Monday 3 July 2023

Dear members of SMA Europe,

In response to your standing request for important risdiplam and SMA clinical development programme updates, we are writing to share news from the Cure SMA Research & Clinical Care Meeting 2023 and Family Conference which took place at the end of June. It was a true honour to connect with so many members of the international SMA Community.

The updates that follow include data on the long-term safety and efficacy of risdiplam, plans to better understand risdiplam use in the real world, and the potential role of combination therapy, which we hope you will find informative. Great progress has been made in recent years and our presentations at the Cure SMA meeting are testament to Roche's continued efforts to address what we know is important to the community and advance care in SMA.

Presentations at Cure SMA Research & Clinical Care Meeting June 28 – 30, 2023 included:

- Long-term efficacy and safety of risdiplam
    - New 4-year data from the ongoing FIREFISH study confirm risdiplam's long-term efficacy and safety profile in children with Type 1 SMA. We presented results which showed that children's abilities to sit, stand and walk improved or were maintained over four years on risdiplam.[1] For more details, please see our press release here.

    - To reach those who couldn't attend previous congresses, we re-presented data from across the risdiplam clinical trial programme, including 4-year efficacy and safety data from SUNFISH.[2,3] Pooled safety data from FIREFISH, SUNFISH, JEWELFISH (open-label extension) and RAINBOWFISH was also presented.[4]

- Real-world evidence generation
    - Results from a study assessing real-world outcomes among patients with SMA who have been treated with risdiplam were presented. Responses were captured via the 2022 Cure SMA Community Update Survey, a web-based questionnaire administered by Cure SMA annually, and included findings across functional outcomes, health-related quality of life (HRQOL) and caregiver burden.[5]

    - The design for a post-authorisation effectiveness study (PAES) in patients with SMA treated with risdiplam in real-world settings was also presented.[6] The study will use secondary data from physician-reported SMA patient registries around the world,

including Europe, and will compare outcomes for patients treated with risdiplam to those of patients not receiving any disease modifying therapy (DMT-naïve patients).

- Designs were presented for two non–interventional studies which aim to gather real-world evidence on the use of risdiplam in adults with SMA aged 25 and over, and in infants with SMA under two months of age. Study sites will be in the US.[7,8]

- Risdiplam and combination treatment
  - At both the Research & Clinical Care Meeting and Family Conference, we shared plans for the design of two new trials that aim to evaluate the safety and efficacy of risdiplam after gene therapy.[9] Enrollment is expected to start in the second half of 2023.

Roche also presented data at the European Paediatric Neurology Society (EPNS) Congress 20-24 June 2023 and is currently at the European Academy of Neurology (EAN) Congress 01 - 04 July 2023. Presentations included 24 month data from the ongoing JEWELFISH study evaluating risdiplam in patients with previously treated SMA, and results from an indirect treatment comparison study which analysed the long-term comparative efficacy and of risdiplam versus nusinersen in children with Type 1 SMA over at least three years of follow-up.

In conclusion

The value of sharing insights, lessons and community connections cannot be overstated. It's what drives our ongoing commitment to advancing care in SMA. Yet advances in our collective understanding of SMA treatment and care are thanks to the SMA community's ongoing support and participation. Our gratitude goes out to all those living with SMA, their caregivers and healthcare providers, and we thank you for your continued partnership.

If you have any questions about the information provided above, please do not hesitate to reach out.

Sincerely,

Louisa Danielle Townson

Louisa Townson, on behalf of the Roche Global SMA Team
Global Patient Partnerships Director, Rare Diseases

References

1. Baranello G, et al. FIREFISH Parts 1 and 2: 4-year efficacy and safety of risdiplam in Type 1 spinal muscular atrophy. Presented at Cure SMA Research & Clinical Care Meeting 2023
2. Day JW, et al. SUNFISH Parts 1 and 2: 4-year efficacy and safety of risdiplam in Types 2 and 3 spinal muscular atrophy (SMA). Presented at Cure SMA Research & Clinical Care Meeting 2023
3. Chiriboga CA, et al. JEWELFISH: 24-month safety, pharmacodynamic and exploratory efficacy data in non-treatment-naïve patients with SMA receiving treatment with risdiplam. Presented at Cure SMA Research & Clinical Care Meeting 2023

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4. Chiriboga CA, et al. Safety update: Risdiplam clinical trial program for spinal muscular atrophy. Presented at Cure SMA Research & Clinical Care Meeting 2023
5. To TM , et al. A cross-sectional examination of outcomes data for risdiplam-treated individuals with SMA using the 2022 CURE SMA community update survey. Presented at Cure SMA Research & Clinical Care Meeting 2023
6. Salem L, et al. A prospective, observational, long-term post-authorisation effectiveness study of risdiplam in patients with SMA. Presented at Cure SMA Research & Clinical Care Meeting 2023
7. Shapouri S, et al. Real-world treatment with risdiplam in adults with SMA: a multicenter study. Presented at Cure SMA Research & Clinical Care Meeting 2023
8. Moawad D, et al. Real-world use of risdiplam for the treatment of spinal muscular atrophy in infants under 2 months of age in the US. Presented at Cure SMA Research & Clinical Care Meeting 2023
9. Guittari CJ, et al. Exploration of the use of risdiplam administration in patients with SMA who previously received gene therapy. Presented at Cure SMA Research & Clinical Care Meeting 2023