Treatment Effects Among Patients with Type 2 and Type 3 SMA:

Directly Reported by Patients and Caregivers from the TOPAZ Clinical Trial

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TOPAZ (NCT03921528)

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Disclosures & Disclaimers

- The TOPAZ trial is sponsored by Scholar Rock, a biopharmaceutical company developing and investigating apitegromab in a clinical development program for the treatment of Spinal Muscular Atrophy (SMA).
- Apitegromab has not been approved by the US Food and Drug Administration (FDA), the European Commission, or any other health authority.
- The safety and effectiveness of apitegromab have not been established.

- George Nomikos, MD, PhD is an employee and shareholder of Scholar Rock, Inc.

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EVIDERA Qualitative Study Background

- Current SMN targeted treatments have shown improvements in motor function; however, unmet need remains.[1]
- Inhibition of myostatin (an important negative regulator of skeletal muscle growth) has the potential to improve muscle function in patients with SMA.[2,3]
  - Apitegromab is an investigational selective inhibitor of myostatin activation.
  - TOPAZ, a phase 2 trial (NCT03921528) of apitegromab reported safety and positive efficacy motor function endpoints in patients with Types 2 and 3 SMA at 12 months.[4]
    - 24 Month data from the Extension period of TOPAZ will be presented by Dr Crawford, Friday, June 17 in the Clinical Drug Development Session.
- Patients with SMA typically experience adverse quality of life (QoL) impacts.
- Evidera aims to gain insights into potential treatment benefits by collecting/analyzing the patient's and caregiver's qualitative observations in addition to the Quality of Life Assessments utilized during apitegromab treatment in the TOPAZ trial through 24 months.
  - Signs/symptoms prior to and after the trial (e.g., breathing, ability to clear lungs, respiratory infections, swallowing, fatigue, mobility, balance, muscle tightness, communication, urinary/bowel, skin, etc).

*Baseline data was collected retrospectively; 1. Bowerman M, et al. *Dis Model Mech.* 2017;10(8):943-954; 2. Long KK, O'Shea KM, Khairallah RJ, et al. *Hum Mol Genet.* 2019;28:1076-1089. Available:https://pubmed.ncbi.nlm.nih.gov/30481286/ 3. Pirruccello-Straub, et al. *Sci Rep.* 2018;8:229. 4. Place A, et al. *Eu J Neurol.* 2021;28(Suppl1) 207–334:(EPR-184).

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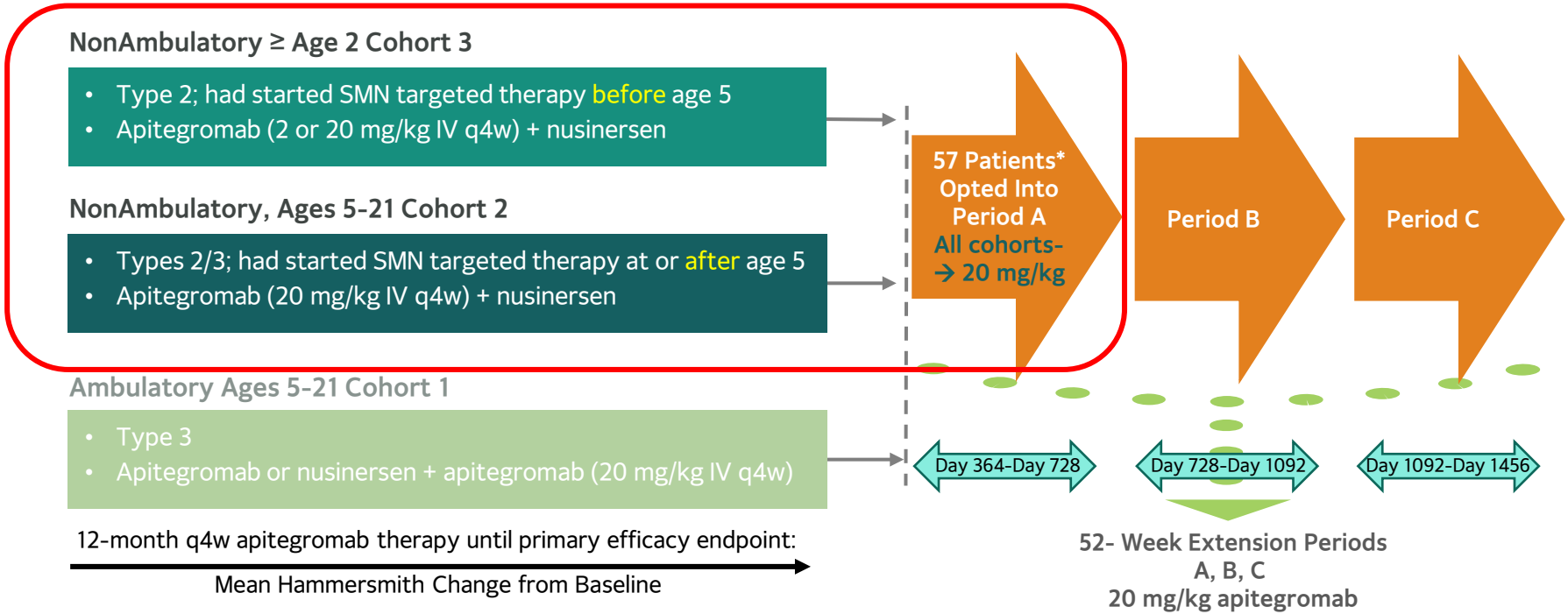
TOPAZ Phase 2 Trial Design, Including Open Label Extension Periods: Three Cohorts to Identify Therapeutic Opportunities

All SMA Types 2/3, cohorts defined by age and ambulatory status at time of enrollment



*Excludes one patient from Cohort 1 who discontinued from the trial; 57/58 Completed Treatment Period and Enrolled in Extension Period A; 2 Withdrew Consent in Extension Period A; 55 Completed Extension Period A and Enrolled into Extension Period B Place A, et al. *Eu J Neurol.* 2021;28(Suppl1) 207–334:(EPR-184).

TOPAZ Showed that Apitegromab was Associated with Motor Function Improvements in Nonambulatory Patients with Types 2 and 3 SMA after 12 Months of Treatment[1]

	Primary endpoint: Mean Change in HFMSE at 12 mo (95% CI):	**Secondary endpoint**: Any point change in HFMSE	**Secondary endpoint**: Mean Change in RULM at 12 mo (95% CI):	**Secondary endpoint**: Any point change in RULM
Non-ambulatory Types 2 & 3*	**Increase of 3.6 (1.2, 6.0)**	**72% (23/32) achieved ≥1 pt** **42% (13/32) achieved ≥3 pt HFMSE change**	**Increase of 1.3 (0.2, 2.3)**	**48% (15/31) achieved ≥1 pt** **40% (12/31) achieved ≥2 pt RULM change**

Safety

- Five most frequently reported TEAEs†: headache (24%), URTI (22%), pyrexia (22%), cough (22%), and nasopharyngitis (21%)
- Incidence and severity of AEs were consistent with the underlying patient population and nusinersen

*ITT, Intent to Treat population; †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. TEAE rates are across all patients in TOPAZ trial; CI, Confidence Interval; HFMSE, Hammersmith functional motor scale expanded; mo, month; RULM, Revised upper limb module. URTI, upper respiratory tract infection. 1. Data on File, ScholarRock. 2. Rouault F, et al. *Neuromuscul Disord.* 2017;27:428-38. 3. Coratti G, et al. *Muscle Nerve.* 2019; 59: 426–430.

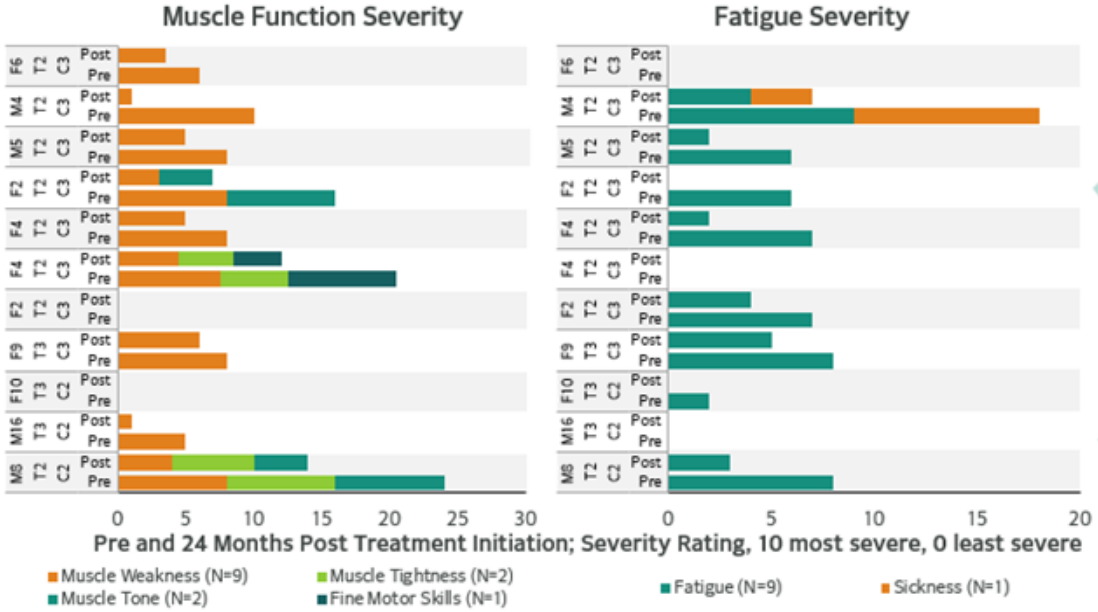
Evidera Qualitative Interview Methods

- Protocol
  - Evidera stand-alone qualitative interview study protocol that included a semi-structured interview guide.
- Site Contracting
  - Evidera entered into stand-alone contracts with TOPAZ sites.
  - Up to 15 participants (TOPAZ patients or their caregivers) from six US sites were invited after trial initiation to participate in a telephone interview about patient experiences at baseline and at approximately 24 months after trial initiation.
- Ethics Review
  - The protocol was submitted to a central IRB for approval (Advarra) and to local IRBs, as needed.
- Analysis
  - Qualitative data (transcripts) are analyzed using a software called ATLAS.ti that helps organize data by themes across interviews.
  - Themes can be quantified by participant.

QoL Results Suggest that Treatment with Apitegromab in TOPAZ May Decrease the Severity of Muscle and Fatigue Sign and Symptom Scores in Individual Patients

"… She has more **recently gained the ability to crawl**… She has the **ability to play** …and walk around on her knees. She is also **able to lift her arms**, that was one of the first things we noticed.."

"I would say like **consistent muscle strength**... we would always notice more than often like a couple of weeks before starting you would see a regression… And since then, **we haven't been seeing those dips**."



"It was every time she stood up or if we tried to get her to move around even on the floor, she would stop doing things… Meaningful is her **being able to stand up from a seated position**… She took **five steps on her own, independently**…"

"But I mean it definitely is a **big play in fatigue** because **prior…she was more tired** and not want to do it."

Preliminary results suggest apitegromab may improve muscle and fatigue function-related QoL in nonambulatory patients with Types 2 or 3 SMA, further exploration is required

ID: Male/Female-Age-Type 2/Type 3 – Cohort. Data on File, Scholar Rock, Inc. Pre-treatment and Post treatment severity of effects

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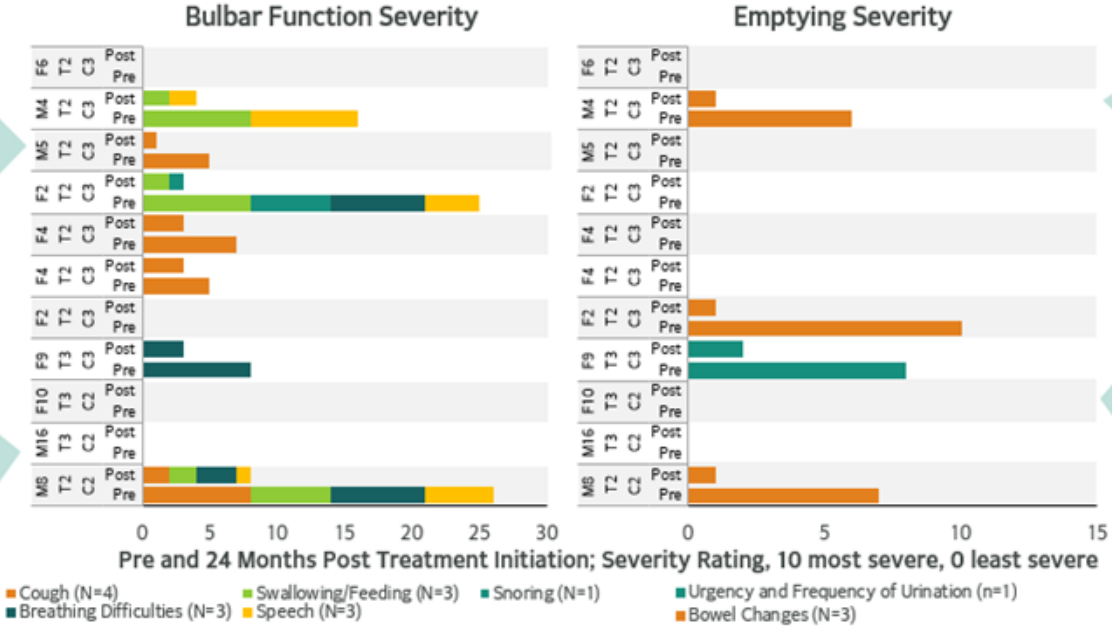
QoL Results Suggest That Treatment with Apitegromab in TOPAZ May Decrease the Severity of Bulbar Function and Emptying Difficulties in Individual Patients

"...the fact that the ***scoliosis has stopped progressing is another huge thing***... But little things like the scoliosis and the ***pulmonology improvements*** are actually huge things that have led us to see that ***there is strengthening happening***."

"...Like if she looks down and it's [her head] heavy, she'll use her hand to help her. But for the most part, ***she can use her own neck muscles to lift her head***, which is phenomenal*"



"Helping her with the ***bowel movement and with mobility***. ...***her muscles, like gained muscle strength***.†"

"...that's probably the biggest thing I've noticed in change... I would say she used to have ***urge sensation in the past,*** whereas now... ***It's not really as of an unexpected*** situation.†"

Preliminary results suggest that apitegromab may help improve bladder, bowel and bulbar functional-related QoL, further exploration is required

ID: Male/Female-Age-Type 2/Type 3 – Cohort. Data on File, Scholar Rock, Inc; *Lifting head improves bulbar functions, such as breathing, eating, speaking. †Bowel and bladder emptying lead to fewer visits to hospital ; Pre-treatment and post treatment severity of effects

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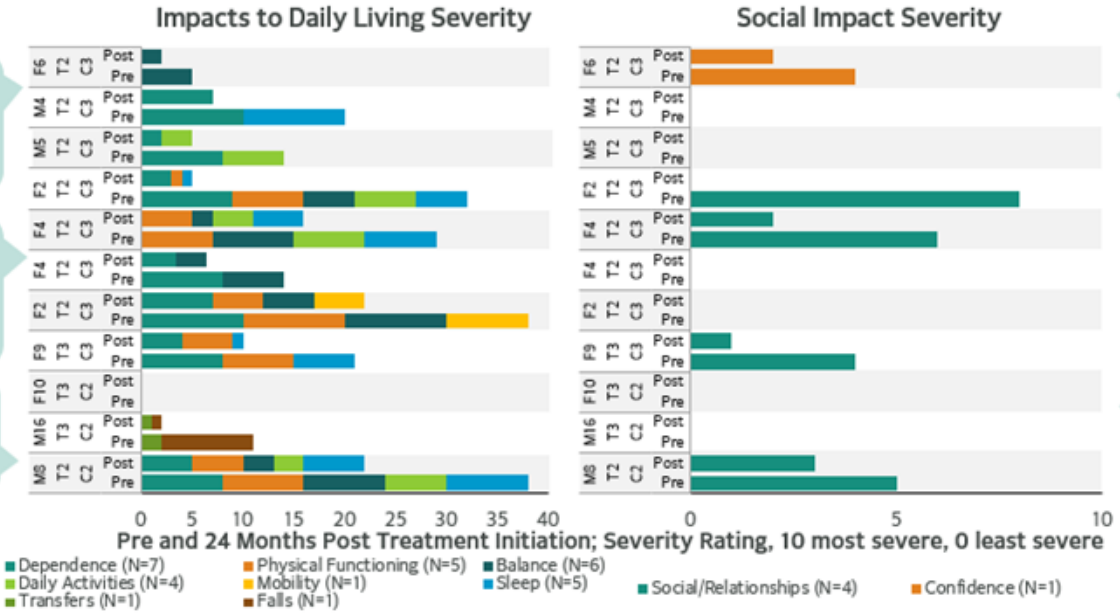
QoL Results Suggest That Treatment with Apitegromab in TOPAZ May Decrease the Severity to Social and Daily Living Activity Impacts in Individual Patients

"She is able to **wipe herself now on the potty,** she has the **balance and the control to lean over** and do the whole **motion without falling**."

"... our child has improved... **fine motor gains, recover from sickness faster; Improvements in daily life are significant** even if not measurable in the trial...."

"... I hold myself better, **no shaking while transferring, and no issues falling***. I am able to hold myself steady more...."



"Just **being able to do more** of the little things, **the little small motor skills things** that she wants to **be independent** doing, like **opening things** or just **live the everyday life of playing with her friends**..."

"...my daughter...**has improved her quality of life**, has **improved her independence**...she wouldn't be the person that she is today."

Preliminary results suggest apitegromab may help improve QoL related to activities of daily living in nonambulatory patients with type 2 or 3 SMA, further exploration is required

ID: Male/Female-Age-Type 2/Type 3 – Cohort. Data on File, Scholar Rock, Inc; *Fewer falls from transferring lead to fewer hospitalization visits; Pre-treatment and Post treatment severity of effects.

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Summary

- Results of a Quality of Life (QoL) assessment of patients with SMA suggest that apitegromab may help improve function- related QoL measures, though further exploration is required.
- Qualitative interviews with patients and caregivers presented here may be helpful in gaining a deeper understanding of patient experiences of SMA, such as signs and symptoms and potential meaningful benefits observed during apitegromab treatment in the TOPAZ trial.
- We acknowledge the inherent limitations that the observational nature of open label qualitative interview studies may hold, including susceptibility to multiple sources of bias, such as recall, routine recruitment bias, proxy estimation by caregivers, small sample size, and heterogeneity that limits the generalizability of results, etc.
- Nonetheless, real-world data studies can serve complementary roles to current controlled trials and can help to inform future research and design of clinical trials (e.g., endpoints of interest to the patients/caregivers).
- Apitegromab has the potential to be the first muscle-directed approach to address QoL improvements in SMA; further exploration is warranted.

Acknowledgments

- Many thanks to all the patients who participate in these studies, and their caregivers/ families, healthcare professionals and patient advocacy groups.
- We thank our collaborators EVIDERA, Medpace, Chris Yun, ChilliPharm, BBK, CRECare.
- We thank the TOPAZ investigators, trial staff, and scientific advisors.
- We thank ScholarRock Research and Development Teams.