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): October 27, 2020

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)

620 Memorial Drive, 2nd Floor, Cambridge, MA 02139
(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 October 27, 2020, Scholar Rock Holding Corporation (the "Company") issued a press release announcing positive six-month interim analysis results from the SRK-015 TOPAZ Phase 2 clinical trial. 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.

On October 27, 2020, the Company will host a conference call and webcast at 8:00 am ET on Tuesday, October 27, 2020 to discuss the interim analysis from the SRK-015 TOPAZ Phase 2 clinical trial. A copy of the presentation slides 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 October 27, 2020
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: October 27, 2020

By: /s/ Junlin Ho
Junlin Ho
Senior Vice President, Head of Legal

Scholar Rock Announces Positive Proof-of-Concept Data from TOPAZ Phase 2 Trial Interim Analysis of SRK-015 in Patients with Type 2 and Type 3 Spinal Muscular Atrophy

- Motor function improvements were observed for all three SRK-015 treatment cohorts in the primary efficacy endpoints (Hammersmith scale scores) at six-months; top-line data from the 12-month treatment period are anticipated in 2Q21

- SRK-015 dose response in the primary efficacy endpoint was observed in the randomized, double-blind cohort, with high dose attaining a 5.6 point mean improvement at six-months over baseline compared to low dose attaining a 2.4 point mean improvement over baseline

- First clinical data showing the potential therapeutic benefits of Scholar Rock's innovative scientific platform of inhibiting the activation of latent myostatin

- First demonstration of the therapeutic potential of the Company's proprietary approach of targeting the latent forms of growth factors

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

CAMBRIDGE, Mass.--(BUSINESS WIRE)--October 27, 2020--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 six-month interim analysis results from the TOPAZ Phase 2 clinical trial. Treatment with SRK-015 led to improvements in Hammersmith scale scores (primary efficacy endpoint) in all three cohorts of patients with Type 2 and Type 3 Spinal Muscular Atrophy (SMA). Dose response in the primary efficacy endpoint was observed across all evaluated timepoints in the double-blind, randomized portion of the trial (Cohort 3). The high-dose arm of Cohort 3 attained a 5.6 point mean improvement from baseline in the Hammersmith Functional Motor Scale Expanded (HFMSE) as compared to the low dose arm, which attained a 2.4 point mean improvement at the six-month interim analysis timepoint. No safety signals were identified from the interim analysis.

"These interim results are important because they demonstrate the potential of this muscle-directed approach to improve motor function of individuals with Type 2 and Type 3 SMA," said Thomas Crawford, M.D., Professor of Neurology at the Johns Hopkins University School of Medicine and Lead Investigator of the TOPAZ trial. "In the last few years, we've celebrated the remarkable success in treating SMA with SMN-upregulating approaches that stabilize against neurodegeneration. These findings highlight the potential for a whole new approach to SMA therapy, used in conjunction with the SMN-enhancing therapies, to address the persistent and significant unmet needs of individuals weakened by SMA."

"This is an exciting and important step towards establishing SRK-015 as the potential first muscle-directed therapy for patients with SMA, while also providing important validation of our scientific approach of targeting the latent forms of growth factors," said Yung Chyung, M.D., Chief Medical Officer of Scholar Rock. "These interim data support the continuation of the TOPAZ trial and we look forward to engaging with regulatory authorities regarding our registrational trial plans."

TOPAZ Phase 2 Six-Month Interim Results

SRK-015 is a highly 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 U.S. and Europe. The trial is evaluating the safety and efficacy of intravenous SRK-015 dosed every four weeks (Q4W) over a 12-month treatment period. A pre-planned interim analysis was conducted following a six-month treatment period across all three study cohorts. Three patients (one in Cohort 2 and two in Cohort 3) each missed three doses of SRK-015 and the six-month interim analysis timepoint due to COVID-19-related site access restrictions; the six-month timepoint from these patients was not included in the interim analysis.

At the six-month interim analysis timepoint:

- Mean increases from baseline in Hammersmith scale scores were observed in all three cohorts.

  - 67% of total patients achieved ≥1 point improvement in Hammersmith scores.

- Substantial proportion of patients in each cohort achieved a ≥3 point increase in Hammersmith scores.

  - 35% of total patients achieved ≥3 point increase in Hammersmith scores.

Dose response in the primary efficacy endpoint was observed in the randomized, double-blind cohort; numerically greater improvements in HFMSE scores were observed for high-dose (20 mg/kg) arm across all evaluated timepoints.

Detailed Summary of Interim Results by Cohort

Cohort 1: This open-label, single-arm cohort enrolled 23 patients with ambulatory Type 3 SMA. Patients are being treated with 20 mg/kg of SRK-015 Q4W either as a monotherapy or in conjunction with an approved SMN upregulator therapy (nusinersen). The primary objectives of the cohort are to assess safety and the mean change from baseline in Revised Hammersmith Scale (RHS).

At baseline, patients across both subgroups of patients had a mean age of 12.6 years (range 7-21 years) and a RHS score of 49.6 (range 26-63) out of a total possible score of 69. Patients in the SRK-015 monotherapy group had a mean age of 12.1 years (range 7-19 years) and a mean RHS score of 47.6 (range 26-63). Patients in the group treated with SRK-015 and receiving an SMN upregulator (nusinersen) had a mean age of 13.1 years (range 7-21 years) and a mean RHS score of 51.3 (range 43-62). One patient discontinued from the trial for reasons that were assessed to be unrelated to SRK-015 but was included in the intent-to-treat interim analysis.

At the six-month interim analysis timepoint:

- Mean change from baseline in RHS score:

  - SRK-015 pooled (n = 23): +0.5 points (95% CI of -1.1, +2.2)

  - SRK-015 monotherapy (n = 11): +0.7 points (95% CI of -2.5, +4.0)

  - SRK-015 + nusinersen (n = 12): +0.3 points (95% CI of -1.4, +2.0)

- Proportion of patients attaining ≥1 point increase in RHS score:

  - SRK-015 pooled: 52% (12/23)

  - SRK-015 monotherapy: 64% (7/11)

  - SRK-015 + nusinersen: 42% (5/12)

- Proportion of patients attaining ≥3 point increase in RHS score:

  - SRK-015 pooled: 26% (6/23)

  - SRK-015 monotherapy: 36% (4/11)

  - SRK-015 + nusinersen: 17% (2/12)

- Proportion of patients attaining ≥5 point increase in RHS score:

  - SRK-015 pooled: 9% (2/23)

  - SRK-015 monotherapy: 9% (1/11)

  - SRK-015 + nusinersen: 8% (1/12)

Cohort 2: This open-label, single-arm cohort enrolled 15 patients with a mean age of 11.7 years (range 8-19 years) with Type 2 or non-ambulatory Type 3 SMA and who are already receiving treatment with an approved SMN upregulator. Patients are being treated with 20 mg/kg of SRK-015 Q4W in conjunction with an approved SMN upregulator therapy (nusinersen). At baseline, patients had a mean HFMSE score of 22.7 (range 13-39) out of a total possible score of 66. One patient missed three doses of SRK-015 and the six-month interim analysis timepoint due to COVID-19-related site access restrictions; the six-month timepoint from this patient was not included in the interim analysis. The primary objectives of the cohort are to assess safety and the mean change from baseline in HFMSE.

At the six-month interim analysis timepoint:

- Mean change from baseline in HFMSE score (n = 14): +1.4 points (95% CI of +0.1, +2.7)
- Proportion of patients attaining ≥1 point increase in HFMSE score: 71% (10/14)
- Proportion of patients attaining ≥3 point increase in HFMSE score: 21% (3/14)
- Proportion of patients attaining ≥5 point increase in HFMSE score: 14% (2/14)
- Improvements in HFMSE scores progressively increased over the six-month treatment period, and a plateau in improvement appears to not have yet been reached. Twelve-month data may provide additional insights evaluating the potential for durability of effect and for further motor function gains.

Cohort 3: This randomized**,** double-blind, 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 (2 mg /kg SRK-015 Q4W) or high dose (20 mg/kg SRK-015 Q4W); both treatment arms are in conjunction with an approved SMN upregulator therapy (nusinersen). Two patients (one in high-dose arm and one in low-dose arm) each missed three doses of SRK-015 and the six-month interim analysis timepoint due to COVID-19-related site access restrictions; the six-month timepoint from these patients was not included in the interim analysis. The primary objectives of the cohort are to assess safety and the mean change from baseline in HFMSE.

At baseline, patients in the high-dose arm had a mean age of 3.8 years (range 2-6 years) and mean HFMSE score of 23.5 (range 14-42) out of a total possible score of 66 points, while patients in the low dose arm had a mean age of 4.1 years (range 2-6 years) and a mean HFMSE score of 26.1 (range 12-44).

At the six-month interim analysis timepoint:

- Mean change from baseline in HFMSE score:

  - 20 mg/kg dose (n = 9): +5.6 points (95% CI of +2.5, +8.7)

  - 2 mg/kg dose (n = 9): +2.4 points (95% CI of -0.9, +5.8)

- Proportion of patients attaining ≥1 point increase in HFMSE score:

  - 20 mg/kg dose: 100% (9/9)

  - 2 mg/kg dose: 67% (6/9)

- Proportion of patients attaining ≥3 point increase in HFMSE score:

  - 20 mg/kg dose: 67% (6/9)

  - 2 mg/kg dose: 44% (4/9)

- Proportion of patients attaining ≥5 point increase in RHS score:

  - 20 mg/kg dose: 56% (5/9)

  - 2 mg/kg dose: 33% (3/9)

Greater improvement achieved with high dose: Patients treated with high dose (20 mg/kg) achieved numerically greater improvements from baseline in HFMSE scores as compared to the low dose (2 mg/kg) at all assessed timepoints (week 8, week 16, and the six-month interim analysis timepoint).

- Numerically greater improvements with high dose were observed both in terms of mean change from baseline and in proportions of patients attaining ≥3 point increase in HFMSE score.

Plateau in improvement appears to not have yet been reached: Improvements in HFMSE scores progressively increased over the six-month treatment period. Twelve-month data may provide additional insights evaluating the potential for durability of effect and for further motor function gains.

PK and PD results are supportive of the observed dose response in efficacy:

- Treatment with the high dose led to higher levels of drug exposure than with the low dose.

- Treatment with high dose achieved higher levels of target engagement, and treatment with low dose did not attain full target saturation.

Overall Safety and Tolerability: No safety signals were identified during the interim analysis.

- Incidence and severity of adverse events were consistent with underlying patient population and background therapy.

- Five most frequently reported TEAEs: Headache, upper respiratory tract infection, pyrexia, nasopharyngitis, and cough.

- No grade 3 (severe) or higher adverse events were reported.

- One patient (Cohort 1) experienced a serious treatment-emergent adverse event (TEAE) of Grade 2 viral upper respiratory tract infection leading to hospitalization. The event was resolved without sequelae and was assessed by the trial investigator as unrelated to study drug.

- 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 study drug.

Top-line data from the 12-month treatment are expected in the second quarter of 2021. Twelve-month data may provide additional insights evaluating the potential for durability of effect and for further motor function gains.

As of October 23, 2020, 39 of 39 patients who have completed the 12-month treatment period have opted into the extension period.

Conference Call/Webcast:
Scholar Rock will host a conference call and audio webcast to discuss the SRK-015 TOPAZ Phase 2 clinical trial interim data 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: 1856917. 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 90 days following the presentation.

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 SRK-015
SRK-015 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. Scholar Rock believes the inhibition of the activation of myostatin with SRK-015 may promote a clinically meaningful increase in muscle strength. A Phase 2 clinical trial in patients with Type 2 and Type 3 SMA is ongoing. The U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation (ODD) and Rare Pediatric Disease (RPD) designation, and the European Commission (EC) has granted Orphan Medicinal Product Designation, to SRK-015 for the treatment of SMA. The effectiveness and safety of SRK-015 have not been established and SRK-015 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 platformfor 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/).

Scholar Rock® is a registered trademark of Scholar Rock, Inc.

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 SRK-015, 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 SRK-015, , 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 data from the TOPAZ final analysis will be inconsistent with the data observed in the interim analysis, 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, 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 TOPAZ clinical trial, 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, 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 Contact:
Investors/Media
Catherine Hu
chu@scholarrock.com
917-601-1649

TOPAZ Interim Analysis: SRK-015 Demonstrates Clinical Proof-of-Concept in Spinal Muscular Atrophy

October 27, 2020

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 SRK-015 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 in a manner consistent with preclinical data 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 timeline, competition from others developing products for similar uses, the preliminary nature of interim clinical 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 Quarterly Report on Form 10-Q for the quarter ended June 30, 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.

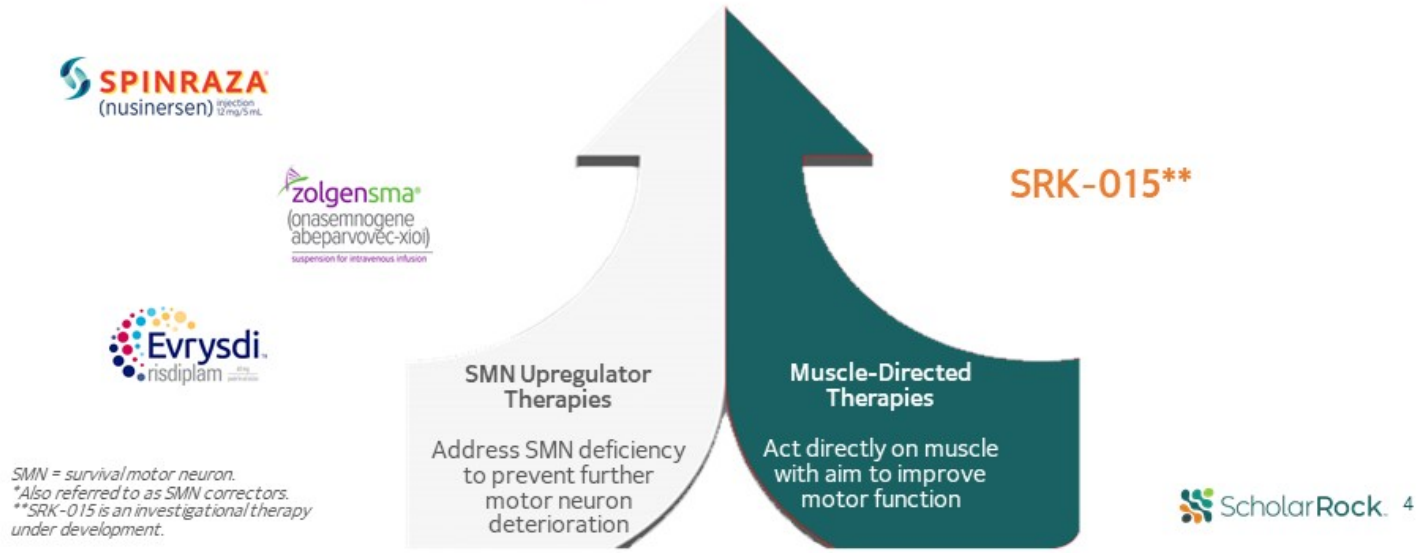
ScholarRock

Agenda

Opening Remarks	Tony Kingsley, President & CEO
Trial Design and Baseline Characteristics	Yung Chyung M.D., Chief Medical Officer
6-month Interim Efficacy and Safety Results	Yung Chyung M.D., Chief Medical Officer
Summary and Next Steps	Tony Kingsley, President & CEO
Questions and Answers	Tony Kingsley, President & CEO Yung Chyung M.D., Chief Medical Officer Ted Myles, Chief Financial Officer

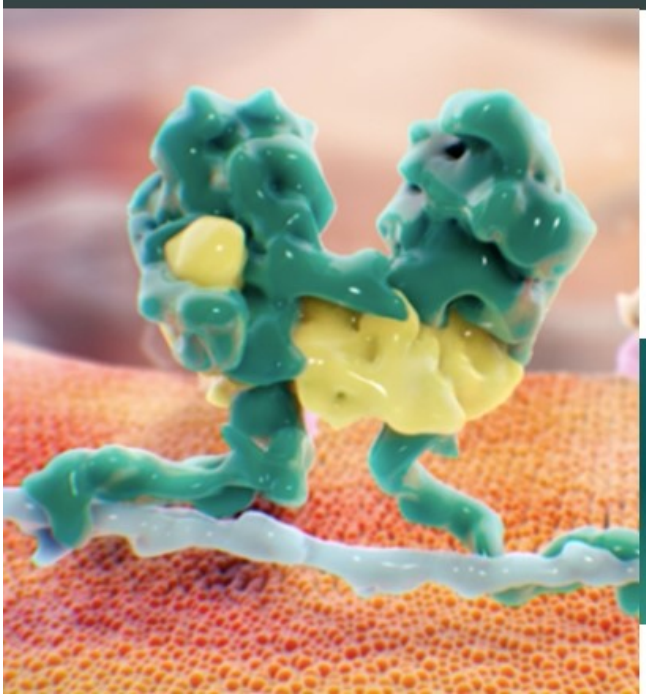
SRK-015 Has Potential to Pioneer a New Treatment Era to Improve Motor Function in Patients with SMA

SMN Upregulator Therapies + Muscle-Directed Therapy (SRK-015) Could Potentially Enhance Outcomes for Patients*



SMN = survival motor neuron.
**Also referred to as SMN correctors.*
***SRK-015 is an investigational therapy under development.*

SRK-015: Highly Selective Inhibitor of the Activation of Pro and Latent Myostatin



- Fully human monoclonal antibody (mAb)
- Half-life of ~23-33 days
- Avoids related growth factors (e.g. GDF11, BMP9, Activin A)

- Rare Pediatric Disease Designation for SMA granted by FDA
- Orphan Drug Designation for SMA granted by the FDA
- Orphan Medicinal Product Designation for SMA granted by the European Commission

Highlights of strong patent portfolio protecting SRK-015:

- **US Patent 10,751,413 (expiry in 2037)**: Covers composition of matter and methods of use for SRK-015
- **US Patent 9,758,576 (expiry in 2034):** Covers mAbs that inhibit the activation of myostatin precursor
- **US 10,287,345 (expiry in 2037):** Treatment methods for various myostatin-related conditions

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 for exquisite selectivity

First demonstration of the therapeutic potential of inhibiting the latent forms of growth factors

TOPAZ Interim Analysis Results Demonstrate Proof-of-Concept

Multiple lines of evidence supporting the potential clinical effect of SRK-015

	Ambulatory Patients (Revised Hammersmith Scale)			Non-Ambulatory Patients (Hammersmith Functional Motor Scale Expanded)		
	Cohort 1			Cohort 2*	Cohort 3*	
	20 mg/kg pooled (n=23)	20 mg/kg monotherapy (n=11)	20 mg/kg +nusinersen (n=12)	20 mg/kg +nusinersen (n=14)	2 mg/kg +nusinersen (n=9)	20 mg/kg +nusinersen (n=9)
Mean change from baseline (95% CI)	0.5 (-1.1, 2.2)	0.7 (-2.5, 4.0)	0.3 (-1.4, 2.0)	1.4 (0.1, 2.7)	2.4 (-0.9, 5.8)	5.6 (2.5, 8.7)
# (%) patients achieving ≥1-pt increase	12/23 (52%)	7/11 (64%)	5/12 (42%)	10/14 (71%)	6/9 (67%)	9/9 (100%)
# (%) patients achieving ≥3-pt increase	6/23 (26%)	4/11 (36%)	2/12 (17%)	3/14 (21%)	4/9 (44%)	6/9 (67%)

✓ **Mean improvements from baseline in HFMSE/RHS observed in each of the 3 cohorts**

- 67% of total patients achieved ≥1-point improvement in Hammersmith scores

✓ **Substantial proportion of patients in each cohort attained ≥3-point improvement in HFMSE/RHS**

- High bar and uncommon to observe in any given patient
- 35% of total patients achieved ≥3-point improvement in Hammersmith scores

✓ **Dose response demonstrated in Cohort 3** *(randomized, double-blind, parallel arm design)*

- Greater improvements in HFMSE scores for high-dose arm across evaluated timepoints
- Supportive PK/PD results; high dose led to higher drug exposure and target engagement

**3 patients (1 in Cohort 2 and 2 in Cohort 3) each missed 3 doses of SRK-015 and the 6-month interim analysis timepoint due to COVID-19-related site access restrictions; the six-month timepoint from these patients was not included in the interim analysis.*
Data on file. Scholar Rock, Inc. Cambridge, MA

Phase 2 Trial Design and Baseline Characteristics

Yung Chyung, M.D.
Chief Medical Officer

TOPAZ

ScholarRock

Next Era of SMA Treatment: Muscle-Directed Therapy

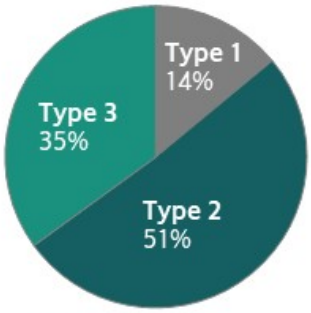
Overall Prevalence of 30,000-35,000 in U.S. and Europe

Type 1:
- Infant-onset
- Usually fatal without treatment

Type 2 and non-ambulatory Type 3:
- Later-onset but still early childhood
- Severe deficits in motor function
- SMN upregulators appear to primarily stabilize disease course

Ambulatory Type 3:
- Typically childhood-onset
- Wide range of motor function deficits; limited mobility and substantial morbidity
- SMN upregulators appear to primarily stabilize disease course

Relative Prevalence Among Patients Living With SMA



TOPAZ trial focuses on Type 2 and Type 3 SMA

Unmet need would be served by a therapy that:

- Improves motor function
- Safety profile that enables chronic dosing, including in the pediatric population
- Low drug administration burden
- Applicable across SMA types

HFMSE = Hammersmith Functional Motor Scale Expanded

SRK-015 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 SRK-015 IV Q4W • 12-month treatment period	• N= 15; ages 5-21 • Open-label, single-arm • 20 mg/kg SRK-015 IV Q4W • 12-month treatment period	• N= 20; ages ≥2 • Double-blind, randomized (1:1) to 2 mg/kg or 20 mg/kg SRK-015 IV Q4W • 12-month treatment period
Patients	• Ambulatory Type 3 SMA • Two subgroups: 1) Receiving background nusinersen 2) SRK-015 monotherapy	• Type 2 or non-ambulatory Type 3 SMA • Receiving background nusinersen	• Type 2 SMA • Receiving background nusinersen (initiated before age 5)
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 SRK-015 in improving motor function

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

Baseline Characteristics

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

*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

Key Strengths of TOPAZ Trial Design and Conduct

- **Large and diverse group of study sites for a rare disease trial**
  - Patients enrolled across 16 study sites in the U.S. and Europe
  - Patient enrollment was not skewed to any one site for any cohort or across the study
- **Primary efficacy endpoints are well-validated outcome measures**
  - Hammersmith Functional Motor Scale Expanded (HFMSE) was specifically designed for SMA and served as primary efficacy endpoint in Phase 3 CHERISH trial of nusinersen
  - Revised Hammersmith Scale (RHS) is very similar to the HFMSE, with some modification to reduce ceiling effects in assessing patients who are ambulatory
- **Efficacy assessments are being conducted in a rigorous fashion:**
  - Standardized conduct of Hammersmith scale assessments; extensive training of all trial sites
  - Assessors of the Hammersmith scale measures are blinded to baseline and prior visit scores
- **Embedded randomized, double-blind portion of trial (Cohort 3) to evaluate dose response between high and low dose arms of SRK-015**

Six-Month Interim Analysis Results

Yung Chyung, M.D.
Chief Medical Officer

TOPAZ Interim Analysis Results Demonstrate Proof-of-Concept

Multiple lines of evidence supporting the potential clinical effect of SRK-015

	Ambulatory Patients (Revised Hammersmith Scale)			Non-Ambulatory Patients (Hammersmith Functional Motor Scale Expanded)		
	Cohort 1			Cohort 2*	Cohort 3*	
	20 mg/kg pooled (n=23)	20 mg/kg monotherapy (n=11)	20 mg/kg +nusinersen (n=12)	20 mg/kg +nusinersen (n=14)	2 mg/kg +nusinersen (n=9)	20 mg/kg +nusinersen (n=9)
Mean change from baseline (95% CI)	0.5 (-1.1, 2.2)	0.7 (-2.5, 4.0)	0.3 (-1.4, 2.0)	1.4 (0.1, 2.7)	2.4 (-0.9, 5.8)	5.6 (2.5, 8.7)
# (%) patients achieving ≥1-pt increase	12/23 (52%)	7/11 (64%)	5/12 (42%)	10/14 (71%)	6/9 (67%)	9/9 (100%)
# (%) patients achieving ≥3-pt increase	6/23 (26%)	4/11 (36%)	2/12 (17%)	3/14 (21%)	4/9 (44%)	6/9 (67%)

✓ **Mean improvements from baseline in HFMSE/RHS observed in each of the 3 cohorts**

- 67% of total patients achieved ≥1-point improvement in Hammersmith scores

✓ **Substantial proportion of patients in each cohort attained ≥3-point improvement in HFMSE/RHS**

- High bar and uncommon to observe in any given patient
- 35% of total patients achieved ≥3-point improvement in Hammersmith scores

✓ **Dose response demonstrated in Cohort 3** *(randomized, double-blind, parallel arm design)*

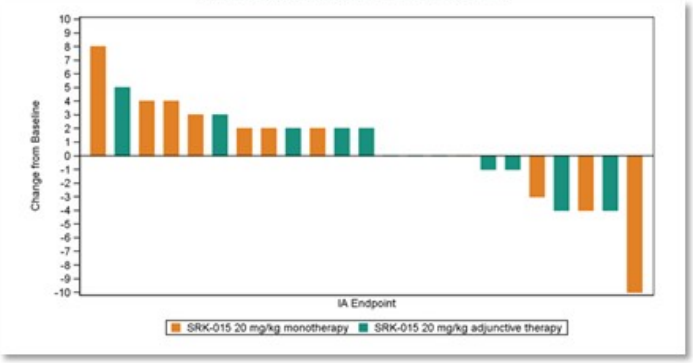
- Greater improvements in HFMSE scores for high-dose arm across evaluated timepoints
- Supportive PK/PD results; high dose led to higher drug exposure and target engagement

**3 patients (1 in Cohort 2 and 2 in Cohort 3) each missed 3 doses of SRK-015 and the 6-month interim analysis timepoint due to COVID-19-related site access restrictions; the six-month timepoint from these patients was not included in the interim analysis.*
Data on file. Scholar Rock, Inc. Cambridge, MA

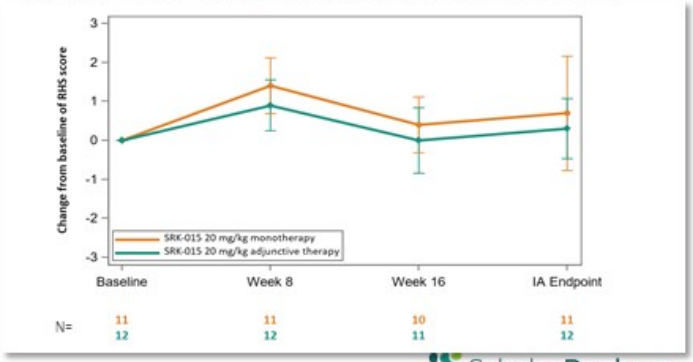
Cohort 1: Improvement in RHS Observed with Both SRK-015 Monotherapy and as Add-on to Background Nusinersen

Ambulatory Type 3 SMA	SRK-015 (20 mg/kg) pooled (n=23)	SRK-015 (20 mg/kg) monotherapy (n=11)	SRK-015 (20 mg/kg) +nusinersen (n=12)
Mean change from baseline in RHS (95% CI)	0.5 (-1.1, 2.2)	0.7 (-2.5, 4.0)	0.3 (-1.4, 2.0)
# (%) patients achieving ≥1-pt increase in RHS	12/23 (52%)	7/11 (64%)	5/12 (42%)
# (%) patients achieving ≥3-pt increase in RHS	6/23 (26%)	4/11 (36%)	2/12 (17%)
# (%) patients achieving ≥5-pt increase in RHS	2/23 (9%)	1/11 (9%)	1/12 (8%)

Individual RHS responses



Mean (±SEM) change from baseline in RHS scores

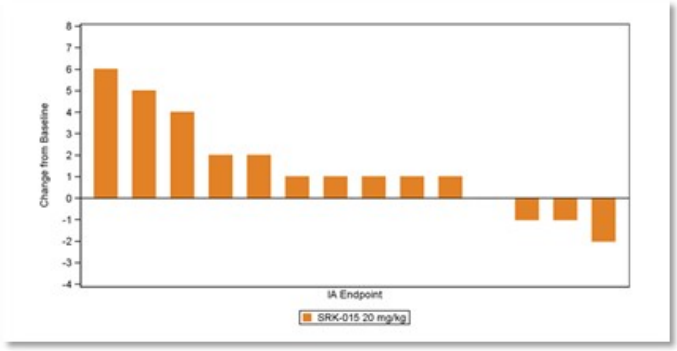


Data on file. Scholar Rock, Inc. Cambridge, MA

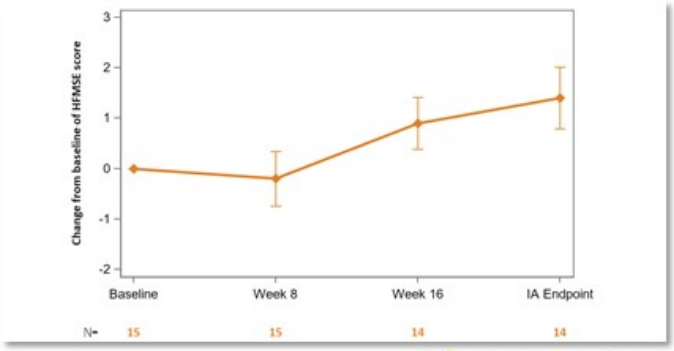
Cohort 2: Meaningful and Consistent Improvements in HFMSE Observed in Type 2 and Non-Ambulatory Type 3 SMA

Type 2 and Non-Ambulatory Type 3 SMA	SRK-015 (20 mg/kg) + nusinersen (n=14)
Mean change from baseline in HFMSE (95% CI)	1.4 (0.1, 2.7)
# (%) patients achieving ≥1-pt increase in HFMSE	10/14 (71%)
# (%) patients achieving ≥3-pt increase in HFMSE	3/14 (21%)
# (%) patients achieving ≥5-pt increase in HFMSE	2/14 (14%)

Individual HFMSE responses



Mean (±SEM) change from baseline in HFMSE scores



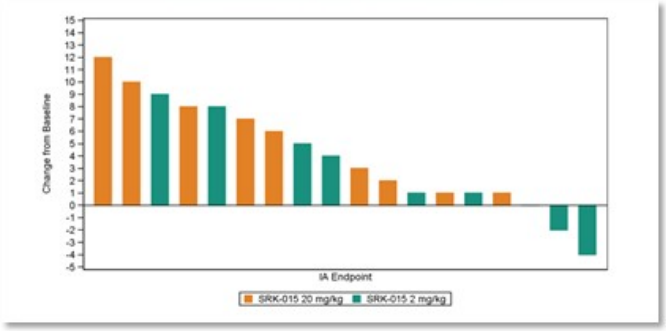
Data on file. Scholar Rock, Inc. Cambridge, MA

Cohort 3: SRK-015 High Dose Showed Substantially Greater Improvements in HFMSE scores Than Low Dose

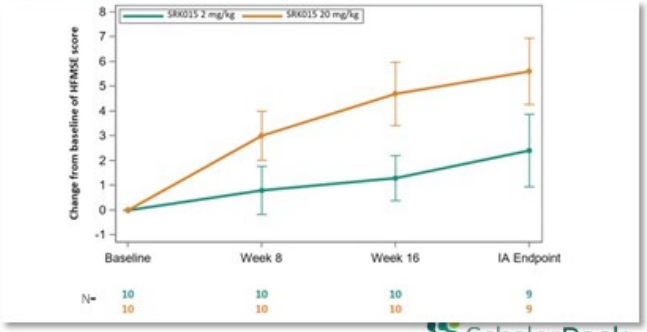
Cohort 3 has a randomized, double-blind, parallel arm design embedded within TOPAZ

Type 2 SMA	SRK-015 low dose (2 mg/kg) +nusinersen (n=9)	SRK-015 high dose (20 mg/kg) +nusinersen (n=9)
Mean change from baseline in HFMSE (95% CI)	2.4 (-0.9, 5.8)	5.6 (2.5, 8.7)
# (%) patients achieving ≥1-pt increase in HFMSE	6/9 (67%)	9/9 (100%)
# (%) patients achieving ≥3-pt increase in HFMSE	4/9 (44%)	6/9 (67%)
# (%) patients achieving ≥5-pt increase in HFMSE	3/9 (33%)	5/9 (56%)

Individual HFMSE responses



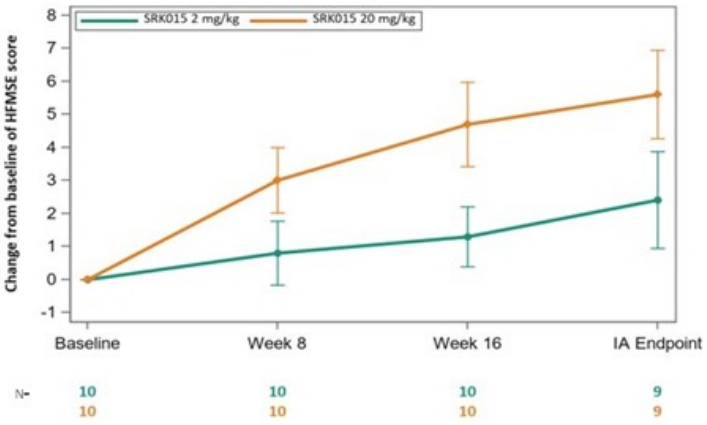
Mean (±SEM) change from baseline in HFMSE scores



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

Cohort 3: Time Course Data Supportive of Dose Response

Mean (±SEM) change from baseline in HFMSE scores



- High-dose arm outperformed low-dose arm numerically across the timepoints
- Plateau in improvement appears to not yet have been reached at the 6-month interim analysis timepoint
- 12-month and extension data enable evaluating the potential for durability of effect and for further motor function gains

Greater improvements in HFMSE scores observed with high dose (20 mg/kg) across all timepoints

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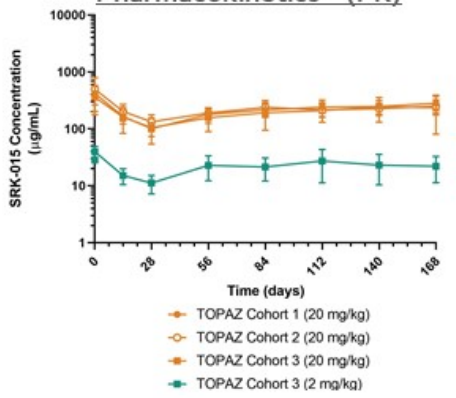
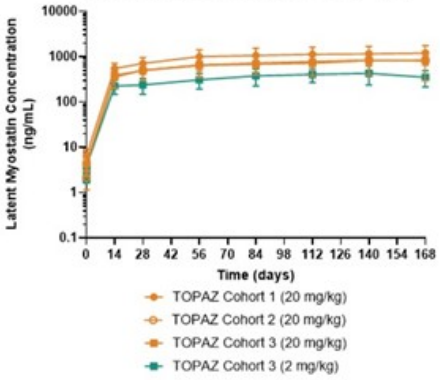
Pharmacokinetic and Pharmacodynamic Data are Supportive of Clinically Observed Dose Response

Pharmacokinetics* (PK)



- Well-behaved PK profile consistent with that commonly observed with monoclonal antibodies
- Drug exposure was dose proportional

Pharmacodynamics (PD)



- Target engagement by SRK-015 was confirmed
- Low dose (2 mg/kg) yielded lower level of target engagement and did not achieve full target saturation

High dose (20 mg/kg) yielded higher levels of drug exposure and target engagement than low dose (2 mg/kg)

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

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

No Safety Signals Identified from Interim Analysis

Treatment-emergent adverse events (TEAEs)	SRK-015 2 mg/kg dose (n=10)	SRK-015 20 mg/kg dose (n=48)	Total (n=58)
Any TEAE	9 (90%)	40 (83.3%)	49 (84.5%)
Any Serious TEAE	0 (0.0%)	1 (2.1%)	1 (1.7%)
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%)	0 (0.0%)	0 (0.0%)

- **Five most frequently reported TEAEs:** Headache, upper respiratory tract infection, pyrexia, nasopharyngitis, and cough.
- **1 serious TEAE (Cohort 1):** Assessed by trial investigator as unrelated to SRK-015. Grade 2 viral upper respiratory infection (prior history) and was hospitalized. Event resolved without sequelae.
- **1 study drug discontinuation (Cohort 1)**: Assessed by trial investigator as unrelated to SRK-015. Grade 2 leg muscle fatigue (developed prior to enrollment). Withdrew consent after ~2 months on trial.

Incidence and severity of AEs are consistent with 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.
Data on file. Scholar Rock, Inc. Cambridge, MA

TOPAZ Interim Analysis Results Demonstrate Proof-of-Concept

1. Multiple lines of evidence supporting the potential clinical effect of SRK-015

- **Dose response demonstrated in randomized, double-blind, parallel arm Cohort 3**
  - High-dose arm showed greater improvements in HFMSE scores
  - Supportive PK/PD results
- **Cohort 2 observed improvements from baseline**
  - In population for which SMN upregulator therapy alone offers motor function stabilization rather than improvement
- **Substantial % of patients in each cohort attained ≥3-pt increase in Hammersmith score**
  - High bar and uncommon to observe in any given patient

2. SRK-015's broad and meaningful therapeutic potential in SMA

- **Mean improvements in Hammersmith scores observed across all 3 cohorts**
- **Most patients experienced an improvement (≥1-pt increase in Hammersmith scores)**
  - Cohort 1: 52% (pooled)
  - Cohort 2: 71%
  - Cohort 3: 100% high dose, 67% low dose
- **Potential for durability and further improvements**
  - Effects observed through 6 months of treatment
  - Plateau in improvement has not yet been observed in Cohorts 2 or 3
  - 12-month and extension data enable evaluation for potential durability of effect and further improvements

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

Summary and Next Steps

Tony Kingsley
President & CEO

Beyond the TOPAZ Interim Analysis

TOPAZ

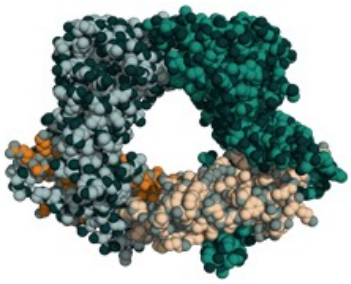
- **Top-line data for 12-month treatment period expected 2Q21**
  - Longer-term evaluation of efficacy for potential durability of clinical effect and continued motor function gains
  - Longer-term safety, PK, PD, and anti-drug antibody
- **39 of 39 patients who have completed 12-month study have opted into the extension period (as of October 23, 2020)**
- **Registrational trial preparations ongoing**
- **Look forward to meeting with regulatory authorities to discuss regulatory path**

Interim results highlight SRK-015's potential as an important treatment for patients with SMA

Unlocking the Potential of the Scholar Rock R&D Engine

TGFβ Superfamily: More than 30 Related Growth Factors that Mediate Diverse Biological Processes

Targeting the latent forms of growth factors



Scholar Rock seeks to unlock the therapeutic potential of modulating growth factor biology

Emerging Insights

Demonstration of proof-of-concept for SRK-015 in SMA

Validation of therapeutic potential for blocking the activation of latent myostatin with SRK-015

Validation of therapeutic potential in targeting latent forms of growth factors

Opportunities Beyond TOPAZ

- Broader exploration of SMA types, age range, and background SMN therapies
- Potential for motor function improvement in other neuromuscular disorders
- Exploration of additional indications related to broader myostatin and fast-twitch fiber biology
- Antibodies against the latent forms of additional well-validated targets in oncology (e.g. SRK-181 program) and fibrosis
- Discovery platform to generate mAbs against other latent growth factors

Differentiated Pipeline with a Series of Anticipated Milestones