Media & Investor Release

European Commission approves Roche's Evrysdi for babies under two months old with spinal muscular atrophy (SMA)

- **Evrysdi available to treat people of all ages with SMA in the European Union, including babies from birth[1]**
- **Approval is based on interim data from ongoing RAINBOWFISH trial showing majority of Evrysdi-treated babies were able to stand and walk within timeframes typical of healthy babies by 12 months' treatment[2,3]**
- **Evrysdi is the only non-invasive SMA therapy and is approved in 100 countries with more than 11,000 patients treated globally**

Basel, 29 August 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the European Commission has approved the extension of the Evrysdi® (risdiplam) European Union (EU) marketing authorisation to include infants with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four SMN2 copies from birth to below two months.[1] Interim data from the ongoing RAINBOWFISH trial in pre-symptomatic babies from birth to six weeks with Type 1 SMA supported the marketing authorisation extension.

"The SMA community welcomes the European Commission's decision to extend the use of Evrysdi from birth," said Dr Nicole Gusset, President & CEO of SMA Europe. "Preserving motor neurons from the earliest age possible and preventing their irreversible loss can have a substantial impact on a person's future ability to move and function. We look forward to continued collaborative efforts to improve diagnosis, including newborn screening, and ensuring all individuals living with SMA have access to medicines."

"With this label extension, we can treat babies soon after birth with Evrysdi, allowing them the greatest chance to achieve the milestones of sitting, standing and walking, similar to healthy children," said Levi Garraway, M.D., Ph. D., Roche's Chief Medical Officer and Head of Global Product Development.

The European Commission approval is based on the RAINBOWFISH interim analysis (n=18), which included six babies with 2 or 3 copies of the SMN2 gene who completed at least one year of study assessments. Of these, 100% (6/6) were able to sit after one year of treatment with Evrysdi, 67% (4/6) could stand and 50% (3/6) could walk independently. All infants were alive at 12 months without permanent ventilation.

The RAINBOWFISH data show that the safety profile of Evrysdi in pre-symptomatic babies is consistent with the safety profile seen in previous trials with symptomatic SMA patients. The most common adverse reactions were fever, diarrhoea, rash, upper respiratory tract infection

(including nasopharyngitis, rhinitis), lower respiratory tract infection (including pneumonia, bronchitis), constipation, vomiting and cough.

Evrysdi was initially approved in Europe in March 2021 for the treatment of patients aged two months or older.[4] The approval was based on clinical trial data from the pivotal SUNFISH and FIREFISH studies.

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 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 100 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=26), 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.

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.

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 endeavour 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] European Commission. Evrysdi. Available at: https://ec.europa.eu/health/documents/community-register/html/h1531.htm Accessed August 2023.
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[3] Day JW, et al. Advances and limitations for the treatment of spinal muscular atrophy. BMC Pediatr. 2022;22(1):632.
[4] Evrysdi (risdiplam). Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/evrysdi-epar-product-information_en.pdf Accessed August 2023.

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