Deep Insights Advancing Impactful Medicines

40th Annual J.P. Morgan Healthcare Conference

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ScholarRock

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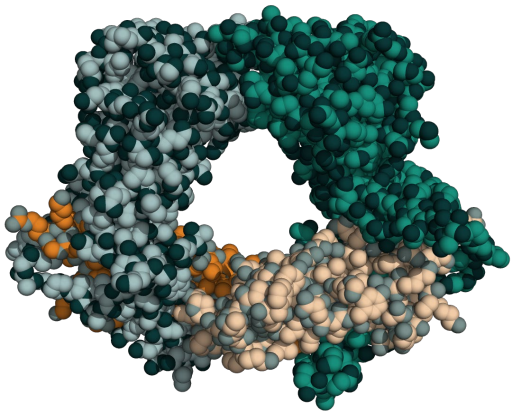
ScholarRock™

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

Scholar Rock's Target

Growth Factor Precursor (Latent Form)



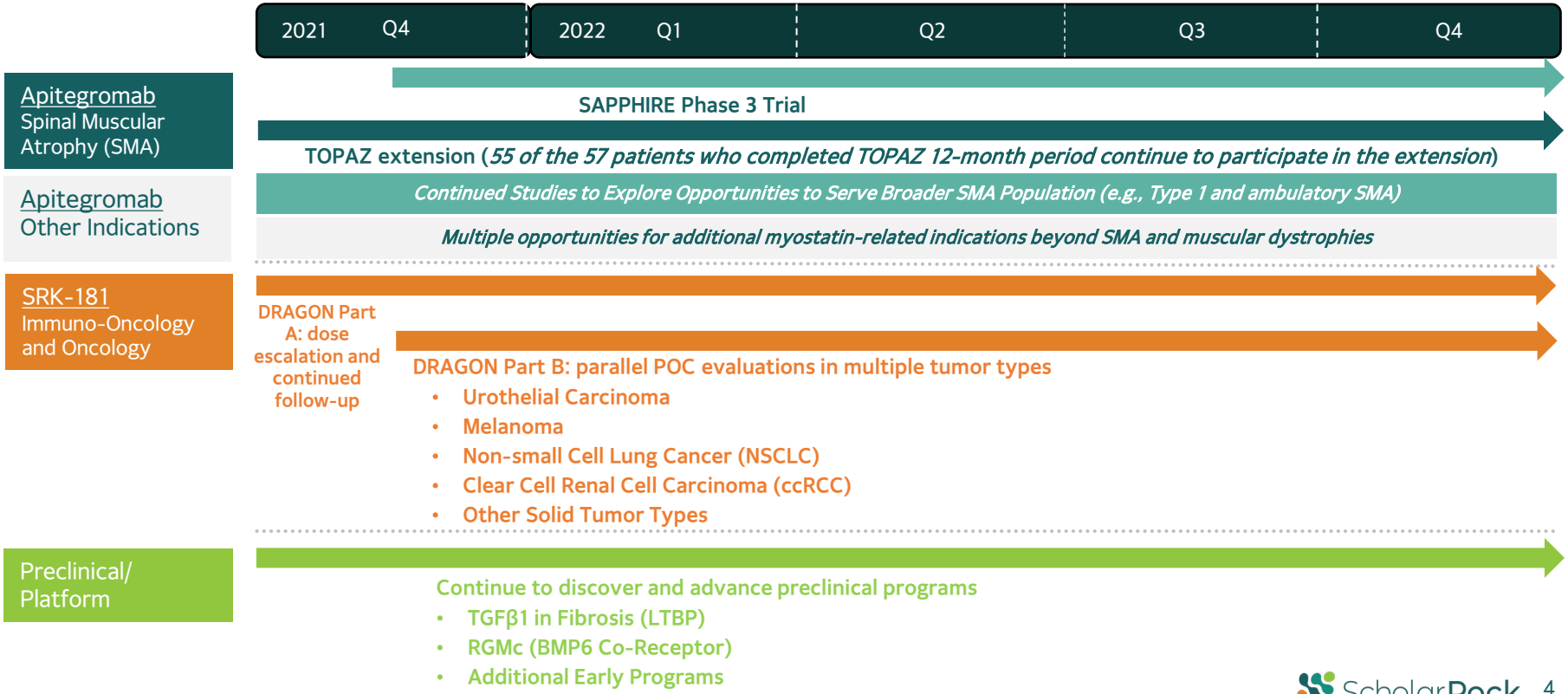
Scholar Rock's R&D Platform

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

Portfolio Spanning All Stages of Discovery and Development



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

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 60 mg powder for oral solution	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)

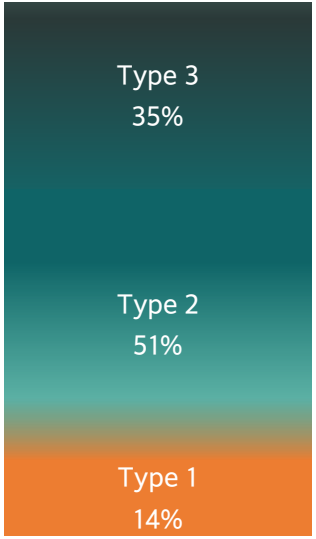
Patients continue to experience major functional impairments despite utilization of SMN upregulators

*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

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

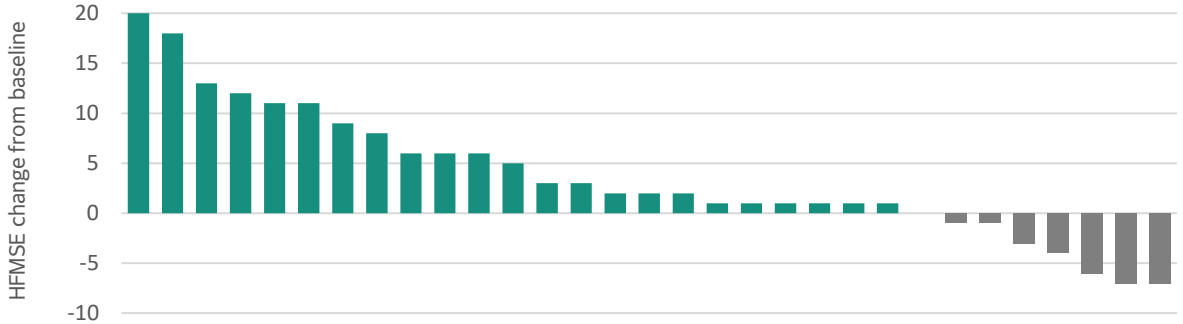
Represents ~2/3 of overall patient population

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

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*

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

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

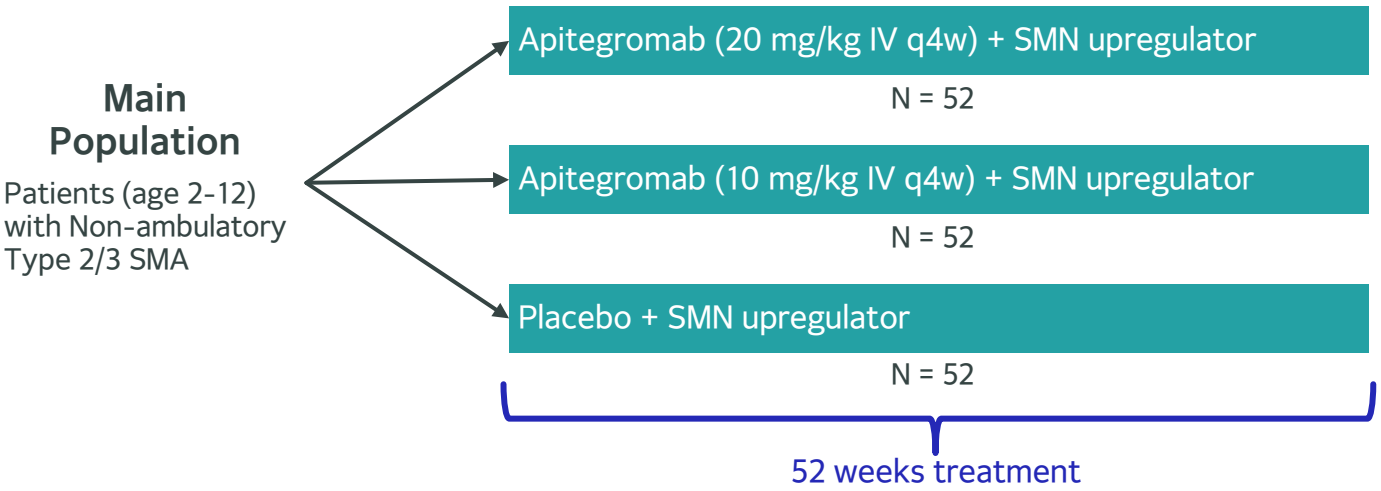
Transformative Potential as Add-on for Apitegromab

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

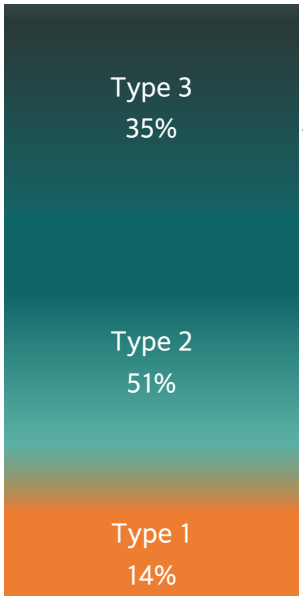
Additional Data Opportunities

- 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

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



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

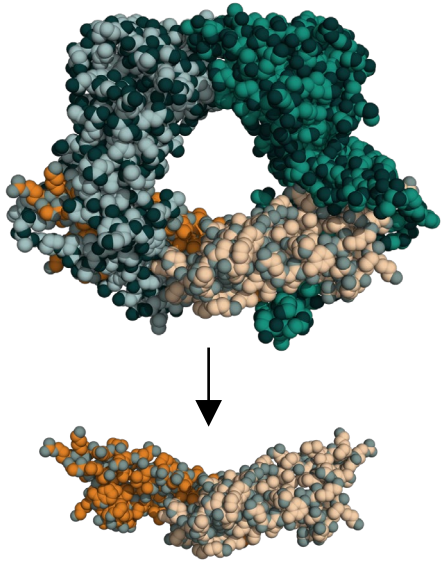
- Highest incidence population and growing prevalence due to SMN upregulator treatment
- TOPAZ showed benefits of early treatment suggesting potential in Type 1 patients

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

ScholarRock

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

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

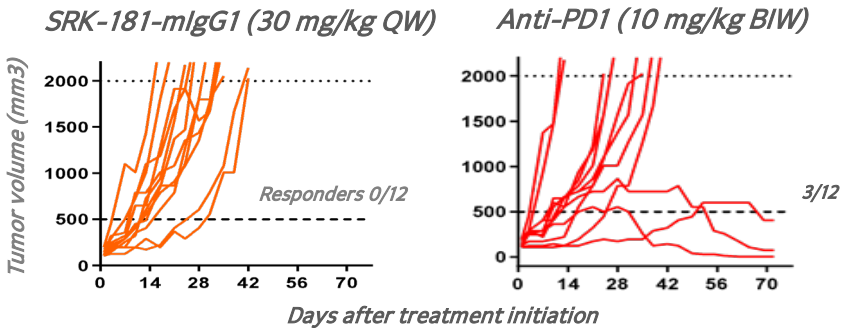
	SRK-181*	Bifunctional TGFβ/CPI	ALK5 Inhibitor	Nonselective TGFβ antibody
Selectivity for TGFβ1: potential for wider therapeutic window and improved safety	✓	X	X	X
Ability to combine with any anti-PD-(L)1	✓	X	✓	✓
Ability to optimize dosing of each component of combination therapy	✓	X	✓	✓
Activity spatially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

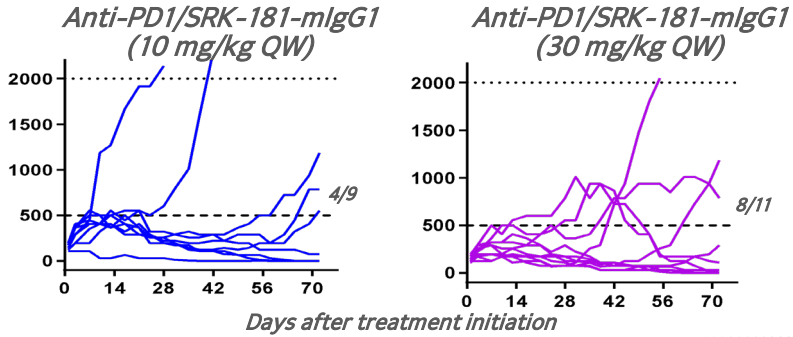
TGFβ1 Blockade with SRK-181-mIgG1 Rendered Preclinical Tumor Models Susceptible to Anti-PD1 Therapy

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

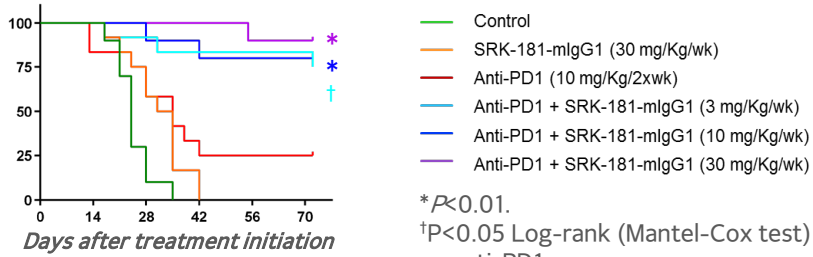
Tumor Regression: Monotherapy



Tumor Regression: Combination Therapy



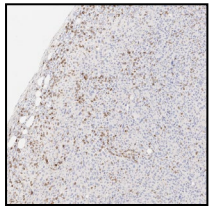
Survival Benefit



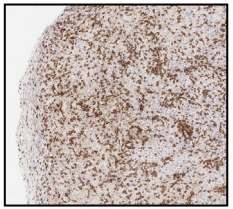
*P<0.01.
†P<0.05 Log-rank (Mantel-Cox test) vs anti-PD1.

Overcoming immune exclusion

Anti-PD1



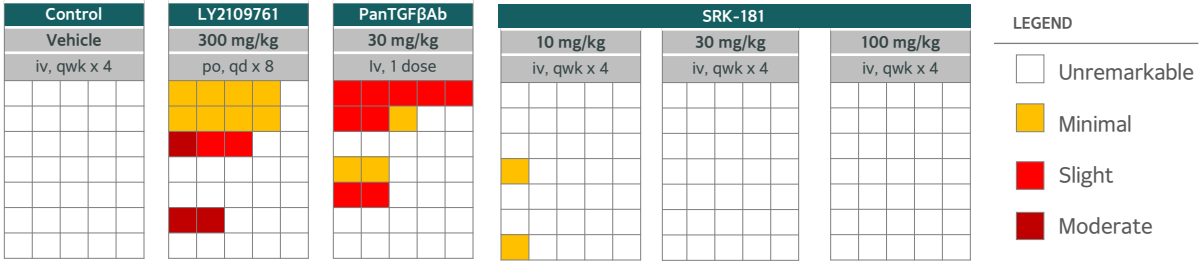
Anti-PD1/ SRK-181-mIgG1 led to influx of CD8+ cells in preclinical bladder tumor model



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 Isoform Specificity of SRK-181 Improved Preclinical Toxicity Profile

Microscopic observations in heart
Valvulopathy
Atrium—Mixed cell infiltrate
Myocardium—Degeneration/necrosis
Myocardium—Hemorrhage
Myocardium—Mixed cell infiltrate, base
Coronary artery—Necrosis with inflammation
Cardiomyocyte—Necrosis/inflammatory cell infiltrate



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

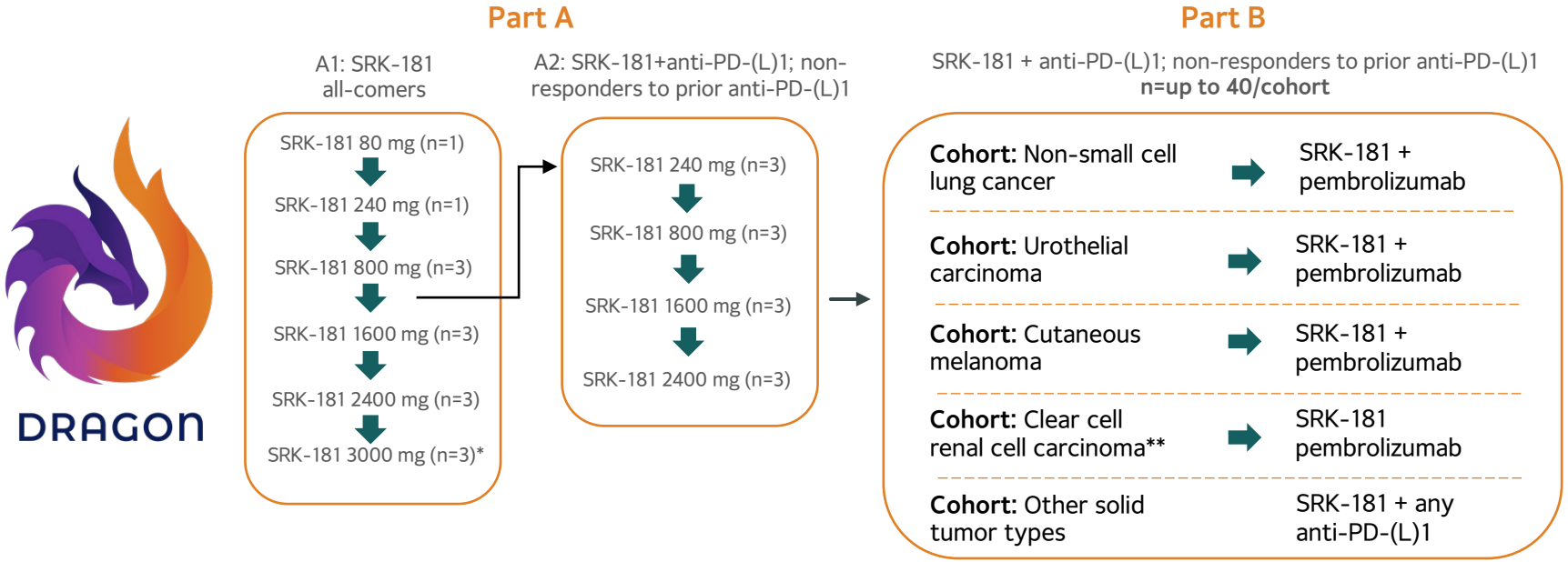
4-week GLP toxicology studies:

- 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.

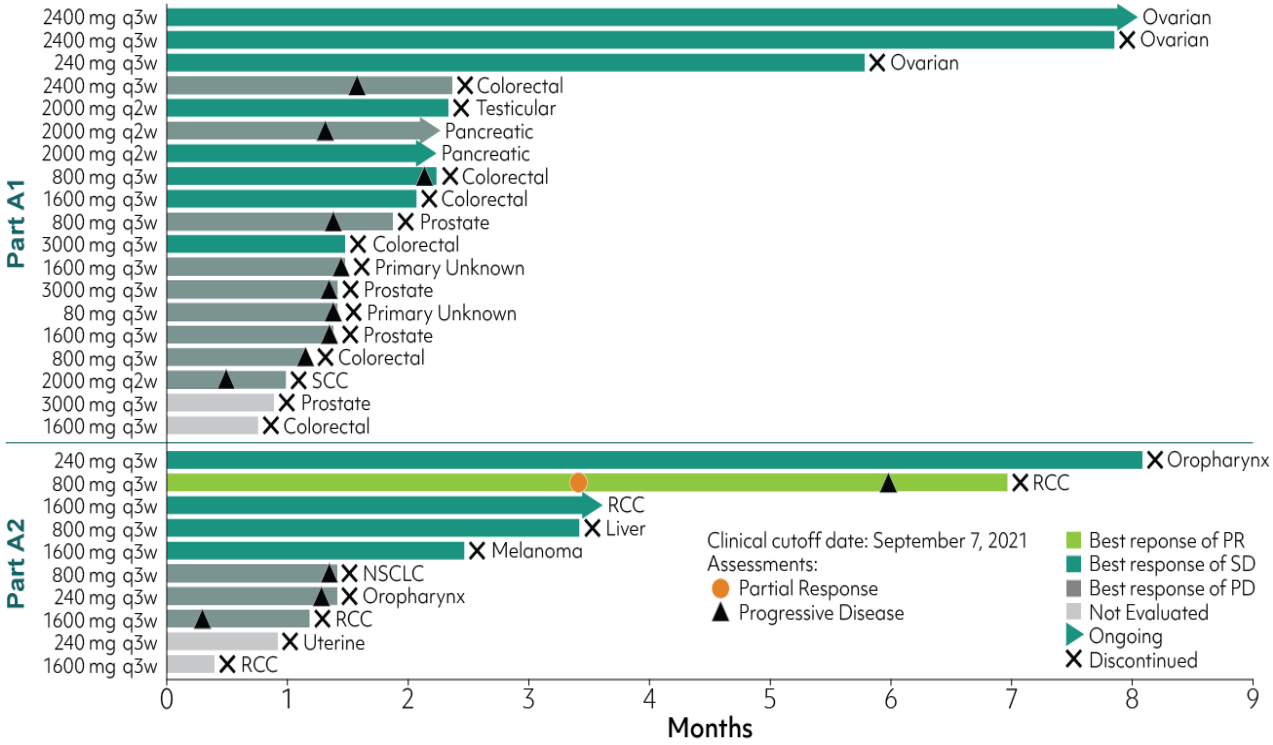
DRAGON Phase 1 POC Trial to Evaluate SRK-181's Ability to Overcome Primary Resistance to Checkpoint Inhibitors



Note: In Part A, SRK-181 is administered q3w, with the exception of a 2000 mg q2w cohort in Part A1. In Part B, SRK-181 is administered at 1500 mg q3w for combination with anti-PD-(L)1 therapy dosed q3w (or at 1000 mg q2w for combination with anti-PD-[L]1 therapy dosed q2w)
* 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: 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.

Biomarker Strategies Employed in DRAGON Trial

Multiple tissue-based and circulating biomarker analyses to be evaluated in DRAGON study

Immunophenotyping
Assessment of immune landscape

Examples:

- Histochemical characterization tumor immune contexture (e.g. CD8+)
  - Classification of inflamed, excluded or immune desert tumors and tumor nests
  - Ability of SRK-181 to overcome tumor immune exclusion
- Analysis of immune response markers (e.g. PD-L1)
- Changes to intra-tumoral and/or circulating immune cell contexture (MDSC)

TGFβ1 pathway evaluation
Assessment of signaling pathway

- Show evidence of the SRK-181 target engagement
  - e.g. circulating TGFβ1 levels
- TGFβ pathway modulation:
  - e.g. Histochemical analysis of pSMAD
  - e.g. RNA based TGFβ gene signatures and pathway analyses

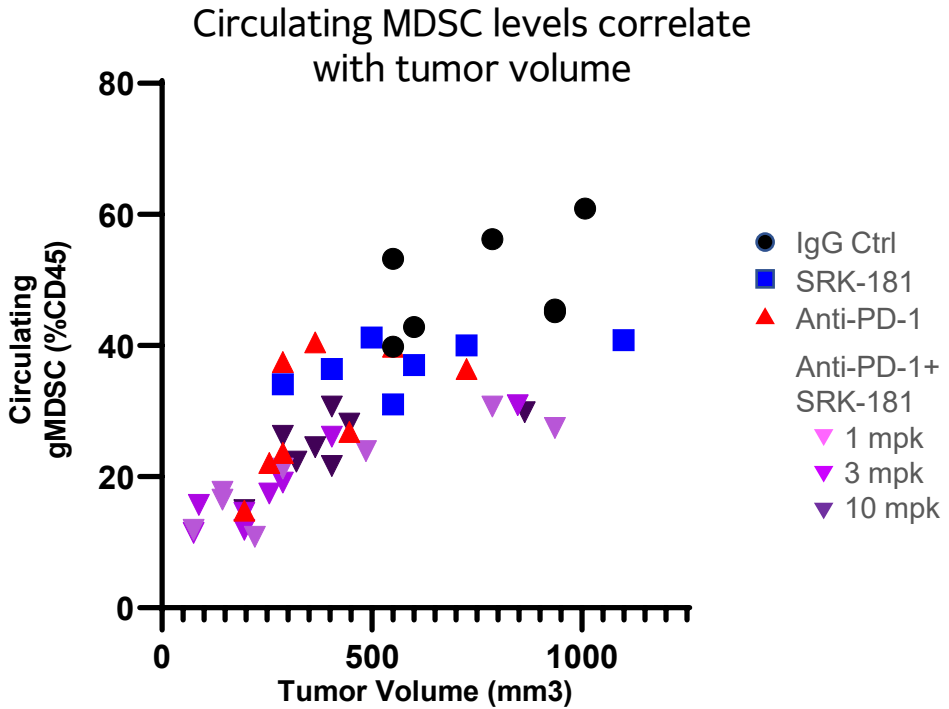
Preclinical data provide scientific rationale to evaluate peripheral samples for evidence of SRK-181 activity

Immunophenotyping
Assessment of immune landscape

Measurement of MDSCs in circulation may provide indirect evidence of drug action on the tumor

- Myeloid-derived suppressor cells (MDSCs) have immune suppressive functions
- SRK-181 plus anti-PD1 combination drive MDSC levels down significantly in the tumor microenvironment
- Reductions in circulating MDSC levels correlate with reduced tumor volume following SRK-181 and anti-PD1 treatment in MBT-2 tumor model

Both tumoral and circulatory MDSC are being evaluated in the DRAGON study



MBT-2 bladder tumor model IgG, anti-PD-1 and SRK-181-mIgG1 dosed d1, d7
Analysis on day 10

New Horizons in TGFβ Selectivity

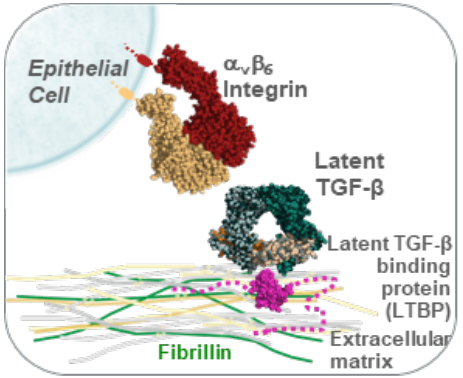
ScholarRock

Selectively Targeting Large Latent Complexes To Achieve Context-Dependent TGFβ1 Inhibition

- Large latent complexes present TGFβ1 though covalent interaction with "presenting molecules" which are cell-type specific
  - LTBP1 and LTBP3 present TGFβ in connective tissue
  - GARP and LRRC33 present TGFβ on the cell surface of immune cells
- Antibodies that *selectively* block TGFβ1 activation in different contexts may allow fine-tuning of therapeutic index
  - LTBP-selective targeting for fibrosis
  - GARP/LLRC33-selective targeting for immunomodulation
- Scholar Rock has identified a portfolio of antibodies that selectively bind TGFβ1 in a context dependent manner

Fibrotic Tissue

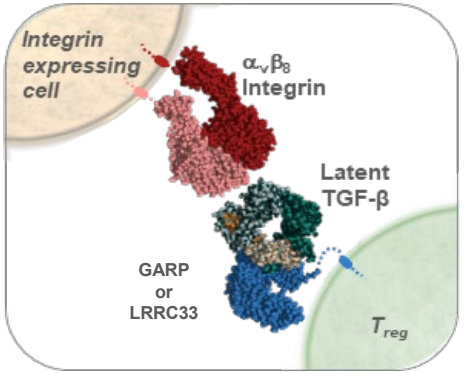
LTBP1 and LTBP3 present TGFβ1 in connective tissue



Immune Cells

GARP presents TGFβ1 on Tregs

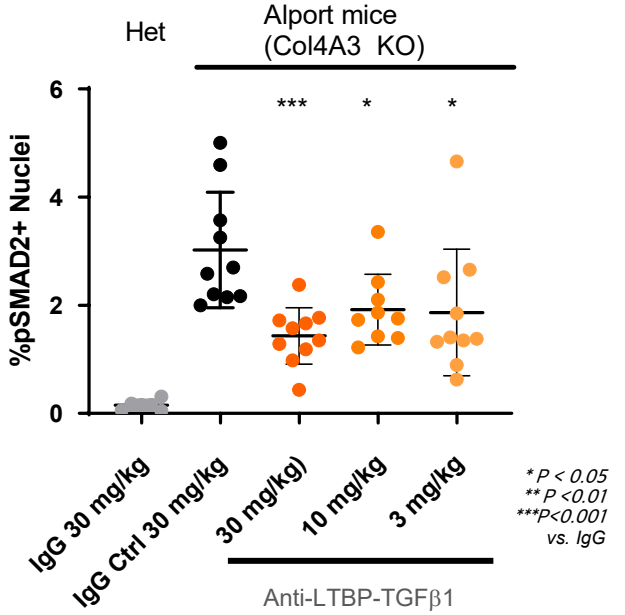
LRRC33 presents TGFβ1 on macrophages



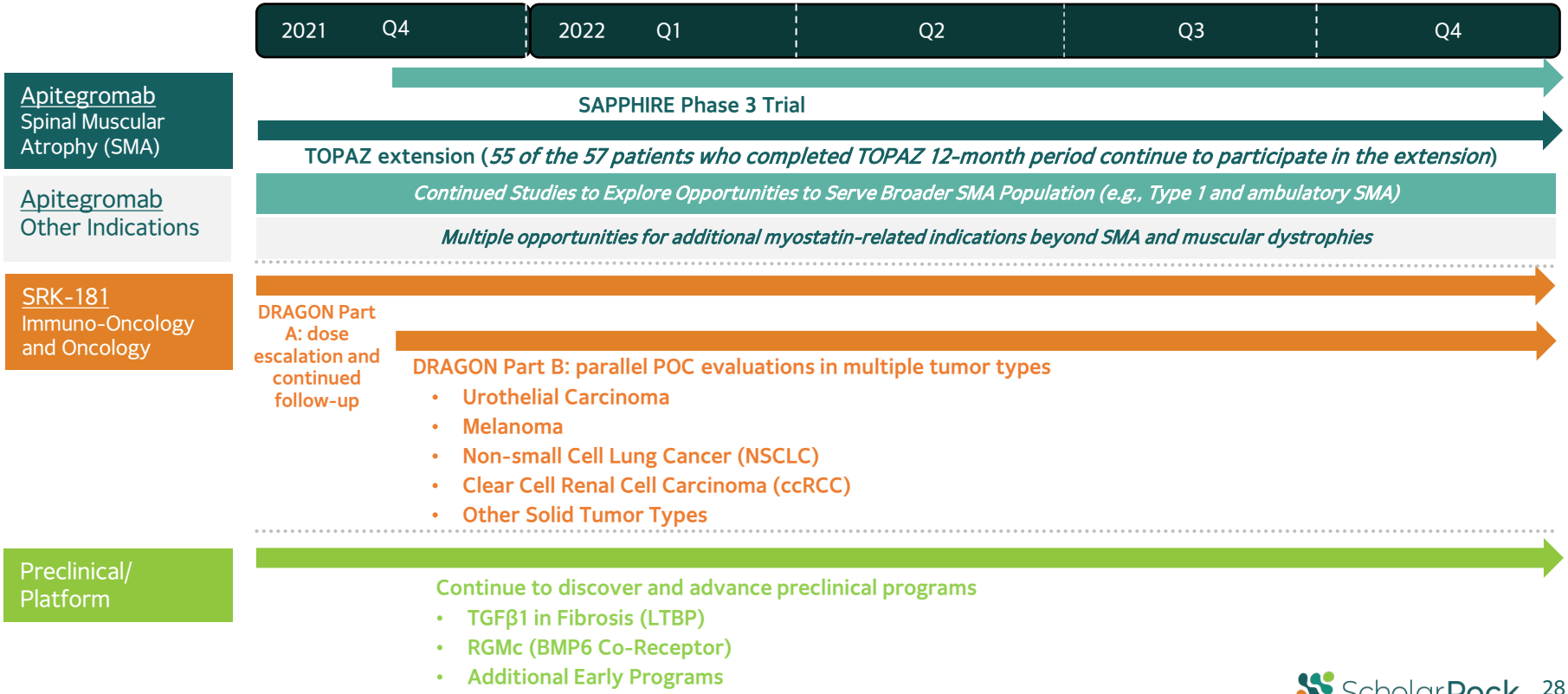
Specificity for LTBP-Selective Context Maintains Anti-Fibrotic Activity

- Antifibrotic efficacy and safety demonstrated in multiple rodent models of kidney fibrosis with context selective LTBP-TGFβ1 antibody
- LTBP-selective inhibition is as effective as context-independent inhibition suggesting that LTBP-drive TGFβ1 is driving fibrosis
- Rat adenine-induced diet model:
  - Reduction of fibrosis observed via decrease in collagen and hydroxyproline staining
  - Improved kidney function observed via reduction of plasma BUN and creatinine
  - Significant reduction in multiple TGFβ related pro-fibrotic gene expression
- Mouse model of Alport's Disease (*Col4A3*$^{-/-}$):
  - Suppression of SMAD2 phosphorylation; indicative of inhibition of TGFβ signaling

Anti-LTBP-TGFβ1 suppresses TGFβ1 signaling in Alport mouse kidney



Portfolio Spanning All Stages of Discovery and Development



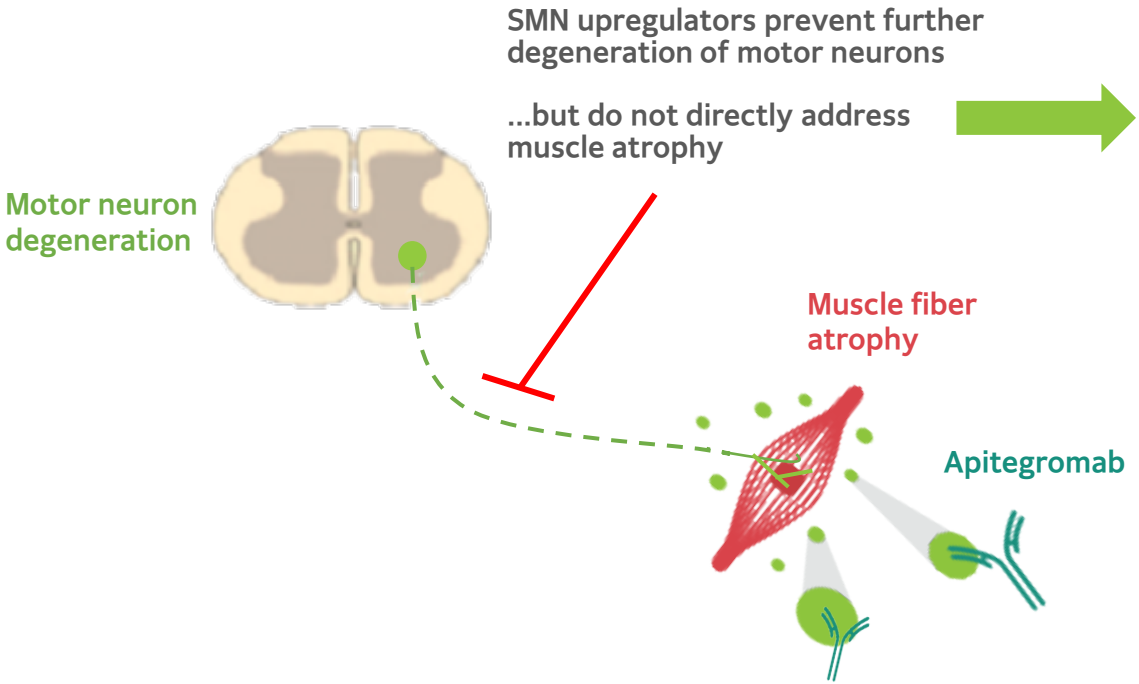
Appendix

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

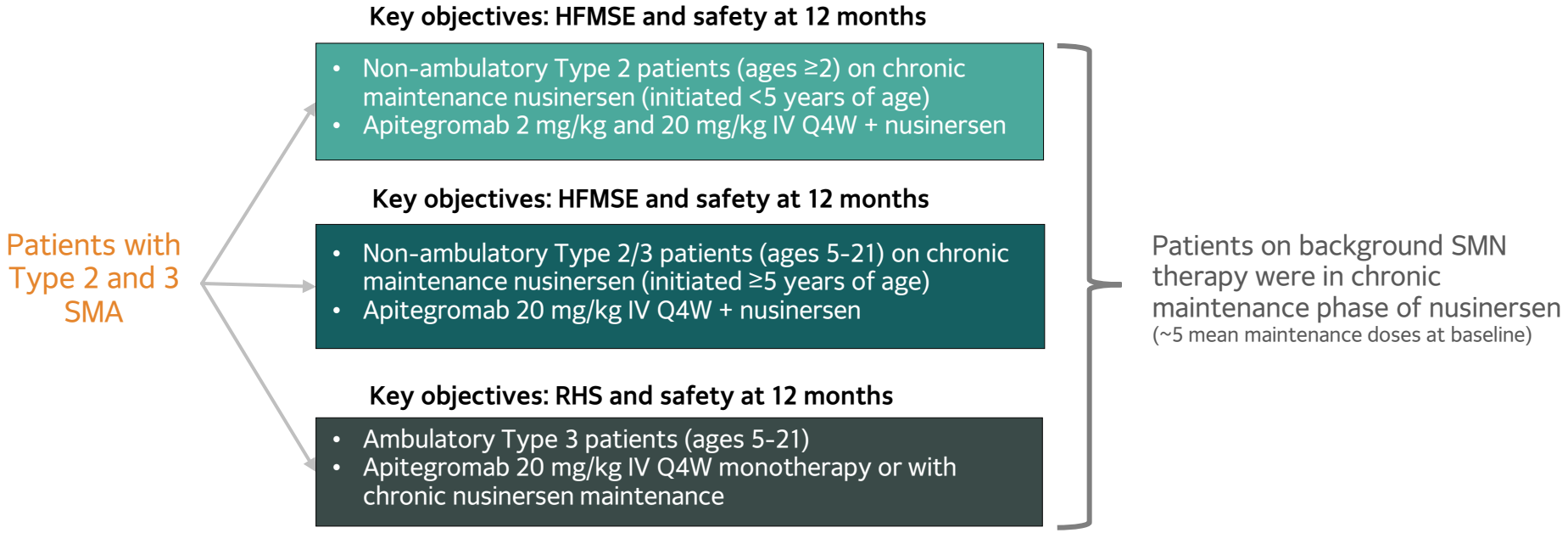


Apitegromab is a muscle-directed approach aimed at improving motor function

- 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

Apitegromab Phase 2 Trial Design



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

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

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)

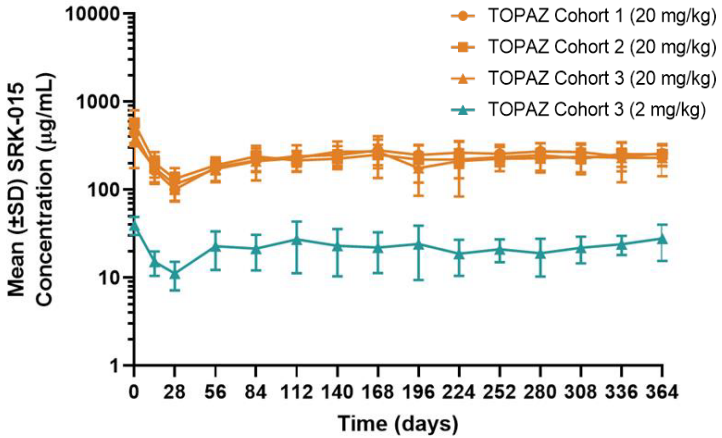
Majority maintained or improved

- 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

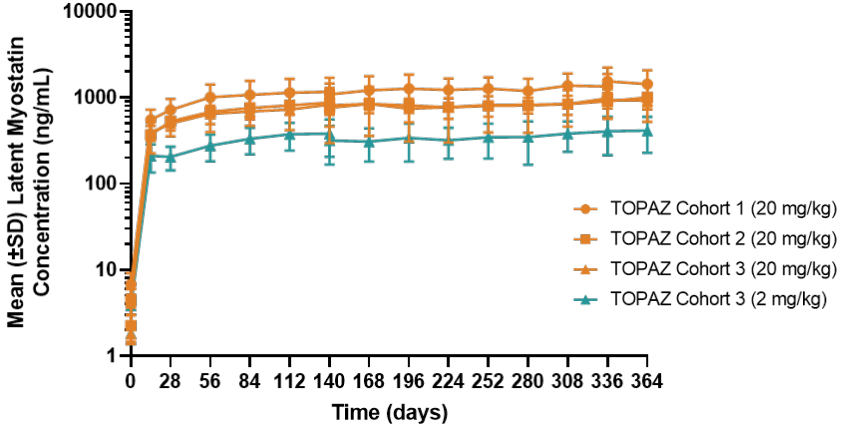
Pharmacokinetic and Pharmacodynamic Data are Supportive of Clinically Observed Effects

Pharmacokinetics* (PK)



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

Pharmacodynamics (PD)



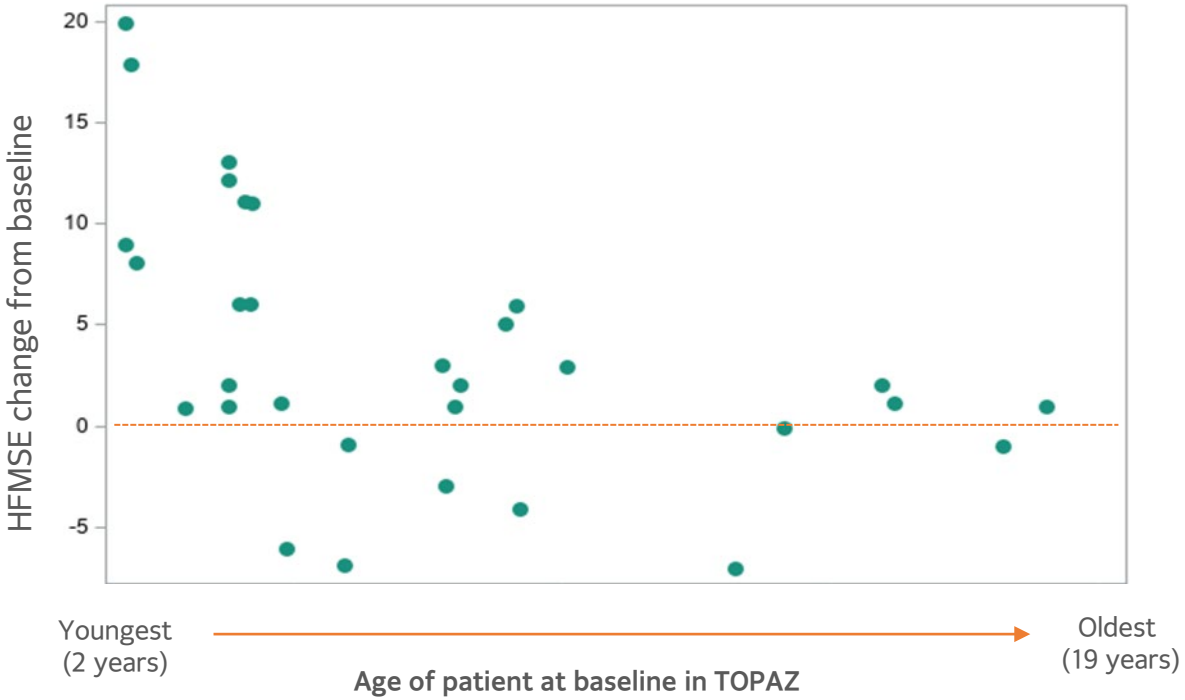
- Both 2 mg/kg and 20 mg/kg doses yielded high levels of target engagement (>100-fold increase from baseline)
- 20 mg/kg dose offers relatively higher magnitude of target engagement than 2 mg/kg dose

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

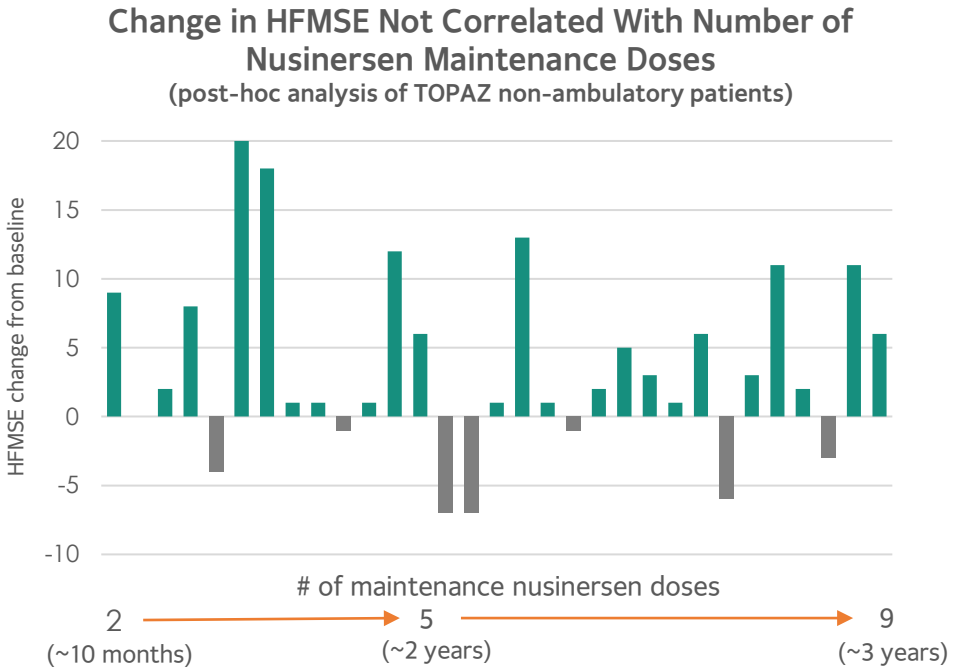
Data on file. Scholar Rock, Inc. Cambridge, MA

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



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)

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

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

Following 12 months of apitegromab treatment…

Sitting without support

Hands & knees crawling

Standing with assistance

Walking with assistance

Standing alone

Walking alone

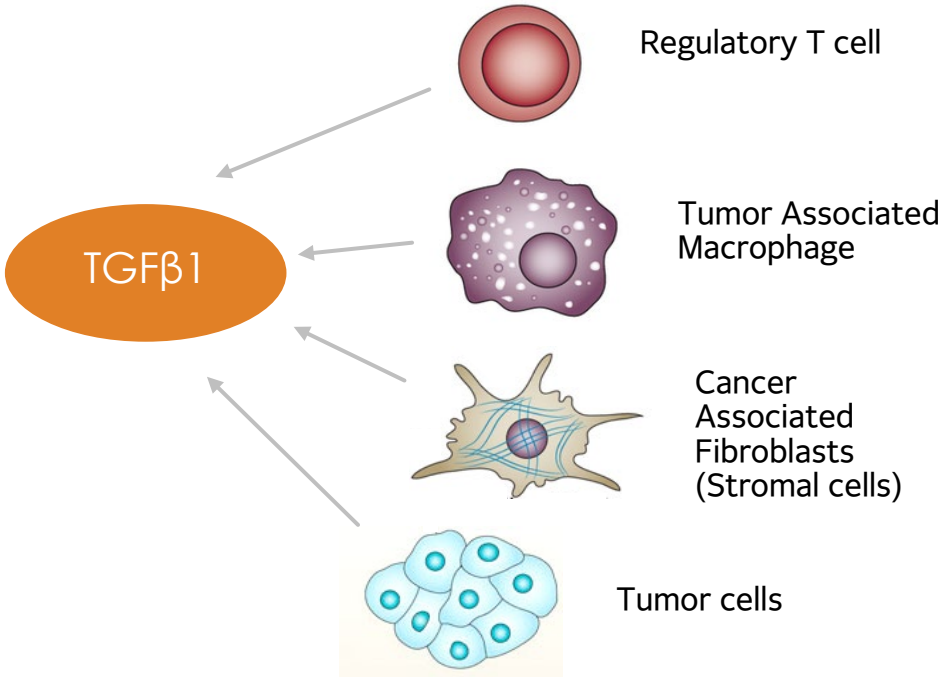
WHO motor milestone analysis included all patients who completed the 12-month treatment period, including 4 patients who missed 3 doses of apitegromab due to COVID-19-related site access restrictions. Median baseline score for both non-ambulatory cohorts was 1.0.

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.

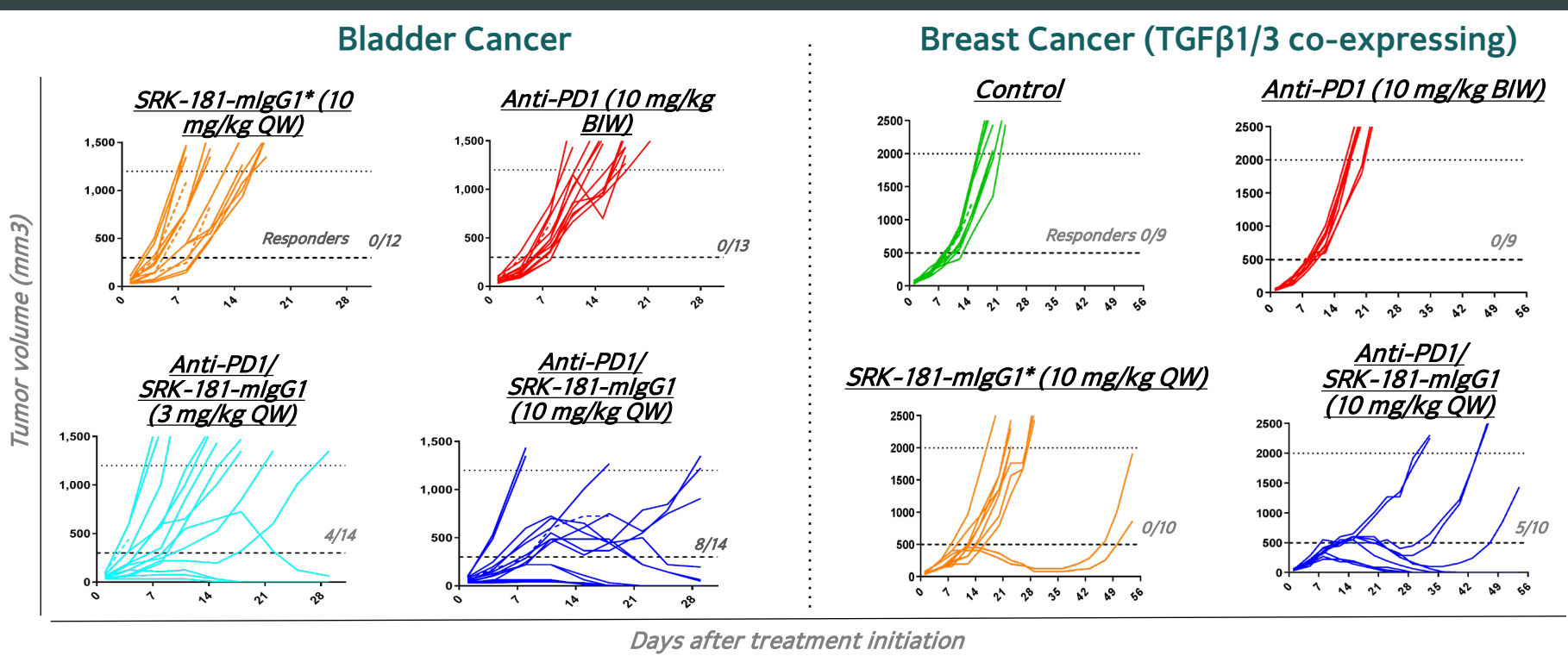
Inhibition of TGFβ1: Multipronged Approach for Immuno-Oncology

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

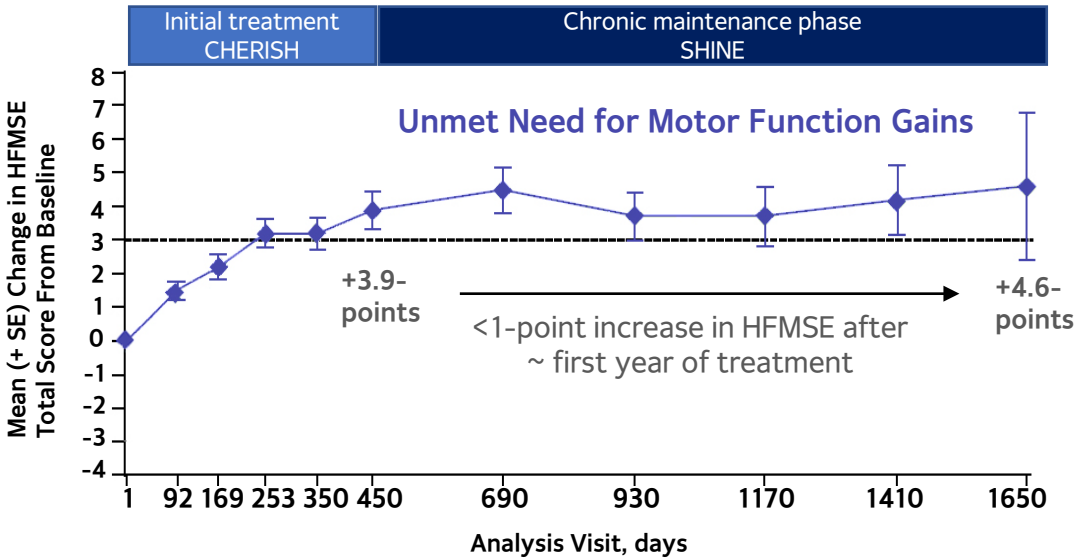


Preclinical data published in *Science Translational Medicine*. Martin CJ, et al. *Sci Transl Med*. 2020 Mar 25;12(536):eaay8456. https://scholarrock.com/platform/publications/.

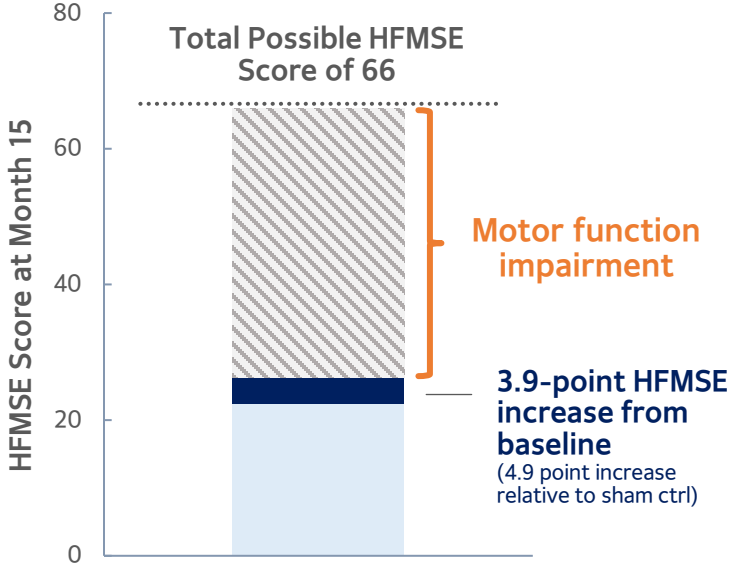
**SRK-181-mIgG1 is the murine version of SRK-181; responder defined as tumor size <25% endpoint volume at study end.*

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…

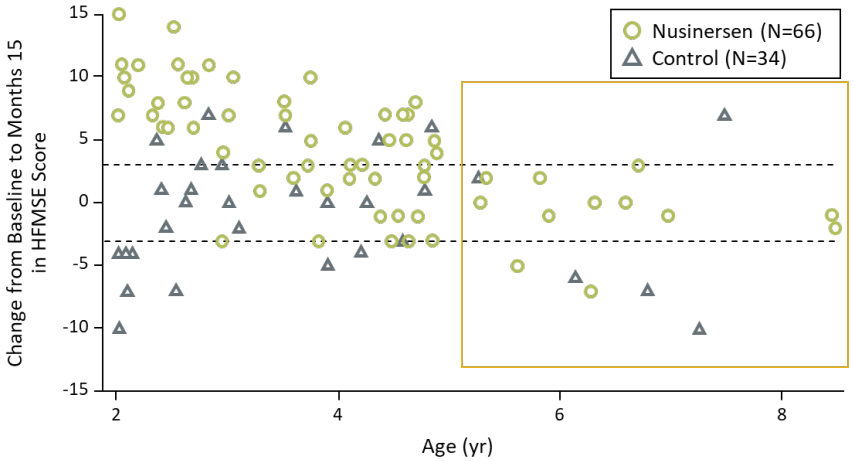


Mean improvement in HFMSE experienced in nusinersen Phase 3 CHERISH trial

"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*

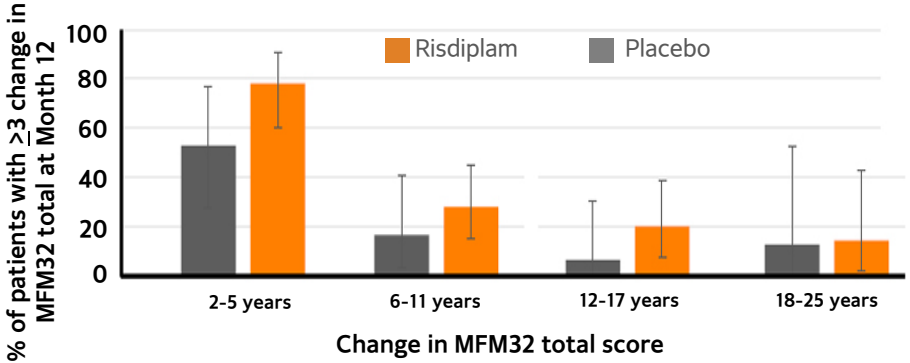
Nusinersen CHERISH Trial in Later-Onset SMA†



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

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

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]

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

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

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

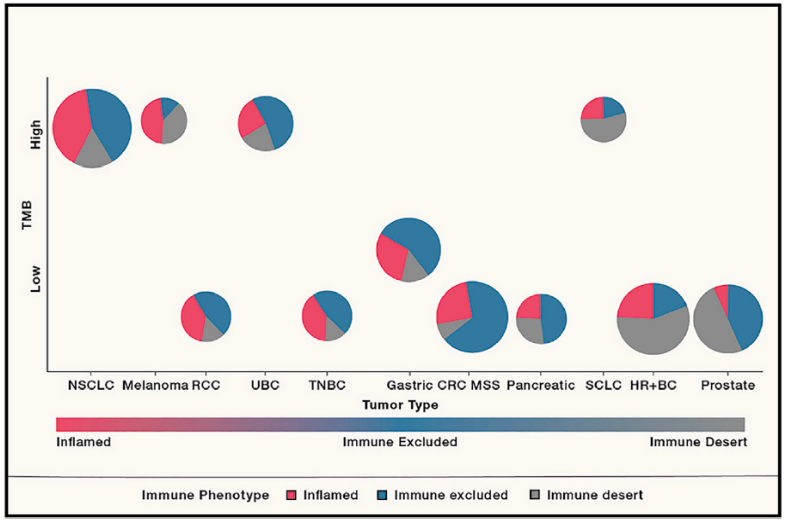
June 2019: *"Merck to Acquire Tilos Therapeutics: Merck Gains Portfolio of Investigational Antibodies Modulating TGFβ"*

- $773 million total potential deal value

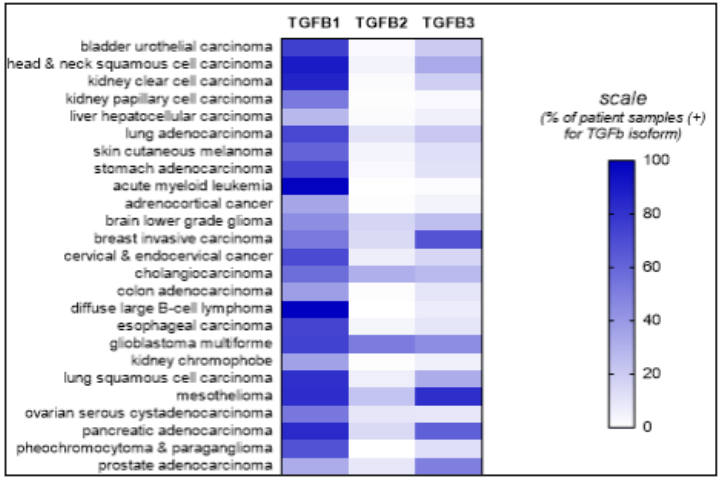
August 2020: *"Bristol Myers Squibb Enters Agreement to Acquire Forbius TGF-beta Program"*

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

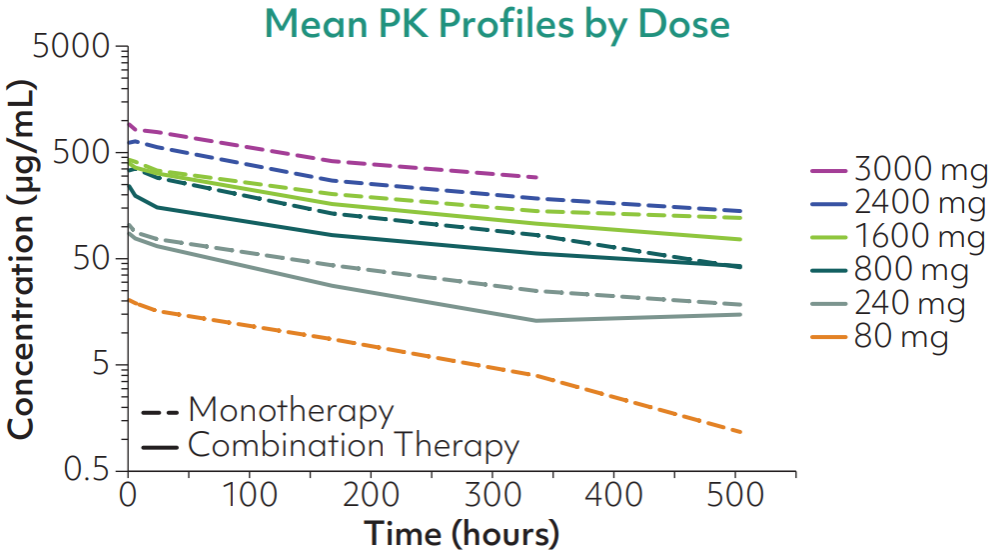
†Priti H, et al. Top 10 challenges in cancer immunotherapy. *Immunity.* 2020 Jan 14:52(1):17-35. https://doi.org/10.1016/j.immuni.2019.12.011.
*Source: National Cancer Institute - Cancer Genome Atlas Program.

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