Scholar Rock Announces Initiation of Patient Dosing in Phase 2 Trial of SRK-015 in Spinal Muscular Atrophy

May 8, 2019

- *Dosing of patients has commenced in TOPAZ, the Phase 2 clinical trial of SRK-015 in Type 2 and Type 3 Spinal Muscular Atrophy (SMA)*
- *Preliminary PK/PD data from a subset of patients are anticipated by year-end 2019*
- *Interim safety and efficacy analysis of a subset of patients with six months of treatment expected in 1H20; top-line results for the full 12-month treatment period are expected beginning 4Q20*

CAMBRIDGE, Mass., May 08, 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 the initiation of patient dosing in the Phase 2 clinical trial of SRK-015, a highly specific inhibitor of myostatin activation, in Type 2 and Type 3 Spinal Muscular Atrophy (SMA). All patients will receive SRK-015 once every four weeks either as a monotherapy or in conjunction with an approved SMN upregulator therapy. This Phase 2 trial is supported by interim results from the Phase 1 trial in healthy volunteers that showed favorable safety and tolerability, pharmacodynamic (PD), and pharmacokinetic (PK) results as well as preclinical data that highlight the promising potential of myostatin as a drug target in SMA.

“Despite real advances improving upon the natural history of SMA with therapies that increase levels of the deficient SMN protein, individuals with SMA nonetheless experience a range of weakness from mild to profound,” said Thomas Crawford, M.D., Professor of Neurology at Johns Hopkins and Lead Principal Investigator of the TOPAZ trial. “Muscle-directed therapy is the next step towards addressing residual weakness in individuals with SMA. I believe SRK-015 holds real promise to potentially improve their overall motor function.”

“The initiation of patient dosing in our Phase 2 TOPAZ study marks an important milestone towards our goal of establishing SRK-015 as the first muscle-directed therapy to help address the functional deficits that continue to affect patients with SMA despite available therapies,” said Yung Chyung, M.D., Chief Medical Officer of Scholar Rock. “Results from this Phase 2 trial will further our understanding on the potential clinical benefits of targeting the latent form of myostatin and open up the possibility of investigating other neuromuscular disorders.”

TOPAZ Phase 2 Trial Design

The Phase 2 proof-of-concept trial will evaluate 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., Canada, and Europe across three distinct and parallel cohorts.

- **Cohort 1** has an open-label, single-arm design and will enroll approximately 20 patients ages 5 through 21 with ambulatory Type 3 SMA. Patients will be treated with 20 mg/kg of SRK-015 Q4W as monotherapy or in conjunction with an approved SMN upregulator therapy. The primary objectives of the cohort are to assess safety and the mean change from baseline in Revised Hammersmith Scale (RHS) over 12 months of treatment. Key secondary assessments include the proportion of patients attaining various thresholds of change from baseline in RHS and change from baseline in 6-minute walk test (6MWT).

- **Cohort 2** has an open-label, single-arm design and will enroll approximately 15 patients ages 5 through 21 with Type 2 or non-ambulatory Type 3 SMA and who are already receiving treatment with an approved SMN upregulator. Patients will be treated with 20 mg/kg of SRK-015 Q4W in conjunction with an approved SMN upregulator therapy. The primary objectives of the cohort are to assess safety and the mean change from baseline in Hammersmith Functional Motor Scale Expanded (HFMSE) over 12 months of treatment. Key secondary assessments include the proportion of patients attaining various thresholds of change from baseline in HFMSE and change from baseline in Revised Upper Limb Module (RULM).

- **Cohort 3** has a randomized, double-blind, parallel arm design and will evaluate the effects of SRK-015 in the setting of early intervention with an SMN upregulator therapy. This cohort will enroll approximately 20 patients with Type 2 SMA who are at least two years of age and initiated treatment with an approved SMN upregulator before five years of age. Patients will be randomized 1:1 to be treated with either 2 mg/kg or 20 mg/kg of SRK-015 Q4W. The primary objectives of the cohort are to assess safety and the mean change from baseline in HFMSE over 12 months of treatment. Key secondary measures include the proportion of patients attaining various thresholds of change from baseline in HFMSE and change from baseline in RULM.

  In cohort 3, a low dose arm of 2 mg/kg has been included for dose exploration purposes. The relationship between drug exposure and therapeutic effect over time may be evaluated by characterizing and comparing the time course of clinical

effect for the 2 mg/kg and 20 mg/kg arms.

An interim analysis is planned for each cohort, encompassing a subset of patients with at least six months of treatment exposure. These interim results by cohort are expected in the first half of 2020. Top-line results for the full 12-month treatment period are expected starting in the fourth quarter of 2020 and through the first quarter of 2021. In addition, analyses of preliminary pharmacokinetic (PK) and pharmacodynamic (PD) data from a subset of patients are planned by the end of 2019.

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 muscle mass and 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. 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/).

Scholar Rock® is a registered trademark of Scholar Rock, Inc.

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 Annual Report on Form 10-K for the quarter and full year ended December 31, 2018, 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.

Scholar Rock Contact:
Investors/Media
Catherine Hu, 917-601-1649
chu@scholarrock.com

Media Contact:
The Yates Network
Kathryn Morris, 914-204-6412
kathryn@theyatesnetwork.com

SCHOLAR ROCK

Source: Scholar Rock