Scholar Rock Presents Data for SRK-015 at the SMA Europe 2nd International Scientific Congress

February 6, 2020

CAMBRIDGE, Mass., Feb. 06, 2020 (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 two poster presentations on SRK-015, a highly specific inhibitor of the activation of latent myostatin, at the SMA Europe 2nd International Scientific Congress being held in Paris-Evry, France. The two posters will highlight key preclinical and Phase 1 clinical data for SRK-015 as well as preliminary demographics, baseline characteristics, and pharmacokinetic (PK)/pharmacodynamic (PD) data from the TOPAZ Phase 2 proof-of-concept trial evaluating SRK-015 for the treatment of patients with Type 2 and Type 3 Spinal Muscular Atrophy (SMA).

"We are pleased to be presenting preclinical and clinical data for SRK-015 at the SMA Europe Congress as we continue to advance the development of SRK-015 towards a goal of improving motor function in patients with SMA," said Yung Chyung, M.D., Chief Medical Officer of Scholar Rock. "With the recent completion of enrollment in the TOPAZ Phase 2 trial, we now await the interim safety and efficacy results that are expected mid-year for an early look at the potential of SRK-015 in addressing the continued functional deficits experienced by patients with SMA despite treatment with SMN upregulators."

TOPAZ Phase 2 Proof-of-Concept Trial Details and Preliminary PK/PD Data

A Phase 2 Study to Evaluate the Efficacy and Safety of SRK-015 in Patients with Later-Onset Spinal Muscular Atrophy (TOPAZ): An Introduction

- Poster P7: Thursday, February 6, 2020 at 5:00–6:00pm (local time)

Preliminary TOPAZ demographic and baseline characteristics:

- *(Based on data entered and source verified as of January 8, 2020)*
- Enrollment in the TOPAZ trial has been completed with a total of 58 patients enrolled across 19 sites in the U.S. and Europe;
    - Cohort 1 enrolled 23 patients with ambulatory Type 3 SMA
    - Cohort 2 enrolled 15 patients with Type 2 or non-ambulatory Type 3 SMA
    - Cohort 3 enrolled 20 patients with Type 2 SMA
- Preliminary demographic and baseline characteristic data are in-line with published data with nusinersen and ensure appropriate inclusion of patients with Type 2 and Type 3 SMA.
- Mean age at informed consent was 12.7 years in Cohort 1 (n=19), 11.8 years in Cohort 2 (n=12), and 4.0 years in Cohort 3 (n=20).
- Mean Revised Hammersmith Scale (RHS) score at screening in Cohort 1 was 47.4 (n=10).
- Mean Hammersmith Functional Motor Scale Expanded (HFMSE) score at screening in Cohort 2 and 3 were 22.5 (n=12) and 24.8 (n=16), respectively.

Preliminary PK/PD analysis (as of data cutoff in November 2019):

- 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.
- 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.

Preclinical and Phase 1 Healthy Volunteer Clinical Data[(1)]

Clinical Development of SRK-015, a Fully Human Anti-proMyostatin Monoclonal Antibody, for the Treatment of Later-Onset Spinal Muscular Atrophy

- Poster P10: Thursday, February 6, 2020 at 5:00–6:00pm (local time)

Preclinical studies[2]:

- Improved muscle strength following administration of muSRK-015P (mouse analog of SRK-015) in mouse models of early and late SMN restoration. Treatment with muSRK-015P resulted in 20%-51% increases in maximal torque (at ≥ 40 Hz) of the plantar flexor muscle group and a greater percentage of muscle fibers compared to treatment with placebo (vehicle).
- Multi-fold increase in serum latent myostatin levels following treatment with muSRK-015P in both early and late SMN restoration mouse models confirm the presence of the latent myostatin target in a modeled diseased setting.
- Relative dose-proportional accumulation of serum latent myostatin, demonstrating target engagement, in rats and cynomolgus monkeys following administration of SRK-015 compared to no meaningful change with placebo.
- Well-behaved pharmacokinetic (PK) profile displayed across animal species (adult rats and cynomolgus monkeys).

Phase 1 healthy volunteer trial[3]:

- SRK-015 was well-tolerated with no apparent safety signals and no dose-limiting toxicities were identified up to the highest evaluated dose of 30 mg/kg.
- Robust and sustained target engagement, along with durable saturation, following administration of SRK-015 in both the single-ascending and multiple-ascending dose portions of the Phase 1 trial.
- Well-behaved PK profile, supporting dosing once every 4-weeks, which is being evaluated in the ongoing Phase 2 trial.

Both posters can be accessed at: https://scholarrock.com/platform/publications/

1. Preclinical, Phase 1, and preliminary TOPAZ PK/PD data are not predictive of efficacy and safety outcomes in the ongoing TOPAZ Phase 2 trial and any future clinical trials.
2. Long, K., O'Shea, K., Khairallah, R., et al. Specific Inhibition of Myostatin Activation is Beneficial in Mouse Models of SMA Therapy, *Human Molecular Genetics*, ddy382, https://doi.org/10.1093/hmg/ddy382
3. Scholar Rock. Data on file. 2019

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 Scholar Rock's future expectations, plans and prospects, including without limitation, Scholar Rock's expectations regarding the timing of its clinical trials for SRK-015; the potential of SRK-015 to address certain patient unmet needs; and the ability of any product candidate to perform in humans in a manner consistent with nonclinical or preclinical study data. 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 Scholar Rock's ability to provide the financial support, resources and expertise necessary to identify and develop product candidates on the expected timeline; preclinical data and results may not be predictive of clinical results; Scholar Rock's dependence on third parties for development and manufacture of product candidates including to supply any clinical trials; 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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