Orchard Therapeutics Reports Third Quarter 2019 Financial Results and Achievement of Key 2019 Milestones for Neurometabolic and Primary Immune Deficiencies Franchises

November 6, 2019

ASH Abstracts Published Today Confirm Achievement of All Key Endpoints in Wiskott-Aldrich Syndrome Registrational Trial and Demonstrate Consistency of Data Between the Fresh and Cryopreserved Formulations of Investigational Gene Therapies

Marketing Authorization Application in EU for Metachromatic Leukodystrophy on Track for Near-Term Submission Following Recent Presentation of Cryopreservation Data

Ended the Third Quarter of 2019 with Approximately $366.2M in Total Cash and Investments

Conference Call Scheduled for Today at 4:30 p.m. ET

BOSTON and LONDON, Nov. 06, 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 and business highlights for the quarter ended September 30, 2019, as well as the achievement of certain corporate milestones for the primary immune deficiencies franchise.

“We made important clinical and operational progress at Orchard over the past quarter, advancing our three lead programs toward regulatory submissions while moving additional programs through earlier stages of clinical development,” said Mark Rothera, president and chief executive officer of Orchard Therapeutics. “The data presented at several major medical conferences throughout the quarter showcase the profound impact that our hematopoietic stem cell-based gene therapies may have across multiple life-threatening diseases. We are working with care and urgency to make these therapies broadly available to patients who need them.”

Recent Achievements for the Neurometabolic Franchise

Metachromatic Leukodystrophy (MLD):

- Presented engraftment data in four patients receiving the cryopreserved formulation of OTL-200 for the treatment of MLD at the European Society of Gene & Cell Therapy (ESGCT) Annual Congress. The initial data showed that cellular engraftment using a cryopreserved formulation was similar to that observed using a fresh formulation, with the longest patient having 12 months of follow-up since treatment. Link to the full release here.
- In addition, an integrated analysis of 29 patients receiving the OTL-200 fresh formulation, which demonstrated positive clinical effects in the treatment of MLD and a consistent safety profile, was presented at the Society for the Study of Inborn Errors of Metabolism (SSIEM) 2019 Symposium. Link to the full release here.
- The company is on-track for a near-term Marketing Authorization Application (MAA) submission for OTL-200.

Mucopolysaccharidosis type I (MPS-I):

- Presented data from the ongoing proof-of-concept trial of OTL-203 for MPS-I at SSIEM. Evidence of engraftment and overexpression of the alpha-l-iduronidase (IDUA) enzyme in the peripheral blood and cerebrospinal fluid (CSF) was seen at the time of analysis in the six patients treated. Link to the full release here.
  -- An abstract has been accepted with updated proof-of-concept data for an oral presentation at the 61st American Society of Hematology (ASH) Annual Meeting in December.
  -- The study is expected to enroll eight patients by the first half of 2020, with primary endpoint results expected after one year of follow-up.

Sanfilippo Syndrome type A (MPS-IIIA):

- The clinical trial application for a proof-of-concept trial at the Royal Manchester Children’s Hospital (RMCH) for Orchard’s MPS-IIIA program (OTL-201) was recently accepted and enrollment is expected to begin later this year.
- This trial utilizes the same technology and procedures that were used to treat the first MPS-IIIA patient with *ex vivo*

hematopoietic stem cell-based (HSC) gene therapy at RMCH under a “Specials” license.

- The patient treated under the “Specials” license continues to do well approximately 10 months after treatment, according to a statement made this week by the Manchester University NHS Foundation Trust.
  -- Six-month results indicate early evidence of metabolic correction with supranormal N-sulfoglucosamine sulfohydrolase (SGSH) enzyme activity in peripheral leukocytes and reduction of glycosaminoglycans (GAGs) in the urine, CSF and plasma.

Upcoming Data Presentations for Primary Immune Deficiencies Franchise

- As announced in a separate release this morning, the company will present data from two registrational programs (OTL-103 for the treatment of Wiskott-Aldrich Syndrome (WAS) and OTL-101 for the treatment of adenosine deaminase severe combined immunodeficiency (ADA-SCID)) at the ASH meeting in December. Highlights include:
  -- OTL-103 for WAS**:** The registrational trial has met its key primary and secondary endpoints (n=8 at three years) with data from an integrated analysis (n=17) reinforcing the treatment benefits of gene therapy and durability of effect in additional patients. Successful engraftment was observed within three months, leading to an increase in WAS protein expression and a vector copy number that has been maintained for up to eight years.
  -- OTL-101 for ADA-SCID: Similar profiles and engraftment have been observed between the cryopreserved and fresh formulations of OTL-101, which represents an important achievement toward the future regulatory filing and potential approval of this investigational gene therapy and a key step toward global patient availability.

Third Quarter 2019 Financial Results

Cash, cash equivalents and investments as of September 30, 2019, were $366.2 million compared to $335.9 million as of December 31, 2018. The increase was primarily driven by proceeds from the company’s public equity offering in June 2019 and a credit facility entered in May 2019, partially offset by the net cash used to fund operations in the nine months ended September 30, 2019. During the three months ended September 30, 2019, the company’s cash used to fund operations included the paydown of accrued liabilities as of June 30, 2019, for the upfront payment and a milestone payment related to the license of a clinical-stage MPS-I program, or OTL-203.

During the three months ended September 30, 2019, the company recognized $1.9 million in revenue related to European sales of Strimvelis®, the first gene therapy approved by the European Medicines Agency for ADA-SCID.

Research and development expenses were $28.5 million for the three months ended September 30, 2019 compared to $27.7 million in the same period in 2018. 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 milestone payments under the company’s agreements with third parties, and personnel costs to support these activities. The company expects R&D expenses to continue to increase as its programs advance through development.

Selling, general and administrative expenses were $14.2 million for the three months ended September 30, 2019, compared to $7.5 million in the same period in 2018. The increase was primarily due to increased investment to prepare for the potential commercialization of multiple late-stage programs, as well as higher costs to support public company operations.

Net loss attributable to ordinary shareholders was $36.7 million for the three months ended September 30, 2019, compared to $33.9 million in the same period in 2018. The increase in net loss as compared to the prior year was primarily due to higher costs related to pre-launch activities on the company’s later-stage programs in development and expenses associated with being a public company, partially offset by higher interest income. The company had 97.8 million weighted average ordinary shares outstanding for the three months ended September 30, 2019.

The company expects that its existing cash, cash equivalents and investments will enable funding of its anticipated operating and capital expenditure requirements into the second half of 2021.

“Orchard is well positioned to enter its next phase of growth as a company with potentially multiple commercial-stage gene therapies, building on a proven track record in identifying and treating patients with Strimvelis, the first *ex vivo* HSC gene therapy on the market,” said Frank Thomas, Orchard’s chief financial officer and chief business officer. “Having treated multiple patients with Strimvelis this quarter at a single center in Milan, Italy, we have deepened our understanding of the support required for patients and families along their treatment journey, successfully secured reimbursement for cross-border healthcare delivery within Europe and completed the manufacturing and release process scheduled and tailored for each individual patient. We look forward to expanding these capabilities and applying key learnings to future commercial gene therapies at multiple centers around the world using cryopreserved formulations of our future products, if approved.”

Conference Call & Webcast Information

Orchard will host a conference call and live webcast with slides today at 4:30 p.m. ET to discuss the third quarter results and recent and upcoming business activities. To participate in the conference call, please dial 1-866-987-6504 (domestic) or +1-602-563-8620 (international) and refer to conference ID 8413109. 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.

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," 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, the therapeutic potential of Orchard's product candidates, including the product candidate or candidates referred to in this release, Orchard's expectations regarding the timing of regulatory submissions for approval of its product candidates, including the product candidate or candidates referred to in this release, 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 the second half of 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 risk that any one or more of Orchard's product candidates, including the product candidate or candidates referred to in this release, will not be successfully developed or commercialized, the risk of cessation or delay of any of Orchard's ongoing or planned 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, the receipt of restricted marketing approvals, and the risk of 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
(In thousands, except share and per share amounts)
(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Product sales, net	$ 1,918	$ 1,387	$ 1,918	$ 1,387
Costs and operating expenses:				
Cost of product sales	614	280	614	280
Research and development	28,493	27,731	86,464	187,893
Selling, general and administrative	14,223	7,466	38,687	19,414
Total costs and operating expenses	43,330	35,477	125,765	207,587
Loss from operations	(41,412)	(34,090)	(123,847)	(206,200)
Total other income (expense), net	2,481	935	3,468	1,336
Net loss before income tax	(38,931)	(33,155)	(120,379)	(204,864)
Income tax (expense) benefit	2,194	(733)	2,373	(568)
Net loss attributable to ordinary shareholders	(36,737)	(33,888)	(118,006)	(205,432)
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (0.38)	$ (3.29)	$ (1.29)	$ (20.27)
Weighted average number of ordinary shares outstanding, basic and diluted	97,817,847	10,294,498	91,553,803	10,132,334

Condensed Consolidated Balance Sheets
(In thousands)
(unaudited)

	September 30,	December 31,

	2019	2018
Assets		
Current assets:		
Cash and cash equivalents	$ 35,478	$ 335,844
Marketable securities	330,677	—
Trade and other receivables	5,006	2,153
Prepaid expenses and other assets	8,326	6,935
Research and development tax credit receivable, current	13,988	10,585
Total current assets	393,475	355,517
Property and equipment, net	5,714	5,476
Research and development tax credit receivable	8,240	—
Other assets	7,310	5,049
Total assets	$ 414,739	$ 366,042
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	$ 11,595	$ 18,125
Accrued expenses and other current liabilities	32,712	29,780
Total current liabilities	44,307	47,905
Long-term debt, net	24,609	—
Other long-term liabilities	6,079	6,799
Total liabilities	74,995	54,704
Total shareholders' equity	339,744	311,338
Total liabilities and shareholders' equity	$ 414,739	$ 366,042

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