Scholar Rock Reports Apitegromab Meets Primary Endpoint in Phase 3 SAPPHIRE Study in Patients with Spinal Muscular Atrophy (SMA)

October 7, 2024

- *Apitegromab met primary endpoint with statistically significant and clinically meaningful improvement in motor function as measured by the gold standard Hammersmith Functional Motor Scale Expanded (HFMSE) for patients with SMA receiving apitegromab versus placebo (current standard of care) at week 52*
- *30.4% of patients receiving apitegromab had >3 point improvement in HFMSE versus 12.5% of patients on placebo*
- *Patients receiving apitegromab demonstrated early motor function improvement compared to placebo from the first measured time point at 8 weeks, benefit observed at 52 weeks as measured by HFMSE*
- *Patients receiving apitegromab experienced clinically meaningful benefit in motor function across all age groups (ages 2-21)*
- *Favorable safety profile in SAPPHIRE consistent with apitegromab's long-term safety profile observed in the Phase 2 TOPAZ trial with >48 months of treatment experience in SMA patients*
- *Scholar Rock plans to submit a U.S. Biologics License Application and European Union marketing authorisation application in Q1 2025*
- *Scholar Rock to host Investor Call today at 8:00 AM ET*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 7, 2024-- Scholar Rock (NASDAQ: SRRK), a late-stage biopharmaceutical company focused on advancing innovative treatments for spinal muscular atrophy (SMA), cardiometabolic disorders, and other serious diseases where protein growth factors play a fundamental role, today announced positive topline results from the Phase 3 SAPPHIRE clinical trial (NCT05156320) evaluating the efficacy and safety of apitegromab, an investigational muscle-targeted therapy, in patients with SMA.

The study achieved its primary endpoint demonstrating a statistically significant and clinically meaningful improvement for apitegromab versus placebo in motor function as measured by the gold standard HFMSE in SMA patients on chronic dosing of standard of care therapies (either nusinersen or risdiplam). Based upon the similar pharmacological profile of the 20 mg/kg and 10 mg/kg doses of apitegromab, the statistical analysis plan was prespecified to analyze both the combined dose (10 mg/kg and 20 mg/kg) compared to placebo, and 20 mg/kg dose each compared to placebo. Statistical significance is achieved per the prespecified statistical analysis plan (Hochberg multiplicity adjustment) where the p-value (≤0.025) is more rigorous if only one prespecified analysis crosses the statistical significance boundary of ≤ 0.05.

- In the main efficacy population (ages 2-12), 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 10 mg/kg of apitegromab (n=53) showed an improvement of 2.2 points (nominal p=0.0121) compared to placebo.

- Based upon PK/PD data from the SAPPHIRE trial, similar levels of target engagement were observed for the 10 mg/kg and 20 mg/kg dose groups.

Motor function outcomes were meaningful and consistent across the main efficacy population and in the ages 13-21 exploratory population, favored apitegromab (n=22) compared to placebo (n=10). Thirty percent of patients receiving apitegromab had ≥3 point improvement in HFMSE versus 12.5% of patients on placebo. Patients receiving apitegromab demonstrated early motor function improvement compared to placebo from the first measured time point at 8 weeks, benefit expanded at 52 weeks as measured by HFMSE. Following trial completion, 98 percent of SAPPHIRE patients (185/188) enrolled in the ongoing ONYX open-label expansion study.

"We are thrilled that apitegromab met the primary endpoint in our Phase 3 SAPPHIRE clinical study. The results clearly demonstrate robust and clinically meaningful improvement in motor function in patients with SMA," said Jay Backstrom, M.D., MPH, President and Chief Executive Officer of Scholar Rock. "At Scholar Rock, we are working with urgency to deliver the potentially transformative benefits of apitegromab to children and adults with SMA in the US, Europe, and around the world."

Treatment with apitegromab was well-tolerated across all age groups. There were no clinically relevant differences in the adverse event profile by dose, 10 mg/kg versus 20 mg/kg. No new safety findings were observed in the SAPPHIRE clinical trial; the profile was consistent with that observed in the Phase 2 TOPAZ clinical trial, including an extension study which had over four years of treatment as of the cut-off date. Serious adverse events (SAEs) were consistent with the underlying disease and current standard of care received by patients; no SAEs were assessed as related to apitegromab. There were no study drug discontinuations due to adverse events.

"We are grateful to the families and investigators who participated in our trials. The positive Phase 3 SAPPHIRE trial, along with over 4 years of TOPAZ clinical trial data, clearly demonstrate the potentially transformative benefit of apitegromab to drive clinically meaningful improvements in motor

function as measured by HFMSE in a broad SMA population, where motor function would normally be expected to generally decline over time," said Jing Marantz, M.D., Ph.D., Chief Medical Officer at Scholar Rock. "We look forward to submitting our applications to the FDA and the EMA in Q1 2025."

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. The Company plans to submit a U.S. Biologics License Application (BLA) and a European Union marketing authorisation application (MAA) in Q1 2025.

"It's a great day for people living with SMA and their families. These encouraging trial results mark a critical milestone for the SMA community," said Kenneth Hobby, President of Cure SMA. "Declining motor function and hopes for reversing losses associated with muscle weakness are significant unmet needs, impacting activities of daily living, from breathing, eating, self-care, to working and social interactions. We need an approved therapy that can support motor function and further improve daily activities for people with 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. Preliminary baseline characteristics from the trial will be presented during a poster presentation at the upcoming 29th Annual Congress of the World Muscle Society on Friday, October 11, 2024, being held in Prague, Czech Republic.

Conference Call Information

Scholar Rock will hold an investor conference call today, October 7 at 8:00 am ET. To access the live conference call, participants may register here. The live audio webcast of the call will be available under "Events and Presentations" in the Investor Relations section of the Scholar Rock website at http://investors.scholarrock.com. To participate via telephone, please register here. Upon registration, all telephone participants will receive a confirmation email detailing how to join the conference call, including the dial-in number along with a unique passcode and registrant ID that can be used to access the call. An archived replay of the webcast will be available on the Company's website for approximately 90 days.

Presentation at Annual Congress of the World Muscle Society

Scholar Rock will present baseline characteristics from the SAPPHIRE trial in a poster presentation at the 29th Annual Congress of the World Muscle Society. Details of the presentation are as follows:

Title: Apitegromab in Spinal Muscular Atrophy: baseline characteristics of participants enrolled in the phase 3 SAPPHIRE study
Presentation type: Poster presentation
Presenter: Thomas O. Crawford, M.D., Professor of Neurology and Pediatrics, Johns Hopkins University
Date and time: Friday, October 11, 2024, 3:45 PM CET
Location: Prague, Czech Republic

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 muscle-targeted treatment candidate to demonstrate clinical proof-of-concept in spinal muscular atrophy (SMA). Myostatin, a member of the TGFβ superfamily of growth factors, is expressed primarily by skeletal muscle cells, and the absence of its gene is associated with an increase in muscle mass and strength in multiple animal species, including humans. Scholar Rock believes that its highly selective targeting of pro- and latent forms of myostatin with apitegromab may lead to a clinically meaningful improvement in motor function in patients with 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 who are receiving current standard of care (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.

About SMA

Spinal muscular atrophy (SMA) is a rare, genetic neuromuscular disease that afflicts an estimated 30,000 to 35,000 people in the United States and Europe. The disease is characterized by the loss of motor neurons, atrophy of the voluntary muscles of the limbs and trunk, and progressive muscle weakness. While there has been progress in the development of therapeutics that address the loss of motor neurons, there continues to be a high unmet need for therapies that directly address the progressive muscle weakness that leads to loss of motor function in SMA.

About Scholar Rock

Scholar Rock is a biopharmaceutical company that discovers, develops, and delivers life-changing therapies for people with serious diseases that have high unmet need. As a global leader in the biology of the transforming growth factor beta (TGFβ) superfamily of cell proteins and named for the visual resemblance of a scholar rock to protein structures, the clinical-stage company is focused on advancing innovative treatments where protein growth factors are fundamental. Over the past decade, Scholar Rock has created a pipeline with the potential to advance the standard of care for neuromuscular disease, cardiometabolic disorders, cancer, and other conditions where growth factor-targeted drugs can play a transformational role.

This commitment to unlocking fundamentally different therapeutic approaches is powered by broad application of a proprietary platform, which has developed novel monoclonal antibodies to modulate protein growth factors with extraordinary selectivity. By harnessing cutting-edge science in disease spaces that are historically under-addressed through traditional therapies, Scholar Rock works every day to create new possibilities for patients. Learn more about our approach at ScholarRock.com and follow @ScholarRock and on LinkedIn.

Availability of Other Information About Scholar Rock

Investors and others should note that we communicate with our investors and the public using our company website www.scholarrock.com, including, but not limited to, company disclosures, investor presentations and FAQs, Securities and Exchange Commission filings, press releases, public conference call transcripts and webcast transcripts, as well as on Twitter and LinkedIn. The information that we post on our website or on Twitter or LinkedIn could be deemed to be material information. As a result, we encourage investors, the media and others interested to review the information that we post there on a regular basis. The contents of our website or social media shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended.

Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding Scholar Rock's future expectations, plans and prospects, including without limitation, Scholar Rock's expectations regarding its growth, strategy, progress and timing of its clinical trials for apitegromab, and indication selection and development timing, including the timing of any regulatory submissions, the therapeutic potential, clinical benefits and safety of any product candidates, expectations regarding timing, success and data announcements of current ongoing preclinical and clinical trials, its cash runway, expectations regarding the achievement of important milestones, the ability of any product candidate to perform in humans in a manner consistent with earlier nonclinical, preclinical or clinical trial data, and the potential of its product candidates and proprietary platform. The use of words such as "may," "might," "could," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "project," "intend," "future," "potential," or "continue," and other similar expressions are intended to identify such forward-looking statements. All such forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, without limitation, whether the results from the Phase 3 SAPPHIRE trial will be sufficient to support regulatory approval, that the full results from the Phase 3 SAPPHIRE trial may differ from the topline data, that preclinical and clinical data, including the results from the Phase 2 or Phase 3 clinical trial of apitegromab, are not predictive of, may be inconsistent with, or more favorable than, data generated from future or ongoing clinical trials of the same product candidates; the data generated from Scholar Rock's nonclinical and preclinical studies and clinical trials; information provided or decisions made by regulatory authorities; competition from third parties that are developing products for similar uses; Scholar Rock's ability to obtain, maintain and protect its intellectual property; Scholar Rock's dependence on third parties for development and manufacture of product candidates including, without limitation, to supply any clinical trials; and Scholar Rock's ability to manage expenses and to obtain additional funding when needed to support its business activities and establish and maintain strategic business alliances and new business initiatives, and our ability to continue as a going concern; as well as those risks more fully discussed in the section entitled "Risk Factors" in Scholar Rock's Quarterly Report on Form 10-Q for the quarter ended June 30, 2024, as well as discussions of potential risks, uncertainties, and other important factors in Scholar Rock's subsequent filings with the Securities and Exchange Commission. Any forward-looking statements represent Scholar Rock's views only as of today and should not be relied upon as representing its views as of any subsequent date. All information in this press release is as of the date of the release, and Scholar Rock undertakes no duty to update this information unless required by law.

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