Corporate Presentation

GH Research PLC (NASDAQ: GHRS)

January 2025

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Pipeline

PROGRAMS	INDICATION	Stage of Development: 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

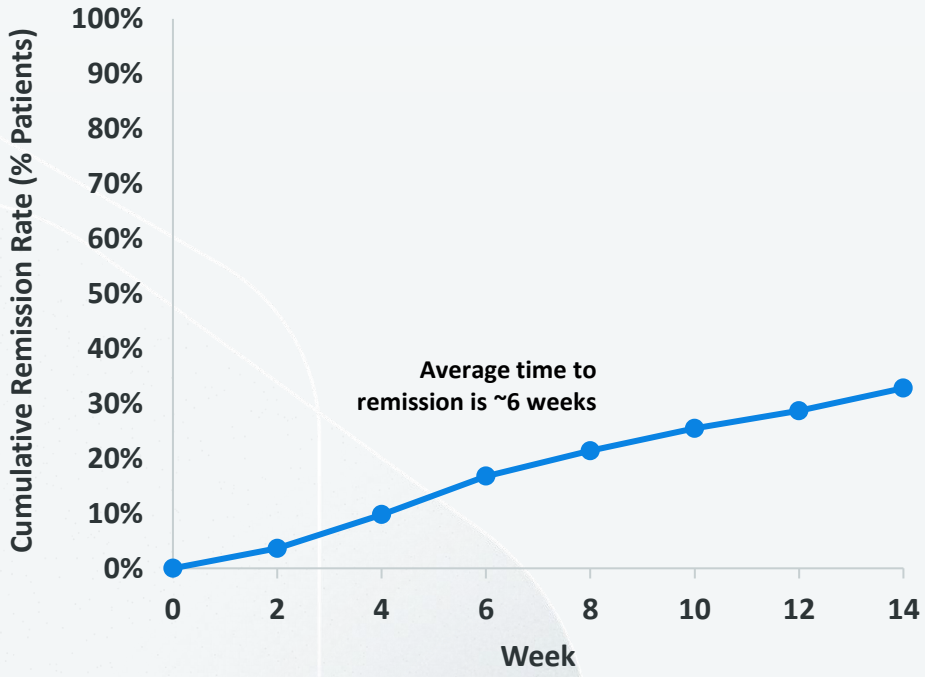
Complete Ongoing

**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

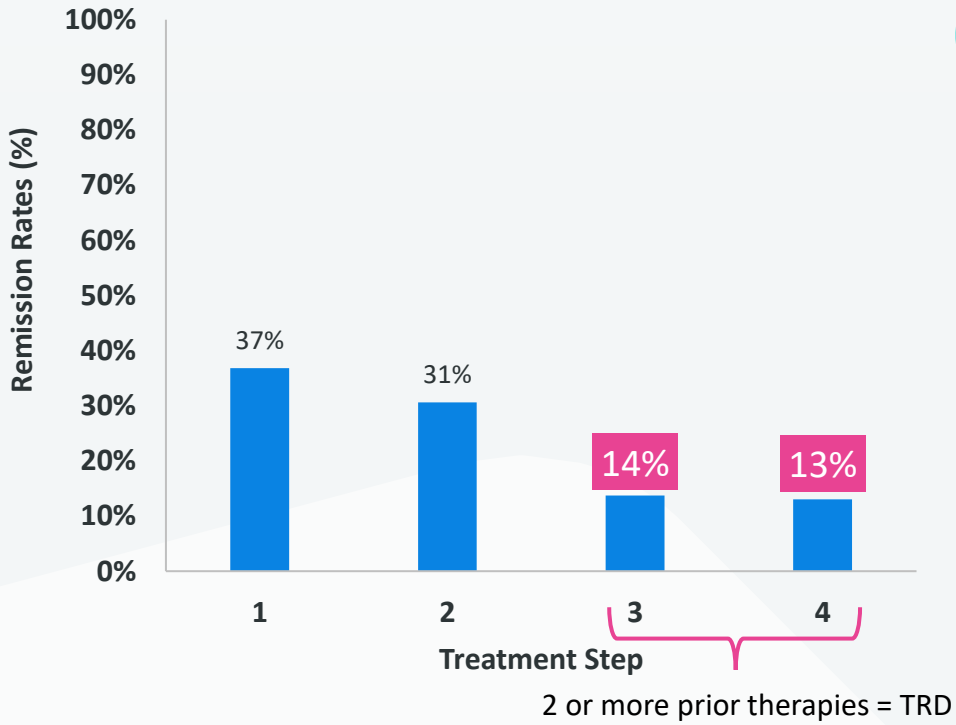
Established Therapies are Slow-Acting

(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

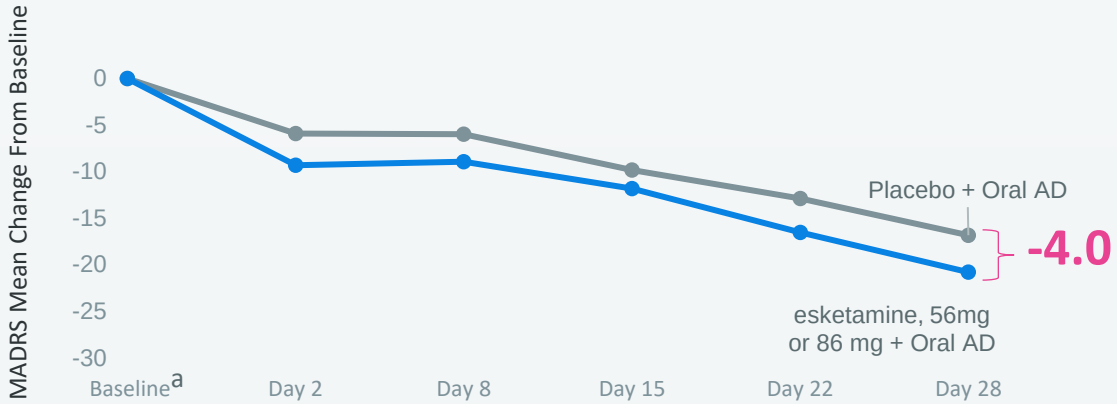
Company estimates based on sources 1,2,3
Abbreviations: MDD = Major Depressive Disorder

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

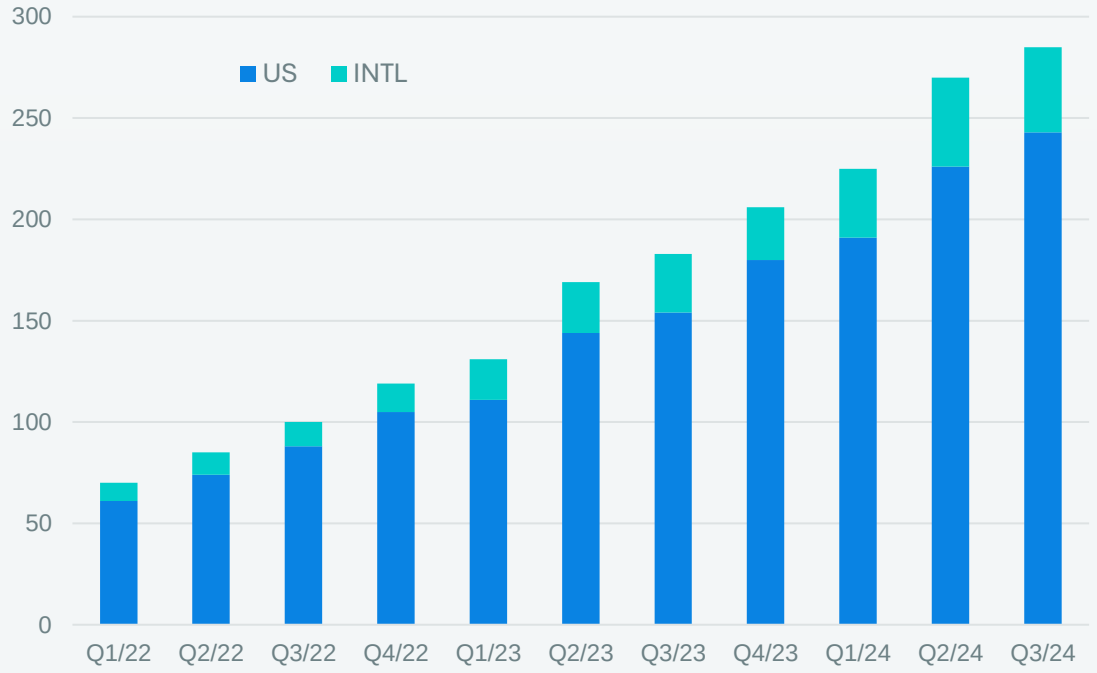
(TRANSFORM-2 Trial Primary Endpoint, Difference of LS Means)



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

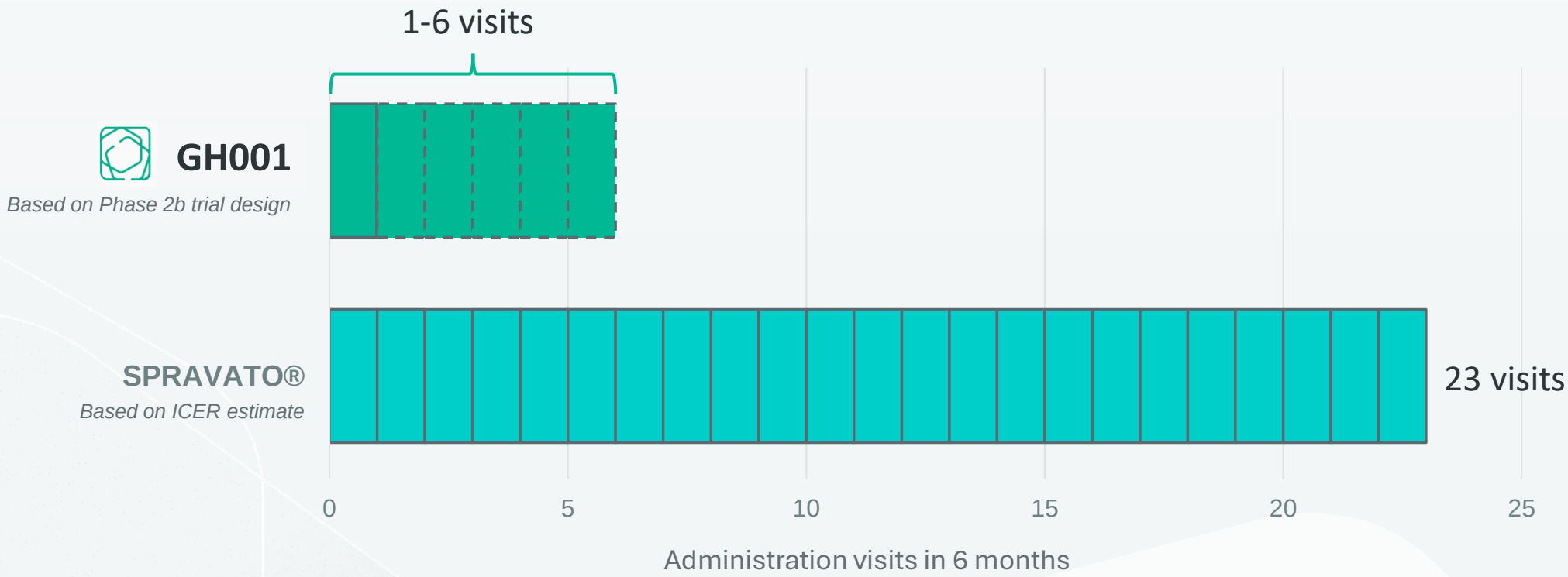
The GH001 Aspirational Profile

	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

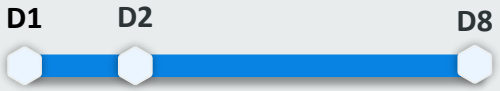
GH001-HV-101[1]
(Healthy Volunteers)

Single-Dose Part (Open-Label)

- GH001 2 mg (n=4)
- GH001 6 mg (n=6)
- GH001 12 mg (n=4)
- GH001 18 mg (n=4)

IDR Part (Open-Label)

- GH001 IDR (6, 12, 18 mg) up to 3 doses, 3h interval (n=4)



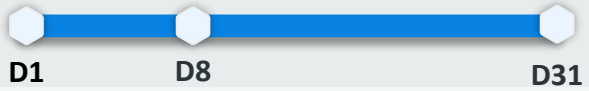
GH001-HV-103[2]
(Healthy Volunteers)

Single-Dose Part (Double-Blind)

- GH001 6 mg (n=8+2 placebo)
- GH001 12 mg (n=8+2 placebo)
- GH001 18 mg (n=8+2 placebo)

IDR Part (Open-Label)

- GH001 IDR (6, 12, 18 mg) up to 3 doses, 1h interval (n=8)
- GH001 IDR (6, 12, 18 mg) up to 3 doses, 2h interval (n=8)



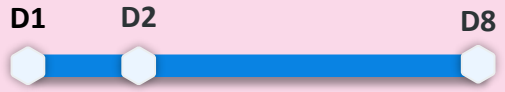
GH001-TRD-102[3]
(Treatment-Resistant Depression)

Phase 1 (Single-Dose, Open-Label)

- GH001 12 mg (n=4)
- GH001 18 mg (n=4)

Phase 2 (IDR, Open-Label)

- GH001 IDR (6, 12, 18 mg) up to 3 doses, 3h interval (n=8)

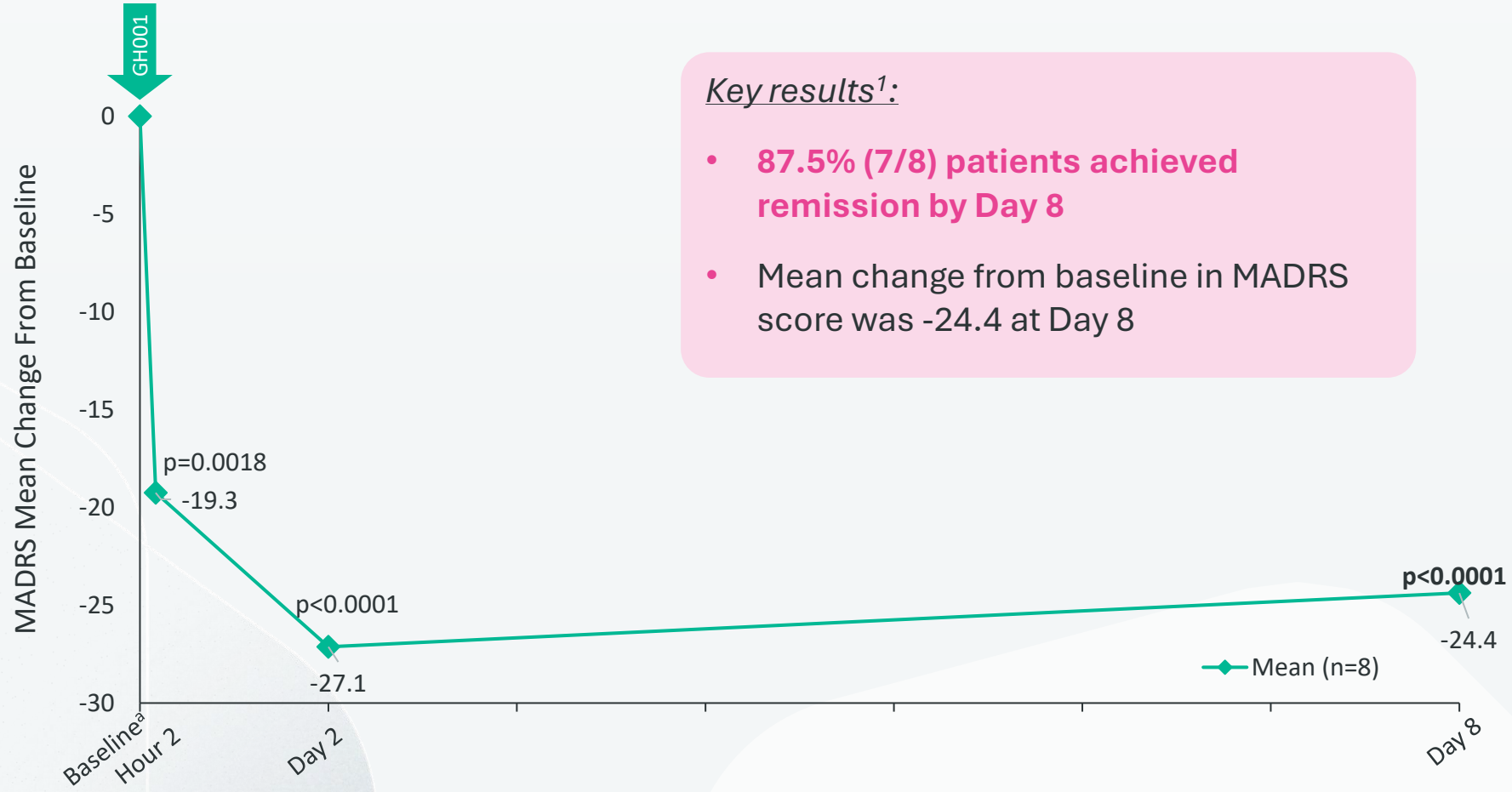


Abbreviations: D = Day; h = Hour; IDR = Individualized dosing regimen; TRD = Treatment-Resistant Depression.

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.

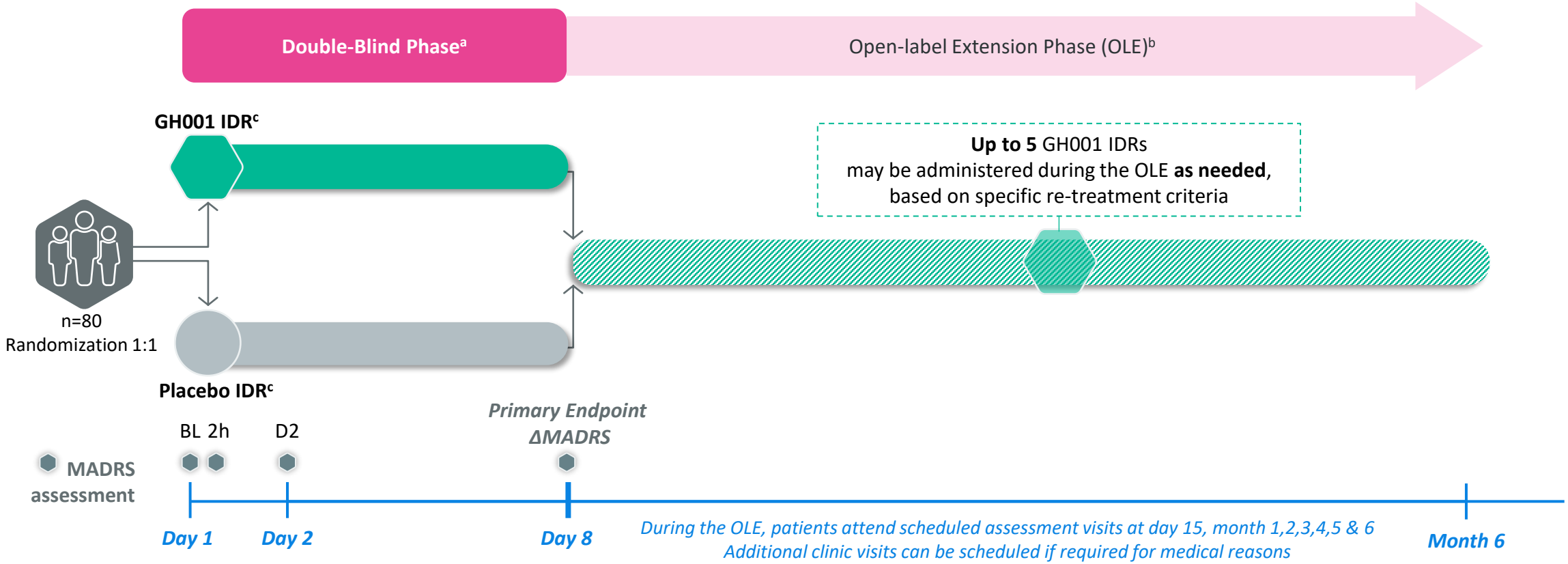
Phase 2b Trial in Treatment-Resistant Depression GH001-TRD-201

(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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