Scholar Rock Announces Publication of Phase 1 Clinical Trial Data Evaluating Apitegromab in Healthy Volunteers in the Journal Advances in Therapy

May 11, 2021

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 11, 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 announced that findings from its Phase 1 trial evaluating the safety and pharmacologic profile of apitemograb in healthy volunteers were published in the peer-reviewed journal *Advances in Therapy.* Apitegromab is a selective inhibitor of myostatin activation that is being developed for the treatment of spinal muscular atrophy (SMA).

“The Phase 1 data provided an important foundation to support advancing the development of apitegromab and we are excited to share these detailed results through a publication in this peer-reviewed journal,” said Yung Chyung, M.D., Chief Medical Officer of Scholar Rock. “We recently announced positive top-line results from the TOPAZ Phase 2 trial, demonstrating apitegromab’s transformative potential to improve the persistent motor function impairments experienced by patients with Type 2 and Type 3 SMA and look forward to advancing the development of apitegromab in SMA.”

The objectives of the Phase 1, double-blind, placebo-controlled study were to assess the safety, immunogenicity, pharmacokinetics (PK), and pharmacodynamics (PD as measured by serum latent myostatin levels) of apitegromab to support future clinical studies. A total of 66 healthy volunteers were enrolled and randomized to receive either intravenous (IV) apitegromab or placebo at doses between 1 mg/kg and 30 mg/kg. Key findings shared in *Advances in Therapy* include:

- Single- and multiple-ascending doses of apitegromab were safe and well-tolerated at IV doses up to 30 mg/kg. No anti-drug antibodies were detected in subjects receiving apitegromab.
- Apitegromab demonstrated a linear, dose-proportional PK profile and a half-life of 24-31 days across the evaluated doses.
- Apitegromab demonstrated dose-dependent increases in serum latent myostatin concentrations as well as durable target saturation.
    - Mean serum latent myostatin levels increased and plateaued between day 14-28 following single doses of up to 10 mg/kg and between day 42-56 for 20 mg/kg and 30 mg/kg doses. This contrasts with mean serum latent myostatin levels remaining at or near baseline levels following placebo.
    - For subjects who received multiple doses of apitegromab (every 2 weeks for a total of three doses), mean serum latent myostatin concentrations remained elevated through the third dose and began to decline by day 56 for the 10 mg/kg and 20 mg/kg doses and day 84 for the 30 mg/kg dose.

The data from this Phase 1 study, as well as preclinical data, supported advancing the development of apitegromab to the TOPAZ Phase 2 trial, which evaluated apitegromab’s potential to improve motor function in patients with Type 2 and Type 3 SMA. Scholar Rock recently announced positive 12-month top-line data from the TOPAZ trial demonstrating the transformative therapeutic potential of apitegromab in patients with Type 2 and Type 3 SMA. A Phase 3 registrational trial is anticipated to initiate by the end of 2021.

About Apitegromab
Apitegromab is a selective inhibitor of the activation of myostatin and is an investigational product candidate for the treatment of patients with spinal muscular atrophy (SMA). Myostatin, a member of the TGFβ superfamily of growth factors, is expressed primarily by skeletal muscle cells, and the absence of its gene is associated with an increase in muscle mass and strength in multiple animal species, including humans. Scholar Rock believes that inhibiting myostatin activation with apitegromab may promote a clinically meaningful improvement in motor function in patients with SMA. The U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation (ODD) and Rare Pediatric Disease (RPD) designation, and the European Medicines Agency (EMA) has granted Priority Medicines (PRIME) Designation and Orphan Medicinal Product Designation, to apitegromab for the treatment of SMA. The efficacy and safety of apitegromab have not been established and apitegromab has not been approved for any use by the FDA or any other regulatory agency.

About SMA
Spinal muscular atrophy (SMA) is a rare, and often fatal, genetic disorder that typically manifests in young children. An estimated 30,000 to 35,000 patients are afflicted with SMA in the United States and Europe. It is characterized by the loss of motor neurons, atrophy of the voluntary muscles of the limbs and trunk and progressive muscle weakness. The underlying pathology of SMA is caused by insufficient production of the SMN (survival of motor neuron) protein, essential for the survival of motor neurons, and is encoded by two genes, SMN1 and SMN2. While there has been progress in the development of therapeutics that address the underlying SMA genetic defect, via SMN-dependent pathways, there continues to be a high unmet need for therapeutics that directly address muscle atrophy.

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/).

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 the potential of SRK-181, 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, the potential of its proprietary platform, and its intellectual property protection. 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 possibility that data from the TOPAZ clinical trial will be inconsistent with the data observed in subsequent clinical trials, 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 including its clinical trials, as well as 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, 2020 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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