Positive Topline Results from Pivotal Phase 3 SAPPHIRE Trial of Apitegromab in Spinal Muscular Atrophy (SMA)

October 7, 2024

ScholarRock

Agenda

Introduction	**Jay Backstrom, M.D., MPH,** President & Chief Executive Officer
SAPPHIRE Results	**Jing Marantz, M.D. Ph.D.,** Chief Medical Officer
Concluding Remarks	**Jay Backstrom, M.D., MPH,** President & Chief Executive Officer
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 growth, strategy, progress and timing of its clinical trials for apitegromab, and indication selection and development timing, including the timing of any regulatory submissions or commercial launch, the therapeutic potential, clinical benefits and safety of any product candidates, expectations regarding timing, success and data announcements of current ongoing preclinical and clinical trials, its 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, whether the results from the Phase 3 SAPPHIRE trial will be sufficient to support regulatory approval, that the full results from the Phase 3 SAPPHIRE trial may differ from the topline data, that preclinical and clinical data, including the results from the Phase 2 or Phase 3 clinical trial of apitegromab, 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; 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; and Scholar Rock's ability to manage expenses and to obtain additional funding when needed to support its business activities and establish and maintain strategic business alliances and new business initiatives, and our ability to continue as a going concern; 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 June 30, 2024, 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 presentation is as of the date of the presentation, and Scholar Rock undertakes no duty to update this information unless required by law.

This presentation discusses product candidates that are under clinical study, and which have not yet been approved for marketing by the FDA or any other regulatory agency. No representation or warranty, express or implied, is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied.

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 is an investigational drug candidate under evaluation. Apitegromab has not been approved for any use by the FDA or any other regulatory agency and the safety and efficacy of apitegromab has not been established.

ScholarRock

Introduction

Jay Backstrom, M.D., MPH
President & Chief Executive Officer

Our Purpose: Create Possibilities for Those Living with Spinal Muscular Atrophy (SMA)

> Muscle is everything. I want to live knowing that I have the strength **to take care of myself** if left alone.
>
> - Lyza

Positive Phase 3 SAPPHIRE Trial: Transformative Benefit in SMA

MET PRIMARY ENDPOINT:

1.8
POINT IMPROVEMENT
in HFMSE* vs. placebo
(p=0.0192)

CONSISTENT
clinically meaningful benefit across **all age groups (2-21)**

30%
of apitegromab patients
ACHIEVED ≥3
POINT IMPROVEMENT IN HFMSE†

FAVORABLE SAFETY profile consistent with >48 months experience in Phase 2 TOPAZ trial

Apitegromab has the potential to alter the course of SMA

* Based on apitegromab combined dose (10 mg/kg and 20 mg/kg) + SOC versus placebo + SOC
† 12.5% of patients on placebo + SOC achieved a ≥3-point improvement in HFMSE
SOC=Standard of care (i.e., nusinersen or risdiplam)

Phase 3 SAPPHIRE Topline Results

Jing Marantz, M.D., Ph.D.
Chief Medical Officer

ScholarRock

Study Design

SAPPHIRE

Randomized, double-blind, placebo-controlled, parallel arm design (n=188)

Patients on standard of care (nusinersen or risdiplam)

SCREENING

MAIN POPULATION (n=156)

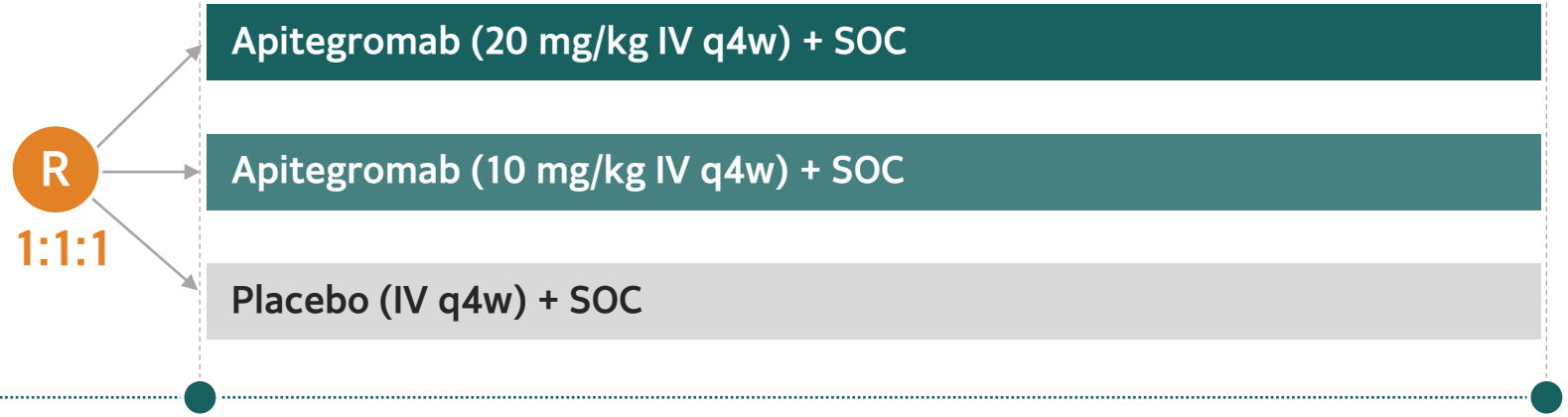
Ages 2-12

With nonambulatory Types 2 and 3 SMA

Stratified to ensure balanced allocation across the three arms:

1. Age at SOC initiation (age < 5 vs. age ≥ 5)
2. SOC (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 Study Objectives

Exploratory Population (n = 32, age 13-21)

Stratified by SOC, randomized 2:1 between apitegromab 20 mg/kg vs placebo
Endpoints: Safety & exploratory efficacy

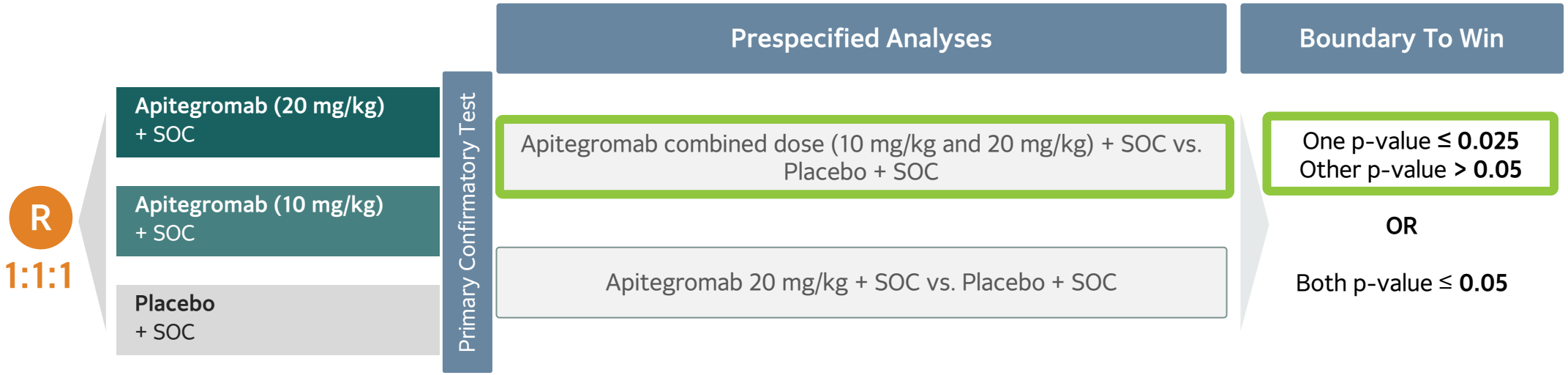
Separate open-label extension study (after patients complete 12-month treatment period)
Safety & exploratory long-term efficacy

ClinicalTrials.gov Identifier: NCT05156320
HFMSE=Hammersmith Functional Motor Scale Expanded; RULM=Revised Upper Limb Module; WHO: World Health Organization Motor Developmental Milestones; R=randomization; SMA=spinal muscular atrophy; SOC=standard of care; PK/PD=pharmacokinetics/pharmacodynamics; ADA=anti-drug antibodies.

Prespecified Statistical Analysis Plan

Primary Objective

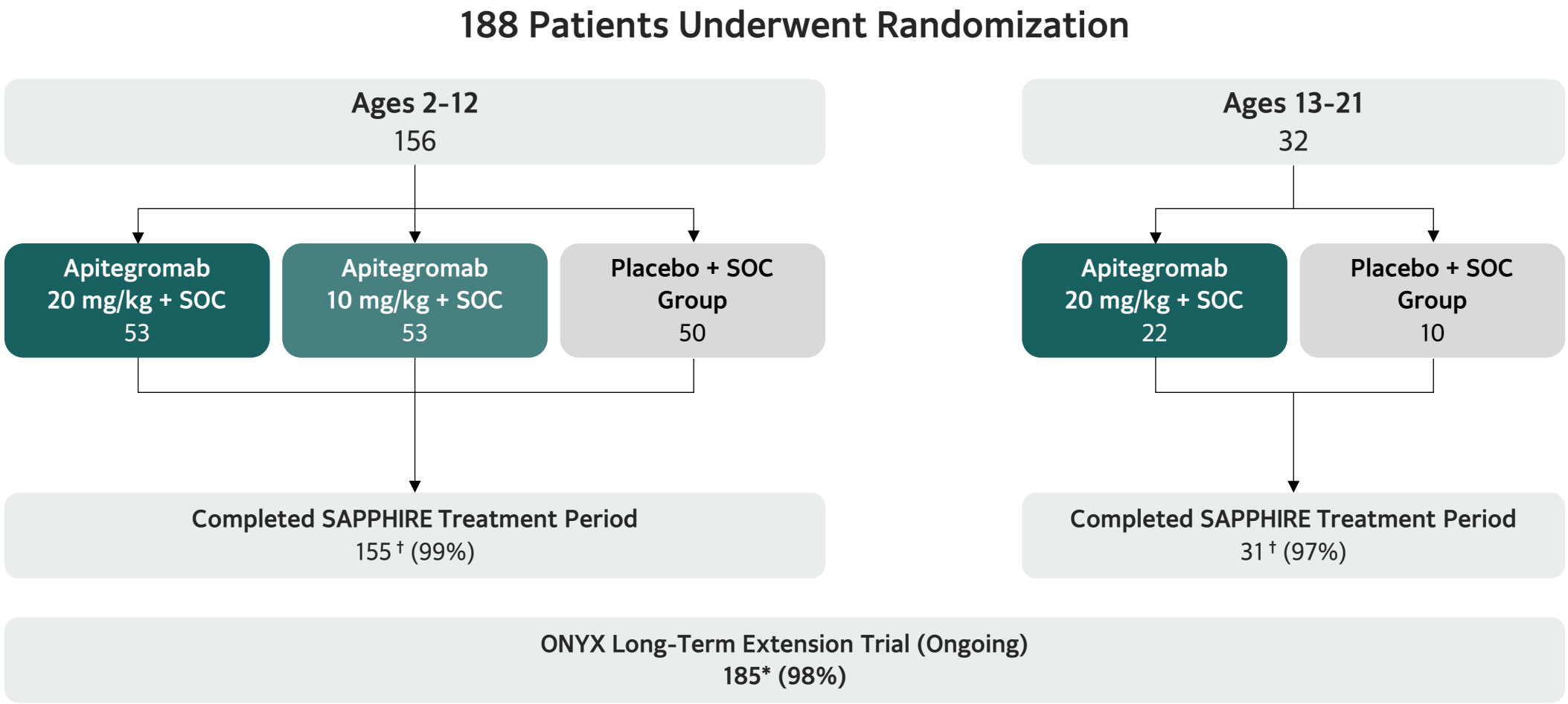
To assess the efficacy of apitegromab compared with placebo using HFMSE in patients 2 through 12 years old



- Prespecified analyses to assess dose: combined apitegromab doses (10 mg/kg + 20 mg/kg), 20 mg/kg, and 10 mg/kg; 10 mg/kg and 20 mg/kg expected to be similar based on insights from TOPAZ
- Primary confirmatory test evaluates HFMSE for combined dose and 20 mg/kg concurrently by Hochberg, followed by RULM, HFMSE ≥ 3 proportion, WHO for 20 mg/kg, then HFMSE, RULM, HFMSE ≥ 3, WHO for 10 mg/kg dose in a hierarchical order

The Hochberg procedure (Hochberg 1988) was used to test: 1) apitegromab combined dose (10 mg/kg and 20 mg/kg) vs placebo and 2) apitegromab 20 mg/kg dose vs placebo concurrently for the primary endpoint as the primary confirmatory test. The hierarchical testing procedure was applied to account for multiple confirmatory tests for the primary endpoint and key secondary endpoints. The testing procedure first evaluated the primary confirmatory test, followed by analyses of key secondary endpoints for apitegromab 20 mg/kg, and then the analyses of primary endpoint and key secondary endpoints for apitegromab 10 mg/kg.
SOC=standard of care

98% of Patients Continue on Long-Term Extension



*1 patient from 2-12 age group opted not to enroll in the ONYX study.

† 1 subject (1%) in the 20 mg/kg apitegromab arm in the 2-12 age group withdrew consent. 1 subject (3%) in the 20 mg/kg apitegromab arm in the 13-21 age group withdrew consent. Neither withdrew consent due to an adverse event.

SOC=standard of care.

Baseline Demographics and Disease Characteristics Well Balanced

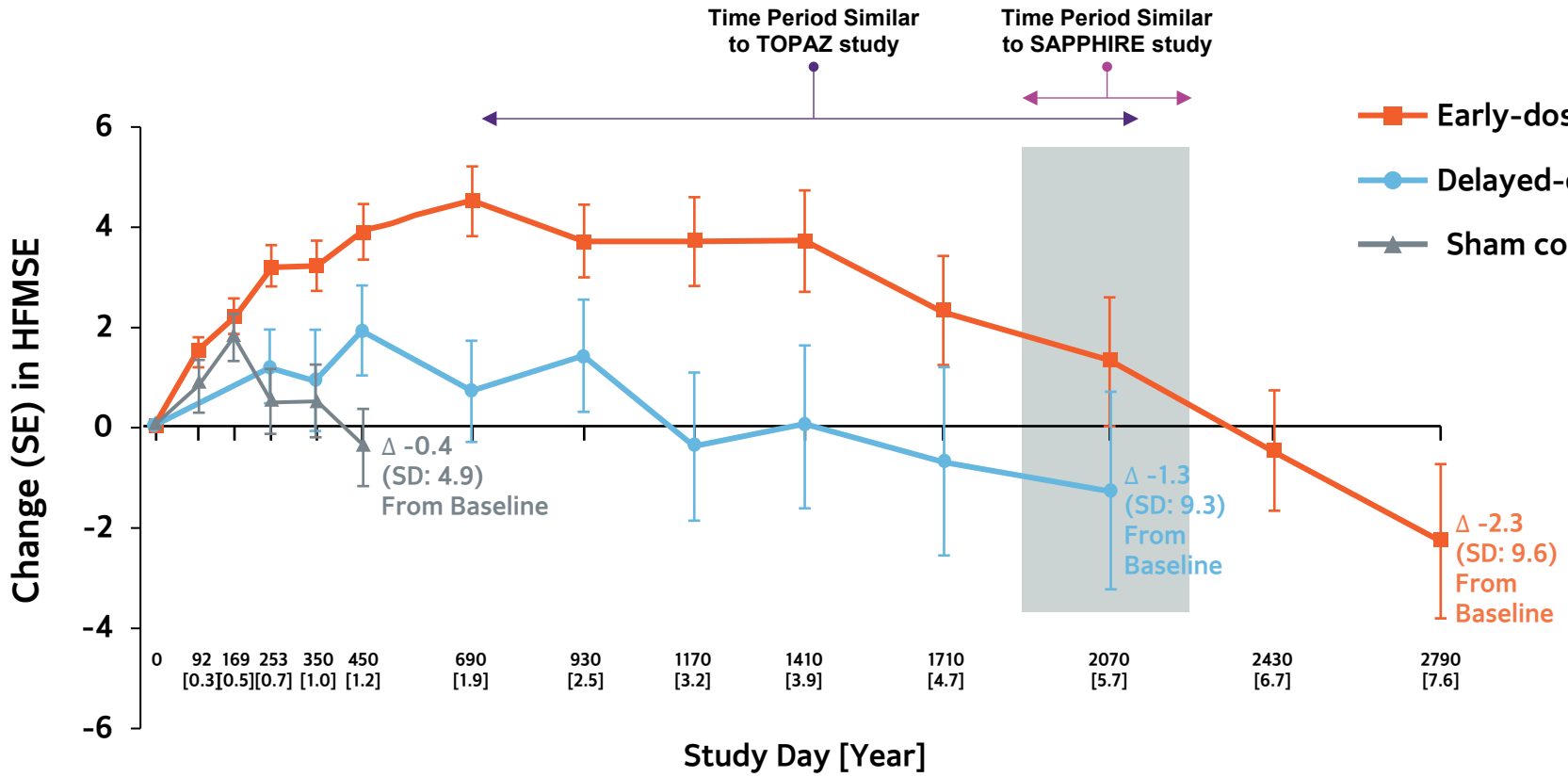
	Ages 2-12				Ages 13-21	
	Placebo + SOC (N = 50)	Apitegromab 10 mg/kg + SOC (N = 53)	Apitegromab 20 mg/kg + SOC (N = 53)	Apitegromab + SOC (N = 106)	Placebo + SOC (N = 10)	Apitegromab 20 mg/kg + SOC (N = 22)
Female Sex, n (%)	25 (50.0)	23 (43.4)	26 (49.1)	49 (46.2)	5 (50.0)	15 (68.2)
Age at Screening – years, mean (range)	8.1 (3, 12)	7.4 (2, 12)	7.9 (2, 12)	7.6 (2, 12)	15.2 (13, 18)	16.1 (13, 21)
SMN Therapy at Randomization						
Nusinersen / Risdiplam (%)	80 / 20	75.5 / 24.5	77.4 / 22.6	76.4 / 23.6	60 / 40	54.5 / 45.5
Duration of Nusinersen / Risdiplam – years, mean	5.5 / 2.7	4.4 / 3.0	5.3 / 3.5	4.8 / 3.2	6.7 / 3.3	5.9 / 3.8
SMN Therapy Initiation Age, <5 / ≥5 years (%)	88 /12	86.8 / 13.2	84.9 / 15.1	85.8 / 14.2	N/A	N/A
Number of SMN Therapies, 1 / 2 (%)	86 / 14	86.8 / 13.2	84.9 / 15.1	85.8 / 14.2	80 / 20	90.9 / 9.1
SMA Type, Type 2 /3 (%)	94 / 6	83 / 17	90.6 / 9.4	86.8 / 13.2	60 / 40	40.9 / 59.1
SMN2 Copy Number, 2 / 3 / 4 (%)	4 / 90 / 2	11.3 / 77.4 / 7.5	7.5 / 86.8 / 5.7	9.4 / 82.1 / 6.6	0 / 80 / 10	4.5 / 59.1 / 13.6
Baseline HFMSE Score, mean (range)	27.8 (9, 46)	25.5 (9, 48)	25.5 (10, 43)	25.5 (9, 48)	22.8 (10, 45)	20.6 (8, 43)
History of Scoliosis (%)	70	71.7	71.7	71.7	90	86.4

KEY TAKEAWAYS

- Study population was broadly representative of SMA population
- Patients on the advanced phase of their SMN therapy journey

Max=Maximum; Min=Minimum; SD=standard deviation; SMN=Survival Motor Neuron; SMA=Spinal Muscular Atrophy, SOC=standard of care.

Despite Chronic SMN Therapy, SMA Patients Continue To Lose Function Over Time



Early-dosed (CHERISH/SHINE)	n=	84	84	84	84	83	76	83	83	79	74	75	54	61	39
Delayed-dose (SHINE)	n=	42			40	18	24	37	37	35	29	30	22		
Sham control (CHERISH)	n=	42	41	41	41	42	39								

SMN-targeted therapies prevent further degeneration of motor neurons[1], yet lack any direct impact on muscle atrophy

Substantial room for improvement in the current approved treatment landscape exists

Finkel RS et al. "Final Safety and Efficacy Data From the SHINE Study in Participants With Infantile-Onset and Later-Onset SMA." Presented at Cure SMA Annual Conference, July 2024
*Patient age based on those received active treatment (mean or median)
1. This information from third-party studies is provided for background purposes only and is not intended to convey or imply a comparison to the SAPPHIRE clinical trial results
SMN=survival motor neuron

Primary Endpoint Met

Clinically Meaningful and Statistically Significant Improvement in HFMSE

Change from Baseline in HFMSE Total Score

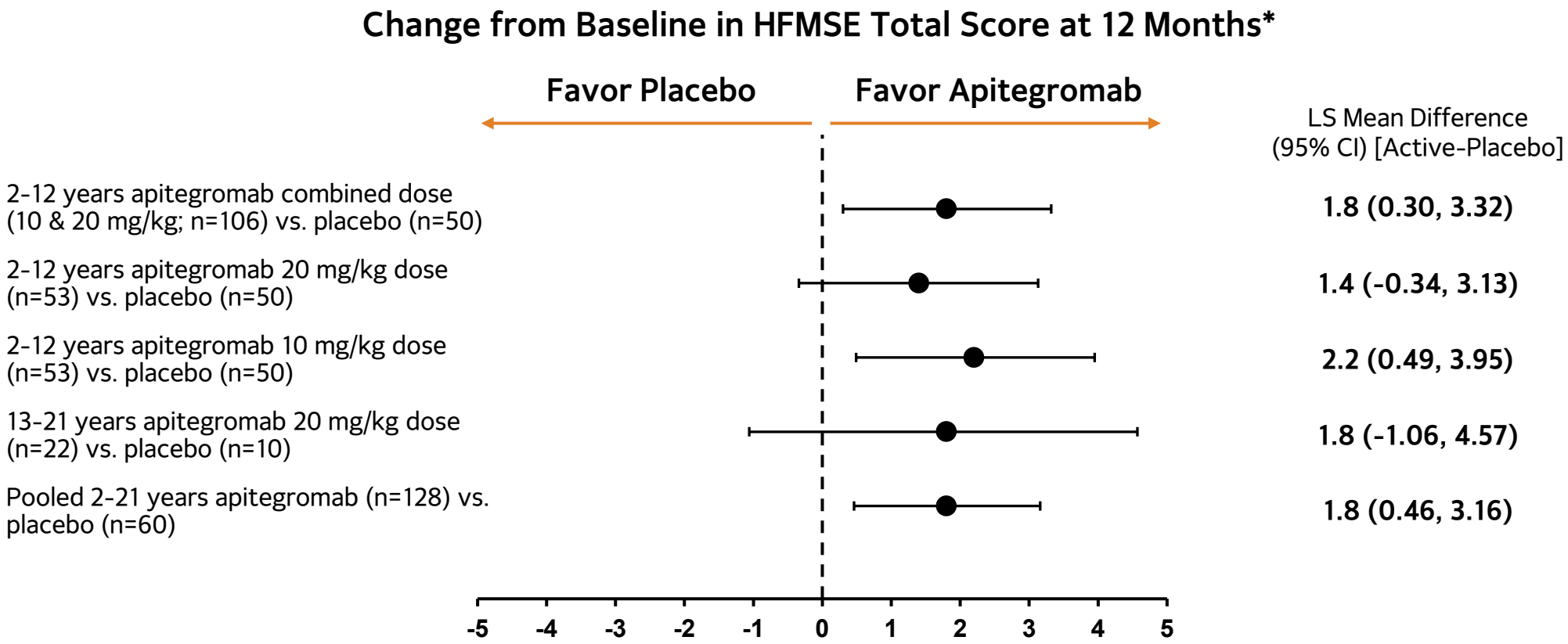
Analysis	n	Results (vs Placebo, n=50)	Unadjusted *P*-value	
Apitegromab 10+20 mg/kg combined	106	**1.8**	**0.0192***	✓
Apitegromab 20 mg/kg	53	1.4	0.1149*	
Apitegromab 10 mg/kg	53	2.2	0.0121**	

Primary Analysis

Achieved Statistical Significance

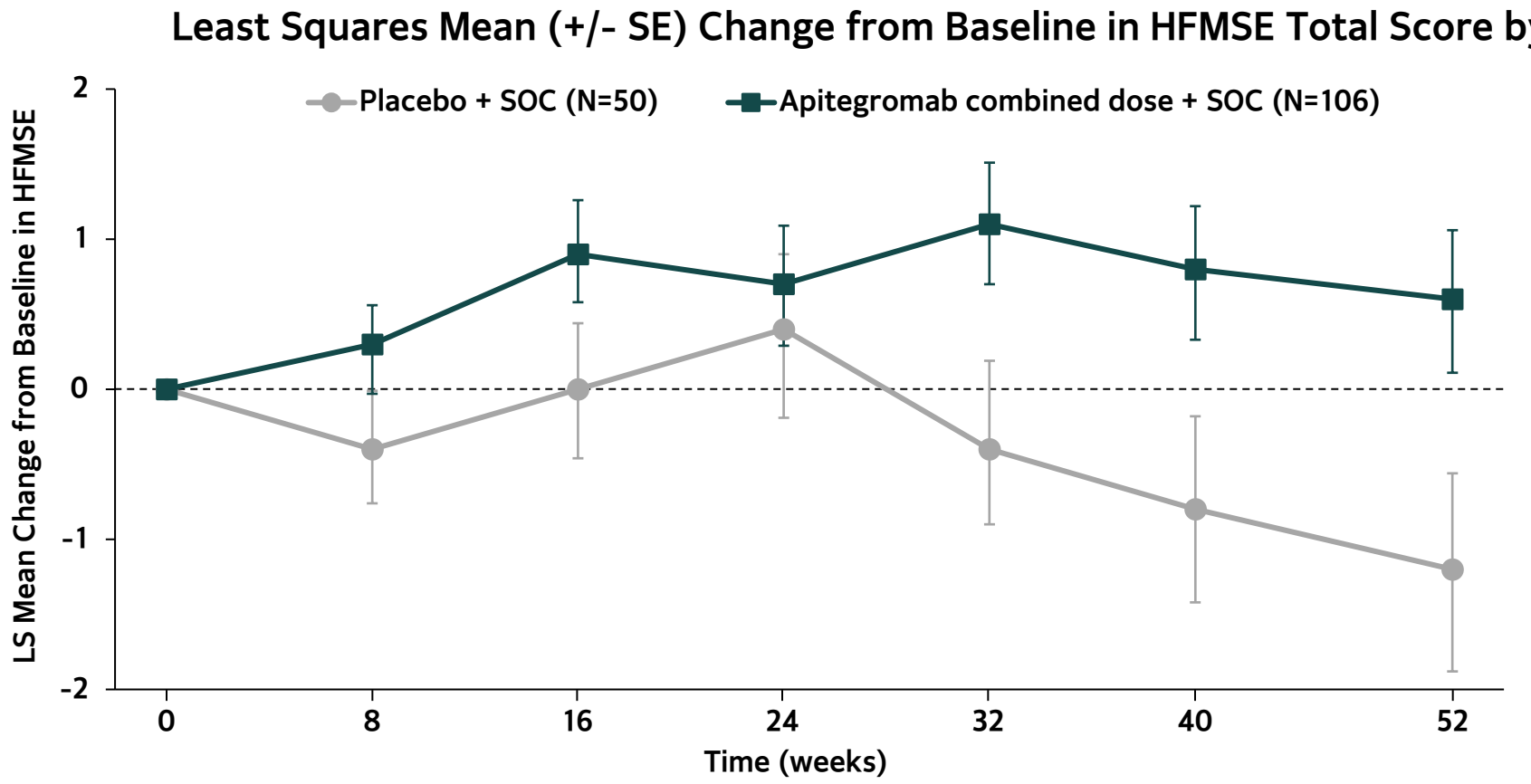
*Hochberg method prespecified for multiplicity adjustment; **nominal p value
HFMSE=Hammersmith Functional Motor Scale Expanded.

Improvement in HFMSE Consistent Across Doses and Age Groups



CI=Confidence Interval; EXP=Exploration Subpopulation; HFMSE=Hammersmith Functional Motor Scale Expanded; SOC=standard of care.
*n values at 12-month endpoint

Early and Increasing HFMSE Improvement vs. Placebo



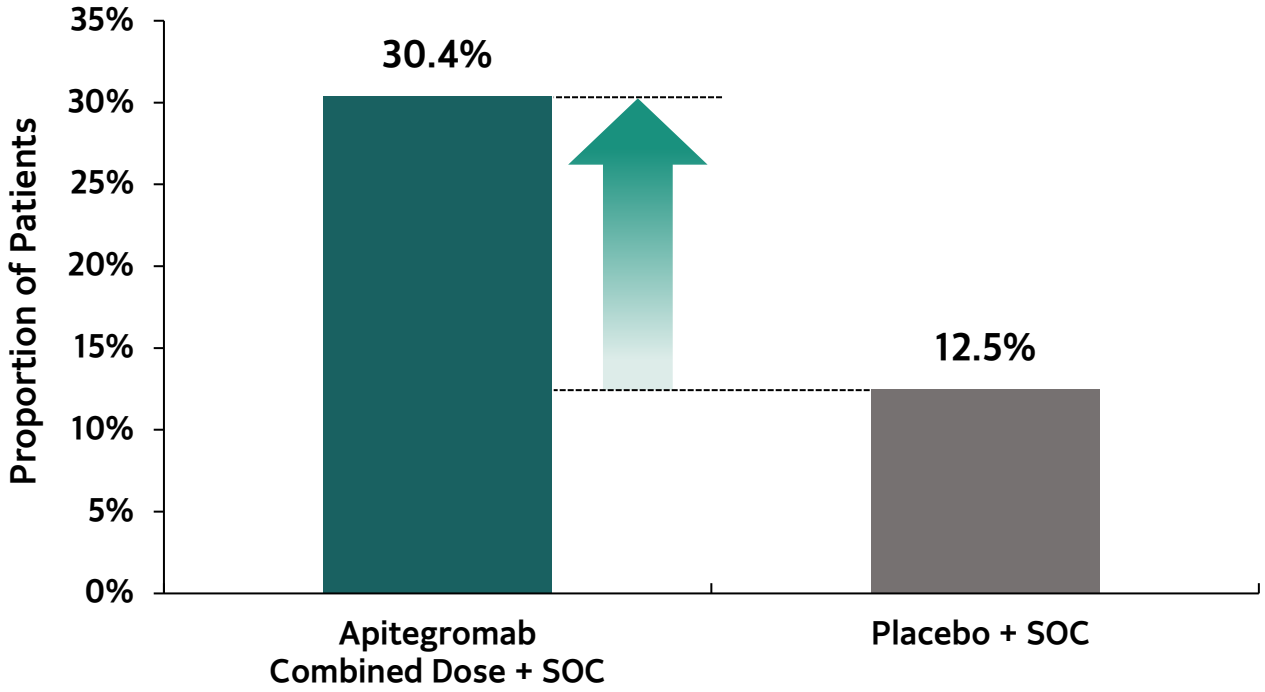
Placebo + SOC	50	50	50	48	50	49	48
Apitegromab + SOC	106	105	105	101	102	102	102

Apitegromab-treated patients improved on HFMSE, while placebo patients declined on HFMSE over 12 months

CI=Confidence Interval; EXP=Exploration Subpopulation; HFMSE=Hammersmith Functional Motor Scale Expanded; LS=Least Squares; MEP=Main Efficacy Population; SOC=standard of care.

30% of Apitegromab Patients Achieved ≥3 Points on HFMSE

≥3 Point Improvement in HFMSE



n/N	31/102	6/48

Proportion of patients achieving ≥3 Point Improvement in HFMSE was higher for apitegromab vs. placebo in combined dose (odds ratio 3.0, p=0.0256)

HFMSE=Hammersmith Functional Motor Scale Expanded; SOC=standard of care.

Well-Tolerated Safety Consistent With Established Profile Observed in Phase 2 TOPAZ Trial

	Ages 2-12				Ages 13-21	
Summary of Adverse Events (AE)	**Placebo + SOC** (N = 50) n (%)	**Apitegromab 10 mg/kg + SOC** (N = 53) n (%)	**Apitegromab 20 mg/kg + SOC** (N = 53) n (%)	**Apitegromab + SOC** (N = 106) n (%)	**Placebo + SOC** (N = 10) n (%)	**Apitegromab 20 mg/kg + SOC** (N = 22) n (%)
AE	43 (86.0)	51 (96.2)	46 (86.8)	97 (91.5)	9 (90.0)	19 (86.4)
SAE	5 (10.0)	9 (17.0)	12 (22.6)	21 (19.8)	1 (10.0)	0
AE Grade ≥ 3	5 (10.0)	9 (17.0)	11 (20.8)	20 (18.9)	1 (10.0)	1 (4.5)
AE Leading to treatment discontinuation	0	0	0	0	0	0
AE Leading to study withdrawal	0	0	0	0	0	0

- AE ≥20% incidence in apitegromab-treated patients were pyrexia, nasopharangitis, cough, vomiting, upper respiratory track infection, and headache
- SAEs pneumonia and dehydration were infrequent (<8%) and deemed unrelated to apitegromab

KEY TAKEAWAYS

- There were no clinically relevant differences in the adverse event profile by dose, 10 mg/kg vs 20 mg/kg
- SAEs were consistent with underlying disease and standard of care, and none were assessed as related to apitegromab
- There were no study drug discontinuations due to adverse events

AE=Adverse Event; SOC=standard of care. All AEs are coded using the MedDRA version 26.1.

Potential to Transform Standard of Care in SMA

Clear and Meaningful Improvement

1.8-point improvement in HFMSE (p=0.0192) compared to placebo

Patients improving on apitegromab vs. declining on placebo

Potential to be Suitable for Broad SMA Population*

Broadly representative study population

Improvement across all age groups (2-21)

Well-tolerated Safety Profile

Favorable safety profile supports durability of treatment

>48 months treatment experience in SMA[1]

[1] Based on TOPAZ patients receiving combination therapy after 4 years of treatment. Data cutoff date: April 2024
* If approved by regulatory authorities

Conclusion

Jay Backstrom, M.D., MPH
President & Chief Executive Officer

ScholarRock

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

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.

Innovating a New Era in the Treatment of Spinal Muscular Atrophy

Scholar Rock has an industry-leading, highly selective antibody engineering platform that has succeeded where others have failed.

Apitegromab is the first and only muscle targeted therapy to show clinically meaningful and statistically significant functional improvement in SMA.

Apitegromab is also the first and only anti-myostatin therapy to demonstrate a functional improvement in a pivotal Phase 3 study.

Apitegromab Has the Potential to Transform Standard of Care in SMA

MET PRIMARY ENDPOINT:

1.8
POINT IMPROVEMENT
in HFMSE* vs. placebo
(p=0.0192)

CONSISTENT
clinically meaningful benefit across **all age groups (2-21)**

30%
of apitegromab patients
ACHIEVED ≥3
POINT IMPROVEMENT IN HFMSE†

FAVORABLE SAFETY profile consistent with >48 months experience in Phase 2 TOPAZ trial

Scholar Rock is working with a sense of urgency to bring apitegromab to SMA patients

* Based on apitegromab combined dose (10 mg/kg and 20 mg/kg) + SOC versus placebo + SOC
† 12.5% of patients on placebo + SOC achieved a ≥3-point improvement in HFMSE
SOC=Standard of care (i.e., nusinersen or risdiplam)

Upcoming Planned Key Milestones

Apitegromab Regulatory Submissions

- Submit FDA and EMA applications in Q1 2025
- Request priority review (FDA) and accelerated assessment (EMA)

Myostatin Clinical Momentum

- Obesity: EMBRAZE readout expected in Q2 2025
- SMA: Under 2 study initiation planned for mid-2025

EMBRAZE

OPAL

Apitegromab Commercial Launch in SMA*

- US launch in Q4 2025 and EU launch to follow

* If approved by relevant health authorities

Q&A Session

Thank you!