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): November 30, 2021

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

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

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

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

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

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

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

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

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

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

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

Item 7.01. Regulation FD Disclosure.

On November 30, 2021, Scholar Rock Holding Corporation (the "Company") issued a press release announcing the design of its Phase 3 SAPPHIRE clinical trial evaluating apitegromab in non-ambulatory patients with Type 2 and Type 3 Spinal Muscular Atrophy (SMA). A copy of the press release is being furnished as Exhibit 99.1 to this Report on Form 8-K.

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, as amended (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, 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.

Item 8.01. Other Events.

The Company will participate in the 33rd Annual Piper Sandler Virtual Healthcare Conference on November 30th-December 2nd, 2021. A copy of the Company's current corporate slide presentation is being filed herewith as Exhibit 99.2 to this 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 99.2.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release issued by the Company on November 30, 2021, furnished hereto.
99.2	Presentation Slide Deck

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: November 30, 2021

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

Exhibit 99.1

Scholar Rock Announces Design of Phase 3 SAPPHIRE Clinical Trial Evaluating Apitegromab in Non-Ambulatory Patients with Type 2 and Type 3 Spinal Muscular Atrophy (SMA)

– Phase 3 trial is a randomized, double-blind, placebo-controlled trial of apitegromab as add-on to background SMN therapy in non-ambulatory Type 2/3 SMA

– Trial design is informed by the positive results from the prior TOPAZ trial, including a new exploratory analysis of patients 2-12 years old with non-ambulatory Type 2/3 SMA

CAMBRIDGE, Mass.--(BUSINESS WIRE)--November 30, 2021--Scholar Rock (NASDAQ: SRRK), a clinical-stage biopharmaceutical company focused on the treatment of serious diseases in which protein growth factors play a fundamental role, today announced the study design for SAPPHIRE, a Phase 3 trial of apitegromab, a selective inhibitor of the activation of latent myostatin. This pivotal trial will evaluate the efficacy and safety of apitegromab in patients with non-ambulatory Type 2 and Type 3 spinal muscular atrophy (SMA), which is estimated to represent approximately two-thirds of the overall SMA patient population. Study start-up activities for SAPPHIRE have commenced.

“Despite the important progress in SMA treatment offered by SMN therapies, there continues to be significant unmet medical need, and we believe that apitegromab has the potential to improve motor function as add-on to background SMN therapy and transform the lives of patients with SMA,” said Nagesh Mahanthappa, Ph.D., Interim CEO. “We are excited to advance to the pivotal trial phase of apitegromab development through SAPPHIRE.”

SAPPHIRE Trial Design

SAPPHIRE is a randomized, double-blind, placebo-controlled, phase 3 clinical trial. Approximately 156 patients aged 2-12 years old with non-ambulatory Type 2/3 SMA are anticipated to be enrolled in the main efficacy population. 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 added on top of background SMN treatment. Patients receiving the background SMN treatment of nusinersen as well as patients receiving background SMN treatment of risdiplam will both be eligible for enrollment.

Additional key elements of the study design include the following:

- At baseline, all patients will be required to be in the chronic maintenance phase of SMN treatment, corresponding to $\geq$ 6 months of prior treatment in the case of risdiplam or $\geq$ 10 months of prior treatment in the case of nusinersen.
- Randomization will be stratified by both the background SMN treatment (nusinersen vs. risdiplam) as well as the age at which SMN treatment had been initiated (< 5 years vs. $\geq$ 5 years).
- The primary efficacy endpoint will evaluate the mean change from baseline in the Expanded Hammersmith Functional Motor Scale (HFMSE) total score after 12 months of treatment.
- Additional endpoints will evaluate safety, proportion of patients with $\geq$3-point HFMSE increase, Revised Upper Limb Module (RULM), and World Health Organization (WHO) motor developmental milestones, pharmacokinetics, pharmacodynamics, anti-drug antibody, and other outcome measures.

In addition, the trial provides the opportunity for an interim analysis when at least 50% of patients in the main efficacy population (age 2-12 years) have completed 12 months of treatment.

Separately from the main efficacy population, an exploratory population of 48 patients aged 13-21 years old with non-ambulatory Type 2/3 SMA will be evaluated. These patients will be randomized 2:1 to receive either apitegromab 20 mg/kg or placebo added to background SMN treatment with nusinersen or risdiplam. 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.

To further characterize apitegromab in SMA, upon completion of the 12-month treatment period, all patients will be offered the option of enrolling in an open-label extension study. In this open-label extension, the safety and tolerability of apitegromab will be evaluated, along with an exploratory characterization of longer-term efficacy. In addition, the TOPAZ extension continues to follow patients from TOPAZ and evaluate the longer-term efficacy and safety of apitegromab. Among the 57 patients who completed the 12-month TOPAZ treatment period, 55 patients continue to participate in the extension period as of November 30, 2021.

SAPPHIRE is planned to enroll across 55 sites globally, including in the U.S. and Europe, and study start-up activities have commenced. For more information about SAPPHIRE, visit www.clinicaltrials.gov.

“We are encouraged and motivated by the positive results of the TOPAZ Phase 2 proof of concept trial, which informed the design of SAPPHIRE to evaluate the therapeutic potential of apitegromab in SMA,” said Yung Chyung, M.D., CMO. “Building on the solid foundation of TOPAZ, our Phase 3 trial and the broader program are aimed at advancing the development of apitegromab towards our aspiration of transforming the lives of patients with SMA.”

TOPAZ Insights Inform Key Elements of the SAPPHIRE Design

The SAPPHIRE design was informed by results from the TOPAZ phase 2 proof of concept trial of apitegromab in patients with Type 2 and Type 3 SMA. Key features of the SAPPHIRE design include the following:

- SAPPHIRE enrolls patients with non-ambulatory Type 2/3 SMA, which was the population of individuals observed to have the largest HFMSE increases from baseline in TOPAZ.
- Selection of the age 2-12 population in SAPPHIRE was informed by the positive efficacy results of an exploratory post hoc analysis from TOPAZ, as described in further detail below.
- SAPPHIRE will use the same primary efficacy endpoint (mean HFMSE change from baseline) as had been used in TOPAZ.
- SAPPHIRE will use the same treatment duration (12 months) as had been used in TOPAZ.
- SAPPHIRE will evaluate apitegromab at 20 mg/kg, which was observed in TOPAZ to have a greater effect than the 2 mg/kg dose both in terms of efficacy and pharmacodynamics. As it is possible that an intermediate dose of apitegromab between 2 and 20 mg/kg may offer comparable effects as the 20 mg/kg dose, SAPPHIRE will include an apitegromab 10 mg/kg arm. 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.

Exploratory Analysis of Age 2-12 Non-Ambulatory Patients from TOPAZ

This exploratory post hoc analysis from TOPAZ pooled together patients from both non-ambulatory cohorts (patients who had initiated their background nusinersen therapy at the age of < 5 years and patients who had initiated their background nusinersen therapy at the age of ≥ 5 years). Patients in this subset of the intent-to-treat population were in the age range of 2-12 years old and had been treated with 20 mg/kg of apitegromab.

The 12-month apitegromab results from this age 2-12 years old exploratory analysis of the pooled non-ambulatory cohorts in TOPAZ include the following:

- N= 16 total, with 50% of these patients being from the cohort of background nusinersen initiated at age < 5 years and 50% of these patients being from the cohort of background nusinersen initiated at age ≥ 5 years
- All patients were in the chronic maintenance phase of nusinersen treatment. Data from the SHINE study suggest that the effects of nusinersen upon HFMSE generally plateau after initial increases.[1]
- Mean HFMSE change from baseline was 4.4-point increase (95% CI of 1.3, 7.4)
- 81% (13/16) of patients had ≥ 1-point increase in HFMSE
- 56% (9/16) of patients had ≥ 3-point increase in HFMSE
- Among the older subset of patients (individuals who had started their background nusinersen at the age of ≥ 5 years) in this analysis, 75% (6/8) of patients had ≥ 1-point increase in HFMSE and 50% (4/8) of patients had ≥ 3-point increase in HFMSE

About Apitegromab

Apitegromab is a selective inhibitor of the activation of myostatin and is an investigational product candidate for the treatment of patients with 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 (FTD), Orphan Drug (ODD) and Rare Pediatric Disease (RPD) 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/).

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 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, SRK-181, 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," "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 preclinical and clinical data, including the 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, the data generated from Scholar Rock's nonclinical and preclinical studies and clinical trials, information provided or decisions made by regulatory authorities, competition from third parties that are developing products for similar uses, Scholar Rock's ability to obtain, maintain and protect its intellectual property, Scholar Rock's dependence on third parties for development and manufacture of product candidates including to supply any clinical trials, Scholar Rock's ability to manage expenses and to obtain additional funding when needed to support its business activities and establish and maintain strategic business alliances and new business initiatives, and the impacts of public health pandemics such as COVID-19 on business operations 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 September 30, 2021, as well as discussions of potential risks, uncertainties, and other important factors in Scholar Rock's subsequent filings with the Securities and Exchange Commission. Any forward-looking statements represent Scholar Rock's views only as of today and should not be relied upon as representing its views as of any subsequent date. All information in this press release is as of the date of the release, and Scholar Rock undertakes no duty to update this information unless required by law.

[1] This information from a third-party study is provided for background purposes only and is not intended to convey or imply a comparison to the TOPAZ clinical trial results.

Contacts

Scholar Rock Contacts:
Investors
Stephanie Ascher
Stern Investor Relations, Inc.
Stephanie.Ascher@sternir.com
212-362-1200

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

Deep Insights, Impactful Medicines

December 1-2, 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 apitegromab, SRK-181, and other product candidates and indication selection and development timing, its cash runway, 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," "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 for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. 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 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 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 and Part B of the Phase 1 trial of SRK-181, respectively, 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, the success of Scholar Rock's current and potential future collaborations, including its collaboration with Gilead, 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 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 September 30, 2021, 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.

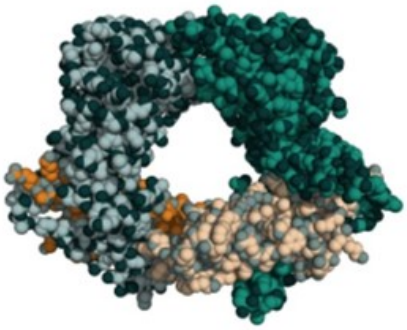
ScholarRock.

2021 Momentum to Carry into 2022 Across Portfolio

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

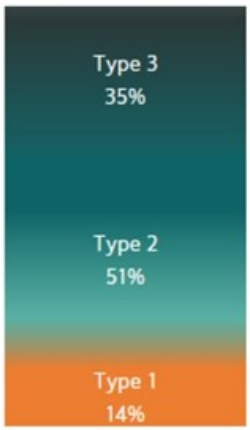
Apitegromab Positioned to be Next Potential Transformative Therapy for Patients with SMA

ScholarRock.

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 showed transformative potential 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)*
Lallyet al, OrphanetJournal of Rare Diseases, 2017

Potential to Pioneer a New Treatment Era: Opportunity for Muscle-Directed Therapy to Complement SMN Upregulators

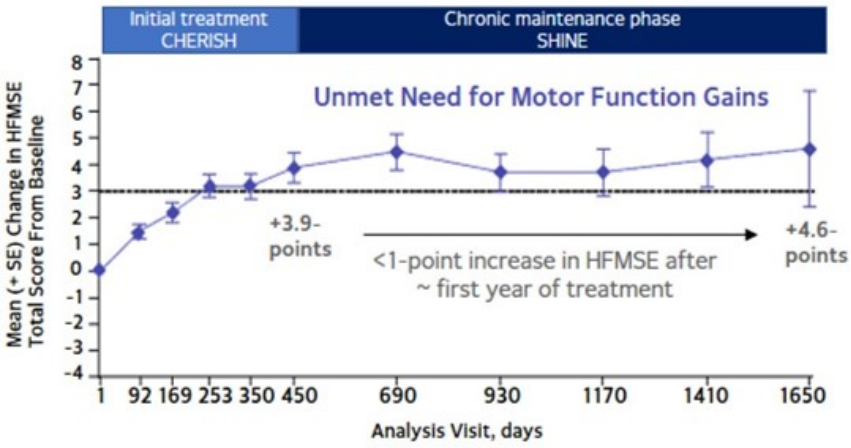
	SPINRAZA® (nusinersen) injection 12 mg/5 mL	Evrysdi® risdiplam	zolgensma® (onasemnogene abeparvovec-xioi) suspension for intravenous infusion
Phase 3 Trial Design	• Non-ambulatory Type 2/3 • 2-12 years of age • **Primary endpoint:** Mean change from baseline in HFMSE at 15 months	• Non-ambulatory Type 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	• SMA in patients less than 2 years of age
Market Penetration	• >11,000* patients treated WW • $2+ billion in revenues (LTM)	• ~4,000** patients treated WW • ~CHF243 million in revenues (1H21)	• ~1,200*** patients treated WW • ~$1.2 billion in revenues (LTM)

Patients continue to experience major functional impairments despite utilization of SMN upregulators

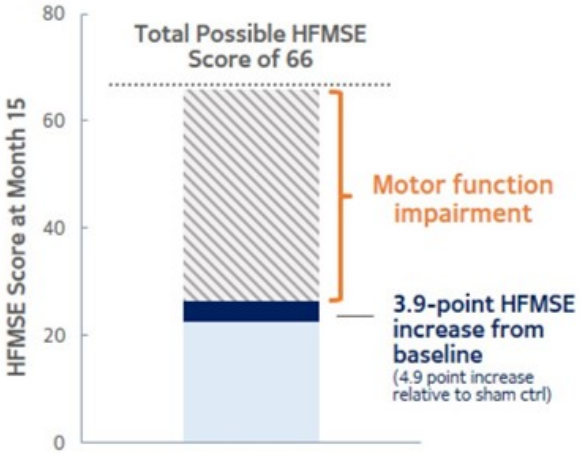
*As of Biogen 2Q21 financial update on 7/22/21; includes patients treated worldwide in post-marketing setting, expanded access program, and clinical trials.
**As of Roche 1H21 financial update on 7/22/21; includes patients treated worldwide between clinical trials, commercial, and compassionate use program.
***As of Novartis 2Q21 financial update on 7/21/21; commercially, via managed access programs and in clinical trials
HFMSE = Hammersmith Functional Motor Scale Expanded; MFM-32 = Motor Function Measure – 32 items

Patients with Type 2 and 3 SMA Continue to Experience Major Functional Deficits Despite Improvement from SMN Therapy*

Plateauing of HFMSE gains apparent following initial treatment effects for nusinersen...



Significant motor function deficits still present...

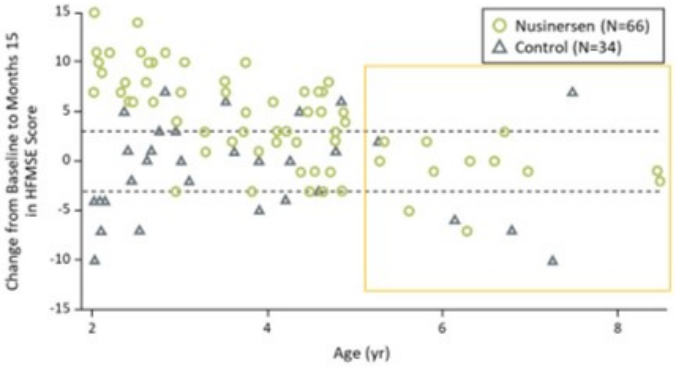


Mean improvement in HFMSE experienced in nusinersen Phase 3 CHERISH trial

"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.

Non-Ambulatory Type 2/3 SMA:
Majority of Patients Started on SMN Rx After Age 5 Do Not Experience Motor Function Increases*

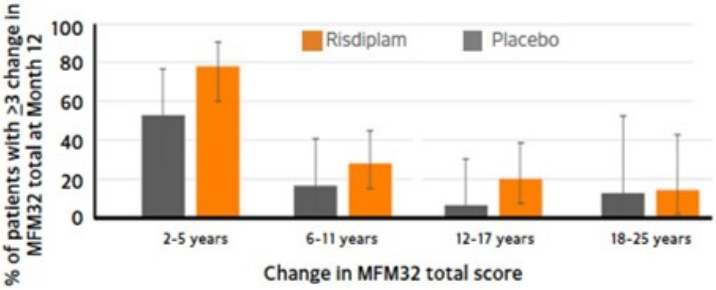
Nusinersen CHERISH Trial in Later-Onset SMA†



In patients with later-onset SMA who were age ≥5 at screening…

- Primary benefit of nusinersen - stabilization of motor function
- Majority of patients do not experience HFMSE increases

Risdiplam SUNFISH Trial in Later-Onset SMA††



- Low percentage of patients over the age of 5 achieved ≥3-point increase on MFM32 scale, even with risdiplam treatment
- HFMSE secondary endpoint showed a mean 0.58-point improvement over placebo (not statistically significant)

† *Source:* Mercuri E, et.al. Nusinersen versus sham control in later-onset spinal muscular atrophy. *N Engl J Med.* 2018;378:625-635.
† †Efficacy and safety of risdiplam (RG7916) in patients with Type 2 or non-ambulant Type 3 spinal muscular atrophy (SMA) Roche/PTC Therapeutics
*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

TOPAZ Top-Line Data Showed Apitegromab's Transformative Potential in Patients with Type 2/3 SMA

✓ Majority of non-ambulatory patients* experienced HFMSE increases from apitegromab as add-on during chronic maintenance phase of SMN therapy

✓ Apitegromab led to HFMSE improvements in both non-ambulatory cohorts (including patients started on nusinersen at age ≥ 5)

At 12 months	Mean HFMSE increase	≥1-point increase	≥3-point increase
Initiated background nusinersen age <5**	+7.1 points	88% (7/8) of patients	63% (5/8) of patients
Initiated background nusinersen age ≥5	+0.6 points	64% (9/14) of patients	29% (4/14) of patients

** Pooled cohorts of non-ambulatory patients treated with apitegromab 20 mg/kg and 2 mg/kg*
***Non-ambulatory patients who initiated background nusinersen at a young age of <5 years and treated with apitegromab 20 mg/kg dose*

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.

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

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

SAPPHIRE Phase 3 Design Optimized by Insights from TOPAZ

TOPAZ Learnings	SAPPHIRE Design Elements
Largest HFMSE gains observed in the non-ambulatory Type 2/3 SMA cohorts	• Study population: Non-ambulatory Type 2/3 SMA • Primary efficacy endpoint: HFMSE
Exploratory age 2-12 analysis in non-ambulatory Type 2/3 showed transformative potential	• Age 2-12 will be main efficacy population
HFMSE gains evident by 12 months of treatment	• 12 month treatment duration
Dose response seen (greater effect observed with 20 mg/kg over 2 mg/kg)	• 20 mg/kg apitegromab dose • To explore potential that dose between 2 and 20 mg/kg may be comparable to 20 mg/kg, will also evaluate 10 mg/kg arm

SAPPHIRE Phase 3 Design Optimized by Insights from TOPAZ

TOPAZ Learnings	SAPPHIRE Design Elements
Largest HFMSE gains observed in the non-ambulatory Type 2/3 SMA cohorts	• Study population: Non-ambulatory Type 2/3 SMA • Primary efficacy endpoint: HFMSE
Exploratory age 2-12 analysis in non-ambulatory Type 2/3 showed transformative potential	• Age 2-12 will be main efficacy population
HFMSE gains evident by 12 months of treatment	• 12 month treatment duration
Dose response seen (greater effect observed with 20 mg/kg over 2 mg/kg)	• 20 mg/kg apitegromab dose • To explore potential that dose between 2 and 20 mg/kg may be comparable to 20 mg/kg, evaluating 10 mg/kg arm

TOPAZ Age 2-12 Exploratory Analysis (Non-Ambulatory Type 2/3 SMA)

Analysis overview*:

- Pooled patients (n =16) of age 2-12 years from the intent-to-treat population of the two non-ambulatory cohorts
  1) Nusinersen initiated at age < 5 years: n = 8
  2) Nusinersen initiated at age ≥ 5 years: n = 8
- 12 months of apitegromab 20 mg/kg as add-on to background nusinersen
- Patients were all in chronic maintenance phase of nusinersen
- HFMSE change from baseline

*Exploratory, post hoc analysis

TOPAZ Age 2-12 Analysis* in Pooled Non-Ambulatory Cohorts

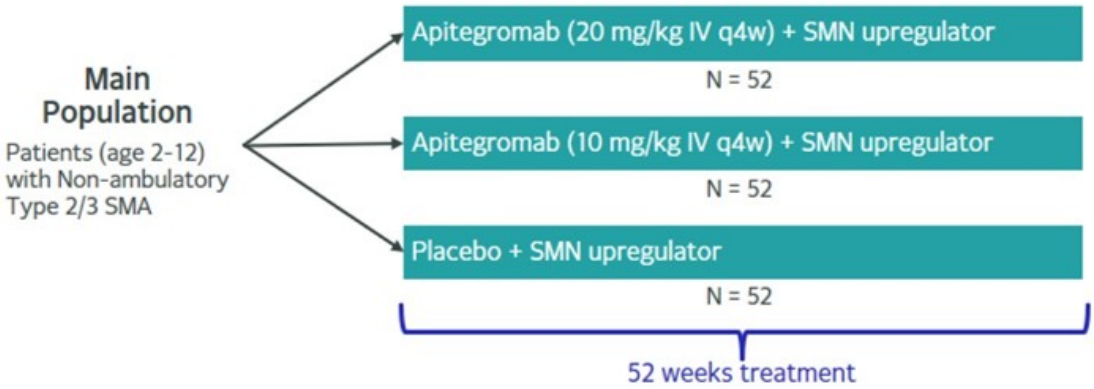
Transformative Potential as Add-on for Apitegromab

Non-Ambulatory Type 2/3 SMA (Apitegromab 20 mg/kg; Intent-to-Treat Population)	**Age 2-12 years (n=16)**
Mean HFMSE change from baseline (95% CI)	**+4.4** **(1.3, 7.4)**
# (%) patients with ≥1-pt increase in HFMSE	**13/16 (81%)**
# (%) patients with ≥3-pt increase in HFMSE	**9/16 (56%)**

- Mean HFMSE increase of 4.4 points, with majority experiencing ≥ 3-point increases on top of background SMN therapy
- HFMSE gains also notable in subset of individuals in this analysis who had started background nusinersen at age ≥ 5: 75% (6/8) with ≥ 1-point increase and 50% (4/8) with ≥ 3-point increase

*Exploratory, post hoc analysis

SAPPHIRE (Phase 3) Trial Overview



SAPPHIRE

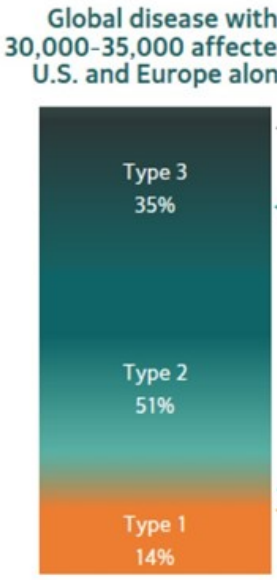
- Randomized, double-blind, placebo-controlled, parallel arm design
- Add-on to background SMN therapy (enrolling patients on nusinersen as well as patients on risdiplam)
- Primary efficacy endpoint: mean HFMSE change from baseline at 12 months
- Study start-up activities commenced

SAPPHIRE Details

Main population	• Age 2-12, non-ambulatory Type 2 and Type 3 SMA • Chronic maintenance phase of SMN Rx (minimum prior duration of treatment before screening of 10 mo's for nusinersen or 6 mo's for risdiplam) • Stratified randomization to ensure balanced allocation: 1) age at SMN Rx initiation (age < 5 vs age ≥ 5) 2) background SMN Rx (nusinersen vs. risdiplam)
Endpoints	• Primary efficacy: HFMSE • Add'l efficacy measures: RULM, WHO, other outcome measures • Safety, PK/PD, ADA
Analysis	• Topline readout based upon main efficacy population (age 2-12) and focused upon apitegromab 20 mg/kg* vs. placebo • Interim analysis opportunity when ≥ 50% of patients in main efficacy population have completed 12 months
Additional Data Opportunities	• Open-label extension (after patients complete 12-month period); focused upon safety & exploratory longer-term efficacy • Exploratory population (age 13-21): n=48 (2:1 randomization between apitegromab 20 mg/kg vs placebo, as add-on to background SMN Rx); focused upon safety & exploratory 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

Additional Therapeutic Opportunities May Be Pursued With Separate Development Strategies



C

Ambulatory patients

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

A

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

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

B

Type 1 SMA, 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

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

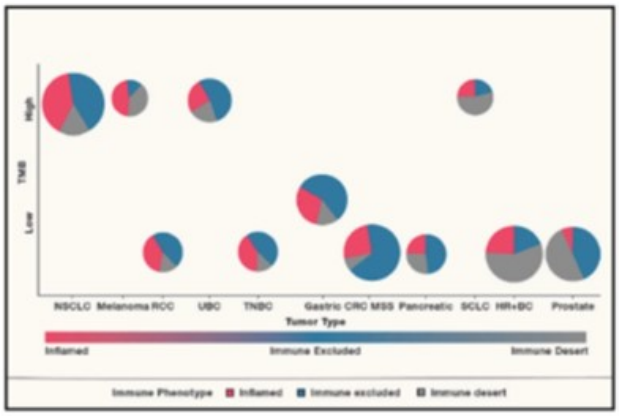
Rik Derynck[1,2,✉], Shannon J. Turley[4,✉] and Rosemary J. Akhurst[2,✉]

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

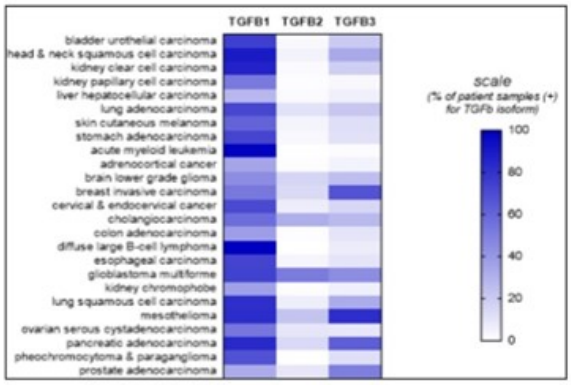
August 2020: *"Bristol Myers Squibb Enters Agreement to Acquire Forbius TGF-beta Program"*

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*



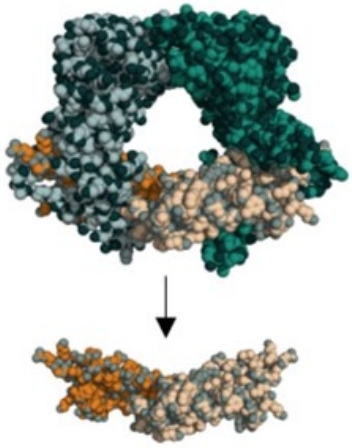
Human Tumor Analyses Reveal TGFβ1 as Most Likely Driver of TGFβ Signaling Pathway in Cancers

[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



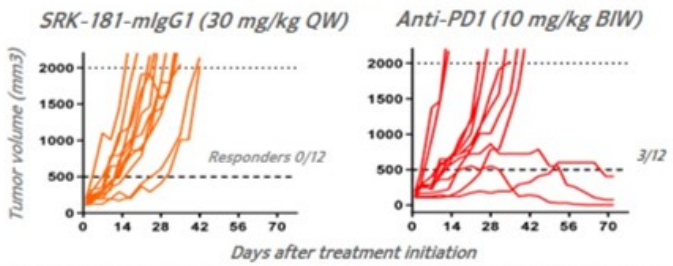
Traditional target:
"Mature" growth factor

- ✓ **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

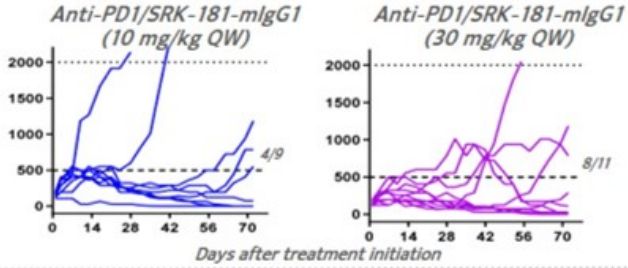
TGFβ1 Blockade with SRK-181-mIgG1 Rendered Preclinical Tumor Models Susceptible to Anti-PD1 Therapy

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

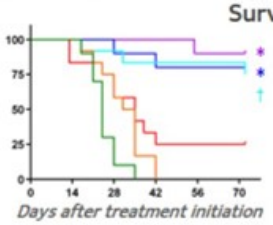
Tumor Regression: Monotherapy



Tumor Regression: Combination Therapy



Survival Benefit



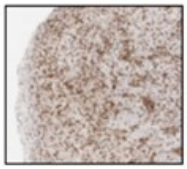
- Control
- SRK-181-mIgG1 (30 mg/Kg/wk)
- Anti-PD1 (10 mg/Kg/2xwk)
- Anti-PD1 + SRK-181-mIgG1 (3 mg/Kg/wk)
- Anti-PD1 + SRK-181-mIgG1 (10 mg/Kg/wk)
- Anti-PD1 + SRK-181-mIgG1 (30 mg/Kg/wk)

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

Overcoming immune exclusion

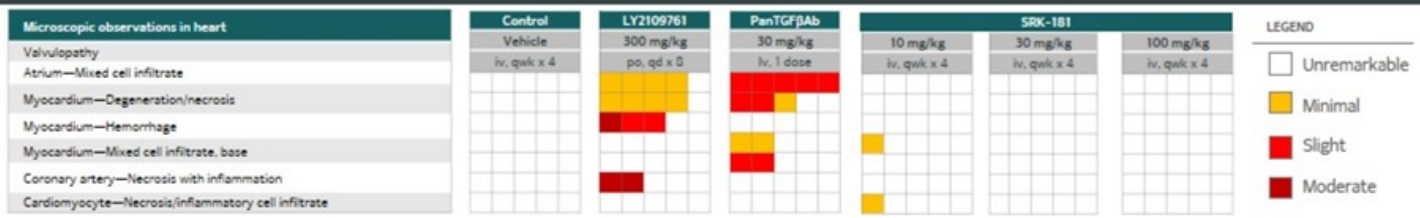
Anti-PD1

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 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

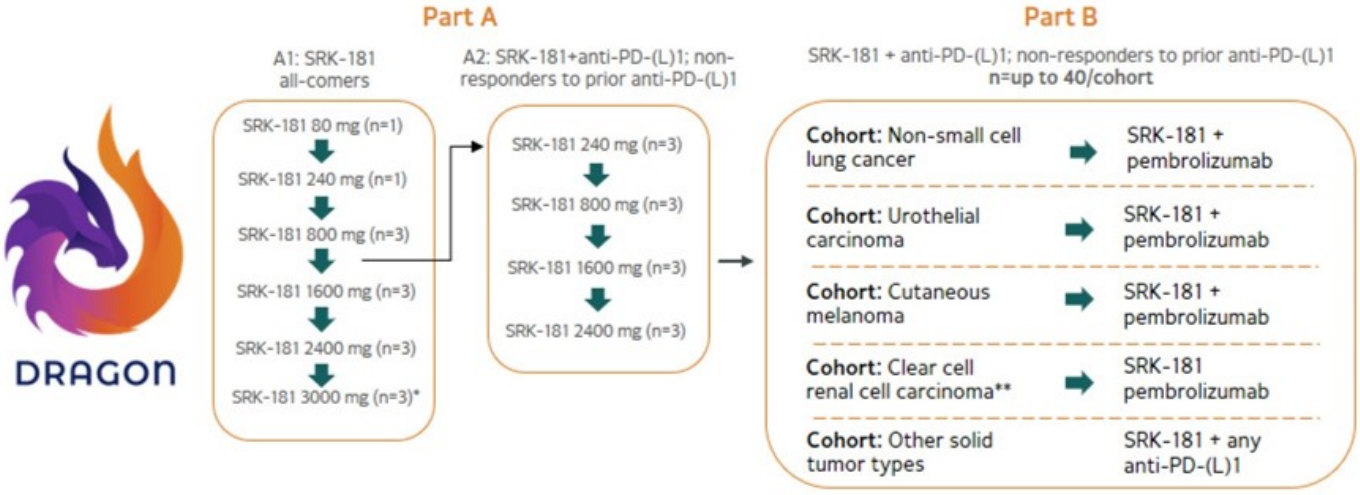
Preclinical data published in *Science Translational Medicine*. Martin CJ, et al. *Sci Transl Med* 2020 Mar 25:12(536): eaay8456.
*Source: Anderton MJ, et al. Induction of heart valve lesions by small-molecule ALK5 inhibitors. *Toxicol Pathol.* 2011:39: 916-924.; and Stauber AJ, et al. Nonclinical safety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

SRK-181 Therapeutic Hypothesis: Potential Advantages of Latent TGFβ1 Inhibitor

	SRK-181*	Bifunctional TGFβ/CPI	ALK5 Inhibitor	Nonselective TGFβ antibody
Selectivity for TGFβ1: potential for wider therapeutic window and improved safety	✓	X	X	X
Ability to combine with any anti-PD-(L)1	✓	X	✓	✓
Ability to optimize dosing of each component of combination therapy	✓	X	✓	✓
Activity spatially distinct from anti-PD-(L)1 in tissue	✓	X	✓	✓

SRK-181 is an investigational product candidate currently being evaluated in DRAGON phase 1 clinical trial. The efficacy and safety of SRK-181 have not been established.

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



DRAGON

* A cohort of 2000 mg Q2W (n=3) was also evaluated.
**The clear cell RCC cohort will also explore the effects of SRK-181 in patients with relapsed response after anti-PD-(L)1 treatment.

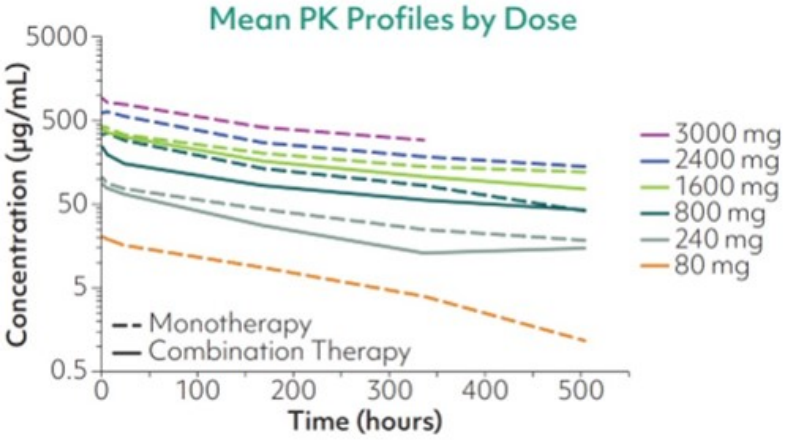
NCT04291079 on www.clinicaltrials.gov.

DRAGON Part A: Dose Escalation Update and Safety Data

- Median number of prior lines of therapy was 4 (range 1, 9) for Part A1 and 4 (range 2, 6) for Part A2
- No dose-limiting toxicities have been observed with SRK-181 in Part A (as of Oct. 12, 2021), evaluating doses as high as the following thus far:
  - Part A1 : doses up to 3000 mg Q3W and 2000 mg Q2W as a monotherapy
  - Part A2: 1600 mg Q3W in combination with anti-PD-(L)1 therapy
- Most common (>10%) treatment-related TEAEs* of any grade were fatigue, decreased appetite, and nausea (Part A1) and rash maculo-papular (Part A2)

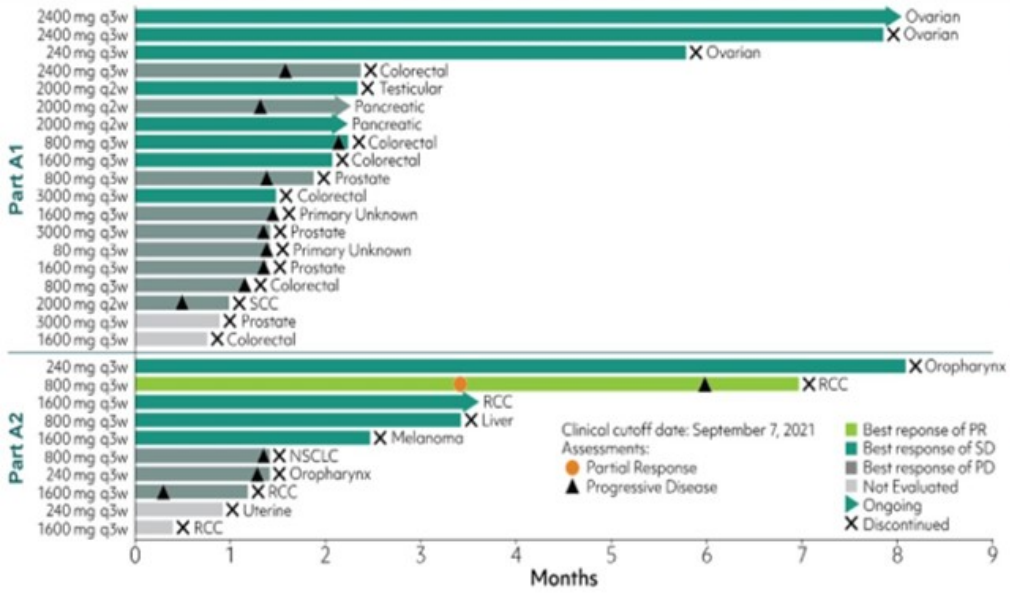
*TEAE = treatment-emergent adverse event

DRAGON Part A: Preliminary Pharmacokinetics (PK) Summary of SRK-181



- SRK-181 displayed typical monoclonal antibody PK characteristics
- Based on a power model, dose-proportional PK was observed for SRK-181
- The $T_{1/2}$ of SRK-181 was 5.4 to 10.7 days

DRAGON Part A: Preliminary Anti-Tumor Effects*



Part A1 (n=19)

- 8 patients had best response of stable disease (SD)
- 3 ovarian cancer patients had best response of SD, with tumor regressions in 2 of these individuals

Part A2 (n=10)

- At 800 mg q3w, 1 partial response (PR) was observed in patient with anti-PD-1-resistant renal cell carcinoma (RCC)
- 4 patients had best response of SD including 1 oropharynx cancer patient with tumor regression

*Preliminary anti-tumor effects were assessed using RECIST1.1 and reported based upon local investigator reads

DRAGON Has Advanced to Part B to Test Proof of Concept for SRK-181 in Overcoming Anti-PD-(L)1 Resistance

- Part B dose selected based upon Part A data & PK modeling: 1500 mg q3w*
  - Estimated to offer drug exposure at levels exceeding those hypothesized as needed for anti-tumor effect based on preclinical data and PK modeling
- Part B encompasses multiple POC cohorts (enrolling up to 40 patients each)
  - Enrolling patients with primary resistance to anti-PD-(L)1 therapy
  - Enriched with solid tumor types for which it is hypothesized there may be higher potential for early efficacy signals based upon translational and preclinical insights
  - Additional Part B cohort of clear cell renal cell carcinoma (ccRCC) being added based on emerging insights, including preliminary data from Part A

*For patients receiving anti-PD-(L)1 therapy dosed at q2w frequency, SRK-181 will be dosed at 1000 mg q2w

NCT04291079 on www.clinicaltrials.gov.

2021 Momentum to Carry into 2022 Across Portfolio

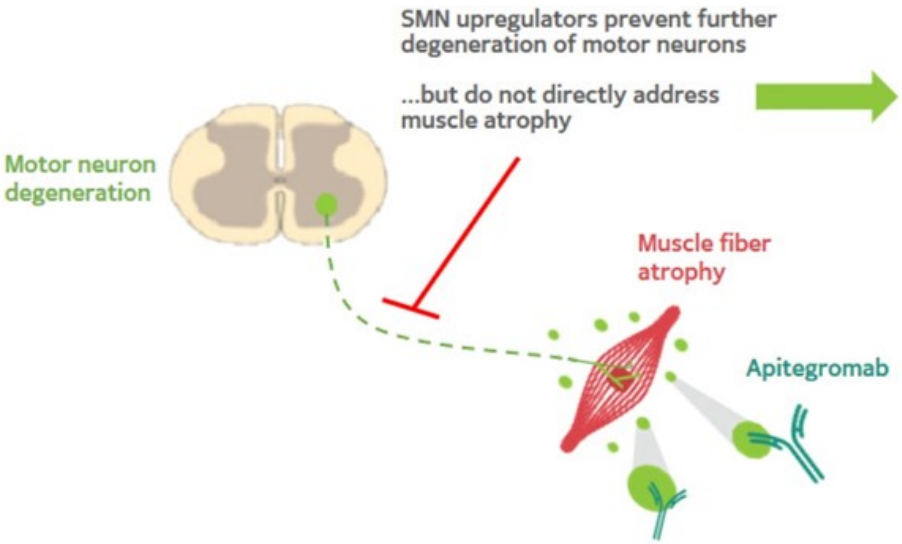
Appendix

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

Apitegromab: Muscle-Directed Therapy Aimed at Complementing SMN Upregulators



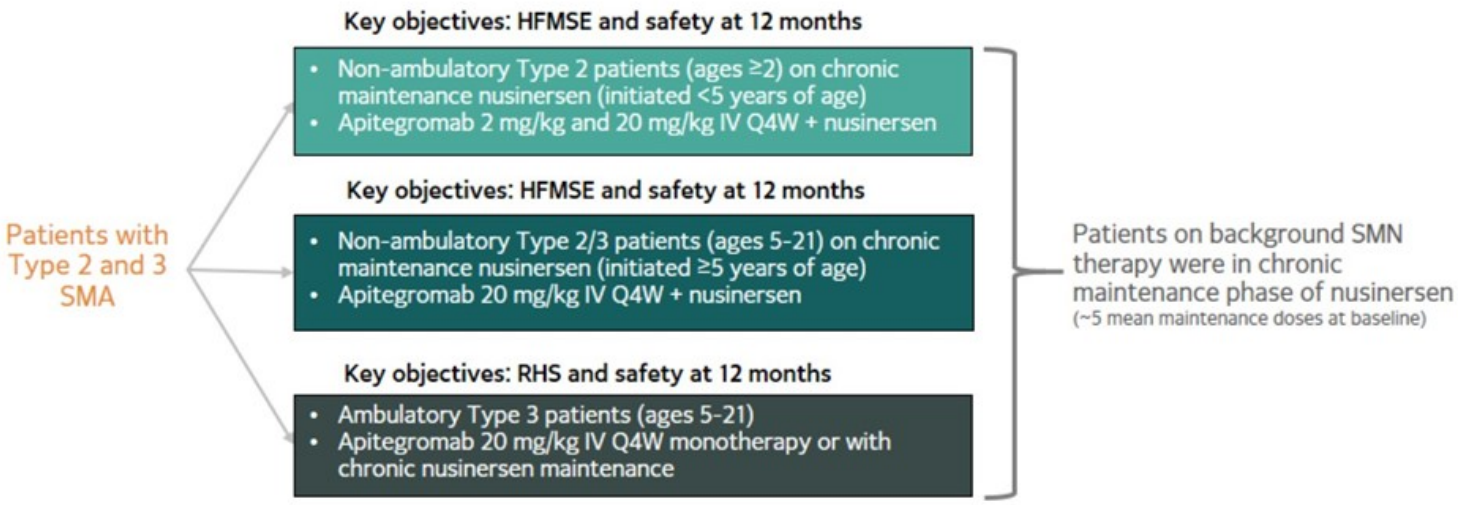
Adapted from images courtesy of the SMA Foundation

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

Apitegromab Phase 2 Trial Design

TOPAZ



55 of the 57* patients who completed TOPAZ 12-month period continue to participate in the extension

*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 and initiated nusinersen <5 years			Non-Ambulatory, Ages 5-21	Ambulatory, Ages 5-21		
	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 at baseline (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 Type 2 Cohort:
Initiated nusinersen age <5

TOPAZ

Apitegromab (20 mg/kg) + nusinersen	n=8
Mean change from baseline in HFMSE (95% CI)	+7.1 (1.8, 12.5)
# (%) patients achieving:	
≥1-pt increase in HFMSE	7/8 (88%)
≥3-pt increase in HFMSE	5/8 (63%)
≥5-pt increase in HFMSE	5/8 (63%)
Baseline characteristics: mean (min, max)	n=10
Age	3.8 (2, 6)
HFMSE score	23.5 (14, 42)
# of nusinersen maintenance doses	5.4 (3, 8)

Sizable increases in HFMSE observed in patients already treated with chronic maintenance nusinersen

- 88% (7/8) improved
- 63% (5/8) with ≥5-point increase
- 38% (3/8) with >10-point increase
- Continuous and durable improvements observed through 12-months of treatment

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

Non-Ambulatory Type 2/3 Cohort:
Initiated nusinersen age ≥5

TOPAZ

Apitegromab (20 mg/kg) + nusinersen	Per Protocol Population* (n=13)	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%)
≥3-pt increase in HFMSE	4/13 (31%)	4/14 (29%)
≥5-pt increase in HFMSE	2/13 (15%)	2/14 (14%)
Baseline characteristics: mean (min, max)	n=15	
Age	11.7 (8, 19)	
HFMSE score	22.7 (13, 39)	
# of nusinersen maintenance doses	5.1 (2, 9)	

Majority of patients improved in HFMSE (despite initiating background nusinersen age ≥5)

- ~2/3 with ≥1-point increase
- ~30% with ≥3-point increase
- Durability of effect observed through 12-months of treatment

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

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

	Apitegromab 20 mg/kg monotherapy	Apitegromab 20 mg/kg + nusinersen
Mean change from baseline in RHS (95% CI)	-0.4 (-3.9, 3.1)	-0.3 (-2.0, 1.4)
# (%) patients achieving:		
≥0-pt increase in RHS	6/11 (55%)	7/12 (58%)
≥1-pt increase in RHS	4/11 (36%)	5/12 (42%)
≥3-pt increase in RHS	3/11 (27%)	2/12 (17%)
Baseline characteristics: mean (min, max)	n=11	n=12
Age	12.1 (7, 19)	13.1 (7, 21)
HFMSE score	47.6 (26, 63)	51.3 (43, 62)
# of nusinersen maintenance doses	n/a	5.6 (2, 8)

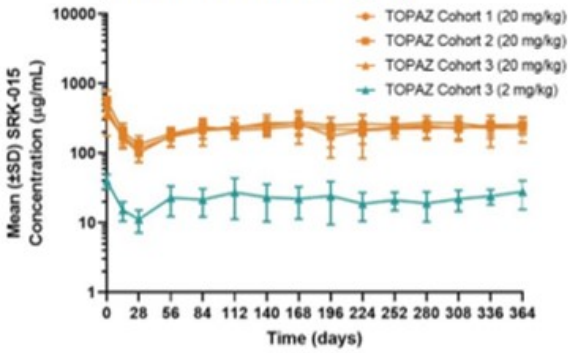
Majority maintained or improved

- 57% (13/23) with ≥0-point increase
- 39% (9/23) with ≥1-point increase
- Up to 8-point increase observed
- Results contrast with declines typically observed with natural history of ambulatory patients

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

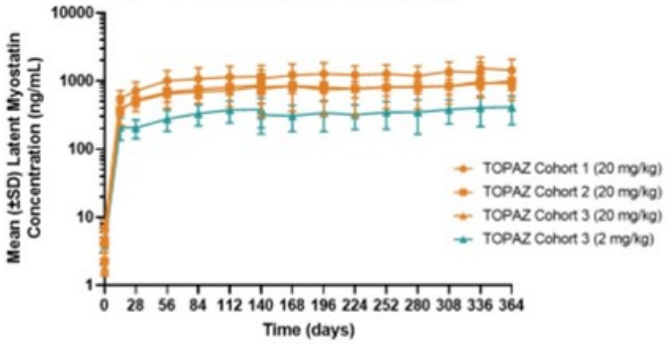
Pharmacokinetic and Pharmacodynamic Data are Supportive of Clinically Observed Effects

Pharmacokinetics* (PK)



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

Pharmacodynamics (PD)



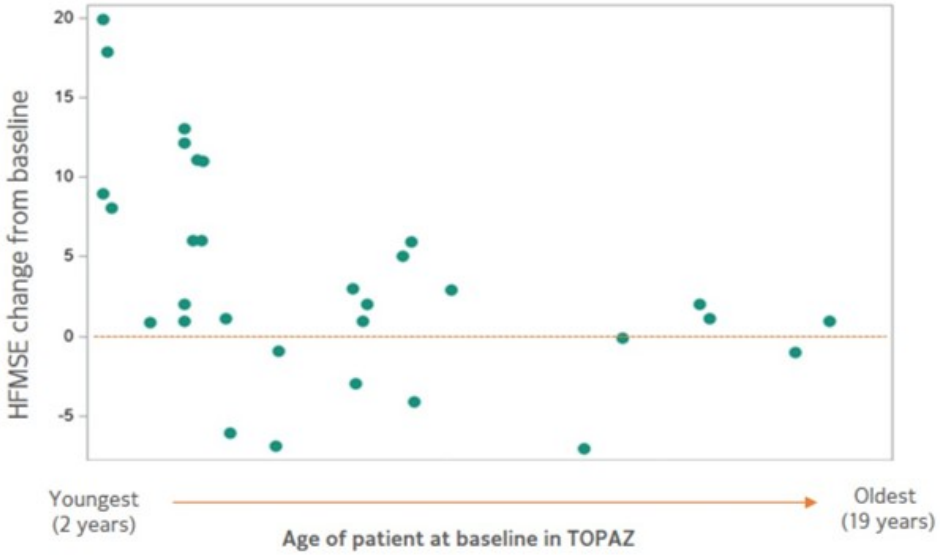
- Both 2 mg/kg and 20 mg/kg doses yielded high levels of target engagement (>100-fold increase from baseline)
- 20 mg/kg dose offers relatively higher magnitude of target engagement than 2 mg/kg dose

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

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

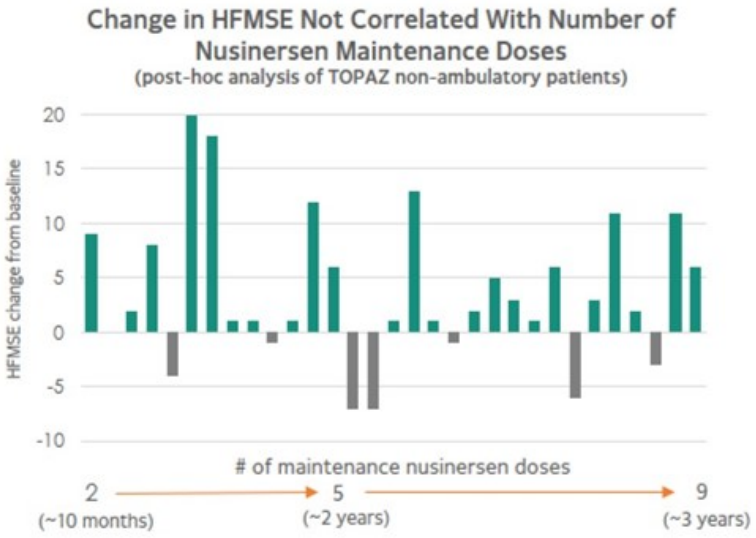
Data on file. Scholar Rock, Inc. Cambridge, MA

HFMSE Improvements Observed Across Age Range of Non-Ambulatory Patients with Relatively Larger Gains from Earlier Treatment



**Pooled cohorts of non-ambulatory patients treated with apitegromab 20 mg/kg and 2 mg/kg; excludes 4 patients who each missed 3 doses of apitegromab due to COVID-19-related site access restrictions and were not included in the primary (intent-to-treat) analysis.*
Data on file. Scholar Rock, Inc. Cambridge, MA

Increases in HFMSE Not Correlated with Duration of Prior Nusinersen Treatment



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

Further data suggesting increases in HFMSE may be attributable to apitegromab

- No correlation between duration of prior nusinersen treatment and change in HFMSE
- Patients in TOPAZ were already in chronic maintenance phase of nusinersen (mean of ~2 years at enrollment)

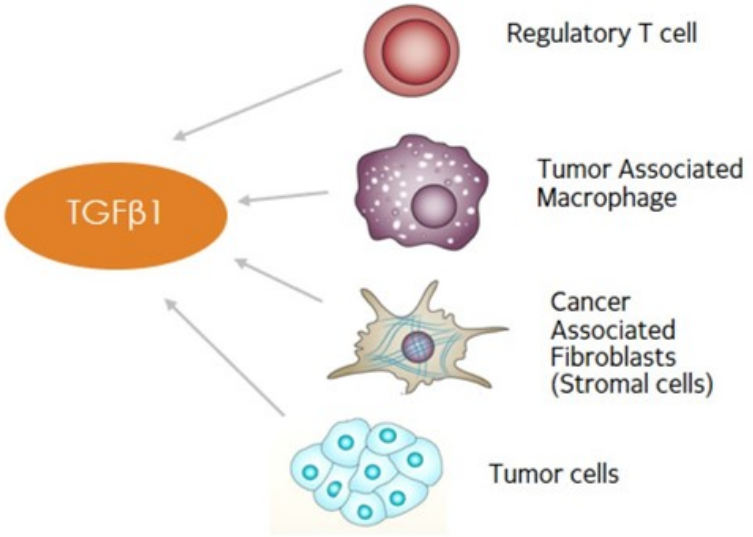
WHO Motor Development Milestone Achievements Further Support Apitegromab's Potential to Improve Motor Function

Non-ambulatory Type 2/3 Patients	Pooled	Initiated nusinersen age <5	Initiated nusinersen age ≥5
# of patients gaining ≥1 WHO motor milestone(s)	7/35	4/20	3/15

WHO motor milestone analysis included all patients who completed the 12-month treatment period, including 4 patients who missed 3 doses of apitegromab due to COVID-19-related site access restrictions. Median baseline score for both non-ambulatory cohorts was 1.0.
1 patient (initiated nusinersen age ≥5) gained 2 new motor milestones and 1 patient (initiated nusinersen age <5, 20 mg/kg) gained 3 new motor milestones
Pictures are not of patients with SMA and are not meant to be representative of patients with SMA. Data on file. Scholar Rock, Inc. Cambridge, MA.

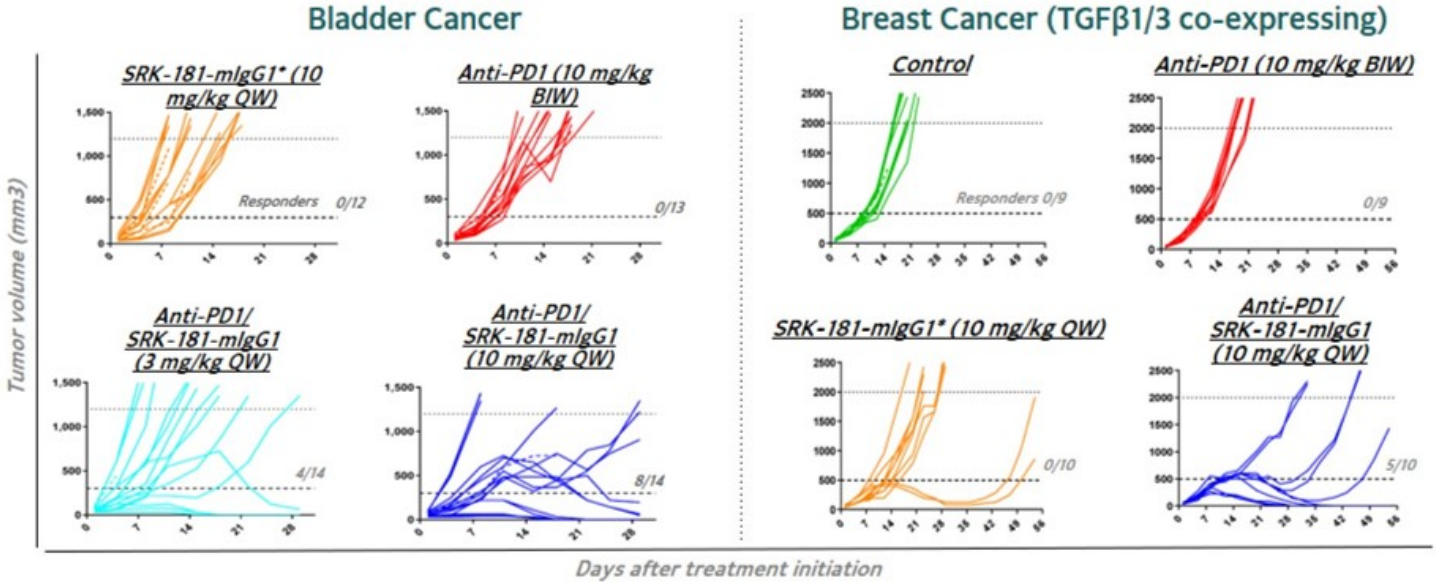
Inhibition of TGFβ1: Multipronged Approach for Immuno-Oncology

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



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.*