



## Clinical trial results:

### A Multicenter, Open-Label Study to Evaluate the Pharmacokinetics, Tolerability, and Safety of a Single Dose of Staccato Alprazolam in Adolescent Study Participants With Epilepsy

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2022-002523-36 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 05 April 2022  |

#### Results information

|                                |                   |
|--------------------------------|-------------------|
| Result version number          | v1 (current)      |
| This version publication date  | 28 September 2022 |
| First version publication date | 28 September 2022 |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | UP0100 |
|-----------------------|--------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04857307 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | UCB Biopharma SRL   |
| Sponsor organisation address | Allée de la Recherche 60, Brussels, Belgium, 1070                                 |
| Public contact               | Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com |
| Scientific contact           | Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com |

Notes:

#### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-003043-PIP01-21 |
| 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                       | 05 May 2022   |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 05 April 2022 |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 05 April 2022 |
| Was the trial ended prematurely?                     | No            |

Notes:

## General information about the trial

Main objective of the trial:

- To evaluate the pharmacokinetic (PK) of alprazolam in adolescent study participants with epilepsy following single inhaled dose of Staccato alprazolam
- To evaluate the safety and tolerability of Staccato alprazolam in adolescent study participants with epilepsy

Protection of trial subjects:

During the conduct of the study all participants were closely monitored.

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

Not applicable

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 28 April 2021 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 14 |
| Worldwide total number of subjects   | 14                |
| EEA total number of subjects         | 0                 |

Notes:

### Subjects enrolled per age group

|   |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 14 |
| Adults (18-64 years)                      | 0  |
| From 65 to 84 years                       | 0  |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

The study started to enroll study participants in April 2021 and concluded in April 2022.

### Pre-assignment

Screening details:

Participant Flow refers to the Safety Set.

### Period 1

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

### Arms

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Staccato Alprazolam |
|------------------|---------------------|

Arm description:

Participants received staccato alprazolam inhalation powder on Day 1. Participants were followed up to Day 9.

|  |                     |
|--|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | Staccato Alprazolam |
| Investigational medicinal product code | UCB7538             |
| Other name                             |                     |
| Pharmaceutical forms                   | Inhalation powder   |
| Routes of administration               | Inhalation use      |

Dosage and administration details:

Participants received staccato alprazolam on Day 1.

|                                       |                     |
|---------------------------------------|---------------------|
| <b>Number of subjects in period 1</b> | Staccato Alprazolam |
| Started                               | 14                  |
| Completed                             | 14                  |

## Baseline characteristics

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Staccato Alprazolam |
|-----------------------|---------------------|

Reporting group description:

Participants received staccato alprazolam inhalation powder on Day 1. Participants were followed up to Day 9.

| Reporting group values                   | Staccato Alprazolam | Total |  |
|--|---------------------|-------|--|
| Number of subjects                       | 14                  | 14    |  |
| Age Categorical<br>Units: participants   |                     |       |  |
| <=18 years                               | 14                  | 14    |  |
| Between 18 and 65 years                  | 0                   | 0     |  |
| >=65 years                               | 0                   | 0     |  |
| Age Continuous<br>Units: years           |                     |       |  |
| arithmetic mean                          | 15.1                |       |  |
| standard deviation                       | ± 1.9               | -     |  |
| Sex: Female, Male<br>Units: participants |                     |       |  |
| Female                                   | 12                  | 12    |  |
| Male                                     | 2                   | 2     |  |

## End points

### End points reporting groups

|   |                     |
|---|---------------------|
| Reporting group title   | Staccato Alprazolam |
| Reporting group description:  |                     |
| Participants received staccato alprazolam inhalation powder on Day 1. Participants were followed up to Day 9. |                     |

### Primary: Maximum plasma concentration (Cmax) following single inhaled dose of Staccato alprazolam

|  |   |
|--|---|
| End point title  | Maximum plasma concentration (Cmax) following single inhaled dose of Staccato alprazolam <sup>[1]</sup> |
| End point description:   |   |
| Cmax was defined as the maximum observed plasma concentration. Pharmacokinetic Set (PKS) included all study participants who received at least 1 dose of IMP and had at least 1 observable PK measurement. |   |
| End point type   | Primary   |
| End point timeframe:   |   |
| Plasma samples were taken on Day 1, predose and then at 2 minutes, 10 minutes, 30 minutes, 1 hour, 2 hours, 6 hours, 24 hours, and 36 hours postdose   |   |
| 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 was planned for this study. Results were summarized in tables as descriptive statistics only.  |   |

|   |                     |  |  |  |
|---|---------------------|--|--|--|
| <b>End point values</b>                             | Staccato Alprazolam |  |  |  |
| Subject group type                                  | Reporting group     |  |  |  |
| Number of subjects analysed                         | 14                  |  |  |  |
| Units: nanogram/milliliter                          |                     |  |  |  |
| geometric mean (geometric coefficient of variation) | 35.50 (± 57.8)      |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Area under the plasma concentration-time curve from zero to the last quantifiable concentration (AUC(0-t)) following single inhaled dose of Staccato alprazolam

|  |  |
|--|--|
| End point title  | Area under the plasma concentration-time curve from zero to the last quantifiable concentration (AUC(0-t)) following single inhaled dose of Staccato alprazolam <sup>[2]</sup> |
| End point description:   |  |
| AUC(0-t) was defined as area under the plasma concentration-time curve from zero to the last quantifiable concentration. Pharmacokinetic Set included all study participants who received at least 1 dose of IMP and had at least 1 observable PK measurement. |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| Plasma samples were taken on Day 1, predose and then at 2 minutes, 10 minutes, 30 minutes, 1 hour,   |  |

2 hours, 6 hours, 24 hours, and 36 hours postdose

Notes:

[2] - 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 was planned for this study. Results were summarized in tables as descriptive statistics only.

| End point values                                    | Staccato Alprazolam |  |  |  |
|---|---------------------|--|--|--|
| Subject group type                                  | Reporting group     |  |  |  |
| Number of subjects analysed                         | 14                  |  |  |  |
| Units: hour*nanogram/milliliter                     |                     |  |  |  |
| geometric mean (geometric coefficient of variation) | 278.2 (± 36.2)      |  |  |  |

### Statistical analyses

No statistical analyses for this end point

#### Primary: Area under the plasma concentration-time curve from time 0 to infinity (AUC) following single inhaled dose of Staccato alprazolam

|                 |  |
|-----------------|--|
| End point title | Area under the plasma concentration-time curve from time 0 to infinity (AUC) following single inhaled dose of Staccato alprazolam <sup>[3]</sup> |
|-----------------|--|

End point description:

AUC was defined as area under the plasma concentration-time curve from time 0 to infinity. Pharmacokinetic Set included all study participants who received at least 1 dose of IMP and had at least 1 observable PK measurement. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Plasma samples were taken on Day 1, predose and then at 2 minutes, 10 minutes, 30 minutes, 1 hour, 2 hours, 6 hours, 24 hours, and 36 hours postdose

Notes:

[3] - 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 was planned for this study. Results were summarized in tables as descriptive statistics only.

| End point values                                    | Staccato Alprazolam |  |  |  |
|---|---------------------|--|--|--|
| Subject group type                                  | Reporting group     |  |  |  |
| Number of subjects analysed                         | 12                  |  |  |  |
| Units: hour*nanogram/milliliter                     |                     |  |  |  |
| geometric mean (geometric coefficient of variation) | 280.0 (± 35.8)      |  |  |  |

### Statistical analyses

No statistical analyses for this end point

#### Primary: Apparent total body clearance (CL/F) following single inhaled dose of

## Staccato alprazolam

|                 |  |
|-----------------|--|
| End point title | Apparent total body clearance (CL/F) following single inhaled dose of Staccato alprazolam <sup>[4]</sup> |
|-----------------|--|

End point description:

CL/F was defined as apparent total body clearance. Pharmacokinetic Set included all study participants who received at least 1 dose of IMP and had at least 1 observable PK measurement. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Plasma samples were taken on Day 1, predose and then at 2 minutes, 10 minutes, 30 minutes, 1 hour, 2 hours, 6 hours, 24 hours, and 36 hours postdose

Notes:

[4] - 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 was planned for this study. Results were summarized in tables as descriptive statistics only.

| End point values                                    | Staccato Alprazolam |  |  |  |
|---|---------------------|--|--|--|
| Subject group type                                  | Reporting group     |  |  |  |
| Number of subjects analysed                         | 12                  |  |  |  |
| Units: Liter/hour                                   |                     |  |  |  |
| geometric mean (geometric coefficient of variation) | 7.144 (± 35.8)      |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of participants with treatment-emergent adverse events (TEAEs)

|                 |  |
|-----------------|--|
| End point title | Percentage of participants with treatment-emergent adverse events (TEAEs) <sup>[5]</sup> |
|-----------------|--|

End point description:

A TEAE was defined as any AE with a start date/time on or after the dose of treatment or any unresolved event already present before administration of treatment that worsened in intensity following exposure to the treatment. Safety Set consisted of all study participants who received at least 1 dose of IMP.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline (Day 1) till end of Safety Follow-up (up to Day 9)

Notes:

[5] - 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 was planned for this study. Results were summarized in tables as descriptive statistics only.

| End point values                  | Staccato Alprazolam |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 14                  |  |  |  |
| Units: percentage of participants |                     |  |  |  |
| number (not applicable)           | 21.4                |  |  |  |



## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of participants with serious treatment-emergent adverse events (serious TEAEs)

|                 |  |
|-----------------|--|
| End point title | Percentage of participants with serious treatment-emergent adverse events (serious TEAEs) <sup>[6]</sup> |
|-----------------|--|

End point description:

A TEAE was defined as any AE with a start date/time on or after the dose of treatment or any unresolved event already present before administration of treatment that worsened in intensity following exposure to the treatment. A serious adverse event (SAE) was defined as any untoward medical occurrence that, at any dose: a. Resulted in death, b. Is life-threatening, c. Required inpatient hospitalization or prolongation of existing hospitalization, d. Resulted in persistent disability/incapacity, e. Is a congenital anomaly/birth defect, f. Important medical events. Safety Set consisted of all study participants who received at least 1 dose of IMP.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline (Day 1) till end of Safety Follow-up (up to Day 9)

Notes:

[6] - 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 was planned for this study. Results were summarized in tables as descriptive statistics only.

| End point values                  | Staccato Alprazolam |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 14                  |  |  |  |
| Units: percentage of participants |                     |  |  |  |
| number (not applicable)           | 0                   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From Baseline (Day 1) till end of Safety Follow-up (up to Day 9)

Adverse event reporting additional description:

A TEAE was defined as any AE with a start date/time on or after the dose of treatment or any unresolved event already present before administration of treatment that worsened in intensity following exposure to the treatment. Safety Set was analyzed for TEAEs.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Staccato Alprazolam |
|-----------------------|---------------------|

Reporting group description:

Participants received staccato alprazolam inhalation powder on Day 1. Participants were followed up to Day 9.

| Serious adverse events                            | Staccato Alprazolam |  |  |
|---|---------------------|--|--|
| Total subjects affected by serious adverse events |                     |  |  |
| subjects affected / exposed                       | 0 / 14 (0.00%)      |  |  |
| number of deaths (all causes)                     | 0                   |  |  |
| number of deaths resulting from adverse events    | 0                   |  |  |

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

| Non-serious adverse events                            | Staccato Alprazolam |  |  |
|---|---------------------|--|--|
| Total subjects affected by non-serious adverse events |                     |  |  |
| subjects affected / exposed                           | 3 / 14 (21.43%)     |  |  |
| Nervous system disorders                              |                     |  |  |
| Dysgeusia   |                     |  |  |
| subjects affected / exposed                           | 3 / 14 (21.43%)     |  |  |
| occurrences (all)                                     | 3                   |  |  |
| Somnolence  |                     |  |  |
| subjects affected / exposed                           | 3 / 14 (21.43%)     |  |  |
| occurrences (all)                                     | 4                   |  |  |
| Dizziness   |                     |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 2 / 14 (14.29%) |  |  |
| occurrences (all)                               | 2               |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Cough   |                 |  |  |
| subjects affected / exposed                     | 2 / 14 (14.29%) |  |  |
| occurrences (all)                               | 2               |  |  |
| Hiccups   |                 |  |  |
| subjects affected / exposed                     | 2 / 14 (14.29%) |  |  |
| occurrences (all)                               | 2               |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment  |
|-----------------|--|
| 12 January 2022 | Protocol Amendment 3, dated 12 Jan 2022, was a substantial amendment that was implemented after 6 participants had been enrolled in the study. The main purpose of this amendment was to decrease the burden on study participants, their families, and clinical sites by allowing study participants to leave the clinic after the 6-hour postdose safety assessments and PK blood sampling and return to the clinic for the 24- and 36-hour postdose assessments, at the discretion of the Investigator. This change in the study conduct was supported by results from the first set of study participants (N=6, including at least 2 adolescent participants with body weight <50kg) enrolled in UP0100. Careful review of these results by the study safety monitoring committee (SMC) did not reveal any safety concerns that would preclude discharge of UP0100 study participants after the 6-hour postdose assessments. Edits were made to clarify removal of the 12-hour time point for assessment of vital signs, peripheral oxygen saturation (SpO2), and sedation/sleepiness (by visual analog scale [VAS]) from the Schedule of Assessments and other applicable sections of the protocol. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The PK endpoint measures of geometric mean are presented with percentage geometric coefficients of variation.

Notes: