Media Release

Roche provides regulatory update on risdiplam for the treatment of spinal muscular atrophy (SMA)

- **U.S. Food and Drug Administration (FDA) extends review time for risdiplam following agreed submission of additional data, including SUNFISH Part 2**
- **Roche has submitted filing applications for risdiplam in seven countries with submission in China imminent**
- **Risdiplam is being investigated in infants, children and adults with Type 1, 2 or 3 SMA**

Basel, 07 April 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY), today announced that the U.S. Food and Drug Administration (FDA) has extended the Prescription Drug User Fee Act (PDUFA) date for its review of the New Drug Application (NDA) of risdiplam with a decision expected by August 24, 2020. The extension is a result of the recent submission of additional data by Roche, including data from the pivotal SUNFISH Part 2 study, in close collaboration with the FDA. These data were recently presented at the 2nd International Scientific and Clinical Congress on Spinal Muscular Atrophy.

In November 2019, the FDA granted Priority Review for risdiplam with a decision for approval expected by May 24, 2020. In February 2020, based on discussions with the FDA, Roche submitted additional data which could help ensure access to risdiplam for a broad range of people living with the condition, if approved. This included 12-month efficacy and safety data from the pivotal SUNFISH Part 2 study (n=180), the only placebo-controlled study ever undertaken in people aged 2-25 years with Type 2 or 3 SMA. Given the volume of additional data submitted, the FDA requires more time for review.

“We strongly believe in the potential of risdiplam as a new therapeutic option and recognize that unmet need remains in the treatment of SMA,” said Levi Garraway, M.D., Ph.D., chief medical officer and head of Global Product Development. “We are working closely with the FDA to support the review of risdiplam. Our goal is to bring this therapy to infants, children and adults living with SMA as quickly as possible."

As part of our continued commitment to people living with SMA, Roche is pleased to announce that we have also submitted in Brazil, Chile, Indonesia, Russia, South Korea and Taiwan. Filing in China is imminent and we are currently on track to submit a Marketing Authorization Application (MAA) to the European Medicines Agency in mid-2020 as well as other international markets.

Roche leads the clinical development of risdiplam, an investigational, orally administered survival motor neuron-2 (SMN2) splicing modifier for SMA, as part of a collaboration with the SMA Foundation and PTC Therapeutics. Risdiplam is being studied in a broad clinical trial programme in SMA, with patients ranging from birth to 60 years old, and includes patients previously treated with other SMA-targeting therapies. The clinical trial population is designed to represent the broad, real-world spectrum of people living with this disease with the aim of ensuring access for all appropriate patients.

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About SMA
Spinal muscular atrophy (SMA) is a severe, inherited, progressive neuromuscular disease that causes devastating muscle atrophy and disease-related complications. It is the most common genetic cause of infant mortality and one of the most common rare diseases, affecting approximately one in 11,000 babies. SMA leads to the progressive loss of nerve cells in the spinal cord that control muscle movement. 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.

SMA is caused by a mutation in the survival motor neuron 1 (SMN1) gene that results in a deficiency of SMN protein. SMN protein is found throughout the body and increasing evidence suggests SMA is a multi-system disorder and the loss of SMN protein may affect many tissues and cells, which can stop the body from functioning.

About risdiplam
Risdiplam is an investigational survival motor neuron-2 (SMN2) splicing modifier for SMA and is an orally administered liquid. It is designed to durably increase and sustain SMN protein levels both throughout the central nervous system and in peripheral tissues of the body. It is being evaluated for its potential ability to help the SMN2 gene produce more functional SMN protein throughout the body.

Risdiplam is currently being evaluated in four multicentre trials in people with SMA:

- 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.
- 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. The primary objective of Part 1 was to assess the safety profile of risdiplam in infants and determine the dose for Part 2. Part 2 is a pivotal, single-arm study of risdiplam in 41 infants with Type 1 SMA treated for 24 months, followed by an open-label extension. Enrolment for Part 2 was completed in November 2018. The primary objective of Part 2 is 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).
- JEWELFISH (NCT03032172) – an open-label exploratory trial in people with SMA aged 6 months–60 years who have been previously treated with SMA-directed therapies. The study has completed recruitment.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 Roche in neuroscience
Neuroscience is a major focus of research and development at Roche. The company's goal is to develop treatment options based on the biology of the nervous system to help improve the lives of people with chronic and potentially devastating diseases.

Roche has more than a dozen investigational medicines in clinical development for diseases that include multiple sclerosis, spinal muscular atrophy, neuromyelitis optica spectrum disorder, Alzheimer's disease, Huntington's disease, Parkinson's disease, Duchenne muscular dystrophy and autism.

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 eleventh 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 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 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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