Orchard Therapeutics Provides Business Update and Reports 2022 Financial Results

March 6, 2023

OTL-200 pre-BLA meeting granted for second quarter of 2023 following productive clinical Type B meeting with the U.S. Food and Drug Administration (FDA)

Strategic financing from leading healthcare investors provides up to $188 million of additional capital upon achievement of key milestones

$18.8M of Libmeldy revenue in 2022 with growth expected in 2023 from ongoing commercial expansion activities in Europe

Newborn screening studies have confirmed three cases of metachromatic leukodystrophy (MLD) with 96,000 babies screened globally to date

Company to webcast conference call today at 8:00 a.m. ET

BOSTON and LONDON, March 06, 2023 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today announced business updates along with its financial results for the quarter and year ended December 31, 2022. The company will host a live webcast at 8:00 a.m. ET that will be available under “News & Events” in the Investors & Media section of the company's website at www.orchard-tx.com. Analysts wishing to participate in the question and answer session should use this link. A replay of the webcast will be archived on the Orchard website following the presentation.

“We are already building tremendous momentum in 2023 across all aspects of our portfolio and business operations,” said Bobby Gaspar, M.D., Ph.D., chief executive officer. “We look forward to the scheduled pre-BLA meeting for OTL-200 with the U.S. FDA to align on the path towards a potential regulatory submission in MLD. Moreover, the strategic financing we announced earlier today provides the capital and resources necessary to progress Libmeldy (OTL-200) while continuing to maximize the opportunities for our HSC gene therapy platform, including our next-in-line MPS programs, and our research in larger indications where current treatment options are limited or do not exist.”

Frank Thomas, president and chief operating officer, added, “Our strategy and portfolio have attracted new capital from a strategic group of investors who recognize the potential of our HSC gene therapy platform. Today, we entered into an innovative financing arrangement that provides, with its initial closing, capital to fund the potential regulatory submission and launch of OTL-200 in the U.S. In addition, the deal structure could enable additional capital priced at increasing premiums to today’s share price upon the achievement of upcoming regulatory milestones. In total, the transaction brings in up to $188 million of new capital that would offset financing needs for the foreseeable future, especially as we expect to grow our revenues to a level that could sustain our business.”

U.S. Regulatory Update

- *OTL-200 for MLD:* In early-2023, the company held a productive Type B meeting with the U.S. FDA which provided clarity on the clinical package for a potential biologics license application (BLA) submission for OTL-200, approved as Libmeldy® (atidarsagene autotemcel) by the European Commission (EC) and Medicines and Healthcare products Regulatory Agency (MHRA) for the treatment of early-onset MLD.

  Based on the outcome of the Type B meeting, Orchard Therapeutics subsequently requested a pre-BLA meeting which has been scheduled for the second quarter of 2023. Pending the outcome of the multidisciplinary pre-BLA meeting, the company now anticipates a potential BLA submission in mid-2023.

Libmeldy Commercial Activities in Europe

- *Newborn Screening:* Three genetically confirmed cases of MLD have been identified following the screening of approximately 96,000 newborns globally to date. One of these cases has been assessed clinically and referred for treatment with Libmeldy with the other two more recently identified patients pending clinical assessment. The identification of treatment-eligible patients from newborn screening (NBS) pilots provides the prospective evidence to help determine the true incidence of MLD and supplies critical data necessary for the adoption of national NBS in key countries. In total, six studies actively screening newborns have initiated in Europe, the Middle East and the United States.

- *Geographic Expansion:* In February 2023, Orchard Therapeutics reached an agreement with the New Therapies (NT) Council which will result in reimbursed access to Libmeldy for all MLD patients who fall within the scope of the European marketing authorization in Sweden. Libmeldy received the strongest possible recommendation for use by the NT Council following the successful completion of a health economic evaluation by FINOSE, a health technology assessment consortium between Finland, Norway and Sweden. Additional reimbursement discussions are ongoing in several other countries or regions across Europe including Spain, France, and the Beneluxa region, among others, to secure reimbursed access for eligible MLD patients.

Recent Clinical and Research Milestones

- Fifteen presentations from across the company's neurometabolic portfolio were featured at the 19th Annual WORLD*Symposium* ™ which took place February 22-26, 2023, in Orlando, Florida. Data highlights included results from an updated integrated analysis of 39 patients with early-onset MLD treated with investigational OTL-200 in the clinical development program with more than 10 years of follow up in the earliest treated patients (median 6.15 years). The composite primary endpoint of severe motor impairment-free survival used in the analysis was developed through ongoing discussions with the U.S. FDA and has been agreed to as clinically meaningful.

  In addition to the updated integrated analysis, there were multiple presentations highlighting various newborn screening efforts to support the timely and accurate diagnosis of MLD, and several investigator-initiated presentations detailing results of patients from Europe, the U.S. and South America who were treated with OTL-200 on a compassionate use basis with drug product supplied from a European commercial manufacturer, demonstrating the potential for global supply from a centralized current good manufacturing practice (cGMP) manufacturing site.

Other Business Updates

- In February 2023, the company announced plans to change the ratio of its American Depositary Shares (ADSs) to its ordinary shares from the current ADS ratio of one ADS to one ordinary share to a new ADS ratio of one ADS to ten ordinary shares. The company anticipates that the ADS ratio change will be effective on or about March 10, 2023. For the company's ADS holders, the change in the ADS ratio will have the same effect as a one-for-ten reverse ADS split and is intended to enable the company to regain compliance with the Nasdaq minimum bid price requirement.

Updated Anticipated 2023 Milestones

Orchard Therapeutics has outlined the following key milestones expected for 2023:

- *Libmeldy:* Secure reimbursement agreements in at least one additional market 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 MLD:* Conduct pre-BLA meeting with FDA in the second quarter in advance of an anticipated BLA submission in mid-year.
- *OTL-203 for mucopolysaccharidosis type I Hurler's (MPS-IH) :* Initiate a global, registrational trial in the second half following clearance of an investigational new drug (IND) application by FDA in late 2022.
- *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 preclinical PoC data in the first half and initiate IND-enabling activities in advance of a planned IND filing in 2024.
- Advance the company's other preclinical programs, which includes a program partnered with and funded by Pharming Group N.V. in hereditary angioedema (HAE), OTL-105.

Fourth Quarter 2022 Financial Results

Revenue from 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. Total revenue for the fourth quarter of 2022 was $7.0 million compared to $0.5 million in the same period in 2021. The cost of product sales, which includes the cost of manufacturing, royalties to third parties and non-cash amortization, was $2.4 million during the fourth quarter of 2022.

Research and development expenses were $25.5 million for the three months ended December 31, 2022, compared to $23.3 million in the same period in 2021, an increase of 9%. 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.

Selling, general and administrative expenses were $10.6 million for the three months ended December 31, 2022, compared to $13.6 million in the same period in 2021, a decrease of 22%. The decline resulted primarily from the realization of savings and associated reduction in G&A expenditures from the restructuring announced in March 2022.

Loss from operations was $31.6 million in the three months ended December 31, 2022, compared to a loss from operations of $36.4 million in the corresponding period of 2021, a decrease of 13%. The reduction resulted from both increased revenue from sales of Libmeldy as well as reduced operating expenses following the March 2022 corporate restructuring.

During the three months ended December 31, 2022, the U.S. dollar weakened against the British pound and Euro, resulting in $22.7 million of unrealized gains on certain intercompany balances denominated in currencies other than the U.S. dollar. Most of the company's cash balance has been and continues to be held in U.S. dollars.

Net loss was $7.9 million for the three months ended December 31, 2022, compared to $36.3 million in the same period in 2021. The company had approximately 126.9 million ordinary shares outstanding as of December 31, 2022.

Cash, cash equivalents and investments as of December 31, 2022, were $143.8 million, with $32.4 million of debt outstanding, compared to $220.1

million and $32.9 million of debt outstanding as of December 31, 2021. These cash figures do not include any of the proceeds anticipated to be raised through today's announced financing. The cash burn rate was $2.9 million for the three months ended December 31, 2022. Excluding offsets from one-time receipts of tax credits and real estate escrow funds, the cash burn rate would have been $23.4 million for the quarter.

Outlook for 2023

Moving forward, the company expects its cash burn rate in 2023 to continue declining as compared to 2022 due to an anticipated increase in revenue from Libmeldy product sales and ongoing management of operating expenses. The company expects R&D expenses to decrease in 2023 as compared to 2022 following the completion of pre-BLA regulatory activities for OTL-200. In addition, the company expects SG&A expenses to decrease slightly in 2023 as compared to 2022 with incremental investments in the commercialization of Libmeldy to be offset by further reductions in G&A expenses.

With the $34 million of up-front proceeds from today's financing, the company expects that its existing cash, cash equivalents and investments will fund its anticipated operating, debt service and capital expenditure requirements into 2025, with the potential for additional runway extension upon subsequent closings from today's financing.

Use of Non-GAAP Financial Measures
Orchard has presented certain non-GAAP financial measures, including its cash burn rate. Management believes this non-GAAP information is useful for investors, taken in conjunction with Orchard's GAAP financial statements, because it provides greater transparency regarding Orchard's operating performance. Management uses these measures, among others, to assess and analyze operational results and trends and to make financial and operational decisions. Non-GAAP information is not prepared under a comprehensive set of accounting rules and should only be used to supplement your understanding of Orchard's operating results as reported under GAAP, not as a substitute for GAAP information. In addition, these non-GAAP financial measures are unlikely to be comparable with non-GAAP information provided by other companies.

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 of Libmeldy, 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 European Medicines Agency (EMA) website.

Libmeldy is approved in the European Union, UK, Iceland, Liechtenstein and Norway. OTL-200 is an investigational therapy in the U.S.

Libmeldy was developed in partnership with the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) in Milan, Italy.

About Orchard Therapeutics
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 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 is advancing a pipeline spanning preclinical, 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's 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 (SEC) 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 forward-looking statements, which are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements. Such forward-looking statements may also be identified by words such as "anticipates," "potential," "expects" or similar expressions. Forward-looking statements include express or implied statements relating to, among other things: Orchard's expectations with respect to the financing arrangement's size, terms and effect on its business; the therapeutic potential of Orchard's products and product candidates; Orchard's expectations regarding the timing of regulatory submissions for approval of its product candidates, including the timing of BLA submission for OTL-200, the timing of interactions with regulators, the timing of the expected registrational study for OTL-203 for MPS-IH; the timing of announcement of preclinical and clinical data for

Orchard's product candidates, and the likelihood that such data will be positive and support further clinical development and regulatory approval of Orchard's product candidates; the likelihood of approval of Orchard's product candidates by the applicable regulatory authorities; the ability of Orchard to meet its anticipated 2023 milestones, including securing reimbursed access to Libmeldy, expanding newborn screen activities, initiating OTL-203 registrational trial and reporting preclinical and clinical data for OTL-104 and OTL-201, respectively; Orchard's expectations with respect to the timing and effect of the ADS ratio change and with respect to the continued listing on Nasdaq of its ADSs; Orchard's estimates and expectations with respect to its financial performance, including revenue, expenses, trend of cash-burn rates and cash-runway; and Orchard's business and product development strategy and goals, commercial plans and expansion expectations. 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 products will not be successfully commercialized, the risk that Orchard will not maintain marketing approval, and the risk that long-term adverse safety findings may be discovered. 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 most recent annual or quarterly report filed with the 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.

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

	Three Months Ended December 31,	
	2022	**2021**
Revenue:		
Libmeldy product sales	$ 5,811	$ —
Strimvelis product sales	582	—
Collaboration revenue	593	483
Total revenue	6,986	483
Costs and operating expenses:		
Cost of product sales	2,433	—
Research and development	25,545	23,346
Selling, general and administrative	10,600	13,552
Total costs and operating expenses	38,578	36,898
Loss from operations	(31,592)	(36,415)
Other income (expense):		
Interest income	857	63
Interest expense	(933)	(683)
Other income (expense), net	22,656	811
Total other income (expense), net	22,580	191
Loss before income taxes	(9,012)	(36,224)
Income tax benefit (expense)	1,129	(125)
Net loss	$ (7,883)	$ (36,349)
Net loss per share, basic and diluted	$ (0.06)	$ (0.29)
Weighted average number of shares outstanding, basic and diluted	128,211,374	127,519,427

Condensed Consolidated Balance Sheet Data
(In thousands)
(Unaudited)

	December 31, 2022	**December 31, 2021**
Assets		
Current assets:		
Cash and cash equivalents	$ 68,424	$ 55,912
Marketable securities	75,326	164,195
Accounts receivable	8,467	1,480
Prepaid expenses and other current assets	9,986	23,011
Research and development tax credit receivable	5,942	30,723
Total current assets	168,145	275,321
Operating lease right-of-use-assets	22,774	24,316
Property and equipment, net	8,138	4,767
Restricted cash	4,215	4,266
Intangible assets, net	3,560	4,149

Other assets	12,075	9,590
Total assets	$ 218,907	$ 322,409
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 9,318	$ 10,008
Accrued expenses and other current liabilities	34,437	24,318
Deferred revenue, current	959	346
Operating lease liabilities	6,424	7,335
Notes payable, current	9,429	786
Total current liabilities	60,567	42,793
Notes payable, long-term	22,991	32,086
Deferred revenue, net of current portion	10,315	12,519
Operating lease liabilities, net of current portion	19,246	19,278
Other long-term liabilities	7,524	5,783
Total liabilities	120,643	112,459
Total shareholders' equity	98,264	209,950
Total liabilities and shareholders' equity	$ 218,907	$ 322,409

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