17 August 2020

Dear SMA Europe members,

We are pleased to be in touch again so soon following the positive FDA announcement last week - this time to share an important milestone on our European regulatory submission. The European Medicines Agency (EMA) has validated the Marketing Authorization Application (MAA) for risdiplam for the proposed use in patients with spinal muscular atrophy (SMA). As part of our ongoing partnership and following your request to receive important and timely updates about Roche's SMA clinical development programme, we wanted to share this news and update with you.

The risdiplam MAA filing is based on data from the FIREFISH and SUNFISH studies which evaluate the efficacy and safety of risdiplam in symptomatic infants with Type 1 SMA aged 2 to 7 months and in people with Types 2 or 3 SMA aged 2 to 25 years, respectively. In addition, the submission incorporates safety data from JEWELFISH, a trial in people with all types of SMA aged 1 to 60 years previously treated with other SMA therapies.

Validation of the MAA confirms that the submission is accepted and begins the formal scientific evaluation process by EMA's Committee for Medicinal Products for Human Use (CHMP). The EMA has granted the marketing application with accelerated assessment, which means that the evaluation process can be reduced from 15 to 9 months, if the accelerated assessment timetable is maintained.

Risdiplam was granted PRIME (PRIority MEdicines) designation by the EMA in 2018 and Orphan Drug Designation in 2019. In addition to our filing in Europe, we have existing regulatory applications under review in Australia, Brazil, Canada, Chile, China, Indonesia, Russia, South Korea and Taiwan.

We thank everyone in the community, especially the patients and families who participate in our studies, the patient groups and the clinical trial sites and staff around the world who have supported and worked with us to achieve this important milestone. We look forward to providing further updates about the risdiplam programme as they become available.

If you have any other questions about this update, please do not hesitate to contact me.

Sincerely,

Fani Petridis

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

Questions & Answers

1. **What does the MAA process include?**
   The European Medicines Agency (EMA) is responsible for the scientific evaluation of centralised marketing authorisation applications (MAA). Once granted by the European Commission, the centralised marketing authorisation is valid in all European Union (EU) Member States, Iceland, Norway and Liechtenstein.

   For more details, visit EMA's website.

2. **When do you expect regulatory approval in Europe?**
   The EMA has granted the marketing application with accelerated assessment, which means that the evaluation process can be reduced from 15 to 9 months, if the accelerated assessment timetable is maintained.

3. **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.

4. **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 actively 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.

5. **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 allows 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.

6. **What is PRIME designation?**
   PRIME is a scheme launched by the European Medicines Agency (EMA) to enhance support for the development of medicines that target an unmet medical need. This voluntary scheme is based on enhanced interaction and early dialogue with developers of promising medicines, to optimise development plans and speed up evaluation so these medicines can reach patients earlier. Through PRIME, the Agency offers early and proactive support to medicine developers to optimise the generation of robust data on a medicine's benefits and risks and enable accelerated assessment of medicines applications.

   Source: https://www.ema.europa.eu/en/human-regulatory/research-development/prime-priority-medicines

7. **What is Orphan Drug Designation?**
   Orphan Drug Designation is a status assigned to a medicine intended for use against a rare condition. The medicine must fulfil certain criteria for designation as an orphan medicine so that it can benefit from incentives such as protection from competition once on the market.

   Source: https://www.ema.europa.eu/en/glossary/orphan-designation

8. **What is Accelerated Assessment?**
   Accelerated assessment reduces the timeframe for the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) to review a marketing-authorisation application. Applications may be eligible for accelerated assessment if the CHMP decides the product is of major interest for public health and therapeutic innovation.

   Source: https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/accelerated-assessment