company expects to leverage cross-border and treatment abroad reimbursement pathways in both Europe and markets such as the Middle East and Turkey. Activities are also underway to drive timely MLD patient identification and access, including disease

awareness, genetic testing and newborn screening studies, which have started or are on track to initiate in five countries in 2021.

The company also provided an update concerning the impact of the COVID-19 pandemic on certain development activities. These include restrictions to laboratory access at Orchard and third-party service providers, which is impacting the timeline to develop a specific functional potency assay for OTL-103 in WAS, as requested by the FDA. As a result, the company now expects to file a BLA for OTL-103 in the U.S. in 2022. Orchard is utilizing the benefits provided under OTL-103's RMAT designation and plans to continue interacting with the FDA in 2021 to confirm the data package for the BLA filing. In addition, with several of the follow-up visits associated with the company's active clinical trials impacted by COVID-19 travel restrictions and other trial site limitations, Orchard is using alternative data collection approaches to capture the necessary data to support future regulatory filings.

Frank Thomas, president and chief operating officer continued, "Starting 2021 with a clear set of strategic priorities is crucial to our ability to effectively manage the business while fueling Orchard's continued growth. Our launch preparations for Libmeldy not only mark our evolution towards a fully integrated company but establish a common manufacturing, commercial and operational infrastructure to support multiple future potential products. This work is complemented by our exciting proof-of-concept and research pipeline that we look forward to advancing internally or in partnership."

Key 2020 Achievements
Orchard's key 2020 achievements are highlighted below.

- **CEO transition and strategy update:** Appointed company founder Bobby Gaspar, M.D., Ph.D., as chief executive officer and implemented a new strategic plan to realize the potential of the HSC gene therapy approach.
- **Libmeldy (OTL-200) EU approval:** Received full marketing authorization from the European Commission (EC) for Libmeldy for eligible patients with early-onset MLD.
- **OTL-200 IND submission**: Received FDA clearance for the Investigational New Drug (IND) application for OTL-200 for the treatment of MLD.
- **OTL-203 in MPS-I:** Presented interim data, including clinical outcomes, from the OTL-203 POC trial.
- **OTL-201 in MPS-IIIA:** Dosed the first three patients in the OTL-201 POC trial.
- **Stable cell line technology:** Secured a license for GlaxoSmithKline's proprietary lentiviral stable cell line technology for use in the OTL-103 program in WAS and OTL-300 program in transfusion-dependent beta thalassemia.
- **New research programs:** Announced new research programs in GRN-FTD, NOD2- CD and amyotrophic lateral sclerosis (ALS) at the company's first R&D investor event.

Cash Guidance
The company ended 2020 with approximately $192 million of cash and investments. The company expects that its cash, cash equivalents and marketable securities as of December 31, 2020 will enable the funding of its currently anticipated operating expenses and capital expenditure requirements into the first half of 2022. This excludes the $50 million expected to be available under the company's credit facility and any non-dilutive capital received from potential future partnerships or priority review vouchers.

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 EMA website.

Libmeldy is not approved outside of 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 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, including its plans and expectations for the commercialization of Libmeldy, the therapeutic potential of Libmeldy (OTL-200) and Orchard's product candidates, including the product candidates referred to in this release, 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, the likelihood that data from clinical trials will be positive and support further clinical development and regulatory approval of Orchard's product candidates, and Orchard's financial condition and cash runway into the first half of 2022. 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 Libmeldy, 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 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 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, including the risk that Orchard may not secure adequate pricing or reimbursement to support continued development or commercialization of Libmeldy; 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.

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