



## Clinical trial results:

### A Phase 3 Randomized, Double-blind, Placebo-controlled, Multi-center Study to Assess the Efficacy and Safety of Viltolarsen in Ambulant Boys with Duchenne Muscular Dystrophy (DMD).

#### Summary

EudraCT number	2019-002076-13
Trial protocol	GB SE ES NL GR IT NO
Global end of trial date	19 October 2023

#### Results information

Result version number	v1 (current)
This version publication date	16 November 2024
First version publication date	16 November 2024

#### Trial information

##### Trial identification

Sponsor protocol code	NS-065/NCNP-01-301
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04060199
WHO universal trial number (UTN)	-
Other trial identifiers	US IND: 127474

Notes:

#### Sponsors

Sponsor organisation name	NS Pharma, Inc.
Sponsor organisation address	140 East Ridgewood Avenue Suite 280s, Paramus, United States, 07652-3914
Public contact	Legal team, NS Pharma, Inc. , +1 2019863860, legal@nspharma.com
Scientific contact	Trial information team, NS Pharma, Inc. , +1 8666774276, trialinfo@nspharma.com

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 October 2023
Global end of trial reached?	Yes
Global end of trial date	19 October 2023
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To compare the efficacy of viltolarsen administered intravenously at a weekly dose of 80 mg/kg over a 48-week treatment period vs. placebo controls in ambulant boys ages 4 to <8 years with DMD using Time to Stand Test from supine (TTSTAND) as a measure of strength and function.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and with all applicable laws and regulations of the locale and country where the study was conducted, and in compliance with Good Clinical Practice Guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 April 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Ukraine: 1
Country: Number of subjects enrolled	Türkiye: 11
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Russian Federation: 10
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	Japan: 1
Country: Number of subjects enrolled	China: 12
Country: Number of subjects enrolled	Chile: 3
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Greece: 3
Country: Number of subjects enrolled	Italy: 4
Worldwide total number of subjects	77
EEA total number of subjects	22

Notes:

<b>Subjects enrolled per age group</b>	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	77
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Screening includes assessments to confirm eligibility (review of inclusion/exclusion criteria and review to confirm the DMD diagnosis and appropriate mutations).

### Period 1

Period 1 title	Treatment and follow up (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Viltolarsen

Arm description:

All randomized subjects who received 80 mg/kg Viltolarsen injection once weekly over a 48-week period.

Arm type	Experimental
Investigational medicinal product name	Viltolarsen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 80 mg/kg Viltolarsen intravenous infusions once weekly over a 48-week period.

<b>Arm title</b>	Placebo
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Arm description:

All randomized subjects who received saline solution as intravenous infusions administered once weekly over a 48-week period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received saline solution as intravenous infusions administered once weekly over a 48-week period.

<b>Number of subjects in period 1</b>	Viltolarsen	Placebo
Started	38	39
Completed	36	38
Not completed	2	1
Patient Relocation	1	-
Protocol deviation	1	1

## Baseline characteristics

### Reporting groups

Reporting group title	Viltolarsen
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Reporting group description:

All randomized subjects who received 80 mg/kg Viltolarsen injection once weekly over a 48-week period.

Reporting group title	Placebo
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Reporting group description:

All randomized subjects who received saline solution as intravenous infusions administered once weekly over a 48-week period.

Reporting group values	Viltolarsen	Placebo	Total
Number of subjects	38	39	77
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	38	39	77
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	38	39	77

## End points

### End points reporting groups

Reporting group title	Viltolarsen
Reporting group description: All randomized subjects who received 80 mg/kg Viltolarsen injection once weekly over a 48-week period.	
Reporting group title	Placebo
Reporting group description: All randomized subjects who received saline solution as intravenous infusions administered once weekly over a 48-week period.	
Subject analysis set title	Viltolarsen mITT population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All randomized patients who received at least 1 dose of Viltolarsen and had a baseline assessment and at least 1 post baseline efficacy assessment.	
Subject analysis set title	Placebo mITT population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All randomized patients who received at least 1 dose of placebo and had a baseline assessment and at least 1 post baseline efficacy assessment.	

### Primary: Primary: Change from baseline in Time to Stand

End point title	Primary: Change from baseline in Time to Stand
End point description:	
End point type	Primary
End point timeframe: 49 weeks	

End point values	Viltolarsen mITT population	Placebo mITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	35		
Units: Velocity				
least squares mean (standard error)	0.009 (± 0.0096)	0.013 (± 0.0096)		

### Statistical analyses

Statistical analysis title	Primary analysis: Time to Stand
Comparison groups	Viltolarsen mITT population v Placebo mITT population

Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
Method	mixed-effect model for repeated measures
Parameter estimate	Mean difference (final values)
Point estimate	-0.004
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-0.03
upper limit	0.022
Variability estimate	Standard error of the mean
Dispersion value	0.013



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All AEs occurring during the course of the study (starting from signing informed consent to study completion) until the follow-up telephone call, 30 days following the last administration of study drug.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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### Reporting groups

Reporting group title	Viltolarsen
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Reporting group description:

All randomized subjects who received 80 mg/kg Viltolarsen injection once weekly over a 48-week period.

Reporting group title	Placebo
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Reporting group description:

All randomized subjects who received saline solution as intravenous infusions administered once weekly over a 48-week period.

Serious adverse events	Viltolarsen	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 38 (5.26%)	3 / 39 (7.69%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 38 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 38 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Adverse drug reaction	Additional description: Prolonged hospitalization after zoledronate infusion: nausea, dizziness, vomiting, and fever.		

subjects affected / exposed	1 / 38 (2.63%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Gastrointestinal disorders</b>			
Vomiting			
subjects affected / exposed	0 / 38 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Infections and infestations</b>			
Influenza			
subjects affected / exposed	0 / 38 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	Viltolarsen	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 38 (97.37%)	33 / 39 (84.62%)	
<b>Vascular disorders</b>			
Haematoma			
subjects affected / exposed	0 / 38 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
<b>General disorders and administration site conditions</b>			
Pyrexia			
subjects affected / exposed	10 / 38 (26.32%)	13 / 39 (33.33%)	
occurrences (all)	12	19	
Fatigue			
subjects affected / exposed	3 / 38 (7.89%)	1 / 39 (2.56%)	
occurrences (all)	3	1	
Influenza like illness			

subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	2 / 39 (5.13%) 3	
Administration site extravasation subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 39 (5.13%) 2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 38 (31.58%)	5 / 39 (12.82%)	
occurrences (all)	15	7	
Rhinorrhoea			
subjects affected / exposed	6 / 38 (15.79%)	2 / 39 (5.13%)	
occurrences (all)	7	2	
Rhinitis allergic			
subjects affected / exposed	3 / 38 (7.89%)	1 / 39 (2.56%)	
occurrences (all)	4	1	
Investigations			
Blood triglycerides increased			
subjects affected / exposed	4 / 38 (10.53%)	2 / 39 (5.13%)	
occurrences (all)	6	2	
Protein urine present			
subjects affected / exposed	2 / 38 (5.26%)	3 / 39 (7.69%)	
occurrences (all)	3	5	
Blood cholesterol increased			
subjects affected / exposed	2 / 38 (5.26%)	2 / 39 (5.13%)	
occurrences (all)	4	2	
Beta 2 microglobulin urine increased			
subjects affected / exposed	1 / 38 (2.63%)	2 / 39 (5.13%)	
occurrences (all)	1	3	
Blood fibrinogen increased			
subjects affected / exposed	2 / 38 (5.26%)	1 / 39 (2.56%)	
occurrences (all)	2	1	
Crystal urine present			
subjects affected / exposed	1 / 38 (2.63%)	2 / 39 (5.13%)	
occurrences (all)	1	3	
Urine protein/creatinine ratio increased			

subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 3	1 / 39 (2.56%) 1	
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	5 / 38 (13.16%) 6	4 / 39 (10.26%) 4	
Contusion subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 4	1 / 39 (2.56%) 1	
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3	2 / 39 (5.13%) 2	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3	5 / 39 (12.82%) 8	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 4	1 / 39 (2.56%) 3	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	9 / 38 (23.68%) 10	7 / 39 (17.95%) 13	
Vomiting subjects affected / exposed occurrences (all)	11 / 38 (28.95%) 12	3 / 39 (7.69%) 3	
Abdominal pain subjects affected / exposed occurrences (all)	4 / 38 (10.53%) 10	6 / 39 (15.38%) 11	
Nausea subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	3 / 39 (7.69%) 4	
Abdominal pain upper			

subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	1 / 39 (2.56%) 1	
Constipation subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	2 / 39 (5.13%) 2	
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 39 (5.13%) 2	
Faeces soft subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 39 (5.13%) 2	
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	3 / 39 (7.69%) 3	
Eczema subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3	0 / 39 (0.00%) 0	
Dermatitis allergic subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	0 / 39 (0.00%) 0	
Pruritus subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 39 (5.13%) 2	
Renal and urinary disorders			
Haematuria subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	2 / 39 (5.13%) 3	
Urine abnormality subjects affected / exposed occurrences (all)	4 / 38 (10.53%) 5	0 / 39 (0.00%) 0	
Pyelocaliectasis subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	2 / 39 (5.13%) 2	
Musculoskeletal and connective tissue disorders			

Pain in extremity subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 4	2 / 39 (5.13%) 2	
Back pain subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	2 / 39 (5.13%) 3	
Arthralgia subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 39 (5.13%) 3	
Myalgia subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	2 / 39 (5.13%) 4	
Infections and infestations			
COVID-19 subjects affected / exposed occurrences (all)	12 / 38 (31.58%) 13	12 / 39 (30.77%) 13	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	10 / 38 (26.32%) 18	9 / 39 (23.08%) 13	
Nasopharyngitis subjects affected / exposed occurrences (all)	9 / 38 (23.68%) 25	7 / 39 (17.95%) 16	
Rhinitis subjects affected / exposed occurrences (all)	6 / 38 (15.79%) 10	3 / 39 (7.69%) 5	
Gastroenteritis subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 4	4 / 39 (10.26%) 4	
Influenza subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	3 / 39 (7.69%) 3	
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 3	2 / 39 (5.13%) 2	
Bronchitis			

subjects affected / exposed	1 / 38 (2.63%)	2 / 39 (5.13%)	
occurrences (all)	1	2	
Hordeolum			
subjects affected / exposed	0 / 38 (0.00%)	3 / 39 (7.69%)	
occurrences (all)	0	3	
Gastroenteritis viral			
subjects affected / exposed	0 / 38 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Pharyngitis			
subjects affected / exposed	2 / 38 (5.26%)	0 / 39 (0.00%)	
occurrences (all)	2	0	
Pneumonia			
subjects affected / exposed	0 / 38 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	3	
Tonsillitis			
subjects affected / exposed	0 / 38 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Varicella			
subjects affected / exposed	0 / 38 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 38 (2.63%)	2 / 39 (5.13%)	
occurrences (all)	1	2	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported