Positive Phase 2 Topaz Trial Extension Data Demonstrate Sizable and Sustained Motor Function Improvement at 24 Months with Apitegromab for Non-Ambulatory Patients with Types 2 and 3 Spinal Muscular Atrophy (SMA)

June 17, 2022

- *Sizable and sustained improvement in Hammersmith Functional Motor Scale-Expanded (HFMSE) scores observed at 24 months*
- *Substantial increase in Revised Upper Limb Module (RULM) scores observed at 24 months*
- *No serious safety risks identified over 24 months*
- *Enrollment progressing in pivotal Phase 3 SAPPHIRE registrational trial*
- *Scholar Rock to host webcast today at 8:30 a.m. ET*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 17, 2022-- 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 after 24-months of treatment, which support sustained and continued improvement with apitegromab for non-ambulatory patients with Types 2 and 3 SMA receiving an SMN therapy. Detailed results are being presented by Thomas Crawford, M.D. of Johns Hopkins Medicine and the lead principal investigator of the TOPAZ trial, during a podium presentation at the Cure SMA Research & Clinical Care Meeting today at 11:20 a.m. PST.

"The 24-month results provide long-term data and evidence, underscoring the findings of the 12-month primary treatment period of the TOPAZ trial in which patients receiving apitegromab experienced sizable motor function gains," said George Nomikos, M.D., Ph.D., Senior Vice President of Clinical Sciences, Head of Muscle Therapeutic Area of Scholar Rock. "This durability and continued increase in motor function support the transformative potential of apitegromab for patients suffering with SMA."

"These data support apitegromab's potential to meaningfully improve the lives of non-ambulatory patients with Types 2 and 3 SMA," said Nagesh Mahanthappa, Ph.D., Founding Chief Executive Officer & President of Scholar Rock. "As a company, we are dedicated to the SMA community and are urgently enrolling patients in our ongoing pivotal Phase 3 SAPPHIRE trial."

TOPAZ evaluated apitegromab across a broad age range (2-21 years) of patients with Types 2 and 3 SMA. All 35 non-ambulatory patients (Cohorts 2 and 3) and 12 of 23 ambulatory patients (Cohort 1) were receiving nusinersen maintenance therapy. The primary efficacy endpoint for the non-ambulatory population was mean change from baseline in HFMSE. Additional endpoints included mean change from baseline in RULM, an assessment specifically designed for upper limb function in patients with SMA. The HFMSE is a validated measure for the assessment of gross motor function in SMA, while the RULM is validated to evaluate upper limb motor performance by evaluating tasks which correspond to the ability to perform various everyday activities with their hands and arms.

For this 24-month evaluation, an observed case analysis was conducted, which pooled all the non-ambulatory patients (Cohorts 2 and 3) and was based upon the available data for given timepoints. This analysis population included patients receiving either low dose (2 mg/kg) or high dose (20 mg/kg) apitegromab (inclusive of patients in Cohort 3 who switched from 2 mg/kg to 20 mg/kg in Year 2) and did not exclude any patients who had missed apitegromab doses due to study site access restrictions from COVID-19.

Non-ambulatory patients (age range of 2 to 21 years old) with valid HFMSE assessments had sizable, sustained gains in HFMSE scores at 24 months from baseline (prior to first dose of apitegromab), while RULM scores continued to increase at 24 months. The mean change from baseline results for non-ambulatory patients showed:

	12-Month Data	**24-Month Data Pooled non-ambulatory pts**	**24-Month Data *excluding pts w/scoliosis surgery**
Mean Change from Baseline in HFMSE (95% CI)	**3.6 points** (95% CI: 1.2, 6.0) N=32	**4.0 points** (95% CI: 1.5, 6.5) N=29	**4.4 points** (95% CI: 2.0, 6.9) N=28

Mean Change from Baseline in RULM (95% CI)	**1.3 points** (95% CI: 0.2, 2.3) N=31	**1.9 points** (95% CI: 0.8, 3.0) N=33	**2.3 points** (95% CI: 1.2, 3.4) N=30

**Three patients in the non-ambulatory group underwent scoliosis surgery in year 2, which has been reported to negatively impact HFMSE scores for a considerable period afterwards[1]. This analysis excluded post-surgery data of these patients.*

Dose response continued to be observed across the 24 months of apitegromab administration based upon HFMSE scores and pharmacodynamic data (target engagement as measured by serum latent myostatin concentrations), with signs that there may be further HFMSE increases as non-ambulatory patients originally receiving the low dose switched to the high dose treatment.

Data at 24-months for ambulatory patients with Type 3 SMA (Cohort 1) suggest stability of Revised Hammersmith Scale (RHS) scores in patients receiving 20 mg/kg of apitegromab and nusinersen. The mean RHS change from baseline at 24-months was -0.7 points (95% CI: -3.1, 1.7) for the apitegromab and nusinersen subgroup (n=10) and -2.8 points (95% CI: -8.4, 2.8) for the apitegromab monotherapy subgroup (n=11). A subset of individuals in Cohort 1(n=21) had RHS improvements, as reflected by 42.9% (9/21) and 23.8% (5/21) of patients having ≥1-point and ≥3-point RHS increases from baseline at 24 months respectively.

Of the 55 patients who completed the 24-month TOPAZ extension period, 54 have opted to continue treatment in the 36-month extension period.

Consistent with the 12-month safety data, no serious safety risks were identified as part of the analysis of the cumulative 24-month data. The incidence and severity of adverse events were consistent with the underlying patient population and background therapy. The five most common treatment-emergent adverse events (TEAEs) were headache, pyrexia, upper respiratory tract infection, cough, and nasopharyngitis. No deaths or serious adverse reactions have been observed with apitegromab. A total of 14 serious TEAEs have been reported over the 24-month treatment period, all assessed by the respective trial investigator as unrelated to apitegromab.

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

Title: TOPAZ Extension: 24-Month Efficacy and Safety of Apitegromab in Patients with Later-Onset Spinal Muscular Atrophy (Type 2 and Type 3 SMA)

Presenter: Thomas Crawford, M.D., lead principal investigator of the TOPAZ trial and Professor of Neurology and Pediatrics; Johns Hopkins University.

Clinical Drug Development Session: June 17 at 11:20 - 11:40 a.m. PST (Abstract #28)

Conference Call/Webcast:

Scholar Rock will host a conference call and audio webcast to discuss topline 24-month data from the Phase 2 TOPAZ clinical trial on June 17, 2022 at 8:30 a.m. Eastern Time. To participate in the call, please dial 833-519-1308 (domestic) or 914-800-3874 (international) and refer to conference ID: 6495684. A webcast of the call will also be 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 180 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 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 non-ambulatory 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 non-ambulatory 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. In this subpopulation of older individuals with SMA, the safety and tolerability of apitegromab will be characterized, and efficacy will also be evaluated in an exploratory, nonpowered manner. SAPPHIRE is expected to enroll 55 sites in the U.S. and Europe. For more information about SAPPHIRE, visit www.clinicaltrials.gov.

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 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, 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 function.

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/). 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, including extension periods, of apitegromab are not predictive of, may be inconsistent with, or more favorable than, data generated from future clinical trials of the same product candidate, 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 such as COVID-19 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, 2022, 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.

[1] Dunaway Young, Sally et al. ‘Scoliosis Surgery Significantly Impacts Motor Abilities in Higher-functioning Individuals with Spinal Muscular Atrophy’. *Journal of Neuromuscular Disease.* 1 Jan. 2020: 183–192.

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Scholar Rock:

Investors
Rushmie Nofsinger
Scholar Rock
rnofsinger@scholarrock.com
ir@scholarrock.com
857-259-5573

Media
Ariane Lovell
Finn Partners
ariane.lovell@finnpartners.com
media@scholarrock.com
917-565-2204

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