Positive Ph2 EMBRAZE Trial

Demonstrating Preservation of Lean Mass with Highly Selective Anti-Myostatin Inhibitor During Tirzepatide-Induced Weight Loss

June 18, 2025

Today's Speakers

David L. Hallal
Chief Executive Officer

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President, Research & Development

Agenda

TOPIC	SPEAKER
Scholar Rock's Leading Anti-Myostatin Platform	**David L. Hallal** Chief Executive Officer
EMBRAZE Trial Results	**Akshay Vaishnaw**, M.D., Ph.D. President of R&D
Q&A Session	

Forward-Looking Statements

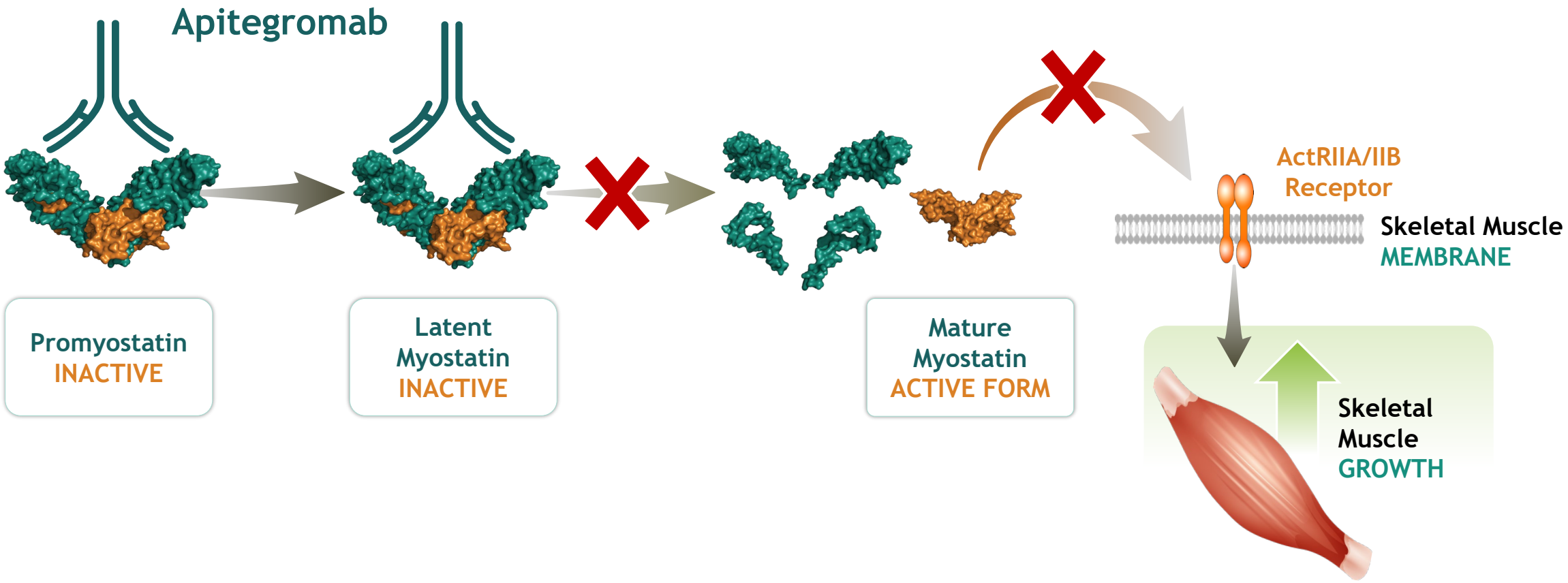
Various statements in this presentation concerning the future expectations, plans and prospects of Scholar Rock Holding Corporation and Scholar Rock, Inc. (collectively, “Scholar Rock”), including without limitation, Scholar Rock’s expectations regarding its strategy, its product candidate selection and development timing, including timing for the initiation of and reporting results from its preclinical studies and clinical trials for apitegromab, SRK-439, and other product candidates and indication selection and development timing, the ability of any product candidate to perform in humans in a manner consistent with earlier nonclinical, preclinical or clinical trial data, expectations relating to commercial launch timing in the United States and in Europe, expectations regarding the achievement of important milestones, 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 whether the results from the Phase 3 SAPPHIRE trial will be sufficient to support regulatory approval, 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; 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, including from the EMBRAZE clinical trial; 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; its ability to establish or maintain strategic business alliances; its ability to receive priority or expedited regulatory review or to obtain regulatory approval of apitegromab; its ability to expand globally and the anticipated commercial launch in the United States of apitegromab in the fourth quarter of 2025; 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, 2024, and Quarterly Report on Form 10-Q for the quarter ended March 31, 2025 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, linavonkibart, SRK-256, SRK-373, 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, linavonkibart, SRK-256, SRK-373, and SRK-439 have not been established.

Scholar Rock is a Global Leader in Selectively Targeting Myostatin

Apitegromab's Unique Upstream Mechanism of Action



Sources: Long KK, et al. Hum Mol Genet. 2019;28:1076-1089; Pirruccello-Straub M, et al. Sci Rep. 2018;8:2292.

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Spinal Muscular Atrophy (SMA)

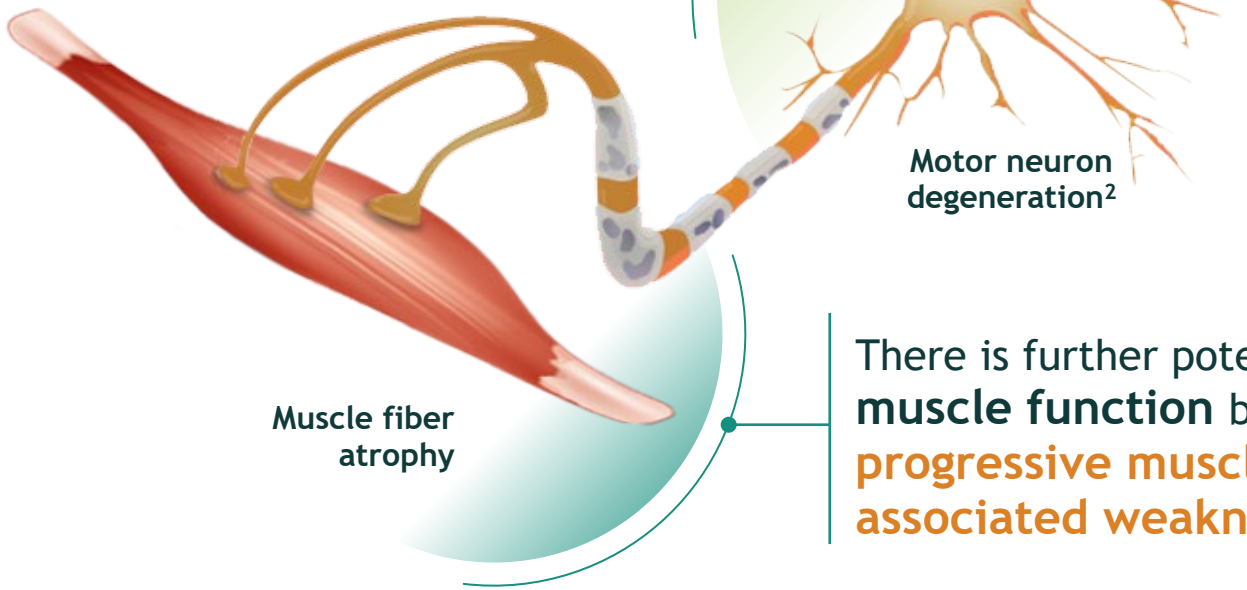
Motor Neuron Degeneration and Muscle Atrophy

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.

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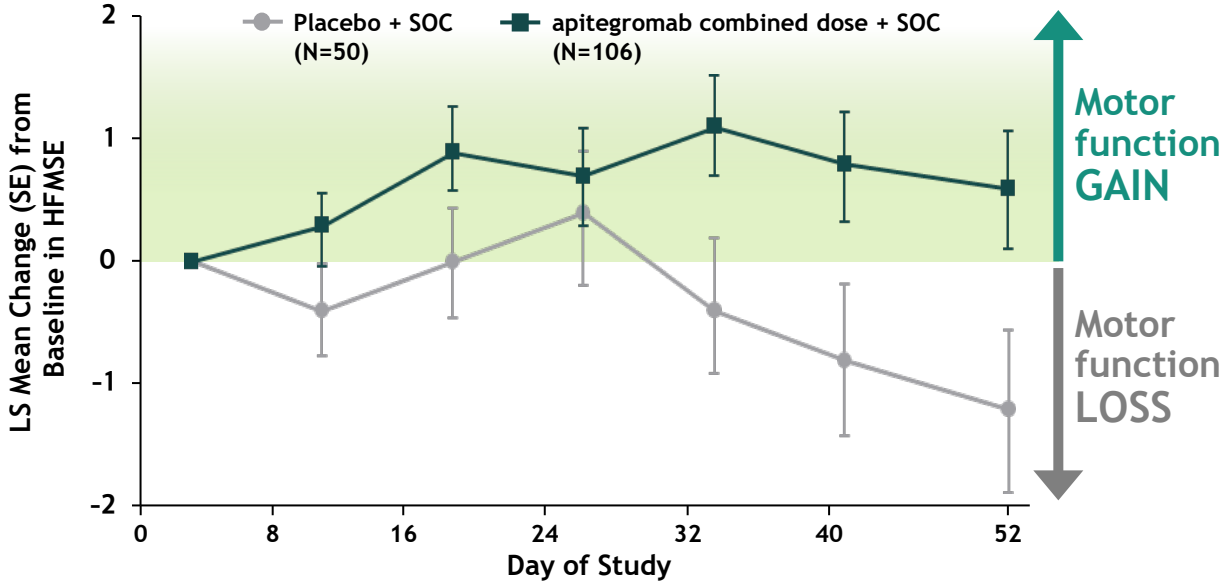
Positive Phase 3 SAPPHIRE Data

Apitegromab in SMA

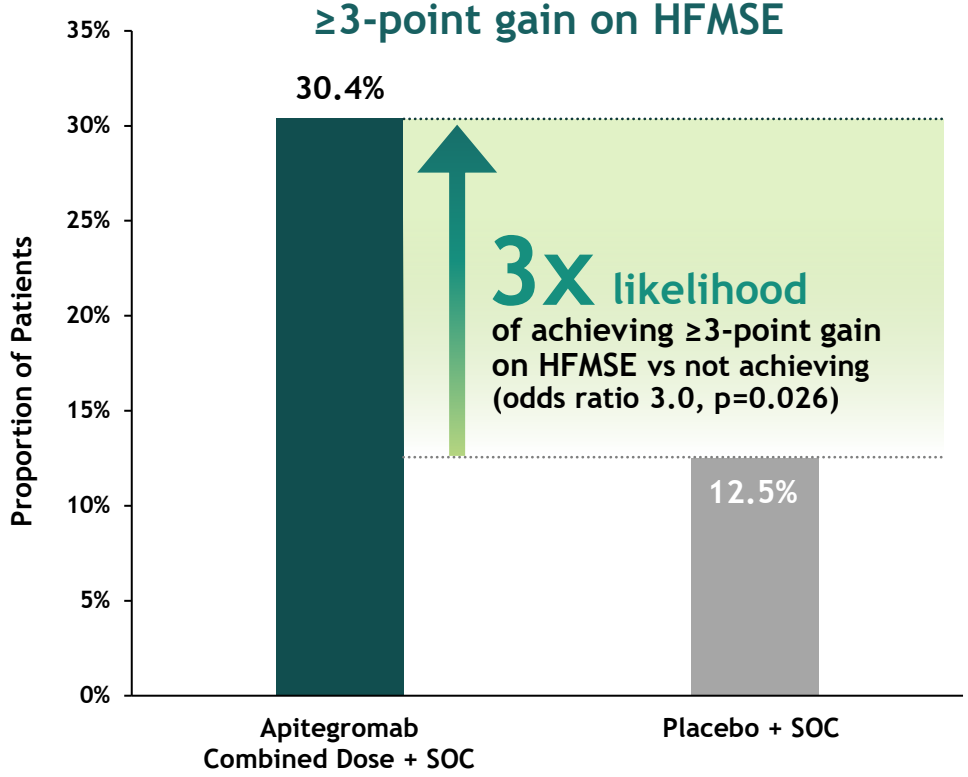
Apitegromab-treated patients improved on HFMSE over 12 months

compared to placebo patients (p=0.019)



placebo + SOC	n=	50	50	50	48	50	49	48
apitegromab + SOC	n=	106	105	105	101	102	102	102

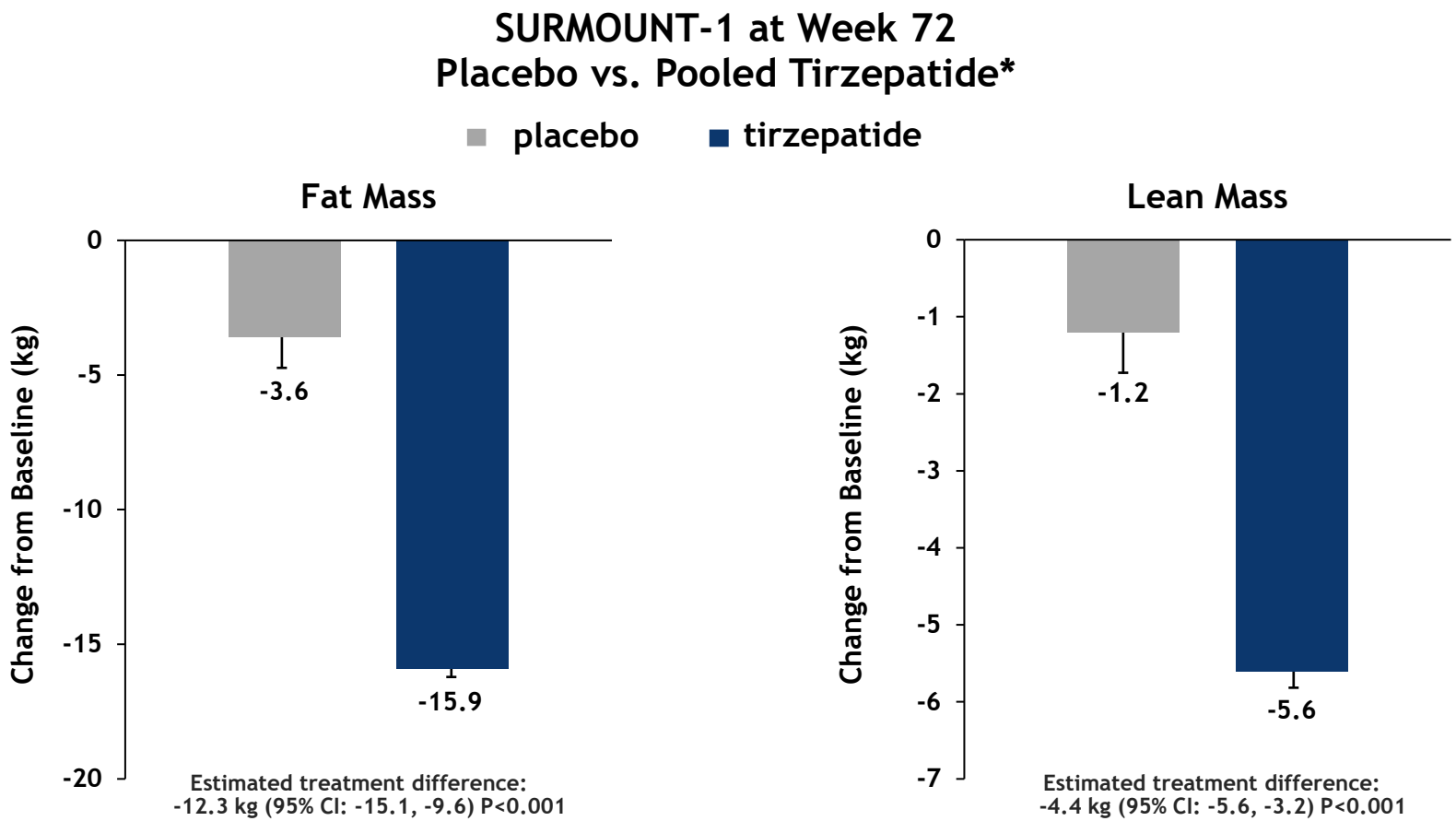
≥3-point gain on HFMSE



n/N	31/102	6/48

- All SAPPHIRE patients randomized to apitegromab or placebo were on background SMN-targeted therapy (nusinersen or risdiplam)
- Well tolerated safety profile consistent with underlying disease and the SMN-targeted therapy

Significant Loss of Lean Body Mass with Tirzepatide



n=	36	124
Baseline (kg)	49.4	46.6

n=	36	124
Baseline (kg)	53.0	50.6

Look, M., et al. Body composition changes during weight reduction with tirzepatide in the SURMOUNT-1 study of adults with obesity or overweight. Diabetes Obes Metab. 2025;1-10. DOI: 10.1111/dom.16275

*Tirzepatide group is pooled tirzepatide 5, 10, and 15 mg.

EMBRAZE Demonstrated Improved Overall Body Composition with Apitegromab

EMBRAZE

Study achieved goals

54.9%
STATISTICALLY SIGNIFICANT
LEAN MASS PRESERVATION
COMPARED TO GIP/GLP-1 MONOTHERAPY
(*p*=0.001)

WEIGHT & FAT MASS LOSS CONSISTENT
WITH GIP/GLP-1 MONOTHERAPY

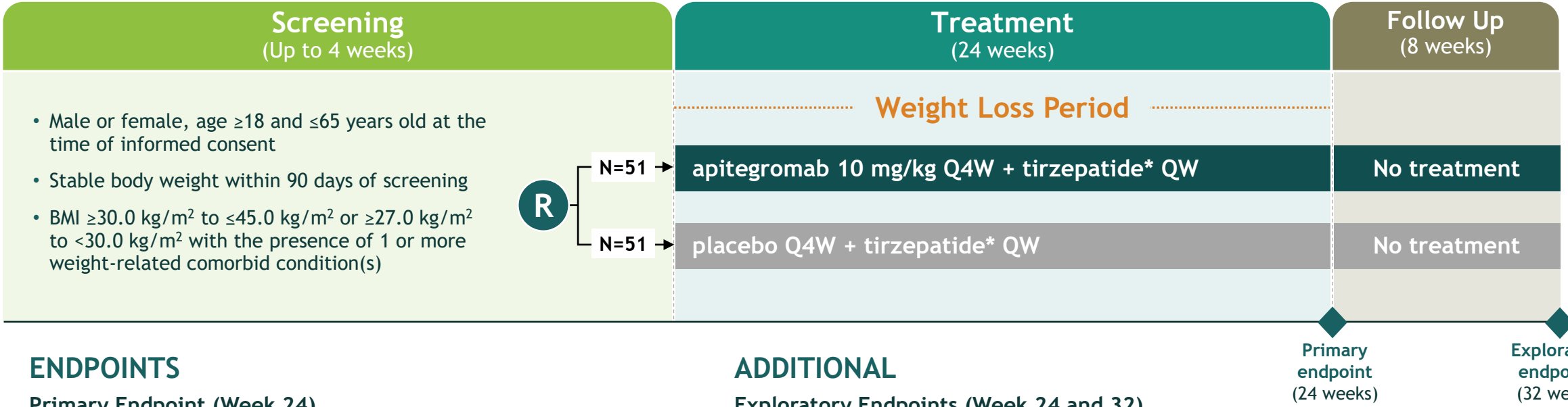
ENCOURAGING SAFETY PROFILE

Trial demonstrated ~30% of tirzepatide-induced weight loss was due to lean mass loss

Phase 2 EMBRAZE Trial Design: Treatment Over 24 Weeks

EMBRAZE

Randomized, double-blind, placebo-controlled (n=102 enrolled)
Enrolled patients who are overweight or obese



ENDPOINTS

Primary Endpoint (Week 24)
Change from baseline in lean mass by DEXA scan

Secondary Endpoints
Additional weight loss measures, safety & tolerability, PK/PD

ADDITIONAL

Exploratory Endpoints (Week 24 and 32)

- Physical function
- Cardiometabolic parameters
- Safety

*Study designed allowed for semaglutide and tirzepatide. Due to expedited enrollment and timing of semaglutide clinical supply, all enrolled patients received tirzepatide.
Apitegromab dose regimen will be 10 mg/kg Q4W, based on projected exposure in the obese population comparable to that of 20 mg/kg Q4W in SMA.
Tirzepatide and semaglutide dose regimen will follow the United States Prescribing Information.

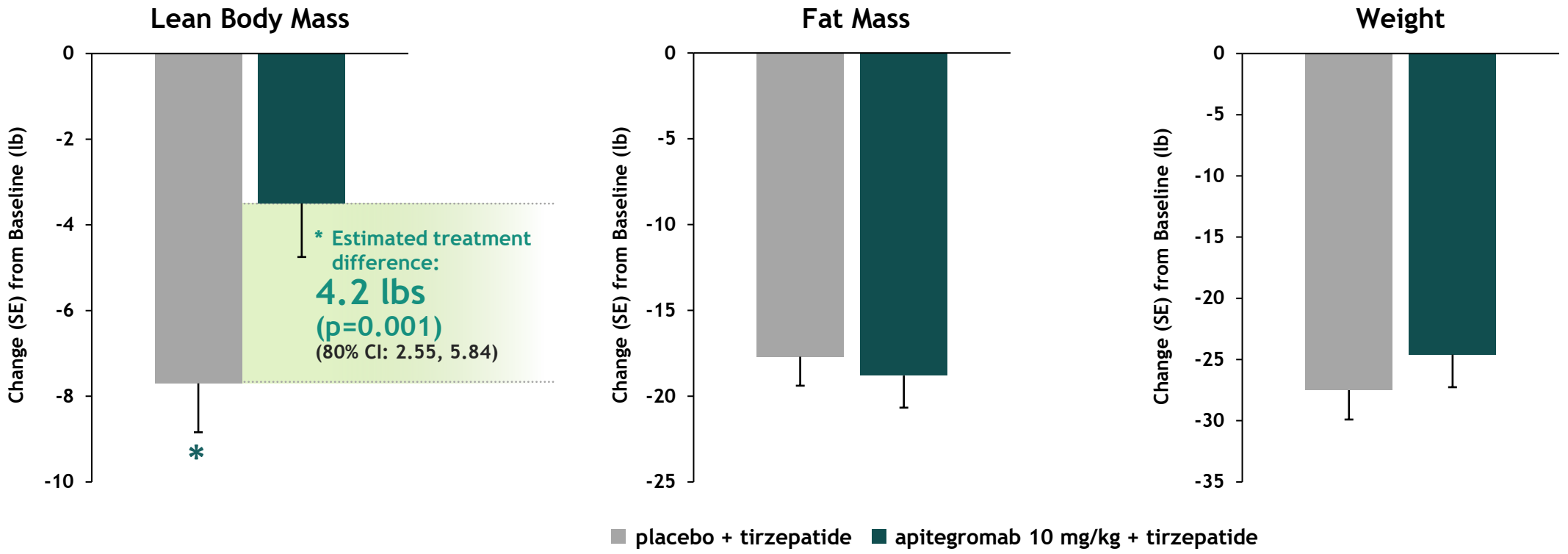
Participant Demographics and Characteristics

Randomized / ITT Population

	placebo + tirzepatide Q4W N=51	apitegromab 10 mg/kg Q4W + tirzepatide N=51
Female sex, n (%)	41 (80.4)	43 (84.3)
Mean age at screening, years (min, max)	42.6 (18, 64)	44.2 (21, 63)
Mean BMI, kg/m^2 (SD)	36.4 (3.87)	34.4 (4.09)
≥30, n (%)	51 (100)	48 (94.1)
Lean body mass, kg (SD)	49.6 (8.05)	48.3 (9.90)
Body fat mass, kg (SD)	45.1 (9.19)	41.3 (8.76)
Mean weight, kg (SD)	98.8 (14.43)	93.2 (14.92)
Prediabetes, n (%)	19 (37.3)	17 (33.3)

KEY TAKEAWAYS Baseline demographics and disease characteristics were well balanced across treatment groups

Combining with Apitegromab Significantly Improved Lean Mass Preservation Compared with Tirzepatide Alone



KEY TAKEAWAYS

- 30% of tirzepatide-induced weight loss was due to loss of lean mass
- Apitegromab in combination with tirzepatide resulted in 54.9% preservation of lean mass
- Weight and fat mass loss consistent with placebo + tirzepatide alone

Analysis based on participants who completed treatment and had a Week 24 DEXA scan. Means based on a linear regression model controlling for baseline lean body mass, baseline weight, age, and sex.

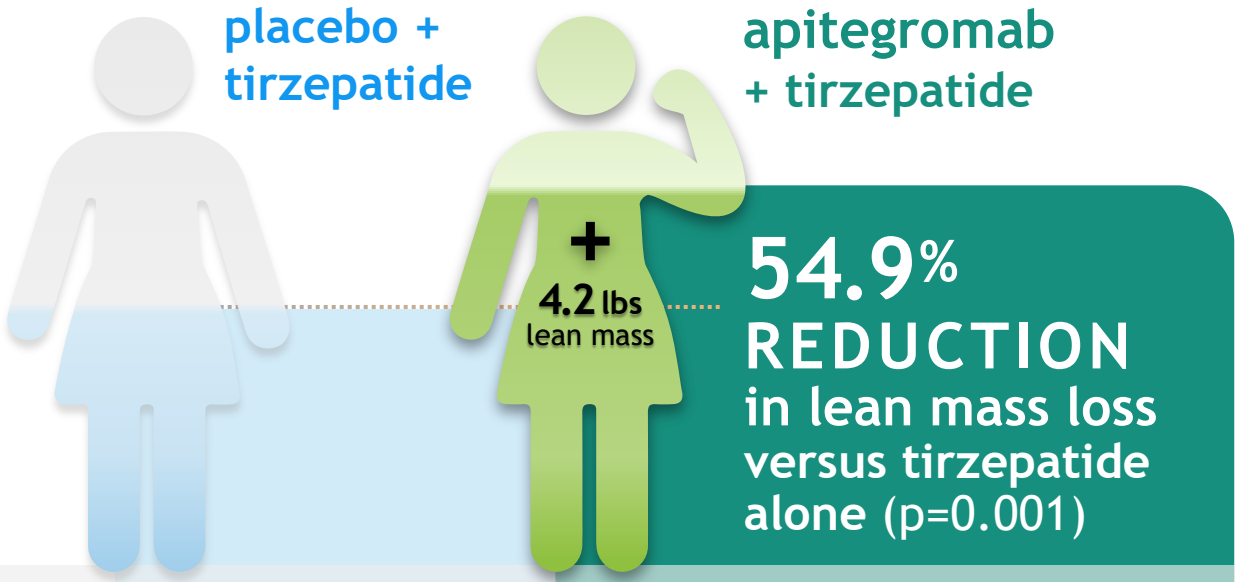
Encouraging Safety Profile

Subjects With at Least 1, n(%)	placebo + tirzepatide N=51	apitegromab 10mg/kg + tirzepatide N=51
AE	**36 (70.6)**	**39 (76.5)**
Study Drug-Related AE	19 (37.3)	22 (43.1)
Tirzepatide-Related AE	30 (58.8)	30 (58.8)
SAE	**1 (2.0)**	**1 (2.0)**
Study Drug-Related SAE	0	0
Tirzepatide-Related SAE	0	1 (2.0)
AE Grade ≥3	**3 (5.9)**	**2 (3.9)**
AE Leading to Study Drug Discontinuation	**3 (5.9)**	**2 (3.9)**

KEY TAKEAWAYS

- Incidence of adverse events generally similar between apitegromab and placebo
- AEs, SAEs, and AEs leading to discontinuation balanced; none related to apitegromab

EMBRAZE Proof-of-Concept Study Achieved Goals

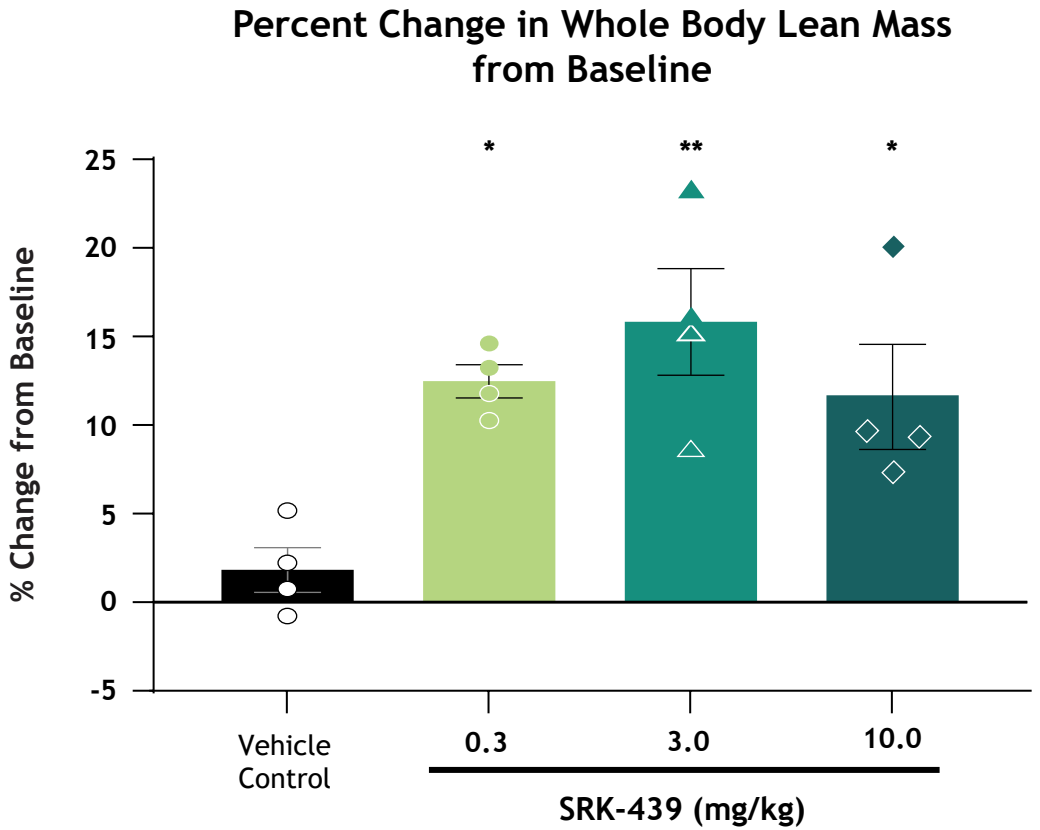


Combining apitegromab 10 mg/kg with tirzepatide over 24 weeks

Higher quality of weight loss observed

Apitegromab generally well tolerated and consistent with safety profile observed in other clinical trials

SRK-439 Significantly Increased Lean Mass At All Doses Tested in Nonhuman Primates



All tested doses of SRK-439 demonstrated a statistically significant increase in lean body mass vs vehicle

- Data highlights potency of SRK-439, achieving maximum target engagement and maximum efficacy at the lowest dose tested
- **IND submission anticipated in 2H 2025**

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*p<0.05, **p<0.01

Delivering on Our Priorities to Drive Long-Term Growth

1 Apitegromab Regulatory Approvals & Commercialization

US: PDUFA Sept 22; Execute Successful Commercial Launch*

EU: MAA mid-2026; Advance Launch Preparedness

ROW: Expand Globally

*Pending regulatory approval

2 Expand in Additional Rare, Severe & Debilitating Neuromuscular Diseases

Apitegromab Development Program: Building a Pipeline in a Product

SRK-439: IND in 2H 2025

3 Disciplined Capital Allocation

Efficient Commercial Build

Phase Investments to Support Potential Future High-value Commercial & Pipeline Initiatives

Leverage Highly Innovative Anti-myostatin Platform

Q&A