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, 2025.

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 ☐

INFORMATION CONTAINED IN THIS REPORT ON FORM 6-K

On January 10, 2025, GH Research PLC (the "Company") announced primary endpoint met in two phase 2a POC trials with GH001 and completion of all FDA requests to address IND hold with no findings of respiratory toxicity in non-rodents, and made available an updated investor presentation on its website. A copy of the press release is exhibited hereto as Exhibit 99.1 and a copy of the investor presentation is attached hereto as Exhibit 99.2.

The fact that this press release and investor presentation is being made available and furnished herewith should not be deemed an admission as to the materiality of any information contained in the materials. The information contained in the press release and investor presentation is being provided as of January 10, 2025, and the Company does not undertake any obligation to update the presentation in the future or to update forward-looking statements to reflect subsequent actual results.

INCORPORATION BY REFERENCE

This Report on Form 6-K (other than Exhibit 99.2 hereto), including Exhibit 99.1 hereto, shall be deemed to be incorporated by reference into the registration statement on Form S-8 (Registration No. 333-270422) and the registration statement on Form F-3 (Registration No 333-270418) of the Company and to be a part thereof from the date on which this report is filed, to the extent not superseded by documents or reports subsequently filed or furnished.

EXHIBIT INDEX

Exhibit No.	Description
99.1	Press release dated January 10, 2025
99.2	Corporate Presentation for January 2025

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 10, 2025

GH Research PLC

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

Exhibit 99.1

GH Research Announces Primary Endpoint Met in Two Phase 2a POC Trials with GH001 and Completion of All FDA Requests to Address IND Hold with No Findings of Respiratory Toxicity in Non-Rodents

- Primary endpoint met in phase 2a POC trial in postpartum depression with a MADRS reduction from baseline of –35.4 points ($p<0.0001$, n=10) and 100% of patients in remission at Day 8
- Primary endpoint met in phase 2a POC trial in bipolar II disorder with a current major depressive episode with a MADRS reduction from baseline of –16.8 points ($p=0.0099$, n=6) and 33% of patients in remission at Day 8
- In both trials, GH001 was well tolerated and no treatment-related serious adverse events were reported
- Inhalation toxicology study in a non-rodent species was completed with no histology findings in the respiratory tract of any dogs in the study at any dose level
- Additional inhalation toxicology study in rats was completed supporting our position that respiratory tract histology findings are rat specific
- Our response to FDA's request for additional device design verification information is being prepared
- Full response to the IND hold planned to be submitted in mid-2025
- Top-line data from our randomized, double-blind, placebo-controlled Phase 2b trial in TRD on track to be announced in Q1 2025

Dublin, Ireland, January 10, 2025 – GH Research PLC (Nasdaq: GHRS), a clinical-stage biopharmaceutical company dedicated to transforming the treatment of psychiatric and neurological disorders, today provided updates on its business and highlighted key upcoming milestones.

Primary Endpoint Met in Phase 2a Proof-of-Concept Trial in PPD

The primary endpoint of the Phase 2a proof-of-concept (POC) trial for GH001 in postpartum depression (PPD) was met with a significant reduction from baseline of –35.4 points (96.3%) in Montgomery–Åsberg Depression Rating Scale (MADRS) total score on Day 8 after administration of GH001 ($p<0.0001$). On Day 8, 100% of patients were in remission (MADRS ≤ 10).

GH001 led to an ultra-rapid antidepressant effect with a significant reduction in MADRS score at 2 hours after administration of –31.4 points ($p<0.0001$) and on Day 2 of –36.0 points ($p<0.0001$).

The trial recruited 10 patients with PPD. All patients were administered an individualized dosing regimen (IDR) of up to three escalating doses of GH001. There was no psychotherapeutic intervention in this trial. The mean total MADRS score on Day 8 was 1.3 and all 10 patients were in remission.

GH001 was well tolerated and no treatment-related serious adverse events were reported. All treatment-emergent adverse events (TEAEs) were mild or moderate.

Primary Endpoint Met in Phase 2a Proof-of-Concept Trial in BDII

The primary endpoint of the Phase 2a POC trial for GH001 in bipolar II disorder with a current major depressive episode (BDII) was met with a significant reduction from baseline of –16.8 points (51.9%) in MADRS total score on Day 8 after administration of GH001 ($p=0.0099$). On Day 8, 33.3% of patients were in remission (MADRS ≤ 10).

GH001 led to an ultra-rapid antidepressant effect with a reduction in MADRS score at 2 hours after administration of –16.3 points (p=0.0006) and on Day 2 of -13.3 points (p=0.0299).

The trial recruited 6 patients with BDII. All patients were administered an IDR of up to three escalating doses of GH001. There was no psychotherapeutic intervention in this trial.

GH001 was well tolerated and no treatment-related serious adverse events were reported. The majority of TEAEs were mild or moderate and there were no reported TEAEs of hypomania or mania.

Update on IND for GH001

As previously announced, our Investigational New Drug Application (IND) for GH001 administered using our proprietary aerosol delivery device has been placed on clinical hold by the U.S. Food and Drug Administration (FDA), with the FDA requesting that we provide (i) an inhalation toxicology study in a non-rodent species and an additional inhalation toxicology study in rats, (ii) additional device design verification information and (iii) updates to our investigator brochure, to resolve the hold.

The requested additional inhalation toxicology study in a non-rodent species has now been completed. The pathology report concludes that there are no histology findings in the respiratory tract of any dogs at any dose level evaluated in the study.

The requested additional inhalation toxicology study in rats has now been completed which showed histology findings consistent with our previously completed study in rats. This supports our position that these findings are rat specific.

Based on previously announced FDA interactions, the response to their request for additional device design verification information is being prepared and, together with the completion of the inhalation toxicology studies, provides the final piece of information requested by the agency.

We are preparing to engage with the FDA in advance of providing a full response to the IND hold which we plan to submit in mid-2025.

Business Updates

GH001 in Patients with TRD

As previously announced, we completed enrolment of the double-blind phase of our randomized, double-blind, placebo-controlled Phase 2b trial in 80 treatment-resistant depression (TRD) patients in the third quarter of 2024, with top-line data on track to be announced in the first quarter of 2025. This trial also includes a 6-month open-label extension which is on track for completion of last patient visit in the first quarter of 2025.

Cash Position

Cash, cash equivalents, other financial assets and marketable securities were $182.6 million as of December 31, 2024, compared to cash, cash equivalents, other financial assets and marketable securities of $222.7 million as of December 31, 2023.

About GH Research PLC

GH Research PLC is a clinical-stage biopharmaceutical company dedicated to transforming the treatment of psychiatric and neurological disorders. GH Research PLC's initial focus is on developing its novel and proprietary mebufotenin therapies for the treatment of patients with treatment-resistant depression (TRD).

About GH001

Our lead product candidate, GH001, is formulated for mebufotenin administration via a proprietary inhalation approach. Based on the observed clinical activity in our completed phase 1/2 GH001-TRD-102 trial, where 87.5% of patients with TRD achieved ultra-rapid remission with our GH001 individualized single-day dosing regimen in the Phase 2 part of the trial, we believe that GH001 has the potential to change the way TRD is treated today.

About Notation for Trial Timepoints

In relation to our clinical trials we have previously referred to the day of dosing as Day 0 (D0), the day after dosing as Day 1 (D1), and the seventh day after dosing as Day 7 (D7). In this press release, and going forward, we shall refer to the day of dosing as Day 1 (D1), the day after dosing as Day 2 (D2) and the seventh day after dosing as Day 8 (D8).

Forward-Looking Statements

This press release contains statements that are, or may deemed to be, forward-looking statements. All statements other than statements of historical fact included in this press release, including statements regarding our future results of operations and financial position, business strategy, product candidates, research pipeline, ongoing and currently planned preclinical studies and clinical trials, regulatory submissions and approvals, research and development costs, timing and likelihood of success, as well as plans and objectives of management for future operations are forward-looking statements. Forward-looking statements appear in a number of places in this press release and include, but are not limited to, statements regarding our intent, belief or current expectations. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. Such statements are subject to risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including, but not limited to, those described in our filings with the U.S. Securities and Exchange Commission. No assurance can be given that such future results will be achieved. Such forward-looking statements contained in this document speak only as of the date of this press release. We expressly disclaim any obligation or undertaking to update these forward-looking statements contained in this press release to reflect any change in our expectations or any change in events, conditions, or circumstances on which such statements are based unless required to do so by applicable law. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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GH
RESEARCH
Corporate Presentation
GH Research PLC (NASDAQ: GHRS)
January 2025
2025© GH Research PLC
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Disclaimer Regarding Forward-Looking Statements

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This presentation does not constitute an offer to sell or the solicitation of an offer to buy securities, nor shall there be any sale of securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

This presentation contains forward-looking statements, all of which are qualified in their entirety by this cautionary statement. Many of the forward-looking statements contained herein can be identified by the use of forward-looking words such as "may", "anticipate", "believe", "could", "expect", "should", "plan", "intend", "estimate", "will", "potential" and "ongoing", among others, although not all forward-looking statements contain these identifying words.

Any statements contained herein that do not describe historical facts are forward-looking statements that are based on management's expectations and are subject to certain factors, risks and uncertainties that may cause actual results, outcomes, timing and performance to differ materially from those expressed or implied by such statements. These factors, risks and uncertainties include, but are not limited to: the costs and uncertainties associated with GH Research's research and development efforts; the inherent uncertainties associated with the conduct, timing and results of nonclinical and clinical studies of GH Research's product candidates; GH Research's expectations related to the clinical hold on the GH001 IND, including plans and expectations for progressing any nonclinical programs and any other work to lift the clinical hold and the timing required to lift such clinical hold; GH Research's ability to obtain, maintain, enforce and defend issued patents; the adequacy of GH Research's capital resources, the availability of additional funding and GH Research's cash runway; and other factors, risks and uncertainties described in GH Research's filings with the U.S. Securities and Exchange Commission.

Except as otherwise noted, these forward-looking statements speak only as of the date of this presentation, and GH Research undertakes no obligation to update or revise any of such statements to reflect events or circumstances occurring after this presentation. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond GH Research's control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in any such forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. GH Research cautions you not to place undue reliance on the forward-looking statements contained in this presentation.

Pipeline

PROGRAMS	INDICATION	PRECLINICAL	PHASE 1	PHASE 2a	PHASE 2b	PHASE 3	CURRENT STATUS	MILESTONES
GH001 *Mebufotenin for inhalation administration*	Treatment-Resistant Depression (TRD)						Phase 2b RDBPC DB phase completed Phase 1 PK trial with proprietary device ongoing	Phase 2b OLE completion in Q1 Phase 1 PK trial completion Lift FDA clinical hold in the US
GH002 *Mebufotenin for i.v. administration*	Psychiatric or Neurological Disorder						Phase 1 HV trial completed	Completed
OTHER INDICATIONS								
GH001	Postpartum Depression (PPD)						Phase 2a POC	Completed
	Bipolar II Disorder* (BDII)						Phase 2a POC	Completed

Cash, cash equivalents, other financial assets and marketable securities were $182.6 million as of December 31, 2024

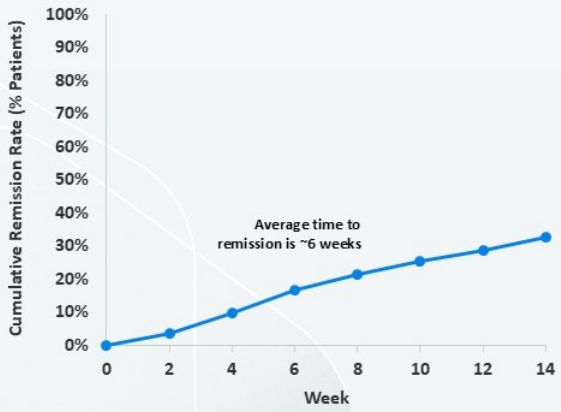
Complete Ongoing

**Bipolar II disorder with a current major depressive episode*
Abbreviations: i.v. = intravenous; RDBPC = Randomized, Double-Blind, Placebo-Controlled; PK = Pharmacokinetics; OLE = Open-Label Extension; FDA = U.S. Food and Drug Administration; HV = Healthy Volunteer; POC = Proof-of-Concept

The Problem for Patients with Depression

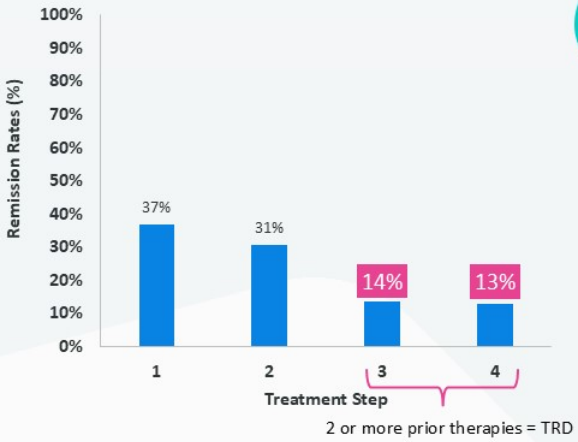
Established Therapies are Slow-Acting

(STAR*D study, Remission Rate Over Time, Treatment Step 1 = Citalopram)



... Remission Rates in TRD < 15%

(STAR*D study, Remission Rates Treatment Steps 1 to 4)



Adapted from Trivedi et al., Am J Psychiatry 2006 and Rush et al., Am J Psychiatry 2006
Abbreviations: TRD = Treatment-Resistant Depression

Large and Open Depression Market in the EU and US

First Line MDD
- Diagnosed: ~**48M**
  - Treated (pharmacotherapy ± psychotherapy): ~**24M**

Second Line MDD
- Non-response to first line: ~**13M**

Treatment-Resistant Depression (TRD)
- Non-response to two prior lines: ~**9M**

Patients cycle through ineffective therapies for TRD

Company estimates based on sources 1,2,3
Abbreviations: MDD = Major Depressive Disorder

Sources: 1) NIMH major depression statistics; 2) Wittchen et al., Eur Neuropsychopharmacol 2011; 3) Rush et al., Am J Psychiatry 2006

SPRAVATO® has been established as a $1-5Bn drug in interventional psychiatry

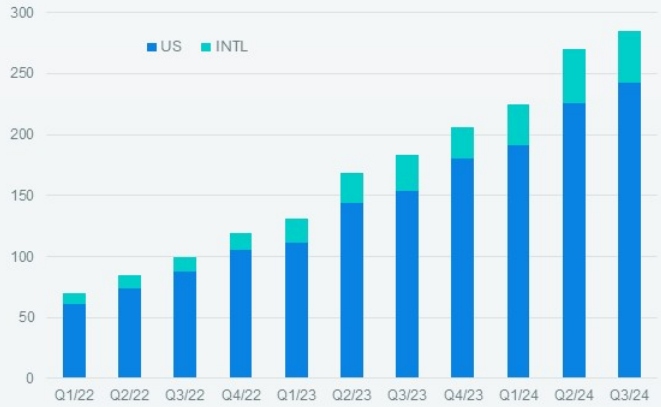
-4.0 MADRS Points Mean Δ to Control Group

(TRANSFORM-2 Trial Primary Endpoint, Difference of LS Means)

Estimated **40 administration visits** per year:

- In-clinic
- Mandatory 2-hour post-dose monitoring
- No driving or operating heavy machinery until next day
- No psychotherapeutic intervention required

Approved for TRD in Conjunction with an Oral AD



Quarterly sales, $M; Estimated annual WAC of **$32,400**

Abbreviations: MADRS = Montgomery–Åsberg Depression Rating Scale; TRD = Treatment-Resistant Depression; LS = Least Square; AD = Antidepressant; WAC = Wholesale Acquisition Cost
[a]Baseline mean MADRS = 37

Sources: 1) Popova et al., Am J Psychiatry 2019; 2) Institute for Clinical and Economic Review (ICER) Final Evidence Report, 2019; 3) SPRAVATO® Prescribing Information; 4) Johnson & Johnson Quarterly Earnings Reports, 2022-2024

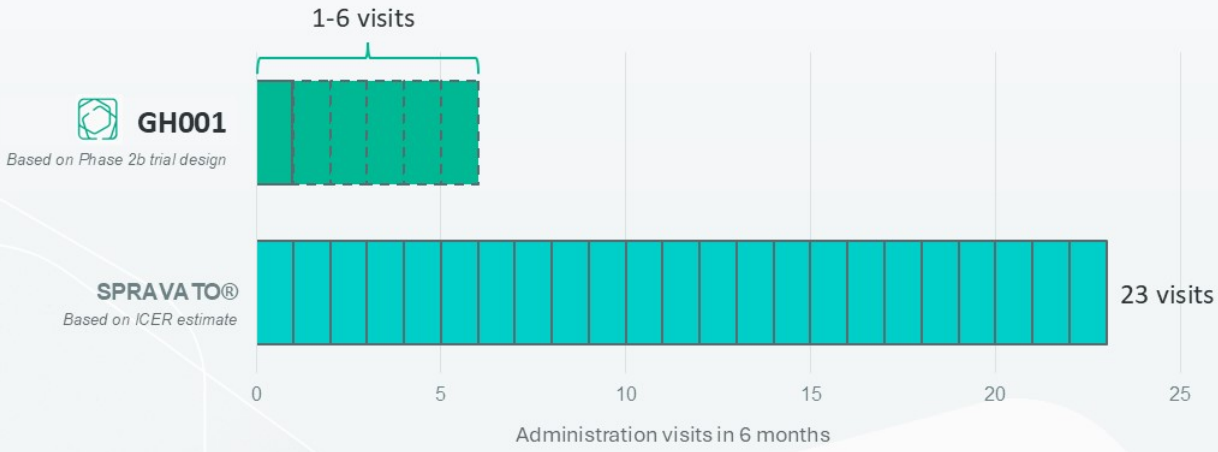
The GH001 Aspirational Profile

	GH001	SPRAVATO®
Maximize **Day 2 Response Rate**	✓✓✓✓	✓
Optimize **Day 8 Primary Endpoint**	✓✓✓✓	✓
Optimize **Fewer Administration Visits / Greater Durability**	✓✓✓✓	✓
Minimize **Post-Discharge Restrictions**	None	No driving or operating machinery until the next day after a restful sleep

GH001 features based on clinical data generated to-date, and treatment model as per the protocol currently being investigated in GH001-TRD-201
SPRAVATO features based on Ph3 clinical trial data, and treatment model as per FDA label (1) and Johnson & Johnson Access, Coding and Reimbursement Guidelines (2)

Sources: 1) SPRAVATO® Prescribing Information; 2) Johnson & Johnson Spravato Access, Coding and Reimbursement Guide

>75% reduction in administration visits with GH001

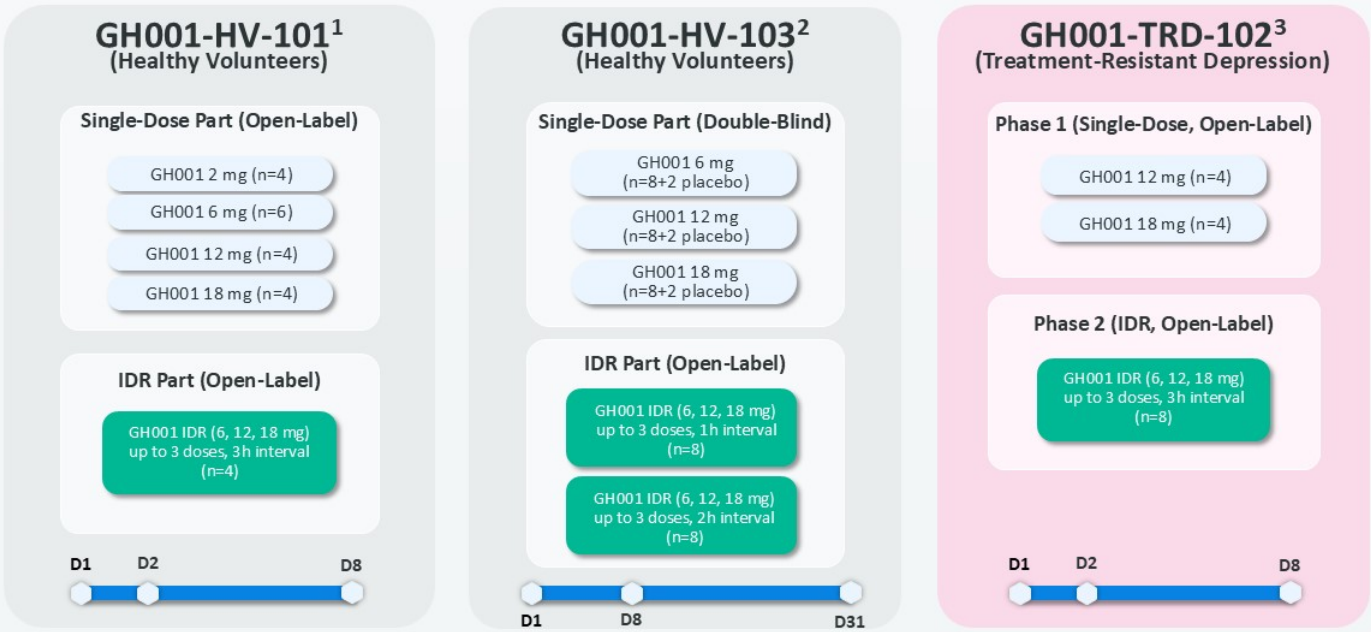


Assumptions:
SPRAVATO®: Assumes 23 administration visits, as per standard initiation protocol of 8 & 4 sessions in months 1 & 2, respectively, and ICER assumed maintenance treatment frequency of 2.86 treatments per month for months 3-6 (1,2,3);
Note: To-date, no head-to-head comparisons of any competing products to any of our product candidates in any clinical trial have been completed

Abbreviations: ICER = Institute for Clinical and Economic Review

Sources: 1) Johnson & Johnson Spravato Access, Coding and Reimbursement Guide; 2) ICER Spravato Final Evidence Report; 3) Janssenscience.com, Dosage and Administration of Spravato, Duration of Therapy

Completed GH001 Phase 1 Clinical Trials: Trial Design

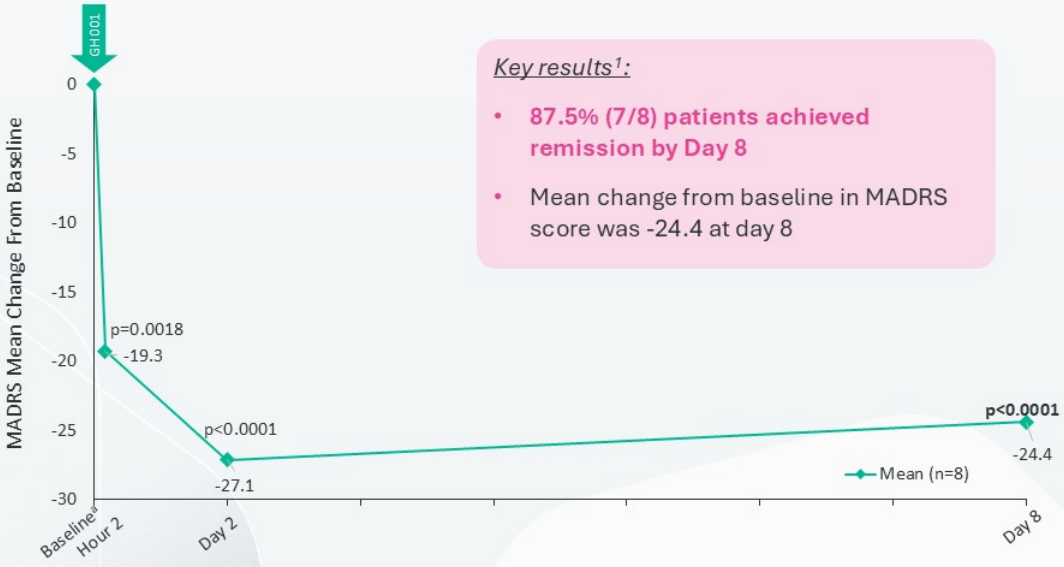


Abbreviations: D = Day; h = Hour; IDR = Individualized dosing regimen; TRD = Treatment-Resistant Depression.

Sources: 1) Reckweg JT, et al. Eur Psychiatry. 2022; 2) GH Research, Data on file; 3). Reckweg JT, et al. Front. Psychiatry. 2023

GH001-TRD-102 | Efficacy of the GH001 IDR

Phase1/2 trial of GH001 in TRD (completed)



Key results[1]:

- **87.5% (7/8) patients achieved remission by Day 8**
- Mean change from baseline in MADRS score was -24.4 at day 8

Abbreviations: MADRS = Montgomery–Åsberg Depression Rating Scale; IDR = Individualized dosing regimen

[a]Baseline mean MADRS = 32.

Sources: 1) Reckweg JT, et al. Front. Psychiatry. 2023.

Safety and Tolerability of GH001 in Completed Phase 1 Trials

GH001-HV-101[1], GH001-HV-103[2], and GH001-TRD-102[3]

Safety Parameters, n (% of population)	Overall Population (n=78)
Any TEAE	50 (64%)
Headache	19 (24%)
Anxiety	12 (15%)
Nausea	8 (10%)
Fatigue	7 (9%)
Any Serious AE	0 (0%)
Any AE leading to trial/drug withdrawal	0 (0%)
Death	0 (0%)

TEAEs by Severity, no. of events	Overall Population (n=78)
Total number of TEAEs	105
Mild TEAEs	97
Moderate TEAEs	8
Severe TEAEs	0

- Overall, **inhalation of GH001 was well tolerated** across completed trials with **no severe or serious adverse events** reported and with TEAEs observed in 64.1% of subjects
- 92.4% of TEAEs were **mild in severity**
- **No noteworthy changes in vital signs were observed**; transient increases in heart rate and blood pressure shortly after GH001 administration were not clinically significant
- **Safety assessments**, including laboratory analyses, psychiatric scales, electrocardiogram, and cognitive function tests **showed no clinically meaningful changes**

Abbreviations: AE = Adverse event; TEAE = Treatment-emergent adverse event.

Sources: 1) Reckweg JT, et al. Eur Psychiatry. 2022; 2) GH Research, Data on file; 3) Reckweg JT, et al. Front. Psychiatry. 2023.

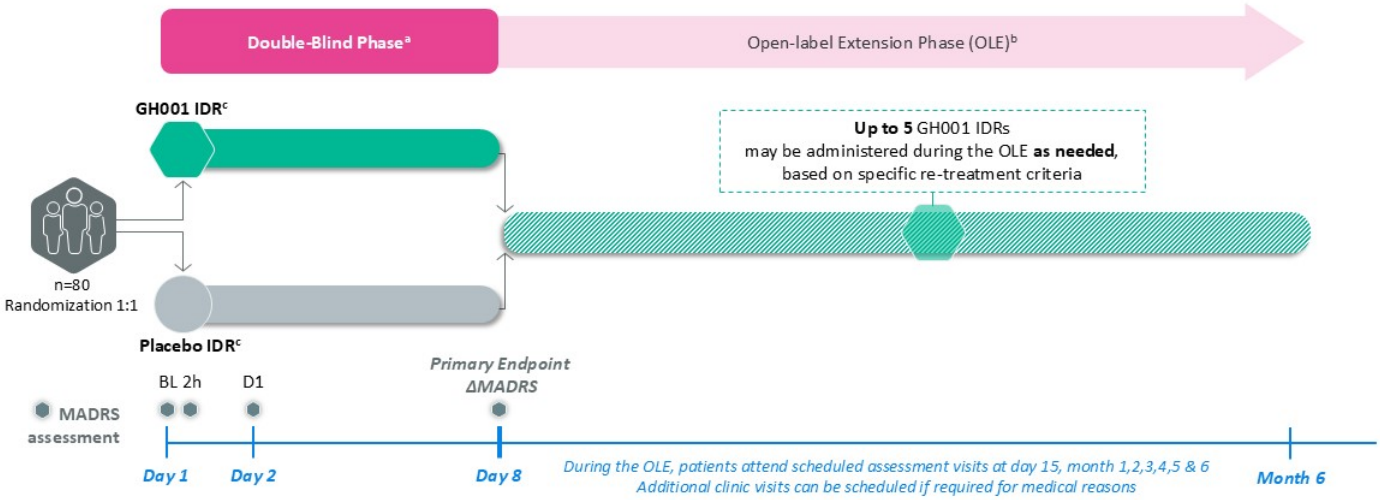
Phase 2b Trial in Treatment-Resistant Depression GH001-TRD-201

(Initiated)

EudraCT Number: 2022-000574-26

GH001-TRD-201 Trial Design

Phase 2b trial in patients with TRD, n=80[1]



Abbreviations: D = Day; h = Hour; BL = Baseline; IDR = Individualized dosing regimen; M = Month; MADRS = Montgomery–Åsberg Depression Rating Scale; OLE = Open-label extension; TRD = Treatment-resistant depression.

[a] The double-blind phase was a fixed duration of 7 days (± 1 day) after an IDR with visits on D1, D2 and D8. After the double-blind phase there was a variable duration until a potential GH001 IDR in the OLE.

[b]During the OLE, additional clinic visits can be scheduled if required for medical reasons. [c]The GH001 IDR consists of up to 3 increasing doses (6, 12, 18 mg) and the placebo IDR consists of up to three placebo doses. As in previously completed trials, the GH001-TRD-201 trial will be conducted under the supervision of a healthcare provider, but without any planned psychotherapeutic interventions before, during, or after dosing.

Sources: 1) NCT05800860. (2024). A Trial of GH001 in Patients With Treatment-Resistant Depression. ClinicalTrials.gov. Accessed August 23, 2024.

Three-Layer Protection Strategy

LAYER 1: REGULATORY EXCLUSIVITY

FDA:	5 years	(+2.5 years paragraph IV stay)
EMA:	10 years	(+1 year for new indication)

LAYER 2: PATENTS

Granted patents and patent applications relating to mebufotenin, including:

- Novel uses in various disorders (including inhaled, nasal, buccal, sublingual, i.v., i.m., s.c. routes)
- Novel aerosol compositions of matter
- Novel manufacturing methods and novel salt forms
- Novel device-related aspects

LAYER 3: TECHNICAL

Complex bioequivalence for systemically-acting inhalation/intranasal products with high intra- and inter-subject variability

Abbreviations: FDA = U.S. Food and Drug Administration; EMA = European Medicines Agency; i.v. = intravenous; i.m. = intramuscular; s.c. = subcutaneous

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