



Clinical trial results:

A Phase 2b, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy, Safety, and Tolerability of MIN-101 in Patients With Negative Symptoms of Schizophrenia, Followed by a 24-Week, Open-Label Extension.

Summary

EudraCT number	2014-004878-42
Trial protocol	LV EE RO BG
Global end of trial date	02 September 2016

Results information

Result version number	v1 (current)
This version publication date	27 September 2018
First version publication date	27 September 2018

Trial information

Trial identification

Sponsor protocol code	MIN-101C03
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Minerva Neurosciences, Inc.
Sponsor organisation address	1601 Trapelo Road, Suite 286, Waltham, United States, 02451
Public contact	Joseph Reilly, Minerva Neurosciences, Inc., 1 6176007380, jreilly@minervaneurosciences.com
Scientific contact	Jay Saoud, Minerva Neurosciences, Inc., 1 6176007375, jsaoud@minervaneurosciences.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	20 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 September 2016
Global end of trial reached?	Yes
Global end of trial date	02 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of MIN-101 compared to placebo in improving the negative symptoms of schizophrenia as measured by the change from Baseline in the Positive and Negative Syndrome Scale (PANSS) negative subscale score of the pentagonal model over 12 weeks of treatment.

Protection of trial subjects:

Prior to initiation of the study, the study protocol and associated documentation were reviewed and approved by an Independent Ethics Committee (IEC). This study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practices (GCP) and applicable regulatory requirements. Subjects or their legally acceptable representatives provided their written consent to participate in the study after having been informed about the nature and purpose of the study, participation/termination conditions, and risks and benefits of treatment.

Personal data from subjects enrolled in this study was limited to those data necessary to investigate the efficacy, safety, quality, and utility of the investigational study agent(s) used in this study, and were collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data privacy protection laws and regulations. Moreover, safety evaluations were performed during the study to ensure patient safety.

Background therapy:

The most commonly taken concomitant medications (by >4% of subjects) were the benzodiazepines lorazepam (11 subjects, 4.5%) and phenazepam (10 subjects, 4.1%); both were used as rescue medications allowed by the study protocol.

Evidence for comparator: -

Actual start date of recruitment	02 March 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Romania: 56
Country: Number of subjects enrolled	Bulgaria: 37
Country: Number of subjects enrolled	Estonia: 1
Country: Number of subjects enrolled	Latvia: 11
Country: Number of subjects enrolled	Russian Federation: 36
Country: Number of subjects enrolled	Ukraine: 103
Worldwide total number of subjects	244
EEA total number of subjects	105

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)	244
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Enrolled subjects were recruited for this study at 44 study centers in 6 countries (Bulgaria, Estonia, Latvia, Romania, Russia, and Ukraine).

Pre-assignment

Screening details:

Subjects were screened for eligibility to participate in the study within 28 days before dosing.

Pre-assignment period milestones

Number of subjects started	342 ^[1]
Number of subjects completed	244

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Adverse event, non-fatal: 1
Reason: Number of subjects	Consent withdrawn by subject: 6
Reason: Number of subjects	Physician decision: 2
Reason: Number of subjects	Lost to follow-up: 1
Reason: Number of subjects	Screening failure: 82
Reason: Number of subjects	Subject moved out of area: 1
Reason: Number of subjects	Other: 5

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The number of subjects reported to have started the pre-assignment period include screened subjects (N=342); however, the worldwide number only includes the number of subjects enrolled (i.e., randomized) (N=244).

Period 1

Period 1 title	12-Week Double-Blind Study Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

Study drug was packaged using a double-dummy, double-blind design.

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:

Administered in a single dose in the morning at approximately the same time each day, in fasting condition, and 2 hours before a light breakfast. Tablets were to be swallowed whole with water and not

divided, crushed, chewed, or placed in water.

Arm title	MIN-101 32 mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MIN-101
Investigational medicinal product code	MIN-101
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The daily dose consisted of 2 tablets identically matched in appearance (one MIN-101 32 mg tablet and one Placebo tablet). The study drug was to be administered in a single dose in the morning at approximately the same time each day, in fasting condition, and 2 hours before a light breakfast. Tablets were to be swallowed whole with water and not divided, crushed, chewed, or placed in water.

Arm title	MIN-101 64 mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MIN-101
Investigational medicinal product code	MIN-101
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The daily dose consisted of 2 tablets (two MIN-101 32 mg tablets). The study drug was to be administered in a single dose in the morning at approximately the same time each day, in fasting condition, and 2 hours before a light breakfast. Tablets were to be swallowed whole with water and not divided, crushed, chewed, or placed in water.

Number of subjects in period 1	Placebo	MIN-101 32 mg	MIN-101 64 mg
Started	83	78	83
Completed	44	45	53
Not completed	39	33	30
Consent withdrawn by subject	13	12	5
Other	1	1	1
Subject moved out of area	-	2	-
Unsatisfactory treatment response	17	11	11
Adverse event	3	3	8
Non-compliance with study medication	1	-	-
Lost to follow-up	1	2	1
Protocol deviation	3	2	4

Period 2

Period 2 title	Whole Study Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

Whole study period includes 12 week randomized double-blind phase and 24-week open-label phase.

Arms

Are arms mutually exclusive?	Yes
Arm title	MIN-101 32 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	MIN-101
Investigational medicinal product code	MIN-101
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The daily dose consisted of 2 tablets identically matched in appearance (one MIN-101 32 mg tablet and one Placebo tablet). The study drug was to be administered in a single dose in the morning at approximately the same time each day, in fasting condition, and 2 hours before a light breakfast. Tablets were to be swallowed whole with water and not divided, crushed, chewed, or placed in water.

Investigational medicinal product name	MIN-101
Investigational medicinal product code	MIN-101
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The daily dose consisted of 2 tablets identically matched in appearance (one MIN-101 32 mg tablet and one Placebo tablet). The study drug was to be administered in a single dose in the morning at approximately the same time each day, in fasting condition, and 2 hours before a light breakfast. Tablets were to be swallowed whole with water and not divided, crushed, chewed, or placed in water.

Arm title	MIN-101 64 mg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	MIN-101
Investigational medicinal product code	MIN-101
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The daily dose consisted of 2 tablets (two MIN-101 32 mg tablets). The study drug was to be administered in a single dose in the morning at approximately the same time each day, in fasting condition, and 2 hours before a light breakfast. Tablets were to be swallowed whole with water and not divided, crushed, chewed, or placed in water.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered in a single dose in the morning at approximately the same time each day, in fasting condition, and 2 hours before a light breakfast. Tablets were to be swallowed whole with water and not divided, crushed, chewed, or placed in water.

Investigational medicinal product name	MIN-101
Investigational medicinal product code	MIN-101
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The daily dose consisted of 2 tablets (two MIN-101 32 mg tablets). The study drug was to be administered in a single dose in the morning at approximately the same time each day, in fasting condition, and 2 hours before a light breakfast. Tablets were to be swallowed whole with water and not divided, crushed, chewed, or placed in water.

Arm title	Placebo to MIN-101
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MIN-101
Investigational medicinal product code	MIN-101
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The daily dose consisted of 2 tablets identically matched in appearance (one MIN-101 32 mg tablet and one Placebo tablet). The study drug was to be administered in a single dose in the morning at approximately the same time each day, in fasting condition, and 2 hours before a light breakfast. Tablets were to be swallowed whole with water and not divided, crushed, chewed, or placed in water.

Investigational medicinal product name	MIN-101
Investigational medicinal product code	MIN-101
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The daily dose consisted of 2 tablets (two MIN-101 32 mg tablets). The study drug was to be administered in a single dose in the morning at approximately the same time each day, in fasting condition, and 2 hours before a light breakfast. Tablets were to be swallowed whole with water and not divided, crushed, chewed, or placed in water.

Number of subjects in period 2	MIN-101 32 mg	MIN-101 64 mg	Placebo to MIN-101
Started	45	53	44
Completed	28	32	28
Not completed	17	21	16
Consent withdrawn by subject	9	9	6
Adverse event, non-fatal	2	2	2
Unsatisfactory treatment response	4	5	5
Noncompliance with study drug	-	-	1
Lost to follow-up	1	4	2

Protocol deviation	1	1	-
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Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	MIN-101 32 mg
Reporting group description: -	
Reporting group title	MIN-101 64 mg
Reporting group description: -	

Reporting group values	Placebo	MIN-101 32 mg	MIN-101 64 mg
Number of subjects	83	78	83
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	83	78	83
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	40	39.8	40.6
standard deviation	± 10.2	± 10.2	± 10.6
Gender categorical			
Units: Subjects			
Female	35	37	35
Male	48	41	48
Race			
Units: Subjects			
Caucasian	83	78	83
Height			
Height measured only at Screening Visit.			
Units: cm			
arithmetic mean	172.5	170.9	171.5
standard deviation	± 8.6	± 9.7	± 8.2
Weight			
Subjects were weighed clothed (lightly) and without shoes.			
Units: kg			
arithmetic mean	77.42	74.16	75.25
standard deviation	± 14.21	± 16.60	± 13.70
BMI			
The BMI was calculated and presented using the following formula: BMI = (weight in kg/height in m2).			
Units: kg/m2			

arithmetic mean	26.0389	25.2967	25.5814
standard deviation	± 4.4749	± 4.4992	± 4.3349

Reporting group values	Total		
Number of subjects	244		
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)	244		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	107		
Male	137		
Race			
Units: Subjects			
Caucasian	244		
Height			
Height measured only at Screening Visit.			
Units: cm			
arithmetic mean			
standard deviation	-		
Weight			
Subjects were weighed clothed (lightly) and without shoes.			
Units: kg			
arithmetic mean			
standard deviation	-		
BMI			
The BMI was calculated and presented using the following formula: BMI = (weight in kg/height in m2).			
Units: kg/m2			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	MIN-101 32 mg
Reporting group description: -	
Reporting group title	MIN-101 64 mg
Reporting group description: -	
Reporting group title	MIN-101 32 mg
Reporting group description: -	
Reporting group title	MIN-101 64 mg
Reporting group description: -	
Reporting group title	Placebo to MIN-101
Reporting group description: -	

Primary: Change from Baseline to Week 12 in PANSS Negative Symptoms Subscale (Pentagonal Structure Model)

End point title	Change from Baseline to Week 12 in PANSS Negative Symptoms Subscale (Pentagonal Structure Model)
End point description: Change from Baseline to Week 12 in PANSS negative subscale score of the pentagonal structure model using mixed model repeated measures (MMRM) analysis, intent-to-treat population.	
End point type	Primary
End point timeframe: Positive and Negative Syndrome Scale (PANSS) negative subscale score of the pentagonal structure model assessment data were collected at Screening, Baseline, Weeks 2, 4, 8, and 12.	

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	-1.53 (± 0.47)	-3.07 (± 0.49)	-3.50 (± 0.48)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in PANSS
Statistical analysis description: MMRM with treatment (placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subject nested in treatment as a random effect with Baseline value as covariate. An unstructured covariance matrix was used.	
Comparison groups	MIN-101 32 mg v MIN-101 64 mg v Placebo

Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.024 ^[1]
Method	Mixed models analysis

Notes:

[1] - MIN-101 32 mg vs Placebo: $p \leq 0.0240$

MIN-101 64 mg vs Placebo: $p \leq 0.0036$

Secondary: Change from Baseline to Week 12 in CGI-S

End point title	Change from Baseline to Week 12 in CGI-S
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End point description:

Change from Baseline to Week 12 in Clinical Global Impression - Severity Scale Score (CGI-S), intent-to-treat (ITT) population. Least-squares mean are from an analysis of covariance (ANCOVA) of ranked data with treatment (Placebo, MIN-101 32 mg, MIN-101 64 mg) as a factor, and Baseline value as covariate.

End point type	Secondary
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End point timeframe:

Clinical Global Impression - Severity (CGI-S) assessment data were collected at Screening, Baseline, Weeks 4, 8, and 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	152.38 (\pm 8.81)	131.32 (\pm 9.08)	123.87 (\pm 8.81)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in CGI-S
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Statistical analysis description:

Change from Baseline to Week 12 in Clinical Global Impression - Severity (CGI-S) Score using analysis of covariance (ANCOVA) of ranked data, with treatment (Placebo, MIN-101 32 mg, MIN-101 64 mg), as a factor and Baseline value as covariate.

Comparison groups	Placebo v MIN-101 32 mg v MIN-101 64 mg
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.0982 ^[2]
Method	ANCOVA

Notes:

[2] - MIN-101 32 mg vs Placebo: $p \leq 0.0982$

MIN-101 64 mg vs Placebo: $p \leq 0.0234$

Secondary: Clinical Global Impression - Global Improvement Scale Scores

End point title	Clinical Global Impression - Global Improvement Scale Scores
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End point description:

Change in Clinical Global Impression - Improvement Scale Score (CGI-I) with CGI-S as Baseline value,

intent-to-treat (ITT) population. Least-squares mean are from an analysis of covariance (ANCOVA) of ranked data with treatment (Placebo, MIN-101 32 mg, MIN-101 64 mg) as a factor, and Baseline value as covariate.

End point type	Secondary
End point timeframe:	
Clinical Global Impression - Global Improvement assessment data were collected at Weeks 4, 8, and 12.	

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	155.19 (\pm 9.50)	139.02 (\pm 9.79)	115.02 (\pm 9.50)	

Statistical analyses

Statistical analysis title	Clinical Global Impression - Improvement Scores
Statistical analysis description:	
Clinical Global Impression - Improvement Scores using analysis of covariance (ANCOVA) of ranked data, with treatment (Placebo, MIN-101 32 mg, MIN-101 64 mg), as a factor and Baseline value as covariate.	
Comparison groups	Placebo v MIN-101 32 mg v MIN-101 64 mg
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.2378 ^[3]
Method	ANCOVA

Notes:

[3] - MIN-101 32 mg vs Placebo: $p \leq 0.2378$

MIN-101 64 mg vs Placebo: $p \leq 0.0032$

Secondary: Change from Baseline to Week 12 in BACS Total Verbal Fluency Score

End point title	Change from Baseline to Week 12 in BACS Total Verbal Fluency Score
End point description:	
Change from Baseline to Week 12 BACS using mixed model repeated measures (MMRM) analysis, intent-to-treat population.	
End point type	Secondary
End point timeframe:	
Brief Assessment of Cognition in Schizophrenia (BACS) assessment data were collected at Baseline, Week 4, and Week 12.	

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	78	83	
Units: NA				
least squares mean (standard error)	0.98 (± 1.27)	5.76 (± 1.29)	4.37 (± 1.29)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in BACS Total
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Statistical analysis description:

MMRM with treatment (placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subject nested in treatment as a random effect with Baseline value as covariate. An unstructured covariance matrix was used.

Comparison groups	Placebo v MIN-101 32 mg v MIN-101 64 mg
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.292 ^[4]
Method	Mixed models analysis

Notes:

[4] - MIN-101 32 mg vs Placebo: $p \leq 0.292$

MIN-101 64 mg vs Placebo: $p \leq 0.5446$

Secondary: Change from Baseline to Week 12 in PANSS Total Score

End point title	Change from Baseline to Week 12 in PANSS Total Score
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End point description:

Change from Baseline to Week 12 in PANSS total score analysis using model from mixed-model repeated measures (MMRM) analysis, ITT population.

End point type	Secondary
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End point timeframe:

Positive and Negative Syndrome Scale (PANSS) total score assessment data were collected at Screening, Baseline, Weeks 2, 4, 8, and 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	-0.56 (± 1.25)	-3.66 (± 1.28)	-5.83 (± 1.26)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in PANSS Total
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Statistical analysis description:

MMRM with treatment (placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subject nested in treatment as a random effect

with Baseline value as covariate. An unstructured covariance matrix was used.

Comparison groups	Placebo v MIN-101 32 mg v MIN-101 64 mg
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.0819 ^[5]
Method	Mixed models analysis

Notes:

[5] - MIN-101 32 mg vs Placebo: $p \leq 0.0819$

MIN-101 64 mg vs Placebo: $p \leq 0.0031$

Secondary: Change from Baseline to Week 12 in PANSS General Psychopathology Subscore

End point title	Change from Baseline to Week 12 in PANSS General Psychopathology Subscore
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End point description:

Change from Baseline in Positive and Negative Syndrome Scale (PANSS) General Psychopathology Scale Total Score of the 3 factors analysis using mixed model repeated measures (MMRM), intent-to-treat population.

End point type	Secondary
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End point timeframe:

Positive and Negative Syndrome Scale (PANSS) General Psychopathology Scale Total Score assessment data were collected at Screening, Baseline, Weeks 2, 4, 8, and 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	-0.05 (± 0.61)	-1.07 (± 0.62)	-2.58 (± 0.62)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in PANSS GP Score
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Statistical analysis description:

MMRM with treatment (placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subject nested in treatment as a random effect with Baseline value as covariate. An unstructured covariance matrix was used.

Comparison groups	Placebo v MIN-101 32 mg v MIN-101 64 mg
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.2359 ^[6]
Method	Mixed models analysis

Notes:

[6] - MIN-101 32 mg vs Placebo: $p \leq 0.2359$

MIN-101 64 mg vs Placebo: $p \leq 0.0034$

Secondary: Change from Baseline to Week 12 in PANSS Negative Scale Total Score

End point title	Change from Baseline to Week 12 in PANSS Negative Scale
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	Total Score
End point description:	
Change from Baseline in Positive and Negative Syndrome Scale (PANSS) Negative Scale Total Score of the 3 factor analysis using mixed model repeated measures (MMRM), intent-to-treat population.	
End point type	Secondary
End point timeframe:	
Positive and Negative Syndrome Scale (PANSS) Negative Scale Total Score assessment data were collected at Screening, Baseline, Weeks 2, 4, 8, and 12.	

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	-1.71 (± 0.41)	-3.35 (± 0.43)	-3.82 (± 0.42)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in PANSS NS Score
Statistical analysis description:	
MMRM with treatment (placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subject nested in treatment as a random effect with Baseline value as covariate. An unstructured covariance matrix was used.	
Comparison groups	Placebo v MIN-101 32 mg v MIN-101 64 mg
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.0064 ^[7]
Method	Mixed models analysis

Notes:

[7] - MIN-101 32 mg vs Placebo: $p \leq 0.0064$
MIN-101 64 mg vs Placebo: $p \leq 0.0004$

Secondary: Change from Baseline to Week 12 in PANSS Positive Scale Total Score

End point title	Change from Baseline to Week 12 in PANSS Positive Scale Total Score
End point description:	
Change from Baseline in Positive and Negative Syndrome Scale (PANSS) Positive Scale Total Score of the 3 factors analysis using mixed model repeated measures (MMRM), intent-to-treat population.	
End point type	Secondary
End point timeframe:	
Positive and Negative Syndrome Scale (PANSS) Positive Scale Total Score assessment data were collected at Screening, Baseline, Weeks 2, 4, 8 and 12.	

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	0.99 (± 0.44)	0.46 (± 0.45)	0.36 (± 0.44)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in PANSS PS Score
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Statistical analysis description:

MMRM with treatment (placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subject nested in treatment as a random effect with Baseline value as covariate. An unstructured covariance matrix was used.

Comparison groups	Placebo v MIN-101 32 mg v MIN-101 64 mg
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.4018 ^[8]
Method	Mixed models analysis

Notes:

[8] - MIN-101 32 mg vs Placebo: $p \leq 0.4018$

MIN-101 64 mg vs Placebo: $p \leq 0.3067$

Secondary: Change from Baseline to Week 12 in PANSS Positive Factor

End point title	Change from Baseline to Week 12 in PANSS Positive Factor
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End point description:

Change from Baseline in PANSS Positive Factor of the pentagonal model using mixed model repeated measures (MMRM) analysis, intent-to-treat population.

End point type	Secondary
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End point timeframe:

Positive and Negative Syndrome Scale (PANSS) Positive Factor assessment data were collected at Screening, Baseline, Weeks 2, 4, 8, and 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	0.29 (± 0.31)	0.58 (± 0.32)	-0.25 (± 0.31)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in PANSS PF Score
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Statistical analysis description:

MMRM with treatment (placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subject nested in treatment as a random effect

with Baseline value as covariate. An unstructured covariance matrix was used.

Comparison groups	MIN-101 32 mg v MIN-101 64 mg v Placebo
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.5045 [9]
Method	Mixed models analysis

Notes:

[9] - MIN-101 32 mg vs Placebo: $p \leq 0.5045$

MIN-101 64 mg vs Placebo: $p \leq 0.2146$

Secondary: Change from Baseline to Week 12 in PANSS Activation Factor

End point title	Change from Baseline to Week 12 in PANSS Activation Factor
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End point description:

Change from Baseline in Positive and Negative Syndrome Scale (PANSS) Activation Score of the pentagonal model using mixed model repeated measures (MMRM), intent-to-treat population.

End point type	Secondary
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End point timeframe:

Positive and Negative Syndrome Scale (PANSS) Activation Factor assesment data were collected at Screening, Baseline, Weeks 2, 4, 8, and 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	1.09 (± 0.35)	-0.05 (± 0.36)	-0.17 (± 0.36)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in PANSS AF Score
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Statistical analysis description:

MMRM with treatment (placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subject nested in treatment as a random effect with Baseline value as covariate. An unstructured covariance matrix was used.

Comparison groups	Placebo v MIN-101 32 mg v MIN-101 64 mg
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.024 [10]
Method	Mixed models analysis

Notes:

[10] - MIN-101 32 mg vs Placebo: $p \leq 0.0240$

MIN-101 64 mg vs Placebo: $p \leq 0.0118$

Secondary: Change from Baseline in PANSS Dysphoric Mood Factor

End point title	Change from Baseline in PANSS Dysphoric Mood Factor
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End point description:

Change from Baseline in Positive and Negative Syndrome Scale (PANSS) Dysphoric Mood Factor of the

pentagonal model using mixed model repeated measures (MMRM), intent-to-treat population.

End point type	Secondary
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End point timeframe:

Positive and Negative Syndrome Scale (PANSS) Dysphoric Mood Factor assessment data were collected at Screening, Baseline, Weeks 2, 4, 8, and 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	-0.07 (\pm 0.31)	-0.32 (\pm 0.32)	-1.04 (\pm 0.32)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in PANSS DM Score
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Statistical analysis description:

MMRM with treatment (placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subject nested in treatment as a random effect with Baseline value as covariate. An unstructured covariance matrix was used.

Comparison groups	Placebo v MIN-101 32 mg v MIN-101 64 mg
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.5644 ^[11]
Method	Mixed models analysis

Notes:

[11] - MIN-101 32 mg vs Placebo: $p \leq 0.5644$

MIN-101 64 mg vs Placebo: $p \leq 0.0266$

Secondary: Change from Baseline to Week 12 in PANSS Autistic Preoccupation Factor

End point title	Change from Baseline to Week 12 in PANSS Autistic Preoccupation Factor
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End point description:

Change from Baseline in Positive and Negative Syndrome Scale (PANSS) Autistic Preoccupation Factor of the pentagonal model using mixed model repeated measures (MMRM), intent-to-treat population.

End point type	Secondary
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End point timeframe:

Positive and Negative Syndrome Scale (PANSS) Autistic Preoccupation Factor assessment data were collected at Screening, Baseline, Weeks 2, 4, 8, and 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	-0.65 (± 0.34)	-0.85 (± 0.35)	-1.21 (± 0.34)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in PANSS AP Score
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Statistical analysis description:

MMRM with treatment (placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subject nested in treatment as a random effect with Baseline value as covariate. An unstructured covariance matrix was used.

Comparison groups	Placebo v MIN-101 32 mg v MIN-101 64 mg
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.67 ^[12]
Method	Mixed models analysis

Notes:

[12] - MIN-101 32 mg vs Placebo: $p \leq 0.6700$

MIN-101 64 mg vs Placebo: $p \leq 0.2408$

Secondary: Change from Baseline to Week 12 in BNSS Total Score

End point title	Change from Baseline to Week 12 in BNSS Total Score
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End point description:

Change from Baseline in Brief Negative Symptom Scale (BNSS) Total Score using mixed model repeated measures (MMRM) analysis, intent-to-treat population.

End point type	Secondary
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End point timeframe:

Brief Negative Symptom Scale (BNSS) Total Score assessment data were collected at Baseline, Weeks 2, 4, 8, and 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	-3.23 (± 0.90)	-5.44 (± 0.93)	-6.94 (± 0.92)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in BNSS Total
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Statistical analysis description:

MMRM with treatment (placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subject nested in treatment as a random effect

with Baseline value as covariate. An unstructured covariance matrix was used.

Comparison groups	Placebo v MIN-101 32 mg v MIN-101 64 mg
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.0869 ^[13]
Method	Mixed models analysis

Notes:

[13] - MIN-101 32 mg vs Placebo: $p \leq 0.0869$

MIN-101 64 mg vs Placebo: $p \leq 0.0040$

Other pre-specified: Change from Baseline to Week 12 in PSP Total Score

End point title	Change from Baseline to Week 12 in PSP Total Score
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End point description:

Change from Baseline in Personal and Social Performance (PSP) Total Score using mixed model repeated measures (MMRM), intent-to-treat population.

End point type	Other pre-specified
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End point timeframe:

Personal and Social Performance (PSP) Total Score assessment data were collected at Baseline, and Weeks 4 and 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	-0.67 (± 0.27)	-1.16 (± 0.28)	-1.89 (± 0.28)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in PSP Total Score
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Statistical analysis description:

MMRM with treatment (placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subject nested in treatment as a random effect with Baseline value as covariate. An unstructured covariance matrix was used.

Comparison groups	Placebo v MIN-101 32 mg v MIN-101 64 mg
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.201 ^[14]
Method	Mixed models analysis

Notes:

[14] - MIN-101 32 mg vs Placebo: $p \leq 0.2010$

MIN-101 64 mg vs Placebo: $p \leq 0.0016$

Other pre-specified: Change from Baseline to Week 12 in Sheehan-STS Total Score

End point title	Change from Baseline to Week 12 in Sheehan-STS Total Score
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End point description:

The SSTS was adapted from the Suicidality Module of the MINI Structured Diagnostic Interview for DMS-IV. SSTS is an 8-item scale that can be administered by the clinician or the subject through self-report. Each item was scored on a 5-point Likert scale (0=not at all, 1=a little, 2=moderately, 3=very, and 4=extremely). Data from SSTS was analyzed as individual item scores, suicidal ideation subscale score (sum of scores from items 2, 3, and 4, plus score from item 5 if ≤ 1), suicidal behavior subscale score (sum of scores from items 6, 7a, and 8, plus score from item 5 if > 1), and total score. On the basis of data collected using SSTS, potential suicide-related events were categorized by the investigator.

End point type	Other pre-specified
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End point timeframe:

Sheehan Suicidality Tracking Scale (SSTS) scores were collected at Screening, Baseline, Day 2, and Weeks 2, 4, 8, 12, 12 \pm 1-2 days, 14, 18, 24, 30, 36, and 37. SSTS scores are presented here for Week 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	54	
Units: NA				
arithmetic mean (standard error)	-0.1 (\pm 0.1)	0.0 (\pm 0.0)	0.0 (\pm 0.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline to Week 12 in AIMS Score - Upper Extremities

End point title	Change from Baseline to Week 12 in AIMS Score - Upper Extremities
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End point description:

The AIMS was used as a safety assessment in this study to detect involuntary movements as potential adverse effects. Items were scored on a 5-point scale (0=none, 1=minimal, may be extreme normal, 2=mild, 3=moderate, 4=severe).

End point type	Other pre-specified
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End point timeframe:

Abnormal Involuntary Movement Scale (AIMS) scores were collected at Screening, Baseline, and Weeks 4, 8, 12, 18, 24, 30, 36, and 37. AIMS scores are presented here for Week 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	54	
Units: NA				
arithmetic mean (standard error)	0.1 (\pm 0.0)	-0.1 (\pm 0.0)	0.0 (\pm 0.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline to Week 12 in AIMS Score - Lower Extremities

End point title	Change from Baseline to Week 12 in AIMS Score - Lower Extremities
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End point description:

The AIMS was used as a safety assessment in this study to detect involuntary movements as potential adverse effects. Items were scored on a 5-point scale (0=none, 1=minimal, may be extreme normal, 2=mild, 3=moderate, 4=severe).

End point type	Other pre-specified
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End point timeframe:

Abnormal Involuntary Movement Scale (AIMS) scores were collected at Screening, Baseline, and Weeks 4, 8, 12, 18, 24, 30, 36, and 37. AIMS scores are presented here for Week 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	54	
Units: NA				
arithmetic mean (standard error)	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline to Week 12 in AIMS Score - Muscles of Facial Expression

End point title	Change from Baseline to Week 12 in AIMS Score - Muscles of Facial Expression
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End point description:

The AIMS was used as a safety assessment in this study to detect involuntary movements as potential adverse effects. Items were scored on a 5-point scale (0=none, 1=minimal, may be extreme normal, 2=mild, 3=moderate, 4=severe).

End point type	Other pre-specified
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End point timeframe:

Abnormal Involuntary Movement Scale (AIMS) scores were collected at Screening, Baseline, and Weeks 4, 8, 12, 18, 24, 30, 36, and 37. AIMS scores are presented here for Week 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	54	
Units: NA				
arithmetic mean (standard error)	0.0 (± 0.0)	-0.1 (± 0.0)	-0.1 (± 0.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline to Week 12 in AIMS Score - Lips and Perioral Area

End point title	Change from Baseline to Week 12 in AIMS Score - Lips and Perioral Area
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End point description:

The AIMS was used as a safety assessment in this study to detect involuntary movements as potential adverse effects. Items were scored on a 5-point scale (0=none, 1=minimal, may be extreme normal, 2=mild, 3=moderate, 4=severe).

End point type	Other pre-specified
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End point timeframe:

Abnormal Involuntary Movement Scale (AIMS) scores were collected at Screening, Baseline, and Weeks 4, 8, 12, 18, 24, 30, 36, and 37. AIMS scores are presented here for Week 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	54	
Units: NA				
arithmetic mean (standard error)	0.0 (± 0.0)	-0.1 (± 0.1)	0.0 (± 0.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline to Week 12 in AIMS Score - Jaw

End point title	Change from Baseline to Week 12 in AIMS Score - Jaw
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End point description:

The AIMS was used as a safety assessment in this study to detect involuntary movements as potential adverse effects. Items were scored on a 5-point scale (0=none, 1=minimal, may be extreme normal, 2=mild, 3=moderate, 4=severe).

End point type	Other pre-specified
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End point timeframe:

Abnormal Involuntary Movement Scale (AIMS) scores were collected at Screening, Baseline, and Weeks 4, 8, 12, 18, 24, 30, 36, and 37. AIMS scores are presented here for Week 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	54	
Units: NA				
arithmetic mean (standard error)	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline to Week 12 in AIMS Score - Tongue

End point title	Change from Baseline to Week 12 in AIMS Score - Tongue
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End point description:

The AIMS was used as a safety assessment in this study to detect involuntary movements as potential adverse effects. Items were scored on a 5-point scale (0=none, 1=minimal, may be extreme normal, 2=mild, 3=moderate, 4=severe).

End point type	Other pre-specified
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End point timeframe:

Abnormal Involuntary Movement Scale (AIMS) scores were collected at Screening, Baseline, and Weeks 4, 8, 12, 18, 24, 30, 36, and 37. AIMS scores are presented here for Week 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	54	
Units: NA				
arithmetic mean (standard error)	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline to Week 12 in AIMS Score - Severity of Abnormal Movements

End point title	Change from Baseline to Week 12 in AIMS Score - Severity of Abnormal Movements
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End point description:

The AIMS was used as a safety assessment in this study to detect involuntary movements as potential adverse effects. Items were scored on a 5-point scale (0=none, 1=minimal, may be extreme normal, 2=mild, 3=moderate, 4=severe).

End point type	Other pre-specified
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End point timeframe:

Abnormal Involuntary Movement Scale (AIMS) scores were collected at Screening, Baseline, and Weeks 4, 8, 12, 18, 24, 30, 36, and 37. AIMS scores are presented here for Week 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	54	
Units: NA				
arithmetic mean (standard error)	0.1 (± 0.0)	-0.1 (± 0.0)	0.0 (± 0.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline to Week 12 in AIMS Score - Incapacitation due to Abnormal Movements

End point title	Change from Baseline to Week 12 in AIMS Score - Incapacitation due to Abnormal Movements
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End point description:

The AIMS was used as a safety assessment in this study to detect involuntary movements as potential adverse effects. Items were scored on a 5-point scale (0=none, 1=minimal, may be extreme normal, 2=mild, 3=moderate, 4=severe).

End point type	Other pre-specified
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End point timeframe:

Abnormal Involuntary Movement Scale (AIMS) scores were collected at Screening, Baseline, and Weeks 4, 8, 12, 18, 24, 30, 36, and 37. AIMS scores are presented here for Week 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	54	
Units: NA				
arithmetic mean (standard error)	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline to Week 12 in AIMS Score - Patient Awareness of Abnormal Movements

End point title	Change from Baseline to Week 12 in AIMS Score - Patient Awareness of Abnormal Movements
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End point description:

The AIMS was used as a safety assessment in this study to detect involuntary movements as potential adverse effects. Items were scored on a 5-point scale (0=none, 1=minimal, may be extreme normal, 2=mild, 3=moderate, 4=severe).

End point type	Other pre-specified
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End point timeframe:

Abnormal Involuntary Movement Scale (AIMS) scores were collected at Screening, Baseline, and Weeks 4, 8, 12, 18, 24, 30, 36, and 37. AIMS scores are presented here for Week 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	54	
Units: NA				
arithmetic mean (standard error)	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline to Week 12 in AIMS Score - Neck, Shoulders, Hips

End point title	Change from Baseline to Week 12 in AIMS Score - Neck, Shoulders, Hips
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End point description:

The AIMS was used as a safety assessment in this study to detect involuntary movements as potential adverse effects. Items were scored on a 5-point scale (0=none, 1=minimal, may be extreme normal, 2=mild, 3=moderate, 4=severe).

End point type	Other pre-specified
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End point timeframe:

Abnormal Involuntary Movement Scale (AIMS) scores were collected at Screening, Baseline, and Weeks 4, 8, 12, 18, 24, 30, 36, and 37. AIMS scores are presented here for Week 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	54	
Units: NA				
arithmetic mean (standard deviation)	0.0 (± 0.0)	0.0 (± 0.0)	-0.1 (± 0.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline to Week 12 in CDSS Total Score

End point title	Change from Baseline to Week 12 in CDSS Total Score
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End point description:

Change from Baseline to Week 12 in Calgary Depression Scale for Schizophrenia (CDSS) scores, intent-to-treat population. Least-squares mean are from a mixed model repeated measures (MMRM) with treatment (Placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subjects nested in treatment as a random effect with Baseline value as covariates. An unstructured covariance matrix was used.

End point type	Other pre-specified
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End point timeframe:

Calgary Depression Scale for Schizophrenia scores for exploratory endpoint were collected at Screening, Baseline, Weeks 2, 4, 8, and 12.

End point values	Placebo	MIN-101 32 mg	MIN-101 64 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	79	
Units: NA				
least squares mean (standard error)	0.04 (± 0.22)	-0.37 (± 0.22)	-0.75 (± 0.21)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 12 in CDSS Total
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Statistical analysis description:

MMRM with treatment (placebo, MIN-101 32 mg, MIN-101 64 mg), visit, pooled study center, and treatment-by-visit interaction terms as fixed effects, subject nested in treatment as a random effect with Baseline value as covariate. An unstructured covariance matrix was used.

Comparison groups	Placebo v MIN-101 32 mg v MIN-101 64 mg
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.1756 ^[15]
Method	Mixed models analysis

Notes:

[15] - MIN-101 32 mg vs Placebo: $p \leq 0.1756$

MIN-101 64 mg vs Placebo $p \leq 0.0091$

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from time of signed informed consent until completion of last study-related procedure.

Adverse event reporting additional description:

Adverse events (AEs) were classified as treatment-emergent AEs (TEAEs) if the AEs were not present before the first dose or were present before first dose by increased in severity on or after first dose.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Placebo - Whole Study Period
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Reporting group description: -

Reporting group title	MIN-101 32 mg - Whole Study Period
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Reporting group description: -

Reporting group title	MIN-101 64 mg Whole Study Period
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Reporting group description: -

Serious adverse events	Placebo - Whole Study Period	MIN-101 32 mg - Whole Study Period	MIN-101 64 mg Whole Study Period
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 83 (4.82%)	6 / 103 (5.83%)	2 / 102 (1.96%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 83 (0.00%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 83 (0.00%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 83 (0.00%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	1 / 83 (1.20%)	3 / 103 (2.91%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric decompensation			
subjects affected / exposed	1 / 83 (1.20%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute psychosis			
subjects affected / exposed	0 / 83 (0.00%)	1 / 103 (0.97%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	0 / 83 (0.00%)	1 / 103 (0.97%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3.5 %

Non-serious adverse events	Placebo - Whole Study Period	MIN-101 32 mg - Whole Study Period	MIN-101 64 mg Whole Study Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 83 (31.33%)	36 / 103 (34.95%)	45 / 102 (44.12%)
Cardiac disorders			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 83 (0.00%)	0 / 103 (0.00%)	5 / 102 (4.90%)
occurrences (all)	0	0	5
Psychiatric disorders			
Headache			
subjects affected / exposed	2 / 83 (2.41%)	6 / 103 (5.83%)	6 / 102 (5.88%)
occurrences (all)	2	6	6
Anxiety			
subjects affected / exposed	3 / 83 (3.61%)	5 / 103 (4.85%)	5 / 102 (4.90%)
occurrences (all)	3	5	5
Insomnia			

subjects affected / exposed	4 / 83 (4.82%)	4 / 103 (3.88%)	6 / 102 (5.88%)
occurrences (all)	4	4	6
Somnolence			
subjects affected / exposed	0 / 83 (0.00%)	3 / 103 (2.91%)	4 / 102 (3.92%)
occurrences (all)	0	3	4
Schizophrenia			
subjects affected / exposed	7 / 83 (8.43%)	1 / 103 (0.97%)	1 / 102 (0.98%)
occurrences (all)	7	1	1
Agitation			
subjects affected / exposed	3 / 83 (3.61%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences (all)	3	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported