



## 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)                          | EMA-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

|                  |                                                      |
|------------------|------------------------------------------------------|
| <b>Arm title</b> | 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.

|                                       |                                                      |
|---------------------------------------|------------------------------------------------------|
| <b>Number of subjects in period 1</b> | 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:<br>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) <sup>[1]</sup> |
| End point description:<br>Treatment Emergent Serious Adverse Events        |                                                      |
| End point type                                                             | Primary                                              |
| End point timeframe:<br>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 conditions | 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) at scheduled 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 <sup>[2]</sup>                                     |  |  |  |
| 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 ( $\pm$ 0.00)    |  |  |  |
| Day 150EOI (960mcg/kg) (3 subjects)    | 2045.67 ( $\pm$ 1009.85) |  |  |  |
| Day 150EOI (1200mcg/kg) (3 subjects)   | 3173.33 ( $\pm$ 656.53)  |  |  |  |
| Month 66 EOI (1200mcg/kg) (2 subjects) | 2450.00 ( $\pm$ 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 <sup>[3]</sup>                                     |  |  |  |
| Units: umol/mmol                         |                                                      |  |  |  |
| arithmetic mean (standard deviation)     |                                                      |  |  |  |
| Baseline (8 subjects)                    | 21.1 ( $\pm$ 12.89)                                  |  |  |  |
| Day 4 Change from Baseline (8 subjects)  | -1.7 ( $\pm$ 12.70)                                  |  |  |  |
| Day 7 Change from Baseline (8 subjects)  | -7.8 ( $\pm$ 9.70)                                   |  |  |  |
| Day 14 Change from Baseline (8 subjects) | -2.2 ( $\pm$ 14.51)                                  |  |  |  |
| Day 28 Change from Baseline (7 subjects) | 2.8 ( $\pm$ 14.17)                                   |  |  |  |
| Day 57 Change from Baseline (7 subjects) | -3.0 ( $\pm$ 10.29)                                  |  |  |  |
| Day 67 Change from Baseline (5 subjects) | -5.7 ( $\pm$ 11.78)                                  |  |  |  |
| Day 87 Change from Baseline (6 subjects) | -9.6 ( $\pm$ 11.70)                                  |  |  |  |
| Day 97 Change from Baseline (6 subjects) | -9.0 ( $\pm$ 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)

|                                                 |                                                                  |  |  |  |
|-------------------------------------------------|------------------------------------------------------------------|--|--|--|
| <b>End point values</b>                         | Subjects<br>Receiving<br>rcPMP and<br>transitioned to<br>ORGN001 |  |  |  |
| Subject group type                              | Reporting group                                                  |  |  |  |
| Number of subjects analysed                     | 8 <sup>[4]</sup>                                                 |  |  |  |
| 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)

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|                             |                                                                  |  |  |  |
|-----------------------------|------------------------------------------------------------------|--|--|--|
| <b>End point values</b>     | Subjects<br>Receiving<br>rcPMP and<br>transitioned to<br>ORGN001 |  |  |  |
| Subject group type          | Reporting group                                                  |  |  |  |
| Number of subjects analysed | 8 <sup>[5]</sup>                                                 |  |  |  |
| 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

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

| <b>Non-serious adverse events</b>                                                                                                                | Subjects Receiving<br>rcPMP and<br>transitioned to<br>ORGN001 |  |  |
|--------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|--|--|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed                                                          | 8 / 8 (100.00%)                                               |  |  |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps)<br>Melanocytic naevus<br>subjects affected / exposed<br>occurrences (all) | 1 / 8 (12.50%)<br>1                                           |  |  |
| Pyogenic granuloma<br>subjects affected / exposed<br>occurrences (all)                                                                           | 1 / 8 (12.50%)<br>1                                           |  |  |
| Vascular disorders<br>Haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                                            | 1 / 8 (12.50%)<br>1                                           |  |  |
| Venous thrombosis<br>subjects affected / exposed<br>occurrences (all)                                                                            | 1 / 8 (12.50%)<br>1                                           |  |  |
| Phlebitis<br>subjects affected / exposed<br>occurrences (all)                                                                                    | 1 / 8 (12.50%)<br>1                                           |  |  |
| Cyanosis<br>subjects affected / exposed<br>occurrences (all)                                                                                     | 1 / 8 (12.50%)<br>3                                           |  |  |
| Surgical and medical procedures<br>Central venous catheterisation<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 8 (12.50%)<br>1                                           |  |  |
| General disorders and administration<br>site conditions<br>Catheter site pain<br>subjects affected / exposed<br>occurrences (all)                | 2 / 8 (25.00%)<br>4                                           |  |  |
| Catheter site discharge<br>subjects affected / exposed<br>occurrences (all)                                                                      | 2 / 8 (25.00%)<br>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<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 8 (12.50%)<br>1 |  |  |
| Product issues<br>Device dislocation<br>subjects affected / exposed<br>occurrences (all)   | 3 / 8 (37.50%)<br>6 |  |  |
| Device leakage<br>subjects affected / exposed<br>occurrences (all)                         | 2 / 8 (25.00%)<br>2 |  |  |
| Device occlusion<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 8 (12.50%)<br>1 |  |  |
| Investigations<br>Blood iron decreased<br>subjects affected / exposed<br>occurrences (all) | 1 / 8 (12.50%)<br>1 |  |  |
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)           | 1 / 8 (12.50%)<br>1 |  |  |
| Cardiac murmur<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 8 (12.50%)<br>1 |  |  |
| Culture urine positive<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 8 (12.50%)<br>2 |  |  |
| Heart rate increased<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 8 (12.50%)<br>1 |  |  |
| Procalcitonin increased<br>subjects affected / exposed<br>occurrences (all)                | 1 / 8 (12.50%)<br>1 |  |  |
| Vitamin D decreased<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 8 (12.50%)<br>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            | 1 / 8 (12.50%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Salivary hypersecretion                |                |  |  |
| subjects affected / exposed            | 1 / 8 (12.50%) |  |  |
| occurrences (all)                      | 2              |  |  |
| Teething                               |                |  |  |
| subjects affected / exposed            | 1 / 8 (12.50%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Vomiting                               |                |  |  |
| subjects affected / exposed            | 6 / 8 (75.00%) |  |  |
| occurrences (all)                      | 11             |  |  |
| Skin and subcutaneous tissue disorders |                |  |  |
| Dry skin                               |                |  |  |
| subjects affected / exposed            | 1 / 8 (12.50%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Erythema                               |                |  |  |
| subjects affected / exposed            | 1 / 8 (12.50%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Keratosis pilaris                      |                |  |  |
| subjects affected / exposed            | 1 / 8 (12.50%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Livedo reticularis                     |                |  |  |
| subjects affected / exposed            | 1 / 8 (12.50%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Petechiae                              |                |  |  |
| subjects affected / exposed            | 1 / 8 (12.50%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Purpura                                |                |  |  |
| subjects affected / exposed            | 1 / 8 (12.50%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Rash                                   |                |  |  |
| subjects affected / exposed            | 3 / 8 (37.50%) |  |  |
| occurrences (all)                      | 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             | 2 / 8 (25.00%) |  |  |
| occurrences (all)                       | 8              |  |  |
| Urinary tract infection bacterial       |                |  |  |
| subjects affected / exposed             | 1 / 8 (12.50%) |  |  |
| occurrences (all)                       | 2              |  |  |
| Varicella                               |                |  |  |
| subjects affected / exposed             | 2 / 8 (25.00%) |  |  |
| occurrences (all)                       | 2              |  |  |
| Vascular device infection               |                |  |  |
| subjects affected / exposed             | 2 / 8 (25.00%) |  |  |
| occurrences (all)                       | 6              |  |  |
| Viral infection                         |                |  |  |
| subjects affected / exposed             | 5 / 8 (62.50%) |  |  |
| occurrences (all)                       | 9              |  |  |
| Viral tonsillitis                       |                |  |  |
| subjects affected / exposed             | 1 / 8 (12.50%) |  |  |
| occurrences (all)                       | 1              |  |  |
| Viral upper respiratory tract infection |                |  |  |
| subjects affected / exposed             | 2 / 8 (25.00%) |  |  |
| occurrences (all)                       | 2              |  |  |
| Bronchitis viral                        |                |  |  |
| subjects affected / exposed             | 1 / 8 (12.50%) |  |  |
| occurrences (all)                       | 1              |  |  |
| Metabolism and nutrition disorders      |                |  |  |
| Dehydration                             |                |  |  |
| subjects affected / exposed             | 1 / 8 (12.50%) |  |  |
| occurrences (all)                       | 1              |  |  |
| Diabetic ketoacidosis                   |                |  |  |
| subjects affected / exposed             | 1 / 8 (12.50%) |  |  |
| occurrences (all)                       | 1              |  |  |
| Iron deficiency                         |                |  |  |
| subjects affected / exposed             | 1 / 8 (12.50%) |  |  |
| occurrences (all)                       | 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:

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## **Interruptions (globally)**

Were there any global interruptions to the trial? No

## **Limitations and caveats**

None reported