Orchard Therapeutics Reports First Quarter 2023 Financial Results and Announces Initiation of Rolling Submission for Biologics License Application of OTL-200 for Metachromatic Leukodystrophy to U.S. FDA

May 15, 2023

OTL-200 Biologics License Application (BLA) submission completion anticipated in mid-2023

Libmeldy revenue and commercial patients treated expected to grow year-over-year in 2023

New clinical data in MPS-I and MPS-IIIA and pre-clinical data in genetic subsets of frontotemporal dementia and Crohn's to be presented this week at ASGCT

Closed initial $34M of potential $188M in proceeds as part of strategic financing and ended Q1 2023 with $146M of cash and investments and runway into 2025

BOSTON and LONDON, May 15, 2023 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today announced various business accomplishments along with its financial results for the quarter ended March 31, 2023.

"Following multiple productive interactions this year with the FDA on our clinical and CMC packages, I am delighted to announce the initiation of our OTL-200 rolling BLA submission with the filing of the first module," said Bobby Gaspar, M.D., Ph.D., chief executive officer. "Alongside a successful Libmeldy launch in Europe, where we continue to see steady progress on MLD patient identification, referral and reimbursement, our robust HSC gene therapy pipeline continues to make significant advancements, as demonstrated by our presence at this week's ASGCT meeting. Multiple oral presentations feature our clinical work in rare neurodegenerative disorders such as MPS-IH and MPS-IIIA, and we are excited to highlight our first presentations supporting pre-clinical efficacy in the progranulin form of frontotemporal dementia and pre-clinical proof-of-concept in NOD2-Crohn's disease. Together, our commercial, clinical and pre-clinical programs provide many opportunities for value creation as we build a sustainable gene therapy business."

Regulatory Progress for OTL-200

- *OTL-200 for MLD:* The company held a productive pre-BLA meeting with the U.S. Food and Drug Administration (FDA) which led to the initiation of a rolling BLA for OTL-200 for the treatment of early-onset metachromatic leukodystrophy (MLD). OTL-200 is approved as Libmeldy® (atidarsagene autotemcel) by the European Commission (EC) and Medicines and Healthcare products Regulatory Agency (MHRA). Orchard expects to complete the OTL-200 rolling submission in mid-2023 and has requested priority review, which if granted would put the company on track for a potential U.S. approval in the first half of 2024.

Libmeldy Commercialization and Newborn Screening

- The company has secured reimbursement agreements for Libmeldy in three new markets so far in 2023. Most recently, both the Finnish National Health Insurance System and Icelandic Health Insurance have accepted the price negotiated for Libmeldy by FINOSE, a health technology assessment consortium in the Nordic region. Eligible MLD patients in Finland and Iceland will be referred to the company's treatment center in Sweden (where an agreement was signed earlier this year) once fully qualified.
- Four patients have either received treatment or are currently undergoing treatment with Libmeldy so far in 2023, including the first patient identified via an MLD newborn screening study. Additional patients have been identified, referred, and are also expected to be treated in the second half of the year.
- The company is pleased to continue supporting research in newborn screening for MLD with eight prospective studies actively screening to date. Additionally, Orchard is a founding member of BeginNGS at Rady Children's Institute for Genomic Medicine, San Diego, where cutting-edge genomic technology will be used to continue to advance the science of newborn screening.

Chief commercial officer Braden Parker added, "We have been successful in driving reimbursed access to Libmeldy on multiple fronts, including via cross border pathways in countries before a formal reimbursement agreement has been signed, and are pleased with the pace of our expansion in the Nordic region. Based on the number of patients currently in the referral and treatment process, we are on track to meet our goal of year-over-year revenue growth in 2023 with reimbursement levels per patient in the range of those seen in 2022."

Upcoming Data Presentations

- Six presentations from across the company's HSC gene therapy portfolio will be featured at the American Society of Gene and Cell Therapy (ASGCT) Annual Meeting taking place May 16-20, 2023, in Los Angeles, California. Featured

presentations include:

- New and updated data on skeletal outcomes from the proof-of-concept (PoC) study (n=8) of OTL-203 in the Hurler subtype of mucopolysaccharidosis type I (MPS-IH) where follow-up of the earliest treated patients now exceeds four years.
- New and updated biochemical and early neurocognitive results from the ongoing PoC study (n=5) of OTL-201 in mucopolysaccharidosis type IIIA (MPS-IIIA), also known as Sanfilippo syndrome type A where follow-up of the earliest treated patients now exceeds 2.5 years.
- The first data supporting pre-clinical efficacy from the OTL-204 research program addressing the progranulin form of frontotemporal dementia (GRN-FTD).
- Two posters demonstrating the therapeutic potential of HSC gene therapy to address a refractory form of Crohn's disease (NOD2-CD) and chronic autoimmune disorders.

March 2023 Financing

In March 2023, the company entered into an innovative financing arrangement with RA Capital and other investors that could bring in up to $188 million at increasing valuations following the achievement of U.S. regulatory milestones for OTL-200 for MLD. The company expects the proceeds from the financing to offset capital needs for the foreseeable future, taking into account expected revenue growth from Libmeldy and approval of OTL-200 in the U.S. The initial closing in March 2023 provided $34 million in new capital and the investors have committed to invest an additional $34 million in the second quarter of 2023, subject to receipt of shareholder approval and minutes from the company's recent pre-BLA meeting.

Remaining 2023 Expected Milestones

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

- *Libmeldy:* Establish qualified treatment centers in Sweden, Spain and Saudi Arabia. Expand newborn screening activities throughout Europe, the U.S. and the Middle East. Beyond the agreements in the Nordic region, additional discussions to secure reimbursed access for eligible MLD patients are ongoing in several other countries across Europe.
- *OTL-200 for MLD:* Complete a rolling BLA submission mid-year in advance of a potential U.S. approval in the first half of 2024.
- *OTL-203 for MPS-IH:* Initiate a global, multi-center registrational trial in the second half of 2023.
- *OTL-201 for MPS-IIIA:* Report new biochemical and clinical data from the ongoing proof-of-concept (PoC) study at the upcoming ASGCT annual meeting.
- *OTL-104 for NOD2-Crohn's disease :* Report pre-clinical PoC data at the upcoming ASGCT annual meeting and initiate IND / CTA-enabling activities.
- Advance the company's other pre-clinical programs, which includes the OTL-204 program in the progranulin form of FTD and the OTL-105 program partnered with and funded by Pharming Group N.V. in hereditary angioedema (HAE).

First Quarter 2023 Financial Results

Revenue from Libmeldy was $0.5 million for the three months ended March 31, 2023 compared to $5.1 million in the same period in 2022. The revenue recognized in the period was lower than that of prior periods due to unique characteristics of our confidential reimbursement agreements which vary by country. The cost of product sales, which includes the cost of manufacturing, royalties to third parties and non-cash amortization, was $0.4 million during the first quarter of 2023 compared to $1.6 million in the same period as 2022.

Research and development expenses were $16.0 million for the three months ended March 31, 2023, compared to $28.2 million in the same period in 2022, a decrease of 43%. The decline resulted from the company taking proactive steps to prioritize its portfolio in 2022 and realign its R&D organization with a more focused strategy. R&D expenses include the costs of clinical trials and pre-clinical 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 $11.1 million for the three months ended March 31, 2023, compared to $13.3 million in the same period in 2022, a decrease of 16%. The decline resulted primarily from the realization of savings in G&A expenditures from the restructuring announced in March 2022.

Loss from operations was $26.3 million in the three months ended March 31, 2023, compared to a loss from operations of $37.6 million in the corresponding period of 2022, a decrease of 30%. The reduction resulted primarily from lower operating expenses following the March 2022 corporate restructuring.

Total other income (expense) was $8.8 million for the three months ended March 31, 2023. The U.S. dollar weakened against the British pound and Euro, resulting in $5.6 million of realized and 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. In addition, the company incurred a $3.9 million gain relating to the fair value remeasurements of the value of warrants and other liabilities that were issued in connection with the strategic financing in March 2023. These warrants and liabilities will continue to be remeasured in future periods resulting in non-cash gains or losses based on a number of valuation assumptions on the underlying financial instruments.

Net loss was $17.4 million for the three months ended March 31, 2023, compared to $44.3 million in the same period in 2022, a reduction of 61%. The company had approximately 184.3 million ordinary shares, equivalent to 18.4 million American Depositary Shares, outstanding as of March 31, 2023.

The company expects its cash used to fund operations in 2023 to decline as compared to 2022 due to an anticipated increase in revenue from Libmeldy product sales, realization of savings from the March 2022 restructuring, and ongoing management of operating expenses.

Cash, cash equivalents and investments as of March 31, 2023, were $146.3 million, with $30.1 million of debt outstanding, compared to $143.8 million and $32.4 million of debt outstanding as of December 31, 2022. 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 the March 2023 financing.

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 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'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 March 2023 financing, including the amount and timing of future proceeds and the 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 timeline for completion of the company's rolling 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 pre-clinical 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 including OTL-200; the ability of Orchard to meet its anticipated 2023 milestones, as further described in this release; 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 Orchard does not receive the shareholder votes necessary to close the second tranche of the March 2023 financing on the timeline we expect to or at all; the risk that the minutes from Orchard's recent pre-BLA meeting expressly advise the Company not to proceed with a BLA submission, which would prevent or delay the closing of the second tranche of the financing the risk that the investors in the March 2023 do not exercise their warrants; the risk that Orchard will need to undertake additional work before completing its BLA submission for OTL-200; the risk that Orchard's BLA submission for OTL-200 is not accepted on the timeline that we expect or at all; the risk that our revenues will be less than we anticipate, which could happen if Orchard treats fewer patients with Libmeldy than we currently anticipate; the risk that our future expenses are greater than we currently anticipate; the risk that Orchard is unable to set up additional qualified treatment centers and newborn screening or is delayed in doing so; 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 March 31,	
	2023	**2022**
Revenue:		
Libmeldy product sales	$ 534	$ 5,059
Collaboration revenue	703	465
Total revenue	1,237	5,524
Costs and operating expenses:		
Cost of product sales	367	1,571
Research and development	15,993	28,234
Selling, general and administrative	11,135	13,299
Total costs and operating expenses	27,495	43,104
Loss from operations	(26,258)	(37,580)
Other income (expense):		
Interest income	1,029	69
Interest expense	(957)	(675)
Changes in fair value of warrants and unit liabilities	3,852	—
Other income (expense), net	4,910	(6,052)
Total other income (expense), net	8,834	(6,658)
Loss before income taxes	(17,424)	(44,238)
Income tax benefit (expense)	12	(58)
Net loss	$ (17,412)	$ (44,296)
Net loss per share, basic and diluted	$ (0.12)	$ (0.35)
Weighted average number of shares outstanding, basic and diluted	141,809,004	127,694,785

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

	March 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 61,487	$ 68,424
Marketable securities	84,828	75,326
Accounts receivable	—	8,467
Prepaid expenses and other current assets	13,810	9,986
Research and development tax credit receivable	6,075	5,942
Total current assets	166,200	168,145
Operating lease right-of-use-assets	21,904	22,774
Property and equipment, net	8,149	8,138
Research and development tax credit receivable, non-current	769	—
Restricted cash	4,215	4,215
Intangible assets, net	3,518	3,560
Other assets	12,262	9,590
Total assets	$ 217,017	$ 218,907
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 8,772	$ 9,318
Accrued expenses and other current liabilities	27,984	34,437
Deferred revenue, current	634	959
Operating lease liabilities	6,467	6,424

Notes payable, current	9,429	9,429
Total current liabilities	53,286	60,567
Notes payable, long-term	20,717	22,991
Deferred revenue, net of current portion	10,779	10,315
Operating lease liabilities, net of current portion	16,657	19,246
Warrant and unit liabilities from financing	6,186	—
Other long-term liabilities	7,737	7,524
Total liabilities	115,362	120,643
Total shareholders' equity	101,655	98,264
Total liabilities and shareholders' equity	$ 217,017	$ 218,907

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