Clinical trial results:
A Randomized, Stratified, Double-blind, Placebo-Controlled Study to Investigate the Efficacy, Safety and Tolerability of JNJ-55308942 in Bipolar Depression

Summary

EudraCT number	2021-004790-31
Trial protocol	ES PL
Global end of trial date	17 May 2024

Results information

Result version number	v1 (current)
This version publication date	30 May 2025
First version publication date	30 May 2025

Trial information

Trial identification

Sponsor protocol code	55308942BIP2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05328297
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)	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	17 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the efficacy of JNJ-55308942 compared to placebo on symptoms of depression in subjects with bipolar disorder (BD) in an major depressive episode (MDE) at Week 6.

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	03 June 2022
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	Canada: 1
Country: Number of subjects enrolled	Poland: 60
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United States: 46
Worldwide total number of subjects	114
EEA total number of subjects	67

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)	114

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 116 subjects were randomised in this study, out of which 114 received treatment. Out of 114 subjects, 92 completed the study.

Pre-assignment

Screening details:

A total of 116 subjects were randomised in this study, out of which 114 received treatment. Out of 114 subjects, 92 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

Blinding implementation details:

Subjects and investigators were blinded to treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	JNJ-55308942

Arm description:

During double-blind (DB) treatment phase, subjects received JNJ-55308942 capsule, orally once daily from Day 1 (Week 0) up to 6 weeks. Subjects were then followed up for up to 2 weeks after their last dose (up to Day 56).

Arm type	Experimental
Investigational medicinal product name	JNJ-55308942
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

A single JNJ-55308942 capsule once daily from Day 1 up to 6 weeks during DB phase.

Arm title	Placebo

Arm description:

During DB treatment phase, subjects received placebo capsule (matching to JNJ-55308942), orally once daily from Day 1 (Week 0) up to 6 weeks. Subjects were then followed up for up to 2 weeks after their last dose (up to Day 56).

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

Dosage and administration details:

A single JNJ-55308942 matching placebo capsule once daily from Day 1 up to 6 weeks during DB phase.

Number of subjects in period 1	JNJ-55308942	Placebo
Started	54	60
Completed	42	50
Not completed	12	10
Consent withdrawn by subject	4	3
Adverse event, non-fatal	5	7
Lost to follow-up	1	-
Lack of efficacy	1	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	JNJ-55308942
Reporting group description:	
During double-blind (DB) treatment phase, subjects received JNJ-55308942 capsule, orally once daily from Day 1 (Week 0) up to 6 weeks. Subjects were then followed up for up to 2 weeks after their last dose (up to Day 56).	
Reporting group title	Placebo
Reporting group description:	
During DB treatment phase, subjects received placebo capsule (matching to JNJ-55308942), orally once daily from Day 1 (Week 0) up to 6 weeks. Subjects were then followed up for up to 2 weeks after their last dose (up to Day 56).	

Reporting group values	JNJ-55308942	Placebo	Total
Number of subjects	54	60	114
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	39.28	40.18	
standard deviation	± 13.603	± 12.664	-
Gender categorical Units: Subjects			
Male	16	27	43
Female	38	33	71

End points

End points reporting groups

Reporting group title	JNJ-55308942
Reporting group description:	
During double-blind (DB) treatment phase, subjects received JNJ-55308942 capsule, orally once daily from Day 1 (Week 0) up to 6 weeks. Subjects were then followed up for up to 2 weeks after their last dose (up to Day 56).	
Reporting group title	Placebo
Reporting group description:	
During DB treatment phase, subjects received placebo capsule (matching to JNJ-55308942), orally once daily from Day 1 (Week 0) up to 6 weeks. Subjects were then followed up for up to 2 weeks after their last dose (up to Day 56).	

Primary: Change from Baseline in Montgomery-Asberg Depression Rating Scale (MADRS) Total Score up to Week 6

End point title	Change from Baseline in Montgomery-Asberg Depression Rating Scale (MADRS) Total Score up to Week 6
End point description:	
MADRS was a clinician-rated scale designed to measure depression severity and detect changes due to antidepressant (AD) treatment. MADRS evaluated reported sadness, apparent sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. The scale consisted 10 items, each was scored from 0 (item not present or normal) to 6 (severe or continuous presence of symptoms), with higher score indicating more severe condition. MADRS total score was the sum of scores from individual question items and it ranged from 0 to 60, with higher scores indicated more severe conditions. Negative change in MADRS total score indicated improvement. Full analysis set (FAS) included all randomised subjects who received at least 1 dose of study intervention and had both baseline and at least 1 postbaseline MADRS measurement.	
End point type	Primary
End point timeframe:	
From Baseline (Day 1) up to Week 6	

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	59		
Units: Units on a scale				
arithmetic mean (standard deviation)	-16.0 (± 10.43)	-15.4 (± 9.81)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Statistical Analysis 1	
Comparison groups	JNJ-55308942 v Placebo

Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.438
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	Least Square Mean difference
Point estimate	-0.3
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-2.84
upper limit	2.23
Variability estimate	Standard error of the mean
Dispersion value	1.96

Secondary: Change from Baseline in Snaith-Hamilton Pleasure Scale (SHAPS) Total Score up to Week 6

End point title	Change from Baseline in Snaith-Hamilton Pleasure Scale (SHAPS) Total Score up to Week 6

End point description:

Change from baseline in SHAPS total score up to Week 6 were reported. The SHAPS was a reliable, valid, and unidimensional instrument used to assess hedonic capacity in adults with Major Depressive Disorder (MDD). It is a 14-item, self-report tool with a completion time below 5 minutes. Each of the items had a set of 4 response categories: 1 = definitely agree/strongly agree, 2 = agree, 3 = disagree, and 4 = strongly disagree. The SHAPS total score was the sum of the 14 item scores, which ranged from 14 to 56. A higher SHAPS total score indicated higher levels of current anhedonia. Negative changes in the SHAPS total score indicated improvement. FAS included all randomised subjects who received at least 1 dose of study intervention and had both baseline and at least 1 postbaseline MADRS measurement. Here, 'N' (subjects analysed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to Week 6

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	50		
Units: Units on a scale				
arithmetic mean (standard deviation)	-8.2 (± 6.87)	-8.3 (± 8.69)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in MADRS Total Score up to Week 6 (Diagnosis Subgroup Analysis)

End point title	Change from Baseline in MADRS Total Score up to Week 6 (Diagnosis Subgroup Analysis)

End point description:

Diagnosis subgroup analysis included subjects with bipolar type I or II. MADRS was clinician-rated scale designed to measure depression severity and detect changes due to AD treatment. MADRS evaluated reported sadness, apparent sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Scale consist 10 items, each scored from 0 (item not present or normal) to 6 (severe or continuous presence of symptoms); higher score indicated more severe condition. MADRS total score was sum of scores from individual question items and ranged from 0-60; higher scores indicated more severe conditions. Negative change in MADRS total score indicated improvement. FAS was used. 'N' (subjects analysed): number of subjects evaluable for this endpoint and 'n' (number analysed): subjects analysed at specified categories.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to Week 6

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	50		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Bipolar type I (n=33, 37)	-15.5 (± 11.02)	-15.3 (± 10.06)		
Bipolar type II (n=9, 13)	-17.7 (± 8.20)	-15.7 (± 9.47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in MADRS Total Score up to Week 6 (Genetic Subgroup Analysis)

End point title	Change from Baseline in MADRS Total Score up to Week 6 (Genetic Subgroup Analysis)

End point description:

Genetic subgroup analysis: subjects with bipolar depression with P2RX7 Gain of Function single nucleotide polymorphism mutation genotype: heterozygous or homozygous. MADRS was clinician-rated scale designed to measure depression severity and detect changes due to AD treatment. MADRS evaluated reported sadness, apparent sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Scale consist 10 items, each scored from 0 (item not present or normal) to 6 (severe or continuous presence of symptoms); higher score indicated more severe condition. MADRS total score was sum of scores from individual question items and ranged from 0-60; higher scores indicated more severe conditions. Negative change in MADRS total score indicated improvement. FAS was used. 'N' (subjects analysed):number of subjects evaluable for this endpoint and 'n' (number analysed):subjects analysed at specified categories.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to Week 6

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	50		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Genotype: Heterozygous (n=31, 34)	-15.2 (± 9.45)	-16.5 (± 10.22)		
Genotype: Homozygous (n=11, 16)	-18.2 (± 13.06)	-13.1 (± 8.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in MADRS Total Score up to Week 6 (Biomarker Subgroup Analysis)

End point title	Change from Baseline in MADRS Total Score up to Week 6 (Biomarker Subgroup Analysis)

End point description:

Biomarker subgroup analysis included specific (3-Marker Model [3MM]) biomarker profile: Yes or No. 3MM biomarker profile: serum C-reactive protein >3 mg/Liter(L) and soluble interleukin-6 receptor >25 micrograms(mcg)/L or tumor necrosis factor >4 nanograms(ng)/L at baseline. MADRS evaluated reported sadness, apparent sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Scale consist 10 items, each scored from 0 (item not present or normal) to 6 (severe or continuous presence of symptoms); higher score indicated more severe condition. MADRS total score was sum of scores from individual question items and ranged from 0-60; higher scores indicated more severe conditions. Negative change in MADRS total score indicated improvement. FAS was used. 'N' (subjects analysed): number of subjects evaluable for this endpoint and 'n' (number analysed): subjects analysed at specified categories.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to Week 6

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	49		
Units: Units on a scale				
arithmetic mean (standard deviation)				
3MM biomarker profile: Yes (n=11, 22)	-12.5 (± 9.04)	-13.9 (± 10.77)		
3MM biomarker profile: No (n=31, 27)	-17.2 (± 10.75)	-16.6 (± 9.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-emergent Clinically Important Abnormalities in Vital Signs

End point title	Number of Subjects with Treatment-emergent Clinically Important Abnormalities in Vital Signs

End point description:

Vital signs included pulse rate (abnormally low [AL]:<50 beats per minute[bpm] with >15 bpm decrease from baseline and abnormally high [AH]: >100 bpm with >15 bpm increase from baseline),Systolic blood pressure (SBP; AL: <90 millimeters of mercury[mmHg] with >20 mmHg decrease from baseline and AH: >180 mmHg with >20 mmHg increase from baseline), Diastolic BP (DBP; AL: <50 mmHg with >15 mmHg decrease from baseline and AH: >105 mmHg with >15 mmHg increase from baseline), temperature (AL: <35.5 and AH: >37.5 degree Celsius [C]), respiratory rate (AH: >20 breaths per minute),and weight (planned to analyzed at Weeks 6 and 8 only; AL: decrease from baseline >7% and AH: increase from baseline >7%). TE abnormalities in vital signs: those abnormalities that occurred at or after first dose administration. Safety analysis set: all randomised subjects who took at least 1 dose of study intervention. 'N': number of subjects evaluable for this endpoint. 'n': subject analysed at specified categories.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 6, and 8 (Follow-up/Early Withdrawal)

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	56		
Units: Subjects				
Pulse:<50 and >15 bpm decrease: Week 1 (n=49, 56)	0	0		
Pulse:>100 and >15 bpm increase: Week 1 (n=49,56)	0	0		
SBP: <90 and >20 mmHg decrease: Week 1 (n=49,56)	0	0		
SBP: >180 and >20 mmHg increase: Week 1(n=49,56)	0	0		
DBP: <50 and >15 mmHg decrease: Week 1 (n=49,56)	0	0		
DBP: >105 and >15 mmHg increase: Week 1(n=49,56)	0	0		
Temperature:<35.5 degree C:Week 1 (n=49,56)	0	0		
Temperature:>37.5 degree C:Week 1 (n=49,56)	0	0		
Respiratory Rate>20breaths/minute:Week1(n=49,5	0	0		
Pulse:<50 and >15 bpm decrease: Week 2 (n=45, 56)	0	0		
Pulse:>100 and >15 bpm increase: Week 2 (n=45,56)	0	0		
SBP: <90 and >20 mmHg decrease: Week 2 (n=45,56)	0	0		
SBP: >180 and >20 mmHg increase: Week 2(n=45,56)	0	0		
DBP: <50 and >15 mmHg decrease: Week 2 (n=45,56)	0	0		

DBP: >105 and >15 mmHg increase: Week 2(n=45,56)	0	0		
Temperature:<35.5 degree C:Week 2 (n=45,56)	0	0		
Temperature:>37.5 degree C:Week 2 (n=45,56)	0	0		
Respiratory Rate>20breaths/minute:Week2(n=45,5	0	1		
Pulse:<50 and >15 bpm decrease: Week 4(n=44,50)	0	0		
Pulse:>100 and >15 bpm increase:Week 4(n=44,50)	0	0		
SBP:<90 and >20 mmHg decrease: Week 4 (n=44,50)	0	0		
SBP:>180 and >20 mmHg increase: Week 4(n=44,50)	0	0		
DBP: <50 and >15 mmHg decrease: Week 4 (n=44,50)	0	0		
DBP:>105 and >15 mmHg increase: Week 4(n=44,50)	0	0		
Temperature:<35.5 degreeC:Week 4 (n=44,50)	0	0		
Temperature:>37.5 degreeC:Week 2 (n=45,56)	0	0		
Respiratory Rate>20breaths/minute:Week4(n=44,5	0	0		
Pulse:<50 and >15 bpm decrease: Week 6(n=42, 50)	0	0		
Pulse:>100 and >15 bpm increase: Week 6(n=42, 50)	0	0		
SBP:<90 and >20mmHg decrease: Week 6(n=42,50)	0	0		
SBP:>180 and >20mmHg increase: Week 6(n=42,50)	0	0		
DBP:<50 and >15mmHg decrease: Week 6(n=42,50)	0	0		
DBP:>105 and >15mmHg increase: Week 6(n=42,50)	0	0		
Temperature:<35.5 degreeC:Week 6 (n=42,50)	0	0		
Temperature:>37.5 degreeC:Week 6 (n=42,50)	0	0		
Respiratory Rate>20breaths/minute:Week6(n=42,5	0	0		
Weight:Decrease >7%:Week 6 (n=42,50)	0	0		
Weight:Increase >7%:Week 6 (n=42,50)	0	1		
Pulse:<50 and >15 bpm decrease:Week 8(n=42, 48)	0	0		
Pulse:>100 and >15 bpm increase:Week 8(n=42, 48)	1	0		
SBP:<90 and >20mmHg decrease:Week 8 (n=42,48)	0	0		
SBP:>180 and >20mmHg increase:Week 8(n=42,48)	0	1		
DBP:<50 and >15mmHg decrease:Week 8 (n=42,48)	0	1		
DBP:>105 and >15mmHg increase:Week 8(n=42,48)	0	0		
Temperature:<35.5 degreeC:Week 8 (n=42,48)	0	0		

Temperature:>37.5 degreeC:Week 8 (n=42,48)	0	0		
Respiratory Rate>20breaths/minute:Week8(n=42,4	0	0		
Weight:Decrease >7%:Week 8 (n=42,48)	1	0		
Weight:Increase >7%:Week 8 (n=42,48)	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Laboratory Values in Male Hormone: Inhibin B

End point title	Change From Baseline in Clinical Laboratory Values in Male Hormone: Inhibin B

End point description:

Change from baseline in clinical laboratory values in male hormone (Inhibin B) were reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here, 'N' (subjects analysed) signifies number of subjects evaluable for this endpoint. Here, 'n' (number analysed) is defined as subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 4, 6, and 8 (Follow-up/Early Withdrawal)

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	25		
Units: nanograms per liter (ng/L)				
arithmetic mean (standard deviation)				
Week 4 (n=15, 22)	-5.9 (± 30.45)	3.1 (± 22.15)		
Week 6 (n=14, 21)	-2.1 (± 30.02)	-1.8 (± 31.09)		
Week 8 (n=14, 21)	-1.2 (± 28.25)	7.3 (± 19.60)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Laboratory Values in Male Hormone: Luteinizing Hormone

End point title	Change From Baseline in Clinical Laboratory Values in Male Hormone: Luteinizing Hormone

End point description:

Change from baseline in clinical laboratory values in male hormone (luteinizing hormone) were reported.

Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here, 'N' (subjects analysed) signifies number of subjects evaluable for this endpoint. Here, 'n' (number analysed) is defined as subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 4, 6, and 8 (Follow-up/Early Withdrawal)

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	27		
Units: International units per liter (IU/L)				
arithmetic mean (standard deviation)				
Week 4 (n=15, 24)	0.15 (± 1.814)	0.29 (± 1.513)		
Week 6 (n=15, 24)	-0.11 (± 1.677)	0.63 (± 2.719)		
Week 8 (n=15, 25)	-0.35 (± 1.638)	0.84 (± 2.103)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Laboratory Values in Male Hormone: Prolactin

End point title	Change From Baseline in Clinical Laboratory Values in Male Hormone: Prolactin

End point description:

Change from baseline in clinical laboratory values in male hormone (prolactin) were reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here, 'N' (subjects analysed) signifies number of subjects evaluable for this endpoint. Here, 'n' (number analysed) is defined as subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Weeks 4, 6, and 8 (Follow-up/Early Withdrawal)

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	27		
Units: micrograms per liter (mcg/L)				
arithmetic mean (standard deviation)				
Week 4 (n=15, 24)	0.347 (± 2.4360)	1.803 (± 3.6211)		
Week 6 (n=15, 24)	0.551 (± 3.1575)	1.465 (± 5.3742)		
Week 8 (n=15, 25)	-0.160 (± 3.8622)	1.748 (± 3.9231)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Laboratory Values in Male Hormones: Sex Hormone Binding Globulin, Testosterone (Free), Testosterone (High Sensitivity), and Testosterone (Low Sensitivity)

End point title	Change From Baseline in Clinical Laboratory Values in Male Hormones: Sex Hormone Binding Globulin, Testosterone (Free), Testosterone (High Sensitivity), and Testosterone (Low Sensitivity)

End point description:

Change from baseline in clinical laboratory values in male hormones (sex hormone binding globulin, testosterone [free], testosterone [high sensitivity], and testosterone [low sensitivity]) were reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here, 'N' (subjects analysed) signifies number of subjects evaluable for this endpoint. Here, 'n' (number analysed) is defined as subjects analysed at specified categories.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Weeks 4, 6, and 8 (Follow-up/Early Withdrawal)

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	27		
Units: nanomoles per Litre (nmol/L)				
arithmetic mean (standard deviation)				
Sex Hormone Binding Globulin: Week 4 (n=14, 23)	-1.976 (± 7.1297)	-0.574 (± 8.5796)		
Sex Hormone Binding Globulin: Week 6 (n=14, 23)	-4.020 (± 7.4992)	-0.274 (± 9.2454)		
Sex Hormone Binding Globulin: Week 8 (n=14, 24)	-2.520 (± 7.8489)	1.058 (± 6.6109)		
Testosterone, Free: Week 4 (n=12, 15)	0.005 (± 0.0677)	0.030 (± 0.0995)		
Testosterone, Free: Week 6 (n=13, 18)	-0.010 (± 0.0731)	0.037 (± 0.1084)		
Testosterone, Free: Week 8 (n=13, 16)	0.031 (± 0.0763)	0.046 (± 0.0877)		
Testosterone, High Sensitivity: Week 4 (n=14, 24)	-0.797 (± 3.3271)	0.357 (± 5.5917)		
Testosterone, High Sensitivity: Week 6 (n=15, 24)	-1.262 (± 3.6807)	0.842 (± 5.6815)		
Testosterone, High Sensitivity: Week 8 (n=15, 25)	0.604 (± 3.7718)	1.416 (± 4.3083)		
Testosterone, Low Sensitivity: Week 4 (n=14, 24)	-0.791 (± 3.8886)	0.854 (± 5.9616)		
Testosterone, Low Sensitivity: Week 6 (n=14, 24)	-1.532 (± 4.5203)	1.380 (± 5.9515)		

Testosterone, Low Sensitivity: Week 8 (n=14, 24)	1.116 (± 4.8452)	1.728 (± 4.6578)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal Laboratory Values: Serum Chemistry

End point title	Number of Subjects With Abnormal Laboratory Values: Serum Chemistry

End point description:

Number of subjects with abnormal laboratory values: serum chemistry were reported. It included: aspartate aminotransferase (high), alanine aminotransferase (high), bilirubin (high/low), and alkaline phosphatase (high/low). Only categories with data were reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here, 'n' (number analysed) is defined as subjects analysed at specified categories.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 6, and 8 (Follow-up/Early Withdrawal)

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	60		
Units: Subjects				
Aspartate Aminotransferase (High):Week 2(n=44,55)	2	2		
Aspartate Aminotransferase (High):Week 4(n=43,50)	0	2		
Aspartate Aminotransferase (High):Week 6(n=42,49)	1	0		
Aspartate Aminotransferase (High):Week 8(n=47,50)	0	2		
Alanine Aminotransferase (High): Week 2 (n=45,56)	1	3		
Alanine Aminotransferase (High): Week 4 (n=42,50)	2	3		
Alanine Aminotransferase (High): Week 6 (n=41,49)	2	1		
Alanine Aminotransferase (High): Week 8 (n=47,49)	1	2		
Bilirubin (Low): Week 2 (n=45, 56)	4	9		
Bilirubin (High): Week 2 (n=45, 56)	1	0		
Bilirubin (Low): Week 4 (n=43, 50)	8	7		
Bilirubin (Low): Week 6 (n=42, 50)	5	4		
Bilirubin (High): Week 6 (n=42, 50)	2	0		
Bilirubin (Low): Week 8 (n=47, 50)	3	5		
Bilirubin (High): Week 8 (n=47, 50)	1	0		
Alkaline Phosphatase (Low): Week 2 (n=45, 56)	1	0		

Alkaline Phosphatase (High): Week 2 (n=45, 56)	3	5		
Alkaline Phosphatase (Low): Week 4 (n=42, 50)	1	0		
Alkaline Phosphatase (High): Week 4 (n=42, 50)	0	3		
Alkaline Phosphatase (Low): Week 6 (n=42, 49)	1	0		
Alkaline Phosphatase (High): Week 6 (n=42, 49)	1	6		
Alkaline Phosphatase (Low): Week 8 (n=47, 50)	1	0		
Alkaline Phosphatase (High): Week 8 (n=47, 50)	4	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormal Laboratory Values: Hematology

End point title	Number of Subjects With Clinically Significant Abnormal Laboratory Values: Hematology

End point description:

Number of subjects with clinically significant abnormal laboratory values: hematology were reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 6, and 8 (Follow-up/Early Withdrawal)

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	60		
Units: Subjects				
Week 2	0	0		
Week 4	0	0		
Week 6	0	0		
Week 8	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormal Laboratory Values: Urinalysis

End point title	Number of Subjects With Clinically Significant Abnormal Laboratory Values: Urinalysis

End point description:

Number of subjects with clinically significant abnormal laboratory values: urinalysis were reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 6, and 8 (Follow-up/Early Withdrawal)

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	60		
Units: Subjects				
Week 2	0	0		
Week 4	0	0		
Week 6	0	0		
Week 8	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects with Treatment-emergent Adverse Events (TEAEs)

End point description:

Number of subjects with TEAEs were reported. An adverse event (AE) is any untoward medical occurrence in a clinical study subjects who administered a medicinal (investigational or non-investigational) product and does not necessarily have a causal relationship with the treatment. A TEAE defined as an AE that occurred at or after the first dose administration up to day of the last dose plus 30 days. Safety analysis set included all randomized subjects who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Day 1 (Week 0) up to 30 days after the last dose (up to 11 weeks)

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	60		
Units: Subjects	22	28		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-emergent Abnormalities in Electrocardiograms (ECGs)

End point title	Number of Subjects with Treatment-emergent Abnormalities in Electrocardiograms (ECGs)

End point description:

Number of subjects with treatment-emergent abnormalities in ECGs were reported. It included ECG mean heart rate (abnormally low [AL]: <50 and abnormally high [AH]: >100 beats per minute [bpm]), PR Interval (AL: <120 and AH: >200 milliseconds [msec]), QRS Duration (AL: <60 and AH: >120 msec), and QT Interval (AL: <200 and AH: >500 msec). Treatment-emergent abnormalities in ECGs is defined as those abnormalities that occurred at or after the first dose administration. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here, 'n' (number analysed) is defined as subjects analysed at specified categories.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 6, and 8 (Follow-up/Early Withdrawal)

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	60		
Units: Subjects				
ECG Mean Heart Rate: <50 bpm: Week 1 (n=48, 56)	1	0		
ECG Mean Heart Rate: >100 bpm: Week 1 (n=48, 56)	0	0		
PR Interval: <120 msec: Week 1 (n=48, 56)	0	1		
PR Interval: >200 msec: Week 1 (n=48, 56)	1	0		
QRS Duration: <60 msec: Week 1 (n=48, 56)	0	1		
QRS Duration: >120 msec: Week 1 (n=48, 56)	1	0		
QT Interval: <200 msec: Week 1 (n=48, 56)	0	0		
QT Interval: <500 msec: Week 1 (n=48, 56)	0	0		
ECG Mean Heart Rate: <50 bpm: Week 2 (n=44, 56)	0	0		
ECG Mean Heart Rate: >100 bpm: Week 2 (n=44, 56)	1	1		
PR Interval: <120 msec: Week 2 (n=44, 56)	0	0		
PR Interval: >200 msec: Week 2 (n=44, 56)	1	2		
QRS Duration: <60 msec: Week 2 (n=44, 56)	0	1		
QRS Duration: >120 msec: Week 2 (n=44, 56)	0	1		
QT Interval: <200 msec: Week 2 (n=44, 56)	0	0		
QT Interval: <500 msec: Week 2 (n=44, 56)	0	0		
ECG Mean Heart Rate: <50 bpm: Week 4 (n=44, 50)	0	0		
ECG Mean Heart Rate: >100 bpm: Week 4 (n=44, 50)	1	0		

PR Interval: <120 msec: Week 4 (n=44, 50)	0	1		
PR Interval: >200 msec: Week 4 (n=44, 50)	0	0		
QRS Duration: <60 msec: Week 4 (n=44, 50)	0	1		
QRS Duration: >120 msec: Week 4 (n=44, 50)	1	0		
QT Interval: <200 msec: Week 4 (n=44, 50)	0	0		
QT Interval: <500 msec: Week 4 (n=44, 50)	0	0		
ECG Mean Heart Rate: <50 bpm: Week 6 (n=41, 50)	0	0		
ECG Mean Heart Rate: >100 bpm: Week 6 (n=41, 50)	0	0		
PR Interval: <120 msec: Week 6 (n=41, 50)	0	0		
PR Interval: >200 msec: Week 6 (n=41, 50)	0	0		
QRS Duration: <60 msec: Week 6 (n=41, 50)	0	4		
QRS Duration: >120 msec: Week 6 (n=41, 50)	0	0		
QT Interval: <200 msec: Week 6 (n=41, 50)	0	0		
QT Interval: <500 msec: Week 6 (n=41, 50)	0	0		
ECG Mean Heart Rate: <50 bpm: Week 8 (n=50, 52)	0	0		
ECG Mean Heart Rate: >100 bpm: Week 8 (n=50, 52)	0	0		
PR Interval: <120 msec: Week 8 (n=50, 52)	1	0		
PR Interval: >200 msec: Week 8 (n=50, 52)	0	0		
QRS Duration: <60 msec: Week 8 (n=50, 52)	1	2		
QRS Duration: >120 msec: Week 8 (n=50, 52)	0	1		
QT Interval: <200 msec: Week 8 (n=50, 52)	0	0		
QT Interval: <500 msec: Week 8 (n=50, 52)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Young Mania Rating Scale (YMRS) Total Score

End point title	Change from Baseline in Young Mania Rating Scale (YMRS) Total Score

End point description:

Change from baseline in YMRS total score were reported. The YMRS was designed to measure the severity of manic symptoms, to gauge the effect of treatment on mania severity, and to detect a return of manic symptoms (for example relapse or recurrence). YMRS had 11 items : 4 items (irritability, speech, thought content, and disruptive/aggressive behavior) were graded on a scale of 0 to 8 and the remaining 7 items (elevated mood, increased motor activity, sexual interest, sleep, language-thought

disorder, appearance, and insight) were graded on a scale of 0 to 4. Higher scores indicated greater symptom severity. Responses were summed to yield YMRS total score ranged from 0 to 60 , with higher scores reflecting greater severity of mania. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here, 'N' (subjects analysed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to Week 6

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	50		
Units: Units on a scale				
arithmetic mean (standard deviation)	-1.2 (± 2.23)	-1.1 (± 1.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Reported Suicidal Ideation (SI) or Suicidal Behavior (SB) Using With Columbia Suicide Severity Rating Scale (C-SSRS) Score

End point title	Number of Subjects Who Reported Suicidal Ideation (SI) or Suicidal Behavior (SB) Using With Columbia Suicide Severity Rating Scale (C-SSRS) Score

End point description:

C-SSRS is a clinician-rated instrument that reports severity of both SI and SB. SI categories : 1 (wish to be dead), 2 (nonspecific active suicidal thoughts), 3 (active SI with any methods [not plan] without intent to act), 4 (active SI with some intent to act, without specific plan), and 5 (active SI with specific plan and intent). SB categories: 6 (preparatory acts or behavior), 7 (aborted attempt), 8 (interrupted attempt), 9 (actual attempt), and 10 (suicide). An additional category for non-suicide: non-suicidal self-injurious behavior. SI/SB was indicated by "yes" answer to any listed categories. Score of 0 (no SI/SB) was assigned. Maximum score of 1 to 10 was assigned if SI/SB was present. Scoring was grouped into 3 categories: No SI or behavior (0), SI (score 1 to 5), and SB (score 6 to 10), with higher scores indicating more severe ideation/behavior. Safety set was used. Here, 'N' (subjects analysed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to Week 8

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	59		
Units: Subjects				
Suicidal ideation (SI)	3	6		
Suicidal behavior (SB)	1	0		
No SI/SB	49	53		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Global Impression-Severity Scale (CGI-S) Score

End point title	Change from Baseline in Clinical Global Impression-Severity Scale (CGI-S) Score

End point description:

Change from baseline in CGI-S score were reported. The CGI-S provides an overall clinician-determined summary measure of the severity of the subject's illness that takes into account all available information, including knowledge of the subject's history, psychosocial circumstances, symptoms, behavior, and the impact of the symptoms on the subject's ability to function. The CGI-S is a 7-point global assessment scale that measures the clinician's impression of the severity of mental illness exhibited by a subject, and rated on a scale of 1 to 7: 1=normal (not at all ill); 2=borderline mentally 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 CGI-S score indicate improvement. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here, 'N' (subjects analysed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to Week 6

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	50		
Units: Units on a scale				
arithmetic mean (standard deviation)	-1.9 (± 1.49)	-1.7 (± 1.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of JNJ-55308942

End point title	Plasma Concentrations of JNJ-55308942[1]

End point description:

Plasma concentrations of JNJ-55308942 were reported. Pharmacokinetics (PK) analysis set included all subjects who received at least 1 dose of JNJ-55308942 and had at least 1 valid blood sample drawn for PK analysis. Here, 'n' (number analysed) is defined as subjects analysed at specified categories. Data for this endpoint was not planned to be collected and analysed for placebo arm.

End point type	Secondary

End point timeframe:

Predose, 1.5 hours and 4 hours post-dose on Week 0 (Day 1), Weeks 1 (Day 8), 2 (Day 15), 4 (Day

29), and 6 (Day 43)

Notes:

[1] - 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: Descriptive statistics for this endpoint were planned to be analysed for specified arm only as the other arm was the placebo.

End point values	JNJ-55308942			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: Nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Week 0 (Day 1): Predose (n=51)	0.00 (± 0.000)			
Week 0 (Day 1): 1.5 hours postdose (n=53)	406.13 (± 162.407)			
Week 0 (Day 1): 4 hours postdose (n=49)	407.72 (± 133.461)			
Week 1 (Day 8): Predose (n=46)	531.20 (± 200.351)			
Week 1 (Day 8): 1.5 hours postdose (n=46)	868.01 (± 296.255)			
Week 1 (Day 8): 4 hours postdose (n=46)	892.54 (± 219.210)			
Week 2 (Day 15): Predose (n=44)	561.32 (± 194.184)			
Week 2 (Day 15): 1.5 hours postdose (n=44)	930.59 (± 265.581)			
Week 2 (Day 15): 4 hours postdose (n=44)	919.86 (± 213.028)			
Week 4 (Day 29): Predose (n=42)	528.90 (± 144.580)			
Week 4 (Day 29): 1.5 hours postdose (n=44)	885.50 (± 249.562)			
Week 4 (Day 29): 4 hours postdose (n=44)	872.80 (± 208.734)			
Week 6 (Day 43): Predose (n=41)	535.80 (± 160.568)			
Week 6 (Day 43): 1.5 hours postdose (n=39)	862.31 (± 240.540)			
Week 6 (Day 43): 4 hours postdose (n=41)	883.51 (± 209.413)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient Reported Outcomes Measurement Information System (PROMIS) Score - Ability to Participate in Social Roles and Activities (APS) T-Scores

End point title	Change from Baseline in Patient Reported Outcomes Measurement Information System (PROMIS) Score - Ability to Participate in Social Roles and Activities (APS) T-Scores

End point description:

Change from baseline in PROMIS score - ability to participate in social roles and activities T-Scores were reported. The PROMIS - APS item bank assesses the perceived ability to perform one’s usual social roles and activities. The item bank did not use a time frame (for example, over the past seven days) when

assessing the APS. The Short Form 4a included 4 items that represent this concept. Each question had 5 response options ranging in value from 1 to 5 with higher scores indicating better social function. Total raw score for short form was calculated by summing the values of the response to each question, so for the 4-item form, the lowest possible raw score was 4; the highest possible raw score was 20. The total raw score was converted to a T score with a mean of 50 and a standard deviation of 10. FAS was used. Here, 'n' (number analysed) is defined as subjects analysed at specified categories.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Weeks 1, 2, 3, 4, 5, and 6

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	59		
Units: t-score				
arithmetic mean (standard deviation)				
PROMIS-APS T-score: Week 1 (n=48, 57)	2.51 (± 5.682)	1.69 (± 6.859)		
PROMIS-APS T-score: Week 2 (n=45, 56)	5.33 (± 6.901)	4.49 (± 9.174)		
PROMIS-APS T-score: Week 3 (n=42, 52)	6.52 (± 8.226)	5.00 (± 8.884)		
PROMIS-APS T-score: Week 4 (n=43, 49)	9.12 (± 9.018)	6.07 (± 8.369)		
PROMIS-APS T-score: Week 5 (n=41, 47)	9.47 (± 8.248)	4.90 (± 9.296)		
PROMIS-APS T-score: Week 6 (n=42, 50)	10.50 (± 8.211)	6.12 (± 8.412)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Generalized Anxiety Disorder 7 (GAD-7) Total Score

End point title	Change from Baseline in Generalized Anxiety Disorder 7 (GAD-7) Total Score

End point description:

Change from baseline in GAD-7 total score were reported. GAD-7 is a brief and validated 7-item self-reported questionnaire for assessment of overall GAD. Subjects responded to each item using a 4-point scale with response categories of 0=not at all, 1=several days, 2=more than half the days, and 3=nearly every day, with a higher score representing a more severe condition. Item responses were summed to yield GAD-7 total score which ranged of 0 to 21, where higher scores indicated more anxiety. FAS included all randomised subjects who received at least 1 dose of study intervention and had both the baseline and at least 1 postbaseline MADRS measurement. Here, 'n' (number analysed) is defined as subjects analysed at specified categories.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Weeks 2, 4, and 6

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	59		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2 (n=45, 56)	-3.8 (± 5.08)	-4.2 (± 5.76)		
Week 4 (n=44, 50)	-5.0 (± 6.59)	-4.5 (± 5.14)		
Week 6 (n=42, 50)	-5.7 (± 6.21)	-5.7 (± 5.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient Health Questionnaire-9 (PHQ-9) Total Score

End point title	Change from Baseline in Patient Health Questionnaire-9 (PHQ-9) Total Score

End point description:

Change from baseline in PHQ-9 total score were reported. PHQ-9 is 9-item, self-report scale assessed depressive symptoms. Each item was rated on 4-point scale (0=Not at all, 1=several days, 2=more than half days, 3=nearly every day. The subject's item responses were summed to provide PHQ-9 total score (range of 0 to 27) with higher scores indicating greater severity of depressive symptoms. FAS included all randomised subjects who received at least 1 dose of study intervention and had both the baseline and at least 1 postbaseline MADRS measurement. Here, 'N' (subjects analysed) signifies number of subjects evaluable for this endpoint. Here, 'n' (number analysed) is defined as subjects analysed at specified categories.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Weeks 1, 2, 3, 4, 5, and 6

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	59		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 1 (n=48, 57)	-2.8 (± 4.24)	-3.1 (± 5.45)		
Week 2 (n=45, 56)	-5.2 (± 5.64)	-4.7 (± 6.63)		
Week 3 (n=41, 52)	-6.4 (± 6.25)	-5.1 (± 6.90)		
Week 4 (n=43, 49)	-7.0 (± 6.38)	-6.1 (± 6.81)		
Week 5 (n=41, 47)	-8.2 (± 6.59)	-5.2 (± 7.21)		
Week 6 (n=42, 50)	-9.0 (± 6.79)	-7.0 (± 7.41)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in MADRS Total Score up to Week 6 (Subgroup of Subjects with Messenger Ribonucleic Acid [mRNA] Transcript Levels)

End point title	Change from Baseline in MADRS Total Score up to Week 6 (Subgroup of Subjects with Messenger Ribonucleic Acid [mRNA] Transcript Levels)

End point description:

Subgroup included subjects with mRNA transcript levels (exceeded medium level for both P2RX7 and IL-1-beta). MADRS was clinician-rated scale designed to measure depression severity and detect changes due to AD treatment. MADRS evaluated reported sadness, apparent sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Scale consist 10 items, each was scored from 0 (item not present or normal) to 6 (severe or continuous presence of symptoms); higher score indicated more severe condition. MADRS total score was sum of scores from individual question items; ranged: 0-60; higher scores indicated more severe conditions. Negative change in MADRS total score indicated improvement. FAS was used. 99999 refer to mean and standard deviation (SD) were not calculable because planned analysis was terminated as reliable data could not be produced using single step polymerase chain reaction method.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to Week 6

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	59		
Units: Units on a scale				
arithmetic mean (standard deviation)	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in MADRS Total Score up to Week 6 (Concomitant Medication Subgroup Analysis)

End point title	Change from Baseline in MADRS Total Score up to Week 6 (Concomitant Medication Subgroup Analysis)

End point description:

Concomitant medication subgroup analysis included subjects with BD not taking any mood stabilizer or antipsychotic, taking a mood stabilizer alone, taking antipsychotic alone, and taking a combination of mood stabilizer and an antipsychotic. MADRS measures depression severity, detects changes due to AD treatment. It consists of 10 items (evaluate apparent sadness, reported sadness, inner tension, sleep, appetite, concentration, lassitude, interest level, pessimistic thoughts, suicidal thoughts), scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms), summed for a total possible score of 0 to 60. Higher scores indicate more severe conditions. Negative change in score indicates improvement. FAS was used for the analysis. 99999 refer to standard deviation not estimable for single subject and 99999 at n=0 signifies no subject was available for the analysis.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to Week 6

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	50		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Not taking mood stabilizer/antipsychotic(n=11,19)	-15.5 (± 13.18)	-16.2 (± 9.69)		
Taking a mood stabilizer alone (n=29,30)	-16.3 (± 9.82)	-15.6 (± 9.47)		
Taking an antipsychotic alone (n=1,1)	-13.0 (± 99999)	5.0 (± 99999)		
Combination: mood stabilizer+antipsychotic(n=1,0)	-13.0 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Achieved Response at Week 6

End point title	Number of Subjects Who Achieved Response at Week 6

End point description:

Number of subjects who achieved response at Week 6 were reported. Response was defined as greater than or equal to (>=)50% improvement in MADRS total score from baseline. MADRS was a clinician-rated scale designed to measure depression severity and detect changes due to AD treatment. The MADRS evaluated reported sadness, apparent sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. The scale consist of 10 items each of which was scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms),with higher score indicating a more severe condition. The MADRS total score was the sum of scores from individual question items and it ranged from 0 to 60, with higher scores indicated more severe conditions. Negative change in MADRS total score indicated improvement. FAS was used.

End point type	Secondary

End point timeframe:

Week 6

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	59		
Units: Subjects	27	31		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Achieved Remission at Week 6

End point title	Number of Subjects Who Achieved Remission at Week 6

End point description:

Number of subjects who achieved remission at Week 6 were reported. Remission was defined as MADRS total score <=12. MADRS was a clinician-rated scale designed to measure depression severity and detect changes due to AD treatment. The MADRS evaluated reported sadness, apparent sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. The scale consist of 10 items each of which was scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms),with higher score indicating a more severe condition. The MADRS total score was the sum of scores from individual question items and it ranged from 0 to 60, with higher scores indicated more severe conditions. Negative change in MADRS total score indicated improvement. FAS was used.

End point type	Secondary

End point timeframe:

Week 6

End point values	JNJ-55308942	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	59		
Units: Subjects	25	30		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality: From screening (-28 days) up to end of study (up to 12 weeks); SAEs and Other AEs: From Day 1 (Week 0) up to 30 days after the last dose (up to 11 weeks)

Adverse event reporting additional description:

All-cause mortality was analysed on all randomized subjects in the study. SAEs and Other AEs were analysed on safety analysis set that 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	Placebo

Reporting group description:

During DB treatment phase, subjects received placebo capsule (matching to JNJ-55308942), orally once daily from Day 1 (Week 0) up to 6 weeks. Subjects were then followed up for up to 2 weeks after their last dose (up to Day 56).

Reporting group title	JNJ-55308942

Reporting group description:

During double-blind (DB) treatment phase, subjects received JNJ-55308942 capsule, orally once daily from Day 1 (Week 0) up to 6 weeks. Subjects were then followed up for up to 2 weeks after their last dose (up to Day 56).

Serious adverse events	Placebo	JNJ-55308942	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 60 (5.00%)	2 / 54 (3.70%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Intentional Overdose			
subjects affected / exposed	1 / 60 (1.67%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Suicide Attempt			
subjects affected / exposed	0 / 60 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 60 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			
subjects affected / exposed	1 / 60 (1.67%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Behaviour Disorder			
subjects affected / exposed	1 / 60 (1.67%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	JNJ-55308942	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 60 (16.67%)	6 / 54 (11.11%)	
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 60 (6.67%)	3 / 54 (5.56%)	
occurrences (all)	4	4	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 60 (5.00%)	2 / 54 (3.70%)	
occurrences (all)	3	2	
Vomiting			
subjects affected / exposed	3 / 60 (5.00%)	1 / 54 (1.85%)	
occurrences (all)	3	1	
Nausea			

subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 5	4 / 54 (7.41%) 4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 February 2022	The rational for this amendment was to remove the safety, tolerability, and efficacy preview (STEP) interview, Patient-Reported Outcomes Measurement Information System (PROMIS) - social isolation and Patient and Global Impression of Severity for Depression(PGI-S), to add clarification on the antidepressant treatment history-short form (ATHF-SF), to replace the DARS with the Snaith-Hamilton Pleasure Scale (SHAPS), to replace the SMDDS with the Patient Health Questionnaire (PHQ-9), and the use of the AiCure application, to add the digital health assessment by the AiCure app, and to add the urine drug screen (UDS) to every visit.
04 July 2022	The rational for this amendment was to add clarifications on timing of self-rating assessments, downloading of apps, prohibited concomitant therapy. To add recommendations on order of events and when the second pharmacogenomics sample could be taken. To add Canada as a new country where TruCulture sampling would be performed, provided flexibility on the country list where TruCulture assay or determination of peripheral blood mononuclear cells (PBMCs) inflammatory profiles could be performed and to remove Russia where we were provisioning phones to all subjects.
27 July 2022	The rational for this amendment was to change the definition of a treatment-emergent adverse events (TEAE) on regulatory request.
25 January 2023	The rational for this amendment was to allow for operational efficiency the prescreening visit would be removed from the study and the prescreening assessment, a blood sample for P2RX7 genotyping, would be part of the screening phase.
18 August 2023	The rational for this amendment was Antipsychotics approved for bipolar depression (BD), however not effective for treating the current major depressive episode, whether taken alone or in combination with a mood stabilizer might be permitted. AiCure services for medication compliance and meal intake were discontinued and replaced with Q1.6 for medication reminders. Vendor names were removed from the body of the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported