Orchard Therapeutics Highlights 2020 Strategic Priorities

January 13, 2020

Commercial Preparations on Track for Potential 2020 EU Launch of OTL-200 for Metachromatic Leukodystrophy (MLD) with U.S. Regulatory Filing Expected Late 2020 / Early 2021

Initiation of Rolling U.S. Regulatory Filing for OTL-101 (ADA-SCID) Planned for 1H 2020;
U.S. and EU Regulatory Filings of OTL-103 (WAS) Expected in 2021

MPS-I and MPS-IIIA Proof-of-Concept Clinical Trials Ongoing with Additional Data Expected in 2020

New Research and Discovery Initiatives Expand Portfolio's Potential into Larger Neurodegenerative Diseases

$325M in Cash and Investments to Support Execution on Strategic Priorities in 2020 and Beyond

BOSTON and LONDON, Jan. 13, 2020 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today outlined the company's strategic priorities and recent progress in conjunction with its attendance at the 38 th Annual J.P. Morgan Healthcare Conference in San Francisco.

Mark Rothera, Orchard's president and chief executive officer, will present a business overview on Tuesday, January 14, 2020 at 11:30 a.m. PT that will be webcast live at ir.orchard-tx.com. He will summarize the company's strong fundamentals and differentiated approach to gene therapy utilizing gene-corrected hematopoietic stem cells (HSCs), with a special focus on the launch strategy for OTL-200 in metachromatic leukodystrophy (MLD) and newly announced research and discovery initiatives.

"2020 has the potential to be a watershed year for Orchard as we work to bring the benefits of our gene therapy approach and expertise to patients," Rothera said. "We are preparing diligently for the anticipated EU regulatory approval of OTL-200 for MLD while building the commercial team and executing our go-to-market strategy that will help ensure broad patient access. At the same time, we are readying our first regulatory filings in the U.S. and advancing multiple clinical-stage programs through important milestones, while also exploring the potential for gene-corrected HSCs in a broader range of severe disorders, including non-rare indications. With an unrelenting focus on execution, our organization is highly motivated to bring these investigational therapies to patients around the world."

2020 Corporate Priorities
Orchard has outlined the following three high-level corporate goals for 2020:

1. Obtain approval for and launch OTL-200 for the treatment of MLD in Europe and prepare for a biologics license application (BLA) filing in the U.S.;
2. Advance two registrational programs in primary immune deficiencies toward regulatory filings; and
3. Investigate the potential of our *ex vivo* HSC gene therapy platform approach in a broad set of neurodegenerative diseases and other new therapeutic areas, including ongoing proof-of-concept clinical trials in mucopolysaccharidosis type I (MPS-I) and mucopolysaccharidosis type IIIA (MPS-IIIA).

Obtain Approval for and Launch OTL-200 for MLD in Europe
In preparation for a potential European approval in the second half of 2020, Orchard plans to establish the global infrastructure needed to support awareness and adoption of OTL-200. Orchard is putting in place a focused commercial team to serve as the backbone for the potential launch of OTL-200, as well as future product launches. A BLA filing for OTL-200 in the U.S. is planned for late 2020 or early 2021.

- Activities are underway to drive timely patient identification and access, including disease awareness, genetic testing and newborn screening pilots.
- The company continues to qualify treatment centers with specialized expertise in transplant and disease area knowledge across key geographies.
- The commercial supply chain for OTL-200 is being established, with the capacity and logistics to support an anticipated launch.
- The company has received stakeholder input on its value philosophy, as well as a set of guiding principles that will underpin Orchard's pricing and market access strategy.

Advance Two Registrational Programs Toward Upcoming Regulatory Filings
In support of its lead primary immune deficiency programs:

- The company plans to initiate a rolling BLA filing in the U.S. for OTL-101 in adenosine deaminase severe combined immunodeficiency (ADA-SCID) in the first half of 2020 with anticipated completion of the filing within 12 months.
- The company anticipates BLA and MAA regulatory filings for OTL-103 in Wiskott-Aldrich Syndrome (WAS) in the U.S. and EU in 2021.

Investigate the Potential of ex vivo HSC Gene Therapy in Additional Neurodegenerative Diseases and New Therapeutic Areas
Orchard has entered into an agreement with Dr. Alessandra Biffi, a leading expert in gene therapy, chair of the pediatric hematology, oncology and stem cell transplant division at Padua University and co-director of the gene therapy program at Dana Farber/Boston Children's Cancer and Blood Disorders Center, to support the expansion of its portfolio into additional areas of critical need for patients, including new programs for rare and non-rare neurodegenerative diseases. The company has also initiated in-house discovery programs to explore the application of *ex vivo* HSC gene therapy in other therapeutic areas.

Dr. Biffi commented, "Developing gene therapies for diseases with central nervous system involvement, such as neurometabolic and other neurodegenerative diseases, has been a challenge in the field. I am thrilled to partner with Orchard to continue development of this innovative gene therapy technology and, together, look forward to advancing potentially transformative treatments for these devastating diseases."

As part of the agreement, Dr. Biffi will serve as senior scientific advisor of neurometabolic diseases at Orchard. Dr. Biffi's previous role at the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) included the discovery and initiation of the OTL-200 program for MLD and the OTL-203 program for MPS-I.

In addition, Orchard plans to continue to advance the following clinical-stage neurometabolic programs currently underway in MPS-I and MPS-IIIA:

- The OTL-203 proof-of-concept clinical trial in MPS-I, which is being conducted at SR-Tiget, has reached its initial enrollment target of eight study participants. One-year follow-up results for the first eight patients, including the primary endpoints, are anticipated in 2021, with interim data planned for presentations at medical conferences during 2020.
- Enrollment has initiated in a proof-of-concept clinical trial for OTL-201 in MPS-IIIA, conducted by the Royal Manchester Children's Hospital. The trial is expected to enroll up to five patients in 2020 with interim data expected in 2020 and 2021.

Key 2019 Achievements
Orchard achieved each of its 2019 corporate milestones, with key achievements highlighted below.

- **MLD European MAA submission:** The Marketing Authorization Application (MAA) for OTL-200 for MLD was filed and accepted for review by the European Medicines Agency (EMA) in November 2019, ahead of previous guidance.
- **Cryopreserved gene therapy formulations:** Similar engraftment profiles have been observed between the cryopreserved and fresh formulations of OTL-200 for MLD and OTL-101 for ADA-SCID, which represents an important achievement toward the potential approvals of these investigational gene therapies and a key step toward global patient availability.
- **WAS registrational data set:** The registrational trial for OTL-103 for WAS met its key primary and secondary endpoints (n=8 at three years), including the elimination of severe bleeding episodes and a significant reduction in the frequency of severe infections.
- **MPS-I global license:** Orchard signed an exclusive license with Fondazione Telethon and Ospedale San Raffaele in Milan, Italy, for a clinical-stage HSC gene therapy program — OTL-203, a treatment for MPS-I that has shown promising early data in an ongoing proof-of-concept clinical trial.

Cash Guidance
The company ended 2019 with approximately $325 million of cash and investments. The company expects that its cash, cash equivalents and marketable securities as of December 31, 2019 will enable the company to fund its currently anticipated operating expenses and capital expenditure requirements into the second half of 2021, which includes the capital investment required to build-out a new manufacturing facility operated by Orchard in Fremont, CA.

Presentation at 38th Annual J.P. Morgan Healthcare Conference
Orchard will webcast its corporate presentation from the 38th Annual J.P. Morgan Healthcare Conference in San Francisco on Tuesday, January 14, 2020 at 11:30 a.m. PT. A live webcast of the presentation will be available under "News & Events" in the Investors & Media section of the company's website at orchard-tx.com. A replay of the webcast will be archived on the Orchard website following the presentation.

About Orchard
Orchard Therapeutics is a global gene therapy leader dedicated to transforming the lives of people affected by rare diseases through innovative, potentially curative gene therapies. Our *ex vivo* autologous gene therapy approach harnesses the power of genetically-modified blood stem cells and seeks to permanently correct the underlying cause of disease in a single administration. The company has one of the deepest gene therapy pipelines in the industry and is advancing seven clinical-stage programs across multiple therapeutic areas where the disease burden on children, families and caregivers is immense and current treatment options are limited or do not exist, including inherited neurometabolic disorders, primary immune deficiencies and blood disorders.

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.com/orchard_tx and www.linkedin.com/company/10276396), 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," "expects," "plans," "intends," "projects," and "future" or similar expressions that are intended to identify forward-looking statements. Forward-looking statements include express or implied statements relating to, among other things, the company's business strategy and goals, the therapeutic potential of Orchard's product candidates, including the product candidate or candidates referred to in this release, Orchard's expectations regarding the timing of regulatory submissions for approval of its product candidates, including the product candidate or 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, the timing of announcement of clinical data for its product candidates and 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 the second half of 2021. 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, the risks and uncertainties include, without limitation: the risk that any one or more of Orchard's product candidates, including the product candidate or 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 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, the receipt of restricted marketing approvals, and the risk of delays in Orchard's ability to commercialize its product candidates, if approved. 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 annual report on Form 20-F for the year ended December 31, 2018, as filed with the U.S. Securities and Exchange Commission (SEC) on March 22, 2019, 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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