Clinical trial results:
A Phase II Open-label, Multicenter Extension Study to Assess the Long-term Safety and Efficacy of Vamorolone in Boys with Duchenne Muscular Dystrophy (DMD)

Summary

EudraCT number	2016-004263-38
Trial protocol	SE GB
Global end of trial date	26 April 2018

Results information

Result version number	v1 (current)
This version publication date	30 March 2019
First version publication date	30 March 2019

Trial information

Trial identification

Sponsor protocol code	VBP15-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02760277
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ReveraGen BioPharma Inc.
Sponsor organisation address	155 Gibbs Street, Rockville, United States, 20850
Public contact	Vice President, Operations, ReveraGen BioPharma Inc., +1 215 680 8286, jesse.damsker@reveragen.com
Scientific contact	Vice President, Operations, ReveraGen BioPharma Inc., +1 215 680 8286, jesse.damsker@reveragen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001794-PIP02-16
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	14 September 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 April 2018
Global end of trial reached?	Yes
Global end of trial date	26 April 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives:
1. To evaluate the long-term safety and tolerability of vamorolone, administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period, in boys ages 4-7 years with DMD;
2. To compare the efficacy, as measured by the Time to Stand Test (TTSTAND), of vamorolone administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period vs. untreated DMD historical controls in boys ages 4-7 years with DMD; and
3. To compare the safety, as measured by body mass index (BMI) z-score, of vamorolone administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period vs. prednisone-treated historical controls in boys ages 4-7 years with DMD.

Protection of trial subjects:

The trial will be conducted in accordance with the International Conference on Harmonisation E6 Guideline for Good Clinical Practice; The United States FDA Code of Federal Regulations, Title 21 CFR Part 312, and the US Health Insurance Portability and Accountability Act of 1996. The Parent/guardian of each participant must consent in writing for participant to be enrolled.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 July 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 20
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Israel: 5
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	Australia: 5
Worldwide total number of subjects	48
EEA total number of subjects	11

Notes:

Subjects enrolled per age group	
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)	48
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:

Only those who have participated in the VBP13-003 trial are able to participate in the 003 trial.

Pre-assignment

Screening details:

Subject has previously completed study VBP15-002 up to and including the Week 4 Follow-up assessments within 8 weeks prior to enrollment.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose level group 1

Arm description:

0.25 mg/kg/day for 24 weeks

Arm type	Experimental
Investigational medicinal product name	Vamorolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Vamorolone 4% oral suspension

Arm title	Dose level Group 2

Arm description:

0.75 mg/kg/day for 24 weeks

Arm type	Experimental
Investigational medicinal product name	Vamorolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Vamorolone 4% oral suspension

Arm title	Dose level Group 3

Arm description:

2.0 mg/kg/day for 24 weeks

Arm type	Experimental

Investigational medicinal product name	Vamorolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:
Vamorolone 4% suspension

Arm title	Dose level Group 4

Arm description:
6.0 mg/kg/day for 24 weeks

Arm type	Experimental
Investigational medicinal product name	Vamorolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:
Vamorolone 4% oral suspension

Number of subjects in period 1	Dose level group 1	Dose level Group 2	Dose level Group 3
Started	12	12	12
Completed	12	12	12

Number of subjects in period 1	Dose level Group 4
Started	12
Completed	12

Baseline characteristics

Reporting groups	
Reporting group title	Dose level group 1
Reporting group description: 0.25 mg/kg/day for 24 weeks	
Reporting group title	Dose level Group 2
Reporting group description: 0.75 mg/kg/day for 24 weeks	
Reporting group title	Dose level Group 3
Reporting group description: 2.0 mg/kg/day for 24 weeks	
Reporting group title	Dose level Group 4
Reporting group description: 6.0 mg/kg/day for 24 weeks	

Reporting group values	Dose level group 1	Dose level Group 2	Dose level Group 3
Number of subjects	12	12	12
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)	12	12	12
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	12	12	12

Reporting group values	Dose level Group 4	Total	
Number of subjects	12	48	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	12	48	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	

85 years and over	0	0	

Gender categorical Units: Subjects			
Female	0	0	
Male	12	48	

End points

End points reporting groups

Reporting group title	Dose level group 1
Reporting group description: 0.25 mg/kg/day for 24 weeks	
Reporting group title	Dose level Group 2
Reporting group description: 0.75 mg/kg/day for 24 weeks	
Reporting group title	Dose level Group 3
Reporting group description: 2.0 mg/kg/day for 24 weeks	
Reporting group title	Dose level Group 4
Reporting group description: 6.0 mg/kg/day for 24 weeks	

Primary: Overall Summary of Adverse Events as Assessed by CTCAE Version 4.03

End point title	Overall Summary of Adverse Events as Assessed by CTCAE Version 4.03[1]

End point description:

Treatment-emergent adverse events (TEAEs) are defined as any adverse event or worsening of an existing conditions after initiation of the investigational product and through the subject's last study visit (study completion or early termination). Serious adverse events were recorded for up to 30 days after the final administration of study drug; To evaluate the long-term safety and tolerability of vamorolone, administered orally at daily doses up to 6.0 mg/kg/day over a 24- week Treatment Period, in boys ages 4-7 years with DMD.

End point type	Primary

End point timeframe:

24 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Treatment levels were not compared.

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: Number of Events Reported				
Total Number of AEs	48	44	54	73
Total Number of TEAEs	48	44	54	72
Subjects with Any TEAE	10	10	11	11
Subjects with Any Drug Related TEAE	1	2	4	5
Subjects with Any CTCAE Grade 3 or Higher TEAE	0	0	0	2
Discontinuation of Study Drug due to TEAE	0	0	0	0
Subjects with Any Serious TEAE	0	1	0	2
Death	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Muscle function measured by Time to Stand Test (TTSTAND)- Velocity

End point title	Muscle function measured by Time to Stand Test (TTSTAND)-Velocity

End point description:

To compare the efficacy, as measured by the Time to Stand Test (TTSTAND), of vamorolone administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period vs. untreated DMD historical controls in boys ages 4-7 years with DMD

End point type	Primary

End point timeframe:

24 weeks

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: rises/second				
arithmetic mean (standard deviation)				
002 Baseline	0.18 (± 0.065)	0.24 (± 0.090)	0.22 (± 0.082)	0.19 (± 0.056)
003 Baseline	0.15 (± 0.045)	0.22 (± 0.077)	0.24 (± 0.078)	0.22 (± 0.070)
003 Week 12	0.18 (± 0.072)	0.23 (± 0.102)	0.24 (± 0.089)	0.22 (± 0.075)
003 Week 12 Change from 002 Baseline	-0.01 (± 0.061)	0.00 (± 0.054)	0.02 (± 0.066)	0.02 (± 0.034)
003 Week 24	0.18 (± 0.081)	0.24 (± 0.114)	0.26 (± 0.108)	0.24 (± 0.086)
003 Week 24 Change from 002 Baseline	-0.01 (± 0.066)	0.00 (± 0.062)	0.05 (± 0.061)	0.04 (± 0.045)

Statistical analyses

Statistical analysis title	Week 24 Change from 002 baseline
Comparison groups	Dose level Group 2 v Dose level group 1 v Dose level Group 3 v Dose level Group 4

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0192 [2]
Method	Mixed models analysis

Notes:

[2] - Group 1 compared to Group 3

Primary: Safety as Measured by BMI Z-score

End point title	Safety as Measured by BMI Z-score

End point description:

To compare the safety, as measured by body mass index (BMI) z-score, of vamorolone administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period vs. prednisone-treated historical controls in boys ages 4-7 years with DMD.

End point type	Primary

End point timeframe:

24 weeks

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: unitless				
arithmetic mean (standard deviation)				
002 Baseline	1.165 (± 0.6219)	0.703 (± 1.0738)	1.200 (± 0.5325)	0.695 (± 0.7189)
003 Week 12	1.103 (± 0.6457)	0.494 (± 1.0680)	1.261 (± 0.3981)	1.011 (± 0.7034)
003 Week 12 Change from 002 Baseline	-0.062 (± 0.2438)	-0.209 (± 0.4078)	0.062 (± 0.3886)	0.174 (± 0.5826)
003 Week 24	1.004 (± 0.6381)	0.493 (± 1.1696)	1.242 (± 0.4596)	1.330 (± 0.5857)
003 Week 24 Change from 002 Baseline	-0.161 (± 0.3234)	-0.210 (± 0.3629)	0.043 (± 0.3849)	0.493 (± 0.6363)

Statistical analyses

Statistical analysis title	Week 24 Change from 002 baseline
Comparison groups	Dose level group 1 v Dose level Group 2 v Dose level Group 3 v Dose level Group 4
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [3]
Method	Mixed models analysis

Notes:

[3] - Dose level group 1 vs. dose level group 4

Secondary: Serum Pharmacodynamics Biomarkers Measured by Levels of ACTH

End point title	Serum Pharmacodynamics Biomarkers Measured by Levels of ACTH

End point description:

To investigate the effects of vamorolone, administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period vs. prednisone-treated historical controls, on serum pharmacodynamic (PD) biomarkers of safety (insulin resistance, adrenal axis suppression, and bone turnover). SomaScan aptamer panels testing 1,200 serum proteins were used to discover a candidate set of prednisone-responsive biomarkers, with a subset of these validating in a longitudinal sample set (individual DMD patients pre/post steroid treatment). These PD biomarkers were assigned to a safety panel or efficacy panel based on comparison to normal controls and information concerning the function of each protein.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: pg/mL				
arithmetic mean (standard deviation)				
002 Baseline	18.3 (± 2.96)	18.0 (± 6.88)	21.1 (± 6.13)	19.3 (± 8.67)
003 Baseline	15.9 (± 4.52)	18.6 (± 4.56)	18.2 (± 5.29)	18.4 (± 9.73)
003 Week 8	13.0 (± 6.25)	7.1 (± 5.84)	7.8 (± 4.42)	6.5 (± 5.23)
003 Week 8 Change from 002 Baseline	-5.3 (± 6.92)	-10.5 (± 9.32)	-13.3 (± 7.33)	-13.5 (± 7.84)
003 Week 8 Percent Change from 002 Baseline	-27.1 (± 40.94)	-54.2 (± 36.34)	-61.9 (± 21.34)	-67.7 (± 24.09)
003 Week 16	12.2 (± 4.93)	9.0 (± 5.86)	9.0 (± 14.18)	9.0 (± 4.49)
003 Week 16 Change from 002 Baseline	-6.2 (± 6.34)	-9.1 (± 9.89)	-12.0 (± 15.42)	-12.2 (± 8.16)
003 Week 16 Percent Change from 002 Baseline	-30.6 (± 35.64)	-42.8 (± 44.91)	-55.7 (± 64.72)	-56.0 (± 22.61)
003 Week 24	19.8 (± 6.32)	14.0 (± 3.88)	15.7 (± 9.63)	11.3 (± 7.52)
003 Week 24 Change from 002 Baseline	0.6 (± 6.63)	-4.0 (± 5.48)	-5.4 (± 11.09)	-6.3 (± 7.78)
003 Week 24 Percent Change from 002 Baseline	4.9 (± 37.93)	-18.6 (± 19.99)	-21.3 (± 50.74)	-34.3 (± 49.52)
003 Week 26-29	9.5 (± 7.26)	0 (± 0)	0 (± 0)	0 (± 0)
003 Week 26-29 Change from 002 Baseline	-7.8 (± 4.19)	0 (± 0)	0 (± 0)	0 (± 0)
003 Week 26-29 Percent Change from 002 Baseline	-49.5 (± 33.00)	0 (± 0)	0 (± 0)	0 (± 0)

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Pharmacodynamics Biomarkers Measured by Levels of Fasting Glucose

End point title	Serum Pharmacodynamics Biomarkers Measured by Levels of Fasting Glucose

End point description:

To investigate the effects of vamorolone, administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period vs. prednisone-treated historical controls, on serum pharmacodynamic (PD) biomarkers of safety (insulin resistance, adrenal axis suppression, and bone turnover). SomaScan aptamer panels testing 1,200 serum proteins were used to discover a candidate set of prednisone-responsive biomarkers, with a subset of these validating in a longitudinal sample set (individual DMD patients pre/post steroid treatment). These PD biomarkers were assigned to a safety panel or efficacy panel based on comparison to normal controls and information concerning the function of each protein.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: mg/dL				
arithmetic mean (standard deviation)				
002 Baseline	87.5 (± 9.44)	88.9 (± 18.71)	89.3 (± 7.91)	92.3 (± 8.19)
003 Week 12	81.5 (± 5.61)	81.7 (± 4.35)	84.3 (± 8.13)	86.5 (± 5.57)
003 Week 12 Change from 002 Baseline	-6.8 (± 8.29)	-7.6 (± 19.22)	-5.1 (± 9.01)	-5.2 (± 9.21)
003 Week 12 Percent Change from 002 Baseline	-7.0 (± 8.95)	-5.8 (± 13.93)	-5.3 (± 9.41)	-5.0 (± 9.95)
003 Week 24	80.8 (± 6.56)	80.8 (± 4.08)	81.3 (± 7.94)	84.6 (± 6.53)
003 Week 24 Change from 002 Baseline	-6.3 (± 11.97)	-9.0 (± 20.87)	-8.1 (± 10.28)	-7.8 (± 9.44)
003 Week 24 Percent Change from 002 Baseline	-6.1 (± 13.69)	-7.0 (± 15.41)	-8.6 (± 10.73)	-7.9 (± 9.96)

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Pharmacodynamics Biomarkers Measured by Levels of Fasting Insulin

End point title	Serum Pharmacodynamics Biomarkers Measured by Levels of Fasting Insulin

End point description:

To investigate the effects of vamorolone, administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period vs. prednisone-treated historical controls, on serum pharmacodynamic (PD) biomarkers of safety (insulin resistance, adrenal axis suppression, and bone turnover). SomaScan aptamer panels testing 1,200 serum proteins were used to discover a candidate set of prednisone-responsive biomarkers, with a subset of these validating in a longitudinal sample set (individual DMD patients pre/post steroid treatment). These PD biomarkers were assigned to a safety panel or efficacy panel based on comparison to normal controls and information concerning the function of each protein.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: UIU/mL				
arithmetic mean (standard deviation)				
002 Baseline	5.54 (± 3.651)	3.09 (± 2.033)	3.40 (± 1.548)	3.96 (± 2.027)
003 Week 12	4.17 (± 3.167)	2.97 (± 1.669)	3.89 (± 2.189)	6.97 (± 3.526)
003 Week 12 Change from 002 Baseline	-1.13 (± 3.822)	-0.14 (± 1.756)	0.49 (± 2.592)	2.97 (± 2.277)
003 Week 12 Percent Change from 002 Baseline	-12.70 (± 50.989)	9.35 (± 64.450)	50.96 (± 135.187)	85.79 (± 76.416)
003 Week 24	4.23 (± 2.560)	3.12 (± 1.788)	4.82 (± 3.393)	7.21 (± 2.374)
003 Week 24 Change from 002 Baseline	-1.67 (± 4.478)	0.34 (± 2.898)	1.36 (± 3.262)	3.26 (± 2.862)
003 Week 24 Percent Change from 002 Baseline	-15.83 (± 50.754)	53.32 (± 121.763)	60.57 (± 114.769)	121.34 (± 107.414)

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Pharmacodynamics Biomarkers Measured by Levels of HbA1c

End point title	Serum Pharmacodynamics Biomarkers Measured by Levels of HbA1c

End point description:

To investigate the effects of vamorolone, administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period vs. prednisone-treated historical controls, on serum pharmacodynamic (PD) biomarkers of safety (insulin resistance, adrenal axis suppression, and bone turnover). SomaScan aptamer panels testing 1,200 serum proteins were used to discover a candidate set of prednisone-responsive biomarkers, with a subset of these validating in a longitudinal sample set (individual DMD patients pre/post steroid treatment). These PD biomarkers were assigned to a safety panel or efficacy panel based on comparison to normal controls and information concerning the function of each protein.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: Percent Hemoglobin A1C				
arithmetic mean (standard deviation)				
002 Baseline	5.18 (± 0.260)	5.22 (± 0.244)	5.19 (± 0.124)	5.23 (± 0.231)
003 Week 8	5.18 (± 0.226)	5.33 (± 0.250)	5.28 (± 0.204)	5.25 (± 0.216)
003 Week 8 Change from 002 Baseline	0.00 (± 0.128)	0.12 (± 0.153)	0.09 (± 0.198)	0.00 (± 0.100)
003 Week 8 Percent Change from 002 Baseline	0.06 (± 2.470)	2.28 (± 3.008)	1.79 (± 3.864)	0.02 (± 1.927)
003 Week 16	5.26 (± 0.239)	5.35 (± 0.238)	5.26 (± 0.156)	5.31 (± 0.270)
003 Week 16 Change from 002 Baseline	0.08 (± 0.204)	0.14 (± 0.225)	0.07 (± 0.130)	0.05 (± 0.113)

003 Week 16 Percent Change from 002 Baseline	1.70 (± 3.989)	2.72 (± 4.457)	1.30 (± 2.505)	1.03 (± 2.147)
003 Week 24	5.15 (± 0.302)	5.22 (± 0.221)	5.13 (± 0.160)	5.24 (± 0.254)
003 Week 24 Change from 002 Baseline	-0.10 (± 0.220)	0.00 (± 0.186)	-0.07 (± 0.130)	-0.02 (± 0.154)
003 Week 24 Percent Change from 002 Baseline	-1.89 (± 4.081)	0.08 (± 3.628)	-1.27 (± 2.525)	-0.33 (± 2.895)
003 Week 26-29	5.07 (± 0.208)	0 (± 0)	0 (± 0)	0 (± 0)
003 Week 26-29 Change from 002 Baseline	-0.07 (± 0.208)	0 (± 0)	0 (± 0)	0 (± 0)
003 Week 26-29 Percent Change from 002 Baseline	-1.25 (± 3.942)	0 (± 0)	0 (± 0)	0 (± 0)

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Pharmacodynamics Biomarkers Measured by Levels of Osteocalcin

End point title	Serum Pharmacodynamics Biomarkers Measured by Levels of Osteocalcin

End point description:

To investigate the effects of vamorolone, administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period vs. prednisone-treated historical controls, on serum pharmacodynamic (PD) biomarkers of safety (insulin resistance, adrenal axis suppression, and bone turnover). SomaScan aptamer panels testing 1,200 serum proteins were used to discover a candidate set of prednisone-responsive biomarkers, with a subset of these validating in a longitudinal sample set (individual DMD patients pre/post steroid treatment). These PD biomarkers were assigned to a safety panel or efficacy panel based on comparison to normal controls and information concerning the function of each protein.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: ng/mL				
arithmetic mean (standard deviation)				
002 Baseline	37.94 (± 11.622)	35.66 (± 6.800)	41.17 (± 5.617)	44.36 (± 5.979)
003 Baseline	39.20 (± 14.136)	41.84 (± 8.552)	47.91 (± 6.648)	42.81 (± 10.851)
003 Week 8	36.21 (± 10.374)	41.78 (± 13.856)	44.45 (± 7.439)	41.55 (± 5.446)
003 Week 8 Change from 002 Baseline	-1.60 (± 8.849)	6.13 (± 10.440)	3.28 (± 8.325)	-2.01 (± 8.898)
003 Week 8 Percent Change from 002 Baseline	-1.16 (± 22.132)	16.51 (± 27.717)	9.34 (± 23.470)	-2.82 (± 20.662)
003 Week 16	39.01 (± 9.620)	42.23 (± 9.393)	44.60 (± 9.534)	39.39 (± 6.972)
003 Week 16 Change from 002 Baseline	1.07 (± 9.916)	6.57 (± 6.709)	3.43 (± 10.718)	-4.17 (± 8.494)

003 Week 16 Percent Change from 002 Baseline	7.48 (± 31.539)	18.93 (± 20.384)	10.09 (± 26.893)	-8.52 (± 19.797)
003 Week 24	38.80 (± 6.292)	51.41 (± 11.265)	51.98 (± 9.372)	49.08 (± 7.771)
003 Week 24 Change from 002 Baseline	-1.34 (± 11.289)	15.75 (± 10.211)	10.81 (± 7.542)	5.29 (± 7.858)
003 Week 24 Percent Change from 002 Baseline	2.52 (± 26.344)	46.30 (± 32.470)	26.61 (± 17.650)	13.10 (± 19.573)
003 Week 26-29	40.10 (± 18.729)	0 (± 0)	0 (± 0)	0 (± 0)
003 Week 26-29 Change from 002 Baseline	-1.23 (± 17.943)	0 (± 0)	0 (± 0)	0 (± 0)
003 Week 26-29 Percent Change from 002 Baseline	-0.58 (± 49.574)	0 (± 0)	0 (± 0)	0 (± 0)

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Pharmacodynamics Biomarkers Measured by Levels of P1NP

End point title	Serum Pharmacodynamics Biomarkers Measured by Levels of P1NP

End point description:

To investigate the effects of vamorolone, administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period vs. prednisone-treated historical controls, on serum pharmacodynamic (PD) biomarkers of safety (insulin resistance, adrenal axis suppression, and bone turnover). SomaScan aptamer panels testing 1,200 serum proteins were used to discover a candidate set of prednisone-responsive biomarkers, with a subset of these validating in a longitudinal sample set (individual DMD patients pre/post steroid treatment). These PD biomarkers were assigned to a safety panel or efficacy panel based on comparison to normal controls and information concerning the function of each protein.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: ng/mL				
arithmetic mean (standard deviation)				
002 Baseline	555.8 (± 184.72)	480.7 (± 118.20)	508.2 (± 94.36)	511.5 (± 106.50)
003 Baseline	573.8 (± 251.02)	489.3 (± 121.66)	492.0 (± 81.92)	566.3 (± 149.32)
003 Week 8	511.6 (± 190.94)	459.8 (± 101.93)	485.2 (± 105.12)	402.7 (± 70.46)
003 Week 8 Change from 002 Baseline	-20.3 (± 120.32)	-22.9 (± 128.79)	-23.0 (± 96.84)	-105.6 (± 121.07)
003 Week 8 Percent Change from 002 Baseline	-3.5 (± 24.14)	-1.1 (± 27.39)	-2.8 (± 20.99)	-18.1 (± 19.46)
003 Week 16	481.9 (± 159.93)	431.8 (± 81.25)	455.7 (± 99.50)	488.5 (± 130.11)

003 Week 16 Change from 002 Baseline	-73.8 (± 109.31)	-42.4 (± 109.07)	-52.5 (± 104.05)	-19.8 (± 130.12)
003 Week 16 Percent Change from 002 Baseline	-12.1 (± 18.25)	-5.1 (± 25.62)	-8.6 (± 20.91)	-2.3 (± 26.63)
003 Week 24	457.1 (± 129.21)	471.1 (± 121.10)	565.5 (± 158.89)	526.2 (± 130.18)
003 Week 24 Change from 002 Baseline	-30.8 (± 113.64)	2.1 (± 165.16)	57.3 (± 150.36)	8.7 (± 88.95)
003 Week 24 Percent Change from 002 Baseline	-6.2 (± 22.42)	6.3 (± 38.81)	13.2 (± 30.95)	2.2 (± 18.51)
003 Week 26-29	619.0 (± 379.07)	0 (± 0)	0 (± 0)	0 (± 0)
003 Week 26-29 Change from 002 Baseline	-152.0 (± 331.46)	0 (± 0)	0 (± 0)	0 (± 0)
003 Week 26-29 Percent Change from 002 Baseline	-16.5 (± 42.70)	0 (± 0)	0 (± 0)	0 (± 0)

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Pharmacodynamics Biomarkers Measured by Levels of CTX

End point title	Serum Pharmacodynamics Biomarkers Measured by Levels of CTX

End point description:

To investigate the effects of vamorolone, administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period vs. prednisone-treated historical controls, on serum pharmacodynamic (PD) biomarkers of safety (insulin resistance, adrenal axis suppression, and bone turnover). SomaScan aptamer panels testing 1,200 serum proteins were used to discover a candidate set of prednisone-responsive biomarkers, with a subset of these validating in a longitudinal sample set (individual DMD patients pre/post steroid treatment). These PD biomarkers were assigned to a safety panel or efficacy panel based on comparison to normal controls and information concerning the function of each protein.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: pg/mLd				
arithmetic mean (standard deviation)				
002 Baseline	871.0 (± 160.85)	935.8 (± 286.50)	936.8 (± 256.25)	889.3 (± 186.68)
003 Baseline	915.9 (± 263.13)	964.4 (± 319.26)	949.8 (± 303.76)	989.2 (± 216.29)
003 Week 8	897.1 (± 365.45)	933.3 (± 330.20)	928.3 (± 333.11)	825.5 (± 164.36)
003 Week 8 Change from 002 Baseline	26.1 (± 368.76)	-31.6 (± 236.34)	-8.5 (± 248.82)	-59.6 (± 259.08)
003 Week 8 Percent Change from 002 Baseline	3.9 (± 39.76)	-1.2 (± 26.23)	0.2 (± 26.94)	-2.4 (± 30.39)

003 Week 16	885.4 (± 261.53)	912.8 (± 305.08)	939.8 (± 157.17)	953.7 (± 199.53)
003 Week 16 Change from 002 Baseline	-2.6 (± 304.50)	-46.3 (± 321.06)	3.0 (± 244.17)	102.3 (± 230.44)
003 Week 16 Percent Change from 002 Baseline	2.2 (± 33.71)	-1.2 (± 32.64)	5.4 (± 26.64)	15.6 (± 35.06)
003 Week 24	1109.3 (± 287.92)	1235.6 (± 295.79)	1248.7 (± 308.90)	1237.0 (± 277.20)
003 Week 24 Change from 002 Baseline	212.3 (± 318.86)	295.6 (± 357.93)	346.5 (± 327.16)	321.4 (± 264.65)
003 Week 24 Percent Change from 002 Baseline	26.2 (± 35.61)	39.8 (± 43.14)	43.0 (± 38.40)	37.5 (± 31.68)
003 Week 26-29	1059.3 (± 536.26)	0 (± 0)	0 (± 0)	0 (± 0)
003 Week 26-29 Change from 002 Baseline	569.5 (± 28.99)	0 (± 0)	0 (± 0)	0 (± 0)
003 Week 26-29 Percent Change from 002 Baseline	73.4 (± 18.15)	0 (± 0)	0 (± 0)	0 (± 0)

Statistical analyses

No statistical analyses for this end point

Secondary: Muscle Strength, Mobility, and Functional Exercise Capacity as Measured by Time to Climb Test (TTCLIMB)- Velocity

End point title	Muscle Strength, Mobility, and Functional Exercise Capacity as Measured by Time to Climb Test (TTCLIMB)- Velocity

End point description:

To investigate the effects of vamorolone, administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period, on muscle strength, mobility and functional exercise capacity vs. historical controls as measured by Time to Climb Test (TTCLIMB) in boys ages 4-7 years with DMD.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: tasks/ second				
arithmetic mean (standard deviation)				
002 Baseline	0.20 (± 0.054)	0.29 (± 0.147)	0.29 (± 0.164)	0.24 (± 0.086)
003 Baseline	0.20 (± 0.065)	0.29 (± 0.168)	0.31 (± 0.144)	0.25 (± 0.082)
003 Week 12	0.21 (± 0.064)	0.34 (± 0.238)	0.31 (± 0.157)	0.26 (± 0.095)
003 Week 12 Change from 002 Baseline	0.01 (± 0.044)	0.05 (± 0.115)	0.02 (± 0.107)	0.02 (± 0.051)
003 Week 24	0.20 (± 0.071)	0.30 (± 0.166)	0.34 (± 0.148)	0.29 (± 0.097)
003 Week 24 Change from 002 Baseline	0.00 (± 0.076)	0.01 (± 0.066)	0.04 (± 0.090)	0.05 (± 0.061)

Statistical analyses

No statistical analyses for this end point

Secondary: Muscle Strength, Mobility, and Functional Exercise Capacity as Measured by Time to Run/Walk 10 Meters Test (TTRW)- Velocity

End point title	Muscle Strength, Mobility, and Functional Exercise Capacity as Measured by Time to Run/Walk 10 Meters Test (TTRW)- Velocity

End point description:

To investigate the effects of vamorolone, administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period, on muscle strength, mobility and functional exercise capacity vs. historical controls as measured by Time to Run/Walk Test (TTRW) in boys ages 4-7 years with DMD.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: meters/second				
arithmetic mean (standard deviation)				
002 Baseline	1.60 (± 0.312)	1.77 (± 0.367)	1.84 (± 0.347)	1.64 (± 0.279)
003 Baseline	1.57 (± 0.371)	1.78 (± 0.414)	1.86 (± 0.418)	1.72 (± 0.295)
003 Week 12	1.54 (± 0.306)	1.77 (± 0.550)	1.97 (± 0.503)	1.88 (± 0.341)
003 Week 12 Change from 002 Baseline	-0.06 (± 0.261)	0.00 (± 0.307)	0.13 (± 0.316)	0.26 (± 0.297)
003 Week 24	1.55 (± 0.384)	1.84 (± 0.486)	1.90 (± 0.321)	1.89 (± 0.378)
003 Week 24 Change from 002 Baseline	-0.05 (± 0.311)	0.06 (± 0.210)	0.06 (± 0.210)	0.27 (± 0.254)

Statistical analyses

No statistical analyses for this end point

Secondary: Muscle Strength, Mobility, and Functional Exercise Capacity as Measured by North Star Ambulatory Assessment (NSAA)

End point title	Muscle Strength, Mobility, and Functional Exercise Capacity as Measured by North Star Ambulatory Assessment (NSAA)

End point description:

To investigate the effects of vamorolone, administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period, on muscle strength, mobility and functional exercise capacity vs. historical controls as measured by North Star Ambulatory Assessment (NSAA) in boys ages 4-7 years with DMD.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: total score				
arithmetic mean (standard deviation)				
002 Baseline	19.0 (± 5.13)	20.5 (± 5.58)	20.0 (± 4.95)	19.7 (± 4.94)
003 Baseline	20.1 (± 7.30)	20.8 (± 5.66)	21.7 (± 3.87)	20.4 (± 4.01)
003 Week 12	19.3 (± 5.60)	21.2 (± 6.45)	21.0 (± 5.13)	20.4 (± 5.41)
003 Week 12 Change from 002 Baseline	0.3 (± 2.06)	0.7 (± 2.71)	1.0 (± 2.56)	0.5 (± 2.38)
003 Week 24	19.8 (± 7.09)	21.6 (± 7.23)	22.3 (± 3.80)	22.3 (± 5.76)
003 Week 24 Change from 002 Baseline	0.8 (± 2.83)	1.1 (± 2.94)	2.3 (± 1.78)	2.5 (± 2.62)

Statistical analyses

No statistical analyses for this end point

Secondary: Muscle Strength, Mobility, and Functional Exercise Capacity vs. Historical Controls as Measured by 6-minute Walk Test (6MWT)

End point title	Muscle Strength, Mobility, and Functional Exercise Capacity vs. Historical Controls as Measured by 6-minute Walk Test (6MWT)

End point description:

To investigate the effects of vamorolone, administered orally at daily doses up to 6.0 mg/kg over a 24-week Treatment Period, on muscle strength, mobility and functional exercise capacity vs. historical controls as measured by 6-minute Walk Test (6MWT) in boys ages 4-7 years with DMD.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Dose level group 1	Dose level Group 2	Dose level Group 3	Dose level Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: meters				
arithmetic mean (standard deviation)				
002 Baseline	316.2 (± 59.47)	331.5 (± 52.76)	353.9 (± 65.40)	336.8 (± 63.18)
003 Baseline	294.3 (± 60.62)	332.2 (± 56.83)	341.1 (± 49.42)	335.1 (± 80.13)
003 Week 12	312.9 (± 60.93)	358.7 (± 71.47)	393.7 (± 59.72)	369.9 (± 69.47)
003 Week 12 Change from 002 Baseline	6.0 (± 28.81)	20.8 (± 38.09)	39.8 (± 35.61)	27.6 (± 42.0)
003 Week 24	306.2 (± 68.08)	350.4 (± 64.23)	383.1 (± 63.38)	372.6 (± 69.12)
003 Week 24 Change from 002 Baseline	-11.6 (± 29.45)	18.9 (± 41.08)	29.2 (± 35.91)	43.9 (± 43.72)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events, including Serious Adverse Events (SAEs), and concomitant medications will be assessed at each study visit and
recorded throughout the study starting from Treatment Period Day 1.

Adverse event reporting additional description:

Adverse events will be summarized overall and by dose level, system organ class (SOC) and preferred term (using the Medical Dictionary for Regulatory Activities [MedDRA]); by dose level and relationship to study medication; and by dose level and intensity (CTCAE grade).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Dose Group 1
Reporting group description: -	
Reporting group title	Dose Group 2
Reporting group description: -	
Reporting group title	Dose Group 3
Reporting group description: -	
Reporting group title	Dose Group 4

Reporting group description: -

Serious adverse events	Dose Group 1	Dose Group 2	Dose Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Reproductive system and breast disorders			
Testicular torsion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Dose Group 4		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 12 (16.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Reproductive system and breast disorders			
Testicular torsion			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Dose Group 1	Dose Group 2	Dose Group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 12 (83.33%)	10 / 12 (83.33%)	11 / 12 (91.67%)
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	2 / 12 (16.67%)	7 / 12 (58.33%)	5 / 12 (41.67%)
occurrences (all)	2	7	5
Thirst			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Testicular torsion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 12 (8.33%)	4 / 12 (33.33%)	1 / 12 (8.33%)
occurrences (all)	1	4	1
Epistaxis			

subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hypoxia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 12 (0.00%)	2 / 12 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
abnormal behaviour			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Emotional disorder			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Personality change			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Stereotypy			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Tic			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood cortisol abnormal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urine output increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Weight increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Foot fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Human bite			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Laceration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	1 / 12 (8.33%)	2 / 12 (16.67%)	0 / 12 (0.00%)
occurrences (all)	1	2	0
Tendon injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture			

subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Left ventricular dysfunction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
Presyncope			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Psychomotor hyperactivity			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Eye disorders			
Excessive eye blinking			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain upper			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1

Diarrhoea			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	2	0	2
Faeces discoloured			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Lip swelling			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)	1 / 12 (8.33%)	3 / 12 (25.00%)
occurrences (all)	1	1	3
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dermatitis contact			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hypertrichosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			

subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Swelling face			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Uriticaria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Tendon pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			

subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	1	0	2
Ear infection			
subjects affected / exposed	1 / 12 (8.33%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gastroenteritis viral			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hordeolum			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Otitis media			
subjects affected / exposed	1 / 12 (8.33%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Pharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Pharyngitis streptococcal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Sinusitis bacterial			

subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Staphylococcal skin infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
Viral infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 12 (33.33%)	4 / 12 (33.33%)	7 / 12 (58.33%)
occurrences (all)	4	4	7
Enterobiasis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Eye infection			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hyperlipidaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Neck pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Dose Group 4		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)		
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Thirst			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Testicular torsion			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Epistaxis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypoxia			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Upper-airway cough syndrome			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
abnormal behaviour			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Emotional disorder			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Personality change			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Stereotypy			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Tic			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Investigations			
Blood cortisol abnormal			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Urine output increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Foot fracture			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Human bite			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Laceration			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Muscle strain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Tendon injury			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Upper limb fracture			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Cardiac disorders			

Left ventricular dysfunction subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Presyncope subjects affected / exposed occurrences (all) Psychomotor hyperactivity subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1		
Eye disorders Excessive eye blinking subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0		
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Abdominal Pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 2 / 12 (16.67%) 2 2 / 12 (16.67%) 2 1 / 12 (8.33%) 1		

Faeces discoloured			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Gastrointestinal disorder			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Lip swelling			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Dermatitis contact			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypertrichosis			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Rash pruritic			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Swelling face			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Uriticaria			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Endocrine disorders			
Cushingoid			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Pain in jaw			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Tendon pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Ear infection			

subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Gastroenteritis				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Gastroenteritis viral				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Gastrointestinal infection				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Hordeolum				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Influenza				
subjects affected / exposed	3 / 12 (25.00%)			
occurrences (all)	3			
Otitis media				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Pharyngitis				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Pharyngitis streptococcal				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Sinusitis				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Sinusitis bacterial				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Staphylococcal skin infection				

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Viral infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	5 / 12 (41.67%)		
occurrences (all)	5		
Enterobiasis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Eye infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hyperlipidaemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Vitamin D deficiency			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported