Orchard Therapeutics Celebrates Global Progress toward Advancing Newborn Screening for MLD on International Neonatal Screening Day

June 28, 2024

A nomination to add MLD to the U.S. Recommended Uniform Screening Panel has been submitted by a multi-disciplinary expert working group

Norway becomes the first country to include MLD on its national newborn screening program

Numerous publications in the first half of 2024 provide critical evidence demonstrating MLD fulfills the necessary criteria for inclusion in NBS programs around the world

TOKYO, LONDON and BOSTON, June 28, 2024 (GLOBE NEWSWIRE) -- Orchard Therapeutics, recently acquired by Kyowa Kirin with the goal of accelerating the delivery of new gene therapies to patients around the globe, today announced a number of updates pertaining to the advancement of universal newborn screening (NBS) for metachromatic leukodystrophy (MLD).

NBS is widely considered one of the most successful public health programs worldwide. In the U.S., approximately 1 in 500 newborns have a condition that can be diagnosed through NBS, and more than 8,000 infants have the potential to receive life-saving treatment due to this public health program annually.[i]

MLD is an ultra-rare, rapidly progressive, irreversible and ultimately fatal neurometabolic disease that affects approximately one in 100,000 live births. It is caused by an error in the gene responsible for encoding the enzyme arylsulfatase A (ARSA) leading to neurological damage and developmental regression. In the most severe form of MLD, babies develop normally but in late infancy start to rapidly lose the ability to walk, talk and interact with the world around them. These children eventually deteriorate into a vegetative state, which may require 24-hour intensive care, and the majority pass away within five years of symptom onset, creating an enormous emotional and financial burden on the family.

Recently, the U.S. Food and Drug Administration (FDA) approved the first and only treatment for eligible children with early-onset MLD which is marketed by Orchard Therapeutics. The same treatment has previously been approved by the European Commission (EC), UK Medicines and Healthcare products Regulatory Agency (MHRA), and Swiss Agency for Therapeutic Products (Swissmedic).

“Building on foundational work to establish a method for identifying MLD through newborn screening, there has been tremendous progress over the past few years to advance screening efforts around the world,” said Leslie Meltzer, Ph.D., chief medical officer of Orchard Therapeutics. “As with many rare, life-threatening diseases, early detection and diagnosis is key to ensuring the best possible outcomes for patients. We recognize the valuable contributions of researchers, physicians, patient advocates and families to help ensure the pace of newborn screening coincides with biomedical innovation, and we look forward to continuing to support the efforts of the broader community to accelerate MLD NBS globally.”

Nomination to add MLD to the U.S. Recommended Uniform Screening Panel submitted by multi-disciplinary expert working group

A multi-disciplinary expert working group of advocates, clinicians, public health professionals, and scientists from the MLD community has submitted a nomination to add MLD to the U.S. Recommended Uniform Screening Panel (RUSP), a national guideline comprising a list of medical conditions for which the federal government recommends all newborns are screened for at birth. States use the RUSP to inform decisions about which conditions to include in their respective NBS panels.

The nomination was submitted on June 27 to the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC), part of the Health Resources and Services Administration (HRSA) within the U.S. Department of Health and Human Services (HHS). The submission of the nomination initiates the review process during which the committee will analyze the evidence presented about the benefit of NBS for MLD. Considerations will include the availability of an effective and precise screening test to detect newborns with the condition, the potential to treat eligible children with confirmed diagnoses of MLD, and the clinical utility of pre-symptomatic diagnosis. Once a new condition is added to the RUSP, adoption and implementation is then carried out at the state level. As of today, 12 states have RUSP alignment legislation intended to expedite the process of adding new conditions to state NBS panels once approved by the HHS Secretary.

A critical element of this process requires evidence generated by pilot studies. Currently, eleven prospective investigator-initiated NBS studies for MLD, most of which are funded by Orchard Therapeutics, are active throughout the U.S., Europe and the Middle East, with more than 300,000 newborns screened to date. Five positive screens have been detected cumulatively in these studies, all of which resulted in confirmed diagnoses of MLD. Most recently, a prospective study initiated in Ospedale Buzzi in Milan, Italy, which will offer NBS for MLD for babies born in the Lombardy region.

“The submission of the RUSP nomination for MLD is a monumental step toward implementing newborn screening for this devastating disease in the U.S.,” said Paul Orchard, M.D., a pediatric blood and marrow transplant physician at M Health Fairview and professor in the Division of Pediatric Blood and Marrow Transplantation and Cellular Therapy Program at the University of Minnesota Medical School. “Newborn screening on a broad scale will prove critical for MLD, as it is the only practical means of identifying patients prior to the onset of symptoms, which is key to achieving optimal outcomes. I have seen first-hand the disparity of outcomes for treated versus untreated children, and I believe we are obligated to provide those with MLD the best opportunity for a meaningful life through early diagnosis and intervention.”

Norway becomes the first country in the world to add MLD to its national newborn screening program

In addition, following completion of public consultation, the Ministry of Health and Care Services in Norway has added MLD to its expanded national

NBS panel. This makes Norway the first country in the world to implement national NBS for MLD.

"We commend the Norwegian Ministry of Health and Care Services for recognizing the immense and urgent medical need and becoming the first country in the world to add MLD to its national screening program," said Charlotte Chanson, executive director of global diagnostics and newborn screening at Orchard Therapeutics. "We are highly encouraged with the progress advancing national NBS programs globally and are confident in the strength of nomination packages given the overwhelming evidence demonstrating that MLD fulfills the Wilson and Jungner NBS criteria. We look forward to continuing to support efforts aimed at advancing similar programs in other European countries."

Robust package of necessary evidence has been generated to support the implementation of universal NBS for MLD

Multiple manuscripts have been published in the first half of 2024 underscoring the need, feasibility and cost-effectiveness of newborn screening for MLD. These manuscripts provide critical evidence demonstrating MLD fulfills the necessary criteria to be included in national NBS programs. Highlights, include:

- Consensus guidelines developed by a panel of MLD experts to establish best practices for the monitoring and management of metachromatic leukodystrophy in the U.S. were published in the March 2024 issue of *Cytotherapy*.
- A real-time Delphi procedure detailing European consensus-based recommendations for clinical management for NBS-identified MLD cases were published in the March 2024 edition of the *European Journal of Paediatric Neurology*. Consensus-based recommendations for NBS in MLD will enhance harmonized management and facilitate integration in national screening programs.
- Findings from a pre-pilot study conducted in the UK which resulted in the identification of a late-infantile MLD case. The results, published in the May 2024 issue of *Molecular Genetics and Metabolism*, add to the growing compendium of international evidence supporting the need for NBS to enable early detection and diagnosis of MLD.
- A manuscript published in the May 2024 edition of *Molecular Genetics and Metabolism* detailing the high-specificity of the screening assay developed to detect MLD is precise, ready for deployment, and can be multiplexed with several other inborn errors of metabolism already tested in NBS centers worldwide.
- A health economic analysis demonstrating that newborn screening for MLD is a cost-effective use of UK's National Health Service (NHS) resources using a willingness-to-pay threshold appropriate to the severity of the disease. The findings, published in the June 2024 *International Journal of Neonatal Screening*, support the addition of MLD to the routine newborn screening program in the country.

Recognizing International Neonatal Screening Day

The announcement of these updates coincides with International Neonatal Screening Day, which is observed annually on June 28 in recognition of the birthday of Dr. Robert Guthrie, a microbiologist who, in the 1960s, established the filter paper blood spot card and developed an assay to screen newborns for phenylketonuria (PKU) in the U.S. His work and advocacy revolutionized the detection of children with congenital disorders and spawned modern newborn screening programs around the world.

Orchard Therapeutics is proud to support the community in its efforts and help generate the data necessary to enable the implementation of universal NBS for MLD globally.

About MLD
MLD is a rare and life-threatening inherited disease of the body's metabolic system estimated to occur in approximately one in every 100,000 live births based on existing literature. MLD is caused by an error 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.[ii]

About Orchard Therapeutics
Orchard Therapeutics, a Kyowa Kirin company, is a global gene therapy leader focused on ending the devastation caused by genetic and other severe diseases 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 with a single treatment.

Founded in 2015, Orchard's roots go back to some of the first research and clinical developments involving HSC gene therapy. Our team has played a central role in the evolution of this technology from a promising scientific idea to a potentially life-transforming reality. Today, Orchard is advancing a pipeline of 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.

For more information, please visit www.orchard-tx.com.

About Kyowa Kirin
Kyowa Kirin aims to discover novel medicines with life-changing value. As a Japan-based Global Specialty Pharmaceutical Company, we have invested in drug discovery and biotechnology innovation for more than 70 years and are currently working to engineer the next generation of antibodies and cell and gene therapies with the potential to help patients affected by a severe or rare disease. A shared commitment to our values, to sustainable growth, and to making people smile unites us across our four regions – Japan, Asia Pacific, North America, and EMEA/International. You can learn more about the business of Kyowa Kirin at www.kyowakirin.com.

[i] *Gaviglio et. al. Infants with Congenital Diseases Identified through Newborn Screening—United States, 2018–2020. International Journal of Neonatal Screening. 2023, 9(2), 23;* https://doi.org/10.3390/ijns9020023

[ii] *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, 25(5), 572-580;* http://doi.org/10.1177/0883073809341669

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