Roche's risdiplam meets primary endpoint in pivotal SUNFISH trial in people with type 2 or 3 spinal muscular atrophy

- **Study demonstrated statistically significant improvements in the overall study population with Type 2 or 3 SMA**
- **No treatment related safety findings leading to withdrawal seen in any risdiplam trial to date**
- **Data will be shared with health authorities globally, including the U.S. Food and Drug Administration (FDA)**

Basel, 11 November 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive data from the pivotal Part 2 of SUNFISH, a study evaluating risdiplam in people aged 2-25 years with Type 2 or 3 spinal muscular atrophy (SMA). The study met its primary endpoint of change from baseline in the Motor Function Measure 32 (MFM-32) scale after one year of treatment with risdiplam, compared to placebo. No treatment related safety findings leading to study withdrawal have been seen in any risdiplam trial to date. Safety for risdiplam was consistent with its known safety profile and no new safety signals were identified.

"The positive outcome of this trial is an important milestone for people with Type 2 or 3 SMA, too many of whom remain untreated," said Levi Garraway, M.D., Ph. D., Roche's Chief Medical Officer and Head of Global Product Development. "SUNFISH is the largest placebo-controlled study ever undertaken in Type 2 or 3 SMA patients. We thank the SMA community for their partnership and look forward to sharing these results with regulators and bringing risdiplam to people living with this condition."

Risdiplam is an investigational survival motor neuron-2 (SMN2) splicing modifier, designed to durably increase and sustain SMN protein levels both throughout the central nervous system and peripheral tissues of the body. Roche leads the clinical development of risdiplam as part of a collaboration with the SMA Foundation and PTC Therapeutics. Data from the SUNFISH study will be presented at an upcoming medical congress.

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 SMA-targeting therapies. The clinical trial population represents the broad real-world spectrum of people living with this disease with the aim of ensuring access for all appropriate patients.

About the SUNFISH Study
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.

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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, orally administered liquid survival motor neuron-2 (SMN-2) splicing modifier for SMA. It is designed to durably increase and sustain SMN protein levels both throughout the central nervous system and 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) – as above. Results will be presented at an upcoming medical congress.
- 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). Part 2 is ongoing.
- 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 is currently recruiting.
- 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 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 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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