June 12, 2020

Dear Members of SMA Europe,

As part of our ongoing partnership and following your request to receive important and timely information about the risdiplam clinical development program, we are pleased to share with you updates from Part 1 of our pivotal SUNFISH trial as well as from our pre-treated study JEWELFISH. The new data were presented today at the virtual Cure SMA Annual Conference, 8-12 June, 2020. Please find a short summary below. For more information, please access the press release at the following location:
https://www.roche.com/media/releases/med-cor-2020-06-12.htm

Roche today presented two-year data from Part 1 of its pivotal SUNFISH trial in people aged 2-25 years with Type 2 or 3 spinal muscular atrophy. The results of an exploratory efficacy analysis show risdiplam significantly improved motor function after 24 months of treatment compared to natural history data, as assessed by the Motor Function Measure (MFM) scale. In a weighted analysis comparing the data with a robust natural history comparator cohort, the MFM total change from baseline at month 24 was greater in patients receiving risdiplam (3.99 point difference (95% CI: 2.34, 5.65) $p < 0.0001$). These results are consistent with the results of the pivotal Part 2 of the trial at 12 months in non-ambulatory patients which demonstrated that change from baseline in total MFM32 score was greater in people treated with risdiplam, compared to placebo (1.55 point mean difference; $p=0.0156$).

SUNFISH is a large (n=231) global two-part study in children and adults. The dose-finding SUNFISH Part 1 (n=51) includes a broad patient population ranging from individuals unable to sit to those capable of walking, as well as people with scoliosis or joint contractures.

In addition, preliminary 12 month data from JEWELFISH, a trial in people with all types of SMA aged 6 months to 60 years previously treated with other SMA therapies, showed that treatment with risdiplam led to rapid and sustained increases in SMN protein levels. In more detail, among the patients who completed 12 months of treatment with risdiplam, a median two-fold increase in SMN protein versus baseline was observed (n=18). Enrolment for the JEWELFISH study, assessing safety and pharmacodynamic data in previously treated patients with SMA, who are now receiving risdiplam, is complete (n=174).

To date there have been no drug-related safety findings leading to withdrawal from either trial and the overall adverse event profile is similar to that observed in risdiplam trials of patients not previously treated with a SMA-targeting therapy.

In November 2019, the U.S Food and Drug Administration granted Priority Review for risdiplam with an expected decision on approval by August 24, 2020.

We want to thank you for your continued partnership and everyone in the community, especially the patients and families who have participated in the risdiplam clinical development programme. We would not be where we are today without you! We look forward to providing further updates as they become available.

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 Director, Global Patient Partnership - Rare Diseases (SMA)