

15 March 2018

Roche SMA Programme Update Start of pivotal part of FIREFISH for babies with Type 1 SMA

Dear SMA Community

We are very pleased to share an update of the Roche SMA programme. We have two investigational molecules in development for people with SMA, olesoxime and RG7916. Both molecules are given by mouth (or g-tube) and work in different ways.

RG7916

RG7916 is an SMN2 splicing modifier and is being studied in three ongoing clinical studies, FIREFISH, SUNFISH and JEWELFISH.



RG7916 is developed in collaboration with PTC Therapeutics and the SMA Foundation.

FIREFISH for babies with Type 1 SMA – Start of Part 2

FIREFISH is evaluating RG7916 in babies aged 1-7 months with Type 1 SMA. It is an open label study, all babies receive RG7916 and there is no placebo.

FIREFISH has two parts: Part 1 assessed the safety profile of RG7916 at different dose levels and demonstrated that RG7916 was safe and well tolerated at all dose levels. In Part 1 we also measured the concentration of RG7916 and the SMN protein level in blood. This has allowed us to confirm the dose of RG7916 to be investigated in Part 2. Participants in Part 1 continue to receive RG7916 in an open-label extension phase.

Part 2 of FIREFISH is now underway and will assess the efficacy and safety of RG7916 in approximately 40 babies. Part 2 of the trial has a duration of two years, after which all babies will continue to receive RG7916 until it is available in their country. The primary analysis of the efficacy and safety of RG7916 is taking place after all patients have completed 1 year of treatment.

Recruitment into FIREFISH Part 2 has begun in Belgium, France and Italy. Additional countries and sites will be progressively opened following Health Authority and Ethics Committee approvals.

If positive, data from FIREFISH may be used to support Health Authority submissions and potential approval and access to RG7916.

Studies for people with Type 2 and 3 SMA

SUNFISH is a clinical study for people with Type 2 and 3 SMA, non-ambulant, aged 2-25 years. SUNFISH is also a two part study. Part 1 has already been completed. In Part 2, we are assessing the safety and efficacy of RG7916 in type 2 and 3 SMA. Part 2 is ongoing in Europe and additional countries and sites will be opened throughout 2018, following Health Authority and Ethics Committee approvals. If positive, data from SUNFISH may be used to support Health Authority submissions and potential approval and access to RG7916.

JEWELFISH is an exploratory study assessing safety and tolerability of RG7916 in people with Type 2 and 3 SMA who have previously taken part in a study with another SMN2-targeting molecule. Recruitment is ongoing in study centers in Europe and in the US.

RG7916 has been well tolerated in all studies to date and no participants have left a study due to drug-related safety findings. We will be sharing more information from all ongoing studies at scientific conferences in the coming months.

OLESOXIME

Olesoxime supports the function of mitochondria, the power houses of cells, therefore supporting the continued function of cells.

The OLEOS study is an ongoing open-label extension study with non-ambulant Type 2 and 3 SMA patients who took part in earlier olesoxime studies. Patients will be followed over several years.



We are working on plans for a phase 3 study with olesoxime and will update you on these plans in the second half of 2018.

You can find further information and recruiting study centers for both RG7916 and olesoxime on www.clinicaltrials.gov (search for SUNFISH, FIREFISH, JEWELFISH or olesoxime) www.clinicaltrialsregister.eu and on www.roche-sma-clinicaltrials.com.

Thank you to the patients and families participating in clinical studies. Thank you too to the Patient Organisations for your contribution to advancing research in SMA. With your support, we progress our clinical studies in SMA with utmost speed and quality and we look forward to providing further updates to the community.

A handwritten signature in black ink, appearing to read 'S. Jethwa', is positioned above the text 'Best regards'.

Best regards

Sangeeta Jethwa, MD, on behalf of the Roche SMA team
Head, Patient Partnership, Rare Diseases
Roche Pharma Research & Early Development
Roche Innovation Centre Basel, Switzerland