

## **PRIME designation granted by European Medicines Agency for Roche's risdiplam for treatment of spinal muscular atrophy (SMA)**

- **Risdiplam has the potential to be the first oral medicine for the treatment of SMA Types 1, 2 and 3; a rare and debilitating genetic disease most commonly diagnosed in children**
- **European Medicines Agency PRIME (PRiority MEDicines) status is granted to medicines that may offer a major therapeutic advantage over existing treatments, or benefit patients without treatment options**
- **Risdiplam is currently being investigated in three global, multicentre clinical trials in all types of SMA**

Basel, 17 December 2018 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Medicines Agency (EMA) has granted PRIME (PRiority MEDicines) designation for the company's investigational oral medicine risdiplam (RG7916) for the treatment of people with SMA. PRIME designation is granted by the EMA to support data generation and development plans for promising medicines, providing a pathway for accelerated evaluation by the agency, and thus potentially enabling them to reach patients earlier.<sup>[1]</sup> Risdiplam, an orally administered, survival motor neuron-2 (SMN2) gene splicing modifier, has shown improvements in motor function in people with SMA Types 1, 2 and 3.<sup>[2,3]</sup> An increasing body of clinical evidence suggests that SMA is a multisystem disorder, and the loss of SMN protein may affect many tissues and cells beyond the central nervous system.<sup>[4]</sup> Risdiplam is systemically distributed and designed to durably increase SMN protein levels in the central nervous system and throughout the body.<sup>[5]</sup>

Roche leads the clinical development of risdiplam as part of a collaboration with the SMA Foundation and PTC Therapeutics.

“SMA is the leading genetic cause of death in young children, and families and clinicians continue to seek alternative treatment options for this progressively debilitating and life-threatening disease,” said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. “The EMA's decision to grant PRIME designation recognises the potential of the oral systemic agent risdiplam to deliver clinically meaningful results for patients and address a continuing medical need in SMA.”

PRIME designation for risdiplam is based on data from Part 1 of the pivotal studies FIREFISH (evaluating safety and determining dosage in infants with Type 1 SMA) and SUNFISH (in children and adults with Type 2 and 3 SMA) as well as a continuing medical need for alternative treatments and administration options for patients with SMA.

Interim data from Part 1 of the FIREFISH study, shared at the World Muscle Society Congress (WMS) 2018, showed that infants with Type 1 SMA treated with risdiplam met developmental milestones, including sitting without support.<sup>[3]</sup>

<b>Motor function and milestones achieved in FIREFISH Part 1*<sup>[3]</sup></b>	
Measurement after 8 months of treatment	Patients (n=14)
Patients sitting with or without support, as defined by the Hammersmith Infant Neurological Examination (HINE-2), % (n)	43% (6)
Patients sitting without support, as defined by HINE-2, % (n)	21% (3)

\*Data cut-off: 7 September 2018

Nineteen of 21 risdiplam-treated patients (90%) remained alive with two having discontinued due to the fatal progression of their disease.<sup>[3]</sup> No infant required a tracheostomy or permanent ventilation since study initiation, and no infant has lost the ability to swallow.<sup>[3]</sup> The most common adverse events were fever (pyrexia; 52.4%), diarrhoea (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%).<sup>[3]</sup>

Interim data from Part 1 of the SUNFISH study in Type 2 and 3 SMA, also presented at WMS 2018, demonstrated a median >2-fold increase in SMN protein levels in the blood following 12 months of treatment.<sup>[2]</sup> Of the patients treated with risdiplam for at least 1 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.

<b>Motor function achieved in SUNFISH Part 1*<sup>[2]</sup></b>			
Endpoint	>12 months' treatment		
Motor Function Measure (MFM)	All patients (n=30)	Age 2–11 (n=17)	Age 12–24 (n=13)
Proportion of patients who achieved improvement (i.e. a change from baseline in MFM score $\geq 3$ ), % (n)	63.3% (19)	76.5% (13)	46.2% (6)

\*Data cut-off: 6 July 2018

Serious adverse events were nausea (4%), upper respiratory tract infection (4%) and vomiting (4%).<sup>[2]</sup>

To date there have been no drug-related safety findings leading to withdrawal from the FIREFISH or SUNFISH studies.

## **About SMA**

SMA is a severe, inherited, progressive neuromuscular disease that causes devastating muscle atrophy and disease-related complications.<sup>[6]</sup> 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.<sup>[7]</sup> SMA leads to the progressive loss of nerve cells in the spinal cord that control muscle movement.<sup>[4]</sup> 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.<sup>[8]</sup>

SMA is caused by a mutation in the survival motor neuron 1 (SMN1) gene that results in a deficiency of SMN protein.<sup>[4]</sup> SMN protein plays an important role throughout the body and increasing evidence suggests that the loss of SMN protein may affect many tissues and cells, which can stop the body from functioning.<sup>[9]</sup>

## **About risdiplam**

Risdiplam is an investigational, oral medicine that is systemically distributed and designed to durably increase SMN protein levels in the central nervous system and throughout the body.<sup>[5]</sup> It is designed to help the SMN2 gene produce more functional SMN protein, to better support motor neurons and muscle function.<sup>[5]</sup>

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

- FIREFISH (NCT02913482) – an open-label, two-part seamless 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 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).
- SUNFISH (NCT02908685) – 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. Enrolment for Part 2 was completed in September 2018 with 180 randomised patients.
- JEWELFISH (NCT03032172) – an open-label exploratory trial in people with all types of SMA aged 6 months–60 years who have been previously treated with SMN-targeting therapy, including olesoxime.

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

### **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 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](http://www.roche.com).

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