Orchard Therapeutics Reports 2020 Financial Results and Reviews Recent Accomplishments

March 2, 2021

$150M Strategic Financing Supports Execution into the First Half of 2023

OTL-203 Achieves Proof of Concept (POC) in MPS-I Hurler Syndrome (MPS-IH); Registrational Trial Planned to Initiate by Year End 2021

OTL-200 U.S. Filing Strategy for Metachromatic Leukodystrophy (MLD) Expected by Mid-2021

R&D Organizational Leadership Changes Announced

BOSTON and LONDON, March 02, 2021 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today reported financial results for the year ended December 31, 2020, as well as recent accomplishments, 2021 strategic priorities and upcoming milestones, and related organizational leadership updates.

Frank Thomas, president and chief operating officer said, “It is gratifying to witness the positive momentum Orchard has already established in early 2021 driven by solid execution. Our compelling data in neurodegenerative disorders at the WORLD*Symposium* and successful completion of the $150 million financing exemplify this recent progress and showcase a growing appreciation for the potential of HSC gene therapy. We look forward to continuing our work in the year ahead and delivering further benefit for patients and our shareholders."

Recent Accomplishments

February 2021

- Executed a $150 million private investment in public equity (PIPE) financing at a price of $6.22 per share with several existing and new investors with expertise in healthcare, including RA Capital Management, Avidity Partners, Casdin Capital, Farallon Capital, and Surveyor Capital (a Citadel company), among others. The link to the full release is available here.
- Presented data from multiple neurometabolic programs at the 2021 WORLD*Symposium*. The link to the full release is available here.
    - Interim data for OTL-203 showing positive clinical results in multiple disease manifestations of MPS-IH was highlighted. All eight patients treated with OTL-203 showed stable cognitive function, motor function and growth within the normal range at multiple data points post-treatment. Treatment with OTL-203 has been generally well-tolerated with a safety profile consistent with the selected conditioning regimen.
    - An oral presentation featuring supportive biomarker data from the first three patients in the ongoing OTL-201 POC study for mucopolysaccharidosis type IIIA (MPS-IIIA, or Sanfilippo syndrome) was also featured. The treatment has been generally well-tolerated in the first three patients with no treatment-related serious adverse events (SAEs), and all transplant-related SAEs and adverse events have resolved.

January 2021

- Appointed Braden Parker as chief commercial officer. Mr. Parker most recently served as Orchard’s senior vice president and general manager for North America and has more than 20 years of experience in the healthcare industry, including commercial leadership roles at Celgene, NPS Pharma (Shire) and PTC Therapeutics, where he led the company’s U.S. product launch in Duchenne muscular dystrophy and oversaw strategic planning for the gene therapy business.
- Received Regenerative Medicine Advanced Therapy (RMAT) designation for OTL-200 from the U.S. Food and Drug Administration (FDA) for early-onset MLD. This designation has the potential to enhance regulatory interactions in the U.S. and open an expedited path to a biologics license application (BLA) filing.
- Secured partnerships with two leading regional specialty pharmaceutical companies to broaden access to Libmeldy (OTL-200) for eligible patients with MLD in the Middle East & Turkey.

2021 Corporate Priorities and Upcoming Milestones

Orchard previously outlined the following key corporate objectives and upcoming expected milestones:

1. Build a successful commercial business in hematopoietic stem cell (HSC) gene therapy
    - Launch Libmeldy (OTL-200) for the treatment of eligible patients with early-onset MLD in Europe in the first half of 2021
    - Complete additional interactions with the FDA by mid-2021 to determine the path to a BLA filing for OTL-200

- File an Marketing Authorization Application (MAA) for OTL-103 in Wiskott-Aldrich syndrome (WAS) with the European Medicines Agency by year-end 2021; followed by a BLA filing in the U.S. in 2022

2. Continue to lead the development of gene therapies for neurodegenerative disorders by advancing two POC programs in MPS-IH and MPS-IIIA
    - Initiate a registrational trial for OTL-203 for MPS-IH by year-end 2021
    - Complete enrollment in the five-patient POC trial for OTL-201 for MPS-IIIA
    - Present additional clinical data from the OTL-203 and OTL-201 POC trials
3. Investigate the potential of HSC gene therapy in larger indications
    - Announce new preclinical 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

Organizational Leadership Updates

Given the progress on key development programs, Anne Dupraz has been appointed to the expanded role of chief development officer. In addition to overseeing the company's regulatory strategy, Ms. Dupraz will lead product development with the goal of ensuring a seamless approach to moving Orchard's programs through to potential regulatory approval. Ms. Dupraz possesses more than 20 years of experience in the clinical and regulatory fields and has deep expertise in advanced therapies, having been involved in more than 50 different tissue, cell and gene-based therapy development programs in her career.

Ran Zheng, chief technical officer, and Andrea Spezzi, chief medical officer, are stepping down from their respective leadership positions with Orchard to pursue other opportunities. Orchard has initiated a global search for permanent replacements for both of these roles.

Fourth Quarter 2020 Financial Results

Research and development expenses were $22.6 million for the three months ended December 31, 2020, compared to $30.9 million in the same period in 2019. R&D expenses include the costs of clinical trials and preclinical work on the company's portfolio of investigational gene therapies, as well as costs related to regulatory, manufacturing, license fees and milestone payments under the company's agreements with third parties, and personnel costs to support these activities. The company expects R&D expenses to grow slightly in the upcoming periods as the company continues to advance its programs through later stages of development.

Selling, general and administrative expenses were $16.2 million for the three months ended December 31, 2020, compared to $18.5 million in the same period in 2019. The decrease was primarily due to realization of savings associated with an updated strategy and corporate restructuring announced in May 2020.

Net loss attributable to ordinary shareholders was $33.6 million for the three months ended December 31, 2020, compared to $45.4 million in the same period in 2019. The decline in net loss as compared to the prior year was primarily due to savings realized in our operating expenses as a result of the company's updated strategy and corporate restructuring. The company had 98.3 million ordinary shares outstanding as of December 31, 2020.

Thomas continued, "Our burn rate has declined from prior periods as we see the positive impact of our May 2020 corporate restructuring take hold, providing a longer runway and greater financial flexibility, aided by our recent financing. We are investing to support execution for the highest value programs in our portfolio while also dedicating capital to our longer-term strategy to expand into larger indications.

Cash, cash equivalents and investments as of December 31, 2020, were $191.9 million compared to $325.0 million as of December 31, 2019, with the decrease primarily driven by cash used to fund operations in 2020. In the fourth quarter of 2020, the cash used to fund operations was approximately $12.0 million after the receipt of approximately $19.2 million from R&D tax credit refunds related to 2019 qualifying activities under the tax code in the UK. The company expects that its cash, cash equivalents and investments as of December 31, 2020, along with gross proceeds of $150.0 million from the February 2021 private placement, will support its currently anticipated operating expenses and capital expenditure requirements into the first half of 2023. This cash runway excludes the $50 million 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 potential U.S. approvals.

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 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, 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.

Consolidated Statements of Operations Data
(In thousands, except share and per share data)
(Unaudited)

	Three months ended December 31,	
	2020	**2019**
Product sales, net	$ —	$ 595
Costs and operating expenses:		
Cost of product sales	—	191
Research and development	22,648	30,899
Selling, general and administrative	16,226	18,531
Total costs and operating expenses	38,874	49,621
Loss from operations	(38,874)	(49,026)
Other income (expense):		
Interest income	279	1,843

Interest expense	(575)	(633)
Other income, net	5,635	2,533
Total other income, net	5,339	3,743
Net loss before income tax	(33,535)	(45,283)
Income tax expense	(85)	(133)
Net loss attributable to ordinary shareholders	$ (33,620)	$ (45,416)

Consolidated Balance Sheet Data
(in thousands)
(Unaudited)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 55,135	$ 19,053
Marketable securities	136,813	305,937
Trade receivables	878	1,442
Prepaid expenses and other current assets	13,365	8,530
Research and development tax credit receivable, current	17,344	14,934
Total current assets	223,535	349,896
Non-current assets:		
Operating lease right-of-use assets	29,815	19,415
Property and equipment, net	4,781	7,596
Research and development tax credit receivable	—	13,710
Other long-term assets	22,806	8,664
Total non-current assets	57,402	49,385
Total assets	$ 280,937	$ 399,281
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	$ 8,823	$ 11,984
Accrued expenses and other current liabilities	28,943	37,980
Operating lease liabilities	8,934	5,892
Notes payable, current	4,861	—
Total current liabilities	51,561	55,856
Notes payable, long-term	20,204	24,699
Operating lease liabilities, non-current	24,168	15,320
Other long-term liabilities	6,570	4,213
Total liabilities	102,503	100,088
Shareholders’ equity:	178,434	299,193
Total liabilities and shareholders’ equity	$ 280,937	$ 399,281

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