GH Research

Corporate Presentation

GH Research PLC (NASDAQ: GHRS)

November 2022

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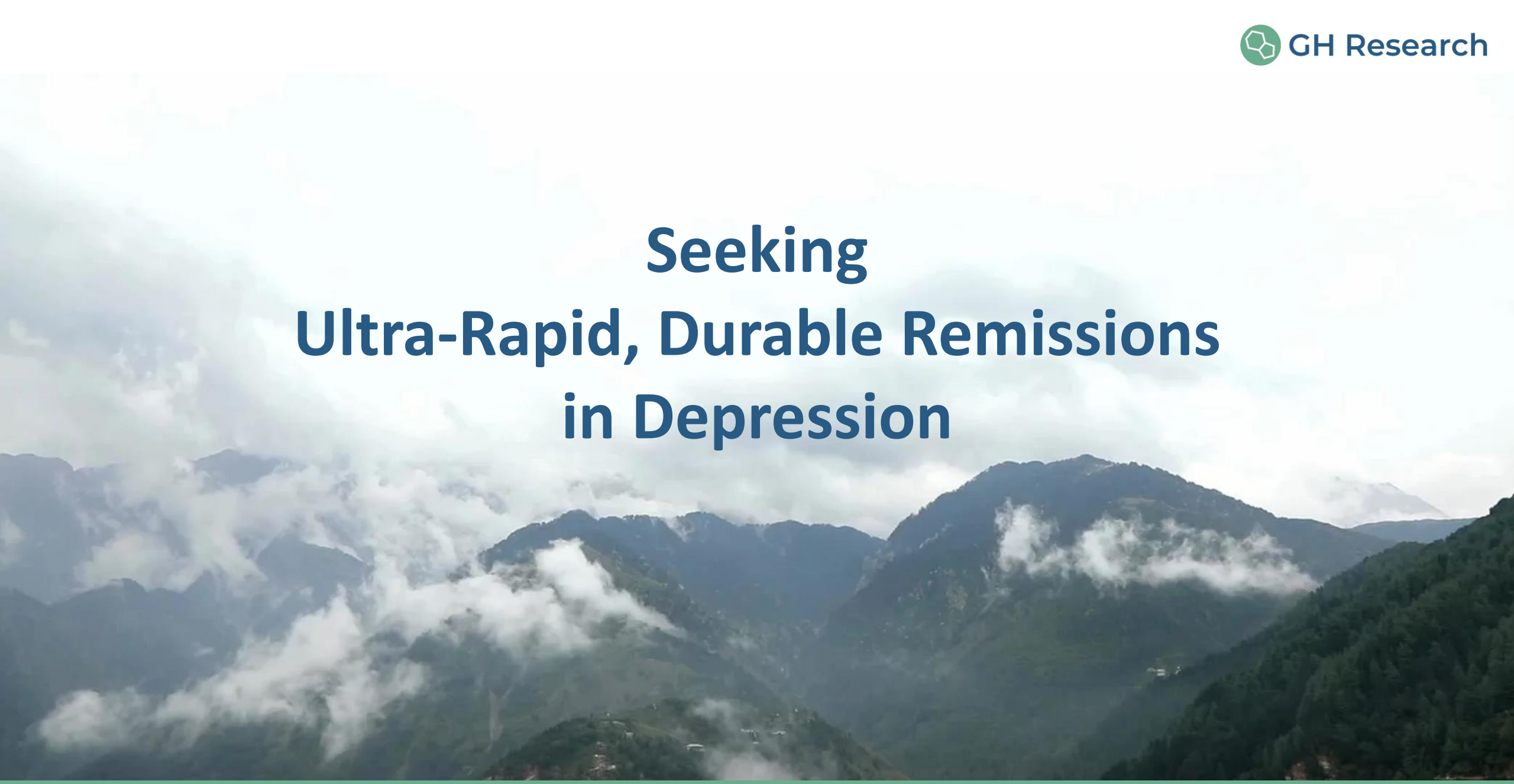
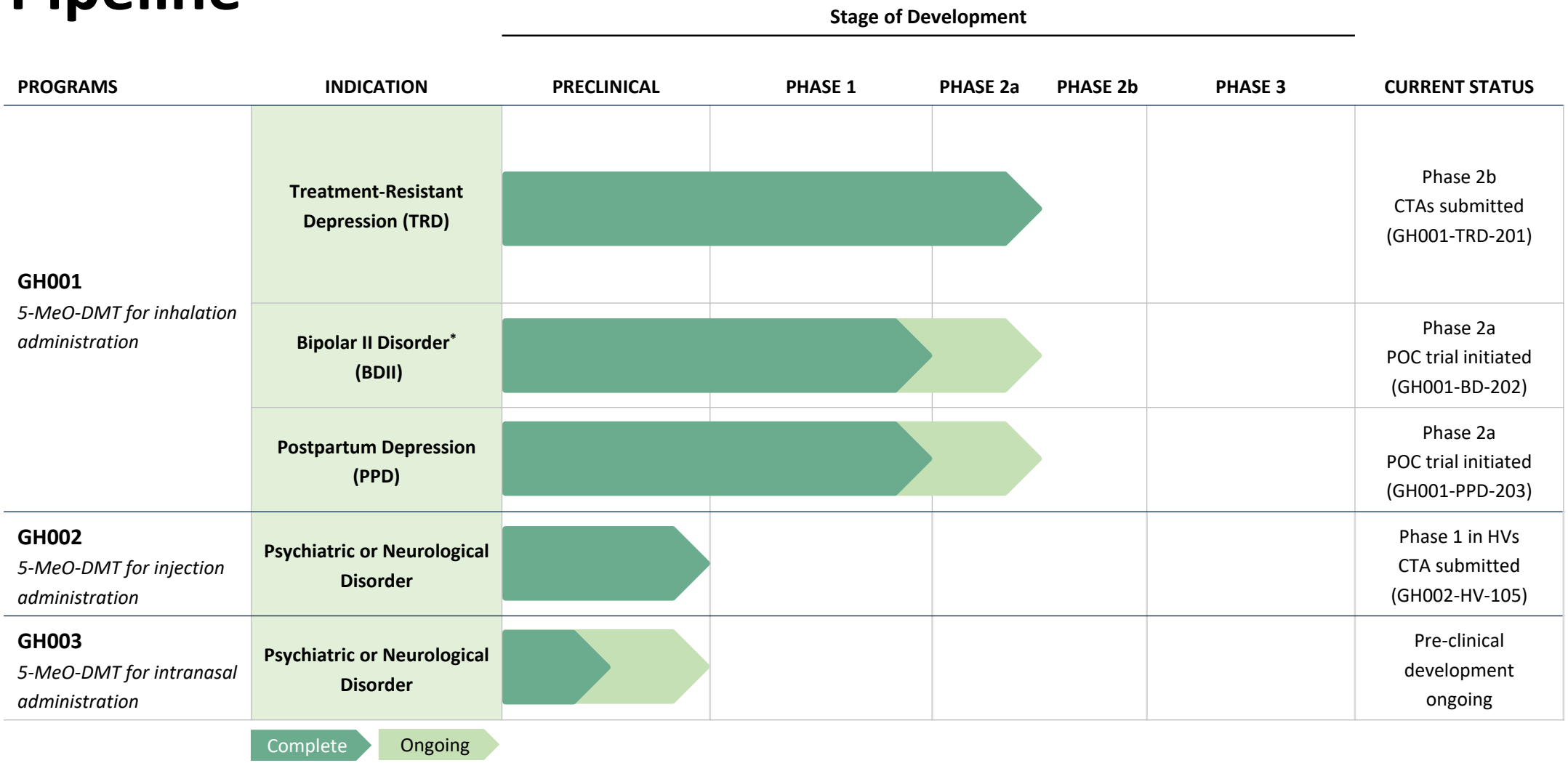


Seeking
Ultra-Rapid, Durable Remissions in Depression

Pipeline

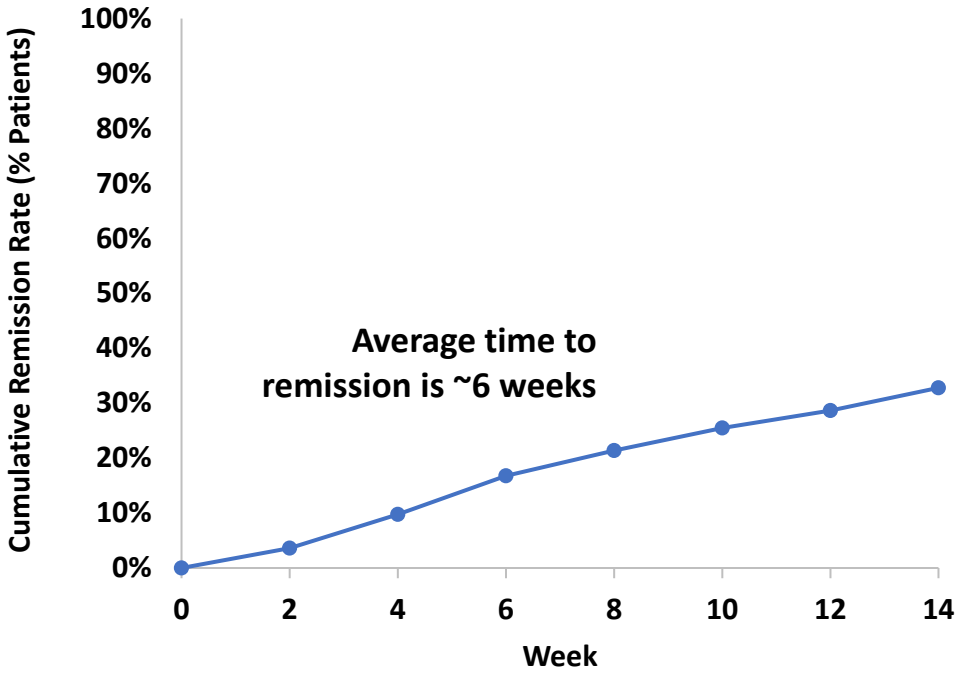


*Bipolar II disorder with a current major depressive episode; 5-MeO-DMT, 5-Methoxy-N,N-Dimethyltryptamine; CTA, Clinical Trial Application; POC, Proof-of-Concept; HV, Healthy Volunteer

The Problem for Patients with Depression

Established Therapies are Slow-Acting

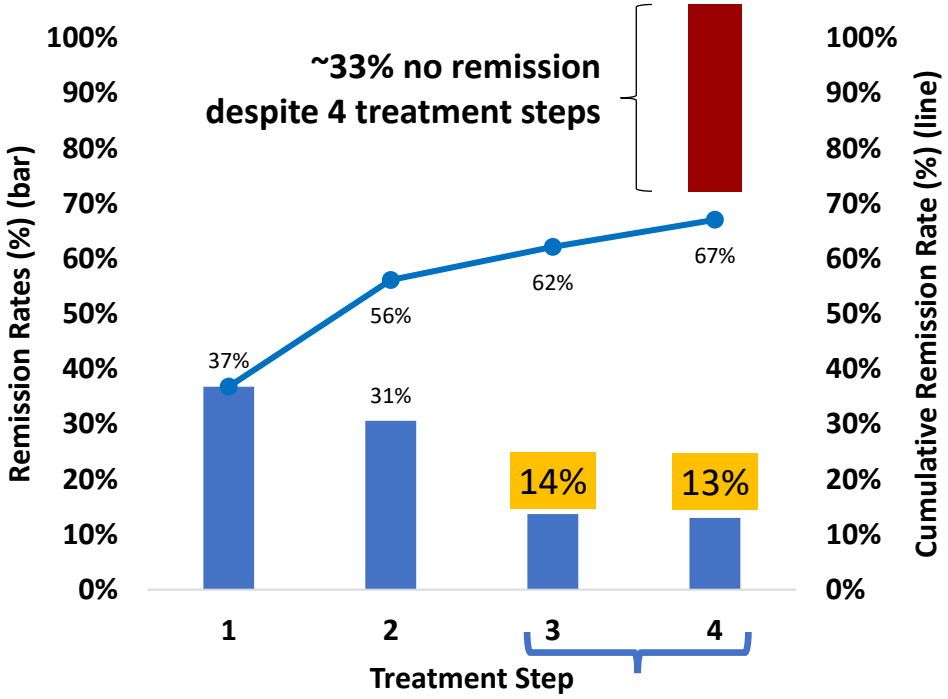
(STAR*D study, Remission Rate Over Time, Treatment Step 1 = Citalopram)



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

... Remission Rates in TRD < 15%

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



2 or more prior therapies = TRD

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)

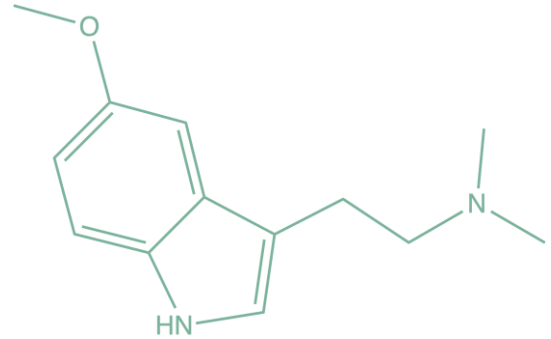
- Non-response to two prior lines: **~9M**

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

5-MeO-DMT and GH001

- 5-MeO-DMT (5-Methoxy-N,N-Dimethyltryptamine)
  - Naturally-occurring psychoactive substance from tryptamine class
  - **Highly potent** agonist on 5-HT1A and 5-HT2A receptors
  - **Psychoactive effects with ultra-rapid onset** (within seconds) **and short duration** (5 to 30 min)
  - **High propensity to induce peak experiences (PE), which may be a surrogate marker for therapeutic effects**

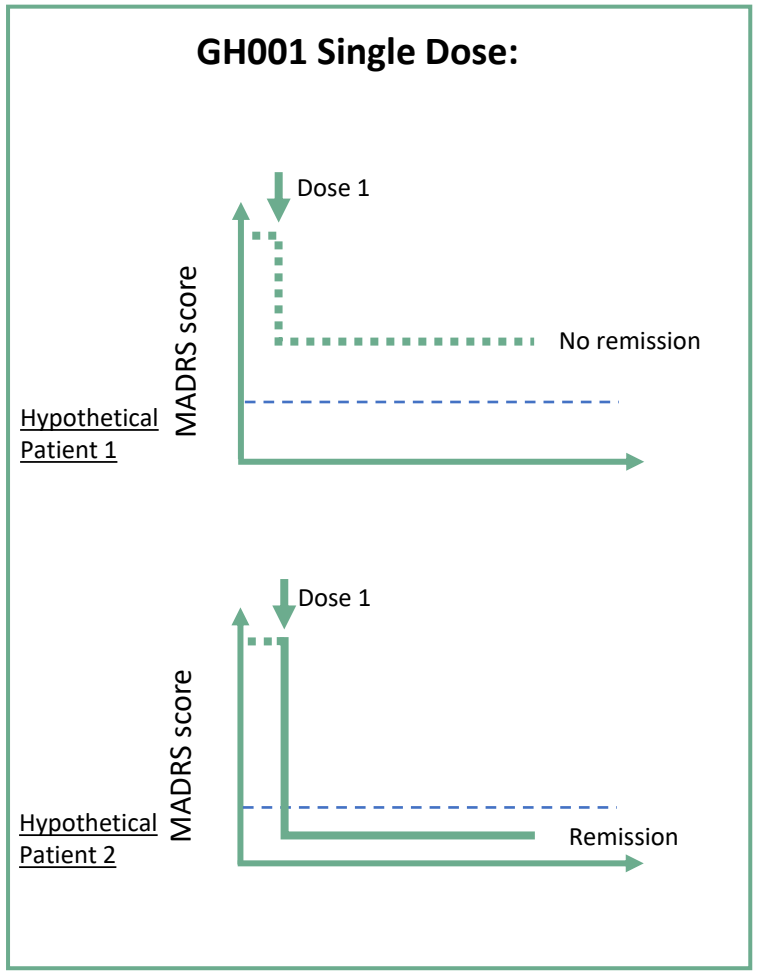


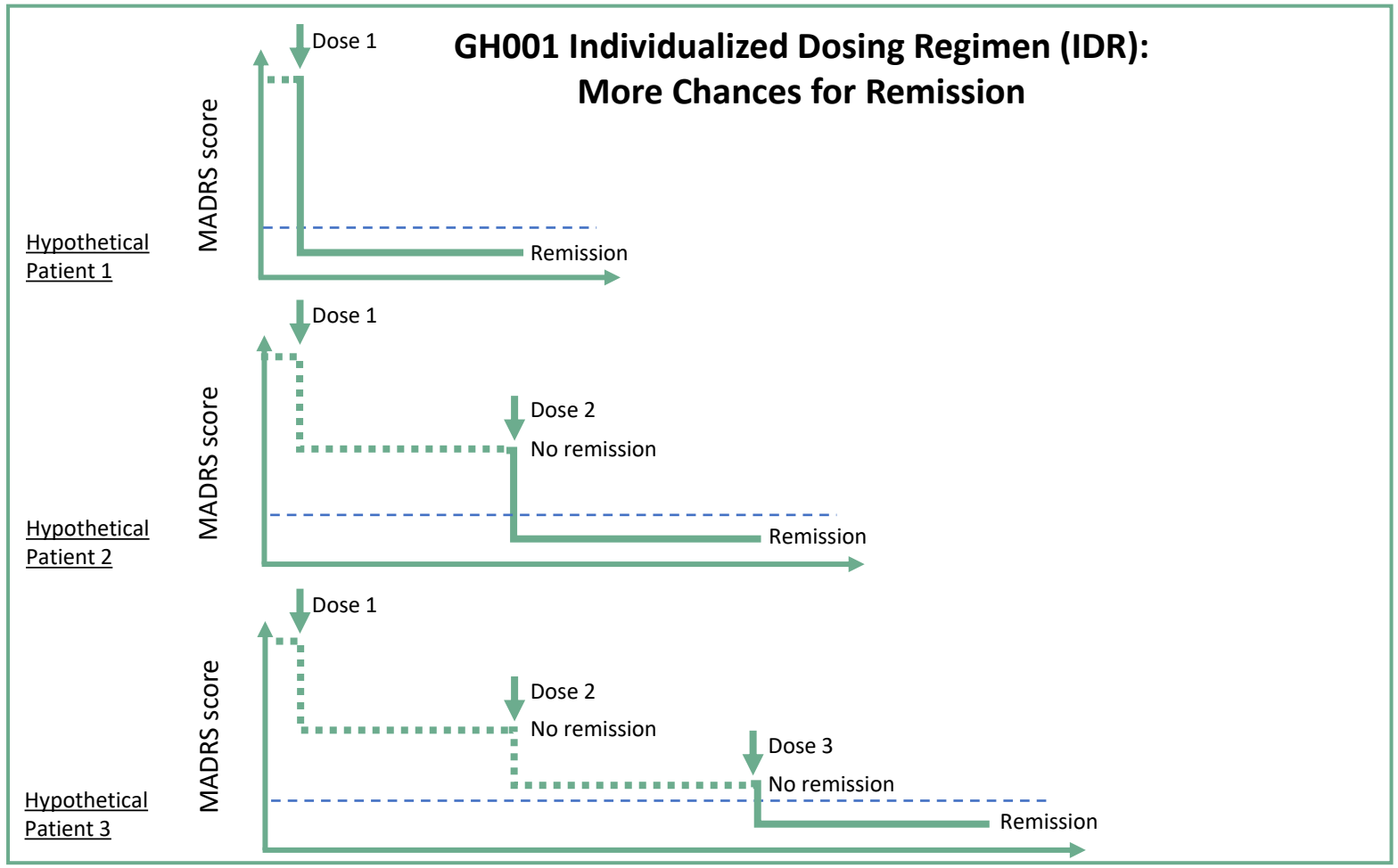
5-MeO-DMT

- GH001 (5-MeO-DMT administration via a proprietary inhalation approach)
  - **Intraday individualized dosing regimen for maximization of ultra-rapid remissions**
  - **Single visit initial treatment,** with no structured psychotherapy
  - Potential for **convenient and infrequent retreatment**

Foundational IP

GH001 – Individualized Dosing Regimen (IDR) Designed to Achieve Ultra-Rapid and Durable Remissions





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

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

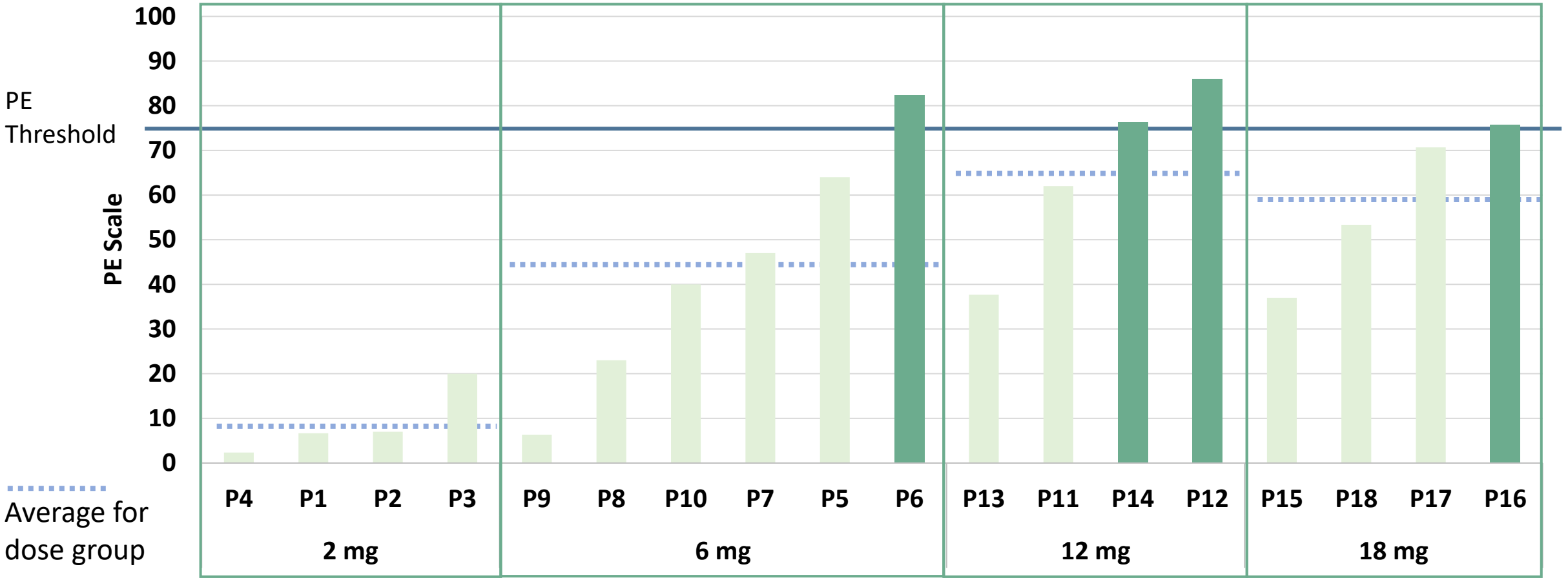
- **No SAEs**
- **All ADRs mild, except two moderate (*)**
- **All ADRs resolved spontaneously**
- **Inhalation well-tolerated**
- No noteworthy changes in vital parameters, except for temporary, non-clinically relevant increase in heart rate and blood pressure shortly after administration of GH001
- 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	n	n	n	n	n
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				

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

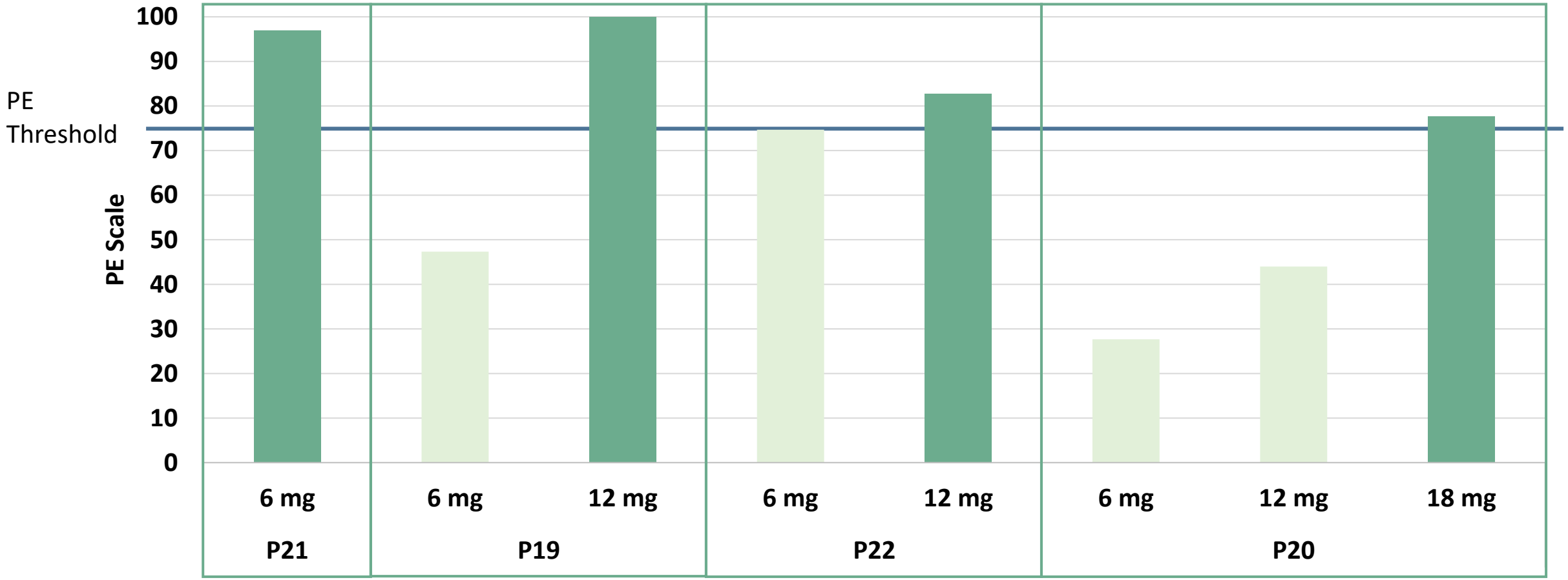
[1]6 mg (N=1); 6-12 mg (N=2); 6-12-18 mg (N=1)

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



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 2-hrs PE Scale Safety	MADRS 1-day Cognitive function Safety	MADRS 7-day Cognitive function Safety

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

[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

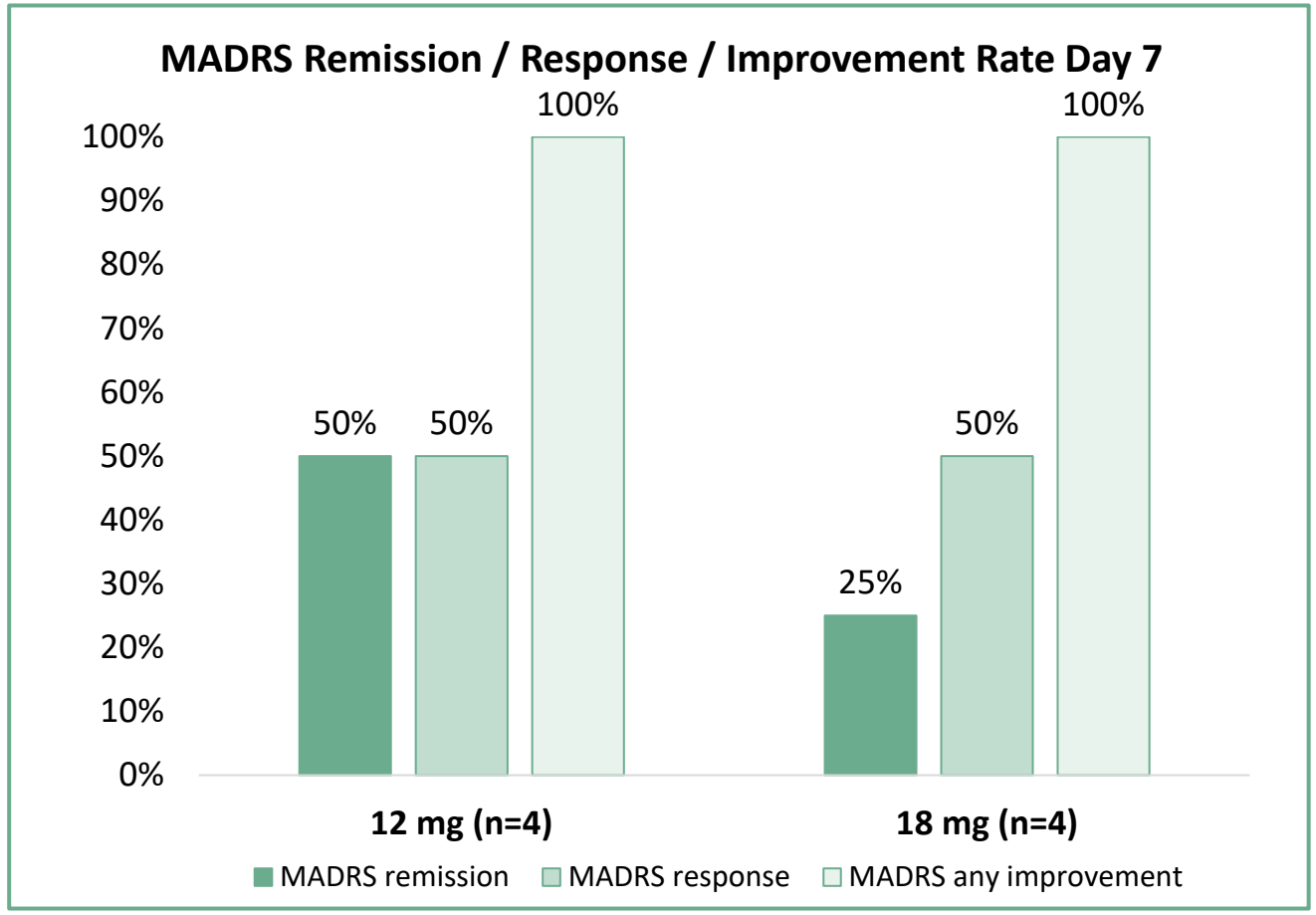
- **No SAEs**
- **All ADRs mild, except three moderate***
- **All ADRs resolved spontaneously**
- **Inhalation well-tolerated**
- No noteworthy changes in vital parameters, except for temporary, non-clinically relevant increase in heart rate and blood pressure shortly after administration of GH001
- 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	**n**	**n**	**n**
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

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

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

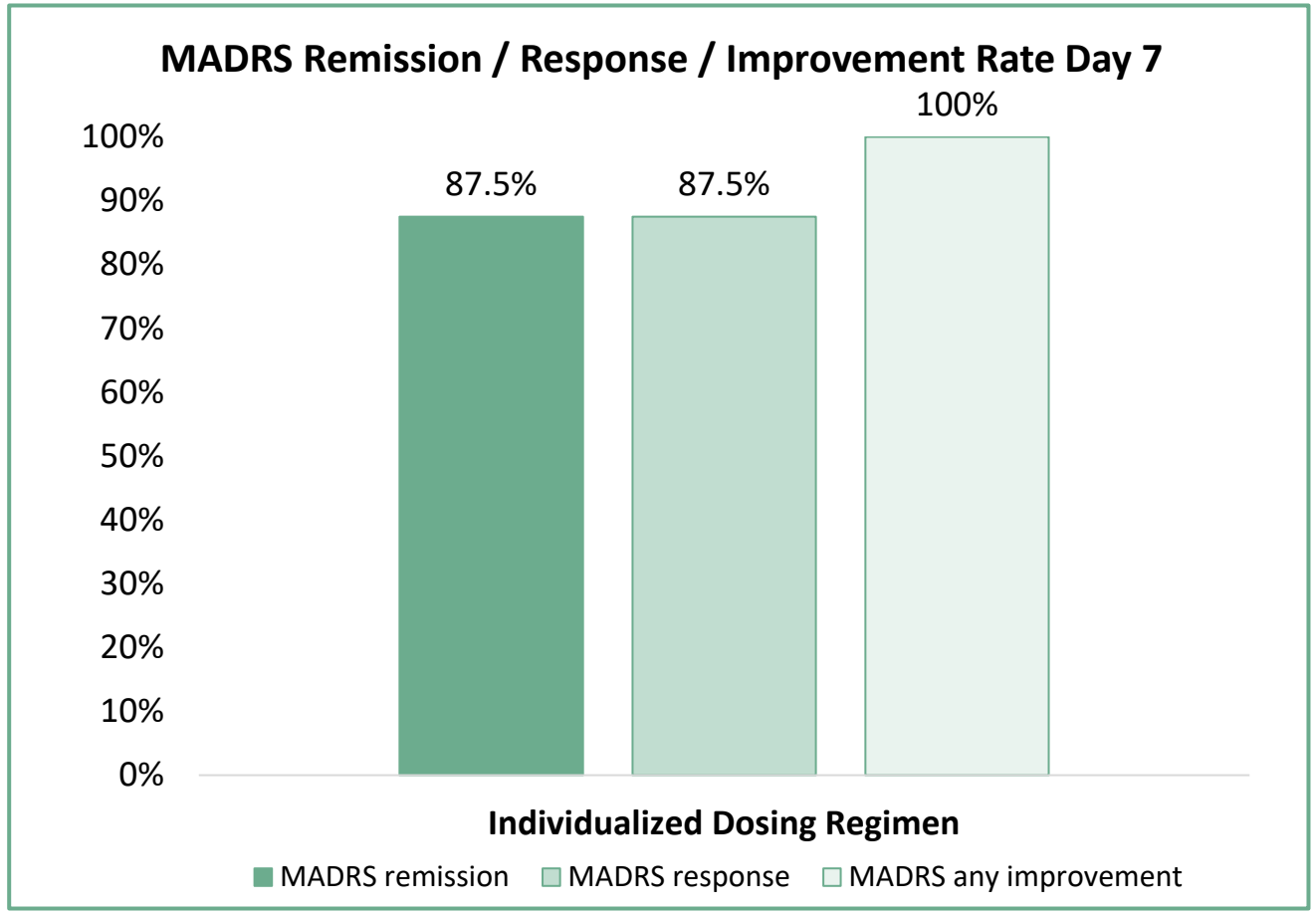
Phase 1 (Single Dose) – Efficacy (MADRS)



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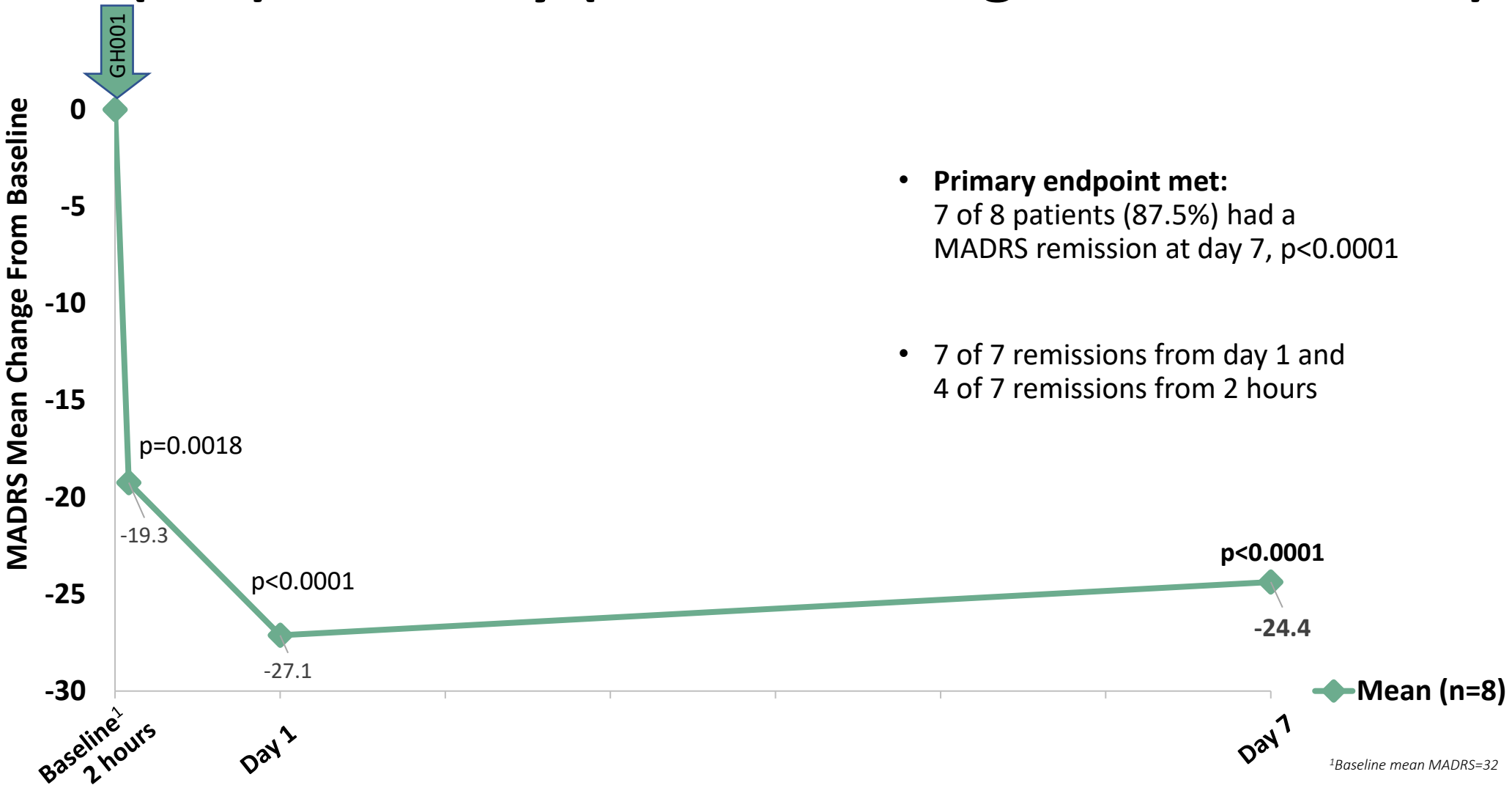
Phase 2 (IDR) – Efficacy (MADRS Change from Baseline)



- **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

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

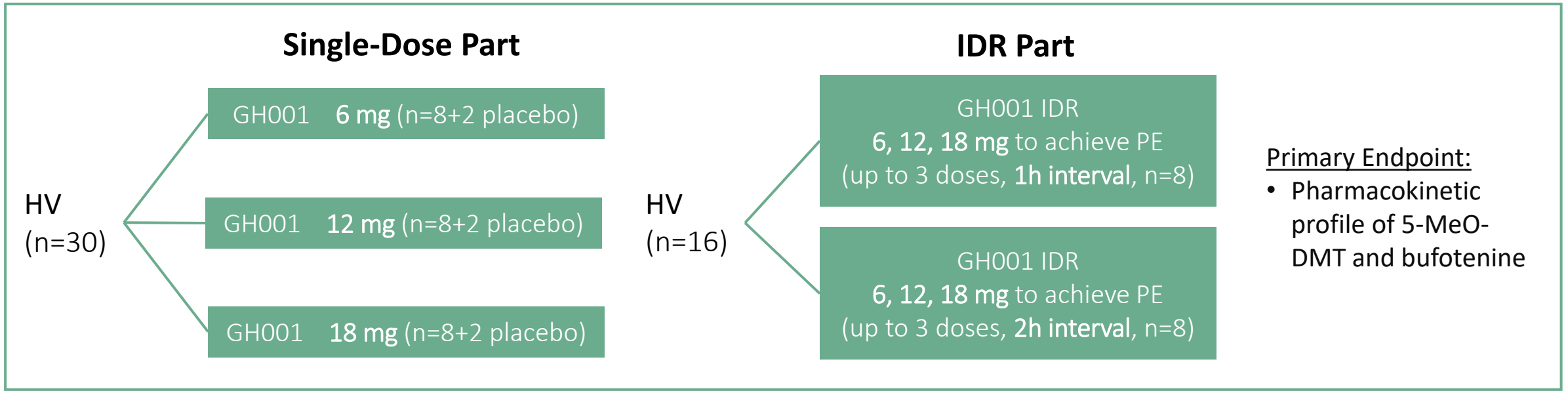
	Phase 2 (IDR)	Phase 1 (Single Dose) 12 mg	Phase 1 (Single Dose) 18 mg
MADRS Remission Rate Day 7	87.5% (7 of 8)	50% (2 of 4)	25% (1 of 4)
Mean MADRS Change Day 7	-24.4 (-76%)	-21.0 (-65%)	-12.5 (-40%)
Rate of PE	87.5% (7 of 8)	50% (2 of 4)	0% (0 of 4)
Mean PE Score	90.4 (at final dose)	58.2	59.1

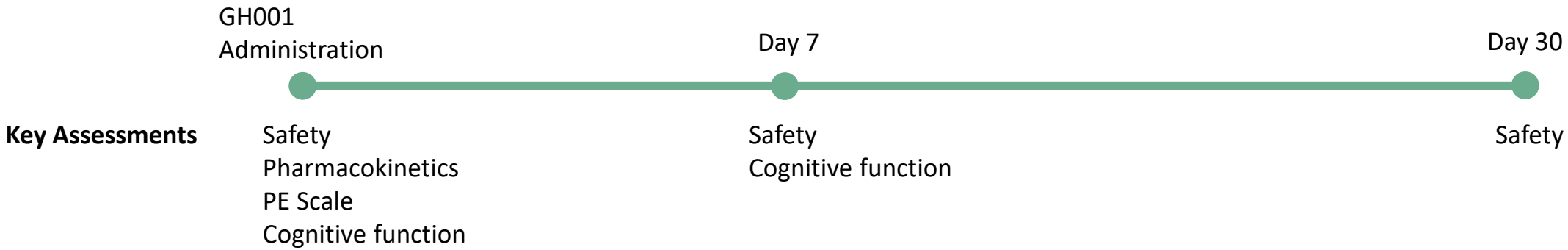
PE, Peak Experience; MADRS, Montgomery-Åsberg Depression Rating Scale
IDR, Individualized Dosing Regimen

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

(Completed)

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





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	**n**	**n**	**n**	**n**	**N**	**n**
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			

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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)

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

Several patent applications filed:

- Novel aerosol compositions of matter of 5-MeO-DMT
- Novel manufacturing methods and novel salt forms of 5-MeO-DMT
- Novel uses of 5-MeO-DMT in various disorders (including inhaled, nasal, buccal, sublingual, i.v., i.m., s.c. routes)

LAYER 3: TECHNICAL

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

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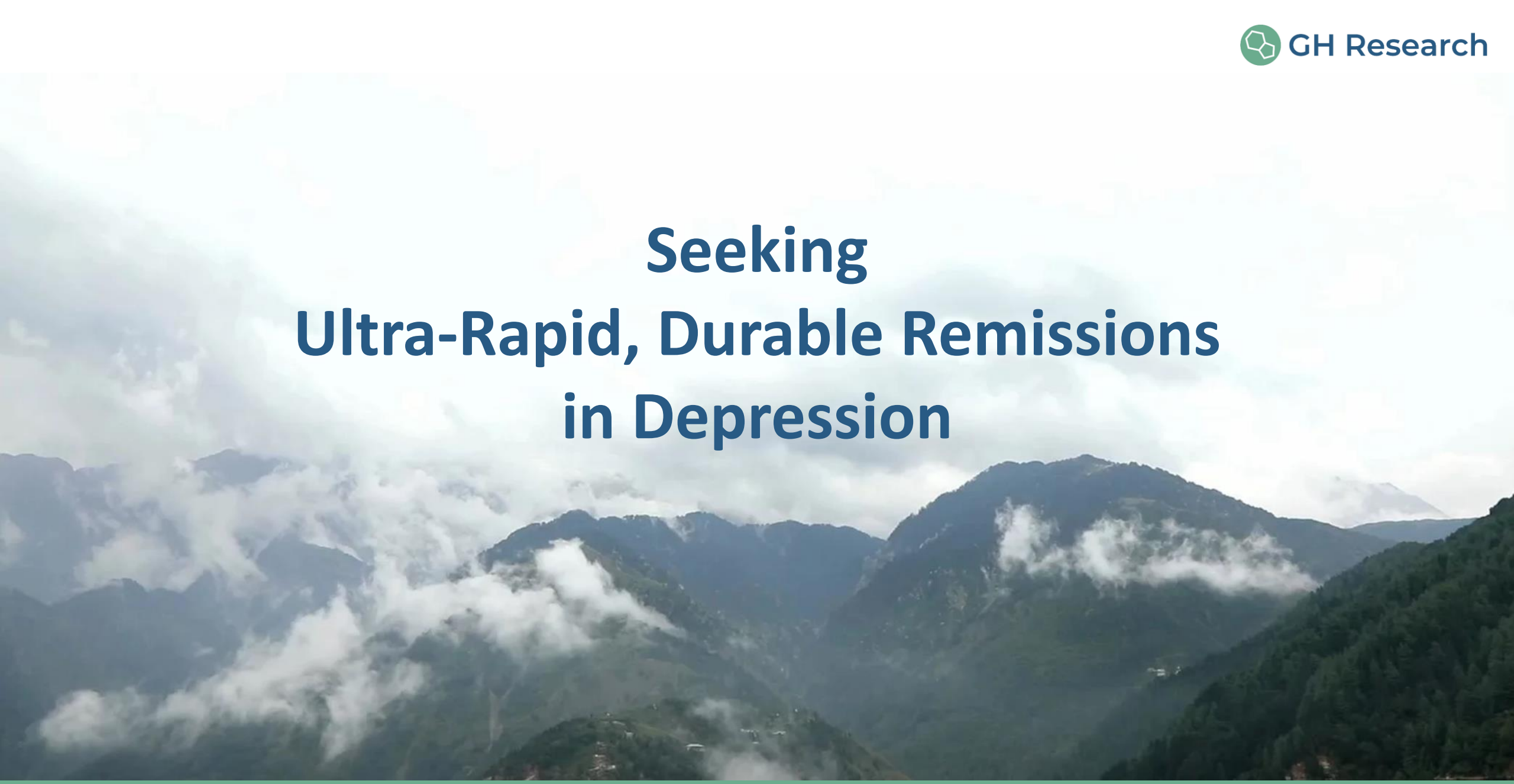
Anticipated Milestones and Financial Overview

- GH001
  - Initiate multi-center, randomized, controlled Phase 2b trial in TRD in 1Q 2023
  - Submit U.S. IND for GH001 in TRD in 1Q 2023
  - Complete proof-of-concept Phase 2a trials in BDII and in PPD by the end of 2023
- GH002
  - Initiate Phase 1 clinical pharmacology trial in healthy volunteers in 4Q 2022
- 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



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