



Scholar Rock to Develop Cancer Immunotherapy Product Candidate, SRK-181, a Selective Inhibitor of TGFβ1 Activation, to Overcome Checkpoint Inhibitor Resistance

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Selective inhibition of TGFβ1 activation enables immune cell entry into the tumor microenvironment in preclinical models, demonstrating potential for overcoming a key mechanism of primary resistance to cancer immunotherapies

Company advances immuno-oncology candidate based on strength of preclinical data and human translational insights, with plans to initiate a Phase 1 trial in patients with solid tumors in mid-2020

CAMBRIDGE, Mass., March 12, 2019 (GLOBE NEWSWIRE) -- [Scholar Rock](#) Holding Corporation (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 that it has selected SRK-181, a highly specific inhibitor of TGFβ1 activation, as the first product candidate in its TGFβ1 cancer immunotherapy program based on the strength of its preclinical data and human translational insights. Scholar Rock has initiated manufacturing and is progressing preclinical development efforts with plans to initiate a Phase 1 trial in patients with solid tumors in mid- 2020.

"Given that a majority of cancer patients fail to respond to checkpoint blockade therapies, we are eager to advance the next product candidate from our pipeline of growth factor modulators to potentially address a key mechanism of pre-existing resistance," said Nagesh Mahanthappa, Ph.D., President and CEO of Scholar Rock. "A growing body of evidence strongly implicates elevated TGFβ1 activity as a cause of immunotherapy failure, and we see tremendous potential for SRK-181 to expand the number of patients who could benefit from checkpoint blockade therapies by potently and selectively inhibiting the activation of TGFβ1."

SRK-181 is a fully human antibody designed to bind to, and prevent the activation of, latent TGFβ1 with high affinity and high selectivity, as evidenced by minimal or no binding to latent TGFβ2 and latent TGFβ3 isoforms. Several important factors led to the decision to advance SRK-181 as a clinical development product candidate for the treatment of tumors resistant to checkpoint blockade therapies (CBTs), such as anti-PD1 antibodies. These factors include:

- TGFβ signaling has been implicated as a culprit in primary resistance to CBTs in multiple peer-reviewed studies.
- Translational data analyses by Scholar Rock highlight the prominent expression of TGFβ1 in many human tumor types, such as bladder cancer, non-small cell lung cancer and melanoma, for which CBTs have either been approved or demonstrated clinical activity in trials.
- Clinical correlation and preclinical model data suggest that TGFβ1 excludes effector cell entry into the tumor, thereby limiting immune system access to tumor cells.
- Preclinical studies in syngeneic mouse tumor models resistant to CBT show SRK-181-mIgG1 (the murine version of SRK-181), when combined with anti-PD1 antibodies, permitted effector T cell infiltration and expansion into the tumor microenvironment and led to tumor regression or control as well as significant survival benefit.
- A 28-day pilot toxicology study of SRK-181 in adult rats showed no observed drug-related toxicity up to a weekly dose of 100 mg/kg for 4 weeks.

Detailed preclinical results for SRK-181-mIgG1 (formerly referred to as SRTβ1-Ab3) were presented at the Society for Immunotherapy of Cancer (SITC) 33rd Annual Meeting in November 2018. The poster presented at SITC can be accessed by visiting the Scholar Rock website at <http://www.scholarrock.com/platform/publications/>. Additional preclinical data for SRK-181-mIgG1 will be presented at the 2019 American Association for Cancer Research Annual Meeting scheduled to take place March 29 to April 3, 2019 in Atlanta, GA.

About SRK-181

SRK-181 is a highly specific inhibitor of TGFβ1 activation being developed to overcome primary resistance to checkpoint blockade therapies (CBTs). 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 CBT, TGFβ1 is implicated as a key contributor to exclude immune cell entry into the tumor microenvironment, thereby preventing normal immune function. By overcoming this immune cell exclusion, SRK-181 has the potential to induce tumor regression when administered in conjunction with CBT.

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 potential of SRK-181 in cancer immunotherapy and the timeline for and progress in developing SRK-181. 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 testing of SRK-181 may not be predictive of the results or success of clinical trials, the development of SRK-181 will take longer and/or cost more than planned, SRK-181 will not receive regulatory approval 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, 2018, 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.

Scholar Rock Contact:

Investors/Media

Catherine Huchu huchu@scholarrock.com

917-601-1649

Media Contact:

The Yates Network

Kathryn Morris kathryn@theyatesnetwork.com

914-204-6412



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