Scholar Rock Announces Initiation of Patient Dosing in Phase 1 Proof-of-Concept Immuno-Oncology Trial of SRK-181 to Overcome Primary Resistance to Anti-PD-(L)1 Therapy

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- Dosing of patients with locally advanced or metastatic solid tumors has commenced in the DRAGON Phase 1 clinical trial of SRK-181, a highly specific inhibitor of latent TGFβ1 activation

- Update on dose escalation is expected in the fourth quarter of 2020; clinical response and safety data anticipated in 2021

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 5, 2020-- 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 the initiation of patient dosing in the DRAGON Phase 1 dose escalation and dose expansion clinical trial of SRK-181 in patients with locally advanced or metastatic solid tumors. SRK-181 is a potent and highly selective inhibitor of latent TGFβ1 activation and is being developed to increase responses to immunotherapy by overcoming primary resistance to anti-PD-1 or anti-PD-L1 antibody therapy.

“Based on emerging evidence in the field from human and preclinical data implicating TGFβ1 as a key culprit in primary resistance to anti-PD-(L)1 therapy, we are excited to be investigating a rational approach to combination immunotherapy,” said Yung Chyung, M.D., Chief Medical Officer of Scholar Rock. “Our team’s focus and determination to advance SRK-181 and this Phase 1 trial, particularly as the evolving COVID-19 pandemic has resulted in various challenges, has been truly impressive. We remain committed to our mission of developing important therapies for patients and the initiation of dosing in this proof-of-concept trial represents an important milestone for us and our TGFβ1 platform.”

DRAGON Phase 1 Proof-of-Concept Trial

The DRAGON Phase 1 open-label, dose escalation and dose expansion clinical trial is evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and efficacy of SRK-181 in adult patients with locally advanced or metastatic solid tumors enrolled across multiple sites in the U.S. The two-part trial consists of a dose escalation portion (Part A) for SRK-181 as both a single agent and in combination with approved anti-PD-(L)1 therapy, followed by a dose expansion portion (Part B) evaluating SRK-181 in combination with approved anti-PD-(L)1 therapy in multiple tumor-specific cohorts. Intravenous (IV) SRK-181 is administered every 3 weeks (Q3W) and additional dosing regimens may be explored.

Due to the COVID-19 pandemic and the anticipated pace of enrollment, Scholar Rock now plans to provide an update on dose escalation of SRK-181 as a single agent as well as in combination with anti-PD-(L)1 therapy in the fourth quarter of 2020. Clinical response and safety data are anticipated in 2021. Timing of data read-outs may be further impacted by COVID-19-related disruptions.

Part A Dose Escalation: Part A of the Phase 1 trial assesses SRK-181 both as a single agent and in combination with approved anti-PD-(L)1 therapy and will be conducted in a staggered fashion. The safety, PK, and activity of SRK-181 will be evaluated, including effects upon biomarkers, such as CD8 T cell infiltration, based on biopsies before and after treatment.

Part A1 evaluates SRK-181 as a single agent in patients with locally advanced or metastatic solid tumors. The dose escalation will follow a modified 3+3 design and assess doses starting at 80 mg up to 2400 mg (based on an average body weight of approximately 80 kg).

Part A2 evaluates SRK-181 in combination with anti-PD-(L)1 therapy in patients with locally advanced or metastatic solid tumors that exhibit primary resistance to anti-PD-(L)1 antibodies. Lack of response is characterized as either stable disease or progressive disease following at least three cycles of treatment with an approved anti-PD(L)1 therapy, either alone or in combination with chemotherapy. Patients must have received their most recent dose of anti-PD-(L)1 therapy within six months of enrollment. In combination with SRK-181, patients will be treated with the same anti-PD-(L)1 therapy that they had previously tried and did not experience a response. The dose escalation will follow a 3+3 design and assess doses up to 2400 mg.

Part B Dose Expansion: Part B of the trial consists of multiple parallel cohorts to evaluate the anti-tumor activity of SRK-181 in combination with anti-PD-(L)1 therapy. The target indications are expected to include non-small cell lung cancer, urothelial carcinoma, and cutaneous melanoma, amongst other solid tumor types.

Each cohort will enroll up to 40 patients with locally advanced or metastatic solid tumors for which anti-PD-(L)1 therapy is approved and have demonstrated primary resistance, characterized as a lack of response (stable or progressive disease) following at least three cycles of treatment. Patients must have received their most recent dose of anti-PD-(L)1 therapy within six months of enrollment. Similar to Part A2, patients will be treated with SRK-181 in combination with the same anti-PD-(L)1 therapy that they had previously tried and did not experience a response.

About SRK-181

SRK-181 is a potent and highly 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 tumors, particularly for those tumors where checkpoint therapies are currently approved. Based on analyses of human tumors that are resistant to anti-PD-(L)1 therapy, data suggests TGFβ1 is a key contributor to excluding immune cell entry into the tumor microenvironment, thereby preventing normal immune function. By overcoming this immune cell exclusion, Scholar Rock believes SRK-181 has the potential to induce tumor regression when administered in combination with anti-PD-(L)1 therapy. A Phase 1 proof-of-concept clinical trial in patients with locally advanced or metastatic solid tumors is ongoing. The effectiveness and safety of SRK-181 have not been established and SRK-181 has not been approved for any use by the FDA or any other regulatory agency.

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 therapies. 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.

Forward-Looking Statement

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, expectations regarding the potential of Scholar Rock's platform, TGFβ programs and molecules and progress, timing and design of its clinical trials, and the impact of COVID-19 on its clinical trials and its business and operations in general. 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 preclinical data and results may not be predictive of clinical results or the success of Scholar Rock's platform and those risks more fully discussed in the section entitled "Risk Factors" in Scholar Rock's Annual Report on Form 10-K for the year ended December 31, 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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