



Clinical trial results:

A Randomized, Double-blind, Parallel-group Trial to Investigate the Safety and Efficacy of GWP42003-P Versus Placebo as Adjunctive Therapy in Participants with Schizophrenia Experiencing Inadequate Response to Ongoing Antipsychotic Treatment

Summary

EudraCT number	2019-003369-16
Trial protocol	ES PL
Global end of trial date	16 March 2022

Results information

Result version number	v2 (current)
This version publication date	09 July 2023
First version publication date	01 April 2023
Version creation reason	<ul style="list-style-type: none">New data added to full data set New data were included in the Adverse Event section

Trial information

Trial identification

Sponsor protocol code	GWAP19030
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04421456
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GW Research Ltd
Sponsor organisation address	Sovereign House, Vision Park, Histon, Cambridge, United Kingdom, CB24 9BZ
Public contact	Clinical Trial Disclosure & Transparency, GW Research Ltd, +1 215-832-3750, ClinicalTrialDisclosure@JazzPharma.com
Scientific contact	Clinical Trial Disclosure & Transparency, GW Research Ltd, +1 215-832-3750, ClinicalTrialDisclosure@JazzPharma.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	16 March 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	16 March 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the efficacy of GWP42003 P versus placebo after 12 weeks of treatment
- To evaluate the safety and tolerability of GWP42003 P

Protection of trial subjects:

This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki, the ICH Harmonised Guideline: Integrated Addendum to ICH E6(R1): Guideline for GCP E6(R2), the EU Clinical Trials Directive, the EU GCP Directive and the clinical study regulations adopting European Commission Directives into national legislation.

The protocol, protocol amendments, informed consent form, Investigator's Brochure, and other relevant documents (eg, advertisements) were submitted to the Institutional Review Board/Independent Ethics Committee (IRB/IEC) by the investigator and reviewed and approved by the IRB/IEC before the study was initiated.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 August 2020
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	Poland: 3
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United States: 68
Country: Number of subjects enrolled	Serbia: 21
Worldwide total number of subjects	95
EEA total number of subjects	6

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)	95
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 95 participants who met all inclusion and no exclusion criteria were enrolled in the study and were randomized to the Placebo Run-in Period. Eighteen participants failed the Placebo Run-in Period. A total of 77 participants were randomized to 1 of 2 GWP42003-P doses or placebo treatment at a 2:2:1:1 ratio at 33 clinic centers.

Pre-assignment

Screening details:

Once enrolled, participants were randomized to treatment following a single-blind, 2-week Placebo Run-in Period. A total of 95 participants were included the Placebo Run-in Period; 18 participants failed the Placebo Run-in Period. A total of 77 participants were randomized to the Treatment Period.

Period 1

Period 1 title	Randomized Placebo Run-in Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Arm title	Pooled Placebo
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Arm description:

Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive a matching placebo per day for 12 weeks.

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

Dosage and administration details:

Oral dose of matched placebo

Number of subjects in period 1	Pooled Placebo
Started	95
Completed	77
Not completed	18
Placebo run-in failures	18

Period 2

Period 2 title	Randomized Treatment Period
Is this the baseline period?	Yes ^[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
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Arm title	GWP42003-P 300 mg
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Arm description:

Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive an oral dose of GWP42003-P 300 milligrams (mg) per day for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	GWP42003-P
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Oral dose of GWP42003-P 150 mg administered twice daily

Arm title	GWP42003-P 1000 mg
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Arm description:

Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive an oral dose of GWP42003-P 1000 milligrams (mg) per day for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	GWP42003-P
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Oral dose of GWP42003-P 500 mg administered twice daily

Arm title	Pooled Placebo
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Arm description:

Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive a matching placebo per day for 12 weeks.

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

Dosage and administration details:

Oral dose of matched placebo

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The baseline period is the Treatment Period where patients were randomized to either GWP42003-P (300 mg or 1000 mg) or placebo.

Number of subjects in period 2^[2]	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo
Started	27	24	26
Completed	23	19	19
Not completed	4	5	7
Withdrawal of parent/legal representative consent	1	-	1
Adverse event, non-fatal	-	1	-
Not specified	-	1	3
Lost to follow-up	2	2	1
Participant non-compliance	1	1	2

Notes:

[2] - The number of subjects reported to be in the baseline 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 worldwide number of patients included 95 participants who were enrolled in the study and randomized to the Placebo Run-in Period. Eighteen participants failed the Placebo Run-in Period. Therefore, a total of 77 participants were randomized to the Treatment Period and is considered the baseline period.

Baseline characteristics

Reporting groups

Reporting group title	GWP42003-P 300 mg
Reporting group description: Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive an oral dose of GWP42003-P 300 milligrams (mg) per day for 12 weeks.	
Reporting group title	GWP42003-P 1000 mg
Reporting group description: Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive an oral dose of GWP42003-P 1000 milligrams (mg) per day for 12 weeks.	
Reporting group title	Pooled Placebo
Reporting group description: Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive a matching placebo per day for 12 weeks.	

Reporting group values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo
Number of subjects	27	24	26
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)	27	24	26
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	37.5	39.2	38.7
standard deviation	± 7.53	± 8.21	± 8.87
Gender categorical Units: Subjects			
Female	6	7	7
Male	21	17	19

Reporting group values	Total		
Number of subjects	77		
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)	77		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	20		
Male	57		

End points

End points reporting groups

Reporting group title	Pooled Placebo
Reporting group description: Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive a matching placebo per day for 12 weeks.	
Reporting group title	GWP42003-P 300 mg
Reporting group description: Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive an oral dose of GWP42003-P 300 milligrams (mg) per day for 12 weeks.	
Reporting group title	GWP42003-P 1000 mg
Reporting group description: Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive an oral dose of GWP42003-P 1000 milligrams (mg) per day for 12 weeks.	
Reporting group title	Pooled Placebo
Reporting group description: Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive a matching placebo per day for 12 weeks.	

Primary: Least Square Mean Change From Baseline in the Positive and Negative Symptoms Scale Total (PANSS-T) Score

End point title	Least Square Mean Change From Baseline in the Positive and Negative Symptoms Scale Total (PANSS-T) Score
End point description: The PANSS-T is a medical scale used for measuring symptom severity of participants with schizophrenia or related psychotic disorder. It is a 30-item rating instrument that assesses the positive and negative symptoms of schizophrenia as well as symptoms of general psychopathology. Individual items are rated on a 7-point scale, where 1 = absent and 7 = extreme. A PANSS-T score is derived from the sum of the 30 items and the total score ranges from 30 to 210, where higher scores represent worse outcome. The least square mean change from baseline is being reported and negative values indicate an improvement in outcome.	
End point type	Primary
End point timeframe: Baseline up to Week 12	

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: units on a scale				
least squares mean (standard error)				
PANSS-T Score	-10.49 (± 1.64)	-10.69 (± 1.75)	-8.74 (± 1.78)	

Statistical analyses

Statistical analysis title	GWP42003-P 300 mg vs Pooled placebo
Comparison groups	GWP42003-P 300 mg v Pooled Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.4528
Method	Mixed-effects repeated measures model
Parameter estimate	Least square mean difference
Point estimate	-1.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.35
upper limit	2.84
Variability estimate	Standard error of the mean
Dispersion value	2.33

Notes:

[1] - The repeated measures model includes stratification factors (sex and region), associated baseline, visit, randomised treatment arm and visit by treatment arm interaction as fixed effects and visit repeated within each participant as a repeated effect. For the PANSS-T score, baseline PANSS-P, baseline PANSS-N, and baseline PANSS-G are included in the model as fixed effects for the associated baseline instead of baseline PANSS-T.

Statistical analysis title	GWP42003-P 1000 mg vs Pooled placebo
Comparison groups	GWP42003-P 1000 mg v Pooled Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	= 0.4226
Method	Mixed-effects repeated measures model
Parameter estimate	Least square mean difference
Point estimate	-1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.76
upper limit	2.85
Variability estimate	Standard error of the mean
Dispersion value	2.44

Notes:

[2] - The repeated measures model includes stratification factors (sex and region), associated baseline, visit, randomised treatment arm and visit by treatment arm interaction as fixed effects and visit repeated within each participant as a repeated effect. For the PANSS-T score, baseline PANSS-P, baseline PANSS-N, and baseline PANSS-G are included in the model as fixed effects for the associated baseline instead of baseline PANSS-T.

Primary: Least Square Mean Change From Baseline in the PANSS Positive Subscale (PANSS-P) Score

End point title	Least Square Mean Change From Baseline in the PANSS Positive Subscale (PANSS-P) Score
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End point description:

The PANSS 'P' Scale was calculated as the sum of the items prefixed with an P, 7 items in total, i.e. delusions, conceptual disorganization, hallucinatory behavior, excitement, grandiosity, suspiciousness/persecution and hostility. Individual items are rated on a 7-point scale, where 1 = absent

and 7 = extreme. The least square mean change from baseline is being reported and negative values indicate an improvement in outcome.

End point type	Primary
End point timeframe:	
Baseline up to Week 12	

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: units on a scale				
least squares mean (standard error)				
PANSS-P Score	-3.16 (± 0.59)	-3.75 (± 0.63)	-2.53 (± 0.62)	

Statistical analyses

Statistical analysis title	GWP42003-P 300 mg vs Pooled Placebo
Comparison groups	Pooled Placebo v GWP42003-P 300 mg
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	= 0.4479
Method	Mixed-effects repeated measures model
Parameter estimate	Least square mean difference
Point estimate	-0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.25
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.83

Notes:

[3] - The repeated measures model includes stratification factors (sex and region), associated baseline, visit, randomised treatment arm and visit by treatment arm interaction as fixed effects and visit repeated within each participant as a repeated effect.

Statistical analysis title	GWP42003-P 1000 mg vs Pooled Placebo
Comparison groups	GWP42003-P 1000 mg v Pooled Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority ^[4]
P-value	= 0.1616
Method	Mixed-effects repeated measures model
Parameter estimate	Least square mean difference
Point estimate	-1.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.92
upper limit	0.49
Variability estimate	Standard error of the mean
Dispersion value	0.87

Notes:

[4] - The repeated measures model includes stratification factors (sex and region), associated baseline, visit, randomised treatment arm and visit by treatment arm interaction as fixed effects and visit repeated within each participant as a repeated effect.

Primary: Least Square Mean Change From Baseline in the PANSS Negative Subscale (PANSS-N) Score

End point title	Least Square Mean Change From Baseline in the PANSS Negative Subscale (PANSS-N) Score
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End point description:

The PANSS 'N' Scale will be calculated as the sum of the items prefixed with an N, 7 items in total, i.e. blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation and stereotyped thinking. Individual items are rated on a 7-point scale, where 1 = absent and 7 = extreme. The least square mean change from baseline is being reported and negative values indicate an improvement in outcome.

End point type	Primary
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End point timeframe:

Baseline up to Week 12

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: units on a scale				
least squares mean (standard error)				
PANSS-N Score	-2.64 (± 0.53)	-1.57 (± 0.56)	-2.33 (± 0.58)	

Statistical analyses

Statistical analysis title	GWP42003-P 300 mg vs Pooled Placebo
Comparison groups	GWP42003-P 300 mg v Pooled Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority ^[5]
P-value	= 0.6787
Method	Mixed-effects repeated measures model
Parameter estimate	Least square mean difference
Point estimate	-0.31

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	1.18
Variability estimate	Standard error of the mean
Dispersion value	0.76

Notes:

[5] - The repeated measures model includes stratification factors (sex and region), associated baseline, visit, randomised treatment arm and visit by treatment arm interaction as fixed effects and visit repeated within each participant as a repeated effect.

Statistical analysis title	GWP42003-P 1000 mg vs Pooled Placebo
Comparison groups	GWP42003-P 1000 mg v Pooled Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority ^[6]
P-value	= 0.3351
Method	Mixed-effects repeated measures model
Parameter estimate	Least square mean difference
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	2.3
Variability estimate	Standard error of the mean
Dispersion value	0.78

Notes:

[6] - The repeated measures model includes stratification factors (sex and region), associated baseline, visit, randomised treatment arm and visit by treatment arm interaction as fixed effects and visit repeated within each participant as a repeated effect.

Primary: Least Square Mean Change From Baseline in the PANSS General Subscale (PANSS-G) Score

End point title	Least Square Mean Change From Baseline in the PANSS General Subscale (PANSS-G) Score
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End point description:

The PANSS 'G' Scale will be calculated as the sum of the items prefixed with a G, 16 items in total, i.e. somatic concerns, anxiety, guilt feelings, tension, mannerisms and posturing, depression, motor retardation, uncooperativeness, unusual thought content, disorientation, poor attention, lack of judgment and insight, disturbance of volition, poor impulse control, preoccupation and active social avoidance. Individual items are rated on a 7-point scale, where 1 = absent and 7 = extreme. The least square mean change from baseline is being reported and negative values indicate an improvement in outcome.

End point type	Primary
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End point timeframe:

Baseline up to Week 12

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: units on a scale				
least squares mean (standard error)				
PANSS-G Score	-4.78 (± 1.03)	-4.91 (± 1.10)	-3.68 (± 1.09)	

Statistical analyses

Statistical analysis title	GWP42003-P 300 mg vs Pooled Placebo
Comparison groups	GWP42003-P 300 mg v Pooled Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority ^[7]
P-value	= 0.4504
Method	Mixed-effects repeated measures model
Parameter estimate	Least square mean difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.96
upper limit	1.76
Variability estimate	Standard error of the mean
Dispersion value	1.45

Notes:

[7] - The repeated measures model includes stratification factors (sex and region), associated baseline, visit, randomised treatment arm and visit by treatment arm interaction as fixed effects and visit repeated within each participant as a repeated effect.

Statistical analysis title	GWP42003-P 1000 mg vs Pooled Placebo
Comparison groups	GWP42003-P 1000 mg v Pooled Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority ^[8]
P-value	= 0.4195
Method	Mixed-effects repeated measures model
Parameter estimate	Least square mean difference
Point estimate	-1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.22
upper limit	1.76
Variability estimate	Standard error of the mean
Dispersion value	1.52

Notes:

[8] - The repeated measures model includes stratification factors (sex and region), associated baseline, visit, randomised treatment arm and visit by treatment arm interaction as fixed effects and visit repeated within each participant as a repeated effect.

Primary: Least Square Mean Change From Baseline in the Clinical Global Impression of Severity (CGI-S) Score

End point title	Least Square Mean Change From Baseline in the Clinical Global Impression of Severity (CGI-S) Score
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End point description:

The CGI-S is a 7-point scale used to rate the severity of participants' illness at the time of assessment. Considering total clinical experience, a participant will be assessed on severity of mental illness at the time of rating 0 = not assessed; 1 = normal, not at all ill; 2 = borderline mentally ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; or 7 = among the most extremely ill participants. The least square mean change from baseline is being reported and negative values indicate an improvement in outcome.

End point type	Primary
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End point timeframe:

Baseline up to Week 12

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: units on a scale				
least squares mean (standard error)				
CGI-S Score	-0.47 (± 0.11)	-0.50 (± 0.12)	-0.45 (± 0.12)	

Statistical analyses

Statistical analysis title	GWP42003-P 300 mg vs Pooled Placebo
Comparison groups	GWP42003-P 300 mg v Pooled Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority ^[9]
P-value	= 0.885
Method	Mixed-effects repeated measures model
Parameter estimate	Least square mean difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.35
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.16

Notes:

[9] - The repeated measures model includes stratification factors (sex and region), associated baseline, visit, randomised treatment arm, visit by treatment arm interaction and visit by associated baseline interaction as fixed effects and visit repeated within each participant as a repeated effect.

Statistical analysis title	GWP42003-P 1000 mg vs Pooled Placebo
Comparison groups	GWP42003-P 1000 mg v Pooled Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority ^[10]
P-value	= 0.7808
Method	Mixed-effects repeated measures model
Parameter estimate	Least square mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.16

Notes:

[10] - The repeated measures model includes stratification factors (sex and region), associated baseline, visit, randomised treatment arm, visit by treatment arm interaction and visit by associated baseline interaction as fixed effects and visit repeated within each participant as a repeated effect.

Primary: Number of Participants With Minimally or Better Clinical Global Impression of Improvement (CGI-I) Score at Week 12

End point title	Number of Participants With Minimally or Better Clinical Global Impression of Improvement (CGI-I) Score at Week 12
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End point description:

The CGI-I is a 7-point scale used to rate the improvement of participants' condition at the time of assessment. Compared to the patient's condition at baseline, the participants' condition was rated as 1 = very much improved since initiation of treatment; 2 = much improved; 3 = minimally improved; 4 = no change from baseline; 5 = minimally worse; 6 = much worse; 7 = very much worse since the initiation of treatment. Higher scores indicate a worse outcome. The number of participants with minimally or better improvements (score of 3 or better) are being reported.

End point type	Primary
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End point timeframe:

Week 12

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: number of participants				
number (not applicable)				
Minimally or Better CGI-I Score	17	12	15	

Statistical analyses

Statistical analysis title	GWP42003-P 300 mg vs Pooled Placebo
Comparison groups	GWP42003-P 300 mg v Pooled Placebo

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6707
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.412
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.288
upper limit	6.924

Statistical analysis title	GWP42003-P 1000 mg vs Pooled Placebo
Comparison groups	GWP42003-P 1000 mg v Pooled Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4883
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.576
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.121
upper limit	2.744

Secondary: Mean Change From Baseline in Body Weight

End point title	Mean Change From Baseline in Body Weight
End point description:	
End point type	Secondary
End point timeframe:	
Baseline up to Week 12	

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: kg				
arithmetic mean (standard deviation)				
Body weight	-0.03 (± 3.09)	-0.14 (± 1.98)	1.37 (± 1.28)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Body Mass Index (BMI)

End point title	Mean Change From Baseline in Body Mass Index (BMI)
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End point description:

End point type	Secondary
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End point timeframe:

Baseline up to Week 12

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: kg/m ²				
arithmetic mean (standard deviation)				
Body mass index	0 (± 0.98)	-0.04 (± 0.66)	0.45 (± 0.45)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Waist Circumference

End point title	Mean Change From Baseline in Waist Circumference
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End point description:

End point type	Secondary
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End point timeframe:

Baseline up to Week 12

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: centimeters				
arithmetic mean (standard deviation)				
Waist circumference	0.41 (± 5.36)	-0.53 (± 2.07)	1.34 (± 3.13)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Blood Pressure

End point title	Mean Change From Baseline in Blood Pressure
End point description:	
End point type	Secondary
End point timeframe:	
Baseline up to Week 12	

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: mmHg				
arithmetic mean (standard deviation)				
Diastolic blood pressure	1.7 (± 6.19)	0 (± 7.05)	-0.2 (± 5.71)	
Systolic blood pressure	0.3 (± 9.38)	0 (± 8.41)	0.3 (± 5.66)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Heart Rate

End point title	Mean Change From Baseline in Heart Rate
End point description:	
End point type	Secondary
End point timeframe:	
Baseline up to Week 12	

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: beats/minute				
arithmetic mean (standard deviation)				
Heart rate	1.0 (\pm 8.46)	-3.1 (\pm 9.13)	0.1 (\pm 6.52)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Respiratory Rate

End point title	Mean Change From Baseline in Respiratory Rate
End point description:	
End point type	Secondary
End point timeframe:	
Baseline up to Week 12	

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: breaths/minute				
arithmetic mean (standard deviation)				
Respiratory rate	-0.6 (\pm 2.13)	0.1 (\pm 1.37)	0 (\pm 1.45)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Temperature

End point title	Mean Change From Baseline in Temperature
End point description:	
End point type	Secondary
End point timeframe:	
Baseline up to Week 12	

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: Celsius				
arithmetic mean (standard deviation)				
Temperature	-0.07 (± 0.34)	0.06 (± 0.20)	-0.02 (± 0.19)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes From Baseline in Clinical Laboratory Test Results

End point title	Number of Participants With Clinically Significant Changes From Baseline in Clinical Laboratory Test Results
End point description:	
End point type	Secondary
End point timeframe:	
Baseline up to Week 12	

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	19	19	
Units: number of participants				
number (not applicable)				
Supine systolic blood pressure, Day 85: <-20	0	0	0	
Supine systolic blood pressure, Day 85: >20	1	0	0	
Supine diastolic blood pressure, Day 85: <-10	0	1	0	
Supine diastolic blood pressure, Day 85: >10	2	1	0	
Heart rate, Day 85: <-20	0	0	0	
Heart rate, Day 85: >20	0	0	0	
Weight, Day 85: ≤-7%	2	1	0	
Weight, Day 85: ≥7%	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Defined Flagged Electrocardiogram (ECG)

Parameter Values

End point title	Number of Participants With Defined Flagged Electrocardiogram (ECG) Parameter Values
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End point description:

End point type	Secondary
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End point timeframe:

Baseline up to Week 12

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27	24	26	
Units: number of participants				
number (not applicable)				
QTcF interval, Day 85: >450 msec	0	1	0	
QTcF interval, Day 85: >480 msec	0	0	0	
QTcF interval, Day 85: >500 msec	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Suicidal Ideation or Behavior Based on The Columbia Suicide Severity Rating Scale (CSSRS)

End point title	Number of Participants With Suicidal Ideation or Behavior Based on The Columbia Suicide Severity Rating Scale (CSSRS)
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End point description:

The C-SSRS is a short questionnaire that is used to assess suicidal ideation (5 questions) and behavior (5 questions) since last patient visit. The questionnaire is completed by participants answering yes or no to each question.

End point type	Secondary
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End point timeframe:

Baseline (screening) up to Day 85

End point values	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27	24	26	
Units: number of participants				
number (not applicable)				
Screening: Ideation, Wish to be dead	1	0	0	
Screening: Ideation, Non-specific active thoughts	0	0	0	
Screening: Ideation, Active any method no intent	0	0	0	

Screening: Ideation, Active intent to act, no plan	0	0	0	
Screening: Ideation, Active specific plan/intent	0	0	0	
Screening: Behavior, Preparatory acts or behavior	0	0	0	
Screening: Behavior, Aborted attempt	0	0	0	
Screening: Behavior, Interrupted attempt	0	0	0	
Screening: Behavior, Actual attempt	0	0	0	
Screening: Behavior, Completed suicide	0	0	0	
Day 14: Ideation, Wish to be dead	0	1	0	
Day 14: Ideation, Non-specific active thoughts	0	0	0	
Day 14: Ideation, Active any method no intent	0	0	0	
Day 14: Ideation, Active intent to act, no plan	0	0	0	
Day 14: Ideation, Active specific plan/intent	0	0	0	
Day 14: Behavior, Preparatory acts or behavior	0	0	0	
Day 14: Behavior, Aborted attempt	0	0	0	
Day 14: Behavior, Interrupted attempt	0	0	0	
Day 14: Behavior, Actual attempt	0	0	0	
Day 14: Behavior, Completed suicide	0	0	0	
Day 29: Ideation, Wish to be dead	1	1	0	
Day 29: Ideation, Non-specific active thoughts	0	1	0	
Day 29: Ideation, Active any method no intent	0	1	0	
Day 29: Ideation, Active intent to act, no plan	0	0	0	
Day 29: Ideation, Active specific plan/intent	0	0	0	
Day 29: Behavior, Preparatory acts or behavior	0	0	0	
Day 29: Behavior, Aborted attempt	0	0	0	
Day 29: Behavior, Interrupted attempt	0	0	0	
Day 29: Behavior, Actual attempt	0	0	0	
Day 29: Behavior, Completed suicide	0	0	0	
Day 85: Ideation, Wish to be dead	0	0	0	
Day 85: Ideation, Non-specific active thoughts	0	0	0	
Day 85: Ideation, Active any method no intent	0	0	0	
Day 85: Ideation, Active intent to act, no plan	0	0	0	
Day 85: Ideation, Active specific plan/intent	0	0	0	
Day 85: Behavior, Preparatory acts or behavior	0	0	0	
Day 85: Behavior, Aborted attempt	0	0	0	
Day 85: Behavior, Interrupted attempt	0	0	0	
Day 85: Behavior, Actual attempt	0	0	0	
Day 85: Behavior, Completed suicide	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events (AEs) were collected from baseline up to end of study, approximately 1 year 8 months.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	GWP42003-P 300 mg
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Reporting group description:

Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive an oral dose of GWP42003-P 300 milligrams (mg) per day for 12 weeks.

Reporting group title	GWP42003-P 1000 mg
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Reporting group description:

Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive an oral dose of GWP42003-P 1000 milligrams (mg) per day for 12 weeks.

Reporting group title	Pooled Placebo (Treatment Period)
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Reporting group description:

Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive a matching placebo per day for 12 weeks.

Reporting group title	Pooled Placebo (Placebo Run-in Period)
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Reporting group description:

Clinically stable schizophrenia participants experiencing inadequate response to antipsychotic treatment who were randomized to receive a matching placebo for 2 weeks (including participants who failed the placebo run-in period).

Serious adverse events	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo (Treatment Period)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 27 (7.41%)	2 / 24 (8.33%)	1 / 26 (3.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Hospitalization			
subjects affected / exposed	0 / 27 (0.00%)	0 / 24 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			

subjects affected / exposed	0 / 27 (0.00%)	1 / 24 (4.17%)	0 / 26 (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
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 27 (7.41%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronavirus infection			
subjects affected / exposed	0 / 27 (0.00%)	1 / 24 (4.17%)	0 / 26 (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

Serious adverse events	Pooled Placebo (Placebo Run-in Period)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 95 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Surgical and medical procedures			
Hospitalization			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronavirus infection			

subjects affected / exposed	0 / 95 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	GWP42003-P 300 mg	GWP42003-P 1000 mg	Pooled Placebo (Treatment Period)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 27 (11.11%)	3 / 24 (12.50%)	3 / 26 (11.54%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 27 (3.70%)	3 / 24 (12.50%)	3 / 26 (11.54%)
occurrences (all)	1	3	3
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 27 (7.41%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Pooled Placebo (Placebo Run-in Period)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 95 (0.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences (all)	0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 95 (0.00%)		
occurrences (all)	0		

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? Yes

Date	Interruption	Restart date
16 March 2022	The study was terminated based on a business decision by the Sponsor.	-

Notes:

Limitations and caveats

None reported