Pivotal SAPPHIRE Trial Data Published in The Lancet Neurology: Apitegromab Demonstrated Significant Motor Function Gains for Children and Adults with SMA on SMN-Targeted Treatment

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- *First and only muscle-targeted SMA therapy to demonstrate statistically significant, clinically meaningful improvements on the gold-standard HFMSE scale (p=0.019) versus placebo, with consistent benefits across pre-specified subgroups (age, type of SMN-targeted treatment, and SMN-targeted treatment initiation age) and region*
- *30.4% of patients receiving apitegromab had ≥ 3-point improvement in HFMSE versus 12.5% of patients on placebo, despite all study patients receiving chronic, ongoing SMN-targeted treatment*
- *19.6% of patients receiving apitegromab had ≥ 4-point improvement in their HFMSE score versus 6.3% of patients on placebo, despite all study patients receiving chronic, ongoing SMN-targeted treatment*
- *Treatment with apitegromab was well-tolerated across all age groups, consistent with the established safety profile*
- *FDA accepted the apitegromab BLA under priority review with a PDUFA target action of September 22, 2025*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 14, 2025-- Scholar Rock (NASDAQ: SRRK), a late-stage biopharmaceutical company focused on developing and commercializing apitegromab for children and adults with spinal muscular atrophy (SMA) and other severe and debilitating neuromuscular diseases, announced today that positive study results from the pivotal Phase 3 SAPPHIRE trial **(NCT05156320)** were published in the peer-reviewed journal *The Lancet Neurology*. The data showed that children and adults with SMA had improved motor function with apitegromab—as measured by the gold-standard Hammersmith Functional Motor Scale Expanded (HFMSE)—and decreased motor function with placebo despite all participants receiving ongoing survival motor neuron (SMN)-targeted treatment.

"The robust apitegromab data reinforce that effective SMA treatment regimens should address both motor neuron preservation and muscle function," said Akshay Vaishnaw, M.D., Ph.D., President of R&D, Scholar Rock. "To improve outcomes and support activities like breathing, eating, swallowing, standing and walking, which require muscle strength and motor function, a comprehensive approach targeting both components of the disease is critical. The SAPPHIRE findings support the value of muscle-targeted therapies for children and adults living with SMA."

Data from this publication were previously presented at the 2025 **Muscular Dystrophy Association Clinical & Scientific Conference** and 2025 **Cure SMA Research and Clinical Care Meeting**. The full manuscript, "Efficacy and safety of apitegromab in nonambulatory type 2 or type 3 spinal muscular atrophy (SAPPHIRE): a phase 3, double-blind, randomised, placebo-controlled trial" is available online and will appear in the August 13, 2025 print issue of *The Lancet Neurology.* Thomas O. Crawford, MD, Professor of Neurology, Johns Hopkins University School of Medicine is the principal investigator of the SAPPHIRE study and is the lead author on the manuscript.

The 52-week Phase 3 SAPPHIRE clinical trial enrolled 188 patients aged 2-21 with SMA who were receiving an SMN-targeted treatment (either nusinersen or risdiplam) to evaluate the safety and efficacy of apitegromab in improving motor function. **As reported, the Phase 3 SAPPHIRE trial met its primary endpoint,** achieving a statistically significant and clinically meaningful improvement in motor function (measured by HFMSE) for patients receiving apitegromab versus placebo, despite all participants receiving chronic, ongoing SMN-targeted treatment.

Apitegromab was well-tolerated across all age groups, with no new safety findings observed. The safety profile was consistent with that observed in the Phase 2 TOPAZ clinical trial, including an extension study with over four years of treatment as of the cut-off date.

Key highlights include:

- The mean difference in change from baseline in HFMSE was 1.8 points (p=0.019) for all patients receiving apitegromab 10 mg/kg and 20 mg/kg (n=106) compared to placebo (n=50) in the 2–12-year-old efficacy population. Patients receiving 20 mg/kg of apitegromab (n=53) showed a 1.4 point mean difference compared to placebo (p=0.11).
- Analysis performed in the ages 2–21-year-old population showed clinically meaningful and consistent improvement in HFMSE with apitegromab across pre-specified subgroups (age, type of SMN-targeted treatment, age at SMN-targeted treatment initiation) and geographic region.
- For secondary endpoints measured on patients aged 2-12 receiving apitegromab (10 mg/kg and 20 mg/kg) or placebo, the following improvements were observed:
    - 30.4% of patients receiving apitegromab had ≥ 3-point improvement in HFMSE versus 12.5% of patients on placebo at 52 weeks.

- 19.6% of patients receiving apitegromab had ≥4-point improvement in HFSME versus 6.3% of patients on placebo at 52 weeks.
- Positive trends were observed across other motor function outcome measures, including Revised Upper Limb Module (RULM) and World Health Organization (WHO) motor development milestones.

The Company submitted a Biologics License Application (BLA) application for apitegromab to the FDA, which has been accepted under priority review with a target action date of September 22, 2025, under the Prescription Drug User Fee Act (PDUFA). Apitegromab is also under review by the European Medicines Agency (EMA).

In anticipation of potential regulatory approvals, Scholar Rock is planning for a U.S. commercial launch of apitegromab for SMA in 2025, with European launch projected in 2026.

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. The trial also enrolled 32 patients aged 13-21 years old. These patients were randomized 2:1 to receive either apitegromab 20 mg/kg or placebo every 4 weeks for 12 months.

About SMA
Spinal muscular atrophy (SMA) is a rare, severe, genetic neuromuscular disease that affects an estimated 30,000 to 35,000 people in the United States and Europe. The disease is characterized by the irreversible loss of motor neurons, atrophy of the voluntary muscles of the limbs and trunk, and progressive muscle wasting that causes continuous motor function decline throughout life and can diminish the independence of both children and adults. 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 late-stage biopharmaceutical company focused on developing and commercializing apitegromab for children and adults with spinal muscular atrophy (SMA) and other severe and debilitating neuromuscular diseases. As a global leader in the biology of the transforming growth factor beta (TGFβ) superfamily, the company is named for the visual resemblance of a scholar rock to protein structures. Our 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 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 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 obtain regulatory approval of apitegromab; and the anticipated commercial launch in the United States of apitegromab in 2025 and new business initiatives; 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, 2025, 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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