



Basel, Thursday April 14th, 2016

Dear Nicole,

As requested, please find hereunder responses to your questions on olesoxime. Over the last months we have been in contact with the United States (US) Food and Drug Administration (FDA) and the European Medicines Agency (EMA). The FDA and EMA are the two regulatory agencies responsible for the approval of drugs in the US and Europe respectively. Both agencies also provide advice and guidance to pharmaceutical companies on development pathways to move an investigational drug towards an approved therapy. The scientific advice received from both agencies on the current clinical evidence package of olesoxime is similar in its conclusion and final:

- The currently available clinical evidence is not sufficient to conclusively determine the benefit / risk profile for the treatment of SMA
- Both the US and EU health authorities have requested additional efficacy evidence for olesoxime, by means of an additional study

As a result of this advice, Roche will be conducting a Phase 3 study of olesoxime in people with SMA Type 2 and Type 3. The additional study is the only possible way to generate the clinical evidence as requested by regulatory authorities in order to establish the benefit / risk profile of olesoxime and support regulatory submissions. The inevitable consequence of this request is a delay, linked to the time needed to run the necessary study. Filing for olesoxime is therefore anticipated in 2020.

We are conscious of the emotional distress linked to the progressive nature of SMA and the urgent need for treatment options. Like you, families and people with SMA, we are extremely disappointed by the news of a delay. At this moment in time we are thinking of all the people with SMA we have had the chance to meet over the last year, to all the parents, siblings and wider families, and people in the Patient Associations. To all of you, we would like to state firmly that our objective remains unchanged and that we are doing everything we can to bring a therapeutic option to people and families with SMA, as soon as possible.

Hence, our objective is to start the Phase 3 study as soon as possible. We are already working on the study protocol and study implementation aspects. We will involve a number of SMA Patient Associations into the discussions. We remain confident in the potential of olesoxime for people with SMA and will continue to advance the clinical development through the OLEOS & Phase 3 studies. At this stage, we are unable to commit to any pre-approval access programmes or requests for compassionate use. For more information on the criteria for pre-approval access, please refer to [Roche's Position on Pre-Approval Access to Investigational Medicinal Products*](#).

We are conscious of the need to answer the SMA community's questions on our developments and are committed to providing regular updates on our progress.

Respectfully yours,
Roche

* www.roche.com/position_on_pre_approval_access_on_investigational_medicinal_products.pdf