Scholar Rock Reports Positive Phase 2 EMBRAZE Trial Results Demonstrating Statistically Significant Preservation of Lean Mass with Apitegromab During Tirzepatide-Induced Weight Loss

June 18, 2025

- *Patients receiving apitegromab with tirzepatide over 24 weeks showed a 54.9% preservation of lean mass (+4.2 lbs of lean mass) versus tirzepatide alone (p=0.001)*
- *Patients receiving apitegromab with tirzepatide over 24 weeks lost 18.8 lbs of fat mass while those on tirzepatide alone lost 17.7 lbs of fat mass*
- *Patients receiving apitegromab with tirzepatide over 24 weeks lost 12.3% of body weight while those on tirzepatide alone lost 13.4% of body weight*
- *Higher quality of weight loss observed for patients receiving apitegromab with tirzepatide (85% fat mass/15% lean mass) compared to tirzepatide alone (70% fat mass/30% lean mass)*
- *Apitegromab was generally well tolerated, and the encouraging safety profile was consistent with the safety profile observed in prior clinical studies*
- *Company to host Conference Call today at 8:00 AM EDT*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 18, 2025-- Scholar Rock (NASDAQ: SRRK), a late-stage biopharmaceutical company focused on developing and commercializing apitegromab for patients with spinal muscular atrophy (SMA) and additional severe and debilitating neuromuscular diseases, today announced positive results from the Phase 2 EMBRAZE proof-of-concept trial assessing apitegromab in combination with tirzepatide to preserve lean mass during tirzepatide-induced weight loss. The trial demonstrated that 30% of total weight loss with tirzepatide alone was due to lean mass loss. Apitegromab therapy (10 mg/kg) with tirzepatide preserved an additional 4.2 pounds (1.9 kilograms) or 54.9% (p=0.001) of lean mass compared to tirzepatide alone, leading to higher quality weight loss. Apitegromab with tirzepatide was generally well tolerated by participants.

“GLP therapies have been an effective and important innovation for individuals living with obesity and cardiometabolic disorders; however, these treatments can result in substantial loss of lean muscle mass for patients, leading to unwanted health risks,” said Akshay Vaishnaw, M.D., Ph.D., President of R&D, Scholar Rock. “We are pleased that the EMBRAZE trial accomplished its objective by achieving its primary endpoint. The results validated our hypothesis that our platform of highly selective myostatin inhibitors has the potential to support healthier weight loss for millions of patients on GLP therapies by safely preserving lean mass.”

Dr. Vaishnaw added, “While this is an exciting development for our platform, we remain focused on preparing for the launch of apitegromab, and following its potential approval in SMA, we look forward to studying it in a range of neuromuscular diseases with high unmet need. Further, there is great potential with SRK-439 to be a subcutaneous, anti-myostatin antibody and we look forward to also exploring its potential in various rare, severe debilitating neuromuscular disorders. We remain on track to file an IND application for SRK-439 in the second half of this year to support the first in human study.”

The EMBRAZE trial was designed to assess the ability to preserve lean body mass associated with tirzepatide-induced weight loss in patients with obesity (BMI of ≥30.0 kg/m^2) or overweight (BMI≥27.0 kg/m^2 with one or more weight-related co-morbidities). Treatment was administered over a 24-week period, and patients were randomized into two treatment arms: apitegromab with tirzepatide and placebo with tirzepatide.

Topline results successfully demonstrated proof-of-concept for a highly selective, anti-myostatin antibody to preserve lean mass, thus improving quality of weight loss with tirzepatide therapy. The 24-week data demonstrated the following:

	24 Weeks		
	apitegromab 10 mg/kg + tirzepatide (n=43)	**placebo + tirzepatide (n=44)**	**Difference apitegromab vs. placebo**
Change in Lean Mass (SE)	**-1.6 (0.57) kg**	**-3.5 (0.52) kg**	**1.9 (0.58) kg**
	-3.4 (1.25) lbs	**-7.6 (1.14) lbs**	**4.2 (1.27) lbs**

			(p=0.001) 54.9% preservation
Total Mass Loss due to Lean Mass Loss (SE) in %	**14.6 (3.19) %**	**30.2 (2.89) %**	**-15.6 (3.23) %**
Change in Fat Mass (SE)	**-8.5 (0.85) kg** **-18.8 (1.87) lbs**	**-8.0 (0.77) kg** **-17.7 (1.70) lbs**	**-0.5 (0.86) kg** **-1.1 (1.90) lbs**
Total Mass Loss due to Fat Mass Loss (SE) in %	**85.3 (3.22) %**	**69.5 (2.93) %**	**15.8 (3.27) %**
Change in body weight (SE) **(% change in body weight)**	**-11.2 (1.21) kg** **-24.6 (2.65) lbs** **(-12.3%)**	**-12.5 (1.09) kg** **-27.5 (2.41) lbs** **(-13.4%)**	**1.3 (1.22) kg** **2.9 (2.69) lbs**

SE = standard error

Lean mass and fat mass were calculated via dual X-ray absorptiometry (DEXA) and body weight was measured with a scale. Analysis based on participants who completed treatment and had a Week 24 DEXA scan. Means based on a linear regression model controlling for baseline lean body mass, baseline weight, age, and sex.

Consistent with prior apitegromab studies, the EMBRAZE trial demonstrated a well tolerated and encouraging safety profile. The incidence of adverse events was generally similar between apitegromab and placebo, with adverse events observed consistent with the known safety profile of tirzepatide. No subjects experienced serious adverse events (SAEs) or discontinuations considered to be related to apitegromab treatment, and there were no deaths.

Participants in both arms completed treatment at 24 weeks and the follow-up period is ongoing. Additional data from the trial will be presented at upcoming medical congresses.

Conference Call Information

Scholar Rock will hold an investor conference call today, June 18 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.

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 2 EMBRAZE Trial in Obesity

EMBRAZE was a randomized, double-blind, placebo-controlled, Phase 2 proof-of-concept trial evaluating the efficacy, safety and pharmacokinetics of apitegromab at 10mg/kg in adults with a body mass index (BMI) of ≥27.0 kg/m^2 (overweight) with at least one weight-related comorbid condition or a BMI of ≥30.0 kg/m^2 (obese) while receiving tirzepatide. The enrollment of EMBRAZE included 100 subjects aged 18-65 who were overweight or living with obesity without diabetes. As part of the study design, the treatment period was 24 weeks, and all subjects received tirzepatide. In addition, all subjects were randomized 1:1 and received either apitegromab 10mg/kg or placebo by intravenous (IV) infusion every four weeks during the 24-week treatment period. The

primary endpoint was change from baseline at Week 24 in lean mass assessed by dual-energy X-ray absorptiometry. Secondary endpoints included additional weight loss measures, safety and tolerability, and pharmacokinetic outcomes. Exploratory endpoints at Weeks 24 and 32 included cardiometabolic parameters (e.g. HbA1c), body composition, and physical function.

About SRK-439

SRK-439 is a novel, preclinical, investigational, subcutaneous 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). Given its optimal profile supported by preclinical data, the Company intends to explore SRK-439's potential in various neuromuscular disorders. 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, the company is named for the visual resemblance of a scholar rock to protein structures. 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 websitewww.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.

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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 timing of any regulatory submissions or approvals, 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, expectations relating to commercial launch timing in the US and in Europe, 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, that preclinical and clinical data, including whether the results from the Phase 3 SAPPHIRE trial will be sufficient to support regulatory approval, that the results from the Phase 2 EMBRAZE trial may not be predictive of, may be inconsistent with, or more favorable than, data generated from future or ongoing clinical trials of the same product candidate; Scholar Rock's ability to manage expenses or provide the financial support, resources and expertise necessary to identify and develop product candidates on the expected timeline; 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; and Scholar Rock's dependence on third parties for development and manufacture of product candidates including, without limitation, to supply any clinical trials 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 March 31, 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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