Scholar Rock Announces Positive Final Results from Phase 1 Clinical Trial of SRK-015 in Healthy Volunteers

June 3, 2019

- SRK-015 was well-tolerated in healthy volunteers across all tested doses, supporting evaluation in the ongoing Phase 2 TOPAZ trial in Spinal Muscular Atrophy (SMA)

- Pharmacodynamic results from the completed multiple-ascending dose portion of the trial show robust and durable target engagement by SRK-015

- Final results from the Phase 1 trial will be presented at the upcoming Cure SMA Annual Conference

CAMBRIDGE, Mass., June 03, 2019 (GLOBE NEWSWIRE) -- Scholar Rock Holding Corporation (NASDAQ: SRRK), a clinical-stage biopharmaceutical company focused on the treatment of serious diseases in which protein growth factors play a fundamental role, today announced positive final top-line results from the Phase 1 clinical trial of its product candidate, SRK-015, a highly specific inhibitor of myostatin activation, in healthy adult volunteers. Consistent with previously announced interim findings, the final results showed robust and sustained target engagement and no apparent safety signals were observed across all tested doses. Detailed results from the Phase 1 trial will be presented at the Cure SMA Annual Conference being held June 28-July 1, 2019 in Anaheim, CA.

“We are pleased to be presenting the Phase 1 SRK-015 trial results at the upcoming Cure SMA annual conference as these data provide initial safety and mechanistic insights for SRK-015 and support our Phase 2 program,” said Yung Chyung, M.D., Chief Medical Officer of Scholar Rock. “With the recent initiation of dosing in the TOPAZ Phase 2 clinical trial, we are now evaluating SRK-015’s potential to address motor functional impairment in patients with spinal muscular atrophy.”

“The pharmacodynamic results from the Phase 1 trial offer initial proof-of-mechanism for Scholar Rock’s unique therapeutic approach of targeting the latent form of growth factors,” said Nagesh Mahanthappa, Ph.D., President and CEO of Scholar Rock. “We have advanced the SRK-015 Phase 2 program in patients with SMA and look forward to the interim safety and efficacy results as well as continuing to progress our robust pipeline of highly specific growth factor modulators across a diverse range of therapeutic areas.”

Phase 1 Final Top-line Results

Safety and Immunogenicity Data. SRK-015 was observed to be well-tolerated in the Phase 1 trial with no dose-limiting toxicities identified up to the highest evaluated dose of 30 mg/kg.

- In the single-ascending dose (SAD) portion of the trial, adverse events (AEs) were observed in 30 percent (9/30) of SRK-015-treated subjects and 50 percent (5/10) of placebo-treated subjects.
- In the multiple-ascending dose (MAD) portion of the trial, AEs were observed in 35 percent (7/20) of SRK-015-treated subjects and 67 percent (4/6) of placebo-treated subjects.
- There were no discontinuations due to a treatment-related AE, no hypersensitivity reactions, and no deaths. A single serious AE (SAE) of gallstone-induced pancreatitis was observed in an SRK-015-treated subject and was assessed by the trial investigator as unrelated to treatment.
- Immunogenicity as evaluated by anti-drug antibody testing was negative for all SRK-015 treated subjects in the trial.

Biomarker/Pharmacodynamic (PD) Data. Target engagement was shown in the Phase 1 trial through increases from baseline in levels of latent myostatin.

- The levels of target engagement attained a plateau after a single dose of SRK-015 at 3 mg/kg or greater, suggesting target saturation. This plateau was sustained up to Day 84 after a single dose at 20 mg/kg.
- This durability of effect was further shown in the MAD portion of the trial, during which the plateau was sustained up to at least Day 140 after three doses given once every two weeks at 20 mg/kg or 30 mg/kg.
- In contrast, no meaningful change was observed in the latent myostatin biomarker concentrations in subjects who received placebo.

PD was evaluated through a proprietary, exploratory biomarker assay developed by Scholar Rock that measures serum concentrations of latent myostatin. This assay was used previously to measure target engagement in preclinical studies in healthy animals and a mouse model of SMA.

Pharmacokinetic (PK) Data. Drug exposure to SRK-015 was dose-proportional and SRK-015’s serum half-life was 23-33 days across dose cohorts. In these respects, SRK-015 displayed a PK profile consistent with what is commonly observed for

monoclonal antibodies.

Phase 1 Trial Design

The randomized, double-blind, placebo-controlled Phase 1 clinical trial was designed to evaluate the safety and tolerability of intravenously administered SRK-015, assess the PK and PD profile, and inform dosing for the Phase 2 trial.

- **Single-Ascending Dose:** Enrolled 40 adult healthy volunteers, randomized 3:1 to receive a single dose of SRK-015 or placebo, and evaluated doses of 1, 3, 10, 20 and 30 mg/kg.
- **Multiple-Ascending Dose:** Enrolled 26 adult healthy volunteers, randomized 3:1 to receive SRK-015 or placebo every two weeks for a total of three doses (Day 0, 14 and 28). The MAD portion of the trial evaluated doses of 10, 20 and 30 mg/kg.

About SRK-015
SRK-015 is a selective inhibitor of the activation of myostatin and is an investigational product candidate for the treatment of patients with spinal muscular atrophy (SMA). Myostatin, a member of the TGF-beta 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. Scholar Rock believes the inhibition of the activation of myostatin with SRK-015 may promote a clinically meaningful increase in motor function. A Phase 2 clinical trial in patients with Type 2 and Type 3 SMA is ongoing. The U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation (ODD), and the European Commission (EC) has granted Orphan Medicinal Product Designation, to SRK-015 for the treatment of SMA. The effectiveness and safety of SRK-015 have not been established and SRK-015 has not been approved for any use by the FDA or any other regulatory agency.

About SMA
Spinal muscular atrophy (SMA) is a rare, and often fatal, genetic disorder that typically manifests in young children. An estimated 30,000 to 35,000 patients are afflicted with SMA in the United States and Europe. It is characterized by the loss of motor neurons, atrophy of the voluntary muscles of the limbs and trunk and progressive muscle weakness. The underlying pathology of SMA is caused by insufficient production of the SMN (survival of motor neuron) protein, essential for the survival of motor neurons, and is encoded by two genes, SMN1 and SMN2. While there has been progress in the development of therapeutics that address the underlying SMA genetic defect, there continues to be a high unmet need for therapeutics that directly address muscle atrophy.

About Scholar Rock
Scholar Rock is a clinical-stage biopharmaceutical company focused on the discovery and development of innovative medicines for the treatment of serious diseases in which signaling by protein growth factors plays a fundamental role. Scholar Rock is creating a pipeline of novel product candidates with the potential to transform the lives of patients suffering from a wide range of serious diseases, including neuromuscular disorders, cancer, fibrosis and anemia. Scholar Rock's newly elucidated understanding of the molecular mechanisms of growth factor activation enabled it to develop a proprietary platform for the discovery and development of monoclonal antibodies that locally and selectively target these signaling proteins at the cellular level. By developing product candidates that act in the disease microenvironment, the Company intends to avoid the historical challenges associated with inhibiting growth factors for therapeutic effect. Scholar Rock believes its focus on biologically validated growth factors may facilitate a more efficient development path. For more information, please visit www.ScholarRock.com or follow Scholar Rock on Twitter (@ScholarRock) and LinkedIn (https://www.linkedin.com/company/scholar-rock/).

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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 future expectations, plans and prospects, including without limitation, expectations regarding the potential of SRK-015 as a therapy in SMA and the timeline for and progress in developing SRK-015. The use of words such as "may," "might," "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 the risks that earlier preclinical and clinical data and testing of SRK-015 may not be predictive of the results or success of additional clinical trials, the development of SRK-015 will take longer and/or cost more than planned, SRK-015 will not receive regulatory approval and those risks more fully discussed in the section entitled "Risk Factors" in Scholar Rock's Quarterly Report on Form 10-Q for th e quarter ended March 31, 2019, 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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