Scholar Rock Announces Initiation of Phase 2 EMBRAZE Trial of Apitegromab in Obesity and New Preclinical Data Supporting SRK-439 in Obesity

May 22, 2024

- *Phase 2 EMBRAZE proof-of-concept trial designed to assess apitegromab's ability to safely preserve lean muscle mass in individuals on GLP-1 receptor agonist therapy for obesity*
- *New preclinical head-to-head comparison shows that SRK-439 is more potent than an anti-ActRII antibody in maintaining lean mass in diet-induced obesity (DIO) mice; lean mass loss with SRK-439, 1mg/kg dose was equivalent to anti-ActRII antibody, 20mg/kg dose*
- *Company hosting Investor Event today in New York City focusing on its selective latent myostatin inhibition programs in Spinal Muscular Atrophy and obesity with presentations from executive leadership and key experts*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 22, 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 the initiation of the Phase 2 EMBRAZE proof-of-concept trial, designed to assess the safety and efficacy of apitegromab, a highly selective myostatin inhibitor, to preserve lean muscle mass in individuals living with obesity and on background therapy of a GLP-1 receptor agonist (GLP-1 RA). The results from this trial will inform the development of SRK-439, a novel investigational selective myostatin inhibitor optimized for the treatment of cardiometabolic disorders, including obesity.

The Company also announced new preclinical data from a head-to-head comparison of SRK-439 and an anti-activin receptor II (anti-ActRII) antibody, which demonstrate SRK-439's potential as best in class in preserving lean mass in patients on GLP-1 RAs. This data will be presented by Mo Qatanani, Ph.D., Chief Scientific Officer, at Scholar Rock's Investor Event, which begins today at 8:30 a.m. ET and is being held in New York City.

"We are thrilled to have initiated the EMBRAZE clinical trial ahead of schedule and to share new data from our SRK-439 program, which we believe further support our hypothesis that selective latent myostatin inhibition has advantages over less selective approaches to safely and effectively maintain lean muscle mass," said Jay Backstrom, M.D., MPH, President and Chief Executive Officer at Scholar Rock. "Selectivity is key in mitigating potential safety concerns for this patient population and we look forward to sharing additional preclinical data at the American Diabetes Association 84th Scientific Sessions in June to support the best-in-class potential of SRK-439."

New SRK-439 Data

For the head-to-head preclinical research study, the Company generated and tested an anti-ActRII antibody (a murine equivalent of bimagrumab), along with a murine equivalent of SRK-439 in a weight-stable diet induced obesity (DIO) mouse model. Mice were given either semaglutide (0.04mg/kg, daily) with an IgG control antibody (weekly, 20mg/kg) or semaglutide (0.04mg/kg, daily) in combination with weekly injections of either SRK-439 (0.3-10mg/kg) or of the anti-ActRII antibody (0.3-20mg/kg). Quantitative nuclear magnetic resonance (qNMR) was used to analyze change in lean mass after four weeks of treatment.

Lean mass differences were significant in all doses of SRK-439 tested, supporting the hypothesis that SRK-439 could be an important therapy to aid in lean mass preservation and is suitable for subcutaneous dosing in a population of adults with obesity.

- SRK-439 attenuated the GLP-1 RA-driven lean mass loss in combination with semaglutide at a dose as low as 0.3 mg/kg (8.3% lean mass loss from baseline).
- Maximal effects observed at all doses over 1 mg/kg (4.2% lean mass loss from baseline at 10mg/kg), as compared to an IgG control + semaglutide (14.1% lean mass loss from baseline).
- Superiority to anti-ActRII antibody was shown in all equivalent doses tested:
    - 3 mg/kg: -4.7% SRK-439 vs. -12.0% for anti-ActRII
    - 1 mg/kg: -5.0% SRK-439 vs. -12.6% for anti-ActRII
    - 0.3 mg/kg: -8.3% SRK-439 vs. -15.4% for anti-ActRII
- Equivalent lean mass preservation was seen at the highest dose tested for both drugs; 10 mg/kg SRK-439 (-4.2%) and 20 mg/kg anti-ActRII (-4.3%).

"The data from this head-to-head comparison show that selectively inhibiting myostatin alone is sufficient to preserve lean mass on a background of GLP-1 RA, in preclinical models. Combined with the positive data observed at low doses of SRK-439, we believe that our selective myostatin approach is the right potential solution to preserve lean muscle mass while avoiding the potential off-target effects observed in less selective programs for this indication. We view this as strong evidence that SRK-439

could have a more favorable benefit/risk profile," said Mo Qatanani, Ph.D., Chief Scientific Officer at Scholar Rock.

Phase 2 EMBRAZE Trial Design

Scholar Rock announced in January that the U.S. Food and Drug Administration cleared the Company's Investigational New Drug (IND) application for EMBRAZE, 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.

Primary data from EMBRAZE are expected in mid-2025 and will inform Scholar Rock's development of SRK-439 towards an anticipated IND filing in 2025.

The presentation from Scholar Rock's Investor Day will be available in the Investors and Media section of Scholar Rock's website. Live webcast of the event may be accessed by visiting the Investors & Media section of the Scholar Rock website at http://investors.scholarrock.com. An archived replay of the webcast will be available on the Company's website for approximately 90 days following the presentations.

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 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 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.

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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 therapeutic potential, clinical benefits and safety thereof, expectations regarding timing, success and data announcements of current ongoing preclinical and clinical trials, 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 the results from the Phase 2a clinical trial of apitegromab, or its preclinical data with respect to SRK-439, 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 or the Phase 2a EMBRAZE clinical trial; 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; 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, 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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