New 36-Month Apitegromab Extension Data Reinforce Long-Term Substantial and Sustained Improvement of Motor Function in Phase 2 TOPAZ Trial Patients with Nonambulatory Spinal Muscular Atrophy

June 30, 2023

- Improvements in patient-reported outcomes consistent with gains in motor function scores

- Safety profile at 36 months consistent with previous reports with no new safety findings; more than 90 percent of nonambulatory patients remained on study

- Enrollment progressing in pivotal Phase 3 SAPPHIRE registrational trial, anticipated completion in Q3 2023

- Scholar Rock to host virtual investor event on July 12 at 9:00 AM EST to discuss the current SMA treatment landscape and apitegromab's potential to advance the standard of care

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 30, 2023-- Scholar Rock (NASDAQ: SRRK), a Phase 3, clinical-stage biopharmaceutical company focused on the treatment of serious diseases in which protein growth factors play a fundamental role, today announced new data from the Phase 2 TOPAZ trial extension period evaluating patient outcomes at 36 months of treatment with apitegromab. These data showed that continued treatment with apitegromab over the extended treatment period was associated with substantial and sustained improvement in motor function, as well as improvements in patient-reported outcome measures in patients with nonambulatory Types 2 and 3 spinal muscular atrophy (SMA) receiving survival motor neuron (SMN)-targeted therapy. Detailed results were presented today by Thomas Crawford, M.D., of Johns Hopkins Medicine, and the lead principal investigator of the TOPAZ trial, during two podium presentations at the Cure SMA Research & Clinical Care Meeting in Orlando, Florida.

"These promising long-term data highlight the therapeutic potential of muscle-targeted therapies, such as apitegromab, to help those with SMA address persistent weakness," said Dr. Crawford. "While SMN-targeted therapies play an important role in preventing further loss of motor neurons, many people still experience persistent or progressive symptoms due to preexisting motor neuron degeneration. Incorporating a muscle-targeted therapy with apitegromab's clinical profile into the treatment paradigm could allow patients to sustain or potentially achieve new gains in motor functioning."

"We are excited to share these new Phase 2 data that support apitegromab's long-term durability of effect and consistent tolerability and safety profile. The results further strengthen our confidence in apitegromab's therapeutic potential for patients with SMA, as well as validate Scholar Rock's unique approach to selectively inhibiting the pro and latent forms of myostatin," said Jay Backstrom, M.D., MPH, President and Chief Executive Officer of Scholar Rock. "In addition to the sustained benefit observed with consistent HFMSE scores, we saw continued improvement in RULM scores, and reductions in fatigue as reported by patients—all of which can be important factors in performing activities of daily living. We remain committed to advancing the standard of care for people with SMA, and we look forward to sharing updates on our pivotal Phase 3 SAPPHIRE trial, which we anticipate will complete enrollment in the third quarter of 2023."

Substantial and Sustained Gains in Motor Function Observed Over the Extended Treatment Period: Nonambulatory patients (ages 2-21) experienced substantial and sustained gains in Hammersmith Functional Motor Scale-Expanded (HFMSE) and Revised Upper Limb Module (RULM) scores over the 36-month extended treatment period from baseline:

	12-Month Data	**24-Month Data**	**36-Month Data**
Mean Change from Baseline in HFMSE (95% Confidence Interval)	**3.6 points** (1.2, 6.0) N=32	**4.2 points** (1.9, 6.6) N=29	**4.0 points** (1.0, 6.9) N=28
Mean Change from Baseline in RULM (95% Confidence Interval)	**1.3 points** (0.2, 2.3) N=31	**2.3 points** (1.2, 3.3) N=31	**2.4 points** (1.1, 3.7) N=27

For the 36-month data, an observed case analysis was conducted, which pooled data for all nonambulatory patients (including those patients on 20 mg/kg of apitegromab for the full duration of the trial, and those who switched from 2 mg/kg to 20 mg/kg at various time intervals in year 2) and was based upon the available data. These analyses exclude data for patients post scoliosis surgery.

Improvement in Patient-Reported Outcomes Consistent with Improvements in Motor Function: Nonambulatory patients (ages 2-21) had improvements in PEDI-CAT (measure of activities of daily living) and PROMIS-Fatigue (a patient-reported outcome tool measuring fatigue) that were consistent and sustained at 36 months. The mean change in PEDI-CAT daily activity domain from baseline at 36 months was 2.2 (95% CI: –0.1, 4.5; N=17), indicating an improvement in the ability to perform daily activities. The mean change in PROMIS-Fatigue from baseline at 36 months was –4.6 (95% CI: –8.7, –0.5; N=14), indicating a decline in fatigue. These improvements in PEDI-CAT and PROMIS-Fatigue were generally consistent with improvements in motor function across the 36 months of the study period.

Consistent Safety Data: Treatment-emergent adverse events (TEAEs) at 36 months were consistent with previous reports at 12 and 24 months, with no new findings after an aggregate of 198 patient-years of exposure. TEAEs were mostly mild-to-moderate in severity, and generally consistent with the underlying patient population and background therapy. The five most common TEAEs were headache, pyrexia, COVID-19, nasopharyngitis, and upper respiratory tract infection. No deaths or suspected unexpected serious adverse reactions or hypersensitivity reactions were observed with

apitegromab at 36 months. A total of 21 serious TEAEs were reported over the 36-month treatment period. No patients displayed positive titers for apitegromab antibodies (ADA).

More than 90 percent of nonambulatory patients remained on treatment in the extension study.

Details of the podium presentations at SMA Research & Clinical Care Meeting are as follows:

Title: Effect of apitegromab on PEDI-CAT and PROMIS-Fatigue questionnaire at 36 months in patients with Type 2 and nonambulatory Type 3 spinal muscular atrophy
Presentation type: Oral presentation
Presenter: Thomas O. Crawford, M.D., Professor of Neurology and Pediatrics, Johns Hopkins University
Date and time: Friday, June 30, 2023, 10:40 AM EST
Location: Disney Swan and Dolphin Hotels, Orlando, FL

Title: Effect of apitegromab on motor function at 36 months in patients with Type 2 and nonambulatory Type 3 spinal muscular atrophy
Presentation type: Oral presentation
Presenter: Thomas O. Crawford, M.D., Professor of Neurology and Pediatrics, Johns Hopkins University
Date and time: Friday, June 30, 2023, 11:00 AM EST
Location: Disney Swan and Dolphin Hotels, Orlando, Florida
For conference information, visit https://www.researchandclinicalcaremeeting.com/

The presentations will be made available in the Publications & Posters section of Scholar Rock's website following the presentation.

Conference Call/Webcast:

Scholar Rock will host a virtual investor event on July 12 at 9:00 AM EST to discuss the current SMA treatment landscape and apitegromab's potential to advance the standard of care for patients with nonambulatory Types 2 and 3 SMA. Click here to register and listen to the webcast. A link to the webcast of this event is also available on the Investors & Media section of the Scholar Rock website at http://investors.scholarrock.com.

An archived replay of the webcast will be available on Scholar Rock's website at: https://scholarrock.com/ for approximately 90 days following the presentation.

About the Phase 2 TOPAZ Trial

The TOPAZ trial is an ongoing proof-of-concept, open-label Phase 2 trial evaluating the safety and efficacy of apitegromab in patients with Types 2 and 3 SMA. In the main treatment period, patients were dosed intravenously every four weeks as monotherapy or with nusinersen, an approved SMN-targeted therapy. The trial enrolled 58 patients in the U.S. and Europe. The primary efficacy endpoints were mean change from baseline in Revised Hammersmith Scale (RHS) score at 12 months for the ambulatory population (Cohort 1), and mean change from baseline in HFMSE score at 12 months for the nonambulatory population (Cohorts 2 and 3). The trial also includes multiple 12-month extension periods designed to evaluate longer-term patient outcomes.

About the Phase 3 SAPPHIRE Trial

SAPPHIRE is an ongoing randomized, double-blind, placebo-controlled, phase 3 clinical trial evaluating the safety and efficacy of apitegromab in nonambulatory patients with Types 2 and 3 SMA who are receiving SMN therapy (either nusinersen or risdiplam). Approximately 156 patients aged 2-12 years old are anticipated to be enrolled in the main efficacy population. These patients will be randomized 1:1:1 to receive for 12 months either apitegromab 10 mg/kg, apitegromab 20 mg/kg, or placebo by intravenous (IV) infusion every 4 weeks. An exploratory population of approximately 48 patients aged 13-21 years old will also separately be evaluated. These patients will be randomized 2:1 to receive either apitegromab 20 mg/kg or placebo. For more information about SAPPHIRE, visit www.clinicaltrials.gov.

About Apitegromab

Apitegromab is an investigational fully human monoclonal antibody inhibiting myostatin activation by selectively binding the pro- and latent forms of myostatin in the skeletal muscle. It is the first muscle-targeted treatment candidate to demonstrate clinical proof of concept in 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 our highly selective targeting of pro- and latent forms of myostatin with apitegromab may lead to a clinically meaningful improvement in motor function in patients with SMA. The U.S. Food and Drug Administration (FDA) has granted Fast Track, Orphan Drug and Rare Pediatric Disease designations, and the European Medicines Agency (EMA) has granted Priority Medicines (PRIME) and Orphan Medicinal Product designations, 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, genetic neuromuscular disease that afflicts an estimated 30,000 to 35,000 people in the United States and Europe. The disease is characterized by the loss of motor neurons, atrophy of the voluntary muscles of the limbs and trunk, and progressive muscle weakness. While there has been progress in the development of therapeutics that address the loss of motor neurons, there continues to be a high unmet need for therapies that directly address the progressive muscle weakness that leads to loss of motor function in SMA.

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/).

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 apitegromab, and other product candidates and indication selection and development timing, 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 2 clinical trial of apitegromab, and are not predictive of, may be inconsistent with, or more favorable than, data generated from future clinical trials of the same product candidates, including, without limitation, the Phase 3 clinical trial of apitegromab in SMA , 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, 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 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 March 31, 2023, 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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