UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER PURSUANT TO RULE 13a-16 OR 15d-16 UNDER THE SECURITIES EXCHANGE ACT OF 1934

For the month of January 2026.

Commission File Number: 001-40530

GH Research PLC

(Exact name of registrant as specified in its charter)

Joshua Dawson House
Dawson Street
Dublin 2
D02 RY95
Ireland
(Address of principal executive office)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

Form 20-F ☒ Form 40-F ☐

GH Research PLC announces the presentation of posters related to its GH001-TRD-201 and GH001-BD-202 clinical trials at the 64th American College of Neuropsychopharmacology (ACNP) annual meeting (the "**Congress**"), which is scheduled to take place from January 12-15, 2026, in Paradise Island, Bahamas.

A copy of the poster to be presented by Sanjay J. Mathew during the Congress is attached hereto as Exhibit 99.1.

A copy of the poster to be presented by Lisa Harding during the Congress is attached hereto as Exhibit 99.2.

A copy of the poster to be presented by Andreas Reif during the Congress is attached hereto as Exhibit 99.3.

EXHIBIT INDEX

99.1	Poster to be presented by Sanjay J. Mathew with Title: Suicidal Ideation and Behavior in Patients with Treatment-Resistant Depression Treated with GH001
99.2	Poster to be presented by Lisa Harding with Title: Rapid Antidepressant Effects of Inhaled GH001 in Treatment-Resistant Depression: Results from a Phase 2b, Double-Blind, Randomized Controlled Trial with 6-Month Follow-Up
99.3	Poster to be presented by Andreas Reif with Title: Results of a Phase 2a Clinical Trial of Inhaled Mebufotenin (GH001) in Patients with Bipolar II Disorder and a Current Major Depressive Episode

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: January 8, 2025

GH Research PLC

By: /s/ Julie Ryan
Name: Julie Ryan
Title: Vice President, Finance

Exhibit 99.1

TH71

Suicidal Ideation and Behavior in Patients with Treatment-Resistant Depression Treated with GH001

Sanjay J. Mathew[1,*], Bernhard T. Baune[2-4], Narcís Cardoner[5], Wiesław J. Cubała[6], Kelly Doolin[7], Rosa Maria Dueñas Herrero[8], David Gregory[7], Luboš Janů[9], John R. Kelly[10,11], Rachael MacIssac[7], Shane J. McInerney[12,13], Alexander Nawka[14], Tomáš Páleníček[15], Víctor Pérez Sola[16-19], Andreas Reif[20,21], Claire Sweeney[7], Madhukar H. Trivedi[22], Velichka Valcheva[7], Eduard Vieta[19,23], Michael E. Thase[24,25]

*Presenting author: Sanjay J. Mathew, Department of Psychiatry and Behavioral Sciences, Texas A&M University Naresh K. Vashisht College of Medicine, Bryan, TX, USA

[1]Department of Psychiatry and Behavioral Sciences, Texas A&M University Naresh K. Vashisht College of Medicine, Bryan, TX, USA; [2]Department of Psychiatry, University of Münster, Münster, Germany; [3]Department of Psychiatry, University of Melbourne, Melbourne, VIC, Australia; [4]The Florey Institute of Neuroscience and Mental Health, Parkville, VIC, Australia; [5]Hospital Santa Creu i Sant Pau, Mental Health Research Group, Institut de Recerca Sant Pau, Universitat Autònoma de Barcelona, CIBERSAM, Barcelona, Spain; [6]Department of Psychiatry, Faculty of Medicine, Medical University of Gdańsk, Gdańsk, Poland; [7]GH Research, Dublin, Ireland; [8]Parc Sanitari Sant Joan de Deu Hospital de Dia de Numancia, Barcelona, Spain; [9]A-Shine SRO, Pilsen, Czechia; [10]Psychedelic Research Group: Trinity College Dublin and Tallaght University Hospital, Dublin, Ireland; [11]Department of Psychiatry, Tallaght University Hospital, Dublin, Ireland; [12]Department of Psychiatry, University Hospital Galway, Galway, Ireland; [13]Department of Psychiatry, University of Galway, Galway, Ireland; [14]Institut Neuropsychiatrické Péče, Praha, Czechia; [15]Psyon s.r.o., Prague, Czechia; [16]Mental Health Institute, Hospital del Mar, Barcelona, Spain; [17]Neurosciences Research Group, Hospital del Mar Research Institute (IMIM), Barcelona, Spain; [18]Department of Psychiatry and Department of Experimental and Health Sciences, Pompeu Fabra University, Barcelona, Spain; [19]Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Instituto de Salud Carlos III, Madrid, Spain; [20]Department of Psychiatry, Psychosomatic Medicine and Psychotherapy, University Hospital Frankfurt – Goethe University, Frankfurt am Main, Germany; [21]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Theodor-Stern-Kai 7, 60596, Frankfurt am Main, Germany; [22]Center for Depression Research and Clinical Care, Peter O'Donnell Jr. Brain Institute and the Department of Psychiatry, University of Texas Southwestern Medical Center, Dallas, TX, USA; [23]Hospital Clinic de Barcelona, Institute of Neuroscience, University of Barcelona, IDIBAPS, CIBERSAM, Barcelona, Catalonia, Spain; [24]Department of Psychiatry, University of Pennsylvania, Philadelphia, PA, USA; [25]Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, PA, USA

Background

- Treatment-resistant depression (TRD) is a debilitating condition that has been defined as a failure to respond to ≥2 adequate treatments for major depressive disorder (MDD)[1]
- Rates of suicidal ideation in patients with TRD are higher than in patients with treatment-responsive MDD (15% vs 6% of patients, respectively)[2]
  - TRD is also associated with higher rates of attempted suicide, all-cause mortality, and deaths by suicide[3]
- There is a significant unmet need for safe and effective therapies for TRD that do not exacerbate suicidal intent
- In a Phase 2b trial, GH001, a synthetic form of mebufotenin (5-MeO-DMT) for pulmonary inhalation, was well tolerated and resulted in rapid and significant improvements in depressive symptoms in patients with TRD

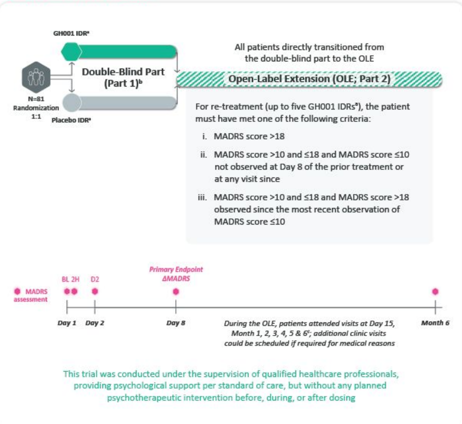
Objective

- We describe the safety effects of GH001 on suicidal ideation and behavior in patients with TRD enrolled in the Phase 2b trial

Methods

- This trial (NCT05800860) included a 7-day, randomized, double-blind part and a 6-month open-label extension (OLE; **Figure 1**)
  - In the double-blind part, patients were randomized 1:1 to receive an individualized dosing regimen (IDR) of up to three escalating doses of GH001 (6, 12, and 18 mg) or placebo IDR on a single day with a 1-hour interval between doses
  - In the OLE, patients received up to five GH001 IDR re-treatments over 6 months as needed, depending on the patient's clinical response and tolerability of previous IDRs
- Trial eligibility criteria excluded patients with suicidal ideation with intent (with items 4 or 5 on the Columbia-Suicide Severity Rating Scale [C-SSRS] endorsed) within the past year, during the screening period, or at baseline; those with suicidal behaviors or non-suicidal self-injury in the past year; and those with a clinical assessment of significant suicide risk
- Suicidal behavior and suicidal ideation were assessed using the C-SSRS at screening; during each treatment period at pre-dose, discharge, Day 2, and Day 8; and at all OLE scheduled visits (Day 15 and monthly up to Month 6/end of treatment)
  - The C-SSRS "baseline/screening" version was used at screening, and the "since last visit" version was used at all subsequent visits
  - Suicidal ideation was defined as "yes" responses to items 1–5 (with items 4 and 5 indicating suicidal ideation with intent), and suicidal behavior was defined as "yes" responses to items 6–10
- Montgomery–Åsberg Depression Rating Scale (MADRS) item 10 (suicidal thoughts) was used to provide further quantification of suicidal ideation, which was indicated by scores ≥2 on a scale from 0–6[4]
- Treatment-emergent adverse events (TEAEs) were assessed at each visit
- Results were analyzed descriptively

Figure 1. Clinical Trial Schematic



[a]A second or third dose was administered if the previous dose was well tolerated according to the trial physician's judgment (based on vital signs and adverse events) and if the patient did not achieve an intense psychoactive effect (peak experience; defined as a mean score of ≥75 on the Peak Experience Scale) following the previous dose. [b]Efficacy assessments were carried out by independent blinded raters in the double-blind part. [c]Patients also attended assessment visits on Day 2 (telephone call) and Day 8 (in-person) after each re-treatment.
Abbreviations: BL = Baseline; D = Day; H = Hour; IDR = Individualized dosing regimen; MADRS = Montgomery–Åsberg Depression Rating Scale.

Results

- Eighty-one patients were randomized (GH001 IDR, 40 and placebo IDR, 41) in the double-blind part, and all transitioned directly into the OLE
- Rates of historic and current suicidal ideation were balanced across treatment groups (**Table 1**)

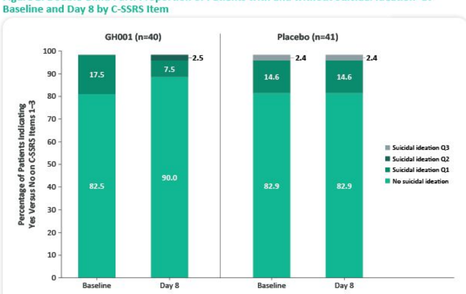
Table 1. Baseline Demographics and Clinical Characteristics

	GH001 (n=40)	Placebo (n=41)
Patient Demographics		
Age, years, mean (SD)	41.6 (11.4)	43.9 (10.9)
Sex, female, n (%)	24 (60.0)	22 (53.7)
Race, White, n (%)	40 (100)	41 (100)
Actively employed, n (%)	33 (82.5)	29 (70.7)
Disease Characteristics		
HAM-D-17 total score, mean (SD)	24.9 (2.6)	24.6 (2.3)
MADRS total score, mean (SD)	29.0 (5.4)	28.2 (4.6)
CGI-S, mean (SD)	4.8 (0.7)	5.0 (0.6)
Suicidality		
Non-suicidal self-injurious behavior		
Lifetime, n (%)	1 (2.5)	0
Past 12 months, n (%)	0	0
Baseline, n (%)	0	0
Suicidal ideation without intent[a]		
Lifetime, n (%)	15 (37.5)	23 (56.1)
Past 12 months, n (%)	10 (25.0)	18 (43.9)
Baseline, n (%)	7 (17.5)	9 (22.0)
Suicidal ideation with intent[a]		
Past 12 months, n (%)	0	0
Baseline, n (%)	0	0
Suicidal behavior[a]		
Past 12 months, n (%)	0	0
Baseline, n (%)	0	0

[a]Suicidal ideation without intent was defined as any "yes" answer to C-SSRS items 1–3; suicidal ideation with intent was defined as any "yes" answer to C-SSRS items 4–5; suicidal behavior was defined as any "yes" answer to C-SSRS items 6–10; patients were counted for each category item to which they answered "yes" and therefore may be counted in more than one item.
Abbreviations: CGI-S = Clinical Global Impression–Severity; C-SSRS = Columbia-Suicide Severity Rating Scale; HAM-D-17 = Hamilton Rating Scale for Depression; MADRS = Montgomery–Åsberg Depression Rating Scale; SD = Standard deviation.

- In the GH001 group, suicidal ideation was reported by seven patients at baseline and four at Day 8 (**Figure 2**)
  - No GH001-treated patients developed new-onset suicidal ideation between baseline and Day 8
  - In the placebo group, five patients reported suicidal ideation both at baseline and at Day 8, two reported suicidal ideation at baseline but not Day 8, and two patients without baseline suicidal ideation reported it at Day 8
- No suicidal behaviors were reported in GH001- or placebo-treated patients at baseline or on any scheduled C-SSRS assessments in the double-blind part

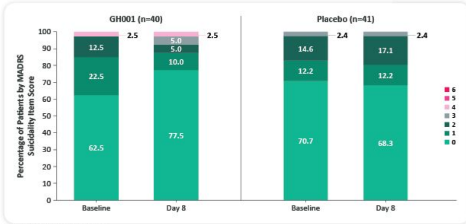
Figure 2. Double-Blind Part: Proportion of Patients with and without Suicidal Ideation[a] at Baseline and Day 8 by C-SSRS Item



[a]Patients responding "yes" to C-SSRS items 1 (wish to be dead), 2 (non-specific active suicidal thoughts), or 3 (active suicidal ideation with any methods); no patients responded "yes" post-dose to items 4 (active suicidal ideation with some intent) or 5 (active suicidal ideation with specific plan).
Abbreviations: C-SSRS = Columbia-Suicide Severity Rating Scale; Q = Question.

- Baseline MADRS item 10 (suicidal thoughts) scores were similar between the two treatment groups, and patients who received GH001 did not report worsening of symptoms on Day 8 of the double-blind part as per MADRS item 10 (**Figure 3**)
  - The median (range) change from baseline to Day 8 in MADRS score for item 10 was 0.0 (–2 to 1) for patients who received GH001 and 0.0 (–1 to 2) for patients who received placebo

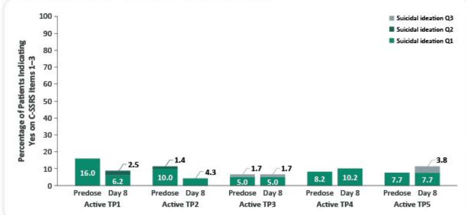
Figure 3. Double-Blind Part: MADRS Suicidality Item 10 Responses at Baseline and Day 8



Higher scores indicate worse symptoms.
Abbreviation: MADRS = Montgomery–Åsberg Depression Rating Scale.

- In the 6-month OLE, the numbers of patients reporting suicidal ideation according to the C-SSRS at all timepoints assessed during the trial were lower than before the first GH001 treatment period; C-SSRS items endorsed during each active treatment period are shown in **Figure 4**

Figure 4. Proportion of Patients Reporting Suicidal Ideation[a] by C-SSRS Item in Each GH001 Treatment Period in the Double-Blind Part and the OLE



[a]Patients responding "yes" to C-SSRS items 1 (wish to be dead), 2 (non-specific active suicidal thoughts), or 3 (active suicidal ideation with any methods); no patients responded "yes" post-dose to items 4 (active suicidal ideation with some intent) or 5 (active suicidal ideation with specific plan).
Abbreviations: C-SSRS = Columbia-Suicide Severity Rating Scale; Q = Question; TP = Treatment period.

- During the OLE, the proportions of patients reporting a score of zero on MADRS item 10 at all timepoints during GH001 treatment were greater than that at baseline of the double-blind part (**Figure 5**)
  - The median (range) change from baseline to Month 6 in MADRS score for item 10 was 0.0 (–3 to 2; n=74)

Figure 5. MADRS Suicidality Item 10 Responses at Baseline and by Month in the OLE

Higher scores indicate worse symptoms.
Abbreviations: ET = End of treatment; MADRS = Montgomery–Åsberg Depression Rating Scale; OLE = Open-label extension.

- No TEAEs of suicidal intent or suicidal behavior occurred throughout the 6-month duration of the trial
- A TEAE of suicidal ideation occurred in one patient; the event lasted 6 hours before resolving spontaneously
  - This TEAE was not accompanied by any changes in C-SSRS score beyond the duration for which the thoughts occurred, and the patient did not report any further TEAEs of suicidal ideation during the trial

Conclusions

- In this double-blind, placebo-controlled trial with a 6-month OLE in patients with TRD who were not at acute risk of suicide at baseline, GH001 was not associated with treatment-emergent events of suicidal ideation with intent or suicidal behavior, or with any increased suicidal ideation as measured by the C-SSRS immediately following treatment or over time for up to 6 months
- These results support that GH001 was generally well tolerated and was associated with significant reductions in depressive symptoms without increasing risk of suicide

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2. Mrazek DA, et al. *Psychiatr Serv*. 2014;65:977-87.
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Presented at the 64th Annual Meeting of the American College of Neuropsychopharmacology (ACNP) | Paradise Island, Bahamas | January 12–15, 2026

TH83

Rapid Antidepressant Effects of Inhaled GH001 in Treatment-Resistant Depression: Results from a Phase 2b, Double-Blind, Randomized, Controlled Trial with 6-Month Follow-Up

Lisa Harding[1,2]*, Bernhard T. Baune[3,4,5], Brian Brennan[6], Narcís Cardoner[7], Rosa Maria Dueñas Herrero[8], David Gregory[6], Luboš Janů[9], John R. Kelly[10,11], Shane J. McInerney[12,13], Alexander Nawka[14], Tomáš Páleníček[15], Víctor Pérez Sola[16-19], Andreas Reif[20,21], Fiona Ryan[6], Claire Sweeney[6], Michael E. Thase[22,23], Madhukar H. Trivedi[24], Velichka Valcheva[6], Eduard Vieta[19,25], Wiesław J. Cubała[26]

*Presenting author: Lisa Harding, Mood Institute, Milton, CT, USA, and Department of Psychiatry, Yale School of Medicine, New Haven, CT, USA

[1]Mood Institute, Milton, CT, USA; [2]Department of Psychiatry, Yale School of Medicine, New Haven, CT, USA; [3]Department of Psychiatry, University of Münster, Münster, Germany; [4]Department of Psychiatry, University of Melbourne, Melbourne, VIC, Australia; [5]The Florey Institute of Neuroscience and Mental Health, Parkville, VIC, Australia; [6]GH Research, Dublin, Ireland; [7]Hospital Santa Creu i Sant Pau, Mental Health Research Group, Institut de Recerca Sant Pau, Universitat Autònoma de Barcelona, CIBERSAM, Barcelona, Spain; [8]Parc Sanitari Sant Joan de Deu Hospital de Dia de Numancia, Barcelona, Spain; [9]A-Shine SRO, Pilsen, Czechia; [10]Psychedelic Research Group: Trinity College Dublin and Tallaght University Hospital, Dublin, Ireland; [11]Department of Psychiatry, Tallaght University Hospital, Dublin, Ireland; [12]Department of Psychiatry, University Hospital Galway, Galway, Ireland; [13]Department of Psychiatry, University of Galway, Galway, Ireland; [14]Institut Neuropsychiatrické Péče, Praha, Czechia; [15]Psyon s.r.o., Prague, Czechia; [16]Mental Health Institute, Hospital del Mar, Barcelona, Spain; [17]Neurosciences Research Group, Hospital del Mar Research Institute (IMIM), Barcelona, Spain; [18]Department of Psychiatry and Department of Experimental and Health Sciences, Pompeu Fabra University, Barcelona, Spain; [19]Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Instituto de Salud Carlos III, Madrid, Spain; [20]Department of Psychiatry, Psychosomatic Medicine and Psychotherapy, University Hospital Frankfurt – Goethe University, Frankfurt am Main, Germany; [21]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Theodor-Stern-Kai 7, 60596 Frankfurt am Main, Germany; [22]Department of Psychiatry, University of Pennsylvania, Philadelphia, PA, USA; [23]Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, PA, USA; [24]Center for Depression Research and Clinical Care, Peter O'Donnell Jr. Brain Institute and the Department of Psychiatry, University of Texas Southwestern Medical Center, Dallas, TX, USA; [25]Hospital Clinic de Barcelona, Institute of Neuroscience, University of Barcelona, IDIBAPS, CIBERSAM, Barcelona, Catalonia, Spain; [26]Department of Psychiatry, Faculty of Medicine, Medical University of Gdańsk, Gdańsk, Poland

Background

- Treatment-resistant depression (TRD) remains one of the most pressing challenges in psychiatry, affecting approximately 30% of patients treated for major depressive disorder (MDD)[1]
- Current therapies for TRD are limited,[2] and there is a large unmet need for treatments that are well tolerated and offer rapid reductions in depressive symptoms and long-term remission
- GH001, a synthetic form of mebufotenin for pulmonary inhalation, has been well tolerated in early-stage trials,[3,4] and shows potential to induce rapid remission of depressive symptoms in patients with TRD[4]

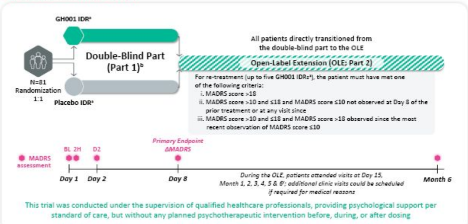
Objective

- This analysis presents the efficacy and safety data for GH001 from a Phase 2b double-blind, placebo-controlled trial in which patients with TRD received up to five re-treatments of GH001 as an individualized dosing regimen (IDR)

Methods

- This two-part, Phase 2b trial (NCT05800860) enrolled patients with TRD (**Figure 1**):
  - Part 1 was a 7-day, double-blind, placebo-controlled part in which patients were randomised 1:1 to receive an IDR of up to three escalating doses of GH001 (6, 12, and 18 mg) or placebo IDR on a single day; there was a 1-hour interval between doses
  - Part 2 was a 6-month open-label extension (OLE) where up to five GH001 IDR re-treatments were administered, depending on the patient's clinical response (re-treatment criteria described in **Figure 1**)
- Patients were required to meet the trial criteria for TRD as assessed by a trial psychiatrist:
  - Recurrent or single major depressive episode without psychotic features, with current episode of ≤2 years and nonresponse to ≥2 and ≤5 oral antidepressant treatments
  - Current major depressive episode based upon the Massachusetts General Hospital – Structured Assessment for Evaluation of Risk (MGH-SAFER) criteria interview
  - 17-Item Hamilton Depression Rating Scale (HAM-D-17) total score ≥20
- The primary endpoint of this trial was mean change in Montgomery-Åsberg Depression Rating Scale (MADRS) total score from baseline to Day 8, as assessed by a blinded rater
- Treatment-emergent adverse events (TEAEs) were assessed throughout the trial

Figure 1. Clinical Trial Design



[a]A second or third dose was administered if the previous dose was well tolerated according to the trial physician's judgment (based on vital signs and adverse events) and if the patient did not achieve an intense psychoactive effect (peak experience; defined as a mean score of ≥75 on the Peak Experience Scale) following the previous dose. [b]Efficacy assessments were carried out by independent blinded raters in the double-blind part. [c]Patients also attended assessment visits on Day 2 (telephone call) and Day 8 (in-person) after each re-treatment.
Abbreviations: BL = Baseline; D = Day; H = Hour; IDR = Individualized dosing regimen; MADRS = Montgomery–Åsberg Depression Rating Scale.

Results

- Eighty-one patients were randomized (GH001 IDR, 40 and placebo IDR, 41) in the double-blind part, and all transitioned directly into the OLE (**Table 1**)

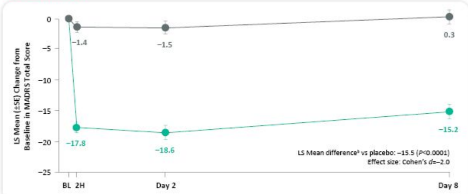
Table 1. Baseline Characteristics and Patient Disposition

	GH001 (N=81)
Patient Demographics	
Age, years, mean (SD)	42.8 (11.2)
Sex, female, n (%)	46 (56.8)
Race, White, n (%)	81 (100)
BMI, kg/m², mean (SD)	26.2 (5.5)
Previously used any psychedelic (lifetime), n (%)	9 (11.1)
Baseline Disease Characteristics	
HAM-D-17 total score, mean (SD)	24.8 (2.5)
MADRS total score, mean (SD)	28.6 (5.0)
MDE History at Baseline	
Number of MDEs	
Mean (SD)	2.1 (1.3)
≥3 MDEs, n (%)	27 (33.3)
Time since first depressive episode, years, mean (SD)	11.7 (9.0)
Duration of current MDE, weeks, mean (SD)	57.1 (78.4)
Patient Disposition, n (%)	
Completed the double-blind part	81 (100)
Received GH001 in the double-blind part	40 (49.4)
Received placebo in the double-blind part	41 (50.6)
Completed the OLE	63 (77.8)
Reasons for Discontinuation During the OLE, n (%)	18 (22.2)
Started additional antidepressant	7 (38.9)
Withdrawal of consent	6 (33.3)
Protocol deviation	2 (11.1)
Other	2 (11.1)
Adverse event	1 (5.6)

Abbreviations: BMI = Body mass index; HAM-D-17 = 17-item Hamilton Depression Rating Scale; MADRS = Montgomery-Åsberg Depression Rating Scale; MDE = Major depressive episode; OLE = Open-label extension; SD = Standard deviation.

- GH001 led to a least squares mean MADRS total score reduction from baseline to Day 8 of −15.5 compared with placebo in the double-blind part (**Figure 2**)

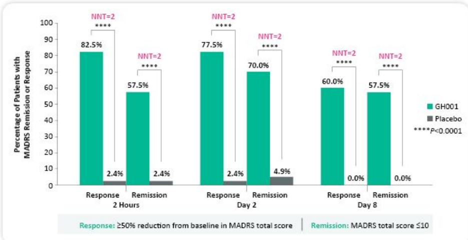
Figure 2. Primary Endpoint: Mean Change in MADRS Total Score from Baseline to Day 8[a] in the Double-Blind Part



[a]FDA guidance notes that efficacy with rapid-acting antidepressants generally should be demonstrated within 1 week, supporting a primary efficacy endpoint within this timeframe.[5] [b]Adjusted for baseline severity of symptoms (MADRS total score).
Abbreviations: BL = Baseline; FDA = Food and Drug Administration; H = Hour; LS = Least squares; MADRS = Montgomery-Åsberg Depression Rating Scale; SE = Standard error.

- GH001 treatment was associated with a 60% response rate and a 57.5% remission rate at Day 8 vs 0% with placebo in the double-blind part (**Figure 3**)

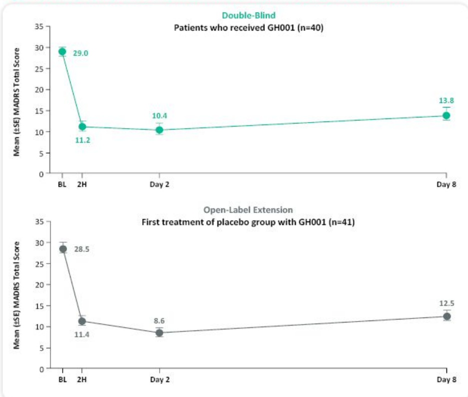
Figure 3. Percentage of Patients with Remission or Response Through Day 8 After Administration of GH001 IDR or Placebo IDR in the Double-Blind Part



Abbreviations: IDR = Individualized dosing regimen; MADRS = Montgomery-Åsberg Depression Rating Scale; NNT = Number needed to treat.

- The reduction in MADRS total score with GH001 observed in the double-blind part was notably reproduced in the placebo group with their first active GH001 treatment in the OLE (**Figure 4**)

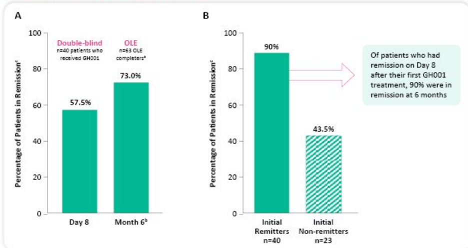
Figure 4. MADRS Total Scores with First GH001 in the Double-Blind Part and the OLE



Abbreviations: BL = Baseline; H = Hour; MADRS = Montgomery-Åsberg Depression Rating Scale; OLE = Open-Label extension; SE = Standard error.

- During the double-blind part, 57.5% of patients who received GH001 were in remission at Day 8; of the 63 patients who completed the OLE, 46 (73.0%) were in remission at 6 months (**Figure 5A**)
  - Patients who completed the OLE received a mean of four treatments across the 6 months (double-blind part and the OLE), with 63.5% (40/63) requiring one to four treatments during the 6 months
  - Among patients who completed the OLE who were in remission on Day 8 after their first active treatment, 90% were in remission at 6 months (**Figure 5B**)

Figure 5. Remission Rate at Day 8 and 6 Months (A) and Remission Rate at 6 Months in OLE Completers by Initial Remission Status (B)



[a]Includes 63 patients who completed the 6-month OLE per protocol (18 patients who discontinued early are excluded). [b]Approximately 6 months post-trial start (median 168 days from Day 1 of double-blind part). [c]Remission was defined as MADRS total score ≤10.
Abbreviations: MADRS = Montgomery-Åsberg Depression Rating Scale; OLE = Open-label extension.

- During the OLE, TEAEs were observed in 72/81 patients (88.9%) and were mostly mild or moderate (**Table 2**); one non–treatment-related serious TEAE (migraine) was reported
- No TEAEs of suicidal intent or suicidal behavior occurred
- The median duration of psychoactive effects after GH001 administration was 11 minutes
- Patients were deemed discharge-ready by 1 hour post-dose at 99% of visits

Table 2. Overall Summary of Adverse Events in the OLE

	GH001 (N=81)	
Summary of Adverse Events		
Any TEAE[a]	72 (88.9)	
Maximum severity of TEAEs		
Mild	28 (34.6)	
Moderate	42 (51.9)	
Severe	2 (2.5)	
Treatment-related TEAEs	65 (80.2)	
Serious TEAEs	1 (1.2)	
Treatment-related serious TEAEs	0	
TEAEs leading to discontinuation	1 (1.2)	
AESI	30 (37.0)	
Death	0	
TEAEs Occurring in >5% of Patients[a]	Overall	Treatment-related
Nausea	37 (45.7)	37 (45.7)
Paresthesia	31 (38.3)	31 (38.3)
Salivary hypersecretion	24 (29.6)	24 (29.6)
Headache	16 (19.8)	11 (13.6)
Muscle tightness	13 (16.0)	13 (16.0)
Feeling cold	12 (14.8)	11 (13.6)
Paresthesia oral	10 (12.3)	10 (12.3)
Upper respiratory tract infection	10 (12.3)	0
Anxiety	9 (11.1)	9 (11.1)
Depression	8 (9.9)	0
Abdominal pain	7 (8.6)	4 (4.9)
Abdominal discomfort	6 (7.4)	4 (4.9)
Affect lability	6 (7.4)	6 (7.4)
Dysgeusia	5 (6.2)	5 (6.2)
Abdominal pain upper	5 (6.2)	4 (4.9)
Fatigue	5 (6.2)	5 (6.2)
Nasopharyngitis	5 (6.2)	0
Palpitations	5 (6.2)	5 (6.2)
Hyperhidrosis	5 (6.2)	3 (3.7)

[a]TEAEs were classified according to the Medical Dictionary of Regulatory Activities (MedDRA version 26.0).
Abbreviations: AESI = Adverse event of special interest; OLE = Open-label extension; TEAE = Treatment-emergent adverse event.

Conclusions

- The primary endpoint was met: GH001 administered as an IDR led to significant MADRS reduction from baseline to Day 8 (−15.5 vs placebo)
- GH001 can maintain long-term remission in TRD, with 73.0% of patients who completed the OLE in remission at 6 months
- GH001 was well tolerated during the 6-month OLE, and no treatment-related serious adverse events occurred

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TU82

Results of a Phase 2a Clinical Trial of Inhaled Mebufotenin (GH001) in Patients with Bipolar II Disorder and a Current Major Depressive Episode

Andreas Reif[1,2], Michael Bauer[3], Max de Leeuw[4], Fabian Devlin[5], Katerina Kriger[6], Padraig O'Grady[6], Philipp Ritter[3,7], Claus Bo Svendsen[6], Michael E. Thase[8,9], Velichka Valcheva[6], Bernhard T. Baune[10,11,12]

[1]Department of Psychiatry, Psychosomatic Medicine and Psychotherapy, University Hospital Frankfurt – Goethe University, Frankfurt am Main, Germany; [2]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Theodor-Stern-Kai 7, 60596, Frankfurt am Main, Germany; [3]Department of Psychiatry and Psychotherapy, Faculty of Medicine, University Hospital Carl Gustav Carus, Dresden, Germany; [4]Department of Psychiatry, Leiden University Medical Center, Leiden, The Netherlands; [5]Mental Health Research for Innovation Centre, Mersey Care NHS Foundation Trust, United Kingdom; [6]GH Research, Dublin, Ireland; [7]Institute of Psychiatry, Psychology and Neuroscience, King's College London, United Kingdom; [8]Department of Psychiatry, University of Pennsylvania, Philadelphia, PA, USA; [9]Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, PA, USA; [10]Department of Psychiatry, University of Münster, Münster, Germany; [11]Department of Psychiatry, University of Melbourne, Melbourne, VIC, Australia; [12]The Florey Institute of Neuroscience and Mental Health, Parkville, VIC, Australia.

Background

- Bipolar II disorder (BDII) is a chronic psychiatric disorder characterized by alternating episodes of hypomania and major depressive episodes (MDE), imposing high burdens of illness on individuals[1]
- The estimated lifetime prevalence rate of BDII is between 0.4 and 5%[2,3]
- Current treatments for depressive symptoms in patients with BDII remain limited, offering insufficient efficacy and tolerability highlighting the need for new therapeutic approaches[4]
- Mebufotenin (5-MeO-DMT) is a rapid acting psychoactive molecule that acts as a non-selective serotonin agonist with highest affinity for the 5-HT_{1A} receptor subtype[5]
- GH001, a synthetic form of mebufotenin for pulmonary inhalation, has been well tolerated in early-stage trials and has shown potential to induce rapid remission of depressive symptoms in patients with treatment-resistant depression (TRD)[6,7]
- The trial presented here is the first in which mebufotenin was administered to patients diagnosed with BDII and a current MDE

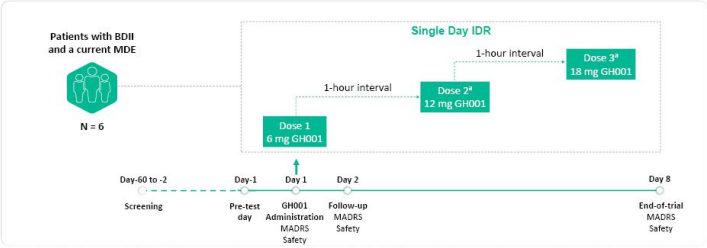
Objective

- To investigate the safety and antidepressant effects of GH001 in adult patients with BDII and a current MDE

Methods

- This Phase 2a, proof-of-concept, open-label trial (NCT05839509) enrolled patients aged 18-64 years who met Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) diagnostic criteria for BDII with a current MDE
- Patients were required to have a Montgomery–Åsberg Depression Rating Scale (MADRS) total score of ≥24 and a Young Mania Rating Scale (YMRS) total score of ≤8 at baseline and prior to dosing on Day 1
- Patients were not permitted to receive any antidepressant medications within 7 days or 5 half-lives, whichever was longer, prior to dosing. Lithium use within 6 months prior to dosing was not permitted, if applicable
- Patients were administered an individualized dosing regimen (IDR) of up to three escalating doses of GH001 (6, 12, and 18 mg) with a 1-hour interval between doses on a single day (Figure 1)
- This trial was conducted under the supervision of qualified healthcare professionals, providing psychological support per standard-of-care, but without any planned psychotherapeutic intervention before, during, or after dosing
- The primary endpoint was change in MADRS total score from baseline to Day 8
- Secondary endpoints included response (≥50% reduction from baseline in MADRS total score), remission (MADRS total score ≤10), Clinical Global Impression-Severity (CGI-S) scale, Bipolar Depression Rating Scale (BDRS), and safety and tolerability

Figure 1. Clinical Trial Design



[a]A second or third dose was administered if the previous dose was well tolerated according to the trial physician's judgement (based on vital signs and adverse events) and if the patient did not achieve an intense psychoactive effect (peak experience; defined as a mean score of ≥75 on the Peak Experience Scale) following the previous dose. Abbreviations: BDII = Bipolar II disorder; IDR = Individualized dosing regimen; MADRS = Montgomery–Åsberg Depression Rating Scale; MDE = Major depressive episode.

Results

Disposition and Demographics

- A total of six patients with BDII and a current MDE were enrolled in this trial. Patient disposition and demographics are presented in Table 1

Table 1. Patient Disposition and Baseline Characteristics

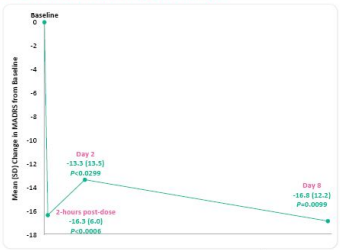
	N=6
Completed trial, n (%)	6 (100)
Discontinued, n (%)	0
Number of previous MDE, mean (SD)	14.0 (12.4)
Duration of current MDE (weeks), mean (SD)	20.8 (22.7)
MADRS total score at baseline, mean (SD)	32.0 (5.1)
Demographics	
Female, n (%)	4 (66.7)
Age (years), mean (SD)	44.2 (9.3)
Height (cm), mean (SD)	174.7 (10.1)
Weight (kg), mean (SD)	76.1 (18.6)
BMI (kg/m²), mean (SD)	24.8 (5.0)
Race, White, n (%)	6 (100)

Abbreviations: BMI = Body mass index; MADRS = Montgomery–Åsberg Depression Rating Scale; MDE = Major depressive episode; SD = Standard deviation.

Efficacy

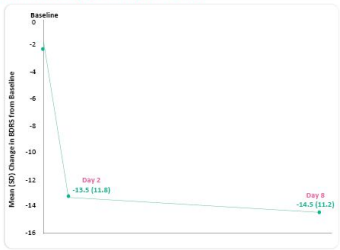
- The primary endpoint was achieved, with a significant reduction from baseline to Day 8 in mean (standard deviation [SD]) MADRS total score of −16.8 (12.2) (P=0.0099; Figure 2)
- Significant reductions in mean (SD) MADRS total score were also observed at 2-hours post-dose (−16.3 [6.0]) and Day 2 (−13.3 [13.5]; Figure 2)
- One-third (33.3%) of patients responded and were in remission on Day 8
- The rapid reduction in the severity of depressive symptoms as assessed by the MADRS, were mirrored in the CGI-S and the BDRS
  - A mean (SD) reduction of −2.5 (1.5) on the CGI-S and −14.5 (11.2) on the BDRS were observed from baseline to Day 8 (Figure 3)

Figure 2. Mean Change in MADRS Total Score From Baseline in Patients With BDII and a Current MDE



Abbreviations: BDII = Bipolar II disorder; MADRS = Montgomery–Åsberg Depression Rating Scale; MDE = Major depressive episode; SD = Standard deviation.

Figure 3. Mean Change in BDRS Total Score From Baseline in Patients With BDII and a Current MDE



Abbreviations: BDII = Bipolar II disorder; BL = Baseline; BDRS = Bipolar Depression Rating Scale; MDE = Major depressive episode; SD = Standard deviation.

Safety

- Treatment-emergent adverse events (TEAEs) were observed in 5/6 patients (83.3%) and were mostly mild in severity (87.5%) with two moderate and one severe events
- Headache (50%), nausea (33.3%) and anxiety (33.3%) were the most frequently reported TEAEs; all other TEAEs occurred in a single patient each
- One severe event of anxiety was reported which subsided within 24 hours; no TEAEs of flashbacks were reported
- There were no treatment-emergent serious adverse events (SAEs), and no patient withdrew from the trial
- There were no clinically significant changes in spirometry after inhalation of GH001
- There was a clinically significant reduction in mean (SD) Brief Psychiatric Rating Scale from baseline to Day 8 (−15.7 [12.0]). There was no clinically relevant worsening of other clinician-rated assessments (based on the Clinical Assessment of Discharge Readiness, Columbia-Suicide Severity Rating Scale, and Modified Observer's Assessment of Alertness and Sedation scales) and all patients were deemed ready for discharge within the same day of dosing
- Following dosing with GH001, YMRS scores remained low and stable, decreasing from 2.2 at baseline to 1.0 by Day 8 (−1.2 [SD=1.5]), indicating no emergence of manic symptoms
- The safety profile observed in this trial was consistent with other completed trials investigating GH001 in TRD and postpartum depression

Table 2. Summary of Safety in Patients with BDII and a Current MDE

	Event #	n (%)
Any TEAE	**18**	**5 (83.3)**
Mild	15	5 (83.3)
Moderate	2	2 (33.3)
Severe	1	1 (16.7)
Treatment-related TEAEs	18	5 (83.3)
Treatment-emergent SAE	0	0
TEAEs by Preferred Term		
Headache	4	3 (50.0)
Nausea	6	2 (33.3)
Anxiety	2	2 (33.3)
Paresthesia	1	1 (16.7)
Agitation	1	1 (16.7)
Hypoaesthesia oral	1	1 (16.7)
Neck pain	1	1 (16.7)
Fatigue	1	1 (16.7)
Cough	1	1 (16.7)

Abbreviations: BDII = Bipolar type II; MDE = Major depressive episode; SAE = Serious adverse event; TEAE = Treatment-emergent adverse event.

Conclusions

- In this trial evaluating the safety and antidepressant effects of GH001 in patients with BDII and a current MDE, the primary endpoint was met: a significant reduction from baseline in MADRS total score was observed on Day 8
- Significant reductions in MADRS total scores were also observed at 2-hours post-dose, supporting the rapid onset of antidepressant effects of GH001
- GH001 administered via inhalation demonstrated a favorable safety profile and was well tolerated in patients with BDII and a current MDE; no treatment-related SAEs were reported

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