# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION

**Washington, D.C. 20549**

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# FORM 8-K

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**CURRENT REPORT**

**Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

Date of Report (Date of earliest event Reported): January 4, 2024

## Scholar Rock Holding Corporation

(Exact Name of Registrant as Specified in Charter)

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

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

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

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

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

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

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

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

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

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

**Item 2.02. Results of Operations and Financial Condition.**

On January 4, 2024, Scholar Rock Holding Corporation (the "Company") issued a press release which contained information regarding the Company's preliminary, unaudited estimate of cash and cash equivalents of approximately $280 million as of December 31, 2023, which is projected to fund the Company's operations into the second half of 2025. This information is preliminary and unaudited. The Company expects to report its audited cash, cash equivalents and marketable securities, as well as other information necessary for a complete understanding of its financial position, in its Annual Report on Form 10-K for the year ended December 31, 2023.

The information in this Item 2.02 is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section. It may only be incorporated by reference in another filing under the Exchange Act or the Securities Act of 1933, as amended, if such subsequent filing specifically references the information furnished pursuant to Item 7.01 and Exhibit 99.1 of this Current Report on Form 8-K.

**Item 7.01. Regulation FD Disclosure.**

On January 4, 2024, the Company announced that management will present at the 42nd Annual J.P. Morgan Healthcare Conference on Tuesday, January 9, 2024 at 1:30 p.m. PT (4:30 p.m. ET). A copy of the presentation slide deck that will be presented is being furnished as Exhibit 99.1 to this report on Form 8-K. A live webcast of the presentation may be accessed by visiting the Investors & Media section of the Scholar Rock website at http://investors.scholarrock.com.

The information in this Item 7.01 and Exhibit 99.1 attached hereto is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liabilities of that section. It may only be incorporated by reference in another filing under the Exchange Act or the Securities Act of 1933, as amended, if such subsequent filing specifically references the information furnished pursuant to Item 7.01 and Exhibit 99.1 of this Current Report on Form 8-K.

**Item 8.01. Other Events.**

On January 4, 2024, the Company issued a press release announcing a corporate update and highlighting priorities for 2024. A copy of this press release is being filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated by reference herein.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits

| Exhibit No. | Description |
|---|---|
| 99.1 | Presentation distributed by Scholar Rock Holding Corporation dated January 8, 2024, furnished hereto. |
| 99.2 | Press Release issued by Scholar Rock Holding Corporation dated January 4, 2024, filed hereto. |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) |

**SIGNATURE**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**Scholar Rock Holding Corporation**

Date: January 8, 2024

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

# Advancing New Possibilities for Patients

## 42nd ANNUAL J.P. MORGAN HEALTHCARE CONFERENCE

JANUARY 9, 2024

ScholarRock

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# 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.

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ScholarRock

ScholarRock

**Emily & Christopher**
living with SMA*


# We are a global leader in harnessing the life-changing potential of TGFß 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.
SMA=Spinal muscular atrophy
*Christopher is a participant in the TOPAZ and ONYX clinical trials.

# 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.


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# Our Approach

Selectivity Drives Success

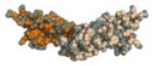
**RIGHT TARGET** → **Validated Biology**

**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



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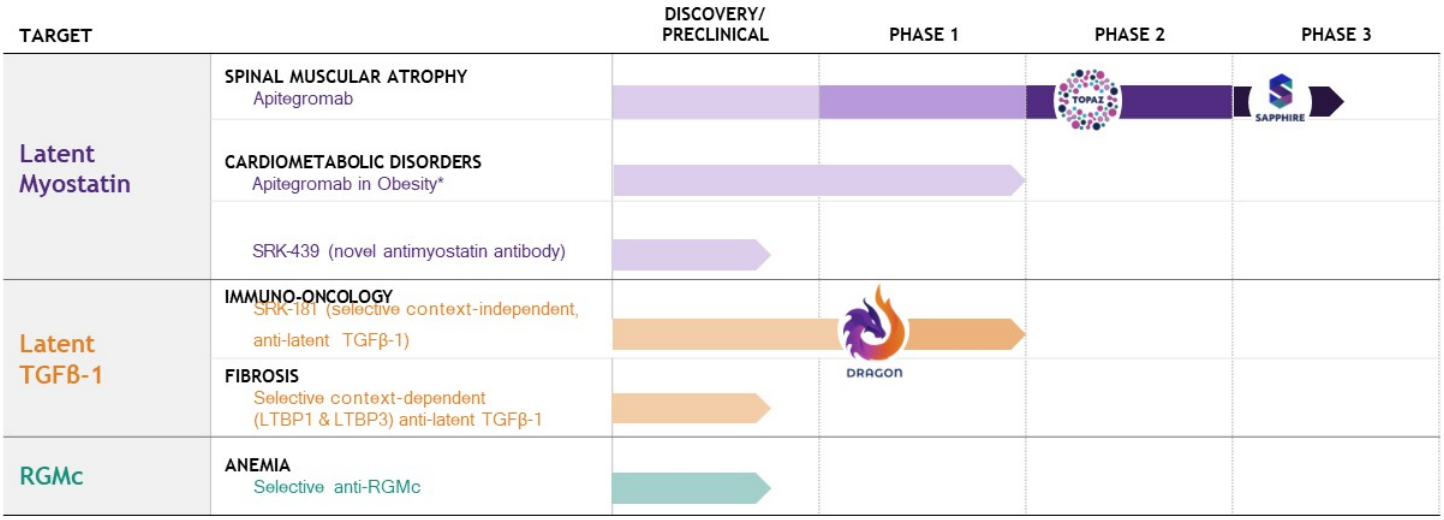
# Advancing a Robust Pipeline with Our Differentiated Platform




**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.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# Antimyostatin Program: Apitegromab in Spinal Muscular Atrophy

ScholarRock™

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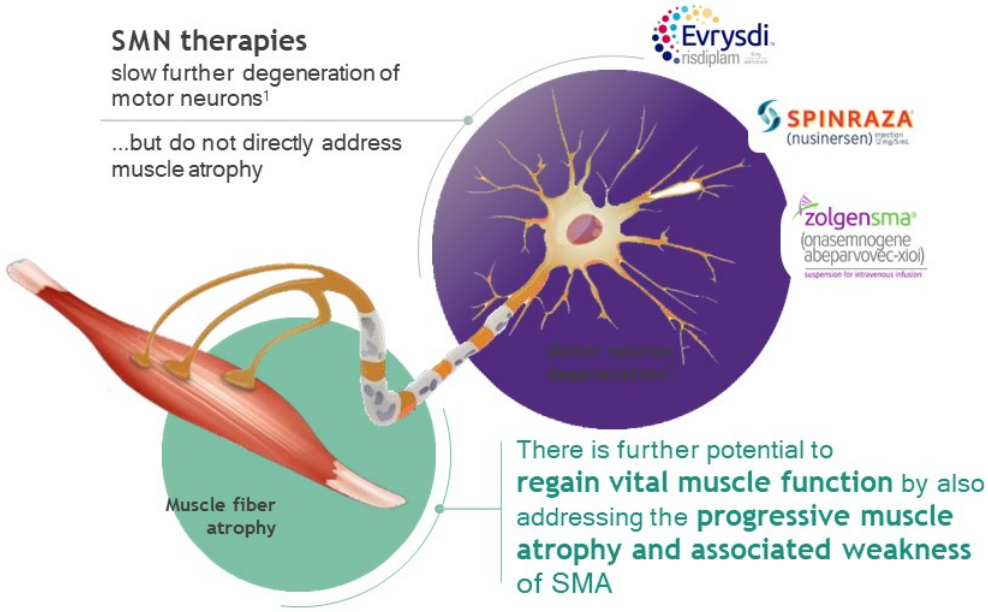
Hallmarks of SMA

# 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




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.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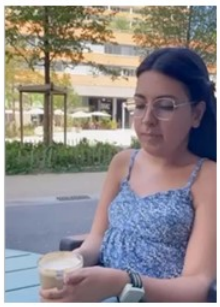
# SMA Leads to Deterioration in Essential Muscle Function



"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/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# 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)

**>13,000 patients** treated WW

**$1.8 billion** annual revenue (LTM)[3]

Evrysdi (risdiplam)

**> 11,000 patients** treated WW

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

zolgensma (onasemnogene abeparvovec-xioi)

**> 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.



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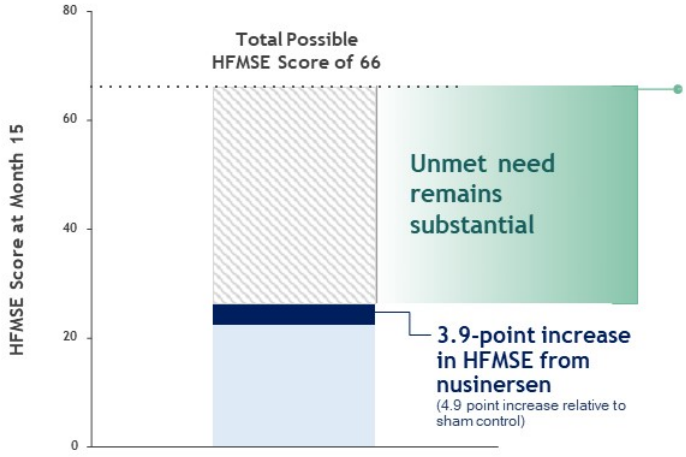
# Muscle-Targeted Therapy: A New Treatment Frontier




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

**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

*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.



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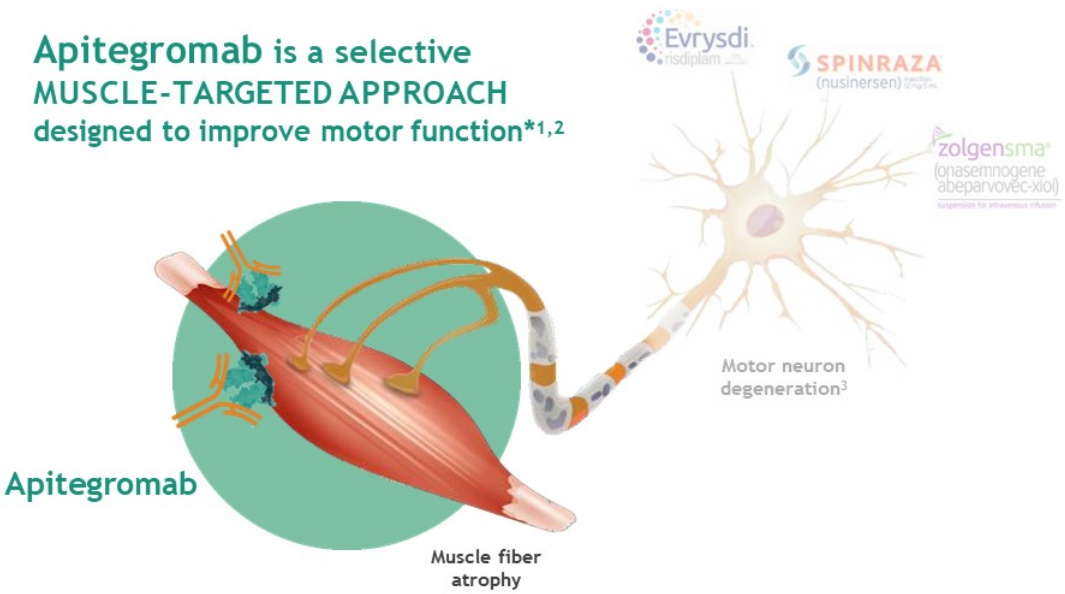
# Apitegromab Offers Significant Potential to Address Unmet Needs

## 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.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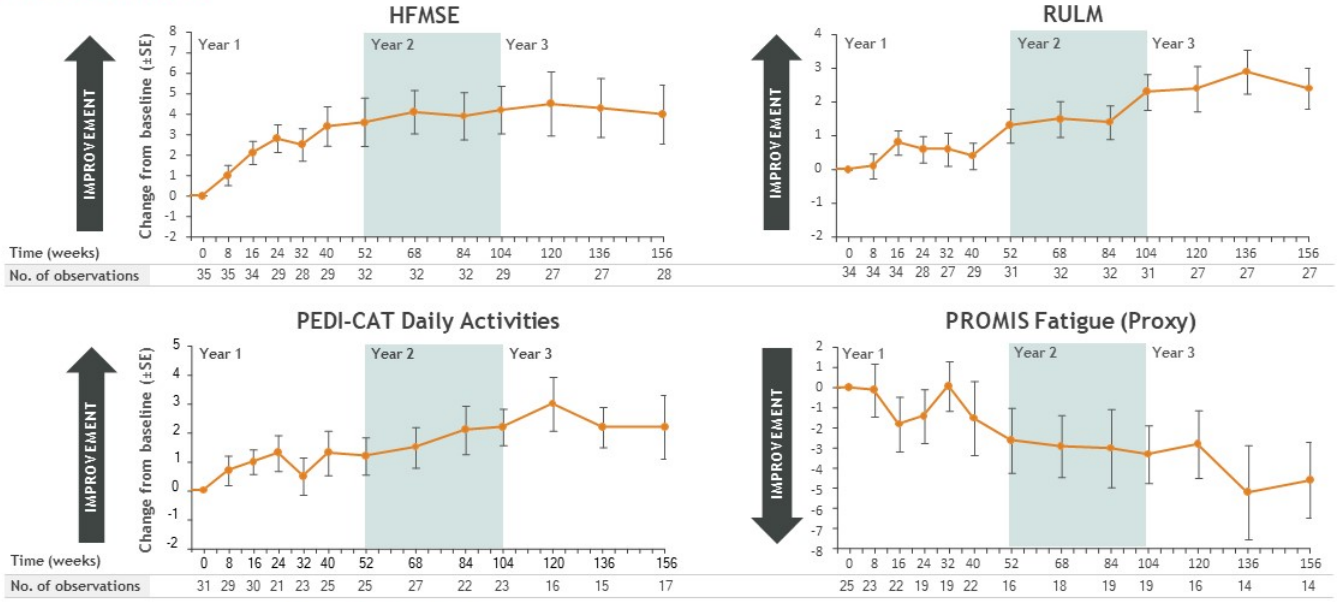
TOPAZ Over 36 Months

# Sustained Functional and PRO Improvements Beyond SMN Treatment




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

PRO=patient reported outcomes; 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. Pooled nonambulatory patients, age 2-21, all doses.
Crawford et al., Cure SMA 2023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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


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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.


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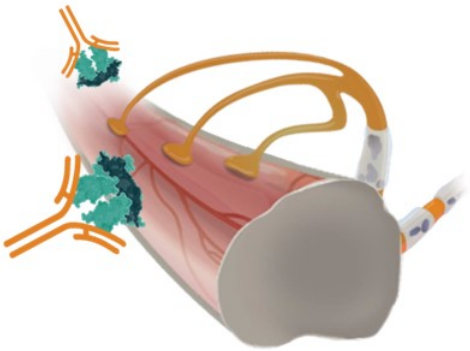
# Apitegromab: Potential to Maximize Outcomes for People Living with Spinal Muscular Atrophy (SMA)

## Transformative Potential to Change the Standard of Care



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

**Phase 3 SAPPHIRE Trial**
**Registrational trial** with topline 12-month data expected in Q4 2024

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

**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.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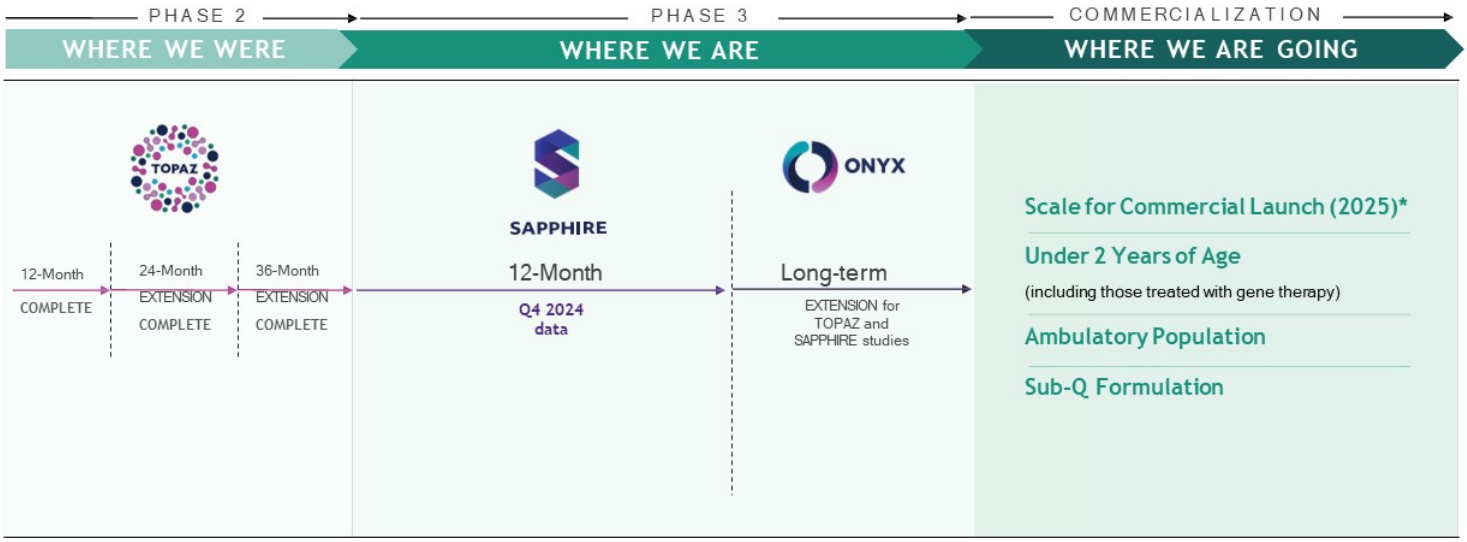
# Expanding to Benefit More People Living with SMA




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

# Antimyostatin Program: Cardiometabolic Disorders

ScholarRock™

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# 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.


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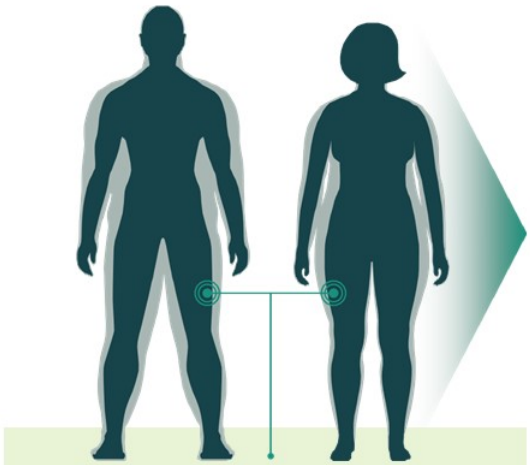
# Loss of Lean Muscle Significant with GLP-1 RA Therapy

## 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.



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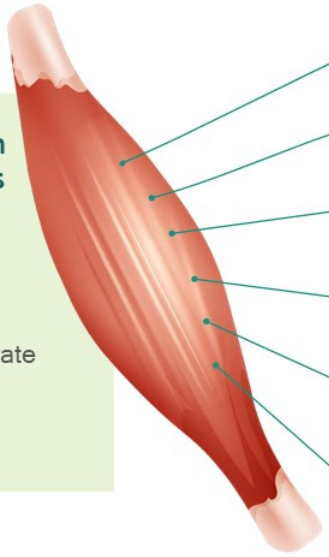
# Maintaining Muscle is Important for Healthy Weight Loss

**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.

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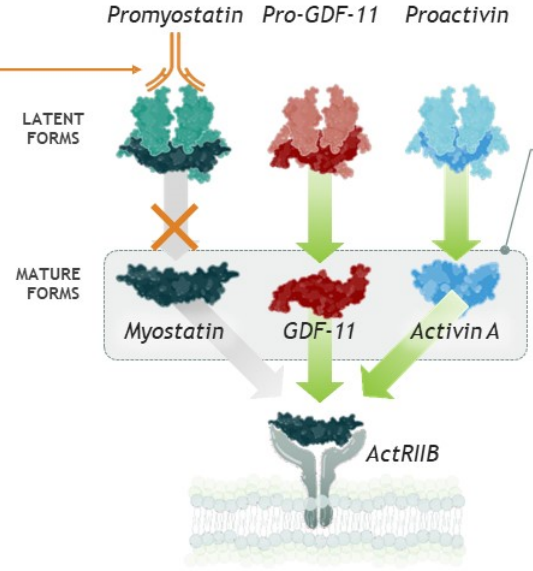
# Our Antibodies Selectively Inhibit Activation of Myostatin

**Apitegromab and SRK-439**

SRRK antibodies do not bind to mature myostatin or any form of GDF11, Activin A, or other TGF-ß 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).



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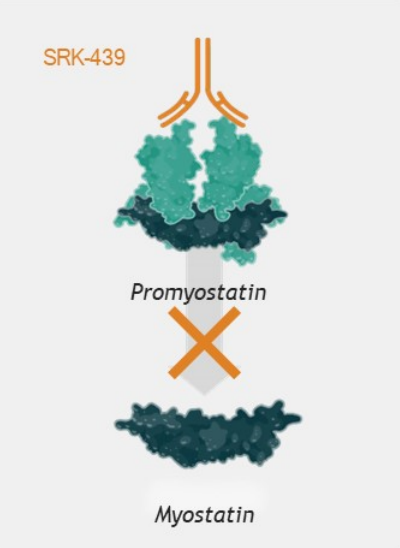
# SRK-439: Novel Myostatin Inhibitor

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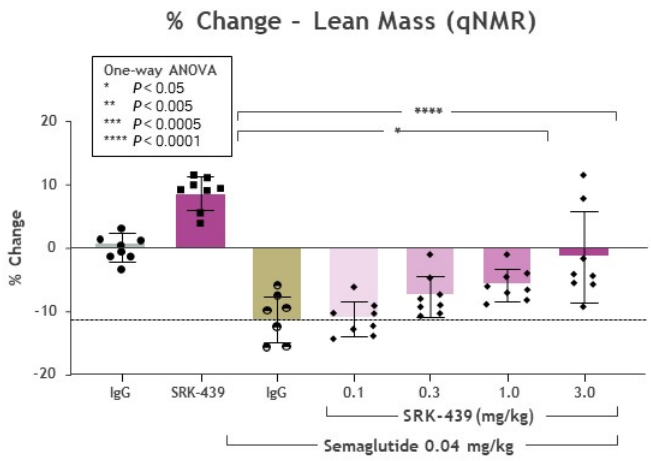
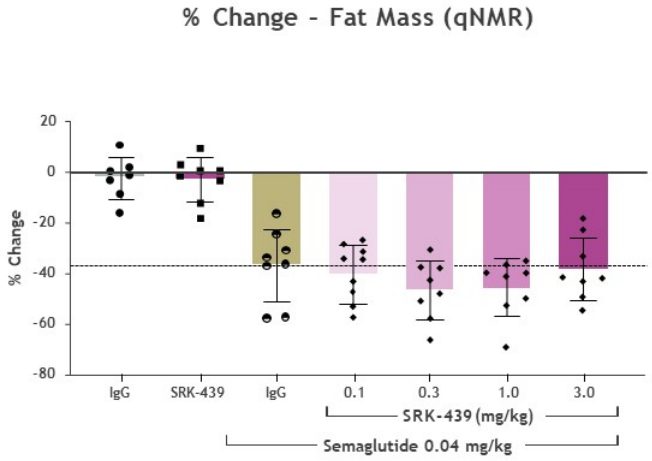
# SRK-439 Reversed Lean Mass Loss and Enhanced Fat Mass Loss Induced by Semaglutide Treatment†




**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.



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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;



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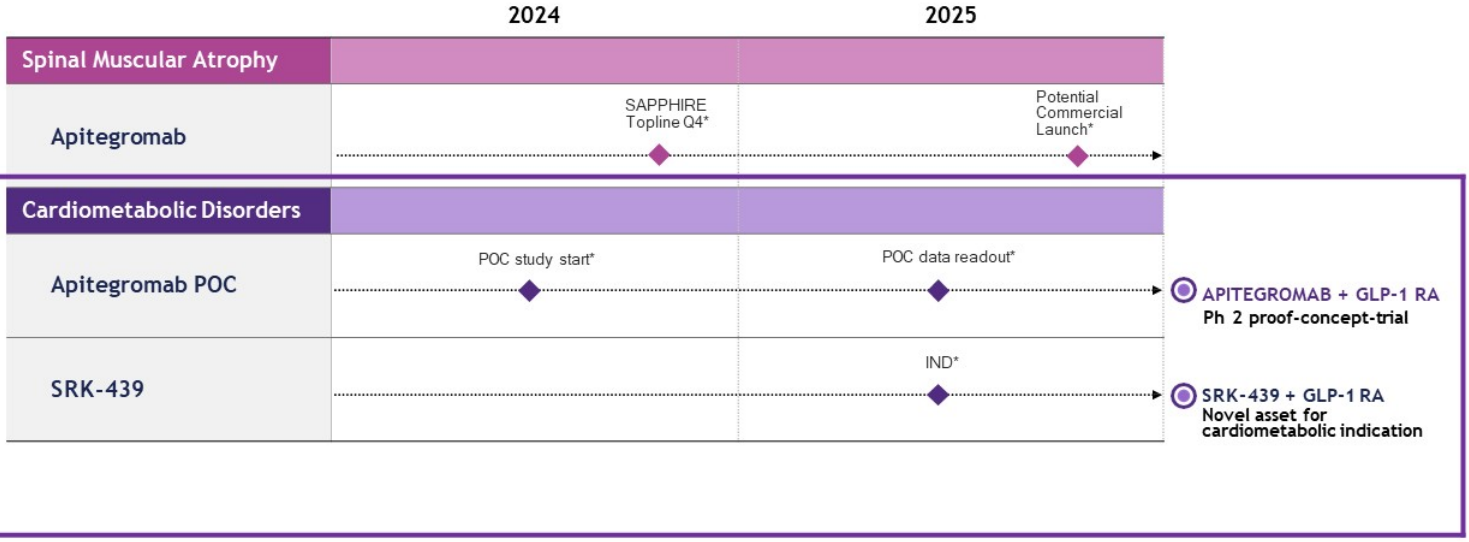
# Expedite Cardiometabolic Program with Ph2 Proof-of-Concept Study of Apitegromab in Obesity

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.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# 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;


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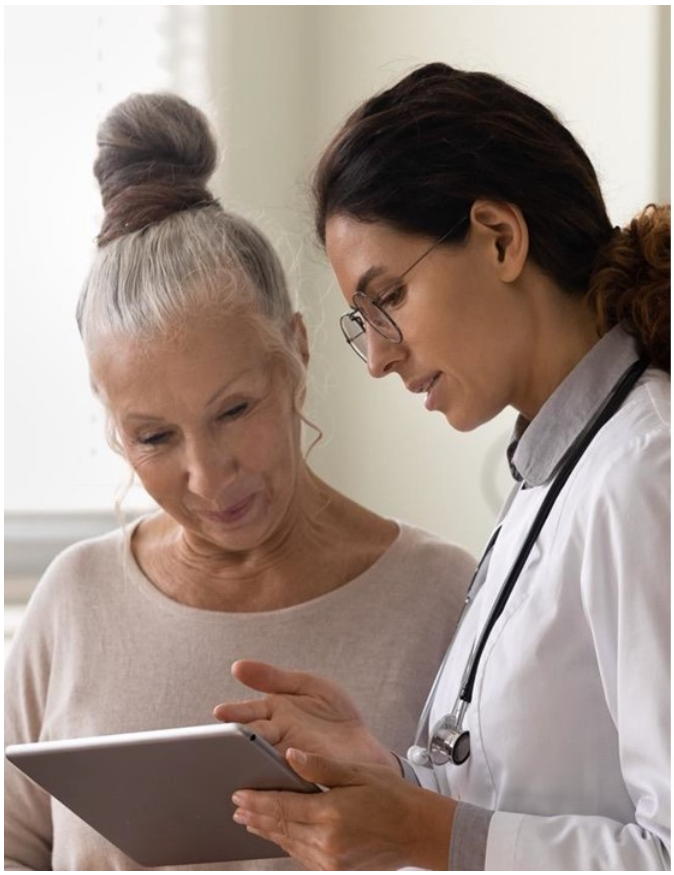

# Appendix

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# Proven Expertise in Anti-Latent TFGB & Antimyostatin Inhibition

FOUNDATION FOR SUCCESS

NEXT HORIZON

Antibody discovery technology and deep structural insights

## Antimyostatin Inhibition

### Apitegromab in SMA

In Ph 3 with potential to be first muscle-targeted treatment to advance the standard of care

- ✓ SAPPHIRE data in Q4 2024
- ✓ Commercial launch 2025*

### SRK-439 in Obesity

Novel highly selective antimyostatin to preserve lean muscle & avoid undesirable off-target effects[1-3]

- ✓ IND-enabling studies in 2024
- ✓ File IND in 2025

## Anti-Latent TGFß-1 Inhibition

### SRK-181 in Immuno-oncology

Recent for SRK-181 data supports proof of concept and validates scientific hypothesis of selective targeting

### Fibrosis

Selective context-dependent (LTBP1 & LTBP3) anti-latent TGFβ-1

* Contingent upon receipt of regulatory approval.

IND=Investigational new drug; SMA=Spinal muscular atrophy; LTBP1=Latent transforming growth factor beta binding protein 1; LTBP3=Latent transforming growth factor beta binding protein 3; TGFβ-1=Transforming growth factor beta-1.

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.

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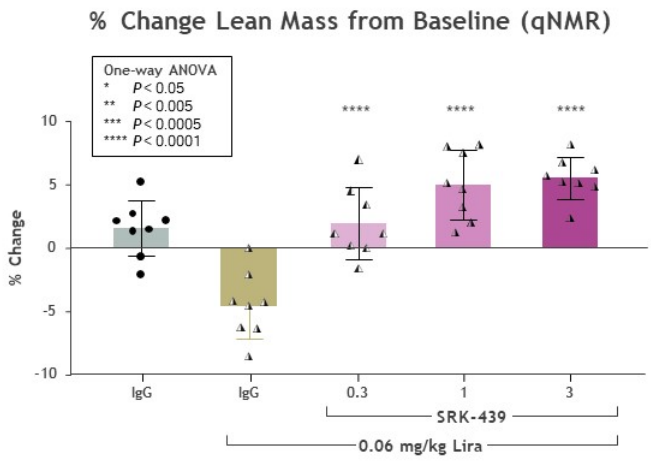
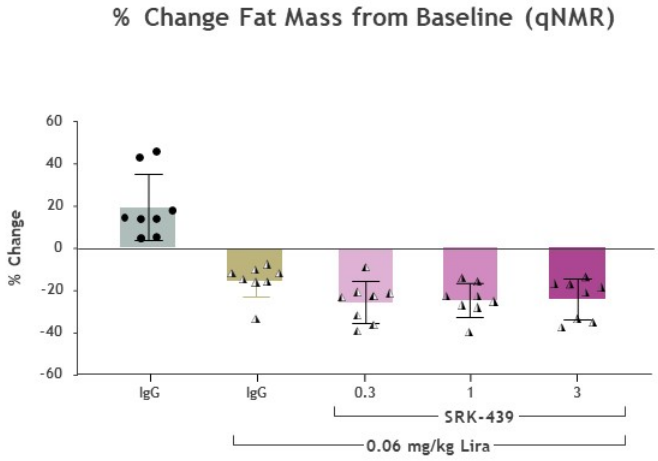
# SRK-439 Maintained Lean Mass When Combined with GLP-1 RA Therapy†




**Increased Lean Mass Gain vs GLP-1 RA Alone**

**Improved Fat Mass Loss vs GLP-1 RA Alone**

ANOVA=Analysis of variance; GLP-1 RA=Glucagon-like peptide-1 receptor agonist; IgG=Immunoglobulin G; qNMR=Quantitative nuclear magnetic resonance.

† In Mouse Diet Induced Obesity (DIO) Model.

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).



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# SRK-181: Targeting Latent TGFB1 to Overcome Immunotherapy Resistance

## 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)



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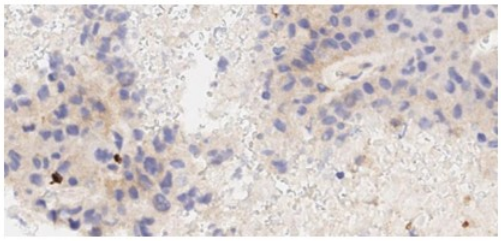
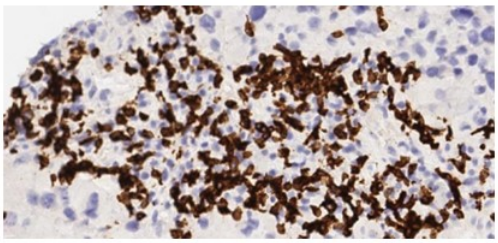
# Promising Anti-tumor Activity in Heavily Pretreated ccRCC Patients; Biomarker Data Supports Proof of Mechanism Across Multiple Tumor Types

## CD8 Stain - Melanoma

Pre-Treatment

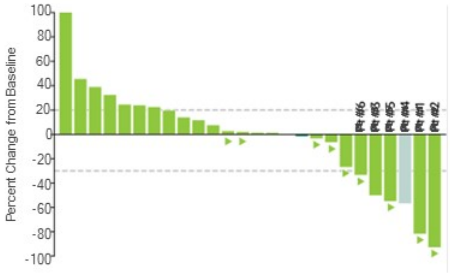


Post-Treatment

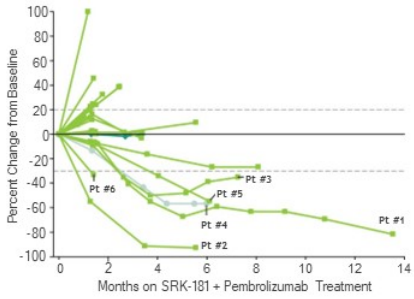


## Continued Tolerability & Promising Anti-Tumor Activity in ccRCC Patients*

Best Response in Target Lesions




Change in Tumor Volume Over Time




ccRCC=Clear cell renal cell carcinoma
Data cutoff August 29, 2023
*28 patients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# Scholar Rock Provides Corporate Update and Highlights Priorities for 2024

***- Advancing industry-leading antimyostatin pipeline, comprised of multiple, novel assets with unparalleled selectivity, to treat spinal muscular atrophy (SMA) and cardiometabolic disorders***

***- Completed enrollment for apitegromab pivotal Phase 3 SAPPHIRE trial in patients with SMA; topline data anticipated in 4Q 2024***

***- Apitegromab Phase 2 proof-of-concept trial in obesity expected to commence in mid-2024***

***- Presenting new preclinical data on SRK-439, a novel investigational myostatin inhibitor for the treatment of obesity, at Keystone Symposia in February***

***- Scholar Rock reports year-end cash and cash equivalents of approximately $280 million***

***- Presenting at the 42nd Annual J.P. Morgan Healthcare Conference on Tuesday, January 9, 2024 at 1:30 p.m. PT (4:30 p.m. ET)***

CAMBRIDGE, Mass.--(BUSINESS WIRE)--January 4, 2024--Scholar Rock (NASDAQ: SRRK), a late-stage biopharmaceutical company focused on advancing innovative treatments for spinal muscular atrophy (SMA), cardiometabolic disorders, and other serious diseases where protein growth factors play a fundamental role, today provided recent corporate updates and highlighted upcoming priorities for 2024.

“We were pleased with our progress in 2023 as we advanced our industry leading antimyostatin pipeline with apitegromab and SRK-439 and have great momentum heading into 2024. With enrollment completed for our Phase 3 SAPPHIRE trial for patients with spinal muscular atrophy, we expect topline data in Q4 this year,” said Jay Backstrom, M.D., MPH, President and Chief Executive Officer of Scholar Rock. “Additionally, we are thrilled with the planned initiation in mid-2024 of an apitegromab Phase 2 proof-of-concept trial in patients with obesity and on GLP-1 therapies that aims to establish the importance of selective, safe myostatin inhibition to preserve lean muscle mass as part of healthy weight loss.”

**2024 Priorities:**

**SPINAL MUSCULAR ATROPHY**

**Apitegromab** is an investigational, fully human monoclonal antibody that inhibits myostatin activation by selectively binding the pro- and latent forms of myostatin in skeletal muscle and is being developed as a potential first muscle-targeted therapy for the treatment of SMA. Apitegromab is the only muscle-targeted therapy to show clinical proof-of-concept in SMA.

- **Planning to announce Phase 3 SAPPHIRE clinical trial topline data in 4Q 2024**. SAPPHIRE is a randomized, double-blind, placebo-controlled clinical trial evaluating apitegromab in patients with nonambulatory Types 2 and 3 SMA on either nusinersen or risdiplam. If the trial is successful and apitegromab is approved, the Company expects to initiate a commercial product launch in 2025.
- **Continue to progress the ONYX long-term extension study for patients from both the TOPAZ and SAPPHIRE studies.**

**CARDIOMETABOLIC DISORDERS**

**SRK-439** is a novel, preclinical, investigational myostatin inhibitor that has high in vitro affinity for pro- and latent myostatin and maintains myostatin specificity (i.e., no GDF11 or Activin-A binding), and is initially being developed for the treatment of obesity.

- **Initiating a Phase 2 proof-of-concept trial with apitegromab in combination with a GLP-1 receptor agonist (GLP-1 RA) in obesity in mid-2024.** As part of the Company’s strategy to advance the development of SRK-439, it plans to initiate a Phase 2 proof-of-concept trial with apitegromab in combination with a GLP-1 RA, subject to IND clearance. Data from the clinical trial are expected in mid-2025 and will be used to guide clinical development of SRK-439. The Company plans to file an IND for SRK-439 for the treatment of obesity in 2025.
- **Presenting preclinical SRK-439 data in a poster presentation at Keystone Symposia** at the *Obesity: Causes and Consequences* meeting on February 5, 2024, in Vancouver, BC, Canada.

**2023 Highlights:**

- Completed enrollment of apitegromab pivotal Phase 3 SAPPHIRE trial.
- Presented TOPAZ 36-month extension trial data at the Cure SMA Research & Clinical Care Meeting in June, and at the 28th Annual Congress of the World Muscle Society in October, which showed long-term substantial and sustained improvements in motor function and patient-reported outcome measures in patients with nonambulatory Types 2 and 3 SMA receiving survival motor neuron (SMN) therapy.
- Initiated the ONYX trial, a long-term extension study for patients from both the TOPAZ and SAPPHIRE studies, which remains ongoing.
- Announced plans to expand into cardiometabolic disorders with SRK-439, starting with a Phase 2 proof-of-concept trial evaluating apitegromab in obesity to inform development of SRK-439.
- Presented SRK-181 Phase 1 DRAGON trial clinical and biomarker data at the SITC 38th Annual Meeting, which showed favorable tolerability and promising anti-tumor activity in heavily pretreated patients with clear cell renal cell carcinoma (ccRCC) resistant to anti-PD-1. The Company believes these data support proof-of-concept and completed enrollment of the DRAGON trial in December. The Company will provide additional clinical data updates as they become available in 2024.
- Completed an equity financing of $98 million in October. As of December 31, 2023, Scholar Rock reported cash, cash equivalents, and marketable securities of approximately $280 million, which is projected to fund the Company’s operations into the second half of 2025.

“We are excited to enter 2024 with several important near-term milestones ahead of us. As the leader in selective myostatin inhibition, we believe we are well positioned to deliver significant value to patients living with spinal muscular atrophy and the millions of people suffering from the wide array of health challenges stemming from cardiometabolic and obesity disorders. We are highly encouraged by our potential to advance the standard of care where muscle-targeted therapies can play a role in addressing unmet patient needs,” said Ted Myles, Chief Operating Officer and Chief Financial Officer.

**J.P. Morgan Healthcare Conference Presentation and Webcast**

Scholar Rock management will highlight these updates in a corporate presentation at the 42nd Annual J.P. Morgan Healthcare Conference on Tuesday, January 9, 2024, at 1:30 p.m. PT (4:30 p.m. ET). A live webcast of the presentation may be accessed by visiting the Investors & Media section of the Scholar Rock website at http://investors.scholarrock.com. An archived replay of the webcast will be available on the Company’s website for approximately 90 days following the presentation.

**About Scholar Rock**

Scholar Rock is a biopharmaceutical company that discovers, develops, and delivers life-changing therapies for people with serious diseases that have high unmet need. As a global leader in the biology of the transforming growth factor beta (TGFβ) superfamily of cell proteins and named for the visual resemblance of a scholar rock to protein structures, the clinical-stage company is focused on advancing innovative treatments where protein growth factors are fundamental. Over the past decade, Scholar Rock has created a pipeline with the potential to advance the standard of care for neuromuscular disease, cardiometabolic disorders, cancer, and other conditions where growth factor-targeted drugs can play a transformational role.

Scholar Rock is the only company to show clinical proof-of-concept for a muscle-targeted treatment in spinal muscular atrophy (SMA). This commitment to unlocking fundamentally different therapeutic approaches is powered by broad application of a proprietary platform, which has developed novel monoclonal antibodies to modulate protein growth factors with extraordinary selectivity. By harnessing cutting-edge science in disease spaces that are historically under-addressed through traditional therapies, Scholar Rock works every day to create new possibilities for patients. Learn more about our approach at ScholarRock.com and follow @ScholarRock and on LinkedIn.

**Availability of Other Information About Scholar Rock**

Investors and others should note that we communicate with our investors and the public using our company website www.scholarrock.com, including, but not limited to, company disclosures, investor presentations and FAQs, Securities and Exchange Commission filings, press releases, public conference call transcripts and webcast transcripts, as well as on Twitter and LinkedIn. The information that we post on our website or on Twitter or LinkedIn could be deemed to be material information. As a result, we encourage investors, the media and others interested to review the information that we post there on a regular basis. The contents of our website or social media shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended.

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**Forward-Looking Statements**

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding Scholar Rock’s future expectations, plans and prospects, including without limitation, Scholar Rock’s expectations regarding its growth, strategy, progress, results and timing of its clinical trials for apitegromab and SRK-181 and its preclinical programs, including SRK-439, regulatory feedback including with respect to the IND submitted in connection with the planned Phase 2 trial of SRK-439 in combination with GLP-1 RAs in obesity, and indication selection and development timing, including the therapeutic potential, clinical benefits and safety thereof, expectations regarding timing, success and data announcements of current ongoing preclinical and clinical trials, its expected cash and cash equivalents as of December 31, 2023 and cash runway, expectations regarding the achievement of important milestones, the ability of any product candidate to perform in humans in a manner consistent with earlier nonclinical, preclinical or clinical trial data, and the potential of its product candidates and proprietary platform. The use of words such as “may,” “might,” “could,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” or “continue,” and other similar expressions are intended to identify such forward-looking statements. All such forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, without limitation, that preclinical and clinical data, including the results from the Phase 2 clinical trial of apitegromab, or Part A or Part B of the Phase 1 clinical 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 candidates, including, without limitation, the Phase 3 clinical trial of apitegromab in SMA or Part B of the Phase 1 clinical trial of SRK-181; Scholar Rock’s ability to provide the financial support, resources and expertise necessary to identify and develop product candidates on their expected timelines; the data generated from Scholar Rock’s nonclinical and preclinical studies and clinical trials; information provided or decisions made by regulatory authorities; competition from third parties that are developing products for similar uses; Scholar Rock’s ability to obtain, maintain and protect its intellectual property; Scholar Rock’s dependence on third parties for development and manufacture of product candidates including, 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 public health pandemics such as COVID-19 on business operations and expectations, as well as those risks more fully discussed in the section entitled "Risk Factors" in Scholar Rock’s Quarterly Report on Form 10-Q for the quarter ended September 30, 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.

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