Scholar Rock Announces New Preclinical Data for SRK-439 Showing Significant Lean Mass Increase and Enhanced Fat Mass Loss with Metformin

November 4, 2024

- Preclinical data show that SRK-439 increased lean mass and lowered fat mass gain in mice receiving metformin

- Data support that Scholar Rock's unique approach to selective myostatin inhibition could improve body composition in people living with obesity and on an existing background treatment

- Scholar Rock's industry-leading anti-myostatin portfolio includes SRK-439 and apitegromab, the first investigational anti-myostatin therapy to show improved motor function in Spinal Muscular Atrophy (SMA) in a Phase 3 trial

- Obesity program progressing with Phase 2 EMBRAZE trial on track for readout in Q2 2025

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Nov. 4, 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 new preclinical data that support the potential of SRK-439, a highly selective investigational antimyostatin antibody, to increase lean mass and lower fat mass gain when taken with metformin. These data will be presented by Melissa Fulham, Ph.D., of Scholar Rock, at the ObesityWeek conference in San Antonio, Texas on November 5.

"These new data build upon a robust body of evidence demonstrating the potential of selective myostatin inhibition as an important therapeutic approach," said Jay Backstrom, M.D., MPH, President and Chief Executive Officer at Scholar Rock. "These latest SRK-439 data support our hypothesis that a highly selective approach to targeting myostatin inhibition could have positive effects on body composition in people living with obesity and associated comorbidities like diabetes, and also underscore the value within Scholar Rock's platform. We are looking forward to providing more updates on the exciting advancements in our cardiometabolic program, including our Phase 2 EMBRAZE trial topline data in the second quarter of 2025."

Preclinical study design

The research study tested a murine equivalent of SRK-439 in a diet-induced obesity (DIO) mouse model. All mice were given a high-fat diet, followed by either metformin (50 mg/kg daily) or control (water) for four weeks. Following that four-week period, mice in metformin and control groups were given either an IgG control antibody (10 mg/kg weekly) or SRK-439 (10 mg/kg weekly for younger mice and 3 mg/kg weekly for older mice) for another four weeks. To assess whether effects were persistent across age ranges, this study design was repeated in two age groups: both young (10-week-old) and mature (22-week-old) DIO mice.

Quantitative nuclear magnetic resonance (qNMR) was used to analyze change in lean mass at baseline, after four weeks of metformin treatment, and every two weeks following treatment with SRK-439 or IgG control.

Changes in body composition in the presence or absence of metformin

The group that received SRK-439 on the background of metformin showed a significant increase in lean mass versus the group receiving metformin alone, and this result was consistent across age groups. Key findings supporting the potential for SRK-439 in advancing healthier weight management include:

- Young animals treated with SRK-439 and metformin demonstrated a 2-fold increase in lean mass over the duration of the study compared to the lean mass increase in the metformin group and in IgG controls (31.6% increase from baseline vs. 15.1%, $p<0.0001$).
- In older metformin-treated animals, the increase in lean mass in the SRK-439 treated animals compared to IgG controls was 50-fold (10.2% lean mass increase from baseline versus 0.2% in IgG controls, $p<0.0001$), owing primarily to the limited lean mass growth in the IgG control group over the duration of the study due to the age of the animals.
- In young mice, the combination treatment of SRK-439 and metformin also resulted in lower fat mass gain (68.2% increase from baseline) than metformin alone (114% increase from baseline; $p<0.05$).
- In older mice, SRK-439 showed a trend toward reduced fat mass gain when combined with metformin, as compared to metformin alone (10.6% increase from baseline vs 18.4%; not statistically significant).

"These new preclinical data show that selectively inhibiting myostatin in combination with metformin increased lean mass—and this effect was robust even in the older treatment group that was more weight stable," said Mo Qatanani, PhD, Chief Scientific Officer at Scholar Rock. "In addition, we observed that when we combined SRK-439 and metformin in younger mice, the effect of lowering fat mass gain was greater than with either therapy alone. Taken together, this is compelling evidence suggesting that SRK-439 has the potential to improve body composition and contribute to healthier weight management in the context of both obesity and type 2 diabetes. These exciting data advance the science of obesity research and continue to differentiate Scholar Rock's pipeline and anti-myostatin programs."

Poster Presentation Information

Title: SRK-439 Selectively Inhibits Myostatin to Promote Healthy Body Composition During Metformin Therapy
Presentation type: Poster presentation
Presenter: Melissa Fulham, Ph.D., Senior Scientist II, Scholar Rock
Date and time: Tuesday, November 5, 2024, 2:30 PM CT
Location: Henry B. González Convention Center, San Antonio, TX

For conference information, visit https://obesityweek.org/.

The slides from the presentation are available in the Publications & Posters section of Scholar Rock's website.

About EMBRAZE

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 binds to pro- and latent myostatin with high affinity and is selective for myostatin (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. 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.

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 indication selection and development timing, including the timing of any regulatory submissions, 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, its cash runway, 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, whether the results from the Phase 3 SAPPHIRE trial will be sufficient to support regulatory approval, that the full results from the Phase 3 SAPPHIRE trial may differ from the topline data, that preclinical and clinical data, including the results from the Phase 2 or 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; 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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