Scholar Rock Presents New Preclinical Data Demonstrating Potential Benefit of SRK-439 for Healthy Weight Loss Management

February 6, 2024

- *Preclinical findings presented at Keystone Symposia show lean mass preservation, fat mass loss, and improved glucose metabolism*
- *Scholar Rock's novel myostatin inhibitor, SRK-439, is part of its growing, industry-leading portfolio of innovative, highly selective anti-myostatin treatments under development*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Feb. 6, 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 showing the potential of SRK-439 to preserve lean mass and improve metabolic health as part of healthy weight loss. These data showed that SRK-439 maintained lean mass and improved fat mass loss when used in combination with a GLP-1 receptor agonist (GLP-1 RA; in separate experiments with semaglutide and liraglutide) in diet-induced obesity (DIO) mice. SRK-439 treatment also led to incremental lowering of fasting glucose beyond the levels seen with semaglutide alone. Detailed results were presented by Melissa Fulham, PhD, of Scholar Rock, at the Keystone Symposia's *Obesity: Causes and Consequences* meeting in Vancouver, BC, Canada on February 5.

"These preclinical data showing that SRK-439 preserves lean mass and improves fat mass loss provide compelling scientific rationale to study SRK-439 in combination with GLP-1 RA therapies for healthy weight loss management," said Jay Backstrom, M.D., MPH, President and CEO of Scholar Rock. "We believe that preserving lean muscle mass through our highly selective approach to myostatin inhibition in combination with GLP-1 RA therapy has the potential to transform the management of weight loss. We look forward to initiating our proof-of-concept study with apitegromab in combination with GLP-1 RA therapy in obesity as we also continue to advance SRK-439 to clinic."

In January, Scholar Rock announced that the U.S. Food and Drug Administration cleared the company's Investigational New Drug (IND) application for its Phase 2 proof-of-concept trial of apitegromab to treat obesity in patients taking a GLP-1 RA. Trial initiation is on track for mid-2024, and data from the apitegromab Phase 2 trial are expected in mid-2025. In parallel, Scholar Rock is developing SRK-439, a novel investigational selective myostatin inhibitor, optimized for the treatment of obesity.

Selectivity and affinity: SRK-439 works by selectively binding to the pro- and latent forms of myostatin, as confirmed through in vitro ELISA testing that shows SRK-439 does not bind to closely related TGFβ family members GDF11 and Activin A, both of which, if inhibited, have potentially detrimental effects outside of the muscle. The studies confirmed that SRK-439 binds to latent myostatin with 0.579 nM affinity. This selectivity and affinity, along with favorable developability characteristics and durable pharmacokinetics suggests that SRK-439 could be suitable for dosing in a subcutaneous formulation and in a low dose volume in a population of adults with obesity.

Changes in body weight, lean mass, and fat mass: Quantitative nuclear magnetic resonance (qNMR) was used to analyze body composition in DIO mice in two separate experiments. In the first, mice received either liraglutide, 0.06 mg/kg daily, or liraglutide, at the same dose, plus SRK-439 in either a 0.3, 1.0, or 3.0 mg/kg weekly dose. In the second experiment, DIO mice received either semaglutide, 0.04 mg/kg daily or semaglutide, at the same dose, plus SRK-439 in either a 0.1, 0.3, 1.0, or 3.0 mg/kg weekly dose. Total body weight, lean mass, and fat mass were assessed. As expected, both liraglutide and semaglutide reduced body weight in DIO mice compared to baseline. SRK-439 diminished the GLP-1 RA-driven lean mass loss in combination with semaglutide (–7.55% to –1.43% change from baseline in lean mass) and with liraglutide (1.98% to 5.55% from baseline). These results were dose-dependent: lean mass was preserved more as the dose of SRK-439 increased. SRK-439 also improved fat mass loss (–36.60% to –46.32% from baseline with semaglutide; –17.31% to –19.04% from baseline with liraglutide).

Results below are shown for the 3 mg/kg dose group of SRK-439 as compared to the IgG control group in each experiment (IgG + semaglutide or IgG + liraglutide), with the full results available on the poster in the Posters and Presentations section of the Scholar Rock website.

	Experiment 1: Liraglutide		Experiment 2: Semaglutide	
	IgG Control	SRK-439 (3mg/kg)	IgG Control	SRK-439 (3mg/kg)
Change in Lean Mass from Baseline	–4.5% (n=8; p<0.0001)	5.6% (n=8; p<0.0001)	–11.3% (n=8; P<0.0001)	–1.4% (n=8; p<0.0001)
Change in Fat Mass from Baseline	0.4% (n=8; p<0.001)	–18.6% (n=8; ns)	–36.6% (n=8; ns)	–37.99 (n=8; ns)

Changes in fasting glucose Fasting glucose was measured on Day 18 of the study in DIO mice that had received treatment with either semaglutide or semaglutide in combination with SRK-439. Mean fasting glucose levels were lower in mice receiving SRK-439, with results for 0.3, 1.0, and 3.0 mg/kg reaching significance compared to semaglutide + IgG control alone (103.0 – 107.8 mg/dL; p<0.05).

For conference information, visit https://www.keystonesymposia.org/.

The poster is available in the Publications & Posters section of Scholar Rock's website.

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 obesity. Based on preclinical data, SRK-439 has the potential to support healthier weight management by preserving lean mass. 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, results and timing of its clinical trials for apitegromab and its preclinical programs, including SRK-439, 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 data 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; Scholar Rock's ability to provide the financial support, resources and expertise necessary to identify and develop product candidates on their expected timelines; 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; 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 the impacts of public health pandemics such as COVID-19 on business operations and expectations, 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 September 30, 2023, 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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