Clinical trial results:
A phase 1/2 study of GH001 in patients with treatment-resistant depression

Summary

EudraCT number	2018-004208-20
Trial protocol	NL
Global end of trial date	06 November 2021

Results information

Result version number	v1 (current)
This version publication date	12 April 2025
First version publication date	12 April 2025

Trial information

Trial identification

Sponsor protocol code	GH001-TRD-102

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04698603
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GH Research Ireland Limited
Sponsor organisation address	28 Baggot Street Lower, Dublin 2, Dublin, Ireland, D02 NX43
Public contact	Padraig O'Grady, GH Research Ireland Limited, clinicaltrials@ghres.com
Scientific contact	Padraig O'Grady, GH Research Ireland Limited, clinicaltrials@ghres.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	11 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 November 2021
Global end of trial reached?	Yes
Global end of trial date	06 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective of Part A (Phase 1): To assess the safety and tolerability of single-day, single dosing of GH001 in a controlled environment in patients with treatment-resistant depression (TRD).
Primary objective of Part B (Phase 2): To assess the effects of single-day, multiple dose of GH001 on the severity of depression.

Protection of trial subjects:

This trial was conducted according to the code of ethics on human experimentation established by the Declaration of Helsinki (1964) and amended in Fortaleza (2013), the International Council for Harmonization guidelines on good clinical practice, and current regulatory regulations (Medical Research Involving Human Subjects Act [Wet Medisch-wetenschappelijk Onderzoek met Mensen or WMO in Dutch]). Before a patient participated in the trial, written informed consent was obtained. The patient was asked to read a patient information section of the consent form that was approved by the Medical Ethics Committee and to sign it to indicate consent to participate in the trial. Informed consent was obtained before the initiation of any trial procedures for each patient. A Study Safety Group (SSG) was established to monitor the safety of the trial population and to advise the sponsor on modifications to the protocol and/or the continuation of the trial. The SSG members evaluated the safety and efficacy data from all patients at each review timepoint. The doses in Part 1 and Part 2 of the trial were chosen based on SSG evaluation of data from a previously conducted trial with GH001 (GH001-HV-101). Additionally, the results from Part 1 of this trial were reviewed by the SSG and provided further information to inform the doses to be used in Part 2.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 January 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	Netherlands: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	16
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were enrolled from a single site in the Netherlands. Potential patients for the trial were identified from the ongoing clinical practice of the trial psychiatrist or registered psychologist. There was also a Dutch-language website and Dutch-language internet advertisements and social media materials were used to assist with recruitment.

Pre-assignment

Screening details:

A total of 250 potential participants were prescreened, 67 of whom subsequently underwent medical and psychiatric screening. Of these, 49 were excluded as they did not meet eligibility criteria, or as the trial had concluded. A total of 16 patients were enrolled, all of whom were dosed and completed the trial. There were no withdrawals.

Period 1

Period 1 title	Part A - Phase 1
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

The trial part was an open-label design, so no blinding or randomization was performed. However, to avoid expectancy effects, patients were not informed of the name of the active molecule or their specific dose administered.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A - 12 mg

Arm description:

Patients received a single dose of GH001 12 mg.

Arm type	Experimental
Investigational medicinal product name	Mebufotenin
Investigational medicinal product code	GH001
Other name	5-MeO-DMT
Pharmaceutical forms	Inhalation vapour, solution
Routes of administration	Inhalation use

Dosage and administration details:

Single dose of GH001 12 mg administered via inhalation through a mouthpiece.

Arm title	Part A - 18 mg

Arm description:

Patients received a single dose of GH001 18 mg.

Arm type	Experimental
Investigational medicinal product name	Mebufotenin
Investigational medicinal product code	GH001
Other name	5-MeO-DMT
Pharmaceutical forms	Inhalation vapour, solution
Routes of administration	Inhalation use

Dosage and administration details:

Single dose of GH001 18 mg administered via inhalation through a mouthpiece.

Number of subjects in period 1[1]	Part A - 12 mg	Part A - 18 mg
Started	4	4
Completed	4	4

Notes:

[1] - 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 Sponsor has reviewed this and does not see any discrepencies.

Period 2

Period 2 title	Part B - Phase 2
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

The trial was an open-label design, so no blinding or randomization was performed. However, to avoid expectancy effects, patients were not informed of the name of the active molecule or their specific dose administered.

Arms

Arm title	Part B - Individualized Dosing Regimen

Arm description:

In Part B, a dose-escalation regimen (IDR) was applied. The patients received at least one and up to three doses of GH001 in a single day. If no peak experience (PE) was achieved with 6 mg doses, and the 6 mg dose level was well tolerated, a higher dose (12 mg) was administered; if no PE was achieved with 12 mg doses, and the 12 mg dose level was well tolerated, a third dose (18 mg) was administered. Any subsequent dose was administered approximately 3 hours after the prior dose.

Arm type	Experimental
Investigational medicinal product name	Mebufotenin
Investigational medicinal product code	GH001
Other name	5-MeO-DMT
Pharmaceutical forms	Inhalation vapour, solution
Routes of administration	Inhalation use

Dosage and administration details:

Up to three doses of GH001 administered via inhalation through a mouthpiece.

Number of subjects in period 2	Part B - Individualized Dosing Regimen
Started	8
Completed	8

Baseline characteristics

Reporting groups	
Reporting group title	Part A - 12 mg
Reporting group description:	
Patients received a single dose of GH001 12 mg.	
Reporting group title	Part A - 18 mg
Reporting group description:	
Patients received a single dose of GH001 18 mg.	

Reporting group values	Part A - 12 mg	Part A - 18 mg	Total
Number of subjects	4	4	8
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)	4	4	8
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	34.8	32.0	
standard deviation	± 12.82	± 12.57	-
Gender categorical Units: Subjects			
Female	2	2	4
Male	2	2	4
Race Units: Subjects			
White	4	4	8
Height Units: centimetre			
arithmetic mean	175.3	175.0	
standard deviation	± 13.00	± 7.39	-
Weight Units: kilogram(s)			
arithmetic mean	73.50	68.63	
standard deviation	± 13.10	± 17.09	-
BMI Units: kilogram(s)/square metre			
arithmetic mean	24.00	22.20	
standard deviation	± 3.39	± 4.17	-

Subject analysis sets

Subject analysis set title	Part B - Phase 2
Subject analysis set type	Full analysis

Subject analysis set description:

Part B - Phase 2

Reporting group values	Part B - Phase 2		
Number of subjects	8		
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)	8		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean	33.0		
standard deviation	± 11.01		
Gender categorical Units: Subjects			
Female	3		
Male	5		
Race Units: Subjects			
White	8		
Height Units: centimetre			
arithmetic mean	177.4		
standard deviation	± 9.47		
Weight Units: kilogram(s)			
arithmetic mean	75.00		
standard deviation	± 14.54		
BMI Units: kilogram(s)/square metre			
arithmetic mean	23.65		
standard deviation	± 3.09		

End points

End points reporting groups

Reporting group title	Part A - 12 mg
Reporting group description:	
Patients received a single dose of GH001 12 mg.	
Reporting group title	Part A - 18 mg
Reporting group description:	
Patients received a single dose of GH001 18 mg.	
Reporting group title	Part B - Individualized Dosing Regimen
Reporting group description:	
In Part B, a dose-escalation regimen (IDR) was applied. The patients received at least one and up to three doses of GH001 in a single day. If no peak experience (PE) was achieved with 6 mg doses, and the 6 mg dose level was well tolerated, a higher dose (12 mg) was administered; if no PE was achieved with 12 mg doses, and the 12 mg dose level was well tolerated, a third dose (18 mg) was administered. Any subsequent dose was administered approximately 3 hours after the prior dose.	
Subject analysis set title	Part B - Phase 2
Subject analysis set type	Full analysis
Subject analysis set description:	
Part B - Phase 2	

Primary: The safety and tolerability of GH001 administered via inhalation after vaporization as evaluated by a panel of measures: AE reporting, safety laboratory analyses, vital signs, ECG, BPRS, CADSS, C-SSRS, PVT and DSST*†

End point title	The safety and tolerability of GH001 administered via inhalation after vaporization as evaluated by a panel of measures: AE reporting, safety laboratory analyses, vital signs, ECG, BPRS, CADSS, C-SSRS, PVT and DSST*†[1]

End point description:

AE=Adverse event, ECG=Electrocardiogram, BPRS=Brief Psychiatric Rating Scale, CADSS=Clinician Administered Dissociative States Scale, C SSRS=Columbia-Suicide Severity Rating Scale; PVT=Psychomotor Vigilance Test and DSST=Digit Symbol Substitution Test.
* Primary endpoint for Part A of the trial
†No clinically significant trends or abnormalities were observed for vital signs, ECG, BPRS, CADSS, C SSRS, PVT and DSST.

End point type	Primary

End point timeframe:

From Day 1 through to the end of the trial (Day 7).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparison group.

End point values	Part A - 12 mg	Part A - 18 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Number and percentage				
Number of ADRs	5	4		
Number of subjects with ADRs	3	3		
Number of subjects with any SAE	0	0		
Number of subjects with an AE leading to withdrawa	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: The effect of GH001 on the severity of depression, as evaluated by the proportion of patients in remission (MADRS ≤10) at 7 days after dosing*

End point title	The effect of GH001 on the severity of depression, as evaluated by the proportion of patients in remission (MADRS ≤10) at 7 days after dosing*[2]

End point description:

MADRS=Montgomery-Åsberg Depression Rating Scale
*Primary endpoint for Part B of the trial

End point type	Primary

End point timeframe:

From Day 1 through to the end of the trial (Day 7).

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This trial was not compared with another group and there is no option to state this. The primary endpoint (proportion of patients in remission [MADRS>/=] on Day 7) was compared to baseline.

End point values	Part B - Individualized Dosing Regimen			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Number, percentage				
Number of patients in remission (MADRS ≤10)	7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Day 1 through to the end of the trial (Day 7).	
Adverse event reporting additional description:	
Data presented here is for treatment-emergent adverse events (TEAEs), defined as any AE that began or worsened on or following the start of dosing.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	Part A - 12 mg
Reporting group description: -	
Reporting group title	Part A - 18 mg
Reporting group description: -	
Reporting group title	Part B - IDR
Reporting group description: -	

Serious adverse events	Part A - 12 mg	Part A - 18 mg	Part B - IDR
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Part A - 12 mg	Part A - 18 mg	Part B - IDR
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	3 / 4 (75.00%)	7 / 8 (87.50%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Headache			
subjects affected / exposed	2 / 4 (50.00%)	1 / 4 (25.00%)	3 / 8 (37.50%)
occurrences (all)	2	1	3
Paraesthesia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Sensory disturbance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	3 / 8 (37.50%)
occurrences (all)	0	0	3
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Feeling abnormal			
subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	0 / 8 (0.00%)
occurrences (all)	1	2	8
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	2 / 8 (25.00%)
occurrences (all)	0	1	2
Flashback			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	2 / 8 (25.00%)
occurrences (all)	1	1	2
Depressive symptom			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Muscle spasms			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Muscle discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 September 2019	a. Summary of GH001-HV-101 trial results included. b. Dose range in Part A specified.
26 November 2019	a. Appendix 2.1 (standalone document) amended to update list of excluded concomitant medications.
24 December 2019	a. Revised exclusion criterion to clarify assessment of suicidality risk.
24 September 2020	a. Changes to trial endpoints.
27 April 2021	a. Dose regimen in Part B specified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/34912222