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): May 26, 2021

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

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

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

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

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

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

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

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	SRRK	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 8.01. Other Events.

The Company from time to time provides business updates to members of the investment community and other parties. A copy of the Company's current corporate slide presentation is being filed herewith as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.1.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Presentation slide deck, furnished hereto.

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: May 26, 2021

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

Deep Insights, Impactful Medicines

May 2021

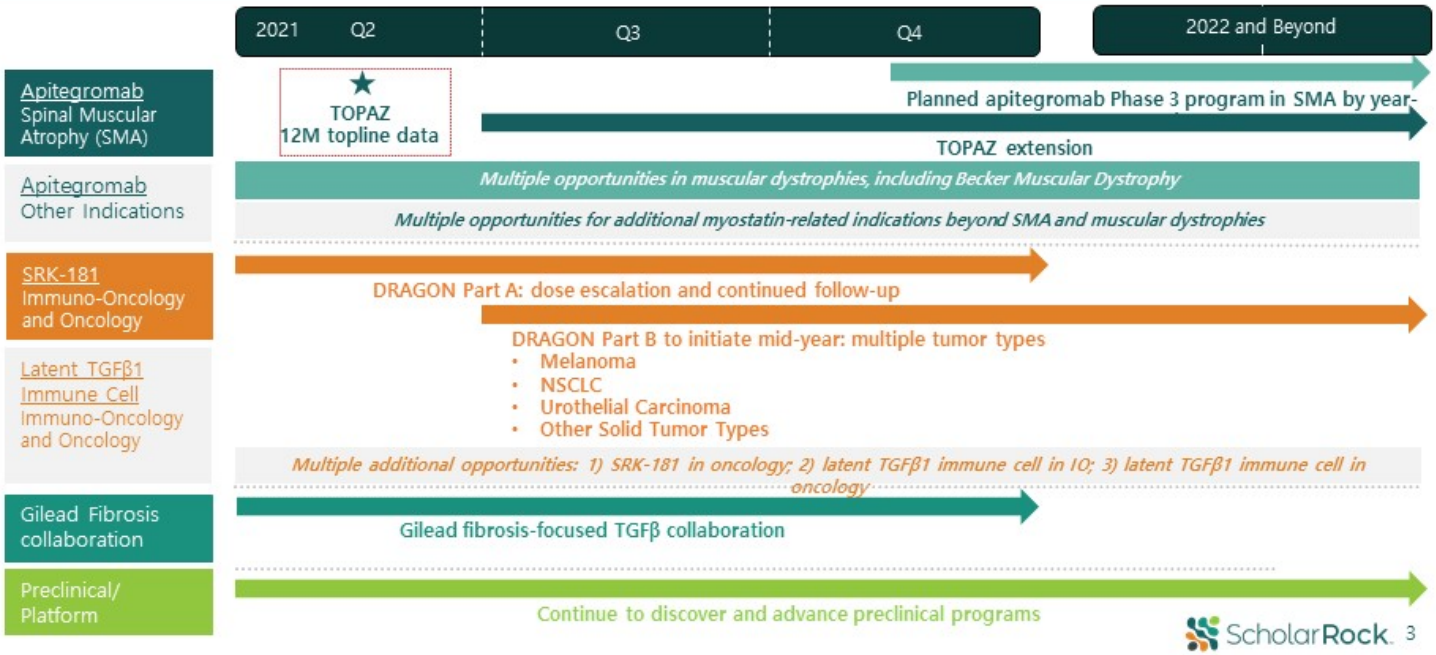
ScholarRock

Disclaimers

Various statements in this presentation concerning the future expectations, plans and prospects of Scholar Rock, Inc. ("Scholar Rock"), including without limitation, Scholar Rock's expectations regarding its strategy, its product candidate selection and development timing, including timing for the initiation of and reporting results from its clinical trials for its product candidates, its disease indication selection and timing for such selection, the ability of apitegromab (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, preclinical and clinical data, including the 12-month top-line results from the Phase 2 trial of apitegromab, are not predictive of, are inconsistent with, or more favorable than, data generated from future clinical trials of the same product candidate, including the planned Phase 3 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, information provided or decisions made by regulatory authorities differ from the company's expectations, competition from third parties that are developing products for similar uses, Scholar Rock's ability to identify and develop multiple product candidates on the expected timeline, the impacts of the COVID-19 pandemic, 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 March 31, 2021, 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.

Scholar Rock

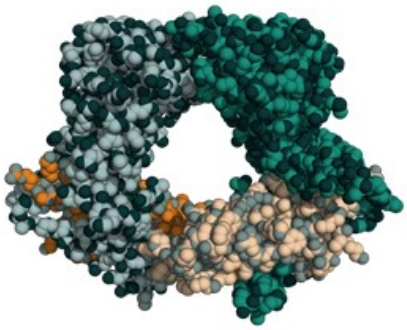
2021: Potential for Another Transformative Year



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

Scholar Rock's Target

Growth Factor Precursor (Latent Form)



Scholar Rock's R&D Platform

Transform Medical Practice

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

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

Apitegromab: Transformative Potential Demonstrated in TOPAZ Phase 2 Trial for Patients with Type 2 and 3 SMA

TOPAZ

ScholarRock.

Apitegromab Positioned to be Next Potential Transformative Therapy for Patients Suffering with SMA

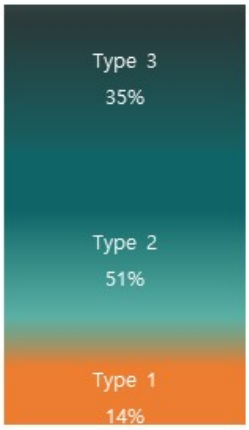
- ✓ Spinal Muscular Atrophy (SMA) remains a devastating and debilitating illness despite the availability of SMN upregulators
  - To improve motor function, a muscle-directed approach like apitegromab is needed to complement the disease stabilizing effects of SMN upregulators
- ✓ Apitegromab demonstrated transformative potential in SMA through the TOPAZ Phase 2 trial, especially in non-ambulatory Type 2 and 3 patients
  - **Patients 2-6 years of age**: +7.1-point increase in HFMSE and 63% attained a ≥3-point increase with 20 mg/kg dose
  - **Patients 8-19 years of age**: +1.2-point* increase in HFMSE and 31% attained a ≥3-point increase
  - Non-ambulatory Type 2 and 3 patients represent ~2/3 of overall population
- ✓ TOPAZ results offer exciting path forward for investigating apitegromab in a rational, targeted, and efficient Phase 3 trial in non-ambulatory Type 2 and 3 patients

**Per-protocol: excludes patient with concomitant exposure to an acetylcholinesterase inhibitor not permitted per the TOPAZ protocol*

Spinal Muscular Atrophy Overview

Global disease with 30,000-35,000 affected in U.S. and Europe alone

- Significant, progressive motor function impairment, many lose ambulation
- Severe, progressive disabilities and Unable to walk independently
- Infantile onset; unable to sit up independently



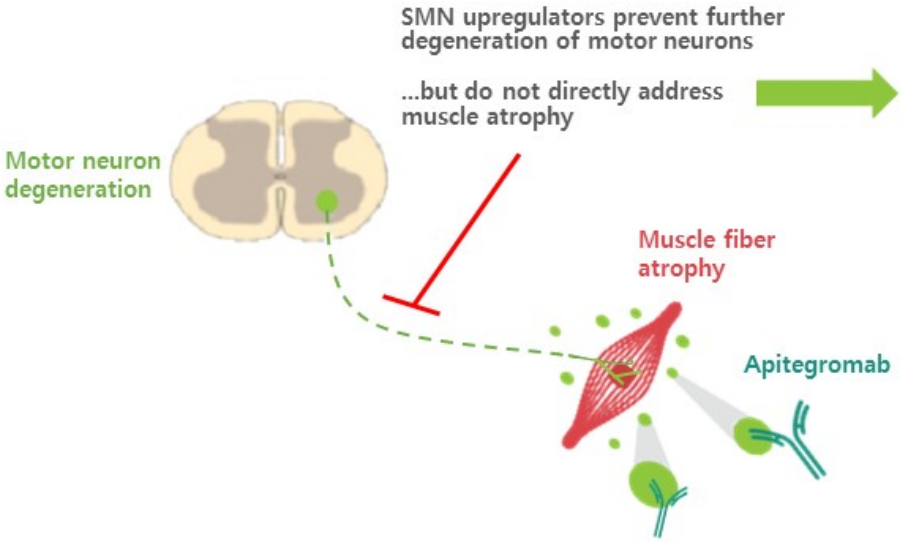
TOPAZ* 12-month results demonstrated transformative efficacy in non-ambulatory Type 2 and 3 patients

Represents ~2/3 of overall patient population

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

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

Apitegromab: Muscle-Directed Therapy Aimed at Complementing SMN Upregulators



Apitegromab is a muscle-directed approach aimed at improving motor function

- Myostatin is a negative regulator of skeletal muscle growth
- Apitegromab is a fully human, mAb that specifically binds to proforms of myostatin and inhibits myostatin activation

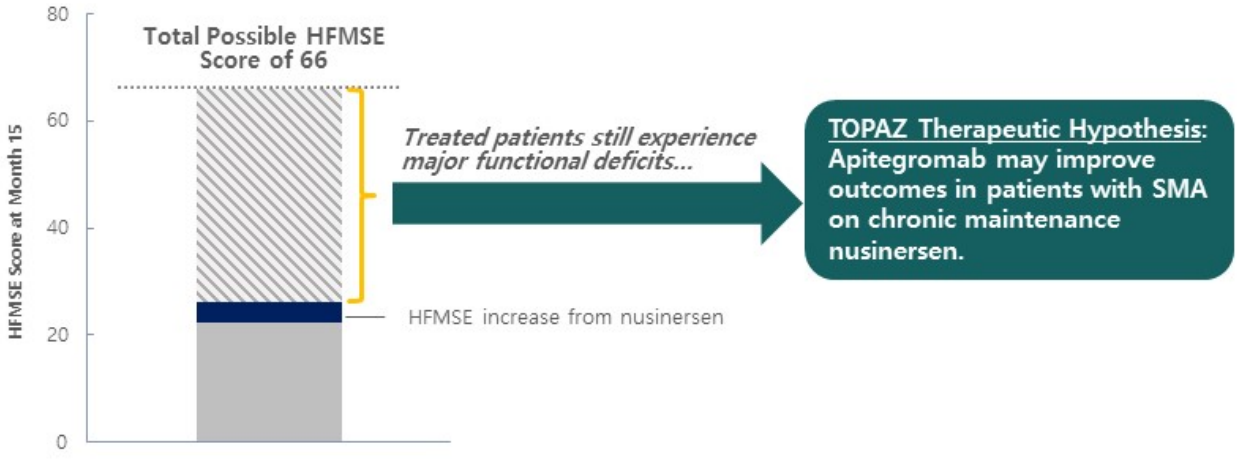
Adapted from images courtesy of the SMA Foundation

Stage is Set for New Treatment Era: *Muscle-Directed Therapy + SMN Upregulators*

	SPINRAZA (nusinersen) injection 12 mg/5 mL	Evrysdi risdiplam	zolgensma (onasemnogene abeparvovec-xioi) suspension for intravenous infusion
Phase 3 Trial Design	• Non-ambulatory Type 2/3 • 2-12 years of age • **Primary endpoint:** Mean change from baseline in HFMSE at 15 months	• Non-ambulatory Type 2/3 • 2-25 years of age • **Primary endpoint:** Mean change from baseline in MFM-32 at 12 months	• Infantile-onset Type 1 • <6 months of age • **Primary endpoints:** Ability to sit independently and event-free survival
Indication	• Type 1, 2, and 3 SMA in pediatric and adult patients	• Type 1, 2, 3 SMA in patients 2 months of age and older	• Approved for SMA less than 2 years of age
Market Penetration	• >11,000* patients treated WW • $2+ billion in revenues (LTM)	• ~3,000** patients treated WW • ~CHF135 million in revenues (LTM)	• ~1,200*** patients treated WW • ~$1.1 billion in revenues (LTM)
Persistent Need	• Major functional deficits remain • HFMSE improvements only in younger patients and rapidly plateaus	• Major functional deficits remain • Increases in MFM-32 primarily limited to youngest patients • HFMSE effects not as pronounced	• Limited data and eligibility for use beyond very young patients

*As of 1Q21 financial update on 4/22/21; includes patients treated worldwide in post-marketing setting, expanded access program, and clinical trials.
**As of 1Q21 financial update on 4/21/21; includes patients treated worldwide between clinical trials, commercial, and compassionate use

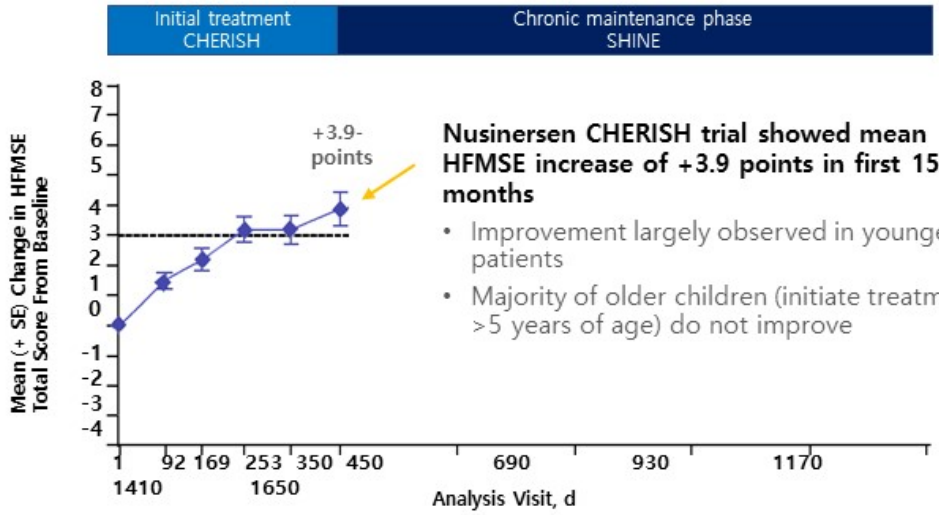
Patients Continue to Experience Major Functional Deficits Despite Availability of Multiple SMN Upregulator Therapies



Mean improvement in HFMSE score experienced by patients with non-ambulatory Type 2/3 SMA in the Phase 3 CHERISH clinical trial of nusinersen

Source: 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.

Non-Ambulatory Type 2/3 SMA: Nusinersen Offers HFMSE Increases Primarily in First Year of Treatment



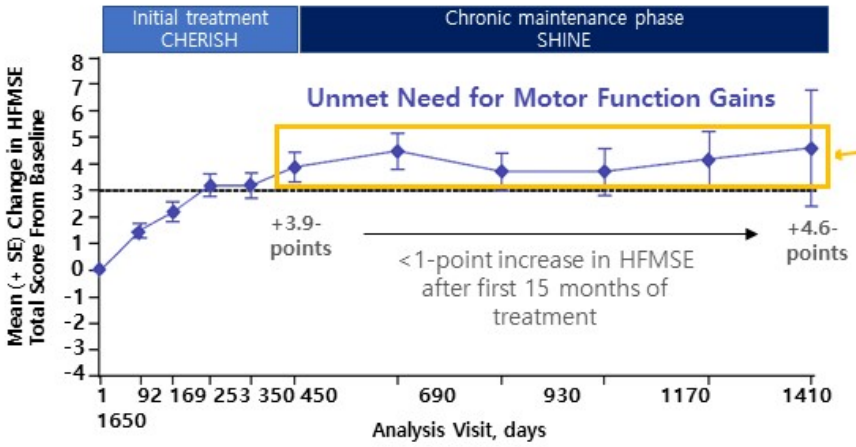
Nusinersen CHERISH trial showed mean HFMSE increase of +3.9 points in first 15 months

- Improvement largely observed in younger patients
- Majority of older children (initiate treatment >5 years of age) do not improve

Most nusinersen-treated patients in CHERISH were <5 years at therapy initiation

"Longer-term treatment with nusinersen: results in later-onset spinal muscular atrophy from the SHINE study" P.257, World Muscle Society Congress 202
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.

Plateauing of Nusinersen Effect Observed Post Initial 15 Months of Treatment in Non-Ambulatory Type 2/3 SMA



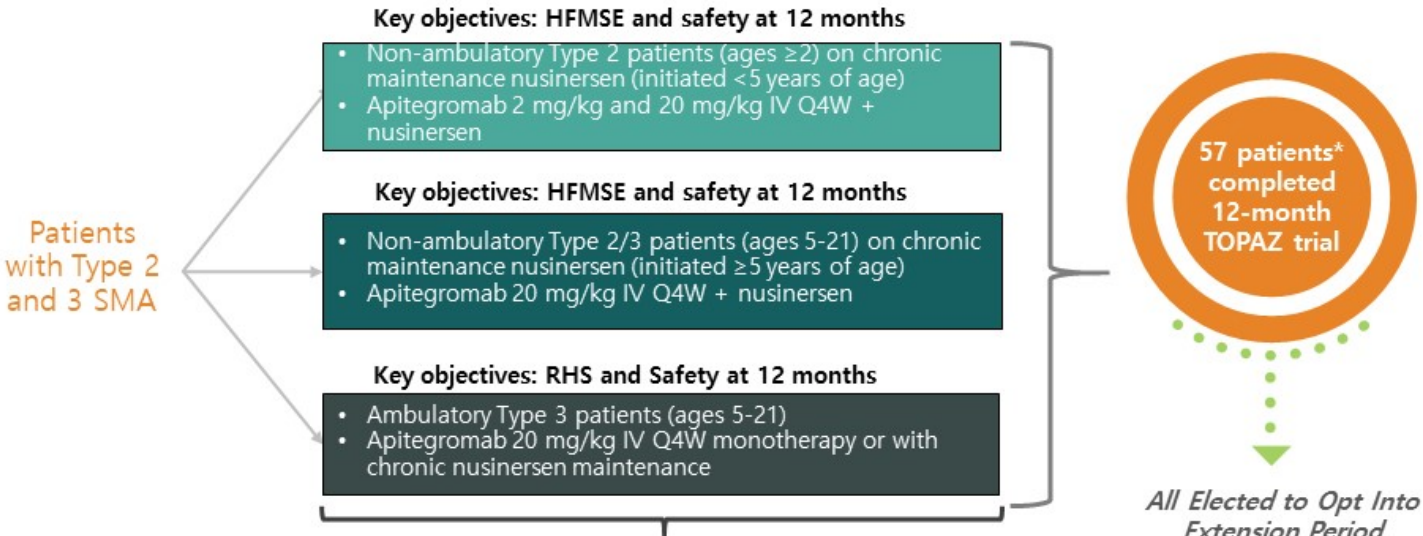
Most nusinersen-treated patients in CHERISH were <5 years at therapy initiation

Nusinersen observed plateauing of improvement during chronic maintenance phase...

"Longer-term treatment with nusinersen: results in later-onset spinal muscular atrophy from the SHINE study" P.257, World Muscle Society Congress 2020
This third-party information is provided for background only and is not intended to convey or imply a comparison to the TOPAZ clinical trial results.

Apitegromab Phase 2 Trial Design

TOPAZ



**Excludes one patient from Cohort 1 that discontinued from the trial*

Baseline Characteristics

Nusinersen-treated patients well into chronic maintenance phase

TOPAZ

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

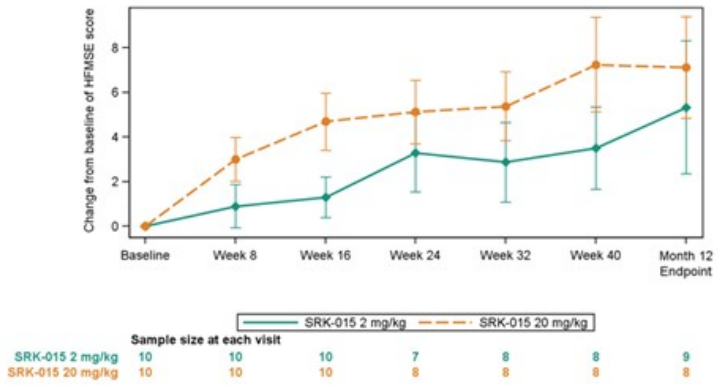
*Data not available for all patients
**Patient who discontinued study for reasons unrelated to study drug
HFMSE=Hammersmith Functional Motor Scale Expanded; RHS=Revised Hammersmith Scale

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

Non-Ambulatory Cohort (Ages 2-6): Sizable HFMSE Increases of Up to 20-points

TOPAZ

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



Sample size at each visit							
SRK-015 2 mg/kg	10	10	10	7	8	8	9
SRK-015 20 mg/kg	10	10	10	8	8	8	8

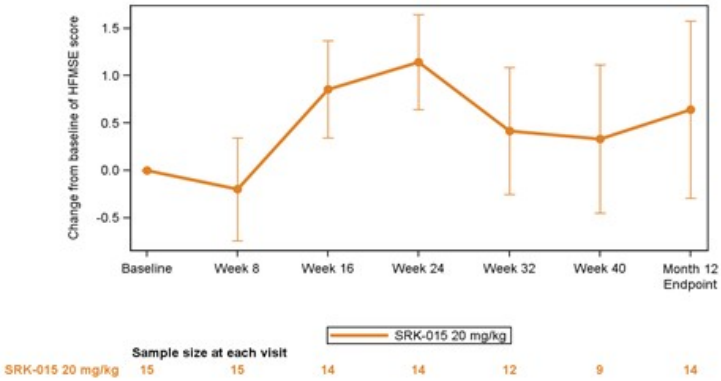
Data on file. Scholar Rock, Inc. Cambridge, MA

- 35% (6/17) with >10-point increase in HFMSE
  - Up to 20-point increases in HFMSE observed
- Sizable, dose-dependent increases in HFMSE observed in patients already on chronic maintenance nusinersen
  - Durable and continuous improvements observed through 12-months
- CHERISH and SHINE nusinersen studies suggest substantial HFMSE increases do not occur in younger patients following first year of treatment

Non-Ambulatory Cohort (Ages 8-19): Majority of Patients Attained Increases in HFMSE

TOPAZ

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



- Majority of patients attained increases in HFMSE
  - ~30% achieved ≥3-point increase in HFMSE
  - Durability of effect observed through 12-months
- Improvements not seen with other therapies in this older patient population
  - Patients already on chronic maintenance nusinersen
- CHERISH data suggest older patients on average observe declines and rarely observe a 3-point increase in HFMSE

Patient had concomitant exposure to an acetylcholinesterase inhibitor, which is not permitted per the TOPAZ trial protocol
Data on file. Scholar Rock, Inc. Cambridge, MA

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

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

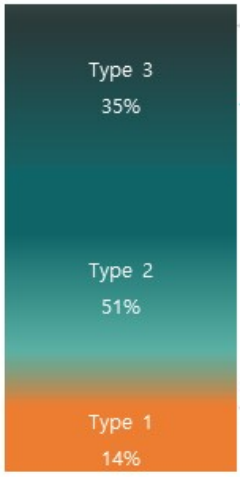
- **Five most frequently reported TEAEs*:** Headache (24%), pyrexia (22%), upper respiratory tract infection (22%), cough (22%), and nasopharyngitis (21%).
- SAEs, Grade 3 AEs and AE leading to early study discontinuation were all assessed by investigators as unrelated to study drug
- **Anti-drug antibodies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

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

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

Initial Regulatory Strategy Focuses on Non-Ambulatory Patients on Background SMN Therapy

Global disease with 30,000-35,000 affected in U.S. and Europe alone



1

Apitegromab in non-ambulatory Type 2 and 3 with background SMN upregulators

- Represents 2/3 of overall patients
- Many patients already treated with or are eligible for SMN upregulator therapy
- Improvements in motor function on top of SMN upregulators observed in TOPAZ

2

Type 1 patients, including those treated with gene therapy

- Highest incidence population and growing prevalence due to SMN upregulator treatment
- TOPAZ showed benefits of early treatment suggesting potential in Type 1 patients

3

Ambulatory patients

- Smaller population but high unmet need as benefits of SMN regulators not well-established
- TOPAZ suggests potential clinical benefit in subset patients

Anticipated Focus of Phase 3 Trial

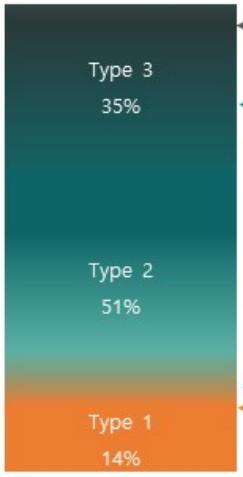
Preliminary Thoughts on Apitegromab Phase 3 Trial Design

Registrational trial design subject to regulator interactions and feedback

Design	• 12-month treatment period • Apitegromab IV Q4W as add-on to nusinersen or risdiplam • TOPAZ data support investigation of 20 mg/kg dose
Subjects	• Non-ambulatory Type 2 and Type 3 SMA • Pediatric population in chronic maintenance phase of SMN therapy
Key Objectives	• HFMSE • Safety
Timeline	• Aim to initiate by end of 2021

Additional Opportunities May Be Pursued With Separate Regulatory Strategies

Global disease with 30,000-35,000 affected in U.S. and Europe alone



3

Ambulatory patients

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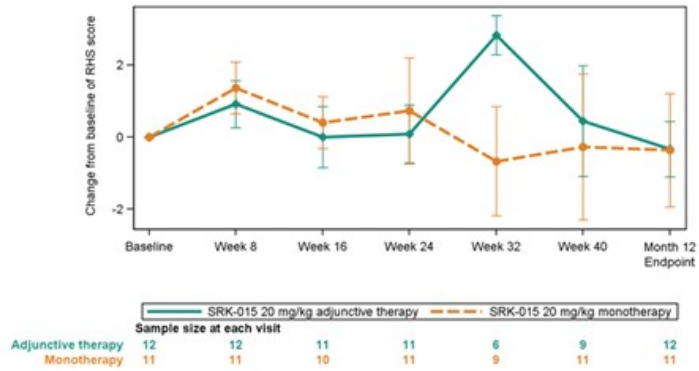
2

Type 1 patients, including those treated with gene therapy

- Highest incidence population and growing prevalence due to SMN upregulator treatment
- TOPAZ showed benefits of early treatment suggesting potential in Type 1 patients

Majority of Ambulatory Patients Maintained or Improved in RHS Score from Baseline

Ambulatory Type 3 SMA (Intent-to-Treat Population)	Apitegromab (20 mg/kg) monotherapy (n=11)	Apitegromab (20 mg/kg) + nusinersen (n=12)	Pooled (n=23)
Mean change from baseline in RHS (95% CI)	-0.4 (-3.9, 3.1)	-0.3 (-2.0, 1.4)	-0.3 (-2.1, 1.4)
# (%) patients achieving ≥0-pt increase in RHS	6/11 (55%)	7/12 (58%)	13/23 (57%)
# (%) patients achieving ≥1-pt increase in RHS	4/11 (36%)	5/12 (42%)	9/23 (39%)
# (%) patients achieving ≥3-pt increase in RHS	3/11 (27%)	2/12 (17%)	5/23 (22%)



- Majority of patients maintained or improved
  - 57% (13/23) with ≥0-point increase in RHS
  - 39% (9/23) with ≥1-point increase in RHS
  - Increases of up to 8-points observed
- Potential signal for therapeutic benefit observed in this population

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

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

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

Plan to present 12-month top-line data and additional analyses at medical congresses in coming months

*Excludes one patient from Cohort 1 that discontinued from the trial

SRK-181: Potential Transformative Backbone for a New Era of Cancer Immunotherapy

DRAGON

Significant Interest in Potential Role of TGFβ Inhibition in Immuno-Oncology

Nature (online), Feb. 14, 2018.

TGFβ attenuates tumour response to PD-L1 blockade by contributing to exclusion of T cells

Sanjeev Mariathasan[1]*, Shannon J. Turley[1]*, Dorothee Nickles[1]*, Alessandra Castiglioni[1], Kobe Yuen[1], Yulei Wang[1], Edward E. Kadel III[1], Hartmut Koeppen[1], Jillian L. Astarita[1], Rafael Cubas[1], Suchit Jhunjhunwala[1], Romain Banchereau[1], Yagai Yang[1], Yinghui Guan[1], Cecile Chalouni[1], James Ziai[1], Yasin Şenbabaoğlu[1], Stephen Santoro[1], Daniel Sheinson[1], Jeffrey Hung[1], Jennifer M. Giltnane[1], Andrew A. Pierce[1], Kathryn Mesh[1], Steve Lianoglou[1], Johannes Riegler[1], Richard A. D. Carano[1], Pontus Eriksson[2], Mattias Höglund[2], Loan Somarriba[3], Daniel L. Halligan[3], Michiel S. van der Heijden[4], Yohann Loriot[5], Jonathan E. Rosenberg[6], Lawrence Fong[7], Ira Mellman[1], Daniel S. Chen[1], Marjorie Green[1], Christina Derleth[1], Gregg D. Fine[1], Priti S. Hegde[1], Richard Bourgon[1] & Thomas Powles[8]

February 2019: *"GSK and Merck KGaA, Darmstadt, Germany announce global alliance to jointly develop and commercialise M7824, a novel immunotherapy with potential in multiple difficult-to-treat cancers"*

- €300 million upfront and up to €3.7 billion total

June 2019: *"Merck to Acquire Tilos Therapeutics: Merck Gains Portfolio of Investigational Antibodies Modulating TGFβ"*

- $773 million total potential deal value

Article

Cell

Genomic and Transcriptomic Features of Response to Anti-PD-1 Therapy in Metastatic Melanoma

Authors

Willy Hugo, Jesse M. Zaretsky, Lu Sun, Douglas B. Johnson, Antoni Ribas, Roger S. Lo

Volume 165, Issue 1, 24 March 2016, Pages 35-44

NATURE REVIEWS | CLINICAL ONCOLOGY

TGFβ biology in cancer progression and immunotherapy

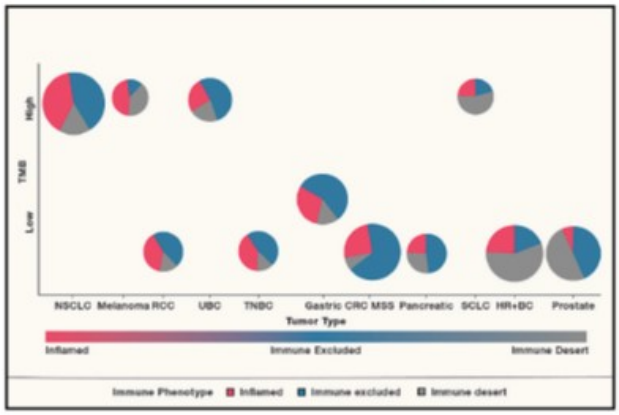
Rik Derynck[1,2,3✉], Shannon J. Turley[4✉] and Rosemary J. Akhurst[2,3✉]

July 24, 2020: https://doi.org/10.1038/ s41571-020-0403-1

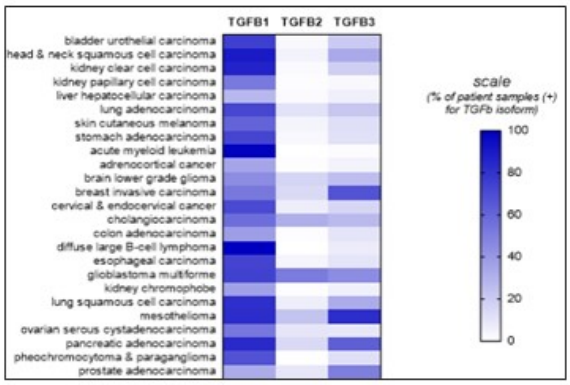
August 2020: *"Bristol Myers Squibb Enters Agreement to Acquire Forbius TGF-beta Program"*

Emerging Evidence Implicates TGFβ1 as Driving Primary Resistance to Checkpoint Inhibitors

Substantial % of solid tumors exhibit immune exclusion



Cancer Genome Atlas RNAseq analysis of >10,000 samples spanning 33 tumor types*

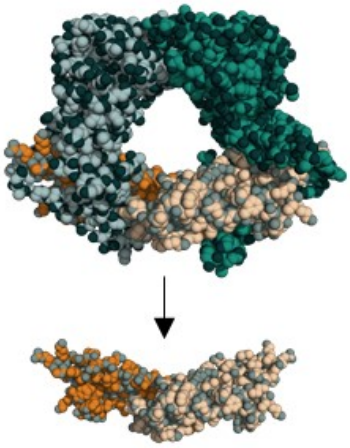


Human Tumor Analyses Reveal TGFβ1 as Most Likely Driver of TGFβ Signaling Pathway in Cancers

[1]Priti H, et al. Top 10 challenges in cancer immunotherapy. *Immunity.* 2020 Jan 14:52(1):17-35. https://doi.org/10.1016/j.immuni.2019.12.011.
*Source: National Cancer Institute - Cancer Genome Atlas Program.

SRK-181: Unique TGFβ1-Selective Approach to Overcoming Checkpoint Inhibitor Resistance

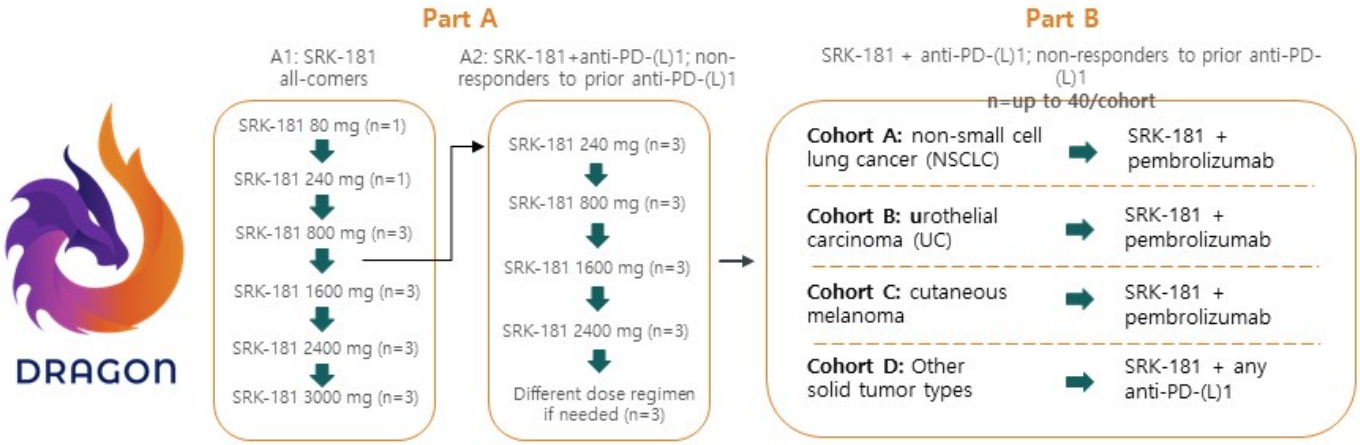
Scholar Rock's Target
SRK-181: Latent TGFβ1 Inhibitor



Traditional target:
"Mature" growth factor

- ✓ **Inhibits TGFβ1 pathway** - implicated in CPI resistance
- ✓ **Highly selective targeting** - avoids inhibiting latent TGFβ2 and TGFβ3 isoforms
- ✓ **Aimed at increasing therapeutic window** – potentially avoids toxicities associated with non-selective TGFβ inhibition
- ✓ **Therapeutic flexibility** - pair with any CPI and optimize dosing of each component of combination therapy

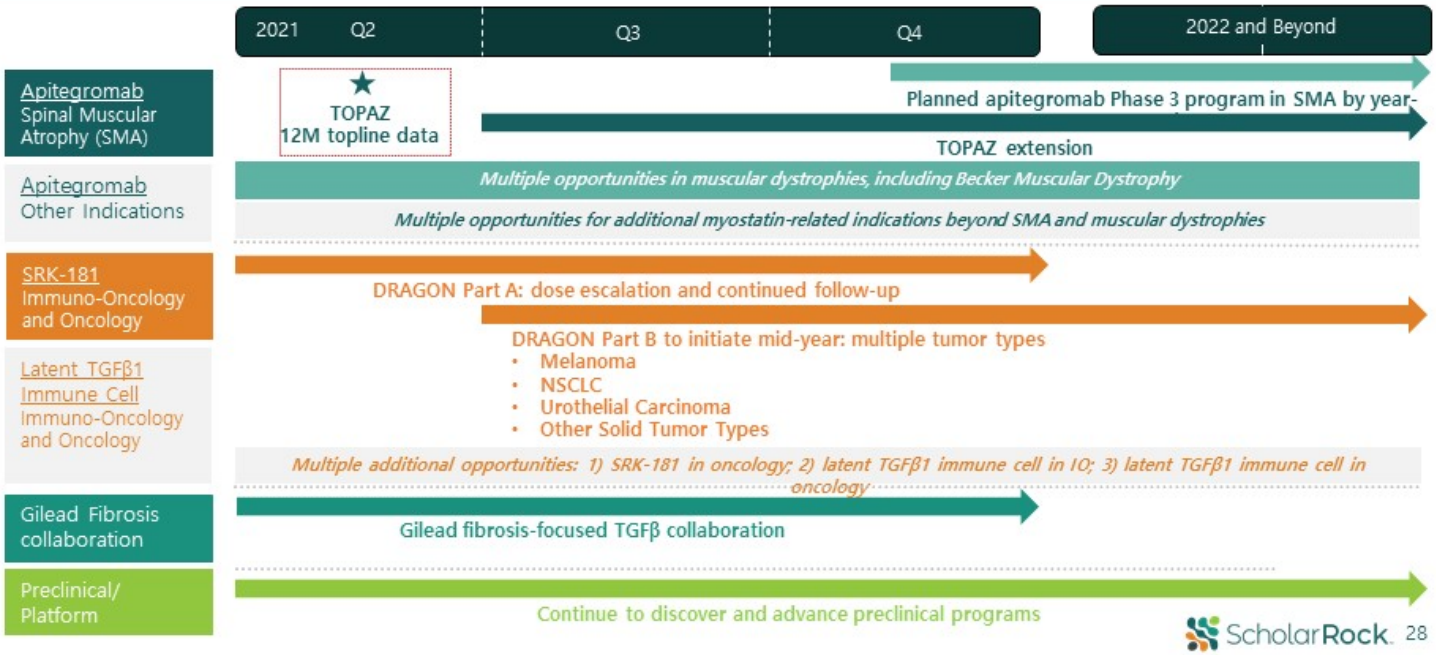
DRAGON Phase 1 POC Trial to Evaluate SRK-181's Ability to Overcome Primary Resistance to Checkpoint Inhibitors



- As of March 9, 2021:
  - Part A1: 3000 mg Q3W dose being evaluated
  - Part A2: 1600 mg Q3W dose being evaluated
- Part B initiation planned mid-year
- Initial clinical response and safety data anticipated by year-end 2021

NCT04291079 on www.clinicaltrials.gov.

2021: Potential for Another Transformative Year



Appendix

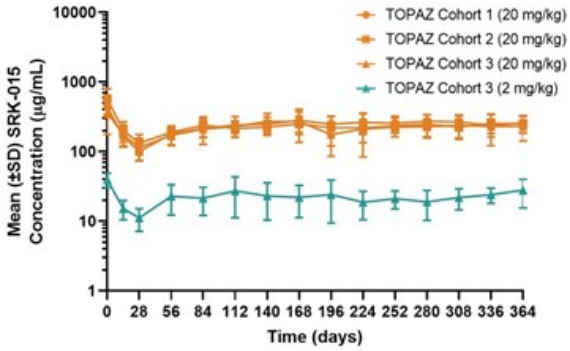
ScholarRock

Apitegromab: Pairing the latent form with important translational insights

Scholar Rock's Guiding Principles for Neuromuscular Indication Selection	Key Characteristics of Spinal Muscular Atrophy (SMA)
Younger population	Genetic disorder with onset in childhood
At least partially intact innervation and no structural muscle abnormalities	Partial neural connectivity and atrophied muscles that largely retain structural integrity
Need for increase in fast-twitch muscle fibers	Substantial deficit in fast-twitch fibers
Clinical trial endpoint driven by fast-twitch fiber function	Fast-twitch fiber function has a prominent role in SMA outcome measures

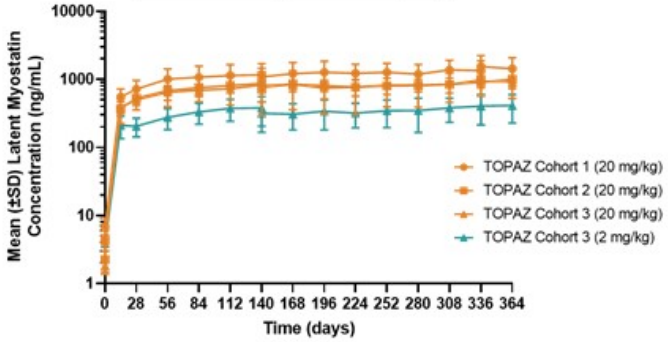
Pharmacokinetic and Pharmacodynamic Data are Supportive of Clinically Observed Effects

Pharmacokinetics* (PK)



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

Pharmacodynamics (PD)



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

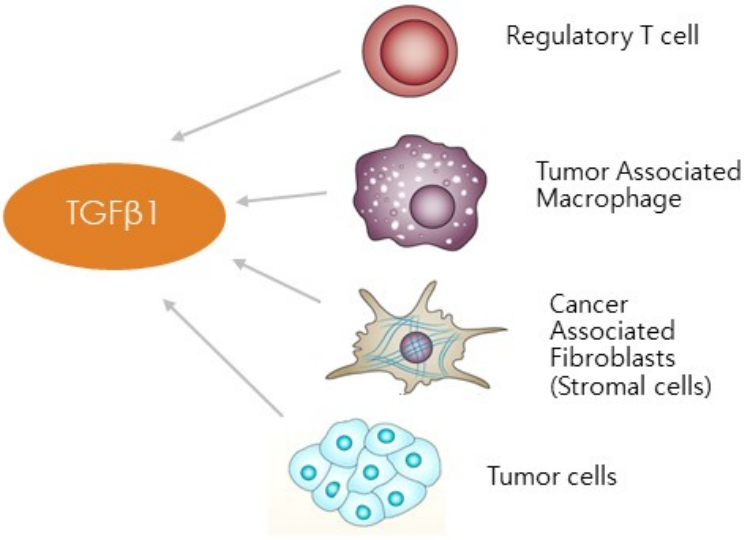
High levels of target engagement achieved by both doses, with relatively higher absolute levels with high dose

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

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

Inhibition of TGFβ1: Multipronged Approach for Immuno-Oncology

TGFβ1 is a key driver of immune system evasion by cancer cells

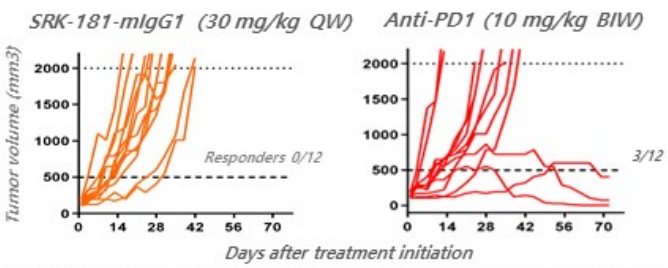


- Pathway analysis in patient tumors points to TGFβ1 as major determinant of primary resistance to anti-PD-(L)1 therapy
- TGFβ1 creates 'immune excluded' tumor microenvironment

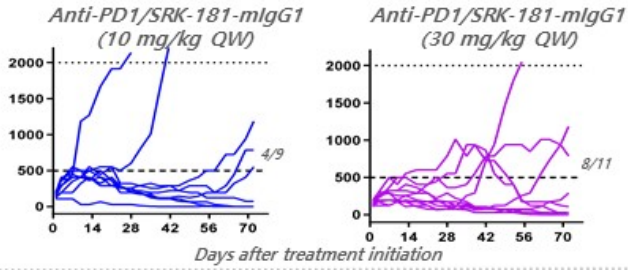
TGFβ1 Blockade with SRK-181-mIgG1 Rendered Preclinical Tumor Models Susceptible to Anti-PD1 Therapy

Melanoma (Cloudman S91) model: Combination treatment led to tumor regression and survival benefit

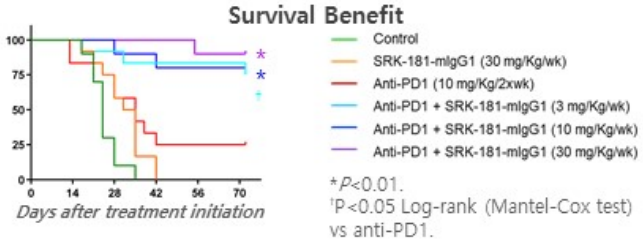
Tumor Regression: Monotherapy



Tumor Regression: Combination Therapy



Survival Benefit

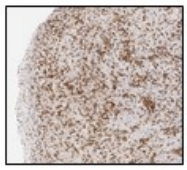


* $P<0.01$.
† $P<0.05$ Log-rank (Mantel-Cox test) vs anti-PD1.

Overcoming immune exclusion

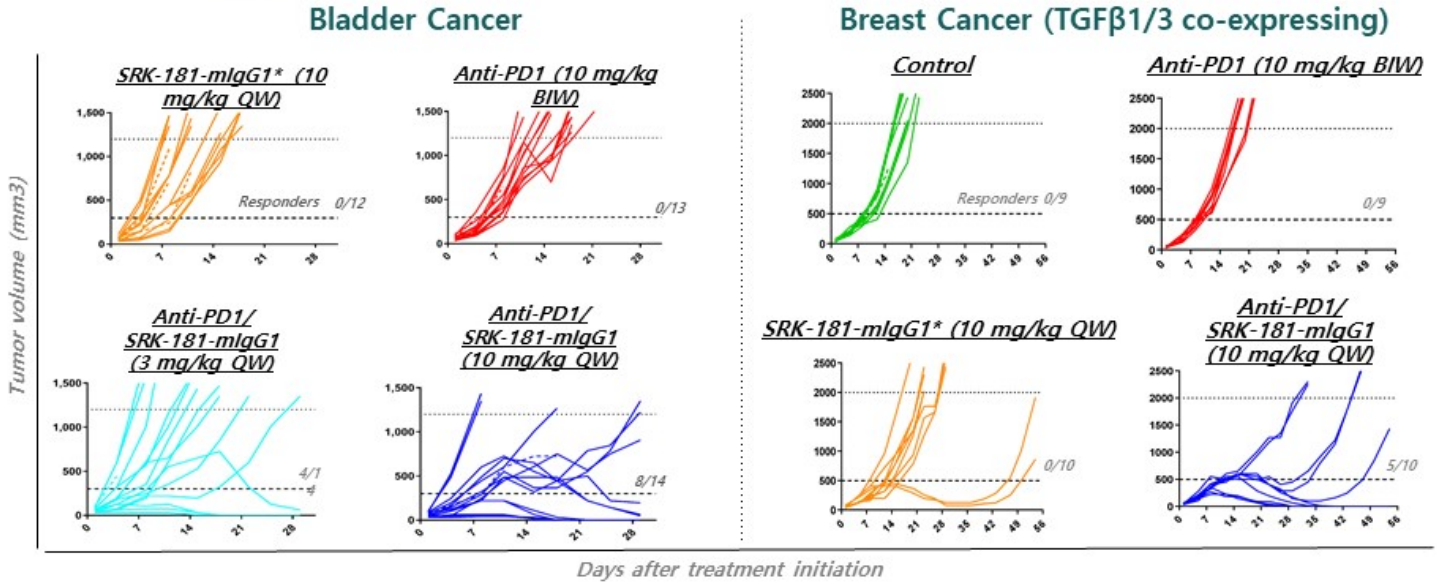
Anti-PD1

Anti-PD1/ SRK-181-mIgG1 led to influx of CD8+ cells in preclinical bladder tumor model



Preclinical data published in *Science Translational Medicine*. Martin CJ, et al. *Sci Transl Med.* 2020 Mar 25;12(536):eaay8456. https://scholarrock.com/platform/publications.

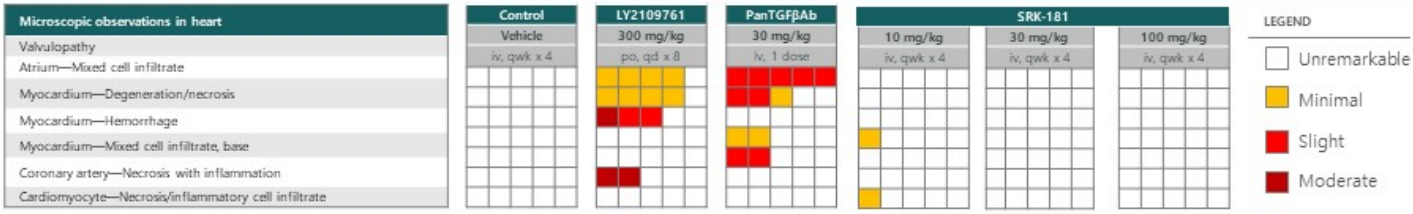
TGFβ1 Blockade with SRK-181-mIgG1 Rendered Preclinical Tumor Models Susceptible to Anti-PD1 Therapy



Preclinical data published in *Science Translational Medicine*. Martin CJ, et al. *Sci Transl Med*. 2020 Mar 25;12(536):eaay8456. https://scholarrock.com/platform/publications/.

**SRK-181-mIgG1 is the murine version of SRK-181; responder defined as tumor size <25% endpoint volume at study end.*

TGFβ1 Isoform Specificity of SRK-181 Improved Preclinical Toxicity Profile



Repeat dose pilot toxicology study in adult female Sprague Dawley rats:

- Cardiac findings were exhibited in animals dosed with a pan-TGFβ antibody or LY2109761 (inhibitor of ALK5, common TGFβ receptor kinase) as expected based on published data†
- No cardiotoxicities (valvulopathy) were noted with SRK-181
  - NOAEL for SRK-181 was the highest dose evaluated of 100 mg/kg QW

4-week GLP toxicology studies:

- Rats: NOAEL for SRK-181 was up to highest evaluated dose of 200 mg/kg QW
- Non-human primates: NOAEL for SRK-181 was up to highest evaluated dose of 300 mg/kg QW

Selectivity of SRK-181 offers potential to overcome toxicity and dose-limiting challenges of non-selective TGFβ pathway approaches

Preclinical data published in *Science Translational Medicine*. Martin CJ, et al. *Sci Transl Med* 2020 Mar 25;12(536): eaay8456.
*Source: Anderton MJ, et al. Induction of heart valve lesions by small-molecule ALK5 inhibitors. *Toxicol Pathol* 2011;39: 916-924.; and Stauber AJ, et al. Nonclinical safety evaluation of a transforming growth factor β Receptor I kinase inhibitor in Fischer 344 rats and beagle dogs. *J Clin Pract* 2014: 4:3.