Scholar Rock Presents TOPAZ Phase 2 Data Showing the Transformative Potential of Apitegromab in Patients with Type 2 and 3 Spinal Muscular Atrophy (SMA) at the 2021 Virtual SMA Research & Clinical Care Meeting

June 11, 2021

- Majority (74%) of patients with non-ambulatory Type 2 and Type 3 SMA achieved a clinical improvement in Hammersmith Functional Motor Scale Expanded (HFMSE) after 12 months

- New exploratory analysis of TOPAZ data found no correlation between duration of prior nusinersen treatment and increases in HFMSE, adding support that observed motor function improvements may be attributable to apitegromab

- Company to host KOL event and panel discussion on apitegromab's therapeutic potential in patients with SMA on June 15, 2021 at 10:00 am ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 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 an oral presentation of TOPAZ Phase 2 trial results by the lead principal investigator, Thomas Crawford, M.D. of Johns Hopkins Medicine, at the Cure SMA Annual SMA Conference. In the TOPAZ trial, treatment with apitegromab in conjunction with nusinersen in patients with Type 2 and 3 SMA led to meaningful motor function improvements of up to 20 points as measured by HFMSE. New exploratory analyses being presented further support apitegromab's potential to improve motor function in patients with SMA.

"The TOPAZ results show that apitegromab has promising potential to benefit the large portion of individuals with SMA who still manifest muscle weakness," said Thomas Crawford, M.D., Professor of Neurology at the Johns Hopkins School of Medicine and Lead Investigator of the TOPAZ trial. "In recent years, there have been some really remarkable advances in therapy for SMA that increase the low levels of SMN protein in motor neurons. But these findings suggest the fortunate streak for SMA therapeutics can potentially continue, this time targeting the persistent weakness in a complementary fashion at the level of muscle."

SMA remains a devastating and debilitating disease despite the utilization of SMN upregulators that prevent further motor neuron deterioration. A muscle-directed approach such as apitegromab, a selective inhibitor of myostatin activation, has the potential to complement SMN upregulators and address motor function impairments in patients with SMA. Scholar Rock's TOPAZ Phase 2 trial (NCT03921528) evaluated apitegromab across a broad age range (2-21 years) of patients with Type 2 and 3 SMA. With the exception of some ambulatory patients who received apitegromab as a monotherapy, patients enrolled in TOPAZ were receiving chronic maintenance doses of nusinersen. Both non-ambulatory cohorts had received more than 5.0 mean maintenance doses or approximately 2 years of treatment at baseline. Clinical data from the CHERISH and SHINE studies of nusinersen offer background insights into this patient population.[1] These studies observed that nusinersen-treated patients primarily experienced stabilization or only slight increases in HFMSE scores beyond the initial 15-month treatment period.[2] In addition, even in the initial 15-month treatment period, patients who initiated nusinersen treatment age ≥5 on average experienced declines in HFMSE and rarely attained a ≥3-point increase in HFMSE in a 12-month timeframe.[3]

Results following 12-months of treatment with apitegromab added to background nusinersen therapy, in the TOPAZ trial, included:

- Majority (74%, 23/31) of non-ambulatory patients showed a clinical improvement (≥1-point increase) in Hammersmith Functional Motor Scale Expanded (HFMSE).
- In the non-ambulatory cohort of patients (mean age 3.8) on background nusinersen started earlier in life (<5 years of age), treatment with apitegromab 20 mg/kg led to sizeable increases in HFMSE.
    - Mean increase from baseline was +7.1 points.
    - 88% (7/8) of patients improved (attained a ≥1-point increase).
    - 63% (5/8) of patients attained a ≥5-point increase.
    - 38% (3/8) of patients attained a >10-point increase.
    - Patients had received approximately two years of prior nusinersen treatment at the time of enrollment (5.4 mean maintenance doses) and were in the chronic maintenance phase of nusinersen therapy during the TOPAZ trial.
- In the non-ambulatory cohort of patients (mean age 11.7) on background nusinersen started later in life (≥5 years of age), treatment with apitegromab 20 mg/kg led to an increase in HFMSE, contrasting with declines experienced on average by this patient population without treatment.
    - Mean increase from baseline was +0.6 points by intent-to-treat analysis and +1.2 points by per-protocol analysis.
    - 64% (9/14) of patients improved (attained a ≥1-point increase).
    - 29% (4/14) of patients attained a ≥3-point increase.
    - Patients had received approximately two years of prior nusinersen treatment at the time of enrollment (5.1 mean maintenance doses) and were in the chronic maintenance phase of nusinersen therapy during the TOPAZ trial.
- A post-hoc analysis across all non-ambulatory patients showed no correlation between change in HFMSE score at 12 months and duration of prior nusinersen therapy, providing further evidence that improvements in motor function may be

attributed to apitegromab.

- WHO Motor Development Milestones, a high bar assessment representing major functional achievements, were gained by seven of 35 non-ambulatory patients treated with apitegromab and nusinersen, including three patients who initiated background nusinersen therapy later in life (≥5 years of age).
    - Five patients achieved one new WHO motor milestone, including one patient gaining the ability to walk independently and one patient gaining the ability to stand independently.
    - One patient achieved two new WHO motor milestones (hands and knees crawling and standing with assistance).
    - One patient achieved three new WHO motor milestones (hands and knees crawling, standing with assistance, and walking with assistance).
- The five most frequently reported treatment-emergent adverse events (AEs) included headache, pyrexia, upper respiratory tract infection, cough, and nasopharyngitis. Incidence and severity of AEs were consistent with the underlying patient population and background therapy.
- Data from additional exploratory endpoints are being analyzed and will be presented in the future, such as at medical and scientific conferences.

A randomized, double-blind, placebo-controlled Phase 3 trial is anticipated to initiate by the end of 2021 and is expected to evaluate apitegromab as an add-on to nusinersen or risdiplam in patients with non-ambulatory Type 2 and Type 3 SMA.

"We are delighted to share the TOPAZ trial results at the annual Cure SMA conference, including new exploratory analyses that further highlight apitegromab's transformative potential to improve motor function in patients with SMA," said Yung Chyung, M.D., Chief Medical Officer of Scholar Rock. "These results offer insights that advance our thinking and plans for a rational, targeted and efficient Phase 3 trial."

Details for the virtual Cure SMA oral presentation are as follows:

- **Title:** TOPAZ: A Phase 2 Study to Evaluate the Efficacy and Safety of Apitegromab (SRK-015) in Patients with Later-Onset Spinal Muscular Atrophy (Type 2 and Type 3 SMA): Topline Results
- **Presenter:** Thomas Crawford, M.D. Co-Director, Muscular Dystrophy Association Clinic and Professor of Neurology and Pediatrics, Johns Hopkins Medicine (Lead TOPAZ Principal Investigator)
- **Clinical Drug Development Session:** Virtual oral presentation on June 11, 2021 at 2:00pm CST

Conference Call/Webcast:

Scholar Rock will host a KOL event and panel discussion to discuss apitegromab's therapeutic potential in patients with SMA on June 15, 2021 at 10:00 a.m. Eastern Time. 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.

[1]This information from third-party studies is provided for background purposes only and is not intended to convey or imply a comparison to the TOPAZ clinical trial results.
2 Source: "Longer-term treatment with nusinersen: results in later-onset spinal muscular atrophy from the SHINE study" P.257, World Muscle Society Congress 2020
3 Source: Mercuri E, et.al. Nusinersen versus sham control in later-onset spinal muscular atrophy. N Engl J Med. 2018;378:625-635.

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 (FTD), Orphan Drug (ODD) and Rare Pediatric Disease (RPD) 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, fibrosis and anemia. 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/).

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 expectations regarding its growth, strategy, progress and timing of its clinical trials and the ability of any product candidate to perform in humans in a manner consistent with earlier nonclinical, preclinical or clinical trial data. 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 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 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, 2021, 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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