New Roche data for Evrysdi show improved motor function in pre-symptomatic babies after one year and confirm safety profile in previously treated people with spinal muscular atrophy (SMA)

- **Data from JEWELFISH, the first trial in a diverse population aged 1 to 60 years with SMA who received prior treatment, showed a consistent safety profile and >2-fold increase in SMN protein levels**
- **Pre-symptomatic babies with SMA treated with Evrysdi for at least one year were able to sit, stand and walk in preliminary data from RAINBOWFISH study**
- **Evrysdi has proven efficacy in adults, children and babies two months and older and is now approved in 44 countries worldwide**

Basel, 11 June 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new interim data from two studies of Evrysdi® (risdiplam); JEWELFISH and RAINBOWFISH. Data from JEWELFISH, an ongoing open-label study primarily evaluating the safety of Evrysdi in people aged 1 to 60 years who have been previously treated with another SMA-targeting therapy, including nusinersen and onasemnogene abeparvovec, showed the safety profile of Evrysdi and increase in SMN protein levels are consistent with those observed in other Evrysdi studies.

Interim exploratory efficacy data from JEWELFISH also suggest stabilization in motor function at one year of treatment as measured by change from baseline in motor function measure (MFM 32). A recent survey from SMA Europe showed that almost 97% of people living with SMA reported disease stabilisation as progress.

Preliminary efficacy data from RAINBOWFISH, an ongoing open label study evaluating Evrysdi in babies from birth to six weeks with pre-symptomatic SMA, showed that infants treated for 12 months achieved age appropriate motor milestones, including sitting, standing and walking, and improvements in motor function. These data will be presented at the 2021 Virtual SMA Research & Clinical Care Meeting from June 9-11 2021.

“These data from JEWELFISH add to the growing body of evidence supporting the use of Evrysdi in patients from one to 60 years of age,” said Levi Garraway, M.D., Ph. D., Roche’s Chief Medical Officer and Head of Global Product Development. “Moreover, the early findings from RAINBOWFISH in pre-symptomatic babies under two months old are very encouraging. Altogether, we are hopeful that Evrysdi will continue to help address unmet treatment needs of the diverse SMA community.”

The JEWELFISH study enrolled the broadest patient population ever studied in an SMA trial, including patients with SMA Types 1-3 who received prior treatment across a wide range of age and disease severities.

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Of the 174 people enrolled, 30% were teenagers and 35% adults, 62% had a HFMSE* score of less than 10 at baseline, 80% had scoliosis and 47% had undergone scoliosis surgery. Seventy-six people had previously been treated with nusinersen and 14 with onasemnogene abeparvovec. Evrysdi led to a sustained >2-fold increase in median SMN protein levels versus baseline in all patients who received prior treatment, irrespective of which treatment was previously received or SMA type.

The overall AE profile of Evrysdi treatment in pre-treated patients was consistent with that of treatment-naïve patients in FIREFISH and SUNFISH. The most common adverse events in all patients were upper respiratory tract infection (17%), pyrexia (17%), headache (16%), nausea (12%), diarrhea (11%), nasopharyngitis (10%) and vomiting (8%). The most common serious adverse events were pneumonia (2%) lower respiratory tract infection (2%), upper respiratory tract infection (2%) and respiratory failure (2%). There were no treatment-related adverse events leading to withdrawal or treatment discontinuation in JEWELFISH, with some patients receiving treatment for more than three years. The study is ongoing and the primary analysis will be conducted at month 24.

"Data from the JEWELFISH study, which included a diverse patient population with a high degree of motor impairment, show that Evrysdi has a favourable safety profile in patients previously treated with an SMA-targeting therapy," said Dr Claudia Chiriboga, Professor of Neurology and Pediatrics, Department of Neurology, Columbia University Medical Center, New York, USA. "Importantly, the data also suggest a stabilisation of motor function in trial participants. As a progressive disease, untreated patients with SMA typically show a decline in motor function over time."

Roche also presented preliminary efficacy data from RAINBOWFISH, which showed that of the five babies treated with Evrysdi for at least 12 months, all achieved sitting without support, rolling and crawling. Of the five, two had two SMN copies and three had >2 copies. Four of the infants were able to stand unaided and walk independently. In addition, four babies reached a maximum score of 64 on the CHOP-INTEND** scale, and one scored 63. Data on the primary endpoint, the number of infants sitting without support for at least five seconds, will be reported when all primary analysis patients have reached one year of treatment. Recruitment for RAINBOWFISH is ongoing.

The most common adverse events were nasal congestion (33%), cough (25%), teething (25%), vomiting (25%), eczema (17%), abdominal pain (17%), diarrhea (17%), gastroenteritis (17%), papule (rash; 17%) and pyrexia (fever; 17%). There were no adverse events leading to withdrawal or study discontinuation.

*Hammersmith Functional Motor Scale Expanded
**Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders

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 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 PRIME designation by the European Medicines Agency (EMA) in 2018 and Orphan Drug Designation by the U.S Food and Drug Administration in 2017. Evrysdi has been approved in 44 countries and submitted in a further 32 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 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 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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