Media & Investor Release

Positive new data for Roche's Evrysdi in largest trial ever undertaken in patients with previously-treated spinal muscular atrophy (SMA)

- **New two-year Evrysdi data show improvement or maintenance of motor function in people with SMA, a progressive neuromuscular disease that can be fatal**
- **The JEWELFISH study enrolled the broadest and most diverse patient population ever studied in an SMA trial**
- **Longer-term safety data consistent with that previously seen in earlier trials and low study drop-out rate**
- **Evrysdi has proven efficacy in babies, children and adults, with more than 7,000 patients treated to date worldwide**

Basel, 12 October 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new two-year data from the JEWELFISH study evaluating Evrysdi® (risdiplam) in people with Type 1, 2 or 3 SMA aged 6 months to 60 years at time of enrolment. Patients had been previously treated with other approved or investigational SMA-targeting therapies, including nusinersen (Spinraza(R)) or onasemnogene abeparvovec (Zolgensma(R)). Data showed Evrysdi improved or maintained motor function and led to rapid increases in SMN protein levels which were sustained after 2-years of treatment. These data will be presented at the 27th World Muscle Society (WMS) congress, 11-15 October 2022.

"The consistent safety profile and exploratory efficacy we have seen in the JEWELFISH study, the largest ever conducted in previously treated patients, reinforces Evrysdi as a meaningful treatment option across SMA populations," said Dr. Claudia Chiriboga, Professor of Neurology and Pediatrics, Department of Neurology, Columbia University Medical Center, New York, USA. "The findings add to our confidence when making treatment decisions for previously-treated patients in need."

The JEWELFISH study enrolled the broadest and most diverse patient population ever studied in an SMA trial. Of the 174 people enrolled, 36% (n=63) were adults, 63% (n=105) had a Hammersmith Functional Motor Scale Expanded (HFMSE) score of less than 10 at baseline, meaning their disease was very severe, and 83% (n=139) had scoliosis. Forty-four percent (n=76) of those enrolled had previously been treated with nusinersen (Spinraza), 41% (n=71) with olesoxime*, 8% (n=14) with onasemnogene abeparvovec (Zolgensma) and 7% (n=13) with RG7800*.

People with SMA are unable to produce enough survival motor neuron (SMN) protein, leading to debilitating and potentially fatal muscle weakness. The study showed Evrysdi led to a two-fold increase in median SMN protein levels versus baseline after 4 weeks of treatment in all

patient groups, irrespective of previous treatment. The SMN protein levels achieved after 4 weeks of treatment were maintained for over two years.

Observed through exploratory efficacy endpoints, the study also suggests maintenance of motor function was sustained at two-years of treatment as measured by change from baseline in Motor Function Measure 32 (MFM-32), Revised Upper Limb Module (RULM) and HFMSE total scores compared to the natural history of SMA in untreated patients. A recent survey conducted by patient advocacy group SMA Europe, more than 96% of people with SMA viewed disease stabilization as progress in terms of their expectations of treatment.

“These important data demonstrate the safety and efficacy of Evrysdi in a broad, real-world population of people previously treated with an SMA-targeting therapy, ” said Levi Garraway, M.D, Ph.D, Roche’s Chief Medical Officer and Head of Global Products. “Those enrolled in JEWELFISH had very severe disease, with over 80% having scoliosis, so maintaining motor function–especially for a progressive disease–can be potentially life-changing.”

The overall adverse event (AE) and serious adverse event (SAE) profiles observed with Evrysdi treatment in JEWELFISH were reflective of underlying disease. The rate of AEs decreased by more than 50% between the first and second 6-month period, and then remained stable thereafter. The rate of SAEs, including pneumonia, decreased throughout the 24-month period, with a total reduction of more than 50% by the second year. The most common AEs (reported in ≥ 12% of all patients:n=173) were pyrexia (24%), upper respiratory tract infection (21%), headache (18%), nasopharyngitis (16%), diarrhoea (14%), nausea (13%) and cough (12%). The most common SAEs (reported in less than >2% of all patients) were pneumonia (3%) respiratory failure (2%), respiratory distress (2%), lower respiratory tract infection (2%) and upper respiratory tract infection (2%). The most common AEs/SAEs were consistent with those observed in treatment-naïve patients in our other three trials. Low rates of discontinuation from the study were observed, with a 5% rate per year over the 24-month period.

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 SMN protein in the central nervous system (CNS) and peripheral tissues. 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. In 2021 Evrysdi was awarded Drug Discovery of the Year by the British Pharmacological Society as well as the Society for Medicines Research award for Drug Discovery. Evrysdi is currently approved in 91 countries and the dossier is under review in a further 18 countries.

Evrysdi is currently being evaluated in five 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 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 ongoing.

- MANATEE (NCT05115110) – a global phase 2/3 clinical study to evaluate the safety and efficacy of GYM329 (RO7204239), an anti-myostatin molecule targeting muscle growth, in combination with Evrysdi for the treatment of SMA in patients 2-10 years of age. The FDA Office of Orphan Products Development granted GYM329 Orphan Drug Designation for the treatment of patients with SMA in December 2021. 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, spinal muscular atrophy, neuromyelitis optica spectrum disorder, Alzheimer's disease, Huntington's disease, Parkinson's disease and Duchenne muscular dystrophy. 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

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

In recognizing our endeavor to pursue a long-term perspective in all we do, Roche has been named one of the most sustainable companies in the pharmaceuticals industry by the Dow Jones Sustainability Indices for the thirteenth consecutive year. This distinction also reflects our efforts to improve access to healthcare together with local partners in every country we work.

Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan.

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**RG7800 and olesoxime are no longer in development as investigational treatments for patients with SMA.*

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