



## Clinical trial results:

### A Short-term Exploratory Study to Evaluate Safety, Tolerability, and Pharmacokinetics of Seltorexant as Adjunctive Therapy to Antidepressants in Adolescents with Major Depressive Disorder Who Have an Inadequate Response to an SSRI and Psychotherapy

#### Summary

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2021-000567-77          |
| Trial protocol           | Outside EU/EEA ES IT SE |
| Global end of trial date | 08 April 2024           |

#### Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 12 March 2025  |
| First version publication date | 24 October 2024  |
| Version creation reason        | <ul style="list-style-type: none"><li>New data added to full data set</li></ul> Secondary end points |

#### Trial information

##### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | 42847922MDD1016 |
|-----------------------|-----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04951609 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Janssen Research & Development, LLC  |
| Sponsor organisation address | 920 Route 202 South, Raritan, New Jersey, United States, 08869                             |
| Public contact               | Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com |
| Scientific contact           | Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com |

Notes:

#### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-002746-PIP01-20 |
| 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                       | 08 April 2024 |
| Is this the analysis of the primary completion data? | No            |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 08 April 2024 |
| Was the trial ended prematurely?                     | Yes           |

Notes:

## General information about the trial

Main objective of the trial:

The main objective was to assess the safety and tolerability of seltorexant as adjunctive therapy to an antidepressant in adolescents with major depressive disorder (MDD), in short-term compared with placebo.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 02 September 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 | Spain: 5          |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Country: Number of subjects enrolled | Italy: 2          |
| Country: Number of subjects enrolled | United States: 22 |
| Worldwide total number of subjects   | 30                |
| EEA total number of subjects         | 7                 |

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) | 30 |
| Adults (18-64 years)      | 0  |
| From 65 to 84 years       | 0  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 31 subjects were randomised, out of which only 30 subjects were treated with either study intervention or placebo. One subject was randomised to seltorexant treatment but was not treated with the study intervention.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Double blind                   |
| Roles blinded                | Subject, Investigator          |

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Placebo |

Arm description:

Subjects received a single oral dose of placebo (matching to seltorexant) tablet once daily at bedtime from Day 1 to Week 6.

|  |          |
|--|----------|
| Arm type                               | Placebo  |
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

Subjects received a single oral dose of placebo (matching to seltorexant) tablet once daily at bedtime from Day 1 to Week 6.

|                  |                             |
|------------------|-----------------------------|
| <b>Arm title</b> | Seltorexant 10 mg and 20 mg |
|------------------|-----------------------------|

Arm description:

Subjects with body weight greater than or equal to ( $\geq$ ) 45 kilograms (kg) received a single oral dose of seltorexant 20 milligrams (mg) tablet once daily at bedtime and subjects with body weight  $\geq 30$  kg to less than ( $<$ ) 45 kg received seltorexant 10 mg tablet once daily at bedtime from Day 1 to Week 6. Subjects continued with their baseline selective serotonin reuptake inhibitor (SSRI) antidepressant (fluoxetine or escitalopram) treatment at same dose as it was prior to entering the study.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Seltorexant  |
| Investigational medicinal product code | JNJ-42847922 |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Subjects received a single oral dose of seltorexant 20 mg or 10 mg tablet once daily at bedtime based on the body weight from Day 1 to Week 6.

| <b>Number of subjects in period 1</b> | Placebo | Seltorexant 10 mg<br>and 20 mg |
|---------------------------------------|---------|--------------------------------|
| Started                               | 7       | 23                             |
| Completed                             | 6       | 22                             |
| Not completed                         | 1       | 1                              |
| Consent withdrawn by subject          | 1       | -                              |
| Adverse event, non-fatal              | -       | 1                              |

## Baseline characteristics

### Reporting groups

|   |                             |
|---|-----------------------------|
| Reporting group title   | Placebo                     |
| Reporting group description:<br>Subjects received a single oral dose of placebo (matching to seltorexant) tablet once daily at bedtime from Day 1 to Week 6.  |                             |
| Reporting group title   | Seltorexant 10 mg and 20 mg |
| Reporting group description:<br>Subjects with body weight greater than or equal to ( $\geq$ ) 45 kilograms (kg) received a single oral dose of seltorexant 20 milligrams (mg) tablet once daily at bedtime and subjects with body weight $\geq 30$ kg to less than ( $<$ ) 45 kg received seltorexant 10 mg tablet once daily at bedtime from Day 1 to Week 6. Subjects continued with their baseline selective serotonin reuptake inhibitor (SSRI) antidepressant (fluoxetine or escitalopram) treatment at same dose as it was prior to entering the study. |                             |

| Reporting group values                      | Placebo    | Seltorexant 10 mg and 20 mg | Total |
|---|------------|-----------------------------|-------|
| Number of subjects                          | 7          | 23                          | 30    |
| Title for AgeCategorical<br>Units: subjects |            |                             |       |
| Children (2-11 years)                       | 0          | 0                           | 0     |
| Adolescents (12-17 years)                   | 7          | 23                          | 30    |
| Adults (18-64 years)                        | 0          | 0                           | 0     |
| From 65 to 84 years                         | 0          | 0                           | 0     |
| 85 years and over                           | 0          | 0                           | 0     |
| Title for AgeContinuous<br>Units: years     |            |                             |       |
| arithmetic mean                             | 15.9       | 15                          |       |
| standard deviation                          | $\pm 1.07$ | $\pm 1.54$                  | -     |
| Title for Gender<br>Units: subjects         |            |                             |       |
| Female                                      | 5          | 17                          | 22    |
| Male  | 2          | 6                           | 8     |

## End points

### End points reporting groups

|   |                             |
|---|-----------------------------|
| Reporting group title   | Placebo                     |
| Reporting group description:<br>Subjects received a single oral dose of placebo (matching to seltorexant) tablet once daily at bedtime from Day 1 to Week 6.  |                             |
| Reporting group title   | Seltorexant 10 mg and 20 mg |
| Reporting group description:<br>Subjects with body weight greater than or equal to ( $\geq$ ) 45 kilograms (kg) received a single oral dose of seltorexant 20 milligrams (mg) tablet once daily at bedtime and subjects with body weight $\geq 30$ kg to less than ( $<$ ) 45 kg received seltorexant 10 mg tablet once daily at bedtime from Day 1 to Week 6. Subjects continued with their baseline selective serotonin reuptake inhibitor (SSRI) antidepressant (fluoxetine or escitalopram) treatment at same dose as it was prior to entering the study. |                             |

### Primary: Double-blind Phase: Number of Subjects with Treatment Emergent Adverse Events (TEAEs)

|   |  |
|---|--|
| End point title   | Double-blind Phase: Number of Subjects with Treatment Emergent Adverse Events (TEAEs) <sup>[1]</sup> |
| End point description:<br>An adverse event (AE) was any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. Treatment-emergent adverse events were any AE occurring at or after the initial administration of study intervention through 2 days after the last administration of study intervention. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. |  |
| End point type  | Primary  |
| End point timeframe:<br>From start of treatment (Day 1) up to Week 6  |  |
| Notes:<br>[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.<br>Justification: Only descriptive data was planned to be reported for this endpoint.   |  |

| End point values            | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|-----------------------------|-----------------|-----------------------------|--|--|
| Subject group type          | Reporting group | Reporting group             |  |  |
| Number of subjects analysed | 7               | 23                          |  |  |
| Units: subjects             | 2               | 9                           |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Double-blind Phase: Number of Subjects with Treatment Emergent Adverse Event of Special Interest (AESIs)

|   |   |
|---|---|
| End point title   | Double-blind Phase: Number of Subjects with Treatment Emergent Adverse Event of Special Interest (AESIs) <sup>[2]</sup> |
| End point description:<br>An adverse event (AE) any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal |   |

relationship with the intervention. Treatment-emergent adverse events were any AE occurring at or after the initial administration of study intervention through 2 days after the last administration of study intervention. AESIs were significant AEs that were judged to be of special interest because of clinical importance, known or suspected class effects, or based on nonclinical signals. Adverse events of special interest were cataplexy, sleep paralysis, complex, and sleep-related behaviors (parasomnias), new suicidal behavior or suicidal ideation. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention.

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

End point timeframe:

From start of treatment (Day 1) up to Week 6

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: Only descriptive data was planned to be reported for this endpoint.

| End point values            | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|-----------------------------|-----------------|-----------------------------|--|--|
| Subject group type          | Reporting group | Reporting group             |  |  |
| Number of subjects analysed | 7               | 23                          |  |  |
| Units: subjects             | 0               | 1                           |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Double-blind Phase: Number of Symptoms as Assessed by Pediatric Adverse Event Rating Scale (PAERS)

|                 |   |
|-----------------|---|
| End point title | Double-blind Phase: Number of Symptoms as Assessed by Pediatric Adverse Event Rating Scale (PAERS) <sup>[3]</sup> |
|-----------------|---|

End point description:

Number of symptoms as assessed by PAERS were reported. The PAERS was a patient-rated scale designed to assess adverse events occurring in pediatric subjects treated with psychotropic medication in clinical studies. Individual PAERS (patient-reported version) items rated on symptoms and severity of symptoms. PAERS scale consisted of 45 items (43 specific signs and symptoms and 2 to be specified). Individual items were rated on a scale of "0" (mild) to "4" (extreme). Safety analysis set included all randomised subjects who took at least 1 dose of study intervention.

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

End point timeframe:

Baseline, Day 15, Day 29, and end of double-blind phase (Week 6)

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: Only descriptive data was planned to be reported for this endpoint.

| End point values            | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|-----------------------------|-----------------|-----------------------------|--|--|
| Subject group type          | Reporting group | Reporting group             |  |  |
| Number of subjects analysed | 7               | 23                          |  |  |
| Units: number of symptoms   |                 |                             |  |  |
| Baseline: Mild              | 55              | 177                         |  |  |
| Baseline: Moderate          | 59              | 134                         |  |  |
| Baseline: Severe            | 30              | 82                          |  |  |
| Baseline: Extreme           | 21              | 43                          |  |  |
| Day 15: Mild                | 79              | 172                         |  |  |



|   |    |     |  |  |
|---|----|-----|--|--|
| Day 15: Moderate                                | 33 | 90  |  |  |
| Day 15: Severe                                  | 13 | 59  |  |  |
| Day 15: Extreme                                 | 9  | 26  |  |  |
| Day 29: Mild                                    | 83 | 154 |  |  |
| Day 29: Moderate                                | 31 | 81  |  |  |
| Day 29: Severe                                  | 5  | 39  |  |  |
| Day 29: Extreme                                 | 2  | 19  |  |  |
| End of double-blind phase (Week 6):<br>Mild     | 74 | 161 |  |  |
| End of double-blind phase (Week 6):<br>Moderate | 25 | 82  |  |  |
| End of double-blind phase (Week 6):<br>Severe   | 9  | 35  |  |  |
| End of double-blind phase (Week 6):<br>Extreme  | 2  | 16  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Double-blind Phase: Number of Subjects with Abnormalities in Clinical Laboratory Values

|                 |  |
|-----------------|--|
| End point title | Double-blind Phase: Number of Subjects with Abnormalities in Clinical Laboratory Values <sup>[4]</sup> |
|-----------------|--|

End point description:

Number of subjects with abnormalities in clinical laboratory values (hematology, and serum chemistry) were reported. Only those categories in which at least one subject had data are reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

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

End point timeframe:

From start of treatment (Day 1) up to end of double-blind phase (Week 6)

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: Only descriptive data was planned to be reported for this endpoint.

| End point values                      | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|---------------------------------------|-----------------|-----------------------------|--|--|
| Subject group type                    | Reporting group | Reporting group             |  |  |
| Number of subjects analysed           | 6               | 22                          |  |  |
| Units: subjects                       |                 |                             |  |  |
| Chemistry: Alkaline Phosphatase: high | 0               | 1                           |  |  |
| Chemistry: Cholesterol: high          | 1               | 3                           |  |  |
| Chemistry: LDL Cholesterol: high      | 0               | 1                           |  |  |
| Chemistry: Phosphate: high            | 0               | 2                           |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Double-blind Phase: Number of Subjects with Abnormalities in Electrocardiogram (ECG)

|                 |   |
|-----------------|---|
| End point title | Double-blind Phase: Number of Subjects with Abnormalities in Electrocardiogram (ECG) <sup>[5]</sup> |
|-----------------|---|

End point description:

Number of subjects with abnormalities in ECG were reported. The ECG parameters included heart rate, PR interval, QRS interval, QT interval, and corrected QT (QTc). Only those categories in which at least one subject had data are reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

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

End point timeframe:

Pre-dose (Day 1) and end of double-blind phase (Week 6)

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: Only descriptive data was planned to be reported for this endpoint.

| End point values                              | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|---|-----------------|-----------------------------|--|--|
| Subject group type                            | Reporting group | Reporting group             |  |  |
| Number of subjects analysed                   | 7               | 23                          |  |  |
| Units: subjects                               |                 |                             |  |  |
| Pre-dose (Day 1) (n=7, 23)                    | 3               | 0                           |  |  |
| End of double-blind phase (Day 43): (n=6, 23) | 2               | 4                           |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Double-blind Phase: Number of Subjects with Abnormalities in Vital Signs

|                 |   |
|-----------------|---|
| End point title | Double-blind Phase: Number of Subjects with Abnormalities in Vital Signs <sup>[6]</sup> |
|-----------------|---|

End point description:

Number of subjects with abnormalities in vital sign (blood pressure [systolic and diastolic blood pressure] and temperature) were reported. Only those categories in which at least one subject had data are reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Units for blood pressure: millimetre of mercury (mmHg).

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

End point timeframe:

From start of treatment (Day 1) up to end of double-blind phase (Week 6)

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: Only descriptive data was planned to be reported for this endpoint.

| End point values                   | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|------------------------------------|-----------------|-----------------------------|--|--|
| Subject group type                 | Reporting group | Reporting group             |  |  |
| Number of subjects analysed        | 7               | 23                          |  |  |
| Units: subjects                    |                 |                             |  |  |
| Systolic Blood Pressure: >130 mmHg | 0               | 3                           |  |  |
| Systolic Blood Pressure: <90 mmHg  | 1               | 2                           |  |  |
| Diastolic Blood Pressure: >80 mmHg | 0               | 2                           |  |  |
| Diastolic Blood Pressure: <50 mmHg | 0               | 0                           |  |  |
| Temperature: >37.7 Celsius (C)     | 0               | 0                           |  |  |
| Temperature: <35.5 C               | 1               | 0                           |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Double-blind Phase: Change from Baseline in Physical Examination: Body Weight

|                 |  |
|-----------------|--|
| End point title | Double-blind Phase: Change from Baseline in Physical Examination: Body Weight <sup>[7]</sup> |
|-----------------|--|

End point description:

Change from baseline in physical examination: waist circumference was reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

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

End point timeframe:

Baseline (Day 1), and end of double-blind phase (Week 6)

Notes:

[7] - 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: Only descriptive data was planned to be reported for this endpoint.

| End point values                     | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|--------------------------------------|-----------------|-----------------------------|--|--|
| Subject group type                   | Reporting group | Reporting group             |  |  |
| Number of subjects analysed          | 6               | 23                          |  |  |
| Units: kilograms (kg)                |                 |                             |  |  |
| arithmetic mean (standard deviation) | -1.40 (± 1.333) | 1.15 (± 1.736)              |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects with Suicidality Assessment Using the Columbia Suicide Severity Rating Scale (C-SSRS) Score

|                 |   |
|-----------------|---|
| End point title | Number of Subjects with Suicidality Assessment Using the Columbia Suicide Severity Rating Scale (C-SSRS) Score <sup>[8]</sup> |
|-----------------|---|

End point description:

C-SSRS scale reported at least one occurrence of any suicidal behavior and ideation. Suicidal behavior:

reporting any of 5 items: suicide, actual attempt, interrupted attempt, aborted attempt, preparatory acts or behavior. Suicidal ideation: consists of 5 yes/no items: wish to be dead, non-specific active suicidal thoughts, active suicidal ideation with any methods (not plan) without intent to act, active suicidal ideation with some intent to act, without specific plan, active suicidal ideation with specific plan and intent. An event of suicidal ideation or behavior were scored on a scale of 0 (no suicidal ideation or behavior) to 10 (suicide) based on highest response at the given time point. Worsening of suicidal ideation indicated an increase in severity of suicidal ideation. Only those categories in which at least 1 subject had data are reported. Safety analysis set was analysed. Here, "n"(number of subjects analysed) signifies number of subjects analysed at specified categories.

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

End point timeframe:

Baseline (Day 1[D1]), Day 8, Day 15, Day 29, and end of double-blind phase (Week 6)

Notes:

[8] - 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: Only descriptive data was planned to be reported for this endpoint.

| End point values                                   | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|--|-----------------|-----------------------------|--|--|
| Subject group type                                 | Reporting group | Reporting group             |  |  |
| Number of subjects analysed                        | 7               | 23                          |  |  |
| Units: subjects                                    |                 |                             |  |  |
| D1: No suicidal ideation or behavior:<br>n=7, 23   | 7               | 18                          |  |  |
| D1: Wish to be dead: n=7, 23                       | 0               | 1                           |  |  |
| D1:Non-specific active suicidal thoughts:n=7, 23   | 0               | 3                           |  |  |
| D1:Suicidal ideation without plan & intent: n=7,23 | 0               | 1                           |  |  |
| D8:No suicidal ideation or behavior(n=7, 23)       | 7               | 21                          |  |  |
| D8: Non-specific active suicidal thoughts(n=7, 23) | 0               | 2                           |  |  |
| D15: No suicidal ideation or behavior(n=7, 23)     | 7               | 20                          |  |  |
| D15:Non-specific active suicidal thoughts:n=7, 23  | 0               | 2                           |  |  |
| D15: Suicidal ideation intent without plan:n=7,23  | 0               | 1                           |  |  |
| D29:No suicidal ideation or behavior (n=6, 23)     | 6               | 18                          |  |  |
| D29: Wish to be dead (n=6, 23)                     | 0               | 2                           |  |  |
| D29:Non-specific active suicidal thoughts:n=6, 23  | 0               | 2                           |  |  |
| D29:Suicidal ideation without plan & intent:n=6,23 | 0               | 1                           |  |  |
| D43:No suicidal ideation or behavior(n=6, 22)      | 6               | 18                          |  |  |
| D43: Wish to be dead (n=6, 22)                     | 0               | 2                           |  |  |
| D43:Non-specific active suicidal thoughts (n=6,22) | 0               | 2                           |  |  |
| D43:Non-suicidal self-injurious behavior(n=6, 22)  | 0               | 1                           |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Withdrawal Symptoms Assessment Using the Physician Withdrawal Checklist (PWC-20)

|                 |   |
|-----------------|---|
| End point title | Withdrawal Symptoms Assessment Using the Physician Withdrawal Checklist (PWC-20) <sup>[9]</sup> |
|-----------------|---|

#### End point description:

PWC-20 was a reliable, sensitive instrument having 20-items used to assess potential withdrawal symptoms following cessation of treatment. Items were loss of appetite, nausea-vomiting, diarrhea, anxiety-nervousness, irritability, dysphoric mood-depression, insomnia, fatigue, poor coordination, restlessness, diaphoresis, tremor, dizziness, headaches, stiffness, weakness, increased acuity sound smell touch (IASST), paresthesia, difficulty concentrating-, remember, derealization. Each item score ranged from 0 (not present) to 3 (severe). Total score ranges from 0-60, where higher score indicates more severe symptoms. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

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

#### End point timeframe:

End of double-blind phase (Week 6), Follow-up 1 (Day 45), Follow-up 2 (Day 54)

#### Notes:

[9] - 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: Only descriptive data was planned to be reported for this endpoint.

| End point values                                | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|---|-----------------|-----------------------------|--|--|
| Subject group type                              | Reporting group | Reporting group             |  |  |
| Number of subjects analysed                     | 6               | 23                          |  |  |
| Units: Units on a scale                         |                 |                             |  |  |
| arithmetic mean (standard deviation)            |                 |                             |  |  |
| End of double-blind phase (Week 6)<br>(n=6, 23) | 2.7 (± 3.78)    | 6.9 (± 6.43)                |  |  |
| Follow-up 1 (Day 45) (5, 22)                    | 4.2 (± 3.90)    | 4.1 (± 6.57)                |  |  |
| Follow-up 2 (Day 54) (6, 23)                    | 5.7 (± 6.65)    | 5.6 (± 5.29)                |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Double-blind Phase: Menstrual Cycle Tracking: Duration of Menses and Length of Menstrual Cycle

|                 |  |
|-----------------|--|
| End point title | Double-blind Phase: Menstrual Cycle Tracking: Duration of Menses and Length of Menstrual Cycle <sup>[10]</sup> |
|-----------------|--|

#### End point description:

Menstrual cycles were tracked during the study in female adolescents or subjects who have at least one menses' using a subject diary and subject's verbal report. Menstrual cycle duration was measured by the number of days subjects noted menstruating in their diary entry. Menstrual cycle length was assessed as the number of days between menstrual cycles (i.e., days between the start of a menstrual period and the start of the next consecutive menstrual period) from baseline to end of double-blind phase (Week 6). Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified categories.

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

End point timeframe:

From baseline (Day 1) up to end of double-blind phase (Week 6)

Notes:

[10] - 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: Only descriptive data was planned to be reported for this endpoint.

| End point values                     | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|--------------------------------------|-----------------|-----------------------------|--|--|
| Subject group type                   | Reporting group | Reporting group             |  |  |
| Number of subjects analysed          | 3               | 15                          |  |  |
| Units: days                          |                 |                             |  |  |
| arithmetic mean (standard deviation) |                 |                             |  |  |
| Duration of menses (n=3, 13)         | 6.0 (± 1.00)    | 6.8 (± 3.06)                |  |  |
| Length of cycle (n=2, 15)            | 62.0 (± 2.83)   | 45.9 (± 19.12)              |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in the Children's Depression Rating Scale (CDRS) Total Score

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in the Children's Depression Rating Scale (CDRS) Total Score |
|-----------------|---|

End point description:

Change from baseline in the CDRS total score were reported. The CDRS-R was a validated 17-item, clinician-rated instrument that measured the severity of a subject's depressive symptoms. The CDRS-R total score was the sum of the responses to 17 questions, ranged from 17 to 113. Each scale item was scored from 1 to 5 or 1 to 7. The highest possible score is 113 (the most severe measure of depression), and the lowest is 17 (not suffering from depression). Higher scores represent a more severe condition. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and end of double-blind phase (Week 6)

| End point values                     | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|--------------------------------------|-----------------|-----------------------------|--|--|
| Subject group type                   | Reporting group | Reporting group             |  |  |
| Number of subjects analysed          | 6               | 22                          |  |  |
| Units: Units on a scale              |                 |                             |  |  |
| arithmetic mean (standard deviation) | -22.0 (± 9.86)  | -21.3 (± 12.45)             |  |  |

## Statistical analyses

**Secondary: Change from Baseline in Montgomery Asberg Depression Rating Scale (MADRS) Score**

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Montgomery Asberg Depression Rating Scale (MADRS) Score |
|-----------------|---|

## End point description:

Change from baseline in MADRS score were reported. The MADRS scale score was a 10-item clinician-administered scale designed to measure depression severity and to detect changes due to antidepressant treatment using the 10 items followed: apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, & suicidal thoughts. Each item scored from 0 (no symptoms or normal) to 6 (symptoms of maximum severity), & the sum of scores of individual question items at a given time point ranged from 0 to 60. Higher scores indicated more severe condition. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Baseline (Day 1) and end of double-blind phase (Week 6)

| End point values                     | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|--------------------------------------|-----------------|-----------------------------|--|--|
| Subject group type                   | Reporting group | Reporting group             |  |  |
| Number of subjects analysed          | 6               | 22                          |  |  |
| Units: Units on a scale              |                 |                             |  |  |
| arithmetic mean (standard deviation) | -17.2 (± 10.42) | -14.6 (± 9.22)              |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change from Baseline in Clinical Global Impression- severity (CGI-S) Score Over Time**

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Clinical Global Impression- severity (CGI-S) Score Over Time |
|-----------------|--|

## End point description:

Change from baseline in the CGI-S score were reported. The CGI-S provided an overall clinician-determined summary measure of the severity of the subject's illness. The CGI scale is an investigator-rated evaluation that assesses the severity of a subject's illness on a 7-point scale, ranged from 1 (normal, not at all ill) to 7 (among the most extremely ill subjects). Considering total clinical experience with the depression population, a subject was assessed on severity of illness at the time of rating according to: 1=normal (not at all ill); 2=borderline ill; 3=mildly ill; 4=moderately ill; 5=markedly ill; 6=severely ill; 7=among the most extremely ill subjects. Higher scores indicated more severe condition. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here, "n"(number analysed) signifies number of subjects analysed at specified timepoints.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Baseline (Day 1), Day 15, Day 29, end of double-blind phase (Week 6)

| End point values                     | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|--------------------------------------|-----------------|-----------------------------|--|--|
| Subject group type                   | Reporting group | Reporting group             |  |  |
| Number of subjects analysed          | 7               | 23                          |  |  |
| Units: units on a scale              |                 |                             |  |  |
| arithmetic mean (standard deviation) |                 |                             |  |  |
| Day 15 (n=7, 23)                     | -1.7 (± 1.11)   | -0.7 (± 0.75)               |  |  |
| Day 29 (n=6,23)                      | -2.0 (± 1.26)   | -1.2 (± 1.00)               |  |  |
| Week 6 (n=6, 22)                     | -2.0 (± 1.26)   | -1.6 (± 1.14)               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Subjective Sleep Assessment (Patient Reported Outcome Measurement Information System-Pediatric-Sleep Disturbance [PROMIS-Pediatric-SD])

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Subjective Sleep Assessment (Patient Reported Outcome Measurement Information System-Pediatric-Sleep Disturbance [PROMIS-Pediatric-SD]) |
|-----------------|---|

End point description:

The PROMIS-Pediatric-SD was a static 8 item questionnaire used to assess self-reported perceptions of sleep quality. Each item has 5 responses scored on a 5 level Likert-type scale. The 8-item short form were used, in which responses were scored 1 to 5 for each item. For the 8-item form, the lowest possible raw score is 8; the highest possible raw score is 40. Lower scores indicate less sleep disturbance. The "direction" of the responses was not the same for all questions, i.e., sometimes a response of "always" indicated more sleep disturbance and sometimes a response of "always" indicated less sleep disturbance. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and end of double-blind phase (Week 6)

| End point values                     | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|--------------------------------------|-----------------|-----------------------------|--|--|
| Subject group type                   | Reporting group | Reporting group             |  |  |
| Number of subjects analysed          | 6               | 22                          |  |  |
| Units: Units on a scale              |                 |                             |  |  |
| arithmetic mean (standard deviation) | -3.93 (± 9.074) | -8.41 (± 8.618)             |  |  |

### Statistical analyses



**Secondary: Change from Baseline on Objective Sleep Assessment Actigraphy: Total Sleep Time**

|                 |   |
|-----------------|---|
| End point title | Change from Baseline on Objective Sleep Assessment Actigraphy: Total Sleep Time |
|-----------------|---|

## End point description:

Change from baseline on objective sleep assessment actigraphy: total sleep time were reported. Objective sleep parameters were measured using actigraphy. Total sleep time was defined as the number of scored sleep epochs (an epoch equals 30 to 60 seconds), in minutes. Full analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Week 1, Week 2, Week 3, Week 4, Week 5, and Week 6

| End point values                     | Placebo           | Seltorexant 10 mg and 20 mg |  |  |
|--------------------------------------|-------------------|-----------------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group             |  |  |
| Number of subjects analysed          | 5                 | 17                          |  |  |
| Units: minutes (min)                 |                   |                             |  |  |
| arithmetic mean (standard deviation) |                   |                             |  |  |
| Week 1 (N=5, 17)                     | 32.62 (± 48.351)  | -25.22 (± 116.136)          |  |  |
| Week 2 (n=5, 14)                     | 30.82 (± 76.472)  | -20.64 (± 95.390)           |  |  |
| Week 3 (n=5,12)                      | 11.44 (± 55.639)  | 5.61 (± 83.844)             |  |  |
| Week 4 (n=5,11)                      | 17.98 (± 35.690)  | 10.14 (± 79.563)            |  |  |
| Week 5 (n=4,12)                      | -17.28 (± 30.116) | 23.68 (± 68.934)            |  |  |
| Week 6 (n=4,12)                      | 23.18 (± 51.956)  | 24.72 (± 38.304)            |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change from Baseline on Objective Sleep Assessment Actigraphy: Number of Wake Bouts**

|                 |   |
|-----------------|---|
| End point title | Change from Baseline on Objective Sleep Assessment Actigraphy: Number of Wake Bouts |
|-----------------|---|

## End point description:

Change from baseline on objective sleep assessment actigraphy: number of wake bouts were reported. Objective sleep parameters were measured using actigraphy. A wake bout was an epoch or continuous epochs (an epoch equals 30 to 60 seconds) scored as awake. Full analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 1, Week 2, Week 3, Week 4, Week 5, and Week 6

| End point values                     | Placebo          | Seltorexant 10 mg and 20 mg |  |  |
|--------------------------------------|------------------|-----------------------------|--|--|
| Subject group type                   | Reporting group  | Reporting group             |  |  |
| Number of subjects analysed          | 5                | 17                          |  |  |
| Units: number of wake bouts          |                  |                             |  |  |
| arithmetic mean (standard deviation) |                  |                             |  |  |
| Week 1 (N=5, 17)                     | 3.54 (± 10.971)  | -2.29 (± 14.181)            |  |  |
| Week 2 (n=5,14)                      | 8.96 (± 16.954)  | -1.69 (± 11.511)            |  |  |
| Week 3 (n=5, 12)                     | 5.72 (± 18.522)  | 2.92 (± 8.492)              |  |  |
| Week 4 (n=5, 11)                     | 1.54 (± 12.002)  | 2.94 (± 12.360)             |  |  |
| Week 5 (n=4, 12)                     | -9.18 (± 15.027) | 1.93 (± 8.405)              |  |  |
| Week 6 (n=4, 12)                     | 1.93 (± 4.562)   | 2.76 (± 8.464)              |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline on Objective Sleep Assessment Actigraphy: Sleep Efficiency

|                 |   |
|-----------------|---|
| End point title | Change from Baseline on Objective Sleep Assessment Actigraphy: Sleep Efficiency |
|-----------------|---|

End point description:

Change from baseline on objective sleep assessment actigraphy: sleep efficiency was reported. Objective sleep parameters were measured using actigraphy. Sleep efficiency was scored total sleep time divided by total time in bed minus total invalid time, multiplied by 100, in percentages. Full analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 1, Week 2, Week 3, Week 4, Week 5, and Week 6

| End point values                     | Placebo         | Seltorexant 10 mg and 20 mg |  |  |
|--------------------------------------|-----------------|-----------------------------|--|--|
| Subject group type                   | Reporting group | Reporting group             |  |  |
| Number of subjects analysed          | 5               | 17                          |  |  |
| Units: percentage                    |                 |                             |  |  |
| arithmetic mean (standard deviation) |                 |                             |  |  |
| Week 1 (N=5,17)                      | 0.02 (± 0.045)  | -0.01 (± 0.075)             |  |  |

|                 |                |                 |  |  |
|-----------------|----------------|-----------------|--|--|
| Week 2 (N=5,14) | 0.00 (± 0.071) | 0.01 (± 0.027)  |  |  |
| Week 3 (N=5,12) | 0.02 (± 0.045) | -0.01 (± 0.051) |  |  |
| Week 4 (N=5,11) | 0.02 (± 0.045) | -0.01 (± 0.030) |  |  |
| Week 5 (N=4,12) | 0.03 (± 0.050) | 0.01 (± 0.067)  |  |  |
| Week 6 (N=4,12) | 0.08 (± 0.096) | -0.02 (± 0.039) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline on Objective Sleep Assessment Actigraphy: Sleep Onset Latency

|                 |  |
|-----------------|--|
| End point title | Change from Baseline on Objective Sleep Assessment Actigraphy: Sleep Onset Latency |
|-----------------|--|

End point description:

Change from baseline on objective sleep assessment actigraphy: sleep onset latency was reported. Objective sleep parameters were measured using actigraphy. Sleep onset latency was time between the start of a given rest interval and the following sleep start time, in minutes. Full analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 1, Week 2, Week 3, Week 4, Week 5, and Week 6

| End point values                     | Placebo           | Seltorexant 10 mg and 20 mg |  |  |
|--------------------------------------|-------------------|-----------------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group             |  |  |
| Number of subjects analysed          | 5                 | 17                          |  |  |
| Units: minutes                       |                   |                             |  |  |
| arithmetic mean (standard deviation) |                   |                             |  |  |
| Week 1 (N=5, 17)                     | -8.04 (± 25.258)  | 1.44 (± 33.390)             |  |  |
| Week 2 (n=5, 14)                     | -14.06 (± 19.382) | -6.25 (± 11.835)            |  |  |
| Week 3 (n=5, 12)                     | -11.56 (± 26.961) | -7.99 (± 12.198)            |  |  |
| Week 4 (n=5, 11)                     | -11.44 (± 22.834) | -7.75 (± 13.613)            |  |  |
| Week 5 (n=4, 12)                     | -7.85 (± 9.035)   | -8.10 (± 16.855)            |  |  |
| Week 6 (n=4, 12)                     | -21.75 (± 21.807) | -7.41 (± 13.201)            |  |  |

## Statistical analyses

**Secondary: Change from Baseline on Objective Sleep Assessment Actigraphy: Wake After Sleep Onset**

|                 |   |
|-----------------|---|
| End point title | Change from Baseline on Objective Sleep Assessment Actigraphy: Wake After Sleep Onset |
|-----------------|---|

## End point description:

Change from baseline on objective sleep assessment actigraphy: Wake after sleep onset was reported. Objective sleep parameters were measured using actigraphy. Wake after sleep onset was the number of epochs of the given sleep interval scored as wake by the actigraphy software, in minutes. Full analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Week 1, Week 2, Week 3, Week 4, Week 5, and Week 6

| End point values                     | Placebo          | Seltorexant 10 mg and 20 mg |  |  |
|--------------------------------------|------------------|-----------------------------|--|--|
| Subject group type                   | Reporting group  | Reporting group             |  |  |
| Number of subjects analysed          | 5                | 17                          |  |  |
| Units: minutes                       |                  |                             |  |  |
| arithmetic mean (standard deviation) |                  |                             |  |  |
| Week 1 (N=5, 17)                     | 10.56 (± 14.227) | -0.42 (± 19.384)            |  |  |
| Week 2 (N=5, 14)                     | 20.56 (± 27.744) | 0.76 (± 14.792)             |  |  |
| Week 3 (N=5, 12)                     | 18.70 (± 15.566) | 8.05 (± 14.490)             |  |  |
| Week 4 (N=5, 11)                     | 14.06 (± 11.631) | 8.88 (± 15.866)             |  |  |
| Week 5 (N=4, 12)                     | -3.28 (± 6.338)  | 2.30 (± 17.768)             |  |  |
| Week 6 (N=4, 12)                     | 3.28 (± 11.261)  | 6.73 (± 17.272)             |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change From Baseline in Subjective Sleep Related Impairment (PROMIS-Pediatric- Sleep-Related Impairment [SRI])**

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Subjective Sleep Related Impairment (PROMIS-Pediatric- Sleep-Related Impairment [SRI]) |
|-----------------|--|

## End point description:

Change from baseline in PROMIS-Pediatric-SRI were reported. The PROMIS-SRI 8 items score was used to assess self-reported daytime perceptions of alertness, sleepiness, and tiredness during usual waking hours, and the perceived functional impairments during wakefulness associated with sleep problems or impaired alertness and assessed on a 5 level Likert-type scale. The 8-item short form used in this study, scored 1 to 5 for each item. For the 8-item form, the lowest possible raw score is 8; the highest possible raw score is 39. Total raw score for a short form with all questions answered equals sum of the values of response to each question. Higher overall score indicated more sleep disturbance. Safety analysis set

included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), and end of double-blind phase (Week 6)

| End point values                     | Placebo               | Seltorexant 10 mg and 20 mg |  |  |
|--------------------------------------|-----------------------|-----------------------------|--|--|
| Subject group type                   | Reporting group       | Reporting group             |  |  |
| Number of subjects analysed          | 6                     | 22                          |  |  |
| Units: units on a scale              |                       |                             |  |  |
| arithmetic mean (standard deviation) | -12.12 ( $\pm$ 8.055) | -6.60 ( $\pm$ 7.616)        |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma Concentration of Seltorexant and an Active Metabolite of Seltorexant

|                 |   |
|-----------------|---|
| End point title | Plasma Concentration of Seltorexant and an Active Metabolite of Seltorexant <sup>[11]</sup> |
|-----------------|---|

End point description:

Plasma concentration of seltorexant and an active metabolite of seltorexant were reported. Population analysed included all subjects who received study intervention and had at least 1 plasma concentration data value after study intervention intake. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From 8 to 14 hours post last dose in Week 6

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was planned to be reported for the specified arms only

| End point values                        | Seltorexant 10 mg and 20 mg |  |  |  |
|---|-----------------------------|--|--|--|
| Subject group type                      | Reporting group             |  |  |  |
| Number of subjects analysed             | 12                          |  |  |  |
| Units: nanograms per millilitre (ng/mL) |                             |  |  |  |
| arithmetic mean (standard deviation)    |                             |  |  |  |
| Total Seltorexant                       | 42.7 ( $\pm$ 52.8)          |  |  |  |
| Active metabolite                       | 54.5 ( $\pm$ 53.1)          |  |  |  |

## Statistical analyses



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From start of treatment (Day 1) up to end of double-blind phase (Week 6)

Adverse event reporting additional description:

Safety analysis set included all randomised subjects who took at least 1 dose of study intervention.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

### Reporting groups

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | Seltorexant 10 mg and 20 mg |
|-----------------------|-----------------------------|

Reporting group description:

Subjects with body weight greater than or equal to ( $\geq$ ) 45 kilograms (kg) received a single oral dose of seltorexant 20 milligrams (mg) tablet once daily at bedtime and subjects with body weight  $\geq 30$  kg to less than ( $<$ ) 45 kg received seltorexant 10 mg tablet once daily at bedtime from Day 1 to Week 6. Subjects continued with their baseline SSRI antidepressant (fluoxetine or escitalopram) treatment at same dose as it was prior to entering the study.

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received a single oral dose of placebo (matching to seltorexant) tablet once daily at bedtime from Day 1 to Week 6.

| Serious adverse events                            | Seltorexant 10 mg and 20 mg | Placebo       |  |
|---|-----------------------------|---------------|--|
| Total subjects affected by serious adverse events |                             |               |  |
| subjects affected / exposed                       | 0 / 23 (0.00%)              | 0 / 7 (0.00%) |  |
| number of deaths (all causes)                     | 0                           | 0             |  |
| number of deaths resulting from adverse events    |                             |               |  |

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

| Non-serious adverse events                            | Seltorexant 10 mg and 20 mg | Placebo        |  |
|---|-----------------------------|----------------|--|
| Total subjects affected by non-serious adverse events |                             |                |  |
| subjects affected / exposed                           | 6 / 23 (26.09%)             | 2 / 7 (28.57%) |  |
| Nervous system disorders                              |                             |                |  |
| Headache  |                             |                |  |
| subjects affected / exposed                           | 3 / 23 (13.04%)             | 1 / 7 (14.29%) |  |
| occurrences (all)                                     | 5                           | 1              |  |
| General disorders and administration site conditions  |                             |                |  |

|   |                     |                     |  |
|---|---------------------|---------------------|--|
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 23 (4.35%)<br>1 | 1 / 7 (14.29%)<br>1 |  |
| Gastrointestinal disorders                                    |                     |                     |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all) | 2 / 23 (8.70%)<br>3 | 1 / 7 (14.29%)<br>1 |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)    | 2 / 23 (8.70%)<br>4 | 1 / 7 (14.29%)<br>1 |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment  |
|---------------|--|
| 27 March 2023 | The purpose of the protocol amendment dated 27-Mar-2023 was to align the protocol criteria more with current clinical practices and to increase feasibility of the study conduct. Due to subject feedback to sites regarding length and number of visits, adjustments were made to the visits as noted in the protocol amendment to allow for visit flexibility through remote assessment. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported