Roche's Evrysdi continues to improve motor function and survival in babies with Type 1 Spinal Muscular Atrophy (SMA)

- **More than twice as many babies (61% vs. 29%) were able to sit without support for at least five seconds after 24 months compared to 12 months of treatment**
- **Evrysdi increased survival and reduced need for permanent ventilation**
- **Evrysdi has proven efficacy across adults, children and babies 2 months and older**

Basel, 15 April 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new 2-year data from Part 2 of FIREFISH, a Phase 2/3 global study evaluating Evrysdi™ (risdiplam) in infants aged 1-7 months at enrollment with symptomatic Type 1 spinal muscular atrophy (SMA). The data showed Evrysdi continued to improve motor function between months 12 and 24, including the ability to sit without support. The study also showed Evrysdi continued to improve survival, improve ability to feed orally and reduce the need for permanent ventilation*. Exploratory data suggested Evrysdi continued to improve the ability to swallow and reduce hospitalisations compared to the natural course of Type 1 SMA. Safety for Evrysdi was consistent with its established safety profile. These longer-term data build upon one-year pivotal findings from FIREFISH Part 2 and will be presented at the 73rd American Academy of Neurology (AAN) Annual Meeting being held virtually April 17-22, 2021.

"The natural course of Type 1 SMA shows us that, sadly, without treatment children are never able to sit without support and typically don't survive beyond the age of two," said FIREFISH investigator Dr. Basil Darras, Professor of Neurology at Harvard Medical School and Director of the Spinal Muscular Atrophy Program at Boston Children's Hospital. "It is encouraging to see that infants continued to improve after 12 months of treatment, with twice as many of those who received Evrysdi for two years able to sit without support for at least five seconds. Infants treated with Evrysdi also experienced a range of improvements in motor function abilities, a reduction in serious events typically caused by disease progression, such as the need for permanent ventilation or hospitalisation, and increased rate of survival."

The primary endpoint of the study was the percentage of infants able to sit without support for at least five seconds at month 12. At 12 months, infants treated with Evrysdi demonstrated improved ability to sit without support for at least five and 30 seconds. Twenty-four month data showed continued improvements from month 12, with 61% (25/41) vs. 29% (12/41) able to sit without support for at least five seconds and 44% (18/41) vs. 17% (7/41) able to sit without support for at least 30 seconds, as assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development Third Edition (BSID-III). Importantly, infants treated with Evrysdi maintained the ability to feed orally (92%; 35/38) at month 24. Further, exploratory data suggest similar maintenance in ability to swallow (95%; 36/38). In the natural course of the disease, infants with Type 1 SMA older than 12 months generally require feeding support.

*No tracheostomy or BiPAP ≥16 hours per day continuously for >3 weeks or continuous intubation >3 weeks, in the absence of, or following the resolution of, an acute reversible event

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Ninety-three percent of infants (38/41) were alive after 24 months of treatment. Eighty-three percent of patients (34/41) were alive and free from permanent ventilation after 24 months, an improvement compared to the natural course of the disease. There were no new deaths between months 12 and 24. Without treatment, the median age of death or permanent ventilation is 13.5 months. In addition, fewer hospitalisations were observed during the second year of treatment with Evrysdi compared with the natural course of the disease, with 34% of infants (14/41) not requiring hospitalisation during 24 months of treatment. Additional findings suggested that Evrysdi continued to improve measures of the Hammersmith Infant Neurological Examination 2 (HINE-2) at month 24 vs. month 12, including being able to hold their head upright (63% vs. 44%), roll from supine to prone (44% vs. 10%), stand with support (15% vs. 5%) and walk* (4% vs. 2%). Continued improvements were also observed in CHOP-INTEND** total score, with a larger percentage of patients achieving a score of at least 40 by month 24 (76%; 31/41) than month 12 (56%; 23/41). In the natural course of the disease, children with Type 1 SMA rarely reach a CHOP-INTEND total score of 40 points.

"These data highlight the real-world impact of this transformative medicine in babies with the most severe form of SMA. For example, all infants alive after 24 months of treatment were able to swallow which can help them to feed orally rather than through a tube," said Levi Garraway, M.D., Ph. D., Chief Medical Officer and Head of Global Product Development. "These results increase our understanding of how this first-of-its-kind treatment can extend the lives of babies with Type 1 SMA, providing much needed hope for their families."

The adverse events and serious adverse events observed were consistent with previous studies. The most common adverse events were upper respiratory tract infection (54%), pneumonia (46%), pyrexia (44%), constipation (29%), nasopharyngitis (17%), bronchitis (15%), diarrhea (15%) and rhinitis (12%). The incidence of serious pneumonia declined by approximately 3-fold between the first and second 12-month periods of FIREFISH Part 2. The most common serious adverse events were pneumonia (39%) and respiratory distress (7%). There were no drug-related adverse events leading to withdrawal or treatment discontinuation.

Roche leads the clinical development of Evrysdi as part of a collaboration with the SMA Foundation and PTC Therapeutics. More than 3,000 patients are now treated with Evrysdi in clinical trial, compassionate use and real-world settings.

*"Walk" includes patients able to "bounce" or "cruise"
**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 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 March 2021, the European Commission (EC) approved 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 has been approved in 39 countries and submitted in a further 33 countries.

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. Patients enrolled in Part 2 received the final dose of Evrysdi defined in Part 1. 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. Patients continued to be evaluated through 24 months of treatment for additional safety and efficacy findings. After 24 months, patients will enter a 3-year open-label extension phase and continue to receive Evrysdi at the same dose.
- 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. Patients in the placebo arm of Part 2 received placebo for 12 months followed by Evrysdi treatment for 12 months. 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

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