Dear SMA Community,

We are excited to announce the design of SAPPHIRE, a Phase 3 clinical trial to further evaluate the safety and efficacy of apitegromab in those living with Spinal Muscular Atrophy (SMA). The SAPPHIRE study is part of Scholar Rock's ongoing development program for apitegromab.

In addition to this statement, Scholar Rock is planning to hold a webinar and answer questions submitted from the community detailing the SAPPHIRE study.

SAPPHIRE trial overview:

SAPPHIRE is a global Phase 3 study which aims to assess the safety and efficacy of apitegromab in conjunction with SPINRAZA® (nusinersen) or EVRYSDI® (risdiplam) in individuals aged 2-21 years with Type 2 or Type 3 non-ambulatory (unable to walk independently) SMA. The trial will have 2 groups of participants with the following estimated number of participants:

- 156 individuals aged 2-12 years.
- 48 individuals aged 13-21 years.

When enrolled, study participants will be randomly assigned to either apitegromab or placebo while continuing their existing treatment with either SPINRAZA® or EVRYSDI® under the supervision of their healthcare provider. The treatment period (when participants will receive apitegromab or placebo) in the trial is planned to be 12 months long. After completing the 12 months, participants will have a 20-week follow-up period or have the option to enroll into an extension study. During the follow-up period, participants will stop taking apitegromab but will continue their treatment with either SPINRAZA® or EVRYSDI®. All participants in the extension study will receive apitegromab while continuing their treatment with either SPINRAZA® or EVRYSDI®.

About apitegromab:

Apitegromab selectively inhibits the activation of myostatin (a protein found in skeletal muscles that restricts muscle growth), which may improve muscle and motor function in people living with SMA.

Apitegromab is an investigational product candidate for the treatment of those living with SMA and has not been approved by the U.S. Food and Drug Administration (FDA) or any other health authority.

Questions and Answers:

What is Myostatin?

- Myostatin is a protein found primarily in skeletal muscle (muscles that connect to your bones) cells. Higher than normal levels of myostatin in the body can decrease muscle mass and strength.

How is apitegromab given?

- Apitegromab is given though an intravenous infusion (directly into a vein over a period of time). In the SAPPHIRE study and the already completed Phase 2 TOPAZ study, apitegromab is infused once every 4 weeks.

Who is eligible to participate in the SAPPHIRE trial?

- The SAPPHIRE study will enroll participants with the following criteria:
    - Aged 2-21 years at the time of screening.
    - Living with non-ambulatory (unable to walk independently) Type 2 or Type 3 SMA. A confirmed, documented diagnosis of 5q SMA will be needed. There are no restrictions on number of SMN2 copies.
    - Able to sit up straight with their head erect for $\geq$ 10 seconds without using their arms.
    - Comfortable receiving medication via intravenous infusion (directly into a vein over a period of time, in this case approximately 1-2 hours).
    - Currently on SPINRAZA® or EVRYSDI®. Participants need to have completed at least 10 months of treatment with SPINRAZA® or at least 6 months of treatment with EVRYSDI® at the time of screening. Those who have taken ZOLGENSMA® (onasemnogene abeparvovec) are not eligible for this trial.

- This is not a comprehensive list of eligibility criteria. A complete list can be found on ClinicalTrials.gov. Please note that the posting on ClinicalTrials.gov is in progress and may not yet be available.

How can I enroll in SAPPHIRE?

- We expect to begin enrolling participants in the coming months. The decision to participate in a clinical trial should be made between an individual and their healthcare provider. Please speak with your healthcare provider if you're interested in this trial. To find the nearest clinical trial site near you or for more information about SAPPHIRE, please visit ClinicalTrials.gov. Please note that the posting on ClinicalTrials.gov is in progress and may not yet be available.

What measurements will be used in the trial?

- The SAPPHIRE trial will assess apitegromab's effect on motor function via the Hammersmith Functional Motor Scale Expanded (HFMSE) and safety (side effects) across all participants. This is not a comprehensive list of all measurements in the SAPPHIRE trial, please visit ClinicalTrials.gov

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Will those who've taken ZOLGENSMA®, are ambulatory, or are Type 1 or Type 4 be allowed to participate in the SAPPHIRE study?

- We recognize that not everyone who's interested in the SAPPHIRE trial will be able to participate. In order to evaluate apitegromab's efficacy in SMA, we need to ensure our trial is focused and well-controlled, which includes restrictions in the eligibility criteria. This allows us to be confident that the effects seen in the trial are due to apitegromab and not something else, while building upon the past apitegromab research. Conducting a clinical trial with a well-defined and similar group of individuals gives the best chance to get strong and conclusive data, which is important in seeking approval from regulatory agencies expeditiously.

Do you plan to study apitegromab in other SMA populations not included in this trial?

- The SAPPHIRE study is part of Scholar Rock's ongoing development program for apitegromab, and we are committed to exploring the use of apitegromab, as an investigational product, in other populations.