Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of NBI-1065845 in Adult Subjects With Major Depressive Disorder (MDD)

Summary

EudraCT number	2021-003989-12
Trial protocol	CZ SK BG PL
Global end of trial date	21 February 2024

Results information

Result version number	v1 (current)
This version publication date	26 October 2025
First version publication date	26 October 2025

Trial information

Trial identification

Sponsor protocol code	NBI-1065845-MDD2024

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05203341
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Neurocrine Biosciences, Inc.
Sponsor organisation address	6027 Edgewood Bend Court, San Diego, United States, 92130
Public contact	Neurocrine Medical Information, Neurocrine Biosciences, Inc., +1 8776413461, medinfo@neurocrine.com
Scientific contact	Neurocrine Medical Information, Neurocrine Biosciences, Inc., +1 8776413461, medinfo@neurocrine.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	05 April 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 January 2024
Global end of trial reached?	Yes
Global end of trial date	21 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of NBI-1065845 compared with placebo in participants with MDD on improving symptoms of depression.

Protection of trial subjects:

The study was conducted in accordance with Good Clinical Practice (GCP), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) GCP guidelines, and the laws and regulations of the countries in which the study was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 December 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 83
Country: Number of subjects enrolled	Poland: 26
Country: Number of subjects enrolled	Slovakia: 14
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	Bulgaria: 24
Country: Number of subjects enrolled	Czechia: 28
Worldwide total number of subjects	183
EEA total number of subjects	100

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)	181
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were randomized 1:1:2 to receive NBI-1065845 as two different doses or placebo orally.

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, Monitor, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

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

Dosage and administration details:

Placebo tablets identical in appearance to the active product were administered in the same manner on an identical schedule as NBI-1065845

Arm title	NBI-1065845 1 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	NBI-1065845
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered once daily

Arm title	NBI-1065845 3 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	NBI-1065845
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered once daily

Number of subjects in period 1	Placebo	NBI-1065845 1 mg	NBI-1065845 3 mg
Started	91	45	47
Received at Least 1 Dose of Study Drug	91	45	47
Completed	79	42	43
Not completed	12	3	4
Physician decision	1	-	-
Consent withdrawn by subject	3	2	1
Adverse event, non-fatal	2	-	1
Not specified	3	-	-
Lost to follow-up	2	1	2
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	183	183	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	47.4		
standard deviation	± 12.4	-	
Gender categorical Units: Subjects			
Female	117	117	
Male	66	66	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	NBI-1065845 1 mg
Reporting group description: -	
Reporting group title	NBI-1065845 3 mg
Reporting group description: -	

Primary: Total Montgomery-Asberg Depression Rating Scale (MADRS) Score Least-Squares Mean Treatment Difference in Change from Baseline to Day 28

End point title	Total Montgomery-Asberg Depression Rating Scale (MADRS) Score Least-Squares Mean Treatment Difference in Change from Baseline to Day 28

End point description:

The least squares mean difference in change from baseline in the total MADRS score at Day 28 between each dose of NBI-1065845 and placebo are presented. A decrease in MADRS score indicated a decrease in the severity of depressive symptoms.
Full analysis set included all randomized participants.

End point type	Primary

End point timeframe:

Baseline to Day 28

End point values	Placebo	NBI-1065845 1 mg	NBI-1065845 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91[1]	45	47	
Units: units on a scale				
least squares mean (confidence interval 95%)	9999 (9999 to 9999)	-4.3 (-7.8 to -0.8)	-3.0 (-6.4 to 0.4)	

Notes:

[1] - No values are expected for LS mean difference for placebo arm (indicated as 9999).

Statistical analyses

Statistical analysis title	NBI-1065845 1 mg

Statistical analysis description:

NBI-1065845 1 mg - Placebo

Comparison groups	Placebo v NBI-1065845 1 mg
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0159
Method	ANCOVA

Statistical analysis title	NBI-1065845 3 mg
Statistical analysis description: NBI-1065845 3 mg - Placebo	
Comparison groups	Placebo v NBI-1065845 3 mg
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0873
Method	ANCOVA

Secondary: Total MADRS Score Least-Squares Mean Treatment Difference in Change from Baseline to Day 56

End point title	Total MADRS Score Least-Squares Mean Treatment Difference in Change from Baseline to Day 56
End point description: The least squares mean difference in change from baseline in the total MADRS score at Day 56 between each dose of NBI-1065845 and placebo are presented. A decrease in MADRS score indicated a decrease in the severity of depressive symptoms. Full analysis set included all randomized participants.	
End point type	Secondary
End point timeframe: Baseline to Day 56	

End point values	Placebo	NBI-1065845 1 mg	NBI-1065845 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79[2]	39	40	
Units: units on a scale				
least squares mean (confidence interval 95%)	9999 (9999 to 9999)	-7.5 (-12.1 to -2.9)	-3.6 (-8.0 to 0.8)	

Notes:

[2] - No values are expected for LS mean difference for placebo arm (indicated as 9999).

Statistical analyses

Statistical analysis title	NBI-1065845 1 mg
Statistical analysis description: NBI-1065845 1 mg - Placebo	
Comparison groups	Placebo v NBI-1065845 1 mg

Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0016
Method	ANCOVA

Statistical analysis title	NBI-1065845 3 mg
Statistical analysis description: NBI-1065845 3 mg - Placebo	
Comparison groups	Placebo v NBI-1065845 3 mg
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1082
Method	ANCOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline through Day 70	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0
Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	NBI-1065845 1 mg
Reporting group description: -	
Reporting group title	NBI-1065845 3 mg
Reporting group description: -	

Serious adverse events	Placebo	NBI-1065845 1 mg	NBI-1065845 3 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 91 (0.00%)	0 / 45 (0.00%)	0 / 47 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Placebo	NBI-1065845 1 mg	NBI-1065845 3 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 91 (23.08%)	9 / 45 (20.00%)	8 / 47 (17.02%)
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 91 (8.79%)	5 / 45 (11.11%)	2 / 47 (4.26%)
occurrences (all)	8	8	5
Somnolence			
subjects affected / exposed	3 / 91 (3.30%)	3 / 45 (6.67%)	0 / 47 (0.00%)
occurrences (all)	3	3	0
Dizziness			
subjects affected / exposed	5 / 91 (5.49%)	0 / 45 (0.00%)	0 / 47 (0.00%)
occurrences (all)	5	0	0

Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	5 / 91 (5.49%) 5	1 / 45 (2.22%) 2	0 / 47 (0.00%) 0
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	2 / 91 (2.20%) 2	1 / 45 (2.22%) 1	3 / 47 (6.38%) 3
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	5 / 91 (5.49%) 6	2 / 45 (4.44%) 2	3 / 47 (6.38%) 3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 July 2021	Global amendment 1.0
24 September 2021	Global amendment 2.0
09 June 2022	Global amendment 3.0
19 November 2022	Global amendment 4.0

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported