



Genentech
A Member of the Roche Group

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Dear SMA Europe members,

As part of our ongoing partnership and following your request to receive updates about the risdiplam clinical development program, we are delighted to share with you a much-anticipated milestone. Today, the U.S. Food and Drug Administration (FDA) has approved risdiplam for the treatment of spinal muscular atrophy (SMA) in adults and children 2 months of age and older. In addition, risdiplam will be known under its brand name Evrysdi™ (ev-RIZ-dee) in the U.S.

Please find a copy of the approval press release [here](#).

The FDA approval is based primarily on data from two studies, which evaluated the efficacy and safety of risdiplam in symptomatic infants with Type 1 SMA aged 2 to 7 months (FIREFISH study) and in people with Types 2 or 3 SMA aged 2 to 25 years (SUNFISH study).

This first health authority approval milestone for risdiplam has been an aspiration since Roche, PTC Therapeutics and the SMA Foundation began collaborating 9 years ago. The strength and resolve of the SMA community has continually inspired us as we developed a new treatment option that has the potential to make a positive impact on patients' lives. Today we celebrate our collective accomplishment.

Our sincere gratitude and appreciation goes out to the many hundreds of patients and families who are participating in our clinical studies, as well as the many patient groups around the world. Thank you for your partnership, trust and continued support that led to this important breakthrough. We are humbled to be part of this resilient community and grateful for everything we have achieved by working together.

In addition to the FIREFISH and SUNFISH trials that were the basis for the approval in the U.S., the ongoing risdiplam clinical development programme involves more than 450 people with SMA. The programme includes pre-symptomatic infants to adults up to 60 years old; participants with a broad spectrum of symptoms and motor function, as well as patients previously treated with other SMA therapies.

Whilst we recognise that this approval in the U.S. is a significant milestone for the SMA community, our unwavering focus remains on continuing to collaborate with health authorities, government agencies and other stakeholders around the world to ensure broad and rapid access to risdiplam to all patients who can benefit from the treatment. As such, we are pleased to inform you that we have existing regulatory applications under review in Brazil, Chile, China, Indonesia, Russia, South Korea and Taiwan; and we hope today's U.S. approval serves as a positive signal for future news around the world. Furthermore, in Europe, a Marketing Authorisation Application submission to the European Medicines Agency (EMA) is imminent.

We expect that you may receive questions from your community about today's news, so we have included some additional information below for you and your members. If you have any other questions about this update, please do not hesitate to contact me. We look forward to providing further updates about the risdiplam programme as they become available.

Sincerely,

Fani Petridis, on behalf of the Roche and Genentech SMA Team
Senior Global Patient Partnership Director, Rare Diseases (SMA)

Questions and Answers

1. What is risdiplam?

Risdiplam is a small molecule that targets the survival of motor neuron-2 (*SMN2*) gene. It is designed to provide sustained increases in survival motor neuron (*SMN*) protein, which plays an important role in the maintenance of specialised nerve cells (called motor neurons) that transmit signals from the brain and spinal cord to skeletal muscles, allowing the body to move. The *SMN* protein is found throughout the body, with highest levels in the spinal cord and the part of the brain that is connected to the spinal cord (the brainstem). In preclinical studies, risdiplam increased *SMN* protein levels both throughout the central nervous system and in peripheral tissues of the body. A liquid medicine, risdiplam is administered once daily at home by mouth or feeding tube if required.

2. What is the risdiplam clinical development programme?

The clinical development programme for risdiplam includes four ongoing clinical trials, FIREFISH, SUNFISH, JEWELFISH and RAINBOWFISH taking place in various countries all over the world. The programme is designed to help advance our understanding of the safety and clinical efficacy of risdiplam in a wide variety of individuals who have SMA, from pre-symptomatic infants to adults aged 60 with varying levels of disease severity, including pre-symptomatic, Types 1, 2, and 3 SMA as well as patients previously treated with other SMA therapies. Roche leads the clinical development programme for risdiplam as part of a collaboration with the SMA Foundation and PTC Therapeutics.

3. What is risdiplam approved for in the U.S.?

The U.S. Food and Drug Administration (FDA) has approved risdiplam for the treatment of spinal muscular atrophy (SMA) in adults and children 2 months of age and older.

4. How many patients have been treated with risdiplam worldwide so far?

More than 450 people have been treated with risdiplam through our clinical development programme. Additional patients have been treated in our Pre-Approval Access/ Compassionate Use Programme, which is currently open in 30 countries.

5. What is the safety profile of risdiplam?

Risdiplam's safety profile has been evaluated across three clinical trials; FIREFISH, SUNFISH and JEWELFISH. The most common adverse reactions observed in patients with later-onset SMA (and more frequent than control) were fever, diarrhea, and rash. In infantile-onset SMA, the most common adverse events were similar to those observed in later-onset SMA patients. In addition, upper respiratory tract infections, pneumonia, constipation, and vomiting were also observed in patients with infantile-onset SMA. There were no treatment-related safety findings leading to participant withdrawal from any study.

6. When are you planning to file for regulatory approval in Europe and the rest of the world?

In Europe, a Marketing Authorisation Application submission to the European Medicines Agency (EMA) is imminent. In addition, we have existing regulatory applications under review in Brazil, Chile, China, Indonesia, Russia, South Korea and Taiwan.

7. When do you expect regulatory approval in Europe and the rest of the world?

The regulatory decision timings are dependent on the procedures of individual country regulatory authorities and therefore, timelines will vary on a country-by-country basis.

8. When will risdiplam be available in my country?

To date, risdiplam has only been approved for use in the U.S., with existing filings ongoing in a number of countries around the world. Regulatory approval is only the first step towards commercial broad availability. National access to medicines requires local authorities to grant both regulatory authorisation and reimbursement, and usually involves many incremental steps. As such, timelines of national reimbursement can vary significantly from country to country and, at the moment, we cannot speculate on timings. Roche is actively collaborating with health authorities, government agencies and

other stakeholders around the world with the aim to ensure broad and rapid access to risdiplam to all patients who can benefit from the treatment.

9. Are there risdiplam clinical studies still recruiting? Where can I obtain further information about the risdiplam studies that are recruiting?

The RAINBOWFISH trial is currently the only study within the risdiplam clinical development programme that is still recruiting. The study is seeking pre-symptomatic infants up to 6 weeks of age. Families should consult with their treating physician if they are interested in taking part in a clinical trial. More information on the RAINBOWFISH trial (NCT03779334), as well as previously recruiting risdiplam trials, can be found on [ClinicalTrials.gov](https://clinicaltrials.gov) and [ForPatient.Roche.com](https://forpatient.roche.com) websites.

10. Is it possible to access risdiplam on compassionate grounds?

Roche announced earlier this year the initiation of a global Pre-Approval Access/ Compassionate Use Programme for risdiplam in countries where applicable laws and regulations allow such Programmes and which fulfil the criteria based on applicable company policy. The Programme is offering patients with the most urgent medical need and no other treatment options the opportunity to access risdiplam through the Pre-Approval Access/ Compassionate Use Programme. The decision to apply for the programme is one that should be made by the treating physician after she/he has explored and discussed all possible options with the patient or family. Please contact your physician for more information.