Media & Investor Release

Four-year follow-up data for Roche's Evrysdi show continued increase in number of children with a severe form of spinal muscular atrophy (SMA) able to sit, stand and walk

- **Data from ongoing FIREFISH study confirm long-term efficacy and safety profile of Evrysdi in children with Type 1 SMA**
- **Ninety-one percent of children were alive at month 48**
- **More than 95% maintained the ability to swallow - without treatment they would have required feeding support and majority would have died within 2 years**
- **Evrysdi is now approved in 99 countries with more than 8,500 patients treated globally**

Basel, 30 June 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today new long-term data for Evrysdi® (risdiplam) from the open-label extension (n=50) of the pivotal FIREFISH study, reinforcing its sustained efficacy and safety profile in children with Type 1 spinal muscular atrophy (SMA). FIREFISH is a two-part study in babies aged 1-7 months at the time of enrolment. After four years of treatment with Evrysdi, many of the babies, now young children, continued to improve their ability to sit, stand and walk without support. All the Evrysdi-treated children who were alive at the time of the primary analysis were still alive at month 48.

Additionally, the majority of infants maintained their ability to feed by mouth and swallow up to month 48. Motor function was 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) and abilities were either maintained or improved over four years of Evrysdi treatment. Without treatment, children with Type 1 SMA are not expected to live past two years of age and are never able to sit without support. These data were presented at the Cure SMA Research & Clinical Care Meeting, June 28 – 30, 2023.

Among the infants treated with Evrysdi (n=58), 37 were able to sit without support for at least 5 seconds at month 48, compared to 35 at month 24 (BSID-III). In addition, 36 infants were able to sit without support for at least 30 seconds at month 48, up from 23 infants at month 24. Between month 24 and month 48, three infants gained the ability to stand alone and one infant gained the ability to walk alone.

"Evrysdi's oral route of administration allows the medicine to be distributed throughout the body, systemically increasing SMN protein production, the lack of which is the underlying cause of SMA," said Dr Giovanni Baranello, UCL Great Ormond Street Institute of Child Health

& Great Ormond Street Hospital, London, UK. “This has shown to help in delivering a meaningful impact on important functions of daily living including motor milestones, feeding and swallowing, which were maintained or improved in this long-term study, while also offering a tolerable safety profile.”

Evrysdi is the first and only small molecule pre-mRNA splicing modifier that targets survival motor neuron-2 (SMN2) for the treatment of SMA, and can be administered at home in liquid form by mouth or by feeding tube.

“The independence that comes with sitting, standing and walking is transformational for children with SMA, and their families, and we are very encouraged by how these skills increased over four years of Evrysdi treatment for many children in this study,” said Levi Garraway, M.D., Ph. D., Chief Medical Officer and Head of Global Product Development. “Nine out of 10 patients in our studies remain on Evrysdi long-term and these data underscore its importance as an option for people with SMA across a broad range of age and disease types.”

No treatment-related adverse events (AEs) led to treatment discontinuation or withdrawal from the study, and the rate of AEs decreased by 71% between the first and fourth 12 month periods. The most common AEs were pyrexia (62%), upper respiratory tract infection (62%) and pneumonia (48%). The rate of hospitalisations decreased over the study period.

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 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 other functions such as swallowing, speaking, breathing 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 99 countries and the dossier is under review in a further 18 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. 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=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

Spinal Muscular Atrophy (SMA) is a severe, progressive neuromuscular disease that can be fatal. It affects approximately one in 10,000 babies and is among 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 other functions such as swallowing, speaking, breathing 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, speak or breathe can be significantly diminished or lost.Spinal Muscular Atrophy (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

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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.sel, 02 June 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that

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.

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