Media & Investor Release

New four year data for Roche's Evrysdi reinforce long-term efficacy and safety profile in some of the most severely affected people with types 2 and 3 spinal muscular atrophy (SMA)

- **Data from pivotal SUNFISH study showed increases in motor function observed during the first year were maintained through the fourth year, while the overall rate of adverse events continued to decrease**
- **Data confirm long-term efficacy and safety profile of Evrysdi in a broad range of people with Type 2 and non-ambulant Type 3 SMA**
- **More than 8,500 people—from newborns to the over 60s—have been treated with Evrysdi, which is now approved in more than 90 countries worldwide**

Basel, 20th March 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new long-term data for Evrysdi® (risdiplam) in a broad range of people aged 2-25 years with spinal muscular atrophy (SMA) from the pivotal SUNFISH study[1]. Data confirm increases in motor function were sustained at four years and the overall rate of adverse events continued to decrease over the 48 month period, reinforcing the long-term efficacy and safety of Evrysdi. Participants also reported continuous improvement or stabilisation when independently performing activities of daily living such as eating, drinking and picking up and moving objects. The data were presented at the Muscular Dystrophy Association (MDA) Clinical and Scientific Conference, March 19-22, 2023.

"Preserving long-term independence and the ability to perform daily tasks is an important measure for people living with SMA and their caregivers. It's encouraging to see that Evrysdi has meaningfully affected this aspect of their lives," said Laurent Servais, M.D., Ph.D., Professor of Paediatric Neuromuscular Diseases at the MDUK Oxford Neuromuscular Centre. "This trial included people with Type 2 and 3 SMA, including patients with advanced disease. These latest data make us confident that the improvement observed during the first year of treatment is sustained during four years which contrasts with the decline we would observe in the absence of treatment."

The increase in motor function from baseline observed during the first year of the study was maintained through the fourth year of treatment with Evrysdi, as measured by changes in Motor Function Measure 32 (MFM-32) and Revised Upper Limb Module (RULM). Without treatment, natural history data show that patients with Type 2 or 3 SMA typically show a decline in motor function over time. Evrysdi was well-tolerated over the four-year time period. Adverse events (AEs) and serious adverse events (SAEs) were reflective of the underlying disease. The most commonly reported AEs include headache, fever (pyrexia) and upper

respiratory tract infection. No treatment-related AEs led to withdrawal from the study.

“These new data show that treatment with Evrysdi may help people with Type 2 or 3 SMA to maintain improvements in muscle strength and mobility over the course of several years,” said Levi Garraway, M.D., Ph. D., Chief Medical Officer and Head of Global Product Development. “The longer-term results of this study add to the robust body of findings from our broad clinical trial programme evaluating Evrysdi across a variety of ages, disease severities and treatment histories.”

In addition to bringing Evrysdi to people around the world, Roche also leads its clinical development as part of a collaboration with the SMA Foundation and PTC Therapeutics. Roche is currently investigating Evrysdi in combination with an anti-myostatin molecule targeting muscle growth in the Ph II/III trial Manatee for the treatment of SMA.

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 by mouth or by feeding tube.

Evrysdi is designed to treat SMA by increasing and sustaining the production of SMN protein in the central nervous system (CNS) and peripheral tissues. SMN protein is found throughout the body and is critical for maintaining healthy motor neurons and movement.

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 90 countries and the dossier is under review in a further 16 countries.

Evrysdi is currently being evaluated in five multicentre trials in people with SMA:

- FIREFISH (NCT02913482) – an open-label, two-part pivotal clinical trial in infants with Type 1 SMA. Part 1 was a dose-escalation study in 21 infants with the primary objective of assessing the safety profile of risdiplam in infants and determining the dose for Part 2. Part 2 is a pivotal, single-arm study of risdiplam in 41 infants with Type 1 SMA treated for 2 years, followed by an open-label extension. Enrolment for Part 2 was completed in November 2018. The primary objective of Part 2 was to assess efficacy as measured by the proportion of infants sitting without support after 12 months of treatment, as assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development – Third Edition (BSID-III) (defined

as sitting without support for 5 seconds). The study met its primary endpoint.

- SUNFISH (NCT02908685) – SUNFISH is a two-part, double-blind, placebo-controlled pivotal study in people aged 2-25 years with Types 2 or 3 SMA. Part 1 (n=51) determined the dose for the confirmatory Part 2. Part 2 (n=180) evaluated motor function using the total score of Motor Function Measure 32 (MFM-32) at 12 months. MFM-32 is a validated scale used to evaluate fine and gross motor function in people with neurological disorders, including 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 risdiplam in babies (~n=25), from birth to six weeks of age (at first dose) with genetically diagnosed SMA who are not yet presenting with symptoms. The study is fully enrolled.
- MANATEE (NCT05115110) – a global 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 endeavor 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.

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

References

[1] Oskoui, M et al. SUNFISH Parts 1 and 2: 4-year efficacy and safety of risdiplam in Types 2 and 3 spinal muscular atrophy (SMA). Poster presentation at the 2023 MDA Clinical & Scientific Conference.

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