New two-year data show Roche's Evrysdi (risdiplam) continues to demonstrate improvement or maintenance of motor function in people aged 2-25 with Type 2 or Type 3 Spinal Muscular Atrophy (SMA)

- **SUNFISH Part 2 study population includes broad range of ages and disease severities, representing a real-world spectrum of people living with Type 2 or 3 SMA**
- **Evrysdi is the first and only at home SMA treatment approved by the FDA, and has proven efficacy across adults, children and infants 2 months and older**
- **More than 2,500 patients now treated with Evrysdi in clinical trial, compassionate use and real-world settings**

Basel, 16 March 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new exploratory 2-year longer-term data from Part 2 of SUNFISH, a global placebo-controlled study evaluating Evrysdi™ (risdiplam) in people aged 2-25 years with Type 2 or non-ambulant Type 3 spinal muscular atrophy (SMA). The study suggests that gains in motor function observed with Evrysdi treatment at month 12 continued to improve or were maintained at month 24 across primary and secondary endpoint measures. Based on the natural history of the disease, people with Types 2 and 3 SMA who remain untreated decline in motor function over time. These data will be presented at the 2021 Muscular Dystrophy Association (MDA) Virtual Clinical & Scientific Conference taking place from March 15-18.

"These results build on the one-year findings from the SUNFISH trial and importantly show the durability of improvement or stabilization of motor function through two years of treatment," said SUNFISH principal investigator Eugenio Mercuri, M.D., Ph.D., Department of Pediatric Neurology, Catholic University, Rome, Italy. "In addition, with no new safety signals identified, these second year results may support the favorable benefit-risk profile of Evrysdi over a longer period of time."

Patients in SUNFISH Part 2 ranged in age from 2-25 and were treated with Evrysdi (n=120) or placebo and Evrysdi (n=60; patients in the placebo arm received placebo for 12 months followed by Evrysdi treatment for 12 months). The study evaluated a number of exploratory 24-month endpoints, which provide important insights into motor function and its impact on daily life. Findings demonstrated that Evrysdi:

- Maintained motor function improvements between months 12 and 24 as measured by Motor Function Measure (MFM-32)*.
- Increased motor function as measured by Revised Upper Limb Module (RULM)** and the Hammersmith Functional Motor Scale-Expanded (HFMSE)*** between months 12 and 24.
- Stabilized motor function for patients who began treatment with Evrysdi after 12 months of placebo as measured by MFM-32, RULM and HFMSE.
- Increased total score change from baseline, as measured by the caregiver-reported SMAIS**** upper limb module, and the patient-reported SMAIS score stabilized between months 12 and 24.

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"These encouraging results confirm that the efficacy and safety of Evrysdi in people with Type 2 and Type 3 SMA can be sustained over time," said Levi Garraway, M.D., Ph. D., Chief Medical Officer and Head of Global Product Development. "Therefore, these findings further highlight the potential longer-term benefit this first-of-its-kind medicine can have for people of varying ages and levels of SMA disease severity."

Decreases in serious adverse events, high-grade adverse events and treatment-related adverse events were observed in the second year versus the first year in both treatment arms. The most common adverse events observed in the Evrysdi arm and the placebo and Evrysdi arm from 12-24 months were upper respiratory tract infection (15.8% and 10%, respectively), nasopharyngitis (21.7% and 16.7%, respectively), pyrexia (13.3% and 10%, respectively), headache (10% and 16.7%, respectively), diarrhea (7.5% and 10%, respectively), vomiting (11.7% and 13.3%, respectively) and cough (10% and 8.3%, respectively). The most common serious adverse events were pneumonia (6.7% and 0%, respectively) and influenza (0.8% and 0%, respectively).

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 of motor neuron 2 (SMN2) splicing modifier designed to treat SMA by increasing and sustaining 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. Evrysdi is administered daily at home in liquid form by mouth or by feeding tube.

The U.S. Food and Drug Administration (FDA) approved Evrysdi for the treatment of SMA in adults and children 2 months of age and older in August of 2020. In April, the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) recommended the approval of Evrysdi for the treatment of 5q SMA in patients 2 months of age and older, with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four SMN2 copies. Evrysdi 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 approved in seven countries and submitted in 57, including the EU 27 and Norway and Iceland.

Evrysdi is currently being evaluated in four multicenter 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. Enrollment 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, multicenter 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 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 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.

** MFM is a validated scale used to evaluate fine and gross motor function in people with neurological disorders, including SMA. It assesses 32 different motor functions from standing and walking through to use of hands and fingers.*
*** RULM is a scale designed to assess upper limb movement in people with SMA. It can capture progressive muscle weakness across the spectrum of the disease, reflective of the SUNFISH Part 2 study population.*
**** HFMSE is intended to be used in assessing the functional motor abilities of people with SMA who are able to sit and walk.*
***** SMAIS was developed to measure self-reported and caregiver-reported independence.*

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