Roche announces new data for risdiplam in Spinal Muscular Atrophy (SMA) at the World Muscle Society Congress

- **Preliminary findings from Part 1 of the FIREFISH study show that infants with Type 1 SMA are meeting developmental milestones including sitting without support**
- **Preliminary data from Part 1 of the SUNFISH study show improvements in motor function in people with Type 2/3 SMA**
- **No drug-related safety findings leading to withdrawal in risdiplam trials to date**

Basel, 3 October 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced interim clinical data from the dose-finding parts of the pivotal FIREFISH and SUNFISH studies investigating risdiplam (RG7916) in SMA. In the FIREFISH study in Type 1 SMA, six out of 14 infants (43%) were able to sit (with or without support), including three (21%) who achieved unassisted stable sitting after eight months of treatment. In addition, four infants (29%) demonstrated rolling to the side; seven (50%) kicking and six (43%) achieved upright head control. These milestones were assessed according to the Hammersmith Infant Neurological Examination (HINE) Module 2 and are key secondary endpoints in the confirmatory part of FIREFISH.

The data were presented at the 23rd International Annual Congress of the World Muscle Society in Mendoza, Argentina. Roche is leading the clinical development of risdiplam, an oral SMN2 splicing modifier, as part of a collaboration with the SMA Foundation and PTC Therapeutics.

“We are highly encouraged by these data showing infants treated with risdiplam surviving and achieving developmental milestones beyond the natural history of this devastating disease,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “SMA therapies that produce a sustained increase in SMN protein in both the CNS and periphery may provide comprehensive benefits to people diagnosed with SMA, and we look forward to sharing additional data on risdiplam as the clinical program progresses.”

Updated analyses of the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND), a scale developed to assess motor function in infants with Type 1 SMA, demonstrated that eight out of 14 infants in FIREFISH (57%) achieved a score of 40 or above at their eight month visit. Typically, an infant with Type 1 SMA does not demonstrate any motor improvement and can decline during this time period. The median CHOP-INTEND scores increased over time (37.5 at 6 months [n=20] compared to 41.5 at eight months [n=14]). The median age at first dose in FIREFISH was 6.7 months and median treatment duration was 9.5 months. Nineteen out of 21 infants enrolled (90%) remain alive with two having discontinued due to the fatal progression of their disease. Three patients are now over 24 months old. No infant has required a tracheostomy or permanent ventilation since study initiation, and no infant has lost the ability to swallow. The most common adverse events were fever (pyrexia; 52.4%), diarrhea (26.8%), upper respiratory tract infections (19%), ear infections (14.3%), pneumonia (14.3%), constipation (14.3%), vomiting (14.3%), cough (14.3%) and upper respiratory tract inflammation (14.3%).

F. Hoffmann-La Roche Ltd 4070 Basel Switzerland
Investor Relations email: investor.relations@roche.com
Tel. +41 61 68-88880 Fax +41 61 69-10014 www.roche.com

In Part 1 of the SUNFISH study in Type 2 and 3 SMA, SMN protein median increases of greater than 2-fold, as measured in blood, were seen after 12 months. A very broad patient population aged between 2-24 years was included, ranging in functional status from weak non ambulant to strong ambulant, and with varying degrees of scoliosis from none to severe. Twenty-one patients initially received lower doses of risdiplam for at least 12 weeks. Of the patients treated with risdiplam for at least one year (n=30), the median change from baseline in Motor Function Measure (MFM), the primary endpoint in the confirmatory part of SUNFISH and a scale used to assess motor function in neuromuscular diseases, was a 3.1 point improvement. Sixty-three percent of patients experienced an improvement in MFM over baseline of three points or more after one year. Such improvements were seen both in patients under 12 years old (76%; n=17) and above 12 years old (46%; n=13). When considering patients who experienced any amount of improvement over baseline, the percentages were 70% overall, 76% for the younger age group, and 62% for the older patients. Serious adverse events that occurred in two or more of the 51 patients exposed to risdiplam were nausea (4%), upper respiratory tract infection (4%), and vomiting (4%). To date there have been no drug-related safety findings leading to withdrawal from any study.

Follow up is ongoing for the confirmatory Part 2 portions of both the FIREFISH and SUNFISH studies.

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 throughout the body.

About risdiplam

Risdiplam is an investigational, oral medicine that is systemically distributed and designed to increase SMN protein levels in the CNS and throughout the body. It is designed to help the SMN2 gene produce more functional SMN protein, to better support motor neurons and muscle function.

Roche is leading the clinical development of risdiplam in collaboration with the SMA Foundation and PTC Therapeutics. Risdiplam is currently being evaluated in three multicentre trials in people with SMA:

- FIREFISH – an open-label trial in infants aged 1-7 months with Type 1 SMA
- SUNFISH – a double-blind, placebo-controlled trial in children and young adults (2-25 years old) with Type 2 and 3 SMA
- JEWELFISH – an open-label exploratory trial in people aged 12–60 with Type 2 or 3 SMA who have been previously treated with SMN-targeting therapy as part of a clinical study

A new trial, RAINBOWFISH in pre-symptomatic SMA, will be initiated by early 2019.

About FIREFISH
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. 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 approximately 40 infants with Type 1 SMA for 24 months, followed by an open-label extension. 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).

About SUNFISH
SUNFISH is a two-part double-blind, placebo-controlled pivotal clinical trial in children and young adults (2-25 years old) with Type 2 and 3 SMA. Part 1 determined the dose for the confirmatory Part 2 and enrolment in Part 2 completed in September 2018.

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, Alzheimer's disease, spinal muscular atrophy, Parkinson's disease, Huntington's disease and autism spectrum disorder.

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. 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 tenth consecutive year, Roche has been recognised as the most sustainable company 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 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 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.

Roche Investor Relations

Dr. Karl Mahler
Phone: +41 61 68-78503
e-mail: karl.mahler@roche.com

Jon Kaspar Bayard
Phone: +41 61 68-83894
e-mail: jon_kaspar.bayard@roche.com

Dr. Sabine Borngräber
Phone: +41 61 68-88027
e-mail: sabine.borngraeber@roche.com

Dr. Bruno Eschli
Phone: +41 61 68-75284
e-mail: bruno.eschli@roche.com

Dr. Birgit Masjost
Phone: +41 61 68-84814
e-mail: birgit.masjost@roche.com

Dr. Gerard Tobin
Phone: +41 61 68-72942
e-mail: gerard.tobin@roche.com

Investor Relations North America

Loren Kalm
Phone: +1 650 225 3217
e-mail: kalm.loren@gene.com

Lisa Tuomi, Ph.D.
Phone: +1 650 467 8738
e-mail: tuomi.lisa@gene.com