Media & Investor Release

Ad hoc announcement pursuant to Art. 53 LR

Roche announces EMBARK trial in Duchenne muscular dystrophy (DMD) did not reach primary endpoint, but shows positive efficacy outcomes on all timed functional key endpoints

- **Elevidys-treated boys aged 4-7 years with Duchenne showed an increase on the North Star Ambulatory Assessment (NSAA), a measure of motor function, compared to placebo at 52 weeks but the primary endpoint was not met**
- **For all key pre-specified secondary functional endpoints, time to rise and 10-metre walk test across age groups, clinically meaningful and statistically significant treatment benefits were observed**
- **No new safety signals observed, reinforcing the favourable and manageable safety profile observed with Elevidys to date**
- **Further evaluation of data is ongoing and Roche will discuss the path forward with health authorities**

Basel, 30 October 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today topline results from the global, randomised, double-blind Phase 3 EMBARK study of Elevidys™ (delandistrogene moxeparvovec) in ambulatory boys (those who can walk) with Duchenne muscular dystrophy aged 4-7 years. In the study, Elevidys-treated patients improved 2.6 points on their NSAA total score 52 weeks after treatment, compared to 1.9 points in placebo-treated patients (0.65; n=125; P=0.24).

In all pre-specified, timed functional key secondary endpoints, time to rise from floor and 10 metre walk test, clinically meaningful and statistically significant improvements were observed. Both endpoints are prognostic factors for disease progression and loss of ability to walk. Additionally, a clinically meaningful and statistically significant improvement was also observed for the pre-specified secondary endpoint stride velocity 95th centile. This novel digital endpoint, qualified by the European Medicines Agency (EMA), measures speed of walking via a wearable device (Syde®). The time to ascend 4-steps secondary endpoint also demonstrated consistent treatment benefit in favour of Elevidys.

All data are being further analysed and will be discussed with health authorities to determine the path forward. Detailed results from the EMBARK study will be shared at an upcoming scientific congress and a medical journal publication will be pursued.

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"High unmet need remains in Duchenne and we are encouraged by the consistent and meaningful results seen in all key secondary functional endpoints for Elevidys, an innovative gene therapy," said Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development, Roche. "We will work to further analyse the EMBARK results and consult with health authorities as quickly as possible. We sincerely thank all the boys, their families and the wider Duchenne community involved in this important research effort."

All key pre-specified functional secondary endpoints demonstrated robust evidence for a clinically meaningful treatment benefit that was consistent across age groups in Elevidys-treated patients compared to placebo at week 52. These include:

Functional endpoints:

Time to rise (TTR)	**Change vs Placebo LSM Difference (seconds)**
Overall (n=125)	-0.64 (p=0.0025)
Ages 4-5 (n=59)	-0.50
Ages 6-7 (n=66)	-0.78

10-metre walk test	**Change vs Placebo LSM Difference (seconds)**
Overall (n=125)	-0.42 (p=0.0048)
Ages 4-5 (n=59)	-0.33
Ages 6-7 (n=66)	-0.52

LSM = least squares mean

As part of a collaboration agreement Roche is working with Sarepta Therapeutics to transform the future for the Duchenne community, enabling those living with the disease to maintain and protect their muscle function, keeping them stronger for longer. Sarepta is responsible for managing regulatory approval and the commercialisation of Elevidys in the US. Roche is responsible for regulatory approvals and bringing Elevidys to patients across the rest of the world. Sarepta is responsible for the manufacturing of Elevidys and together, the companies are working on a comprehensive joint clinical development plan to maximise the chances of broad approval and access.

Elevidys clinical development programme

- Study 101 evaluating the safety of Elevidys in four ambulatory participants aged between 4-<8 years old with Duchenne. Four-year data show a durable response and consistent safety profile.
- Study 102, a Phase 2 clinical trial evaluating the safety and efficacy of Elevidys in patients with Duchenne aged 4-<8 years.
- Study 103 (ENDEAVOR), a two-part, open-label, Phase 1b study assessing the Elevidys-dystrophin expression and safety of Elevidys in five cohorts of boys with Duchenne representing different stages of disease progression. This study is ongoing.
- Study 301 (EMBARK), a Phase 3 global, randomised, double-blinded and placebo-controlled study of Elevidys in ambulatory Duchenne patients aged 4-<8 years old.
- The ENVOL trial (Study 302) a Phase 2 study in children with Duchenne. The study aims to enrol 21 participants who are under 4 years of age, including newborns. Not yet started.
- The ENVISION trial (Study 303), a Phase 3 study in older ambulatory/non-ambulatory patients which is now recruiting.
- The EXPEDITION long-term (5 year) follow up study (Study 305) of participants who have received Elevidys in a previous clinical study, which is not yet recruiting.

About EMBARK

EMBARK is a multinational, Phase 3, randomised, double-blind, two-part crossover, placebo-controlled study assessing the safety and efficacy of Elevidys in ambulatory boys with a confirmed mutation in the *DMD gene*, aged between 4 and 7 years. Eligible participants received a single dose of Elevidys during either Part 1 or Part 2 of the study. The study is ongoing.

Participants (n=125) received $1.33x10^{14}$ vg/kg of delandistrogene moxeparvovec or placebo. In Part 1, participants were randomised according to age (4-5 or 6-7) or NSAA total score at screening (≤22 or >22) to receive either Elevidys or placebo, with a follow-up period for 52 weeks. In Part 2, participants crossed over - meaning, those who were previously treated with placebo in Part 1 received Elevidys and participants who were previously treated with placebo received Elevidys, with a follow-up period for 52 weeks.

The primary endpoint of the trial was change from baseline in NSAA total score at week 52. Secondary endpoints include:

- The quantity of delandistrogene moxeparvovec micro-dystrophin expression at Week 12 as measured by western blot of biopsied muscle tissue (Part 1)
- Change from baseline to Week 52 in Time to Rise from Floor
- Change from baseline to Week 52 in 10-metre Walk/Run (10MWR)
- Change from baseline to Week 52 in stride velocity 95th centile (as measured by Syde®, a wearable device)

- Change from baseline to Week 52 in 100-metre Walk/Run
- Change from baseline to Week 52 in time to ascend 4 steps

Data not yet available for the following endpoints:

- Change from baseline to Week 52 in Patient-Reported Outcomes Measurement Information System® (PROMIS®) mobility score
- Change from baseline to Week 52 in PROMIS® upper extremity score
- Number of skills gained or improved at Week 52 as measured by the NSAA

About ELEVIDYS™

Elevidys™ (delandistrogene moxeparvovec, also known as SRP-9001) is the first approved disease-modifying therapy for Duchenne and is designed to address the underlying cause of Duchenne through targeted skeletal, respiratory and cardiac muscle expression of shortened dystrophin produced by Elevidys. Elevidys is a one-time treatment administered through a single (one-time) intravenous dose. Elevidys is contraindicated in patients with any deletion in exons 8 and/or 9 in the *DMD gene*.

Elevidys received accelerated approval in the US in June 2023, in the United Arab Emirates in August 2023 and in Qatar in September 2023 for the treatment of ambulant children aged 4 through 5 years with Duchenne, who have a confirmed mutation in the *DMD* gene.

About Duchenne muscular dystrophy

Duchenne is a rare, genetic, muscle-wasting disease that progresses rapidly from early childhood. Approximately 1 in 3,500 - 5,000 boys worldwide are born with Duchenne, while Duchenne in girls is very rare. Everyone who has Duchenne will lose the ability to walk, upper limb, lung and cardiac function and mean life expectancy is 28 years. A diagnosis of DMD will require full-time caregiving which is most often provided by parents, the majority of whom will find it difficult to carry out usual work or household activities and suffer from depression and physical pain.

Duchenne is caused by mutations of the *DMD gene*, which affects the production of the muscle protein, dystrophin. Dystrophin is a critical component of a protein complex that strengthens muscle fibers and protects them from injury during muscle contraction. Due to a genetic mutation in the *DMD gene*, people with Duchenne do not make functional dystrophin; their muscle cells are more sensitive to injury and muscle tissue is progressively replaced with scar tissue and fat.

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 neuromuscular diseases: Duchenne muscular dystrophy, facioscapulohumeral muscular dystrophy, myasthenia gravis and spinal muscular atrophy; neuro immune diseases: multiple sclerosis and neuromyelitis optica spectrum disorder; and neurodegenerative diseases: Alzheimer's disease, Huntington's disease and Parkinson's disease. 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.

In recognising our endeavour to pursue a long-term perspective in all we do, Roche has been named one of the most sustainable companies in the pharmaceuticals industry by the Dow Jones Sustainability Indices for the thirteenth consecutive year. This distinction also reflects our efforts to improve access to healthcare together with local partners in every country we work.

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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