TOPAZ Interim Analysis: SRK-015 Demonstrates Clinical Proof-of-Concept in Spinal Muscular Atrophy

October 27, 2020

ScholarRock™

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Agenda

Opening Remarks	Tony Kingsley, President & CEO
Trial Design and Baseline Characteristics	Yung Chyung M.D., Chief Medical Officer
6-month Interim Efficacy and Safety Results	Yung Chyung M.D., Chief Medical Officer
Summary and Next Steps	Tony Kingsley, President & CEO
Questions and Answers	Tony Kingsley, President & CEO Yung Chyung M.D., Chief Medical Officer Ted Myles, Chief Financial Officer

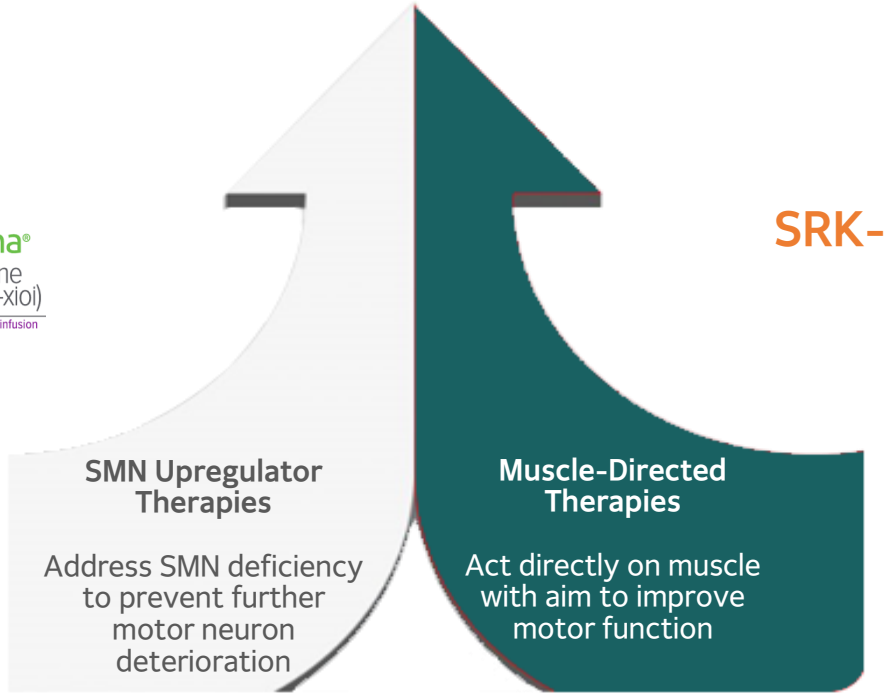
SRK-015 Has Potential to Pioneer a New Treatment Era to Improve Motor Function in Patients with SMA

SMN Upregulator Therapies + Muscle-Directed Therapy (SRK-015) Could Potentially Enhance Outcomes for Patients*

SPINRAZA® (nusinersen) injection 12 mg/5 mL

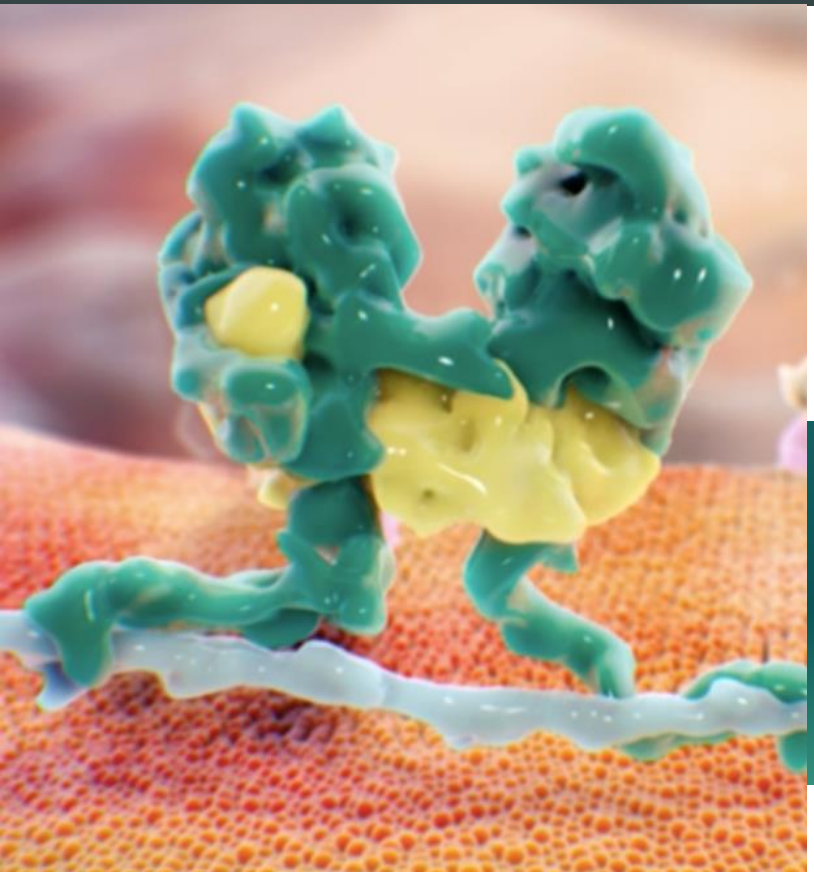
zolgensma® (onasemnogene abeparvovec-xioi) suspension for intravenous infusion

Evrysdi™ risdiplam



SMN = survival motor neuron.
**Also referred to as SMN correctors.*
***SRK-015 is an investigational therapy under development.*

SRK-015: Highly Selective Inhibitor of the Activation of Pro and Latent Myostatin



- Fully human monoclonal antibody (mAb)
- Half-life of ~23-33 days
- Avoids related growth factors (e.g. GDF11, BMP9, Activin A)

- Rare Pediatric Disease Designation for SMA granted by FDA
- Orphan Drug Designation for SMA granted by the FDA
- Orphan Medicinal Product Designation for SMA granted by the European Commission

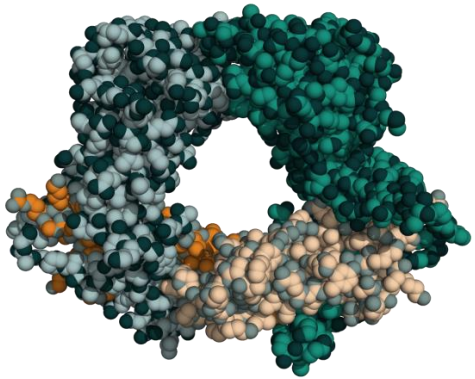
Highlights of strong patent portfolio protecting SRK-015:

- **US Patent 10,751,413 (expiry in 2037**): Covers composition of matter and methods of use for SRK-015
- **US Patent 9,758,576 (expiry in 2034):** Covers mAbs that inhibit the activation of myostatin precursor
- **US 10,287,345 (expiry in 2037):** Treatment methods for various myostatin-related conditions

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

Scholar Rock's Target

Growth Factor Precursor (Latent Form)



Scholar Rock's R&D Platform

Transform Medical Practice

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

First demonstration of the therapeutic potential of inhibiting the latent forms of growth factors

TOPAZ Interim Analysis Results Demonstrate Proof-of-Concept

Multiple lines of evidence supporting the potential clinical effect of SRK-015

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

✓ **Mean improvements from baseline in HFMSE/RHS observed in each of the 3 cohorts**
- 67% of total patients achieved ≥1-point improvement in Hammersmith scores

✓ **Substantial proportion of patients in each cohort attained ≥3-point improvement in HFMSE/RHS**
- High bar and uncommon to observe in any given patient
- 35% of total patients achieved ≥3-point improvement in Hammersmith scores

✓ **Dose response demonstrated in Cohort 3** *(randomized, double-blind, parallel arm design)*
- Greater improvements in HFMSE scores for high-dose arm across evaluated timepoints
- Supportive PK/PD results; high dose led to higher drug exposure and target engagement

**3 patients (1 in Cohort 2 and 2 in Cohort 3) each missed 3 doses of SRK-015 and the 6-month interim analysis timepoint due to COVID-19-related site access restrictions; the six-month timepoint from these patients was not included in the interim analysis.*
Data on file. Scholar Rock, Inc. Cambridge, MA

Phase 2 Trial Design and Baseline Characteristics

Yung Chyung, M.D.
Chief Medical Officer

TOPAZ

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Next Era of SMA Treatment: Muscle-Directed Therapy

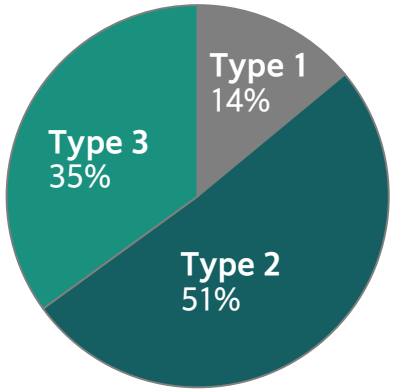
Overall Prevalence of 30,000-35,000 in U.S. and Europe

Type 1:
- Infant-onset
- Usually fatal without treatment

Type 2 and non-ambulatory Type 3:
- Later-onset but still early childhood
- Severe deficits in motor function
- SMN upregulators appear to primarily stabilize disease course

Ambulatory Type 3:
- Typically childhood-onset
- Wide range of motor function deficits; limited mobility and substantial morbidity
- SMN upregulators appear to primarily stabilize disease course

Relative Prevalence Among Patients Living With SMA



TOPAZ trial focuses on Type 2 and Type 3 SMA

Unmet need would be served by a therapy that:

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

HFMSE = Hammersmith Functional Motor Scale Expanded

SRK-015 Phase 2 Trial Design

TOPAZ

	Ambulatory Patients (Revised Hammersmith Scale)	Non-Ambulatory Patients (Hammersmith Functional Motor Scale Expanded)	
	Cohort 1	Cohort 2	Cohort 3
Design	• N= 23; ages 5-21 • Open-label, single-arm • 20 mg/kg SRK-015 IV Q4W • 12-month treatment period	• N= 15; ages 5-21 • Open-label, single-arm • 20 mg/kg SRK-015 IV Q4W • 12-month treatment period	• N= 20; ages ≥2 • Double-blind, randomized (1:1) to 2 mg/kg or 20 mg/kg SRK-015 IV Q4W • 12-month treatment period
Patients	• Ambulatory Type 3 SMA • Two subgroups: 1) Receiving background nusinersen 2) SRK-015 monotherapy	• Type 2 or non-ambulatory Type 3 SMA • Receiving background nusinersen	• Type 2 SMA • Receiving background nusinersen (initiated before age 5)
Primary Objectives	• Safety • Mean change from baseline in RHS	• Safety • Mean change from baseline in HFMSE	• Safety • Mean change from baseline in HFMSE

Evaluate potential of SRK-015 in improving motor function

HFMSE=Hammersmith Functional Motor Scale Expanded; RHS=Revised Hammersmith Scale

Data on file. Scholar Rock, Inc. Cambridge, MA

Baseline Characteristics

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

*data not available for all patients
**patient who discontinued study for reasons unrelated to study drug

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

Key Strengths of TOPAZ Trial Design and Conduct

- **Large and diverse group of study sites for a rare disease trial**
  - Patients enrolled across 16 study sites in the U.S. and Europe
  - Patient enrollment was not skewed to any one site for any cohort or across the study
- **Primary efficacy endpoints are well-validated outcome measures**
  - Hammersmith Functional Motor Scale Expanded (HFMSE) was specifically designed for SMA and served as primary efficacy endpoint in Phase 3 CHERISH trial of nusinersen
  - Revised Hammersmith Scale (RHS) is very similar to the HFMSE, with some modification to reduce ceiling effects in assessing patients who are ambulatory
- **Efficacy assessments are being conducted in a rigorous fashion:**
  - Standardized conduct of Hammersmith scale assessments; extensive training of all trial sites
  - Assessors of the Hammersmith scale measures are blinded to baseline and prior visit scores
- **Embedded randomized, double-blind portion of trial (Cohort 3) to evaluate dose response between high and low dose arms of SRK-015**

Six-Month Interim Analysis Results

Yung Chyung, M.D.
Chief Medical Officer

TOPAZ Interim Analysis Results Demonstrate Proof-of-Concept

Multiple lines of evidence supporting the potential clinical effect of SRK-015

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# (%) patients achieving ≥1-pt increase	12/23 (52%)	7/11 (64%)	5/12 (42%)	10/14 (71%)	6/9 (67%)	9/9 (100%)
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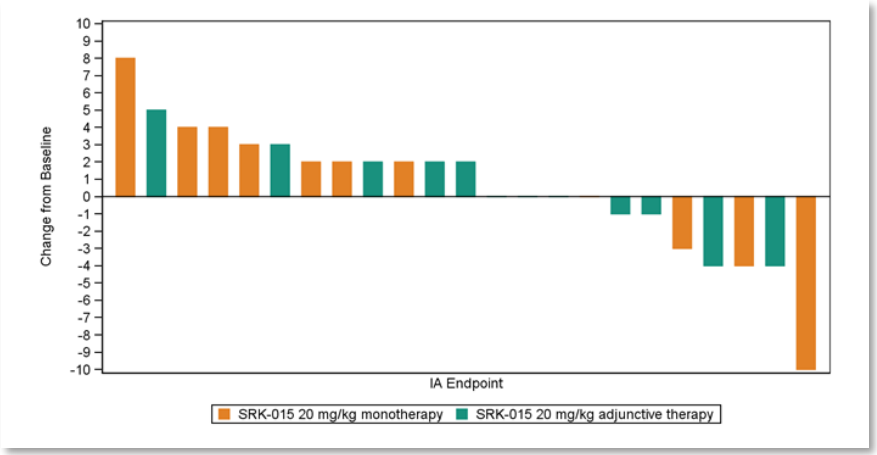
Data on file. Scholar Rock, Inc. Cambridge, MA

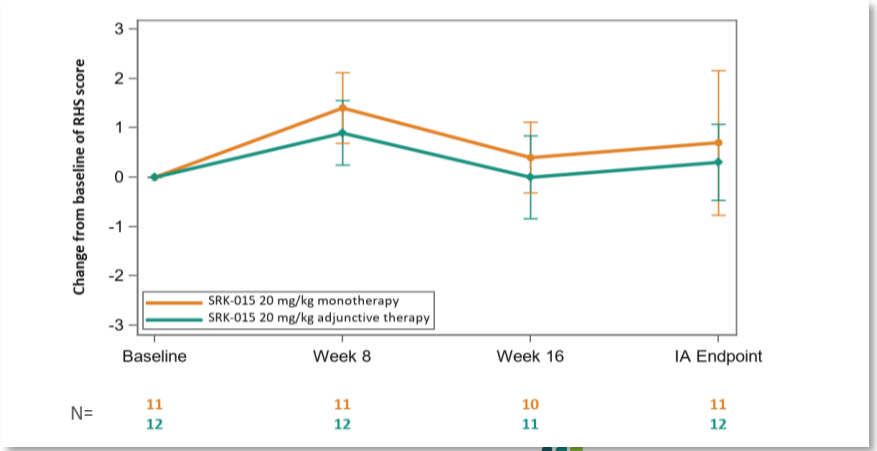
Cohort 1: Improvement in RHS Observed with Both SRK-015 Monotherapy and as Add-on to Background Nusinersen

Ambulatory Type 3 SMA	SRK-015 (20 mg/kg) pooled (n=23)	SRK-015 (20 mg/kg) monotherapy (n=11)	SRK-015 (20 mg/kg) +nusinersen (n=12)
Mean change from baseline in RHS (95% CI)	0.5 (-1.1, 2.2)	0.7 (-2.5, 4.0)	0.3 (-1.4, 2.0)
# (%) patients achieving ≥1-pt increase in RHS	12/23 (52%)	7/11 (64%)	5/12 (42%)
# (%) patients achieving ≥3-pt increase in RHS	6/23 (26%)	4/11 (36%)	2/12 (17%)
# (%) patients achieving ≥5-pt increase in RHS	2/23 (9%)	1/11 (9%)	1/12 (8%)

Individual RHS responses



Mean (±SEM) change from baseline in RHS scores

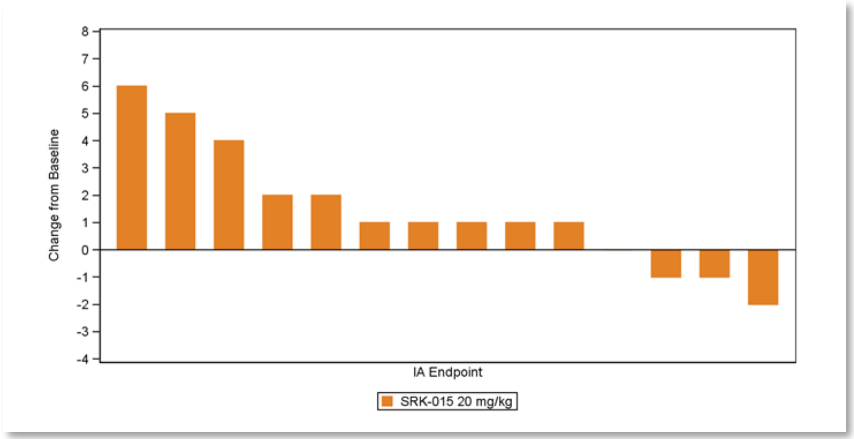


Data on file. Scholar Rock, Inc. Cambridge, MA

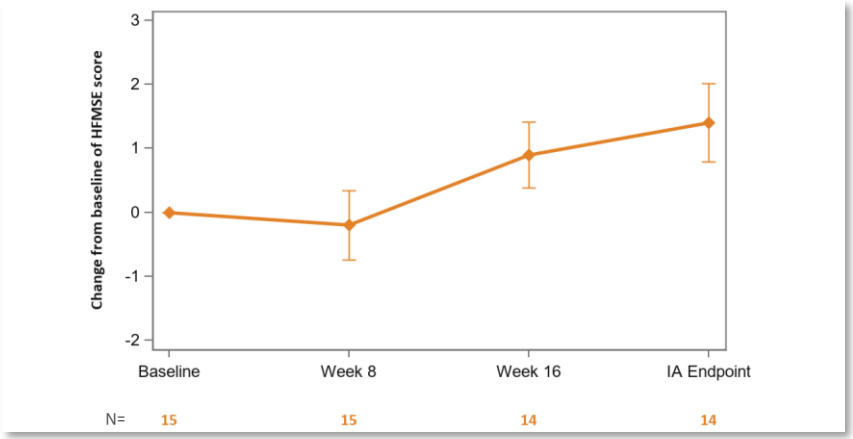
Cohort 2: Meaningful and Consistent Improvements in HFMSE Observed in Type 2 and Non-Ambulatory Type 3 SMA

Type 2 and Non-Ambulatory Type 3 SMA	SRK-015 (20 mg/kg) + nusinersen (n=14)
Mean change from baseline in HFMSE (95% CI)	1.4 (0.1, 2.7)
# (%) patients achieving ≥1-pt increase in HFMSE	10/14 (71%)
# (%) patients achieving ≥3-pt increase in HFMSE	3/14 (21%)
# (%) patients achieving ≥5-pt increase in HFMSE	2/14 (14%)

Individual HFMSE responses



Mean (±SEM) change from baseline in HFMSE scores



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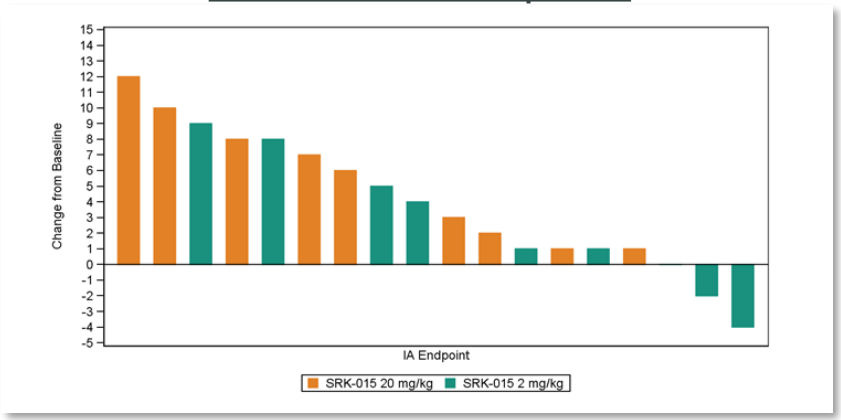
Cohort 3: SRK-015 High Dose Showed Substantially Greater Improvements in HFMSE scores Than Low Dose

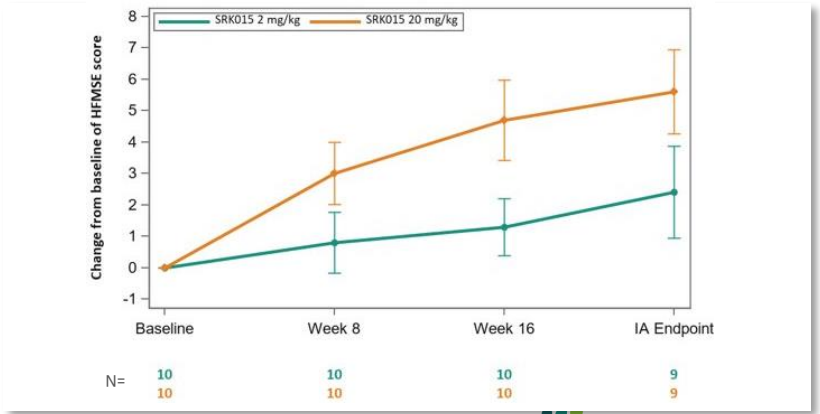
Cohort 3 has a randomized, double-blind, parallel arm design embedded within TOPAZ

Type 2 SMA	SRK-015 low dose (2 mg/kg) +nusinersen (n=9)	SRK-015 high dose (20 mg/kg) +nusinersen (n=9)
Mean change from baseline in HFMSE (95% CI)	2.4 (-0.9, 5.8)	5.6 (2.5, 8.7)
# (%) patients achieving ≥1-pt increase in HFMSE	6/9 (67%)	9/9 (100%)
# (%) patients achieving ≥3-pt increase in HFMSE	4/9 (44%)	6/9 (67%)
# (%) patients achieving ≥5-pt increase in HFMSE	3/9 (33%)	5/9 (56%)

Individual HFMSE responses



Mean (±SEM) change from baseline in HFMSE scores



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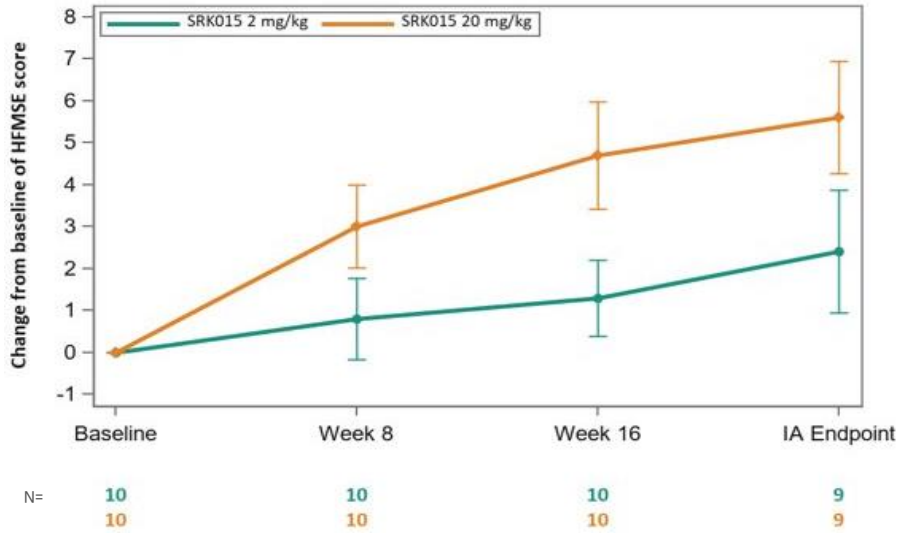
Cohort 3: Time Course Data Supportive of Dose Response

Mean (±SEM) change from baseline in HFMSE scores



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

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

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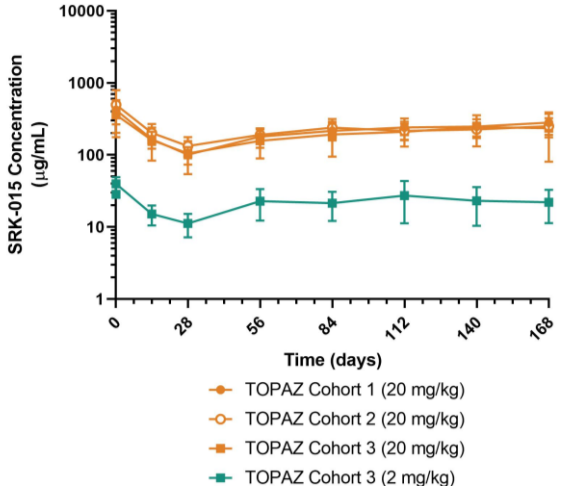
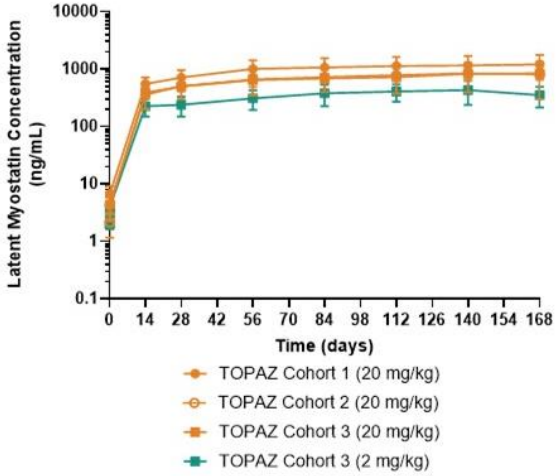
Pharmacokinetic and Pharmacodynamic Data are Supportive of Clinically Observed Dose Response

Pharmacokinetics* (PK)



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

Pharmacodynamics (PD)



- Target engagement by SRK-015 was confirmed
- Low dose (2 mg/kg) yielded lower level of target engagement and did not achieve full target saturation

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

*Starting at day 28, measures are pre-dose trough levels

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No Safety Signals Identified from Interim Analysis

Treatment-emergent adverse events (TEAEs)	SRK-015 2 mg/kg dose (n=10)	SRK-015 20 mg/kg dose (n=48)	Total (n=58)
Any TEAE	9 (90%)	40 (83.3%)	49 (84.5%)
Any Serious TEAE	0 (0.0%)	1 (2.1%)	1 (1.7%)
Any TEAE leading to study drug discontinuation	0 (0.0%)	1 (2.1%)	1 (1.7%)
Any Grade 3 (severe) or higher TEAE	0 (0.0%)	0 (0.0%)	0 (0.0%)

- **Five most frequently reported TEAEs:** Headache, upper respiratory tract infection, pyrexia, nasopharyngitis, and cough.
- **1 serious TEAE (Cohort 1):** Assessed by trial investigator as unrelated to SRK-015. Grade 2 viral upper respiratory infection (prior history) and was hospitalized. Event resolved without sequelae.
- **1 study drug discontinuation (Cohort 1)**: Assessed by trial investigator as unrelated to SRK-015. Grade 2 leg muscle fatigue (developed prior to enrollment). Withdrew consent after ~2 months on trial.

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

Treatment-emergent adverse events (TEAEs) are defined as AEs that start after the first dose of study drug or start prior to the administration of study drug and worsen in severity/grade or relationship to investigational medication after the administration of study drug.
Data on file. Scholar Rock, Inc. Cambridge, MA

TOPAZ Interim Analysis Results Demonstrate Proof-of-Concept

1. Multiple lines of evidence supporting the potential clinical effect of SRK-015

- **Dose response demonstrated in randomized, double-blind, parallel arm Cohort 3**
  - High-dose arm showed greater improvements in HFMSE scores
  - Supportive PK/PD results
- **Cohort 2 observed improvements from baseline**
  - In population for which SMN upregulator therapy alone offers motor function stabilization rather than improvement
- **Substantial % of patients in each cohort attained ≥3-pt increase in Hammersmith score**
  - High bar and uncommon to observe in any given patient

2. SRK-015's broad and meaningful therapeutic potential in SMA

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

Data on file. Scholar Rock, Inc. Cambridge, MA

Summary and Next Steps

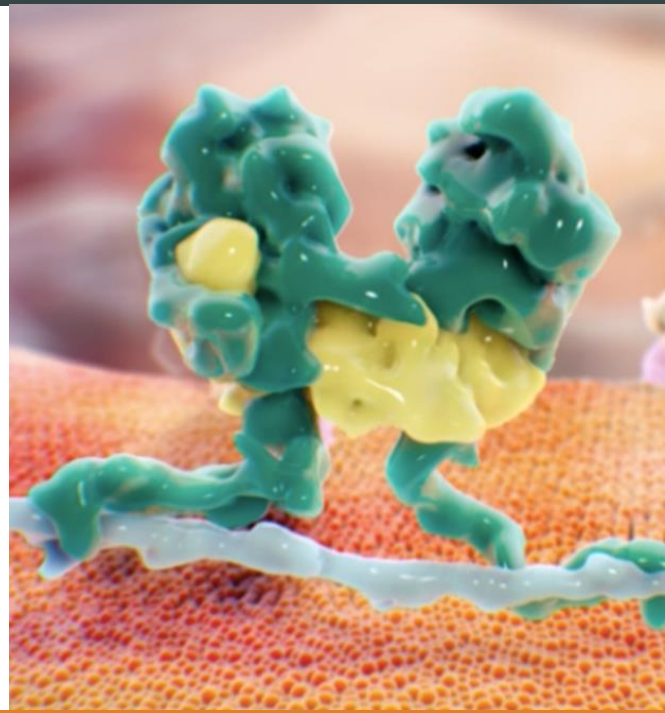
Tony Kingsley

President & CEO

Beyond the TOPAZ Interim Analysis

TOPAZ

- **Top-line data for 12-month treatment period expected 2Q21**
  - Longer-term evaluation of efficacy for potential durability of clinical effect and continued motor function gains
  - Longer-term safety, PK, PD, and anti-drug antibody
- **39 of 39 patients who have completed 12-month study have opted into the extension period (as of October 23, 2020)**
- **Registrational trial preparations ongoing**
- **Look forward to meeting with regulatory authorities to discuss regulatory path**

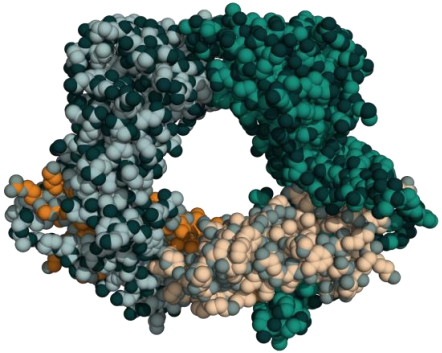


Interim results highlight SRK-015's potential as an important treatment for patients with SMA

Unlocking the Potential of the Scholar Rock R&D Engine

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

Targeting the latent forms of growth factors



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

Emerging Insights

Demonstration of proof-of-concept for SRK-015 in SMA

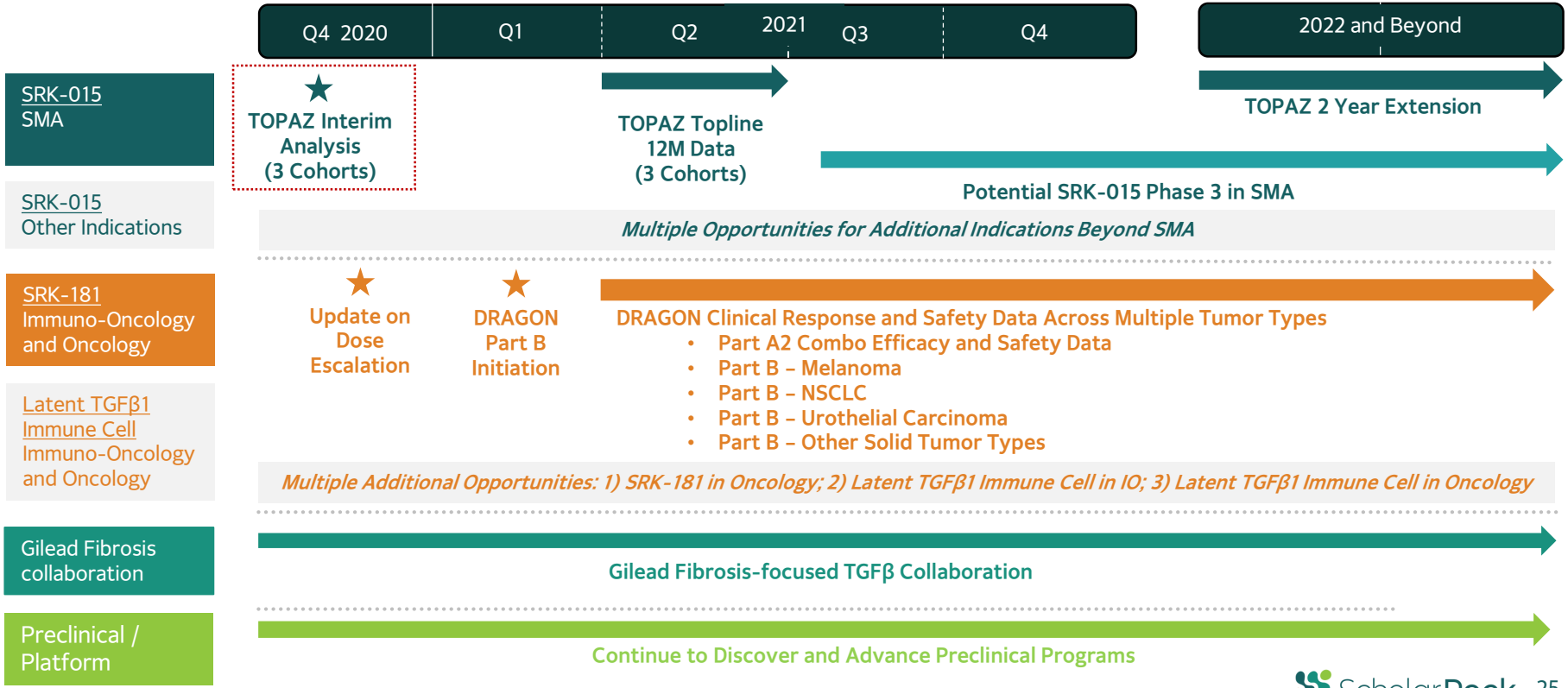
Validation of therapeutic potential for blocking the activation of latent myostatin with SRK-015

Validation of therapeutic potential in targeting latent forms of growth factors

Opportunities Beyond TOPAZ

- Broader exploration of SMA types, age range, and background SMN therapies
- Potential for motor function improvement in other neuromuscular disorders
- Exploration of additional indications related to broader myostatin and fast-twitch fiber biology
- Antibodies against the latent forms of additional well-validated targets in oncology (e.g. SRK-181 program) and fibrosis
- Discovery platform to generate mAbs against other latent growth factors

Differentiated Pipeline with a Series of Anticipated Milestones



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