Media & Investor Release

Roche's Evrysdi (risdiplam) granted FDA priority review for treatment of pre-symptomatic babies under 2 months of age with spinal muscular atrophy (SMA)

- **Interim data submitted to the FDA show majority of pre-symptomatic babies treated with Evrysdi for at least one year were able to sit, stand and walk within timeframes typical of healthy babies, as well as maintain swallowing**
- **Evrysdi is approved in 70 countries and submitted in a further 31 with more than 4,500 patients treated to date**

Basel, 25 January 2022 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the U.S. Food and Drug Administration (FDA) has granted priority review of a supplemental new drug application (sNDA) for the use of Evrysdi® (risdiplam) to treat pre-symptomatic babies under two months of age with spinal muscular atrophy (SMA). The sNDA submission incorporates interim data from the RAINBOWFISH study, which shows the majority of pre-symptomatic babies treated with Evrysdi achieved key milestones such as sitting, standing, walking and maintained the ability to swallow following 12 months of treatment.

"Treating very young babies with Evrysdi before SMA symptoms arise may help them to achieve milestones such as standing and walking within timeframes typical of healthy infants," said Levi Garraway, M.D., Ph. D., Roche's Chief Medical Officer and Head of Global Product Development. "Extending treatment access for the youngest members of the SMA community is crucial and we look forward to working with the FDA on this application."

Evrysdi is designed to treat SMA by increasing and sustaining 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's existing FDA label is for the treatment of SMA in adults, children and babies two months and older. If approved, Evrysdi would be the first medicine administered at-home for pre-symptomatic babies with SMA.

Initial interim data from the RAINBOWFISH study, presented at the World Muscle Society (WMS) Virtual Congress 2021, showed that of the babies included in the interim efficacy analysis, all (5/5), maintained the ability to swallow and were able to feed exclusively orally after 12 months of treatment. Eighty per cent (4/5) treated with Evrysdi for at least 12 months achieved milestones such as standing and walking independently within World Health Organization windows for healthy children. All participants (n=5) met HINE-2* motor milestones of head control, sitting upright, rolling and crawling after 12 months of treatment with Evrysdi.

No treatment related serious adverse events were reported in any of the babies treated with

Evrysdi through the interim safety analysis period (n=12). Four treatment emergent adverse events were reported, and all were resolved or were resolving with ongoing treatment with Evrysdi. The most common adverse events (AEs) were nasal congestion (33%), cough (25%), teething (25%), vomiting (25%), eczema (17%), abdominal pain (17%), diarrhoea (17%), gastroenteritis (17%), papule (17%) and pyrexia (17%). The AEs were reflective of the age of the babies rather than the underlying SMA. The RAINBOWFISH study is currently recruiting.

The latest results from the RAINBOWFISH study will be presented at the Muscular Dystrophy Association (MDA) Clinical and Scientific Conference in March 2022.

Roche leads the clinical development of Evrysdi as part of a collaboration with the SMA Foundation and PTC Therapeutics.

*Hammersmith Infant Neurological Examination, Section 2

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.

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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 70 countries and the dossier is under review in a further 31 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 (inclusion criteria) 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 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 currently recruiting.
- 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 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 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, neuromyelitis optica spectrum disorder, Alzheimer's disease, Huntington's disease, Parkinson's disease, Duchenne muscular dystrophy and autism spectrum disorder. 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

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics, as well as growing capabilities in the area of data-driven medical insights help Roche deliver truly personalised healthcare. Roche is working with partners across the healthcare sector to provide the best care for each person.
Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. In recent years, the company has invested in genomic profiling and real-world data partnerships and has become an industry-leading partner for medical insights.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. More than thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Moreover, for the thirteenth consecutive year, Roche has been recognised as one of the most sustainable companies in the pharmaceutical industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2020 employed more than 100,000 people worldwide. In 2020, Roche invested CHF 12.2 billion in R&D and posted sales of CHF 58.3 billion. 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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