Scholar Rock Presents Data from Part A of the DRAGON Phase 1 Trial Evaluating SRK-181 as Monotherapy and in Combination with Anti-PD-(L)1 for the Treatment of Solid Tumors -- Announces Advancement into Part B

November 12, 2021

- Safety and pharmacokinetic results from Part A dose escalation supported Part B dose selection, which is estimated to offer drug exposure at levels exceeding those hypothesized as needed for anti-tumor effects

- Part B dose expansion portion of the DRAGON trial has been initiated and will assess SRK-181 in combination with an approved anti-PD-(L)1 therapy across multiple solid tumor cohorts to test proof of concept; early efficacy and safety data anticipated in 2022

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Nov. 12, 2021-- 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 presented initial clinical data from Part A of its DRAGON Phase 1 proof-of-concept trial (NCT04291079) at the ongoing 36th Society for Immunotherapy of Cancer (SITC) Annual Meeting (November 10-14, 2021), which supported dose selection and advancement into Part B. The DRAGON trial is investigating SRK-181, a selective inhibitor of TGFβ1 activation, in patients with locally advanced or metastatic solid tumors that have shown primary resistance to checkpoint inhibitor therapies.

The main objectives of DRAGON Part A are to evaluate the safety and tolerability of SRK-181 alone (Part A1) or in combination with anti-PD-(L)1 checkpoint inhibitor therapy (Part A2) and to determine the recommended dose for the Part B dose expansion phase. Part A1 enrolled patients who have experienced treatment failure from available standard of care therapy, and Part A2 enrolled patients who did not respond to prior anti-PD-(L)1 therapy. Based on the safety and pharmacokinetic data from Part A, Scholar Rock has initiated Part B, which is evaluating SRK-181 dosed 1500 mg every three weeks (Q3W) in patients receiving an approved anti-PD-(L)1 therapy dosed Q3W and 1000 mg every two weeks (Q2W) in patients receiving an approved anti-PD-(L)1 therapy dosed Q2W.

“While checkpoint inhibitor therapy has definitely advanced the treatment of cancer, resistance to this type of therapy remains a very significant unmet medical need,” said Nagesh Mahanthappa, Ph.D., Interim CEO. “We are excited that the DRAGON Part A results support moving forward in Part B with a dose of SRK-181 aimed at robustly suppressing TGFβ1 signaling, and look forward to advancing our program to test our hypothesis that SRK-181 can overcome resistance to checkpoint inhibitors thereby increasing the number of patients who may benefit from cancer immunotherapy.”

Details for the virtual e-poster are as follows:

- **Title**: First-in-Human Phase 1 Trial of SRK-181: A Latent TGFβ1 inhibitor, Alone or in Combination with Anti-PD-(L)1 Treatment in Patients with Advanced Solid Tumors (DRAGON trial) (#532). The full abstracts were made available on the SITC website on November 9, 2021.
- **Time:** Virtual e-posters will be on display on the SITC 2021 virtual meeting platform starting November 12, 2021.

Highlights from the DRAGON Part A data presented at SITC include:

- As of September 7, 2021, 29 patients have been dosed in Part A of the trial. The median number of prior lines of therapy was 4 (range 1, 9) for Part A1 and 4 (range 2, 6) for Part A2.
- As of October 12, 2021, no dose-limiting toxicities were observed with SRK-181 in Part A. Doses up to 3000 mg Q3W and 2000 mg Q2W as a monotherapy in Part A1 and 1600 mg Q3W in combination with anti-PD-(L)1 therapy in Part A2 have been evaluated.
- The most common (>10%) treatment-emergent adverse events of any grade related to treatment were fatigue, decreased appetite, and nausea (Part A1) and rash maculo-papular (Part A2).
- Preliminary data showed a pharmacokinetic (PK) profile of SRK-181 consistent with that which is generally observed for monoclonal antibodies.
- Preliminary anti-tumor effects were assessed using RECIST1.1 and reported based upon local investigator reads:
    - Among 19 patients in Part A1 (monotherapy), eight patients had a best response of stable disease (SD). There were three patients with ovarian cancer in Part A1; each of these patients had stable disease, with tumor regression observed in two patients.
    - Among 10 patients in Part A2 (combination therapy), one patient with renal cell carcinoma (RCC) who had a lack of response to prior anti-PD-1 therapy had a partial response (PR) after treatment with SRK-181 dosed 800 mg Q3W in combination with the same anti-PD-1 therapy. In addition, four patients had a best response of SD.

The efficacy and safety of SRK-181 are being evaluated in DRAGON Part B. With early data anticipated to be available in 2022, Part B will enroll and dose patients in multiple proof of concept cohorts conducted in parallel, including urothelial carcinoma (UC),

cutaneous melanoma (MEL), non-small cell lung cancer (NSCLC), as well as a miscellaneous cohort of other solid tumors. Another cohort focusing on patients with clear cell renal cell carcinoma (ccRCC) is being added based on emerging insights, including preliminary data from Part A. Each cohort will enroll up to 40 patients with locally advanced or metastatic solid tumors who have demonstrated primary resistance to anti-PD-(L)1 therapy. The ccRCC cohort will also explore the effects of SRK-181 in patients with relapsed response after anti-PD-(L)1 treatment. Patients in the UC, MEL, NSCLC and ccRCC cohorts will be treated with SRK-181 in combination with pembrolizumab, and patients in the miscellaneous solid tumor cohort will be treated with SRK-181 in combination with any approved anti-PD-(L)1 therapy.

The selection of the Part B dose was based upon safety and PK results from Part A. Patients receiving an approved anti-PD-(L)1 therapy dosed Q3W will be dosed with SRK-181 dosed 1500 mg Q3W, while patients receiving an approved anti-PD-(L)1 therapy dosed Q2W will be dosed with SRK-181 dosed 1000 mg Q2W. Drug exposures from these regimens are anticipated to exceed the levels hypothesized as needed for anti-tumor effects, as predicted from PK modeling and preclinical tumor model data.

“We are pleased by the Part A data, which have enabled the initiation of Part B with a dose regimen aimed at robustly testing the therapeutic hypothesis for SRK-181 in overcoming tumor resistance to anti-PD-(L)1 therapy,” said Yung Chyung, M.D., CMO. “Part B has been specifically enriched with solid tumor types for which we believe there may be a higher potential for early efficacy signals on the basis of translational and preclinical insights.”

About SRK-181
SRK-181 is a selective inhibitor of TGFβ1 activation and is an investigational product candidate being developed to overcome primary resistance to checkpoint inhibitor therapy, such as anti-PD-(L)1 antibodies. TGFβ1 is the predominant TGFβ isoform expressed in many human tumor types. Based on analyses of various human tumors that are resistant to anti-PD-(L)1 therapy, data suggest TGFβ1 is a key contributor to the immunosuppressive tumor microenvironment, excluding and preventing entry of cytotoxic T cells into the tumor, thereby inhibiting anti-tumor immunity [(1)]. Scholar Rock believes SRK-181, which specifically targets the latent TGFβ1 isoform, has the potential to overcome this immune cell exclusion and induce tumor regression when administered in combination with anti-PD-(L)1 therapy while potentially avoiding toxicities associated with non-selective TGFβ inhibition. The DRAGON Phase 1 proof-of-concept clinical trial (NCT04291079) in patients with locally advanced or metastatic solid tumors is ongoing. The efficacy and safety of SRK-181 have not been established. SRK-181 has not been approved for any use by the FDA nor any other regulatory agency.

(1) Martin et al., Sci. Transl. Med. 12: 25 March 2020

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, and fibrosis. Scholar Rock’s approach to targeting 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 and timing of its clinical trials for SRK-181, and indication selection and development timing, its cash runway, the ability of any product candidate to perform in humans in a manner consistent with earlier nonclinical, preclinical or clinical trial data, and the potential of its product candidates and proprietary platform. 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 preclinical and clinical data, including the results from Part A of the Phase 1 trial of SRK-181, are not predictive of, are inconsistent with, or more favorable than, data generated from future clinical trials of the same product candidate, including Part B of the Phase 1 trial of SRK-181, Scholar Rock’s ability to provide the financial support, resources and expertise necessary to identify and develop product candidates on the expected timeline, the data generated from Scholar Rock’s nonclinical and preclinical studies and clinical trials, information provided or decisions made by regulatory authorities, 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 dependence on third parties for development and manufacture of product candidates including to supply any clinical trials, Scholar Rock’s ability to manage expenses and to obtain additional funding when needed to support its business activities and establish and maintain strategic business alliances and new business initiatives, and the impacts of public health pandemics such as COVID-19 on business operations and expectations, as well as 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, 2021, 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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