Roche announces results from Evrysdi (risdiplam) study in infants with Type 1 spinal muscular atrophy (SMA) published in New England Journal of Medicine

- **FIREFISH Part 1 data show treatment with Evrysdi at 12 months helped 90% of these infants survive without permanent ventilation and 33% sit without support, a key motor milestone not normally seen in the natural course of the disease**
- **The FDA approved Evrysdi in August 2020 as the first and only at home SMA treatment with proven efficacy in adults, children and infants 2 months and older**

Basel, 25 February 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the New England Journal of Medicine has published Evrysdi™ (risdiplam) data from the dose finding Part 1 of the pivotal FIREFISH study in infants with symptomatic Type 1 spinal muscular atrophy (SMA). The data show that treatment with Evrysdi at 12 months helped 90% (19/21) of these infants survive without permanent ventilation and 33% (7/21) sit without support for at least 5 seconds, which is not normally seen in the natural course of the disease. The study also found that treatment with Evrysdi increased the levels of survival of motor neuron (SMN) protein by a median 1.9-fold from baseline in the high-dose cohort at 12 months.

"Since Evrysdi was FDA approved in August, we have been inspired by the stories and sense of hope that we have heard from people living with SMA and their families about the impact Evrysdi has had in their lives," said Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development. "The publication of the data in the New England Journal of Medicine reinforces the value of Evrysdi as an important treatment option for SMA."

The exploratory efficacy analysis found that after 12 months of treatment, seven (33%; 7/21) 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). All seven infants who achieved this milestone received the high dose (41%; 7/17), which was the dose selected for the confirmatory Part 2 of the study. Nine of the infants in the high-dose cohort (53%; 9/17) had upright head control after 12 months of treatment, and one infant (6%; 1/17) was able to stand (bearing weight), as assessed by the Hammersmith Infant Neurological Examination Module 2 (HINE-2).

In the low- and high-dose cohorts, no infant lost the ability to swallow over 12 months, and 86% (18/21) were able to feed orally, either exclusively or in combination with a feeding tube at 12 months. In addition, 90% (19/21) of infants were alive without permanent ventilation after 12 months of treatment with Evrysdi. Three infants experienced fatal complications of their disease after approximately one, eight and 13 months of treatment, respectively. An additional infant passed away after the data cut-off with death occurring approximately 3.5 months after receiving the last dose of study drug. None of these have been attributed by the investigator as related to Evrysdi.

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The researchers also assessed motor function with the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND), a scale used for infants with Type 1 SMA. Results showed that 11 out of the 21 infants (52%) had a CHOP-INTEND total score of 40 points or higher. The CHOP-INTEND scale ranges from 0 to 64, with higher scores indicating better function.

The most common adverse events included fever (pyrexia; 52%), upper respiratory tract infections (43%), diarrhea (29%), cough (24%), vomiting (24%), constipation (19%) and pneumonia (19%). In total, 24 serious adverse events were reported as of the clinical data cut-off, with the most common including pneumonia in three infants and respiratory tract infection, viral respiratory tract infection, acute respiratory failure and respiratory distress in two infants each.

Among the 21 infants enrolled in Part 1 of the FIREFISH study, the median duration of treatment was 14.8 months at the time of analysis. The median age at enrollment was 6.7 months and symptom onset between the ages of 28 days to 3 months.

In September 2020, two-year results from FIREFISH Part 1 were presented and the exploratory efficacy data showed 88% of infants treated with Evrysdi were alive and did not require permanent ventilation at two years, and 59% of infants were able to sit without support for at least 5 seconds.

FIREFISH, an open-label, two-part pivotal study, was designed to assess Evrysdi safety, tolerability, efficacy, pharmacokinetics (PK) and pharmacodynamics (PD) in patients aged 1 to 7 months with Type 1 SMA. Part 1 evaluated several doses of Evrysdi and determined the therapeutic dose of 0.2 mg/kg for Part 2.

Evrysdi has been and continues to be studied in more than 450 people as part of a large and robust clinical trial program in SMA.

About Evrysdi™ (risdiplam)
Evrysdi is a survival of motor neuron 2 (SMN2) splicing modifier designed to treat SMA by increasing 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. 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. Evrysdi has been approved in seven countries and submitted in 57, including the EU 27, 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.

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