

## **Roche's Risdiplam meets primary endpoint in pivotal FIREFISH trial in infants with type 1 spinal muscular atrophy**

- **Risdiplam demonstrated statistically significant and medically meaningful motor milestone improvement in infants with Type 1 SMA**
- **No treatment related safety findings leading to withdrawal seen in any risdiplam trial to date**
- **Data will be shared with health authorities globally**

Basel, 23 January 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive topline results from the pivotal Part 2 of the FIREFISH study, evaluating risdiplam in infants aged 1-7 months with Type 1 spinal muscular atrophy (SMA). The primary outcome measure of the study was the proportion of infants sitting without support for at least five seconds at 12-months of treatment, assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development Third Edition (BSID-III). Safety for risdiplam in the FIREFISH study was consistent with its known safety profile and no new safety signals were identified. To date, more than 400 patients have been treated with risdiplam across all studies, with no treatment related safety findings leading to study withdrawal in any risdiplam trial.

“This large, global trial confirms the efficacy of risdiplam in an advanced and difficult-to-treat population, including many infants whose disease had already progressed significantly before starting treatment,” said Levi Garraway, M.D., Ph. D., Roche's Chief Medical Officer and Head of Global Product Development. “We are very encouraged by these results and we look forward to sharing them with regulators. We also thank the entire SMA community for their continued partnership.”

Risdiplam is an investigational survival motor neuron-2 (SMN2) splicing modifier, designed to increase and sustain SMN protein levels throughout the central nervous system and in peripheral tissues. Roche leads the clinical development of risdiplam as part of a collaboration with the SMA Foundation and PTC Therapeutics. Data from the FIREFISH 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.

On November 11 2019, Roche announced positive results from Part-2 of SUNFISH, a study evaluating the efficacy and safety of risdiplam in people aged 2-25 years with Type 2 or 3 SMA. Also in November 2019, the U.S Food and Drug Administration granted Priority Review for risdiplam with a decision for approval by May 24, 2020.

### **About the FIREFISH study**

FIREFISH is a two-part, open-label, pivotal study in infants aged 1-7 months with Type 1 SMA. Part 1 (n=21) assessed the safety profile of risdiplam and determined the dose for Part 2. Part 2 (n=41) assessed efficacy as measured by the proportion of infants sitting without support after 12 months of treatment, and longer, assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development – Third Edition (defined as sitting without support for 5 seconds).

### **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 (SMN-2) 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:

- FIREFISH (NCT02913482) – as above. Results will be presented at an upcoming medical congress.
- SUNFISH (NCT02908685) – a two-part, double-blind, placebo-controlled pivotal clinical trial in people aged 2–25 years with Type 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. Part 2 met its primary endpoint in November 2019. Data will be presented at an upcoming medical congress.
- 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 close to completing 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 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](http://www.roche.com).

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