15 December 2022

Dear members of SMA Europe,

As we are coming to the year's close, and following your request to receive regular updates, we are pleased to share a summary of the progress that has been made in 2022 in collaboration with the spinal muscular atrophy (SMA) community. This includes an overview of the advancement in research and clinical trials, the work to increase access to risdiplam globally and our collaborative efforts with the community. We want to take this opportunity to express our sincere gratitude for your ongoing collaboration and partnership – it is vital to improving care for people living with SMA.

Scientific presentations:
Data from ongoing risdiplam trials were regularly shared throughout the year as part of our commitment to transparency and providing timely access to data. Additionally, this furthers the broader community's collective knowledge about SMA, including the longer-term safety and efficacy profile of risdiplam.

- **SUNFISH –** Three-year data on risdiplam's long-term effectiveness in children and adults with Type 2 or 3 SMA was presented at the Muscular Dystrophy Association (MDA) Clinical and Scientific Conference in March.
- **RAINBOWFISH –** Interim (preliminary) data exploring the use of risdiplam in pre-symptomatic babies was also presented at the MDA Clinical and Scientific Conference.
- **FIREFISH** – Three-year data determining risdiplam's long-term effectiveness and safety in babies with Type 1 SMA was presented at the European Paediatric Neurology Society Congress in April.
- **JEWELFISH –** Two-year data evaluating risdiplam in children and adults with Type 1, 2 or 3 SMA who have previously been treated with other approved or investigational SMA-targeting therapies was presented at the World Muscle Society Congress in October.

Clinical trial updates:

Clinical study recruitment:
- In February 2022, we were pleased to announce that the RAINBOWFISH study completed enrolment. Researchers will analyse overall study data after all study participants complete their 12-month trial period; we expect results in 2023.
- The following risdiplam studies have completed enrolment: FIREFISH, SUNFISH, JEWELFISH and RAINBOWFISH.

Investigational studies:
- Earlier this year the first patient entered into Part 1 of the MANATEE clinical study – a two-part, global Phase 2/3 study evaluating the safety and efficacy of GYM329 (RO7204239), an investigational anti-myostatin antibody targeting muscular growth, in combination with risdiplam. Enrolment is currently ongoing across the activated sites, and our team continues to work to open recruitment at the remaining study sites quickly. Results from Part 1 of the study will indicate if we move forward with Part 2 – the main part of the study, which has the potential for a regulatory application submission.
- We are continuing to explore ways to further increase independence for all people living with SMA. Roche has initiated a new study to investigate the safety, the effect of food, bioavailability,* and bioequivalence† of a new tablet formulation of risdiplam for the fixed (5mg) dose. The estimated primary completion date of the trial is in early 2023.

Regulatory and product updates:
- To more clearly understand and advise patients on risdiplam's storage requirements, we conducted a study to assess how long risdiplam can be stored above the recommended temperature range of 2–8°C. The study showed that, if necessary, constituted risdiplam solution may be stored at room temperature (40°C or 104°F) for no more than a total of 120 hours (5 days). This is an increase of 4 days on the original temperature excursion time of 24 hours. The updated information can be found in the latest European Summary of Product Characteristics.[1]

* Bioavailability: the measure of the drug's ability to be absorbed by the body

† Bioequivalence: the measure of the biochemical similarity of two drugs that share the same chemical compound or active ingredient, and their desired effect on the body

- Furthermore, in May 2022, the U.S. Food and Drug Administration (FDA) approved a label extension for risdiplam to include babies under two months old with SMA, signifying that risdiplam is now approved in the U.S. to treat SMA in children and adults of all ages[2]. In Europe, risdiplam is not yet approved for the treatment of babies under two months of age, however a variation application has been submitted to the European Medicines Agency (EMA).

Access to risdiplam:
Since the approval of risdiplam by the European Medicines Agency (EMA) in 2021, Roche has been working closely with reimbursement and assessment bodies to enable broad and sustainable access and minimise any delay between regulatory approval and national reimbursement.

Risdiplam has now:
- received regulatory approval in over 93 countries[‡]
- been reimbursed in 42 countries,[§] (most recently in Ukraine - the first approval for SMA in that country[3]); additional reimbursement applications are pending in other countries.

Our ongoing commitment:
We recognise the significant challenges the SMA community has faced in Ukraine and other countries impacted by the crisis. Our primary focus has been ensuring uninterrupted access to treatment for all patients who are currently receiving risdiplam, through introducing a global support programme. The programme supports patients who are currently in Ukraine or those who have left the country. We are also honoured to support the tireless efforts led by SMA Europe and its national member organisations to cover the unprecedented needs of people with SMA who are affected by the invasion.

In 2022, the global *SMA My Way* programme celebrated one year since its launch. We are passionate about continuing to collaborate with the community to provide a dedicated space to share experiences, helping people in all parts of the community to live with SMA their way.

At the same time, we are grateful for your continuous partnership in advancing the care landscape globally:
- SMA Europe and Roche have embarked on a new partnership to conduct a benchmarking study that will measure how care is currently provided for adults living with SMA across the 23 countries where SMA Europe members are based. Through this project, we aim to increase understanding of the gaps and best practices in care for SMA and introduce recommendations of solutions and evidence-based policy changes that can improve care and overall quality of life of adults living with SMA.
- We are proud to be long-standing members of two important collaboration initiatives led by SMA Europe; the European Alliance for Newborn Screening in SMA, advocating for the adoption of newborn screening in Europe, and OdySMA, an initiative aimed at revealing and addressing the challenges of access to SMA treatments and care, ensuring that "*no one is left behind*".
- We are pleased to support the expansion of the STEP-IN Educational Program, a professional development program for physical therapists. The program is being developed by clinical researchers at Columbia University Medical Center (CUMC) in collaboration with Cure SMA to enhance expertise of evaluation techniques in the assessment and management of SMA in South America.

We thank you for your continued commitment to partnering with us and wish you all a very happy holiday season and all the best for the New Year.

Sincerely,

Fani Petridis

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

[‡] U.S., EU (EU 27 + Norway + Iceland + Liechtenstein), Albania, Argentina, Aruba, Australia, Azerbaijan, Bangladesh, Belarus, Brazil, Canada, Chile, China, Costa Rica, Cuba, Dominican Republic, Ecuador, Egypt, El Salvador, Georgia, Guatemala, Guyana, Honduras, Hong-Kong, India, Indonesia, Israel, Japan, Kazakhstan, Kosovo, Kuwait, Iran, Libya, Macau, Malaysia, Mexico, Moldova, Montenegro, New Zealand, Nicaragua, North Macedonia, Oman, Pakistan, Palestine, Panama, Paraguay Peru, Philippines, Qatar, Russia, Saudi Arabia, Serbia, Singapore, Sint-Maarten, South Africa, South-Korea, Switzerland, Taiwan, Thailand, Trinidad & Tobago, Ukraine, UAE, UK, Uruguay

[§] Australia, Austria, Bahrain, Belgium, Bulgaria, Canada, Croatia, Denmark England, Wales & Northern Ireland, Estonia, France, Georgia, Germany, Iceland, Iran, Iraq, Israel, Italy, Japan, Kazakhstan, Kuwait, Latvia, Libya, North Macedonia, Norway, Paraguay, Poland, Qatar, Romania, Russia, Saudi Arabia, Scotland, Serbia, Slovakia, Slovenia, Sweden, Switzerland, Ukraine, United Arab Emirates, U.S., Uruguay and Uzbekistan

References

[1] Evrysdi: Summary of product characteristics. Accessed: https://www.ema.europa.eu/documents/product-information/evrysdi-epar-product-information_en.pdf Last accessed: December 2022.

[2] Evrysdi: Summary of product characteristics. Accessed: https://www.ema.europa.eu/documents/product-information/evrysdi-epar-product-information_en.pdf Last accessed: December 2022.

[3] Ukraine Ministry of Health. Accessed: https://moz.gov.ua/article/news/vpershe-v-ukraini-pacientam-budut-bezoplatno-dostupni-liki-proti-spinalnoi-mjazovoi-atrofii Last accessed: December 2022.