October 24, 2024

Dear members of the SMA Community,

We are pleased to share positive news that topline results from the Phase 3 SAPPHIRE clinical study showed that our investigational treatment, apitegromab, improved motor function in people living with spinal muscular atrophy (SMA) who are currently on SMN-targeted therapy.

We would like to express our gratitude to the patients, families and investigators who participated in the SAPPHIRE study, and to all who contributed to this research achievement. We continue to be motivated everyday by the passion and resilience of the SMA community and are committed to doing our utmost to accelerate new breakthroughs.

For more than a decade, Scholar Rock has been pursuing therapeutic possibilities to address significant unmet needs in SMA. These study results are an important milestone, as they help us advance our commitment to addressing specific needs expressed by the SMA community and work towards the regulatory approval of apitegromab, potentially as the first muscle-targeted therapy for SMA.

The Phase 3 SAPPHIRE clinical data showed clinically meaningful and statistically significant improvements in motor function in our main study group of people ages 2-12 treated with apitegromab compared to those treated with placebo. Motor function was measured by the Hammersmith Functional Motor Scale Expanded (HFMSE), which is validated for assessing motor function in SMA. Participants were already taking an SMN-targeted therapy (nusinersen or risdiplam) and were treated with apitegromab or placebo in the trial.

Specifically, our topline data showed:

- The mean difference in change from baseline in HFMSE was 1.8 points (p=0.0192) for all patients receiving apitegromab 10 mg/kg and 20 mg/kg (n=106) compared to placebo (n=50). Patients receiving 20 mg/kg of apitegromab (n=53) showed a 1.4 point mean difference compared to placebo (p=0.1149).
- The prespecified analysis of the 10 mg/kg dose showed that patients receiving that dose of apitegromab (n=53) had an improvement of 2.2 points (nominal p=0.0121) compared to placebo.
- Apitegromab also showed clinically meaningful and consistent motor function improvements for people ages 13-21, a predefined sub-group in the trial.
- The safety profile of apitegromab in SAPPHIRE was consistent across all age groups. There were no clinically relevant differences in the adverse event profile by dose, 10 mg/kg and 20 mg/kg.

- No new safety findings were observed in the SAPPHIRE clinical trial. The profile was consistent with the Phase 2 TOPAZ clinical study of apitegromab, including an extension study with more than four years of treatment data.

SAPPHIRE was one of the largest studies of its kind, and almost all SAPPHIRE participants (98%) are now enrolled in our ONYX long-term extension trial, where they will continue receiving apitegromab. We believe these topline results – combined with the clinical data we have generated over the past four years from the Phase 2 TOPAZ trial – further emphasize the potential of apitegromab, if approved, to advance the standard of care in SMA. Analyses of the full Phase 3 SAPPHIRE data are ongoing, and Scholar Rock plans to present detailed results at an upcoming medical conference in early 2025.

As you know, the current treatments in SMA have had led to a significant impact on the disease, but there is more to be done to preserve motor function and slow the progression of this disease. Our hope is that the future of SMA will be transformed with an expanded focus on improving muscle strength and function to positively impact the lives of individuals with SMA.

The U.S. Food and Drug Administration (FDA) has previously granted apitegromab Fast Track, Orphan Drug and Rare Pediatric Disease designations, and the European Medicines Agency (EMA) has granted it Priority Medicines (PRIME) and Orphan Medicinal Product designations. Our plan is to file a U.S. Biologics License Application (BLA) and European Union marketing authorisation application (MAA) in Q1 2025 and request priority review. If approved, we expect to initiate a commercial product launch in the U.S. in Q4 2025.

Going forward, we will continue to treat those enrolled in our ongoing ONYX long-term extension study. We also plan to initiate the OPAL trial for apitegromab in children with SMA under 2 years of age in 2025 and will continue to share program updates with the SMA community.

We are now moving with urgency to share this data with regulatory agencies and working collaboratively towards our goal of delivering a muscle-targeted therapy for people living with SMA as soon as possible. **There is no time to waste.**

Sincerely,
The Scholar Rock Team

About Apitegromab
Apitegromab is an investigational fully human monoclonal antibody inhibiting myostatin activation by selectively binding the pro- and latent forms of myostatin in the skeletal muscle. It is the first and only muscle targeted therapy to show clinically meaningful and statistically significant functional improvement in SMA. The U.S. Food and Drug Administration (FDA) has granted Fast Track, Orphan Drug and Rare Pediatric Disease designations, and the European Medicines Agency (EMA) has granted Priority Medicines (PRIME) and Orphan Medicinal Product designations, to apitegromab for the treatment of SMA. Apitegromab has not been approved for any use by the FDA or any other regulatory agency.

About SAPPHIRE
SAPPHIRE was a randomized, double-blind, placebo-controlled Phase 3 clinical trial that evaluated the safety and efficacy of apitegromab in nonambulatory patients with Types 2 and 3 SMA currently

receiving an SMN-targeted therapy (either nusinersen or risdiplam). SAPPHIRE enrolled 156 patients aged 2-12 years old in the main efficacy population. These patients were randomized 1:1:1 to receive for 12 months either apitegromab 10 mg/kg, apitegromab 20 mg/kg, or placebo by intravenous (IV) infusion every 4 weeks. An exploratory population that enrolled 32 patients aged 13-21 years old was also evaluated. These patients were randomized 2:1 to receive either apitegromab 20 mg/kg or placebo.

Frequently Asked Questions

- **What were the SAPPHIRE topline study results?**
  - The Phase 3 SAPPHIRE clinical trial achieved its primary efficacy endpoint, which means the study showed statistically significant and clinically meaningful motor function improvement for patients in the study who were treated with apitegromab compared to placebo. Both patients who received apitegromab and patients who received placebo were on SMN-targeted therapy (nusinersen or risdiplam). The safety profile was consistent with the Phase 2 TOPAZ clinical study of apitegromab, including an extension study with more than four years of treatment data.

- **What patients was apitegromab studied in?**
  - The phase 3 SAPPHIRE study enrolled 156 patients aged 2-12 years old in the main efficacy population. An exploratory population that enrolled 32 patients aged 13-21 years old was also evaluated. The phase 2 TOPAZ study enrolled 35 patients aged 2-21 years old. Scholar Rock's ongoing ONYX long-term extension trial continues to treat patients from SAPPHIRE and TOPAZ, with 98 percent of patients from SAPPHIRE now enrolled in ONYX.

- **What is myostatin?**
  - Myostatin is a protein expressed primarily in skeletal muscle cells to negatively regulate muscle growth. When myostatin is activated, it works alongside other growth factors and hormones to maintain appropriate muscle mass.

- **What happens next?**
  - Scholar Rock plans to file a U.S. Biologics License Application (BLA) and European Union marketing authorisation application (MAA) in Q1 2025 and request priority review.
  - The SAPPHIRE study is now closed and almost all (98%) of patients in the trial have been transferred to our ONYX long-term extension study.
  - In 2025, Scholar Rock plans to initiate a new study called OPAL for apitegromab in patients under the age of 2 years old.

- **When do you expect a response from regulatory agencies?**
  - We are working to share this data with regulatory agencies as soon as possible. The U.S. Food and Drug Administration (FDA) has previously granted apitegromab Fast Track, Orphan Drug and Rare Pediatric Disease designations, and the European Medicines Agency (EMA) has granted it Priority Medicines (PRIME) and Orphan Medicinal Product designations.

- **If I am in the clinical trial, will I still have access to apitegromab?**
  - Yes, through our long-term extension study. Participants in the SAPPHIRE study have the option to continue into our open label extension study, ONYX, and almost all SAPPHIRE participants (98%) are now enrolled in the ONYX study.

- **When will the drug be available to people not in the trial?**
  - Apitegromab is an investigational drug and not approved by the FDA, EMA or any other health authority, so it is not currently available outside of a clinical trial setting. If apitegromab is approved, we anticipate a U.S. commercial launch in Q4 2025.

- **Will there be an EAP program?**
  - As we advance our investigational therapies through clinical development, our goal is to provide access at the appropriate time and in the correct manner for eligible patients. Contact us for more information about our expanded access policy.

- **Where can the SMA community go for further information / updates?**
  - Please visit clinicaltrials.gov or scholarrock.com for more information.