Roche receives positive CHMP opinion for Evrysdi, the first and only at home spinal muscular atrophy (SMA) treatment with proven efficacy in adults, children and infants two months and older

- **In two pivotal clinical studies, Evrysdi showed event-free survival and motor milestone improvements never previously achieved in the natural history of the disease**
- **More than 2,500 patients now treated with Evrysdi in clinical trial, compassionate use and real-world settings**
- **Evrysdi is approved in seven countries, submitted in 30 more**

Basel, 26 February 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) has recommended the approval of Evrysdi™ (risdiplam) for the treatment of 5q spinal muscular atrophy (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. SMA is a leading genetic cause of death in infants and 5q SMA is the most common form of the disease. SMA causes progressive muscle weakness and atrophy, and significant unmet need remains, particularly in adults living with this condition.

The CHMP recommendation was completed under the accelerated assessment pathway, which is offered to medicines deemed to be of major interest for public health and therapeutic innovation. A final decision regarding approval is expected from the European Commission in the next two months and will be applicable to all 27 European Union member states, as well as Iceland, Norway, and Liechtenstein. Evrysdi was approved by the U.S. Food and Drug Administration (FDA) in August 2020.

“Our close partnership with the SMA community has enabled the development of the first ‘at-home’ treatment for SMA in infants, children and adults with varying levels of disease severity, the majority of whom remain untreated,” said Levi Garraway, M.D., Ph. D., Roche’s Chief Medical Officer and Head of Global Product Development. “If approved, Evrysdi would represent a much-needed therapeutic option and we expect it to become the treatment of choice for people living with SMA and their families."

The CHMP recommendation 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.

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. A liquid medicine, Evrysdi is administered daily at home by mouth or feeding tube.

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.

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.

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.

More than 2,500 patients have now been treated with Evrysdi in clinical trials, compassionate use and real world settings, with patients ranging from birth to over 70 years of age and including those previously treated with other SMA-targeting therapies. Roche leads the clinical development of Evrysdi as part of a collaboration with the SMA Foundation and PTC Therapeutics.

Roche is actively engaged with reimbursement and assessment bodies in European countries to enable broad and rapid access to patients in need. Reimbursement dossiers are being submitted in many countries in advance of an expected European Commission decision to minimise any delay in patient access.

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

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 has been approved in seven countries (US, Chile, Brazil, Ukraine, South Korea, Georgia and Russia)

and submitted in a further 30 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 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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