A Phase 2 Study to Evaluate the Efficacy and Safety of SRK-015 in Patients with Later-Onset Spinal Muscular Atrophy (TOPAZ): An Introduction

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Cure SMA
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Disclaimer

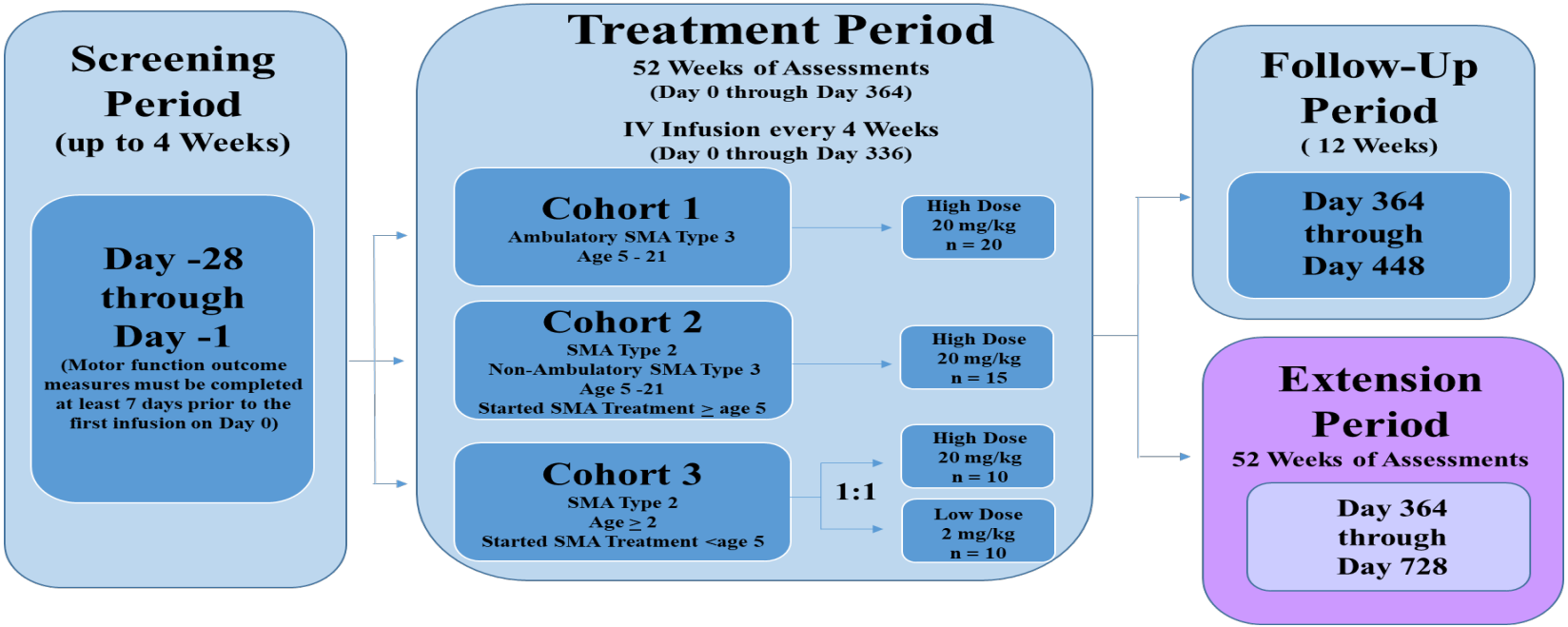
- SRK-015 is an investigational product candidate that is currently being evaluated in a clinical trial

- SRK-015 has not been approved by the U.S. Food and Drug Administration (FDA), the European Commission, or any other health authority, and the safety and effectiveness of this molecule have not been established

Disclosures

- Amy Place is an employee of Scholar Rock and owns equity in the company.

TOPAZ Study Schematic: Treatment Period



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NTC03921528

SRK-015 Phase 2 Trial (TOPAZ): Objectives and Design

	Cohort 1	Cohort 2	Cohort 3
Design	• N= 20; 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 • Receiving treatment with approved SMN upregulator or as monotherapy	• Type 2 or non-ambulatory Type 3 SMA • Receiving treatment with approved SMN upregulator	• Type 2 SMA • Initiated treatment with approved SMN upregulator 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

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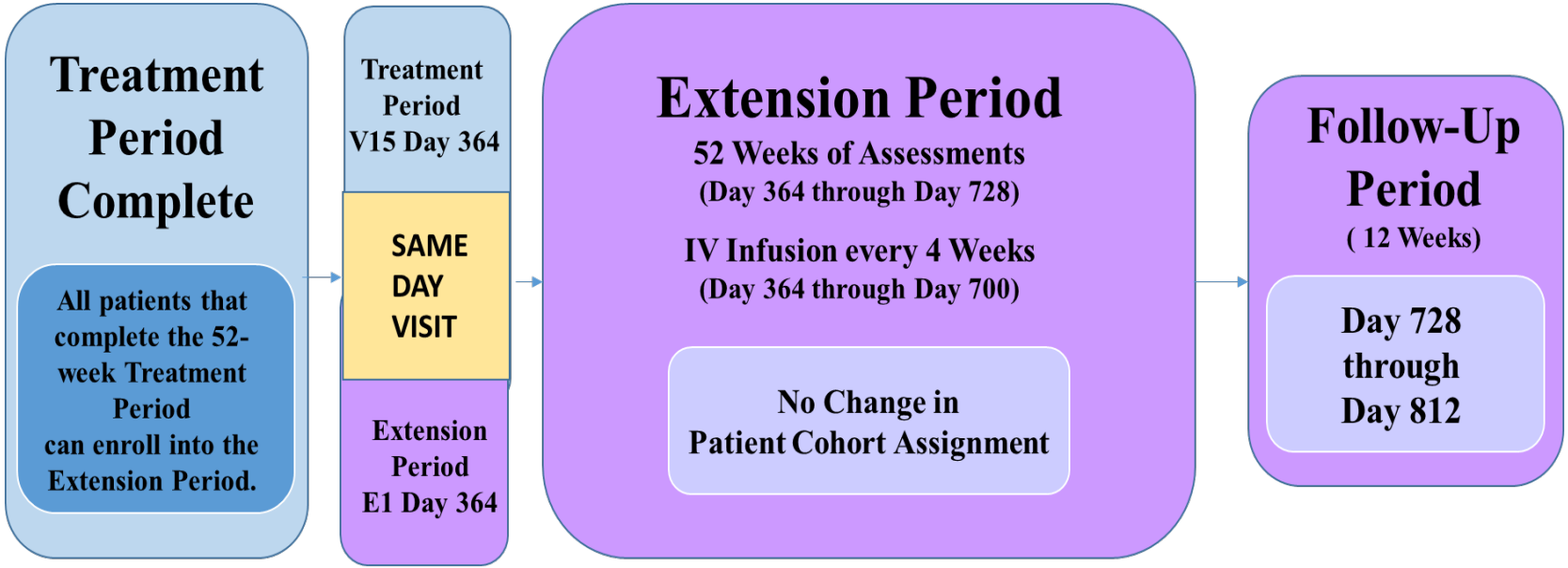
RHS: Revised Hammersmith Scale
HFMSE: Hammersmith Functional Motor Scale Expanded

TOPAZ Study Schematic: Extension Period



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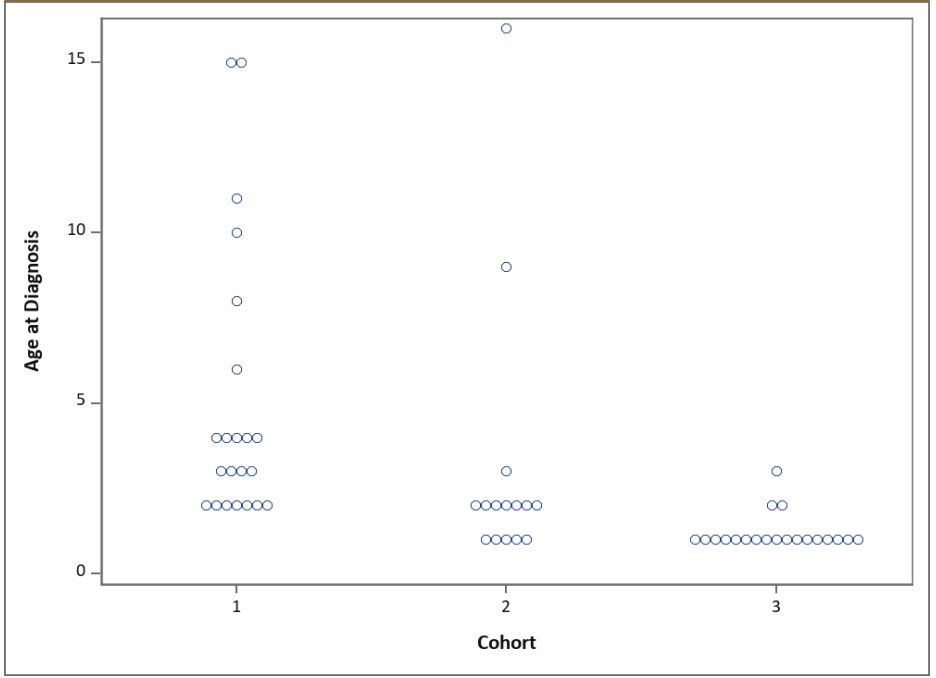
Study Participant Baseline Demographics (1/2)

Age (Years) at Informed Consent by Cohort

Cohort	N	Mean	Std	Min	Med	Max
1	23	12.6	4.53	7	13.0	21
2	15	11.7	3.94	8	10.0	19
3	20	4.0	1.23	2	4.0	6
Total	*58*	*9.4*	*5.31*	*2*	*8.0*	21

Age (Years) at Diagnosis by Cohort



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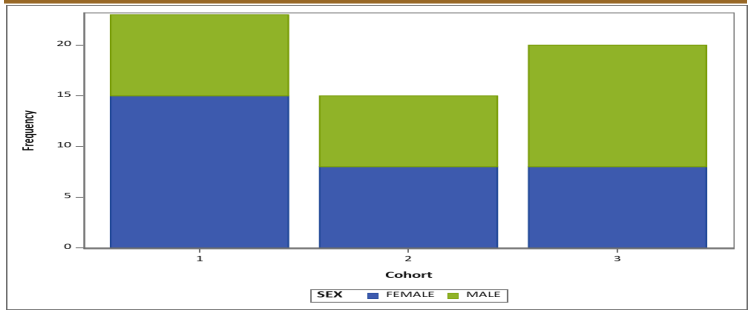
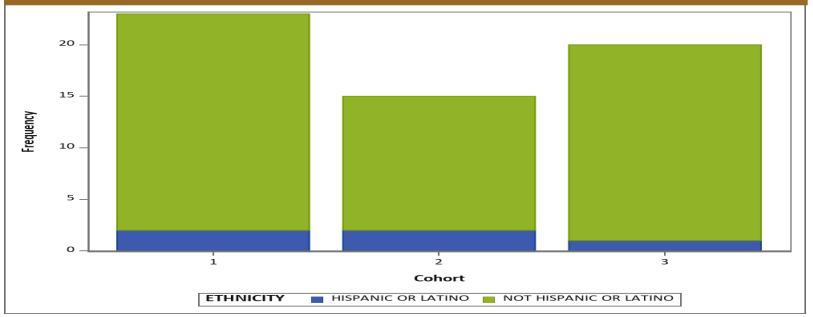
Study Participant Baseline Demographics (2/2)

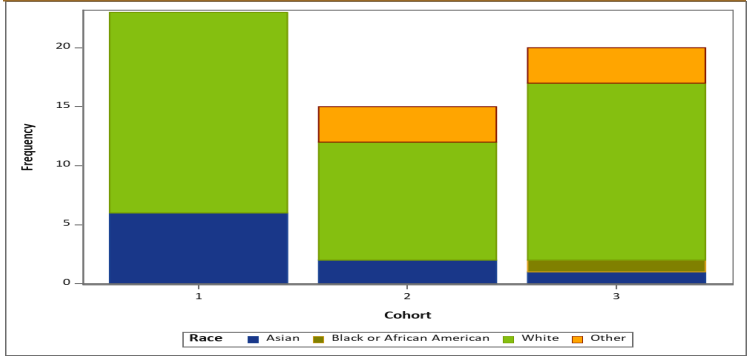
Sex Distribution by Cohort



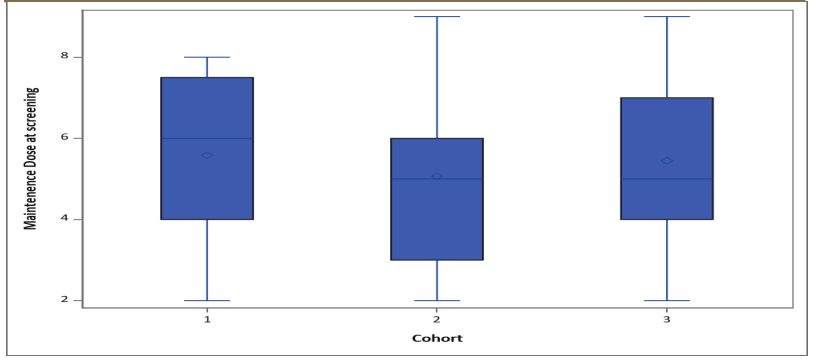
Ethnicity Distribution by Cohort



Race Distribution by Cohort



Maintenance Dose of Nusinersen at Screening†



†Excluded Cohort 1 patients who are not on Nusinersen

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Study Participant Baseline Motor Function

Cohort 1: RHS* Score at Screening

	N	Mean	Std	Min	Med	Max
RHS Score	23	49.0	11.00	25	49	63

Cohort 1: 6 Minute Walk at Screening‡

	N	Mean	Std	Min	Med	Max
Distance Walked (m)	20	260.1	166.85	11	341.0	514

Cohorts 2 and 3: HFMSE at Screening**

Cohort	N	Mean	Std	Min	Med	Max
2	15	22.3	8.98	12	19.0	37
3	19	25.0	9.58	12	22.0	44
Total	*34*	*23.8*	*9.28*	*12*	*21.5*	*44*

*Top RHS score 69 points
**Top HFMSE score 66 points
‡ Only including patients who are ambulatory and completed the test

RHS: Revised Hammersmith Scale
HFMSE: Hammersmith Functional Motor Scale Expanded

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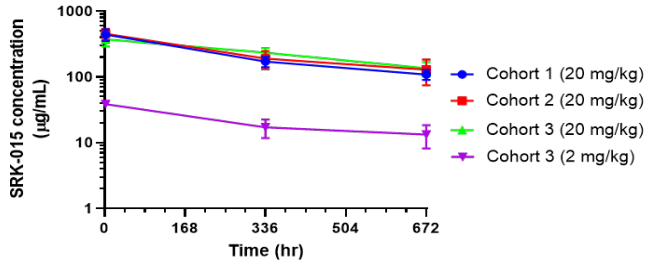
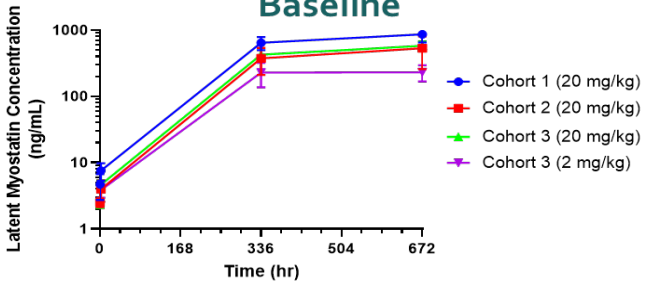
Preliminary TOPAZ Biomarker Data Provide First Demonstration of Target Engagement in SMA

PK Data



Latent Myostatin Change over Baseline



Well-Behaved, Linear PK Profile

- Minimal variability across cohorts
- Dose proportional increase in serum drug exposure between low (2 mg/kg) and high (20 mg/kg) doses

Robust Target Engagement Observed

- ~100-fold increase in serum latent myostatin levels following single 20 mg/kg dose in all cohorts
- Confirms presence of latent myostatin in patients with SMA

Preliminary PK/PD results from planned data cutoff in November 2019 include data from 29 patients (12 in Cohort 1, 8 in Cohort 2, and 9 in Cohort 3). Press release announcing preliminary PK/PD data (Nov 19, 2019) at www.scholarrock.com.

SRK-015 Phase 2 Trial (TOPAZ) Timelines

- All 3 cohorts fully enrolled
- Interim analysis: 6-month treatment period
- Top-line results: 12-month treatment period
- Patients eligible to continue treatment for an additional 12-month extension period
- Results from TOPAZ trial may inform future studies in SMA

SRK-015 has the potential to be the first muscle-directed therapy for patients with SMA

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- Phase 2 trial study investigators, site staff and participants
- Medpace
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  - Yung Chyung
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