Orchard Therapeutics Reports Third Quarter 2021 Financial Results and Highlights Recent Business Updates

November 4, 2021

Updates from OTL-201 Clinical Proof-of-Concept Study in MPS-IIIA and OTL-204 Preclinical Study for GRN-FTD at ESGCT Showcase Potential for HSC Gene Therapy in Multiple Neurodegenerative Disorders

Launch Activities for Libmeldy® Across Key European Countries, including Reimbursement Discussions, Progressing in Anticipation of Treating Commercial Patients

Frank Thomas, President and Chief Operating Officer, to Step Down Following Transition in 2022; Search for a Chief Financial Officer Initiated

Cash and Investments of Approximately $254M Provide Runway into First Half 2023

BOSTON and LONDON, Nov. 04, 2021 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today reported financial results for the quarter ended September 30, 2021, as well as recent business updates and upcoming milestones.

“This quarter, we are pleased by the progress demonstrated by our investigational neurometabolic HSC gene therapy programs with promising preclinical and clinical updates at ESGCT,” said Bobby Gaspar, M.D., Ph.D., chief executive officer of Orchard. “With follow-up in OTL-201 for MPS-IIIA patients now ranging between 6 and 12 months, biomarker data remain highly encouraging, showing supraphysiological enzyme activity and corresponding substrate reductions in the CSF and urine. The launch strategy for Libmeldy is also advancing in Europe with momentum building on reimbursement discussions and patient finding activities.”

Recent Presentations and Business Updates

Data presentations at ESGCT

Clinical and pre-clinical data from across the company’s investigational hematopoietic stem cell (HSC) gene therapy portfolio were featured in two oral and seven poster presentations at the European Society of Gene & Cell Therapy Congress (ESGCT) on October 19-22. Highlights from key presentations are summarized below:

- OTL-201 for Mucopolysaccharidosis type IIIA (MPS-IIIA): A poster presentation featured supportive biomarker data from the first four patients with evaluable results, with duration of follow-up ranging from 6 to 12 months. The treatment has been generally well-tolerated in all enrolled patients (n=5) with no treatment-related serious adverse events (SAEs).
    - Supraphysiological *N-sulphoglucosamine sulphohydrolase (*SGSH) enzyme activity above the normal range was seen in leukocytes and plasma within one to three months in all evaluable patients (n=4).
    - A greater than 90% reduction in urinary glycosaminoglycans (GAGs) was seen within three months in all evaluable patients (n=4).
    - SGSH activity in the cerebrospinal fluid (CSF) increased from undetectable at baseline to within or above the normal range by six months in all patients with available data (n=3).
    - CSF GAGs decreased from baseline in patients with available data (n=3).
- OTL-204 for Progranulin-mutated Frontotemporal Dementia (GRN-FTD):
    - Preliminary *in vivo* data from the preclinical proof-of-concept study showed that murine *GRN-/-* HSPCs, transduced with an LV expressing progranulin under the control of a novel promoter, are able to engraft and repopulate the brain myeloid compartment of FTD mice and to locally deliver the GRN enzyme.

R&D Investor Event Summary

In September, Orchard hosted an R&D investor event highlighting its discovery and research engine in HSC gene therapy, including an update on the OTL-104 program in development for NOD2 Crohn’s disease (NOD2-CD) and potential new applications in HSC-generated antigen-specific regulatory T-cells (Tregs) and HSC-vectorization of monoclonal antibodies (mAbs).

The discussion also covered the differentiated profile of Orchard’s HSC gene therapy approach, which has exhibited favorable safety, long-term durability and broad treatment applicability.

- In particular, Orchard’s lentiviral vector-based HSC gene therapy programs have shown no indication of insertional oncogenesis and no evidence of clonal dominance due to integration into oncogenes. Importantly, the promoters and regulatory elements of Orchard vectors are derived from human (not viral) sequences and are specifically designed to have limited enhancer activity on neighboring genes thereby mitigating the potential for safety concerns.
- In addition, because of the fundamental biological differences between the HSC and adeno-associated virus (AAV) gene therapy approaches, Orchard’s programs have not, to date, seen the safety and durability concerns experienced by the

AAV gene therapy field.

Libmeldy (atidarsagene autotemcel) launch in Europe

Orchard is providing an update on the following key launch activities for Libmeldy in Europe:

- Discussions with health authorities and payors are underway across Europe in key markets including Germany, the UK, France and Italy.
- Qualification of treatment centers is progressing with The University of Tübingen in Germany ready to treat commercial patients and other centers in the final stages of qualification and treatment readiness.
- Disease awareness and patient identification activities continue and have supported patient referrals in major European centers. Orchard's partnerships in the Middle East and Turkey allow for opportunities to treat eligible patients from these territories at qualified European centers.
- Orchard is providing sponsorship for an ongoing newborn screening pilot in Germany and is working with laboratories to implement pilots in Italy, the UK, France and Spain.

Executive organizational update

The company also announced that Frank Thomas will step down from his role as president and chief operating officer, following a transition in 2022. A search for a chief financial officer is underway. Mr. Thomas' other responsibilities will be assumed by existing members of the leadership team in commercial and corporate affairs. Orchard recently strengthened the executive team with the appointments of Nicoletta Loggia as chief technical officer and Fulvio Mavilio as chief scientific officer and the promotion of Leslie Meltzer to chief medical officer.

"I want to extend my gratitude to Frank Thomas for his immense contributions to Orchard," said Gaspar. "During his tenure, Frank oversaw the transition of the organization to a publicly traded company and has managed operations with a focus on cross-company innovation, including his role as a key architect in creating and executing the focused business plan we rolled out in 2020. Along with the entire board of directors and leadership team, I appreciate Frank's commitment to facilitate a smooth transition during this time."

Gaspar continued, "Our search is focused on a CFO to lead the broad strategic planning efforts necessary to capitalize on the full potential of our hematopoietic stem cell gene therapy platform.
We have a strong team in place to aid Orchard's success in this next phase of growth and are well capitalized through the anticipated completion of several value-creating milestones."

Upcoming Milestones

In June 2021, Orchard announced several portfolio updates following recent regulatory interactions for the company's investigational programs in metachromatic leukodystrophy (MLD), Mucopolysaccharidosis type I Hurler syndrome (MPS-IH) and Wiskott-Aldrich syndrome (WAS).

- OTL-200 for MLD in the U.S: Based on feedback received from the U.S. Food and Drug Administration (FDA), the company is preparing for a Biologics License Application (BLA) filing for OTL-200 in pre-symptomatic, early-onset MLD in late 2022 or early 2023, using data from existing OTL-200 patients. This approach and timeline are subject to the successful completion of activities remaining in advance of an expected pre-BLA meeting with FDA, including future CMC regulatory interactions and demonstration of the natural history data as a representative comparator for the treated population.
- OTL-203 for MPS-IH: Orchard is incorporating feedback from FDA and the European Medicines Agency (EMA) into a revised global registrational study protocol, with study initiation expected to occur in 2022.
- OTL-201 for MPS-IIIA: Additional interim data from this proof-of-concept study are expected to be presented at medical meetings in 2022, including early clinical outcomes of cognitive function.
- OTL-103 for WAS: The company expects a MAA submission with EMA for OTL-103 in WAS in 2022, subject to the completion of work remaining on potency assay validation and further dialogue with EMA. The company will provide updated guidance for a BLA submission in the U.S. following additional FDA regulatory interactions.

Third Quarter 2021 Financial Results

Revenue from product sales of Strimvelis were $0.7 million for the third quarter of 2021 compared to $2.0 million in the same period in 2020, and cost of product sales were $0.2 million for the third quarter of 2021 compared to $0.7 million in the same period in 2020. Collaboration revenue was $0.5 million for the third quarter of 2021, resulting from the collaboration with Pharming Group N.V. entered into in July 2021. This revenue represents expected reimbursements for preclinical studies and a portion of the $17.5 million upfront consideration received by Orchard under the collaboration, which will be amortized over the expected duration of the agreement.

Research and development (R&D) expenses were $20.8 million for the third quarter of 2021, compared to $14.7 million in the same period in 2020. The increase was primarily due to higher manufacturing and process development costs for the company's neurometabolic programs and lower R&D tax credits as compared to 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 (SG&A) expenses were $13.0 million for the third quarter of 2021, compared to $13.0 million in the same period in 2020. SG&A expenses are expected to increase in future periods as the company builds out its commercial infrastructure globally to support additional product launches following regulatory approvals.

Net loss was $36.4 million for the third quarter of 2021, compared to $20.3 million in the same period in 2020. The increase in net loss as compared to the prior year was primarily due to higher R&D expenses as well as the impact of foreign currency transaction gains and losses. The company had approximately 125.5 million ordinary shares outstanding as of September 30, 2021.

Cash, cash equivalents and investments as of September 30, 2021, were $254.1 million compared to $191.9 million as of December 31, 2020. The increase was primarily driven by net proceeds of $143.6 million from the February 2021 private placement and $17.5 million in upfront payments from the July 2021 collaboration with Pharming Group N.V., offset by cash used for operating activities and capital expenditures. The company expects that its cash, cash equivalents and investments as of September 30, 2021 will support its currently anticipated operating expenses and capital expenditure requirements into the first half of 2023. This cash runway excludes an additional $67 million that could become 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 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 approved in 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

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 has a deep 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 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, 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 September 30,		Nine months ended September 30,	
	2021	2020	2021	2020
Product sales, net	$ 700	$ 1,998	$ 700	$ 2,595
Collaboration revenue	492	—	492	—
Total revenues	1,192	1,998	1,192	2,595
Costs and operating expenses:				
Cost of product sales	226	667	226	858
Research and development	20,846	14,678	63,631	71,082
Selling, general and administrative	13,039	12,956	41,353	48,760
Total costs and operating expenses	34,111	28,301	105,210	120,700
Loss from operations	(32,919)	(26,303)	(104,018)	(118,105)
Other income (expense):				
Interest income	65	534	349	2,906
Interest expense	(683)	(572)	(1,814)	(1,753)
Other income (expense), net	(4,041)	5,510	(2,049)	(2,223)
Total other income (expense), net	(4,659)	5,472	(3,514)	(1,070)
Net loss before income tax	(37,578)	(20,831)	(107,532)	(119,175)
Income tax (expense) benefit	1,133	541	(704)	816
Net loss	(36,445)	(20,290)	(108,236)	(118,359)
Net loss per share, basic and diluted	$ (0.29)	$ (0.20)	$ (0.88)	$ (1.19)
Weighted average number of ordinary shares outstanding, basic and diluted	127,376,562	99,664,616	122,765,516	99,255,370

Condensed Consolidated Balance Sheet Data

(in thousands)

(Unaudited)

	September 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 74,324	$ 55,135
Marketable securities	179,819	136,813
Trade receivables	1,073	878
Prepaid expenses and other current assets	17,962	13,365
Research and development tax credit receivable, current	18,284	17,344
Total current assets	291,462	223,535
Non-current assets:		
Operating lease right-of-use assets	26,267	29,815
Property and equipment, net	4,756	4,781
Research and development tax credit receivable	11,942	—

Intangible assets, net	4,740	3,076
Other long-term assets	16,490	19,730
Total non-current assets	64,195	57,402
Total assets	$ 355,657	$ 280,937
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	$ 6,096	$ 8,823
Accrued expenses and other current liabilities	28,500	28,943
Deferred revenue	1,392	—
Operating lease liabilities	8,257	8,934
Notes payable, current	—	4,861
Total current liabilities	44,245	51,561
Notes payable, long-term	32,786	20,204
Deferred revenue, net of current portion	11,502	
Operating lease liabilities, non-current	19,800	24,168
Other long-term liabilities	6,026	6,570
Total liabilities	114,359	102,503
Shareholders’ equity:	241,298	178,434
Total liabilities and shareholders’ equity	$ 355,657	$ 280,937

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