11 June 2021

Dear members of SMA Europe,

We are pleased to share new interim data from two studies evaluating risdiplam in people with spinal muscular atrophy (SMA) who have been previously treated with other SMA-targeting therapies (JEWELFISH) and pre-symptomatic babies (RAINBOWFISH). The findings – which we are sharing with you in response to your request to receive regular updates – will be presented at the Cure SMA 2021 Virtual SMA Research & Clinical Care Meeting from June 9-11 2021.

For a more in-depth look at the results, please find the press release here https://www.roche.com/media/releases/med-cor-2021-06-11.htm

JEWELFISH

The first study being presented is JEWELFISH, a trial evaluating the safety, tolerability and efficacy of risdiplam in people living with SMA Types 1-3, aged 1 to 60 years who had been previously treated with another SMA-targeting therapy, including nusinersen and onasemnogene abeparvovec. The JEWELFISH study has enrolled the broadest patient population ever studied in an SMA trial.

In JEWELFISH, the safety of risdiplam was shown to be consistent with previous studies. There were no treatment-related adverse events (AEs) leading to withdrawal or treatment discontinuation with some patients receiving treatment for more than three years. The most common AEs in all patients were upper respiratory tract infection (17%), pyrexia (17%), headache (16%), nausea (12%), diarrhea (11%), nasopharyngitis (10%) and vomiting (8%). The most common serious AEs were pneumonia (2%) lower respiratory tract infection (2%), upper respiratory tract infection (2%) and respiratory failure (2%).

All patients treated with risdiplam showed a sustained >2-fold increase in median SMN protein levels versus baseline (from the start of the trial), irrespective of which treatment was previously received or SMA type. In addition, interim exploratory efficacy data indicated that patients treated with risdiplam showed stabilisation in motor function at one year of treatment, as measured by change from baseline in motor function measure (MFM 32).

The study is open label (participants and researchers are aware of the treatment that is administrated) and ongoing with the full analysis conducted at month 24.

RAINBOWFISH

Preliminary data of the second study, RAINBOWFISH, will also be presented. The study is evaluating the efficacy and safety of risdiplam in babies from birth to six weeks with pre-symptomatic SMA.

All five babies treated with risdiplam for at least 12 months achieved sitting without support, rolling and crawling. Of the five, two had two SMN copies and three had >2 copies. Four of the infants were able to stand unaided and walk independently. In addition, four babies reached a maximum score of 64 on the CHOP-INTEND* scale, and one scored 63. Data on the primary endpoint, the number of infants sitting without support for at least five seconds, will be reported when all primary analysis patients have reached one year of treatment.

In RAINBOWFISH, there were no AEs leading to withdrawal or study discontinuation. The most common AEs were nasal congestion (33%), cough (25%), teething (25%), vomiting (25%), eczema (17%), abdominal pain (17%), diarrhea (17%), gastroenteritis (17%), papule (rash; 17%) and pyrexia (fever; 17%).

RAINBOWFISH is open label and the only Roche-sponsored global clinical trial with risdiplam currently recruiting. More information about the trial and its sites can be found on the ClinicalTrials.gov website (ClinicalTrials.gov Identifier: NCT03779334).

**Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders*

Evaluating risdiplam in such a broad patient population from pre-symptomatic babies to those 60-years-old has only been possible thanks to our close collaboration with the SMA community, so we would like to thank all of our clinical trial participants, as well as SMA Europe and members, like you, for helping to make this clinical programme a reality. We greatly appreciate your continued support.

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

Sincerely,

Fani Petridis

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