



Deep Insights, Impactful Medicines

November 2020



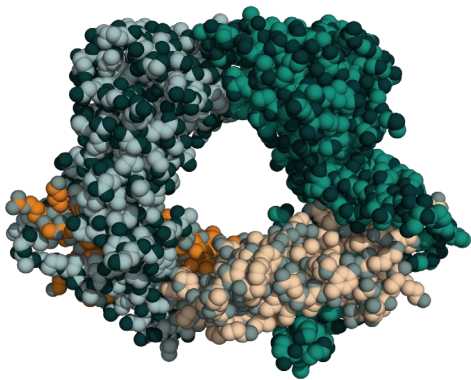
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Various statements in this presentation concerning the future expectations, plans and prospects of Scholar Rock, Inc. ("Scholar Rock"), including without limitation, Scholar Rock's expectations regarding its strategy, its product candidate selection and development timing, including timing for the initiation of and reporting results from its clinical trials for its product candidates, its disease indication selection and timing for such selection, the ability of apitegromab (SRK-015) to affect the treatment of patients suffering from Spinal Muscular Atrophy (SMA) either as a monotherapy or in conjunction with the current standard of care, and the ability of SRK-181 to affect the treatment of cancer patients in a manner consistent with preclinical data constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. The use of words such as "may," "might," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "target," "project," "intend," "future," "potential," or "continue," and other similar expressions are intended to identify such forward-looking statements. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including, without limitation, Scholar Rock's ability to provide the financial support and resources necessary to identify and develop multiple product candidates on the expected timeline, competition from others developing products for similar uses, the preliminary nature of interim clinical data, Scholar Rock's ability to obtain, maintain and protect its intellectual property, Scholar Rock's dependence on third parties for development and manufacture of product candidates including to supply any clinical trials, and Scholar Rock's ability to manage expenses and to obtain additional funding when needed to support its business activities and establish and maintain strategic business alliances and new business initiatives as well as those risks more fully discussed in the section entitled "Risk Factors" in the Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, which is on file with the Securities and Exchange Commission, as well as discussions of potential risks, uncertainties, and other important factors in Scholar Rock's subsequent filings with the Securities and Exchange Commission. Any forward-looking statements represent Scholar Rock's views only as of today and should not be relied upon as representing its views as of any subsequent date. Scholar Rock explicitly disclaims any obligation to update any forward-looking statements unless required by law.

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

Scholar Rock's Target

Growth Factor Precursor (Latent Form)



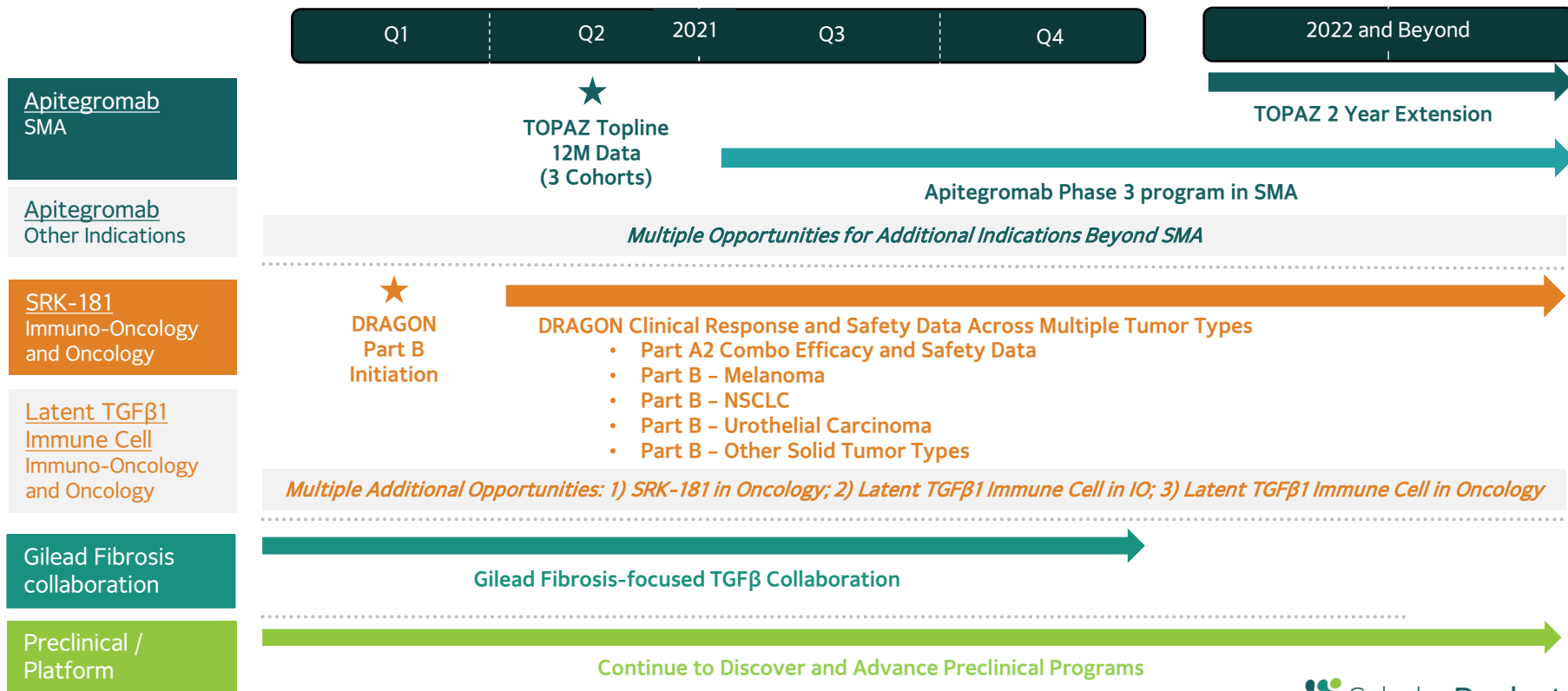
Scholar Rock's R&D Platform

Transform Medical Practice

- Pursue important targets with well-validated biology but are difficult to drug
- Apply revolutionary approach to tough targets
 - Leverage deep insights into structure and function
 - Engineer antibodies for exquisite selectivity

Apitegromab interim analysis data provides first demonstration of the therapeutic potential of inhibiting the latent forms of growth factors

Differentiated Pipeline with a Series of Anticipated Milestones

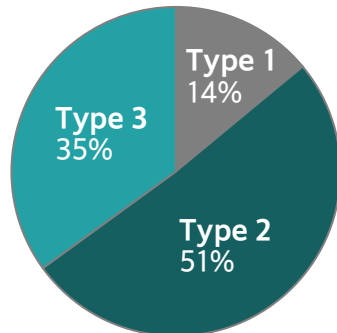


Significant Market Opportunities for Lead Product Candidates

Apitegromab in SMA

*Muscle-directed therapies needed to complement disease-stabilizing benefits of SMN upregulators**

Overall prevalence of patients with SMA in the U.S. and Europe: 30,000-35,000



Approved SMN Upregulators

SPINRAZA
(nusinersen) injection 12 mg/5 mL
(\$2B+ LTM sales)

Biogen

zolgensma
(onasemnogene abeparvovec-xioi)
suspension for intravenous infusion
(\$850M+ LTM sales)

NOVARTIS

Evrysdi
(risdiplam) oral suspension
(FDA approved August 2020)

Genentech
A Member of the Roche Group

SRK-181 in Immuno-Oncology

Significant unmet potential to increase response to checkpoint inhibitors

~20% of patients respond to checkpoint inhibitors (CPIs)[†]



Current checkpoint inhibitor market: \$25B+*

Pfizer

Roche

SANOFI
REGENERON

EMD SERONO

MERCK

Bristol Myers Squibb

AstraZeneca

*Source: Company information, Wall Street research, Evaluate Pharma.

[†]Source: Carretero-Gonzalez A, et al. *Oncotarget*. 2018;9:8706-8715

ScholarRock 5

Apitegromab: Potential First Muscle-Directed Therapy for Spinal Muscular Atrophy



Next Era of SMA Treatment: Muscle-Directed Therapy

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

Type 1:

- Infant-onset
- Usually fatal without treatment

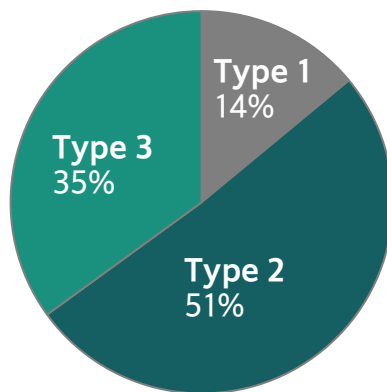
Type 2 and non-ambulatory Type 3:

- Later-onset but still early childhood
- Severe deficits in motor function
- SMN upregulators appear to primarily stabilize disease course

Ambulatory Type 3:

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

*Relative Prevalence Among
Patients Living With SMA*



*TOPAZ trial focuses on
Type 2 and Type 3 SMA*

Unmet need would be served by a therapy that:

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

Apitegromab Phase 2 Trial Design



	Ambulatory Patients (Revised Hammersmith Scale)	Non-Ambulatory Patients (Hammersmith Functional Motor Scale Expanded)	
	Cohort 1	Cohort 2	Cohort 3
Design	- N= 23; ages 5-21 - Open-label, single-arm 20 mg/kg apitegromab IV Q4W 12-month treatment period	- N= 15; ages 5-21 - Open-label, single-arm 20 mg/kg apitegromab IV Q4W 12-month treatment period	- N= 20; ages ≥ 2 - Double-blind, randomized (1:1) to 2 mg/kg or 20 mg/kg apitegromab IV Q4W 12-month treatment period
Patients	- Ambulatory Type 3 SMA - Two subgroups: - Receiving background nusinersen - Apitegromab monotherapy	- Type 2 or non-ambulatory Type 3 SMA - Receiving background nusinersen	- Type 2 SMA - Receiving background nusinersen (initiated before age 5)
Primary Objectives	- Safety - Mean change from baseline in RHS	- Safety - Mean change from baseline in HFMSE	- Safety - Mean change from baseline in HFMSE

Evaluate potential of apitegromab in improving motor function

Baseline Characteristics



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

*data not available for all patients

**patient who discontinued study for reasons unrelated to study drug

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

TOPAZ Interim Analysis Results Demonstrate Proof-of-Concept

Multiple lines of evidence supporting the potential clinical effect of apitegromab

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

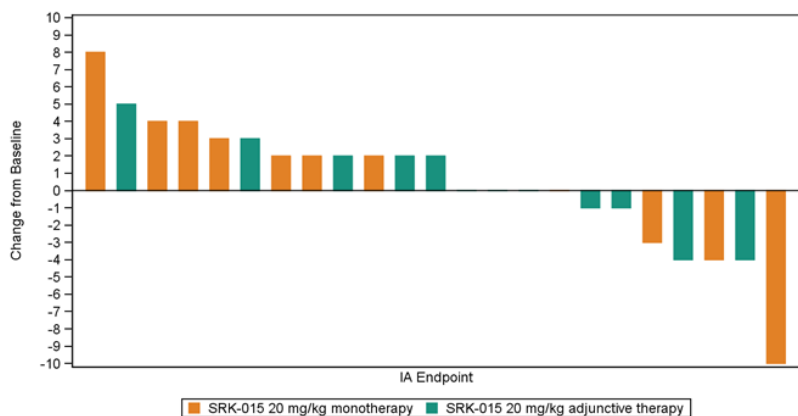
- ✓ **Mean improvements from baseline in HFMSE/RHS observed in each of the 3 cohorts**
 - 67% of total patients achieved ≥1-point improvement in Hammersmith scores
- ✓ **Substantial proportion of patients in each cohort attained ≥3-point improvement in HFMSE/RHS**
 - High bar and uncommon to observe in any given patient
 - 35% of total patients achieved ≥3-point improvement in Hammersmith scores
- ✓ **Dose response demonstrated in Cohort 3 (*randomized, double-blind, parallel arm design*)**
 - Greater improvements in HFMSE scores for high-dose arm across evaluated timepoints
 - Supportive PK/PD results; high dose led to higher drug exposure and target engagement

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

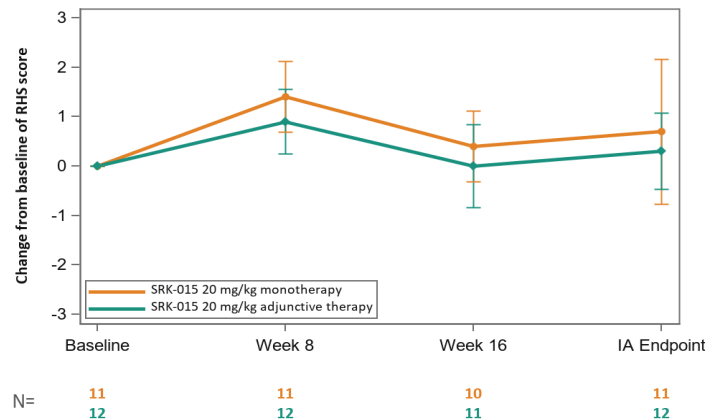
Cohort 1: Improvement in RHS Observed with Both Apitegromab Monotherapy and as Add-on to Background Nusinersen

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

Individual RHS responses



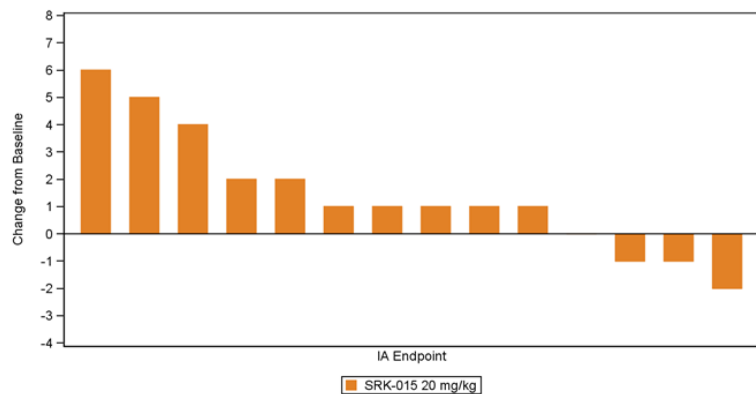
Mean ($\pm$ SEM) change from baseline in RHS scores



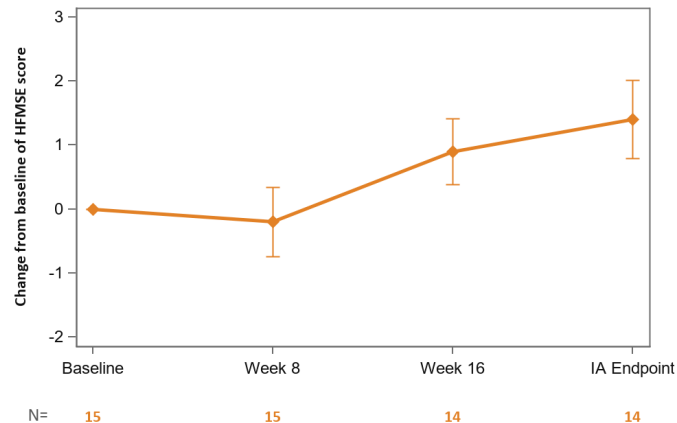
Cohort 2: Meaningful and Consistent Improvements in HFMSE Observed in Type 2 and Non-Ambulatory Type 3 SMA

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

Individual HFMSE responses



Mean ($\pm$ SEM) change from baseline in HFMSE scores

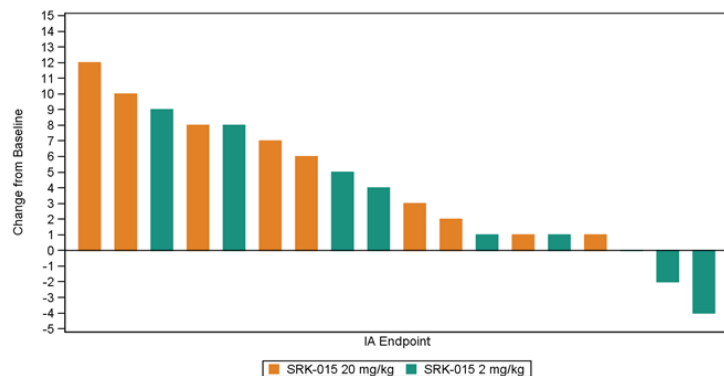


Cohort 3: Apitegromab High Dose Showed Substantially Greater Improvements in HFMSE scores Than Low Dose

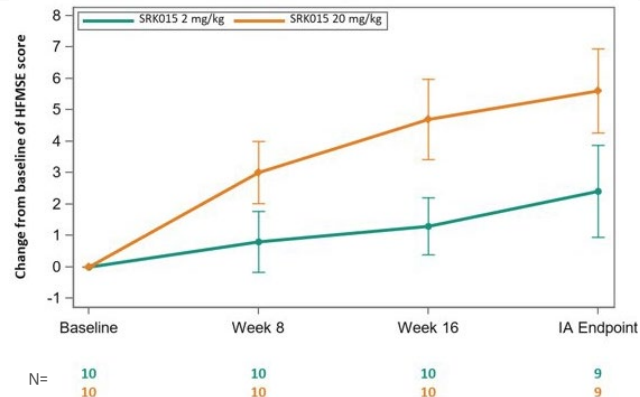
Cohort 3 has a randomized, double-blind, parallel arm design embedded within TOPAZ

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

Individual HFMSE responses

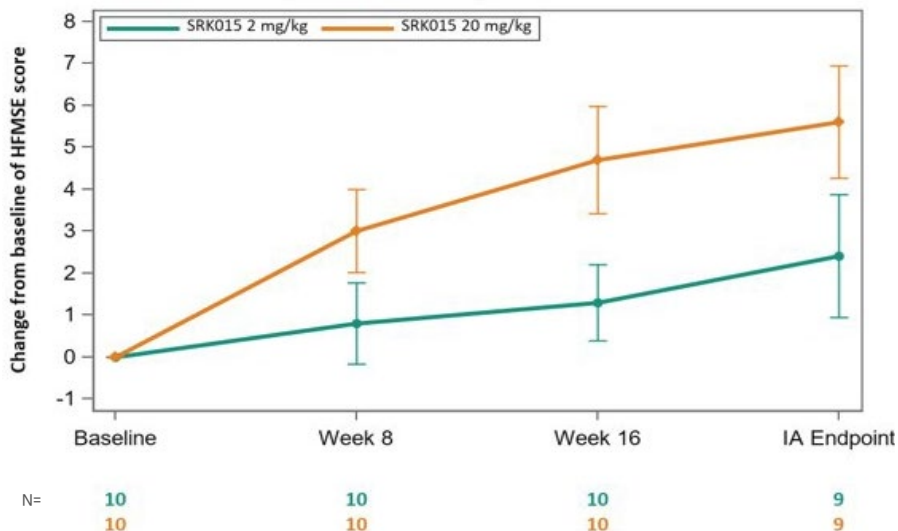


Mean ($\pm$ SEM) change from baseline in HFMSE scores



Cohort 3: Time Course Data Supportive of Dose Response

Mean ($\pm$ SEM) change from baseline in HFMSE scores

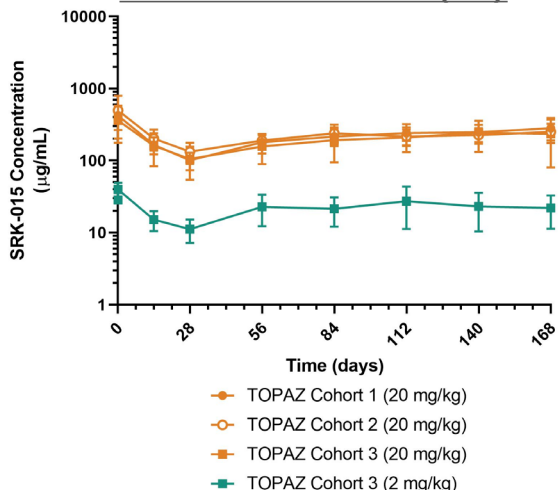


- High-dose arm outperformed low-dose arm numerically across the timepoints
- Plateau in improvement appears to not yet have been reached at the 6-month interim analysis timepoint
- 12-month and extension data enable evaluating the potential for durability of effect and for further motor function gains

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

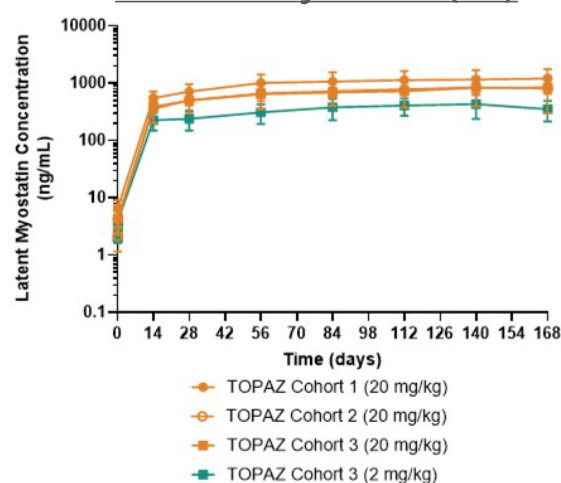
Pharmacokinetic and Pharmacodynamic Data are Supportive of Clinically Observed Dose Response

Pharmacokinetics* (PK)



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

Pharmacodynamics (PD)



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

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

*Starting at day 28, measures are pre-dose trough levels
Apitegromab = non-proprietary name for SRK-015
Data on file. Scholar Rock, Inc. Cambridge, MA

No Safety Signals Identified from Interim Analysis

Treatment-emergent adverse events (TEAEs)	Apitegromab 2 mg/kg dose (n=10)	Apitegromab 20 mg/kg dose (n=48)	Total (n=58)
Any TEAE	9 (90%)	40 (83.3%)	49 (84.5%)
Any Serious TEAE	0 (0.0%)	1 (2.1%)	1 (1.7%)
Any TEAE leading to study drug discontinuation	0 (0.0%)	1 (2.1%)	1 (1.7%)
Any Grade 3 (severe) or higher TEAE	0 (0.0%)	0 (0.0%)	0 (0.0%)

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

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

TOPAZ Interim Analysis Results Demonstrate Proof-of-Concept

1. Strength of study and evidence supporting the potential clinical effect of apitegromab

- **Cohorts 1 & 2 (open-label, single arm):**
 - HFMSE/RHS conduct standardized; assessors blind to prior scores
 - Natural history (even w/ nusinersen) suggests HFMSE/RHS scores usually stable or declining
 - Patients on nusinersen for avg ~2 years prior to enrollment; baselines more typical of natural history (Cohort 1 combo: RHS 51.3, Cohort 2: HFMSE 22.7)
 - Substantial % of patients attained ≥ 3 -pt increase in HFMSE/RHS; high bar and uncommon outcome
- **Cohort 3 (randomized, double-blind, parallel arm):**
 - High-dose arm showed greater improvements in HFMSE
 - Consistency across all timepoints
 - Supportive PK/PD results

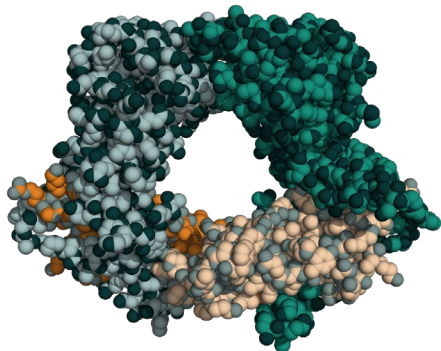
2. Apitegromab's broad and meaningful therapeutic potential in SMA

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

Unlocking the Potential of the Scholar Rock R&D Engine

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

Targeting the latent forms of growth factors



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

Emerging Insights

Demonstration of proof-of-concept for apitegromab in SMA

Validation of therapeutic potential for blocking the activation of latent myostatin with apitegromab

Validation of therapeutic potential in targeting latent forms of growth factors

Opportunities Beyond TOPAZ

- Broader exploration of SMA types, age range, and background SMN therapies
- Exploration of additional myostatin-related indications
- Antibodies against the latent forms of additional well-validated targets in oncology (e.g. SRK-181 program) and fibrosis
- Discovery platform to generate mAbs against other latent growth factors

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



Significant Recent 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 Castiglioni¹, Kobe Yuen¹, Yulei Wang¹, Edward E. Kadel III¹, Hartmut Koeppen¹, Jillian L. Astarita¹, Rafael Cubas¹, Suchit Jhunjhunwala¹, Romain Banchereau¹, Yagai Yang¹, Yinghui Guan¹, Cecile Chalouni¹, James Ziai¹, Yasin Şenbabaoğlu¹, Stephen Santoro¹, Daniel Sheinson¹, Jeffrey Hung¹, Jennifer M. Giltman¹, Andrew A. Pierce¹, Kathryn Mesh¹, Steve Lianoglou¹, Johannes Riegler¹, Richard A. D. Carano¹, Pontus Eriksson², Mattias Höglund², Loan Somarriva³, Daniel L. Halligan³, Michiel S. van der Heijden⁴, Yohann Loriot⁵, Jonathan E. Rosenberg⁶, Lawrence Fong⁷, Ira Mellman¹, Daniel S. Chen¹, Marjorie Green¹, Christina Derleth¹, Gregg D. Fine¹, Priti S. Hegde¹, Richard Bourgon¹ & Thomas Powles⁸

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

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

Article

NATURE REVIEWS | CLINICAL ONCOLOGY

TGFβ biology in cancer progression and immunotherapy

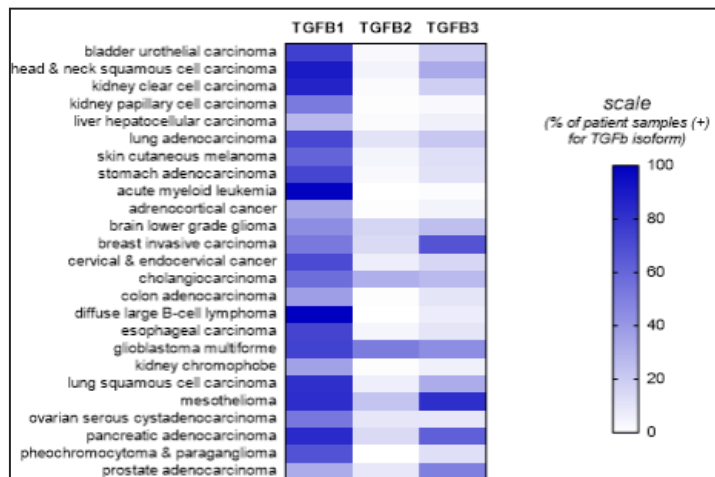
Rik Derynck^{1,2,3}, Shannon J. Turley⁴ and Rosemary J. Akhurst^{1,2,3}

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

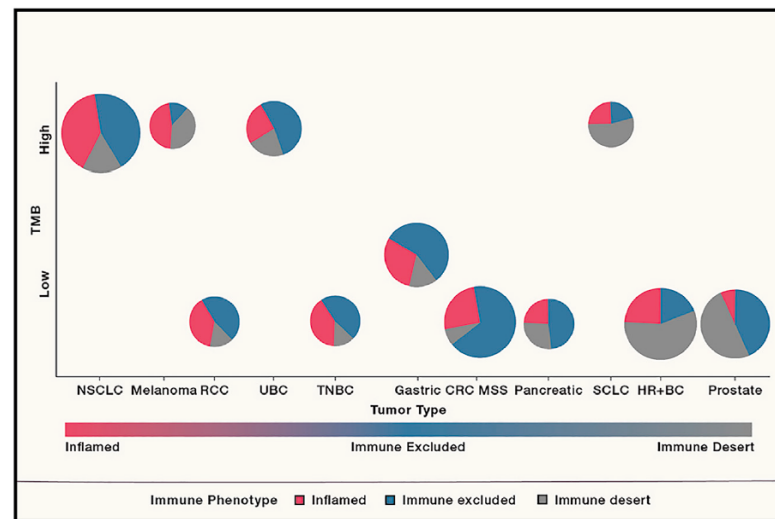
August 2020: *“Bristol Myers Squibb Enters Agreement to Acquire Forbuis TGF-beta Program”*

Broad Potential for TGF β Blockade Across Many Solid Tumors

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



Substantial % of solid tumors exhibit immune exclusion; only ~20% of patients respond to CPIs[†]



Human Tumor Analyses Reveal TGF β 1 as Most Likely Driver of TGF β Pathway Signaling in Cancers

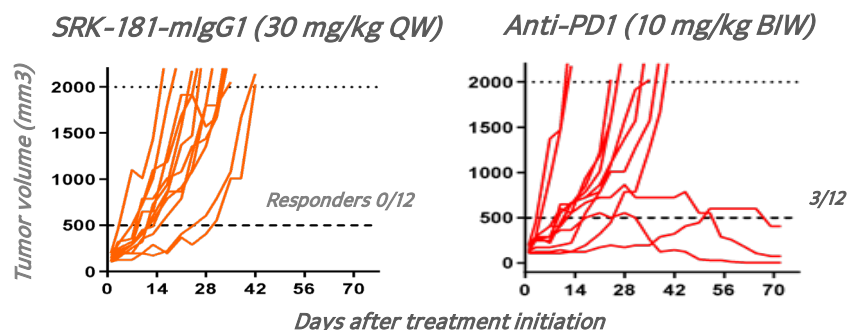
*Source: National Cancer Institute - Cancer Genome Atlas Program.

[†]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>.

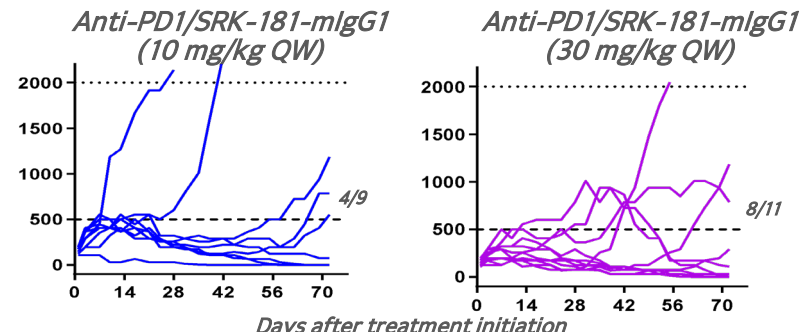
TGF β 1 Blockade with SRK-181-mIgG1 Rendered Preclinical Tumor Models Susceptible to Anti-PD1 Therapy

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

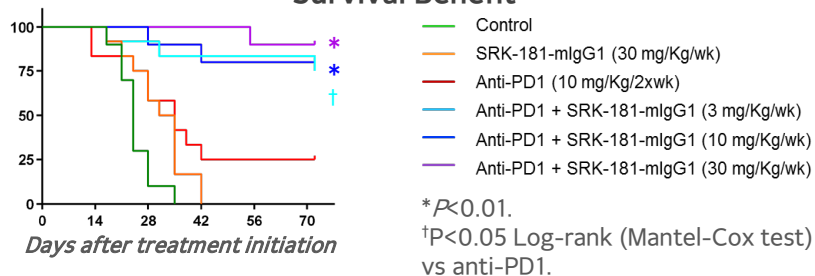
Tumor Regression: Monotherapy



Tumor Regression: Combination Therapy

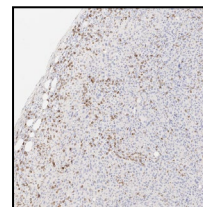


Survival Benefit

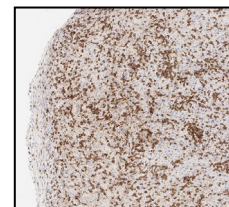


Overcoming immune exclusion

Anti-PD1

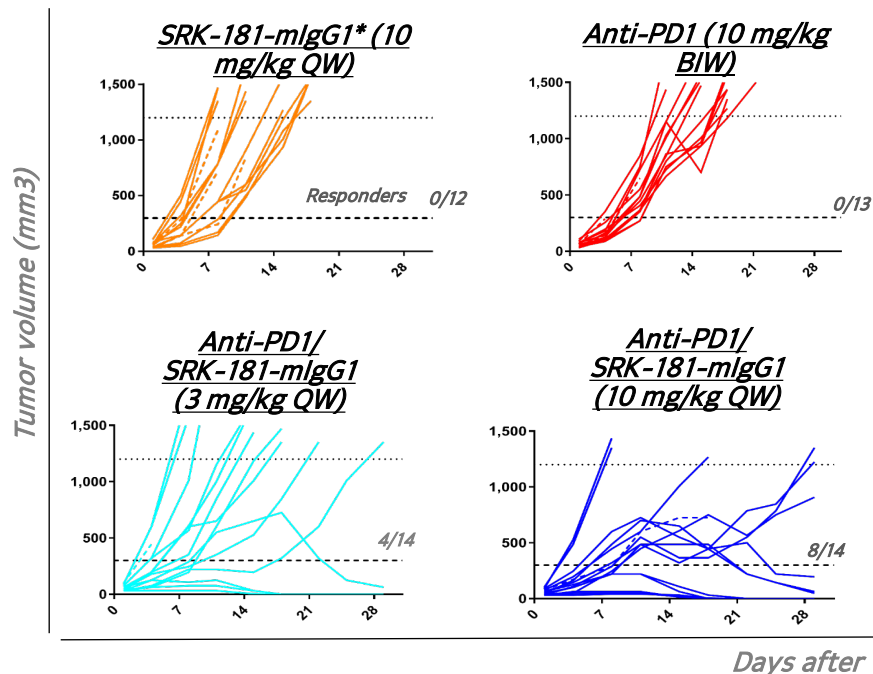


Anti-PD1/ SRK-181-mIgG1 led to influx of CD8+ cells in preclinical bladder tumor model

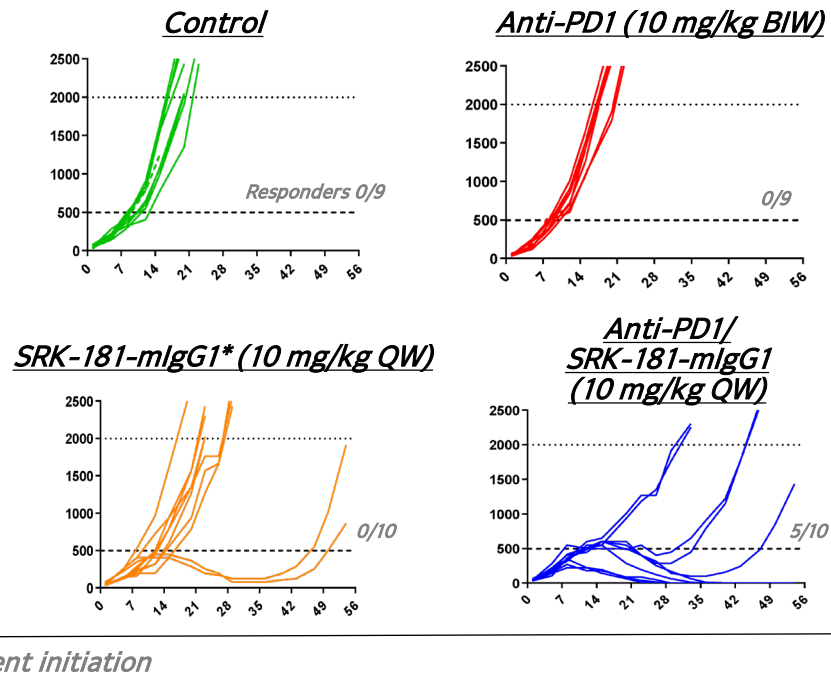


TGF β 1 Blockade with SRK-181-mIgG1 Rendered Preclinical Tumor Models Susceptible to Anti-PD1 Therapy

Bladder Cancer



Breast Cancer (TGF β 1/3 co-expressing)



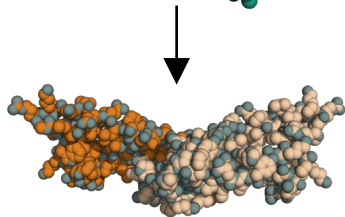
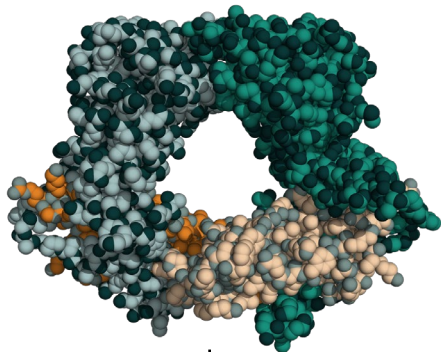
Preclinical data published in *Science Translational Medicine*. Martin CJ, et al. *Sci Transl Med*. 2020 Mar 25;12(536):eaay8456.

<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.

SRK-181: Unique TGF β 1-Selective Approach to Overcoming Checkpoint Inhibitor Resistance

Scholar Rock's Target SRK-181: Latent TGF β 1 Inhibitor



Traditional target:
“Mature” growth factor

- ✓ Inhibits TGF β 1 pathway - implicated in CPI resistance
- ✓ Highly selective targeting - avoids binding to latent TGF β 2 and TGF β 3 isoforms
- ✓ Aimed at increasing therapeutic window - potentially avoids toxicities associated with non-selective TGF β inhibition
- ✓ Therapeutic flexibility - pair with any CPI and optimize dosing of each component of combination therapy

TGFβ1 Isoform Specificity of SRK-181 Improved Preclinical Toxicity Profile

Microscopic observations in heart	Control	LY2109761	PanTGFβAb	SRK-181			LEGEND
	Vehicle	300 mg/kg	30 mg/kg	10 mg/kg	30 mg/kg	100 mg/kg	
	iv, qwk x 4	po, qd x 8	iv, 1 dose	iv, qwk x 4	iv, qwk x 4	iv, qwk x 4	Unremarkable
Valvulopathy							Minimal
Atrium—Mixed cell infiltrate							Slight
Myocardium—Degeneration/necrosis							Moderate
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:

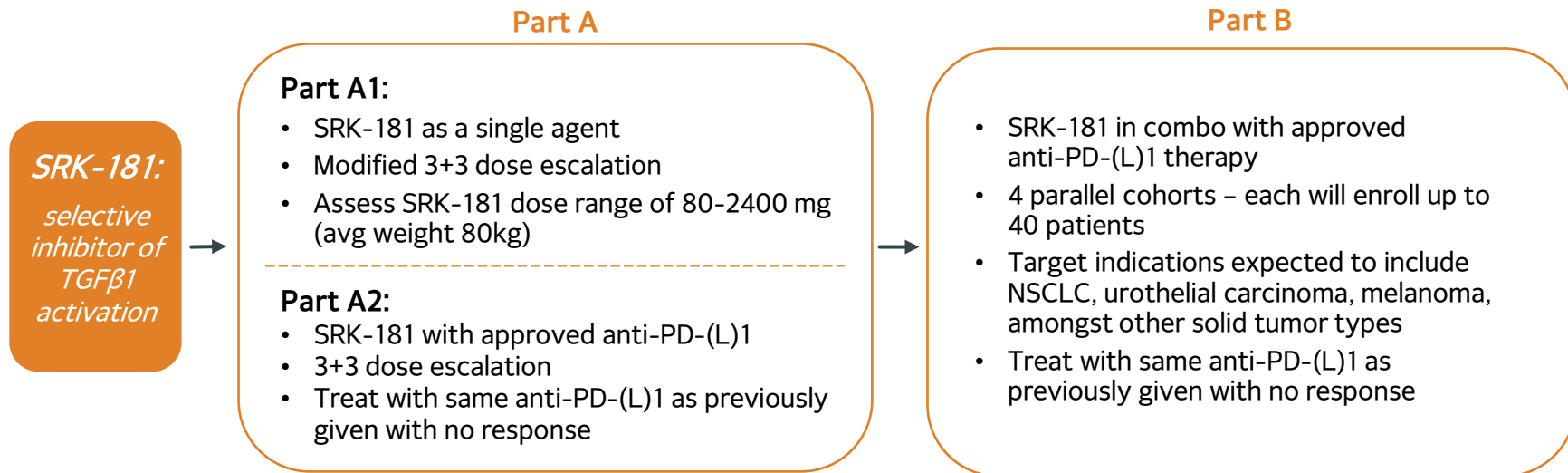
- Rats: NOAEL for SRK-181 was up to highest evaluated dose of 200 mg/kg QW
- Non-human primates: NOAEL for SRK-181 was up to highest evaluated dose of 300 mg/kg QW

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



- Open-label, dose escalation, and dose expansion clinical trial
- Evaluate the efficacy, safety/tolerability, and PK/PD of SRK-181 in combination with approved anti-PD-(L)1 therapy
- Patients with locally advanced or metastatic solid tumors that exhibit primary resistance to anti-PD(L)1 therapy
- Lack of response characterized as stable or progressive disease following ≥3 cycles of anti-PD-(L)1 therapy either alone or in combination with chemotherapy

DRAGON Part A: Commenced Evaluation of SRK-181 with Anti-PD-(L)1 Therapy

DRAGON Part A1

- SRK-181 as a single agent
- Modified 3+3 dose escalation
- Assess SRK-181 dose range of 80-2400 mg (avg weight 80kg)

Safety and PK Data as Single-Agent

- Enables progression to evaluation of combination treatment

DRAGON Part A2

- SRK-181 with approved anti-PD-(L)1
- 3+3 dose escalation
- Focus on patients with primary resistance to single-agent anti-PD-1 or anti-PD-L1
- Treat with same anti-PD-(L)1 as previously given with no response

Potential for Early Efficacy Signals

- Anti-tumor response from combination treatment in individual patients would be unexpected given prior resistance to anti-PD-(L)1 therapy

DRAGON Part B: Multiple Opportunities for Efficacy Signals

DRAGON Part B



- Study population focused on patients already shown to have primary resistance to single-agent CPI
- 4 parallel cohorts; each to enroll up to 40 patients
 - **NSCLC:** SRK-181 + pembrolizumab
 - **Urothelial carcinoma:** SRK-181 + pembrolizumab
 - **Melanoma:** SRK-181 + pembrolizumab*
 - **Additional tumor types:** SRK-181 + anti-PD-(L)1 therapy for which patient experienced primary resistance

Potential for Rapid Path to Proof-of-Concept

- Anti-tumor response and safety with combination treatment
 - Response in individual patients would be unexpected given prior resistance to anti-PD-(L)1 therapy
 - Evaluation of patients with stable or progressive disease
- Ability to evaluate response across multiple tumor types
- Patient population with high unmet medical need
 - Strong proof-of-concept signal could support efficient registrational path

DRAGON Part B initiation planned 1Q21; anti-tumor and safety data expected starting in 2H21

* Planning to open eligibility to patients with history of primary resistance to either pembrolizumab or nivolumab NCT04291079 on www.clinicaltrials.gov.

Differentiated Pipeline with a Series of Anticipated Milestones

