Orchard Therapeutics Announces Expansion of Neurometabolic Disease Portfolio and Reports First Quarter 2019 Financial Results

May 28, 2019

New Collaboration with Fondazione Telethon and Ospedale San Raffaele for Clinical Program in Mucopolysaccharidosis Type I (MPS-I) Using Ex Vivo Autologous Hematopoietic Stem Cell Gene Therapy

Anticipated Marketing Authorization Application (MAA) Submission for the Treatment of Metachromatic Leukodystrophy (MLD) Brought Forward to the First Half of 2020

Clinical Trial in Sanfilippo Syndrome Type A (MPS-IIIA) Now Expected to Start Later This Year

Ended the First Quarter of 2019 with Approximately $300M in Total Cash and Investments; Newly Secured $75 Million Credit Facility Extends Runway into 2021

Conference Call Scheduled for Today at 8:00 a.m. ET

BOSTON and LONDON, May 28, 2019 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a leading commercial-stage biopharmaceutical company dedicated to transforming the lives of patients with serious and life-threatening rare diseases through innovative gene therapies, today announced financial results for the quarter ended March 31, 2019 and provided several program updates related to its neurometabolic disease portfolio. Orchard has brought forward the timeline for key clinical and regulatory milestones for two of its neurometabolic disease programs and, as announced in a separate release this morning, has secured an exclusive worldwide license for a clinical-stage *ex vivo* autologous hematopoietic stem cell (HSC) gene therapy program in Mucopolysaccharidosis Type I (MPS-I).

"The progress we've made advancing *ex vivo* autologous hematopoietic stem cell-based gene therapies aimed at correcting neurometabolic diseases furthers our confidence in the potential of our technology to treat additional serious, often fatal, rare diseases that to date have been difficult or impossible to treat," said Mark Rothera, president and chief executive officer of Orchard. "With today's announcements, including the addition of the MPS-I program, our gene therapy portfolio now includes nine programs from late pre-clinical to commercial stage, with the goal of having three more approved therapies available to transform the lives of children affected by some of these serious rare diseases in the next three years."

Summary of Neurometabolic Franchise Updates

- **Mucopolysaccharidosis Type I (MPS-I):** Orchard has been granted an exclusive worldwide license from Fondazione Telethon and Ospedale San Raffaele to research, develop, manufacture and commercialize an *ex vivo* autologous HSC gene therapy program for the treatment of MPS-I, which will be referred to as OTL-203. The program has currently shown encouraging preliminary data with signs of metabolic correction in patients with the most severe subtype of MPS-I, known as Hurler syndrome, in the ongoing proof-of-concept clinical trial being conducted at San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) in Milan, Italy. As of the data presented at the American Society of Gene & Cell Therapy (ASGCT) annual meeting in April 2019, four patients have been enrolled in the trial with follow-up of up to nine months. The trial is expected to enroll up to eight patients by the first half of 2020. The terms of the license include an upfront cash payment, success-based milestones and royalties on net sales.
- **Metachromatic Leukodystrophy (MLD):** Orchard held a positive Marketing Authorization Application (MAA) pre-submission meeting with the European Medicines Agency (EMA) in early May. The company has brought forward the timeline for the planned submission of an MAA to the EMA for OTL-200 to the first half of 2020 and also expects to file a Biologics License Application (BLA) in the U.S. approximately one year after the MAA submission.
- **Sanfilippo Syndrome Type A (MPS-IIIA):** Last week, the Manchester University NHS Foundation Trust issued a statement that the Royal Manchester Children's Hospital (RMCH) is the first in the world to treat an MPS-IIIA patient with an *ex vivo* HSC gene therapy. This was conducted under a "Specials" license, granted by the UK government for the use of an unlicensed pharmaceutical product in situations of high unmet need when there is no other treatment option available. Orchard holds the license to the MPS-IIIA program (OTL-201) and will support an upcoming proof-of-concept clinical trial, which will be conducted at RMCH, utilizing the same technology and procedures that were used to treat this first MPS-IIIA patient. The trial is expected to begin enrolling patients later this year.

First Quarter Business Milestone Achievements

- Achieved clinical proof-of-concept and presented data for OTL-300 for the treatment of transfusion-dependent beta-thalassemia (TDT). Data presented at ASGCT in April 2019 demonstrated that eight of nine patients had a reduced or eliminated need for transfusions 12 months following treatment, with four of six pediatric patients achieving transfusion independence.
- Presented two- and three-year follow-up data on 20 patients from the OTL-200 registrational trial for MLD, using the fresh

product formulation, at the 45th Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT). In the study, late infantile MLD patients achieved gross motor function scores of 65 and 72 percentage points higher at two and three years following gene therapy than MLD patients in a natural history patient cohort who did not receive gene therapy.
- Dosed the first patient in a clinical trial using the cryopreserved formulation of OTL-103 for patients with Wiskott-Aldrich syndrome (WAS). This program remains on track for BLA and MAA filings in 2021.

First Quarter 2019 Financial Results

Cash, cash equivalents and restricted cash as of March 31, 2019 were $299.2 million compared to $339.7 million as of December 31, 2018. The decrease was primarily driven by cash used to fund operations for the quarter, including a paydown of 2018 accrued expenses and deferred payments for inventory and transition services under the April 2018 agreement with GSK.

Research and development expenses were $17.5 million for the first quarter of 2019, compared to $9.2 million in the same period in 2018. The increase was primarily driven by costs associated with clinical-stage programs acquired from GSK in April 2018. Personnel-related costs increased $4.2 million due to an increase in headcount over the prior year to support our growth and to assist in the further development of our product candidates and pipeline.

Selling, general and administrative expenses were $10.8 million for the first quarter of 2019, compared to $4.5 million in the same period in 2018. The increase was primarily due to personnel costs to support public company operations, including a $1.9 million increase in non-cash share-based compensation expense, as well as costs to market Strimvelis® and prepare for the potential commercialization of the company's three late-stage development programs.

Net loss attributable to ordinary shareholders was $30.7 million in the first quarter of 2019, compared to $15.3 million in the same period in 2018.

Credit Facility

In May, Orchard signed a five-year senior credit facility for up to $75 million with MidCap Financial. Twenty-five million dollars of the facility is to be funded on or around May 28, 2019, with the ability to access the remaining $50 million in two tranches subject to the achievement of certain clinical and regulatory milestones and other customary conditions. The facility provides for an interest-only period of up to 36 months and bears interest at a rate of LIBOR plus 6%.

The company expects that its cash and investments as of March 31, 2019, together with the borrowing capacity from the senior credit facility with MidCap Financial, will fund its anticipated operating and capital expenditure requirements into 2021.

"The MPS-I program is a significant and important addition to our portfolio, enabling us to leverage our expertise in neurometabolic diseases and further extend the potential reach in addressing these conditions," said Frank Thomas, chief financial officer and chief business officer of Orchard. "The $75 million credit facility strengthens our cash position and supports a number of important milestones, with a particular focus on the build-out of an Orchard manufacturing site. In addition, we continue to prepare for three potential product launches and the completion of two registrational trials and three proof-of-concept trials as part of our broader mission to bring gene therapy treatments to patients who need them."

Conference Call & Webcast Information

Orchard will host a conference call and live webcast with slides today at 8:00 a.m. ET to discuss the first quarter results and recent business activities. To participate in the conference call, please dial 1-866-930-5155 (domestic) or 1-409-937-8974 (international) and refer to conference ID 2764629. A live webcast of the presentation will be available under "News & Events" in the "Investors & media" section of the company's website at orchard-tx.com and a replay will be archived on the Orchard website following the presentation.

About Orchard

Orchard Therapeutics is a fully integrated commercial-stage biopharmaceutical company dedicated to transforming the lives of patients with serious and life-threatening rare diseases through innovative gene therapies.

Orchard's portfolio of *ex vivo*, autologous, hematopoietic stem cell (HSC) based gene therapies includes Strimvelis®, a gammaretroviral vector-based gene therapy and the first such treatment approved by the European Medicines Agency for severe combined immune deficiency due to adenosine deaminase deficiency (ADA-SCID). Additional programs for neurometabolic disorders, primary immune deficiencies and hemoglobinopathies are all based on lentiviral vector-based gene modification of autologous HSCs and include three advanced registrational studies for metachromatic leukodystrophy (MLD), ADA-SCID and Wiskott-Aldrich syndrome (WAS), clinical programs for X-linked chronic granulomatous disease (X-CGD), transfusion-dependent beta-thalassemia (TDT) and mucopolysaccharidosis Type I (MPS-I), as well as an extensive preclinical pipeline. Strimvelis, as well as the programs in MLD, WAS and TDT were acquired by Orchard from GSK in April 2018 and originated from a pioneering collaboration between GSK and the San Raffaele Telethon Institute for Gene Therapy in Milan, Italy initiated in 2010.

Orchard currently has offices in the U.K. and the U.S., including London, San Francisco and Boston.

About MidCap Financial

MidCap Financial is a middle market-focused, specialty finance firm that provides senior debt solutions to companies across all industries. MidCap is headquartered in Bethesda, MD, with offices in Chicago and Los Angeles, and provides a broad array of products intended to finance growth and manage working capital. For more information, visit www.midcapfinancial.com.

MidCap Financial refers to MidCap FinCo Designated Activity Company, a private limited company domiciled in Ireland, and its subsidiaries, including MidCap Financial Services, LLC. MidCap Financial Services, LLC employs all personnel and provides sourcing, due diligence and portfolio management services to MidCap FinCo Designated Activity Company pursuant to a services agreement. MidCap Financial is managed by Apollo Capital Management, L.P., a subsidiary of Apollo Global Management, pursuant to an investment management agreement.

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. Such forward-looking statements may be identified by words such as "anticipates," "believes," "expects," "intends," "projects," "anticipates," and "future" or similar expressions that are intended to identify forward-looking statements. Forward-looking statements include express or implied statements relating to, among other things, Orchard's expectations regarding the timing of regulatory submissions for approval of its product candidates, the timing of interactions with regulators and regulatory submissions related to ongoing and new clinical trials for its product candidates, the timing of announcement of clinical data for its product candidates and the likelihood that such data will be positive and support further clinical development and regulatory approval of these product candidates, the likelihood of approval of such product candidates by the applicable regulatory authorities, and the Company's financial condition and cash runway into 2021. 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, the risks and uncertainties include, without limitation: 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, the receipt of restricted marketing approvals, or delays in Orchard's ability to commercialize its product candidates, if approved. 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 annual report on Form 20-F for the year ended December 31, 2018 as filed with the U.S. Securities and Exchange Commission (SEC) on March 22, 2019, 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,	
	2019	**2018**
Costs and operating expenses		
Research and development	$ 17,493	$ 9,171
Selling, general and administrative	10,790	4,527
Total costs and operating expenses	28,283	13,698
Loss from operations	(28,283)	(13,698)
Other income (expense), net	(1,863)	(1,696)
Net loss before income tax	(30,146)	(15,394)
Income tax (expense) benefit	(593)	83
Net loss attributable to ordinary shareholders	(30,739)	(15,311)
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (0.35)	$ (1.53)
Weighted average number of ordinary shares outstanding, basic and diluted	87,010,596	9,983,754

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

	March 31, 2019	**December 31, 2018**
Assets		
Current assets:		
Cash and cash equivalents	$ 295,407	$ 335,844
Trade and other receivables	354	2,153
Prepaid expenses and other assets	6,731	6,935
Research and development tax credit receivable	16,094	10,585
Total current assets	318,586	355,517
Non-current assets:		
Property and equipment, net	5,685	5,476
Restricted cash	3,840	3,837
Other long-term assets	1,208	1,212
Total non-current assets	10,733	10,525
Total assets	$ 329,319	$ 366,042
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	$ 8,384	$ 18,125
Accrued expenses and other current liabilities	26,316	29,780
Total current liabilities	34,700	47,905

Other long-term liabilities	7,143	6,799
Total liabilities	41,843	54,704
Shareholders' equity:	287,476	311,338
Total liabilities and shareholders' equity	$ 329,319	$ 366,042

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Source: Orchard Therapeutics