Media & Investor Release

Five-year data for Roche's Evrysdi show the majority of treated children with a severe form of spinal muscular atrophy (SMA) achieved or maintained the ability to sit, stand or walk

- **After five years of treatment, 91% of children were alive — without treatment, children with Type 1 SMA would not be expected to live past two years of age**
- **96% of Evrysdi-treated children could swallow, 80% could feed without a feeding tube and 59% could sit without support for at least 30 seconds**
- **Evrysdi is now approved in more than 100 countries with over 15,000 patients treated globally**

Basel, 07 June 2024 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today new five-year data confirming the sustained efficacy and safety profile of Evrysdi® (risdiplam) in children with Type 1 spinal muscular atrophy (SMA) from the open-label extension of the pivotal FIREFISH study. By the end of Year 5, 91% of children treated with Evrysdi were alive, 81% were alive without permanent ventilation and the majority were able to sit without support for at least 30 seconds (59%). At the end of year 5, seven children were able to stand, three with support, four unaided and six could walk with support. Without disease modifying treatment, natural history studies indicate that children with Type 1 SMA would not only never be able to reach such milestones, but also not typically live past the age of two. The data were presented at the Cure SMA Research & Clinical Care Meeting, June 5 - 7, 2024.

"These long-term findings confirm the ongoing benefit of Evrysdi for children with Type 1 SMA," said Professor Giovanni Baranello, M.D., UCL Great Ormond Street Institute of Child Health & Great Ormond Street Hospital, London, UK. "Children treated with Evrysdi over five years have maintained or improved their ability to sit, stand and walk - critical skills for development and daily living. An overwhelming majority also maintained the ability to swallow and to eat without a feeding tube."

Motor function abilities, as assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development Third Edition (BSID-III) and Hammersmith Infant Neurological Examination 2 (HINE-2), were maintained or continued to be achieved in those treated with Evrysdi. The FIREFISH results showed most children treated with Evrysdi also maintained their feeding and swallowing abilities; of those assessed at year 5, 96% were able to swallow and 80% were able to feed without a feeding tube.

"This is the final readout of the FIREFISH study, which has provided a wealth of insights and data, helping to firmly establish Evrysdi as an important treatment option, improving the lives of children across the globe living with SMA," said Levi Garraway, M.D., Ph. D., Chief Medical Officer and Head of Global Product Development. "This would not have been possible without

the commitment and dedication of the children and families who participated, as well as numerous healthcare professionals and patient support organisations to whom we are immensely thankful."

No treatment-related adverse events (AEs) led to treatment discontinuation or withdrawal from the study. The overall rate of AEs decreased by 66% between Year 1 and the final year of study. The most common AEs were upper respiratory tract infection (64%), pyrexia (64%) and pneumonia (50%). Hospitalisations declined over the 5-year treatment period and 22% of children did not require hospitalisation at all since beginning treatment with Evrysdi.

Evrysdi is the only oral, non-invasive small molecule SMA treatment designed to be systemically delivered to both the central nervous system (CNS) & peripheral tissues.

Roche leads the clinical development of Evrysdi as part of a collaboration with the SMA Foundation and PTC Therapeutics.

About Evrysdi® (risdiplam)

Evrysdi is a survival motor neuron 2 (*SMN2*) splicing modifier designed to treat SMA caused by mutations in chromosome 5q that lead to survival motor neuron (SMN) protein deficiency. Evrysdi is administered daily at home in liquid form either by feeding tube or by mouth.

Evrysdi is designed to treat SMA by increasing and sustaining the production of SMN protein in the CNS and peripheral tissues. SMN protein is found throughout the body and is critical for maintaining healthy motor neurons and core motor functions such as swallowing, speaking, and breathing.

Evrysdi was granted PRIME designation by the European Medicines Agency (EMA) in 2018 and Orphan Drug Designation by the U.S. Food and Drug Administration in 2017. In 2021, Evrysdi was awarded Drug Discovery of the Year by the British Pharmacological Society as well as the Society for Medicines Research Award for Drug Discovery. Evrysdi is currently approved in more than 100 countries, and the dossier is under review in a further 13 countries.

Evrysdi is currently being, or has been, evaluated in five global multicentre trials in people with SMA:

- FIREFISH (NCT02913482) – an open-label, two-part pivotal clinical trial in infants with Type 1 SMA. Infants were approximately 5.5 months of age (median) at the time of enrollment and of the 58 infants that completed the first year of treatment, 52 entered the open-label extension study.The study met its primary endpoint.
- SUNFISH (NCT02908685) – a two-part, double-blind, placebo-controlled pivotal study in people aged 2-25 years with Types 2 or 3 SMA. The study met its primary endpoint.

- JEWELFISH (NCT03032172) – an open-label exploratory trial designed to assess the safety, tolerability, pharmacokinetics and pharmacodynamics in people with SMA aged 6 months to 60 years who received other investigational or approved SMA therapies for at least 90 days prior to receiving Evrysdi. The study has completed recruitment (n=174).

- RAINBOWFISH (NCT03779334) – an open-label, single-arm, multicentre study, investigating the efficacy, safety, pharmacokinetics, and pharmacodynamics of Evrysdi in babies (n=26), from birth to six weeks of age (at first dose) with genetically diagnosed SMA who are not yet presenting with symptoms. The study met its primary endpoint.

- MANATEE (NCT05115110) – a phase 2/3 clinical study to evaluate the safety and efficacy of GYM329 (RG6237), an anti-myostatin molecule targeting muscle growth, in combination with Evrysdi for the treatment of SMA in patients 2-10 years of age. The FDA Office of Orphan Products Development granted GYM329 Orphan Drug Designation for the treatment of patients with SMA in December 2021. The study is currently recruiting.

About SMA

SMA is a severe, progressive neuromuscular disease that can be fatal. It affects approximately one in 10,000 babies and is the leading genetic cause of infant mortality. SMA is caused by a mutation of the survival motor neuron 1 (*SMN1*) gene, which leads to a deficiency of SMN protein. This protein is found throughout the body and is essential to the function of nerves that control muscles and movement. Without it, nerve cells cannot function correctly, leading to muscle weakness over time. Depending on the type of SMA, an individual's physical strength and their ability to walk, eat or breathe can be significantly diminished or lost.

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.

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 fifteenth 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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