# Scholar Rock Provides Corporate Update and Outlines Key R&D Priorities for 2020

January 10, 2020

*- Completed enrollment of TOPAZ Phase 2 clinical trial of SRK-015 in patients with Type 2 and Type 3 Spinal Muscular Atrophy*

*- Submitted IND application for SRK-181, a potent and selective inhibitor of latent TGFβ1 activation; plan to initiate a Phase 1 proof-of-concept trial in patients with solid tumors in the first quarter of 2020*

*- Advanced strategic collaboration with Gilead focused on fibrosis with successful demonstration of efficacy in preclinical in vivo proof-of-concept studies; earned $25 million milestone payment*

CAMBRIDGE, Mass., Jan. 10, 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 highlighted key accomplishments of the past year and announced R&D priorities for 2020.

**Key Accomplishments:**

- **SRK-015:** highly specific inhibitor of latent myostatin activation being developed for the treatment of Spinal Muscular Atrophy (SMA).
    - Initiated and completed enrollment of the TOPAZ Phase 2 proof-of-concept trial of SRK-015 in patients with Type 2 and Type 3 SMA.
    - Preliminary pharmacokinetic (PK) and pharmacodynamic (PD) data from 29 patients in the TOPAZ trial are consistent with robust target engagement in patients with SMA, providing the first evidence of successful pharmacologic engagement of a latent growth factor in a human disease setting.
    - No clinically significant safety signals had been observed in TOPAZ as of the data cutoff for the preliminary PK/PD analysis.
- **SRK-181:** potent and selective inhibitor of latent transforming growth factor beta 1 (TGFβ1) activation aimed at expanding anti-tumor responses from immunotherapy by overcoming primary resistance to checkpoint inhibitor therapies.
    - Accelerated non-clinical development and submitted an Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA), supporting plans to initiate a Phase 1 proof-of-concept trial in patients with solid tumors in the first quarter of 2020.
    - Demonstrated preclinically that Scholar Rock's highly selective inhibitor of latent TGFβ1 activation rendered resistant solid tumors vulnerable to PD-1 blockade and drove tumor regression in syngeneic mouse tumor models emulating key features of clinically observed primary resistance.
    - Demonstrated preclinically the potential of SRK-181 for reduced toxicity that has historically limited drug exposure from non-selective TGFβ inhibition. In a pilot toxicology study, treatment of adult rats with SRK-181 up to a weekly dose of 100mg/kg for four weeks had an improved toxicity profile and avoided the cardiovascular toxicity observed with a non-selective TGFβ antibody and an ALK5 inhibitor. In addition, no adverse effects were observed up to the highest evaluated dose of 200 mg/kg per week in a 4-week GLP rat toxicology study and 300 mg/kg per week in a 4-week GLP non-human primate toxicology study.
- **Preclinical research programs:**
    - Achieved first milestone and earned a $25 million payment in strategic collaboration with Gilead Sciences, Inc. by demonstrating that highly selective inhibitors of latent TGFβ1 activation are efficacious in relevant preclinical models of fibrotic diseases. Scholar Rock is advancing multiple collaboration programs toward product candidate selection.
    - Continued to progress preclinical pipeline programs for neuromuscular disorders, cancers, fibrosis, and anemias.

"The past 12 months were a time of remarkable progress for Scholar Rock across all of our R&D programs. We rapidly advanced

our SRK-015 program in SMA by completing enrollment in the TOPAZ trial in just eight months, achieved the initial catalytic milestone in our fibrosis-focused collaboration with Gilead, and submitted our IND application for SRK-181 for cancer immunotherapy at the end of the year," said Nagesh Mahanthappa, Ph.D., President and CEO of Scholar Rock. "As we begin 2020 with great momentum, we look forward to further advancing our robust pipeline in the year ahead. Importantly, with the recent implication of TGFβ1 activity as a major checkpoint inhibitor resistance mechanism in patients, we believe that SRK-181 holds unique potential to meaningfully broaden clinical responses to PD-(L)1 inhibitors. With our plans to initiate enrollment of patients with solid tumors in our Phase 1 proof-of-concept trial this quarter, we now expect initial clinical data for SRK-181 as well as for SRK-015 this year."

**2020 R&D Priorities:**

**SRK-015 Program for Spinal Muscular Atrophy:**

- **Interim Safety and Efficacy Data from TOPAZ Phase 2 Proof-of-Concept Trial Expected in Mid-2020.** Scholar Rock plans to report interim safety and efficacy results at six months of treatment exposure for all three fully enrolled cohorts in mid-2020. Top-line data for the full 12-month treatment period are expected beginning in the fourth quarter of 2020 and into the first quarter of 2021.

- **Identification of Second Indication for SRK-015 Planned for 2020.** Scholar Rock continues to evaluate multiple potential opportunities beyond SMA, for which the selective inhibition of the activation of myostatin with SRK-015 may offer therapeutic benefit.

**SRK-181 Program for Immuno-Oncology:**

- **Initiation of SRK-181 Phase 1 Dose Escalation and Dose Expansion Clinical Trial in Patients with Solid Tumors Planned for the First Quarter of 2020.** TGFβ signaling has been implicated in driving immune exclusion, a key culprit of primary resistance to checkpoint inhibitor therapies as described by multiple academic and industrial groups. Scholar Rock is developing SRK-181 as a potential therapy in cancer immunotherapy to broaden responses to anti-PD-(L)1 therapies. In an aim to reduce toxicities associated with non-selective TGFβ inhibition that have historically limited the ability to dose at clinically meaningful levels, SRK-181 has been designed to selectively block the TGFβ1 isoform.

  An IND application for SRK-181 has been submitted to the FDA and Scholar Rock plans to initiate a Phase 1 proof-of-concept trial in the first quarter of 2020 in patients with locally advanced or metastatic solid tumors. The two-part trial will consist of a dose escalation portion for SRK-181 as both a single-agent and in combination with an approved anti-PD-(L)1 antibody, followed by a dose expansion portion evaluating SRK-181 in combination with an approved anti-PD-(L)1 antibody in multiple tumor-specific cohorts, such as urothelial carcinoma, melanoma, non-small cell lung cancer, and other solid tumors. Key objectives of the study include evaluating the safety and pharmacokinetics of SRK-181 and the efficacy of SRK-181 in combination with anti-PD-(L)1 therapy in the treatment of solid tumors exhibiting primary resistance to anti-PD-(L)1 therapy. Initial clinical data from the Phase 1 trial are expected in the second half of 2020 with clinical response and safety data anticipated in 2021.

**Strategic Fibrosis Collaboration with Gilead Sciences:**

- **Further Advance Collaborative Programs Towards Product Candidate Selection.** Scholar Rock has demonstrated in preclinical studies that potent and selective inhibitors of TGFβ1 signaling prevent the activation of the growth factor in the fibrotic matrix and may offer a powerful new approach to suppressing pro-fibrotic signaling in multiple organs. With the recent achievement of the first milestone with the demonstration of efficacy in *in vivo* proof-of-concept studies, Scholar Rock and Gilead are advancing the collaboration with the aim of selecting molecules to be developed as new medicines for patients with fibrotic diseases.

  Gilead has exclusive options to license worldwide rights to product candidates that emerge from three Scholar Rock TGFβ programs. Scholar Rock is responsible for antibody discovery and preclinical research through product candidate nomination, after which, upon exercising the option for a program, Gilead will be responsible for the program's preclinical and clinical development and commercialization. Scholar Rock is eligible to receive up to an additional $1,425 million in potential payments from Gilead as well as high single-digit to low double-digit tiered royalties on sales of potential future products originating from the collaboration.

**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 its growth, strategy, progress; timing of its clinical trials for SRK-015, SRK-181, and other product candidates; indication selection and development timing; the ability of any product candidate to perform in humans in a manner consistent with nonclinical or preclinical study data; progress under its collaboration with Gilead. 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; 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 ability to support its current and potential future collaborations, including its collaboration with Gilead; 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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