16 December 2021

Dear members of SMA Europe,

As we come to the close of 2021, based on your requests to receive regular updates, we would like to provide an overview of our recent work in the community over the past year and a summary of our progress to advancing research and increasing access to risdiplam in Europe and beyond.

Research and clinical trial data updates

Clinical trial data updates:
Transparency and access to results of clinical studies are a commitment that we at Roche take very seriously. Throughout 2021, Roche presented findings from the four ongoing clinical trials of risdiplam in people living with spinal muscular atrophy (SMA). The growing body of data is essential to continue monitoring the longer-term safety and efficacy profile of risdiplam and to furthering our collective scientific knowledge.

SUNFISH - evaluating risdiplam in people aged 2-25 years with Type 2 or non-ambulant Type 3 SMA

- During the 2021 Muscular Dystrophy Association (MDA) Virtual Clinical and Scientific Conference, Roche presented 24-month efficacy and safety data from Part 2 of the SUNFISH study.
- For a more in-depth look at the findings, please access the press release here

FIREFISH - evaluating risdiplam in infants aged 1-7 months at enrolment with symptomatic Type 1 SMA.

- At 73rd American Academy of Neurology (AAN) Annual Meeting, Roche presented 24-month efficacy and safety data from Part 2 of the FIREFISH study.
- For a more in-depth look at the findings, please access the press release here

JEWELFISH - evaluating risdiplam in people with all types of SMA aged 1 to 60 years previously treated with another SMA-targeting therapy, including nusinersen and onasemnogene abeparvovec

- Safety, pharmacodynamic and exploratory efficacy data from the JEWELFISH study were presented during the Cure SMA 2021 Virtual SMA Research & Clinical Care Meeting.
- More information on the data presented can be accessed in the press release here

RAINBOWFISH - evaluating the efficacy and safety of risdiplam in babies from birth to six weeks with pre-symptomatic SMA

- Preliminary efficacy and safety data from the RAINBOWFISH study were shared during the Cure SMA 2021 Virtual SMA Research & Clinical Care.
- For a more in-depth look at the findings, please access the press release here

The data presented further demonstrated a favourable efficacy and safety profile for risdiplam. Our next update will be shared during the SMA Europe Scientific and Clinical Congress 2022 in February, which we are proud to support.

New research and development programs:
In addition to our work in ongoing trials, we also continue to invest in new research and development programs in pursuit of exploring new treatment pathways that can address the ongoing needs in the SMA community. One approach under evaluation is combining treatments that work in different ways, which is believed to have the potential to provide further benefit to people impacted by SMA by addressing the underlying cause and the symptoms of the disease concurrently.[1]

In October, Roche announced the initiation of MANATEE, a two-part, global Phase 2/3 clinical study, which aims to evaluate the safety and efficacy of GYM329 (RO7204239), an investigational anti-myostatin antibody targeting muscle growth in combination with risdiplam. Approximately 15 sites have been selected to participate in Part 1 of MANATEE, which is anticipated to start in early 2022. Whilst the study is currently enrolling ambulant patients aged 2-10 years, we will also be exploring the combination in other patient populations in the future, including non-ambulant patients and in a broader age range. More information regarding the study and its trial sites can be found on ClinicalTrials.gov.

Access to risdiplam

[1] Cure SMA. Scientific Considerations For Drug Combinations. Available at: <https://curesma.wpengine.com/wp-content/uploads/2020/03/03042020_Scientific-Considerations-for-Drug-Combinations_Final_Updated.pdf>

Since the first regulatory approval in the US in August 2020, risdiplam has now been approved in 66 countries worldwide[2], including all 27 European Union member states as well as Iceland, Norway, and Liechtenstein. We are continuing to pursue regulatory approvals and applications are currently under review in 34 additional countries[3], reaching a total of 100 submissions and approvals. To date, more than 4,500 people have been treated with risdiplam in clinical trials, or have received risdiplam commercially and through the compassionate use program, which is open in more than 60 countries.

We recognise that regulatory approval is only the first step towards patient access. Roche is working closely with reimbursement and assessment bodies in European countries and worldwide to minimise any delay between regulatory approval and access to risdiplam and ensure sustainable access. To date, 13 countries [Australia, Denmark, France, Germany, Iraq, Japan, Kuwait, North Macedonia, Qatar, Russia, United States, Serbia, Switzerland] have national reimbursement for the use of risdiplam and an additional 10 countries [Canada, Croatia, England, Estonia, Latvia, New Zealand, Northern Ireland, Sweden, Ukraine, Wales] have positive national assessment decisions (with reimbursement pending). The reimbursement and assessment decisions are specific to each country and we look forward to providing more details as part of OdySMA.

Ongoing commitment

2021 marked 10 years of Roche working in partnership with the SMA community. Over this decade, we have worked collaboratively with our partners in the community to make a difference to the lives of people living with SMA, their families and loved ones. During 2021, Roche worked on a number of collaborative projects through our engagement with you directly and the broader community.

As a company with a relentless focus on transforming outcomes for all patients, we are honoured to be part of two important collaboration initiatives, led by SMA Europe, that aim at improving healthcare and reducing disparities. The first is the European Alliance for Newborn Screening in SMA, founded in 2020, which advocates for the inclusion of SMA in all newborn screening tests in Europe in order to expedite the time to a correct diagnosis, which is vital to preventing the onset of disability and in maintaining the best possible quality of life. Recently, Germany and Norway became the first two European countries to announce nationwide newborn screening for SMA, and many other countries are taking bold steps towards achieving that goal. In addition, we are pleased to expand our partnership with SMA Europe and support OdySMA in our joint efforts to address the challenges of access to SMA treatments and care across Europe and ensure that no subgroup is left untreated.

At the same time, Roche has continued investing in advancing our collective knowledge on important topics including the adaptation of standards of care and building capabilities in Health Technology Assessment. By strengthening connectivity, exchanging best practices and learnings, we can help further the work to address unsolved challenges and take a step towards delivering equal healthcare across the globe.

Finally, it has also been our privilege to work together with the community to launch *SMA My Way*, an online collaboration to support people impacted by SMA by providing a dedicated space for sharing personal experiences, or life-hacks, and empowering one another to celebrate individuality and pursue life goals.

We are proud of the work undertaken together and remain committed to providing our ongoing support for these important efforts.

Thank you for the trust you have placed in us and for your continuous partnership, which has been instrumental in shaping our clinical development programs and delivering solutions that are centered around the community's expectations and needs. We wish everyone in the SMA community a happy holiday season and look forward to continuing our collaboration together in 2022.

Sincerely,

Fani Petridis

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

[2] Approved: US, EU (EU 27 + Norway + Iceland + Liechtenstein), Aruba, Australia, Azerbaijan, Brazil, Chile, China, Canada, Dominican Republic, Ecuador, Egypt, El Salvador, Georgia, Guatemala, Guyana, Honduras, Hong-Kong, India, Indonesia, Israel, Japan, Kuwait, Malaysia, North Macedonia, Paraguay, Peru, Qatar, Russia, Singapore, South-Korea, Switzerland, Thailand, Ukraine, UAE, UK, Uruguay.

[3] Submitted: Albania, Argentina, Belarus, Bolivia, Bosnia-Herzegovina, Botswana, Colombia, Costa Rica, Cuba, Curacao, Jordan, Kazakhstan, Libya, Mauritius, Mexico, Moldova, Montenegro, Morocco, Namibia, Nicaragua, New Zealand, Oman, Panama, Pakistan, Philippines, Saudi Arabia, Serbia, Sint-Maarten, South Africa, Trinidad & Tobago, Turkey, Taiwan, Vietnam, Zambia