Scholar Rock Completes Enrollment in Phase 2 EMBRAZE Proof-of-Concept Trial of Apitegromab in Obesity

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- *Topline results expected in 2Q 2025*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 10, 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 it has completed enrollment in the Phase 2 EMBRAZE trial designed to show proof-of-concept of apitegromab, an investigational selective myostatin inhibitor antibody, to safely preserve lean muscle mass in individuals on GLP-1 receptor agonist (GLP-1 RA) therapy for obesity. Results from this trial are expected in the second quarter of 2025 and will inform the development of SRK-439, a novel, investigational selective myostatin inhibitor, which the Company plans to advance specifically for the treatment of cardiometabolic disorders, including obesity.

EMBRAZE is a randomized, double-blind, placebo-controlled, Phase 2 trial evaluating the efficacy, safety and pharmacokinetics of apitegromab in adults who are overweight or obese without diabetes and taking a GLP-1 RA. The trial fully enrolled participants aged 18-65 to assess the primary endpoint of change in lean mass by DEXA scan at 24 weeks. Initiation of enrollment was announced in May 2024.

“We believe the rapid enrollment of the EMBRAZE trial speaks to the unmet need to preserve lean muscle mass for patients experiencing significant weight loss on GLP-1 therapies. As a leader in myostatin inhibition, Scholar Rock is uniquely positioned to play a meaningful role in the cardiometabolic space. Preserving muscle has the potential to improve the quality of weight loss as well as attenuate the weight regain often observed when people come off GLP-1 therapy,” said Jing Marantz, M.D., Ph.D., Chief Medical Officer at Scholar Rock. “We anticipate reporting results from EMBRAZE in the second quarter of 2025 and plan to use the data to further inform Scholar Rock’s development of SRK-439, which was designed specifically for the treatment of obesity.”

The Company also announced today that it will present new preclinical SRK-439 data in a poster presentation entitled, “SRK-439 Selectively Inhibits Myostatin to Promote Healthy Body Composition During Metformin Therapy” at The Obesity Society’s Annual Meeting at ObesityWeek®, November 3-6, in San Antonio, Texas. Preclinical data presented earlier showed that SRK-439 maintained lean mass and improved fat mass loss when used in combination with a GLP-1 RA in diet-induced obesity (DIO) mice. Preclinical data also supported the potential for SRK-439 to increase lean mass and attenuate fat mass regain, thus contributing to a favorable body composition following withdrawal from GLP-1 RA treatment. The Company plans to file an IND for SRK-439 in 2025.

Apitegromab is being developed as potentially the first muscle-targeted therapy for the treatment of spinal muscular atrophy (SMA) and is the only muscle-targeted therapy to show clinical proof-of-concept in SMA. The Company is on track to report topline data in the fourth quarter of 2024 from the pivotal Phase 3 SAPPHIRE clinical trial in patients with SMA. If the trial is successful and apitegromab is approved by the U.S. Food and Drug Administration (FDA), the Company expects to initiate a commercial product launch in 2025.

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. The efficacy and safety of apitegromab have not been established and apitegromab has not been approved for any use by the FDA or any other regulatory agency.

About the Phase 3 SAPPHIRE Trial in Spinal Muscular Atrophy

SAPPHIRE is an ongoing randomized, double-blind, placebo-controlled, Phase 3 clinical trial evaluating the safety and efficacy of apitegromab in nonambulatory patients with Types 2 and 3 SMA who are receiving SMN-targeted therapy (either nusinersen or risdiplam). SAPPHIRE targeted enrolling approximately 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 targeted enrolling up to 48 patients aged 13-21 years old will also separately be evaluated. These patients were randomized 2:1 to receive either apitegromab 20 mg/kg or placebo. For more information about SAPPHIRE, visit www.clinicaltrials.gov. Apitegromab has not been approved for any use by the US FDA or any other health authority, and its safety and efficacy have not been established.

About the Phase 2 EMBRAZE Trial in Obesity

EMBRAZE is a randomized, double-blind, placebo-controlled, Phase 2 proof-of-concept trial evaluating the efficacy, safety and pharmacokinetics of apitegromab in adults with a body mass index (BMI) of >27 (overweight) or a BMI of >30 (obese) and taking a GLP-1 RA (tirzepatide or semaglutide). The target enrollment of EMBRAZE is 100 subjects aged 18-65 who are overweight or obese without diabetes. As part of the study design, the treatment period is 24 weeks, and all subjects will receive a GLP-1 RA. In addition, all subjects will be randomized 1:1 to receive either apitegromab or

placebo by intravenous (IV) infusion every four weeks during the 24-week treatment period. The primary endpoint is change from baseline at Week 24 in lean mass assessed by dual-energy X-ray absorptiometry. Secondary endpoints include additional weight loss measures, safety and tolerability, and pharmacokinetic outcomes. Exploratory endpoints at Weeks 24 and 32 include cardiometabolic parameters (e.g. HbA1c), body composition, and physical function.

About SRK-439

SRK-439 is a novel, preclinical, investigational myostatin inhibitor that has high in vitro affinity for pro- and latent myostatin and maintains myostatin specificity (i.e., no GDF11 or Activin-A binding), and is initially being developed for the treatment of cardiometabolic disorders, including obesity. Based on preclinical data, SRK-439 has the potential to support healthier weight management by preserving lean mass during weight loss. The efficacy and safety of SRK-439 have not been established and SRK-439 has not been approved for any use by the FDA or any other regulatory agency.

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.

Scholar Rock is the only company to show clinical proof-of-concept for a muscle-targeted treatment in spinal muscular atrophy (SMA). 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 its preclinical programs, including SRK-439, and indication selection and development timing, including the therapeutic potential, clinical benefits and safety thereof, expectations regarding timing, success and data announcements of current ongoing preclinical and clinical trials, 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," "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, that preclinical and clinical data, including the results from the Phase 2 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, including, without limitation, the Phase 3 clinical trial of apitegromab in SMA; 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 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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