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): June 17, 2022

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	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 1.02 Termination of a Material Definitive Agreement.

Scholar Rock Holding Corporation (the "Company") previously entered into an Open Market Sale Agreement℠ (the "Sale Agreement") with Jefferies LLC (the "Sales Agent") on March 9, 2021, pursuant to which the Company was able to issue and sell from time to time in an "at-the-market" offering shares of the Company's common stock, par value $0.001 per share (the "Common Stock"). As of June 16, 2022, 500,000 shares of Common Stock have been issued and sold under the Sale Agreement.

On June 16, 2022, the Company provided notice to the Sales Agent that it was terminating the Sale Agreement, effective immediately. The Sale Agreement provided for termination thereof by either party upon ten (10) calendar days' prior written notice to the other party; however, the Sales Agent has waived such ten (10) day notice requirement. The Company will not incur any early termination penalties in connection with the termination of the Sale Agreement.

Item 7.01. Regulation FD Disclosure.

On June 17, 2022, the Company issued a press release announcing positive 24-month topline results from its TOPAZ Phase 2 clinical trial for apitegromab. A copy of the press release is attached hereto as Exhibit 99.1.

On June 17, 2022, the Company will host a conference call and webcast at 8:30 am ET to discuss the 24-month topline results from the 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. 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.

The information in this report furnished pursuant to Item 7.01 and Exhibit 99.1 shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section nor shall such information be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, 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. It may only be incorporated by reference in another filing under the Exchange Act or the Securities Act of 1933, as amended, if such subsequent filing specifically references the information furnished pursuant to Item 7.01 and Exhibit 99.1 of this report.

Item 8.01. Other Events.

TOPAZ Phase 2 Clinical Trial Update

On June 17, 2022, the Company announced new data from the Phase 2 TOPAZ trial extension period evaluating patient outcomes after 24-months of treatment, which support sustained and continued improvement with apitegromab for non-ambulatory patients with Types 2 and 3 SMA receiving an SMN therapy.

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

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

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

	12-Month Data	**24-Month Data** **Pooled non-ambulatory pts**	**24-Month Data** ***excluding pts w/scoliosis surgery**
Mean Change from Baseline in HFMSE (95% CI)	**3.6 points** (95% CI: 1.2, 6.0) N=32	**4.0 points** (95% CI: 1.5, 6.5) N=29	**4.4 points** (95% CI: 2.0, 6.9) N=28
Mean Change from Baseline in RULM (95% CI)	**1.3 points** (95% CI: 0.2, 2.3) N=31	**1.9 points** (95% CI: 0.8, 3.0) N=33	**2.3 points** (95% CI: 1.2, 3.4) N=30

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

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

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

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

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

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	**Description**
99.1	Press Release issued by Scholar Rock Holding Corporation, dated June 17, 2022
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: June 17, 2022

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

Exhibit 99.1

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

- *Sizable and sustained improvement in Hammersmith Functional Motor Scale-Expanded (HFMSE) scores observed at 24 months*

- *Substantial increase in Revised Upper Limb Module (RULM) scores observed at 24 months*

- *No serious safety risks identified over 24 months*

- *Enrollment progressing in pivotal Phase 3 SAPPHIRE registrational trial*

- *Scholar Rock to host webcast today at 8:30 a.m. ET*

CAMBRIDGE, Mass., June 17, 2022 (BUSINESS WIRE) -- Scholar Rock (NASDAQ: SRRK), a Phase 3, clinical-stage biopharmaceutical company focused on the treatment of serious diseases in which protein growth factors play a fundamental role, today announced new data from the Phase 2 TOPAZ trial extension period evaluating patient outcomes after 24-months of treatment, which support sustained and continued improvement with apitegromab for non-ambulatory patients with Types 2 and 3 SMA receiving an SMN therapy. Detailed results are being presented by Thomas Crawford, M.D. of Johns Hopkins Medicine and the lead principal investigator of the TOPAZ trial, during a podium presentation at the Cure SMA Research & Clinical Care Meeting today at 11:20 a.m. PST.

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

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

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

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

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

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

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

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

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

Conference Call/Webcast:

Scholar Rock will host a conference call and audio webcast to discuss topline 24-month data from the Phase 2 TOPAZ clinical trial on June 17, 2022 at 8:30 a.m. Eastern Time. To participate in the call, please dial 833-519-1308 (domestic) or 914-800-3874 (international) and refer to conference ID: 6495684. A webcast of the call will also be available on the Investors & Media section of the Scholar Rock website at http://investors.scholarrock.com. An archived replay of the webcast will be available on Scholar Rock's website at: https://scholarrock.com/ for approximately 180 days following the presentation.

About the Phase 2 TOPAZ Trial

The TOPAZ trial is an ongoing proof-of-concept, open-label phase 2 trial evaluating the safety and efficacy of apitegromab in patients with Types 2 and 3 SMA. In the main treatment period, patients were dosed intravenously every four weeks as monotherapy or with nusinersen, an approved SMN therapy. The trial enrolled 58 patients in the U.S. and Europe. The primary efficacy endpoints were mean change from baseline in Revised Hammersmith Scale (RHS) score at 12 months for the ambulatory population (Cohort 1), and mean change from baseline in HFMSE score at 12 months for non-ambulatory population (Cohorts 2 and 3). The trial also includes multiple 12-month extension periods designed to evaluate longer-term patient outcomes.

About the Phase 3 SAPPHIRE Trial

SAPPHIRE is an ongoing randomized, double-blind, placebo-controlled, phase 3 clinical trial evaluating the safety and efficacy of apitegromab in non-ambulatory patients with Types 2 and 3 SMA who are receiving SMN therapy (either nusinersen or risdiplam). Approximately 156 patients aged 2-12 years old are anticipated to be enrolled in the main efficacy population. These patients will be randomized 1:1:1 to receive for 12-months either apitegromab 10 mg/kg, apitegromab 20 mg/kg, or placebo by intravenous (IV) infusion every 4 weeks. An exploratory population of approximately 48 patients aged 13-21 years old will also separately be evaluated. These patients will be randomized 2:1 to receive either apitegromab 20 mg/kg or placebo. In this subpopulation of older individuals with SMA, the safety and tolerability of apitegromab will be characterized, and efficacy will also be evaluated in an exploratory, nonpowered manner. SAPPHIRE is expected to enroll 55 sites in the U.S. and Europe. For more information about SAPPHIRE, visit www.clinicaltrials.gov.

About Apitegromab

Apitegromab is a selective inhibitor of the activation of myostatin and is an investigational product candidate for the treatment of patients with spinal muscular atrophy (SMA). Myostatin, a member of the TGFβ superfamily of growth factors, is expressed primarily by skeletal muscle cells, and the absence of its gene is associated with an increase in muscle mass and strength in multiple animal species, including humans. Scholar Rock believes that inhibiting myostatin activation with apitegromab may promote a clinically meaningful improvement in motor function in patients with SMA. The U.S. Food and Drug Administration (FDA) has granted Fast Track, Orphan Drug and Rare Pediatric Disease designations, and the European Medicines Agency (EMA) has granted Priority Medicines (PRIME) and Orphan Medicinal Product designations, to apitegromab for the treatment of SMA. The efficacy and safety of apitegromab have not been established and apitegromab has not been approved for any use by the FDA or any other regulatory agency.

About SMA

Spinal muscular atrophy (SMA) is a rare, and often fatal, genetic disorder that typically manifests in young children. An estimated 30,000 to 35,000 patients are afflicted with SMA in the United States and Europe. It is characterized by the loss of motor neurons, atrophy of the voluntary muscles of the limbs and trunk and progressive muscle weakness. The underlying pathology of SMA is caused by insufficient production of the SMN (survival of motor neuron) protein, essential for the survival of motor neurons, and is encoded by two genes, SMN1 and SMN2. While there has been progress in the development of therapeutics that address the underlying SMA genetic defect, via SMN-dependent pathways, there continues to be a high unmet need for therapeutics that directly address muscle function.

About Scholar Rock

Scholar Rock is a clinical-stage biopharmaceutical company focused on the discovery and development of innovative medicines for the treatment of serious diseases in which signaling by protein growth factors plays a fundamental role. Scholar Rock is creating a pipeline of novel product candidates with the potential to transform the lives of patients suffering from a wide range of serious diseases, including neuromuscular disorders, cancer, and fibrosis. Scholar Rock's approach to targeting the molecular mechanisms of growth factor activation enabled it to develop a proprietary platform for the discovery and development of monoclonal antibodies that locally and selectively target these signaling proteins at the cellular level. By developing product candidates that act in the disease microenvironment, the Company intends to avoid the historical challenges associated with inhibiting growth factors for therapeutic effect. Scholar Rock believes its focus on biologically validated growth factors may facilitate a more efficient development path. For more information, please visit www.ScholarRock.com or follow Scholar Rock on Twitter (@ScholarRock) and LinkedIn (https://www.linkedin.com/company/scholar-rock/). Investors and others should note that we communicate with our investors and the public using our company website www.scholarrock.com, including, but not limited to, company disclosures, investor presentations and FAQs, Securities and Exchange Commission filings, press releases, public conference call transcripts and webcast transcripts, as well as on Twitter and LinkedIn. The information that we post on our website or on Twitter or LinkedIn could be deemed to be material information. As a result, we encourage investors, the media and others interested to review the information that we post there on a regular basis. The contents of our website or social media shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended.

Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding Scholar Rock's future expectations, plans and prospects, including without limitation, Scholar Rock's expectations regarding its growth, strategy, progress and timing of its clinical trials for apitegromab, and other product candidates and indication selection and development timing, the ability of any product candidate to perform in humans in a manner consistent with earlier nonclinical, preclinical or clinical trial data, and the potential of its product candidates and proprietary platform. The use of words such as "may," "might," "could," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "project," "intend," "future," "potential," or "continue," and other similar expressions are intended to identify such forward-looking statements. All such forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, without limitation, that preclinical and clinical data, including the results from the Phase 2 clinical trial, including extension periods, of apitegromab are not predictive of, may be inconsistent with, or more favorable than, data generated from future clinical trials of the same product candidate, including, without limitation, the Phase 3 clinical trial of apitegromab in SMA, Scholar Rock's ability to provide the financial support, resources and expertise necessary to identify and develop product candidates on the expected timeline, the data generated from Scholar Rock's nonclinical and preclinical studies and clinical trials, information provided or decisions made by regulatory authorities, competition from third parties that are developing products for similar uses, Scholar Rock's ability to obtain, maintain and protect its intellectual property, Scholar Rock's dependence on third parties for development and manufacture of product candidates including, without limitation, to supply any clinical trials, Scholar Rock's ability to manage expenses and to obtain additional funding when needed to support its business activities and establish and maintain strategic business alliances and new business initiatives, and the impacts of public health pandemics such as COVID-19 on business operations and expectations, as well as those risks more fully discussed in the section entitled "Risk Factors" in Scholar Rock's Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, as well as discussions of potential risks, uncertainties, and other important factors in Scholar Rock's subsequent filings with the Securities and Exchange Commission. Any forward-looking statements represent Scholar Rock's views only as of today and should not be relied upon as representing its views as of any subsequent date. All information in this press release is as of the date of the release, and Scholar Rock undertakes no duty to update this information unless required by law.

Scholar Rock:

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Apitegromab Upda

Anti-Myostatin Antibody With Transformative Potential in Patie Type 2 and Type 3 SMA

Data extracted April 7, 2022

Disclaimers

Various statements in this presentation concerning the future expectations, plans and prospects of Scholar Rock, Inc. ("Scholar Rock"), inc
limitation, Scholar Rock's expectations regarding its strategy, its product candidate selection and development timing, including timing for
reporting results from its clinical trials for apitegromab, SRK-181, and other product candidates and indication selection and development
runway, the ability of any product candidate to perform in humans in a manner consistent with earlier nonclinical, preclinical or clinical trial
potential of its product candidates and proprietary platform. The use of words such as "may," "could," "might," "will," "should," "expect," "pla
"believe," "estimate," "project," "intend," "future," "potential," or "continue," and other similar expressions are intended to identify such forw
statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. All such forward-loo
based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause act
materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, with
preclinical and clinical data, including the results from the Phase 2 trial of apitegromab or Part A of the Phase 1 trial of SRK-181, are not pre
inconsistent with, or more favorable than, data generated from future clinical trials of the same product candidate, including the Phase 3 c
apitegromab in SMA and Part B of the Phase 1 clinical trial of SRK-181, respectively, Scholar Rock's ability to provide the financial support,
expertise necessary to identify and develop product candidates on the expected timeline, the data generated from Scholar Rock's nonclini
studies and clinical trials, information provided or decisions made by regulatory authorities, competition from third parties that are develo
similar uses, Scholar Rock's ability to obtain, maintain and protect its intellectual property, the success of Scholar Rock's current and pote
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important factors in Scholar Rock's subsequent filings with the Securities and Exchange Commission. Any forward-looking statements rep
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 pre
date of the release, and Scholar Rock undertakes no duty to update this information unless required by law.This presentation and the any
presentation may also contain estimates and other statistical data made by independent parties and by us relating to market size and grow
about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such es
projections, assumptions, and estimates of our future performance and the future performance of the markets in which we compete are n
a high degree of uncertainty and risk.

Agenda

SMA Disease Background & Current Treatment Landscape

Apitegromab TOPAZ Extension Period: 24-Month Data

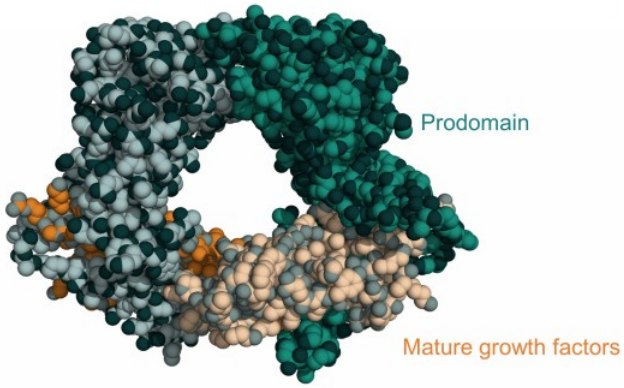
Apitegromab SAPPHIRE Phase 3 Trial Overview

Business Update

Revolutionary Approach to Regulating Highly Sought-
Growth Factors Implicated in Devastating Diseases

Scholar Rock's Target

Growth Factor Precursor (Latent Form)



Scholar Rock's R&D Platf

Transform Medical Practic

- Pursue important targets with well biology but are difficult to drug
- Apply revolutionary approach to t
  - Leverage deep insights into s function
  - Engineer antibodies to delive differentiated therapeutic pr (i.e. exquisite selectivity)

TOPAZ demonstrated the therapeutic potential of inhibiting the latent forms of grow

Sc

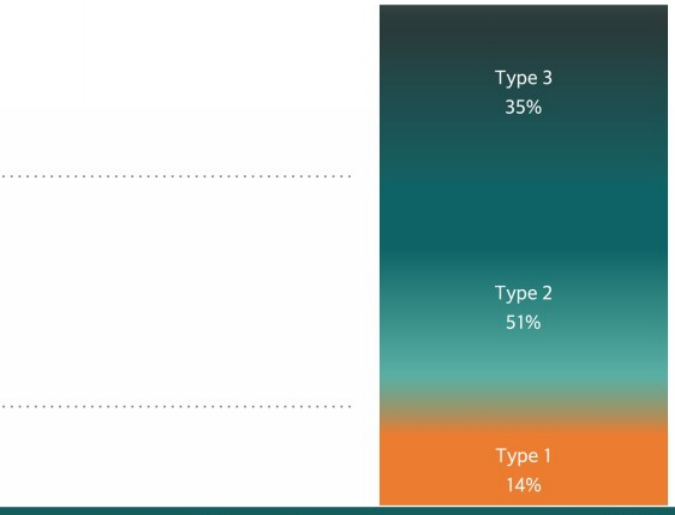
Apitegromab Shows Transformative Potential in Patients with Type 2 and 3 SMA

- Spinal Muscular Atrophy (SMA) remains a devastating and debilitating disease despite utilization of SMN therapies
  - Motor neuron defect with loss of muscle
- Current therapies target motor neuron deterioration; muscle-directed therapy may further improve motor function
- Apitegromab targets myostatin for muscle function
  - Transformative potential in patients with ambulatory Type 2/3 SMA thru the TOPA Phase 2 trial
- Exciting potential path forward for apitegro with the ongoing SAPPHIRE Phase 3 trial
- Further development in Type 1 SMA planned

Apitegromab is an investigational drug candidate being evaluated for the treatment of spinal muscular atrophy. Apitegromab has not been approved for any use by the FDA or any other regulatory agency and its safety and efficacy have not been established.

Spinal Muscular Atrophy Overview

Global disease with 30,000-35,000 affected in U.S. and Europe alone [1,2,3]



TOPAZ* 12-month resu
showed transformati
potential in non-ambula
Types 2 and 3 patien

Represents ~2/3 of ov
patient population

Motor neuron impairment and loss due to SMN genetic deficiency, leading to muscle atrophy a

*TOPAZ Phase 2 trial evaluated patients with Type 2 and 3 SMA (did not include Type 1)

1. Lally et al, Orphanet Journal of Rare Diseases, 2017
2. SMA Europe. SMATracker. About SMA. Accessed January 24, 2022. https://smatracker.eu/what-is-spinal-muscular-atrophy.
3. National Organization for Rare Disorders. Spinal muscular atrophy. Accessed January 24, 2022. https://rarediseases.org/rare-diseases/spinal-muscular-atrophy/.

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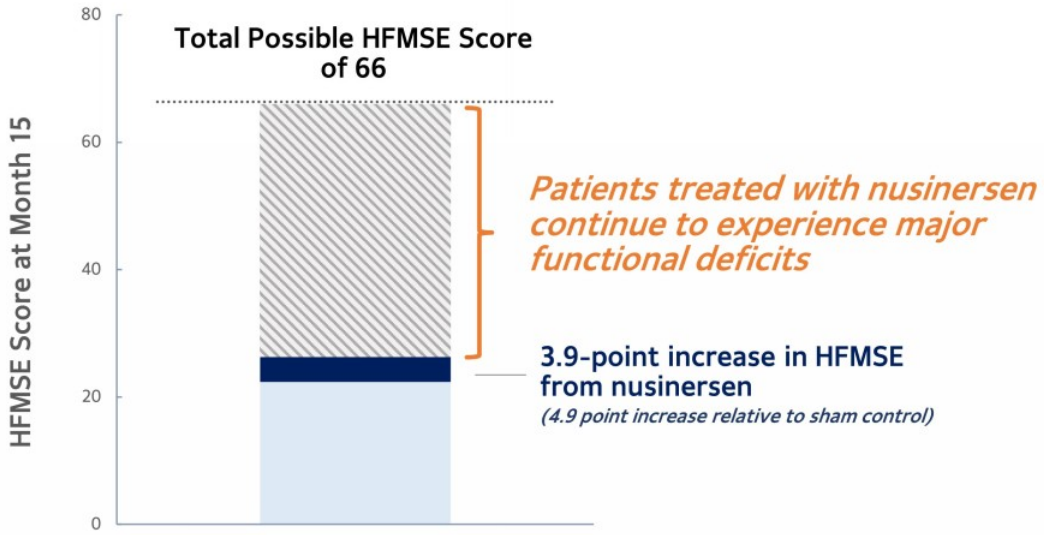
Patients with Types 2 and 3 SMA Continue to Experience Functional Deficits Despite Improvement from Nusinersen



Mean improvement in HFMSE experienced by patients with non-ambulatory Types 2/3 SMA in nusinersen Phase 3 CHERISH trial

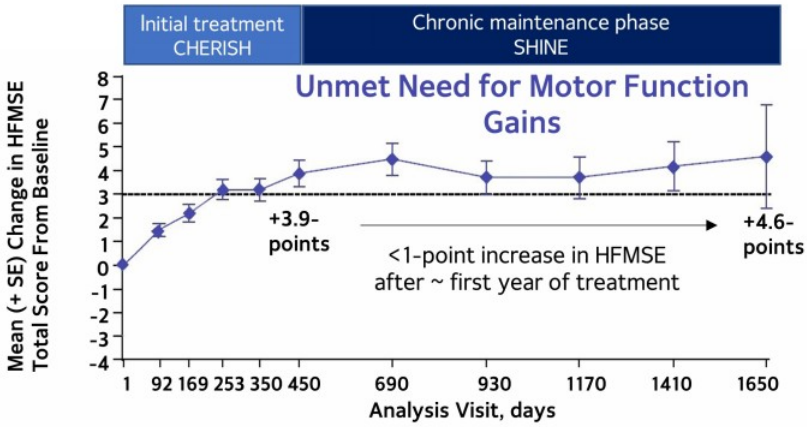
HFMSE=Hammersmith Functional Motor Scale-Expanded

Darras, B., et.al. Nusinersen in later-onset spinal muscular atrophy. Neurology. May 2019; 92 (21) e2492-e2506.

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.

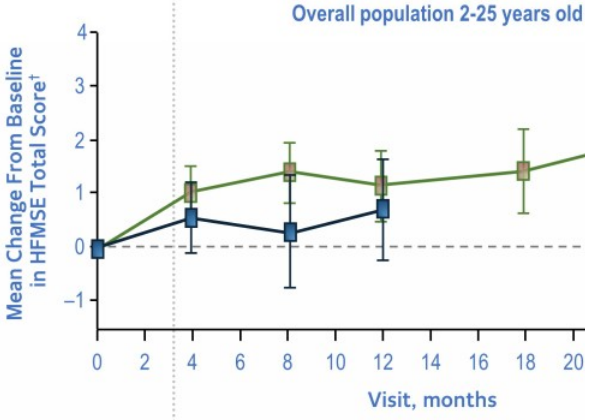
Motor Gains in Patients with Types 2 and 3 SMA on SMN Therapies Plateau After Initial Gains

Plateauing of HFMSE increases observed following initial treatment effects for nusinersen



NUSINERSEN[1]

Plateau of HFMSE increases observed treatment effect of risdiplam, although currently under investigat



RISDIPLAM[2]

HFMSE=Hammersmith Functional Motor Scale-Expanded.

1. Mercuri E, et al. Presented at: World Muscle Society Congress 2020, P. 257
2. Oskoui M, et al. Presented at: 2021 Muscular Dystrophy Association Clinical & Scientific Conference; March 15-18, 2021. Poster 80.

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Summary of TOPAZ Extension Period: 24-Month Data
Sustained Benefit and Evidence of Continued Improvement

❖ Non-Ambulatory Types 2/3 SMA

- **Motor function associated with activities of daily living improved with apitegromab + nu at 24 months:**
  - Sizable and sustained gains in HFMSE scores observed
  - Continued increase in Revised Upper Limb Module (RULM) scores observed
  - Dose response observed over 24 months, with evidence of further motor function ga as low-dose patients switch to high-dose in extension period (2 mg/kg to 20 mg/kg)

❖ Ambulatory Type 3 SMA

- **Stability of Revised Hammersmith Scale (RHS) in patients receiving 20 mg/kg of apitegro nusinersen**
- **Potential motor function gains in subgroups**

❖ No serious safety risks identified to date

- **Five most common treatment-emergent adverse events (TEAEs) were headache, pyrexia respiratory tract infection, cough, and nasopharyngitis**
- **Incidence and types of TEAEs were consistent with underlying disease or nusinersen ther**

❖ Detailed analyses to be presented at Cure SMA (June 2022)

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TOPAZ Phase 2 Trial Design

Ambulatory Patients (Revised Hammersmith Scale)	Non-Ambulatory Patients (Hammersmith Functional Motor Scale Expan	
Cohort 1	Cohort 2	Coh
• 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 ≥ • Double-blind, to 2 mg/kg or apitegromab • 12-month trea
• **Ambulatory Type 3 SMA** • Two subgroups: 1) Receiving nusinersen 2) Apitegromab monotherapy	• **Type 2 or Type 3 SMA** • **Receiving nusinersen (initiated at age 5 or older)**	• **Type 2 SMA** • **Receiving nu (initiated bef**
• Safety • Mean change from baseline in RHS	• Safety • Mean change from baseline in HFMSE	• Safety • Mean change HFMSE

Apitegromab = nonproprietary name for SRK-015
HFMSE=Hammersmith Functional Motor Scale Expanded; RHS=Revised Hammersmith Scale
Data on file. Scholar Rock, Inc. Cambridge, MA

TOPAZ Subject Disposition, Demographics and Baseline Characteristics

	Ambulatory Patients	Cohort 1		NonAmbulatory Patients	Cohort 2	Cohor
		20 mg/kg monotherapy	20 mg/kg + nusinersen		20 mg/kg + nusinersen	2 mg/kg + nusinersen
N (dosed)		11	12		15	10
Mean age at screening (min, max)		12.1 (7, 19)	13.1 (7, 21)		11.7 (8, 19)	4.1 (2, 6)
Mean age at SMA diagnosis (min, max)		5.9 (2, 15)	4.5 (2, 15)		3.1 (1, 16)	1.2 (1, 2)
Female (%)		73%	58%		53%	30%
SMN2 Gene Copy* (#, %)						
2		1 (9%)	0 (0%)			1 (10%)
3		4 (36%)	9 (75%)		11 (73%)	8 (80%)
4		4 (36%)	1 (8%)		2 (13%)	1 (10%)
# of maintenance doses of nusinersen at baseline (min, max)		N/A	5.6 (2, 8)		5.1 (2, 9)	5.5 (2, 9)
Discontinuation(s)		0	2†		1†	0
Scoliosis (#, %)		7 (63.6)	4 (33.3)		11 (73.3)	4 (40%)
Contracture(s) (#, %)		6 (54.5)	7 (58.3)		13 (86.7)	8 (80%)
Mean RHS score (min, max)		47.6 (26, 63)	51.3 (43, 62)			
Mean HFMSE score (min, max)					22.7 (13, 39)	26.1 (12, 44)

*1 patient answered 3-4, 1 patient answered >4 , both patients are in Cohort 1 treated with 20 mg/kg + nusinersen; data not available for all patients.
†1 cohort 1 patient discontinued study in 12M Treatment Period, 1 cohort 1 patient and 1 cohort 2 patient discontinued during 24M Extension Period A. All discontinuat were for reasons unrelated to study drug.
HFMSE=Hammersmith Functional Motor Scale Expanded; RHS=Revised Hammersmith Scale.
Data on File. Scholar Rock, Inc. Cambridge, MA.

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TOPAZ Extension Period Overview

57 of 58 patients completed primary treatment period and enrolled in second year of therapy

- **55 of 57 patients completed**
- High dose (20 mg/kg) patients stayed on high dose
- Low dose (2 mg/kg) patients switched to high dose (20 mg/kg)*
- Four patients had scoliosis surgery during year 2**

54 of 55 pat
remain on tre
as of June 1

*All ten patients switched from low dose to high dose. Time points varied across individual patients.
** Three non-ambulatory patients and one ambulatory patient

Significance of Hammersmith Functional Motor Scale Expanded (HFM

Validated measure assessing the physical abilities of patients with Type

Examples of HFMSE items

Able to touch head above ear level whilst maintaining stable trunk and head position

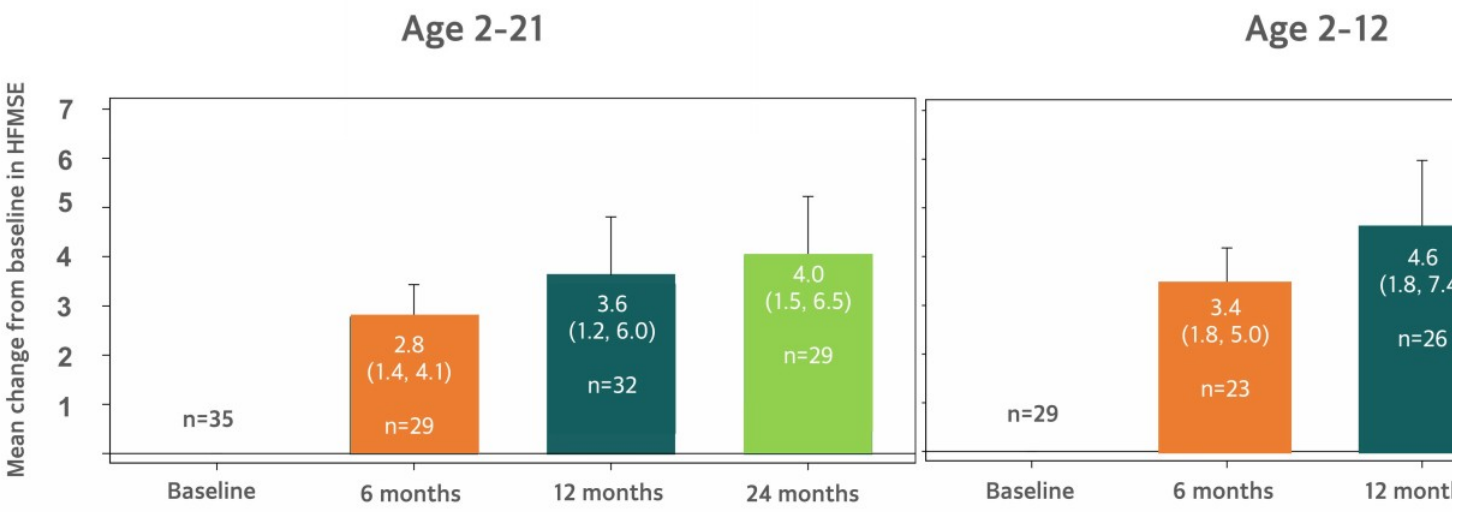
Able to roll from supine to prone over the right side without pulling/pushing on hands

- Consists of 33 items graded on a scale of 0 t unable; 1 denotes performed with modificat adaptation; and 2 denotes without modifica adaptation.
- Item scores are summed to give a total scor maximum of 66. The higher the total score, patient's motor function.
- Examples of items:
  - One hand to head in sitting
  - Rolls supine to prone
  - Lying to sitting
  - Four-point kneeling
  - Supported standing
  - Stepping
  - Ascends 4 stairs with railing

O'Hagen et al. 2007; Glanzman et al. 2011;
Hammersmith Functional Motor Scale Expanded for SMA (HFMSE) Manual, 2019

Sizable, Sustained Increases in HFMSE Observed At 24 Months of Apit

Pooled Non-Ambulatory Patients



Observed Case Analysis is based upon data available for a given timepoint, and this analysis population includes patients treated with the lower dose 2 mg/kg and does not exclude any patients who missed apitegromab doses due to COVID-19 site access restrictions. Error bars represent standard error of the mean (SEM). Values in parentheticals represent 95% confidence interval.

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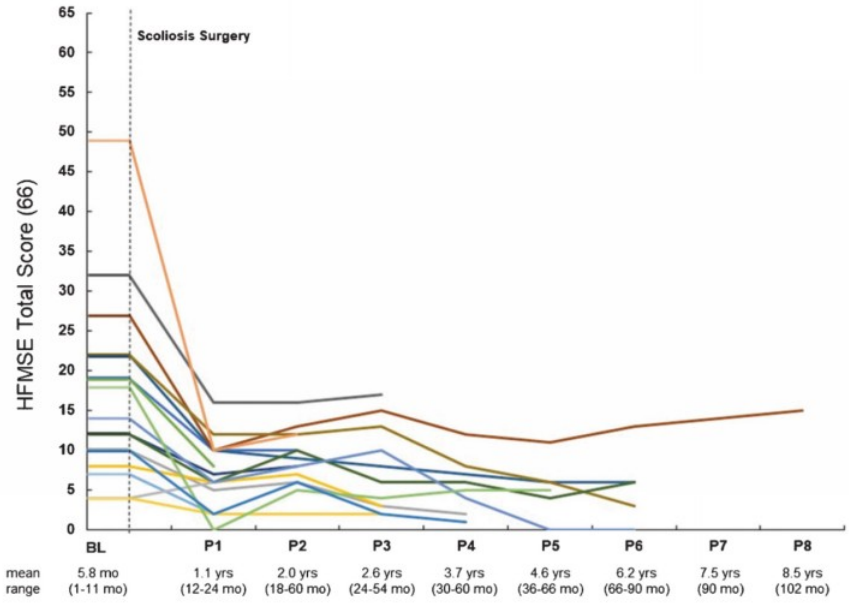
Data on File. Scholar Rock, Inc. Cambridge, MA.

Reported Impact of Scoliosis Surgery on Motor Abilities in SMA

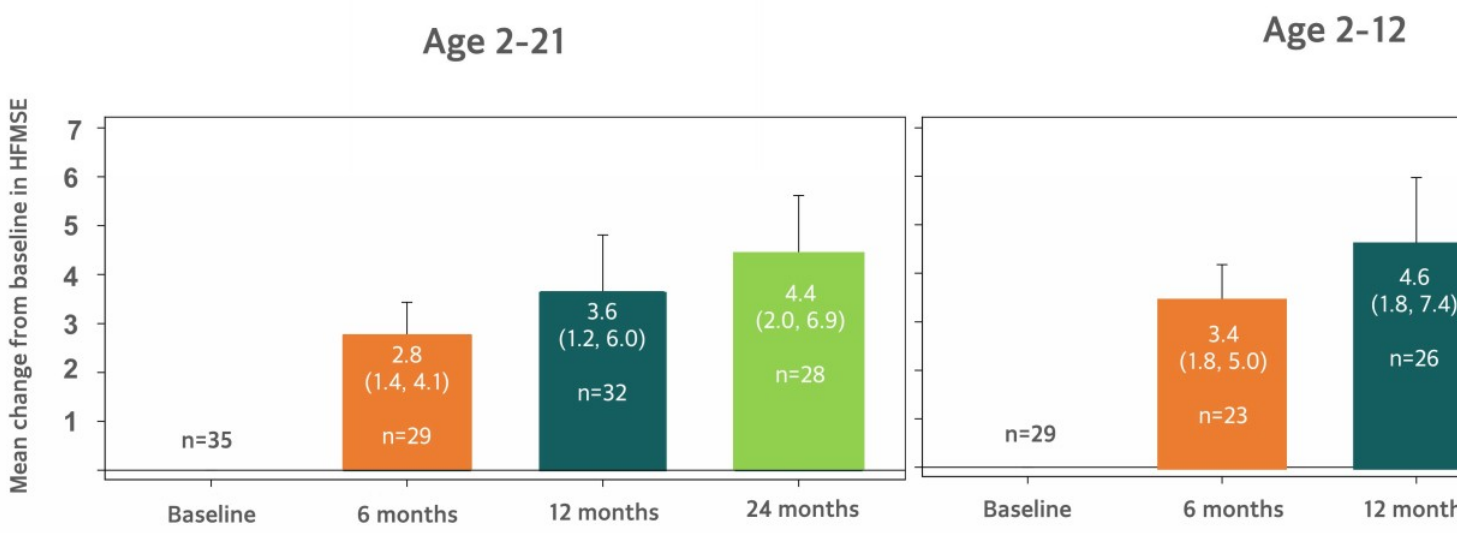
Post-Surgery HFMSE scores Type 2/3 SMA (*Dunaway Young et al. 2020)*



- The vast majority of patients i
  reviewed study lost >3 pts on
  assessed at least 3 months po
  - 14/17 participants lost >3 poin
    = - 12.1, SD = 8.9) on the HFM
    functionally meaningful chang
  - 3/17 participants had minimal
    within ±2 points (mean change
    representing no change or sta
  - 0/17 participants had improve
    2 points post-surgery

Sizable, Sustained Increases in HFMSE Observed At 24 Months of Apit

Pooled Non-Ambulatory Patients Excluding Data Post Scoliosis Surgery



This analysis excludes from the Observed Case Analysis any HFMSE data following scoliosis surgery in TOPAZ. Of the three non-ambulatory patients who had scoliosis surgery, data from one was excluded and the other two did not have valid HFMSE assessments. Error bars represent SEM. Values in parentheticals represent 95% confidence interval.

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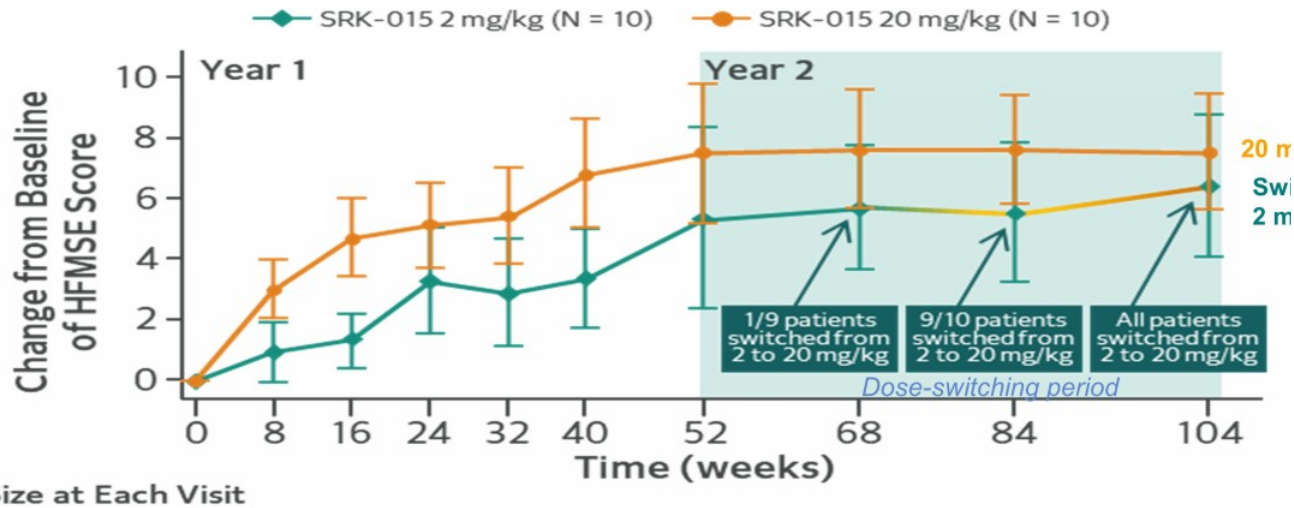
Data on File. Scholar Rock, Inc. Cambridge, MA.

Strong Evidence of Dose Response Observed Over 24 Months
Further Supported by Data from Low Dose to High Dose Switch

Mean Change from Baseline in HFSME Scores Over Time (Cohort 3)
Excludes data after scoliosis surgery



Sample Size at Each Visit

Cohort 3 SRK 2 mg/kg	10	10	10	7	8	9	9	9	10	10
Cohort 3 SRK 20 mg/kg	10	10	10	8	8	10	8	10	10	8

This analysis excludes from the Observed Case Analysis the HFMSE data attained post-scoliosis surgery during TOPAZ. Error bars represent SEM.

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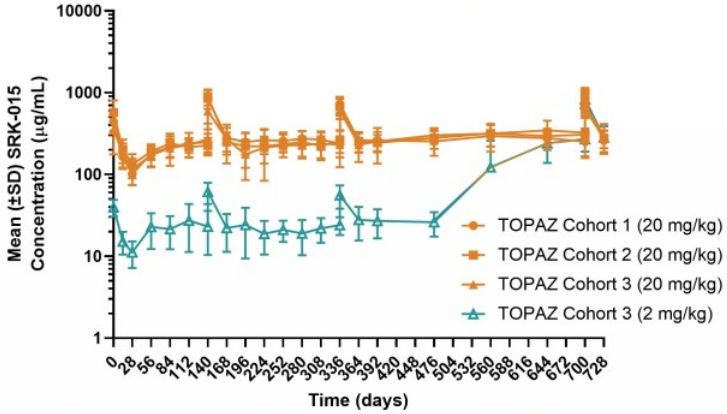
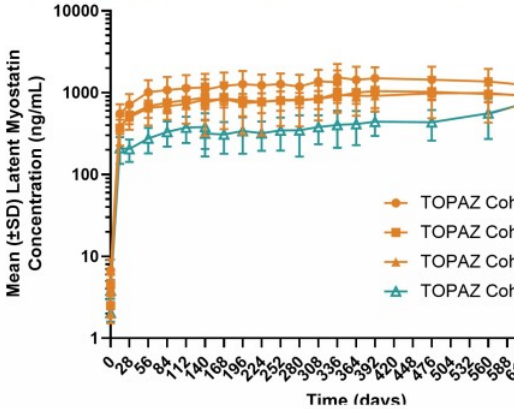
PK and PD Data are Consistent With Clinically Observ Dose Response

Pharmacokinetics* (PK)



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

Target Engagement [Pharmacodynar



- Target engagement by apitegromab was co
- Low-dose (2 mg/kg) yielded lower level of t engagement and did not achieve full target

*Starting at day 28, measures are predose trough levels.
Data on File. Scholar Rock, Inc. Cambridge, MA.

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Significance of the Revised Upper Limb Module (RULM)
Evaluates Motor Performance in Upper Limbs

Examples of RULM items

Able to bring token to cup placed vertically at shoulder height

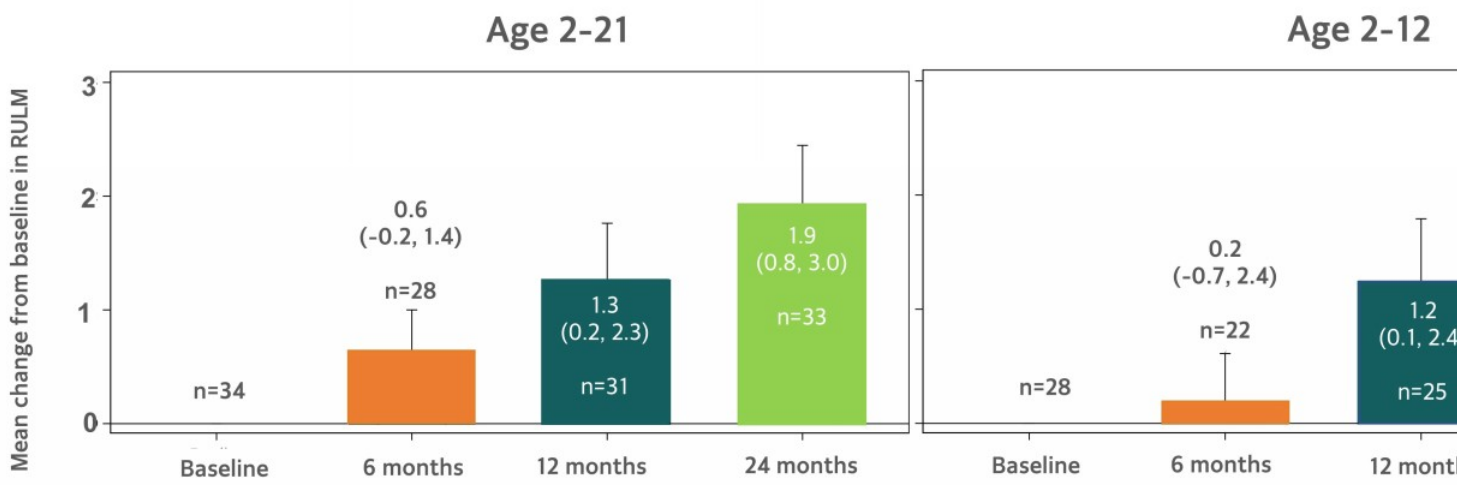
Brings weight at eye level using two hands

- Evaluated upper limb tasks correspond to ab everyday activities
- Except for 1 activity with a binary score, the scored 0 to 2: 0 denotes unable; 1 denotes a modification; and 2 denotes able with no diff
- Maximum score of 37 points (19 task items)
- Examples of items:
  - Putting a coin into a cup
  - Elevating a cup to mouth
  - Picking up a coin
  - Bringing hand to shoulder
  - Lifting up weighted objects
  - Opening a zip lock bag
  - Drawing a line on paper

Mazzone et al. 2017; Pierzchlewicz et al. 2021;
Revised Upper Limb Module for SMA Manual, 2014

Sc

Continued Increase in RULM Observed at 24 Months of Apitegroma
Pooled Non-Ambulatory Patients



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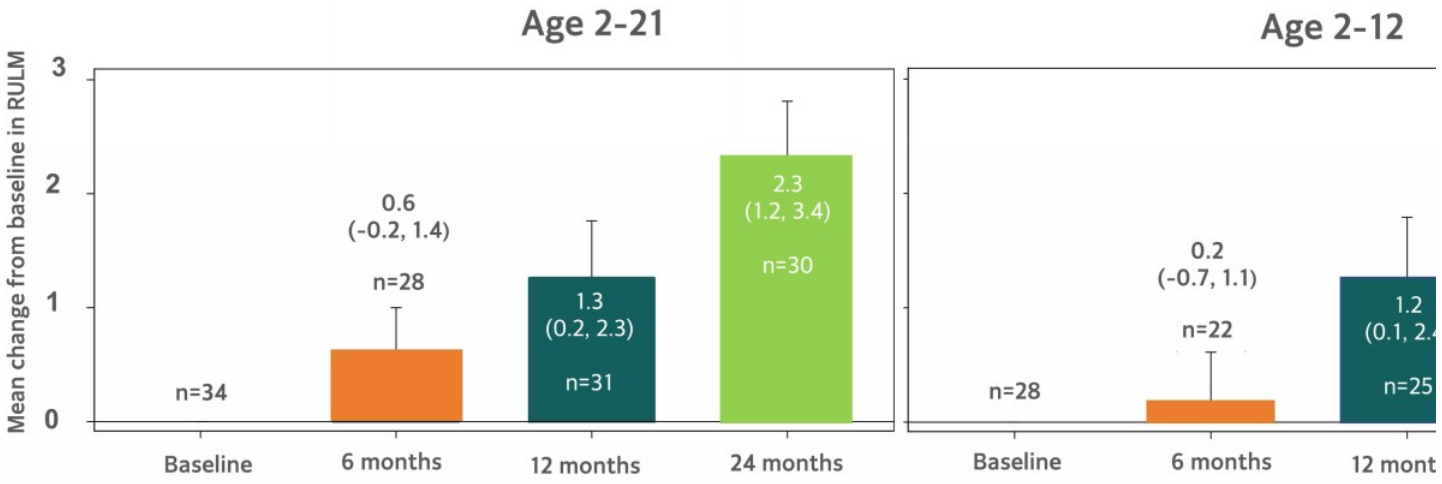
Data on File. Scholar Rock, Inc. Cambridge, MA.

Continued Increase in RULM Observed at 24 Months of Apitegromab

Pooled Non-Ambulatory Patients Excluding Data Post Scoliosis Surgery



This analysis excludes data from 3 non-ambulatory patients after their scoliosis surgery during TOPAZ from the Observed Case Analysis. Error bars represent SEM. Values in parentheticals represent 95% confidence interval.

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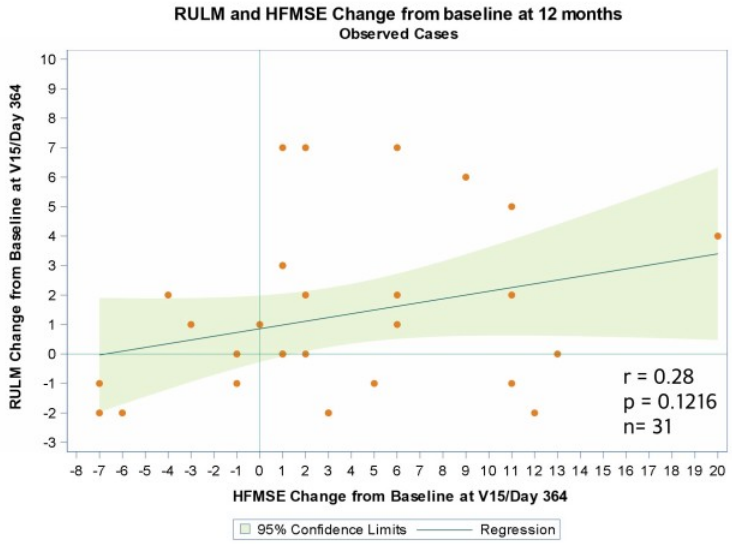
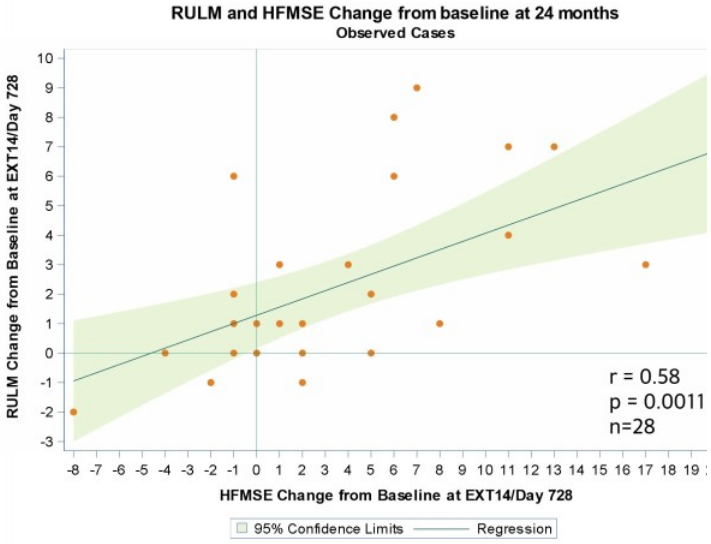
Data on File. Scholar Rock, Inc. Cambridge, MA.

Correlation of HFMSE to RULM Increased Over 24 Months
Pooled Non-Ambulatory Patients

"The observation that the majority of patients in this analysis experienced gains in both the HFMS and RULM over 24 months further supports the therapeutic potential of apitegromab."

-Basil Darras, MD *Associate Neurologist-in-Chief, Boston Children's Hospital; Professor of Neurology, Harvard Medical School; TOPAZ trial Investigator*





This analysis is based on the Observed Case Analysis population. The 12-month graph displays all patients who had a valid measurement at visit 15 (Day 364) and the 24-month graph displays all patients who had a valid measurement at extension visit 14 (Day 728).

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Therapeutic Potential of Apitegromab Observed in the Ambulator SMA Cohort at 24 Months

	Ambulatory Patients (Revised Hammersmith Scale; RHS)		
24 Month Analysis	Cohort 1		
	20 mg/kg pooled (n=21)	20 mg/kg monotherapy (n=11)	20 mg/kg + nusinersen (n=10)
Mean change from baseline (95% CI)	-1.8 (-4.7, 1.1)	-2.8 (-8.4, 2.8)	-0.7 (-3.1, 1.7)
# (%) pts achieving ≥1-pt increase	9/21 (42.9%)	5/11 (45.5%)	4/10 (40%)
# (%) pts achieving ≥3-pt increase	5/21 (23.8%)	3/11 (27.3%)	2/10 (20%)

Observed Case Analysis includes all patients who had a valid measurement at E14 (Day 728). Inclusive of data from 3 patients in apitegromab monotherapy who lost ability to ambulate.

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No Serious Safety Risks Identified Over 24 Months of Apitegroma Treatment

Treatment-Emergent Adverse Events (TEAEs)*	2 mg/kg dose (N=10) n (%)	20 mg/kg dose (N=48) n (%)	T (N n
Any TEAE	10 (100)	45 (93.8)	55
Any Serious TEAE	3 (30)	11 (22.9)	14
Any TEAE leading to study drug discontinuation	0 (0.0)	1 (2.1)	1
Any Grade 3 (severe) or higher TEAE	2 (20)	9 (18.8)	1

- **The incidence and types of treatment-emergent AEs were consistent with the underlying disease or nusinersen therapy**
- **The 5 most common treatment-emergent AEs were headache, pyrexia, upper respiratory tract infection, cough, and nasopharyngit**
- **No deaths or suspected unexpected serious adverse reactions (SUSARs) reported**
- **Adverse events continue to be reported as mostly mild to moderate in severity, as observed in the 12-month analysis**
- **No serious safety risks identified to date**

*Notes: % = 100 x n/N (n=incidence)
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 collected for safety events over the 24-month period and includes patients who switched from 2 mg/kg to 20 mg/kg. Data on file, extracted on April 7, 2022. Scholar Rock, Inc. Cambridge, MA

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- **Stability of Revised Hammersmith Scale (RHS) in patients receiving 20 mg/kg of apitegro nusinersen**
- **Potential motor function gains in subgroups**

❖ No serious safety risks identified to date

- **Five most common treatment-emergent adverse events (TEAEs) were headache, pyrexia respiratory tract infection, cough, and nasopharyngitis**
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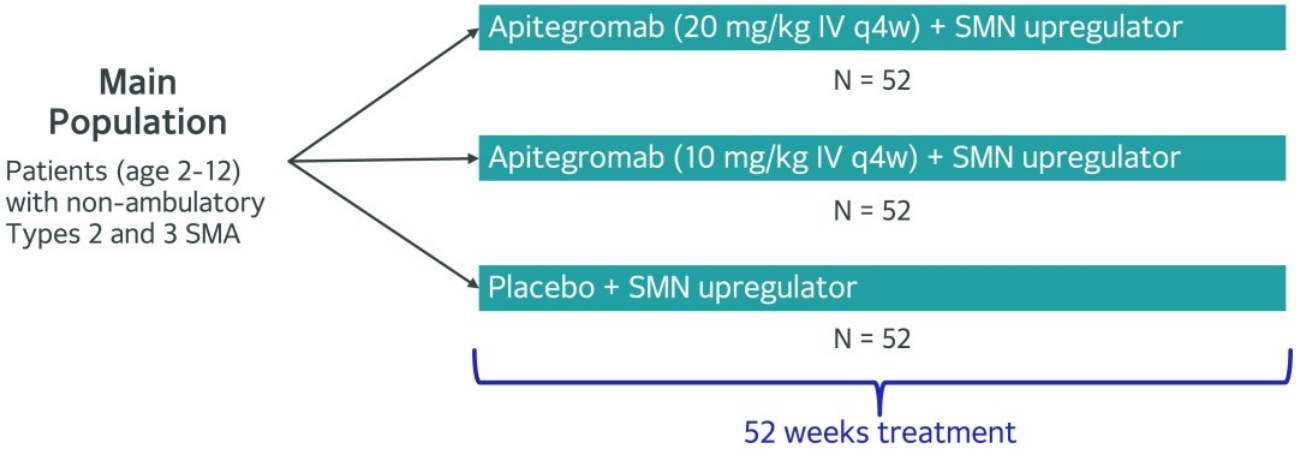
Ongoing SAPPHIRE Phase 3 Trial Overview



- Randomized, double-blind, placebo-controlled, parallel arm design
- Enrolling patients on SMN therapy (nusinersen or risdiplam)
- Primary efficacy endpoint: mean HFMSE change from baseline at 12 months
- Study start-up activities commenced

SAPPHIRE Details

Main population

- Age 2-12, non-ambulatory Type 2 and Type 3 SMA
- Maintenance phase of SMN therapy (nusinersen ≥10 months; risdiplam ≥ 6 mont
- Stratified randomization to ensure balanced allocation: 1) age at SMN Rx initiatic vs age ≥ 5) 2) SMN Rx (nusinersen vs. risdiplam)

Endpoints

- Primary efficacy: HFMSE
- Additional efficacy measures: RULM, WHO, other outcome measures
- Safety, PK/PD, ADA

Analysis

- Topline readout based of main efficacy population (age 2-12) is apitegromab 20 placebo
- Interim analysis opportunity when ≥ 50% of patients in main efficacy population completed 12 months

Additional Data Opportunities

- Exploratory population (age 13-21), in patients using SMN therapy; focused upor exploratory efficacy (n=48; 2:1 randomization between apitegromab 20 mg/kg v
- Separate open-label extension study (after patients complete 12-month period) upon safety & exploratory long-term efficacy

*To control type I error caused by multiple comparisons, the efficacy analysis will first compare the apitegromab 20 mg/kg arm against placebo before any testing of apitegromab 10 mg/kg against placebo.
PK/PD=pharmacokinetics and pharmacodynamics; ADA=anti-drug antibodies

Focused Pipeline of Novel Product Candidates

Potential to transform the lives of patients suffering from a wide range of serious diseases, including neuromu disorders, cancer, and fibrosis

APITEGROMAB

A selective inhibitor of myostatin activation being developed as the potential first muscle-directed therapy for the treatment of spinal muscular atrophy (SMA) in multiple clinical trials

- Phase 2 TOPAZ study (extension portion ongoing)
- Phase 3 SAPPHIRE trial

SAPPH

Phase 3 Piv

SRK-181

A selective inhibitor of latent TGFβ1 activation being developed with the aim of overcoming primary resistance to and increasing the number of patients who may benefit from checkpoint inhibitor therapy

- Potential to become the next transformative therapy for cancer patients
- Phase 1 DRAGON (Part B ongoing)

DRAG

Phase 1 Proof Tri

Discovery-stage pipeline focused on the selective modulation of growth factor signaling

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Key Investment Highlights

Proprietary Platform

- **Designed to discover and develop** monoclonal antibodies that can modulate growth factors with extraordinary selectivity
- **Designed to overcome the challenges** that have plagued traditional approaches by targeting the precursor or latent forms of growth factors

Robust Pipeline

- **Apitegromab (Phase 3)**: potentially transformative therapy to improve motor function for patients with SMA
- **SRK-181 (Phase 1)**: potential to shift the treatment landscape for cancer patients with CPI resistance
- **Discovery-stage pipeline**: focus on myostatin and TGFβ

SAPPHIRE

Phase 3 Pivotal Trial

Phas

Financing Announc

-Fully Funds Sapphire, P
Trial, Continued Advance
Dragon Tria

-Runway Extended

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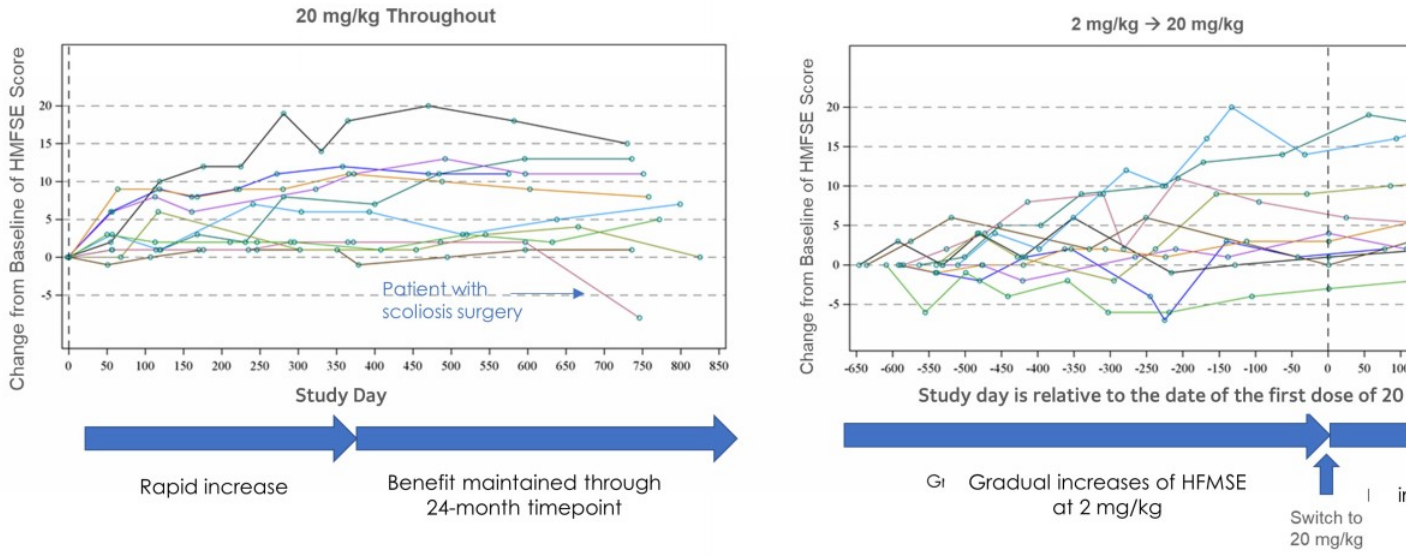
Appendix

Strong Evidence of Dose Response Observed Over 24 Mon
Further Supported by Data from Low Dose to High Dose S

Most patients in Cohort 3 who switched from 2 mg/kg to 20 mg/kg continued to show HFMSE improvement



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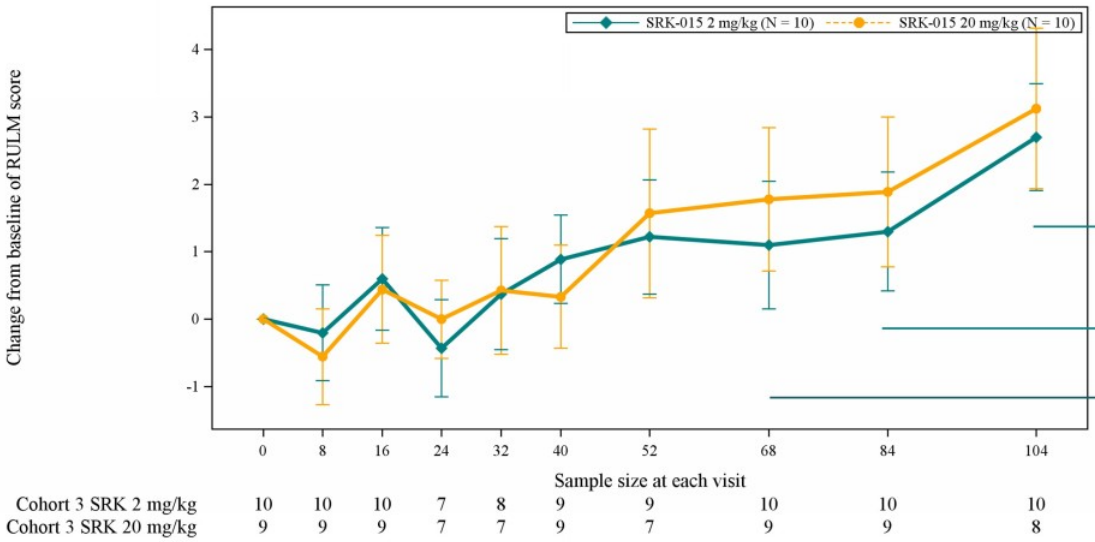
Cohort 3: Mean RULM Score Change Over Time

RULM trended up in low dose arm patients after switch to high dose

Mean Change from Baseline in RULM Scores Over Time (Cohort 3)

Excludes data after scoliosis surgery



Cohort 3 SRK 2 mg/kg	10	10	10	7	8	9	9	10	10	10
Cohort 3 SRK 20 mg/kg	9	9	9	7	7	9	7	9	9	8

A
sw
20

9 of 10
switche
20 mg/k

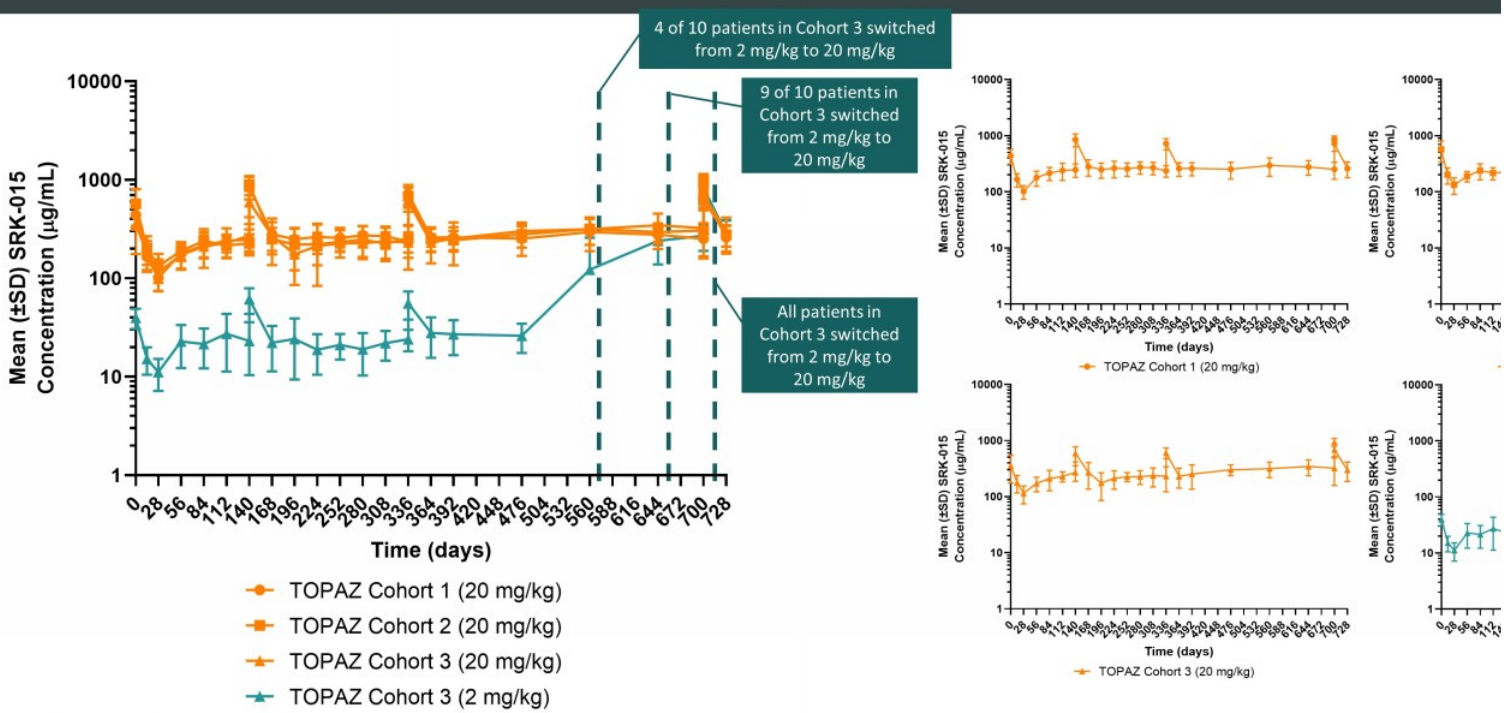
1 of 9 p
switche
20 mg/k

Observed Case Analysis is based upon data available for a given timepoint, and this analysis population includes patients treated with the lower dose 2 mg/kg and does not exclude any patients who missed apitegromab doses due to COVID-19 site access restrictions. Error bars represent standard error of the mean (SEM). Error bars represent SEM.

Apitegromab is an investigational drug candidate being evaluated for the treatment of spinal muscular atrophy. Apitegromab has not been approved for any use by the FDA or any other regulatory agency and its safety and efficacy have not been established.

Sc

PK Data Consistent With Clinically Observed Dose Response



Cohort 3 2 mg/kg Timing Patient Conversion Timeline to 20 mg/kg:

- Day 560: 105-304, 110-301, 110-302, and 114-301
- Day 644: 105-301, 107-302, 118-301, 302-301, and 501-301
- Day 700: 103-301

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TOPAZ Extension Period: 24-Month Patient Dispositic

	Cohort 1 Ambulatory	Non-Ambulatory		
		Cohort 2	Cohort 3	
# Non-Ambulatory Patients (2-21)		15	20	
# Non-Ambulatory Patients (2-12)		9	20	
Dropped Out (0-12 M)	1	0	0	
Dropped Out (12-24 M)	1	1		
Not Having Valid HFMSE testing at Month 24	Not applicable	5*	1**	
Not Having RULM at Month 24	Not applicable	2***	1****	
# of patients scoliosis surgery	1	2*****	1	

**Includes 1 patient who withdrew from study; 1 patient off schedule due to scheduled surgery; 1 patient who had hip pain; 1 patient with femur refused to be in supine position.*

***Patient with bilateral lower extremity cast*

****Includes 1 patient withdrew from study, and 1 patient off schedule due to planned surgery.*

*****Patient was too young for RULM at baseline and RULM was not conducted at following visit.*

******Patients did not have valid HFMSE test at 24 months.*

Overall Safety and Tolerability Profile Over 24 Month Treatment: Serious TEAEs

- Fourteen patients experienced a serious TEAE, all assessed by the respective trial investigator as unrelated to apitegromab:
    - One patient treated with 2 mg/kg dose (Cohort 3) was hospitalized due to adenoidal hypertrophy and tonsillar hypertrophy to perform scheduled adenotonsillectomy (Grade 2). Events resolved without sequelae.
    - Two patients treated with 20 mg/kg dose (both Cohort 1) presented with gait inability considered a significant disability (both Grade 3). Events remain ongoing.
    - One patient treated with 20 mg/kg dose (Cohort 1) was hospitalized with post lumbar puncture syndrome (Grade 2). Event resolved without sequelae.
    - One patient treated with 20 mg/kg dose (Cohort 1) was hospitalized due to viral upper respiratory tract infection (Grade 2). Event resolved without sequelae.
    - Five patients treated with 20 mg/kg dose (one from Cohort 1, three from Cohort 2, and one from Cohort 3) were hospitalized for spinal fusion surgery/ scoliosis/ scoliosis surgery (all Grade 3). All events resolved without sequelae.
    - One patient treated with 20 mg/kg dose (Cohort 1) was hospitalized due to bilateral developmental hip dysplasia and left hip dislocation (both Grade 3). Events resolved without sequelae.
    - One patient treated with 2 mg/kg dose (Cohort 3) was hospitalized due to hip dislocation (Grade 3). Event resolved with sequelae (anxiety and post-operative pain).
    - One patient treated with 20 mg/kg dose (Cohort 3) was hospitalized due to respiratory syncytial virus infection (Grade 2). Events resolved without sequelae.
    - One patient treated with 2 mg/kg dose (Cohort 3) was hospitalized due to vomiting and pneumonia (Grade 3). Events resolved without sequelae.

Overall Safety and Tolerability Profile Over 24 Month Treatment: Non-Serious Grade 3 Events

- Four patients presented with non-serious Grade 3 events, all assessed by the respective trial investigator as unrelated to apitegromab:
    - One patient treated with 20 mg/kg dose (Cohort 1) presented with post lumbar puncture syndrome. Event resolved without sequelae.
    - One patient treated with 20 mg/kg dose (Cohort 2) presented with worsening of scoliosis. Event resolved (with surgery, reported as serious, above) without sequelae.
    - One patient treated with 20 mg/kg dose (Cohort 2) presented with osteopenia. Events remains ongoi
    - One patient treated with 2 mg/kg (Cohort 3) presented with two instances of hypoglycemia and one instance of metabolic acidosis. All events 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.