Media & Investor Release

Roche announces new results from EMBARK demonstrating significant sustained benefits of Elevidys in ambulatory individuals with Duchenne muscular dystrophy (DMD)

- **Across three key functional outcomes, North Star Ambulatory Assessment (NSAA), Time to Rise (TTR) and 10-meter walk/run (10MWR), results were statistically significant and clinically meaningful two years after treatment with Elevidys, compared to a pre-specified propensity-weighted untreated external control group**
- **Functional differences between individuals treated with Elevidys and those in the external control group increased between one year and two years after treatment**
- **No new safety signals observed further reinforcing the consistent and manageable safety profile observed with Elevidys to date**

Basel, 27 January 2025 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today positive topline results from year two of the EMBARK trial, a global, randomised, double-blind phase III study of Elevidys™ (delandistrogene moxeparvovec), the first approved gene therapy for the treatment of individuals with Duchenne muscular dystrophy. Two years after treatment with Elevidys, statistically significant and clinically meaningful improvements were observed across three key motor function measures of NSAA, TTR and 10MWR, when compared to a pre-specified propensity-weighted untreated external control group.* Functional differences between individuals treated with Elevidys and those in the external control group increased between one and two years after dosing. Together, these results demonstrate consistent, sustained benefit in favour of Elevidys.

Detailed results from year two of the EMBARK study will be shared at an upcoming medical meeting and discussed with health authorities. One-year data from part one of the EMBARK study were published in Nature Medicine in October 2024.

“After two years of treatment with Elevidys, we are seeing multiple sustained benefits in the day-to-day lives of these young boys, all of which are indicators of its disease modifying potential in Duchenne,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. "These results, which include improvements in

* The pre-specified external control used contemporary datasets taken from three separate studies in Duchenne, two randomised controlled clinical trials and one natural history study, creating a prospectively defined consolidated comparison group of individuals with Duchenne, matched for variables, including age, steroid usage, baseline NSAA and timed function tests with the EMBARK part one treated patients. The prospectively defined propensity score analysis allows for a robust and rigorous balancing of multiple variables.

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standing, walking and running, represent meaningful progress and we plan to share them with health authorities as quickly as possible."

Individuals treated in part one of EMBARK (n=63) showed clinically meaningful and statistically significant improvements on the NSAA were sustained two years after treatment with Elevidys.

"As Duchenne progresses, children will lose the ability to walk, have difficulty breathing, and develop heart problems, all of which severely impact their health and ability to fully participate in life," said Professor Francesco Muntoni, Director of Dubowitz Neuromuscular Centre, Great Ormond Street Hospital for Children, UK. "Encouraging results from year two of the EMBARK trial suggest that with innovative treatments like Elevidys, the period of mobility and independence can potentially be improved, reducing the physical and emotional challenge Duchenne poses for these young boys and their families."

For individuals treated in part one, two years after treatment, functional motor improvements include:

Functional endpoints (treated in part one)	**Measure compared to the external control group (LSM mean difference)**
NSAA	+2.88 points (improvement), P<0.0001
TTR	-2.06 seconds (improvement), P<0.0033
10MWR	-1.36 seconds (improvement), P<0.0028

Individuals who received a placebo in part one crossed over at 52 weeks and were treated with Elevidys in part two. Despite being one year older than those treated in part one, the crossover treated group (n=59) experienced similar changes 52 weeks after treatment, favouring Elevidys compared to the external control. Individuals treated in part one were between the ages of four and seven years, and in part two, individuals were between the ages of five and nine years.

For individuals treated in part two, one year after treatment, functional motor improvements include:

Functional endpoints (treated in part two)	**Measures compared to the external control (pre-therapy baseline; LSM mean difference)**
NSAA	+2.34 points (improvement), P<0.0001
TTR	-2.70 seconds (improvement), P<0.0001
10MWR	-1.07 seconds (improvement), P=0.0001

Muscle biopsies from a subset of patients taken 64 weeks after dosing in part one showed consistent and sustained expression of micro-dystrophin, as measured by western blot. Muscle pathology on MRI continues to show minimal progression in underlying muscle pathology and remains highly consistent with the functional benefits shown.

No new safety signals were observed, reinforcing the consistent and manageable safety profile of Elevidys to date.

Elevidys is approved for people living with Duchenne aged four years old and over regardless of their ambulatory status in the US, United Arab Emirates (UAE), Qatar, Kuwait, Bahrain and Oman. Elevidys is also approved for the treatment of ambulatory individuals aged four through seven years in Brazil and Israel. Filings have also been submitted to the European Medicines Agency (EMA) and regulatory authorities in Japan, Switzerland, Singapore, Hong Kong and Saudi Arabia.

In 2019, Roche entered into a global collaboration agreement with Sarepta Therapeutics, Inc. to commercialise Elevidys in territories outside the U.S.

Elevidys clinical development programme

- 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.
- 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.
- 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.

- 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.
- 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.
- 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.
- 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). The study Is recruiting.
- 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 EMBARK

EMBARK is a multinational, phase III, 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 four to seven years at the beginning of the trial.

Eligible participants received a single dose of Elevidys during either part one or part two of the study. The study is complete.

Participants (n=126) received $1.33x10^{14}$ vector genomes per kilogram bodyweight (vg/kg) of Elevidys or placebo. In part one, participants were randomised according to age (4-5y or 6-7y) 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 two, participants crossed over - meaning, those who were previously treated with placebo in part one received Elevidys and participants who were previously treated with Elevidys received placebo, 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 included:

- The quantity of Elevidys micro-dystrophin protein expression at Week 12 as measured by western blot of biopsied muscle tissue
- 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 four steps

NSAA is a 17-item rating scale that is used to measure functional motor abilities and monitor disease progression in ambulant children with DMD.

About ELEVIDYS™

Elevidys™ (delandistrogene moxeparvovec, also known as SRP-9001) is the first approved disease-modifying gene 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 intravenous dose. Elevidys is contraindicated in individuals with any deletion in exons 8 and/or 9 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 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 Duchenne 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. As dystrophin is also deficient in vital organ systems such as the cardiovascular and respiratory systems, the effect is thus inevitably fatal, with an average survival limited to the third decade of life.

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.

For more information, please visit www.roche.com.

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