# Media & Investor Release

## CHMP recommends Roche's Evrysdi for babies under two months old with spinal muscular atrophy (SMA)

- **Positive recommendation is based on interim data from ongoing RAINBOWFISH trial which showed majority of Evrysdi-treated babies were able to stand and walk within timeframes typical of healthy babies by 12 months' treatment[1,2]**
- **If approved by the European Commission, Evrysdi will be available to treat people of all ages with SMA in the European Union, including babies from birth**
- **Evrysdi is now approved in 100 countries with more than 8,500 patients treated globally**

Basel, 21 July 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the EU Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion for the extension of the Evrysdi® (risdiplam) European Union (EU) marketing authorisation, which would include infants with genetically confirmed diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four *SMN2* copies, including from birth to below two months.[1] The recommendation is based on an interim analysis from the ongoing RAINBOWFISH trial in pre-symptomatic babies with Type 1 SMA from birth to six weeks. In SMA, early treatment is critical to counteract ongoing and irreversible loss of motor neurons.[3,4,5] A final decision regarding the approval is expected from the European Commission later this year.

"Treating babies with SMA early helps them to carry out daily activities such as sitting, standing, and walking," said Levi Garraway, M.D., Ph. D., Chief Medical Officer and Head of Global Product Development. "This CHMP recommendation is an important step towards treating babies from birth with an oral formulation, and is a testament to Evrysdi's impact on preserving precious muscle function and improving the daily lives of people with SMA."

The CHMP decision is based on the RAINBOWFISH interim analysis (n=18), which included 6 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.

F. Hoffmann-La Roche Ltd
4070 Basel
Switzerland
Group Communications
Roche Group Media Relations
Phone +41 61 688 88 88
www.roche.com

Evrysdi is currently approved in the EU for the treatment of patients aged two months or older.[6]

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=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.

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 Medicines Agency. Evrysdi. Available at https://www.ema.europa.eu/en/medicines/human/summaries-opinion/evrysdi-0. Accessed July 2023.
[2] Finkel RS, et al, on behalf of the RAINBOWFISH Study Group. RAINBOWFISH: Preliminary efficacy and safety data in risdiplam-treated infants with presymptomatic SMA. Poster presented at: Muscular Dystrophy Association Clinical and Scientific Conference. 2022; Nashville, TN.
[3] Day JW, et al. Advances and limitations for the treatment of spinal muscular atrophy. *BMC Pediatr*. 2022;22(1):632.
[4] Dangouloff T, et al. Clinical Evidence Supporting Early Treatment Of Patients With Spinal Muscular Atrophy: Current Perspectives. *Ther Clin Risk Manag*. 2019;15:1153-1161.
[5] Kong L, et al. Impaired prenatal motor axon development necessitates early therapeutic intervention in severe SMA. *Sci Transl Med*. 2021;13(578):eabb6871.
[6] Evrysdi (risdiplam). Summary of Product Characteristics. Available at https://www.ema.europa.eu/en/documents/product-information/evrysdi-epar-product-information_en.pdf. Accessed July 2023.

## Roche Group Media Relations

Phone: +41 61 688 8888 / e-mail: media.relations@roche.com

**Hans Trees, PhD**
Phone: +41 79 407 72 58

**Nathalie Altermatt**
Phone: +41 79 771 05 25

**Karsten Kleine**
Phone: +41 79 461 86 83

**Nina Mählitz**
Phone: +41 79 327 54 74

**Kirti Pandey**
Phone: +49 172 6367262

**Sileia Urech**
Phone: +41 79 935 81 48

## Roche Investor Relations

**Dr. Bruno Eschli**
Phone: +41 61 68-75284
e-mail: bruno.eschli@roche.com

**Dr. Sabine Borngräber**
Phone: +41 61 68-88027
e-mail: sabine.borngraeber@roche.com

**Dr. Birgit Masjost**
Phone: +41 61 68-84814
e-mail: birgit.masjost@roche.com

**Dr. Gerard Tobin**
Phone: +41 61 68-72942
e-mail: gerard.tobin@roche.com

## Investor Relations North America

**Loren Kalm**
Phone: +1 650 225 3217
e-mail: kalm.loren@gene.com