# Phase 1 interim results evaluating the safety, tolerability, pharmacokinetics, and exploratory efficacy of salanersen for spinal muscular atrophy

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# Disclosures

- **DC:** Received funding from Genentech, ReveraGen, Edgewise, and Biohaven, and consulting fees from Arugula Science
- **VAS:** Scientific advisory board member for Biogen, Novartis, Roche, and Scholar Rock
- **KK-J:** Principal investigator in Biogen, Novartis, and Roche clinical studies and has participated in advisory boards for Biogen, Novartis, and Roche
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- **AZ:** Received speaker and consulting honoraria from Biogen, Novartis, and Roche
- **SF, PS, SA, JI, CR, JC, JH, AV-B, SW, WL, YL, RF, LB:** Employees of Biogen and may hold stock


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SMA = spinal muscular atrophy.

# Introduction

- Salanersen (BIIB115) is a novel, intrathecally administered ASO in development for SMA
- Salanersen corrects splicing of *SMN2* pre-mRNA by binding to a region also targeted by nusinersen and is designed to increase SMN protein. Salanersen has a new backbone chemistry that leads to high potency, enabling the potential for high efficacy with once yearly dosing

## Objectives

- To report interim data with at least 1 year follow-up on the safety and exploratory efficacy of salanersen in pediatric participants with SMA previously treated with IV OA from the Phase 1 study (NCT05575011).

ASO = antisense oligonucleotide; OA = onasemnogene abeparvovec; PK, pharmacokinetics; SMA = spinal muscular atrophy; SMN = survival motor neuron; *SMN2* = *survival motor neuron 2*.

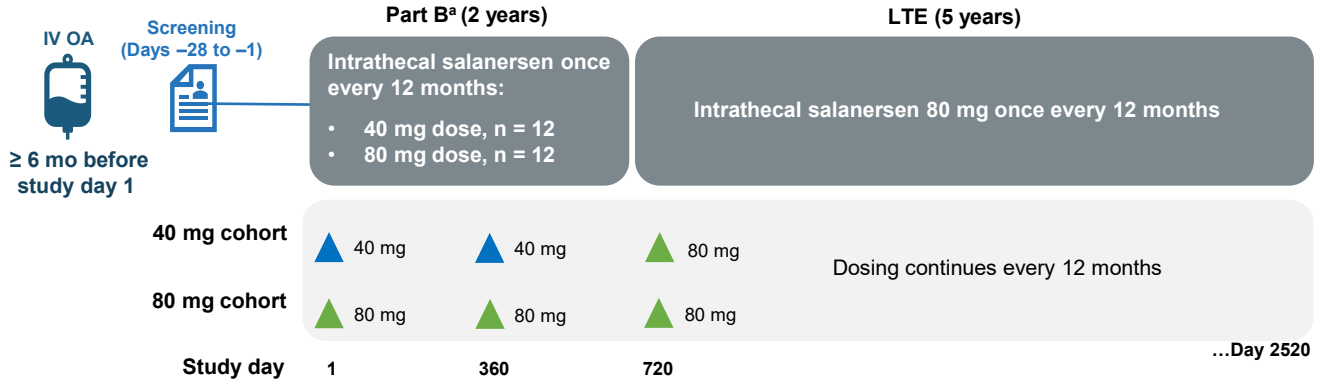
# The Phase 1 Part B open-label study includes participants previously treated with OA

| Inclusion criteria | Exclusion criteria |
|---|---|
| • Genetic documentation of 5q SMA<br>• Aged 0.5–12 years at first salanersen dose<br>• *SMN2* copy number of ≥ 1<br>• Received IV OA ≥ 6 months before first salanersen dose<br>• Suboptimal clinical status per the Investigator[a] | • Severe or serious AEs related to OA ongoing at screening<br>• Permanent ventilation, defined as tracheostomy or ventilation ≥ 16 hours/day continuously for > 21 days in the absence of an acute reversible event<br>• Treatment with risdiplam after receiving OA<br>• Treatment with nusinersen after receiving OA or < 12 months from the first dose of salanersen |

Note: Part A of the study assessed the safety, tolerability, and PK of salanersen in healthy men (data not shown)

[a]In one or more domains: motor function, respiratory function, swallowing or feeding ability for age, and other.
AE = adverse event; IV = intravenous; OA = onasemnogene abeparvovec; SMA = spinal muscular atrophy; *SMN2* = *survival motor neuron 2*.

# All participants receive salanersen every 12 months with routine safety, PK, and efficacy assessments




**Primary endpoint**

- Safety (incidence of AEs/SAEs)

**Key secondary endpoint**

- Pharmacokinetics (serum and CSF)

**Key exploratory endpoints**

- Neurofilament light chain
- WHO motor milestones
- Motor function assessments
  - Older (2-12 years): HFMSE, RULM
  - Younger (0.5 to < 2 years): HINE-2, CHOP-INTEND

[a]In Part B, within each dose cohort, there is an older subgroup (n = 8, aged 2–12 years) and a younger subgroup (n = 4, aged 0.5 to < 2 years). Intracohort dose staggering reviewed safety in 2- to 12-year-olds before dosing 0.5- to < 2-year-olds.

AE = adverse event; CHOP-INTEND = Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; CSF = cerebrospinal fluid; HFMSE = Hammersmith Functional Motor Scale Expanded; HINE-2 = Hammersmith Infant Neurological Examination Section 2; IV = intravenous; LTE, long-term extension; OA = onasemnogene abeparvovec; RULM = Revised Upper Limb Module; SAE = serious adverse event; SMA = spinal muscular atrophy.

# The study enrolled a heterogeneous population with prolonged duration between OA and salanersen

| | | 40 mg Cohort | | 80 mg Cohort | |
|---|---|---|---|---|---|
| | | Younger Participants n = 4 | Older Participants n = 8 | Younger Participants n = 4 | Older Participants n = 8 |
| *SMN2* copy number, n (%) | 2<br>3 | 4 (100.0)<br>0 | 3 (37.5)<br>5 (62.5) | 4 (100.0)<br>0 | 5 (62.5)<br>3 (37.5) |
| Prior therapies, months, median (range) | Age at OA | 2.33 (0.5–3.8) | 12.39 (0.7–59.8) | 0.77 (0.6–5.0) | 16.15 (6.7–58.6) |
| | Age at first salanersen dose, | 16.66 (9.6–23.4) | 39.74 (29.7–99.3) | 15.87 (14.9–18.1) | 56.80 (29.2–96.2) |
| | Time from OA dose to first salanersen dose | 14.34 (8.0–20.7) | 31.43 (10.3–39.5) | 14.56 (13.1–15.4) | 36.88 (14.1–47.9) |
| Participants with motor milestone at baseline (%) | Sitting without support<br>Standing without support<br>Walking with support<br>Walking without support | 1 (25)<br>0<br>0<br>0 | 5 (62.5)<br>2 (25.0)<br>2 (25.0)<br>1 (12.5) | 2 (50.0)<br>0<br>0<br>0 | 6 (75.0)<br>0<br>0<br>0 |

Phase 1 interim analysis data cutoff date: December 2, 2025.
Further details on baseline characteristics are in the Appendix.
OA = onasemnogene abeparvovec; SD = standard deviation; *SMN2 = survival motor neuron 2.*

# No safety concerns or dose-related trends were identified

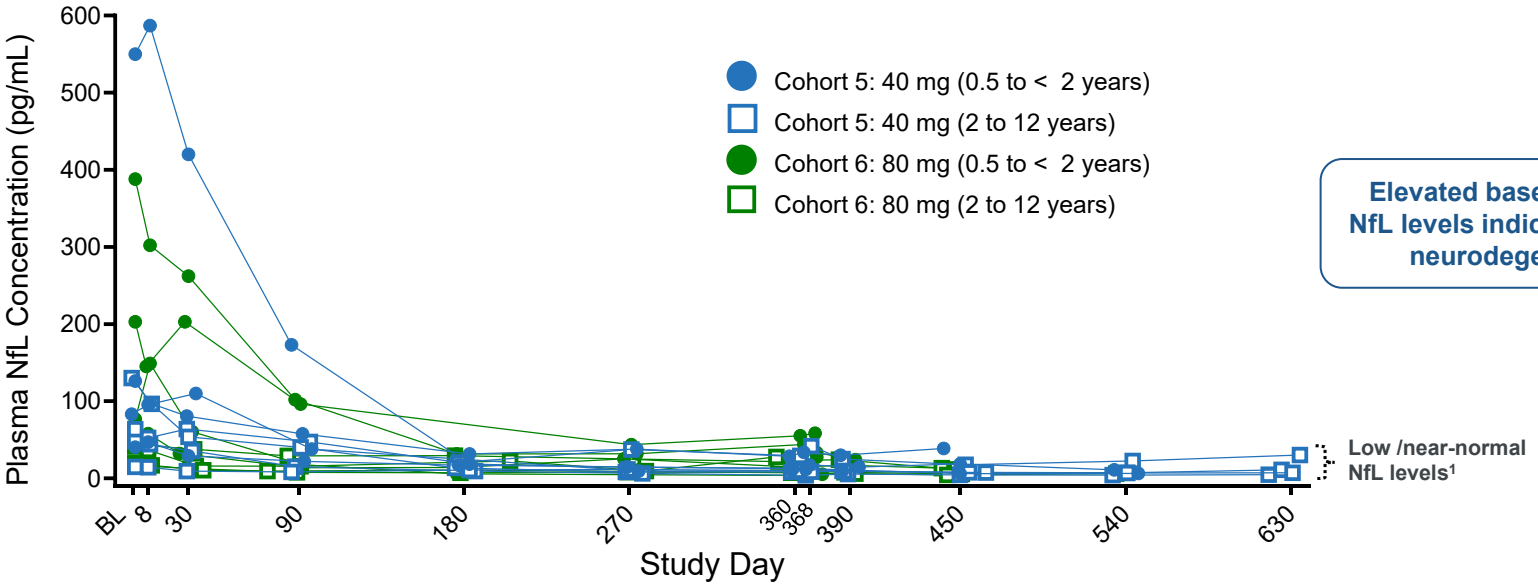
- Salanersen was generally well tolerated at doses of 40 mg and 80 mg
- Most AEs were mild or moderate in severity
- Most AEs and SAEs were events common in the general pediatric population, after lumbar puncture, and in individuals with SMA

| | Overall population N = 24<br>n (%) |
|---|---|
| Any AE | 23 (95.8) |
| Severity[a]<br>Mild<br>Moderate<br>Severe | <br>3 (12.5)<br>13 (54.2)<br>7 (29.2) |
| Treatment-related AE[b,c] | 7 (29.2) |
| SAE | 12 (50.0) |
| Treatment-related SAE | 0 |
| AE leading to treatment withdrawal | 0 |
| AE leading to death | 0 |

Phase 1 interim analysis data cutoff date: December 2, 2025. [a]Participants were counted once at their maximum severity. [b]Related as assessed by the Investigator. [c]Full list of TRAE's are in the Appendix.
AE = adverse event; SAE = serious adverse event; SMA = spinal muscular atrophy; TRAE, treatment-related adverse events.

# Elevated NfL levels at baseline were reduced by 75% at Day 180 and remained low

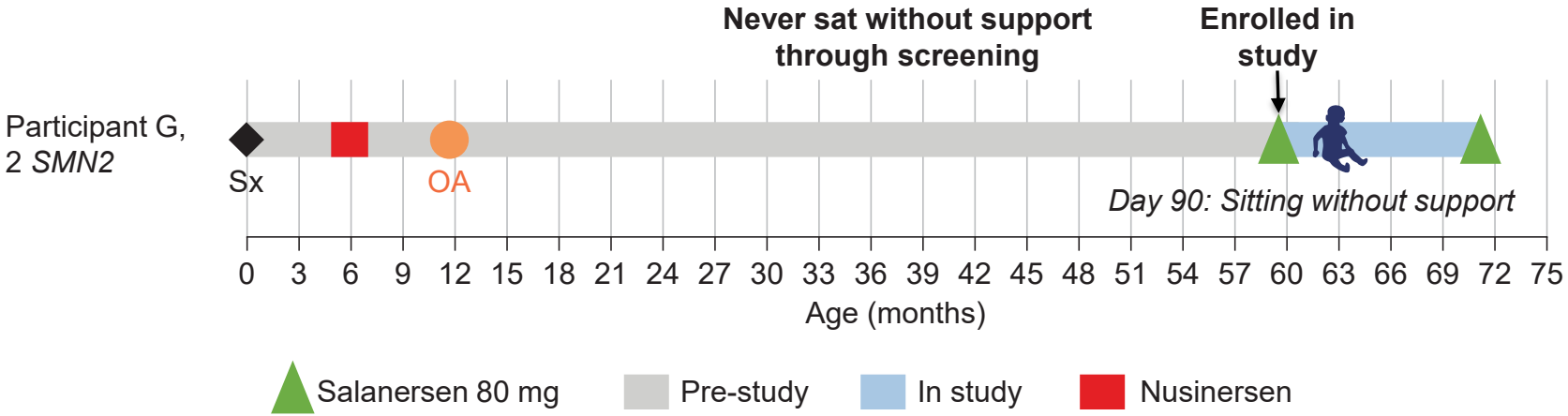
## Plasma NfL concentrations in participants with elevated[a] baseline NfL, n = 16/23[b]




**Elevated baseline plasma NfL levels indicated ongoing neurodegeneration**

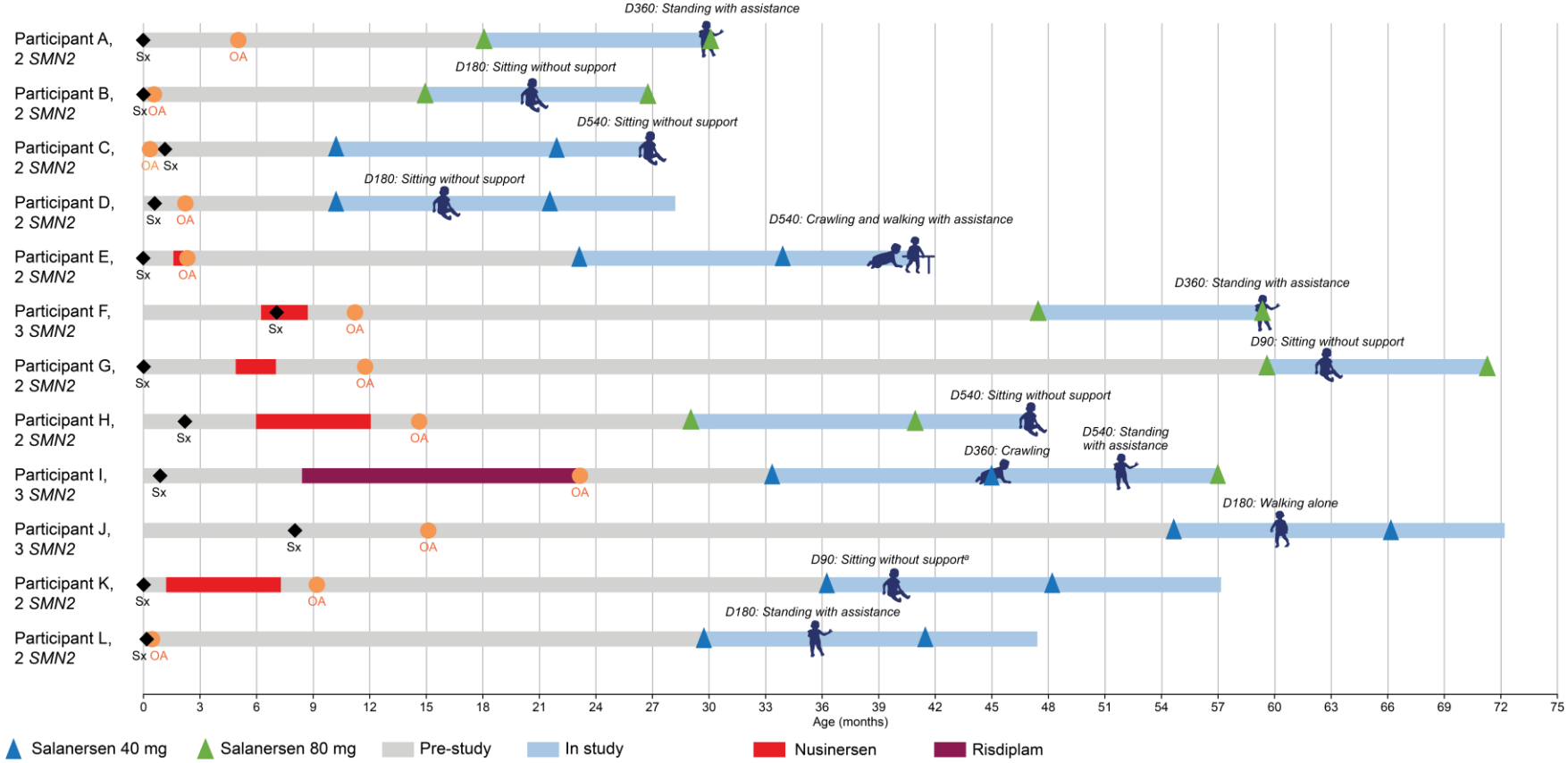
NfL levels are expected to be approximately 5–20% higher in serum as compared with plasma.[2-4]
Plasma NfL levels were measured with a single molecular array (Simoa) immunoassay via the HD-X Analyzer using the NfL v2 Advantage kit (Product# 104073; Quanterix, Lexington, MA, USA). Testing was performed at Charles River Laboratories, Shrewsbury, MA.
[a]Elevated baseline defined as exceeding 95th percentile for serum in neurologically healthy children of similar ages.[1] [b]Baseline values are available for 23 of 24 participants.
BL = baseline; NfL = neurofilament light chain.
1. Bayoumy S *et al. Clin Chem Lab Med* 2024;62:1252–65. 2. Kapoor R *et al. Neurology* 2020;95:436–44. 3. Barro C *et al. Ann Clin Transl Neurol* 2020;7:2508–23. 4. Mayo Clinic Laboratories. Available at: https://neurology.testcatalog.org/show/NFLP. Accessed February 26, 2026.

# Participants gained new WHO motor milestones beyond what would be expected




Sx indicates time of symptom onset.
[a]Participant K sitting without support not replicated in clinic on Days 180 and 630 (unscheduled visit) but present at home per caregiver.
OA = onasemnogene abeparvovec; *SMN2* = *survival motor neuron 2*.

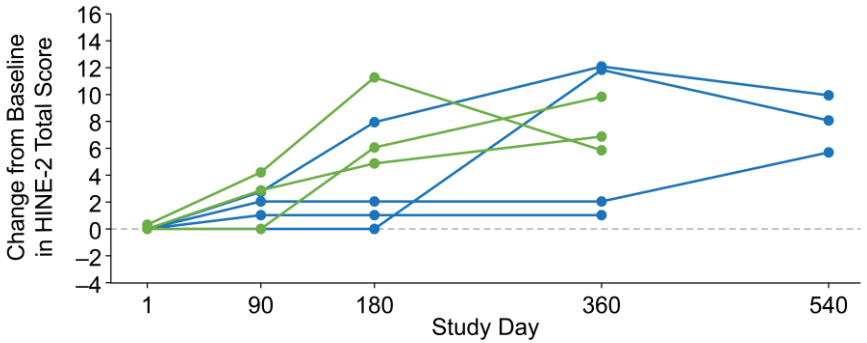
# Half of participants achieved ≥ 1 new WHO motor milestone



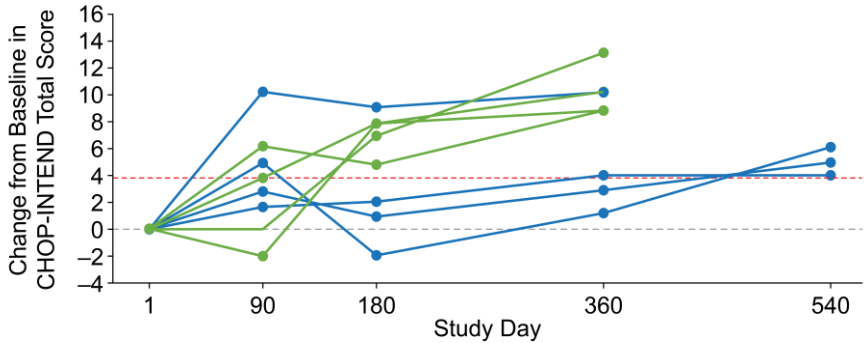

Sx indicates time of symptom onset.
[a]Participant K sitting without support not replicated in clinic on Days 180 and 630 (unscheduled visit) but present at home per caregiver.
D, Day; OA = onasemnogene abeparvovec; *SMN2* = *survival motor neuron 2*.

# Participants experienced improvements in HINE-2 and CHOP-INTEND

## Change from baseline in HINE-2[a]




## Change from baseline in CHOP-INTEND




● Salanersen 40 mg (n = 4) ● Salanersen 80 mg (n = 4)

Minimal clinically importance difference[1]

| HINE-2 scores | 40 mg cohort (n=4) | 80 mg cohort (n=4) |
|---|---|---|
| Baseline score, mean (SD) | 7.3 (7.18) | 7.8 (4.03) |
| Change from baseline to Day 360, mean (SD) | 6.8 (6.08) | 7.7 (2.08) |

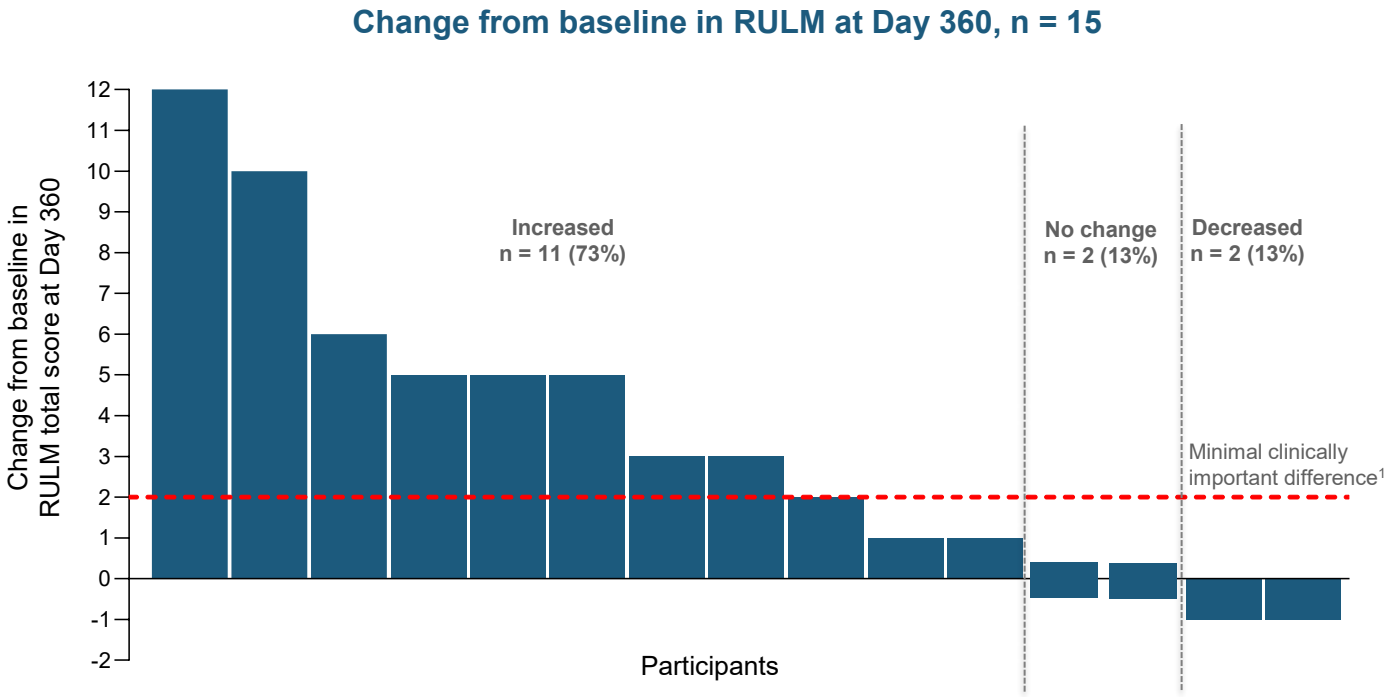
| CHOP-INTEND scores | 40 mg cohort (n=4) | 80 mg cohort (n=4) |
|---|---|---|
| Baseline score, mean (SD) | 45.3 (11.09) | 44.8 (6.95) |
| Change from baseline to Day 360, mean (SD) | 4.5 (3.87) | 10.3 (1.89) |
| Participants with ≥ 4-point improvement at Day 360, n (%) | 2 (50%) | 4 (100%) |

[a]One participant from the 80 mg cohort had missing data at Day 360 visit.

CHOP-INTEND = Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; HINE-2 = Hammersmith Infant Neurological Examination Section 2.

1. Stull DE *et al. J Manag Care Spec Pharm* 2019;25(3-a Suppl):S55.

# Majority of participants improved in RULM at Day 360

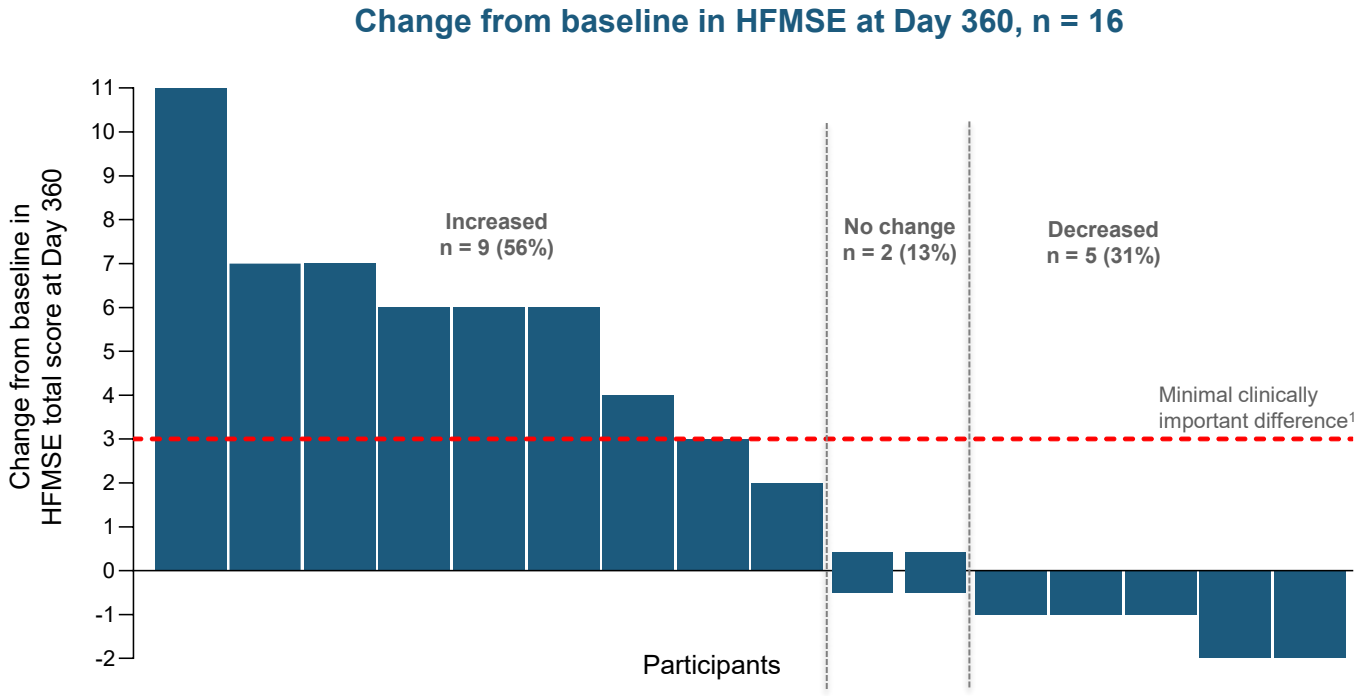



RULM is assessed for participants aged ≥ 2 years at the visit. Given this, participants within the younger age group (0.5- to < 2-years-olds) do not have baseline RULM available prior to the first study dose; therefore, results of the older subgroup (n = 15) only are presented here. One participant did not complete RULM.

pts = points; RULM = Revised Upper Limb Module; SD = standard deviation.

1. Pera MC *et al. Muscle Nerve* 2019;59:426–30.

# Majority of participants improved in HFMSE at Day 360




HFMSE is assessed for participants aged ≥ 2 years at the visit. Given this, participants within the younger age group (0.5- to < 2-year-olds) do not have baseline HFMSE available prior to the first study dose; therefore, results of the older subgroup (n = 16) only are presented here.

HFMSE = Hammersmith Functional Motor Scale Expanded; SD = standard deviation.

1. Swoboda KJ *et al. PLoS One* 2010;5:e12140.

# Summary

Interim Phase 1 safety and exploratory efficacy data continue to be supportive of salanersen development:

- ✓ Salanersen was generally well tolerated at doses of 40 mg and 80 mg
- ✓ Consistent and sustained reductions in plasma NfL were observed across participants with elevated baseline levels, without attenuation of treatment effect
- ✓ While the small sample size and heterogeneity in the study population are limiting, the magnitude and consistency of changes observed across all efficacy outcomes measures are highly suggestive of a clinically relevant impact of salanersen in participants with SMA

**The efficacy and safety of salanersen 80 mg is now being evaluated in Phase 3 studies (STELLAR-1,[1] STELLAR-2,[1] and SOLAR[2]) across a broad population with SMA**

NfL = neurofilament light chain; SMA = spinal muscular atrophy.

1. Crawford TO, *et al*. Presented at the Muscular Dystrophy Association (MDA) Clinical & Scientific Conference, March 8–11, 2026, Orlando, FL. Poster 199M. 2. Shieh P, *et al*. Presented at the Muscular Dystrophy Association (MDA) Clinical & Scientific Conference, March 8–11, 2026, Orlando, FL, USA. Poster 193M.

# Many thanks!

The authors thank the **participants** in the study including the **children** and their **parents/guardians** and **family members**, without whom this effort cannot succeed.

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**Phase 1 Part B Principal Investigators**

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- Astrid Pechmann
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- Valeria Sansone
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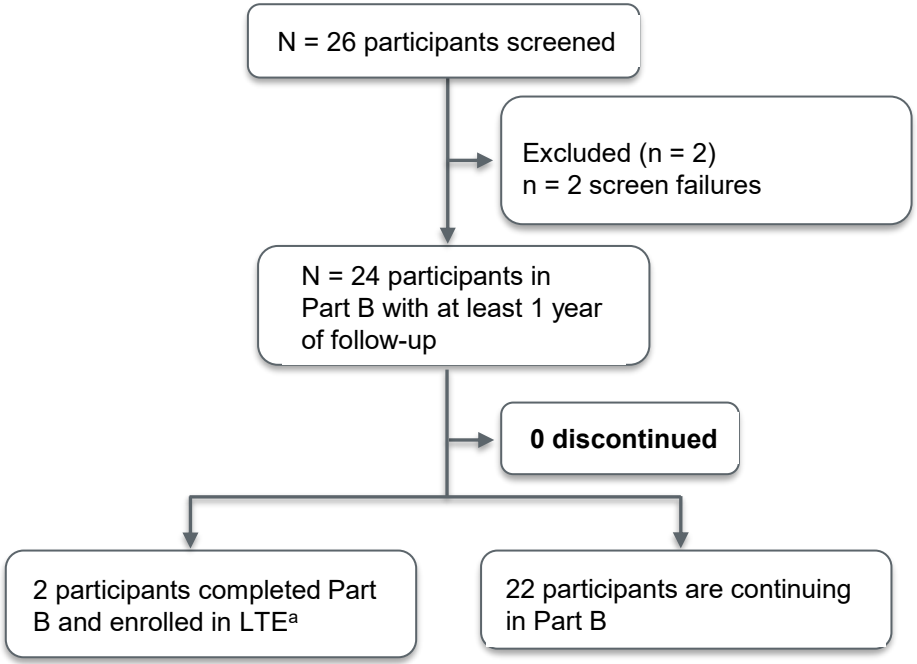
- Andreea Seferian
- Ludo van der Pol
- Andreas Ziegler

# Appendix

# All participants continue in the study with at least 1 year of follow-up as of the interim data cut




[a]At the time of the interim data cut (Dec 2025), 2 participants had completed Part B and 2/2 enrolled in the LTE.

LTE = long-term extension.

# Additional baseline characteristics and SMA history

| | 40 mg | | 80 mg | |
|---|---|---|---|---|
| | Younger Participants n = 4 | Older Participants n = 8 | Younger Participants n = 4 | Older Participants n = 8 |
| Male / female, n (%) | 3 (75.0) / 1 (25.0) | 5 (62.5) / 3 (37.5) | 2 (50.0) / 2 (50.0) | 5 (62.5) / 3 (37.5) |
| Age at SMA symptom onset, months, median (range) | 0.9 (0.0–2.0) | 2.5 (0.0–13.0) | 0.5 (0.0–4.0) | 5.5 (0.0–10.0) |
| Age at SMA diagnosis, months, median (range) | 0.3 (0.2–3.0) | 5.5 (0.0–17.0) | 1.1 (0.7–1.3) | 6.5 (2.0–18.0) |
| Participants who were symptomatic at the time of OA dosing, n (%) | 3 (75.0) | 8 (100.0) | 3 (75.0) | 8 (100.0) |
| HFMSE total score, mean (SD) | – | 23.6 (18.4) | – | 19.0 (9.2) |
| RULM total score, mean (SD) | – | 17.7 (6.8)[a] | – | 18.4 (9.1) |
| HINE-2 total score, mean (SD) | 7.3 (7.18) | – | 7.8 (4.0) | – |
| CHOP-INTEND total score, mean (SD) | 45.3 (11.1) | – | 44.8 (7.0) | – |

[a]Baseline RULM total scores were available for 7 of 8 participants.

CHOP-INTEND = Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; HFMSE = Hammersmith Functional Motor Scale Expanded; HINE-2 = Hammersmith Infant Neurological Examination Section 2; OA = onasemnogene abeparvovec; RULM = Revised Upper Limb Module; SD = standard deviation; SMA = spinal muscular atrophy.

# Treatment-related[a] adverse events (n = 7 participants, 29.2%)

| | 40 mg | | 80 mg | |
|---|---|---|---|---|
| | Younger Participants (n = 4) n (%) | Older Participants (n = 8) n (%) | Younger Participants (n = 4) n (%) | Older Participants (n = 8) n (%) |
| Vomiting | -- | 1 (12.5) | -- | 1 (12.5) |
| Diarrhea | -- | 1 (12.5) | -- | -- |
| Nausea | -- | -- | -- | 1 (12.5) |
| Salivary hypersecretion | 1 (25.0) | -- | -- | -- |
| Fatigue | 1 (25.0) | -- | 1 (25.0) | -- |
| Pyrexia | -- | 1 (12.5) | -- | -- |
| Dizziness | -- | -- | -- | 1 (12.5) |
| Headache | -- | 1 (12.5) | -- | -- |
| Neutropenia | -- | 1 (12.5) | -- | -- |
| Procedural pain | -- | -- | 1 (25.0) | -- |
| Pain in extremity | -- | -- | -- | 1 (12.5) |
| Alopecia | -- | 1 (12.5) | -- | -- |

[a]Related as assessed by the Investigator.

# Salanersen shows dose-dependent serum exposure, rapid decline after peak, and durable levels in CSF

- In Part B, serum exposures increased with dose across 40 mg to 80 mg cohorts
- The overall shape of the serum concentration–time profiles is similar across age groups
  - Concentrations peaked between 2 and 6 hours post-dose, and dropped to < 1% of $C_{max}$ at 7 days post-dose
- As expected, an inverse relationship between serum concentrations and age is observed
- CSF trough concentrations are quantifiable in participants 1 year after the first dose

As of the Phase 1 interim analysis data cutoff date (December 2025), serum data are available to at least Day 390, and CSF data are available for most Part B participants through to Day 360.
$C_{max}$ = maximum concentration; CSF = cerebrospinal fluid.