27 March 2024

Dear members of SMA Europe,

It was wonderful to see so many of you at SMA Europe's 4th Scientific International Congress in Ghent, Belgium, and at the MDA Clinical and Scientific Conference in Orlando, U.S. In response to your request for updates, we are pleased to share a round up of some of the key data for risdiplam presented at these March congresses, including an update on the tablet formulation.

Findings on the risdiplam tablet formulation and next steps

We appreciate the need for care and treatment options that can be selected to suit individuals' needs and preferences. With that in mind, we have been researching a potential tablet formulation of risdiplam as an additional option to the currently available oral solution, in a Phase 1 study completed last year.

The study (NCT04718181) evaluated a tablet formulation of 5mg risdiplam, that could be swallowed whole or dispersed in a small amount of bottled water. Results presented at the SMA Europe congress concluded that, whether swallowed whole or dispersed:

- The tablet formulation resulted in the same concentration of risdiplam in the body as the currently available oral solution
- The tablets may be administered with or without food, as food had no effect on the absorption of the tablets. This was similarly demonstrated for the oral solution
- No new safety signals were identified for the tablet formulation[1]

Regulatory submissions to the European Medicines Agency (EMA) and U.S. Food and Drug Administration (FDA) for the tablet formulation are planned in the first half of 2024.

Independent living and measuring what matters: the SMAIS-ULM and SUNFISH findings

At the SMA Europe congress we presented data looking at the SMA Independence Scale-Upper Limb Module (SMAIS-ULM) by age subgroup in Part 2 of the SUNFISH clinical trial (NCT02908685). Roche developed the SMAIS-ULM in close partnership with CureSMA, SMA Europe, and the SMA Foundation, to measure the level of support needed to perform activities of daily living (ADL) and to better capture the patient and caregiver experience.

The SUNFISH trial was designed to investigate risdiplam in people aged 2-25 years living with Type 2 or non-ambulant Type 3 SMA, with patients and their caregivers reporting SMAIS-ULM scores. A post-hoc analysis of the SMAIS-ULM data showed a larger proportion of those treated with risdiplam (*Patient-reported ≥12–25 years 69.8%; Caregiver-reported 2-25 years 66.4%*) were likely to maintain or gain independence in ADLs than those on placebo (*Patient-reported ≥12–25 years 39.1%; Caregiver-reported 2-25 years 38.3%*). This finding was observed across all age groups.[2]

Fertility and family planning in SMA

The design for a new, observational clinical trial, MARLIN (ISRCTN31399857), was presented at the MDA conference. The study aims to collect patient-reported, fertility-related outcomes in adult males living with SMA who have been treated with risdiplam in the US.[3]

We extend our sincere thanks to the SMA community for your valued support and participation in clinical trials, like those mentioned above, that help advance the understanding of SMA and of risdiplam in SMA. As always, we welcome any questions you may have on these or other ongoing Roche efforts in SMA.

Sincerely,

Louisa Danielle Townson

Louisa Townson, on behalf of the Roche Global SMA Team
Global Patient Partnership

References

1. Kletz H. et al. Bioequivalence and food effect assessment for a new risdiplam tablet formulation in healthy volunteers. Presented at SMA Europe 4th Scientific International Congress 2024
2. Sully K. et al. Post hoc analysis of the SMA Independence Scale-Upper Limb Module (SMAIS-ULM) in individuals with Type 2 and non-ambulant Type 3 SMA using SUNFISH Part 2 data. Presented at SMA Europe 4th Scientific International Congress 2024
3. Dickendesher T et al. Observational Study of Fertility in Risdiplam-Treated Adult Male Patients With Spinal Muscular Atrophy (SMA). Presented at MDA Clinical and Scientific Conference 2024

M-XX-00016785
Date of preparation: March 2024