Media & Investor Release

New three-year data for Roche's Evrysdi (risdiplam) show long-term improvements in survival and motor milestones in babies with Type 1 spinal muscular atrophy (SMA)

- **91% of infants treated with Evrysdi in the FIREFISH study were still alive at three years**
- **Infants treated with Evrysdi maintained or continued to improve in measures of motor function, including their ability to sit without support for 5 and 30 seconds**
- **Evrysdi has proven efficacy in infants and adults, with over 5,000 patients treated to date**

Basel, 29 April 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new three-year data from the FIREFISH study, including one-year data from the open label extension, reinforcing the long-term efficacy and safety of Evrysdi® (risdiplam) in infants with symptomatic Type 1 spinal muscular atrophy (SMA). The data showed an estimated 91% of infants (n=58) treated with Evrysdi were alive after three years of treatment. The Evrysdi-treated infants continued to improve or maintain motor functions, including the ability to swallow, sit without support, stand with support and walk while holding on, between two and three years of treatment. Without treatment, children with Type 1 SMA are never able to sit without support. The study also showed overall continued reductions in serious adverse events (SAEs) and hospitalisations over time.

The FIREFISH study evaluated the efficacy and safety of Evrysdi in infants aged 1-7 months at the time of enrolment with Type 1 SMA. The study was in two parts, with Part 1 being the dose-finding period and Part 2 evaluating the efficacy and safety at the dose selected in Part 1. The pooled population includes participants treated with Evrysdi at the approved dose for a minimum of three years. These long-term data will be presented at the 14th European Paediatric Neurology Society (EPNS) Congress, April 28 – May 2, 2022.

"These long-term results in babies treated with Evrysdi are very encouraging, with the vast majority improving or maintaining motor functions after three years. Without treatment, they would typically not survive beyond two years of age," said Levi Garraway, M.D., Ph. D., Chief Medical Officer and Head of Global Product Development. "Support for the compelling efficacy of Evrysdi continues to grow for a broad range of people, including infants with one of the most severe forms of SMA."

Infants treated with Evrysdi maintained or continued to improve in their ability to sit without support between 24-36 months. Among the infants with an available assessment (n=48) treated with Evrysdi, 32 infants maintained and four gained the ability to sit without support for at least five seconds since month 24, as assessed by the Gross Motor Scale of the Bayley

Scales of Infant and Toddler Development Third Edition (BSID-III). In addition, 20 infants maintained and 15 gained the ability to sit without support for at least 30 seconds. No infant who gained the ability to sit without support lost this ability after three years of treatment. The majority of infants treated with Evrysdi maintained the ability to feed orally and swallow up to month 36.

Most of the infants treated with Evrysdi continued to improve or maintain measures of the Hammersmith Infant Neurological Examination 2 (HINE-2) between 24-36 months, including being able to hold their heads upright (36 maintained, 3 gained and none lost the ability since month 24), pivot while sitting (15 maintained, 11 gained and none lost the ability), stand with support (6 maintained, 5 gained and 1 lost the ability) and walk while holding on (1 maintained, 2 gained and none lost the ability).

The most common adverse events (AEs) were pyrexia (60%), upper respiratory tract infection (57%), pneumonia (43%), constipation (26%), nasopharyngitis (24%), diarrhoea (21%), rhinitis (19%), vomiting (19%) and cough (17%). The most common SAEs were pneumonia (36%), respiratory distress (10%), viral pneumonia (9%), acute respiratory failure (5%) and respiratory failure (5%). The rate of AEs, including pneumonia, continued to decrease over time. The rate of SAEs similarly decreased, with a reduction of approximately 50% after each 12-month treatment period and a 78% reduction between the first and third year of treatment. All AEs and SAEs reported were reflective of the underlying disease and there were no treatment-related AEs leading to withdrawal or treatment discontinuation. The rate of hospitalisations decreased from 1.24 hospitalisations per patient year over 12 months to 0.70 hospitalisations over 36 months. No additional deaths have occurred since the primary analysis of FIREFISH, up to the data cut-off of this analysis (23 Nov 2021).

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 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 79 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 Q2 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 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 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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