Orchard Therapeutics Announces Historic Agreement Making Libmeldy Available by NHS England for MLD Patients

February 4, 2022

First-ever lentiviral hematopoietic stem cell gene therapy approved for reimbursement by NHS England

Two children with early-onset MLD recently treated commercially with Libmeldy in Germany and France

A third eligible patient identified through partnership in Middle East and referred for international reimbursed treatment abroad in Italy

Announcements mark significant milestones for the MLD community and reinforce growing momentum of European launch

BOSTON and LONDON, Feb. 03, 2022 (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today announced it has reached an agreement with the National Health Service (NHS) that enables access to Libmeldy® (atidarsagene autotemcel) for all children with metachromatic leukodystrophy (MLD) in England and Wales who fall within the scope of the European marketing authorization. The agreement coincides with publication of the positive National Institute for Health and Care Excellence's (NICE) final evaluation determination, which recognized the clinical impact and economic benefit of Libmeldy according to the institute's Highly Specialized Technologies (HST) process. In addition, the company announced the first two commercially treated patients in Germany and France under reimbursement mechanisms for early access. A third patient from the Middle East was referred for international reimbursed treatment abroad in Italy.

"Today's landmark agreement with NHS England follows a thoughtful and comprehensive value assessment by NICE and represents a major milestone for the MLD community, Orchard, and the entire field of HSC gene therapy," said Professor Bobby Gaspar, M.D., Ph.D., chief executive officer of Orchard Therapeutics. "We are delighted that NICE and NHS England have recognized the transformational clinical impact and significant economic value of Libmeldy for eligible MLD patients, and thank the leading clinicians and advocates involved for their tireless engagement throughout the process. A deep body of evidence now points to the potential for durable effects in HSC gene therapy for certain severe genetic diseases including MLD. I am grateful for the opportunity we have at Orchard to commercially scale the reach of our therapeutic approach for patients in need—starting with MLD."

MLD is a rare, rapidly progressing, irreversible and fatal genetic disorder caused by a mutation in the *arylsulfatase-A* (*ARSA*) gene that results in the accumulation of fats called sulfatides in the brain, peripheral nerves, and other areas of the body, including the liver, gallbladder and kidneys. Over time, the nervous system is damaged, and children with MLD experience neurological problems such as motor, behavioral and cognitive regression, severe spasticity and seizures. In its most severe form, children quickly lose the ability to walk, talk and interact with the world around them. The majority of these children pass away before adolescence. Libmeldy is the only one-time gene therapy intended to correct the underlying cause of MLD in eligible patients approved in Europe. In clinical studies, Libmeldy resulted in sustained, clinically relevant benefits in children with early-onset MLD by preserving cognitive function and motor development in most patients.

"MLD causes catastrophic physical suffering for affected children and places immense physical, emotional and financial burden on their families," said Georgina Morton, chairperson of ArchAngel MLD Trust. "Previously, there was a dearth of treatment options for this condition, which was mainly managed using supportive care. Our community is deeply appreciative of the NHS and NICE for recognizing the significant medical need in MLD and paving the way for eligible children in England and Wales to now have access to this important therapy. As advocates we are now turning our sights to advancing newborn screening for MLD in order to help as many future MLD affected patients as possible."

Updates on Commercial Momentum in Europe
Since the European Commission approval of Libmeldy, Orchard Therapeutics has continued to build its commercial infrastructure in the region to support patient identification and treatment efforts. Recently, the first two commercially treated patients were infused with Libmeldy at Tübingen University Hospital and the Hôpital Debré in Paris, two of the treatment centers qualified to administer the therapy. Both patients are being treated under reimbursed early access arrangements available in the respective countries while final reimbursement negotiations are ongoing with national authorities. In addition, through the company's commercial partnership with Genpharm, a patient from the Middle East has been identified and referred for reimbursed international treatment abroad at Ospedale San Raffaele in Milan, Italy.

To continue identifying eligible patients in the appropriate treatment window, the company has launched a newborn screening pilot in Germany and is planning additional screening initiatives in other European countries, including Italy, the UK, Spain and France, while it continues to work with its clinical partners to support additional ongoing diagnostic and disease education initiatives throughout the region.

"The early launch momentum we're experiencing with Libmeldy in Europe is very encouraging and confirms the company's strategy to focus on areas of significant need where we believe our HSC gene therapy platform approach has distinct therapeutic potential," said Braden Parker, chief commercial officer of Orchard Therapeutics. "We are pleased with the agreement we've reached with NHS and are committed to working closely and urgently with governments, health authorities and payers in other European countries to enable access for eligible young children in those localities who may benefit from this therapy. These efforts coincide with the fact that for the first time ever eligible children with MLD have received treatment with Libmeldy in the European commercial setting, with another patient in the process of referral and treatment. Our team has worked diligently alongside our partners to reach this moment. I am incredibly proud of their collective efforts and look forward to the next steps in our company's commercial journey."

About MLD
MLD is a rare and life-threatening inherited disease of the body's metabolic system occurring in approximately one in every 100,000 live births. MLD is

caused by a mutation in the *arylsulfatase-A* (*ARSA*) gene that results in the accumulation of sulfatides in the brain and other areas of the body, including the liver, gallbladder, kidneys, and/or spleen. Over time, the nervous system is damaged, leading to neurological problems such as motor, behavioral and cognitive regression, severe spasticity and seizures. Patients with MLD gradually lose the ability to move, talk, swallow, eat and see. In its late infantile form, mortality at five years from onset is estimated at 50 percent and 44 percent at 10 years for juvenile patients.[i]

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 U.S.

Libmeldy was developed in partnership with the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) in Milan, Italy.

About Orchard Therapeutics
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. Such forward-looking statements may be identified by words such as "anticipates," "believes," "expects," "plans," "intends," "projects," and "future" or similar expressions that are intended to identify forward-looking statements. Except for statements of historical fact, information contained herein constitutes forward-looking statements and may include, but is not limited to, the Company's expectations regarding the safety and efficacy of Libmeldy, the Company's ability to establish the infrastructure necessary to enable the treatment of eligible MLD patients, and the adequacy of the Company's supply chain and ability to commercialize Libmeldy. 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 Libmeldy will not be successfully commercialized; the risk that any one or more of Orchard's product candidates, including OTL-200, will not be approved, successfully developed or commercialized; the risk that prior results, such as signals of safety, activity or durability of effect, observed from preclinical studies or clinical trials of Orchard's product candidates will not be repeated or continue in ongoing or future studies or trials involving its product candidates; the risk that the market opportunity for its products or product candidates may be lower than estimated; and the severity of the impact of the COVID-19 pandemic on Orchard's business, including on preclinical and 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.

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[i] *Mahmood et al. Metachromatic Leukodystrophy: A Case of Triplets with the Late Infantile Variant and a Systematic Review of the Literature. Journal of Child Neurology 2010, DOI:* http://doi.org/10.1177/0883073809341669

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