Scholar Rock Reports Preliminary Pharmacokinetic and Pharmacodynamic Data from TOPAZ Phase 2 Trial of SRK-015 for the Treatment of Patients with Spinal Muscular Atrophy

November 19, 2019

- *Biomarker results confirm presence of latent myostatin in patients with SMA, further supporting relevance of drug target in disease*
- *SRK-015 demonstrated robust and dose-dependent target engagement*
- *Data provide first evidence of successful pharmacologic engagement of a latent growth factor in a human disease setting*

CAMBRIDGE, Mass., Nov. 19, 2019 (GLOBE NEWSWIRE) -- Scholar Rock (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 preliminary pharmacokinetic (PK) and pharmacodynamic (PD) results from the TOPAZ Phase 2 proof-of-concept trial of SRK-015 for the treatment of patients with spinal muscular atrophy (SMA). The planned preliminary PK/PD analysis, which includes data from 29 patients with SMA across all three cohorts, showed dose-proportional drug exposure and demonstrated target engagement, as evidenced by dose-dependent increases of up to 100-fold in the serum levels of latent myostatin following SRK-015 treatment (2 mg/kg and 20 mg/kg doses). SRK-015 is a highly selective inhibitor of the precursor, or latent form, of myostatin, and was specifically designed to avoid interactions with related targets such as activins, GDF-11, or BMPs, to potentially improve the therapeutic profile compared to traditional non-selective inhibitors.

“We are pleased with the progress we have made to date towards our goal of developing SRK-015 as a muscle-directed therapy to address the functional deficits that remain a significant unmet need for patients with SMA despite advancements with SMN upregulators,” said Yung Chyung, M.D., Chief Medical Officer of Scholar Rock. “These preliminary PK/PD results positively address two important questions for the program by both confirming the presence of latent myostatin in patients with SMA and further corroborating the ability of SRK-015 to engage this drug target, including in pediatric patients with SMA.”

“These results represent a key milestone for Scholar Rock by showing that we can indeed bring together cutting-edge monoclonal antibody technology with deep structural biology insights to target latent forms of growth factors in the context of human disease,” said Nagesh Mahanthappa, Ph.D., President and CEO of Scholar Rock. “We look forward to building upon these insights as we advance a growing portfolio of product candidates.”

TOPAZ Phase 2 Preliminary PK/PD Results
The Phase 2 proof-of-concept trial is evaluating the safety and efficacy of SRK-015 dosed intravenously every four weeks (Q4W) over a 12-month treatment period. The trial is anticipated to enroll approximately 55 patients with Type 2 or Type 3 SMA in the U.S. and Europe across three distinct cohorts. Patients in Cohorts 1 and 2 are being treated with 20 mg/kg of SRK-015 Q4W and patients in Cohort 3 are randomized to either 20 mg/kg or 2 mg/kg Q4W. The primary objectives of the cohorts are to assess safety and clinically meaningful motor functional outcomes, such as the Revised Hammersmith Scale (RHS) and the Hammersmith Functional Motor Scale Expanded (HFMSE). The TOPAZ trial is ongoing and further details about the trial can be found on clinicaltrials.gov.

The preliminary PK/PD analysis of the TOPAZ trial includes data from 29 patients across the three cohorts; 12 patients in Cohort 1, eight patients in Cohort 2, and nine patients in Cohort 3. These patients had received one dose of SRK-015 and were evaluated for four weeks as of the data cutoff. The preliminary results are as follows:

- Dose-dependent increases of up to 100-fold in serum latent myostatin levels following treatment with SRK-015 (2 mg/kg and 20 mg/kg doses) confirms the presence of latent myostatin in patients with SMA and demonstrates robust target engagement.
- Fold-increases from baseline in serum latent myostatin levels in the first four weeks following SRK-015 treatment were comparable between SMA patients in the TOPAZ trial and healthy adult volunteers in the Phase 1 trial.
- In patients with SMA, SRK-015 displayed a preliminary PK profile exhibiting dose proportionality and low variability, consistent with PK observations from the Phase 1 trial in healthy adult volunteers.
- No clinically significant safety signals had been observed as of the data cutoff for this preliminary PK/PD analysis.

An interim efficacy and safety analysis is planned, encompassing a subset of patients with at least six months of treatment exposure. The interim results are expected in the first half of 2020 with top-line results for the full 12-month treatment period

expected starting in the fourth quarter of 2020 and through the first quarter of 2021.

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 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. Scholar Rock believes the inhibition of the activation of myostatin with SRK-015 may promote a clinically meaningful increase in muscle strength. 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. The Company's two lead product candidates include SRK-015, a selective inhibitor of the activation of myostatin, for the treatment of patients with Spinal Muscular Atrophy and SRK-181, an isoform-selective inhibitor of TGFβ1 activation as a cancer immunotherapy in combination with anti-PD(L)1 antibodies. 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.

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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 clinical trials, interim clinical trial results will differ from final clinical trial results, 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 the quarter ended September 30, 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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Source: Scholar Rock