Orchard Therapeutics Announces Recent Commercial and Regulatory Progress for Late-stage HSC Gene Therapy Programs and Outlines Key 2022 Milestones

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Launch Momentum Building for Libmeldy® in Europe with Health Technology Assessments Progressing Favorably and Treatment Underway for Multiple Commercial Patients

Initiating U.S. BLA Submission for OTL-200 as Early as Year End 2022; Constructive CMC Meeting with FDA Supports Timeline

EU MAA Submission for OTL-103 in Wiskott-Aldrich Syndrome Expected in Mid-2022 Following Productive Regulatory Interactions

Ended 2021 with approximately $220M in Cash and Investments to Support Operations into the First Half of 2023

BOSTON and LONDON, Jan. 10, 2022 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today outlined commercial and regulatory updates and key 2022 milestones in advance of its attendance at the virtual 40th Annual J.P. Morgan Healthcare Conference. These activities and priorities support the company's vision to end the devastation caused by genetic and other severe diseases through the curative potential of HSC gene therapy.

"Looking back at 2021 Orchard has accomplished much, from significant progress in the launch of Libmeldy in Europe, to receiving clarity from regulators on the potential path forward for our MLD, WAS and MPS-IH programs, as well as showcasing new discovery projects through our HAE collaboration with Pharming and at our latest R&D Day," said Bobby Gaspar, M.D., Ph.D., chief executive officer. "There is still work to do, and we are starting 2022 with the same passion and commitment to continue building a company focused on changing the treatment paradigm for patients with severe genetic diseases."

Libmeldy Commercial Updates in Europe

As part of Orchard's objective to build a successful and sustainable commercial business in HSC gene therapy, the company is focused on three foundational pillars of the Libmeldy launch: market access, patient identification and treatment delivery.

- Market access: Health technology assessments (HTAs) are progressing well across Europe. The company is pleased that the HTA bodies have recognized both the severity of MLD and the magnitude of potential therapeutic benefit of Libmeldy to treat this condition. For example, in Germany, Libmeldy is one of only five medicines to ever achieve the highest possible therapeutic benefit rating of "major benefit" for pre-symptomatic MLD patients. Orchard anticipates reaching reimbursement agreements with at least two countries in the first half of 2022.
- Patient identification: Patient identification efforts are progressing well, and two patients, one in France and one in Germany, are in the process of being treated commercially with Libmeldy under reimbursed early access. Activities are also underway to drive a timely MLD diagnosis, including five newborn screening studies or pilots that have launched or are planned in Germany, Italy, the UK, Spain and France.
- Treatment delivery: Four centers with specialized expertise in transplant and disease area knowledge in Germany, Italy, France and the Netherlands are treatment-ready and activation of a fifth center in the UK is in progress.

"As leaders in the field of HSC gene therapy, we are pioneering all aspects of our operations—including how we commercialize and deliver these potentially transformative medicines to the communities we serve," said Braden Parker, chief commercial officer. The foundation and experience we are establishing for this launch will serve us well in 2022 and beyond as we expand geographically."

Regulatory Progress and Upcoming Milestones for OTL-200 and OTL-103

OTL-200 for MLD (U.S.)
Orchard has completed the majority of the activities necessary in advance of a pre-Biologics License Application (BLA) meeting with U.S. Food and Drug Administration (FDA) for OTL-200. In November 2021, a Type B CMC meeting took place with the FDA, the feedback from which confirms a planned BLA submission timeline of late 2022 to early 2023.

OTL-103 for WAS (EU and U.S.)
Following productive regulatory interactions with the European Medicines Agency (EMA) and recent rapporteur and co-rapporteur meetings, Orchard

is preparing for a Marketing Authorization Application (MAA) submission for OTL-103 in Europe in mid-2022. In the U.S., Orchard is planning to interact with FDA in early 2022 to discuss elements of a potential BLA filing package, including development work on a functional potency assay and the clinical dataset.

Orchard is utilizing the benefits provided under FDA's regenerative medicine advanced therapy (RMAT) designation for both OTL-103 and OTL-200's regulatory interactions in the U.S.

Additional 2022 Corporate Priorities

To lead the development of gene therapies for neurodegenerative disorders and investigate the potential of HSC gene therapy in future indications where there is a compelling scientific and clinical rationale, Orchard has outlined the remaining key milestones expected for 2022:

- OTL-203 for MPS-IH: Obtain the necessary regulatory clearance in mid-2022 to enable the initiation of the OTL-203 global registrational study in MPS-IH by year end.
- OTL-201 for MPS-IIIA: Present clinical data, including early clinical outcomes of cognitive function, from the OTL-201 proof-of-concept (POC) trial in the first half of 2022.
- Research programs: Advance the company's preclinical portfolio, which includes programs focused on neurodegenerative disorders (OTL-204 for GRN-FTD and OTL-205 for ALS), immunological diseases (OTL-104 for NOD2-CD and OTL-105 for HAE) and HSC-generated antigen-specific Tregs.

Key 2021 Achievements
Orchard's key achievements from 2021 are highlighted below.

- **Libmeldy (MLD) Europe:**
  - Initiated launch activities including market access discussions and qualifying treatment centers.
  - Established partnerships to identify eligible patients for Libmeldy in the Middle East and Turkey.
- **OTL-200 (MLD) U.S:**
  - Received clarity from FDA on the expected clinical and CMC package for a BLA.
  - Manufactured OTL-200 for use under investigator-initiated compassionate use Investigational New Drug (INDs) at the University of Minnesota, the first clinical site to administer OTL-200 outside of Europe. Orchard also coordinated the successful shipment and release of patients' HSCs between the U.S. treatment site and ACG Biologics' manufacturing facility in Italy.
- **OTL-203 (MPS-IH):**
  - Presented one-year POC data, including clinical outcomes of cognitive function, motor function and growth.
  - Obtained guidance on the design of a global registrational trial through a parallel scientific advice meeting with FDA and EMA.
- **OTL-201 (MPS-IIIA):** Completed enrollment of five patients in the POC trial and presented initial study data.
- **Research and discovery:**
  - Signed a strategic collaboration with Pharming Group N.V. to research, develop, manufacture and commercialize OTL-105, an investigational ex vivo autologous HSC gene therapy for the treatment of hereditary angioedema (HAE).
  - Hosted a virtual R&D event highlighting updates from the OTL-104 program for NOD2 Crohn's disease (NOD2-CD) and potential new applications in HSC-generated antigen-specific regulatory T-cells (Tregs) and HSC-vectorization of monoclonal antibodies.
- **Publications:** Supported two New England Journal of Medicine (NEJM) publications, including interim proof-of-concept results for the OTL-203 program in MPS-IH.
- **Cash position:** Raised $150 million in a strategic financing through a private investment in public equity (PIPE) financing.

Cash Guidance
The company ended 2021 with approximately $220 million of cash and investments. The company expects that its cash, cash equivalents and investments as of December 31, 2021 will support its currently anticipated operating and capital expenditure requirements into the first half of 2023. This cash runway excludes an additional $67 million that could become available under the company's credit facility and any non-dilutive capital received from potential future partnerships or priority review vouchers granted by the FDA following future U.S. approvals.

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

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 GlaxoSmithKline (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 has a deep 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 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 2023. 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, 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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