Media Release

FDA grants priority review to Roche's risdiplam for spinal muscular atrophy

- **Filing submission includes 12-month data from pivotal FIREFISH and SUNFISH trials in a broad population of people living with Types 1, 2 or 3 SMA**

Basel, 25 November 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the U.S. Food and Drug Administration (FDA) has accepted the New Drug Application (NDA) and granted Priority Review for risdiplam, an investigational survival motor neuron-2 (SMN-2) splicing modifier for SMA. Risdiplam is designed to increase and sustain SMN protein levels both throughout the central nervous system and peripheral tissues of the body. The FDA is expected to make a decision on approval by May 24, 2020.

"The FIREFISH and SUNFISH trials were designed to represent the real world spectrum of people living with SMA and include many people previously underrepresented in clinical trials," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We look forward to working closely with the FDA to explore broad access to risdiplam for all individuals in the community who might benefit."

The risdiplam NDA submission incorporates 12-month data from the dose-finding Part 1 sections of the FIREFISH and SUNFISH pivotal studies, as well data from the confirmatory Part 2 of SUNFISH. FIREFISH is an open-label, two-part pivotal clinical trial in infants with Type 1 SMA. Part 1 was a dose-escalation study in 21 infants aged one to seven months. The primary objective of Part 1, which evaluated efficacy as an exploratory endpoint, was to assess the safety profile of risdiplam in infants and determine the dose for Part 2, which is a pivotal, single-arm trial evaluating risdiplam in 41 infants with Type 1 SMA for 24 months, followed by an open-label extension.

SUNFISH is a two-part, double-blind, placebo-controlled pivotal clinical trial in children and young adults (2-25 years old) with Type 2 or 3 SMA. Part 1 determined the dose for the confirmatory Part 2, and evaluated efficacy as an exploratory endpoint. SUNFISH Part 2 is a large placebo-controlled trial evaluating treatment for people with Type 2 or 3 SMA. SUNFISH Part 2 recently met its primary endpoint of change from baseline in the Motor Function Measure 32 (MFM-32) scale.* 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. Results will be presented at an upcoming medical congress.

If approved, risdiplam, an orally administered liquid, would be the first at-home administered medicine for people living with SMA. In addition to the studies included in the NDA submission, risdiplam is being studied in a broad clinical trial programme in SMA, with patients ranging from newborns to 60 years old, and includes patients previously treated with SMA therapies.

**MFM-32 is a validated scale used to evaluate fine and gross motor function in people with neurological disorders, including SMA*

F. Hoffmann-La Roche Ltd 4070 Basel Switzerland | Group Communications Roche Group Media Relations | Tel. +41 61 688 88 88 www.roche.com

Roche leads the clinical development of risdiplam as part of a collaboration with the SMA Foundation and PTC Therapeutics, and would commercialize the medicine in the United States if approved.

Priority Review designation is granted to medicines that the FDA considers to have the potential to provide significant improvements in the safety and effectiveness of the treatment, prevention or diagnosis of a serious disease. Previously, the FDA also granted Orphan Drug Designation for risdiplam in January 2017, followed by Fast Track Designation in April 2017.

About spinal muscular atrophy
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 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 multicenter trials in people with SMA.

- FIREFISH (NCT02913482) – an ongoing open-label, two-part pivotal clinical trial in infants with Type 1 SMA.
- SUNFISH (NCT02908685) – a two-part, double-blind, placebo-controlled pivotal clinical trial in children and young adults (two to 25 years old) with Type 2 or 3 SMA.
- JEWELFISH (NCT03032172) – an open-label exploratory trial in people with SMA Type 1, 2 or 3, aged 6 months to 60 years who have been previously treated with SMN-targeting therapy, gene therapy or olesoxime. 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 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.

Roche Group Media Relations
Phone: +41 61 688 8888 / e-mail: media.relations@roche.com
- Nicolas Dunant (Head)
- Patrick Barth
- Daniel Grotzky
- Karsten Kleine
- Nathalie Meetz
- Barbara von Schnurbein