Media & Investor Release

FDA approves Roche's Evrysdi for use in babies under two months with spinal muscular atrophy (SMA)

- **Approval based on interim RAINBOWFISH data which show pre-symptomatic babies treated with Evrysdi for at least one year were able to sit, stand and walk**
- **Prescribing information updated with FIREFISH data showing the majority of symptomatic babies treated with Evrysdi for at least two years could sit for at least five seconds**
- **Evrysdi has proven efficacy in babies, children and adults with more than 5,000 patients treated to date**

Basel, 31 May 2022 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the U.S. Food and Drug Administration (FDA) has approved a label extension for Evrysdi® (risdiplam) to include babies under two months old with spinal muscular atrophy (SMA). The approval is based on interim efficacy and safety data from the RAINBOWFISH study in newborns, which showed that the majority of pre-symptomatic babies treated with Evrysdi achieved key milestones such as sitting and standing with half walking after 12 months of treatment. Evrysdi is now approved in the US to treat SMA in children and adults of all ages.

Of the babies with 2 or 3 copies of the SMN2 gene (n=6), 100% were able to sit after one year of treatment with Evrysdi, 67% could stand and 50% of infants could walk independently. All infants were alive at 12 months without permanent ventilation.

"The approval of Evrysdi for pre-symptomatic babies is particularly important, as early treatment of SMA, before symptoms start to arise, can help babies to achieve motor milestones," said Richard Finkel, M.D., RAINBOWFISH Principal Investigator and Director of the Experimental Neuroscience Program at St. Jude Children's Research Hospital. "With the inclusion of SMA in newborn screening programmes, this approval provides the opportunity to start treating at home with Evrysdi soon after the diagnosis is confirmed."

As part of the label extension, the Evrysdi prescribing information has also been updated to include recent two-year pooled data from Parts 1 and 2 of the FIREFISH study, which demonstrate long-term efficacy and safety in symptomatic infants with Type 1 SMA. The study enrolled babies aged 1-7 months and after two years of treatment with Evrysdi at the recommended dose (n=58), 60% of infants were able to sit without support* for five seconds, 40% for 30 seconds and 28% of infants were able to stand.**

Without treatment, infants do not achieve these milestones in the natural history of the disease. There were no treatment-related adverse events leading to withdrawal. The most

common adverse reactions were upper respiratory tract infection (including nasopharyngitis, rhinitis), lower respiratory tract infection (including pneumonia, bronchitis), constipation, vomiting, and cough.

“The priority review and subsequent approval of Evrysdi for babies under two months of age speaks to the urgent ongoing need for additional treatment options for babies with SMA,” said Levi Garraway, M.D., Ph. D., Roche’s Chief Medical Officer and Head of Global Product Development. “Because of its efficacy in multiple settings, Evrysdi is now available for people with SMA from pre-symptomatic newborns to older adults. We are proud of this achievement, which has the potential to make a real difference to those living with SMA and their caregivers.”

Evrysdi is approved in 81 countries and the dossier is under review in a further 27 countries. More than 5,000 patients have now been treated worldwide 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 81 countries and the dossier is under review in a further 27 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 previously received other investigational or approved SMA therapies 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 risdiplam 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 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.

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

References

** Bayley Scales of Infant and Toddler Development – Third Edition*
*** Hammersmith Infant Neurological Examination (HINE-2)*

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