

# Biogen - SHINE

An Open-Label Extension Study for Patients With Spinal Muscular Atrophy Who Previously Participated in Investigational Studies of Nusinersen (ISIS 396443)

## Summary

This is a Phase 3 study that evaluates the long-term safety, efficacy, and tolerability of Nusinersen in participants with SMA who have previously participated in other Nusinersen studies.

**Study Number: NCT02594124**

## Description by Biogen

The primary objective is to evaluate the long-term safety and tolerability of nusinersen (ISIS 396443) administered by intrathecal (IT) injection to participants with Spinal Muscular Atrophy (SMA) who previously participated in investigational studies of nusinersen. The secondary objective is to examine the long-term efficacy of nusinersen administered by IT injection to participants with SMA who previously participated in investigational studies of nusinersen.

## Primary Outcome Measures

- Number of participants experiencing Adverse events (AEs) and/or Serious Adverse Events (SAEs) [ Time Frame: Up to Day 1814 ]
- Number of participants with clinically significant vital sign abnormalities [ Time Frame: Up to Day 1814 ]
- Number of participants with clinically significant weight abnormalities [ Time Frame: Up to Day 1814 ]
- Number of participants with clinically significant neurological examination abnormalities [ Time Frame: Up to Day 1814 ]



## Trial Status

Fully recruited

**Locations**  
Melbourne - Melbourne Children's Campus, Fully recruited, Sydney - Children's Hospital, Fully recruited

**Trial Sponsor**  
Biogen

**Age**  
Any age

**SMN2 Copy Numbers Required**  
2 or more

**Mode of delivery**  
IT

**MRI**  
No

**Phase**  
3

**Length Of Participation**  
5 years

**Recruitment Target**  
292

**Therapeutic Category**  
SMN2 Gene upregulation

- Number of participants with clinically significant laboratory assessment abnormalities  
[ Time Frame: Up to Day 1814 ]
- Number of participants with clinically significant coagulation parameter abnormalities  
[ Time Frame: Up to Day 1814 ]
- Number of participants with clinically significant 12-lead electrocardiograms (ECGs) abnormalities  
[ Time Frame: Up to Day 1814 ]
- Change from Baseline in concomitant medications  
[ Time Frame: Up to Day 1814 ]

### Secondary Outcome Measures

- Percentage of participants who attained motor milestones as assessed by World Health Organization (WHO) criteria [ Time Frame: Up to Day 1814 ]
- Percentage of participants who attained motor milestones as assessed by Section 2 of Hammersmith Infant Neurological Examination (HINE)  
[ Time Frame: Up to Day 1814 ]
- Time to death or permanent ventilation  
[ Time Frame: Up to Day 1814 ]
- Percentage of participants not requiring permanent ventilation [ Time Frame: Up to Day 1814 ]
- Change from Baseline in the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) motor function scale  
[ Time Frame: Up to Day 1814 ]
- CHOP-INTEND tests includes 16 items structured to move from easiest to hardest with the grading including gravity eliminated (lower scores) to antigravity movements (higher scores). All item scores range from 0-4.

- Change from Baseline in Hammersmith Functional Motor Scale [ Time Frame: Up to Day 1814 ]
- The HFMSE tests motor function of patients with SMA. The original 20 item Hammersmith Functional Motor Scale was expanded to include 13 additional adapted items from the Gross Motor Function Measure to improve sensitivity for the higher functioning ambulant population.
- Change from Baseline in Revised Upper Limb Module (RULM) [ Time Frame: Up to Day 1814 ]
- Change from Baseline in 6-Minute Walk Test (6MWT) [ Time Frame: Up to Day 1814 ]
- 6MWT: walking up and down a 25 meter track without aids or orthotics as fast as possible for 6 minutes. Lap splits, minute splits and total distance are recorded, in addition to any rests and falls.
- Change from Baseline in Compound Muscular Action Potential (CMAP) [ Time Frame: Up to Day 1814 ]
- CMAP is an electrophysiological technique that can be used to determine the approximate number of motor neurons in a muscle or group of muscles.
- Change from Baseline in body length and/or height (for all participants) [ Time Frame: Up to Day 1814 ]
- Change from Baseline in head circumference (for participants up to 36 months of age) [ Time Frame: Up to Day 1814 ]
- Change from Baseline in chest circumference (for participants up to 36 months of age) [ Time Frame: Up to Day 1814 ]
- Change from Baseline in arm circumference (for participants up to 36 months of age) [ Time Frame: Up to Day 1814 ]

- Proportion of CMAP responders [ Time Frame: Up to Day 1814 ]
- Number of participants with motor milestones achieved [ Time Frame: Up to Day 1814 ]
- Proportion of participants who achieved standing alone [ Time Frame: Up to Day 1814 ]
- Proportion of participants who achieved walking with assistance [ Time Frame: Up to Day 1814 ]
- Number of participants with serious respiratory events [ Time Frame: Up to Day 1814 ]
- Number of participants hospitalized [ Time Frame: Up to Day 1814 ]
- Duration of hospitalizations [ Time Frame: Up to Day 1814 ]
- Change from Baseline in Cobb-Angle on X-Ray of the thoracolumbar spine [ Time Frame: Up to Day 1814 ]
- Change from Baseline in Quality of Life (QOL) Questionnaires [ Time Frame: Up to Day 1814 ]
- Number of Disease-related hospitalizations and AEs [ Time Frame: Up to Day 1814 ]
- Overall survival rate [ Time Frame: Up to Day 1814 ]

## **Can I take part?**

### **Inclusion Criteria**

- ✓ Signed informed consent of parent or guardian and signed informed assent of the participant, if indicated per participant's age and institutional guidelines.
- ✓ Completion of the index study in accordance with the study protocol or as a result of Sponsor decision (e.g., early termination of the index study) within the preceding 16 weeks

## Exclusion Criteria

- ✘ Have any condition or worsening condition which in the opinion of the Investigator would make the participant unsuitable for enrollment, or could interfere with the participant participating in or completing the study
- ✘ Clinically significant abnormalities in hematology or clinical chemistry parameters or electrocardiogram (ECG), as assessed by the Site Investigator, at the Screening visit that would render the participant unsuitable for participation in the study
- ✘ Participant's parent or legal guardian is not willing or able to meet standard of care guidelines (including vaccinations and respiratory syncytial virus prophylaxis if available), nor provide nutritional and respiratory support throughout the study
- ✘ Treatment with another investigational agent, biological agent, or device within one month of Screening, or 5 half-lives of study agent, whichever is longer

Other inclusion/exclusion criteria apply.

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