# Clinical trial results:
# A Multicenter, Double-Blind, Randomized, Parallel-Group, Placebo-Controlled, Adaptive Dose-Finding Study to Evaluate the Efficacy and Safety of JNJ-42847922 as Adjunctive Therapy to Antidepressants in Adult Subjects With Major Depressive Disorder Who Have Responded Inadequately to Antidepressant Therapy

## Summary

| | |
|---|---|
| EudraCT number | 2015-005282-22 |
| Trial protocol | DE FI BG FR |
| Global end of trial date | 19 January 2019 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 02 February 2020 |
| First version publication date | 02 February 2020 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 42847922MDD2001 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03227224 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Janssen Research & Development, LLC |
| Sponsor organisation address | 920 Route 202, South Raritan, United States, NJ 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) | No |
| 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 | 19 January 2019 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 19 January 2019 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the dose-response relationship of up to 3 doses of seltorexant (20, and 40 milligram [mg], with 10 mg added at the interim analysis [IA]) compared with placebo as adjunctive therapy to an antidepressant drug in improving depressive symptoms in subjects with major depressive disorder (MDD) who have had an inadequate response to current antidepressant therapy with a selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI). This study also assessed the safety and tolerability of seltorexant compared with placebo as adjunctive therapy to an antidepressant in subjects with MDD.

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. The informed consent form (ICF) was performed for all subjects and the ICFs were all approved by local/country Independent Review Boards (IRBs) or Ethics Committees (ECs) . Safety evaluations were based upon the adverse events (AEs), vital sign measurements, clinical laboratory test results, physical examinations. Electrocardiogram (ECG), Physician Withdrawal Checklist (PWC)-20, Columbia Suicide Severity Rating Scale (C-SSRS), Arizona Sexual Experiences Scale (ASEX).

Background therapy:

All subjects needed to be on an selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) to participate though the Sponsor did not supply this.

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 31 August 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Bulgaria: 66 |
| Country: Number of subjects enrolled | Germany: 3 |
| Country: Number of subjects enrolled | Finland: 10 |
| Country: Number of subjects enrolled | Japan: 37 |
| Country: Number of subjects enrolled | Russian Federation: 45 |
| Country: Number of subjects enrolled | Ukraine: 39 |
| Country: Number of subjects enrolled | United States: 83 |
| Worldwide total number of subjects | 283 |
| EEA total number of subjects | 79 |

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) | 0 |
| Adults (18-64 years) | 270 |
| From 65 to 84 years | 13 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 434 subjects were screened of which 287 subjects were randomly assigned to receive study treatment. Of the 287 subjects randomly assigned to treatment, 251 subjects completed the study.

### 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 |
| **Arm title** | Placebo |

Arm description:

Subjects received JNJ-42847922 matching placebo capsule once daily orally from Day 1 to Day 41 (Week 6).

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

Dosage and administration details:

Subjects received JNJ-42847922 matching placebo capsules once daily orally from Day 1 to Day 41 (Week 6).

| | |
|---|---|
| **Arm title** | JNJ-42847922 10 milligram (mg) |

Arm description:

Subjects received JNJ-42847922 10 mg capsules once daily orally from Day 1 to Day 41 (Week 6).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | JNJ-42847922 10 mg |
| Investigational medicinal product code | |
| Other name | Seltorexant, MIN-202 |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received JNJ-42847922 10 mg capsules once daily orally from Day 1 to Day 41 (Week 6).

| | |
|---|---|
| **Arm title** | JNJ-42847922 20 mg |

Arm description:

Subjects received JNJ-42847922 20 mg capsules once daily orally from Day 1 to Day 41 (Week 6).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | JNJ-42847922 20 mg |
| Investigational medicinal product code | |
| Other name | Seltorexant, MIN-202 |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received JNJ-42847922 20 mg capsules once daily orally from Day 1 to Day 41 (Week 6).

| **Arm title** | JNJ-42847922 40 mg |
|---|---|

Arm description:

Subjects received JNJ-42847922 40 mg capsules (2*20 mg capsules) once daily orally from Day 1 to Day 41 (Week 6).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | JNJ-42847922 40 mg |
| Investigational medicinal product code | |
| Other name | Seltorexant, MIN-202 |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received JNJ-42847922 40 mg capsules once daily orally from Day 1 to Day 41 (Week 6).

| **Number of subjects in period 1** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg |
|---|---|---|---|
| Started | 137 | 33 | 61 |
| Completed | 123 | 27 | 55 |
| Not completed | 14 | 6 | 6 |
| Adverse event, serious fatal | 1 | - | - |
| Consent withdrawn by subject | 3 | 2 | 3 |
| Adverse event, non-fatal | 1 | 1 | 1 |
| Non-compliance with study drug | 2 | 1 | - |
| Un-specified | 3 | - | - |
| Lost to follow-up | 1 | - | 2 |
| Protocol deviation | 2 | 2 | - |
| Lack of efficacy | 1 | - | - |

| **Number of subjects in period 1** | JNJ-42847922 40 mg |
|---|---|
| Started | 52 |
| Completed | 46 |
| Not completed | 6 |
| Adverse event, serious fatal | - |
| Consent withdrawn by subject | 2 |
| Adverse event, non-fatal | 4 |
| Non-compliance with study drug | - |
| Un-specified | - |
| Lost to follow-up | - |
| Protocol deviation | - |

| | |
|---|---|
| Lack of efficacy | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received JNJ-42847922 matching placebo capsule once daily orally from Day 1 to Day 41 (Week 6). | |
| Reporting group title | JNJ-42847922 10 milligram (mg) |
| Reporting group description: | |
| Subjects received JNJ-42847922 10 mg capsules once daily orally from Day 1 to Day 41 (Week 6). | |
| Reporting group title | JNJ-42847922 20 mg |
| Reporting group description: | |
| Subjects received JNJ-42847922 20 mg capsules once daily orally from Day 1 to Day 41 (Week 6). | |
| Reporting group title | JNJ-42847922 40 mg |
| Reporting group description: | |
| Subjects received JNJ-42847922 40 mg capsules (2*20 mg capsules) once daily orally from Day 1 to Day 41 (Week 6). | |

| Reporting group values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg |
|---|---|---|---|
| Number of subjects | 137 | 33 | 61 |
| Title for AgeCategorical | | | |
| Units: subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 131 | 29 | 59 |
| From 65 to 84 years | 6 | 4 | 2 |
| 85 years and over | 0 | 0 | 0 |
| Title for AgeContinuous | | | |
| Units: years | | | |
| arithmetic mean | 49.6 | 49.4 | 48.5 |
| standard deviation | ± 11.71 | ± 15.31 | ± 13.56 |
| Title for Gender | | | |
| Units: subjects | | | |
| Female | 74 | 20 | 30 |
| Male | 63 | 13 | 31 |

| Reporting group values | JNJ-42847922 40 mg | Total | |
|---|---|---|---|
| Number of subjects | 52 | 283 | |
| Title for AgeCategorical | | | |
| Units: subjects | | | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 51 | 270 | |
| From 65 to 84 years | 1 | 13 | |
| 85 years and over | 0 | 0 | |
| Title for AgeContinuous | | | |
| Units: years | | | |
| arithmetic mean | 48.3 | | |
| standard deviation | ± 10.52 | - | |

| Title for Gender<br>Units: subjects | | | |
|---|---|---|---|
| Female | 28 | 152 | |
| Male | 24 | 131 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received JNJ-42847922 matching placebo capsule once daily orally from Day 1 to Day 41 (Week 6). | |
| Reporting group title | JNJ-42847922 10 milligram (mg) |
| Reporting group description: | |
| Subjects received JNJ-42847922 10 mg capsules once daily orally from Day 1 to Day 41 (Week 6). | |
| Reporting group title | JNJ-42847922 20 mg |
| Reporting group description: | |
| Subjects received JNJ-42847922 20 mg capsules once daily orally from Day 1 to Day 41 (Week 6). | |
| Reporting group title | JNJ-42847922 40 mg |
| Reporting group description: | |
| Subjects received JNJ-42847922 40 mg capsules (2*20 mg capsules) once daily orally from Day 1 to Day 41 (Week 6). | |

### Primary: Change From Baseline to Week 6 in Montgomery-Asberg Depression Rating Scale (MADRS) Total Score at Day 42

| | |
|---|---|
| End point title | Change From Baseline to Week 6 in Montgomery-Asberg Depression Rating Scale (MADRS) Total Score at Day 42 |
| End point description: | |
| MADRS is a clinician-administered scale designed to measure depression severity and detects changes due to antidepressant treatment. The MADRS evaluates the following 10 items: apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Each item is scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms), for a total possible score of 60. Higher scores represent a more severe condition. Full analysis set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here N (numbers of subjects analysed) signifies numbers of subjects evaluable for this endpoint. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline to Day 42 (Week 6) | |

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 124 | 26 | 55 | 47 |
| Units: Units on a score | | | | |
| arithmetic mean (standard deviation) | -12.3 (± 10.95) | -12.2 (± 8.33) | -15.0 (± 12.13) | -14.7 (± 13.29) |

## Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v JNJ-42847922 10 milligram (mg) |
| Number of subjects included in analysis | 150 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.724 |
| Method | Mixed model for repeated measures (MMRM) |
| Parameter estimate | Difference of Least Square Means |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -3.12 |
| upper limit | 4.82 |

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Comparison groups | Placebo v JNJ-42847922 20 mg |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.083 |
| Method | MMRM |
| Parameter estimate | Difference of Least Square Means |
| Point estimate | -3.1 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -6.13 |
| upper limit | -0.16 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Comparison groups | Placebo v JNJ-42847922 40 mg |
| Number of subjects included in analysis | 171 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.424 |
| Method | MMRM |
| Parameter estimate | Difference of Least Square Means |
| Point estimate | -1.5 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -4.7 |
| upper limit | 1.63 |

## Primary: Percentage of Subjects With Treatment-emergent Adverse Events as a Measure of Safety and Tolerability

| End point title | Percentage of Subjects With Treatment-emergent Adverse Events as a Measure of Safety and Tolerability[1] |
|---|---|

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Treatment-emergent were events between administration of study drug and up to Week 8 that were absent before treatment or that worsened relative to pre-treatment state. Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug.

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

End point timeframe:

Up to Week 8

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 statistical analyses was planned to report for this primary end point.

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 137 | 33 | 61 | 52 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 40.9 | 33.3 | 41.0 | 36.5 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects with Clinically Significant Laboratory Abnormalities

| End point title | Percentage of Subjects with Clinically Significant Laboratory Abnormalities[2] |
|---|---|

End point description:

Percentage of subjects with clinically significant laboratory abnormalities were reported. Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, Gamma-glutamyl transferase, Alanine Aminotransferase, Aspartate Aminotransferase, Alkaline Phosphatase, Creatine Kinase, Lactate Dehydrogenase signifies GGT, ALT, AST, ALP, CK, LDH respectively. Here n (number of subjects analyzed) signifies those subjects who were evaluable for specified categories.

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

End point timeframe:

Up to Week 8

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 statistical analyses was planned to report for this primary end point.

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 137 | 33 | 61 | 52 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| ALT: Abnormally high (n=135,31,60,52) | 0 | 0 | 0 | 1.9 |
| Albumin: Abnormally low(n=135,31,60,52) | 0 | 0 | 0 | 0 |
| Albumin: Abnormally high(n=135,31,60,52) | 0 | 0 | 0 | 0 |
| ALP: Abnormally high(n=135,31,60,52) | 0 | 0 | 0 | 0 |
| AST: Abnormally high(n=135,31,60,51) | 0 | 0 | 0 | 0 |
| Bicarbonate: Abnormally low(n=135,31,60,52) | 0 | 0 | 0 | 0 |
| Bicarbonate: Abnormally high(n=135,31,60,52) | 0 | 0 | 0 | 0 |
| Bilirubin: Abnormally high(n=135,31,60,52) | 0 | 0 | 0 | 0 |
| Calcium: Abnormally (n=135,31,60,52) | 0 | 0 | 0 | 0 |
| Calcium: Abnormally high(n=135,31,60,52) | 0 | 0 | 0 | 0 |
| Chloride: Abnormally low(n=134,31,60,52) | 0.7 | 0 | 0 | 0 |
| Chloride: Abnormally high(n=134,31,60,52) | 0 | 0 | 0 | 0 |
| Cholesterol: Abnormally high(n=131,29,56,51) | 0 | 0 | 0 | 0 |
| CK: Abnormally high(n=135,31,60,52) | 0 | 0 | 1.7 | 0 |
| Creatinine: Abnormally high(n=135,31,60,52) | 0 | 0 | 0 | 0 |
| Direct Bilirubin: Abnormally high(n=134,31,60,51) | 0 | 0 | 0 | 0 |
| GGT: Abnormally high(n=135,31,60,52) | 0 | 0 | 0 | 0 |
| Glucose: Abnormally low(n=135,31,60,51) | 0 | 0 | 0 | 0 |
| Glucose: Abnormally high(n=135,31,60,51) | 0 | 0 | 0 | 0 |
| HDL Cholesterol: Abnormally low(n=131,29,55,51) | 2.3 | 6.9 | 1.8 | 2.0 |
| Hemoglobin A1C: Abnormally low(n=132,28,57,51) | 0 | 0 | 0 | 0 |
| Hemoglobin A1C: Abnormally high(n=132,28,57,51) | 0 | 0 | 0 | 0 |
| LDL Cholesterol: Abnormally low(n=131,29,54,51) | 4.6 | 10.3 | 9.3 | 5.9 |
| LDL Cholesterol: Abnormally high(n=131,29,54,51) | 7.6 | 6.9 | 1.9 | 11.8 |
| LDH: Abnormally high(n=133,31,60,51) | 0 | 0 | 0 | 0 |
| Phosphate: Abnormally low(n=135,31,60,51) | 0.7 | 3.2 | 3.3 | 7.8 |
| Phosphate: Abnormally high(n=135,31,60,51) | 0 | 0 | 0 | 0 |
| Potassium: Abnormally low(n=135,31,60,51) | 0 | 0 | 0 | 0 |
| Potassium: Abnormally high(n=135,31,60,51) | 0.7 | 3.2 | 0 | 0 |
| Protein:Abnormally low(n=135,31,60,52) | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Sodium: Abnormally low(n=135,31,60,52) | 0 | 0 | 0 | 0 |
| Sodium: Abnormally high(n=135,31,60,52) | 0 | 0 | 0 | 0 |
| Triglycerides: Abnormally high(n=131,29,55,51) | 0 | 0 | 0 | 0 |
| Urate: Abnormally low(n=135,31,60,52) | 0 | 0 | 0 | 0 |
| Urate: Abnormally high(n=135,31,60,52) | 0 | 0 | 5.0 | 1.9 |
| Urea Nitrogen: Abnormally high(n=135,31,60,52) | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Vital Signs (Systolic Blood Pressure [SBP] and, Diastolic Blood Pressure [DBP])

| End point title | Change from Baseline in Vital Signs (Systolic Blood Pressure [SBP] and, Diastolic Blood Pressure [DBP])[3] |
|---|---|

End point description:

Change from baseline in vital signs (systolic blood pressure [SBP], diastolic blood pressure [DBP]) were reported. Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, n (number of subjects analyzed) signifies those subjects who were evaluable for specified categories. Endpoint (DB) values are from the last measurement within the double-blind period.

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

End point timeframe:

Baseline, Day 8, 22, 42 and Double blind (DB) Endpoint (Up to 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: No statistical analyses was planned to report for this primary end point.

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 137 | 33 | 61 | 52 |
| Units: millimeters of mercury (mmHg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Standing DBP: Day 8 (n=136,32,60,52) | -0.7 (± 6.29) | -0.5 (± 5.22) | 0.7 (± 5.86) | 0.9 (± 6.41) |
| Standing DBP: Day 22 (n=132,29,58,49) | 0.0 (± 6.67) | -1.2 (± 5.92) | -0.4 (± 6.90) | 2.4 (± 7.42) |
| Standing DBP: Day 42 (n=126,28,56,48) | -0.5 (± 6.22) | 0.3 (± 9.16) | -0.8 (± 6.75) | 2.9 (± 7.96) |
| Standing DBP: Endpoint (n=136,32,60,52) | -0.3 (± 6.29) | 0.6 (± 8.98) | -0.6 (± 6.78) | 2.8 (± 7.79) |
| Standing SBP: Day 8 (n=136,32,60,52) | -0.4 (± 8.16) | -0.8 (± 7.19) | 0.2 (± 8.17) | 0.3 (± 9.71) |
| Standing SBP: Day 22 (n=132,29,58,49) | 0.2 (± 7.01) | -1.2 (± 6.55) | -2.7 (± 9.62) | 1.6 (± 11.29) |
| Standing SBP: Day 42 (n=126,28,56,48) | -0.5 (± 7.99) | 1.1 (± 7.92) | -3.2 (± 10.57) | 2.0 (± 9.90) |
| Standing SBP: Endpoint (n=136,32,60,52) | -0.3 (± 8.33) | 1.0 (± 7.42) | -3.1 (± 10.29) | 1.8 (± 9.89) |

| | | | | |
|---|---|---|---|---|
| Supine DBP: Day 8 (n=136,32,60,52) | -0.8 (± 6.32) | -0.9 (± 6.19) | 2.3 (± 6.14) | 1.2 (± 6.67) |
| Supine DBP: Day 22 (n=132,29,58,49) | -0.4 (± 6.81) | -1.8 (± 6.70) | -0.2 (± 7.41) | 2.6 (± 6.81) |
| Supine DBP: Day 42 (n=126,28,56,48) | -0.6 (± 7.10) | -1.6 (± 9.23) | 0.0 (± 8.31) | 2.1 (± 7.50) |
| Supine DBP: Endpoint (n=136,32,60,52) | -0.4 (± 7.08) | -1.4 (± 9.34) | 0.2 (± 8.35) | 2.3 (± 7.39) |
| Supine SBP: Day 8 (n=136,32,60,52) | 0.1 (± 8.19) | 1.6 (± 6.56) | 1.5 (± 9.57) | 0.5 (± 10.19) |
| Supine SBP: Day 22 (n=132,29,58,49) | 0.8 (± 8.14) | 0.3 (± 4.76) | -0.9 (± 10.78) | 2.2 (± 10.08) |
| Supine SBP: Day 42 (n=126,28,56,48) | 0.6 (± 8.88) | -0.5 (± 10.00) | -1.3 (± 10.85) | 1.9 (± 8.35) |
| Supine SBP: Endpoint (n=136,32,60,52) | 0.6 (± 8.81) | -0.3 (± 9.38) | -1.4 (± 10.52) | 1.6 (± 8.58) |

### Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Vital Sign (Pulse Rate [PR])

| End point title | Change from Baseline in Vital Sign (Pulse Rate [PR])[4] |
|---|---|

End point description:

Change from baseline in vital sign (Pulse rate) were reported. Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here n (number of subjects analyzed) signifies those subjects who were evaluable for specified categories. Endpoint (DB) values are from the last measurement within the double-blind period.

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

End point timeframe:

Baseline, Day 8, 22, 42 and DB Endpoint (Up to 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: No statistical analyses was planned to report for this primary end point.

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 137 | 33 | 61 | 52 |
| Units: Beats per Minutes | | | | |
| arithmetic mean (standard deviation) | | | | |
| Standing PR: Day 8 (n=136,32,60,52) | -0.1 (± 7.95) | -0.7 (± 7.07) | 0.9 (± 9.17) | 1.3 (± 9.21) |
| Standing PR: Day 22 (n=132,29,58,49) | 1.4 (± 7.57) | 0.7 (± 7.36) | 1.5 (± 8.27) | 0.3 (± 9.59) |
| Standing PR: Day 42 (n=126,28,56,48) | 0.8 (± 7.99) | -1.4 (± 9.35) | 1.5 (± 8.99) | -0.6 (± 9.04) |
| Standing PR: Endpoint (n=136,32,60,52) | 0.4 (± 8.40) | -1.6 (± 9.27) | 2.1 (± 9.34) | -0.5 (± 9.11) |
| Supine PR: Day 8 (n=136,32,60,52) | 0.0 (± 7.15) | -1.2 (± 7.16) | 0.5 (± 6.23) | 1.7 (± 9.32) |
| Supine PR: Day 22 (n=132,29,58,49) | 1.5 (± 7.61) | -0.7 (± 7.31) | 2.8 (± 7.94) | 0.9 (± 10.55) |
| Supine PR: Day 42 (n=126,28,56,48) | 0.3 (± 8.16) | -2.8 (± 8.67) | 2.4 (± 9.01) | -0.6 (± 9.71) |
| Supine PR: Endpoint (n=136,32,60,52) | 0.2 (± 8.16) | -2.4 (± 8.97) | 2.4 (± 8.78) | -0.5 (± 9.60) |

### Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Vital Sign (Temperature)

| End point title | Change from Baseline in Vital Sign (Temperature)[5] |
|---|---|

End point description:

Change from baseline in vital Sign (temperature) were reported. Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here n (number of subjects analyzed) signifies those subjects who were evaluable for specified categories. Endpoint (DB) values are from the last measurement within the double-blind period.

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

End point timeframe:

Baseline, Day 8, 22, 42 and DB Endpoint (Up to 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: No statistical analyses was planned to report for this primary end point.

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 137 | 33 | 61 | 52 |
| Units: Celsius | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 8 (n=136,32,60,52) | -0.01 (± 0.324) | -0.05 (± 0.274) | 0.02 (± 0.278) | 0.06 (± 0.300) |
| Day 22 (n=132,29,58,48) | -0.02 (± 0.299) | -0.01 (± 0.242) | -0.02 (± 0.332) | 0.02 (± 0.392) |
| Day 42 (n=126,28,56,48) | 0.02 (± 0.326) | -0.04 (± 0.291) | -0.05 (± 0.223) | 0.05 (± 0.445) |
| Endpoint (n=136,32,60,52) | 0.02 (± 0.317) | -0.03 (± 0.276) | -0.06 (± 0.242) | 0.06 (± 0.437) |

### Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Physical Examination (Waist Circumference)

| End point title | Change from Baseline in Physical Examination (Waist Circumference)[6] |
|---|---|

End point description:

Change from baseline in physical examination (waist circumference) was reported. Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

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

End point timeframe:

Baseline and Day 42

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 statistical analyses was planned to report for this primary end point.

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 134 | 32 | 58 | 51 |
| Units: centimeter (cm) | | | | |
| arithmetic mean (standard deviation) | 0.31 (± 2.778) | -0.50 (± 1.972) | 0.00 (± 3.523) | -0.48 (± 9.498) |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Physical Examination (Body Weight)

| End point title | Change from Baseline in Physical Examination (Body Weight)[7] |
|---|---|

End point description:

Change from baseline in physical examination (body weight) was reported. Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

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

End point timeframe:

Baseline and Day 42

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: No statistical analyses was planned to report for this primary end point.

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 134 | 32 | 58 | 51 |
| Units: Kilogram (kg) | | | | |
| arithmetic mean (standard deviation) | 0.19 (± 2.373) | 0.01 (± 1.889) | 0.05 (± 1.563) | 0.61 (± 1.946) |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Physical Examination (Body Mass Index [BMI])

| End point title | Change from Baseline in Physical Examination (Body Mass Index [BMI])[8] |
|---|---|

End point description:

Change from baseline in physical examination (BMI) was reported. Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

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

End point timeframe:

Baseline and Day 42

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: No statistical analyses was planned to report for this primary end point.

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 134 | 32 | 58 | 51 |
| Units: kilogram per meter square (kg/m^2) | | | | |
| arithmetic mean (standard deviation) | 0.07 (± 0.850) | 0.01 (± 0.662) | 0.02 (± 0.553) | 0.22 (± 0.715) |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects with Treatment-emergent Abnormal Electrocardiogram (ECG) Values Outside Pre-defined Limits

| End point title | Percentage of Subjects with Treatment-emergent Abnormal Electrocardiogram (ECG) Values Outside Pre-defined Limits[9] |
|---|---|

End point description:

Percentage of subjects with treatment-emergent abnormal ECG values outside pre-defined limits were reported. Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here n (number of subjects analyzed) signifies those subjects who were evaluable for specified categories. here, sign (<=) indicates less than or equal to and (>=)indicates greater than or equal to.

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

End point timeframe:

Up to Week 8

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: No statistical analyses was planned to report for this primary end point.

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 137 | 33 | 61 | 52 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Heart rate (<=50) (n=134,30,58,50) | 0.7 | 0 | 3.4 | 6.0 |
| Heart rate (>=100) (n=134,30,58,50) | 0.7 | 0 | 1.7 | 0 |
| PR interval (<=120) (n=134,30,58,50) | 0.7 | 0 | 0 | 0 |
| PR interval (>=200) (n=134,30,58,50) | 0.7 | 0 | 1.7 | 6.0 |
| QRS interval (<=60) (n=134,30,58,50) | 0 | 0 | 0 | 0 |
| QRS interval (>=120) (n=134,30,58,50) | 0 | 3.3 | 0 | 0 |
| QT interval (<=200) (n=134,30,58,49) | 0 | 0 | 0 | 0 |
| QT interval (>=500) (n=134,30,58,49) | 0 | 3.3 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects With Most Severe Postbaseline Potentially Suicide-Related Category Using Columbia Suicide Severity Rating Scale (C-SSRS)

| End point title | Percentage of Subjects With Most Severe Postbaseline Potentially Suicide-Related Category Using Columbia Suicide Severity Rating Scale (C-SSRS)[10] |
|---|---|

End point description:

C-SSRS is a clinician rated assessment of suicidal behavior and/or intent. Scale consists of Suicidal Ideation (1-5) (Wish to be Dead [1], Non-specific Active Suicidal Thoughts [2], Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act [3], Active Suicidal Ideation with Some Intent to Act, without Specific Plan [4]and Active Suicidal Ideation with Specific Plan and Intent [5]); and Suicidal Behavior (6-10) (Preparatory Acts or Behavior [6], Aborted Attempt [7], Interrupted Attempt [8], Actual Attempt (non-fatal)[9], Completed Suicide [10]). If no events qualify for a score of 1 to 10, a score of 0 was assigned (0="no event that can be assessed on the basis of C-SSRS"). Higher scores indicate greater severity. Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

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

End point timeframe:

Up to Week 8

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: No statistical analyses was planned to report for this primary end point.

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 136 | 32 | 60 | 51 |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| No Event | 94.9 | 96.9 | 96.7 | 94.1 |
| Suicidal ideation | 5.1 | 3.1 | 3.3 | 5.9 |
| Suicidal behavior | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Sexual Functioning as Measured by Arizona Sexual Experiences Scale (ASEX)

| End point title | Change from Baseline in Sexual Functioning as Measured by Arizona Sexual Experiences Scale (ASEX)[11] |
|---|---|

End point description:

Effect on sexual functioning was assessed using the ASEX. The ASEX is a five-item rating scale that quantifies sex drive, arousal, vaginal lubrication/penile erection, ability to reach orgasm, and satisfaction from orgasm. Each of the 5 items is rated on a 6-point scale, ranging from 1 to 6. The 5 items are summed to create a total score, ranging from 5 to 30, with the higher scores indicating more sexual dysfunction. Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

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

End point timeframe:

Baseline and Day 42

Notes:

[11] - 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 statistical analyses was planned to report for this primary end point.

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 133 | 31 | 58 | 49 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -1.4 (± 4.55) | -2.2 (± 3.62) | -2.4 (± 4.55) | -2.5 (± 4.94) |

### Statistical analyses

No statistical analyses for this end point

## Primary: Physician Withdrawal Checklist-20 (PWC-20) Total Score

| End point title | Physician Withdrawal Checklist-20 (PWC-20) Total Score[12] |
|---|---|

End point description:

Intensity of discontinuation symptoms was assessed (for example: underlying depression; anxiety-nervousness; dysphoric mood/depression; difficulty concentrating; weakness; fatigue-lethargy-lack of energy; irritability), using the Physician Withdrawal Checklist (PWC-20) administered by a trained clinician/rater. Assessment has 20 items evaluated to detect withdrawal symptoms. Symptoms are rated on a scale 0 (No symptom present) and 3 (severe symptoms). Total scores range from 0 to 24 calculated by adding the scores of following 8 items: Nausea-Vomiting, Diarrhea, Poor Coordination, Diaphoresis, Tremor-Tremulousness, Dizziness-Lightheadedness, Increased Acuity Sound Smell Touch, Paresthesias. Higher scores indicating more severe symptoms. Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here n (number of subjects analyzed) signifies the subjects evaluable for specified categories.

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

End point timeframe:

Up to Week 8

Notes:

[12] - 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 statistical analyses was planned to report for this primary end point.

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 137 | 33 | 61 | 52 |
| Units: Units on a score | | | | |
| arithmetic mean (standard deviation) | | | | |
| At Telephone contact (n=134,29,58,49) | 0.9 (± 1.68) | 0.2 (± 0.60) | 0.7 (± 1.60) | 0.5 (± 0.87) |
| At Follow-up visit (n=133,29,57,50) | 0.9 (± 1.91) | 0.4 (± 0.78) | 0.8 (± 1.64) | 0.7 (± 1.25) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline to Day 42 in the MADRS Total Score by Baseline Insomnia Severity Index (ISI) Score

| End point title | Change From Baseline to Day 42 in the MADRS Total Score by Baseline Insomnia Severity Index (ISI) Score |
|---|---|

End point description:

MADRS is a clinician-administered scale designed to measure depression severity and detects changes due to antidepressant treatment. The MADRS evaluates the following 10 items: apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Each item is scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms), for a total possible score of 60 calculated by adding the scores of all 10 items. Higher scores represent a more severe condition. Full analysis set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint. Here, 'n' (number of subjects) signifies those subjects who were evaluable for specific category.

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

End point timeframe:

Baseline and Day 42

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 124 | 26 | 55 | 47 |
| Units: Units on a score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline ISI score per IWRS<15:Day 42(50,21,23,13) | -13.3 (± 10.83) | -12.6 (± 8.01) | -13.0 (± 11.38) | -14.9 (± 12.14) |
| Baseline ISI score per IWRS>=15:Day 42(74,5,32,34) | -11.6 (± 11.06) | -10.4 (± 10.41) | -16.5 (± 12.62) | -14.6 (± 13.87) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Insomnia Severity Index (ISI) Total Score to DB Endpoint (Up to Week 6)

| End point title | Change From Baseline in Insomnia Severity Index (ISI) Total Score to DB Endpoint (Up to Week 6) |
|---|---|

End point description:

The ISI is a commonly used, 7-item psychometrically validated measure used to rate insomnia. Each item is scored 0 (no problem) - 4 (very big problem) with total between 0-28 (absence of insomnia (0-7); sub-threshold insomnia (8-14); moderate insomnia (15-21); and severe insomnia (22-28). The change in ISI total score from baseline at DB endpoint was evaluated. Negative change in score indicates improvement. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here 'N' (number of subjects analyzed) signifies the evaluable subjects for this endpoint. Endpoint (DB) values are from the last measurement within the double-blind period.

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

End point timeframe:

Baseline and DB Endpoint (Up to Week 6)

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 134 | 31 | 58 | 51 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -6.3 (± 6.73) | -4.9 (± 6.22) | -8.7 (± 6.91) | -8.5 (± 8.73) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Response on Depressive Symptoms Scale Based on Montgomery-Asberg Depression Rating Scale (MADRS)

| End point title | Percentage of Subjects With Response on Depressive Symptoms Scale Based on Montgomery-Asberg Depression Rating Scale (MADRS) |
|---|---|

End point description:

Responders are defined with a >=50 percent (%) improvement in the MADRS total score from baseline to a given timepoint. MADRS is a clinician-administered scale designed to measure depression severity and detects changes due to antidepressant treatment. The MADRS evaluates the following 10 items: apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Each item is scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms), for a total possible score of 60. Higher scores represent a more severe condition. Subjects with missing values at a given time point were imputed as non-responders. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug.

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

End point timeframe:

Day 42

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 137 | 33 | 61 | 52 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 28.5 | 24.2 | 41.0 | 38.5 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Remission of Depressive Symptoms Based on Montgomery-Asberg Depression Rating Scale (MADRS)

| End point title | Percentage of Subjects With Remission of Depressive Symptoms Based on Montgomery-Asberg Depression Rating Scale (MADRS) |
|---|---|

End point description:

Subjects with a MADRS total score of less than or equal to (<=)8, <=10, and <=12 at a given time point were considered as remitters. MADRS is a clinician-administered scale designed to measure depression severity and detects changes due to antidepressant treatment. The MADRS evaluates the following 10 items: apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Each item is scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms), for a total possible score of 60. Subjects with missing values at a given time point were imputed as non-responders. Higher scores represent a more severe condition. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'n' (number of subjects) signifies those subjects who were evaluable for specific category.

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

End point timeframe:

Day 42

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 137 | 33 | 61 | 52 |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| MADRS (<=12)(n=137,33,61,52) | 19.0 | 15.2 | 29.5 | 26.9 |
| MADRS (<=10)(n=137,33,61,52) | 17.5 | 9.1 | 26.2 | 26.9 |
| MADRS (<=8)(n=137,33,61,52) | 16.1 | 6.1 | 23.0 | 19.2 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Structured Interview Guide for the Hamilton

## Anxiety Rating Scale (HAM-A) Total Score at Day 42

| End point title | Change From Baseline in Structured Interview Guide for the Hamilton Anxiety Rating Scale (HAM-A) Total Score at Day 42 |
|---|---|

End point description:

HAM-A is a 14-item scale designed to measure anxiety in individuals. Each question reflects a symptom of anxiety and physical as well as mental symptoms are represented. Each of the 14-items in the scale is scored on a 5-point scale, ranging from 0 (a complete lack of that symptom) to 4 (a very severe show of anxiety with that symptom). The total score ranges from 0 to 56, where higher score indicates worsening. Negative change in score indicates improvement. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here 'N' (number of subjects analyzed) signifies the evaluable subjects for this endpoint.

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

End point timeframe:

Baseline and Day 42

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 126 | 27 | 56 | 47 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -8.7 (± 7.92) | -9.9 (± 5.57) | -9.6 (± 9.31) | -9.9 (± 10.17) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Response on Anxiety Symptoms Scale Based on Hamilton Anxiety Rating scale (HAM-A)

| End point title | Percentage of Subjects With Response on Anxiety Symptoms Scale Based on Hamilton Anxiety Rating scale (HAM-A) |
|---|---|

End point description:

Subjects with a >=50 percent (%) improvement in the HAM-A total score from baseline at a given timepoint were considered as responders. HAM-A is a 14-item scale designed to measure anxiety in individuals. Each question reflects a symptom of anxiety and physical as well as mental symptoms are represented. Each of the 14-items in the scale is scored on a 5-point scale, ranging from 0 (a complete lack of that symptom) to 4 (a very severe show of anxiety with that symptom). The total score ranges from 0 to 56, where higher score indicates worsening. Subjects with missing values at a given time point will be imputed as non-responders. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug.

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

End point timeframe:

Day 42

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 137 | 33 | 61 | 52 |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | 37.2 | 57.6 | 50.8 | 46.2 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Clinical Global Impression-Severity (CGI-S) Score at DB Endpoint (Up to Week 6)

| End point title | Change From Baseline in Clinical Global Impression-Severity (CGI-S) Score at DB Endpoint (Up to Week 6) |
|---|---|

End point description:

The CGI-S is a 7-point global assessment scale that measures the clinician's impression of the severity of illness exhibited by a subjects, rating according to: 1=normal (not at all ill); 2=borderline ill; 3=mildly ill; 4=moderately ill; 5=markedly ill; 6=severely ill; and 7=among the most extremely ill subjects. Higher scores indicate worsening. Negative change in score indicates improvement. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, N (number of subjects analyzed) signifies subjects evaluable for this endpoint. Endpoint (DB) values are from the last measurement within the double-blind period.

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

End point timeframe:

Baseline and DB Endpoint (Up to Week 6)

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 135 | 30 | 60 | 52 |
| Units: Units on a scale | | | | |
| median (full range (min-max)) | -1.0 (-5 to 2) | -1.0 (-3 to 1) | -1.0 (-5 to 1) | -1.0 (-5 to 1) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the Sheehan Disability Scale (SDS) at Day 42

| End point title | Change From Baseline in the Sheehan Disability Scale (SDS) at Day 42 |
|---|---|

End point description:

The SDS is a 5-item questionnaire which has been widely used and accepted for assessment of functional impairment and associated disability. The first 3 items assess disruption of (1) work/school, (2) social life, and (3) family life/home responsibilities using a 0-10 rating scale. The scores for the first 3 items are summed to create a total score of 0-30 where a higher score indicates greater impairment. It also has 1 item on days lost from school or work and 1 item on days when underproductive. Negative

change in score indicates improvement. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

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

End point timeframe:

Baseline and Day 42

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 96 | 16 | 30 | 26 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -7.9 (± 6.99) | -7.5 (± 5.19) | -7.9 (± 7.46) | -5.9 (± 9.20) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in the MADRS Total Score at Day 42 in Subjects With Major Depressive Disorder (MDD) With Anxious Distress Versus Subjects With MDD Without Anxious Distress

| End point title | Change From Baseline in the MADRS Total Score at Day 42 in Subjects With Major Depressive Disorder (MDD) With Anxious Distress Versus Subjects With MDD Without Anxious Distress |
|---|---|

End point description:

MADRS is a clinician-administered scale designed to measure depression severity and detects changes due to antidepressant treatment. The MADRS evaluates the following 10 items: apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Each item is scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms), for a total possible score of 60. Higher scores represent a more severe condition. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint. Here, 'n' (number of subjects analyzed) signifies those subjects who were evaluable for specific categories.

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

End point timeframe:

Baseline and Day 42

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 76 | 13 | 31 | 31 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -13.9 (± 11.50) | -11.0 (± 8.67) | -16.9 (± 12.31) | -15.3 (± 13.0) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Salivary Cortisol Levels, Measured Upon Awakening at Days 8, 22 and 42

| End point title | Change From Baseline in Salivary Cortisol Levels, Measured Upon Awakening at Days 8, 22 and 42 |
|---|---|

End point description:

Exposure on the hypothalamic-pituitary-adrenal (HPA) axis in subjects with MDD was evaluated by assessing change in salivary cortisol levels. Biomarker analysis set included all randomized subjects who received at least 1 dose of study drug during the double-blind phase and had biomarker data at baseline. Here, 'n' (number of subjects analyzed) signifies those subjects who were evaluable for specific timepoints.

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

End point timeframe:

Baseline, Day 8, 22 and 42

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 133 | 31 | 59 | 45 |
| Units: nanomole per Liter (nmol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 8 (n=116,26,48,38) | 0.2 (± 8.41) | 0.7 (± 7.24) | 0.0 (± 8.64) | -0.4 (± 6.19) |
| Day 22 (n=117,21,45,38) | 0.4 (± 8.65) | 2.1 (± 6.39) | 0.7 (± 6.75) | 1.0 (± 10.75) |
| Day 42 (n=112,18,45,37) | 1.0 (± 10.85) | 1.5 (± 6.15) | -1.2 (± 6.67) | -0.5 (± 6.69) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma Concentrations of JNJ-42847922 and its Metabolites (M12 and M16)

| End point title | Plasma Concentrations of JNJ-42847922 and its Metabolites (M12 and M16)[13] |
|---|---|

End point description:

Plasma concentrations of JNJ-42847922 and its metabolites (M12 and M16) over time were reported. Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'n' (number of subjects analyzed) signifies those subjects who were evaluable for specific timepoints.

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

End point timeframe:

Day 1: Between 0.25 hours (h) to 1.5 hour, 2 to 4 hours, and 6 to 8 hours post-dose; Day 8 (morning): 6 to 12 hours post evening dose of Day 7

Notes:

[13] - 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: Statistics analysis was not planned for all the arms in the baseline period.

| **End point values** | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 61 | 52 | |
| Units: nanogram per milliliter (ng/mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| JNJ42847922:Day 1,0.25h-1.5h(n=24,46,43) | 181 (± 165) | 277 (± 291) | 535 (± 500) | |
| JNJ42847922: Day 1, 2-4h(n=24,46,43) | 199 (± 113) | 374 (± 232) | 647 (± 325) | |
| JNJ42847922: Day 1, 6-8h(n=24,46,43) | 117 (± 99.3) | 167 (± 179) | 207 (± 169) | |
| JNJ42847922: Day 8, Morning(n=28,59,50) | 52.8 (± 65.8) | 69.4 (± 119) | 104 (± 203) | |
| M12: Day 1,0.25h-1.5h(n=24,46,43) | 118 (± 107) | 194 (± 223) | 357 (± 367) | |
| M12: Day 1, 2-4h(n=24,46,43) | 146 (± 58.8) | 283 (± 185) | 513 (± 284) | |
| M12: Day 1, 6-8h(n=24,46,43) | 105 (± 73.5) | 187 (± 189) | 279 (± 278) | |
| M12: Day 8, Morning(n=28,59,50) | 76.2 (± 79) | 99 (± 133) | 169 (± 251) | |
| M16: Day 1,0.25h-1.5h(n=24,46,43) | 29.1 (± 30.2) | 47 (± 53.4) | 71.4 (± 78.3) | |
| M16: Day 1, 2-4h(n=24,46,43) | 33.3 (± 15.7) | 61.4 (± 35.7) | 101 (± 49.3) | |
| M16: Day 1, 6-8h(n=24,46,43) | 27.5 (± 16.6) | 40.1 (± 31.4) | 70.6 (± 33.6) | |
| M16: Day 8, Morning(n=28,59,50) | 23.7 (± 14.9) | 37.6 (± 36.1) | 61.7 (± 43.7) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Depressive Symptoms Using the Patient Health Questionnaire 9-Item (PHQ-9) at DB Endpoint (Up to Week 6)

| End point title | Change From Baseline in Depressive Symptoms Using the Patient Health Questionnaire 9-Item (PHQ-9) at DB Endpoint (Up to Week 6) |
|---|---|

End point description:

The PHQ-9 is a 9-item, subject Reported Outcome measure to assess depressive symptoms. The scale scores each of the 9 symptom domains of the Diagnostic and Statistical Manual of Mental Disorders-5th Edition (DSM-5) major depressive disorder (MDD) criteria. Each item is rated on a 4 point scale (0=not at all, 1=several days, 2=more than half the days, and 3=nearly every day). The subjects item responses are summed to provide a total score (range of 0 to 27), with higher scores indicating greater severity of depressive symptoms. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

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

End point timeframe:

Baseline and DB Endpoint (Up to Week 6)

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 136 | 32 | 60 | 51 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -7.3 (± 6.14) | -6.2 (± 5.48) | -8.6 (± 6.66) | -7.0 (± 7.64) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Anhedonia Using the Snaith-Hamilton Pleasure Scale (SHAPS) at DB Endpoint (Up to Week 6)

| End point title | Change From Baseline in Anhedonia Using the Snaith-Hamilton Pleasure Scale (SHAPS) at DB Endpoint (Up to Week 6) |
|---|---|

End point description:

The SHAPS is a 14-item, self-report instrument to assess hedonic capacity in adults with MDD. Each of the items has a set of 4 response categories-Definitely Agree (=1), Agree (=2), Disagree (=3), and Definitely Disagree (=4). A total score is created with either of the Disagree responses receiving a score of 1 and either of the Agree responses receiving a score of 0. The subjects item responses are summed to provide a total score ranging from 0 to 14. A higher total SHAPS score indicates higher levels of current anhedonia. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint. Endpoint (DB) values are from the last measurement within the double-blind period.

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

End point timeframe:

Baseline and DB Endpoint (Up to Week 6)

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 136 | 32 | 60 | 51 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -3.6 (± 4.44) | -2.3 (± 4.09) | -4.2 (± 4.50) | -3.2 (± 5.20) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Sleep Disturbance Using the Patient Reported Outcome Measurement Information System-Sleep Disturbance (PROMIS-SD) Short

## Form at DB Endpoint (Up to Week 6)

| End point title | Change From Baseline in Sleep Disturbance Using the Patient Reported Outcome Measurement Information System-Sleep Disturbance (PROMIS-SD) Short Form at DB Endpoint (Up to Week 6) |
|---|---|

End point description:

The PROMIS-SD Short Form subscale consists of a static 8 item questionnaire. It assesses the concepts of sleep initiation (2 items), quality of sleep (3 items), early morning feelings (2 items) and worrying about sleep (1 item). Responses to each of the 8 items range from 1 to 5, and the range of possible summed raw scores is 8 to 40. Higher scores on the PROMIS SD indicate more of the concept measured (disturbed sleep). Negative change in score indicates improvement. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

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

End point timeframe:

Baseline and DB Endpoint (Up to Week 6)

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 136 | 32 | 60 | 51 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -6.4 (± 8.53) | -5.1 (± 8.39) | -10.2 (± 9.21) | -10.9 (± 9.25) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Fatigue Using the Patient Reported Outcome Measurement Information System-Fatigue (PROMIS-F) Short Form subscale at DB Endpoint (Up to Week 6)

| End point title | Change From Baseline in Fatigue Using the Patient Reported Outcome Measurement Information System-Fatigue (PROMIS-F) Short Form subscale at DB Endpoint (Up to Week 6) |
|---|---|

End point description:

The PROMIS-Fatigue Short Form subscale consists of a static 8 item questionnaire. It assesses a range of symptoms from mild subjective feelings of tiredness to an overwhelming, debilitating, and sustained sense of exhaustion that likely decreases one's ability to execute daily activities and function normally in family or social roles. Ratings are done on a 5-item Likert scale ranging from 0 (not at all) to 5 (very much) and 0 (never) to 5(always). Higher scores on the PROMIS F indicate more of the concept measured (fatigue). Negative change in score indicates improvement. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint. Endpoint (DB) values are from the last measurement within the double-blind period.

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

End point timeframe:

Baseline and DB Endpoint (Up to Week 6)

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 136 | 32 | 60 | 51 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -7.7 (± 8.45) | -7.4 (± 8.25) | -9.4 (± 8.62) | -8.0 (± 10.29) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Severity of Depression Using the Patient Global Impression-Severity (PGI-S) at DB Endpoint (Up to Week 6)

| End point title | Change From Baseline in Severity of Depression Using the Patient Global Impression-Severity (PGI-S) at DB Endpoint (Up to Week 6) |
|---|---|

End point description:

The PGI-S is a self-report scale to measure severity of illness (1=none, 2=mild, 3=moderate, 4=severe). Higher score indicates more illness severity. Negative change in score indicates improvement. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint. Endpoint (DB) values are from the last measurement within the double-blind period.

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

End point timeframe:

Baseline and DB Endpoint (Up to Week 6)

| End point values | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 136 | 32 | 60 | 51 |
| Units: Units on a scale | | | | |
| median (full range (min-max)) | -1.0 (-3 to 2) | 0.0 (-2 to 1) | -1.0 (-3 to 1) | -1.0 (-3 to 1) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in European Quality of Life 5 Dimensions (EQ-5D-5L) Heath State Index Total Score at DB Endpoint (Up to Week 6)

| End point title | Change From Baseline in European Quality of Life 5 Dimensions (EQ-5D-5L) Heath State Index Total Score at DB Endpoint (Up to Week 6) |
|---|---|

End point description:

EQ-5D descriptive system comprises of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels of perceived problems (1-no

problem, 2-slight problems, 3-moderate problems, 4-severe problems, 5-extreme problems). The responses to 5 EQ-5D dimensions were scored using a utility-weighted algorithm to derive an EQ-5D health status index score between 0 (death) to 1 (full health). Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, N (number of subjects analyzed) signifies subjects who were evaluable for this endpoint. Endpoint (DB) values are from the last measurement within the double-blind period.

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

End point timeframe:

Baseline and DB Endpoint (Up to Week 6)

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 136 | 32 | 60 | 51 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | 0.188 (± 0.2201) | 0.143 (± 0.1856) | 0.229 (± 0.2084) | 0.158 (± 0.2841) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in EQ-5D-5L Visual Analog Scale (VAS) Total Score at Endpoint (Week 6)

| End point title | Change From Baseline in EQ-5D-5L Visual Analog Scale (VAS) Total Score at Endpoint (Week 6) |
|---|---|

End point description:

EQ-5D-5L (describing and valuing health-related quality of life) descriptive system comprises 5 dimensions of health (mobility, self -care, usual activities, pain/discomfort, and anxiety/depression) to describe the subject's current health state. Each dimension comprises 5 levels with corresponding numeric scores, where 1 indicates no problems, and 5 indicates extreme problems. Higher scores representing a better health state. An increase in the EQ-5D-5L total score indicates improvement. EQ-VAS self-rating records respondent's own assessment of his/her overall health status at time of completion, on scale of 0 (worst health you can imagine) to 100 (best health you can imagine). Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, N (number of subjects analyzed) signifies subjects who were evaluable for this endpoint. Endpoint (DB) values: last measurement within double-blind period.

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

End point timeframe:

Baseline and Endpoint (up to Week 6)

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 136 | 32 | 60 | 51 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | 17.4 (± 20.55) | 8.9 (± 19.34) | 23.4 (± 21.18) | 20.1 (± 23.08) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Work Productivity and Limitations Using the Work Limitations Questionnaire (WLQ) Short Form at DB Endpoint (Up to Week 6)

| End point title | Change From Baseline in Work Productivity and Limitations Using the Work Limitations Questionnaire (WLQ) Short Form at DB Endpoint (Up to Week 6) |
|---|---|

End point description:

The WLQ is a 8-item questionnaire self-report rating scale developed to measure the on-the-job impact of chronic health problems and/or treatment ("work limitations"). It comprises five dimensions of limitations: handling time, physical, mental-interpersonal, productivity loss and output demands. Subjects respond to each item with options ranging from 'Almost all of the time' to 'none of the time', or 'Does not apply to my job'. Each dimension of limitations have a scale score ranging from 0 to 100 with lower score indicating low level of work limitations. Full analysis set included subjects who were randomly assigned to study drug and received at least 1 dose of study drug. Here, 'n' (number of subjects analyzed) signifies those subjects who were evaluable for specific categories. Endpoint (DB) values are from the last measurement within the double-blind period.

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

End point timeframe:

Baseline and DB Endpoint (Up to Week 6)

| **End point values** | Placebo | JNJ-42847922 10 milligram (mg) | JNJ-42847922 20 mg | JNJ-42847922 40 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 137 | 33 | 61 | 52 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Time management (n=104,31,22,32) | -21.3 (± 30.41) | -18.2 (± 28.28) | -21.8 (± 34.46) | -20.8 (± 37.48) |
| Physical demands (n=105,25,33,34) | -15.2 (± 23.64) | -23.5 (± 26.10) | -11.7 (± 31.40) | -14.3 (± 35.37) |
| Mental interpersonal scale (n=109,25,34,33) | -21.2 (± 27.61) | -19.5 (± 25.28) | -26.8 (± 27.89) | -15.9 (± 31.76) |
| Output demand scale (n=103,22,32,30) | -23.9 (± 26.72) | -22.2 (± 27.80) | -20.3 (± 30.08) | -21.7 (± 35.80) |
| Productivity loss (n=99,31,29,29) | -5.1 (± 5.56) | -4.7 (± 5.30) | -4.7 (± 6.16) | -4.6 (± 7.02) |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Up to Week 8 | |
| Adverse event reporting additional description: | |
| Safety analyses set included all subjects who were randomly assigned to study drug and received at least 1 dose of study drug. | |
| Assessment type | Non-systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 21.1 |

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received JNJ-42847922 matching placebo capsules once daily orally from Day 1 to Day 41 (Week 6). | |
| Reporting group title | JNJ-42847922 10 mg |
| Reporting group description: | |
| Subjects received JNJ-42847922 10 mg capsules once daily orally from Day 1 to Day 41 (Week 6). | |
| Reporting group title | JNJ-42847922 20 mg |
| Reporting group description: | |
| Subjects received JNJ-42847922 20 mg capsules once daily orally from Day 1 to Day 41 (Week 6). | |
| Reporting group title | JNJ-42847922 40 mg |
| Reporting group description: | |
| Subjects received JNJ-42847922 40 mg capsules once daily orally from Day 1 to Day 41 (Week 6). | |

| Serious adverse events | Placebo | JNJ-42847922 10 mg | JNJ-42847922 20 mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | 0 / 33 (0.00%) | 0 / 61 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Polycythaemia Vera | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | 0 / 33 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | JNJ-42847922 40 mg | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| number of deaths (all causes) | 0 | | |

| | | | |
|---|---|---|---|
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Polycythaemia Vera | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Placebo | JNJ-42847922 10 mg | JNJ-42847922 20 mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 56 / 137 (40.88%) | 11 / 33 (33.33%) | 25 / 61 (40.98%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 9 / 137 (6.57%) | 2 / 33 (6.06%) | 1 / 61 (1.64%) |
| occurrences (all) | 11 | 2 | 1 |
| Somnolence | | | |
| subjects affected / exposed | 7 / 137 (5.11%) | 1 / 33 (3.03%) | 6 / 61 (9.84%) |
| occurrences (all) | 9 | 1 | 6 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 7 / 137 (5.11%) | 0 / 33 (0.00%) | 0 / 61 (0.00%) |
| occurrences (all) | 8 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 4 / 137 (2.92%) | 1 / 33 (3.03%) | 4 / 61 (6.56%) |
| occurrences (all) | 6 | 2 | 4 |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 137 (0.73%) | 2 / 33 (6.06%) | 1 / 61 (1.64%) |
| occurrences (all) | 3 | 2 | 1 |

| **Non-serious adverse events** | JNJ-42847922 40 mg | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 19 / 52 (36.54%) | | |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Headache<br>subjects affected / exposed<br>occurrences (all)<br><br>Somnolence<br>subjects affected / exposed<br>occurrences (all) | 6 / 52 (11.54%)<br>8<br><br>2 / 52 (3.85%)<br>2 | | |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all) | 1 / 52 (1.92%)<br>1<br><br>3 / 52 (5.77%)<br>3 | | |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all) | 2 / 52 (3.85%)<br>2 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 19 July 2016 | The key reasons for this amendment were: 1) to add a 3rd dosage arm of JNJ-42847922 to Stage 1; 2) to include population pharmacokinetic (PK) and exposure-response analyses at interim analysis; 3) to add the Insomnia Severity Index (ISI) as a continuous variable to be a specific endpoint; 4) to include diagnostic measures of major depressive disorder (MDD) capable of evaluating associated specifiers, such as anxious distress; 5) to update and/or clarify eligibility criteria; and 6) to provide the latest clinical information regarding JNJ-42847922. This amendment was issued before first patient enrolled. |
| 12 October 2016 | The key reasons for this amendment were: 1) to clarify timing of evening dosing to occur at bedtime and at least 3 hours after the last meal; 2) to clarify that pharmacogenomic sampling is optional and to include a separate informed consent form (ICF) for pharmacogenomic sampling; 3) to update and/or clarify eligibility criteria; 4) to update and/or clarify the description of the placebo capsule; 5) to clarify that anticipated events werel not designated in Japan; and 6) to provide the latest clinical information regarding JNJ-42847922. This amendment was issued before first patient enrolled. |
| 27 February 2017 | The key reasons for this amendment were to simplify the dose-finding strategy and reduce the sample size by: 1) removing Stage 2 from the original study design; 2) removing the active comparator (quetiapine) arm from the study; 3) reducing the number of JNJ-42847922 treatment arms. This amendment was issued before first patient enrolled. |
| 21 July 2017 | The key reasons for this amendment were to report preclinical safety data from a 9-month study in dogs, to add instructions to investigators to ensure awareness of preclinical data regarding seizures/convulsions, to increase the sample size of this study, and to prohibit use of ketamine or esketamine for depression prior to or during the study. This amendment was issued before first patient enrolled. |
| 24 April 2018 | To add results of the male and female rat fertility studies. To exclude further enrollment of women of childbearing potential (WOCBP). In addition, other minor changes and clarifications related to study procedures were made. |

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.

During interim analysis, number of subjects with baseline ISI score >=15 was nearing limits. so seltorexant 10 mg was introduced and seltorexant 40 mg was removed from randomization after IA, dose-groups were not balanced when based on ISI score.

Notes: