Orchard Therapeutics Reports First Quarter 2021 Financial Results and Provides Recent Business Updates

May 13, 2021

Commercial Activities Advancing for Upcoming Launch of Libmeldy™ (atidarsagene autotemcel) for Eligible Patients with Early-onset MLD in Germany

Update on OTL-200 U.S. BLA Filing Strategy for MLD on Track for Mid-2021 Following Type B RMAT Meeting with FDA

Recent Publications, Including ADA-SCID Dataset in NEJM and Multiple Oral Presentations at ASGCT, Highlight Broad and Innovative Potential of HSC Gene Therapy

Cash and Investments of Approximately $300M Provide Runway into First Half 2023 Following $150M Financing in February 2021

BOSTON and LONDON, May 13, 2021 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today reported financial results for the quarter ended March 31, 2021, as well as recent business updates and upcoming milestones.

"With Libmeldy, we are on the brink of bringing an important therapy to eligible MLD patients in Germany and look forward to continuing our work to expand commercial availability across Europe while advancing our regulatory discussions in the U.S.," said Bobby Gaspar, M.D., Ph.D., chief executive officer of Orchard. "As a company, we are committed to applying our HSC gene therapy approach to develop therapies for a whole series of severe, often fatal genetic conditions, and consider Libmeldy to be representative of the transformative potential we envision for future gene therapies in our portfolio."

Business Highlights

Libmeldy for metachromatic leukodystrophy (MLD):

- Orchard is providing an update on the following key launch activities for Libmeldy in Germany:
  - An AMNOG dossier has been submitted to the Federal Joint Committee (G-BA: Gemeinsamer Bundeausschuss) to commence the pricing and reimbursement process
  - The University of Tübingen has been selected as the first treatment center and is in the final stage of qualification and treatment readiness
  - Commercial supply, including vector inventory and drug product capacity, has been established through manufacturing partner, AGC Biologics.
  - Orchard has provided sponsorship for a local newborn screening pilot to drive patient identification and disease awareness.
- Similar launch readiness activities are underway in other major European countries including the UK, France, Italy and the Netherlands. The company's partnerships with GenPharm and Gen Ilac in the Middle East and Turkey, respectively, are intended to extend the reach of European qualified treatment centers.
- Consistent with previous guidance, the company is on track to provide a regulatory update on OTL-200 for MLD in the U.S. by mid-year following the receipt of minutes from a planned Type B regenerative medicine advanced therapy (RMAT) meeting with the U.S. Food and Drug Administration (FDA). The purpose of the meeting is to seek input on the path to a submission of a Biologics License Application (BLA) for OTL-200 for the treatment of early-onset MLD.

Recent and Upcoming Data Publications

- Data evaluating the safety and efficacy of Orchard's investigational hematopoietic stem cell (HSC) gene therapy for adenosine deaminase severe combined immunodeficiency (ADA-SCID) was published in the New England Journal of Medicine (NEJM). Results from 50 patients showed 100% overall survival and ≥95% event-free survival (defined as survival in the absence of enzyme replacement therapy reinstitution or rescue allogeneic hematopoietic stem cell transplant) at two and three years of follow up. The link to the full release is available here.
- Seven presentations from Orchard's HSC gene therapy portfolio, including six oral presentations, were featured at the

American Society for Gene and Cell Therapy (ASGCT) 2021 Annual Meeting.
    - The abstracts are available on the ASGCT website and include preliminary results from Orchard's discovery labs in transduction enhancers (TEs) showing improvements in HSC gene therapy manufacturing efficiency. Orchard has developed a novel TE, J-Boost™, and identified and validated several novel transduction protocols using J-Boost in combination with Protamine Sulphate, that increased vector copy number (VCN) by ~9x and transduction efficiency by ~4x. These improvements enable a potential 50-70% reduction in vector usage compatible with several HSC programs across neurometabolic, primary immune deficiency and blood disorders.
- An OTL-203 abstract has been selected as one of the six best submissions to the European Hematology Association (EHA) 2021 Annual Meeting and will be presented as an oral presentation during the Presidential Symposia on June 11, 2021. The abstract is available on the EHA website.

2021 Corporate Priorities and Upcoming Milestones

Orchard continues to expect to achieve the following key corporate objectives and upcoming milestones:

1. Build a successful commercial business in HSC gene therapy

- Launch Libmeldy (OTL-200) for the treatment of eligible patients with early-onset MLD in Europe in 2021
- Complete additional interactions with the FDA by mid-2021 to determine the path to a U.S. BLA filing for OTL-200 in MLD
- File a Marketing Authorization Application (MAA) for OTL-103 in Wiskott-Aldrich syndrome (WAS) with the European Medicines Agency (EMA) by year-end 2021; followed by a BLA filing in the U.S. in 2022

2. Continue to lead the development of investigational gene therapies for neurodegenerative disorders by advancing two proof-of-concept (POC) programs in mucopolysaccharidosis type I hurler syndrome (MPS-IH) and MPS-IIIA (mucopolysaccharidosis type IIIA or Sanfilippo syndrome type A)

- Initiate a registrational trial for OTL-203 for MPS-IH by year-end 2021 following discussion and feedback on study design from FDA and EMA utilizing parallel scientific advice
- 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

First Quarter 2021 Financial Results

Research and development expenses were $21.0 million for the first quarter of 2021, compared to $24.8 million in the same period in 2020. 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 development milestone payments under the company's agreements with third parties, and personnel costs to support these activities.

Selling, general and administrative expenses were $14.1 million for the first quarter of 2021, compared to $20.1 million in the same period in 2020. The decrease was primarily due to realization of savings associated with an updated strategy and corporate restructuring announced in May 2020.

Net loss was $35.2 million for the first quarter of 2021, compared to $50.6 million in the same period in 2020. 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 approximately 123.8 million ordinary shares outstanding as of March 31, 2021.

Cash, cash equivalents and investments as of March 31, 2021, were $298.4 million compared to $191.9 million as of December 31, 2020, with the increase primarily driven by net proceeds of $143.7 million from the February 2021 private placement, offset by cash used for operating activities and capital expenditures. The company expects that its cash, cash equivalents and investments as of March 31, 2021 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 (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 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 severe 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 March 31, 2021, 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.

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

	Three Months Ended March 31,	
	2021	**2020**
Product sales, net	$ —	$ —
Costs and operating expenses:		
Research and development	21,035	24,836
Selling, general and administrative	14,051	20,145
Total costs and operating expenses	35,086	44,981
Loss from operations	(35,086)	(44,981)
Other income (expense):		

Interest income	171	1,480
Interest expense	(538)	(613)
Other income (expense), net	1,358	(6,790)
Total other income (expense), net	991	(5,923)
Net loss before income tax	(34,095)	(50,904)
Income tax (expense) benefit	(1,087)	335
Net loss	(35,182)	(50,569)
Net loss per share, basic and diluted	$ (0.31)	$ (0.51)
Weighted average shares outstanding, basic and diluted	114,829,272	98,713,126

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

	March 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 78,883	$ 55,135
Marketable securities	219,543	136,813
Trade receivables	—	878
Prepaid expenses and other current assets	12,504	13,365
Research and development tax credit receivable	17,493	17,344
Total current assets	328,423	223,535
Non-current assets:		
Operating lease right-of-use-assets	28,700	29,815
Property and equipment, net	4,591	4,781
Research and development tax credit receivable	3,552	—
Other assets	23,847	22,806
Total assets	$ 389,113	$ 280,937
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	$ 7,905	$ 8,823
Accrued expenses and other current liabilities	25,672	28,943
Operating lease liabilities	7,964	8,934
Notes payable, current	6,944	4,861
Total current liabilities	48,485	51,561
Notes payable, long-term	18,208	20,204
Operating lease liabilities	20,847	24,168
Other long-term liabilities	5,993	6,570
Total liabilities	93,533	102,503
Shareholders' equity	295,580	178,434
Total liabilities and shareholders' equity	$ 389,113	$ 280,937

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