Roche presents new 2-year data for Evrysdi (risdiplam) in infants with Type 1 spinal muscular atrophy (SMA)

- **Exploratory efficacy data showed 88% of infants treated with Evrysdi were alive and did not require permanent ventilation at two years**
- **59% of infants were able to sit without support for at least 5 seconds**
- **No new safety signals were identified**
- **In August, the FDA approved Evrysdi for the treatment of SMA in adults and children 2 months and older**

Basel, 28 September 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new 2-year data from Part 1 of the pivotal FIREFISH study of Evrysdi™ (risdiplam) in infants aged 2-7 months with symptomatic Type 1 spinal muscular atrophy (SMA). The 2-year results in infants treated with the therapeutic dose of Evrysdi (17/21) showed that they continued to improve and achieve motor milestones.

This exploratory analysis showed that an estimated 88% of infants were alive and required no permanent ventilation at two years. In addition, at two years, 59% (10/17 vs. 7/17 at 1-year) of infants were able to sit without support for at least 5 seconds, assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development – Third Edition (BSID-III). Sixty-five percent (11/17 vs. 9/17 at 1-year) had maintained upright head control, 29% (5/17 vs. 2/17 at 1-year) could turn themselves over and 30% (5/17 vs. 1/17 at 1-year) were able to stand either supporting weight or with support. After two years of treatment with Evrysdi, 71% (12/17 vs. 10/17 at 1-year) of infants achieved a CHOP-INTEND* score of 40 points or more and all infants increased their score from month 12 to month 24. Of the infants alive at two years (n=14), 100% maintained the ability to swallow and 93% (13/14) were able to feed orally. Safety for Evrysdi in the FIREFISH study was consistent with its previously reported safety profile and no new safety signals were identified. The most common adverse events (n=21) included fever (pyrexia; 71%), upper respiratory tract infection (52%), cough (33%), vomiting (33%), diarrhea (29%) and respiratory tract infection (29%). The most serious adverse event that occurred in 24% of infants was pneumonia.

“We are highly encouraged by the results we are seeing in the second year of treatment with Evrysdi,” said Levi Garraway, M.D., Ph. D., Roche’s Chief Medical Officer and Head of Global Product Development. “These results build on the efficacy and safety demonstrated by Evrysdi in pivotal trials, and we look forward to continued assessments of both survival and motor function during long-term follow up for this first-of-its-kind treatment.”

At the time of the analysis, the youngest infant was 28.4 months and the oldest was 45.1 months of age. The median age at enrollment was 6.3 months. Of the 17 infants treated with the therapeutic dose, two experienced fatal complications of their disease at 8 and 13 months of treatment and one infant was withdrawn from the study and sadly died 3.5 months later. None of these were attributed by the

investigator as related to Evrysdi.

The data were presented at the virtual 25th International Annual Congress of the World Muscle Society.

Evrysdi is being studied in more than 450 people as part of a broad and robust clinical trial programme in SMA, with patients ranging from birth to 60 years old, and includes pre-symptomatic patients and those previously treated with other SMA-targeting therapies. Evrysdi is designed to treat SMA by increasing and sustaining the production of the survival of motor neuron (SMN) protein. SMN protein is found throughout the body and is critical for maintaining healthy motor neurons and movement. Roche leads the clinical development of Evrysdi as part of a collaboration with the SMA Foundation and PTC Therapeutics.

*Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders

About Evrysdi™ (risdiplam)
Evrysdi is a survival of 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.

The FDA approved Evrysdi for the treatment of SMA in adults and children 2 months of age and older. Risdiplam was granted PRIME designation by the European Medicines Agency (EMA) in 2018 and Orphan Drug Designation by FDA and EMA in 2017 and 2019, respectively. At this time, Evrysdi has been filed in 16 international markets: Australia, Brazil, Chile, India, Indonesia, Israel, Kuwait, Macedonia, Malaysia, Russia, Singapore, South Korea, Taiwan, Thailand, Ukraine and the United Arab Emirates. In addition, four health authorities worldwide are currently reviewing the application: Canada, China, EU and Switzerland.

Risdiplam 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 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 in 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 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 (PK) and pharmacodynamics (PD) 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 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 under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best

way possible.

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.

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 eleventh 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 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 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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