Orchard Therapeutics Highlights Recent Progress Across HSC Gene Therapy Portfolio and Outlines Key 2023 Milestones

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Libmeldy® revenue totaled $5.8M in Q4 2022 and $18.8M for the full year with commercial expansion activities continuing in Europe

Clinical Type B meeting with U.S. FDA to take place in early 2023 prior to OTL-200 (MLD) BLA submission

Ended 2022 with approximately $144M in cash and investments and reduced burn rate to support operations into Q2 2024

OTL-203 (MPS-IH) IND application cleared by U.S. FDA with global registrational trial to initiate in the second half of 2023

Preclinical proof-of-concept data for OTL-104 (NOD2-Crohn's disease) expected in the first half of 2023; initiating IND-enabling activities ahead of 2024 filing

BOSTON and LONDON, Jan. 09, 2023 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today announced recent commercial and regulatory accomplishments and outlined key 2023 milestones, highlighting the strong potential of its hematopoietic stem cell (HSC) gene therapy platform to drive value for patients, providers and shareholders.

As a leader in the development, manufacturing and commercialization of HSC gene therapies, Orchard is well-positioned to leverage its expertise to provide potentially curative treatments to people suffering from a broad range of severe diseases with a single administration. To date, over 170 patients have been treated with Orchard's current and former HSC gene therapy programs across seven different diseases, reflecting the broad clinical applicability of the company's approach.

"Orchard's accomplishments in 2022 showcase the depth and strength of our neurometabolic portfolio," said Bobby Gaspar, M.D., Ph.D., chief executive officer. "We right sized our workforce and narrowed the focus of our HSC gene therapy portfolio to concentrate on severe neurometabolic diseases and research programs where alternative treatment options are limited or do not exist. At the same time, we continued to advance our commercialization and access strategy for Libmeldy. From securing reimbursement and treating the first eligible MLD patients commercially in Europe, to constructive engagement with the FDA to finalize the design of our OTL-203 global registrational trial for MPS-IH and presenting the first neurocognitive results from the OTL-201 program in MPS-IIIA, we are well-positioned to end the devastation caused by genetic and other severe diseases for patients and their families."

Gaspar continued, "Looking ahead to the first half of 2023, we will maintain our disciplined strategy and stewardship of capital as we focus on execution and achieving our regulatory and clinical milestones while remaining open to partnership opportunities that could accelerate growth and value creation. We expect our upcoming clinical Type B meeting for OTL-200 for MLD with the FDA to provide further clarity on our anticipated BLA submission. Given the broad potential for our technology, we have a number of exciting prospects in our pipeline, including larger indications such as the NOD2 form of Crohn's disease, and will advance the development of our portfolio prudently as we progress through anticipated near-term milestones."

Key 2023 Priorities

Orchard has outlined the following key milestones expected for 2023:

- Libmeldy: Secure reimbursement agreements in at least two additional markets in Europe and establish qualified treatment centers in Sweden, Spain and Saudi Arabia. Expand newborn screening activities throughout Europe, the U.S. and the Middle East.
- OTL-200 for metachromatic leukodystrophy (MLD): Conduct a clinical Type B meeting with the U.S. Food and Drug Administration (FDA) in early 2023 in advance of an anticipated BLA submission.
- OTL-203 for mucopolysaccharidosis type I Hurler's (MPS-IH) : Initiate a global, registrational trial in the second half of 2023.
- OTL-201 for mucopolysaccharidosis type IIIA (MPS-IIIA): Report additional biochemical and clinical data from the ongoing proof-of-concept (PoC) study.
- OTL-104 for NOD2-Crohn's disease : Report pre-clinical PoC data in the first half of 2023 and initiate IND-enabling activities in advance of a planned 2024 filing.
- Advance the company's other preclinical programs, which includes a program partnered with and funded by Pharming in hereditary angioedema (HAE), OTL-105.

Preliminary Financial Information (unaudited)

Preliminary estimated revenue from product sales of Libmeldy was $5.8 million for the three months ended December 31, 2022, and $18.8 million for the full year ended December 31, 2022.

The company ended 2022 with approximately $144 million of cash and investments. The burn rate was $2.9 million for the fourth quarter of 2022.

Excluding offsets from one-time receipts of tax credits and real estate escrow funds, the burn rate would have been $23.4 million for the quarter. Moving forward, the company expects its burn rate in 2023 to continue declining as compared to 2022 due to an anticipated increase in revenue from Libmeldy product sales, continued savings realized by the March 2022 corporate restructuring, and ongoing management of operating expenses.

The company expects that its cash, cash equivalents and investments as of December 31, 2022 will support its currently anticipated operating and capital expenditure requirements into the second quarter of 2024.

Key 2022 Accomplishments

Business Operations

- Refined the company's HSC gene therapy portfolio and workforce to focus on severe neurometabolic diseases and pre-clinical research programs.
- Reduced the cash burn rate in each successive quarter of 2022 realizing the financial benefits of the March 2022 corporate restructuring, extending the cash runway into the second quarter of 2024.
- Consolidated the company's UK headquarters to a single office and lab location.

Technical Operations Platform

- Achieved a 100 percent success rate releasing drug product at manufacturing partners, treating over 80 patients cumulatively through the end of 2022 across Orchard's late-stage HSC gene therapy programs in commercial and clinical settings.
- The average time for manufacture and release of Libmeldy commercial product was 44 days.
- Advanced the development of a lentiviral vector, suspension-based manufacturing process to enable the more efficient manufacture and release of drug product for the company's HSC gene therapy programs in larger indications with an expected significantly lower cost per patient.

Libmeldy® (atidarsagene autotemcel)

- Reimbursement: Secured agreements in three major European markets (Germany, Italy and the UK) enabling access and reimbursement for all eligible patients with MLD. In addition, the company secured the renewal of the early access program in France, under which the company receives reimbursement for the treatment of any eligible patient with MLD.
- Commercial treatment: Recognized revenue from commercial treatments from markets with reimbursement agreements, early access mechanisms, treatment abroad programs and European cross-border (S2) pathways.
- Newborn screening (NBS): Initiated over a dozen NBS studies in Europe, the Middle East and the U.S.; six studies have screened approximately 85,000 newborns to date. In the fall of 2022, the ARCHIMEDlife study identified the first confirmed case of a patient with MLD from one such study, supplying critical evidence to advance the potential adoption of NBS in key countries.
- Lancet publication: Announced the publication of long-term clinical outcomes for the treatment of children with early-onset MLD in *The Lancet.* A link to the full release is available here.
- As part of the next phase of commercial expansion in Europe, a marketing authorization application (MAA) was accepted for evaluation by the Swiss Agency for Therapeutic Products (Swissmedic) for the potential treatment of eligible patients with early-onset MLD. A link to the full release is available here.

Regulatory and Clinical Achievements for Investigational Therapies

- OTL-200 for MLD: Engaged in a constructive, ongoing dialogue with the FDA throughout 2022 on the components of a planned BLA submission. Separately, patients in the U.S. were treated on compassionate use basis with EU CDMO manufacturing.
- OTL-203 for MPS-IH: Received clearance from the FDA for the Investigational New Drug (IND) application. A link to the full release is available here.
- OTL-201 for MPS-IIIA: Presented early clinical findings, including the first neurocognitive results, from the ongoing PoC study as part of an oral presentation at the 64th American Society of Hematology Annual Meeting & Exposition. Four out of five patients demonstrated gain of cognitive skills in line with development in healthy children with one patient showing a marked improvement compared to disease natural history. A link to the full release is available here.
- OTL-104 for NOD2-CD: Successfully developed and selected a vector design to advance a development candidate to IND-enabling activities using a suspension-based manufacturing process.

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 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. Such forward-looking statements may be identified by words such as "anticipates," "believes," and "expects," or similar expressions, which 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, the therapeutic potential of Orchard's products and product candidates, including the products and product candidates referred to in this release, Orchard's expectations regarding the timing of regulatory submissions for approval of its product candidates, including the product candidates referred to in this release, the timing of interactions with regulators and regulatory submissions related to ongoing and new clinical trials for its product candidates, including the anticipated timing of a Type B meeting with the FDA regarding OTL-200 and an anticipated BLA submission for OTL-200, the timing of a potential registrational study for OTL-203 for MPS-IH, the timing of announcement of clinical data for its product candidates, the likelihood that such data will be positive and support further clinical development and regulatory approval of these product candidates, the likelihood of approval of such product candidates by the applicable regulatory authorities, and the company's financial condition and cash runway into 2024. 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 will not realize the anticipated benefits of its strategic plan or the expected cash savings from its restructuring; 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 or maintain marketing approval from the applicable regulatory authorities for any of Orchard's product candidates or the receipt of restricted marketing approvals; the risk of delays in Orchard's ability to commercialize its product candidates, if approved; the risk that the ongoing and evolving COVID-19 pandemic, or global macroeconomic and geopolitical developments, could affect the company's business; and the risk that the market opportunity for Libmeldy and its product candidates may be lower than estimated or that Orchard may be unable to identify patients for its products on a consistent basis. Given these uncertainties, the reader is advised not to place any undue reliance on such forward-looking statements.

The estimates of revenue and expenses for the three and twelve months ended December 31, 2022 and of cash and investments as of December 31, 2022 are preliminary in nature and unaudited and do not present all information necessary for an understanding of Orchard's financial condition as of December 31, 2022 and its results of operations for the three or twelve months ended December 31, 2022.

Other risks and uncertainties faced by Orchard include those identified under the heading "Risk Factors" in Orchard's most recent annual or quarterly report 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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