GH Research

Corporate Presentation

GH Research PLC (NASDAQ: GHRS)

January 2023

Disclaimer Regarding Forward-Looking Statements

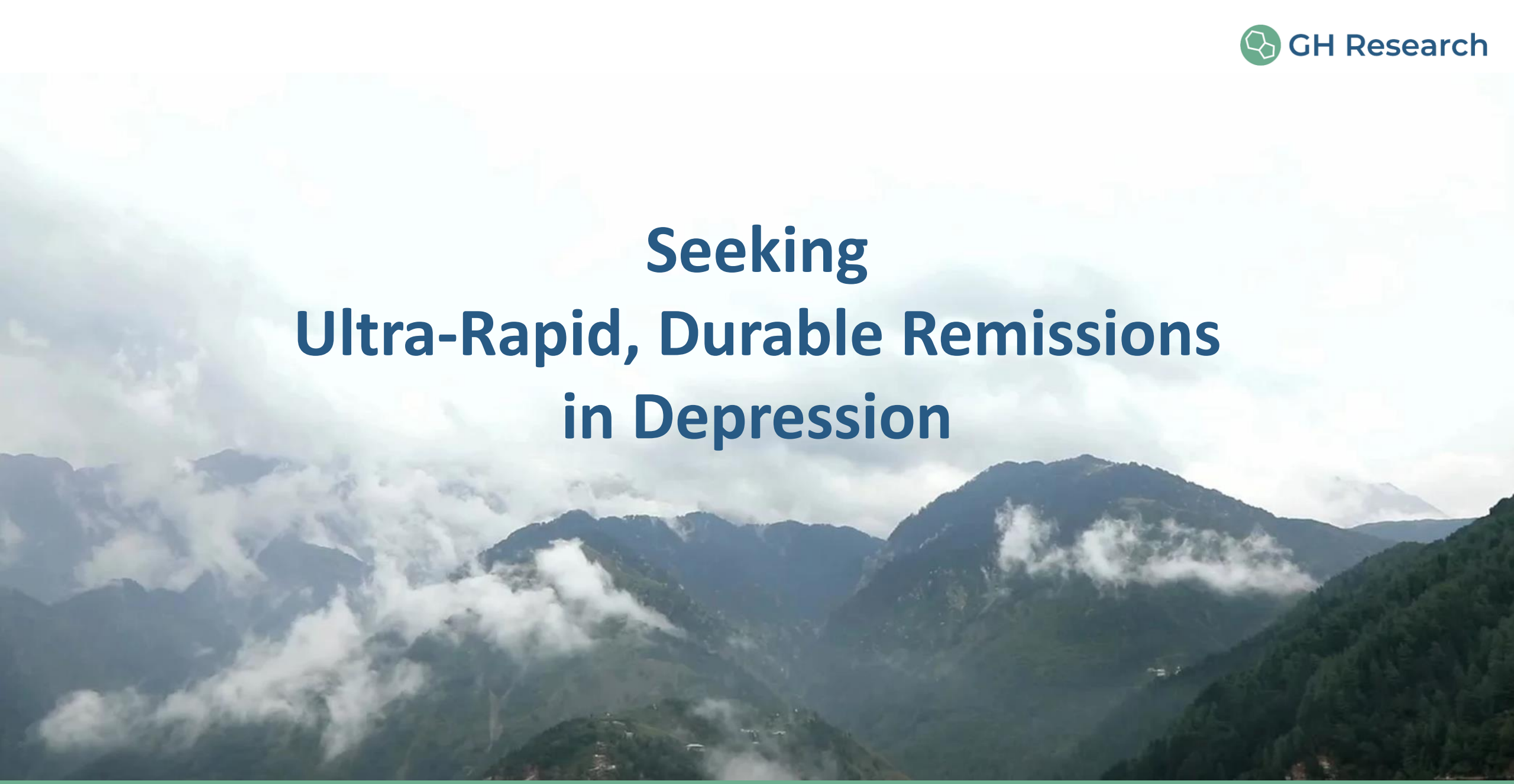
This presentation has been prepared by GH Research PLC ("GH Research") for informational purposes only and not for any other purpose. Nothing contained in this presentation is, or should be construed as, a recommendation, promise or representation by the presenter or GH Research or any director, employee, agent, or adviser of GH Research. This presentation does not purport to be all-inclusive or to contain all of the information you may desire.

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 these 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.

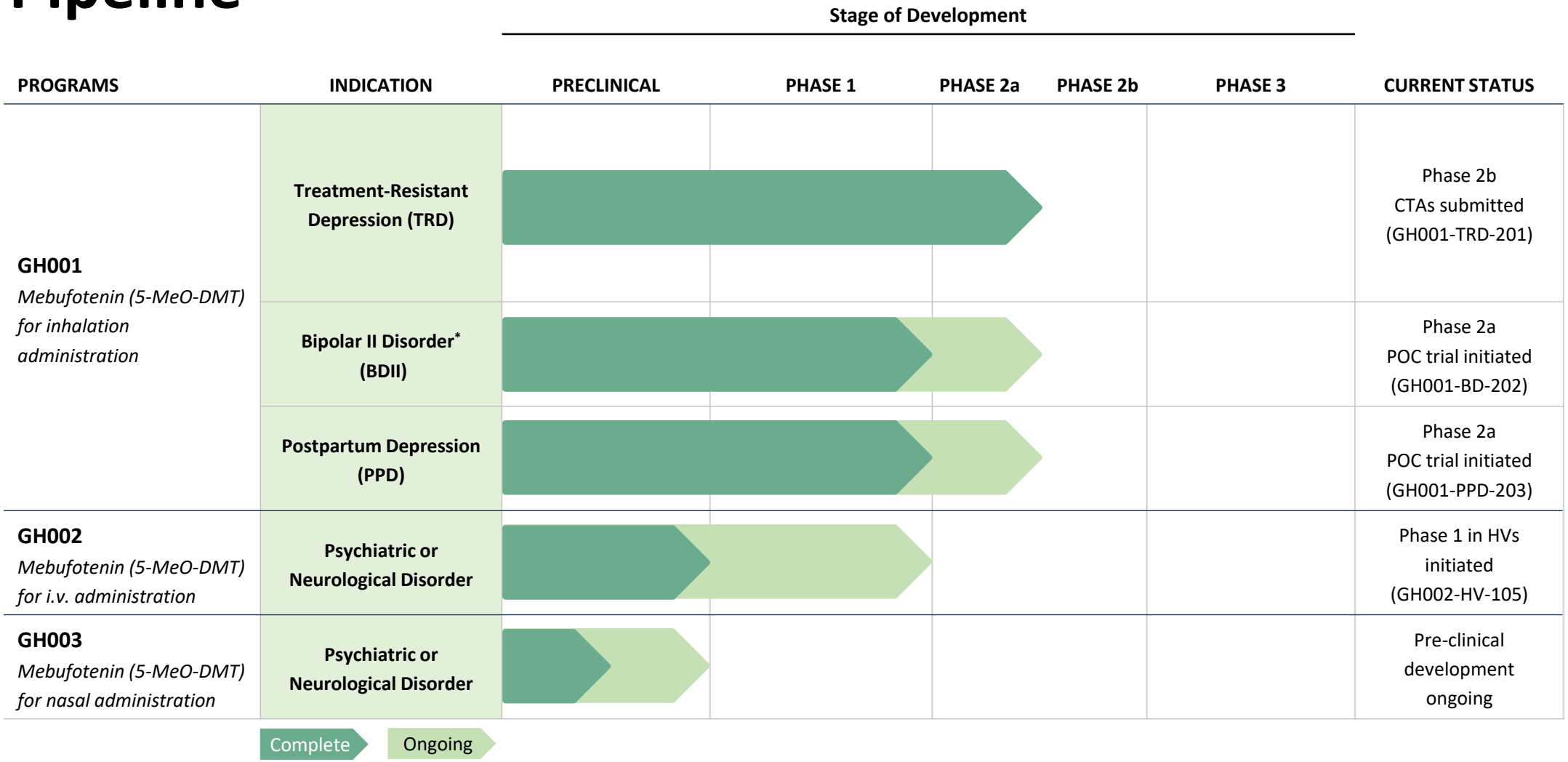
Any statements contained herein that do not describe historical facts are forward-looking statements that are based on management's expectations and are subject to certain factors, risks and uncertainties that may cause actual results, outcomes, timing and performance to differ materially from those 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 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.



Seeking
Ultra-Rapid, Durable Remissions in Depression

Pipeline



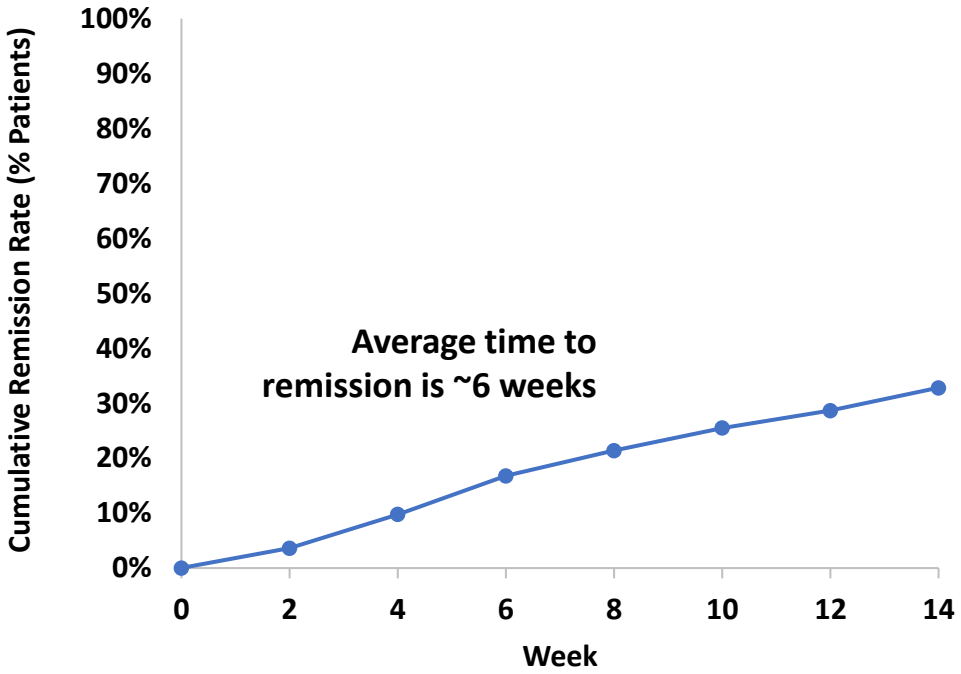
Bipolar II disorder with a current major depressive episode

5-MeO-DMT, 5-Methoxy-N,N-Dimethyltryptamine; i.v., intravenous; CTA, Clinical Trial Application; POC, Proof-of-Concept; HV, Healthy Volunteer

The Problem for Patients with Depression

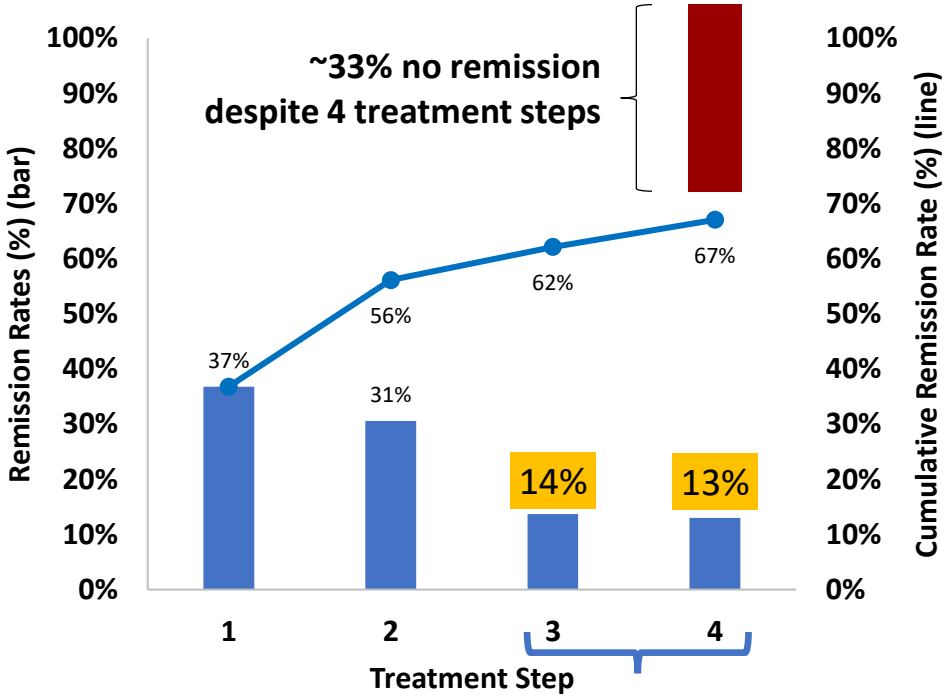
Established Therapies are Slow-Acting

(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)



2 or more prior therapies = TRD

Adapted from Trivedi et al., Am J Psychiatry 2006 and Rush et al., Am J Psychiatry 2006
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)

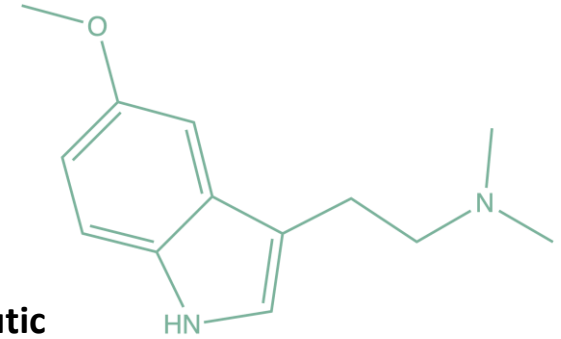
- Non-response to two prior lines: **~9M**

Patients cycle through ineffective therapies for TRD

*Company estimates based on: https://www.nimh.nih.gov/health/statistics/major-depression.shtml; Wittchen et al., The size and burden of mental disorders and other disorders of the brain in Europe 2010, European Neuropsychopharmacology (2011); Rush et al., Acute and Longer-Term Outcomes in Depressed Outpatients Requiring One or Several Treatment Steps: A STAR*D Report, Am J Psychiatry 2006*
MDD, Major Depressive Disorder

Mebufotenin (5-MeO-DMT) and GH001

- Mebufotenin (5-Methoxy-N,N-Dimethyltryptamine, 5-MeO-DMT)
  - Naturally-occurring psychoactive substance from tryptamine class
  - **Highly potent** agonist on 5-HT1A and 5-HT2A receptors
  - **High propensity to induce peak experiences (PE), which may be a surrogate marker for therapeutic effects**



Mebufotenin (5-MeO-DMT)

- GH001 (Mebufotenin administration via a proprietary pulmonary inhalation approach)
  - **Psychoactive effects with ultra-rapid onset** (within seconds) **and short duration** (5 to 30 min)
  - **Intraday individualized dosing regimen (IDR)** for **maximization of ultra-rapid and durable remissions**
  - **Single visit initial treatment,** with no structured psychotherapy
  - Potential for **convenient and infrequent retreatment**

Foundational IP

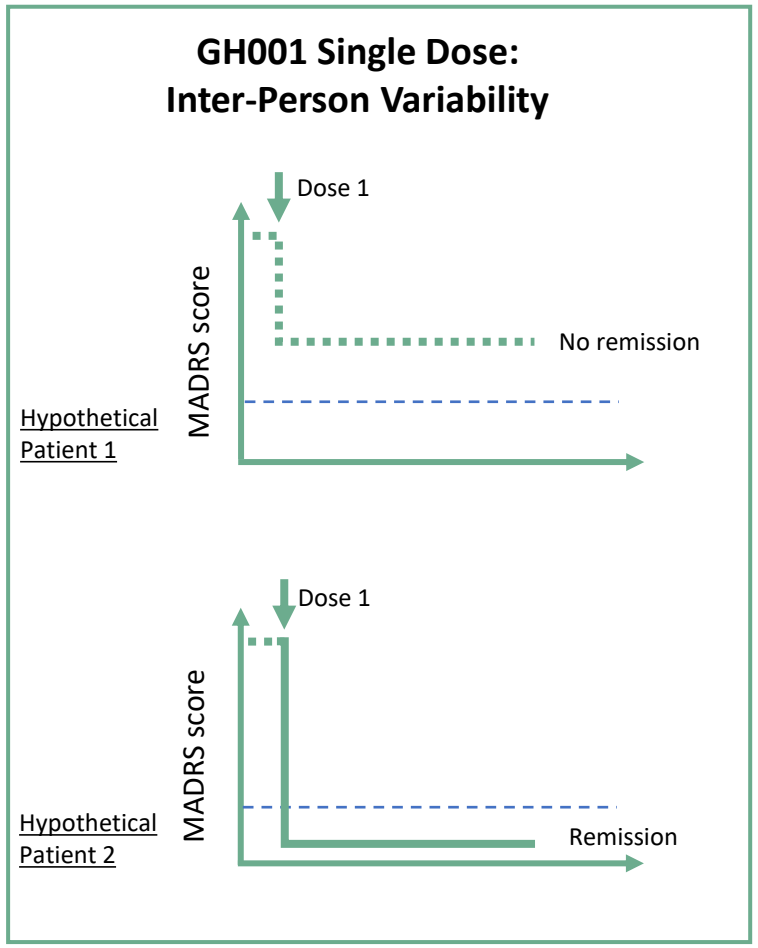

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)
(19) World Intellectual Property Organization
International Bureau
(43) International Publication Date
27 August 2020 (27.08.2020)
WIPO | PCT
(10) International Publication Number
WO 2020/169850 A1

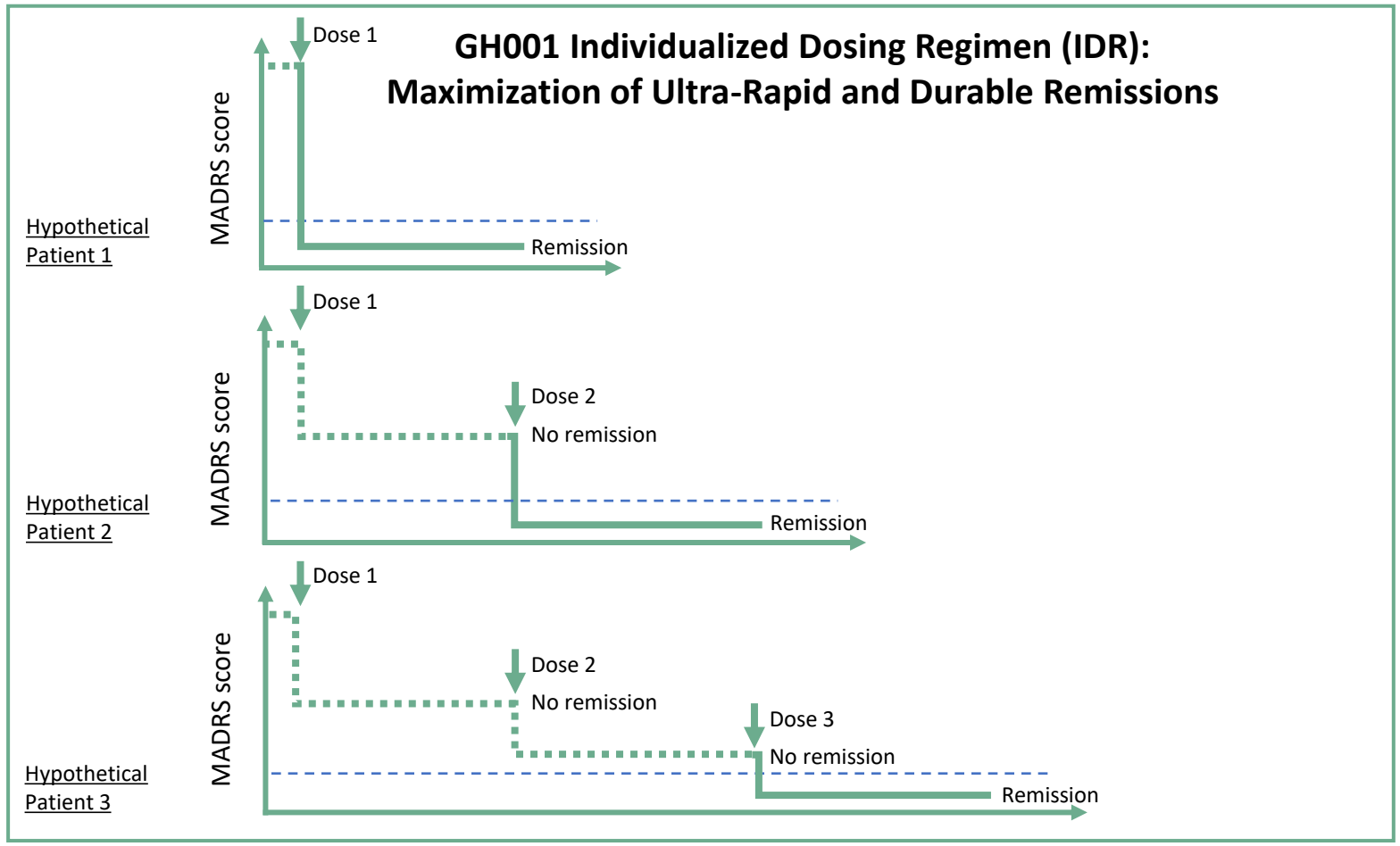
(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)
(19) World Intellectual Property Organization
International Bureau
(43) International Publication Date
27 August 2020 (27.08.2020)
WIPO | PCT
(10) International Publication Number
WO 2020/169851 A1

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)
(19) World Intellectual Property Organization
International Bureau
(43) International Publication Date
02 September 2021 (02.09.2021)
WIPO | PCT
(10) International Publication Number
WO 2021/170614 A1

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)
(19) World Intellectual Property Organization
International Bureau
(43) International Publication Date
24 December 2020 (24.12.2020)
WIPO | PCT
(10) International Publication Number
WO 2020/254584 A1

GH001 – Individualized Dosing Regimen (IDR) for Maximization of Ultra-Rapid and Durable Remissions





MADRS, Montgomery-Åsberg Depression Rating Scale

Phase 1 Trial in Healthy Volunteers
GH001-HV-101

(Completed)

Clinicaltrials.gov ID: NCT04640831

Design of Phase 1 Trial in Healthy Volunteers (GH001-HV-101)

Part A (Single Dose)

HV (n=18)

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

Primary Endpoint:

- Safety until day 7
- Peak Experience Scale (PE Scale)[1]

Part B (IDR)

HV (n=4)

GH001 IDR **6, 12, 18 mg** to achieve PE (up to 3 doses, 3h interval)

Primary Endpoint:

- Safety until day 7
- Peak Experience Scale (PE Scale)[1]

Key Assessments	GH001 Administration	Day 1	Day 7
	Safety PE Scale Cognitive function	Safety	Safety Cognitive function

HV, Healthy Volunteer; PE, Peak Experience; IDR, Individualized Dosing Regimen

[1]*The PE Scale averages answers scored by the subject by marking a visual analogue scale between 0 and 100 for the following three questions: 1. How intense was the experience; 2. To what extent did you lose control; 3. How profound (i.e., deep and significant) was the experience?*

Part A (Single Dose) and Part B (IDR) – Safety

Study Safety Group review

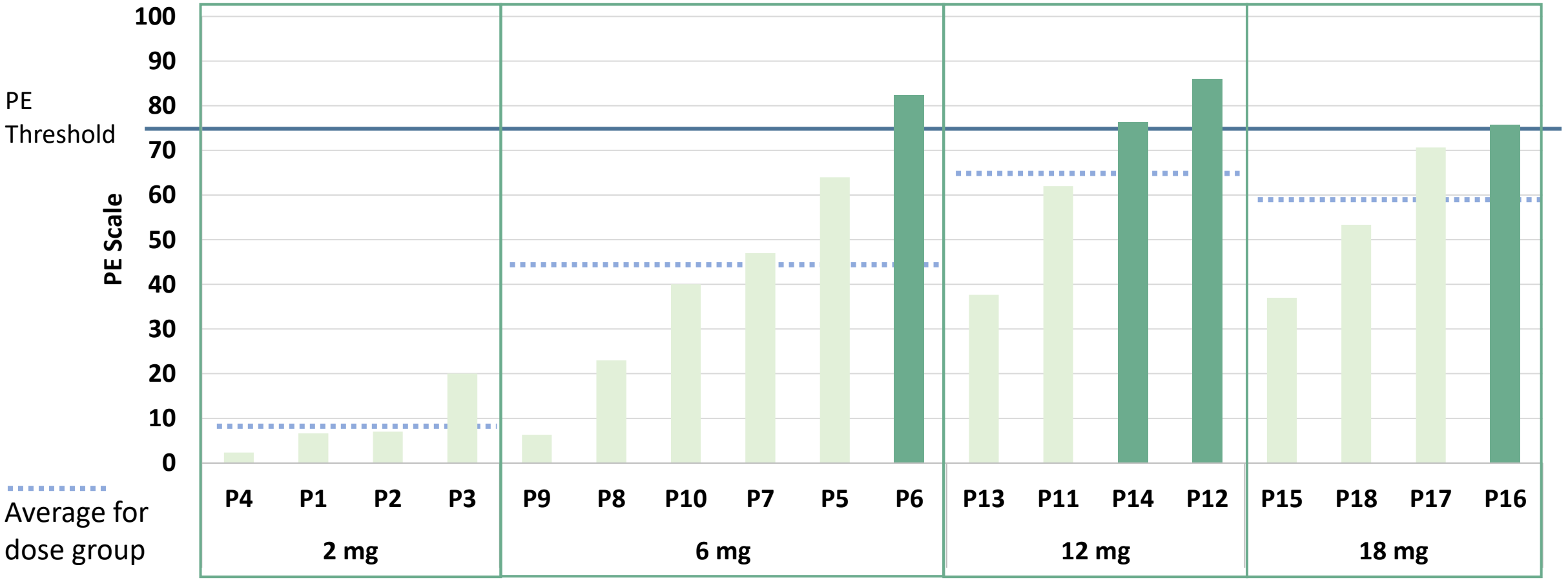
- **No SAEs**
- **All ADRs mild, except two moderate (*)**
- **All ADRs resolved spontaneously**
- **Inhalation well-tolerated**
- No noteworthy changes in vital parameters, except for temporary, non-clinically relevant increase in heart rate and blood pressure shortly after administration of GH001
- No clinically significant changes in safety laboratory analyses, psychiatric safety assessments or measures of cognitive function

ADRs	Part A (Single Dose)				Part B (IDR)
	2 mg (n=4)	6 mg (n=6)	12 mg (n=4)	18 mg (n=4)	IDR[1] (n=4)
MedDRA Preferred Term	Number of Events				
Abnormal dreams				1	
Anxiety		1	1		
Clumsiness		1			
Confusional state		1			
Euphoric mood		1			
Fatigue				1	1*
Feeling hot		1			
Flashback				1	
Hallucination				1	
Head discomfort					1
Headache		2		1	1
Heart rate increased			1*		
Hyperacusis				1	
Insomnia				1	
Mental fatigue				1	
Nausea	2	1		1	2
Vision blurred	1				

SAE, Serious Adverse Event; ADR, Adverse Drug Reaction, an adverse event with a relationship code to the investigational product of definite, probable, or possible, or where code is missing; IDR, Individualized Dosing Regimen

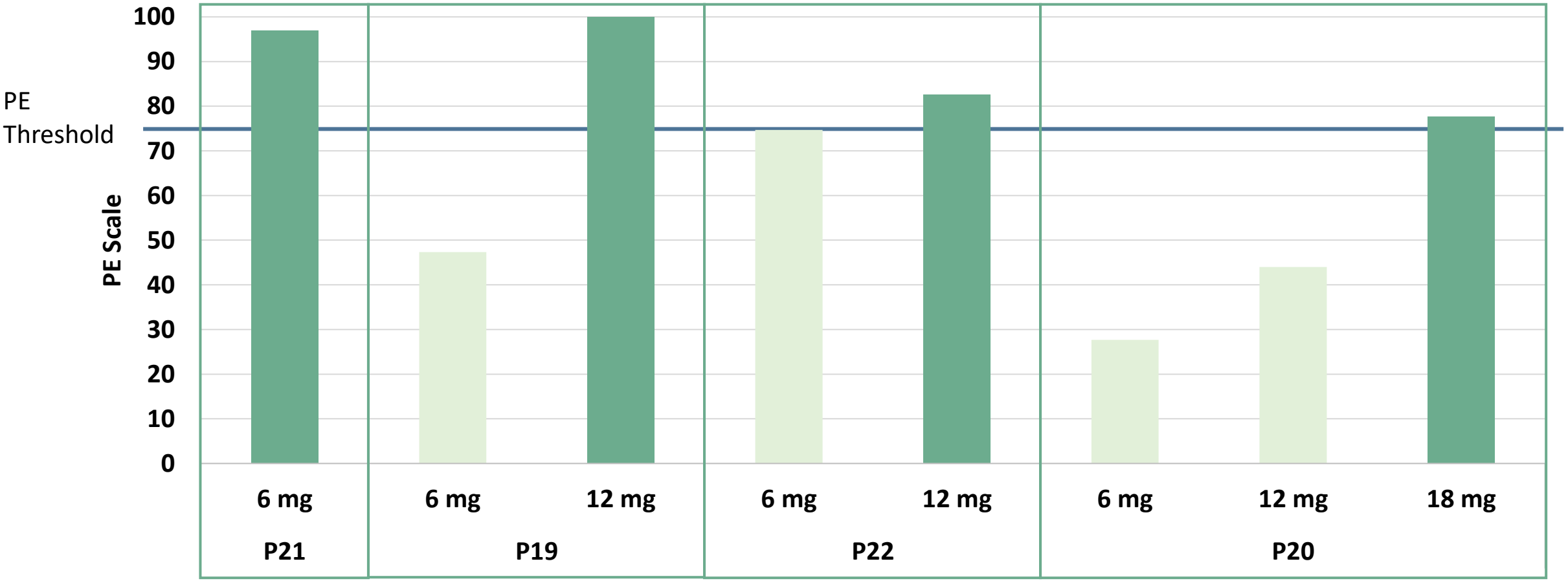
[1]6 mg (n=1); 6-12 mg (n=2); 6-12-18 mg (n=1)

Part A – Peak Experience (PE) Dose-Effects and Inter-Person Variability



PE, Peak Experience

Part B – Peak Experience (PE)
Effect of Intraday Individualized Dosing Regimen (IDR)



PE, Peak Experience

Phase 1/2 Trial in Treatment-Resistant Depression GH001-TRD-102

(Completed)

Clinicaltrials.gov ID: NCT04698603

Design of Phase 1/2 Trial in TRD (GH001-TRD-102)

Phase 1 (Single Dose)

TRD[1] (n=8)

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

Primary Endpoint:

- Safety until day 7

Phase 2 (IDR)

TRD[1] (n=8)

GH001 IDR **6, 12, 18 mg** to achieve PE (up to 3 doses, 3h interval)

Primary Endpoint:

- MADRS remission day 7 (MADRS≤10)

	GH001 Administration	Day 1	Day 7
Key Assessments	MADRS H2 PE Scale Safety	MADRS D1 Cognitive function Safety	MADRS D7 Cognitive function Safety

TRD, Treatment-Resistant Depression; PE, Peak Experience; MADRS, Montgomery-Åsberg Depression Rating Scale; IDR, Individualized Dosing Regimen; H, Hour; D, Day

[1]*Defined as inadequate response to at least two adequate courses of pharmacological therapy or one adequate course of pharmacological therapy and at least one adequate course of evidence-based psychotherapy*

Phase 1 (Single Dose) and Phase 2 (IDR) – Safety

Study Safety Group review

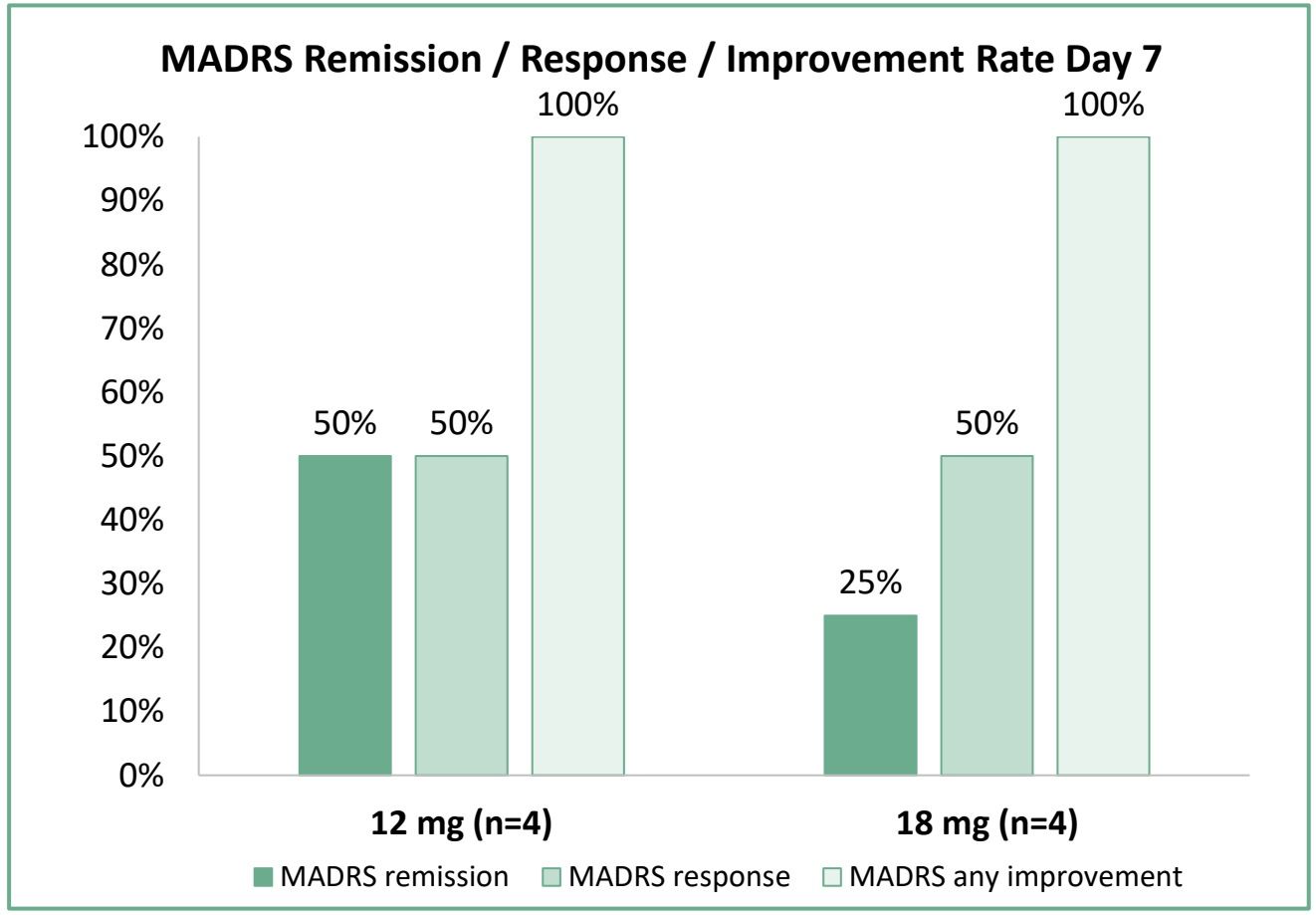
- **No SAEs**
- **All ADRs mild, except three moderate***
- **All ADRs resolved spontaneously**
- **Inhalation well-tolerated**
- No noteworthy changes in vital parameters, except for temporary, non-clinically relevant increase in heart rate and blood pressure shortly after administration of GH001
- No clinically significant changes in safety laboratory analyses, psychiatric safety assessments or measures of cognitive function
- No safety signal relating to suicidal ideation or suicidal behavior, based on C-SSRS and MADRS subscore item “suicidal thoughts”

ADRs	Phase 1 (Single Dose)		Phase 2 (IDR)
	12 mg (n=4)	18 mg (n=4)	IDR[1] (n=8)
MedDRA Preferred Term	**Number of Events**		
Abdominal discomfort			1
Anxiety			2
Depressive symptom			1*
Dizziness	1		
Feeling abnormal	1	1	
Flashback	1	1	2
Headache	2	1	3
Muscle discomfort			1
Muscle spasms		1	
Nausea			2*
Paresthesia			1
Sensory disturbance			3

SAE, Serious Adverse Event; ADR, Adverse Drug Reaction, an adverse event with a relationship code to the investigational product of definite, probable, or possible, or where code is missing; IDR, Individualized Dosing Regimen; C-SSRS, Columbia-Suicide Severity Rating Scale; MADRS, Montgomery-Åsberg Depression Rating Scale

[1]6-12 mg (n=6); 6-12-18 mg (n=2)

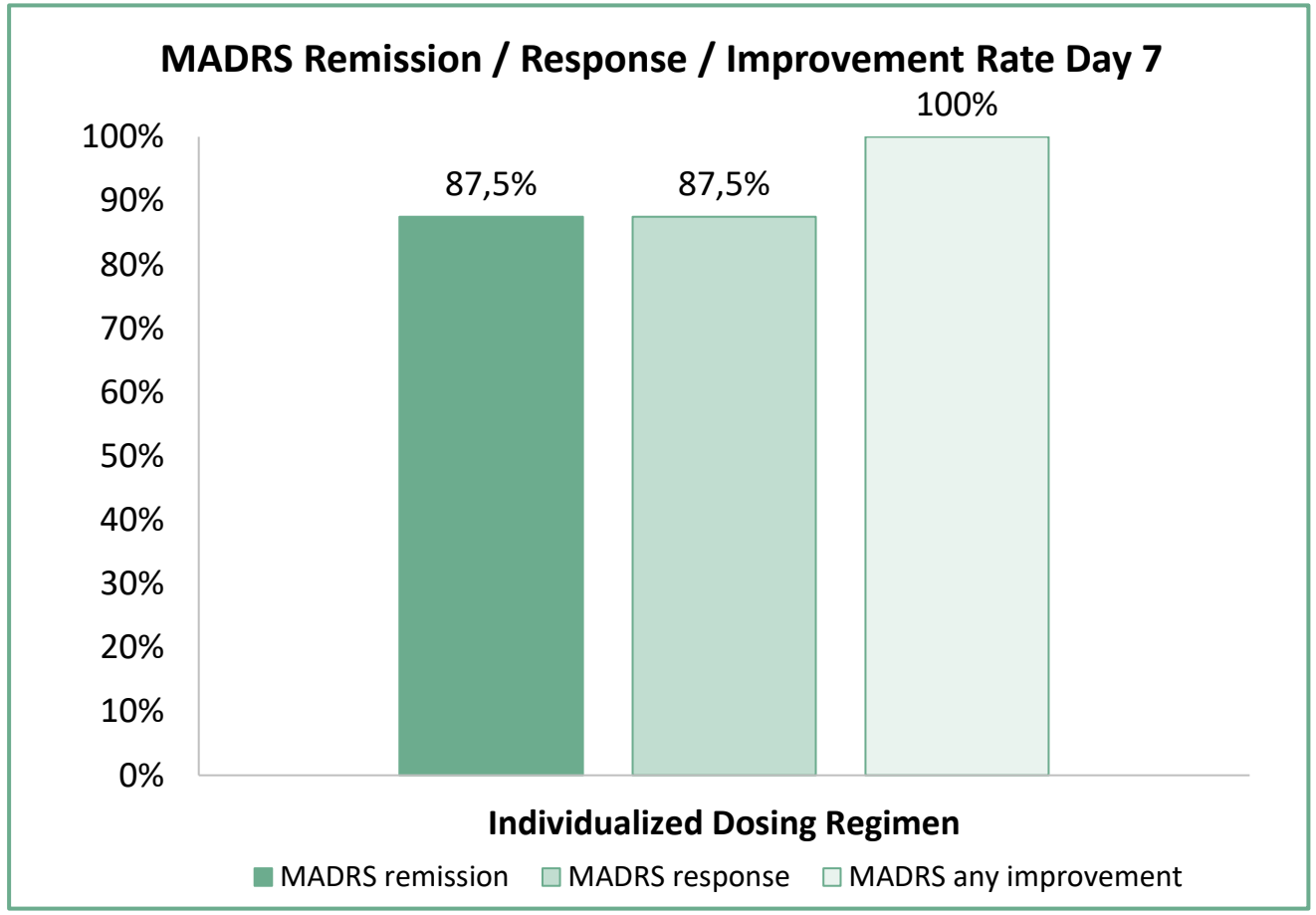
Phase 1 (Single Dose) – Efficacy (MADRS)



- 2 of 4 (50%) in the 12 mg group and 1 of 4 (25%) in the 18 mg group had a MADRS remission at day 7
- 2 of 8 patients had a PE and both had a MADRS remission at day 7

PE, Peak Experience; MADRS, Montgomery–Åsberg Depression Rating Scale
MADRS remission = MADRS of ≤10; MADRS response = Reduction of ≥50% from baseline in MADRS; MADRS any improvement = any reduction from baseline in MADRS.

Phase 2 (IDR) – Efficacy (MADRS)

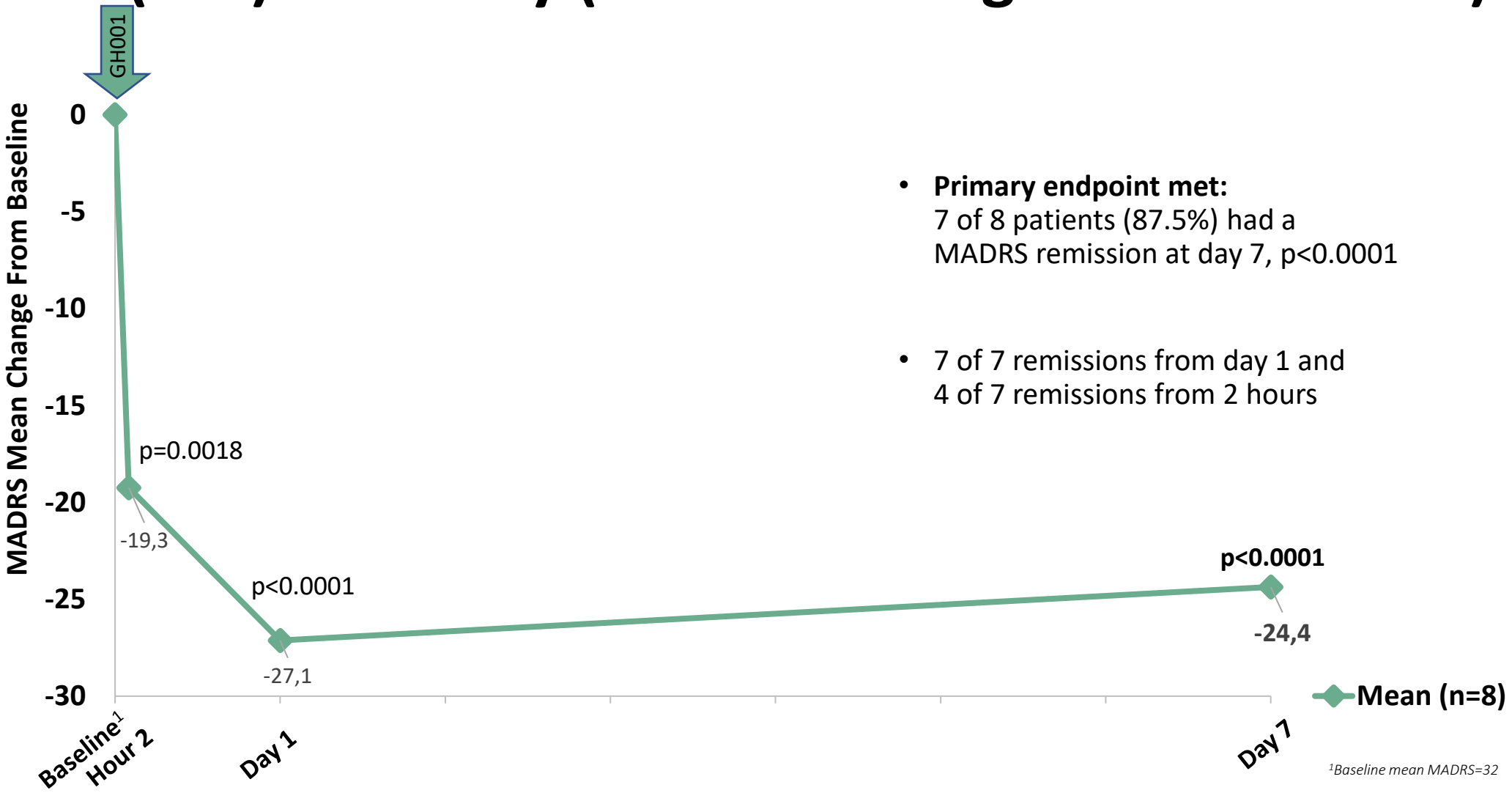


- **Primary endpoint met:**
  7 of 8 patients (87.5%) had a MADRS remission at day 7, p<0.0001

- 7 of 8 patients had a PE and 6 of those had a MADRS remission at day 7

PE, Peak Experience; MADRS, Montgomery–Åsberg Depression Rating Scale
MADRS remission = MADRS of ≤10; MADRS response = Reduction of ≥50% from baseline in MADRS; MADRS any improvement = any reduction from baseline in MADRS.
.

Phase 2 (IDR) – Efficacy (MADRS Change from Baseline)



- **Primary endpoint met:**
  7 of 8 patients (87.5%) had a MADRS remission at day 7, p<0.0001
- 7 of 7 remissions from day 1 and 4 of 7 remissions from 2 hours

[1]*Baseline mean MADRS=32*

MADRS and PE – Observed Improved Outcome in Phase 2 (IDR) vs Phase 1 (Single Dose)

	Phase 2 (IDR)	Phase 1 (Single Dose) 12 mg	Phase 1 (Single Dose) 18 mg
MADRS Remission Rate Day 7	87.5% (7 of 8)	50% (2 of 4)	25% (1 of 4)
Mean MADRS Change Day 7	-24.4 (-76%)	-21.0 (-65%)	-12.5 (-40%)
Rate of PE	87.5% (7 of 8)	50% (2 of 4)	0% (0 of 4)
Mean PE Score	90.4 (at final dose)	58.2	59.1

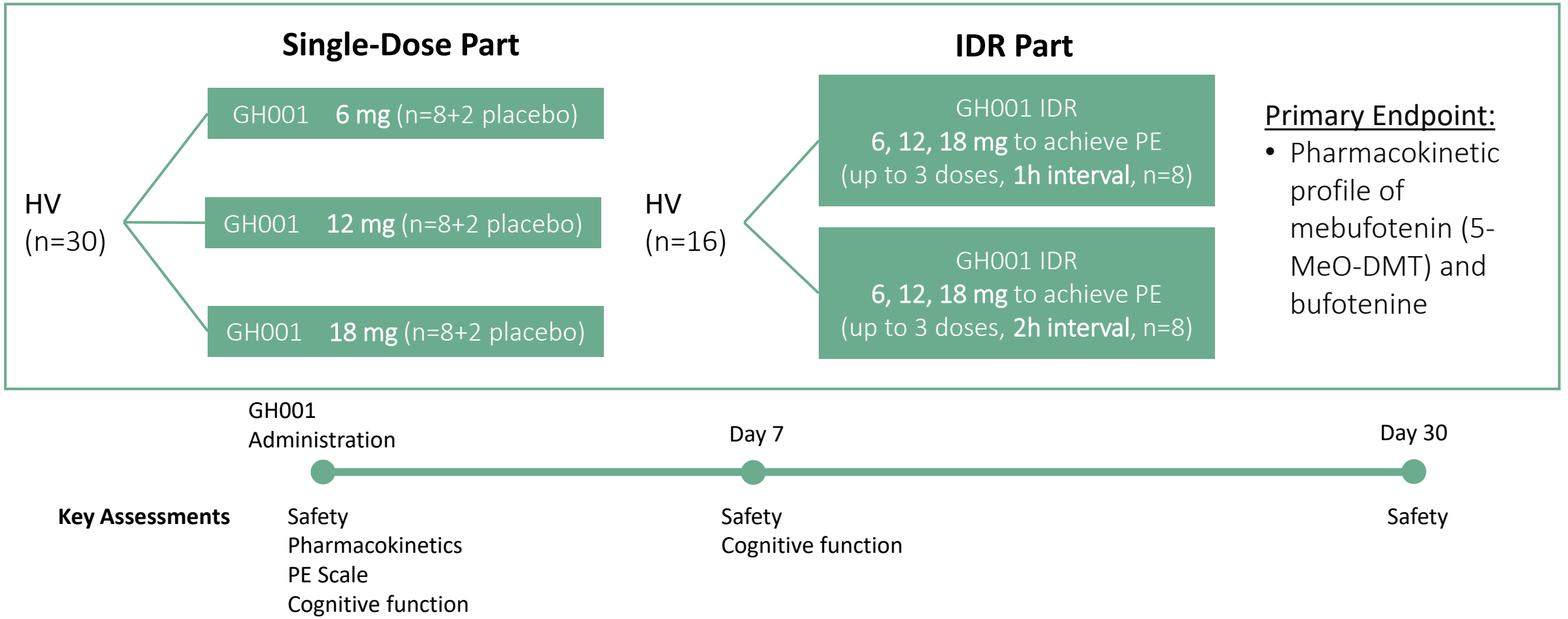
PE, Peak Experience; MADRS, Montgomery-Åsberg Depression Rating Scale; IDR, Individualized Dosing Regimen

Phase 1 Clinical Pharmacology Trial in Healthy Volunteers GH001-HV-103

(Completed)

Clinicaltrials.gov ID: NCT05163691

Design of Phase 1 Clinical Pharmacology Trial in Healthy Volunteers (GH001-HV-103)



HV, Healthy Volunteer; PE, Peak Experience; IDR, Individualized Dosing Regimen

Single Dose and IDR – Safety and Further Results

Safety Review

- **No SAEs**
- **All ADRs mild**
- **All ADRs resolved spontaneously**
- **Inhalation well-tolerated**
- No noteworthy changes in vital parameters, except for temporary, non-clinically relevant increase in heart rate and blood pressure shortly after administration of GH001
- No clinically relevant changes in ECG, safety laboratory analyses, peak flow, cognitive function, psychiatric safety assessments, including the C-SSRS

Further Results

- Pharmacokinetic analyses and psychoactive effect assessments (PE Scale) support that an interval down to 1 hour between individual doses of the IDR is feasible for future clinical trials

ADRs	Single-dose				IDR	
	6 mg (n=8)	12 mg (n=8)	18 mg (n=8)	Placebo (n=6)	1h interval (n=8)[1]	2h interval (n=8)[2]
MedDRA Preferred Term	**Number of Events**					
Abnormal dreams						1
Chest discomfort		1				
Crying			2		2	
Dizziness			1			
Dry mouth	1					
Dyskinesia			1			
Fatigue		1			2	1
Headache	3		1		1	1
Hypoesthesia oral		1				
Paresthesia oral						1
Retching			1			
Somnolence		1				
Tachycardia			2			
Tension						1
Tremor			1			

SAE, Serious Adverse Event; Adverse Drug Reaction, or ADR, an adverse event with a relationship code to the investigational product of definite, probable, or possible, or where code is missing; IDR, Individualized Dosing Regimen; C-SSRS, Columbia-Suicide Severity Rating Scale; PE, Peak Experience

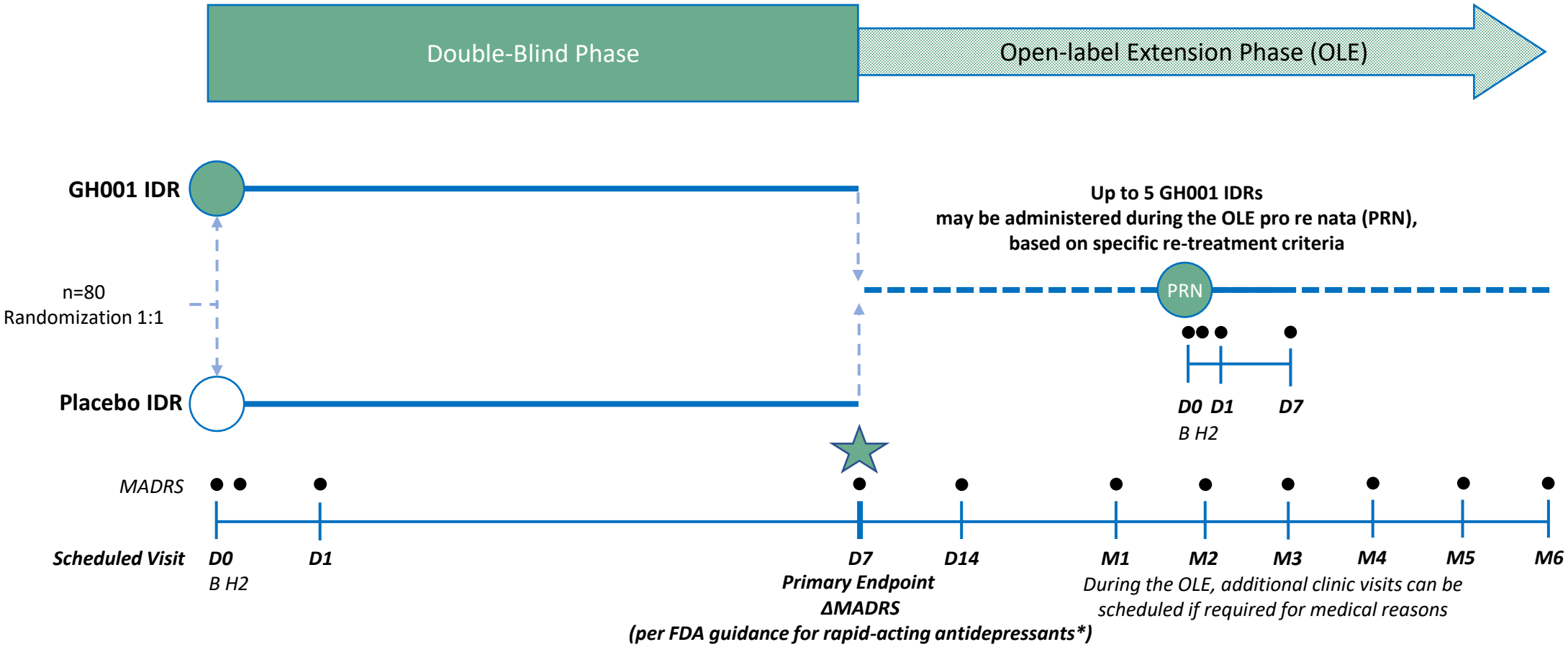
[1]6 mg (n=1), 6-12 mg (n=3); 6-12-18 mg (n=4)
[2]6-12 mg (n=3); 6-12-18 mg (n=5)

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

(Initiation Expected Q1 2023)

EudraCT Number: 2022-000574-26

Design of Phase 2b Trial in TRD (GH001-TRD-201)



*The bold solid lines indicate the fixed duration of 7 days (± 1 day) after an IDR with visits on D0, D1 and D7. The bold dotted line indicates the variable duration until a potential GH001 IDR in the OLE. 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, to achieve a peak experience, given at a 1H interval. 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. IDR, Individualized Dosing Regimen; PRN, pro re nata (as needed); B, Baseline; H, Hour; D, Day; M, Month. *FDA Guidance for Industry: Major Depressive Disorder: Developing Drugs for Treatment*

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

11 patent families filed relating to mebufotenin (5-MeO-DMT), including:

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

LAYER 3: TECHNICAL

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

Board of Directors & Management

Florian Schönharting
MSc
Chairman of the Board, Co-founder

Michael Forer
BA, LLB
Vice-Chairman of the Board

Dermot Hanley
BSC, MBA
Board Member

Duncan Moore
MPhil, PhD
Board Member

Theis Terwey
PD Dr. med.
CEO, Co-founder

Julie Ryan
ACA, MAcc, BComm
VP, Finance

Magnus Halle
BSc
Managing Director, Ireland, Co-founder

Scientific Advisors

Madhukar Trivedi
M.D.
Professor of Psychiatry,
UT Southwestern Medical Center

Michael Thase
M.D.
Professor of Psychiatry, Perelman School of Medicine
University of Pennsylvania

Mark Zimmerman
M.D.
Professor of Psychiatry and Human Behavior,
Brown University

Eduard Vieta
Prof. Dr.
Head, Psychiatry Unit,
Hospital Clínic de Barcelona

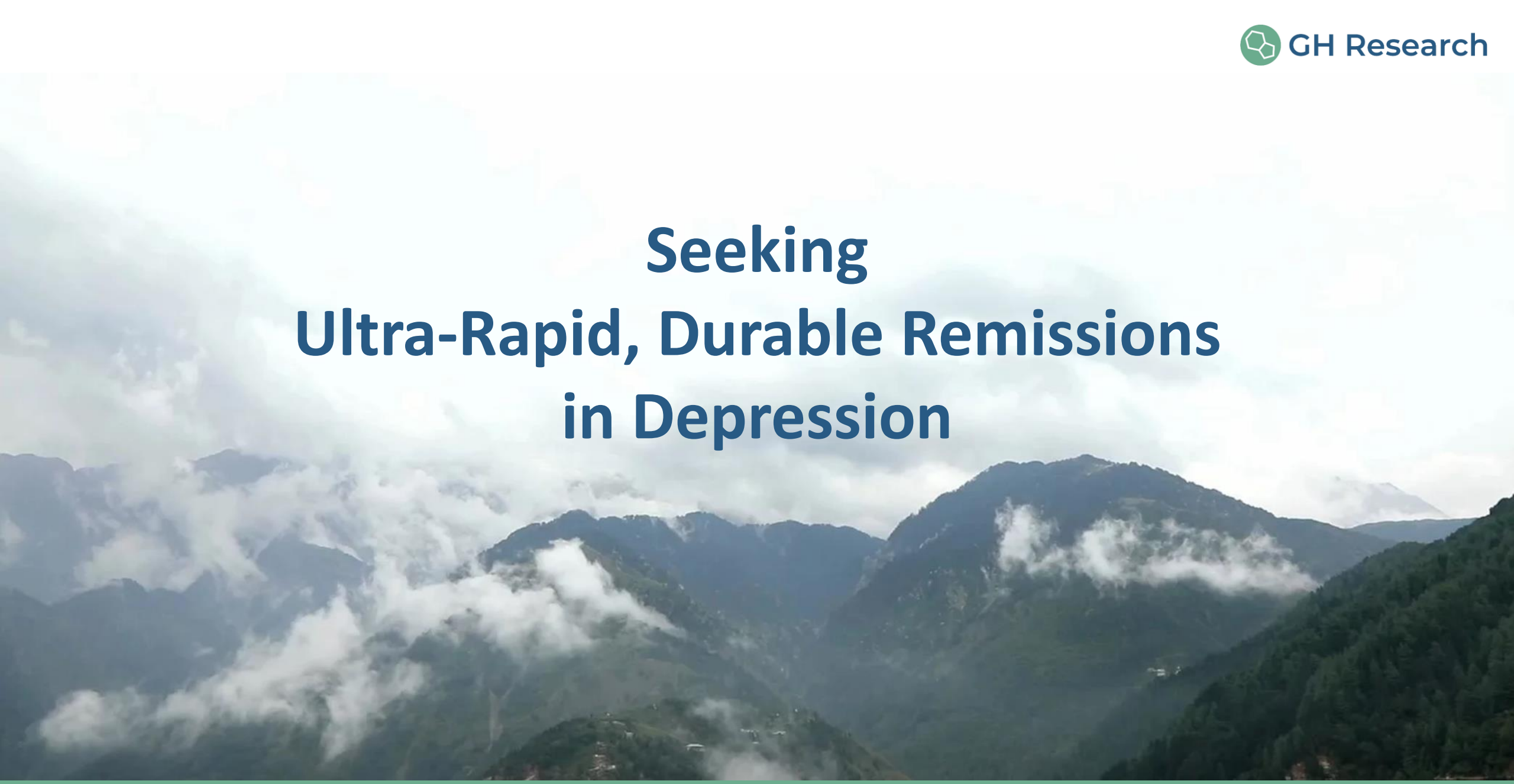
Michael Bauer
Prof. Dr. rer. nat. Dr. med.
Chair, Department of Psychiatry and Psychotherapy,
Technische Universität Dresden

Malek Bajbouj
Prof. Dr. med.
Head, Center for Affective Neuroscience,
Charité, Berlin

Johannes Ramaekers
Prof. Dr.
Professor, Faculty of Psychology
and Neuroscience of Maastricht University

Anticipated Milestones and Financial Overview

- GH001
  - Initiate multi-center, randomized, double-blind, placebo-controlled Phase 2b trial in TRD in Q1 2023
  - Submit U.S. IND for GH001 with proprietary aerosol delivery device in Q3 2023
  - Complete proof-of-concept Phase 2a trials in BDII and in PPD in Q4 2023
- GH002
  - Complete Phase 1 clinical pharmacology trial in healthy volunteers in Q4 2023
- GH003
  - Complete preclinical development
- Financial Overview
  - Cash was $256.9 million as of September 30, 2022
  - We believe existing cash will be sufficient to fund operating expenses and capital expenditure requirements into 2025



Seeking
Ultra-Rapid, Durable Remissions in Depression