Scholar Rock Presents New Phase 3 SAPPHIRE Data at the 2025 Muscular Dystrophy Association Clinical & Scientific Conference

March 16, 2025

- *Primary endpoint showed clinically meaningful improvement in patients with SMA receiving apitegromab as measured by gold standard Hammersmith Functional Motor Scale Expanded (HFMSE) versus placebo (p=0.0192), with consistent outcomes across all major sub-groups including age, SMN-targeted background therapy, and age at initiation of SMN-targeted therapy*
- *Pre-specified secondary endpoint showed that 30.4% of patients receiving apitegromab had ≥ 3-point improvement in HFMSE versus 12.5% of patients on placebo (nominal p-value = 0.0156), despite all study patients receiving ongoing SMN-targeted background therapy*
- *In other pre-specified secondary endpoints, patients with SMA receiving apitegromab showed consistent improvement at 52 weeks compared to placebo as measured by Revised Upper Limb Module (RULM) and WHO motor development milestones despite all study patients receiving ongoing SMN-targeted background therapy*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 16, 2025-- Scholar Rock (NASDAQ: SRRK), a late-stage biopharmaceutical company focused on advancing innovative treatments for neuromuscular diseases, cardiometabolic disorders, and other serious diseases where protein growth factors play a fundamental role, today announced that new efficacy and safety data from the Phase 3 pivotal SAPPHIRE trial (NCT05156320) will be presented in multiple clinical presentations at the 2025 Muscular Dystrophy Association (MDA) Clinical & Scientific Conference in Dallas, Texas. The Phase 3 SAPPHIRE trial evaluated the efficacy and safety of apitegromab, an investigational muscle-targeted therapy that is being developed to provide clinically meaningful improvement in motor function for people living with SMA who are receiving SMN-targeted treatments.

During this week's 2025 MDA Conference, the SAPPHIRE trial presentations highlight new data including secondary endpoint analyses. In addition to achieving the SAPPHIRE trial's primary endpoint as previously announced in October 2024, apitegromab demonstrated a clinically meaningful and consistent benefit in motor function across pre-specified patient subgroups (patient age, SMA background therapy, and patient age at initiation of SMN background therapy). Efficacy was also consistent across patient outcome measures of motor function including Hammersmith Functional Motor Scale Expanded (HFMSE), Revised Upper Limb Module (RULM), and World Health Organization (WHO) motor development milestones.

"While the gains possible with SMN-targeting therapies is dramatic, there remains residual weakness, and functional decline is now evident in many people with SMA. The impact that this weakness has on SMA patients' ability to maintain their daily activities and independence is substantial," said Thomas O. Crawford, M.D., Professor of Neurology and Pediatrics, Johns Hopkins University and SAPPHIRE Principal Investigator. "The findings from the SAPPHIRE trial are very exciting as they support the hypothesis that targeting muscle can provide functional improvement for patients with SMA on top of SMN-targeted therapy. Importantly, the improvements in function were observed consistently across multiple validated metrics used to assess patient functional outcomes in SAPPHIRE."

2025 MDA Conference Phase 3 SAPPHIRE Trial Data Presentation Highlights:

Primary Endpoint (HFMSE) Analysis

- As previously announced, the Phase 3 SAPPHIRE trial 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 patients with SMA on chronic dosing of standard of care therapies (either nusinersen or risdiplam).
- 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) in the main efficacy population (ages 2-12). Patients receiving 20 mg/kg of apitegromab (n=53) showed a 1.4 point mean difference compared to placebo (p=0.1149).
- New analysis performed in the pooled population (ages 2-21) showed clinically meaningful and consistent improvement in HFMSE across pre-specified subgroups (type of SMN-targeted therapy, age at SMN-targeted therapy initiation) and geographic region.

Secondary Endpoints

For secondary endpoints measured on patients ages 2-12 receiving apitegromab (10 mg/kg and 20 mg/kg) or placebo, the following improvements were observed:

- A greater proportion of patients treated with apitegromab had improvements of ≥3 points in their HFMSE scores compared

to placebo with odds ratio of 3.0 (nominal *p-value* = 0.0256). Additionally, 30.4% of patients receiving apitegromab had ≥ 3-point improvement in HFMSE versus 12.5% of patients on placebo (nominal p-value= 0.0156).
- Consistent improvement in motor function with a greater proportion of participants on apitegromab achieving HFMSE improvements versus placebo across all five-point thresholds (from ≥ 0-points to ≥ 4-points) at 52 weeks.
- Consistent improvement across other motor function outcome measures, including RULM and WHO motor development milestones.

Safety and Pharmacokinetics (PK)

- Treatment with apitegromab was well-tolerated across all age groups, consistent with the established safety profile and with no clinically relevant differences by dose.
- Serious adverse events (SAEs) were consistent with underlying disease and SMN-targeted therapy. There were no SAEs assessed as related to apitegromab.
- PK and pharmacodynamic (PD) data demonstrated similar levels of target engagement across the 10 mg/kg and 20 mg/kg dose groups.

"We are looking forward to sharing the SAPPHIRE data with the medical community at the MDA conference in Dallas. These new data from the SAPPHIRE trial reinforce apitegromab's potential as a transformative muscle-targeted therapy by demonstrating statistically significant and clinically meaningful improvements in motor function for individuals living with SMA," said Jay Backstrom, M.D., MPH, President and Chief Executive Officer of Scholar Rock. "Progressive muscle weakness robs many people with SMA of the motor function needed for the most basic activities, despite current SMN-targeted treatments, and the SMA community has clearly been asking for more. We are thrilled with the consistency of clinical benefit demonstrated across important outcome measures in all patient subgroups and now are urgently preparing to commercialize apitegromab in the US, Europe and additional countries where patients with SMA can benefit from therapy."

Additional 2025 MDA Conference Apitegromab Presentation Information:

Oral Presentation

Title: Efficacy and safety of apitegromab in individuals with type 2 and type 3 spinal muscular atrophy evaluated in the phase 3 SAPPHIRE trial
Presenter: Thomas O. Crawford, M.D., Professor of Neurology and Pediatrics, Johns Hopkins University
Location: Hilton Anatole Dallas, Coronado ABCD
Date and time: Wednesday, March 19, 10:45-11:00 a.m. CT

Poster Presentations

Title: Efficacy and safety of apitegromab in individuals with type 2 and type 3 spinal muscular atrophy evaluated in the phase 3 SAPPHIRE trial
Presenter: Thomas O. Crawford, M.D., Professor of Neurology and Pediatrics, Johns Hopkins University
Location: Hilton Anatole Dallas, Trinity Exhibit Hall (Poster #O284)
Date and time: Sunday, March 16 – Tuesday, March 18, 6:00-8:00 p.m. CT

Title: muSRK-015 builds muscle mass and strength in combination with dystrophin upregulation in a mouse model of DMD
Presenter: Adam I. Fogel, Ph.D., Director, Discovery Biology, Scholar Rock
Location: Hilton Anatole Dallas, Trinity Exhibit Hall (Poster #P160)
Date and time: Sunday, March 16 – Tuesday, March 18, 6:00-8:00 p.m. CT

Presentations will be made available in the **Publications & Posters section** of Scholar Rock's website.

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 in spinal muscular atrophy (SMA) to demonstrate clinical success in a pivotal phase 3 clinical trial. 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 the Phase 3 SAPPHIRE Trial
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 were 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 either apitegromab 10 mg/kg, apitegromab 20 mg/kg, or placebo by intravenous (IV) infusion every 4 weeks for 12 months. An exploratory population including 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 every 4 weeks for 12 months.

The SAPPHIRE trial met its primary endpoint for the main efficacy population with a statistically significant 1.8-point improvement (p=0.0192) based on apitegromab combined dose (10 mg/kg and 20 mg/kg) and standard of care (SOC) versus placebo and SOC (Hochberg multiplicity adjustment) as measured by the Hammersmith Functional Motor Scale-Expanded at week 52. Patients receiving 20 mg/kg of apitegromab (n=53) showed a 1.4 point mean difference compared to placebo (p=0.1149). Additional details can be found here.

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 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.

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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 X (formerly known as Twitter) and LinkedIn. The information that we post on our website or on X (formerly known as 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 plans for apitegromab, including expectations relating to commercial launch in the US in the fourth quarter of 2025, and subsequent launch in Europe. 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 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, and may not be sufficient for regulatory approval; Scholar Rock's ability to provide the financial support, resources and expertise necessary to identify and develop product candidates on the expected timeline; the data generated from Scholar Rock's nonclinical 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, supply for apitegromab; 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; its ability to receive priority or expedited regulatory review or to obtain regulatory approval of apitegromab; its ability to expand globally and the anticipated commercial launch in the United States of apitegromab in the fourth quarter of 2025 and new business initiatives; as well as those risks more fully discussed in the section entitled "Risk Factors" in Scholar Rock's Annual Report on Form 10-K for the year ended December 31, 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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