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

August 4, 2021

Regulatory feedback obtained on OTL-200 (MLD) and OTL-203 (MPS-IH) programs

New HAE collaboration with Pharming Group highlights broad potential for HSC gene therapy

Multiple presentations from neurometabolic programs at MPS Symposia including additional follow-up in MPS-IH

Cash and Investments of Approximately $270M Provide Runway into First Half 2023

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

“This past quarter Orchard has shown great progress against multiple core strategic objectives across the portfolio,” said Bobby Gaspar, M.D., Ph.D., chief executive officer of Orchard. “Obtaining regulatory clarity from the FDA on our investigational OTL-200 program in early-onset MLD represents a tremendous step toward making a treatment option available for young patients in the U.S. A second neurodegenerative program in MPS-IH is also advancing toward a pivotal trial, incorporating recent feedback from both the U.S. and EU regulatory agencies. In our earlier stage pipeline, we’re very excited for our new collaboration with Pharming exploring the potential of HSC gene therapy in hereditary angioedema.”

Summary of Recent Publication and Business Updates

Data presentations at MPS 2021

Presentations from investigational hematopoietic stem cell (HSC) gene therapy programs in mucopolysaccharidosis type I Hurler syndrome (MPS-IH) and mucopolysaccharidosis type IIIB (MPS-IIIB) were featured at the 16th International Symposium on MPS and Related Diseases on July 23-25, 2021.

- OTL-203 for MPS-IH: Updated data for OTL-203 showing positive clinical results in multiple disease manifestations of MPS-IH were highlighted in an oral presentation. With follow-up in five of eight patients now out to two years, all patients treated with OTL-203 continue to show stable cognitive and motor function and growth within the normal range throughout the follow-up period. Treatment with OTL-203 has been generally well-tolerated with a safety profile consistent with the selected conditioning regimen.
- OTL-202 for MPS-IIIB: Long-term results following HSC gene therapy in a mouse model of MPS-IIIB were also presented. Significant α-N-acetylglucosaminidase (NAGLU) enzyme expression was seen in the bone marrow, blood plasma and other somatic tissues following gene therapy. Importantly, at six months post-treatment, sufficient expression of NAGLU enzyme was observed in the brain of mice treated with gene therapy, which led to a normalization of heparin sulfate levels and neurological corrections, which was not observed in mice treated with hematopoietic stem-cell transplantation (HSCT).

Collaboration with Pharming Group for hereditary angioedema (HAE)

On July 1, 2021 Orchard Therapeutics and Pharming Group N.V. announced a strategic collaboration to research, develop, manufacture and commercialize OTL-105, a newly disclosed investigational *ex vivo* autologous HSC gene therapy for the treatment of HAE. OTL-105 is designed to increase C1 esterase inhibitor (C1-INH) in HAE patient serum to prevent hereditary angioedema attacks. In preclinical studies, to date, OTL-105 demonstrated high levels of SERPING1 gene expression via lentiviral-mediated transduction in multiple cell lines and primary human CD34+ HSCs. A link to the full announcement can be found here.

- Under the terms of the collaboration, Pharming has been granted worldwide rights to OTL-105 and will be responsible for clinical development, regulatory filings, and commercialization of the investigational gene therapy, including associated costs. Orchard will lead the completion of IND-enabling activities and oversee manufacturing of OTL-105 during pre-clinical and clinical development, which will be funded by Pharming. Orchard received an upfront payment of $17.5 million in the form of cash and an equity investment and is also eligible to receive up to $189.5 million in development, regulatory and sales milestones as well as mid-single to low double-digit royalty payments on future worldwide sales.

Clinical and Regulatory Updates

In June 2021, Orchard announced several portfolio updates following recent regulatory interactions for the company’s investigational programs in metachromatic leukodystrophy (MLD), MPS-IH and Wiskott-Aldrich syndrome (WAS). A link to the full announcement can be found here.

- OTL-200 for MLD: Orchard held a productive meeting with the U.S. Food and Drug Administration (FDA) and has received written feedback concerning the clinical package expected to support a Biologics License Application (BLA) for OTL-200 in

MLD. Based on the feedback from this meeting and previous interactions, the company is preparing for a BLA filing for OTL-200 in pre-symptomatic, early-onset MLD in late 2022 or early 2023, using data from existing patients. This approach and timeline are subject to the successful completion of the remaining regulatory activities in advance of an expected pre-BLA meeting with FDA, including CMC interactions and demonstration of the natural history data as a representative comparator for the treated population.

- OTL-203 for MPS-IH: Orchard received feedback on the design of a global registrational trial for OTL-203 following a parallel scientific advice meeting with FDA and the European Medicines Agency (EMA). The interaction offered guidance on the proposed clinical trial protocol from each of the regulatory agencies, including elements of the trial design, comparator arm and recommended endpoints. Orchard will be incorporating this feedback into a revised global clinical study protocol, with study initiation expected to occur in 2022.
- OTL-201 for MPS-IIIA: The proof-of-concept trial for OTL-201 has met its recruitment goal with the enrollment of a fifth patient. Interim data from this study is expected to be presented at medical meetings in the second half of 2021 and 2022.
- OTL-103 for WAS: Orchard updated its guidance regarding the Marketing Authorization Application (MAA) and BLA submissions for the OTL-103 program in WAS to take into account work remaining on potency assay development and validation. The company now expects a MAA submission in 2022, subject to further dialogue with EMA, and will provide updated guidance for a BLA submission following additional FDA regulatory interactions.

Research Programs

Orchard plans to 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.

Second Quarter 2021 Financial Results

Research and development expenses were $21.8 million for the second quarter of 2021, compared to $31.6 million in the same period in 2020. The decline is primarily due to non-cash impairment charges of $5.7 million taken in the second quarter of 2020 and other savings associated with our corporate restructuring. 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 $14.3 million for the second quarter of 2021, compared to $15.7 million in the same period in 2020. The decrease was primarily due to savings associated with personnel and related changes.

Net loss was $36.6 million for the second quarter of 2021, compared to $47.5 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 May 2020 updated strategy and corporate restructuring. The company had approximately 124 million ordinary shares outstanding as of June 30, 2021.

Cash, cash equivalents and investments as of June 30, 2021, were $269.3 million compared to $191.9 million as of December 31, 2020 and excludes the $17.5 million in upfront payments from the collaboration with Pharming Group N.V. entered into on July 1, 2021. The increase was primarily driven by net proceeds of $143.6 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 June 30, 2021 will support its currently anticipated operating expenses and capital expenditure requirements into the first half of 2023. This cash runway excludes the 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

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 June 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 June 30,		Six months ended June 30,	
	2021	2020	2021	2020
Product sales, net	$ —	$ 597	$ —	$ 597
Costs and operating expenses:				
Cost of product sales	—	191	—	191
Research and development	21,750	31,568	42,785	56,404
Selling, general and administrative	14,263	15,659	28,314	35,804
Total costs and operating expenses	36,013	47,418	71,099	92,399
Loss from operations	(36,013)	(46,821)	(71,099)	(91,802)
Other income (expense):				
Interest income	113	892	284	2,372
Interest expense	(593)	(568)	(1,131)	(1,181)
Other income (expense), net	634	(943)	1,992	(7,733)
Total other income (expense), net	154	(619)	1,145	(6,542)
Net loss before income tax	(35,859)	(47,440)	(69,954)	(98,344)
Income tax (expense) benefit	(750)	(60)	(1,837)	275

Net loss	(36,609)	(47,500)	(71,791)	(98,069)
Net loss per share, basic and diluted	$ (0.29)	$ (0.48)	$ (0.60)	$ (0.99)
Weighted average number of ordinary shares outstanding, basic and diluted	125,952,834	99,251,314	120,421,781	99,048,498

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

	June 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 99,929	$ 55,135
Marketable securities	169,385	136,813
Trade receivables	—	878
Prepaid expenses and other current assets	17,286	13,365
Research and development tax credit receivable	17,589	17,344
Total current assets	304,189	223,535
Non-current assets:		
Operating lease right-of-use-assets	27,874	29,815
Property and equipment, net	4,588	4,781
Research and development tax credit receivable	7,782	—
Other long-term assets	20,325	22,806
Total non-current assets	60,569	57,402
Total assets	$ 364,758	$ 280,937
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	$ 6,520	$ 8,823
Accrued expenses and other current liabilities	26,186	28,943
Operating lease liabilities	8,245	8,934
Notes payable, current	-	4,861
Total current liabilities	40,951	51,561
Notes payable, long-term	32,699	20,204
Operating lease liabilities	20,581	24,168
Other long-term liabilities	6,153	6,570
Total liabilities	100,384	102,503
Shareholders' equity	264,374	178,434
Total liabilities and shareholders' equity	$ 364,758	$ 280,937

Contacts

Investors
Renee Leck
Director, Investor Relations
+1 862-242-0764
Renee.Leck@orchard-tx.com

Media
Benjamin Navon
Director, Corporate Communications
+1 857-248-9454
Benjamin.Navon@orchard-tx.com