UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event Reported): April 6, 2021

Scholar Rock Holding Corporation
(Exact Name of Registrant as Specified in Charter)

Delaware	**001-38501**	**82-3750435**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(I.R.S. Employer Identification Number)

301 Binney Street, 3rd Floor, Cambridge, MA 02142
(Address of Principal Executive Offices) (Zip Code)

(857) 259-3860
(Registrant's telephone number, including area code)

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	SRRK	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2). Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Item 7.01. Regulation FD Disclosure.

On April 6, 2021, Scholar Rock Holding Corporation (the "Company") issued a press release announcing positive 12-month top-line results from the TOPAZ Phase 2 clinical trial evaluating apitegromab in patients with Type 2 and Type 3 spinal muscular atrophy. A copy of the press release is attached hereto as Exhibit 99.1.

The information in this Item 7.01 of Form 8-K, including the accompanying Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act"), or otherwise subject to the liability of such section, nor shall such information be deemed incorporated by reference in any filing under the Securities Act of 1933 or the Exchange Act, regardless of the general incorporation language of such filing, except as shall be expressly set forth by specific reference in such filing.

Item 8.01. Other Events.

The Company will host a conference call and audio webcast at 8:00 am ET on Tuesday, April 6, 2021 to discuss the top-line results from the apitegromab TOPAZ Phase 2 clinical trial. A copy of the presentation slides to be used by the Company during the conference call and webcast is attached hereto as Exhibit 99.2 and is incorporated herein by reference. A live webcast of the conference call may be accessed by visiting the Investors & Media section of the Company's website at http://investors.scholarrock.com.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits:

Exhibit No.	Description
99.1	Press Release issued by Scholar Rock Holding Corporation, dated April 6, 2021
99.2	Presentation Slide Deck
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Scholar Rock Holding Corporation

Date: April 6, 2021

By: /s/ Junlin Ho
Junlin Ho
General Counsel and Corporate Secretary

Exhibit 99.1

Scholar Rock Announces Positive 12-Month Top-Line Results From the TOPAZ Phase 2 Clinical Trial Evaluating Apitegromab in Patients With Type 2 and Type 3 Spinal Muscular Atrophy (SMA)

- Data further demonstrate proof-of-concept for the therapeutic potential of apitegromab in patients with Type 2 and Type 3 SMA

- Phase 3 registrational trial initiation expected by the end of 2021

- European Medicines Agency (EMA) granted Priority Medicines (PRIME) designation to apitegromab, recognizing unmet medical needs of patients with SMA

- Scholar Rock to host webcast today at 8:00am ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)--April 6, 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 positive top-line data from the TOPAZ Phase 2 clinical trial evaluating apitegromab (SRK-015) in patients with Type 2 and Type 3 spinal muscular atrophy (SMA).

“These top-line 12-month data provide further support towards establishing apitegromab as a potential first muscle-directed therapy for patients with SMA,” said Yung Chyung, M.D., Chief Medical Officer of Scholar Rock. “The findings also offer important insights into myostatin biology and our scientific approach of targeting the latent forms of growth factors. We look forward to advancing the development and investigation of apitegromab as we plan to initiate a pivotal trial in SMA by the end of 2021 and explore its potential in additional disease areas.”

Key findings from the 12-month top-line analysis include:

- **Cohort 1:** 5-21 years of age, ambulatory Type 3, 20 mg/kg dose monotherapy and in conjunction with nusinersen:
  - Observed a mean change from baseline in Revised Hammersmith Scale (RHS) of a 0.3-point decline.
  - Majority of patients across the cohort (57%, 13/23 of patients) maintained or improved their motor function, as reflected by a ≥0-point change from baseline in RHS score, and 22% of patients (5/23) attained a ≥3-point increase from baseline.
  - Results suggest potential clinical effect in certain patients in this population.
- **Cohort 2:** 5-21 years of age, Type 2 and non-ambulatory Type 3 who initiated nusinersen ≥5 years old, 20 mg/kg dose:
  - Observed a mean change from baseline in Hammersmith Functional Motor Scale Expanded (HFMSE) of a 0.6-point improvement.
  - Majority of patients (64%, 9/14 of patients) attained a ≥1-point increase from baseline and 29% of patients (4/14) attained a ≥3-point increase from baseline.
  - Results support the potential durability of the improvements in motor function observed at the six-month interim analysis.
- **Cohort 3:** ≥2 years of age, Type 2 who initiated nusinersen <5 years of age:
  - Observed a mean change from baseline in HFMSE of 7.1-point and 5.3-point improvements in the 20 mg/kg dose and the 2 mg/kg dose arms, respectively.
  - Across the full cohort, 59% of patients (10/17) attained a ≥5-point increase and 35% of patients (6/17) attained a >10-point increase from baseline.
  - Results demonstrate further improvements in motor function beyond what had been observed at the six-month interim analysis.
  - Dose response continued to be observed based upon clinical efficacy (HFMSE improvements) and pharmacodynamics (target engagement).
- No safety signals for apitegromab were identified as of the 12-month top-line analysis. The five most frequently reported treatment-emergent adverse events (TEAEs) were headache, pyrexia, upper respiratory tract infection, cough, and nasopharyngitis.
- All 57 patients who completed the 12-month TOPAZ trial have opted into the extension period.

“These 12-month results from the Phase 2 apitegromab TOPAZ trial have built upon the previously announced exciting 6-month interim results,” said Thomas Crawford, M.D., Professor of Neurology at the Johns Hopkins School of Medicine and Lead Investigator of the TOPAZ trial. “There looks to be promising potential for a muscle-directed therapy that will complement the unmet need still evident, and likely emerging, in many individuals with SMA who receive SMN-enhancing therapies. Though much work remains to be done, I believe the results are wonderful news for the SMA community, and I am enthusiastic about the potential that apitegromab may offer for further meaningful functional improvements.”

Detailed summary of the TOPAZ 12-month top-line results by cohort

Apitegromab is a selective inhibitor of the activation of latent myostatin. The TOPAZ Phase 2 proof-of-concept trial enrolled 58 patients with Type 2 and Type 3 SMA across 16 study sites in the United States and Europe. The trial evaluated the safety and efficacy of intravenous apitegromab dosed every four weeks (Q4W) over a 12-month treatment period. Four patients (one in Cohort 2 and three in Cohort 3) each missed three consecutive doses of apitegromab over the course of the 12-month treatment period due to COVID-19-related site access restrictions and are excluded from the prespecified intent-to-treat primary analysis.

Cohort 1: This open-label, single-arm cohort enrolled 23 patients with ambulatory Type 3 SMA. Patients were treated with 20 mg/kg of apitegromab either as a monotherapy or in conjunction with an approved SMN upregulator therapy (nusinersen). The primary objectives of Cohort 1 were to assess safety and the mean change from baseline in RHS following 12 months of treatment.

In Cohort 1 (pooled population), the mean change from baseline in RHS score was a 0.3-point decline. The Cohort 1 efficacy data suggest a potential clinical effect of apitegromab in certain patients in this population, as 57% of patients observed a maintenance or improvement in RHS score (>0-point change from baseline) and 22% of patients achieved at least a 3-point increase in RHS score from baseline.

Cohort 1 (Intent-to-treat population)	**Apitegromab 20 mg/kg monotherapy (n=11)**	**Apitegromab 20 mg/kg + nusinersen (n=12)**	**Apitegromab pooled (n=23)**
Mean change from baseline in RHS score (95% CI)	-0.4 (-3.9, +3.1)	-0.3 (-2.0, +1.4)	-0.3 (-2.1, +1.4)
% of patients attaining ≥0-point increase in RHS score	6/11 (55%)	7/12 (58%)	13/23 (57%)
% of patients attaining ≥1-point increase in RHS score	4/11 (36%)	5/12 (42%)	9/23 (39%)
% of patients attaining ≥3-point increase in RHS score	3/11 (27%)	2/12 (17%)	5/23 (22%)
% of patients attaining ≥5-point increase in RHS score	1/11 (9%)	0/12 (0%)	1/23 (4%)

Cohort 2: This open-label, single-arm cohort enrolled 15 patients with Type 2 or non-ambulatory Type 3 SMA and who were already receiving treatment with an approved SMN upregulator (nusinersen) initiated at age five years or older. One patient missed three consecutive doses of apitegromab due to COVID-19-related site access restrictions and was excluded from the prespecified intent-to-treat primary analysis. The primary objectives of the cohort were to assess safety and the mean change from baseline in HFMSE following 12 months of treatment.

Cohort 2 efficacy data demonstrate improvement of motor function from baseline. The mean change from baseline in HFMSE score was a 0.6-point increase. The majority (64%) of patients achieved at least a 1-point increase in HFMSE and 29% of patients achieved at least a 3-point increase in HFMSE from baseline. Potential durability of effect was observed up to 12 months of treatment.

One patient in Cohort 2 was identified as having received concomitant treatment with an acetylcholinesterase inhibitor before and during the study, which was not permitted by the trial protocol. This patient experienced a 7-point decline in HFMSE score at the 12-month timepoint. In the per protocol analysis conducted in accordance with the prespecified approach, which excludes this patient as well as the patient who missed three consecutive doses due to COVID-19-related site access restrictions, the mean change from baseline in HFMSE score for Cohort 2 was a 1.2-point improvement.

Cohort 2	**Apitegromab 20 mg/kg + nusinersen**	
	Intent-to-treat (n=14)	**Per Protocol (n=13)**
Mean change from baseline in HFMSE score (95% CI)	+0.6 (-1.4, +2.7)	+1.2 (-0.5, 2.9)
% of patients attaining ≥1 point increase in HFMSE score	9/14 (64%)	9/13 (69%)
% of patients attaining ≥3 point increase in HFMSE score	4/14 (29%)	4/13 (31%)
% of patients attaining ≥5 point increase in HFMSE score	2/14 (14%)	2/13 (15%)

Cohort 3: This randomized, double-blind, parallel arm portion of the trial enrolled patients with Type 2 SMA who had initiated treatment with an approved SMN upregulator (nusinersen) before five years of age. Twenty patients were randomized in a 1:1 ratio to receive the low dose (apitegromab 2 mg /kg Q4W) or high dose (apitegromab 20 mg/kg Q4W); both treatment arms were in conjunction with an approved SMN upregulator therapy (nusinersen). Three patients (two in high-dose arm and one in low-dose arm) each missed three consecutive doses of apitegromab due to COVID-19-related site access restrictions and were excluded from the prespecified intent-to-treat primary analysis. The primary objectives of the cohort were to assess safety and the mean change from baseline in HFMSE following 12 months of treatment.

Cohort 3 efficacy data demonstrate further improvements in motor function relative to what was observed at the six-month interim analysis. The mean change from baseline in HFMSE score was a 7.1-point and a 5.3-point improvement for the 20 mg/kg and 2 mg/kg dose arms, respectively. The majority (59%) of patients in Cohort 3 achieved at least a 5-point increase in HFMSE and 35% of patients achieved greater than a 10-point increase in HFMSE over baseline.

Dose response was observed; the 20 mg/kg dose achieved numerically greater mean improvements from baseline in HFMSE scores than the 2 mg/kg dose across all assessed timepoints in the 12-month treatment period. The clinically observed dose response was consistent with the pharmacodynamic (target engagement) results. Both the 20 mg/kg and 2 mg/kg doses yielded high levels of target engagement (>100-fold increase from baseline), but the 20 mg/kg dose led to a relatively higher absolute level of target engagement.

Cohort 3 (Intent-to-treat population)	**Apitegromab 20 mg/kg + nusinersen (n=8)**	**Apitegromab 2 mg/kg + nusinersen (n=9)**	**Apitegromab pooled (n=17)**
Mean change from baseline in HFMSE score (95% CI)	+7.1 (+1.8, +12.5)	+5.3 (-1.5, +12.2)	+6.2 (+2.2, +10.1)
% of patients attaining ≥1-point increase in HFMSE score	7/8 (88%)	7/9 (78%)	14/17 (82%)
% of patients attaining ≥3-point increase in HFMSE score	5/8 (63%)	5/9 (56%)	10/17 (59%)
% of patients attaining ≥5-point increase in HFMSE score	5/8 (63%)	5/9 (56%)	10/17 (59%)
% of patients attaining >10-point increase in HFMSE score	3/8 (38%)	3/9 (33%)	6/17 (35%)

Overall safety and tolerability profile:

- Incidence and severity of adverse events were consistent with the underlying patient population and background therapy.
- Five most frequently reported TEAEs: Headache (24%), pyrexia (22%), upper respiratory tract infection (22%), cough (22%), and nasopharyngitis (21%).
- Five patients experienced a serious treatment-emergent adverse event, all assessed by the respective trial investigator as unrelated to apitegromab:
    - One patient treated with 2 mg/kg dose (Cohort 3) hospitalized due to adenoidal hypertrophy and tonsillar hypertrophy to perform scheduled adenotonsillectomy (Grade 2). Event resolved without sequelae.
    - Two patients treated with 20 mg/kg dose (both Cohort 1) with gait inability considered a significant disability (both Grade 3). Events remain ongoing.
    - One patient treated with 20 mg/kg dose (Cohort 1) hospitalized with post lumbar puncture syndrome (Grade 2). Event resolved without sequelae.
    - One patient treated with 20 mg/kg dose (Cohort 1) hospitalized due to viral upper respiratory tract infection (Grade 2). Event resolved without sequelae.
- One patient (Cohort 1) presented with a non-serious Grade 3 post lumbar puncture syndrome; assessed by trial investigator as unrelated to apitegromab. Event resolved without sequelae.
- One patient (Cohort 1) discontinued from the trial due to Grade 2 muscle fatigue that started prior to initiation of dosing with study drug; assessed by the trial investigator as unrelated to apitegromab.
- Anti-drug antibodies (ADA) were present at low titers following apitegromab treatment in three out of the 58 enrolled patients. No apparent impact on drug exposure was observed and was not associated with any hypersensitivity reactions.

Additional potential disease areas for apitegromab: Scholar Rock believes apitegromab has potential for applicability across multiple SMA types, as well as in other neuromuscular indications. Based upon ongoing indication assessments, the Company has identified Becker Muscular Dystrophy (BMD), which affects approximately 20,000 individuals in the US and EU[a], as the next potential indication for apitegromab. The Company is in the process of planning a proof-of-concept trial with an aim to initiate the trial in 2022. Scholar Rock is continuing to explore other myostatin-related indications for which fast-twitch fibers may play an important role in motor function.

Conference call/webcast:
Scholar Rock will host a conference call and audio webcast to discuss the apitegromab TOPAZ Phase 2 clinical trial top-line results today at 8:00 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: 4196782. 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.

(a) "Muscular Dystrophy: Disease Landscape and Forecast." DRG Reports, June 2020

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[1] and Europe[2]. 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[3]. While there has been progress in the development of therapeutics that address the underlying SMA genetic defect, there continues to be a high unmet need for therapeutics that directly address muscle atrophy.

(1) Lally, C. et al. Indirect estimation of the prevalence of spinal muscular atrophy Type I, II, and III in the United States. Orphanet Journal of Rare Diseases. (2017) 12:175.
(2) Briefing Document to the Clinical Trial Readiness in Spinal Muscular Atrophy (SMA) SMA Europe, TREAT-NMD and European Medicines Agency meeting. Prepared by SMA Europe and TREAT-NMD. November 11, 2016.
(3) Parente, V. and Corti, S. Advances in spinal muscular atrophy therapeutics. Therapeutic Advances in Neurological Disorders. (2018) 11:1.

About Apitegromab
Apitegromab (SRK-015) is a selective inhibitor of the activation of latent 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. Scholar Rock believes the inhibition of the activation of latent myostatin with apitegromab may promote a clinically meaningful improvement in motor function.

The TOPAZ Phase 2 clinical trial in patients with Type 2 and Type 3 SMA is ongoing in the extension phase (NCT03921528). 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 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 https://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 apitegromab, 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, 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 preclinical and clinical data, including the 12-month top-line results from the Phase 2 trial of apitegromab, are not predictive of, are inconsistent with, or more favorable than, data generated from future clinical trials of the same product candidate, including the planned Phase 3 registrational 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 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.

Contacts

Scholar Rock:
Investors:
Catherine Hu
chu@scholarrock.com

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

TOPAZ Phase 2 Trial Top-Line Results

Improvements in Motor Function with Apitegromab for Patients with Spinal Muscular Atrophy (SMA)

April 6, 2021

ScholarRock

Disclaimers

Various statements in this presentation concerning the future expectations, plans and prospects of Scholar Rock, Inc. ("Scholar Rock"), including without limitation, Scholar Rock's expectations regarding its strategy, its product candidate selection and development timing, including timing for the initiation of and reporting results from its clinical trials for its product candidates, its disease indication selection and timing for such selection, the ability of apitegromab to affect the treatment of patients suffering from Spinal Muscular Atrophy (SMA) either as a monotherapy or in conjunction with the current standard of care, and the ability of SRK-181 to affect the treatment of cancer patients constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. The use of words such as "may," "might," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "target," "project," "intend," "future," "potential," or "continue," and other similar expressions are intended to identify such forward-looking statements. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including, without limitation, Scholar Rock's ability to provide the financial support and resources necessary to identify and develop multiple product candidates on the expected timelines, competition from others developing products for similar uses, the preliminary nature of interim clinical data, the possibility that preclinical or clinical data is inconsistent with subsequent data, 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, and 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 as well as those risks more fully discussed in the section entitled "Risk Factors" in the Annual Report on Form 10-K for the year ended December 31, 2020, which is on file with the Securities and Exchange Commission, 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. Scholar Rock explicitly disclaims any obligation to update any forward-looking statements unless required by law.

ScholarRock

Agenda

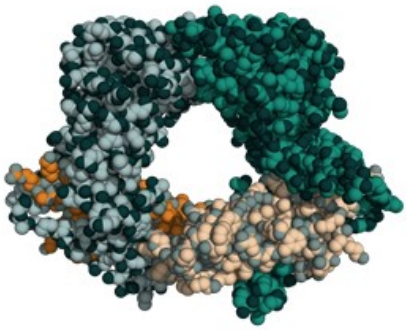
Opening Remarks	Tony Kingsley, President & CEO
Trial Design and Baseline Characteristics Top-line Safety and Efficacy Results	Yung Chyung M.D., Chief Medical Officer
Next Steps for Apitegromab Program	Tony Kingsley, President & CEO Ted Myles, Chief Financial Officer

Questions and Answers

Bringing a Revolutionary Approach to Highly Sought-After Growth Factors Implicated in Devastating Diseases

Scholar Rock's Target

Growth Factor Precursor (Latent Form)



Scholar Rock's R&D Platform

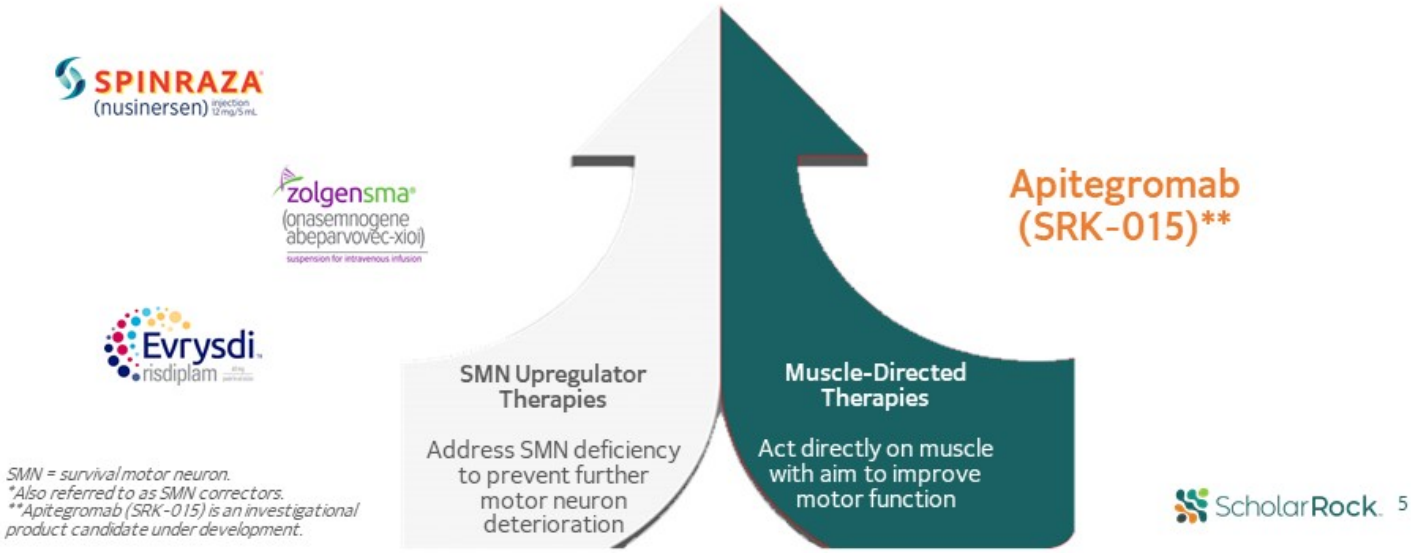
Transform Medical Practice

- Pursue important targets with well-validated biology but are difficult to drug
- Apply revolutionary approach to tough targets
  - Leverage deep insights into structure and function
  - Engineer antibodies to deliver differentiated therapeutic profiles (i.e. exquisite selectivity)

TOPAZ demonstrates the therapeutic potential of inhibiting the latent forms of growth factors

Apitegromab Offers Potential to Pioneer a New Treatment Era to Improve Motor Function in Patients with SMA

SMN Upregulator Therapies + Muscle-Directed Therapy (apitegromab)*
Potential for Enhanced Outcomes for Patients



SMN = survival motor neuron.
**Also referred to as SMN correctors.*
***Apitegromab (SRK-015) is an investigational product candidate under development.*

TOPAZ 12-Month Data Further Support the Potential of Apitegromab in Patients with Type 2 and Type 3 SMA

Adverse events were consistent with the underlying patient population and background therapy

	Cohort 1 Ambulatory Type 3	Cohort 2 Type 2 & non-ambulatory Type 3 (initiated nusinersen ≥5 yrs)	Cohort 3 Type 2 (initiated nusinersen <5 yrs)
TOPAZ 6-month interim results*	• Mean RHS increase from baseline • Majority of patients maintained or improved (≥0-pt change from baseline)	• Mean HFMSE increase from baseline • Majority of patients improved (≥1-pt increase from baseline)	• Mean HFMSE increases from baseline • Majority of patients achieved ≥3-pt increase • Dose response observed
TOPAZ 12-month top-line results	• Mean RHS decline from baseline • Majority of patients maintained or improved (≥0-pt change from baseline)	• Mean HFMSE increase from baseline • Majority of patients improved (≥1-pt increase from baseline) • Sizeable % of patients achieved ≥3-pt increase (29%)	• Further HFMSE increases observed vs. 6-month interim analysis • Majority of patients achieved ≥5-pt increase • Dose response continues to be observed

*Database for HFMSE and RHS scores for the 12-month topline analysis are locked. The 6-month interim analysis was a snapshot and subsequent adjustments by sites investigators resulted in the following changes to the 6-month interim results:
• Cohort 2: Mean change in HFMSE score from baseline was updated to +1.1-points (from +1.4-points). Proportion of patients with ≥3-point increases was updated to 2/14 (from 3/14) and updated to 1/14 (from 2/14) for patients with ≥5-point increases.
• Cohort 3 high dose arm (20 mg/kg): Mean change in HFMSE score from baseline was revised to +5.3-points (from +5.6-points).

Phase 2 Trial Design and 12-Month Top-Line Results

Yung Chyung, M.D.
Chief Medical Officer

TOPAZ

ScholarRock

Apitegromab Phase 2 Trial Design

TOPAZ

	Ambulatory Patients (Revised Hammersmith Scale)	Non-Ambulatory Patients (Hammersmith Functional Motor Scale Expanded)	
	Cohort 1	Cohort 2	Cohort 3
Design	• N= 23; ages 5-21 • Open-label, single-arm • 20 mg/kg apitegromab IV Q4W • 12-month treatment period	• N= 15; ages 5-21 • Open-label, single-arm • 20 mg/kg apitegromab IV Q4W • 12-month treatment period	• N= 20; ages ≥2 • Double-blind, randomized (1:1) to 2 mg/kg or 20 mg/kg apitegromab IV Q4W • 12-month treatment period
Patients	• Ambulatory Type 3 SMA • Two subgroups: 1) Receiving background nusinersen 2) Apitegromab monotherapy	• Type 2 or non-ambulatory Type 3 SMA • Receiving background nusinersen (initiated ≥5 years of age)	• Type 2 SMA • Receiving background nusinersen (initiated before 5 years of age)
Primary Objectives	• Safety • Mean change from baseline in RHS	• Safety • Mean change from baseline in HFMSE	• Safety • Mean change from baseline in HFMSE

Evaluate potential of apitegromab in improving motor function in patients with Type 2 and Type 3 SMA

HFMSE=Hammersmith Functional Motor Scale Expanded; RHS=Revised Hammersmith Scale
Data on file. Scholar Rock, Inc. Cambridge, MA

Considerations in the Conduct and Design of TOPAZ Proof-of-Concept Study

- Main focus of TOPAZ was to assess the potential additive therapeutic benefit of apitegromab on top of background SMN upregulator therapy.*
  - While the protocol allowed the use of any approved SMN upregulator as background therapy, only nusinersen had widespread use during TOPAZ trial enrollment.
- Specifically designed with 3 distinct cohorts to assess apitegromab's potential across patient populations with varying disease severity and different background expectations for disease course.
- Clinical data for nusinersen and natural history data help inform our background expectations for disease course for the different populations evaluated in TOPAZ.
  - These insights further our understanding as we continue to investigate apitegromab in SMA.
- Cohort 3 evaluated two dose arms as we recognized that complete target saturation may not be necessary to achieve therapeutic effect.
  - Low dose of 2 mg/kg was selected to explore this question by aiming for a high level of target engagement but lower than that of the 20 mg/kg dose.

*An apitegromab monotherapy subgroup was included in Cohort 1.

Baseline Characteristics

TOPAZ

	Ambulatory Patients			Non-Ambulatory Patients			
	Cohort 1			Cohort 2	Cohort 3		
	20 mg/kg monotherapy	20 mg/kg +nusinersen	Pooled	20 mg/kg +nusinersen	20 mg/kg +nusinersen	2 mg/kg +nusinersen	Pooled
N	11	12	23	15	10	10	20
Mean age (min, max)	12.1 (7, 19)	13.1 (7, 21)	12.6 (7, 21)	11.7 (8, 19)	3.8 (2, 6)	4.1 (2, 6)	4.0 (2, 6)
Female (%)	73%	58%	65%	53%	50%	30%	40%
SMN2 Gene Copy* (#, %)							
2	1 (9%)	0 (0%)	1 (4%)		1 (10%)	1 (10%)	2 (10%)
3	4 (36%)	9 (75%)	13 (57%)	11 (73%)	8 (80%)	8 (80%)	16 (80%)
4	4 (36%)	1 (8%)	5 (22%)	2 (13%)	0 (0%)	1 (10%)	1 (5%)
Mean # of nusinersen maintenance doses (min, max)	N/A	5.6 (2, 8)	N/A	5.1 (2, 9)	5.4 (3, 8)	5.5 (2, 9)	5.5 (2, 9)
Discontinuation(s)	0	1**	1**	0	0	0	0
Mean RHS score (min, max)	47.6 (26, 63)	51.3 (43, 62)	49.6 (26, 63)				
Mean HFMSE score (min, max)				22.7 (13, 39)	23.5 (14, 42)	26.1 (12, 44)	24.8 (12, 44)

*Data not available for all patients
**Patient who discontinued study for reasons unrelated to study drug
HFMSE=Hammersmith Functional Motor Scale Expanded; RHS=Revised Hammersmith Scale

Data on file. Scholar Rock, Inc. Cambridge, MA

Safety Results from TOPAZ 12-Month Top-Line Analysis Support Evaluation of Apitegromab in Phase 3 Trial

Treatment-emergent adverse events (TEAEs)	Apitegromab 2 mg/kg (n=10)	Apitegromab 20 mg/kg (n=48)	Total (n=58)
Any TEAE	9 (90.0%)	44 (91.7%)	53 (91.4%)
Any Serious TEAE	1 (10.0%)	4 (8.3%)	5 (8.6%)
Any TEAE leading to study drug discontinuation	0 (0.0%)	1 (2.1%)	1 (1.7%)
Any Grade 3 (severe) or higher TEAE	0 (0.0%)	3 (6.2%)	3 (5.2%)

- **Five most frequently reported TEAEs*:** Headache (24%), pyrexia (22%), upper respiratory tract infection (22%), cough (22%), and nasopharyngitis (21%).
- **Anti-drug antibodies (ADA)** were present at low titers following apitegromab treatment in 3 out of 58 enrolled patients. No apparent impact on drug exposure was observed and was not associated with any hypersensitivity reactions.
- No safety signals identified as of the TOPAZ 12-month top-line analysis

Incidence and severity of AEs were consistent with the underlying patient population and background therapy

Treatment-emergent adverse events (TEAEs) are defined as AEs that start after the first dose of study drug or start prior to the administration of study drug and worsen in severity/grade or relationship to investigational medication after the administration of study drug.
**TEAE rates are across all patients in TOPAZ trial*
Data on file. Scholar Rock, Inc. Cambridge, MA

Serious and Severe Treatment-Emergent Adverse Events (TEAEs)

Serious TEAEs; *All Assessed by Trial Investigators as Unrelated to Apitegromab*

2 mg/kg:

- **Cohort 3:** 1 patient hospitalized due to adenoidal and tonsillar hypertrophy and scheduled adenotonsillectomy (Grade 2). Resolved without sequelae.

20 mg/kg:

- **Cohort 1:** 2 patients with gait inability considered a significant disability (both Grade 3). Events remain ongoing.
- **Cohort 1:** 1 patient hospitalized with post lumbar puncture syndrome (Grade 2). Resolved without sequelae.
- **Cohort 1:** 1 patient hospitalized due to viral upper respiratory infection (Grade 2/prior history). Resolved without sequelae.

Other Severe TEAE; *Assessed by Trial Investigator as Unrelated to Apitegromab*

- **Cohort 1:** 1 patient presented with post lumbar puncture syndrome (non-serious Grade 3). Resolved without sequelae.

Study Discontinuation; *Assessed by Trial Investigator as Unrelated to Apitegromab*

- **Cohort 1:** 1 patient withdrew consent after ~2 months in the trial. Grade 2 leg muscle fatigue (developed prior to enrollment).

Treatment-emergent adverse events (TEAEs) are defined as AEs that start after the first dose of study drug or start prior to the administration of study drug and worsen in severity/grade or relationship to investigational medication after the administration of study drug.
Data on file. Scholar Rock, Inc. Cambridge, MA

TOPAZ 12-Month Top-line Results Demonstrate Potential of Apitegromab for Patients with Type 2 and Type 3 SMA

	Ambulatory Patients (Revised Hammersmith Scale)			Non-Ambulatory Patients (Hammersmith Functional Motor Scale Expanded)			
	Cohort 1			Cohort 2*	Cohort 3*		
(Intent-to-Treat Population)	20 mg/kg monotherapy (n=11)	20 mg/kg +nusinersen (n=12)	Pooled (n=23)	20 mg/kg +nusinersen (n=14)	20 mg/kg +nusinersen (n=8)	2 mg/kg +nusinersen (n=9)	Pooled (n=17)
Mean change from baseline (95% CI)	-0.4 (-3.9, 3.1)	-0.3 (-2.0, 1.4)	-0.3 (-2.1, 1.4)	+0.6 (-1.4, 2.7)	+7.1 (1.8, 12.5)	+5.3 (-1.5, 12.2)	+6.2 (2.2, 10.1)
# (%) pts achieving ≥1-pt increase	4/11 (36%)	5/12 (42%)	9/23 (39%)	9/14 (64%)	7/8 (88%)	7/9 (78%)	14/17 (82%)
# (%) pts achieving ≥3-pt increase	3/11 (27%)	2/12 (17%)	5/23 (22%)	4/14 (29%)	5/8 (63%)	5/9 (56%)	10/17 (59%)

✓ **Cohort 1 data suggest potential clinical effect in certain patients in this patient population**
- Mean decline in RHS from baseline
- Majority (57%) maintained or improved in RHS (≥0-point change from baseline) and 22% achieved ≥3-point increase

✓ **Cohort 2 observed improvement of motor function from baseline**
- Mean improvement in HFMSE from baseline; potential durability of improvement apparent up to 12-months
- Majority (64%) achieved ≥1-point increase in HFMSE and sizeable subset (29%) achieved ≥3-point increase

✓ **Cohort 3 observed further improvements in motor function and continued dose response vs. 6-month interim analysis**
- Large mean improvement in HFMSE from baseline in both dose arms; high dose numerically outperformed low dose
- Majority (59%) achieved ≥5-point increase and sizeable subset (35%) achieved >10-point increase in HFMSE

**4 patients (1 in Cohort 2 and 3 in Cohort 3) each missed 3 doses of apitegromab due to COVID-19-related site access restrictions and were not included in the primary (intent-to-treat) analysis.*

Data on file. Scholar Rock, Inc. Cambridge, MA

Cohort 1

ScholarRock.

Background Insights into Ambulatory Type 3 SMA Patients

Coratti et, al. Natural History Study of Ambulatory Type 3 SMA

Baseline characteristics

- 130 patients with ambulatory Type 3 SMA (some patients were lost to follow-up over time)
- Mean age at baseline of 10.05
- Mean HFMSE score of 52.81

12-month assessments

- Mean change in HFMSE from baseline was -0.79 points
- 11 patients lost ambulation - mean age at ambulation loss was 10.21 years (SD±6.43)

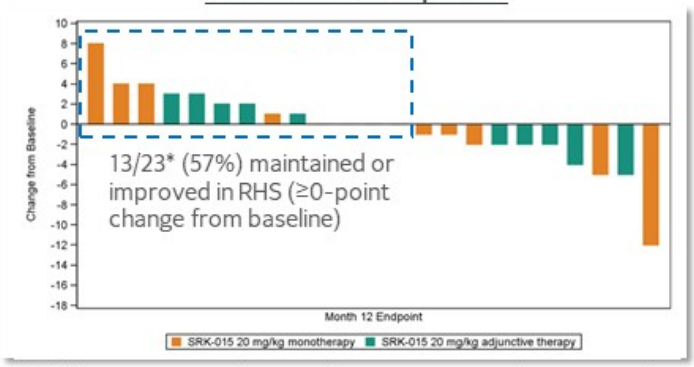
Motor function decline is common in ambulatory Type 3 SMA and can be severe in a subset of patients

Source: Coratti, et, al. Annals of Neurology (2020; 88:1109-1117) DOI: 10.1002/ana.25900
This third-party information is provided for background only and is not intended to convey or imply a comparison to the TOPAZ clinical trial results.

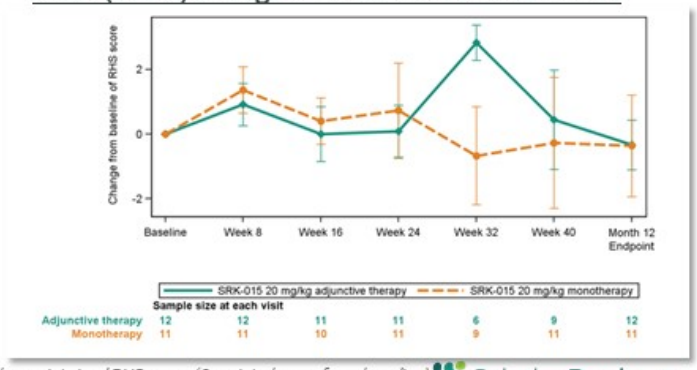
Cohort 1: Mean Decline in RHS at 12-Months but Majority of Patients Maintained or Improved in RHS Score from Baseline

Ambulatory Type 3 SMA (Intent-to-Treat Population)	Apitegromab (20 mg/kg) monotherapy (n=11)	Apitegromab (20 mg/kg) + nusinersen (n=12)	Pooled (n=23)
Mean change from baseline in RHS (95% CI)	-0.4 (-3.9, 3.1)	-0.3 (-2.0, 1.4)	-0.3 (-2.1, 1.4)
# (%) patients achieving ≥1-pt increase in RHS	4/11 (36%)	5/12 (42%)	9/23 (39%)
# (%) patients achieving ≥3-pt increase in RHS	3/11 (27%)	2/12 (17%)	5/23 (22%)
# (%) patients achieving ≥5-pt increase in RHS	1/11 (9%)	0/12 (0%)	1/23 (4%)

Individual RHS responses



Mean (±SEM) change from baseline in RHS scores

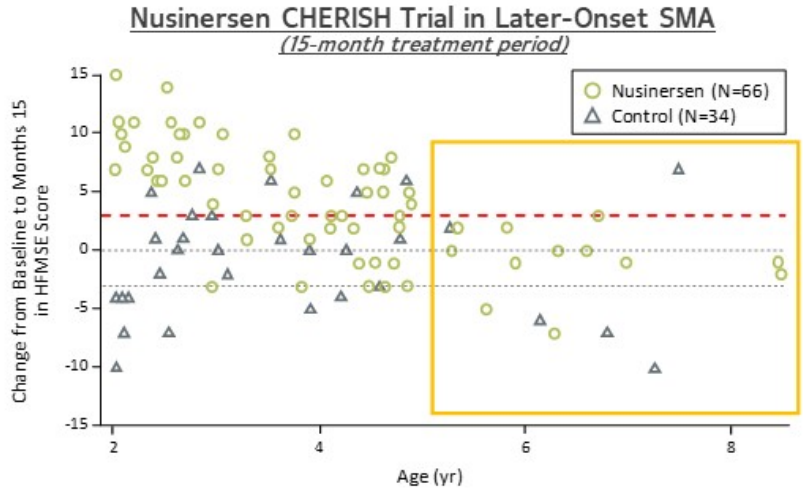


*Includes 2 patients in monotherapy and 2 patients in apitegromab + nusinersen subgroup who maintained RHS score (0-point change from baseline)
Per protocol and sensitivity (all patients) analyses showed similar results to primary intent-to-treat analysis
apitegromab = SRK-015
Data on file. Scholar Rock, Inc. Cambridge, MA

Cohort 2

ScholarRock.

Background Insights Into Non-Ambulatory Later-Onset SMA ≥5 Years of Age



CHERISH clinical trial data*

After 15 months of treatment in patients who started on nusinersen at age ≥5....

- Mean HFMSE decline of >0.5-points
- <15% with ≥3-point increase

Natural history study**

After 12-month follow-up in patients age ≥5...

- Mean HFMSE decline
- <5% with ≥3-point increase

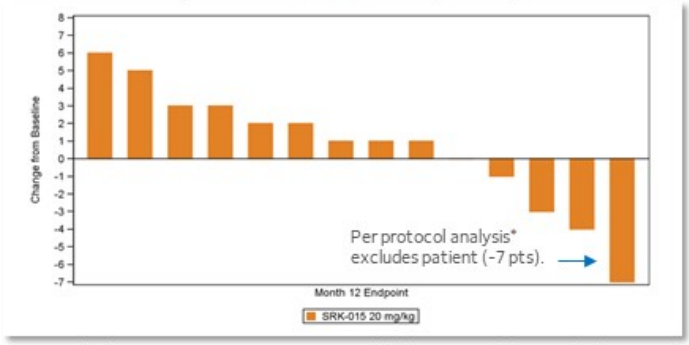
Majority of patients in this age range do not experience HFMSE improvements and rarely achieve a ≥3-point increase

*Mercuri E. et.al. Nusinersen versus sham control in later-onset spinal muscular atrophy. *N Engl J Med.* 2018;378:625-635.
**Mercuri E. et al. Patterns of disease progression in type 2 and 3 SMA: implications for clinical trials. https://doi.org/10.1016/j.nmd.2015.10.006
This third-party information is provided for background only and is not intended to convey or imply a comparison to the TOPAZ clinical trial results.

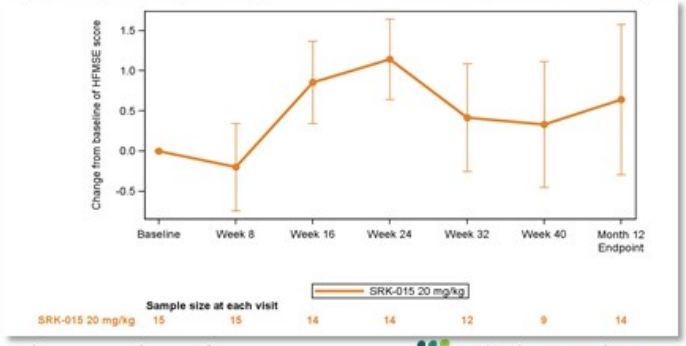
Cohort 2: Improvement in Mean HFMSE at 12-Months with Majority of Patients Achieving ≥1-point Increase

Type 2 and Non-Ambulatory Type 3 SMA	Apitegromab (20 mg/kg) + nusinersen	
	Intent-to-Treat Population (n=14)	Per Protocol Population* (n=13)
Mean change from baseline in HFMSE (95% CI)	+0.6 (-1.4, 2.7)	+1.2 (-0.5, 2.9)
# (%) patients achieving ≥1-pt increase in HFMSE	9/14 (64%)	9/13 (69%)
# (%) patients achieving ≥3-pt increase in HFMSE	4/14 (29%)	4/13 (31%)
# (%) patients achieving ≥5-pt increase in HFMSE	2/14 (14%)	2/13 (15%)

Individual HFMSE responses



Mean (±SEM) change from baseline in HFMSE scores



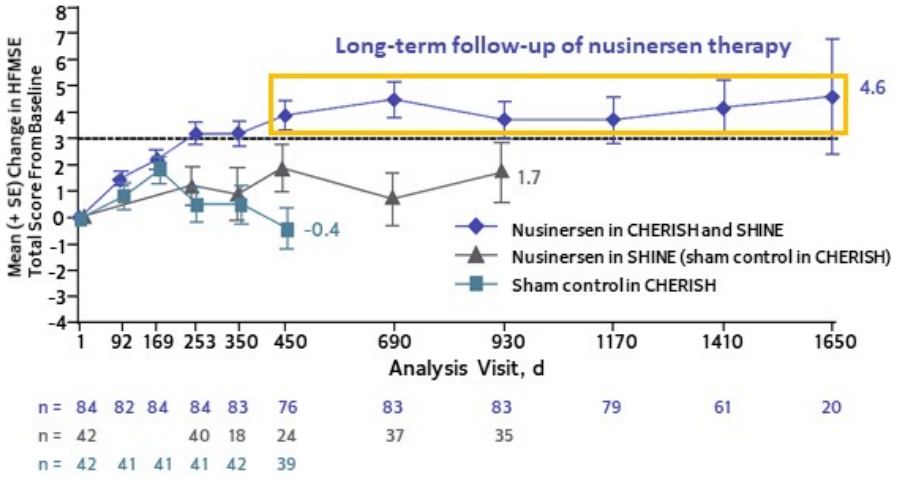
*Patient had concomitant exposure to an acetylcholinesterase inhibitor, which is not permitted per the TOPAZ trial protocol
Sensitivity analysis (all patients) showed similar results to primary intent-to-treat analysis
apitegromab = SRK-015. Data on file. Scholar Rock, Inc. Cambridge, MA

Cohort 3

ScholarRock.

Background Insights Into Non-Ambulatory Later-Onset SMA with Early Initiation of Nusinersen Therapy

Nusinersen SHINE Trial in Later-Onset SMA*



n =	84	82	84	84	83	76	83	83	79	61	20
n =	42			40	18	24	37	35			
n =	42	41	41	41	42	39					

*Most nusinersen-treated patients in CHERISH were under age 5 years at time of therapy initiation

Nusinersen SHINE Trial

SHINE data suggest nusinersen-treated patients primarily stabilize or experience modest and gradual improvement beyond the initial 15 months of therapy

TOPAZ Cohort 3

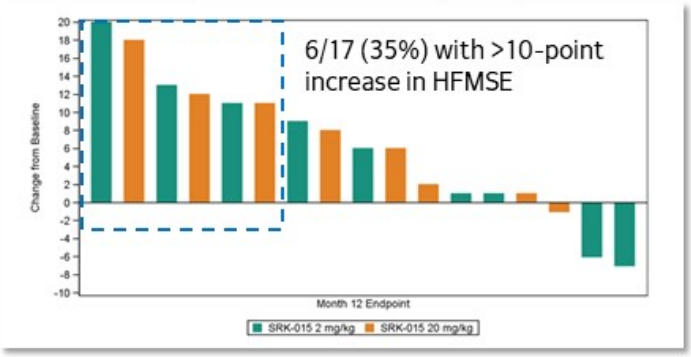
Patients on average had received ~2 years of treatment with nusinersen at baseline and ~3 years by the 12-month analysis timepoint.

Source: Darras, B., et.al. Nusinersen in later-onset spinal muscular atrophy. *Neurology*. May 2019; 92 (21) e2492-e2506.
"Longer-term treatment with nusinersen: results in later-onset spinal muscular atrophy from the SHINE study" P.257, World Muscle Society Congress 2020
This third-party information is provided for background only and is not intended to convey or imply a comparison to the TOPAZ clinical trial results.

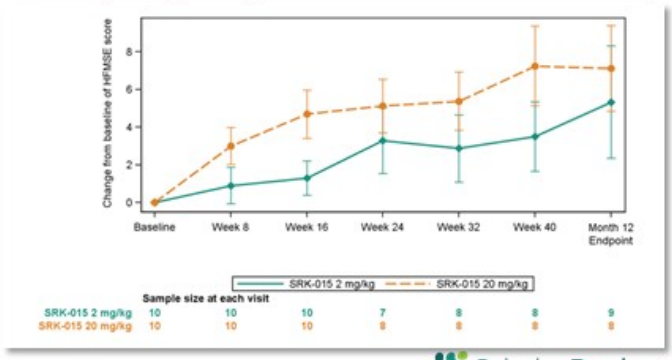
Cohort 3: Sizeable Continued Improvements in Mean HFMSE Observed Across 12 Months

Type 2 SMA (Intent-to-Treat Population)	Apitegromab 20 mg/kg + nusinersen (n=8)	Apitegromab 2 mg/kg + nusinersen (n=9)	Pooled (n=17)
Mean change from baseline in HFMSE (95% CI)	+7.1 (1.8, 12.5)	+5.3 (-1.5, 12.2)	+6.2 (2.2, 10.1)
# (%) patients achieving ≥1-pt increase in HFMSE	7/8 (88%)	7/9 (78%)	14/17 (82%)
# (%) patients achieving ≥3-pt increase in HFMSE	5/8 (63%)	5/9 (56%)	10/17 (59%)
# (%) patients achieving ≥5-pt increase in HFMSE	5/8 (63%)	5/9 (56%)	10/17 (59%)

Individual HFMSE responses



Mean (±SEM) change from baseline in HFMSE scores

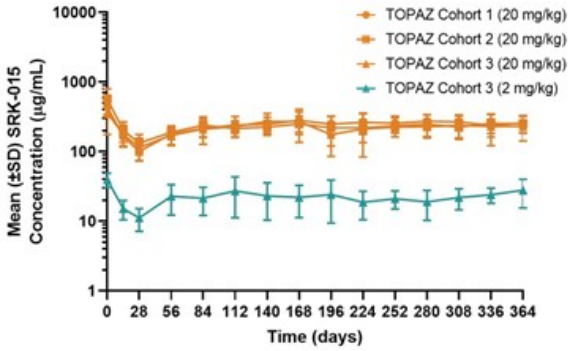


Per protocol and sensitivity (all patients) analyses showed similar results to primary intent-to-treat analysis
apitegromab = SRK-015

Data on file. Scholar Rock, Inc. Cambridge, MA

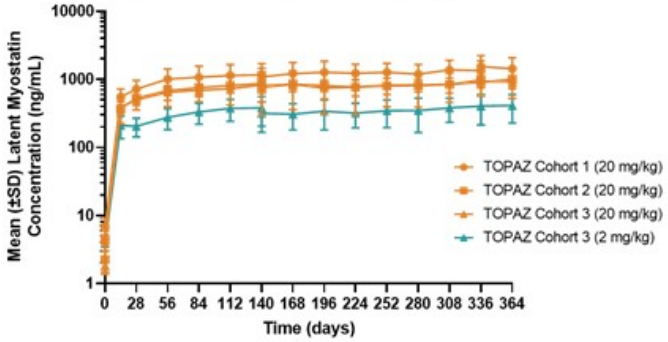
Pharmacokinetic and Pharmacodynamic Data are Supportive of Clinically Observed Effects

Pharmacokinetics* (PK)



- Dose-proportional and sustained drug exposure following chronic administration of apitegromab

Pharmacodynamics (PD)



- Both 2 mg/kg and 20 mg/kg doses yielded high levels of target engagement (>100-fold increase from baseline)
- 20 mg/kg dose offers relatively higher magnitude of target engagement than 2 mg/kg dose

High levels of target engagement achieved by both doses, with relatively higher absolute levels with high dose

*Starting at day 28, measures are pre-dose trough levels

Data on file. Scholar Rock, Inc. Cambridge, MA

12-Month Top-line Results Support the Therapeutic Potential of Apitegromab and Further Development

Cohort 1
- Mean RHS decline from baseline, but majority of patients maintained or improved (≥0-pt change in RHS)
- Potential subset of patients with more pronounced effect (22% with ≥3-pt increase)

Cohort 2
- Mean HFMSE improvement from baseline
- Majority (64%) of patients improved (≥1-pt increase in HFMSE) and sizeable subset (29%) attained ≥3-pt increase in HFMSE

Cohort 3
- Large HFMSE improvements from baseline, with dose response observed
- Majority (59%) of patients attained ≥5-pt increase and sizeable subset (35%) attained >10-pt increase in HFMSE
- PK/PD results support observed dose response

Safety
- No safety signals identified as of the 12-month top-line analysis
- Incidence and severity of AEs were consistent with the underlying patient population and background therapy

All Elected to Opt Into Extension Period

**Excludes one patient from Cohort 1 that discontinued from the trial*
Data on file. Scholar Rock, Inc. Cambridge, MA

1. Plinth/chair sitting
2. Long sitting
3. One hand to head in sitting
4. Two hands to head in sitting
5. Supine to side-lying
6. Rolls prone to supine over R
7. Rolls prone to supine over L
8. Rolls supine to prone over R
9. Rolls supine to prone over L
10. Sitting to lying
11. Props on forearms
12. Lifts head from prone
13. Prop on extended arms
14. Lying to sitting
15. Four-point kneeling
16. Crawling
17. Lifts head from supine
18. Supporting standing
19. Stand unsupported
20. Stepping
21. Right hip flexion in supine
22. Left hip flexion in supine
23. High kneeling to right half kneel
24. High kneeling to left half kneel
25. High kneeling to standing leading with left leg (through right half kneel)
26. High kneeling to standing leading with right leg (through left half kneel)
27. Stand to sitting on the floor
28. Squat
29. Jump 12 inches forward
30. Ascends 4 stairs with railing
31. Descends 4 stairs with railing
32. Ascends 4 stairs without arm support
33. Descends 4 stairs without arm support

http://columbiasma.org/docs/HFMSE_2019_Manual.pdf

Hammersmith Functional Motor Scale Expanded for SMA (HFMSE)

Total achievable score of 66

- 33 distinct measures of an individual's ability to perform various activities
- Quality and execution of each movement is ranked on a scale of 0, 1, 2

ScholarRock.

Next Steps for Apitegromab Program

Tony Kingsley - President & CEO

Ted Myles - CFO & Head of Business Ops

Additional TOPAZ Data and Analyses Will Further Our Understanding of Apitegromab's Potential in SMA

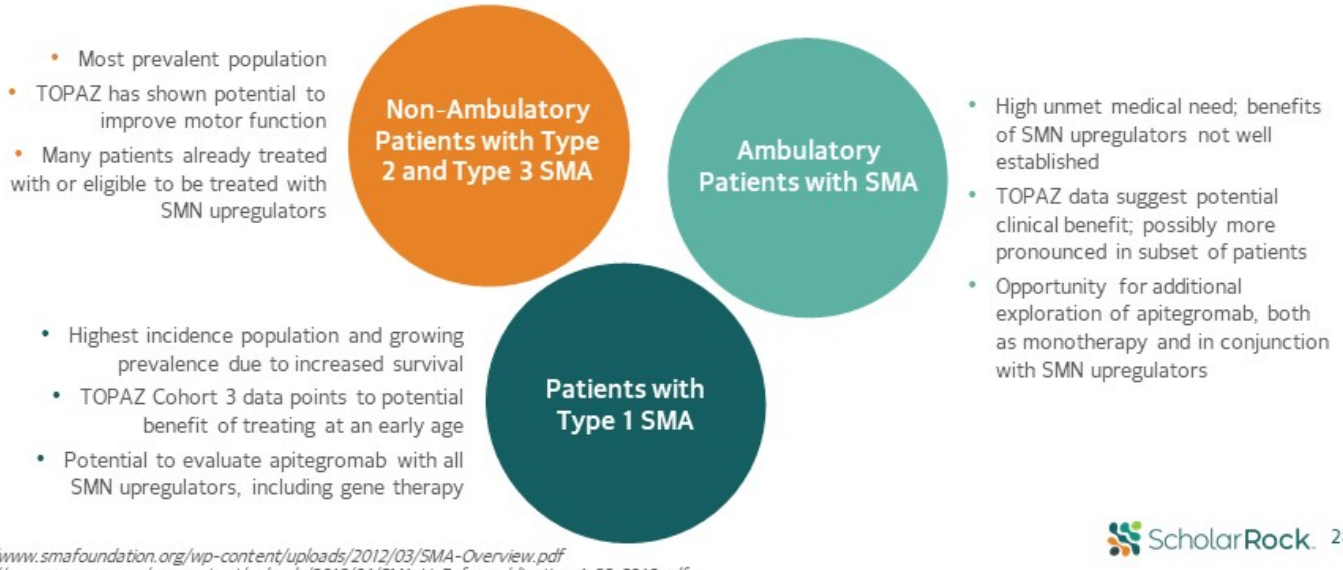
- Exploratory analyses, including patient-level data
- Additional outcome measures
- Additional safety data

Plan to present 12-month top-line data and additional analyses at upcoming medical congresses

Apitegromab Has Broad Potential in SMA…

Global Disease with Overall Prevalence of 30,000-35,000 in U.S. and Europe Alone

Subject to discussions with regulatory authorities; planned Phase 3 trial expected to initiate by year-end

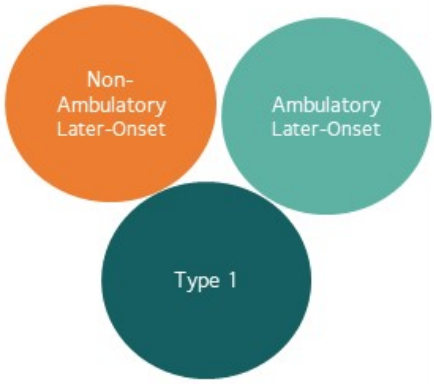


http://www.smafoundation.org/wp-content/uploads/2012/03/SMA-Overview.pdf
https://www.curesma.org/wp-content/uploads/2018/01/SMA-VoP-for-publication-1-22-2018.pdf

…as well as Broad Potential Beyond SMA

Spinal Muscular Atrophy

Leverage TOPAZ findings to conduct **further explorations** in Type 1 and other subpopulations



Muscular Dystrophies

Becker Muscular Dystrophy*

- Prevalence of 15,000-25,000, substantially under-diagnosed in earliest stages
- Younger population with less severe dystrophin deficiency and slower progressing muscle damage

Duchenne Muscular Dystrophy*

- Prevalence of 30,000-40,000 with very severe symptoms and high unmet need
- Progress in the development of next-generation disease-stabilizing therapies may enable add-on muscle-directed approach

Other Dystrophies

- Potential for add-on muscle-directed therapy in other rare dystrophies with less severe phenotypes or upon availability of disease-stabilizing therapies

Additional Indications

Late-onset Pompe Disease**

- Large percentage of patients treated with enzyme replacement therapies (ERTs)
- Existing ERTs may address underlying pathology, but muscle strength remains ongoing challenge

Post-cancer muscle recovery in pediatrics***

- Some children may develop severe muscle wasting from chemotherapy

Glucocorticoid induced myopathy

- Potential benefit for subset of patients unable to discontinue steroid therapy

*"Muscular Dystrophy: Disease Landscape and Forecast." DRG Reports, June 19, 2020
**Enzyme replacement therapy in late-onset Pompe disease: a systematic literature review. Journal of Neuology. 2013
***A Systematic Review of Selected Musculoskeletal Late Effects in Survivors of Childhood Cancer. Current Pediatric Reviews. 2014

Potential for Apitegromab in Becker Muscular Dystrophy (BMD); Aim to Initiate Clinical Trial in 2022

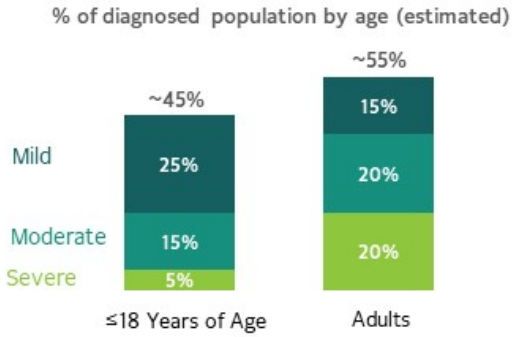
Strong fit for a selective inhibitor of latent myostatin…

Key Scientific Question	BMD Fit
Is patient population young?	Genetic disorder present at birth, with majority of patients identified at young age (before 18)
Are muscles structurally intact?	Less severe dystrophin deficiency and muscle disease than DMD with slower progression
Does disease impact fast-twitch fibers?	BMD causes a substantial deficit in fast-twitch muscle fibers
Is there an established endpoint that relies on fast-twitch fibers?	Several endpoints[1] (NSAA, TTSTAND) dependent on fast-twitch fibers have been used in past pivotal studies of muscular dystrophy therapies

(1)NSAA: North Star Ambulatory Assessment. TTSTAND: Time To Stand
Source: KOL Interviews; Dystrophin levels and clinical severity in Becker muscular dystrophy patients, J Neurol Neurosurg Psychiatry. 2014; Functional changes in Becker muscular dystrophy: implications for clinical trials in dystrophinopathies, Scientific Reports, 2016

… with a sizeable unmet need to be addressed

Estimated Prevalence of 15,000-25,000



- Natural adjacencies to current program in SMA
- Positions apitegromab program for evaluation in a range of other muscular dystrophies (e.g. Duchenne Muscular Dystrophy)

Source: KOL Interviews; Practicing neurologist survey (N=21), 'Muscular Dystrophy: Disease Landscape & Forecast' published Jun 2020

Broad Patent Portfolio Protecting Apitegromab Into Late 2030s; Multiple Designations Granted by FDA/EMA

Highlights of apitegromab patent portfolio:

- **US 10,751,413 (2037)**: Composition of matter and methods of use for apitegromab
- **US 9,758,576 (2034):** Composition of matter claims to mAbs that inhibit the activation of myostatin precursor
- **US 10,307,480 (2035):** Antibodies that selectively inhibit myostatin activation
- **US 10,287,345 (2037):** Treatment methods for various myostatin-related conditions
- **US 10,946,036 (2037):** Covers both add-on and combination therapy with a myostatin inhibitor and a neuronal corrector therapy
- **US 10,882,904 (2036):** Broadly directed to use of apitegromab to achieve certain therapeutic effects; without limiting to specific indications
- **US 9,399,676 (2034):** Methods of producing antibodies that bind pro/latent myostatin

Multiple designations granted by FDA/EMA recognizing the potential for apitegromab to address unmet medical needs in SMA

Rare Pediatric Disease for SMA granted by FDA
Orphan Drug Designation for SMA granted by FDA
Priority Medicines (PRIME) Designation for SMA granted by EMA
Orphan Medicinal Product Designation for SMA granted by EMA

2021: Potential for Another Transformative Year