New Phase 2 TOPAZ Trial Data Indicate Positive Trends in Quality-of-Life Measures Over 24 Months with Apitegromab for Nonambulatory Patients with Types 2 and 3 SMA

October 22, 2022

- Tertiary endpoint data show trends of continuous improvement in activities of daily living, fatigue, and endurance over 24 months

- These data indicate the potential for sustained improvement in quality-of-life measures for patients with symptomatic SMA and offer further evidence of possible durable effects of apitegromab

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 22, 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 quality-of-life (QoL) data from its Phase 2 TOPAZ trial extension period evaluating patient outcomes after 24 months of treatment which indicate stabilization or continued improvement with apitegromab for nonambulatory patients with Types 2 and 3 spinal muscular atrophy (SMA) receiving an SMN-targeted therapy. The data were featured in a podium presentation today by Basil Darras, M.D., Associate Neurologist-in-Chief, Boston Children's Hospital and Professor of Neurology, Harvard Medical School, at the 3rd International Scientific Congress on SMA in Barcelona, Spain (SMA Europe 2022).

"SMA can have a significant impact on the ability to perform daily activities but there is limited research on potential interventions to improve quality-of-life measures, such as increasing muscle endurance and reducing fatigue.[1,2] These positive TOPAZ data indicate sustained improvements of quality-of-life measures over 24 months in the patient population studied," said Jay Backstrom, M.D., M.P.H., Chief Executive Officer of Scholar Rock. **"**As the Phase 3 SAPPHIRE trial advances, these additional TOPAZ trial analyses coupled with the previously reported measures of motor function, such as HFMSE and RULM, continue to yield positive, consistent results, building the case for apitegromab as a promising new treatment option for patients with SMA."

The TOPAZ trial assessed activities of daily living (ADL), fatigue, and muscle endurance by three tertiary endpoint measures:

1. The Pediatric Evaluation of Disability Inventory-Computer Adaptive Test (PEDI-CAT) measures pediatric abilities through three functional domains, daily activities, mobility, and social cognition;[3]
2. Patient Reported Outcome Measurement Information System (PROMIS) measures mild subjective feelings of tiredness to debilitating and sustained feelings of exhaustion, with lower scores reflecting less fatigue;[4,5] and
3. Endurance Shuttle Box and Block Test (ESBBT), a muscle endurance measurement tool, evaluates how fast a patient fatigues with the added measure of endurance[6] and may be complementary to outcome measures that focus on arm motor function, such as the Revised Upper Limb Module (RULM) assessment.

The tertiary endpoint data from these measures show trends of continuous improvement over 24 months. These data are relevant for informing the therapeutic hypotheses being evaluated in the Phase 3 SAPPHIRE trial. Limitations of these exploratory quality-of-life data analyses include small patient sample sizes in an open-label study, and further exploration is warranted. Specifically, the data found:

- Nonambulatory Type 2 patients (aged two or older who began receiving nusinersen maintenance therapy *before* age five) reported stabilization or continuous improvements in ADL up to a mean change from baseline of 3 points (n=14) in PEDI-CAT scores and fatigue up to a mean change from baseline of 5 points (n=10) in PROMIS scores over 24 months of apitegromab.
- Nonambulatory Types 2 and 3 patients (aged five to 21 who began receiving nusinersen maintenance therapy *at or after* age five) reported stabilization or increases in ADL up to a mean change from baseline of 0.7 points (n=8) in PEDI-CAT scores, and less fatigue up to a mean change from baseline of 3.5 points (n=2) in PROMIS scores over 24 months of apitegromab. Additionally, these patients also experienced trends in improvements in fatigability and endurance measures based on mean change in ESBBT activities. The trends of improvement with ESBBT are consistent with the previously reported increases in RULM scores observed in the TOPAZ trial at 24 months.

These findings complement previously reported data from the TOPAZ trial 24-month extension period that demonstrated sustained and durable improvements in motor function as measured by the Hammersmith Functional Motor Scale Expanded (HFMSE) and RULM in patients with nonambulatory Types 2 and 3 SMA.

No safety risks were identified over 24 months of treatment. The incidence and severity of adverse events were consistent with the underlying patient population and nusinersen 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.

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

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 the nonambulatory population (Cohorts 2 and 3). The trial also includes multiple 12-month extension periods designed to evaluate longer-term patient outcomes.

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/).

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," "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 June 30, 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] Wan HWY, Carey KA, D'Silva A, et al. *Orphanet J Rare Dis*. 2020;15:70.
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[6] Cure SMA. Best Practices for Physical Therapists and Clinical Evaluators in Spinal Muscular Atrophy (SMA). 2021. Available at: https://www.curesma.org/wp-content/uploads/2021/09/Clinical-Evaluators-Best-Practices-13-August-2021.pdf.

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Source: Scholar Rock