Media & Investor Release

New data for Roche's Evrysdi (risdiplam) demonstrate long-term efficacy and safety in a broad population of people with spinal muscular atrophy (SMA)

- **Long-term efficacy data from the pivotal SUNFISH study confirm increases in motor function are sustained at three years while adverse events decreased over the same period**
- **Part 2 of SUNFISH showed Evrysdi demonstrated a marked improvement in, or stabilisation of, motor function after two years compared to an untreated external control group**
- **Latest interim results from the RAINBOWFISH study demonstrate that the majority of babies treated with Evrysdi for at least 12 months were able to stand and walk within timeframes typical of healthy babies**
- **More than 5,000 patients have been treated with Evrysdi to date, from newborns to people over 60 years of age**

Basel, 16 March 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new data for Evrysdi® (risdiplam) in spinal muscular atrophy (SMA). Presentations included new three-year data from the SUNFISH study which further confirmed the long-term efficacy and safety of Evrysdi in a broad population of people aged 2-25 years with Type 2 or Type 3 SMA. Additional presentations included exploratory two-year efficacy data from SUNFISH Part 2, demonstrating improvement in or stabilisation of motor function with Evrysdi compared to an untreated external control group. Roche also announced updated interim data from the RAINBOWFISH study in pre-symptomatic babies with SMA under two months of age. The data were presented at the Muscular Dystrophy Association (MDA) Clinical and Scientific Conference, March 13-16, 2022.

"The positive long-term efficacy and safety results for Evrysdi in this broad SMA population are important for physicians as they consider Evrysdi as a treatment option for their patients," said Laurent Servais, M.D., Ph.D., Professor of Paediatric Neuromuscular Diseases at the MDUK Oxford Neuromuscular Centre. "In treating people with SMA, our aim is to enable or preserve their independence and patients in the SUNFISH study reported continuous improvement or stabilisation in the level of help needed for daily living."

In the SUNFISH study, the increase in Motor Function Measure 32 (MFM32) total score from baseline previously observed at year one was maintained through year three in people treated with Evrysdi. The increases in Revised Upper Limb Module (RULM) and Hammersmith Functional Motor Scale Expanded (HFMSE) total scores from baseline were also sustained

between year one and year three.

Evrysdi was well-tolerated over the three-year time period in the SUNFISH study. The overall rate of adverse events (AEs) in SUNFISH decreased over three years, and a trend towards a lower rate of serious adverse events (SAEs) was observed in the third year of treatment. Overall, AEs and SAEs were reflective of the underlying disease and no treatment-related AEs led to withdrawal from the study.

In addition, for the first time an external comparator analysis has been done for SUNFISH two-year data with an untreated control group.

The weighted exploratory analyses of MFM total scores showed that in SUNFISH Part 2, the proportion of patients demonstrating a marked improvement (change ≥3 points) or stabilisation (change ≥0 points) were more likely in patients who were on Evrysdi for 24 months than those in the untreated comparator group. (p=0.025 and p=0.002 respectively).

“We are pleased that these long-term results further reinforce the safety and efficacy of Evrysdi and it is especially encouraging to see that adverse events decreased over time,” said Levi Garraway, M.D., Ph. D., Chief Medical Officer and Head of Global Product Development. “We remain committed to working towards continued access to Evrysdi for all appropriate patients with this progressive disease.”

Updated interim data from the RAINBOWFISH study were also shared, demonstrating the safety and efficacy of Evrysdi for newborns. In January, the U.S. Food and Drug Administration (FDA) granted priority review of a supplemental new drug application (sNDA) for the use of Evrysdi to treat pre-symptomatic babies under two months of age with SMA.

To date, more than 5,000 people have been treated with Evrysdi in clinical trials, compassionate use or real-world settings. 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 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 the survival motor neuron (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 76 countries and the dossier is under review in a further 29 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 (RO7204239), 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 commencing recruitment in Q1 2022.

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 in1896 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 recognizing 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.

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