



Orchard Therapeutics Reports OTL-201 Initial Clinical Data in Sanfilippo Syndrome Type A (MPS-III A)

December 8, 2020

Preliminary results from first patient treated with OTL-201 show over expression of the therapeutic enzyme and decrease in substrate levels three months following gene therapy

BOSTON and LONDON, Dec. 08, 2020 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, yesterday reported initial data from an ongoing proof-of-concept clinical trial evaluating the safety and efficacy of OTL-201, an investigational *ex vivo* autologous hematopoietic stem cell (HSC) gene therapy being studied for the treatment of mucopolysaccharidosis type IIIA (MPS-III A, also known as Sanfilippo syndrome type A). The data were presented as part of an oral presentation given yesterday at the 62nd American Society of Hematology (ASH) Annual Meeting.

"The data presented yesterday represents encouraging progress for patients and families living with MPS-III A, a progressive, life-threatening metabolic disease with no approved treatment options," said Professor Robert Wynn, chief investigator at The Royal Manchester Children's Hospital, part of Manchester University NHS Foundation Trust. "The initial results in the first patient treated provide preliminary evidence of engraftment of cells capable of producing supra-physiological N-sulphoglucosamine sulphohydrolase enzyme expression in multiple lineages. We are eager to continue the follow-up of this patient as well as the investigation of OTL-201 in additional patients and look forward to working in close collaboration with Orchard to advance this program with great urgency on behalf of the MPS community."

Initial Study Results

As of December 2020, preliminary results from the first patient treated with OTL-201 showed promising safety, tolerability, engraftment and biomarker data over a follow up period of three months. Certain data, including engraftment of gene-modified cells as measured by vector copy number, were unavailable at the time of the presentation due to the impact of COVID-19. Specifically, the results showed:

- The treatment was generally well-tolerated with no treatment related adverse events or serious adverse events to date.
- Evidence of hematological engraftment as suggested by recovery of neutrophils and platelets post myeloablative conditioning.
- N-sulphoglucosamine sulphohydrolase (SGSH) enzyme expression reached supra-physiological levels in plasma, total leukocytes and multiple cell subpopulations, including CD3+ and CD15+ cells, within 3 months of receiving OTL-201.
- Reduction of urinary heparan sulfate from 60.8 mg/mmol creatinine at baseline to the normal range by three months post-treatment with gene therapy.

Three patients have been treated in the ongoing proof-of-concept study, which is being sponsored and conducted by [The University of Manchester \(UoM\)](#) and funded by Orchard. The OTL-201 program and this clinical trial follow over a decade of development and pre-clinical work by Brian Bigger, Ph.D., Professor of Cell and Gene Therapy at UoM. Completion of enrollment and the release of additional interim results are expected in 2021.

About OTL-201 and MPS-III A

Mucopolysaccharidosis type IIIA (MPS-III A, also known as Sanfilippo syndrome type A) is a rare and life-threatening metabolic disease. People with MPS-III A are born with a mutation in the *N-sulphoglucosamine sulphohydrolase (SGSH)* gene, which, when healthy, helps the body break down sugar molecules called mucopolysaccharides, including heparan sulfate. The buildup of mucopolysaccharides in the brain and other tissues leads to intellectual disability and loss of motor function. MPS-III A occurs in approximately one in every 100,000 live births. Life expectancy of children born with MPS-III A is estimated to be between 10-25 years.¹ There are currently no approved treatment options for MPS-III A. OTL-201 is an investigational *ex vivo* autologous hematopoietic stem cell gene therapy being studied for the treatment of MPS-III A. It uses a modified virus to insert a functional copy of the *SGSH* gene into a patient's cells.

About Orchard

Orchard Therapeutics is a global gene therapy leader dedicated to transforming the lives of people affected by rare 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](#).

About Manchester University NHS Foundation Trust

Manchester University NHS Foundation Trust is one of the largest NHS trusts in England and a leading provider of specialist healthcare services. Its nine hospitals are home to hundreds of world class clinicians and academic staff committed to finding patients the best care and treatments. This includes Royal Manchester Children's Hospital (RMCH), one of the largest children's hospitals in the UK with an international reputation as a centre of excellence for research and innovation. More information is available at www.mft.nhs.uk.

About The University of Manchester

The University of Manchester, a member of the prestigious Russell Group, is one of the UK's largest single-site universities with more than 40,000

students – including more than 10,000 from overseas. It is consistently ranked among the world's elite for graduate employability. The University is also one of the country's major research institutions, rated fifth in the UK in terms of 'research power' (REF 2014). World-class research is carried out across a diverse range of fields including cancer, advanced materials, global inequalities, energy and industrial biotechnology.

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, the therapeutic potential of Orchard's product candidates, including the product candidate or candidates referred to in this release, and Orchard's expectations regarding its ongoing clinical trial for OTL-201, including the timing of enrollment for such clinical trial and the release of additional clinical data. 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 any one or more of Orchard's product candidates, including the product candidate or 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; and the inability or risk of delays in Orchard's ability to commercialize its product candidates, if approved; 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, 2020, 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.

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¹ Lavery, C., Hendriksz, C.J. & Jones, S.A. Mortality in patients with Sanfilippo syndrome. *Orphanet J Rare Dis* 12, 168 (2017) doi:10.1186/s13023-017-0717-y

