

# Biogen - DEVOTE

## Escalating Dose and Randomized, Controlled Study of Nusinersen (BIIB058) in Participants With Spinal Muscular Atrophy

### Summary

This is a Phase 2 and 3 clinical trial that studies the safety, efficacy, and tolerability of nusinersen at higher doses in participants with SMA. The study is comprised of 3 parts. Part A investigates a high dose of nusinersen (28mg) in nusinersen-naïve participants with late-onset SMA. Part B investigates two different doses of nusinersen (12mg or 50mg) in nusinersen-naïve participants with infantile or late-onset SMA. Part C investigates participants who have previously taken 12mg of nusinersen for 1 year prior to the study; it involves giving an initial dose of 50mg of nusinersen at the start of the study, and subsequently 28mg of nusinersen at later visits in the study.

**Study Number: NCT04089566**

### Description by Biogen

The primary objectives of this study are to examine the clinical efficacy of nusinersen administered intrathecally at higher doses to participants with SMA, as measured by change in Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) total score (Part B); to examine the safety and tolerability of nusinersen administered intrathecally at higher doses to participants with spinal muscular atrophy (SMA) (Parts A and C).

The secondary objectives of this study are to examine the clinical efficacy of nusinersen administered intrathecally at higher doses to participants with SMA (Parts A, B and C); to examine the effect of nusinersen administered intrathecally at higher doses to participants with SMA (Parts A and C); to examine the safety and tolerability of nusinersen administered intrathecally at higher doses to participants with SMA, to examine the effect of



**AUSNMD**

### Trial Status Recruiting

**Locations**  
Melbourne -  
Melbourne Children's  
Campus, Recruiting

**Trial Sponsor**  
Biogen

**Age**  
Any age

**SMA Subtype**  
Type 2, Type 3a,  
Type 3b

**SMN2 Copy  
Numbers  
Required**  
2 or more

**Mode of  
delivery**  
IT

**MRI**  
No

**Phase**  
2+3

**Length Of  
Participation**  
56 weeks

**Recruitment  
Target**  
125

**Therapeutic  
Category**  
SMN2 Gene  
upregulation

nusinersen administered intrathecally at higher doses compared to the currently approved dose in participants with SMA (Part B).

### Primary Outcome Measures

- Part A (nusinersen-naïve participants with late-onset SMA): safety profile
- Part B ( two different doses of nusinersen (12mg or 50mg) in participants with infantile or late-onset SMA): Change from Baseline in CHOP INTEND Total Score
- Part C (participants previously on nusinersen 12mg): safety profile

### Secondary Outcome Measures

- Part A (nusinersen-naïve participants with late-onset SMA):
  - Change from Baseline in Hammersmith Functional Motor Scale - Expanded (HFMSE) Score
  - Change from Baseline in Revised Upper Limb Module (RULM) Score
  - Total Number of New WHO Motor Milestones
  - Change from Baseline in Assessment of Caregiver Experience with Neuromuscular Disease (ACEND)
  - Change from Baseline in Pediatric Quality of Life Inventory™ (PedsQL)
  - Clinical Global Impression of Change (CGIC)
  - Number of Hospitalizations
  - Duration of Hospitalizations

- Change from Baseline in the PASA Scale
- Part B (two different doses of nusinersen (12mg or 50mg) in participants with infantile or late-onset SMA):
  - Percentage of Hammersmith Infant Neurological Examination (HINE) Section 2 Motor Milestone Responders
  - Change from Baseline in HINE Section 2 Motor Milestones Total Score
  - Time to Permanent Ventilation ( 16 hours of ventilation/day continuously for > 21 days in the absence of an acute reversible event)
  - Time to Death (Overall Survival)
  - Change from Baseline in Hammersmith Functional Motor Scale - Expanded (HFMSE) Score
  - Change from Baseline in Revised Upper Limb Module (RULM) Score
  - Total Number of New WHO Motor Milestones
  - Change from Baseline in Assessment of Caregiver Experience with Neuromuscular Disease (ACEND)
  - Change from Baseline in Pediatric Quality of Life Inventory™ (PedsQL)
  - Number of Participants with AEs and SAEs
  - Number of Hospitalizations
  - Duration of Hospitalizations
  - Clinical Global Impression of Change (CGIC)

- Change from Baseline in the Parent Assessment of Swallowing Ability (PASA) Scale
- Change from Baseline in the PASA Scale
- Part C (participants previously on nusinersen 12mg):
  - Change from Baseline in HFMSE Score
  - Change from Baseline in RULM Score
  - Total Number of New WHO Motor Milestones
  - Change from Baseline in ACEND
  - Clinical Global Impression of Change (CGIC)
  - Change from Baseline in PedsQL™
  - Change from Baseline in CHOP INTEND Total Score
  - Change from Baseline in HINE Section 2 Motor Milestones Total Score
  - Number of Hospitalizations
  - Duration of Hospitalizations

## Can I take part?

### Inclusion Criteria

For Part A, B and C:

- ✓ Genetic documentation of 5q SMA (homozygous gene deletion, mutation, or compound heterozygote)

Part A (nusinersen-naïve participants with late-onset SMA):

- ✓ Onset of clinical signs and symptoms consistent with SMA at > 6 months (> 180 days) of age (i.e., later-onset SMA)

- ✓ Age 2 to 15 years, inclusive, at the time of informed consent

Part B ( two different doses of nusinersen (12mg or 50mg) in participants with infantile or late-onset SMA):

- ✓ Participants with SMA symptom onset 6 months ( 180 days) of age (infantile onset) should have age > 1 week to 7 months ( 210 days) at the time of informed consent
- ✓ Participants with SMA symptom onset > 6 months (> 180 days) of age (later onset):
  - ✓ Age 2 to < 10 years at the time of informed consent
  - ✓ Can sit independently but has never had the ability to walk independently
  - ✓ HFMSE score 10 and 54 at Screening

Part C (participants previously on nusinersen 12mg):

- ✓ Participants may be of any age
- ✓ Participants 18 years of age at Screening must be ambulatory
- ✓ Currently on nusinersen treatment at the time of Screening, with the first dose being at least 1 year prior to Screening

#### **Exclusion Criteria**

Part A, B and C:

- ✗ Presence of an untreated or inadequately treated active infection requiring systemic antiviral or antimicrobial therapy at any time during the Screening period
- ✗ Presence of an implanted shunt for the drainage of cerebrospinal fluid (CSF) or of an implanted central nervous system (CNS) catheter

- ✘ Hospitalization for surgery, pulmonary event, or nutritional support within 2 months prior to screening or planned within 12 months after the participant's first dose

Part A (nusinersen-naïve participants with late-onset SMA):

- ✘ Respiratory insufficiency, defined by the medical necessity for invasive or noninvasive ventilation for > 6 hours/day during a 24-hour period, at Screening
- ✘ Medical necessity for a gastric feeding tube
- ✘ Treatment with an investigational drug given for the treatment of SMA, biological agent, or device within 30 days or 5 half-lives of the agent, whichever is longer, prior to screening or anytime during the study; any prior or current treatment with any survival motor neuron-2 (SMN2)-splicing modifier or gene therapy; or prior antisense oligonucleotide treatment, or cell transplantation

Part B ( two different doses of nusinersen (12mg or 50mg) in participants with infantile or late-onset SMA):

- ✘ Treatment with an investigational drug given for the treatment of SMA, biological agent, or device within 30 days or 5 half-lives of the agent, whichever is longer, prior to screening or anytime during the study; any prior or current treatment with any SMN2-splicing modifier or gene therapy; or prior antisense oligonucleotide treatment, or cell transplantation
- ✘ Participants with SMA symptom onset > 6 months (> 180 days) of age (later onset):
  - ✘ Respiratory insufficiency, defined by the medical necessity for invasive or noninvasive ventilation for > 6 hours/day, at screening
  - ✘ Medical necessity for a gastric feeding tube

- ✦ Participants with SMA symptom onset 6 months ( 180 days) of age (infantile onset): Signs or symptoms of SMA present at birth or within the first week after birth.

Part C (participants previously on nusinersen 12mg):

- ✦ Concurrent or previous participation and/or administration of nusinersen in another clinical study

Other inclusion/exclusion criteria apply.

For contact details and to find out more, please refer to [ausnmd.org](https://ausnmd.org).