Deep Insights Advancing Impactful Medicines

Company Overview | March 2024

ScholarRock™

Forward-Looking Statements

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 preclinical studies and clinical trials for SRK-439, 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,” “could,” “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, without limitation, that preclinical and clinical data, including the results from the Phase 2 trial of apitegromab or Part A or Part B of the Phase 1 trial of SRK-181, are not predictive of, may be inconsistent with, or more favorable than, data generated from future or ongoing clinical trials of the same product candidate, including the Phase 3 clinical trial of apitegromab in SMA and Part B of the Phase 1 clinical trial of SRK-181, respectively, Scholar Rock’s ability to provide the financial support, 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, Scholar Rock’s dependence on third parties for development and manufacture of product candidates including, without limitation, to supply any clinical trials, Scholar Rock’s ability to manage expenses and to obtain additional funding when needed to support its business activities and establish and maintain strategic business alliances and new business initiatives, and the impacts of current macroeconomic and geopolitical events, hostilities in Ukraine, increasing rates of inflation and rising interest rates, on business operations and expectations, as well as those risks more fully discussed in the section entitled "Risk Factors" in Scholar Rock’s Form 10-K for the year ended December 31, 2022, and Quarterly Report on Form 10-Q for the quarter ended September 30, 2023, 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.

This presentation may also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we compete are necessarily subject to a high degree of uncertainty and risk.

Apitegromab and SRK-181 are investigational drug candidates under evaluation. Apitegromab, SRK-181, and SRK-439 have not been approved for any use by the FDA or any other regulatory agency and the safety and efficacy of apitegromab, SRK-181 and SRK-439 have not been established.

ScholarRock™

We are a global leader in harnessing the life-changing potential of TGFβ biology

OUR MISSION

To discover, develop, and deliver life-changing therapies by harnessing cutting-edge science to create new possibilities for people living with serious diseases

TGFβ=Transforming growth factor-beta.

Building a Fully Integrated Therapeutics Company

Revolutionary Scientific Platform

- **Pioneers in unparalleled selective** targeting of the **latent forms** of **growth factors**
- Robust pipeline of **novel** assets including **two clinical programs** and a **growing portfolio of preclinical programs**

Transformative Therapeutics in Development

Apitegromab in SMA

Potential therapy in Ph 3 designed to **improve motor function to help address remaining unmet need** after receipt of existing SMA therapies

SRK- 439 in Obesity

Novel antimyostatin antibody with the potential to support **healthier weight management by preserving lean muscle**

SRK-181 in Immuno-Oncology

In Ph 1 development to **overcome resistance to checkpoint inhibitors** in multiple tumor types

Experienced and Focused

- Seasoned team with **track record** of **clinical** and **commercial success**
- **Deep** rare disease, R&D, FDA/EMA approval & launch **experience**
- **Focused, efficient approach** to scaling the organization

SMA=Spinal muscular atrophy; EMA=European Medicines Agency; FDA=United States Food and Drug Administration; R&D=research and development.

Our Approach

Selectivity Drives Success

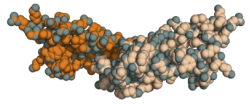
RIGHT TARGET → **Validated Biology**

RIGHT TIME → **Latent Form**

Deep structural insights to validated targets

Industry-leading antibody design and protein engineering to selectively target latent growth factors

Optimized for efficacy and mitigates off-target effects

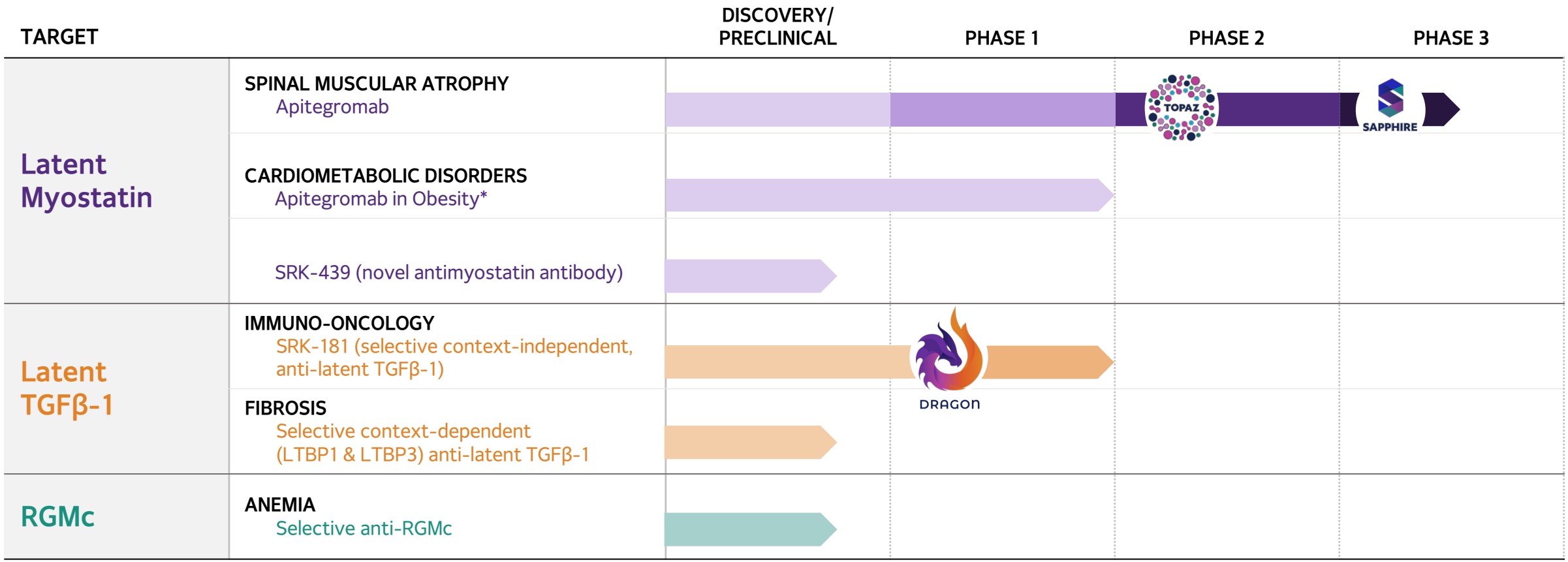


Traditional Target
"mature" active growth factor

Scholar Rock's Target
Latent Growth Factor

ScholarRock

Advancing a Robust Pipeline with Our Differentiated Platform



Potential to transform the lives of people living with a wide range of serious diseases, including neuromuscular disorders, cardiometabolic disorders, oncology, and fibrosis

* Subject to receipt of regulatory authority approval. We plan to utilize data from a previously completed Ph 1 study in healthy volunteers and initiate a Ph 2 POC trial in 2024.

LTBP1=Latent transforming growth factor beta binding protein 1; LTBP3=Latent transforming growth factor beta binding protein 3; POC=Proof of concept; RGMc=Repulsive guidance molecule C; TGFβ-1=Transforming growth factor beta-1.

Antimyostatin Program: Apitegromab in Spinal Muscular Atrophy

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Hallmarks of SMA

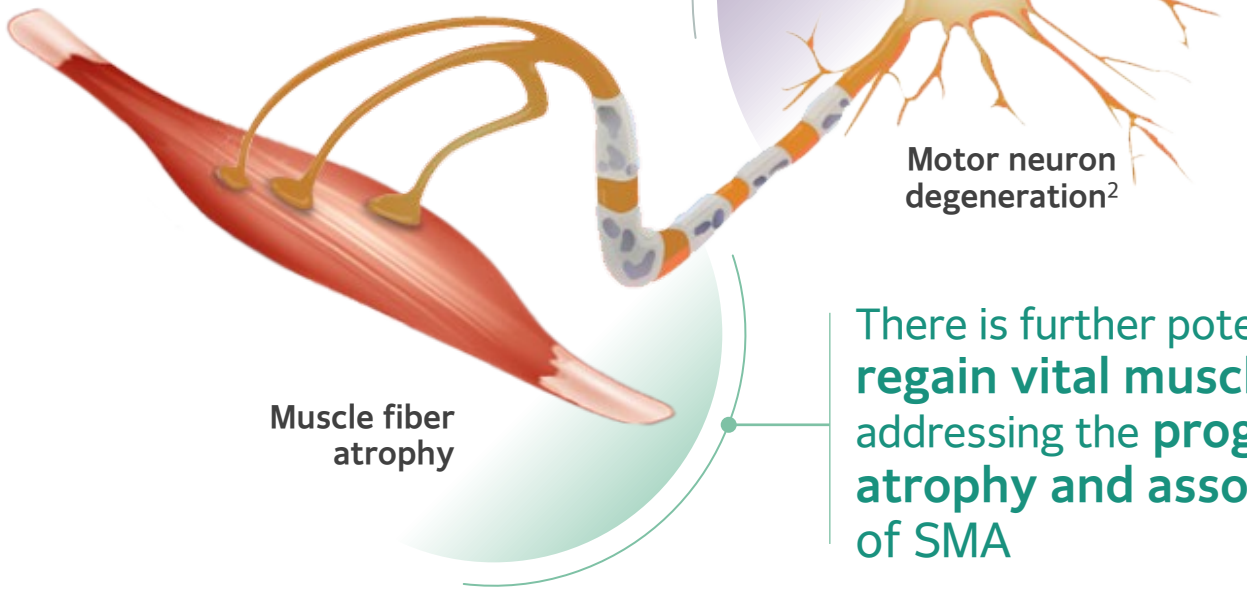
Motor Neuron Loss and Muscle Atrophy Leads to Progressive Muscle Weakness

Spinal Muscular Atrophy

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

SMN therapies
slow further degeneration of motor neurons[1]

...but do not directly address muscle atrophy



There is further potential to **regain vital muscle function** by also addressing the **progressive muscle atrophy and associated weakness** of SMA

SMA=Spinal muscular atrophy; SMN=Survival motor neuron.
1. Hua Y, et al. Nature. 2011;478(7367):123-6.
2. Figure adapted from: SMA Foundation Overview. http://www.smafoundation.org/wp-content/uploads/2012/03/SMA-Overview.pdf.; Accessed April 18, 2021.

SMA Leads to Deterioration in Essential Muscle Function

"What may seem like minimal gains in strength actually translate to **exponential gains in functional abilities.**

I often have to choose between taking a shower and doing homework because **I don't have the energy to do both.**

Small tasks are huge success in my life. If I could lift that 1L bottle of water at work instead of having to find a graduate student to move it for me…**things don't take a ton more muscle, but they are all muscle I still don't have**."

Despite significant advancements, **progressive muscle weakness** remains an unmet need in SMA

Muscle weakness can lead to deterioration in **mobility, swallowing, breathing** and cause **debilitating fatigue**

Quotes are from patient advocates who participated in 2022 Cure SMA FDA Patient-Led Listening Session and not from the pictured individuals. Summary of the listening session can be found on the FDA website at https://www.curesma.org/cure-sma-holds-patient-led-listening-session-with-fda/

SMA Today: More Patients Screened and Treated

GLOBAL DISEASE:

>20,000 affected

in US and Europe[1, 2]

Three treatments to address SMN loss

SPINRAZA® (nusinersen) injection 12 mg/5 mL

>13,000 patients
treated WW

$1.8 billion
annual revenue (LTM)[3]

Evrysdi™ risdiplam 60 mg powder for oral solution

> 11,000 patients
treated WW

~CHF1.4 billion
annual revenue (LTM)[4]

zolgensma® (onasemnogene abeparvovec-xioi) suspension for intravenous infusion

> 3,500 patients
treated WW

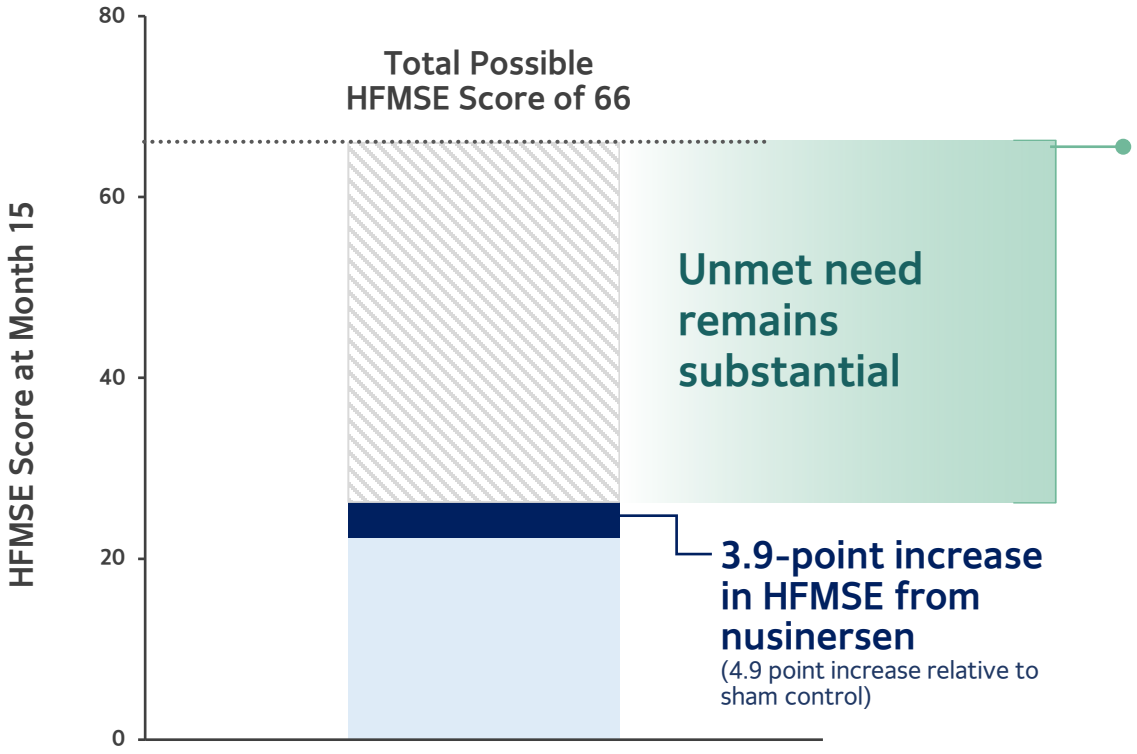
~$1.2 billion
in revenues (LTM)[5]

Established market dynamics support Scholar Rock's first potential commercial launch

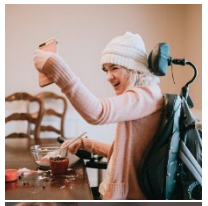
CHF=Swiss franc; LTM=last twelve months; SMA=Spinal muscular atrophy; SMN=Survival motor neuron; WW=worldwide.

1. Cure SMA 2022 Report: 9042022_State-of-SMA_vweb.pdf (curesma.org)
2. Lally et al. Indirect estimation of the prevalence of spinal muscular atrophy Type I, II, and III in the United States. Orphanet J Rare Dis. 2017 Nov 28;12(1):175. doi: 10.1186/s13023-017-0724-z.
3. Revenue as of Biogen 3Q23 financial update; includes patients treated worldwide in post-marketing setting, expanded access program, and clinical trials as of May 2022.
4. Revenue as of Roche 3Q23 financial update; includes patients treated worldwide as of July 2023.
5. Revenue as of Novartis 3Q23 financial update; includes patients treated worldwide including clinical trials, commercially, and managed access programs as of August 2023.

Muscle-Targeted Therapy: A New Treatment Frontier



Patients and caregivers want new therapies to address the following unmet needs[2]:



INCREASE muscle strength

IMPROVE daily activities

STABILIZE or GAIN new motor function

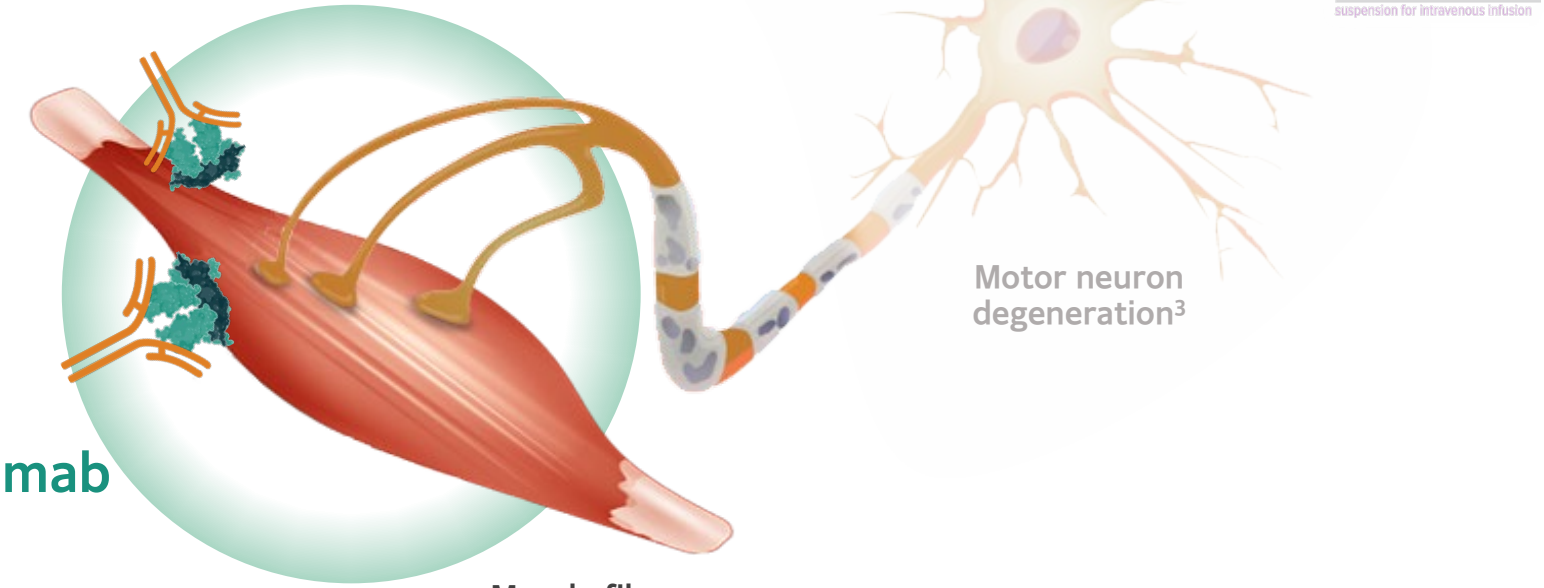
REDUCE fatigue

Mean improvement in HFMSE experienced by patients in nusinersen Phase 3 CHERISH trial[1]

*Percentages represent percent of patients who named these unmet needs when asked, "What are your most significant current unmet needs that you hope new therapies would address?"
HFMSE=Hammersmith Functional Motor Scale-Expanded.
1. Mercuri E et al.; N Engl J Med 2018; 378:625-635; DOI: 10.1056/NEJMoa1710504; cherish trial results; 2. 2022 Community Update Survey, Cure SMA.
This third-party information is provided for background only and is not intended to convey or imply a comparison to the TOPAZ clinical trial results.

Apitegromab Offers Significant Potential to Address Unmet Needs

Apitegromab is a selective
MUSCLE-TARGETED APPROACH
designed to improve motor function*[1,2]



Myostatin is a negative modulator of muscle growth

Strong clinical and preclinical evidence indicates upstream targeting of structurally differentiated pro- and latent myostatin avoids undesirable off-target effects

Apitegromab specifically and only inhibits myostatin and has the potential to build muscle and strength to improve patient outcomes

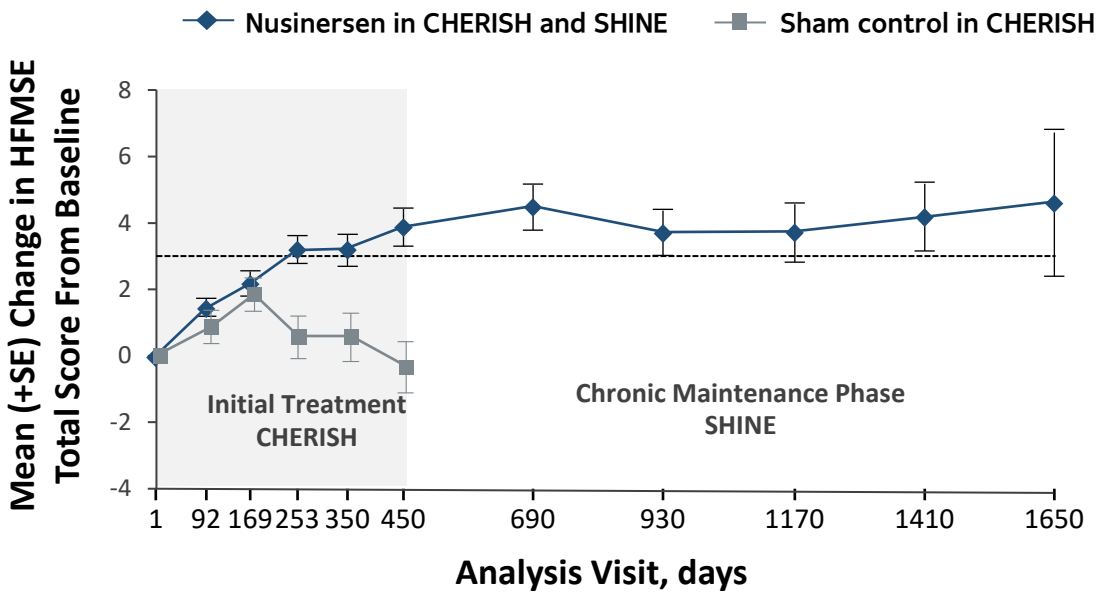
* Based on Animal Model Data; 1. Long KK, et al. Hum Mol Genet. 2019;28(7):1077-1088; 2. Pirruccello-Straub M, et al. Sci Reports. 2018;8(1):2292. doi:10.1038/s41598-018-20524-9 3. Figure adapted from: SMA Foundation Overview. http://www.smafoundation.org/wp-content/uploads/2012/03/SMA-Overview.pdf.; Accessed April 18, 2021. For illustrative purposes only.

Motor Function With SMN Therapies as Assessed by HFMSE

HFMSE appears to Plateau After Initial Gains

Change in HFMSE Over Four Years with Nusinersen[1]

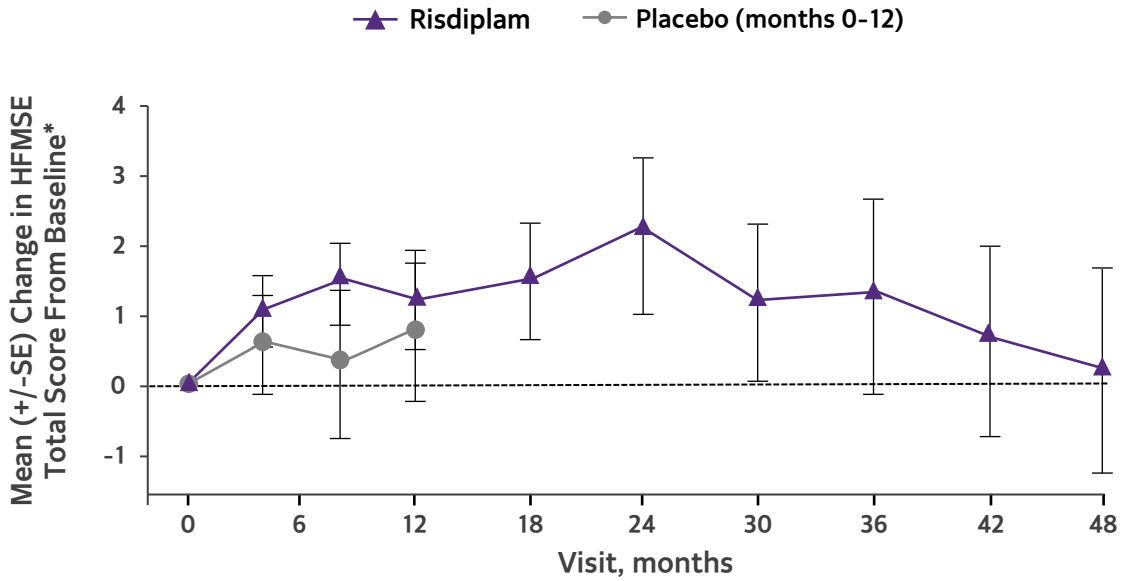
Overall population age 2-12



Nusinersen	n=	84	82	84	84	83	76	83	83	79	61	20
Placebo	n=	42	41	41	42	42	39					

Change in HFMSE* Over Four Years with Risdiplam[2]

Overall population age 2-25



Risdiplam	n=	120	120	119	117	109	106	89	99	101	97
Placebo	n=	60	60	58	58						

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

HFMSE, Hammersmith Functional Motor Scale–Expanded; SE, standard error.
*MFM was primary efficacy endpoint of SUNFISH. HFMSE was a secondary endpoint. 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.

Phase 2 TOPAZ Trial: Safety and Efficacy Data from Muscle-Targeted Treatment Candidate in SMA

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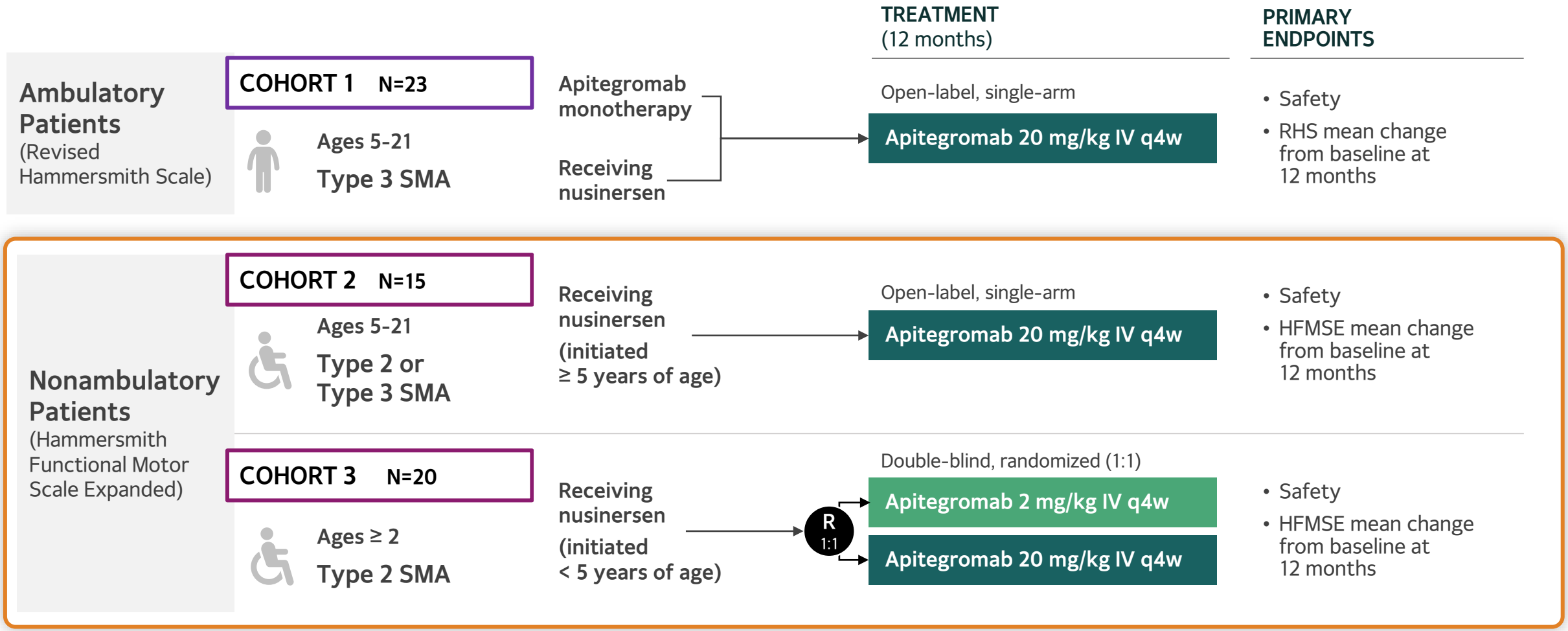
TOPAZ Phase 2 Trial Design[1,2]



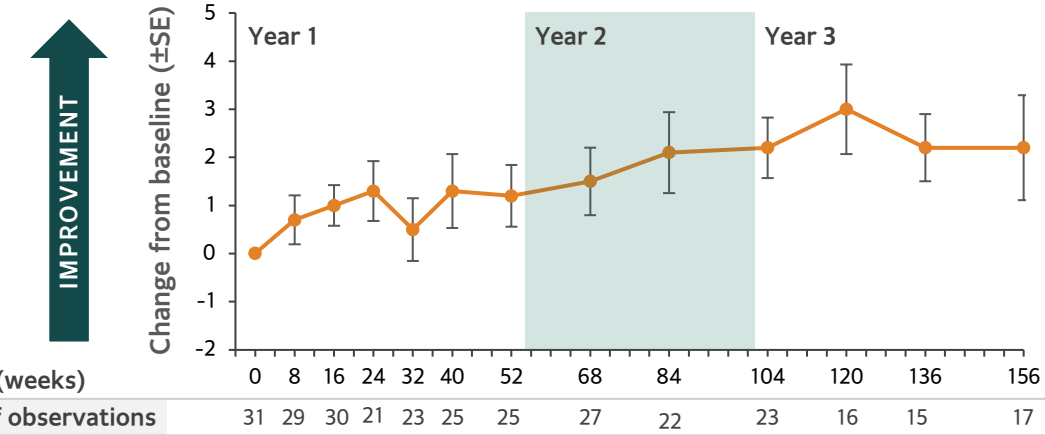
All SMA Types 2/3, cohorts defined by age and present ambulatory status at time of enrollment. HFMSE, Hammersmith Functional Motor Scale Expanded; IV, intravenous; q4w, every 4 weeks; SMA, spinal muscular atrophy; SMN, survival motor neuron.

1. Place A, et al. Eu J Neurol. 2021;28(Suppl1):207-334 (EPR-184). 2. Crawford T, et al. TOPAZ Extension: 24-month Efficacy and Safety of Apitegromab in Patients With Later-onset SMA (Type 2 and Type 3 SMA). Presented at CureSMA Annual Conference; June 16-19, 2022.

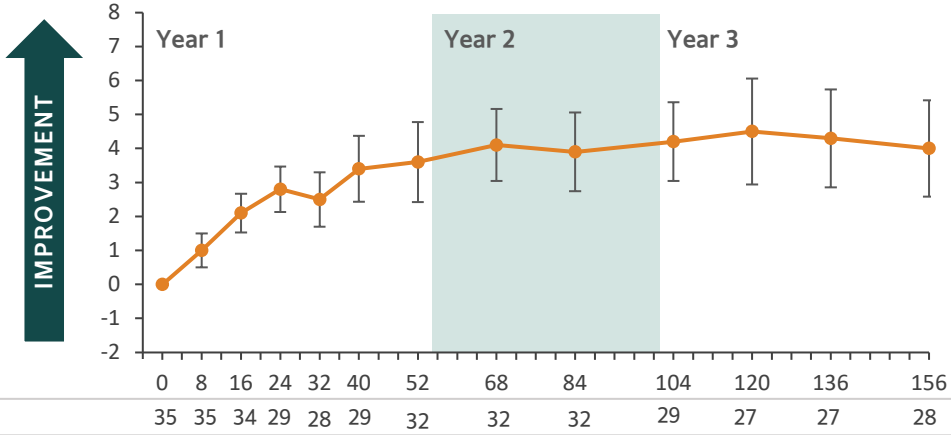
TOPAZ Over 36 Months | Pooled Nonambulatory Patients | Age 2 – 21 | All Doses

Sustained Functional and PRO Improvements Beyond SMN Treatment

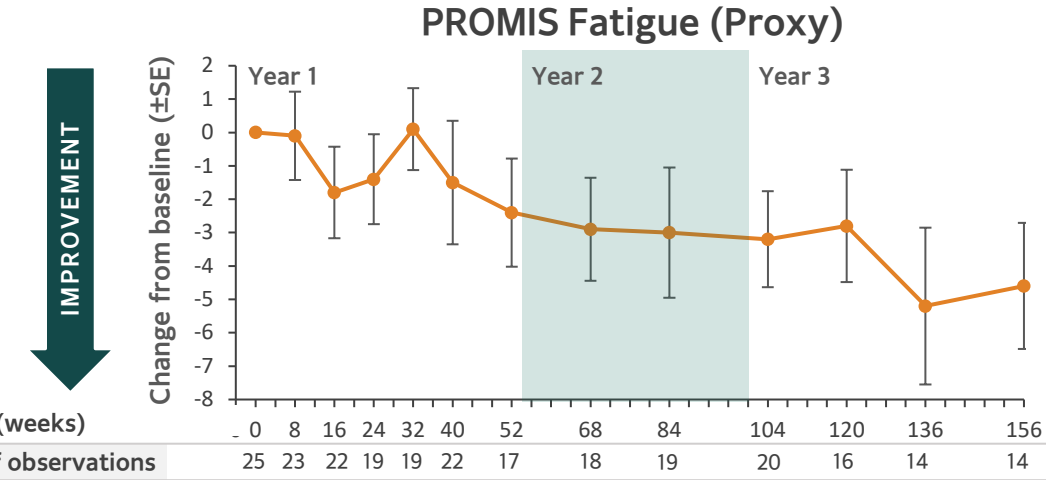
PEDI-CAT Daily Activities



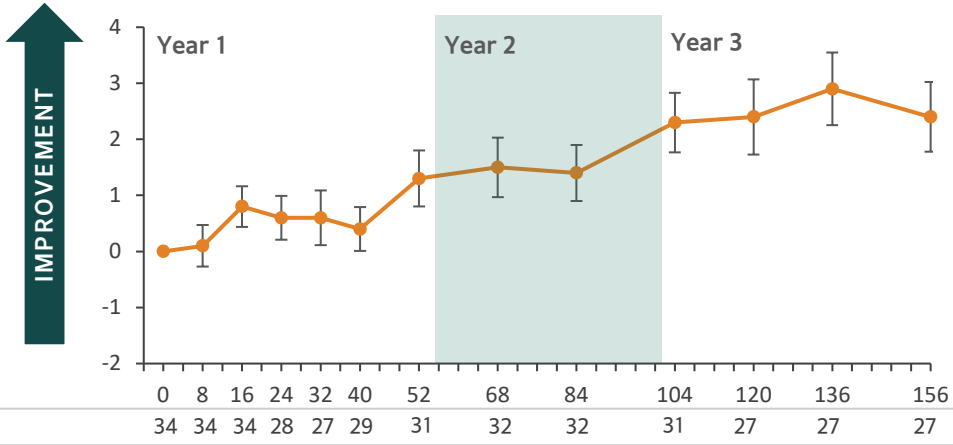
HFMSE



PROMIS Fatigue (Proxy)



RULM



N = 35; Baseline mean age=7.3 |**Prior Time on SMN Rx=24.1m**

HFMSE=Hammersmith Functional Motor Scale Expanded; OC=observed case; PEDI-CAT=Pediatric Evaluation of Disability Inventory Computer Adaptive Test; PROMIS=Patient Reported Outcome Measurement Information System; RULM=Revised upper limb module; SE=standard error of the mean. SMN Rx=SMN therapy. Data on File. Scholar Rock, Inc. Cambridge, MA. Data cutoff date as of March 13, 2023. This analysis excludes data post scoliosis surgery (a known confounding factor interfering with motor function assessment) from seven patients for HFMSE and RULM. The updated PEDI-CAT analysis included additional records (2 at 12 months and 1 at 24 months) that were not available at the time of previous analysis. Apitegromab is an investigational drug candidate being evaluated for the treatment of spinal muscular atrophy. Apitegromab has not been approved for any use by any health authorities and its safety and efficacy have not been established.

TOPAZ Over 36 Months

Well Tolerated Safety Profile & Low Discontinuation Rate

RIGHT TARGET → Myostatin

RIGHT TIME → Latent Form

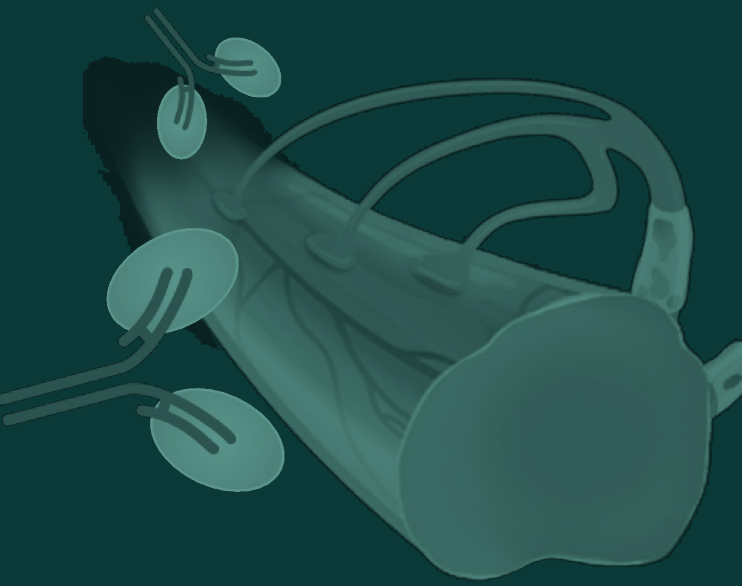
- >90% of patients on combination therapy remained in extension study*
- Treatment-emergent adverse events (TEAEs) were consistent with previous reports with no new findings after 198 patient-years of exposure
  - Most frequently reported TEAEs included headache, pyrexia, COVID-19, nasopharyngitis, & upper respiratory tract infection
  - TEAEs were mostly mild to moderate and generally consistent with the underlying patient population and nusinersen therapy
- No treatment-related serious AEs or hypersensitivity reactions
- No report of positive apitegromab antibodies (ADA)

Crawford et al., Cure SMA 2023

* Excludes patients on monotherapy

Summary of TOPAZ Data

Substantial and Sustained Improvement Over 36 MONTHS



TOPAZ

Data to date has shown substantial clinical benefit that is dose-dependent

Benefit continued to improve or was sustained over 36 months

Consistency across functional scales and patient-reported outcomes

Well tolerated profile and low discontinuation rate supports durability of treatment

TOPAZ data suggest that apitegromab has the potential to transform care in SMA by directly addressing progressive muscle weakness

PRO=Patient Reported Outcome

SAPPHIRE

Sapphire Phase 3 Pivotal Trial

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SAPPHIRE Phase 3 Design is Optimized by Insights from TOPAZ

TOPAZ Learnings

STUDY POPULATION

Substantial HFMSE gains observed in the nonambulatory Type 2/3 SMA cohorts

AGE

Exploratory age 2-12 analysis in nonambulatory Type 2/3 showed transformative potential

DURATION

HFMSE gains substantial by 12 months of treatment

DOSE

Dose response seen (greater effect observed with 20 mg/kg over 2 mg/kg)

Phase 3 SAPPHIRE Trial

Registrational trial with topline 12-month data readout expected in Q4 2024

SAPPHIRE Design Elements

STUDY POPULATION

- Nonambulatory Type 2/3 SMA
- Primary efficacy endpoint: HFMSE

AGE

Age 2-12 main efficacy population
Age 13-21 exploratory population

DURATION

12-month treatment duration

DOSE

- 20 mg/kg apitegromab dose
- 10 mg/kg apitegromab dose

HFMSE=Hammersmith Functional Motor Scale Expanded.

Ongoing SAPPHIRE Phase 3 Trial Overview

SAPPHIRE

Randomized, double-blind, placebo-controlled, parallel arm design (n=204)
Enrolling patients who are on SMN-directed therapy (nusinersen or risdiplam)
Anticipate completing enrollment in 3Q 2023

SCREENING

MAIN POPULATION (n=156)

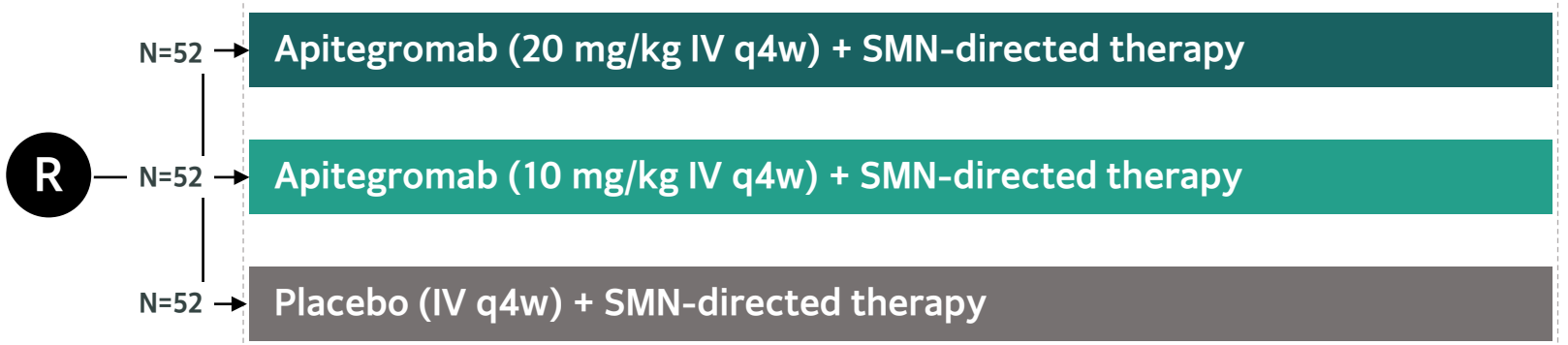
Ages 2-12

With nonambulatory Types 2 and 3 SMA

Stratified to ensure balanced allocation across the three arms:

1. Age at SMN therapy initiation (age < 5 vs age ≥ 5)
2. SMN therapy (nusinersen vs. risdiplam)

TREATMENT (52 weeks)



ENDPOINTS

Primary Efficacy:
Mean HFMSE change from baseline at 12 months

Additional Efficacy Measures:
RULM, WHO, other outcome measures

Safety, PK/PD, ADA

Additional Data Opportunities

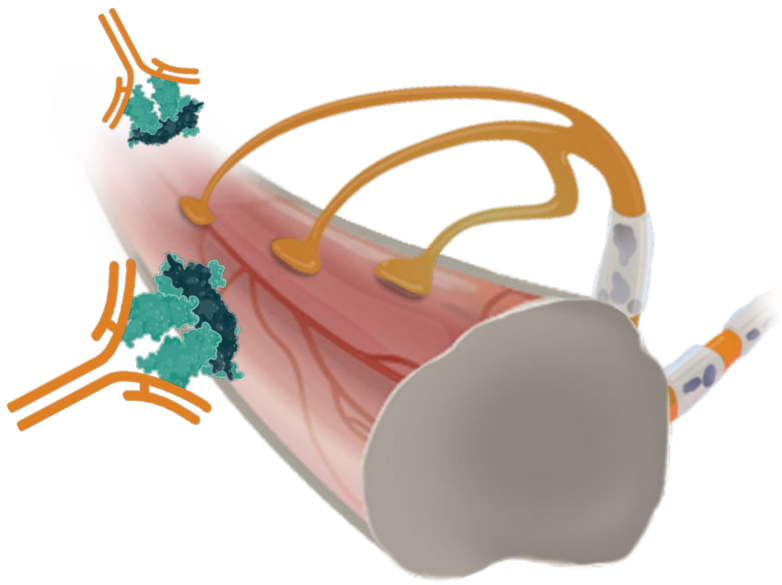
Exploratory population (age 13-21), in patients using SMN therapy
Focused upon safety & exploratory efficacy (n=48; 2:1 randomization between apitegromab 20 mg/kg vs placebo)

Separate open-label extension study (after patients complete 12-month treatment period)
Focused upon safety & exploratory long-term efficacy

ClinicalTrials.gov Identifier: NCT05156320
HFMSE=Hammersmith Functional Motor Scale Expanded; RULM=Revised Upper Limb Module; R=randomization; SMA=spinal muscular atrophy; SMN=survival motor neuron.

Apitegromab: Potential to Maximize Outcomes for People Living with Spinal Muscular Atrophy (SMA)

Transformative Potential to Change the Standard of Care



First and only muscle-targeted investigational treatment to demonstrate clinical proof-of-concept in SMA

SAPPHIRE

Phase 3 SAPPHIRE Trial

Registrational trial with topline 12-month data expected in Q4 2024

TOPAZ

Phase 2 TOPAZ Trial

Demonstrated **substantial and sustained functional improvements** in Type 2 and nonambulatory Type 3 SMA patients

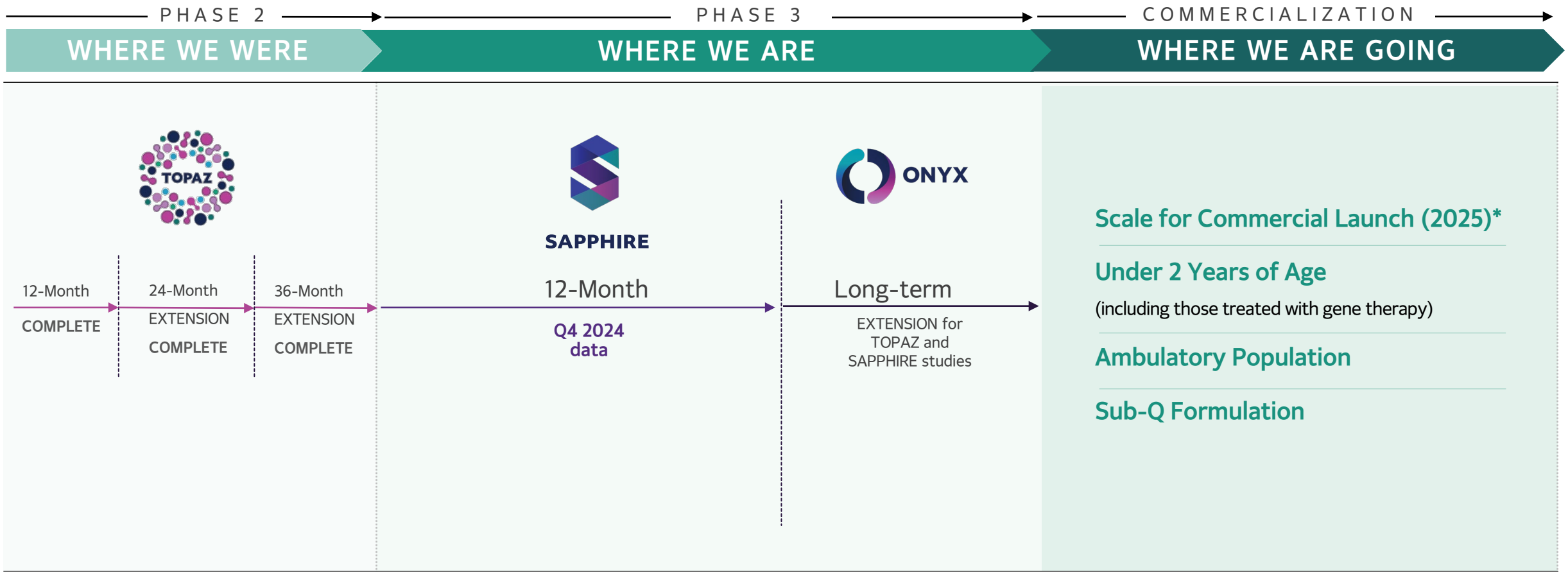
ONYX

ONYX Open-Label Extension Study

Evaluating the **long-term safety and efficacy** of apitegromab in **patients who have completed TOPAZ or SAPPHIRE**

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

Expanding to Benefit More People Living with SMA



*Subject to regulatory approval.
SMA=Spinal muscular atrophy; Sub-Q=Subcutaneous

Next Horizon: Cardiometabolic Disorders

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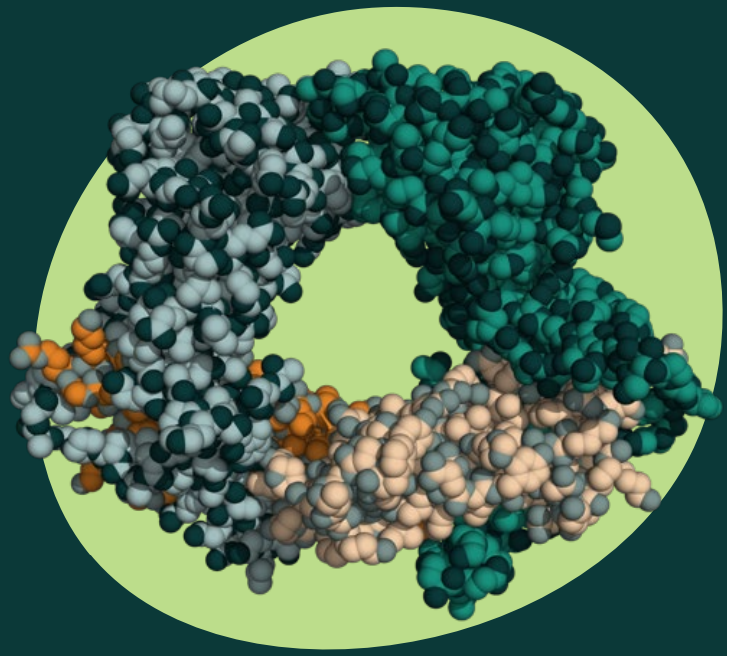
Differentiated Expertise Developing Muscle-Targeted Therapies



Myostatin is a member of the TGFβ superfamily known to be a negative regulator of muscle mass and promotes muscle catabolism

Next Frontier in Antimyostatin

Leveraging Our R&D Platform to Expand into Cardiometabolic Disorders

- Pioneered unique approach to develop antibodies that bind to pro- and latent forms of myostatin with exquisite selectivity and inhibit its activation

- Apitegromab is being developed as a highly selective inhibitor of latent myostatin activation, to enhance muscle growth and function in neuromuscular disorders
  - To date apitegromab has been evaluated in approximately 250 patients ages 2 to 21 living with spinal muscular atrophy (SMA), showing sustained benefit over 36 months, a well tolerated profile and low discontinuation rate

- Discovered multiple additional anti-pro/latent myostatin inhibitory antibodies including:
  - SRK-439: Being developed as a novel, highly potent and selective antibody tailored for cardiometabolic disorders

Obesity is Recognized as a Top Global Public Health Issue

Obesity is a common, serious, and costly chronic disease affecting adults and children worldwide

BY 2030, OBESITY WILL AFFECT:

>1 BILLION
adults

>250 MILLION
children and adolescents[1]

Adult obesity associated with more than **$170 billion in excess costs** annually in the U.S.[2]

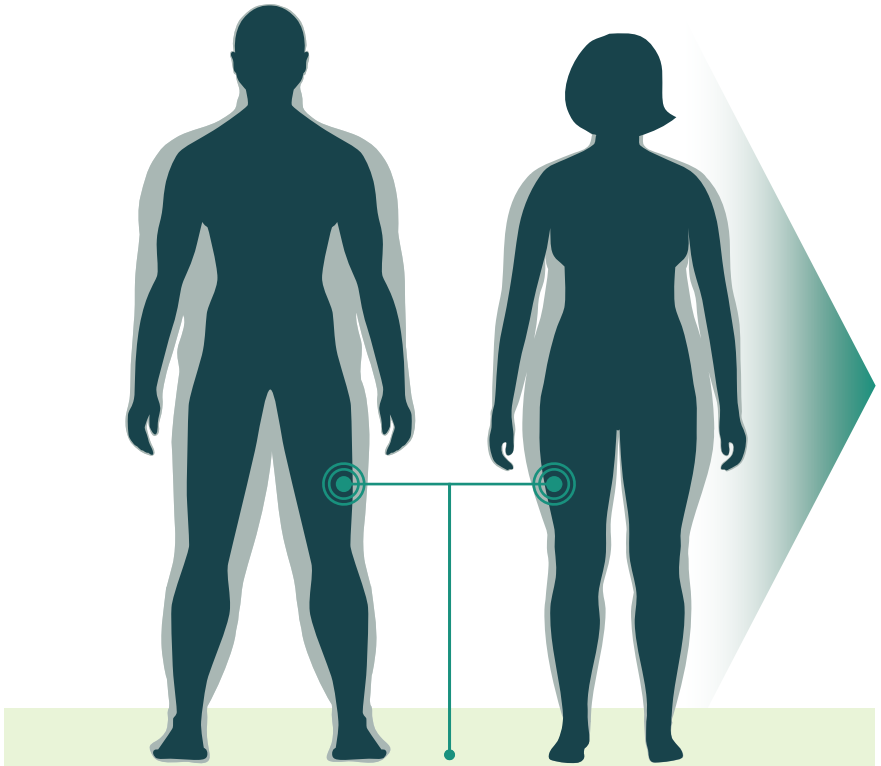
In the US, **1 in 5** children and more than **1 in 3** adults are obese

Obesity can increase the risk of comorbidities, such as some cancers, heart disease, and type 2 diabetes

1. The World Obesity Foundation, World Obesity Atlas 2022; 2. Ward ZJ, Bleich SN, Long MW, Gortmaker SL (2021) Association of body mass index with health care expenditures in the United States by age and sex. PLoS ONE 16(3): e0247307.

Loss of Lean Muscle Significant with GLP-1 RA Therapy

Lean muscle is essential to healthy metabolic function



Significant proportion of weight loss due to loss of lean muscle mass

Current Weight Loss Strategies *Challenged by:*

- Tolerability
- Lack of durability
- **Significant muscle loss**[1-3]

Recently approved **GLP-1 RAs are highly effective** in weight loss & experiencing rapid uptake

But 25%-40% of total body weight loss mediated by GLP-1 RA therapy may be attributed to **loss of lean muscle mass**[2,3]

Preserving lean muscle mass is important to promote long-term metabolic benefits, sustainable weight management and health outcomes[4-7]

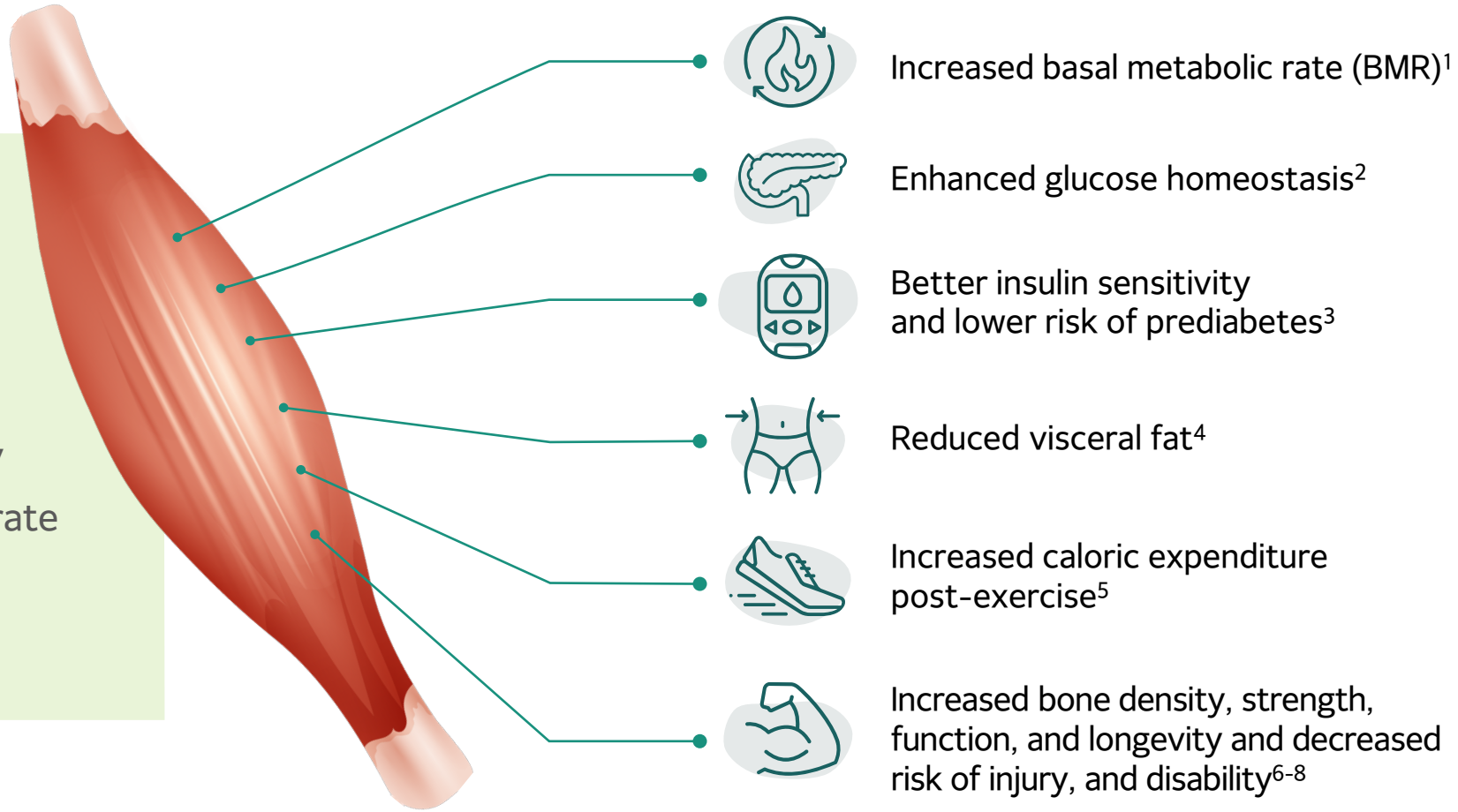
GLP-1 RA=Glucagon-like peptide-1 receptor agonists.

1. Muller TD, et al Anti-obesity drug discovery: advances and challenges. Nature Reviews Drug Discovery 2022; 21, 201–223; 2. Wilding JPH, Batterham RL, Calanna S, et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. N Engl J Med. 2021;384(11):989-1002; 3. Jastreboff AM, et al Tirzepatide Once Weekly for the Treatment of Obesity. NEJM 2022; 387 (3): 205-216; 4. Cava et al. Preserving healthy muscle during weight loss. Adv Nutr 2017;8:511-19; 5. Lundgren JR et al. Healthy Weight Loss Maintenance with Exercise, Liraglutide or Both Combined. NEJM 2021;384:1719-30; 6. Beal JW et al. Dietary weight loss-induced improvements in metabolic function are enhanced by exercise in people with obesity and prediabetes. Nat Metab. 2022;5(7):1221-1235; 7. Dulloo AG, et al How dieting makes some fatter: from a perspective of human body composition autoregulation. Proc Nutr Soc. 2012 Aug;71(3):379-89.

Maintaining Muscle is Important for Healthy Weight Loss

The preservation of lean mass has many benefits for overall health:

- Improved strength
- Improved insulin sensitivity
- Increased basal metabolic rate
- Improved metabolic profile
- Reduced total body fat



- Increased basal metabolic rate (BMR)[1]
- Enhanced glucose homeostasis[2]
- Better insulin sensitivity and lower risk of prediabetes[3]
- Reduced visceral fat[4]
- Increased caloric expenditure post-exercise[5]
- Increased bone density, strength, function, and longevity and decreased risk of injury, and disability[6-8]

GLP-1 RA=Glucagon-like peptide-1 receptor agonist.

1. Aristizabal JC, Freidenreich DJ, Volk BM, et al. Effect of resistance training on resting metabolic rate and its estimation by a dual-energy X-ray absorptiometry metabolic map. Eur J Clin Nutr.2015; 69, 831–836. https://doi.org/10.1038/ejcn.2014.216; 2. Lindegaard B, Hansen T, Hvid T, et al. The effect of strength and endurance training on insulin sensitivity and fat distribution in human immunodeficiency virus-infected patients with lipodystrophy. J Clin Endocrinol Metab. 2008; 93:3860–9; 3. Srikanthan P, Karlamangla AS. Relative muscle mass is inversely associated with insulin resistance and prediabetes. Findings from the third National Health and Nutrition Examination Survey. J Clin Endocrinol Metab. 2011; 96:2898–903. doi: 10.1210/jc.2011-0435; 4. Wewege MA, Desai I, Honey C, et al. The effect of resistance training in healthy adults on Body fat percentage, fat mass and visceral fat: A systematic review and meta-analysis. Sports Med. 2022(Feb);52(2):287-300. doi: 10.1007/s40279-021-01562-2; 5. Zurlo, F., Larson, K., Bogardus, C., et al. Skeletal muscle metabolism is a major determinant of resting energy expenditure. J Clin Invest. 1990;86(5), 1423-1427; 6. Fukushima Y, Kurose S, Shinno H, et al. Importance of lean muscle maintenance to improve insulin resistance by body weight reduction in female patients with obesity. Diabetes Metab J. 2016;40: 147-153; 7. Roh E, Choi KM. Health consequences of sarcopenic obesity: a narrative review. Front. Endocrinol. 2020;11: 332; 8. Volpi E, Nazemi R, Fujita S. Muscle tissue changes with aging. Curr Opin Clin Nutr Metab Care. 2004;7(4): 405-410.

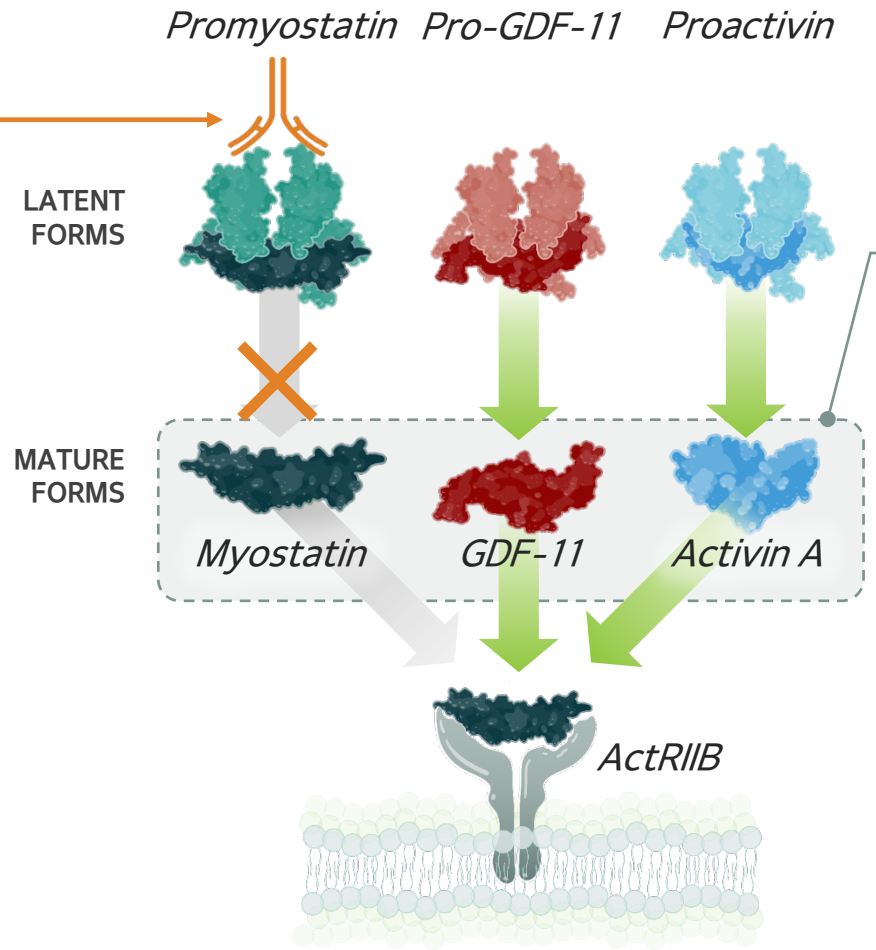
Our Antibodies Selectively Inhibit Activation of Myostatin

Apitegromab and **SRK-439**

SRRK antibodies do not bind to mature myostatin or any form of GDF11, Activin A, or other TGF-β family members

Selectivity is critical to avoid safety concerns

Selective Targeting of Proforms of Myostatin



Broad inhibition of ActRIIb signaling may be problematic:

ActRIIB knockout animals die shortly after birth with developmental defects in respiratory and cardiac organs[1]

Activins are critical in reproductive biology, and inhibition was shown to reduce FSH levels in women[2]

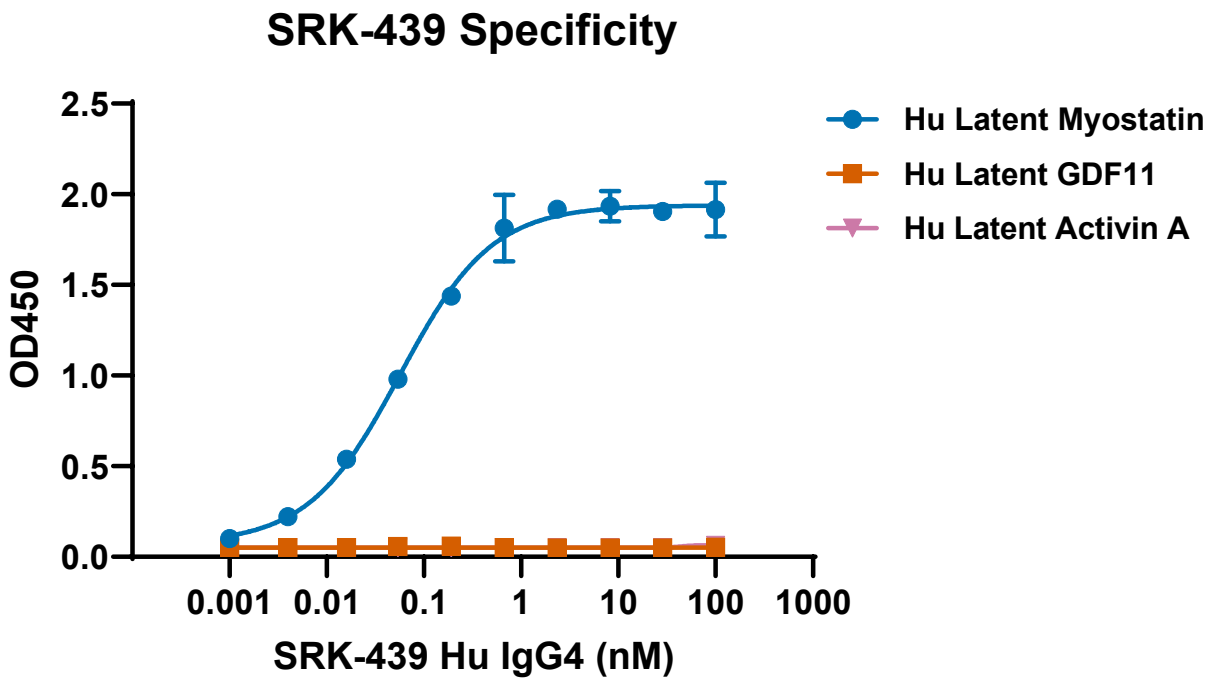
GDF11 loss leads to embryonic lethality, skeletal and kidney formation defects[3]

GDF11 signaling inhibition may have negative impacts on bone[4, 5]

ActRIIB=Activin Receptor IIB; FSH=Follicle stimulating hormone; GDF-11=Growth and differentiation factor 11; TGF-β=Transforming growth factor-beta.

1. Oh SP & Li E. Genes Dev. 1997 Jul 15;11(14):1812-26; 2. Garito T, et al. Clin Endocrinol (Oxf). 2018 Jun;88(6):908-919; 3. McPherron AC et al Nat Genet 1999, 22(3):260-264.; 4. Joonho Suha et al Proc Natl Acad Sci U S A . 2020 Mar 3;117(9):4910-4920; 5, Ravenscroft TA et al. Genet Med 2021 Oct;23 (10):1889-1900).

SRK-439 binds selectivity to Myostatin and not to related family members GDF11 or Activin A



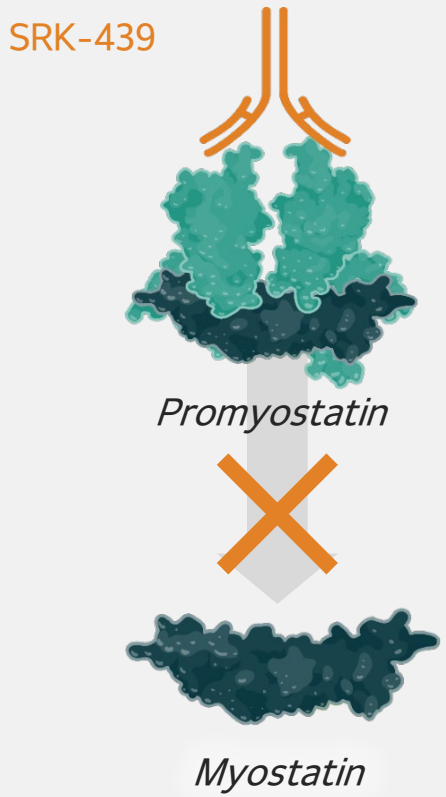
Exquisite selectivity avoids undesirable off-target effects [1-3]

1. Pirruccello-Straub M et al. Blocking extracellular activation of myostatin as a strategy for treating muscle wasting. Sci Reports 2017;8:2922; 2. Welsh BT et al. Preclinical safety assessment and toxicokinetics of apitegromab, an antibody targeting proforms of myostatin for the treatment of muscle-atrophying disease. Int J Tox 2021;40(4):322-336; 3. Barrett D et al. A randomized phase 1 safety, pharmacokinetic and pharmacodynamic study of a novel myostatin inhibitor apitegromab (SRK-015): A potential treatment for spinal muscular atrophy. Adv Ther 2021;38:3203-3222.

ScholarRock

SRK-439: Novel Myostatin Inhibitor

Preclinical candidate in development with potential to address muscle loss associated with weight loss



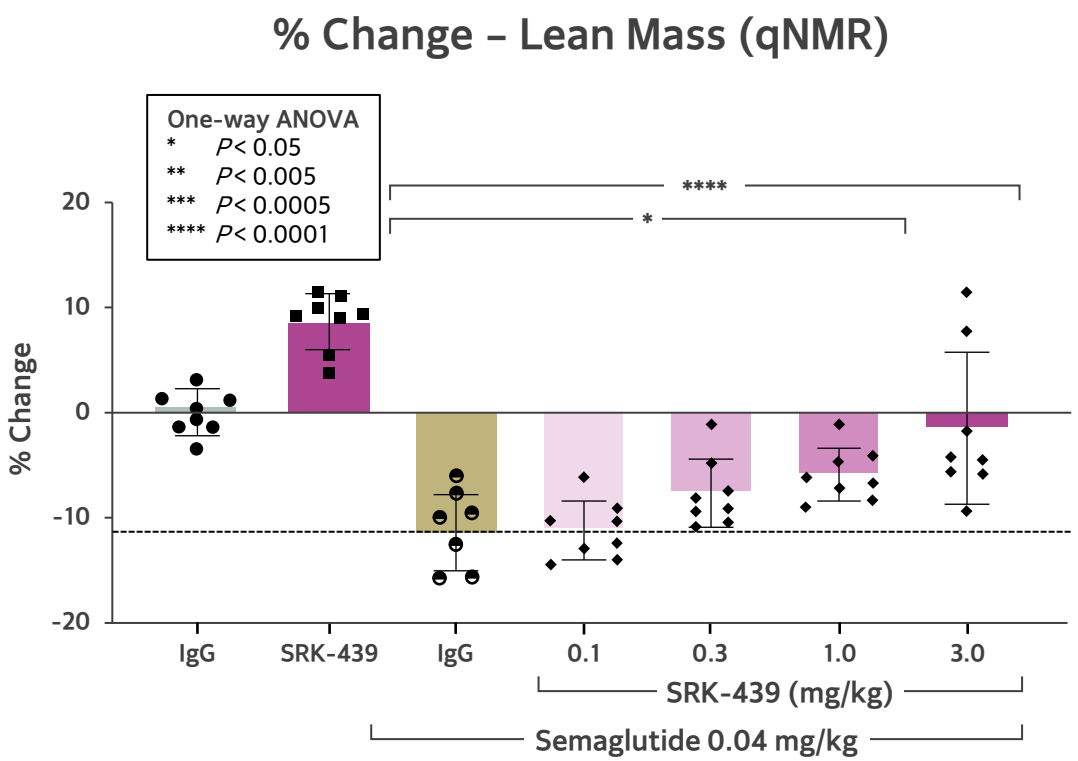
Attractive Properties

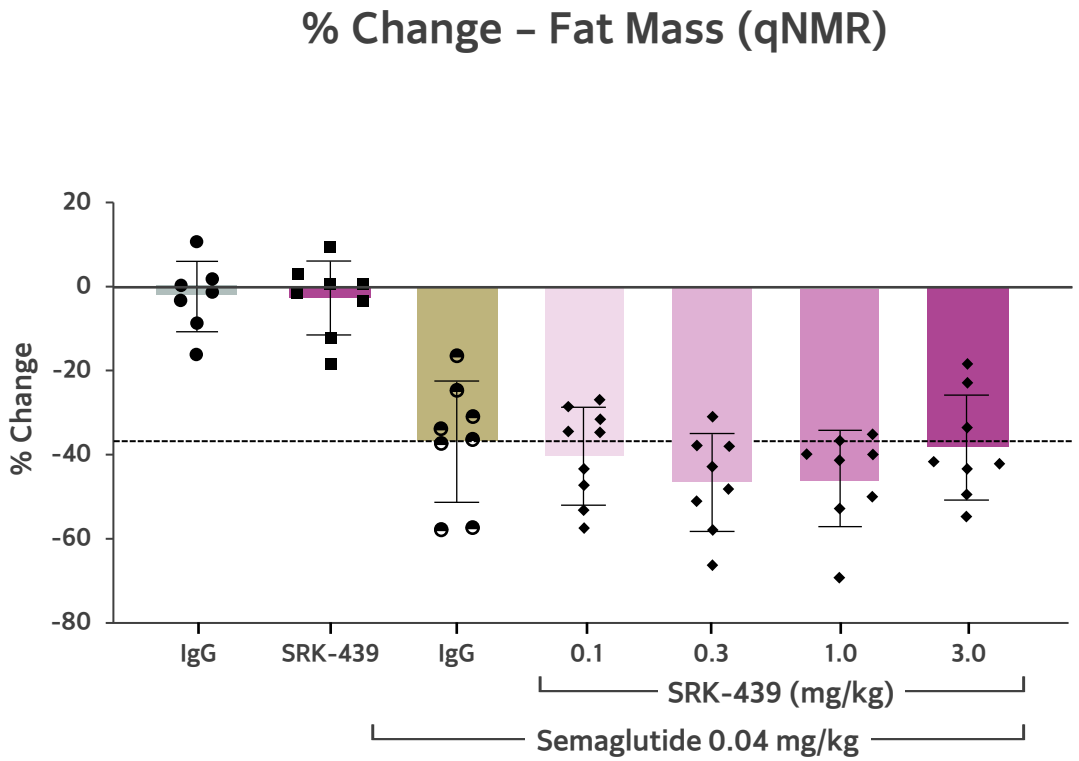
- High *in vitro* affinity for pro- and latent myostatin
- Maintained myostatin specificity (No GDF-11 or Activin-A binding)
- Maintained good developability profile

Optimized for subcutaneous formulation and dosing

mTLL2 IC50: Inhibitory concentration at 50% as measure of in vitro potency of the antibody in its ability to inhibit the activation of latent myostatin by its activating enzyme mammalian tolloid like protease 2 | KD: Equilibrium dissociation constant as a measure of binding affinity of the antibody to latent myostatin.
GDF-11=Growth and differentiation factor 11.

SRK-439 Reversed Lean Mass Loss and Enhanced Fat Mass Loss Induced by Semaglutide Treatment†





Dose-dependent Preservation of Lean Mass with effects seen as low as 0.3mg/kg

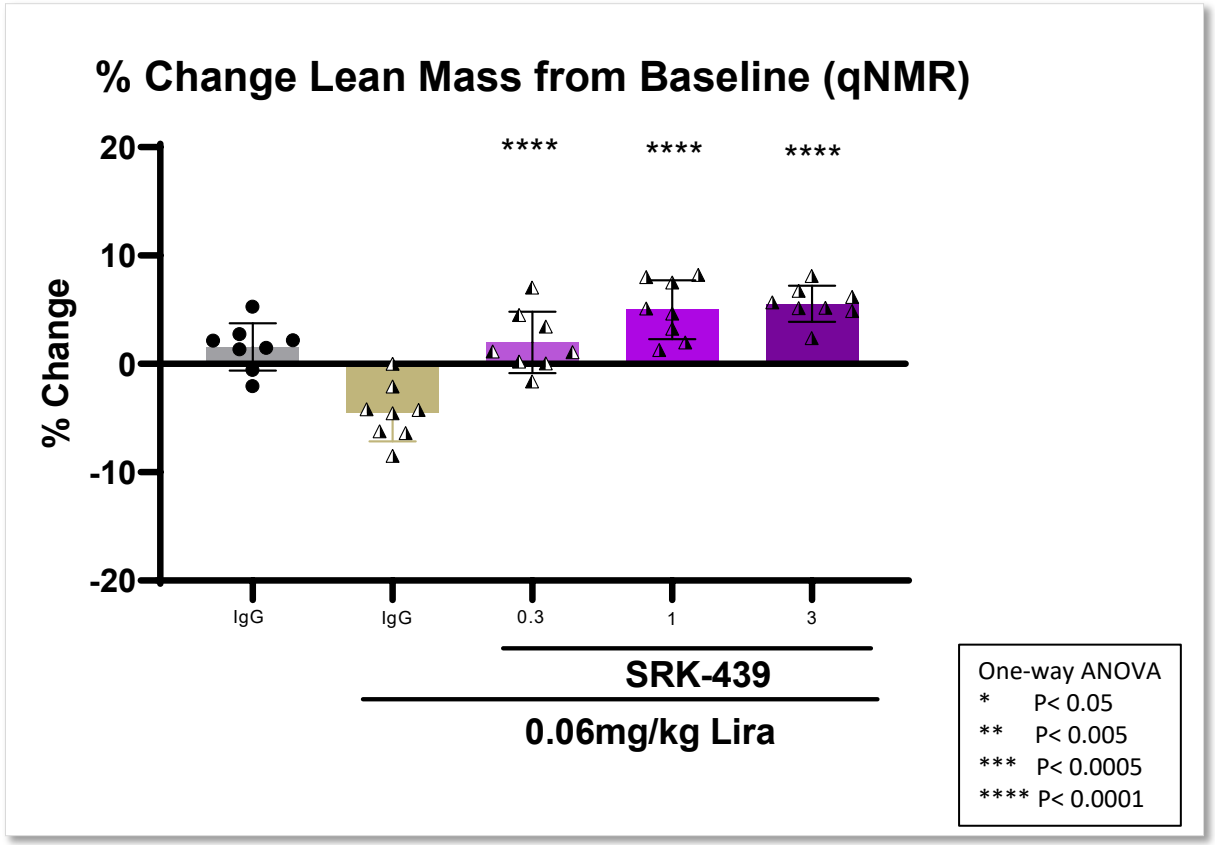
Additional Fat Mass Loss vs Semaglutide Alone

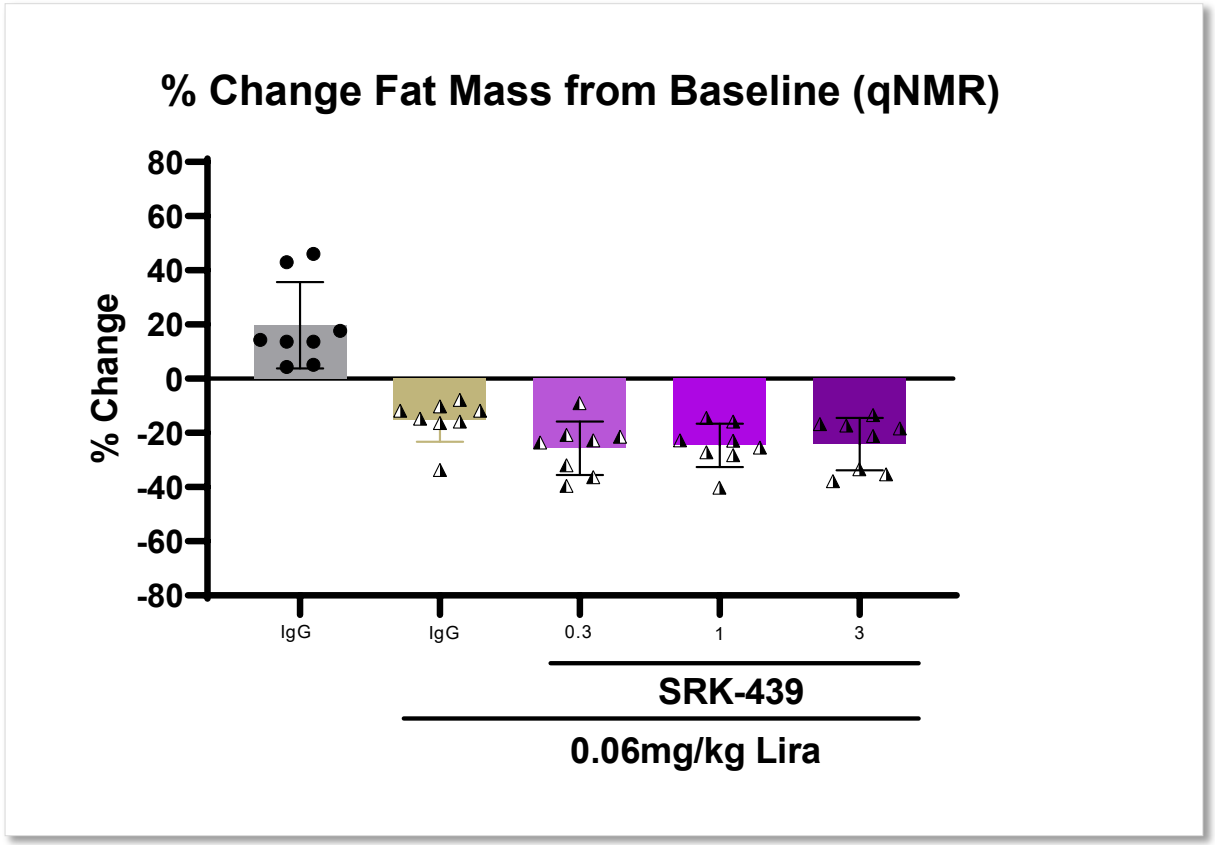
† In Mouse Diet Induced Obesity (DIO) Model.

Figure showed the effects of increasing doses of SRK-439 in combination with semaglutide on lean mass (left panel) and fat mass (right panel) in DIO mouse model as measured by qNMR; statistical analysis was done using one-way ANOVA (Dunnett's multiple comparison test).

ANOVA=Analysis of variance; IgG=Immunoglobulin G; qNMR=Quantitative nuclear magnetic resonance.

SRK-439 Maintained Lean Mass in Mouse Diet Induced Obesity (DIO) Model When Combined with GLP-1 RA Therapy

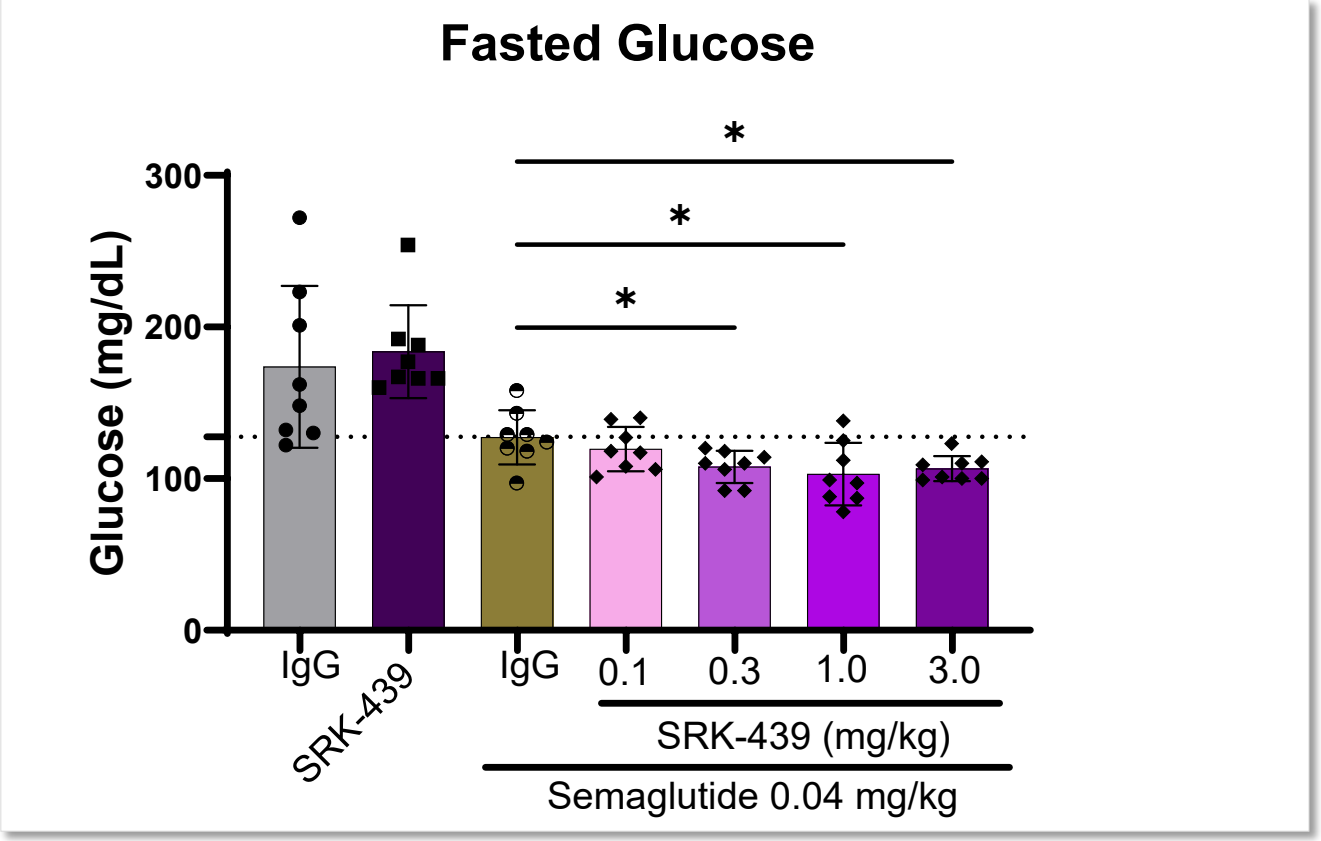




- Increased lean mass gain vs GLP-1 RA alone
- Improved fat mass loss vs GLP-1 RA alone

Figure shows the effects of increasing doses of SRK-439 in combination with liraglutide on lean mass (left panel) and fat mass (right panel) in a 28-day DIO mouse model as measured by qNMR; statistical analysis was done using one-way ANOVA (Dunnett's multiple comparison test).

SRK-439 Further Improves Fasting Blood Glucose in Combination with Semaglutide



**** P< 0.0001
*** P< 0.005
** P< 0.01
* P< 0.05

Statistical analysis: One way ANOVA (Dunnett's multiple comparisons test)

- Semaglutide alone reduces fasting glucose levels as expected
- Combination with SRK-439 further improves fasting glucose levels in a dose-dependent manner highlighting additional improvement in metabolic profile

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Opportunity for Safe, Durable Weight Loss: Add Highly Selective Antimyostatin to GLP-1 RA to Preserve Lean Muscle

Exquisite Selectivity

- Only inhibits myostatin
- Avoids undesirable off-target effects [1-3]

Myostatin Inhibition

Preclinical models demonstrated: increased muscle mass

- Beneficial metabolic effects (insulin sensitivity, basal metabolic rate, reduction in fat mass)[4]

Lean Muscle Retention

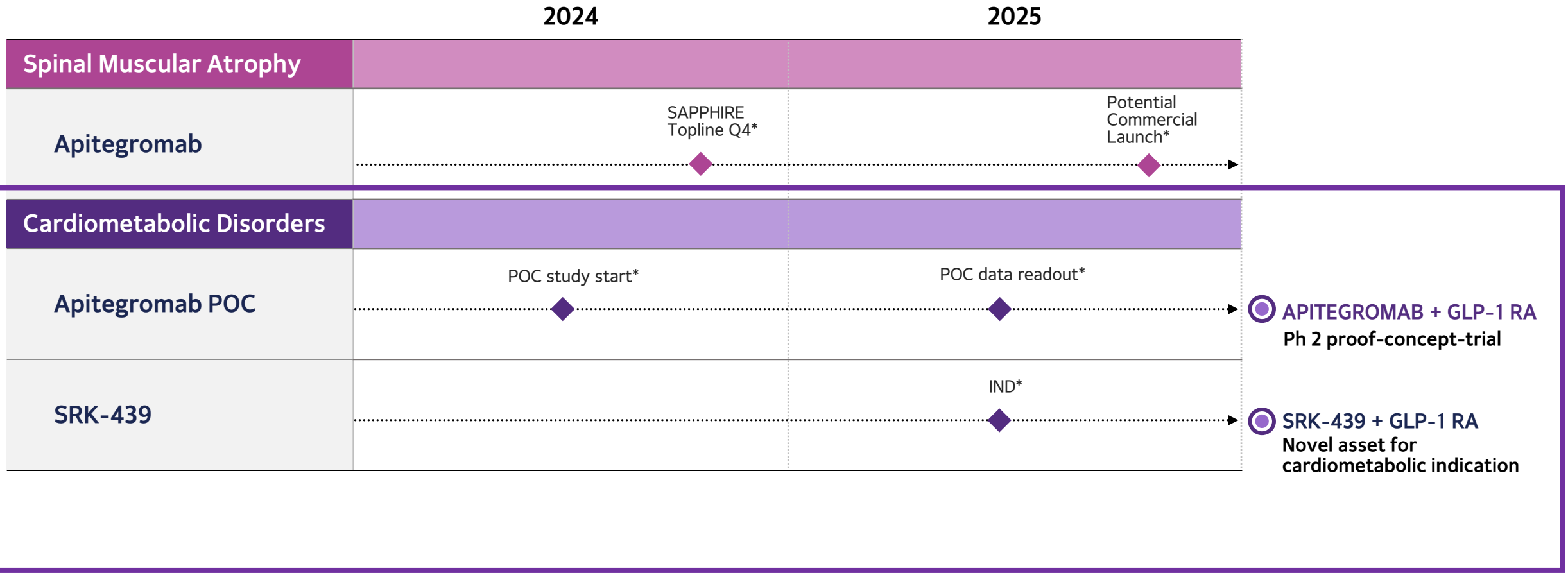
Inhibition of myostatin in combination with GLP-1 RA-driven weight loss may lead to retention of lean muscle mass and combat the counter-regulatory metabolic effects of weight loss

GLP-1 RA=Glucagon-like peptide-1 receptor agonist.

1. Pirruccello-Straub M et al. Blocking extracellular activation of myostatin as a strategy for treating muscle wasting. Sci Reports 2017;8:2922; 2. Welsh BT et al. Preclinical safety assessment and toxicokinetics of apitegromab, an antibody targeting proforms of myostatin for the treatment of muscle-atrophying disease. Int J Tox 2021;40(4):322-336; 3. Barrett D et al. A randomized phase 1 safety, pharmacokinetic and pharmacodynamic study of a novel myostatin inhibitor apitegromab (SRK-015): A potential treatment for spinal muscular atrophy. Adv Ther 2021;38:3203-3222. 4.Yang M et al. Myostatin: A potential therapeutic target for metabolic syndrome. Frontiers in Endocrinology 2023;14:1181913;

Expedite Cardiometabolic Program with Ph2 Proof-of-Concept Study of Apitegromab in Obesity

Creates additional anticipated milestones in next 18-24 months



* Anticipated milestones.
GLP-1 RA=Glucagon-like peptide-1 receptor agonist; IND=Investigational new drug; POC=Proof of concept.

Cardiometabolic Program Summary

Differentiation

- Preclinical data suggests selective mechanism of action that can maintain muscle mass while enhancing fat mass loss, thereby improving metabolic function
- SRK-439: Preclinical data supports the overall target candidate profile to address the cardiometabolic patient population
- Represents a potential new class of treatment

Strong Scientific Rationale

- Strong pre-clinical evidence indicates maintenance or increase in lean muscle mass & enhancement of fat loss when a myostatin selective inhibitor is combined with GLP-1 receptor agonist (GLP-1 RA)
- Scholar Rock has the potential to lead the next frontier in anti-myostatin therapies with pioneered unique approach and differentiated expertise

High Unmet Medical Need & Significant Commercial Opportunity

- Obesity is a growing global epidemic leading to chronic health problems and 4.7M premature deaths annually[1]
- Clinical and commercial landscape evolving quickly amid high unmet need
- Muscle-targeted approach represents a new potential class of treatments

Opportunity

- Expanded investments in pipeline, including to accelerate and advance cardiometabolic program
- Filed composition of matter patent for SRK-439 with projected expiry of 2043

[1]www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

DRAGON

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

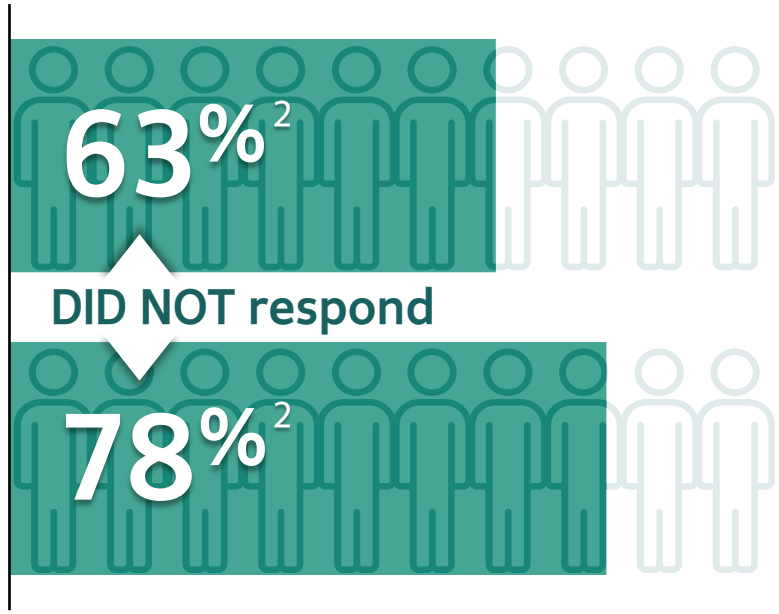
ScholarRock™

Resistance to Checkpoint Inhibitor (CPI) Therapies Remains a Significant Clinical Challenge

7.9–10.4[1]
MILLION
US patients
on CPI therapies

First-line CPI therapy

Second-line (or later) CPI therapy



Clinically derived rationale points to significant opportunity to

increase checkpoint therapy responses by targeting TGFβ-1

1. Source: Gores, M. (2022). *In the eye of the storm: PD-(L)1 inhibitors weathering turbulence* [White paper]. IQVIA. https://www.iqvia.com/library/white-papers/in-the-eye-of-the-storm-pd-l-1-inhibitors-weathering-turbulence
2. Source: Carretero-Gonzalez et al. (2018) Oncotarget 9:8706-8715
Meta-analysis of twelve randomized trials with control arm or adequate safety profile (includes nivolumab, pembrolizumab, and atezolizumab)

Strong Scientific Rationale for the Role of TGFβ Inhibition in Immuno-Oncology

Nature (online), February 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]

Science Translational Medicine, March 25, 2020.

Selective inhibition of TGFβ-1 activation overcomes primary resistance to checkpoint blockade therapy by altering tumor immune landscape

Constance J. Martin, et al.

Vol 12, Issue 536. DOI: 10.1126/scitranslmed.aay8456

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

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, July 24, 2020 NATURE REVIEWS | CLINICAL ONCOLOGY

TGFβ: biology in cancer progression and immunotherapy

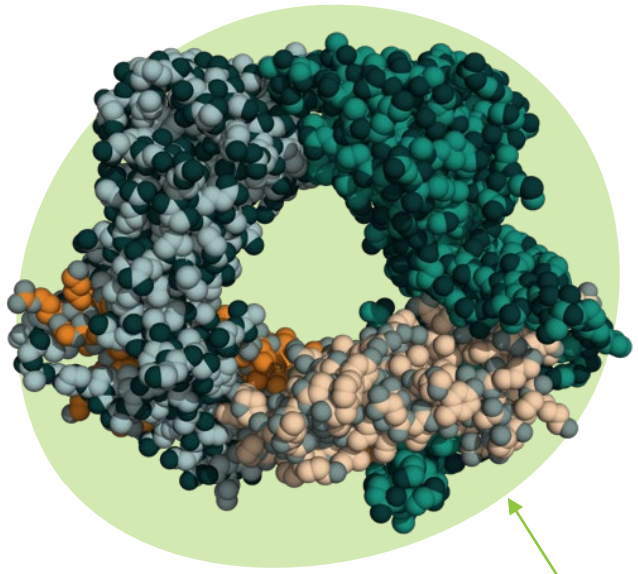
Rik Derynck[1,2,3], Shannon J. Turley[4] and Rosemary J. Akhurst[2,3]

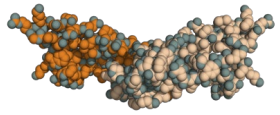
July 24, 2020: https://doi.org/10.1038/ s41571-020-0403-1

August 2022.

"Bristol Myers Squibb Enters Agreement to Acquire Forbius TGF-beta Program"

SRK-181: Unique Latent TGFβ-1 Selective Approach Designed to Overcome Checkpoint Inhibitor Resistance





Traditional Target
"Mature" growth factor

SRK-181: Latent TGFβ-1 Inhibitor

Targets TGFβ-1	**Potential to overcome CPI resistance**	SRK-181 inhibits the TGFβ-1 implicated in check point inhibitor resistance	
Selective to β-1 isoform	**Highly selective to β-1 isoform vs. 2 and 3**	Increases therapeutic window and potentially avoids toxicities associated with non-selective TGFβ inhibition	Other programs target multiple isoforms of TGFβ
Targets the latent form of TGFβ-1	**Increases opportunity to inhibit TGFβ-1**	Selectively targeting the latent form shuts off the growth factor before activation	Most other programs target the mature form of TGFβ-1
Context-independent	**Inhibits all sources of TGFβ-1**	SRK-181 targets all TGFβ-1 sources (LRRC33, GARP and LTBP1 and 3)	Some programs only target one source

1. Wakefield LM, Winokur TS, Hollands RS, Christopherson K, Levinson AD, Sporn MB. Recombinant latent transforming growth factor beta 1 has a longer plasma half-life in rats than active transforming growth factor beta 1, and a different tissue distribution. *J Clin Invest*. 1990 Dec;86(6):1976-84. doi: 10.1172/JCI114932. PMID: 2254455; PMCID: PMC329834.

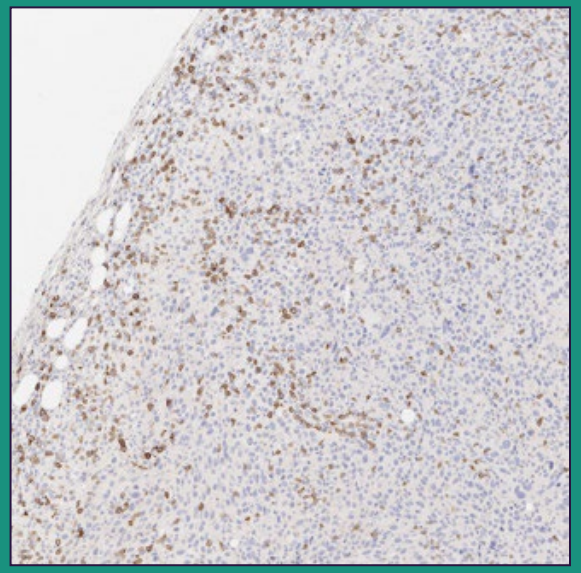
SRK-181-mIgG1 + Anti-PD1 Overcomes Immune Exclusion

Overcoming immune exclusion

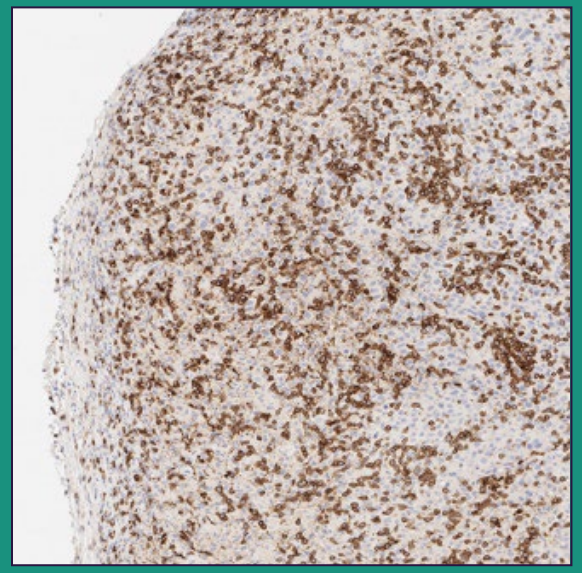
Tumor micro-environment

Anti-PD1

Immune Exclusion



Anti-PD1/ SRK-181-mIgG1

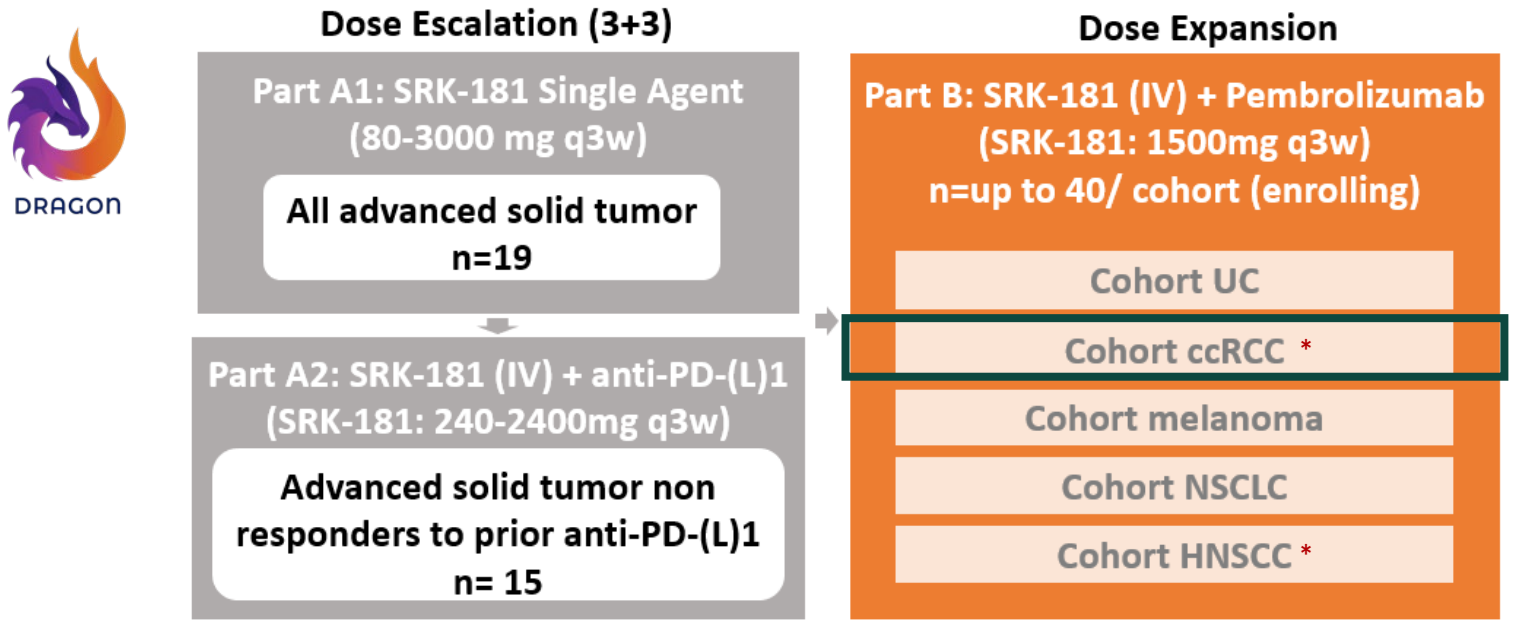


Overcome Exclusion

SRK-181-mIgG1 combination therapy led to influx and amplification of cytotoxic 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.
Data from MBT-2 syngeneic tumor model. Dose 10mg/kg QW for 4 weeks.

SRK-181 | Immuno-Oncology



Eligibility for ccRCC Patients

- >18 years old and ECOG 0–1
- Measurable disease per RECIST v1.1
- At least 1 prior line of anti-PD-1 antibody**
- Part A2:
  - Non-responsive to prior anti-PD-1 with a best response of PD or SD
- Part B:
  - Must have had PD on the most recent prior anti-PD-1 treatment
  - Up to 3 lines of treatment are allowed between the last dose of prior anti-PD-1 treatment

Data from Phase 1 DRAGON Proof-of-Concept Trial

- Supports proof-of-concept for SRK-181 in heavily pre-treated patients with ccRCC resistant to anti-PD-1
- Biomarker data from all cohorts in Part B supports proof-of-mechanism in patients with multiple tumor types

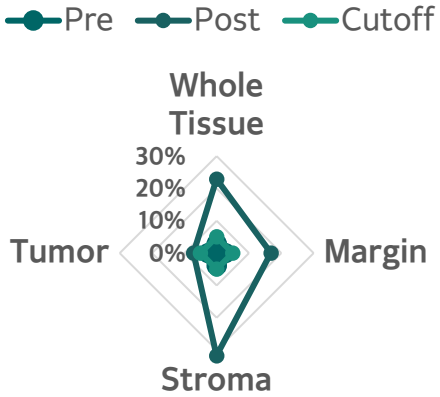
Data as of August 29, 2023

*The clear cell RCC and HNSCC cohorts will also explore the effects of SRK-181 in patients with relapsed response after anti-PD-1 treatment.
1. NCT04291079 on www.clinicaltrials.gov. **ccRCC cohort (n=30): 5 patients received 1 prior line of therapy, 10 patients received 2 prior lines of therapy, and 15 received ≥ 3 lines of therapy. 100% had disease progression from last line of prior therapy.

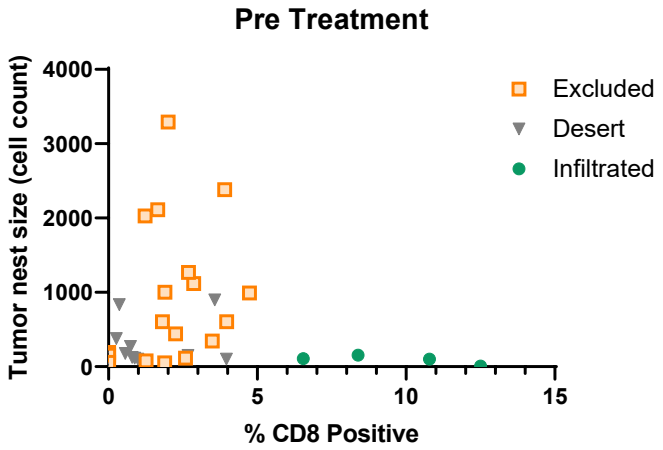
SRK-181 in Combination with Anti-PD1 Increases Infiltration of CD8+ T Cells in Melanoma

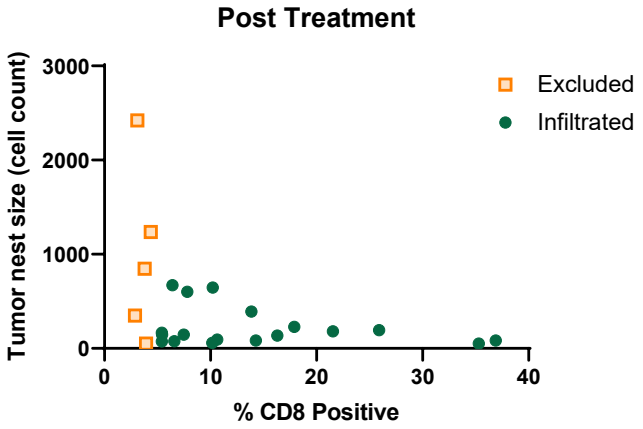
- Paired biopsies from 2 melanoma patients were analyzed for CD8 content.
- An increase in CD8+ T cell infiltration was observed in both biopsy pairs, overcoming an initially excluded or desert phenotype and resulting in more infiltrated tumor nests.
- Shown here is the representative quantification and images from one melanoma patient.

Primary Compartmental Analysis % CD8+ T cells per compartment

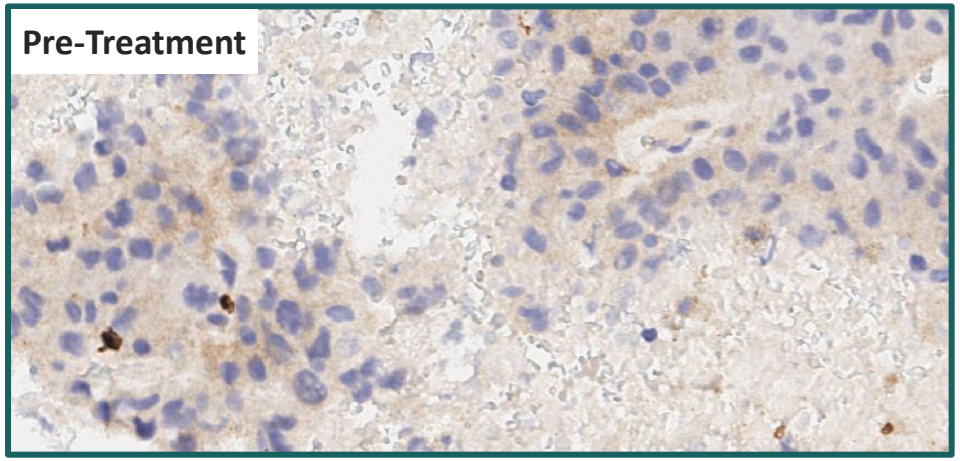


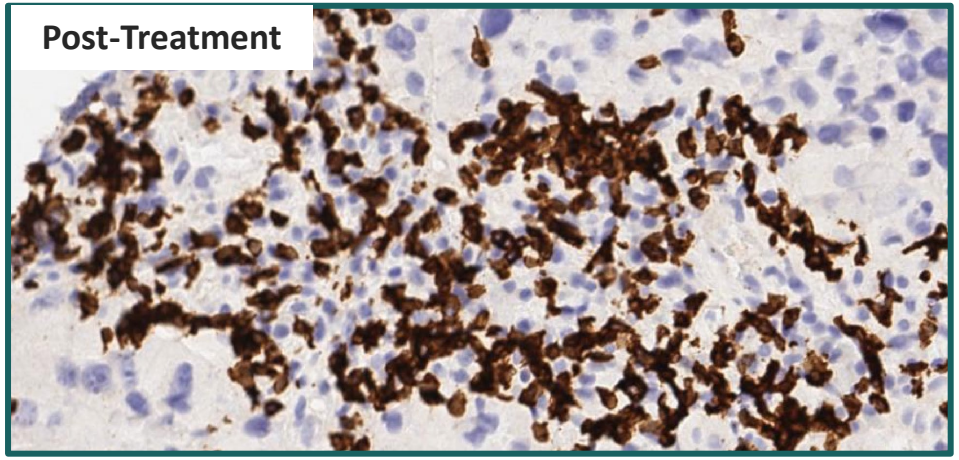
Tumor Nest Analysis



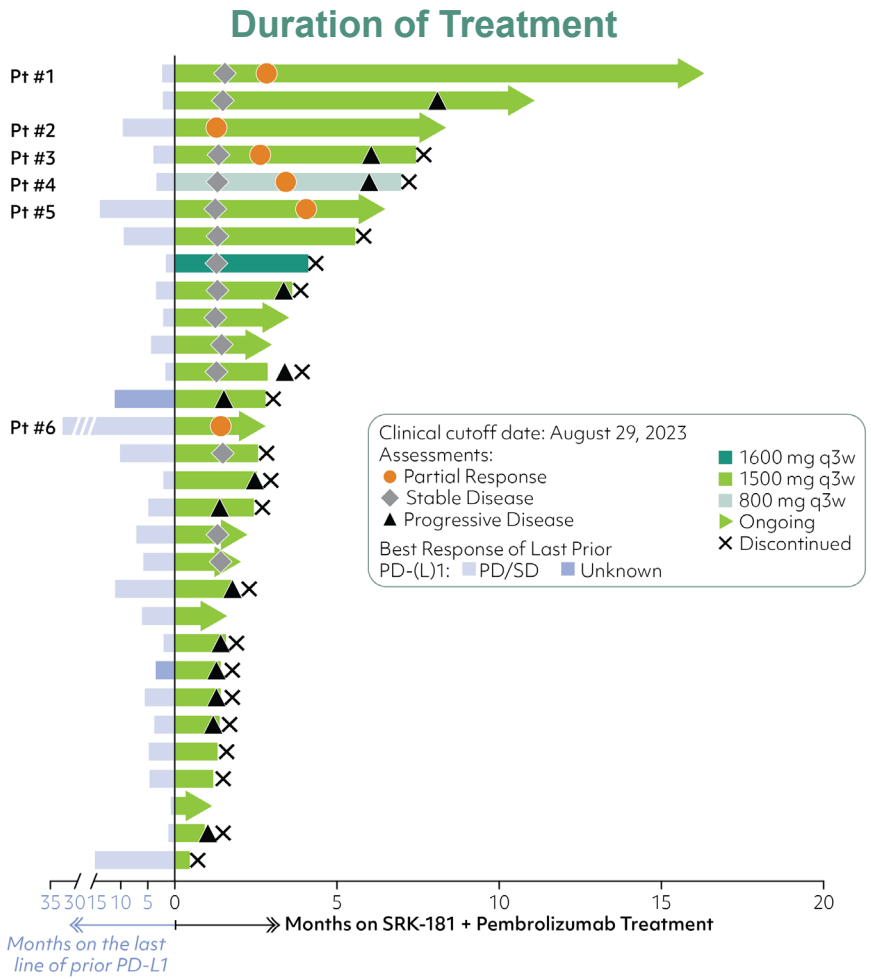


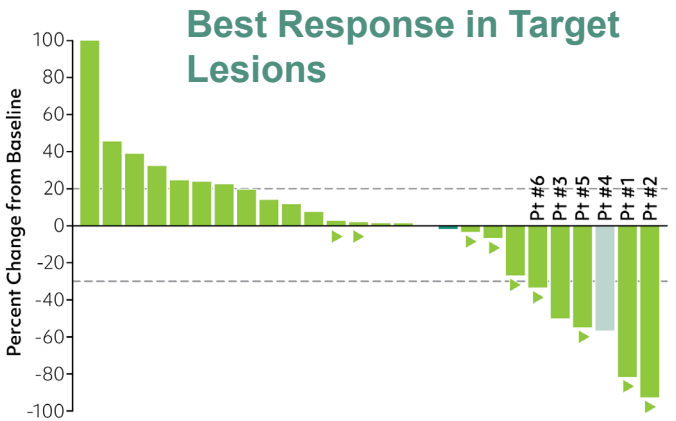
CD8 Stain – Melanoma, Pre and Post Treatment

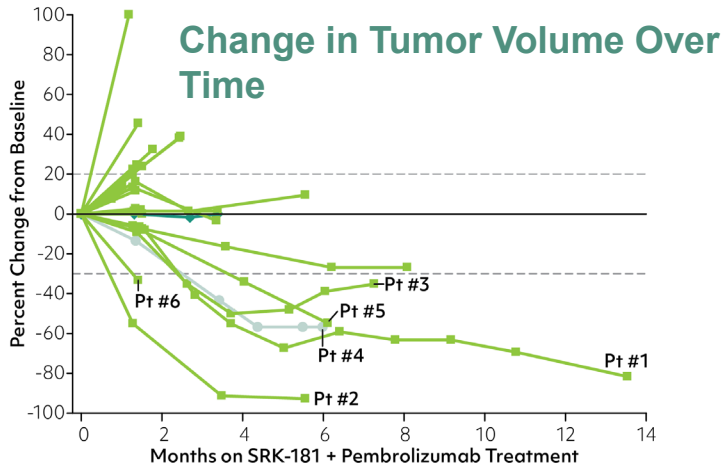




Continued Tolerability & Promising Anti-Tumor Activity
ccRCC Patients







PR=Partial response
SD=Stable disease

SRK-181 + pembrolizumab in ccRCC Patients*

- ORR = **21.4%**
- Disease control rate = **57%**
- **6 PRs** (4 remain on study)
- **33% to 93%** best tumor reduction observed
- **10 SD** patients, 5 of which remain on study
- Combination therapy of SRK-181 + pembrolizumab was **generally well tolerated**

***28 patients; data as of 8/29/23**

SRK-181 Summary

Differentiation

- Monoclonal antibody selectively targeting latent and context-independent binding to TGFβ1
- Novel and highly selective inhibition of TGFβ-1 targeting latent form
- Offers potential to avoid toxicity and dose-limiting challenges of non-selective TGFβ inhibition approaches

Ph1 DRAGON Demonstrated Proof-of-Concept in ccRCC patients

- **Showed objective, durable clinical responses above what is expected from continuing PD-1 alone[1]**
- **Biomarker data supports proof-of-mechanism in multiple tumor types**

NEXT STEPS

Enrollment completed
December 2023

Present ongoing emerging data at future medical meetings

Conduct an end of Phase 1 meeting with regulatory authorities to inform next steps

PD-1=Programmed cell death ligand 1; TGFβ=Transforming growth factor-beta; ccRCC=Clear cell renal cell carcinoma.

1.Sumanta Kumar Pal et al. Atezolizumab plus cabozantinib versus cabozantinib monotherapy for patients with renal cell carcinoma after progression with previous immune checkpoint inhibitor treatment (CONTACT-03): a multicentre, randomised, open-label, phase 3 trial. The Lancet, Volume 402, Issue 10397, 2023, Pages 185-195, https://doi.org/10.1016/S0140-6736(23)00922-4

PD-1/PD-L1)

Fibrosis

ScholarRock™

TGFβ is Established as Key Driver of Fibrosis Across Multiple Diseases

Nature Reviews , April 25, 2016 NATURE REVIEWS | NEPHROLOGY

TGF-β: the master regulator of fibrosis

Xiao-ming Meng[1], David J. Nikolic-Paterson[2] and Hui Yao Lan[3]

Int. J. Mol. Sci. August 27, 2018

Targeting TGF-β Signaling in Kidney Fibrosis

Yoshitaka Isaka

Nature Reviews. August 19, 2014 NATURE REVIEWS | RHEUMATOLOGY

Transforming growth factor β—at the centre of systemic sclerosis

Robert Lafyatis

J. Am. Soc. Nephrol. December 3, 2017

Targeting Anti-TGF-β Therapy to Fibrotic Kidneys with a Dual Specificity Antibody Approach

Steve McGaraughty,* Rachel A. Davis-Taber,† Chang Z. Zhu,* Todd B. Cole,* Arthur L. Nikkel,* Meha Chhaya,† Kelly J. Doyle,* Lauren M. Olson,* Gregory M. Preston,† Chrisine M. Grinnell,† Katherine M. Salte,* Anthony M. Giamis,* Yanping Luo,* Victor Sun,† Andrew D. Goodearl,† Murali Gopalakrishnan,* and Susan E. Lacy†

J Pathol, July 25, 2021

TGF-β as a driver of fibrosis: physiological roles and therapeutic opportunities

Erine H Budi[1], Johanna R Schaub[1], Martin Decaris[1], Scott Turner[1], Rik Derynck[2]

J Receptors Sign Trans, Feb 13, 2020

Inevitable role of TGF-β in progression of nonalcoholic fatty liver disease

Bhagyalakshmi Nair and Lekshmi R. Nath

Proc Am Thorac Soc, July 3, 2006

Transforming Growth Factor β
A Central Modulator of Pulmonary and Airway Inflammation and Fibrosis

Dean Sheppard

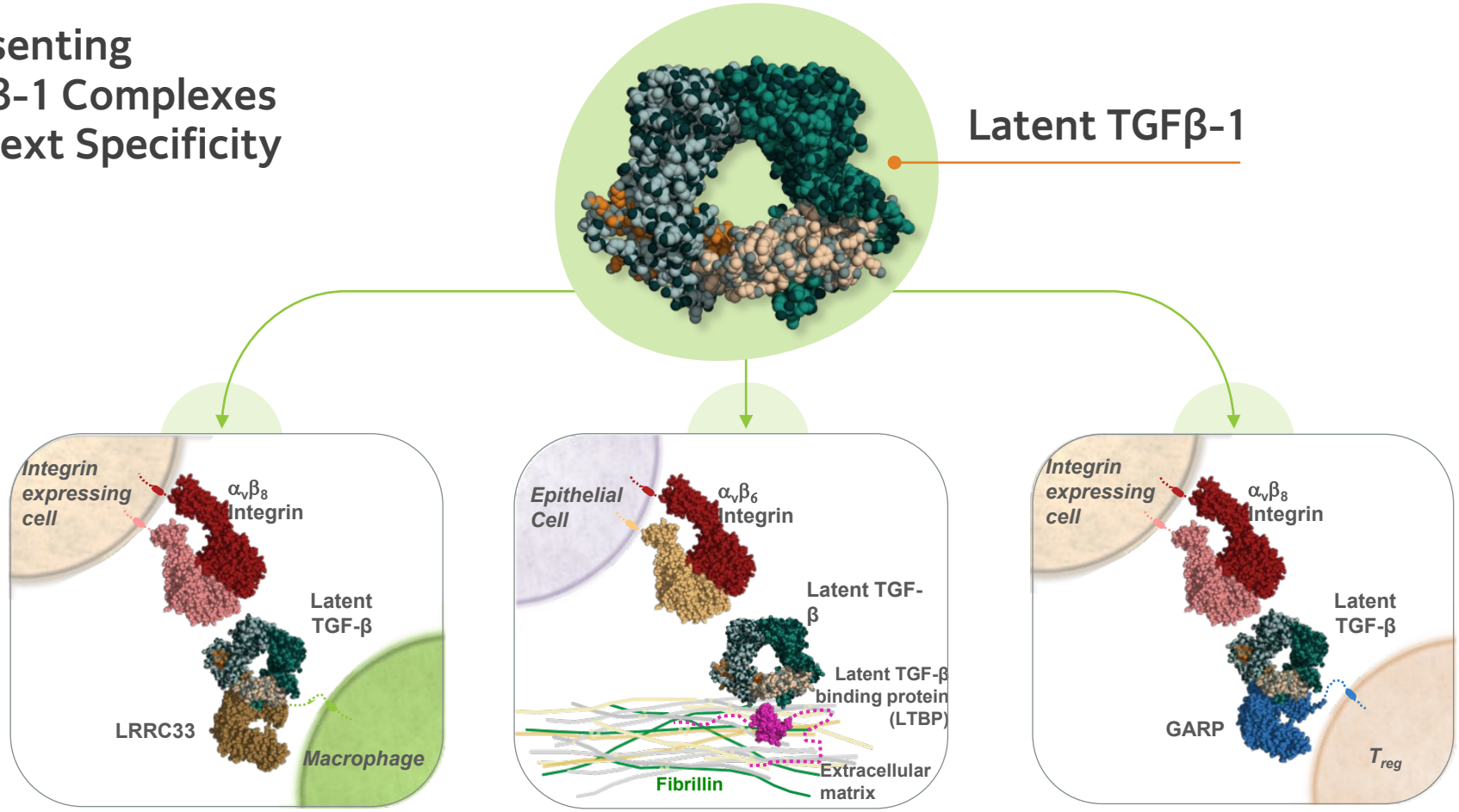
PNAS, February 24, 1986 PNAS

Transforming growth factor type β: Rapid induction of fibrosis and angiogenesis in vivo and stimulation of collagen formation in vitro

ANITA B. ROBERTS* MICHAEL B. SPORN*, RICHARD K. ASSOIAN*, JOSEPH M. SMITH*, NANETTE S. ROCHE*, LALAGE M. WAKEFIELD*, URSULA I. HEINE*, LANCE A. LIOTTA*, VINCENT FALANGA†, JOHN H. KEHRL‡, AND ANTHONY S. FAUCI‡

Targeting Latent TGFβ-1 Complexes Creates Multiple "Handles" For Selectivity

Targeting Presenting Molecule/TGFβ-1 Complexes Provides Context Specificity



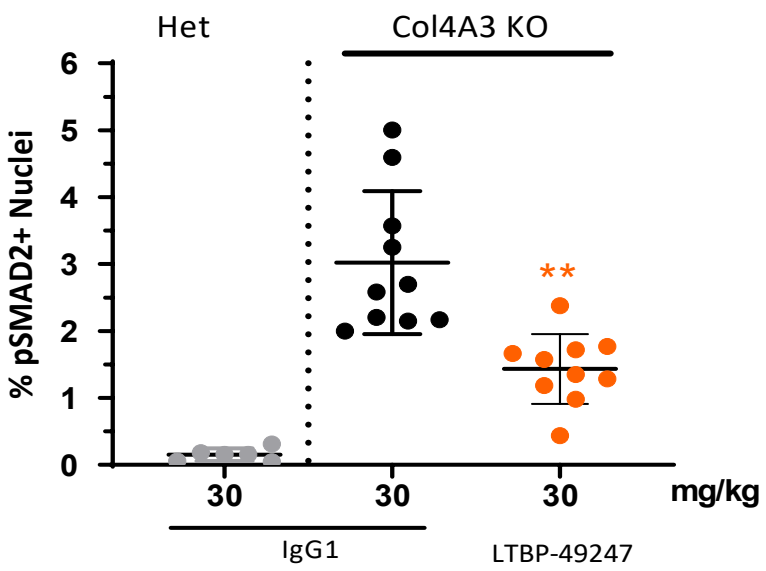
LRRC33 Presents TGFβ on Macrophages

LTBP1 & 3 Present TGFβ in Connective Tissue

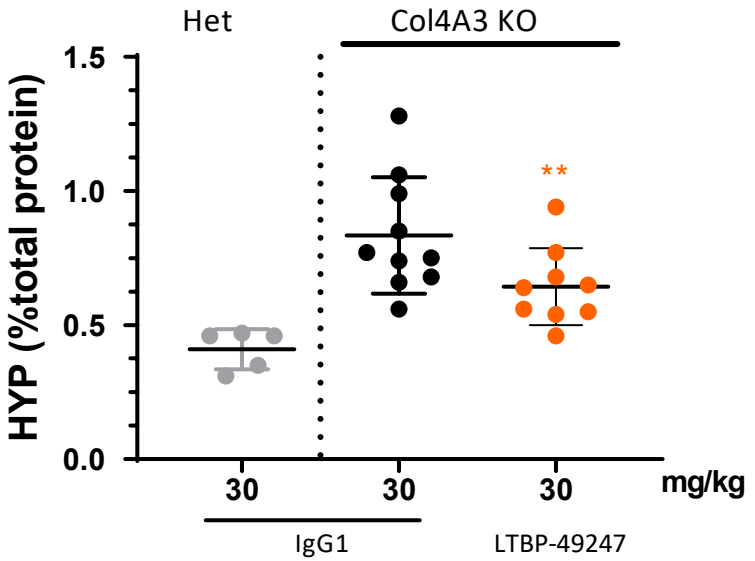
GARP Presents TGFβ on Tregs

LTBP-49247 Reduced TGFβ Signaling and Fibrosis in Preclinical Models of Kidney Fibrosis

LTBP-49247 reduced a TGFβ PD biomarker in kidneys of *Col4a3* KO mice (Alport Syndrome model)



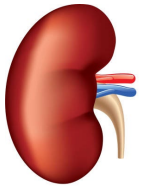
LTBP-49247 reduced fibrosis in kidneys of Alport model



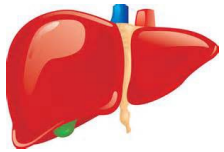
** p < 0.01
One way ANOVA vs. IgG
HYP=hydroxyproline

- Efficacy also seen in rat model of kidney fibrosis
- No observed toxicity in mouse 13-week non-GLP repeat dose study
- Favorable PK in cynomolgus monkeys (t1/2 ~28 days) suggests LTBP-49247 is amenable to clinical subcutaneous dosing with promising developability profile

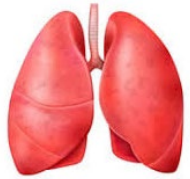
Significant Opportunities to Address High Unmet Need Across Multiple Fibrotic Indications



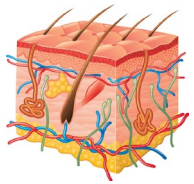
Alport Syndrome (AS)
Focal Segmental Glomerulosclerosis (FSGS)
IgA Nephropathy (IgAN)



Primary Sclerosing Cholangitis (PSC)



Idiopathic Pulmonary Fibrosis (IPF)



Diffuse Cutaneous Systemic Sclerosis (dcSSc)

Collectively, significant commercial potential given large patient population with clear high unmet need given poor outcomes and lack of effective therapeutics

- Significant impact to delay or stop progression to end-stage disease and organ transplant
- Expansion opportunities via other indications given shared etiologies

Iron-Restricted Anemia

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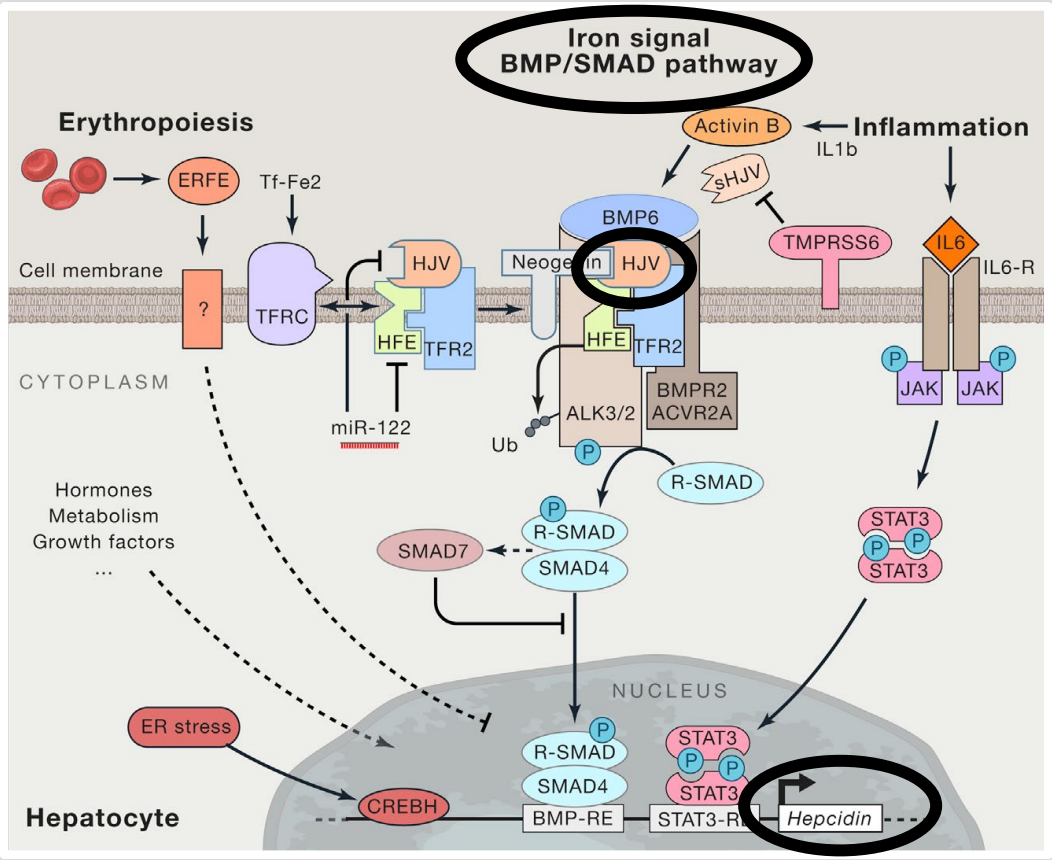
BMP6/RGMc Pathway is a Well Validated Regulator of Systemic Iron Homeostasis



HJV/RGMc is a key player in the regulation of hepcidin expression

- Human mutations in HJV/RGMc establish it as a central player in hepcidin regulation[1]
- Knockout phenotypes and tissue-specific expression pattern demonstrate that its predominant role is in iron homeostasis[2]
- Member of repulsive guidance molecule (RGM) family (RGMa, RGMb, RGMc/HJV) that act as BMP co-receptors to modulate BMP signaling[3]

Anemia of Inflammation/ Chronic Disease

- Elevation of proinflammatory cytokines drives increased hepcidin expression and results in anemia due to functional iron deficiency[4]

Untreated	Ab treated
↑ Hepcidin	↓ Hepcidin
↓ Serum iron	↑ Serum iron

Fig: Muckenthaler, M.U., Rivella, S., Hentze, M.W. and Galy, B. (2017) A Red Carpet for Iron Metaboism. *Cell*, 168(3): 344-361

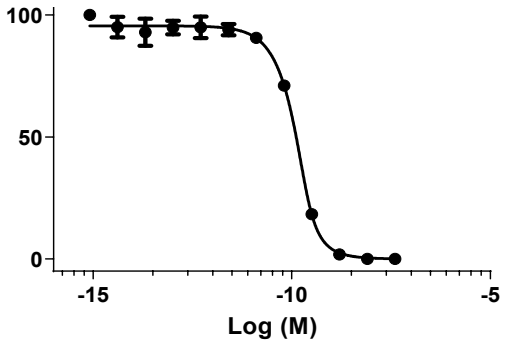
1: *Kuns-Hashimoto R, et al.* (2008) Selective binding of RGMc/hemojuvelin, a key protein in systemic iron metabolism, to BMP-2 and neogenin. *Am J Physiol Cell Physiol* 294(4):C994-C1003
2: *Constante M, et al.. (2007)* Repression of repulsive guidance molecule C during inflammation is independent of Hfe and involves tumor necrosis factor-alpha. *Am J Pathol* 170(2):497-504
3: *Core A.B., et al.* (2014) Hemojuvelin and bone morphogenetic protein (BMP) signaling in iron homeostasis. *Front Pharmacol.* 5:104.
4. Wang CY and Babitt JL. (2016) Hepcidin Regulation in the Anemia of Inflammation. *Curr Opin Hematol* 23(3): 189-197.

HJV-35202: An Investigational High-Affinity Antibody Demonstrating Selective Inhibition of HJV/RGMc and Robust PK/PD in Cynos

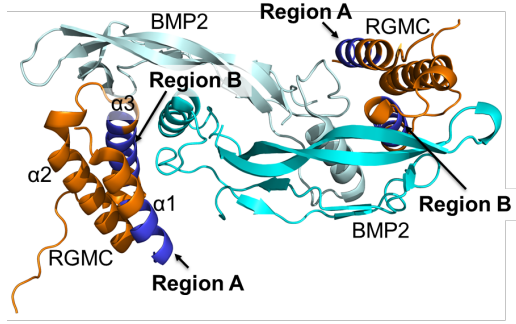
Key Attributes of HJV-35202:[1,2]

- High-affinity antibody
- Specific to RGMc, with mechanism of specificity understood
- Cross-reactive to human, mouse, rat and cyno
- Sustained PD observed in healthy rats and cynos, with clear PK/PD relationship
- Highly manufacturable framework with no sequence liabilities
- Formulatable into a subcutaneous format (150 mg/mL)

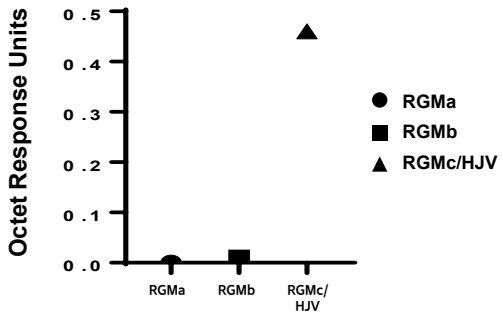
Potent in vitro binding affinity (KD=3.9E-11)



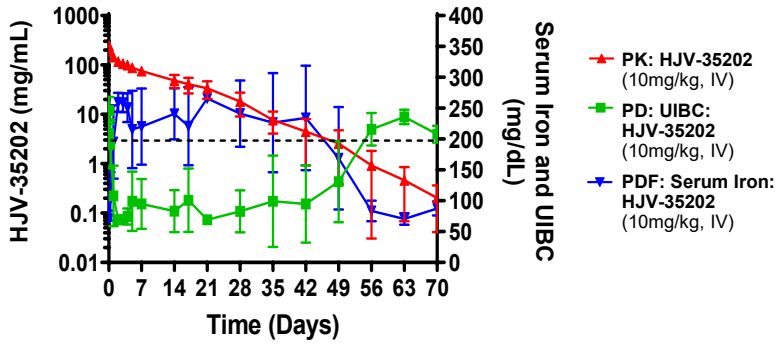
Highly specific to RGMc/HJV with well understood mechanism



Specific to RGMc over other RGM family members

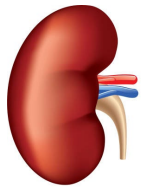


Sustained PD effect in single dose Cyno study



1. Nicholls S.B., et al. Poster: RGMc-selective antibodies modulate iron homeostasis in vivo, *12th International BMP Conference, Tokyo, October 2018*
2. Scholar Rock, Data on File

Significant Opportunities to Target Iron-Restricted Anemias Across Multiple Indications



Chronic Kidney Disease (CKD)

Anemia of Chronic Inflammation (AI)

Myelofibrosis (MF)

Targeting RGMc/HJV for anemia is well validated and relatively de-risked

- High levels of hepcidin, the main regulator of systemic iron metabolism, are associated with anemia across various diseases

Safe and convenient RGMc inhibitor has promise of improving patient outcomes across multiple indications as stand alone or in combination with SoC

- Significant and clear unmet need given lack of approved treatments or severe limitations of current treatments
- Well defined patient population

Collectively, sizeable commercial opportunity given relatively large population

- Potential for rapid POC with clear regulatory path
- Opportunity to build an anemia franchise with initial POC and indication expansion in the future

Key Accomplishments and 2024 Strategic Priorities

2023
ACCOMPLISHMENTS

- COMPLETED SAPPHIRE enrollment
- EXPANDED antimyostatin program into cardiometabolic disorders
- SUCCESSFUL $98M public offering, extending projected runway into second half of 2025

Building on this success,
in 2024 we are focused on

SAPPHIRE Readout in Q4

Prepare for commercialization

Initiate Ph 2 POC trial with apitegromab in obesity

Advance IND-enabling studies for SRK-439

IND=Investigational new drug; POC=Proof of concept;

Appendix

ScholarRock™

Leadership Team: Experienced in Drug Development and Commercialization

Jay Backstrom, MD, MPH
President & CEO

30 years of clinical R&D experience, leading multiple successful regulatory approvals

Ted Myles, MBA
Chief Operating Officer & CFO

25 years of progressive experience in clinical and commercial-stage companies

Jing Marantz, MD, PhD
Chief Medical Officer

20 years of development and medical leadership experience across neurology, hematology/oncology, and rare diseases

Tracey Sacco
Chief Commercial Officer

20 years of commercial leadership experience, including product launch and global commercial strategy

Mo Qatanani, PhD
SVP, Research

15 years of industry experience on the strategic and operational sides of research & development

Caryn Parlavecchio
Chief Human Resources Officer

25 years of experience leading HR, culture transformation, leadership development, DEI, and talent management

Junlin Ho, JD
General Counsel & Corporate Secretary

15 years of experience leading and advising life sciences companies in areas of legal and compliance

Apitegromab Summary

Differentiation

- Potential muscle-targeted therapy in SMA
- Robust body of data supports therapeutic potential

Strong Scientific Rationale

- Strong pre-clinical evidence indicates upstream targeting of structurally differentiated latent myostatin avoids undesirable off-target effects
- Phase 2 TOPAZ trial demonstrated the therapeutic potential of inhibiting the latent forms of growth factors

Clear Clinical Pathway

- TOPAZ has demonstrated sustained motor function gains to date in patients with nonambulatory Types 2 and 3 SMA
- Pivotal Phase 3 SAPPHIRE trial: enrollment completed in Q3 2023; data readout expected in Q4 2024
- FDA has granted Fast Track, Orphan Drug, and Rare Pediatric Disease designations
- European Medicines Agency (EMA) has granted Priority Medicines (PRIME) and Orphan designations

High Unmet Medical Need & Significant Commercial Opportunity

- SMN therapies prevent further degeneration of motor neurons but do not directly address muscle atrophy
- Apitegromab is a muscle-targeted approach and has the potential to address this unmet medical need
- Global SMA treatment market expected to grow in the next five years

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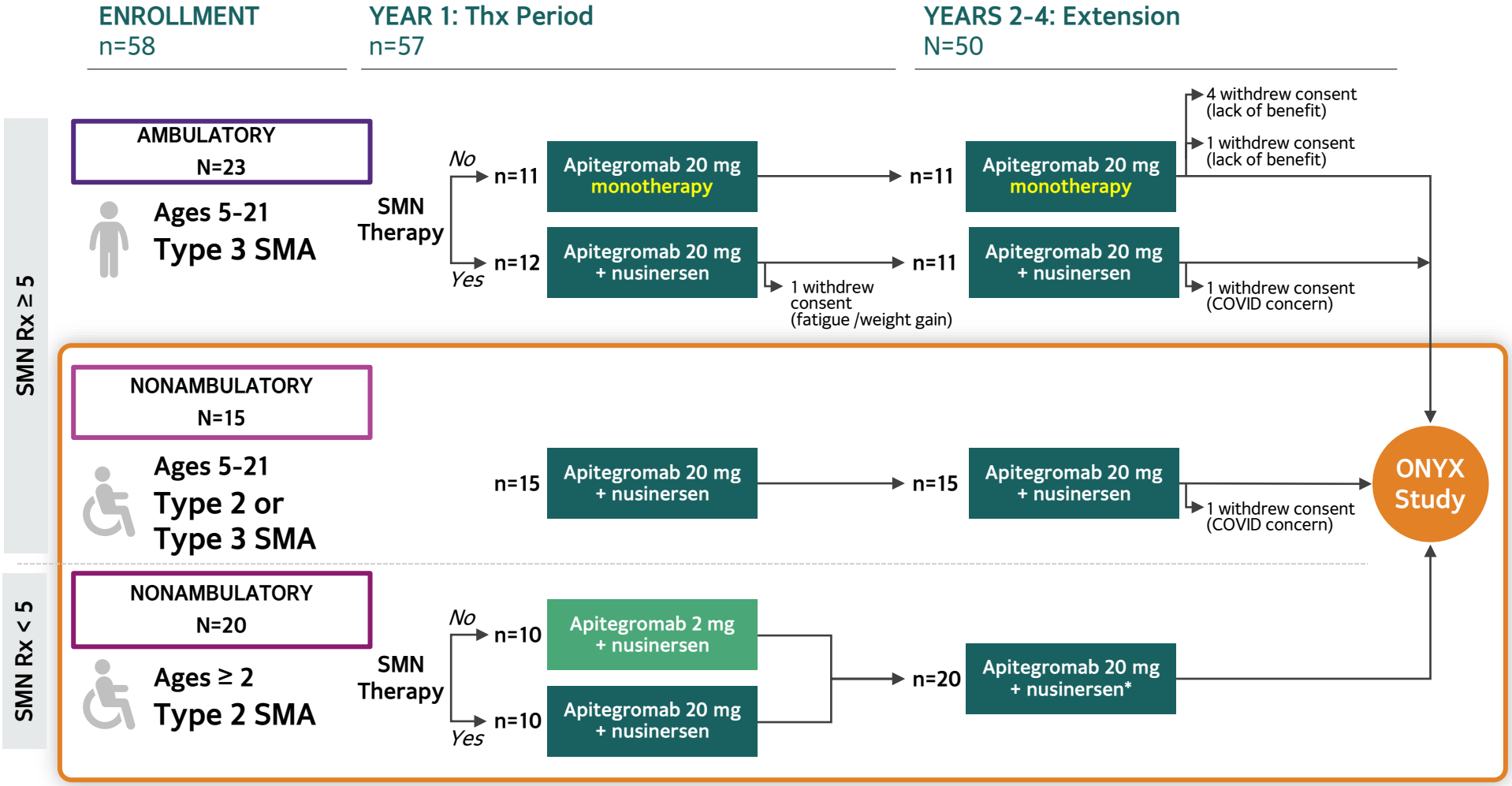
TOPAZ Baseline Characteristics[1,2]

			N (dosed)	Mean age (min, max)	Mean RHS (min, max)	Mean HFMSE (min, max)	Prior Nusinersen, Months Mean (min, max)*	No. of patients with 2,3, or 4 SMN2 copies	Discontinuation(s)
Ambulatory	COHORT 1: Age 5-21	20 mg/kg monotherapy	11	12 (7, 19)	48 (26, 63)		N/A	1, 4, 4	0
		20 mg/kg + nusinersen	12	13 (7, 21)	51 (43, 62)		20 (12, 28)	0, 9, 1	1†
		Pooled	23	13 (7, 21)	50 (26, 63)		N/A	1, 13, 5	1†
Nonambulatory	COHORT 2: Age 5-21	20 mg/kg + nusinersen	15	12 (8, 19)		23 (13, 39)	25 (12, 39)	0, 11, 2	0
	COHORT 3: Age 2+	20 mg/kg + nusinersen	10	4 (2, 6)		24 (14, 42)	24 (10, 34)	1, 8, 0	0
		2 mg/kg + nusinersen	10	4 (2, 6)		26 (12, 44)		1, 8, 1	0
		Pooled	20	4 (2, 6)		25 (12, 44)		2, 16, 1	0

*Patients on average received ~2 years of nusinersen treatment at baseline and ~3 years of nusinersen treatment by the end of the TOPAZ study (12-months). SMN2 copy numbers were not available for all patients. †12-month baseline characteristics recorded in the table, 1-cohort 1 patient and 1- cohort 2 patient discontinued during 24M Extension Period A. All discontinuations were for reasons unrelated to study drug.
HFMSE, Hammersmith Functional Motor Scale–Expanded; max, maximum; min, minimum; RHS, Revised Hammersmith Scale; SMN, survival motor neuron.
1. Crawford T, et al. Neuromuscul Disord. 2022;32(Suppl1):S86-S87. P102. 2. Crawford T, et al. TOPAZ Extension: 24-month Efficacy and Safety of Apitegromab in Patients With Later-onset Spinal Muscular Atrophy (Type 2 and Type 3 SMA). Presented at CureSMA Annual Conference; June 16-19, 2022.

TOPAZ Patient Disposition Over 36 Months



a. Patients stratified based on previous treatment with approved SMN therapy.
b. Patients randomized to receive 2 or 20 mg/kg apitegromab.
*Includes patients who crossed over from 2 mg/kg to 20mg/kg starting week 68 through week 104
** Excludes patients on monotherapy
SMN Rx=SMN therapy.

TOPAZ patient retention

PRIMARY TREATMENT:

58 ENROLLED

57 completed primary treatment period and enrolled in the extension study

- 1 withdrew consent due to fatigue & weight gain

EXTENSION:

57 ENROLLED

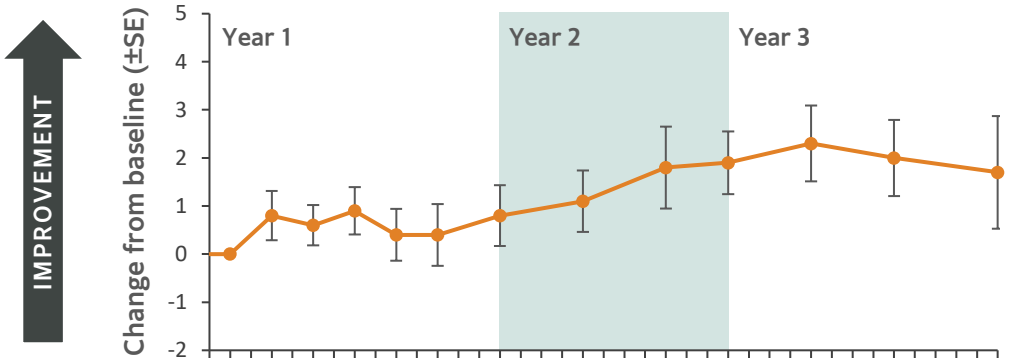
7 discontinued

- 2 due to concerns with COVID-19
- 5 on monotherapy due to lack of benefit
- >90% of patients on combination therapy remained in study**

Pooled Nonambulatory Patients | Age 2 – 12 | All Doses | Over 36 Months

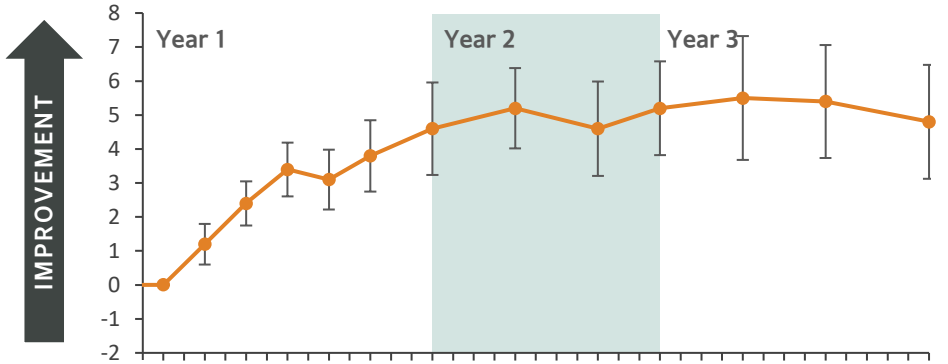
Improvements in PRO Measures Consistent With Motor Function

PEDI-CAT Daily Activities



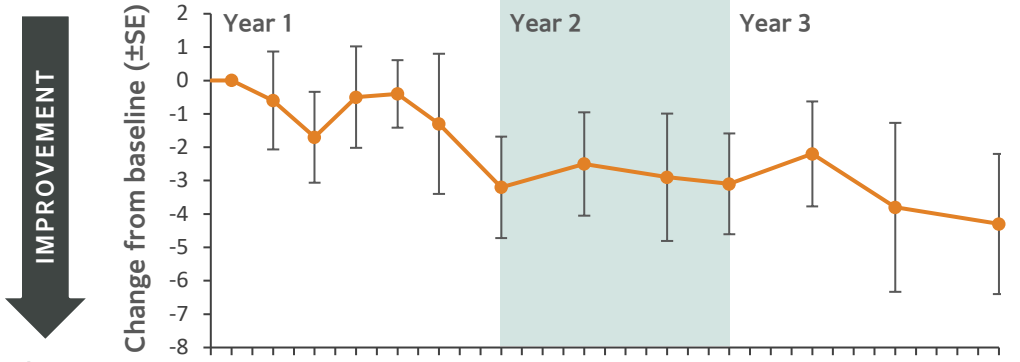
Time (weeks)	0	8	16	24	32	40	52	68	84	104	120	136	156
No. of observations	25	23	24	16	18	20	20	23	18	19	14	13	15

HFMSE



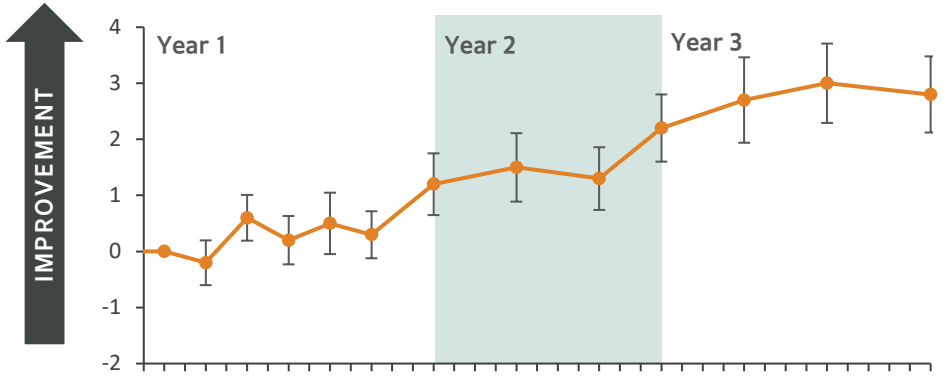
Time (weeks)	0	8	16	24	32	40	52	68	84	104	120	136	156
No. of observations	29	29	29	23	24	26	26	26	26	23	22	22	23

PROMIS Fatigue (Proxy)



Time (weeks)	0	8	16	24	32	40	52	68	84	104	120	136	156
No. of observations	21	19	18	15	15	18	12	16	17	16	13	11	12

RULM



Time (weeks)	0	8	16	24	32	40	52	68	84	104	120	136	156
No. of observations	28	28	28	22	23	26	25	26	26	25	22	22	22

N = 29.; Baseline mean age=5.5 |**Time on SMN Rx=24.6m**

HFMSE=Hammersmith Functional Motor Scale Expanded; OC=observed case; PEDI-CAT=Pediatric Evaluation of Disability Inventory Computer Adaptive Test; PROMIS=Patient Reported Outcome Measurement Information System; RULM=Revised upper limb module; SE=standard error of the mean. SMN Rx=SMN therapy. Data on File. Scholar Rock, Inc. Cambridge, MA. Data cutoff date as of March 13, 2023. Error bars represent standard error (SE). Data cutoff date as of March 13, 2023. The updated PEDI-CAT analysis included additional records (2 at 12 months and 1 at 24 months) that were not available at the time of previous analysis. Apitegromab is an investigational drug candidate being evaluated for the treatment of spinal muscular atrophy. Apitegromab has not been approved for any use by the US FDA or any other health authority, and its safety and efficacy have not been established.

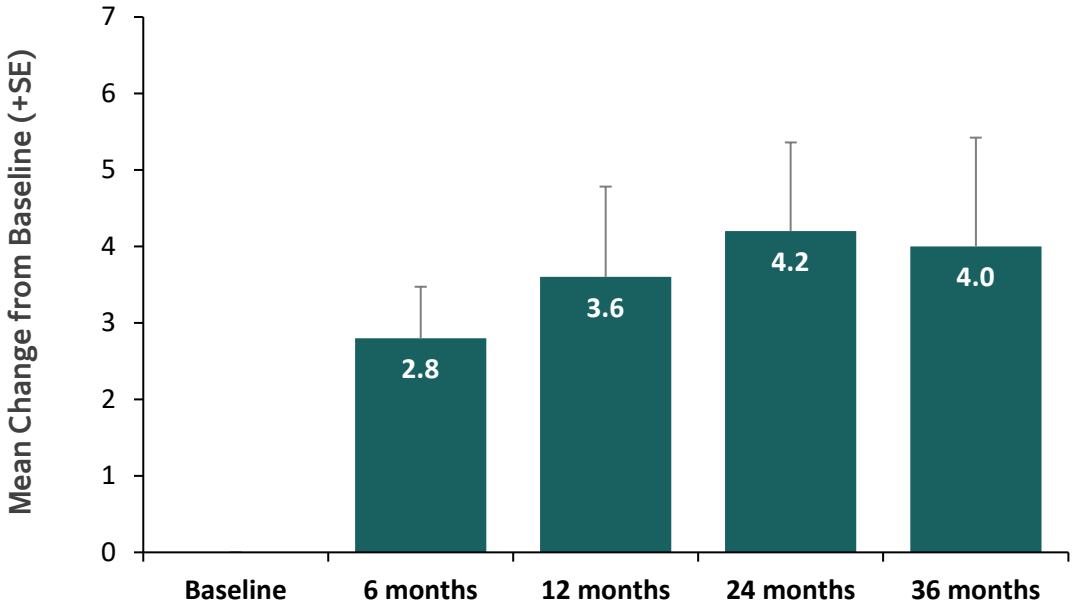
Motor Function Outcomes by HFMSE Over 36 Months

Improvements Were Substantial and Sustained

Pooled Nonambulatory Patients

Age 2-21 Years
All Doses (N=35)

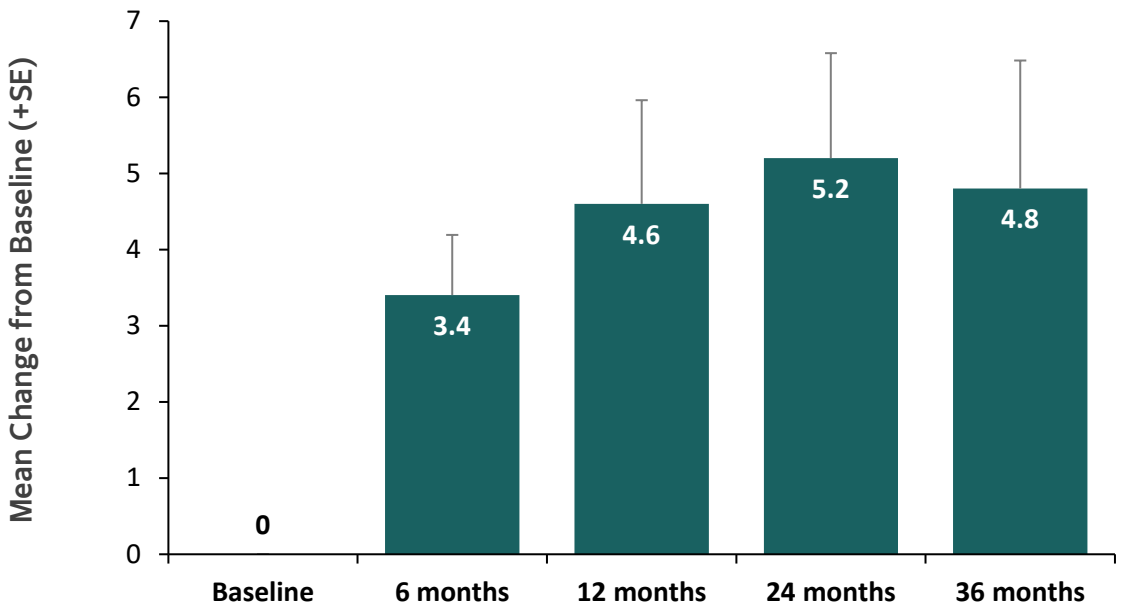
Baseline mean age=7.3 | Time on SMN Rx=24.1m



n=	35	29	32	29	28
95% CI=		(1.4, 4.1)	(1.2, 6.0)	(1.9, 6.6)	(1.0, 6.9)

Age 2-12 Years
All Doses (N=29)

Baseline mean age=5.5 | Time on SMN Rx=24.6m



n=	29	23	26	23	23
95% CI=		(1.8, 5.0)	(1.8, 7.4)	(2.3, 8.0)	(1.3, 8.3)

For the 36-month evaluation, an observed case analysis was conducted, which pooled all the nonambulatory patients (Cohorts 2 and 3) and was based upon the available data for given timepoints. This analysis population included patients receiving either low dose (2 mg/kg) or high dose (20 mg/kg) apitegromab (inclusive of patients in Cohort 3 who switched from 2 mg/kg to 20 mg/kg in Year 2). This analysis excludes data post scoliosis surgery from seven patients. One patient did not conduct HFMSE at time of database lock for 24 months, however, this patient had an unscheduled HFMSE score one month prior to their scheduled visit. In the most recent analysis, this result was included in the 24-month analysis. Error bars represent SE. CI represents confidence interval. SMN Rx=SMN therapy. In the age 2-21 group, 18/28 patients achieved ≥ 1-pt gains, and 11/28 patients ≥ 3-pt gains at 36 months. Data cutoff date as of March 13, 2023. Apitegromab is an investigational drug candidate being evaluated for the treatment of spinal muscular atrophy. Apitegromab has not been approved for any use by the US FDA or any other health authority, and its safety and efficacy have not been established.

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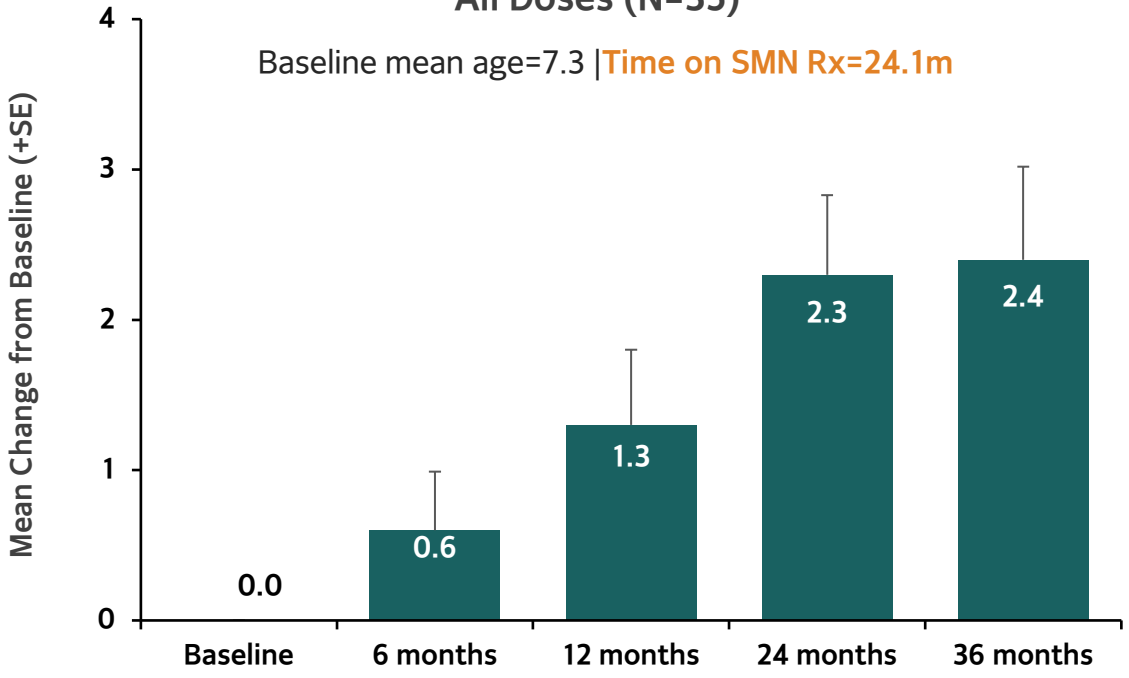
Motor Function Outcomes by RULM Over 36 Months

Improvements Were Substantial and Sustained

Pooled Nonambulatory Patients

Age 2-21 Years
All Doses (N=35)

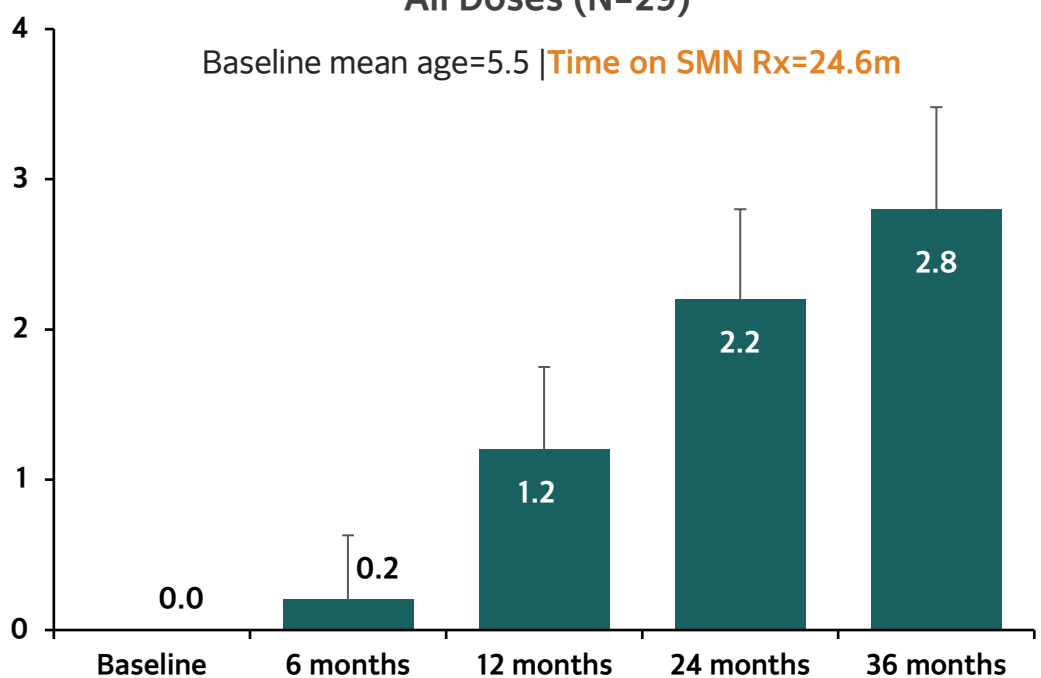
Baseline mean age=7.3 |Time on SMN Rx=24.1m



n=	35	28	31	31	27
95% CI=		(-0.2, 1.4)	(0.2, 2.3)	(1.2, 3.3)	(1.1, 3.7)

Age 2-12 Years
All Doses (N=29)

Baseline mean age=5.5 |Time on SMN Rx=24.6m



n=	29	22	25	25	22
95% CI=		(-0.7, 1.1)	(0.1, 2.4)	(1.0, 3.5)	(1.4, 4.2)

For the 36-month evaluation, an observed case analysis was conducted, which pooled all the nonambulatory patients (Cohorts 2 and 3) and was based upon the available data for given timepoints. This analysis population included patients receiving either low dose (2 mg/kg) or high dose (20 mg/kg) apitegromab (inclusive of patients in Cohort 3 who switched from 2 mg/kg to 20 mg/kg in Year 2). This analysis excludes data post scoliosis surgery from seven patients. One patient did not conduct RULM at month 24, however, had an unscheduled RULM score one month prior to their scheduled visit. In the most recent analysis, this result was included in the 24-month analysis. Error bars represent standard error (SE). CI represents confidence interval. SMN Rx=SMN therapy. In the age 2-21 group, 18/27 patients achieved ≥ 1-pt gains, and 15/27 patients ≥ 2-pt gains at 36 months. Data cutoff date as of March 13, 2023. Apitegromab is an investigational drug candidate being evaluated for the treatment of spinal muscular atrophy. Apitegromab has not been approved for any use by the US FDA or any other health authority, and its safety and efficacy have not been established.

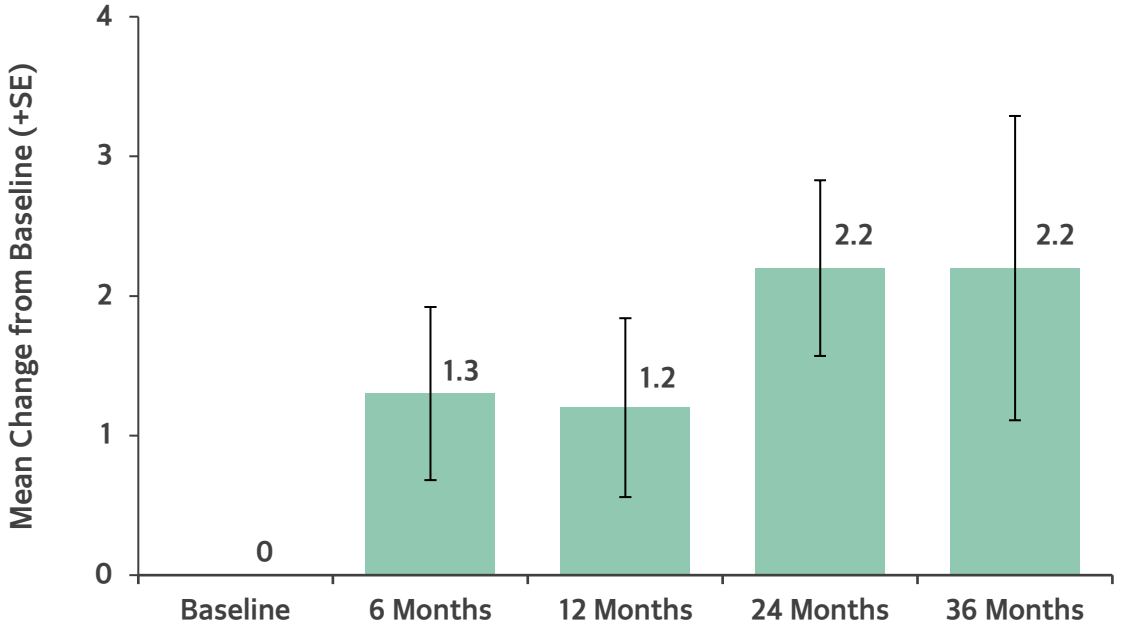
PEDI-CAT Daily Activities Over 36 Months

Improvements Were Substantial and Sustained

Pooled Nonambulatory Patients

Age 2-21 Years
All Doses (N=35)

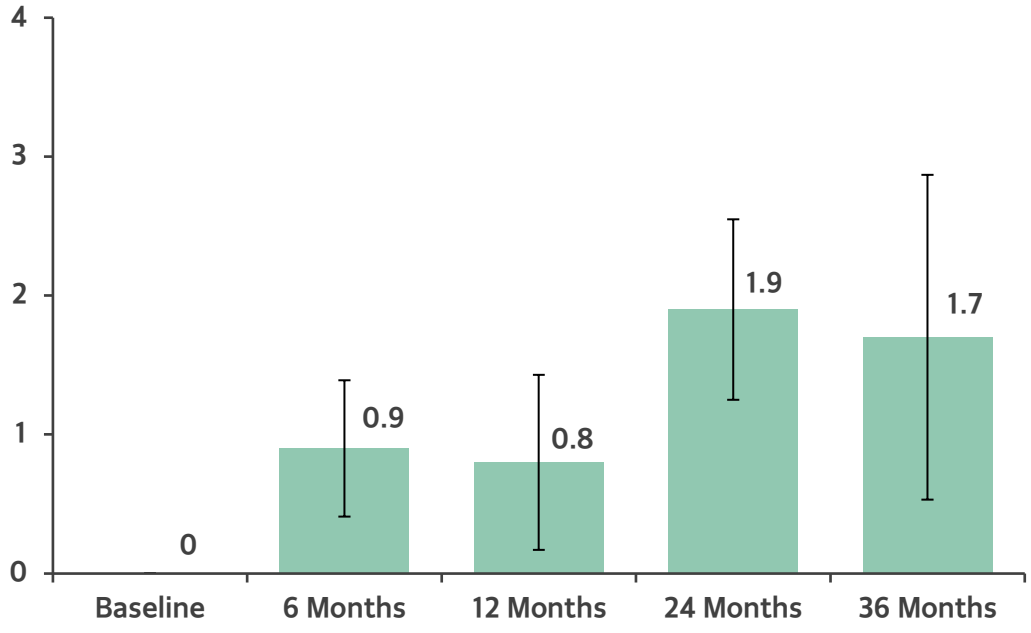
Baseline mean age=7.3 | Time on SMN Rx=24.1m



n=	35	21	25	23	17
95% CI=		(-0.0, 2.6)	(-0.1, 2.6)	(0.9, 3.5)	(-0.1, 4.5)

Age 2-12 Years
All Doses (N=29)

Baseline mean age=5.5 | Time on SMN Rx=24.6m



n=	29	16	20	19	15
95% CI=		(-0.1, 2.0)	(-0.5, 2.1)	(0.5, 3.2)	(-0.8, 4.2)

For the 36-month evaluation, an observed case analysis was conducted, which pooled all the nonambulatory patients (Cohorts 2 and 3) and was based upon the available data for given timepoints. This analysis population included patients receiving either low dose (2 mg/kg) or high dose (20 mg/kg) apitegromab (inclusive of patients in Cohort 3 who switched from 2 mg/kg to 20 mg/kg in Year 2). Error bars represent SE. CI represents confidence interval. SMN Rx=SMN therapy. Data cutoff date as of March 13, 2023. The updated analysis included additional records (2 at 12 months and 1 at 24 months) that were not available at the time of previous analysis. Apitegromab is an investigational drug candidate being evaluated for the treatment of spinal muscular atrophy. Apitegromab has not been approved for any use by the US FDA or any other health authority, and its safety and efficacy have not been established.

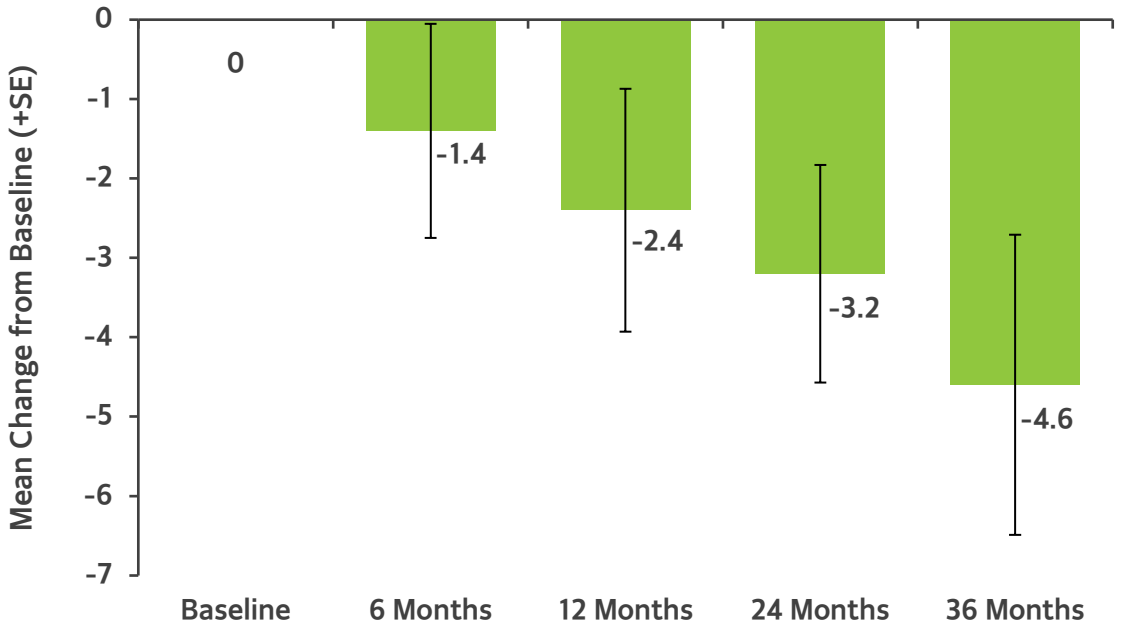
PROMIS Fatigue (Proxy) Over 36 Months

Improvements Were Substantial and Sustained

Pooled Nonambulatory Patients

Age 2-21 Years
All Doses (N=35)

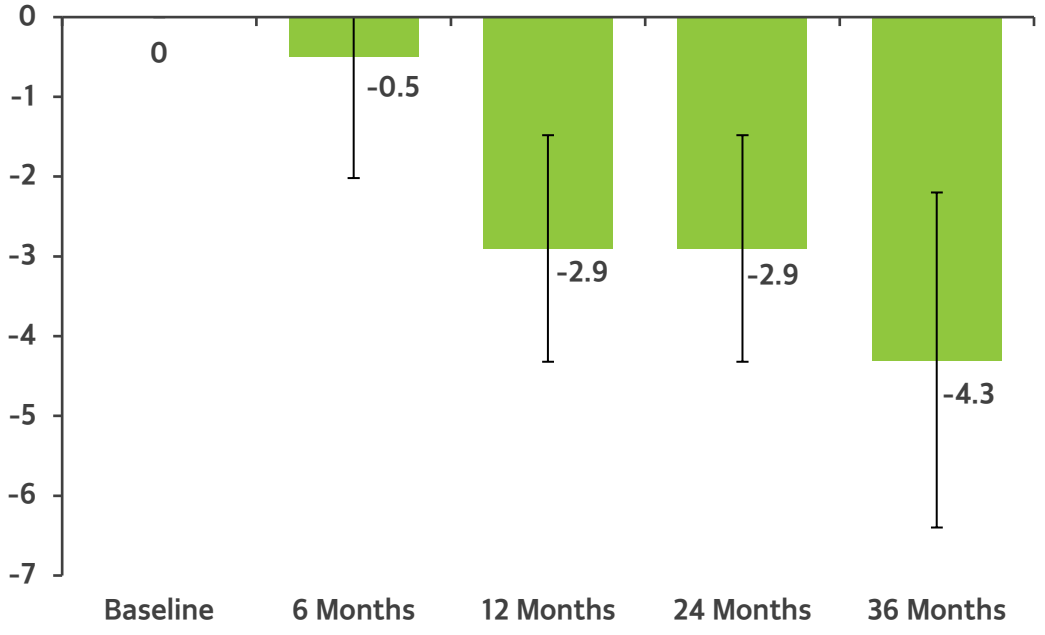
Baseline mean age=7.3 | Time on SMN Rx=24.1m



	Baseline	6 Months	12 Months	24 Months	36 Months
n=	35	19	17	20	14
95% CI=		(-4.3, 1.4)	(-5.7, 0.8)	(-6.0, -0.3)	(-8.7, -0.5)

Age 2-12 Years
All Doses (N=29)

Baseline mean age=5.5 | Time on SMN Rx=24.6m



	Baseline	6 Months	12 Months	24 Months	36 Months
n=	29	15	13	17	12
95% CI=		(-3.7. 2.8)	(-6.0, 0.2)	(-6.0. 0.1)	(-8.9, 0.4)

For the 36-month evaluation, an observed case analysis was conducted, which pooled all the nonambulatory patients (Cohorts 2 and 3) and was based upon the available data for given timepoints. This analysis population included patients receiving either low dose (2 mg/kg) or high dose (20 mg/kg) apitegromab (inclusive of patients in Cohort 3 who switched from 2 mg/kg to 20 mg/kg in Year 2). Error bars represent SE. CI represents confidence interval. SMN Rx=SMN therapy. Data cutoff date as of March 13, 2023. Apitegromab is an investigational drug candidate being evaluated for the treatment of spinal muscular atrophy. Apitegromab has not been approved for any use by the US FDA or any other health authority, and its safety and efficacy have not been established.

Pooled Nonambulatory Patients

New WHO Development Milestones Achieved Over 36 Months

Proportion of patients gaining new milestones in TOPAZ
Cohort 2: BL (0%),12m (20%), 24m (7%), 36m (0%)
Cohort 3 (all doses): BL (0%,) 12m (24%), 24m (26%), 36m (30%)
Cohort 3: Randomized to 20mg/kg dose: 12m (25%), 24m (33%), 36m (40%)
*Includes patients who crossed over from 2 mg/kg to 20mg/kg starting week 68 through week 104.
SMN Rx=SMN therapy. Data cutoff date as of March 13, 2023. Apitegromab is an investigational drug candidate being evaluated for the treatment of spinal muscular atrophy. Apitegromab has not been approved for any use by the US FDA or any other health authority, and its safety and efficacy have not been established.

Key Takeaways

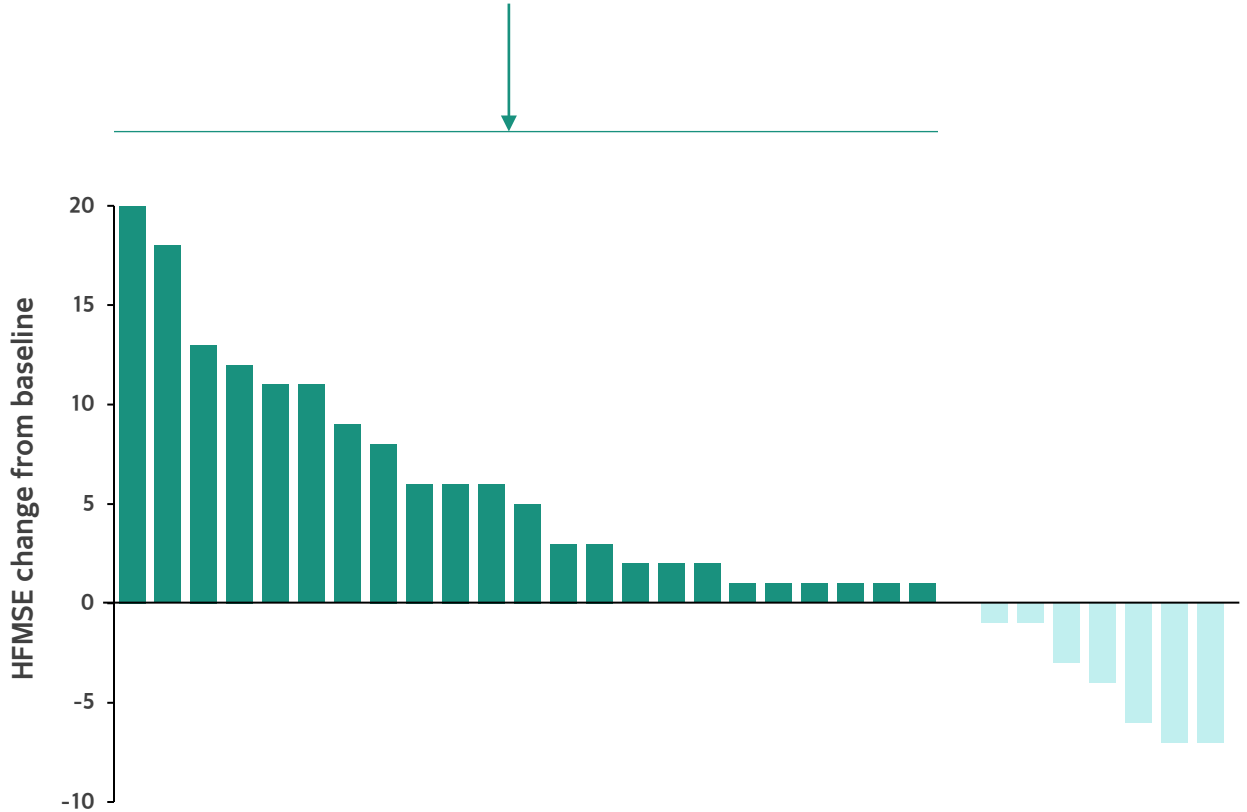
- Patients receiving nusinersen ≥ age 5 mostly maintained WHO milestones
- Patients receiving nusinersen < age 5 improved overall: 6 out of 20 gained new milestones over 36 months

TOPAZ Topline 12-Month Data Showed Apitegromab's

Transformative Potential in Patients with Type 2/3 SMA

Majority of nonambulatory patients* experienced HFMSE increases from apitegromab

during chronic maintenance phase of SMN therapy



Apitegromab led to HFMSE improvements in both nonambulatory cohorts

including patients started on nusinersen at age ≥ 5

	Initiated background nusinersen	
	Age < 5**	Age ≥ 5
Mean HFMSE Increase	+7.1 points	+0.6 points
≥ 1-point Increase % (n/N)	88% (7/8)	64% (9/14)
≥ 3-point Increase % (n/N)	63% (5/8)	29% (4/14)

Crawford T et al. TOPAZ topline results; Presented at CureSMA, 2021 Virtual SMA Research & Clinical Care Meeting; June 9-11, 2021

* Pooled cohorts of nonambulatory patients treated with apitegromab 20 mg/kg and 2 mg/kg

**Nonambulatory patients who initiated background nusinersen at a young age of <5 years and treated with apitegromab 20 mg/kg dose. Apitegromab is an investigational drug candidate being evaluated for the treatment of spinal muscular atrophy. Apitegromab has not been approved for any use by the US FDA or any other health authority, and its safety and efficacy have not been established.

TOPAZ Age 2-12 Analysis* in Pooled Nonambulatory Cohorts (20mg/kg) at 12 Months

Mean Increase of Motor Function Outcomes by HFMSE was Significant

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
- 50% (4/8) with ≥ 3-point increase

Nonambulatory Types 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, n (%)	**13 (81%)**
Patients with ≥ 3-pt increase in HFMSE, n (%)	**9 (56%)**

TOPAZ results showed HFMSE improvement from baseline or RHS stabilization across all three pre-specified cohorts.[1]

No safety signals for apitegromab were identified through month 12 of TOPAZ; the five most frequently reported treatment-emergent adverse events were headache, pyrexia, upper respiratory tract infection, cough, and nasopharyngitis

*Exploratory, post hoc analysis. †For 12-month endpoint, if participants skipped three consecutive doses due to site restrictions caused by COVID-19, records after dose skipping were excluded from analysis. The last observation carried forward was used for other missing data.

1. Crawford T et al. TOPAZ topline results. Presented at Muscular Dystrophy Association, 2023 Clinical & Scientific Conference, March 22, 2023. CI, confidence interval; HFMSE, Hammersmith functional motor scale expanded; SMA, spinal muscular atrophy. Apitegromab is an investigational drug candidate being evaluated for the treatment of spinal muscular atrophy. Apitegromab has not been approved for any use by the US FDA or any other health authority, and its safety and efficacy have not been established.

TOPAZ 12-Month Data | Nonambulatory Type 2 High Dose Cohort

Initiated nusinersen age <5[1,2]

Increases in HFMSE observed in patients already treated with chronic maintenance nusinersen

- Improved: 88% (7/8)
- ≥ 5-point increase: 63% (5/8)
- > 10-point increase: 38% (3/8)

Continuous and durable improvements observed through 12-months of treatment

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)

*This was a primary intent-to-treat (ITT) analysis that, as prespecified, excluded 2 patients who missed 3 doses due to COVID-19 related site access restrictions. An all-patients sensitivity analysis that included those 2 patients had similar results as this primary ITT analysis.

1. Crawford T et al. TOPAZ topline results; Presented at CureSMA, 2021 Virtual SMA Research & Clinical Care Meeting; June 9-11, 2021. 2. Data on file; Scholar Rock. 2022.

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

TOPAZ 12-Month Data | Nonambulatory Type 2/3 Cohort

Initiated nusinersen age ≥5[1,2]

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

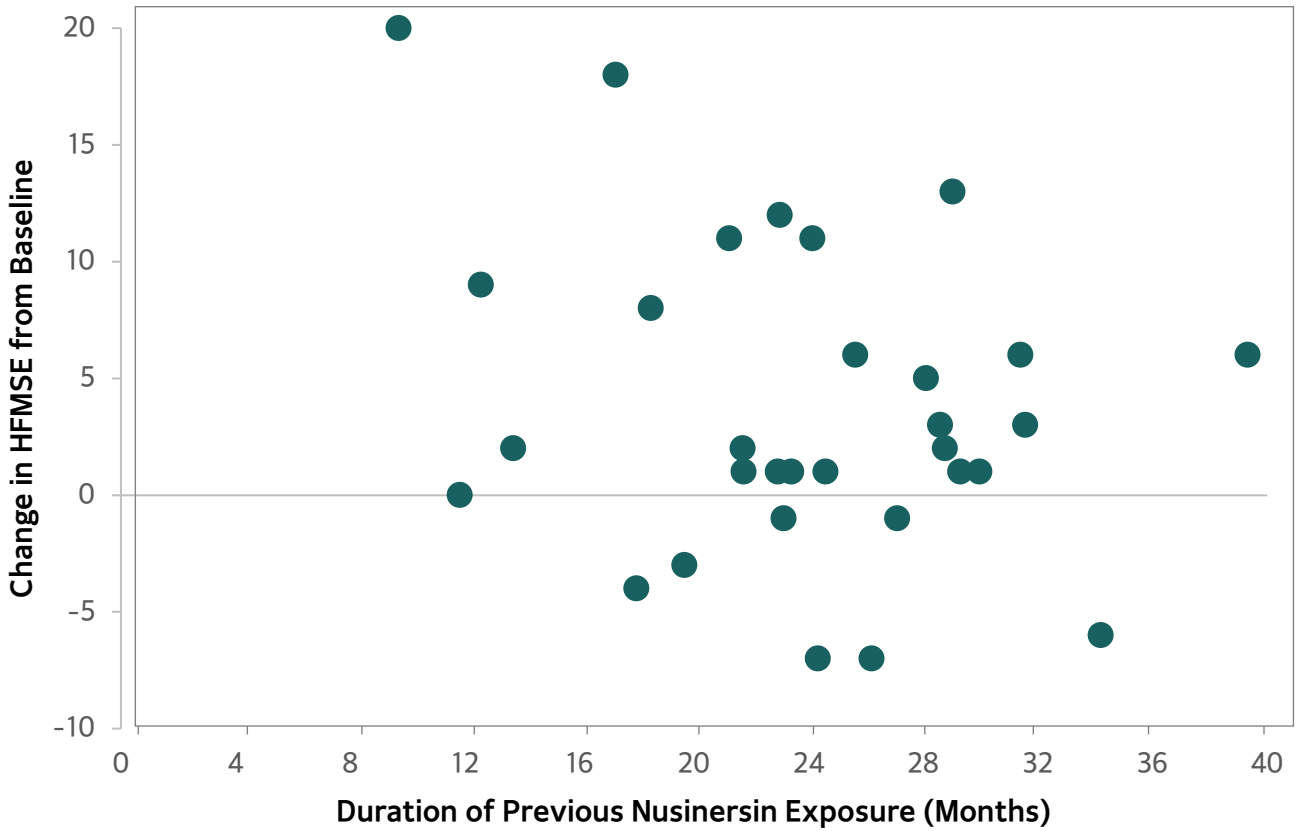
- ≥ 1-point increase: **~67%**
- ≥ 3-point increase: **~30%**

Durability of effect observed through 12-months of treatment

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)	

*Intent-to-treat analysis excluded 1 patient (per prespecified approach) who missed 3 doses due to COVID-19 related site access restrictions; 1 patient who had inadvertently been enrolled who was receiving (and continued to receive) an acetylcholinesterase inhibitor was removed, which is not permitted per the trial protocol; 1. Crawford T et al. TOPAZ topline results; Presented at CureSMA, 2021 Virtual SMA Research & Clinical Care Meeting; June 9-11, 2021. 2. Data on file. Scholar Rock, Inc. Apitegromab is an investigational drug candidate being evaluated for the treatment of spinal muscular atrophy. Apitegromab has not been approved for any use by the US FDA or any other health authority, and its safety and efficacy have not been established.

TOPAZ 12-Month HFMSE Changes and Duration of Prior Nusinersen

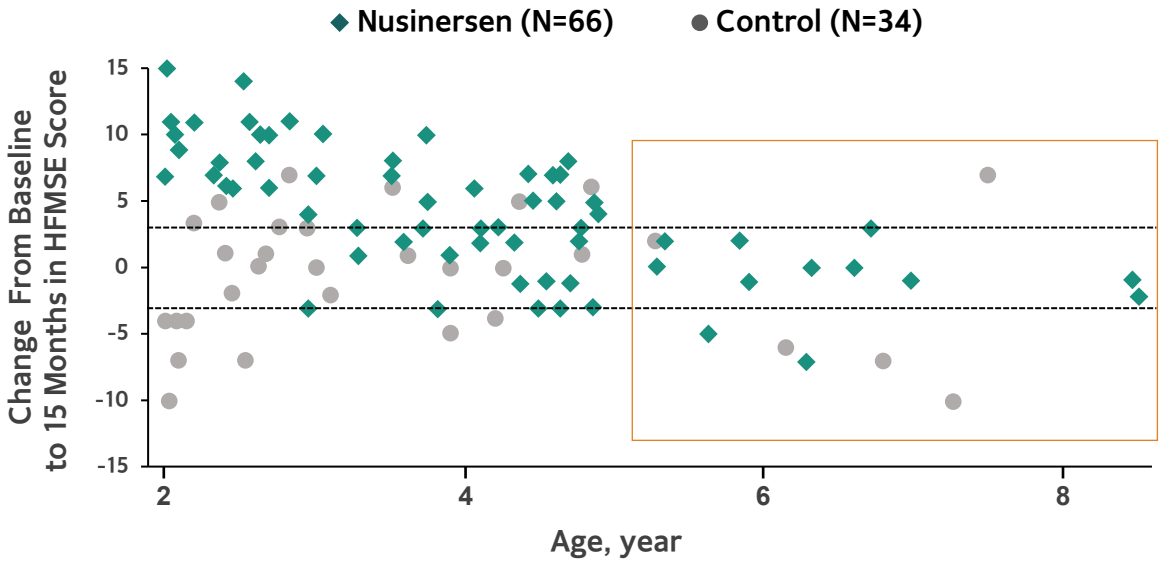


- Patients enrolled were already in the chronic maintenance phase of nusinersen
- Lack of clear correlation between 12-month HFMSE & duration of prior nusinersen exposure in patients aged 2 – 21 suggests motor function improvement mainly attributable to apitegromab

Post hoc analysis: Scatter plot of prior nusinersen treatment duration vs change in HFMSE from baseline; in nonambulatory Types 2 and 3 participants in TOPAZ, there was no clear relationship between duration of nusinersen treatment and change in motor function. Patients skipped 3 or more doses due to COVID-site restrictions excluded; apitegromab is an investigational product candidate under development. HFMSE, Hammersmith Functional Motor Scale–Expanded

Majority of Patients Started on SMN Therapy After Age 5 Do Not Experience Motor Function Increases

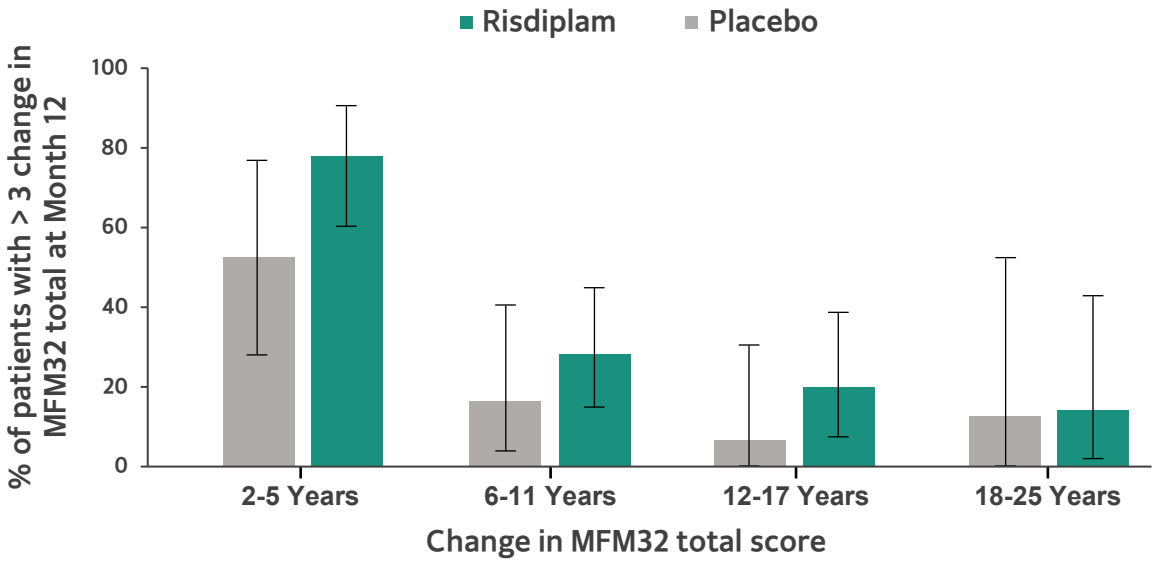
Nusinersen CHERISH Trial in Later-Onset SMA[1]



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[2]



- 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)

1. Mercuri E, et.al. Nusinersen versus sham control in later-onset spinal muscular atrophy. *N Engl J Med.* 2018;378:625-635.
2. 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

Significance of Hammersmith Functional Motor Scale Expanded (HFMSE) and Revised Upper Limb Module (RULM)

HFMSE

Assesses the physical abilities of patients with Types 2/3 SMA

ABLE TO:

Touch Head Above Ear Level
whilst maintaining stable trunk and head

Roll From Supine to Prone
over the right side without pulling/ pushing on hands

33 Items
Graded on scale 0 to 2

0 = unable
1 = performed with modification or adaptation
2 = without modification or adaptation

Item scores are summed to give a total score

The higher the total score, the greater the patient's motor function

Maximum score: 66

Examples of items:

- One hand to head in sitting
- Rolls supine to prone
- Lying to sitting
- Four-point kneeling
- Supported standing
- Stepping
- Ascends 4 stairs with railing

RULM

Evaluates Motor Performance in Upper Limbs

ABLE TO:

Bring Token to Cup
placed vertically at shoulder height

Bring Weight at Eye Level
using two hands

19 Items
Graded on scale 0 to 2
(Except for 1 activity with a binary score)

0 = unable
1 = able with modification
2 = able with no difficulty

Evaluated upper limb tasks correspond to ability to perform everyday activities

Maximum score: 37

Examples of items:

- Putting a coin into a cup
- Elevating a cup to mouth
- Picking up a coin
- Bringing hand to shoulder
- Lifting up weighted objects
- Opening a zip lock bag
- Drawing a line on paper

O'Hagen et al. 2007; Glanzman et al. 2011; Hammersmith Functional Motor Scale Expanded for SMA (HFMSE) Manual, 2019
Mazzone et al. 2017; Pierzchlewicz et al. 2021; Revised Upper Limb Module for SMA Manual, 2014

Activities of Daily Living and Fatigue: Assessed by Three Measures

PEDI-CAT, PROMIS, and ESBBT

Used to assess:

- **ADL**
- **Fatigue**
- **Muscle Endurance**

1 PEDI-CAT:

Measure of activities of daily living

Measures pediatric abilities through 3 functional domains, daily activities, mobility, and social cognitive[1]

- 4-point scale **(1=unable to 4=easy)** assessment of various activities, **higher scores reflect improved abilities**[1,2]
- PEDI-CAT has been validated in SMA, but alone cannot identify small changes in function across all types of SMA[3]

2 PROMIS (Fatigue):

Measure of Patient Fatigue

PRO measurement tool[4]

- Measures mild subjective feelings of tiredness to debilitating and sustained feelings of exhaustion, **with lower scores reflecting less fatigue**[4,5]
- Has been utilized to assess fatigue and fatigability in the Cure SMA database, but has not been fully validated in SMA[5]

3 ESBBT (Fatigability):

Measure of how fast a patient fatigues

Muscle endurance measurement tool[6]

- Part of a series of endurance shuttle tests that include: nine-hole peg test, box and block test, and walk test (ESNHPT, ESBBT, and ESWT)[6]
- Patients are asked to move blocks individually from one box to another in one minute, with **higher numbers of blocks suggesting higher muscle endurance**[6]
- The endurance shuttle tests have been validated for use in patients with SMA[7]

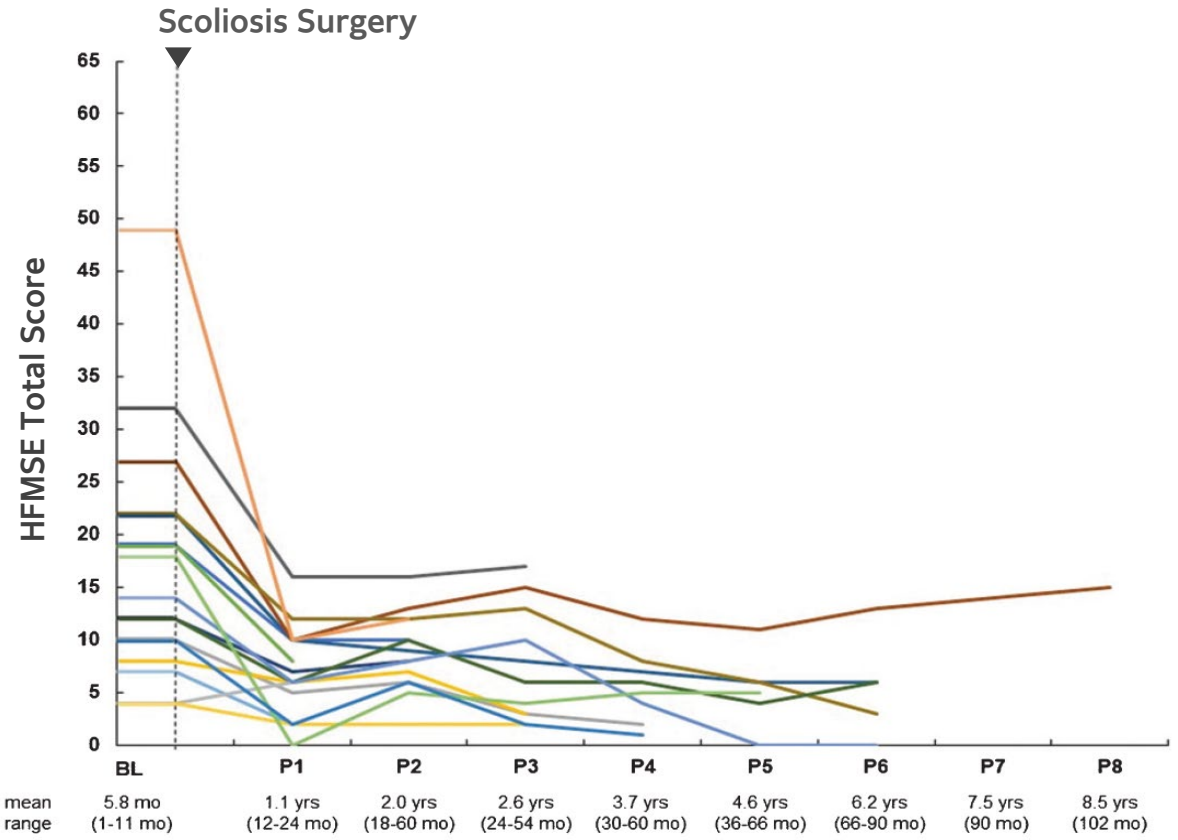
ADL, activities of daily living; ESBBT, endurance shuttle box and block test; ESNHPT, endurance shuttle nine-hole peg test; ESWT, endurance shuttle walk test; PEDI-CAT, pediatric evaluation of disability inventory computer adaptive test; PROMIS, patient-reported outcomes measurement information system; PRO(s), patient-reported outcome(s); SMA, spinal muscular atrophy.

1. Cre Care. PEDI-CAT. Accessed April 26, 2022. https://www.pedicat.com/. 2. Data on file; Scholar Rock. 2022. 3. Pasternak A, et al. *Muscle Nerve*. 2016;54(6):1097-1107. 4. NIH. PROMIS. Accessed April 26, 2022. https://commonfund.nih.gov/promis/index. 5. Belter L, et al. *Orphanet Journal of Rare Diseases*. 2020;15:217. 6. Cure SMA. Best Practices for Physical Therapists and Clinical Evaluators in Spinal Muscular Atrophy (SMA). 2021. Available at: https://www.curesma.org/wp-content/uploads/2021/09/Clinical-Evaluators-Best-Practices-13-August-2021.pdf. 7. Bartels B, et al. *Orphanet Journal of Rare Diseases*. 2020;15:75.

Reported Impact of Scoliosis Surgery on Motor Abilities in SMA

Post-Surgery HFMSE scores Type 2/3 SMA

peer-reviewed study

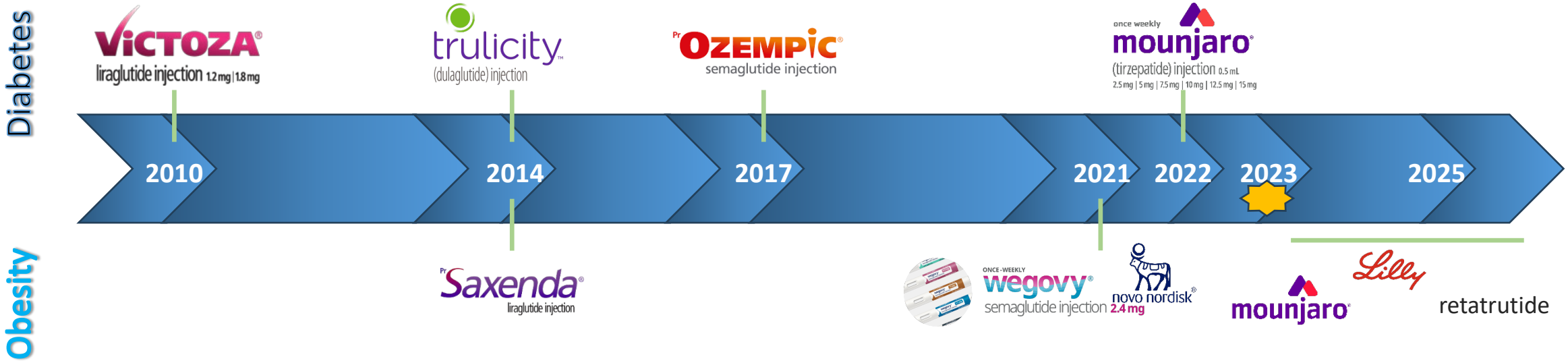


3-month post-surgery assessment

14/17	**Lost >3 points on the HFMSE** (mean change = - 12.1, SD = 8.9)	**Functionally meaningful change**
13/17	Minimal HFMSE changes within ± 2 points (mean change = - 0.7)	No change or stability
0/17	Improvement > 2 points post-surgery	

Dunaway Young et al. 2020

Obesity Landscape is Evolving & Growing: Estimated $70–$100B Annual Revenues by 2035[1]



TODAY

Watch out, Ozempic? Another diabetes drug is 'superior' for weight loss in studies

A. Pawlowski
Mon, September 25, 2023 at 6:46 PM EDT · 7 min read 102

BUSINESS INSIDER

Insurers and drug-industry middlemen are cashing in on the weight-loss drug frenzy

The Washington Post
Democracy Dies in Darkness

Prescriptions for Ozempic and similar drugs have skyrocketed, data shows

Weight-loss drugs like Ozempic and Wegovy may be risky for older people because they melt away all-important muscles, experts say

BY MADISON MULLER AND BLOOMBERG
September 27, 2023 at 4:57 PM EDT

1. Seigerman, ED, et al. "Obesity Exceptionalism: It's different this time." BMO Capital Markets: September 2023

ScholarRock

Recent KOL Interviews: Select Physicians See Value and Benefit in Muscle Maintenance During Weight Loss

Key Opportunities

- **Some key opinion leaders (KOLs) see a lack of standard of care (SOC) in obesity** which leads to significant unmet need in large patient population
- **KOLs see the potential for additional benefit to patients** as sustained results stem from exercise, proper diet and treatment
- **Combination therapy with other weight loss drugs** (GLP-1 RA) may have a synergistic effect on weight loss and benefit overall patient health
- **Patients may experience prolonged weight-loss** and sustained results through the addition of muscle-targeted therapy

"There isn't a set SOC right now for obesity and there clearly needs to be something out there that is standard and addresses the entire scope of the disease. If a company could address both weight loss and muscle maintenance, I think this could improve SOC significantly."

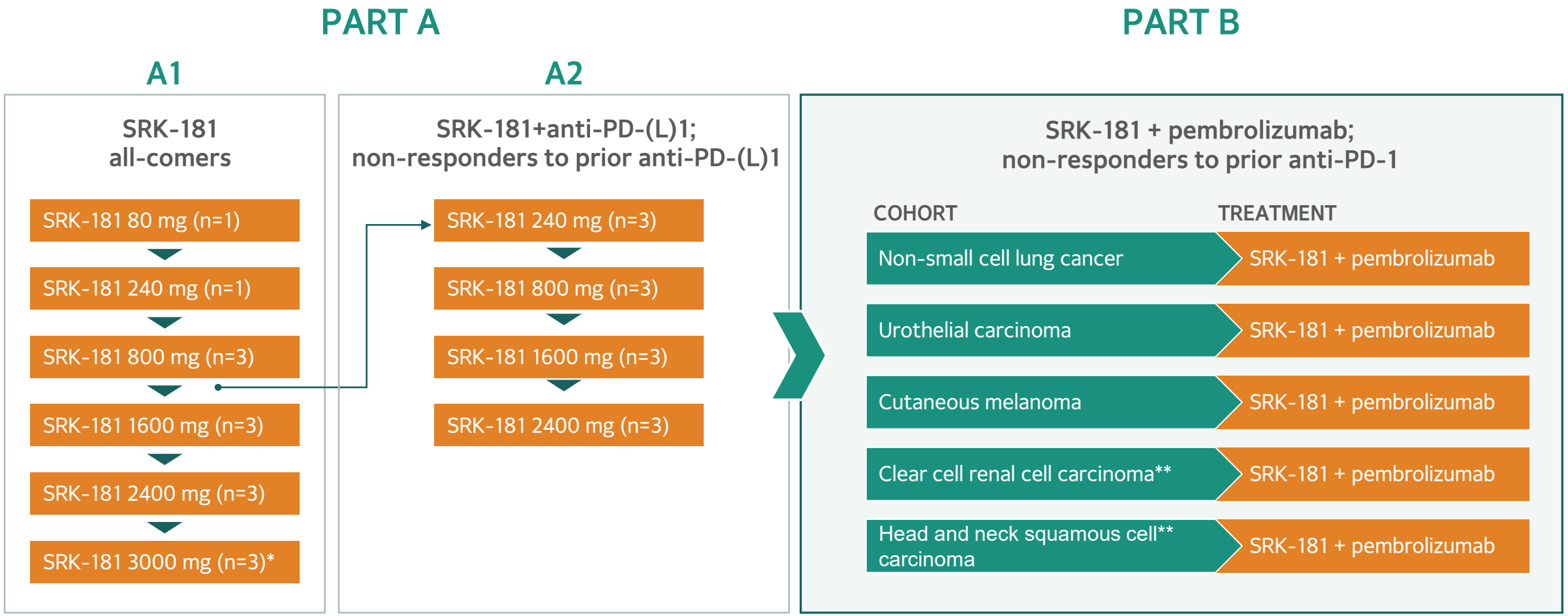
- KOL, PCP

"I do see the importance of muscle mass, and this is something that if I could add to my patient's program, I would in a heartbeat and really think it would make an impact. I have a lot of patients that would benefit from something like this."

- KOL, Endocrinologist

Source: Clarion 2022 Analysis, Clarion KOL interviews

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



* A cohort of 2000 mg Q2W (n=3) was also evaluated.
**The clear cell RCC and HNSCC cohorts will also explore the effects of SRK-181 in patients with relapsed response after anti-PD-1 treatment.
1. NCT04291079 on www.clinicaltrials.gov.

DRAGON Part A: Safety

PART A1 Monotherapy

Treatment-Emergent AEs Related to SRK-181, All Grades >10%

Dose (MG)	80 N=1	240 N=1	800 N=3	1600 N=4	2400 N=3	3000 N=3	2000 N=4	All N=19
Fatigue	0	1	0	0	1	0	1	3 (15.8%)
Decreased Appetite	1	0	1	0	0	0	0	2 (10.5%)
Nausea	1	0	0	0	0	0	1	2 (10.5%)

No DLTs were observed up to 3000 mg q3w and 2000 mg q2w

No Grade 4 or 5 treatment-related AEs occurred

Treatment-related Grade 3 AEs:

- Alanine aminotransferase increased (1 patient)

Treatment-related SAEs:

- None

PART A2 Combination Treatment

Treatment-Emergent AEs Related to SRK-181 or Anti-PD(L)1, All Grades >10%

Dose (MG)	240 N=3	800 N=3	1600 N=6	2400 N=3	All N=15
Rash maculo-papular	1	1	1	2	5 (33.3%)
Pruritus	1	1	1	1	4 (26.7%)
Rash	0	1	0	2	3 (20.0%)
Diarrhea	0	0	2	0	2 (13.3%)
Pemphigoid	0	0	0	2	2 (13.3%)

No DLTs were observed up to 2400 mg q3w

No Grade 4 or 5 treatment-related AEs occurred

Treatment-related Grade 3 AEs:

- Pruritus (2 patients), blister, immune-mediated lung disease, pemphigoid, rash, rash maculo-popular and rash vesicular (1 patient each)

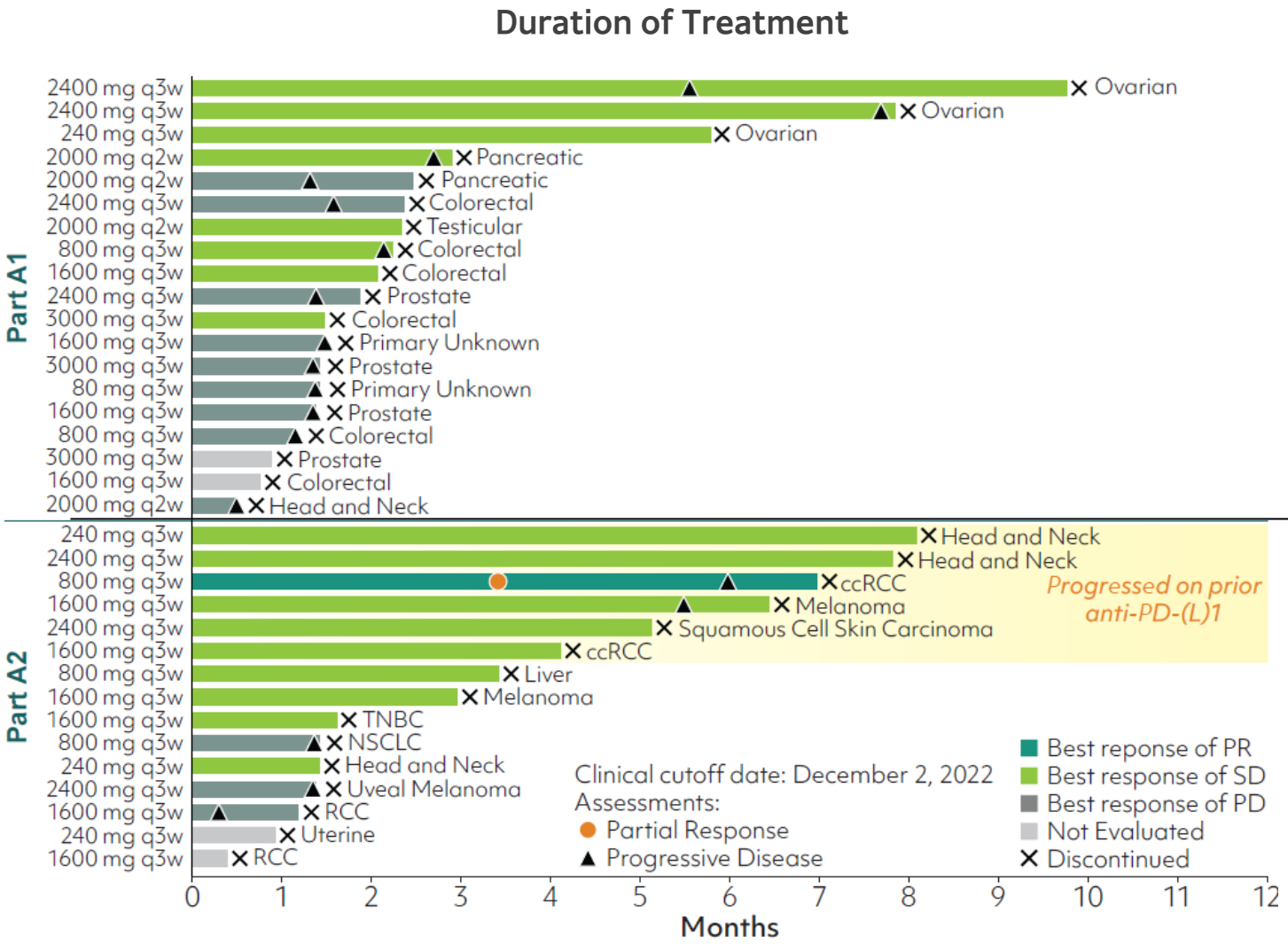
Treatment-related SAEs:

- Blister, pruritus, and rash (all in 1 patient) and immune-mediated lung disease (1 patient)

All dose levels were administered q3w except 2000 mg, which was administered q2w.

Yap T et al. Safety and Efficacy Results of SRK-181, a latent TGFβ1 inhibitor, from a Phase 1 trial (DRAGON Trial); Presented at ESMO-TAT; March 7, 2023. *Clinical cutoff date: December 2, 2022. Response is assessed using RECIST v1.1 by PI; the scan is performed during screening, 6 weeks after first dose, every 9 weeks for the next 6 months of treatment, and every 12 weeks thereafter. SRK-181 is an investigational drug candidate that is being evaluated for the treatment of cancer. SRK-181 has not been approved by the US FDA or any other health authority, and its safety and efficacy have not been established.

DRAGON Part A: Preliminary Efficacy Data*



Part A1 (n=19)

- 8 patients had a best response of stable disease (SD)

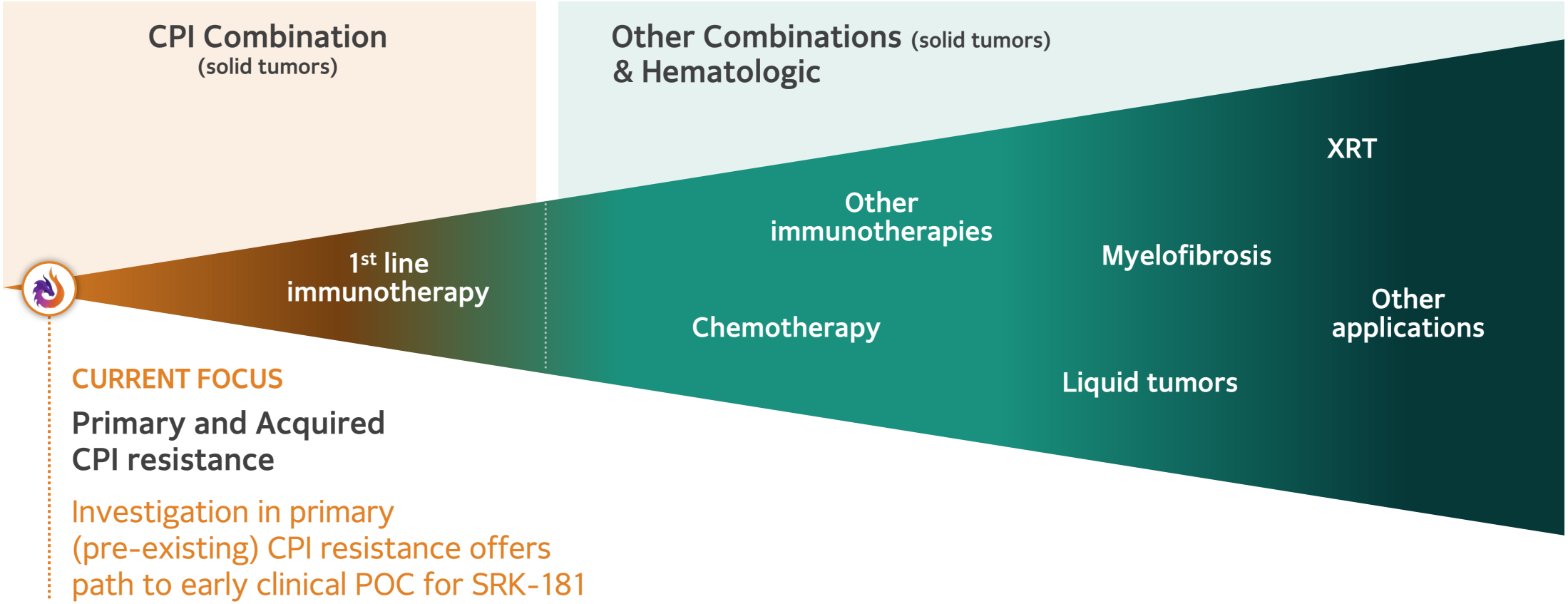
All 3 patients with ovarian cancer were stable for 6-10 months

Part A2 (n=15)

- At 800 mg q3w, 1 partial response (PR) was observed in patient with anti-PD-1-resistant clear cell renal cell carcinoma (ccRCC)
- 9 patients had best response of SD
- 6 patients (green highlight) were stable beyond the 16-week cutoff
  - 1 ongoing patient with head and neck cancer had a 29.4% tumor reduction

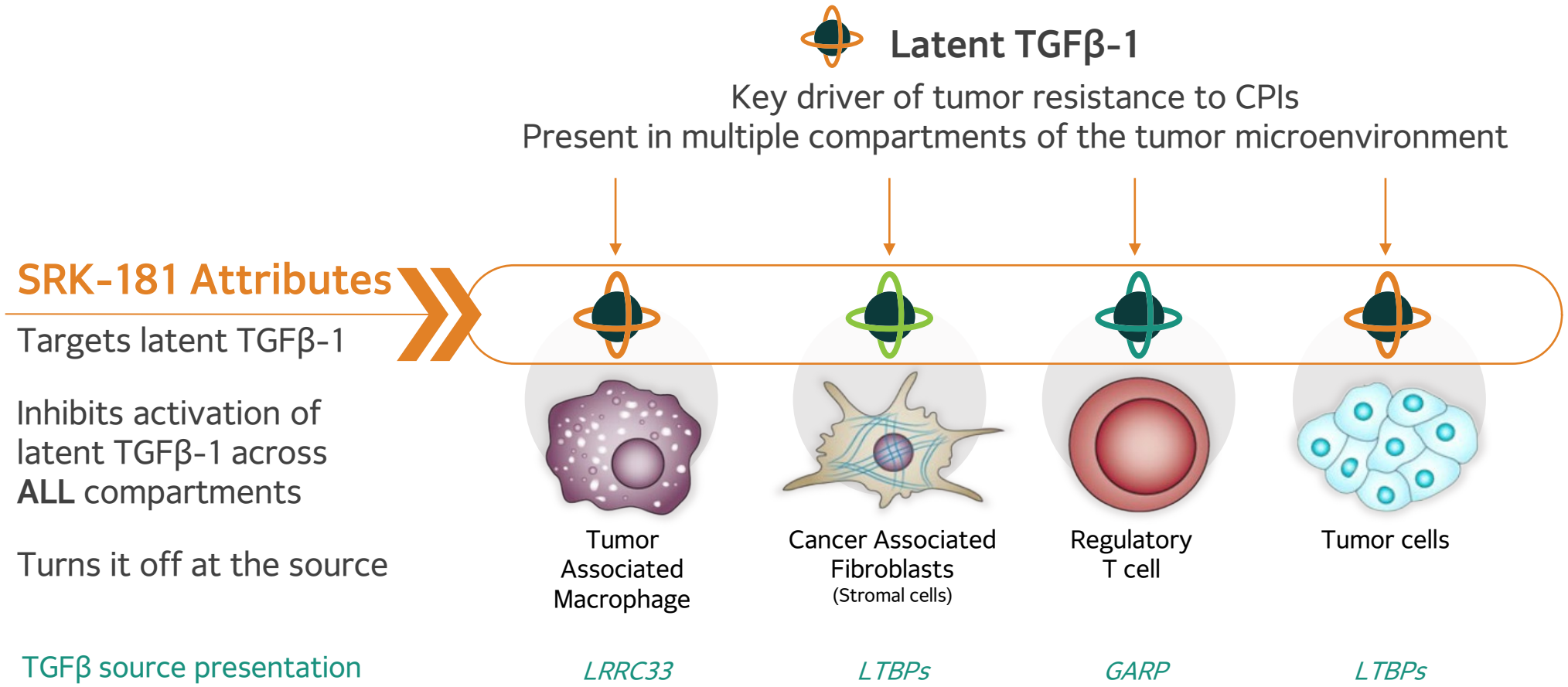
Yap T et al. Safety and Efficacy Results of SRK-181, a latent TGFβ1 inhibitor, from a Phase 1 trial (DRAGON Trial); Presented at ESMO-TAT; March 7, 2023. *Clinical cutoff date: December 2, 2022. Response is assessed using RECIST v1.1 by PI; the scan is performed during screening, 6 weeks after first dose, every 9 weeks for the next 6 months of treatment, and every 12 weeks thereafter. SRK-181 is an investigational drug candidate that is being evaluated for the treatment of cancer. SRK-181 has not been approved by the US FDA or any other health authority, and its safety and efficacy have not been established.

SRK-181: Transformative Potential as the Backbone For Next Era of Cancer Therapy



First in class monoclonal antibody targeting latent and context-independent binding to TGFB-1

Context-Independent: SRK-181 Designed to Inhibit Latent TGFβ-1 Across All Compartments of the Tumor Microenvironment



TGFβ Latent growth factor

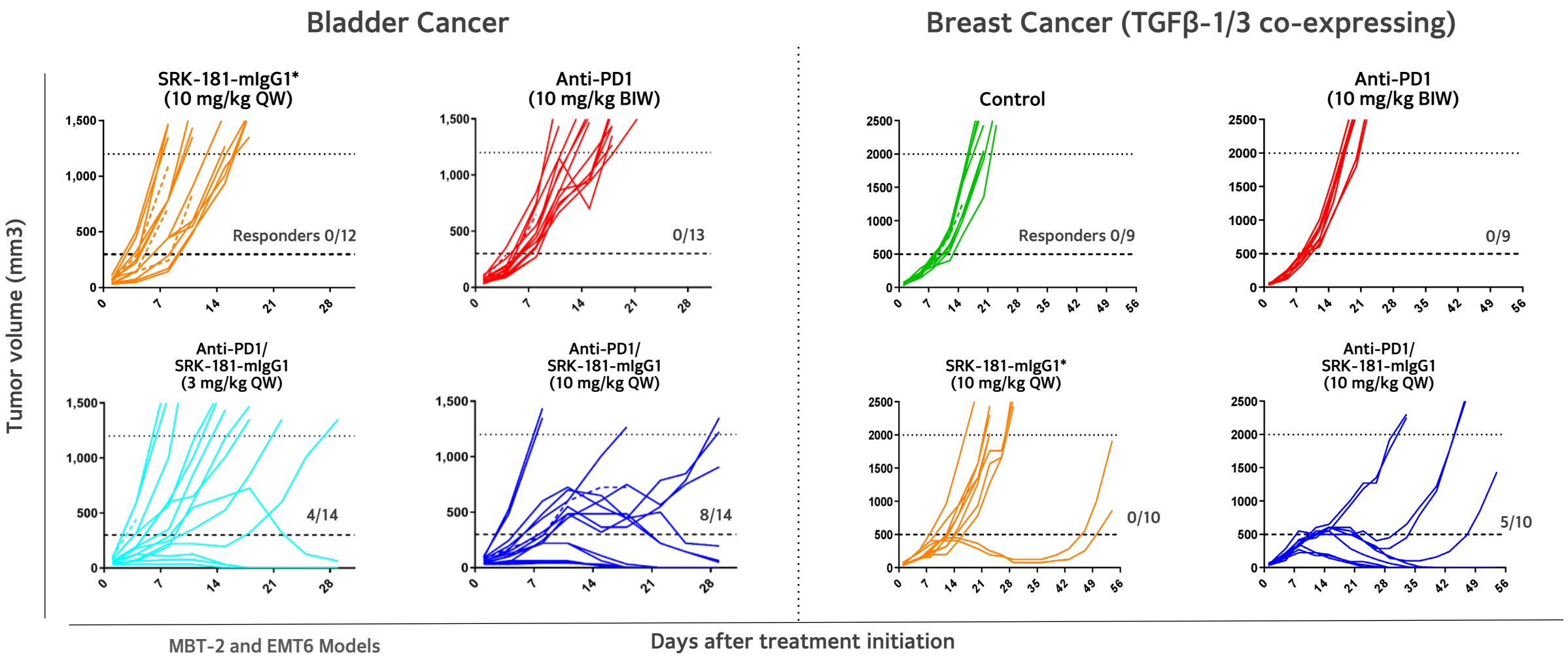
LRRC33: leucine-rich-repeat-containing protein family member 33 | LTBPs: latent transforming growth factor β binding proteins | GARP: glycoprotein A repetitions predominant

SRK-181 Therapeutic Hypothesis: Potential Advantages of Latent TGFβ-1 Inhibitor

	SRK-181*	Bifunctional TGFβ/CPI	ALK5 Inhibitor	Nonselective TGFβ antibody
Selectivity for TGFβ-1: potential for wider therapeutic window and improved safety	✓	✗	✗	✗
Ability to combine with any anti-PD-(L)1	✓	✗	✓	✓
Ability to optimize dosing of each component of combination therapy	✓	✗	✓	✓
Activity spatially distinct from anti-PD-(L)1 in tissue	✓	✗	✓	✓
Inhibits all sources of TGFβ-1 contributing to CPI resistance (Context independent)	✓	✗	✓	✓
Target latent form (Blocks TGFβ-1 activation)	✓	✗	✗	✗

*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.

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

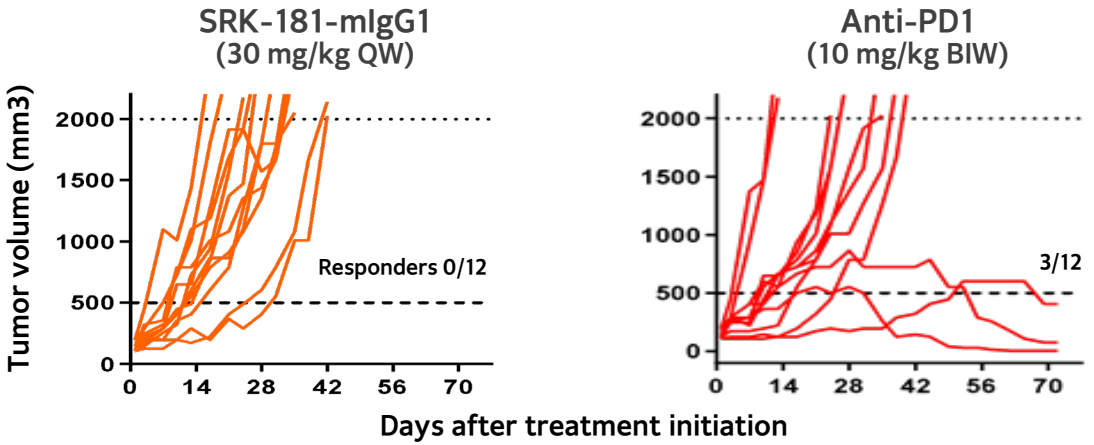


Preclinical data published in Science Translational Medicine. Martin CJ, et al. Sci Transl Med. 2020 Mar 25;12(536):eaay8456.
https://scholarrock.com/platform/publications/.
*SRK-181-mIgG1 is the murine version of SRK-181; responder defined as tumor size <25% endpoint volume at study end.

SRK-181-mIgG1 Combination Treatment Led to Melanoma Tumor Regression and Survival Benefit

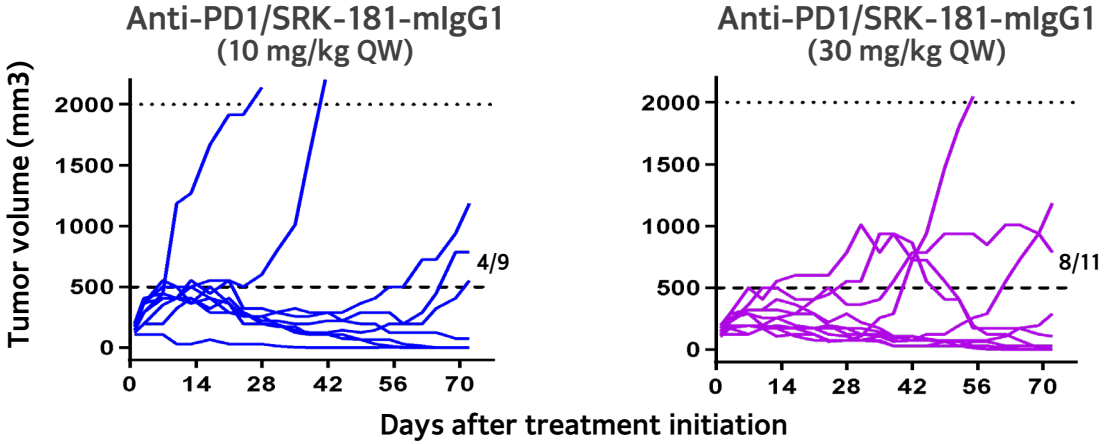
Tumor Regression

Monotherapy

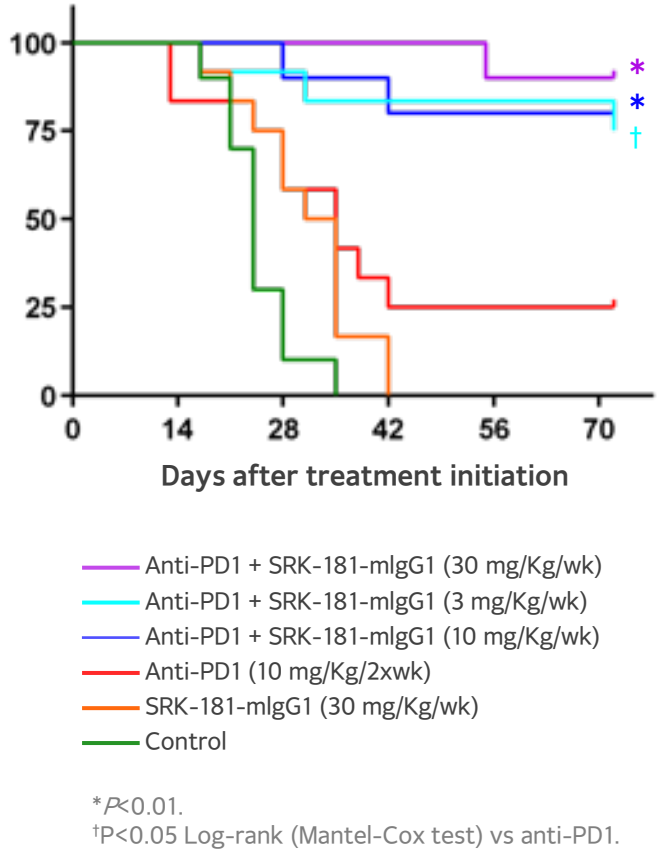


Combination Therapy

Led to tumor regression and survival benefit



Survival Benefit



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

Melanoma (Cloudman S91) 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.

Selectivity of SRK-181 Offers Potential to Overcome Toxicity and Dose-limiting Challenges of Non-selective TGFβ Pathway Approaches

Toxicology:

- Unremarkable
- Minimal
- Slight
- Moderate

Microscopic Observations in Heart	CONTROL Vehicle iv, qwk x 4	LY2109761 300 mg/kg po, qd x 8	PanTGFβAb 30 mg/kg Iv, 1 dose	SRK-181 10 mg/kg iv, qwk x 4	SRK-181 30 mg/kg iv, qwk x 4	SRK-181 100 mg/kg iv, qwk x 4
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				*		

Non-selective TGFβ

Toxicity: Minimal, slight and moderate

Selective TGFβ-1

Toxicity: Minimal

* Not test article related

Repeat Dose Pilot Toxicology Study

Adult female Sprague Dawley rats

Cardiac findings were exhibited
in animals dosed with 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: 100 mg/kg QW
(highest dose evaluated)

4-week GLP toxicology studies

RATS
NOAEL for SRK-181: 200 mg/kg QW
(highest dose evaluated)

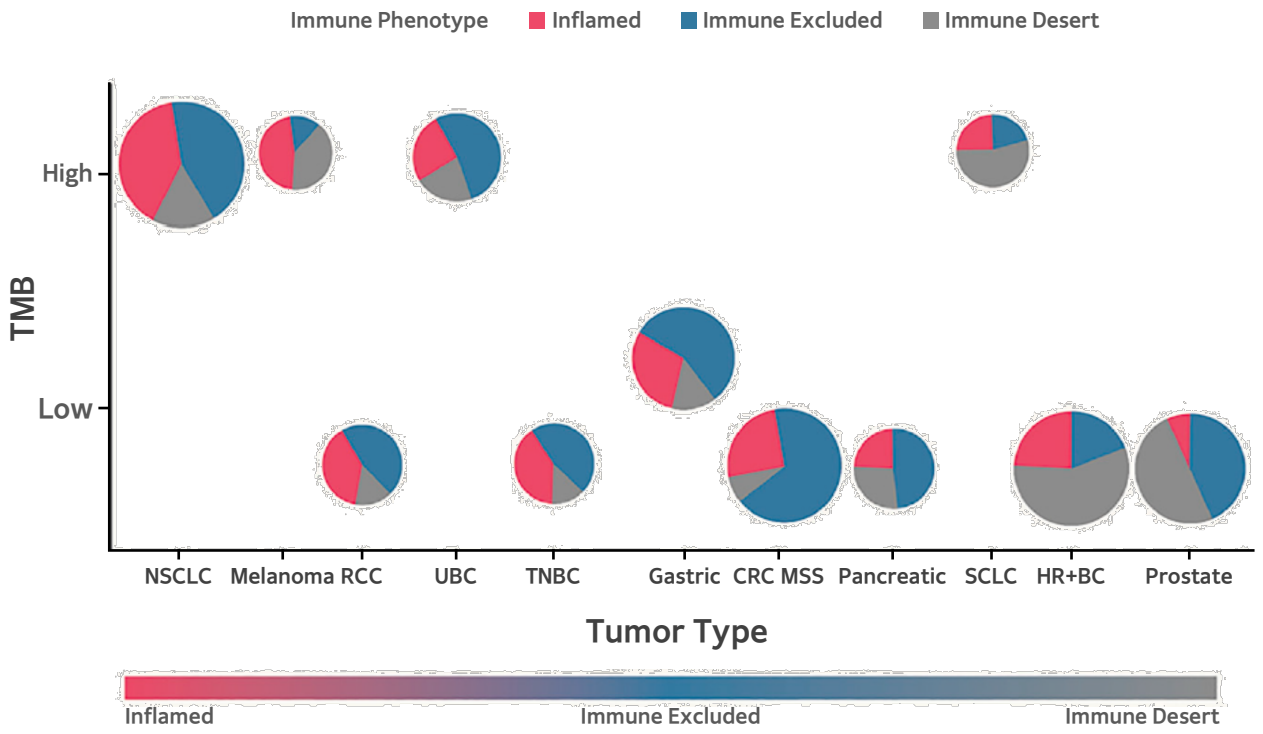
NON-HUMAN PRIMATES
NOAEL for SRK-181: 300 mg/kg
(highest dose evaluated)

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

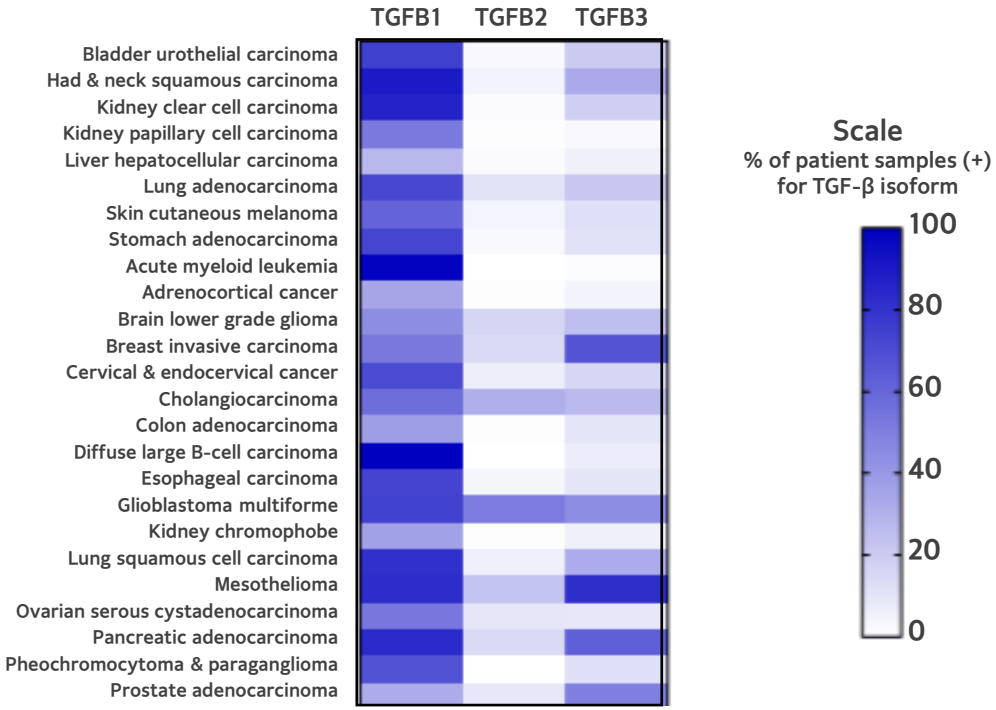
*Source: Anderton MJ, et al. Induction of heart valve lesions by small-molecule ALK5 inhibitors. *Toxicol Pathol*. 2011;39: 916-924.; and Stauber AJ, et al. Nonclinical safety evaluation of a transforming growth factor β Receptor I kinase inhibitor in Fischer 344 rats and beagle dogs. *J Clin Pract*. 2014: 4:3.

Emerging Evidence Implicates TGFβ-1 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 TGFβ-1 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.

Biomarker Strategies Employed in DRAGON Trial

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

Immunophenotyping
Assessment of immune landscape

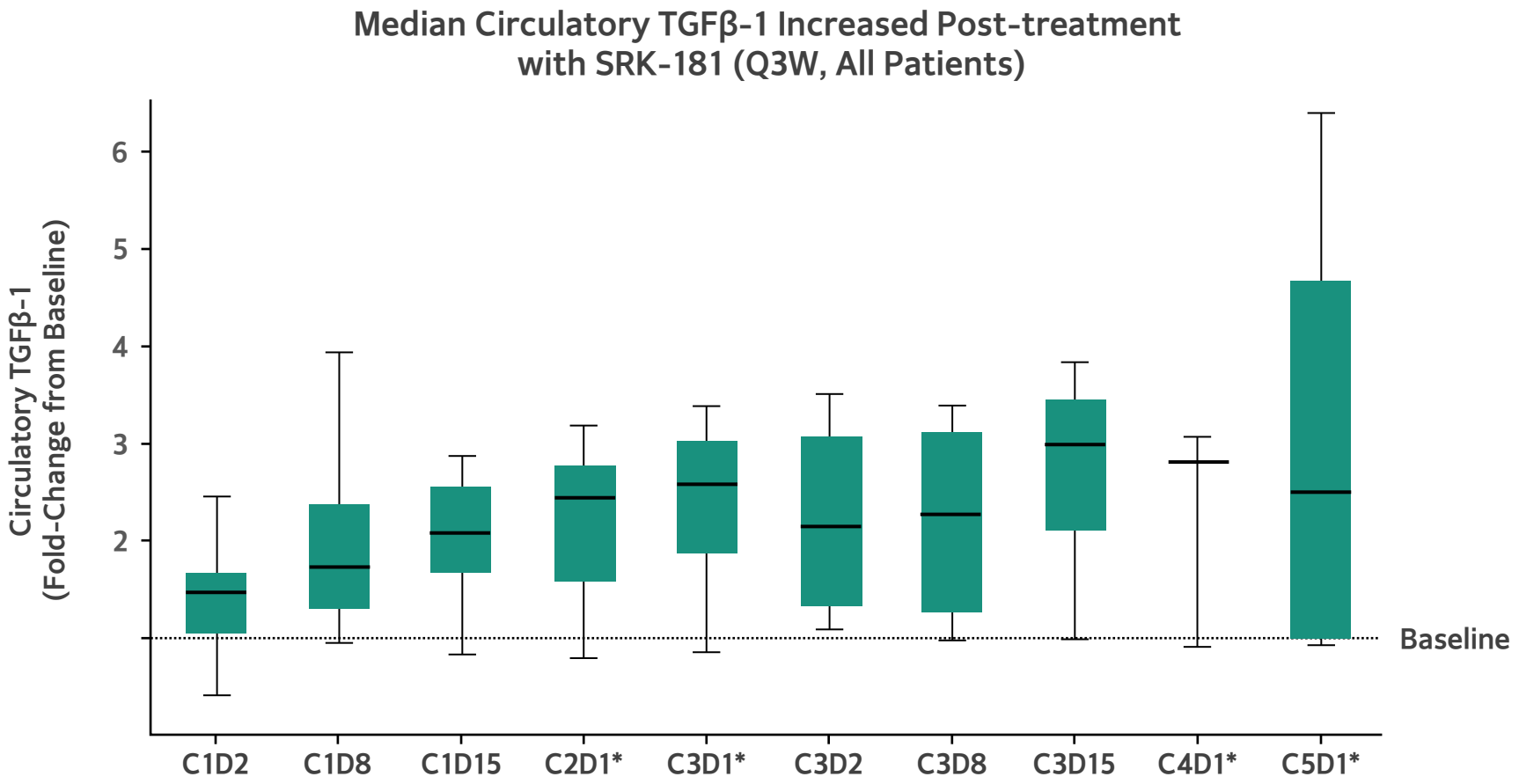
- Higher resolution histochemical characterization of tumor immune contexture (e.g. CD8+)
  - Classification of inflamed, excluded or immune desert tumors and tumor nests
  - Ability of SRK-181 to overcome tumor immune exclusion
- Analysis of immune response markers (e.g. PD-L1)
- Changes to intra-tumoral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

TGFβ-1 pathway evaluation
Assessment of signaling pathway

- Show evidence of the SRK-181 target engagement
  - e.g. circulating TGFβ-1 levels
- TGFβ pathway modulation:
  - e.g. Histochemical analysis of pSMAD
  - e.g. RNA-based TGFβ gene signatures and pathway analyses
- Paired biopsies from the head and neck cohort allow for a potential to accelerate the development path

Clear Evidence of Target Engagement

Pharmacodynamic Biomarker Results for Part A: Circulatory TGFβ-1



Binding to latent TGFβ-1 delays maturity state allowing TGFβ-1 to accumulate in system

Combination treatment with pembrolizumab did not appear to impact circulatory TGFβ-1 levels

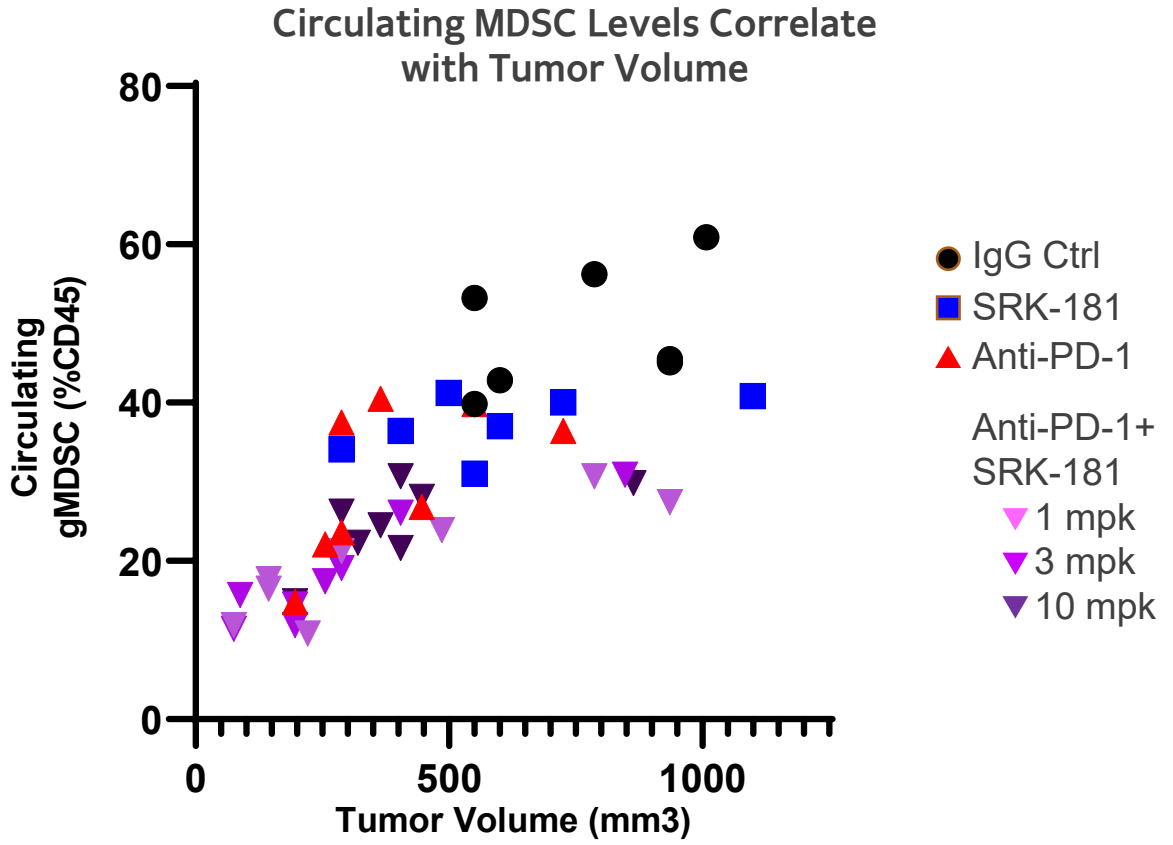
Yap T et al. SRK-181, a latent TGFβ1 inhibitor: safety, efficacy, and biomarker results from the dose escalation portion of a phase I trial (DRAGON trial) in patients with advanced solid tumors (Poster 780); Presented at SITC; Nov. 10-11, 2022. Circulatory TGFβ-1 and PF4 levels were quantitated by using validated ELISA kits from R&D System.12 Because platelet activation during sample processing can lead to elevated TGFβ-1 levels, samples with elevated PF4, a platelet activation biomarker, were excluded from the analysis based on a preliminary cutoff value.
Pre-infusion.
SRK-181 is an investigational drug candidate that is being evaluated for the treatment of cancer. SRK-181 has not been approved by the US FDA or any other health authority, and its safety and efficacy have not been established.

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