Data for Roche's Evrysdi® (risdiplam) published in New England Journal of Medicine shows significant improvement in survival and motor milestones in babies with Type 1 spinal muscular atrophy (SMA)

- **FIREFISH Part 2 study showed treatment with Evrysdi helped babies stay free of permanent ventilation, sit without support and improve across a range of motor milestones**
- **Evrysdi has proven efficacy in adults, children and babies two months and older with over 4,000 patients treated to date**
- **SMA is the leading genetic cause of death in infants**

Basel, 29 July 2021 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the New England Journal of Medicine (NEJM) has published data from FIREFISH Part 2, a pivotal global study evaluating the efficacy and safety of Evrysdi® (risdiplam) in babies aged 1-7 months old with symptomatic Type 1 spinal muscular atrophy (SMA). The study met its primary endpoint with 29% of infants (12/41) sitting without support for at least five seconds* by month 12, a milestone not seen in the natural course of the disease. Safety for Evrysdi in the FIREFISH Part 2 study was consistent with its known safety profile.

"Without treatment, babies with Type 1 SMA are unlikely to survive beyond two years of age," said Professor Laurent Servais, M.D., Ph.D., FIREFISH investigator and Professor of Paediatric Neuromuscular Diseases at the MDUK Oxford Neuromuscular Centre. "Important motor milestones, such as sitting, rolling over and swallowing, are the fundamental building blocks that can help these babies achieve optimal outcomes with Evrysdi, potentially reducing the need for ventilation and increasing the rate of survival.'

At the time of the data analysis, the median duration of treatment with Evrysdi was 15.2 months and the median age was 20.7 months. At month 12, 93% (38/41) of infants were alive and 85% (35/41) were free from permanent ventilation. Without treatment, the median age of death or permanent ventilation was 13.5 months in a natural history cohort. Ninety percent (37/41) had a CHOP-INTEND** score increase of at least 4 points, with 56% (23/41) achieving a score above 40; the median increase was 20 points.

In addition, the study met one of its secondary endpoints with 78% (32/41) of infants classified as HINE-2*** responders, which evaluated motor function through head control, sitting, voluntary grasp, ability to kick, rolling, crawling, standing and walking. Infants were classified as HINE-2 responders if more motor milestones showed improvement than worsened.

"These data published in the New England Journal of Medicine validate results from Part 1 of the FIREFISH study that showed Evrysdi can help babies with SMA reach the significant milestone of sitting without support for at least five seconds," said Levi Garraway, M.D., Ph. D., Roche's Chief Medical Officer and Head of Global Product Development. "These results have been further confirmed in the recently presented 24 month data showing Evrysdi continued to improve motor function, doubling the number of babies able to sit without support from month 12. We will continue to work closely with governments and the SMA

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community to bring Evrysdi to as many people as possible."

Safety for Evrysdi in the FIREFISH Part 2 study was consistent with its known safety profile. The most common adverse events were upper respiratory tract infection (68%), pneumonia (39%), pyrexia (39%), constipation (20%), diarrhoea (10%) and maculopapular rash (10%). The most common serious adverse events were pneumonia (32%), bronchiolitis (5%), hypotonia (5%) and respiratory failure (5%). Three infants experienced fatal complications of their disease within the first three months of treatment. None of these were attributed by the investigator as related to Evrysdi.

In February 2021, 12 month results from the dose finding Part 1 of the FIREFISH study were published in NEJM.

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

*As assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development Third Edition (BSID-III)

**Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders
***Hammersmith Infant Neurological Examination 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.

Evrysdi is designed to treat SMA by increasing and sustaining the production of the survival motor neuron (SMN) protein. SMN protein is found throughout the body and is critical for maintaining healthy motor neurons and movement.

Evrysdi was granted orphan designation by the European Medicines Agency (EMA) in 2019, PRIME designation by the EMA in 2018 and Orphan Drug Designation by the U.S Food and Drug Administration in 2017. Evrysdi has been approved in 54 countries and submitted in a further 33 countries.

Evrysdi is currently being evaluated in four 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 Evrysdi in infants and determining the dose for Part 2. Part 2 is a pivotal, single-arm study of Evrysdi 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.

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, Roche 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 twelfth consecutive year, Roche has been recognised as one of the most sustainable companies in the Pharmaceuticals 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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