Scholar Rock Presents New Data from SRK-181 Phase 1 DRAGON Trial at ASCO 2024 Annual Meeting

June 3, 2024

- *Promising objective response rates (ORR) were observed in multiple tumor types in anti-PD-(L)1 resistant patients*
- *Analysis of baseline biomarker data in clear cell renal cell carcinoma (ccRCC) patients reveals a doubling of the ORR highlighting a potential patient selection strategy*
- *SRK-181 combination with pembrolizumab was generally well tolerated*
- *Company holding conference call to discuss data with Dr. Toni Choueiri on Tuesday, June 4th at 7 a.m. CDT/8 a.m. EST*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 3, 2024-- Scholar Rock (NASDAQ: SRRK), a late-stage biopharmaceutical company focused on advancing innovative treatments for spinal muscular atrophy (SMA), cardiometabolic disorders, and other serious diseases where protein growth factors play a fundamental role, today announced encouraging data from its Phase 1 DRAGON proof-of-concept trial of SRK-181, a selective inhibitor of latent TGFβ1 activation, in combination with pembrolizumab in patients with advanced solid tumors. The results show encouraging responses in heavily pretreated and anti-PD-(L)1 resistant patients across multiple tumor types. Data were shared in an oral presentation during the American Society of Clinical Oncology (ASCO) Annual Meeting on June 3 in Chicago.

“These new data from our SRK-181 program show promising response to treatment with SRK-181 across multiple tumor types and represent further evidence of the value of our highly selective TGFβ platform,” said Jay Backstrom, M.D., MPH, President and Chief Executive Officer of Scholar Rock. “The anti-tumor activity we observed in heavily pretreated cancer patients, most notably in ccRCC and melanoma gives us confidence that SRK-181 could be part of a treatment strategy to overcome immune checkpoint inhibitor-associated resistance. In addition, our new finding that baseline CD8+ infiltration status and elevated baseline regulatory T-cell levels in ccRCC correspond with the twofold increase in response rate has the potential to inform a patient selection strategy. We are very encouraged by these new data and are committed to engaging with the FDA in an end of Phase 1 meeting, while also continuing to evaluate opportunities to partner this important program.”

Safety data continued to show SRK-181 was generally well tolerated
Safety data from all cohorts in the dose expansion phase (Part B; n=78 patients; 1500 mg q3w) continued to show SRK-181 was generally well tolerated when used in combination with pembrolizumab. One Grade 4 treatment-related adverse event (AE) of generalized dermatitis exfoliative was observed in one patient. No Grade 5 treatment-related AEs occurred. The only treatment-related serious adverse event related to SRK-181 or pembrolizumab that occurred in at least 2% of patients was pemphigoid. The most common AEs were rash, pruritis, fatigue, and diarrhea.

Data presented continues to provide objective evidence of anti-tumor activity
Encouraging responses were observed in multiple tumor types, continuing to support proof-of-concept for SRK-181. The response was assessed by principal investigators based on RECIST 1.1 for patients across five cohorts: clear cell renal cell carcinoma (ccRCC), head and neck squamous cell carcinoma (HNSCC), melanoma (MEL), urothelial carcinoma (UC), and non-small cell lung cancer (NSCLC). A summary of anti-tumor activity is presented in the table below; results for NSCLC (n=11) are not included because no response was observed.

Summary of Response Rate in Multiple Tumor Types

	ccRCC (n=30)	HNSCC (n=11)	MEL (n=11)	UC (n=11)
Objective response rate (ORR)	7 (23.3%)	2 (18.2%)	3 (27.3%)	1 (9.1%)
Durability of response (DoR); median (range), months	7.7+ (2.5+, 20.9+)	2.2+ (0.1, 4.3+)	4.9 (1.8, 7.1)	12.9 (12.9, 12.9)

Biomarker findings continue to support proof of mechanism
Tumor infiltration by CD8+ T-cells was measured in multiple tumor types for which paired biopsy samples (i.e., samples before and after treatment for individual patients) were available. The analysis included patients with ccRCC, melanoma, non-small cell lung cancer (NSCLC), head and neck squamous cell carcinoma (HNSCC) or urothelial carcinoma (UC). In 6 out of 9 paired biopsies analyzed, the combination of SRK-181 and pembrolizumab was associated with an enhanced proinflammatory microenvironment, with activated CD8+ T-cells in responding patients across multiple cohorts and the number of activated T-cells correlating with tumor shrinkage.

New biomarker findings in ccRCC could inform patient selection strategy
Notably, the baseline immune contexture unique to ccRCC amongst the cohorts examined has been identified, predictive of clinical response.

An analysis in ccRCC patients showed a positive correlation between baseline CD8+ infiltration status and response rate, with an increase in ORR from 23.3 to 40%, and an improvement in median durability of response (mDoR) from 7.7 to 9.3 months if enrollment had been limited to patients whose tumors were infiltrated by CD8+ T-cells at baseline.

In addition, an independent analysis showed a positive correlation between elevated regulatory T-cell (Treg) levels in ccRCC patients pre-treatment and response rate, with an increase in ORR from 23.3 to 50% and improvement in mDoR from 7.7 to 9.8 months if enrollment had been limited to patients whose tumors had elevated Treg levels at baseline. Together, these results suggest that baseline CD8+ status and Treg levels should be further investigated as a potential future patient selection strategy, aimed to predict ccRCC patients who are likely to respond to SRK-181 and anti-PD-(L)1 combination therapy.

The presentation is available in the Publications & Posters section of Scholar Rock's website.

For conference information, visit https://conferences.asco.org/.

Conference Call Information
Scholar Rock will host a conference call on June 4 at 8 a.m. EST that can be accessed from Events and Presentations page of Scholar Rock's website. Members of Scholar Rock's executive management team will be joined by Dr. Toni Choueiri, M.D., Director of the Lank Center for Genitourinary (GU) Oncology at Dana-Farber Cancer Institute (DFCI). The audio of the conference call can be accessed by registering in advance at the following link: https://register.vevent.com/register/BIca0060fe57734207b3fc21ce38d84a63

About SRK-181
SRK-181 is a selective inhibitor of TGFβ1 activation being developed to overcome primary resistance to checkpoint inhibitor therapy, such as anti-PD-(L)1 antibodies, in advanced cancer. 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 that TGFβ1 is a key contributor to the immunosuppressive tumor microenvironment, excluding and preventing entry of cytotoxic T cells into the tumor, as well as suppressing T cell activity, thereby inhibiting anti-tumor immunity.

SRK-181 specifically targets the latent TGFβ1 isoform in a context-independent manner, designed to enable complete inhibition of TGFβ1 in all compartments within the tumor microenvironment. Scholar Rock believes that SRK-181 has the potential to overcome this immunosuppressive tumor microenvironment and induce tumor regression when administered in combination with anti-PD-(L)1 therapy while potentially avoiding toxicities associated with non-selective TGFβ inhibition. Enrollment of the DRAGON Phase 1 proof-of-concept clinical trial (NCT04291079) was completed in December 2023, and patients who remain on the study continue to be treated. The trial enrolled patients in multiple proof of concept cohorts conducted in parallel, including urothelial carcinoma (UC), cutaneous melanoma (MEL), non-small cell lung cancer (NSCLC), head and neck squamous cell carcinoma (HNSCC), and clear cell renal cell carcinoma (ccRCC). SRK-181 is an investigational product candidate and its efficacy and safety have not been established. SRK-181 has not been approved for any use by the FDA or any other regulatory agency.

About Scholar Rock

Scholar Rock is a biopharmaceutical company that discovers, develops, and delivers life-changing therapies for people with serious diseases that have high unmet need. As a global leader in the biology of the transforming growth factor beta (TGFβ) superfamily of cell proteins and named for the visual resemblance of a scholar rock to protein structures, the clinical-stage company is focused on advancing innovative treatments where protein growth factors are fundamental. Over the past decade, Scholar Rock has created a pipeline with the potential to advance the standard of care for neuromuscular disease, cardiometabolic disorders, cancer, and other conditions where growth factor-targeted drugs can play a transformational role.

Scholar Rock is the only company to show clinical proof of concept for a muscle-targeted treatment in spinal muscular atrophy (SMA). This commitment to unlocking fundamentally different therapeutic approaches is powered by broad application of a proprietary platform, which has developed novel monoclonal antibodies to modulate protein growth factors with extraordinary selectivity. By harnessing cutting-edge science in disease spaces that are historically under-addressed through traditional therapies, Scholar Rock works every day to create new possibilities for patients. Learn more about our approach at ScholarRock.com and follow @ScholarRock and on LinkedIn.

Availability of Other Information About Scholar Rock

Investors and others should note that we communicate with our investors and the public using our company website www.scholarrock.com, including, but not limited to, company disclosures, investor presentations and FAQs, Securities and Exchange Commission filings, press releases, public conference call transcripts and webcast transcripts, as well as on Twitter and LinkedIn. The information that we post on our website or on Twitter or LinkedIn could be deemed to be material information. As a result, we encourage investors, the media and others interested to review the information that we post there on a regular basis. The contents of our website or social media shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended.

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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, including the therapeutic potential, clinical benefits and safety thereof, expectations regarding timing, success and data announcements of current ongoing clinical trials, 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," "could," "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, without limitation, that preclinical and clinical data, including the results from the Phase 1 clinical trial of SRK-181, are not predictive of, may be inconsistent with, or more favorable than, data generated from future or ongoing clinical trials of the same product candidates; 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, without limitation, to supply any clinical trials; and 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; 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 March 31, 2024, 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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