

20th March 2017

Dear SMA community,

At Roche, we are committed to addressing the urgent needs of people living with SMA. We are happy to share this update on our two investigational oral molecules in development, olesoxime and RG7916, and the three trials with RG7916 that are currently recruiting – SUNFISH (Type 2/3), FIREFISH (Type 1) and JEWELFISH (non-naïve Type 2/3).

Olesoxime

- Olesoxime is an orally administered compound that may maintain mitochondrial function and support the continued function of cells
- The European Medicines Agency (EMA) and US Food and Drug Administration (FDA) have recommended that we generate additional benefit/risk data in a Phase III study
- We are considering EMA and FDA feedback on potential plans for a Phase III study with olesoxime and will keep you updated in the coming months

RG7916

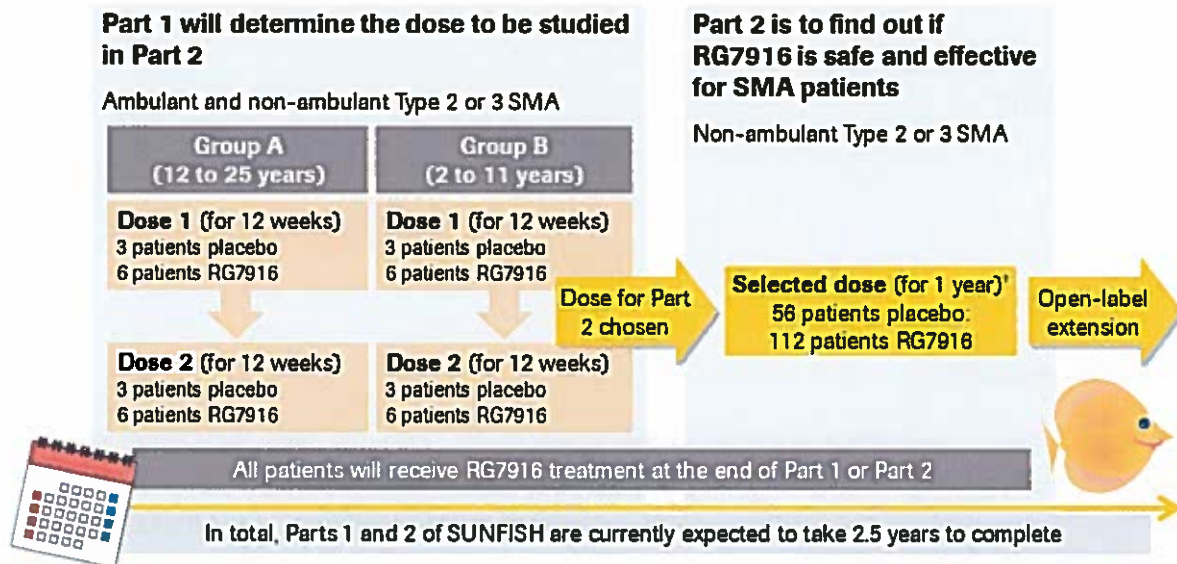
- RG7916 is an SMN2 splicing modifier that is taken orally and distributes widely throughout the whole body
- It is in clinical development in collaboration with PTC Therapeutics and the SMA Foundation
- RG7916 has received Orphan Drug Designation from the FDA*

What clinical trials with RG7916 are currently recruiting?

- Three clinical trials with RG7916 are currently recruiting participants: SUNFISH, FIREFISH and JEWELFISH
- Potential participants would need to meet all the inclusion criteria before enrolment in any RG7916 trial

SUNFISH

- **Aim:** To assess the safety and efficacy of RG7916 in patients with Type 2 or 3 SMA
 - Part 1 will assess how safe and well tolerated RG7916 is at 2 different dose levels
 - Part 2 will assess the efficacy and safety of RG7916 at the dose selected from Part 1
- **Who could enrol?** Children and young adults (2–25 years old) with Type 2 or 3 SMA*
- **Study design:** There are 2 parts to the SUNFISH study



- **Current status:** Planned enrolment is complete for Part 1 Dose level 1 (low dose) of RG7916 in 10 adults and adolescents (Group A), and in 9 children (Group B)[‡]. Part 1 Dose level 2 (higher dose) is currently enrolling patients
- **Safety review:** The safety of study participants is a priority for us. As pre-planned in the study protocol, a Safety Monitoring Committee reviews all safety information from all SUNFISH participants. After reviewing the safety information from the lower dose given to group B in Part 1, the Committee endorsed SUNFISH to advance as planned
- **Future development:** Part 2 is expected to begin in the second half of 2017, including additional countries and sites

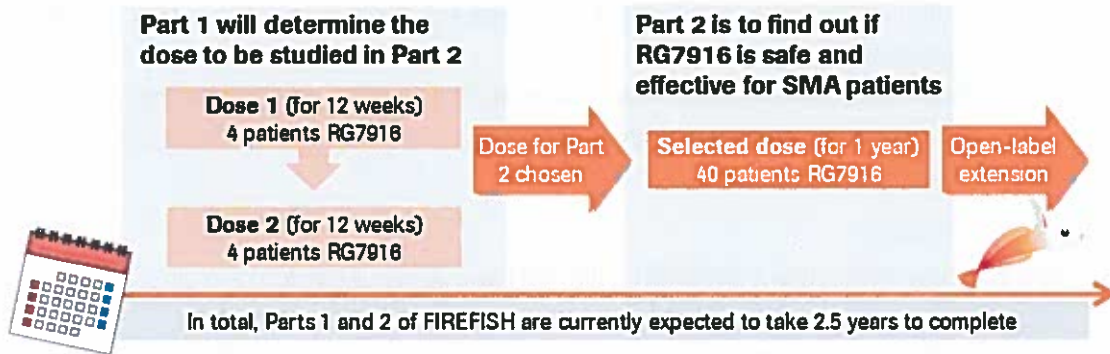
* Potential participants would need to meet the full inclusion criteria before enrolment in SUNFISH

[†] This updated protocol is pending final approval from the regulatory authorities

[‡] Part 1 Dose level 1 Group B may enrol additional patients

FIREFISH

- **Aim:** To assess the safety and efficacy of RG7916 in babies aged 1 to 7 months with Type 1 SMA
 - Part 1 will assess the safety and efficacy of RG7916 at 2 different dose levels
 - Part 2 will assess the efficacy and safety of RG7916 at the dose selected from Part 1
- **Who could enrol?** Babies aged 1 to 7 months with Type 1 SMA*
- **Study design:** There are 2 parts to the FIREFISH study

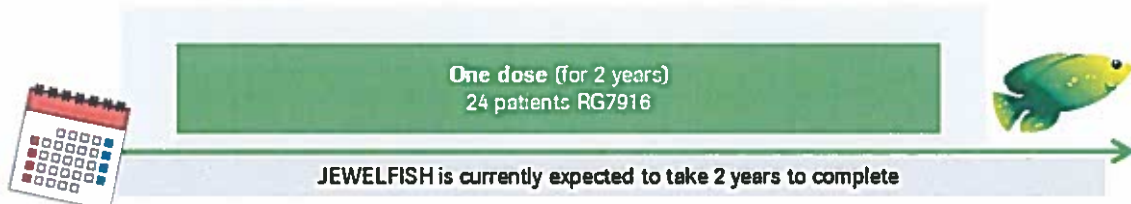


- **Current status:** The first baby was dosed with RG7916 in December 2016, and the study is progressing in Europe. FIREFISH Part 1 will open in additional countries and sites, including the US, in the coming months
- **Safety:** The safety of study participants is a priority for us. As pre-planned in the study protocol, a Safety Monitoring Committee reviews all safety information from all FIREFISH participants
- **Future development:** Part 2 is expected to begin in the second half of 2017, including additional countries and sites

* Potential participants would need to meet the full inclusion criteria before enrolment in FIREFISH

JEWELFISH

- **Aim:** To assess the safety and tolerability of RG7916
- **Who could enrol?** Patients with SMA who have previously received an SMN2-targeting therapy (either as part of the MOONFISH study with RG7800 or a study with another SMN2-targeting therapy)*



- **Current status:** The first patient has received their first dose at a US site
- **Safety:** Safety of study participants is a priority for us. As pre-planned in the study protocol, a Safety Monitoring Committee reviews all safety information from all JEWELFISH participants
- **Future development:** Further screening and enrolment of patients at sites across the US and Europe is planned

* Potential participants would need to meet the full inclusion criteria before enrolment in JEWELFISH

How can I or my family find out how to participate in SUNFISH, FIREFISH or JEWELFISH?

- Please contact your physician if you think you or a family member could be suitable for one of these trials
 - You can also visit <http://www.rocche-sma-clinicaltrials.com/> to read more about our programme
 - Your local patient group may have more information and resources; for a list of organizations go to <http://www.smafoundation.org/about-sma/sma-organizations-worldwide>

How can I find out more?

- You can read more about SUNFISH, FIREFISH and JEWELFISH at www.clinicaltrials.gov and <https://www.clinicaltrialsregister.eu/>
- We will continue to share updates and developments about our studies

If you have any questions, or would like to discuss this further, please contact me at sangeeta.jethwa@roche.com.

Sincerely,



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