26 February 2021

Dear members of SMA Europe,

As part of our ongoing partnership and following your request to receive updates about the risdiplam clinical development programme, we are delighted to share an important milestone on our European regulatory submission. Today, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending the approval of risdiplam for the treatment of 5q spinal muscular atrophy (SMA) in patients 2 months of age and older, with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four SMN2 copies. The positive recommendation followed an accelerated assessment procedure, which is granted by the CHMP to manufacturers when a medicine is expected to be of major public health interest and therapeutic innovation.[1]

The CHMP recommendation is based on data from two pivotal studies, which evaluate 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). Both studies have demonstrated clinically meaningful efficacy of risdiplam with a favorable safety profile. A liquid medicine administered once daily, risdiplam, if approved, will be the first and only treatment for SMA that can be taken at home by mouth or feeding tube, if required.

The CHMP positive opinion is now referred to the European Commission (EC), which grants marketing authorizations for centrally authorized medicines in the European Union (EU). The EC will review the CHMP recommendation and give its final decision within approximately two months.[2] A positive EC decision will mean that risdiplam is approved across all 27 European Union member states, as well as Iceland, Norway and Liechtenstein.

Subject to the approval by the EC, health authorities in each EU and European Economic Area member state will then decide whether to reimburse risdiplam for use in their national health system. Recognizing the persisting unmet need in access to treatment options, Roche is actively engaged with reimbursement and assessment bodies across Europe to align on the requirements for reimbursement decision-making. We are submitting reimbursement dossiers in many countries in advance of the European Commission's expected decision to minimize any delay in patient access.

In addition to our ongoing efforts in Europe, we are working diligently to enable access for patients and families worldwide. Seven countries (United States, Chile, Brazil, Ukraine, South Korea, Georgia and Russia) have already approved risdiplam in the last few months, while we have existing regulatory applications under review for marketing authorization in 27 other countries including: Argentina, Australia, Botswana, Bolivia, Canada, China, Colombia, Indonesia, Israel, Japan, Kuwait, Malaysia, Mauritius, Namibia, New Zealand, North Macedonia, Pakistan, Peru, Qatar, Taiwan, Thailand, Saudi Arabia, South Africa, Singapore, Switzerland, United Arab Emirates and India (where the first step towards approval was granted).

We would like to express our sincere gratitude to the hundreds of people and families who are participating in our clinical studies, to SMA Europe and its member organizations, and to the many other patient groups around the world. Your partnership, trust and continued support has been critical to reaching this important milestone. We are proud to be part of this resilient community and look forward to continuing our collaboration to overcome the challenges that remain in SMA.

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

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

Questions and Answers

Does the CHMP positive opinion mean that risdiplam is now approved in the EU?
Risdiplam is not yet approved in the EU, but the CHMP positive opinion is an important milestone towards EU-wide approval. The European Commission (EC) will now review the CHMP recommendation in order to make the final decision on whether to approve risdiplam.

When do you expect EC approval?
The EC decision usually follows within approximately two months of the CHMP recommendation.[2]

When will risdiplam become available in EU member states?
Regulatory approval is the first step towards commercial availability. Following EC approval, health authorities in each EU and European Economic Area member state will then decide whether to reimburse risdiplam for use in their national health system. Roche is actively engaged with reimbursement and assessment bodies across Europe to align on the requirements for reimbursement decision-making. We are submitting reimbursement dossiers in many countries in advance of the European Commission's decision to minimize any delay in patient access.

Will the COVID-19 pandemic have any impact on the supply of risdiplam once it is licensed?
Throughout the COVID-19 pandemic, our primary focus has been to ensure patient safety, uninterrupted access to treatment and to support the wider community. We are continually assessing the potential implications of COVID-19 to our manufacturing and supply chain operations and we are monitoring the demand for all our therapies to mitigate potential stock out risks. Currently, we are not facing any supply or logistics interruptions for risdiplam due to COVID-19. However, we are taking proactive measures in collaboration with our logistics service providers to ensure the delivery of products to/from affected countries and regions remains as stable as possible.

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.

How many patients have been treated with risdiplam worldwide so far?
More than 2,500 patients have been treated with risdiplam, including clinical trials, compassionate use and real world settings, with patients ranging from birth to over 70 years of age and including those previously treated with other SMA-targeting therapies.

How does today's CHMP announcement affect the ongoing Pre-Approval Access (PAA)/ Compassionate Use (CU) programme?
This announcement does not affect the risdiplam PAA/CU programme. Patients will continue to receive risdiplam as normal and as per applicable country-specific laws and regulations. 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.

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.

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 and ForPatient.Roche.com websites.

References:

1. EMA. Accelerated Assessment. Available at: https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/accelerated-assessment. Last accessed January 2021.
2. Authorisation procedures – The centralised procedure at: https://ec.europa.eu/health/authorisation-procedures-centralised_en. Last accessed February 2021