Media & Investor Release

Ad hoc announcement pursuant to Art. 53 LR

Roche provides safety update on Elevidys™ gene therapy for Duchenne muscular dystrophy in non-ambulatory patients

- **After a thorough clinical review, the benefit-risk for the use of Elevidys in non-ambulatory patients with Duchenne has been re-assessed, following two cases of fatal acute liver failure**
- **Effective immediately, dosing of non-ambulatory patients, irrespective of age, is paused in the clinical setting; dosing of non-ambulatory patients is discontinued in the commercial setting**
- **Roche is working closely with relevant health authorities, investigators and prescribing physicians to ensure they are informed and patient care is being appropriately modified**
- **The benefit-risk of Elevidys treatment in ambulatory Duchenne patients remains positive and treatment guidance is unchanged**

Basel, 15 June 2025 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today new dosing restrictions, effective immediately, for ELEVIDYS™ (delandistrogene moxeparvovec), for non-ambulatory Duchenne muscular dystrophy (DMD) patients, irrespective of age, in both clinical and commercial settings. In the commercial setting, non-ambulatory patients should no longer receive Elevidys. In the clinical trial setting, enrolment and dosing of non-ambulatory patients will be immediately paused until additional risk mitigation measures (e.g. immune modulatory treatment) are implemented in the study protocol. Health authorities, investigators and physicians are being informed so that patient care can be quickly adjusted.

This decision follows careful assessment of two cases in non-ambulatory patients of fatal acute liver failure (ALF), an identified risk of Elevidys and other AAV-mediated gene therapies, which led to a reassessment of the benefit-risk profile as unfavourable for patients with DMD who are non-ambulatory.

The new dosing restrictions do not impact the treatment of ambulatory DMD patients of any age, and the benefit-risk ratio remains positive in the ambulatory patient population.

"We are deeply saddened by the loss of these two young men and are urgently working to mitigate any risks related to the use of Elevidys," said Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development, Roche. "Patient safety is always our highest priority. Therefore, we have recommended halting treatment with Elevidys in non-ambulatory patients with immediate effect."

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DMD is a rare, genetic, muscle-wasting disease that progresses rapidly from early childhood. Duchenne primarily affects males, with 1 in 5,000 boys born worldwide having Duchenne. Everyone with Duchenne will eventually lose the ability to walk, along with upper limb, lung and cardiac function.

The two fatal ALF cases occurred in non-ambulatory patients, out of a total of approximately 140 non-ambulatory patients treated with Elevidys globally to date. Following the first case of fatal ALF, European regulators requested that Roche and Sarepta put temporary clinical holds on Elevidys studies 104 (NCT06241950), 302 (ENVOL, NCT06128564) and 303 (ENVISION Study 303, NCT05310071). The temporary clinical holds are still in effect. Outside of Europe, dosing will be paused, effective immediately, for the ENVISION trial. The dosing restrictions will also go into effect for future dosing of commercial non-ambulatory patients.

Elevidys has been approved by regulatory authorities in eight Roche territories for the treatment of DMD including Bahrain, Brazil, Israel, Japan, Kuwait, Oman, Qatar, and the UAE.

In 2019, Roche entered into a global collaboration agreement with Sarepta Therapeutics, Inc. to commercialise Elevidys in territories outside the U.S. Roche and Sarepta jointly manage the clinical studies for Elevidys. Roche is the sponsor of the ENVOL study; Sarepta is the sponsor for all other studies.

Overview of the Elevidys clinical development programme

Studies in non-ambulatory people with DMD

Ongoing

- ENVISION (Study 303, NCT05881408), a global Phase III study investigating the safety and efficacy of Elevidys in participants who are ambulatory (aged 8 to <18 years old) and non-ambulatory (no age limitation). This study is already on temporary clinical hold in Europe. Outside of Europe, recruitment will be paused.
- ENDEAVOR (Study 103, NCT04626674), a two-part, open-label, Phase Ib study assessing Elevidys micro-dystrophin protein expression and safety of Elevidys in seven cohorts of boys with Duchenne, across different ages, mutations and stages of disease progression. No longer recruiting; long term follow up ongoing.

Studies in ambulatory people with DMD

- Study 101 (NCT03375164), a Phase I/II study evaluating the safety of Elevidys in four ambulatory participants aged 4 to <8 years old with Duchenne. The study is complete.
- Study 102 (NCT03769116), a Phase II clinical trial evaluating the safety and efficacy of Elevidys in patients with Duchenne aged 4 to <8 years. The study is complete.
- Study 104 (NCT06241950), a Phase I open-label, systemic gene delivery study to evaluate the safety, tolerability and expression of Elevidys in association with imlifidase in individuals aged 4 to 9 years with pre-existing antibodies to recombinant

adeno-associated virus serotype, rAAVrh74. The study is on temporary clinical hold in Europe.

- HORIZON (Study 105, NCT06597656), a Phase I open-label, systemic gene delivery study to evaluate the safety, tolerability and expression of Elevidys following plasmapheresis in individuals aged 4 to 8 years with pre-existing antibodies to adeno-associated virus serotype, AAVrh74. The study is recruiting ambulatory patients.
- EMBARK (Study 301, NCT05096221), a multinational, Phase III, randomised, double-blind, placebo-controlled study assessing the safety and efficacy of Elevidys in ambulatory boys aged 4 to 7 years. The study duration is two years. The study is complete.
- ENVOL (Study 302, NCT06128564), a Phase II study evaluating the safety of Elevidys and expression of Elevidys micro-dystrophin protein in young children, including babies and newborns. The study is on temporary clinical hold in Europe and the UK.
- EXPEDITION (Study 305, NCT05967351), a Phase III long-term five-year follow-up study evaluating the safety and efficacy of Elevidys in those who have received Elevidys in a previous clinical study. EXPEDITION is enrolling by invitation.

About Elevidys™ (delandistrogene moxeparvovec)

Elevidys is a one-time treatment administered through a single intravenous dose and the first and only approved gene therapy for Duchenne. It is designed to target the underlying cause of Duchenne by delivering new instructions to cells to produce Elevidys-dystrophin in skeletal, respiratory and cardiac muscles. Elevidys aims to slow the progression of Duchenne by delaying the need for a wheelchair, protecting the heart from damage and a person's ability to breathe without a respirator for as long as possible. Elevidys uses adeno-associated virus (AAV) vector technology and consists of three parts: a transgene, promoter and vector. Its unique construct optimises delivery to all muscle types, including those of interest for Duchenne treatment.

A robust clinical trial programme to understand its potential in a broad range of people with Duchenne, of all ages, ambulatory status and a wide range of *DMD* gene mutations is ongoing. To date, more than 900 individuals with Duchenne have been treated with Elevidys through Roche's clinical development program and in real-world settings. Elevidys has already been approved for the treatment of DMD by 10 regulatory authorities around the world, including the US and Japan. Elevidys is being developed by Roche in collaboration with Sarepta Therapeutics.

About Duchenne muscular dystrophy

Duchenne muscular dystrophy (DMD) is a rare, genetic, muscle-wasting disease that progresses rapidly from early childhood. Duchenne primarily affects males, with 1 in 5,000 boys born worldwide having Duchenne. Everyone with Duchenne will eventually lose the ability to walk, along with upper limb, lung and cardiac function. Average life expectancy is

only 28 years. The physical, emotional and financial impact of Duchenne on those affected, their families and caregivers, is profound.

Duchenne is an X-linked, rare neuromuscular disease caused by pathogenic variants (mutations) in the DMD gene that disrupt the production of functional dystrophin protein, leading to progressive and irreversible muscle weakness, diminished quality of life and premature death. Dystrophin strengthens and protects muscles and without it, normal activity causes excessive damage to muscle cells as they are more sensitive to injury. Over time, muscle tissue is replaced with scar tissue and fat, causing muscles to weaken. Although Duchenne progresses differently in each individual, its devastating trajectory is well established. Those with Duchenne will eventually lose the ability to use and move their limbs, to breathe on their own and are susceptible to respiratory infections. Muscle damage to the heart causes cardiomyopathy, including rhythm abnormalities and heart failure.

Early diagnosis is important for timely intervention to prolong muscle function and preserve quality of life. There is a critical need for disease-modifying treatments that address the underlying cause of DMD before irreversible muscle loss occurs.

About Roche in Neuroscience

Neuroscience is a major focus of research and development at Roche. Our goal is to pursue groundbreaking science to develop new treatments that help improve the lives of people with chronic and potentially devastating diseases.

Roche is investigating more than a dozen medicines for neurological disorders, including multiple sclerosis, spinal muscular atrophy, neuromyelitis optica spectrum disorder, Alzheimer's disease, Huntington's disease, Parkinson's disease and Duchenne muscular dystrophy. Together with our partners, we are committed to pushing the boundaries of scientific understanding to solve some of the most difficult challenges in neuroscience today.

About Roche

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

For over 125 years, sustainability has been an integral part of Roche's business. As a science-driven company, our greatest contribution to society is developing innovative medicines and

diagnostics that help people live healthier lives. Roche is committed to the Science Based Targets initiative and the Sustainable Markets Initiative to achieve net zero by 2045.

Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan.

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