Media Release

FDA approves Roche's Evrysdi tablet as first and only tablet for Spinal Muscular Atrophy (SMA)

- **Evrysdi is the only non-invasive disease-modifying SMA treatment and is approved in over 100 countries**
- **Evrysdi tablet can be stored at room temperature and offers the same demonstrated efficacy and safety as the currently available oral solution**
- **New tablet formulation may provide greater freedom and independence for people with SMA thanks to simplified dose administration**

Basel, 12 February 2025 - Roche (SIX: RO, ROG; OTCQX: RHHBY), announced today that the U.S. Food and Drug Administration (FDA) has approved a New Drug Application (NDA) for an Evrysdi® (risdiplam) tablet for people living with spinal muscular atrophy (SMA). Evrysdi is the only non-invasive disease-modifying treatment for SMA. The 5 mg Evrysdi tablet can either be swallowed whole or dispersed in water.

"Evrysdi has robust potential to modify the SMA disease trajectory, and has already been used to treat thousands of patients to date. This approval marks another significant step forward," said Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development, Roche. "The Evrysdi tablet combines established efficacy with convenience, providing an additional flexible option for SMA management."

The approval of the Evrysdi tablet was based on the results of a bioequivalence study, which demonstrated that the 5 mg tablet, whether swallowed whole or dispersed in non-chlorinated drinking water (e.g., filtered water), and original oral solution provide comparable exposure to risdiplam. This means patients who take the tablet can expect the same established efficacy and safety as the Evrysdi oral solution. The Evrysdi oral solution will remain available for those on other doses of Evrysdi and for those who may prefer the oral solution.

"We cannot underestimate the value that comes with simplifying treatment administration and disease management for people who are living with SMA or those caring for them," said Kenneth Hobby, President of Cure SMA. "This new room temperature stable formulation option offers an additional choice that may more conveniently fit into daily living activities such as working, traveling, and education."

As part of the label extension, the Evrysdi prescribing information has been updated to include guidance on tablet administration and storage.

The new tablet, expected to be available in the coming weeks, is suitable for people two years of age or older who weigh more than 20 kgs (44 lbs).

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*) pre-mRNA splicing modifier designed to treat SMA

caused by mutations in chromosome 5q that lead to survival of motor neuron (SMN) protein deficiency. Evrysdi is administered daily at home or on the go, either in liquid form (by feeding tube or by mouth) or in the form of a tablet (by mouth only, swallowed whole or dispersed in water).

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 core functions.

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 (FDA) 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 more than 100 countries, with more than 16,000 people with SMA treated globally.

Evrysdi is currently being, or has been, evaluated in numerous global multicentre trials in people with SMA:

- FIREFISH (NCT02913482) – an open-label, two-part pivotal clinical trial in infants with Type 1 SMA. Infants were approximately five and a half months of age (median) at the time of enrolment and of the 58 infants that completed the first year of treatment, 52 entered the open-label extension study. The study met its primary endpoint and has concluded after five years of follow up.

- SUNFISH (NCT02908685) – a two-part, double-blind, placebo-controlled pivotal study in people aged two-25 years with Types 2 or 3 SMA. The study met its primary endpoint and has concluded after five years of follow up.

- JEWELFISH (NCT03032172) – an open-label exploratory trial designed to assess the safety, tolerability, pharmacokinetics and pharmacodynamics in people with SMA aged six months to 60 years who 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 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 met its primary endpoint.

- MANATEE (NCT05115110) – a Phase II/III 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 two to ten 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 active.

- HINALEA 1 (NCT05861986) and HINALEA 2 (NCT05861999) – Phase IV clinical studies to evaluate the effectiveness and safety of Evrysdi in patients under two years of age at enrolment, who received onasemnogene abeparvovec gene therapy either pre-

symptomatically or post-symptomatically, following a genetically confirmed diagnosis of 5q–autosomal recessive SMA. The studies are currently recruiting.

- PUPFISH (NCT05808764) – a Phase II, open-label study to investigate the pharmacokinetics and safety of Evrysdi in babies with SMA who are under 20 days of age (at first dose). The study is currently recruiting.

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.

For over 125 years, sustainability has been an integral part of Roche's business. As a science-driven company, our greatest contribution to society is developing innovative medicines and diagnostics that help people live healthier lives. Roche is committed to the Science Based Targets initiative and the Sustainable Markets Initiative to achieve net zero by 2045.

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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