Clinical trial results:
A Phase 2, Multicenter, Multinational, Open-Label, Dose-Escalation Study to Evaluate the Safety and Efficacy of ORGN001 (formerly ALXN1101) in Pediatric Patients with Molybdenum Cofactor Deficiency (MoCD) Type A Currently Treated with Recombinant Escherichia Coli-Derived Cyclic Pyranopterin Monophosphate (rcPMP)

Summary

EudraCT number	2013-002701-56
Trial protocol	GB NL
Global end of trial date	15 August 2022

Results information

Result version number	v1 (current)
This version publication date	17 September 2023
First version publication date	17 September 2023

Trial information

Trial identification

Sponsor protocol code	ALXN1101-MCD-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02047461
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Origin Biosciences (affiliate of BridgeBio)
Sponsor organisation address	Suite 250, 3160 Porter Drive, Palo Alto, CA, United States, 94304
Public contact	Business Development and Operations, Origin Biosciences (affiliate of BridgeBio), +1 650-391-9740,
Scientific contact	Business Development and Operations, Origin Biosciences (affiliate of BridgeBio), +1 650-391-9740,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001491-PIP01-13
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	24 May 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 August 2022
Global end of trial reached?	Yes
Global end of trial date	15 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this clinical study was to evaluate the safety of fosdenopterin over the first 6 months of treatment.

Protection of trial subjects:

The study was conducted in accordance with Good Clinical Practice (GCP) and the Declaration of Helsinki.

Background therapy: -

Evidence for comparator:

A placebo-controlled study would not have been appropriate due to the severity of the untreated disease and the reported improved outcomes of newborn infants with MoCD Type A who were treated with rcPMP. An active comparator study was not feasible due to the lack of an approved treatment for MoCD Type A.

Actual start date of recruitment	01 February 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	72 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Tunisia: 1
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	8
EEA total number of subjects	2

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)	2
Children (2-11 years)	6
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:

A total of 8 subjects were enrolled and analyzed. The subjects were recruited from Australia, Tunisia, the Netherlands, United Kingdom, and USA.

Pre-assignment

Screening details:

Subject screening evaluations were performed at any time during the screening period (Days -21 to -1) before the 1st dose of fosdenopterin. Enrolled patients attended at least 2 study visits for baseline data collection. Subjects continued to receive daily IV infusions of their current rcPMP treatment during the screening period.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Arm title	Subjects Receiving rcPMP and transitioned to ORGN001

Arm description:

Patients currently receiving rcPMP infusions at baseline are transitioned to ORGN001(formerly ALXN1101), starting at their current rcPMP dose and escalating to a target dose of 0.9 mg/kg per protocol

Arm type	Experimental
Investigational medicinal product name	Fosdenopterin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Infusion

Dosage and administration details:

Fosdenopterin (2.5 mg/vial and 12.5 mg/vial), Dose level: same as current dose of rcPMP, IV infusion, approximately 24 (+-3) hours after the last rcPMP treatment, daily.
After 2 months of treatment, Fosdenopterin (2.5 mg/vial and 12.5 mg/vial), Dose level: escalation each month as per protocol (but no more than 240 µg/kg/Day), IV infusion, daily.

Number of subjects in period 1	Subjects Receiving rcPMP and transitioned to ORGN001
Started	8
Completed	8

Baseline characteristics

Reporting groups

Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	8	8	
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)	2	2	
Children (2-11 years)	6	6	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: months			
arithmetic mean	45.2		
standard deviation	± 22.96	-	
Gender categorical Units: Subjects			
Female	5	5	
Male	3	3	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	8	8	
Not Reported	0	0	
Missing/Unknown	0	0	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	3	3	
Black or African American	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
White	5	5	
Other	0	0	
Missing/Unknown	0	0	

End points

End points reporting groups

Reporting group title	Subjects Receiving rcPMP and transitioned to ORGN001
Reporting group description:	
Patients currently receiving rcPMP infusions at baseline are transitioned to ORGN001(formerly ALXN1101), starting at their current rcPMP dose and escalating to a target dose of 0.9 mg/kg per protocol	

Primary: Safety of ORGN001 (Formerly ALXN1101)

End point title	Safety of ORGN001 (Formerly ALXN1101)[1]
End point description:	
Treatment Emergent Serious Adverse Events	
End point type	Primary
End point timeframe:	
Baseline to Study Completion (full study duration)	

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: No formal statistical hypothesis testing will be performed. Efficacy data will be analyzed using descriptive statistics. All data collected during the study will be presented in summary tables, figures, or by-subject data listings. Continuous variables will be summarized using mean, SD, median, minimum, and maximum. Categorical variables will be summarized using percentages and frequency distributions. Graphical displays will be produced as appropriate.

End point values	Subjects Receiving rcPMP and transitioned to ORGN001			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: number of subjects affected				
Gastrointestinal disorders	1			
General disorders and administration site conditio	5			
Infections and infestations	6			
Injury, poisoning and procedural complications	2			
Metabolism and nutrition disorders	2			
Musculoskeletal and connective tissue disorders	1			
Nervous system disorders	2			
Product issues	2			
Respiratory, thoracic and mediastinal disorders	2			
Skin and subcutaneous tissue disorders	1			
Surgical and medical procedures	1			
Vascular disorders	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (Actual Plasma Concentration) of ORGN001 (Formerly ALXN1101)

End point title	Pharmacokinetics (Actual Plasma Concentration) of ORGN001 (Formerly ALXN1101)

End point description:

ORGN001 levels by dose at pre-infusion and end of infusion (EOI) atscheduled timepoints.

Measurement is actual plasma concentration of ORGN001 at measured timepoints,starting at their current rcPMP dose. 6 subjects started at a dose of 240 mcg/kg, 1 subject at 248 mcg/kg, and 1 subject at 280 mcg/kg. (EOI = End of Infusion). 1 subject is missing a pre-infusion dose measurement.

End point type	Secondary

End point timeframe:

First 6 months at each dose level, where available

End point values	Subjects Receiving rcPMP and transitioned to ORGN001			
Subject group type	Reporting group			
Number of subjects analysed	8[2]			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1 Pre-infusion(240mcg/kg) (6 subjects)	3.95 (± 9.68)			
Day 1 Pre-infusion(248mcg/kg) (1 subjects)	0 (± 0)			
Day 1 EOI(240mcg/kg) (6 subjects)	669.00 (± 236.06)			
Day 1 EOI(248mcg/kg) (1 subject)	980.00 (± 0.00)			
Day 1 EOI(280mcg/kg) (1 subject)	770.00 (± 0.00)			
Day 7 EOI(240mcg/kg) (6 subjects)	669.50 (± 246.72)			
Day 7 EOI(248mcg/kg) (1 subject)	694.00 (± 0.00)			
Day 7 EOI(280mcg/kg) (1 subject)	938.00 (± 0.00)			
Day 60 EOI(480mcg/kg) (5 subjects)	880.84 (± 558.56)			
Day 90 EOI(240mcg/kg) (1 subject)	1230.00 (± 0.00)			
Day 90 EOI(480mcg/kg) (1 subject)	762.00 (± 0.00)			
Day 90 EOI(720mcg/kg) (6 subjects)	1888.33 (± 271.10)			
Day 120EOI (480mcg/kg) (1 subject)	2810.00 (± 0.00)			
Day 120EOI (720mcg/kg) (1 subject)	671.00 (± 0.00)			
Day 120EOI (960mcg/kg) (6 subjects)	4213.33 (± 4520.31)			

Day 150EOI (720mcg/kg) (1 subject)	3810.00 (± 0.00)			
Day 150EOI (960mcg/kg) (3 subjects)	2045.67 (± 1009.85)			
Day 150EOI (1200mcg/kg) (3 subjects)	3173.33 (± 656.53)			
Month 66 EOI (1200mcg/kg) (2 subjects)	2450.00 (± 381.84)			

Notes:

[2] - For some [C] there is only 1 patient with data, thus no SD. For each [C], no of subjects differ.

Statistical analyses

No statistical analyses for this end point

Secondary: S-sulfocysteine (Umol/L) Normalized to Urine Creatinine (mmol/L) - Change From Baseline Over Time

End point title	S-sulfocysteine (Umol/L) Normalized to Urine Creatinine (mmol/L) -Change From Baseline Over Time

End point description:

Analyses were performed on urine SSC, a biomarker of the MoCD pathway. Levels of SSC measured in urine were normalized to urine creatinine levels. The observed value, change, and percent change in urine and blood SSC levels from baseline were summarized by visit overtime. Not all subjects had samples taken at each expected timepoint.

End point type	Secondary

End point timeframe:

Until study completion (approx. 72 months)

End point values	Subjects Receiving rcPMP and transitioned to ORGN001			
Subject group type	Reporting group			
Number of subjects analysed	8[3]			
Units: umol/mmol				
arithmetic mean (standard deviation)				
Baseline (8 subjects)	21.1 (± 12.89)			
Day 4 Change from Baseline (8 subjects)	-1.7 (± 12.70)			
Day 7 Change from Baseline (8 subjects)	-7.8 (± 9.70)			
Day 14 Change from Baseline (8 subjects)	-2.2 (± 14.51)			
Day 28 Change from Baseline (7 subjects)	2.8 (± 14.17)			
Day 57 Change from Baseline (7 subjects)	-3.0 (± 10.29)			
Day 67 Change from Baseline (5 subjects)	-5.7 (± 11.78)			
Day 87 Change from Baseline (6 subjects)	-9.6 (± 11.70)			
Day 97 Change from Baseline (6 subjects)	-9.0 (± 11.12)			

Day 117 Change from Baseline (7 subjects)	-12.8 (± 15.58)			
Day 127 Change from Baseline (8 subjects)	-12.2 (± 14.77)			
Day 147 Change from Baseline (8 subjects)	-13.7 (± 11.86)			
Day 157 Change from Baseline (5 subjects)	-14.3 (± 16.87)			
Month 6 Change from Baseline (8 subjects)	-13.6 (± 11.77)			
Month 9 Change from Baseline (8 subjects)	-8.7 (± 17.14)			
Month 12 Change from Baseline (8 subjects)	-8.6 (± 20.15)			
Month 18 Change from Baseline (6 subjects)	-11.4 (± 16.81)			
Month 24 Change from Baseline (6 subjects)	-14.3 (± 14.73)			
Month 30 Change from Baseline (5 subjects)	-11.2 (± 21.28)			
Month 36 Change from Baseline (5 subjects)	-13.2 (± 18.40)			
Month 48 Change from Baseline (5 subjects)	-6.7 (± 6.65)			
Month 60 Change from Baseline (4 subjects)	-17.9 (± 14.59)			
Month 78 Change from Baseline (4 subjects)	-15.6 (± 11.82)			
Month 84 Change from Baseline (1 subject)	-5.3 (± 0.00)			
Month 90 Change from Baseline (2 subjects)	1.7 (± 10.25)			

Notes:

[3] - For some [C] there is only 1 patient with data, thus no SD. For each [C], no of subjects diffe

Statistical analyses

No statistical analyses for this end point

Secondary: Effect of ORGN001 on Neurologic Function Including Motor Examination

End point title	Effect of ORGN001 on Neurologic Function Including Motor Examination

End point description:

Change from baseline on repeated Neurologic examinations such as muscle strength and tone, as well as sensory and reflex exam.

All subjects entering the study had complete examinations throughout the study to identify Normal vs Abnormal Neurologic Function on the parameters presented. Data shown here are from Baseline up to M30. For data from M36 to M90 (final examination), please refer to section 14 of CSR.

End point type	Secondary

End point timeframe:

Until study completion (approx. 72 months)

End point values	Subjects Receiving rcPMP and transitioned to ORGN001			
Subject group type	Reporting group			
Number of subjects analysed	8[4]			
Units: subjects				
Quality of Spontaneous Movement at Baseline (N)	3			
Quality of Spontaneous Movement at Baseline (A)	5			
Quality of Spontaneous Movement at D1 (N)	4			
Quality of Spontaneous Movement at D1 (A)	4			
Quality of Spontaneous Movement at D4 (N)	3			
Quality of Spontaneous Movement at D4 (A)	5			
Quality of Spontaneous Movement at D7 (N)	3			
Quality of Spontaneous Movement at D7 (A)	4			
Quality of Spontaneous Movement at D14 (N)	2			
Quality of Spontaneous Movement at D14 (A)	5			
Quality of Spontaneous Movement at D28 (N)	3			
Quality of Spontaneous Movement at D28 (A)	4			
Quality of Spontaneous Movement at D60 (N)	2			
Quality of Spontaneous Movement at D60 (A)	4			
Quality of Spontaneous Movement at D90 (N)	4			
Quality of Spontaneous Movement at D90 (A)	4			
Quality of Spontaneous Movement at D120 (N)	2			
Quality of Spontaneous Movement at D120 (A)	6			
Quality of Spontaneous Movement at D150 (N)	4			
Quality of Spontaneous Movement at D150 (A)	4			
Quality of Spontaneous Movement at D180 (N)	3			
Quality of Spontaneous Movement at D180 (A)	5			
Quality of Spontaneous Movement at M9 (N)	3			
Quality of Spontaneous Movement at M9 (A)	5			
Quality of Spontaneous Movement at M12 (N)	3			
Quality of Spontaneous Movement at M12 (A)	5			
Quality of Spontaneous Movement at M18 (N)	4			

Quality of Spontaneous Movement at M18 (A)	4			
Quality of Spontaneous Movement at M24 (N)	2			
Quality of Spontaneous Movement at M24 (A)	6			
Quality of Spontaneous Movement at M30 (N)	4			
Quality of Spontaneous Movement at M30 (A)	4			
Dystonic at Baseline (N)	4			
Dystonic at Baseline (A)	4			
Dystonic at D1 (N)	4			
Dystonic at D1 (A)	4			
Dystonic at D4 (N)	5			
Dystonic at D4 (A)	3			
Dystonic at D7 (N)	4			
Dystonic at D7 (A)	3			
Dystonic at D14 (N)	4			
Dystonic at D14 (A)	3			
Dystonic at D28 (N)	4			
Dystonic at D28 (A)	3			
Dystonic at D60 (N)	4			
Dystonic at D60 (A)	2			
Dystonic at D90 (N)	4			
Dystonic at D90 (A)	4			
Dystonic at D120 (N)	4			
Dystonic at D120 (A)	4			
Dystonic at D150 (N)	4			
Dystonic at D150 (A)	4			
Dystonic at D180 (N)	4			
Dystonic at D180 (A)	4			
Dystonic at M9 (N)	4			
Dystonic at M9 (A)	4			
Dystonic at M12 (N)	4			
Dystonic at M12 (A)	4			
Dystonic at M18 (N)	3			
Dystonic at M18 (A)	5			
Dystonic at M24 (N)	4			
Dystonic at M24 (A)	4			
Dystonic at M30 (N)	4			
Dystonic at M30 (A)	4			
Opistonic at Baseline (N)	7			
Opistonic at Baseline (A)	1			
Opistonic at D1 (N)	7			
Opistonic at D1 (A)	1			
Opistonic at D4 (N)	8			
Opistonic at D4 (A)	0			
Opistonic at D7 (N)	7			
Opistonic at D7 (A)	0			
Opistonic at D14 (N)	7			
Opistonic at D14 (A)	0			
Opistonic at D28 (N)	7			

Opistonic at D28 (A)	0			
Opistonic at D60 (N)	6			
Opistonic at D60 (A)	0			
Opistonic at D90 (N)	8			
Opistonic at D90 (A)	0			
Opistonic at D120 (N)	7			
Opistonic at D120 (A)	1			
Opistonic at D150 (N)	8			
Opistonic at D150 (A)	0			
Opistonic at D180 (N)	8			
Opistonic at D180 (A)	0			
Opistonic at M9 (N)	7			
Opistonic at M9 (A)	1			
Opistonic at M12 (N)	7			
Opistonic at M12 (A)	1			
Opistonic at M18 (N)	6			
Opistonic at M18 (A)	2			
Opistonic at M24 (N)	6			
Opistonic at M24 (A)	2			
Opistonic at M30 (N)	6			
Opistonic at M30 (A)	2			
Truncal Tone at Baseline (N)	2			
Truncal Tone at Baseline (A)	5			
Truncal Tone at D1 (N)	3			
Truncal Tone at D1 (A)	5			
Truncal Tone at D4 (N)	2			
Truncal Tone at D4 (A)	5			
Truncal Tone at D7 (N)	2			
Truncal Tone at D7 (A)	5			
Truncal Tone at D14 (N)	2			
Truncal Tone at D14 (A)	5			
Truncal Tone at D28 (N)	3			
Truncal Tone at D28 (A)	4			
Truncal Tone at D60 (N)	3			
Truncal Tone at D60 (A)	3			
Truncal Tone at D90 (N)	3			
Truncal Tone at D90 (A)	5			
Truncal Tone at D120 (N)	3			
Truncal Tone at D120 (A)	5			
Truncal Tone at D150 (N)	2			
Truncal Tone at D150 (A)	6			
Truncal Tone at D180 (N)	2			
Truncal Tone at D180 (A)	6			
Truncal Tone at M9 (N)	2			
Truncal Tone at M9 (A)	6			
Truncal Tone at M12 (N)	3			
Truncal Tone at M12 (A)	5			
Truncal Tone at M18 (N)	3			
Truncal Tone at M18 (A)	5			
Truncal Tone at M24 (N)	2			
Truncal Tone at M24 (A)	6			
Truncal Tone at M30 (N)	2			

Truncal Tone at M30 (A)	6			
Appendicular Tone at Baseline (N)	2			
Appendicular Tone at Baseline (A)	6			
Appendicular Tone at D1 (N)	2			
Appendicular Tone at D1 (A)	6			
Appendicular Tone at D4 (N)	2			
Appendicular Tone at D4 (A)	6			
Appendicular Tone at D7 (N)	2			
Appendicular Tone at D7 (A)	5			
Appendicular Tone at D14 (N)	1			
Appendicular Tone at D14 (A)	6			
Appendicular Tone at D28 (N)	2			
Appendicular Tone at D28 (A)	5			
Appendicular Tone at D60 (N)	1			
Appendicular Tone at D60 (A)	5			
Appendicular Tone at D90 (N)	2			
Appendicular Tone at D90 (A)	6			
Appendicular Tone at D120 (N)	1			
Appendicular Tone at D120 (A)	7			
Appendicular Tone at D150 (N)	1			
Appendicular Tone at D150 (A)	7			
Appendicular Tone at D180 (N)	2			
Appendicular Tone at D180 (A)	6			
Appendicular Tone at M9 (N)	1			
Appendicular Tone at M9 (A)	7			
Appendicular Tone at M12 (N)	2			
Appendicular Tone at M12 (A)	6			
Appendicular Tone at M18 (N)	1			
Appendicular Tone at M18 (A)	7			
Appendicular Tone at M24 (N)	1			
Appendicular Tone at M24 (A)	7			
Appendicular Tone at M30 (N)	1			
Appendicular Tone at M30 (A)	7			
Deep Tendon Reflexes at Baseline (N)	4			
Deep Tendon Reflexes at Baseline (A)	4			
Deep Tendon Reflexes at D1 (N)	3			
Deep Tendon Reflexes at D1 (A)	5			
Deep Tendon Reflexes at D4 (N)	1			
Deep Tendon Reflexes at D4 (A)	6			
Deep Tendon Reflexes at D7 (N)	2			
Deep Tendon Reflexes at D7 (A)	5			
Deep Tendon Reflexes at D14 (N)	2			
Deep Tendon Reflexes at D14 (A)	5			
Deep Tendon Reflexes at D28 (N)	3			
Deep Tendon Reflexes at D28 (A)	4			
Deep Tendon Reflexes at D60 (N)	2			
Deep Tendon Reflexes at D60 (A)	4			
Deep Tendon Reflexes at D90 (N)	3			
Deep Tendon Reflexes at D90 (A)	5			
Deep Tendon Reflexes at D120 (N)	2			
Deep Tendon Reflexes at D120 (A)	6			
Deep Tendon Reflexes at D150 (N)	3			

Deep Tendon Reflexes at D150 (A)	5			
Deep Tendon Reflexes at D180 (N)	4			
Deep Tendon Reflexes at D180 (A)	4			
Deep Tendon Reflexes at M9 (N)	4			
Deep Tendon Reflexes at M9 (A)	4			
Deep Tendon Reflexes at M12 (N)	3			
Deep Tendon Reflexes at M12 (A)	5			
Deep Tendon Reflexes at M18 (N)	2			
Deep Tendon Reflexes at M18 (A)	6			
Deep Tendon Reflexes at M24 (N)	2			
Deep Tendon Reflexes at M24 (A)	6			
Deep Tendon Reflexes at M30 (N)	3			
Deep Tendon Reflexes at M30 (A)	5			
Primitive Reflexes at Baseline (N)	5			
Primitive Reflexes at Baseline (A)	1			
Primitive Reflexes at D1 (N)	4			
Primitive Reflexes at D1 (A)	1			
Primitive Reflexes at D4 (N)	5			
Primitive Reflexes at D4 (A)	1			
Primitive Reflexes at D7 (N)	3			
Primitive Reflexes at D7 (A)	2			
Primitive Reflexes at D14 (N)	2			
Primitive Reflexes at D14 (A)	1			
Primitive Reflexes at D28 (N)	3			
Primitive Reflexes at D28 (A)	1			
Primitive Reflexes at D60 (N)	3			
Primitive Reflexes at D60 (A)	1			
Primitive Reflexes at D90 (N)	4			
Primitive Reflexes at D90 (A)	1			
Primitive Reflexes at D120 (N)	4			
Primitive Reflexes at D120 (A)	0			
Primitive Reflexes at D150 (N)	5			
Primitive Reflexes at D150 (A)	0			
Primitive Reflexes at D180 (N)	5			
Primitive Reflexes at D180 (A)	1			
Primitive Reflexes at M9 (N)	4			
Primitive Reflexes at M9 (A)	2			
Primitive Reflexes at M12 (N)	5			
Primitive Reflexes at M12 (A)	1			
Primitive Reflexes at M18 (N)	6			
Primitive Reflexes at M18 (A)	1			
Primitive Reflexes at M24 (N)	6			
Primitive Reflexes at M24 (A)	1			
Primitive Reflexes at M30 (N)	6			
Primitive Reflexes at M30 (A)	1			
Clonus presence at Baseline (N)	7			
Clonus presence at Baseline (A)	1			
Clonus presence at D1 (N)	7			
Clonus presence at D1 (A)	1			
Clonus presence at D4 (N)	7			
Clonus presence at D4 (A)	1			
Clonus presence at D7 (N)	6			

Clonus presence at D7 (A)	2			
Clonus presence at D14 (N)	6			
Clonus presence at D14 (A)	1			
Clonus presence at D28 (N)	5			
Clonus presence at D28 (A)	2			
Clonus presence at D60 (N)	5			
Clonus presence at D60 (A)	1			
Clonus presence at D90 (N)	6			
Clonus presence at D90 (A)	1			
Clonus presence at D120 (N)	7			
Clonus presence at D120 (A)	1			
Clonus presence at D150 (N)	6			
Clonus presence at D150 (A)	2			
Clonus presence at D180 (N)	6			
Clonus presence at D180 (A)	2			
Clonus presence at M9 (N)	8			
Clonus presence at M9 (A)	0			
Clonus presence at M12 (N)	7			
Clonus presence at M12 (A)	1			
Clonus presence at M18 (N)	6			
Clonus presence at M18 (A)	2			
Clonus presence at M24 (N)	6			
Clonus presence at M24 (A)	2			
Clonus presence at M30 (N)	6			
Clonus presence at M30 (A)	2			
Ambulation at Baseline (N)	4			
Ambulation at Baseline (A)	4			
Ambulation at D1 (N)	4			
Ambulation at D1 (A)	4			
Ambulation at D4 (N)	4			
Ambulation at D4 (A)	4			
Ambulation at D7 (N)	3			
Ambulation at D7 (A)	4			
Ambulation at D14 (N)	3			
Ambulation at D14 (A)	4			
Ambulation at D28 (N)	3			
Ambulation at D28 (A)	4			
Ambulation at D60 (N)	3			
Ambulation at D60 (A)	3			
Ambulation at D90 (N)	4			
Ambulation at D90 (A)	4			
Ambulation at D120 (N)	4			
Ambulation at D120 (A)	4			
Ambulation at D150 (N)	4			
Ambulation at D150 (A)	4			
Ambulation at D180 (N)	4			
Ambulation at D180 (A)	4			
Ambulation at M9 (N)	4			
Ambulation at M9 (A)	4			
Ambulation at M12 (N)	4			
Ambulation at M12 (A)	4			
Ambulation at M18 (N)	4			

Ambulation at M18 (A)	4			
Ambulation at M24 (N)	4			
Ambulation at M24 (A)	4			
Ambulation at M30 (N)	4			
Ambulation at M30 (A)	4			
Communication at Baseline (N)	1			
Communication at Baseline (A)	7			
Communication at D1 (N)	1			
Communication at D1 (A)	7			
Communication at D4 (N)	1			
Communication at D4 (A)	7			
Communication at D7 (N)	1			
Communication at D7 (A)	6			
Communication at D14 (N)	0			
Communication at D14 (A)	7			
Communication at D28 (N)	2			
Communication at D28 (A)	5			
Communication at D60 (N)	2			
Communication at D60 (A)	4			
Communication at D90 (N)	1			
Communication at D90 (A)	7			
Communication at D120 (N)	1			
Communication at D120 (A)	7			
Communication at D150 (N)	2			
Communication at D150 (A)	6			
Communication at D180 (N)	2			
Communication at D180 (A)	6			
Communication at M9 (N)	2			
Communication at M9 (A)	6			
Communication at M12 (N)	2			
Communication at M12 (A)	6			
Communication at M18 (N)	2			
Communication at M18 (A)	6			
Communication at M24 (N)	2			
Communication at M24 (A)	6			
Communication at M30 (N)	2			
Communication at M30 (A)	6			

Notes:

[4] - For D7, 14, 28 -> N=7. For D60, N=6.
(N): Normal/Present/Yes. (A): Abnormal/Absent/No,

Statistical analyses

No statistical analyses for this end point

Secondary: Long-term Safety of ORGN001

End point title	Long-term Safety of ORGN001

End point description:

Change from baseline in Seizure frequency

Number of subjects with Seizures in observation period

End point type	Secondary

End point timeframe:
Until study completion (approx. 72 months)

End point values	Subjects Receiving rcPMP and transitioned to ORGN001			
Subject group type	Reporting group			
Number of subjects analysed	8[5]			
Units: subjects				
Screening (N=7)	3			
Baseline to Month 6 (N=7)	4			
Month 6 to Month 12 (N=8)	3			
Month 12 to Month 18 (N=8)	3			
Month 18 to Month 24 (N=8)	3			
Month 24 to Month 30 (N=8)	3			
Month 30 to Month 36 (N=7)	3			
Month 36 to Month 42 (N=7)	3			
Month 42 to Month 48 (N=7)	3			
Month 48 to Month 54 (N=7)	3			
Month 54 to Month 60 (N=7)	3			
Month 60 to Month 66 (N=7)	3			
Month 66 to Month 72 (N=7)	3			
Month 72 to Month 78 (N=7)	3			
Month 78 to Month 84 (N=6)	2			
Month 84 to Month 90 (N=6)	2			
Month 90 to Month 96 (N=3)	2			

Notes:
[5] - For each timepoint, the number of analyzed subjects differ.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 1 with ORGN001 treatment until study completion, up to Month 90.

Adverse event reporting additional description:

All-cause Mortality is zero in this study because there were no deaths that occurred. SAE Data presented is for all SAEs that occurred during the whole study in all subjects.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Subjects Receiving rcPMP and transitioned to ORGN001

Reporting group description:

Patients currently receiving rcPMP infusions at baseline are transitioned to ORGN001(formerly ALXN1101), starting at their current rcPMP dose and escalating to a target dose of 0.9 mg/kg per protocol

Serious adverse events	Subjects Receiving rcPMP and transitioned to ORGN001		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Postoperative respiratory failure			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Haemorrhage			

subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Central venous catheterisation				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Dystonia				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Complication associated with device				
subjects affected / exposed	4 / 8 (50.00%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			

Catheter site irritation				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Swelling				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Catheter site discharge				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Catheter site extravasation				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Erosive oesophagitis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonitis aspiration				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Upper airway obstruction			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin disorder			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Joint contracture			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Catheter site infection			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular device infection			

subjects affected / exposed	2 / 8 (25.00%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Pneumonia influenzal				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Catheter site abscess				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral upper respiratory tract infection				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rhinovirus infection				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Otitis media				

subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device dislocation				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Device leakage				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Type 1 diabetes mellitus				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Subjects Receiving rcPMP and transitioned to ORGN001		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Pyogenic granuloma			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Venous thrombosis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Phlebitis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Cyanosis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	3		
Surgical and medical procedures			
Central venous catheterisation			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
General disorders and administration site conditions			
Catheter site pain			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	4		
Catheter site discharge			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Catheter site discolouration			

subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Catheter site extravasation				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	2			
Catheter site haemorrhage				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Catheter site irritation				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	5			
Catheter site oedema				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Chills				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	3			
Complication associated with device				
subjects affected / exposed	6 / 8 (75.00%)			
occurrences (all)	16			
Gait disturbance				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Medical device site discomfort				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Medical device site reaction				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	3			
Pain				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Pyrexia				
subjects affected / exposed	7 / 8 (87.50%)			
occurrences (all)	38			
Swelling				

subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Swelling face			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Asthma			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	7		
Asthmatic crisis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Bronchopneumopathy			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	4 / 8 (50.00%)		
occurrences (all)	7		
Epistaxis			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Increased upper airway secretion			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Lung disorder			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Obstructive sleep apnoea syndrome			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Oropharyngeal pain			

subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Pneumonitis aspiration			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Respiratory failure			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	2		
Rhinitis allergic			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Sneezing			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Tachypnoea			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	3		
Upper airway obstruction			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	3		
Wheezing			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Irritability			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		

Sleep disorder subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Product issues Device dislocation subjects affected / exposed occurrences (all) Device leakage subjects affected / exposed occurrences (all) Device occlusion subjects affected / exposed occurrences (all)	 3 / 8 (37.50%) 6 2 / 8 (25.00%) 2 1 / 8 (12.50%) 1		
Investigations Blood iron decreased subjects affected / exposed occurrences (all) C-reactive protein increased subjects affected / exposed occurrences (all) Cardiac murmur subjects affected / exposed occurrences (all) Culture urine positive subjects affected / exposed occurrences (all) Heart rate increased subjects affected / exposed occurrences (all) Procalcitonin increased subjects affected / exposed occurrences (all) Vitamin D decreased subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 2 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Joint dislocation			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Muscle injury			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Post procedural complication			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Post procedural haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Postoperative respiratory failure			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Scar			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Tendon injury			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Thermal burn			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Traumatic haematoma			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Cardiac disorders			
Tachycardia			

subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	2		
Nervous system disorders			
Cerebral atrophy			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Dystonia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	9		
Epilepsy			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Hypertonia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Muscle spasticity			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	2		
Opisthotonus			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Seizure			
subjects affected / exposed	3 / 8 (37.50%)		
occurrences (all)	8		
Tonic convulsion			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Iron deficiency anaemia			

subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Leukocytosis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Lymphadenopathy			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Splenomegaly			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	4		
Tympanic membrane hyperaemia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Eye disorders			
Chalazion			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Eye irritation			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Eye pruritus			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Eye swelling			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Strabismus			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Gastrointestinal disorders			

Abdominal pain				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	2			
Barrett's oesophagus				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Constipation				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	4			
Diarrhoea				
subjects affected / exposed	3 / 8 (37.50%)			
occurrences (all)	5			
Dysphagia				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Erosive oesophagitis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Gastritis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	2			
Gastroesophageal reflux disease				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	2			
Gastrointestinal motility disorder				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Mouth haemorrhage				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Nausea				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	3			
Noninfective gingivitis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			

Retching subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1			
Salivary hypersecretion subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 2			
Teething subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1			
Vomiting subjects affected / exposed occurrences (all)	6 / 8 (75.00%) 11			
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1			
Erythema subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1			
Keratosis pilaris subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1			
Livedo reticularis subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1			
Petechiae subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1			
Purpura subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1			
Rash subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 3			
Rash erythematous				

subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Rash maculo-papular				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	2			
Rash erythematous bilateral				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Skin disorder				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	2			
Seborrhoeic dermatitis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Skin ulcer				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Skin irritation				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Urticaria				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Foot deformity				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	2			
Growth retardation				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	3			
Joint contracture				

subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Kyphoscoliosis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Kyphosis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Blister infected			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	4		
Bullous impetigo			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Catheter site abscess			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Catheter site infection			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	3		
Conjunctivitis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Device related infection			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	3		

Ear infection				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	4			
Ear infection viral				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Eye infection				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Gastroenteritis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Gastroenteritis viral				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	2			
Hordeolum				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	4 / 8 (50.00%)			
occurrences (all)	4			
Lower respiratory tract infection				
subjects affected / exposed	3 / 8 (37.50%)			
occurrences (all)	9			
Nasopharyngitis				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	5			
Oral candidiasis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Otitis media				
subjects affected / exposed	3 / 8 (37.50%)			
occurrences (all)	12			
Otitis media acute				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	8			

Paronychia				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Pharyngitis				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	4			
Pneumonia				
subjects affected / exposed	4 / 8 (50.00%)			
occurrences (all)	12			
Pneumonia influenzal				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Pustule				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Respiratory tract infection				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	3			
Respiratory tract infection viral				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Rhinitis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Rhinovirus infection				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Sepsis				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	2			
Sinusitis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Upper respiratory tract infection				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	5			

Urinary tract infection subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 8		
Urinary tract infection bacterial subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 2		
Varicella subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2		
Vascular device infection subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 6		
Viral infection subjects affected / exposed occurrences (all)	5 / 8 (62.50%) 9		
Viral tonsillitis subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2		
Bronchitis viral subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Diabetic ketoacidosis subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Iron deficiency subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Metabolic alkalosis			

subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Vitamin D deficiency			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2013	Amendment 1 (Version 2.0, 19 November 2013) was implemented to modify the dose-escalation scheme of ALXN1101 to establish the safety and potential additional efficacy of higher doses of cPMP as ALXN1101 and determine the starting dose for future studies.
27 January 2014	Amendment 2 (Version 3.0, 27 January 2014) was implemented to add BP monitoring time points, the option of additional EEGs, and the added responsibility of the DMC to review all dose escalations, removal of references to specific starting doses, update visit windows, and clarify that after dose escalation was complete, a patient could be returned to the prior dose based on the patient's clinical status at the discretion of the treating physician after consultation with the SRC.
01 October 2015	Amendment 3 (Version 4.0, 01 October 2015) was implemented to update the name of the Sponsor, medical monitor, and drug safety physician and revise the section describing the Bayley-III, MRI text, and blood sampling priority list, remove the post-Day 7 BP measurements by home infusion services, and update the AE severity assessment language to align with the protocol template.
09 December 2016	Amendment 4 (Version 5.0, 09 December 2016) was implemented to clarify the process for patient discontinuation in the event that ALXN1101 becomes registered and available as a treatment for MoCD Type A; extend the duration of the extension period; add additional assessments during the extension period; specify the infusion rate of ALXN1101 per FDA feedback on Protocol ALXN1101-202; specify that the NOAEL (10 mg/kg/day) determined from the 14-day adult rat toxicology study was used for dose justification since > 1 NOAEL has been determined across multiple species in nonclinical studies; add 12.5 mg/vial strength, clarify that the dose of ALXN1101 could be re-escalated to the final tolerated dose during the 60-month extension period in patients who were de-escalated for reasons other than PK or safety considerations; add a pre-dose PD sample collection to provide better characterization of PD data during the 60-month extension period; indicate that collection of the pre-dose PD sample would occur before the neurocognitive assessments, add an optional blood PK assessment at 24 hours after EOI on Day 1 and addition of PK assessment at 3 to 4 hours post-EOI at any visit during the 60-month extension period to better characterize PK at the designated time points; add sample blood volume tables during the 60-month extension period, safety follow-up visit, and an unscheduled dose adjustment.
13 January 2017	Amendment 5 (Version 6.0, 13 January 2017) was implemented to specify that a pre-dose PD blood sample was collected 1 time to better distinguish from other PD blood assessments collected at multiple clinical visits during the extension period; add a PK assessment at the EOI and 4 hours post-EOI during the 60-month extension period to better characterize PK; specify that neurological examination would also occur if there was an unscheduled dose adjustment; align the NOAEL across the program, including ALXN1101 IB Edition 4 and Protocol ALXN1101-MCD-202; and add WPPSI-IV assessments during the 60-month extension period to permit a more longitudinal assessment of intelligence for patients ≥ 3 years of age.
23 November 2018	Amendment 5.1 (Version 6.1, 23 November 2018) was implemented to update the drug name (ORGN001), title, Sponsor, and drug manufacturer information to reflect the new Sponsor, Origin Biosciences, Inc., who acquired the program from Alexion in September 2018.

28 June 2019	Amendment 6.0 (Version 7.0, 28 June 2019) was implemented to update Sponsor and medical monitor contact information, update the responsible medical officer, update the new clinical study leader and responsible physician, and remove all references limiting the extension period to 60 months.
03 January 2020	Amendment 7.0 (Version 8.0, 03 January 2020) was implemented to update text for the risk/benefit assessment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported