Roche's Evrysdi approved by European Commission as first and only at home treatment for spinal muscular atrophy

- **Evrysdi has proven efficacy in adults, children and babies two months and older, as shown in two pivotal clinical trials**
- **Roche is actively engaging with health authorities in the EU to achieve broad and rapid access for people with SMA**
- **More than 3,000 patients now treated with Evrysdi in clinical trial, compassionate use and real-world settings**

Basel, 30 March 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Commission (EC) has approved Evrysdi™ (risdiplam) for the treatment of 5q spinal muscular atrophy (SMA) in patients two 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. SMA is a leading genetic cause of death in infants and 5q SMA is the most common form of the disease. The condition causes muscle weakness and progressive loss of movement and significant unmet need remains, particularly in adults living with this condition.

"Today's approval of Evrysdi, the first and only SMA treatment with proven efficacy that can be taken at home, potentially transforms treatment options for a broad range of people with SMA living in the EU," said Levi Garraway, M.D., Ph. D., Roche's Chief Medical Officer and Head of Global Product Development. "By avoiding the need for in-hospital administration, Evrysdi can reduce the treatment burden on those living with SMA, their caregivers and healthcare systems. We thank the SMA community for their partnership, the trust they have placed in us and their unyielding commitment to achieve this significant milestone."

The approval is based on data from two clinical studies, designed to represent a broad spectrum of people living with SMA: FIREFISH in symptomatic Type 1 infants aged 2 to 7 months and SUNFISH in symptomatic Type 2 and 3 children and adults aged 2 to 25 years. SUNFISH is the first and only placebo-controlled trial to include adults with Types 2 and 3 SMA. Evrysdi demonstrated a favourable efficacy and safety profile, with the safety profile established across both trials.

"We welcome today's approval of Evrysdi for people with SMA in Europe, and are proud of the role we have played in its development and of our partnership with Roche," said Dr Nicole Gusset, President of SMA Europe. "A recent survey conducted by SMA Europe showed that a large proportion of people with SMA in the EU were not receiving an approved treatment which leaves them feeling helpless and frustrated. It is vital that we work together with health authorities, regulators and industry to ensure we can get this medicine to the patients who need it as soon as possible."

Roche is working closely with reimbursement and assessment bodies in European countries to enable broad and rapid access to patients in need. Evrysdi will be accessible to patients in Germany in the coming days and in France from early April through the cohort Temporary Authorization for Use. Reimbursement dossiers

have been submitted in many countries in anticipation of today's decision by the European Commission to minimise any delay in patient access.

The decision from the European Commission follows a positive recommendation from the Committee for Medicinal Products for Human Use (CHMP) in February 2021. The review was completed under the accelerated assessment pathway for medicines, which is offered to medicines deemed to be of major interest for public health and therapeutic innovation. This approval is applicable to all 27 European Union member states, as well as Iceland, Norway, and Liechtenstein. Evrysdi was granted PRIME designation by the European Medicines Agency (EMA) in 2018 and Orphan Drug Designation in 2019. Maintenance of Orphan Drug Designation was recently confirmed by the Committee for Orphan Medicinal Products based on the assumption of Evrysdi's significant benefit over existing treatments. Evrysdi has been approved in 38 countries and submitted in a further 33 countries.

Roche leads the clinical development of Evrysdi as part of a collaboration with the SMA Foundation and PTC Therapeutics.

About FIREFISH
In FIREFISH, 29% (12/41; $p<0.0001$ compared to natural history) of infants treated with Evrysdi for 12 months were able to sit without support for at least five seconds, as assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development Third Edition. This is a key motor milestone never achieved in the natural history of Type 1 SMA. In addition, 93% of infants were alive and 85% were event-free (alive with no permanent ventilation). Furthermore, 5% (2/41) of infants were able to stand with support, as measured by the Hammersmith Infant Neurological Examination, and 83% were able to feed orally. Ninety per cent (37/41) had a CHOP-INTEND* score increase of at least 4 points, with 56% (23/41) achieving a score above 40; the median increase was 20 points. The median age at enrolment was 5.3 months.

About SUNFISH
In SUNFISH, children and adults treated with Evrysdi experienced a clinically meaningful and statistically significant improvement in motor function at 12 months (1.55 point mean difference; $p=0.0156$) compared to placebo (1.36 points [95% CI: 0.61, 2.11]; -0.19 points [95% CI: -1.22, 0.84], respectively), as measured by a change from baseline in the Motor Function Measure-32 (MFM-32) total score. Children and adults also experienced significant improvement in upper limb function, a key secondary endpoint, at 12 months (1.59 point mean difference; $p=0.0469$) compared to placebo (1.61 points [95% CI: 1.00, 2.22]; 0.02 points [95% CI: -0.83, 0.87] respectively), as measured by a change from baseline in the Revised Upper Limb Module (RULM). The median age at enrolment was nine years. Patients treated with Evrysdi for 2-years overall experienced maintenance of improvement in motor function between month 12 and month 24. The mean change from baseline for MFM32 was 1.83 (95% CI: 0.74, 2.92) and for RULM was 2.79 (95% CI: 1.94, 3.64).

*Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders

Evrysdi demonstrated a favourable efficacy and safety profile, with the safety profile established across the FIREFISH and SUNFISH trials. The most common adverse events were upper respiratory tract infection, pneumonia, nasopharyngitis, pyrexia, constipation, rhinitis, diarrhoea, headache, cough and vomiting. There were no treatment-related safety findings leading to withdrawal from either study.

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 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 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 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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