GH Research

Corporate Presentation

GH Research PLC (NASDAQ: GHRS)

March 2022

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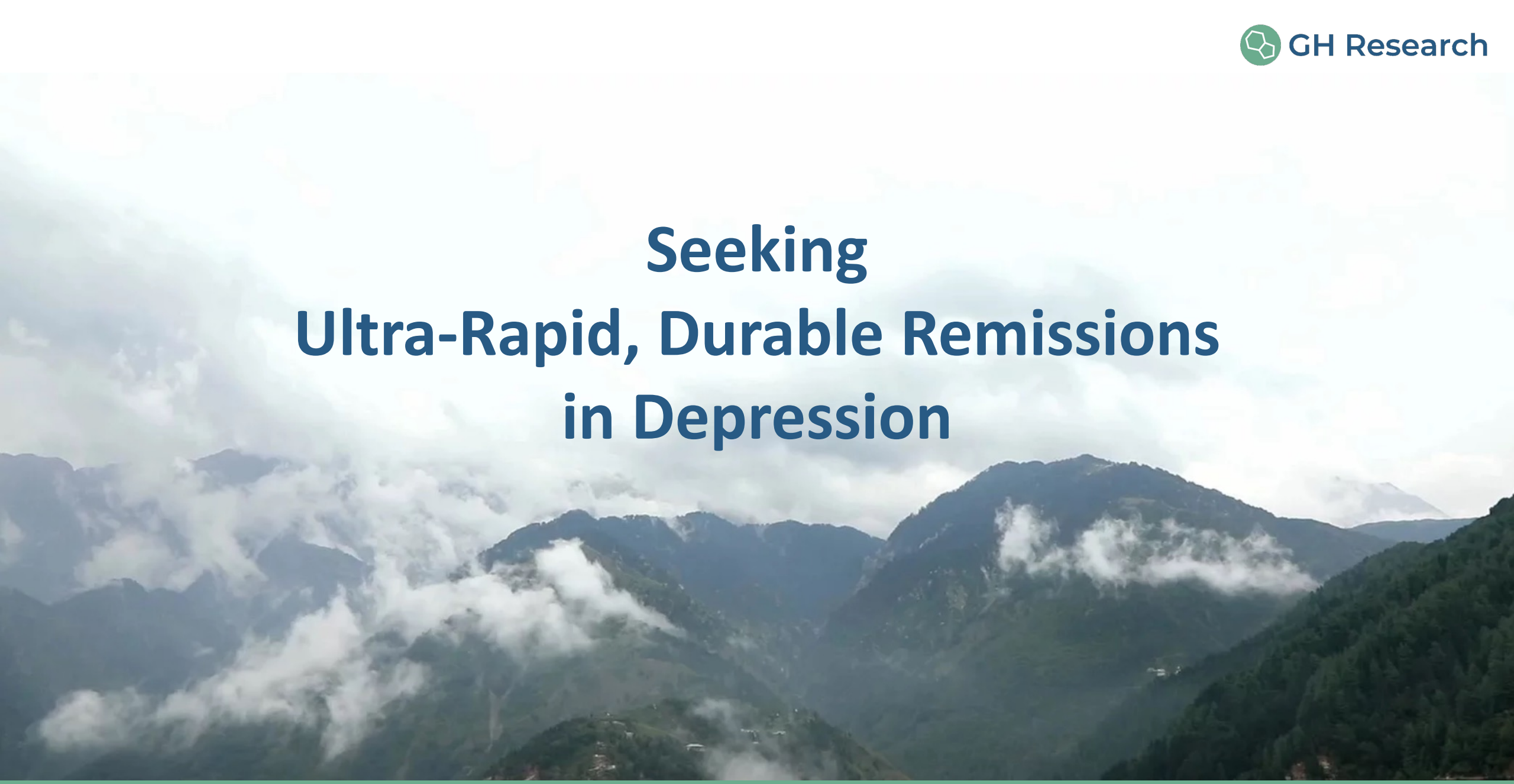
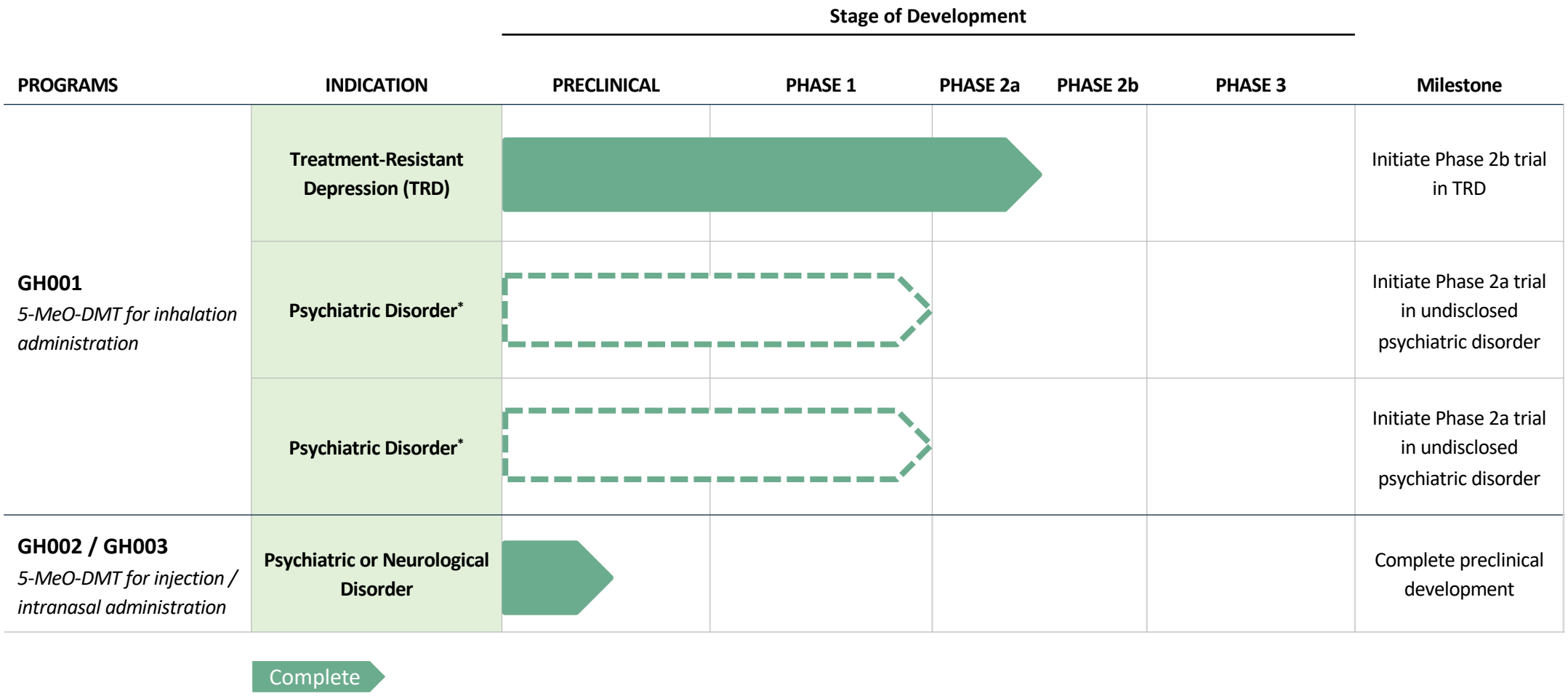


Seeking
Ultra-Rapid, Durable Remissions in Depression

Pipeline

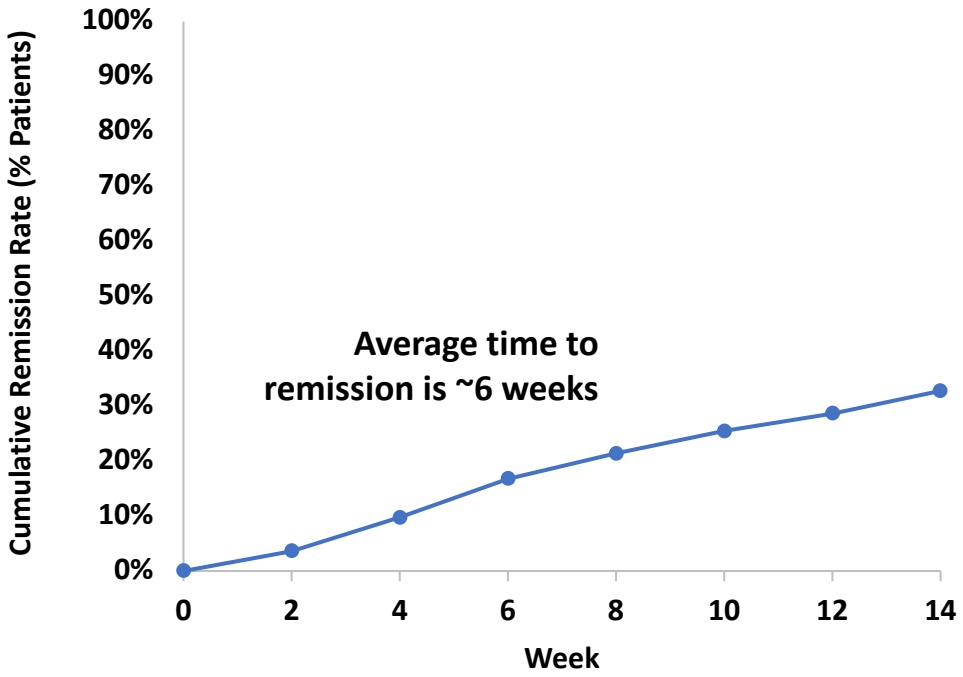


In light of our completed Phase 1 clinical trial of GH001 in healthy volunteers and our completed Phase 1/2 trial in TRD, we plan to request clearance from European regulatory authorities to begin Phase 2a clinical trials in patients with two additional undisclosed psychiatric disorders

The Problem for Patients with Depression

Established Therapies are Slow-Acting

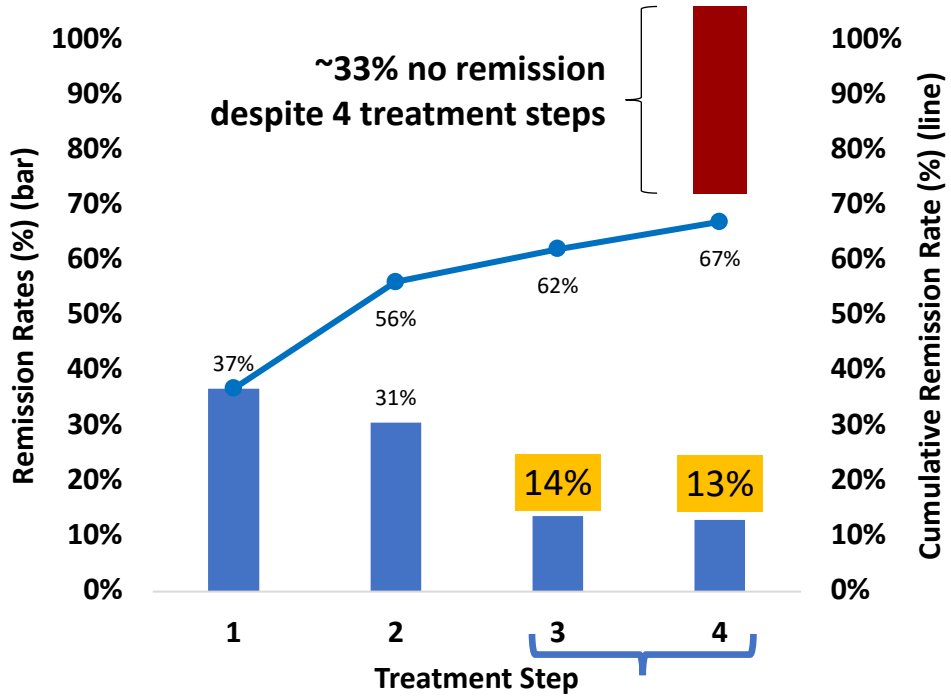
(STAR*D study, Remission Rate Over Time, Treatment Step 1 = Citalopram)



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 =
Treatment-Resistant Depression (TRD)

Large and Open Depression Market 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)

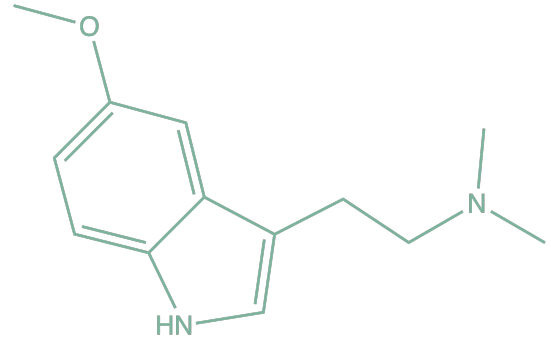
- Non-response to two prior lines: **~9M**

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**

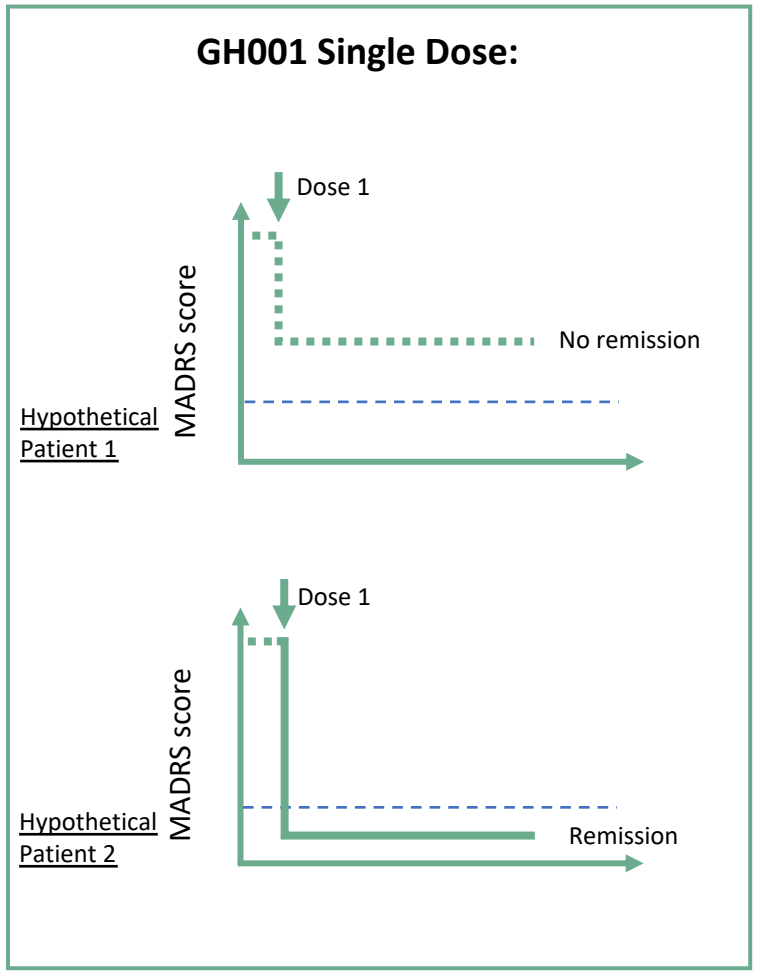


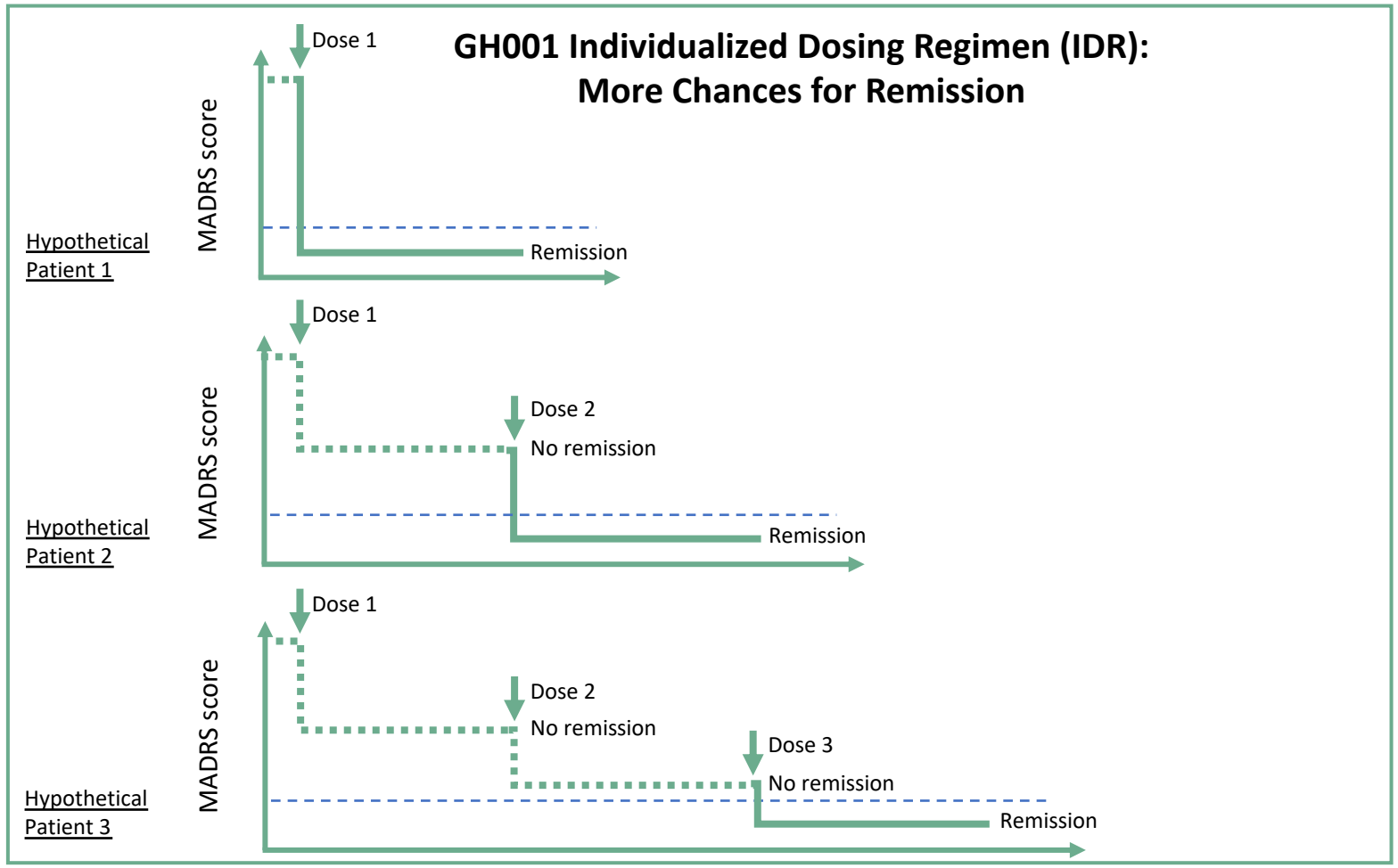
5-MeO-DMT

- 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

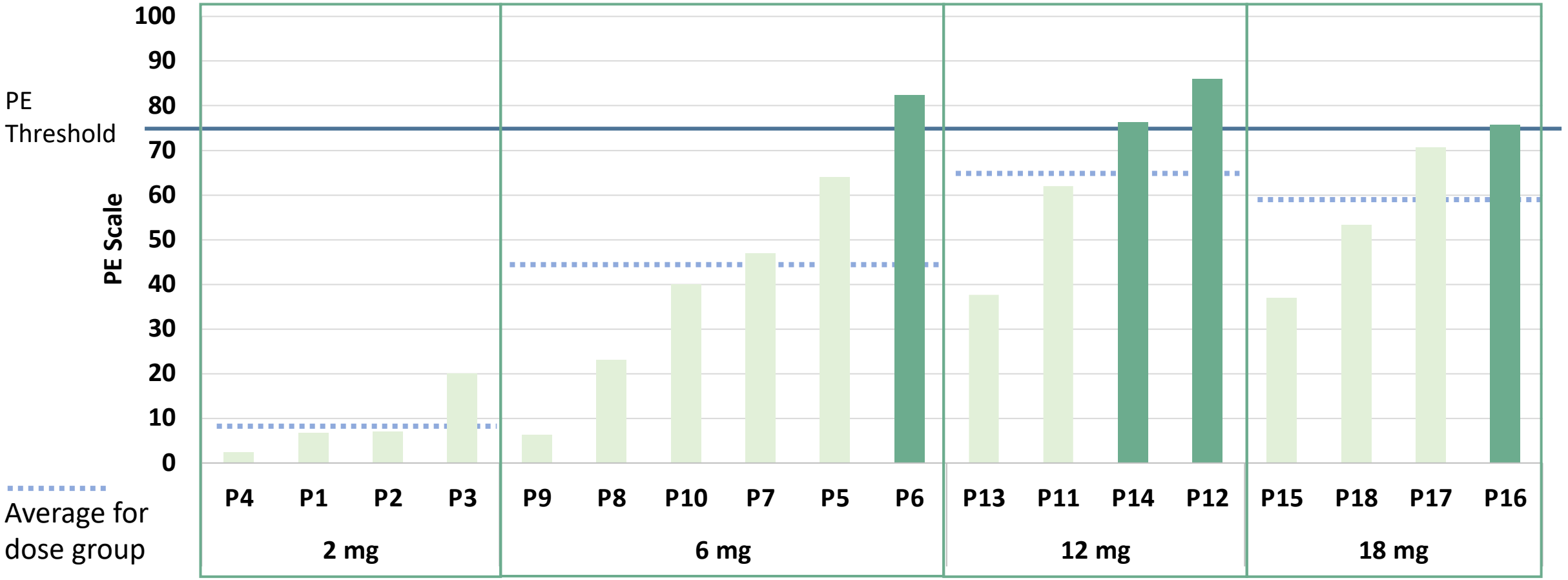
- **No SAEs**
- **All ADRs mild, except two moderate (*)**
- **All ADRs resolved spontaneously**
- **Inhalation well-tolerated**
- No noteworthy changes in vital parameters, except for temporary, non-clinically relevant increase in heart rate and blood pressure shortly after administration of GH001
-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

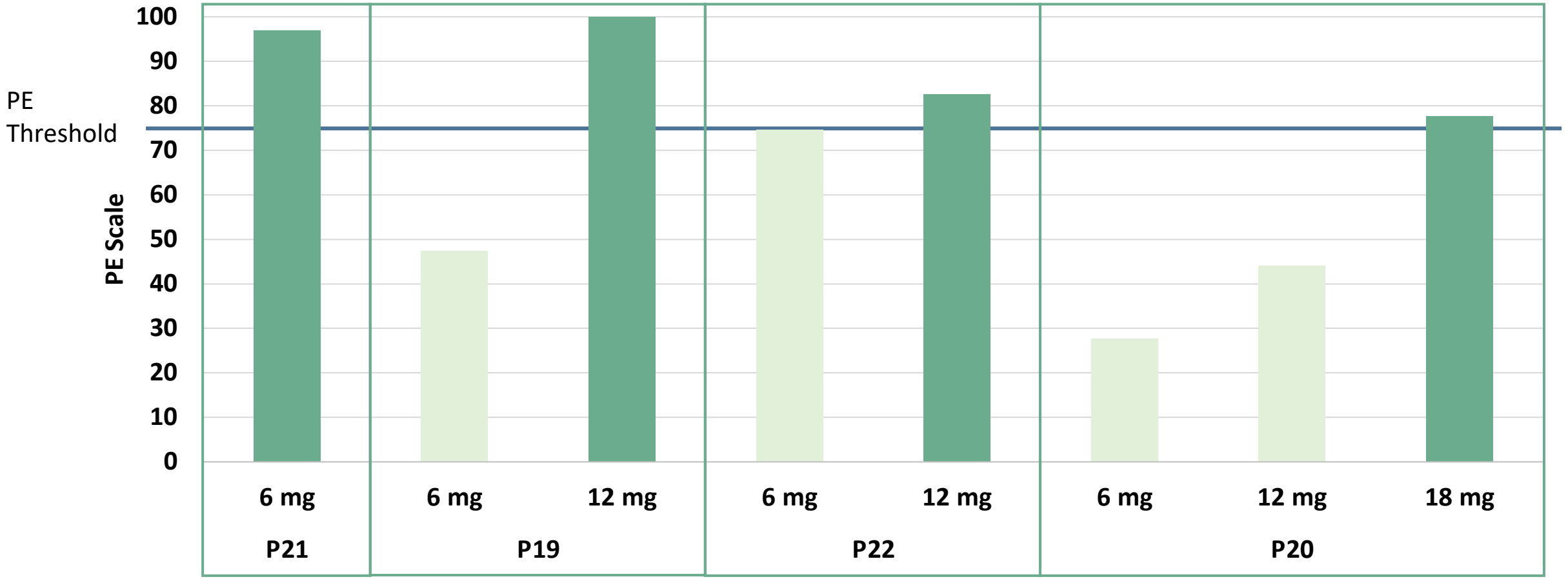
[1]6 mg (N=1); 6-12 mg (N=2); 6-12-18 mg (N=1)

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)

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

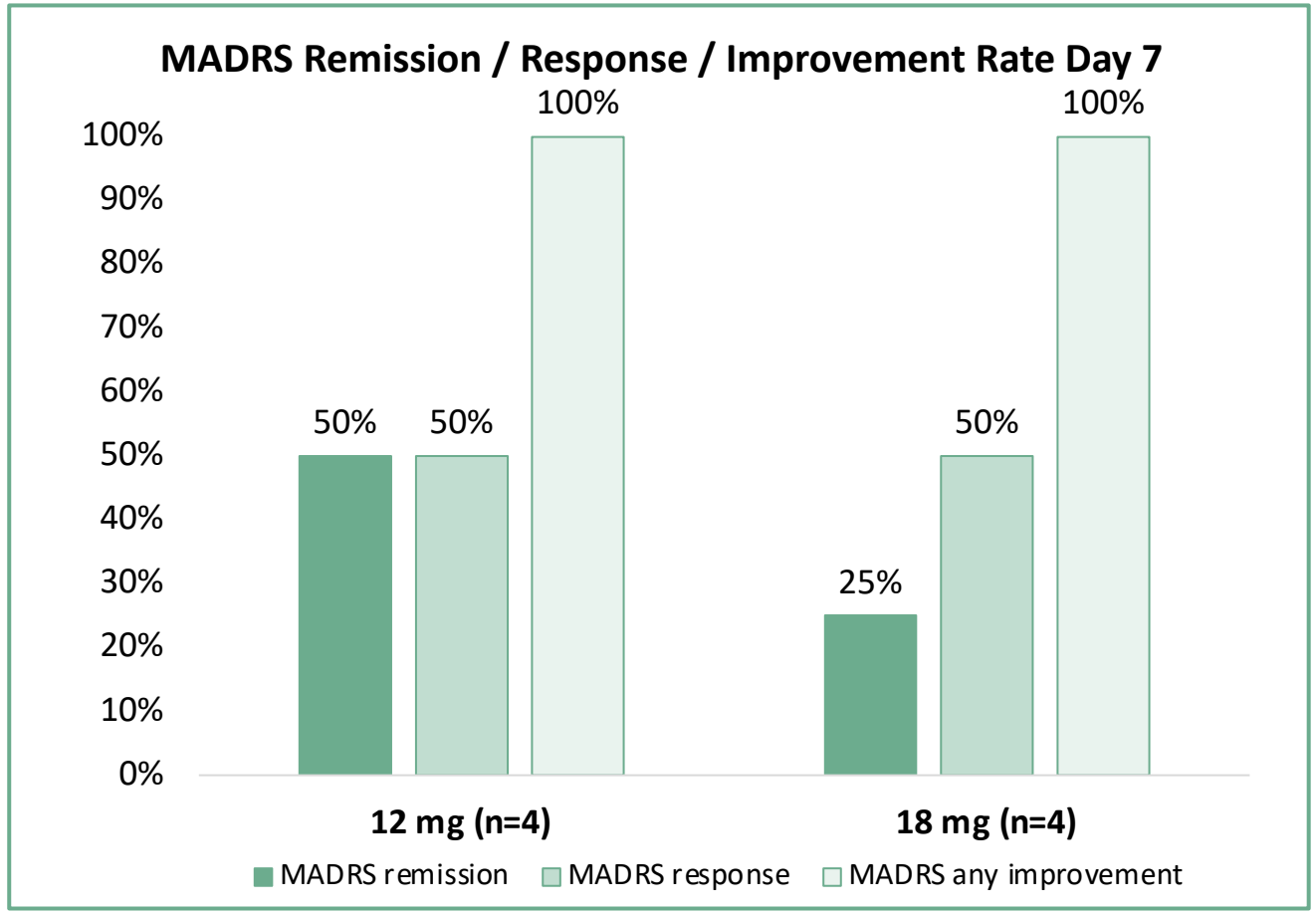
- **No SAEs**
- **All ADRs mild, except three moderate***
- **All ADRs resolved spontaneously**
- **Inhalation well-tolerated**
- No noteworthy changes in vital parameters, except for temporary, non-clinically relevant increase in heart rate and blood pressure shortly after administration of GH001
-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

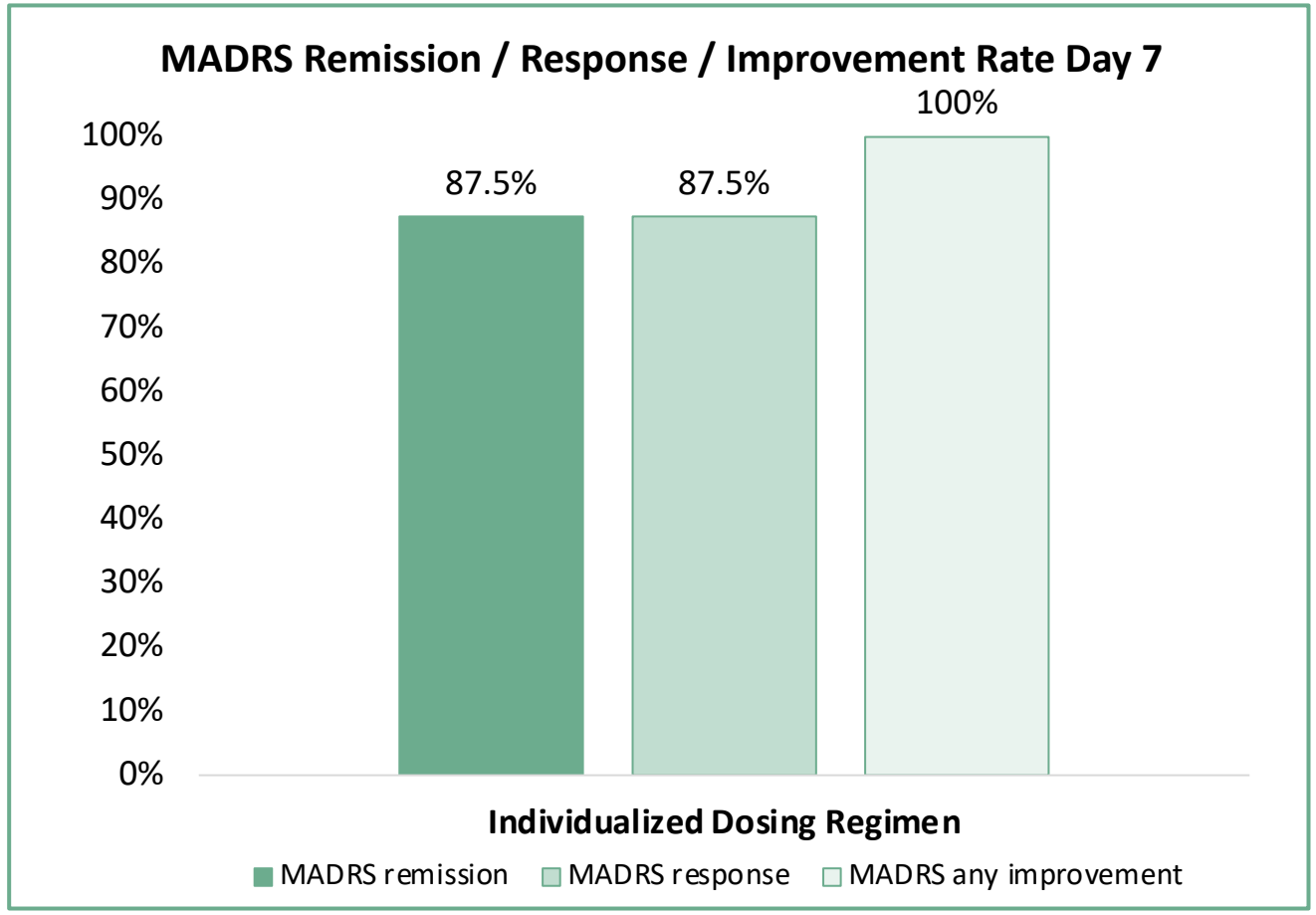
Phase 1 (Single Dose) – Efficacy (MADRS)



- 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.

Phase 2 (IDR) – Efficacy (MADRS)

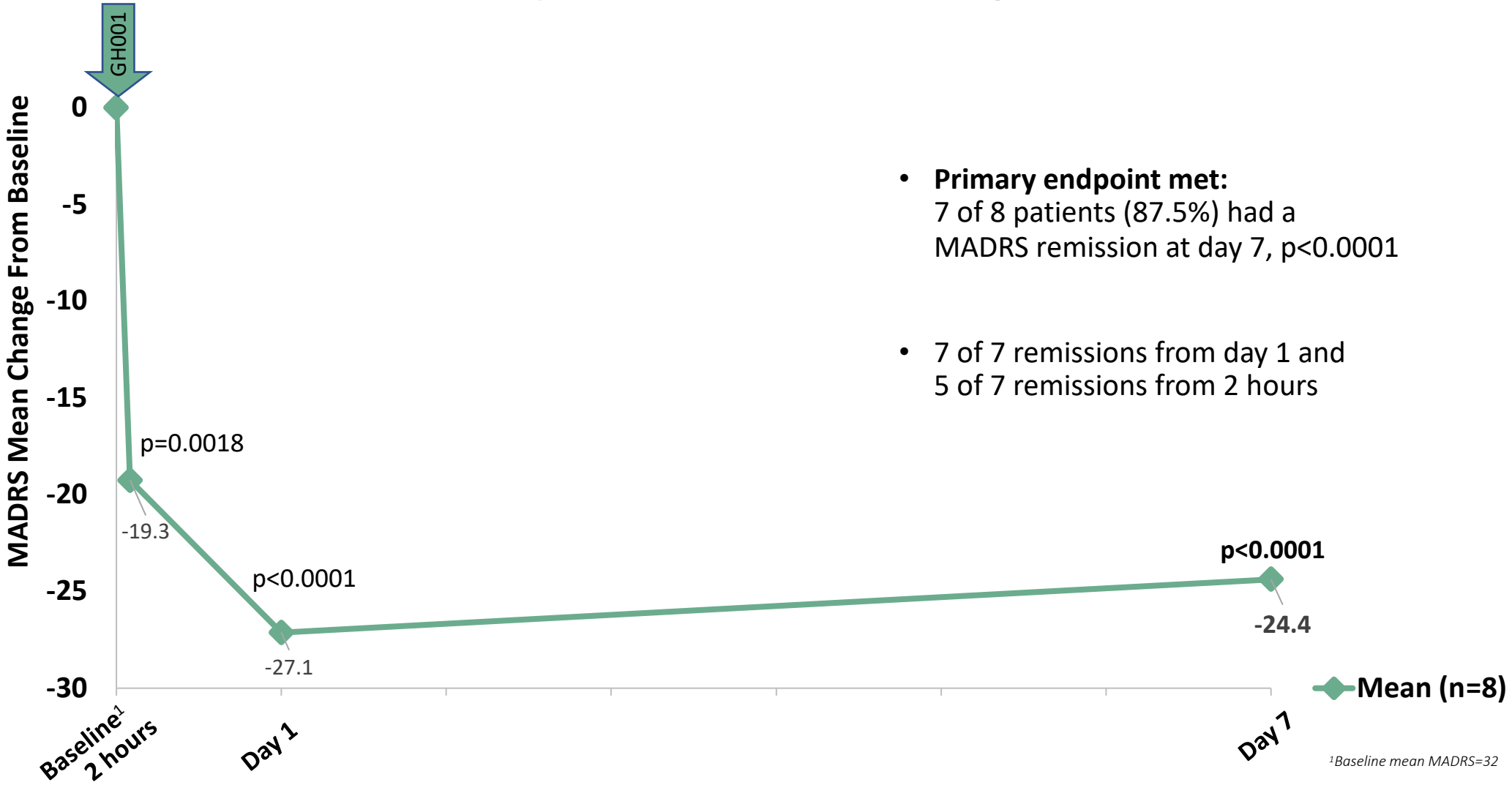


- **Primary endpoint met:**
  7 of 8 patients (87.5%) had a MADRS remission at day 7, p<0.0001

- 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.

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 5 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)

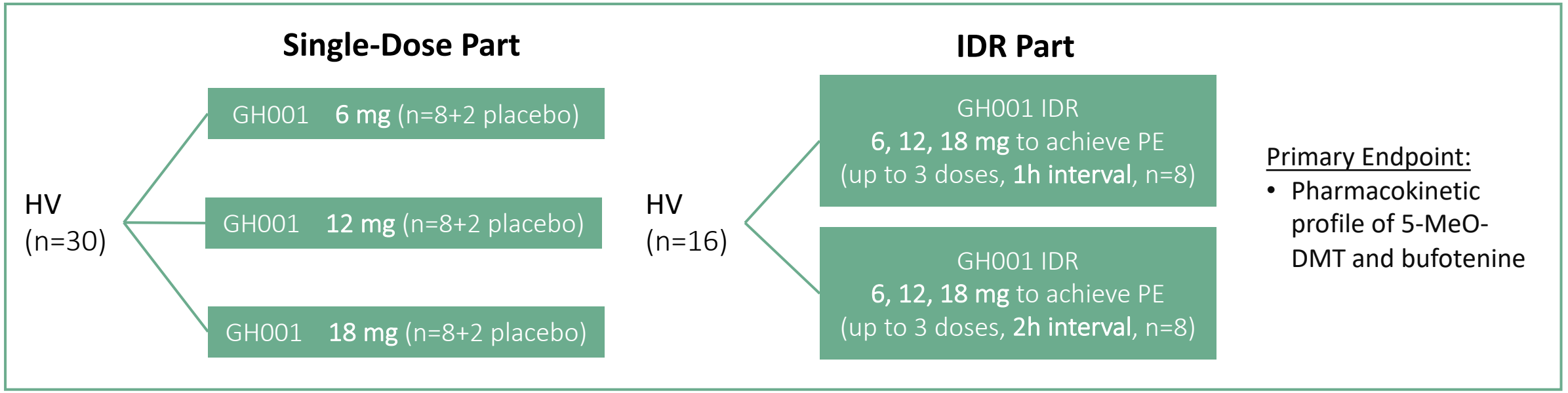
	Phase 2 (IDR)	Phase 1 (Single Dose) 12 mg	Phase 1 (Single Dose) 18 mg
MADRS Remission Rate Day 7	87.5% (7 of 8)	50% (2 of 4)	25% (1 of 4)
Mean MADRS Change Day 7	-24.4 (-76%)	-21.0 (-65%)	-12.8 (-41%)
Rate of PE	87.5% (7 of 8)	50% (2 of 4)	0% (0 of 4)
Mean PE Score	90.4 (at final dose)	58.2	59.1

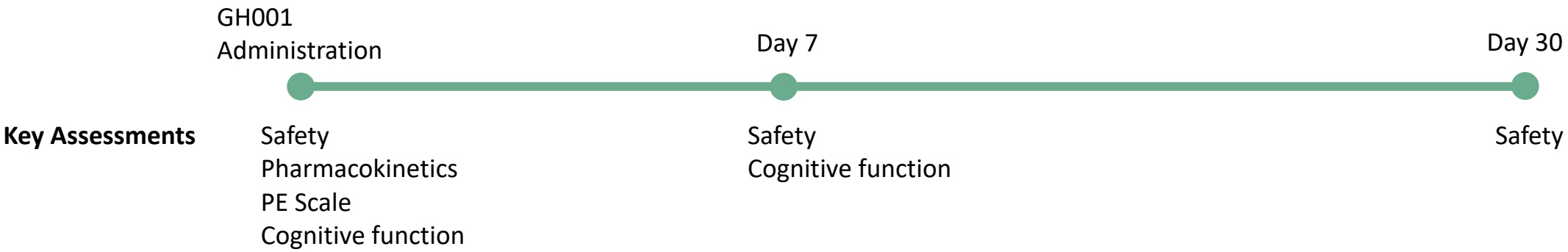
PE, Peak Experience; MADRS, Montgomery-Åsberg Depression Rating Scale
IDR, Individualized Dosing Regimen

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

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 assessment, and psychiatric safety assessments, including the C-SSRS

ADRs	Single-dose				IDR	
	6 mg (N=8)	12 mg (N=8)	18 mg (N=8)	Placebo (N=6)	1h interval (N=8)[2]	2h interval (N=8)[3]
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			

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; Pharmacokinetic analyses and analyses of various secondary endpoints are still ongoing.

[2]6 mg (N=1), 6-12 mg (N=3); 6-12-18 mg (N=4)
[3]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 of 5-MeO-DMT
- Novel uses of 5-MeO-DMT in various disorders (including inhaled, intranasal, i.v., i.m., s.c., and other routes)

LAYER 3: TECHNICAL

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

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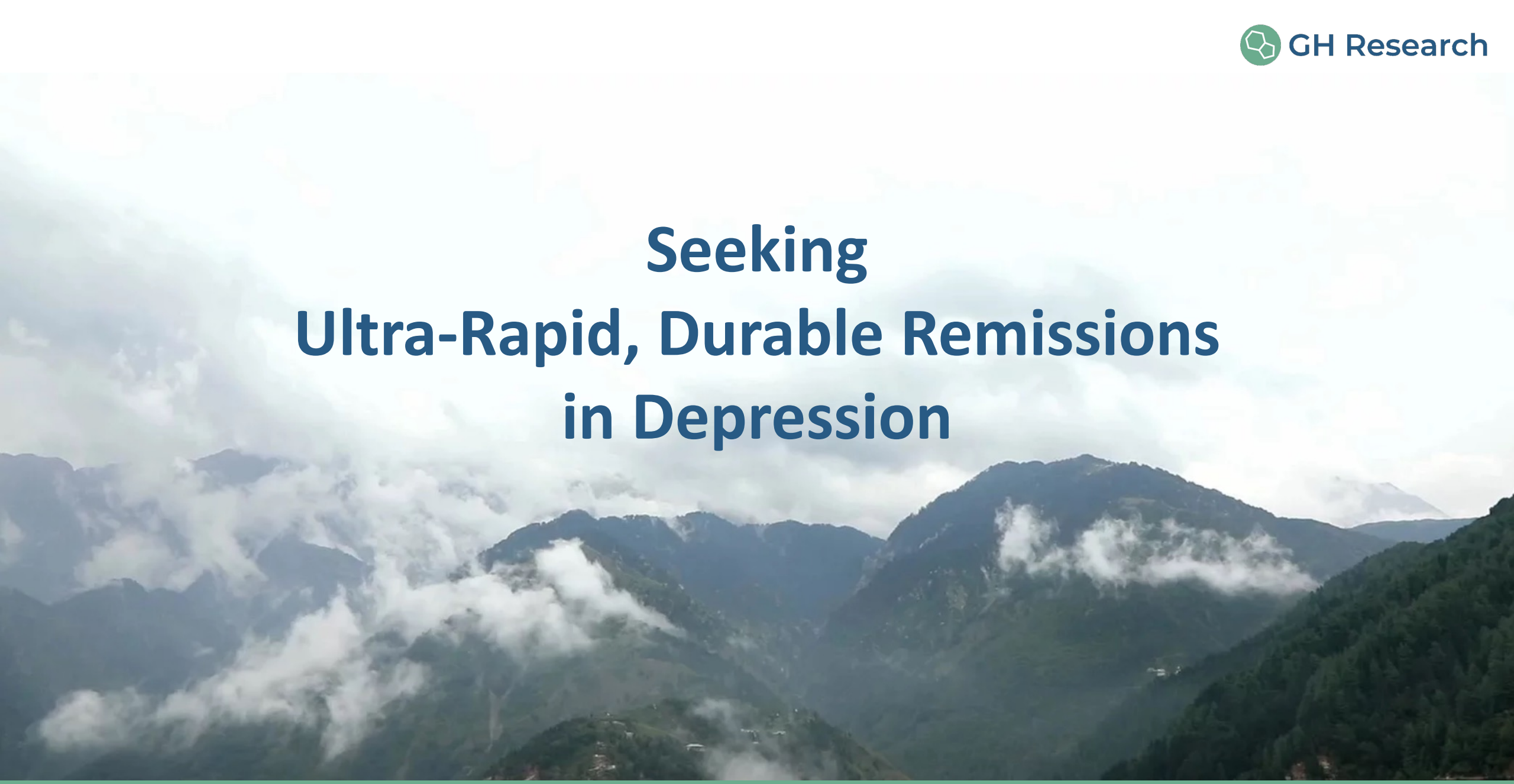
Anticipated Milestones

- GH001
  - Request a pre-IND meeting with the FDA in Q1 2022[1]
  - Initiate randomized, controlled Phase 2b trial in TRD
  - Request regulatory clearance for two Phase 2a trials in two additional psychiatric disorders in Q1 2022
- GH002 and GH003
  - Complete preclinical work and initiate Phase 1 trial in Healthy Volunteers

[1]*EMA Scientific Advice not considered necessary at this time.*



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