



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