Ultra-Rapid, Durable Remission in TRD with Minimal Clinic Burden

GH Research PLC (Nasdaq: GHRS)

March 2026

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Pipeline

Product Candidate	Indication	Preclinical	Phase 1	Phase 2a	Phase 2b	Phase 3	Current Status	Milestone
GH001 *Mebufotenin for **inhalation** administration*	Treatment-resistant depression (TRD)						Phase 2b RDBPC completed Phase 1 PK trial with proprietary device ongoing	Phase 3 initiation in 2026 Phase 1 PK trial completion
	Postpartum depression (PPD)						Phase 2a POC	Completed
	Bipolar II Disorder[a] (BDII)						Phase 2a POC	Completed
GH002 *Mebufotenin for **i.v.** administration*	Psychiatric disorder						Phase 1 HV trial completed	IND submission

Completed

In Planning

Cash, cash equivalents and marketable securities were $280.7 million as of December 31, 2025

[a]Bipolar II disorder with a current major depressive episode.

Abbreviations: HV = Healthy volunteer; IND = Investigational New Drug; i.v. = Intravenous; PK = Pharmacokinetics; POC = Proof-of-concept; RDBPC = Randomized, double-blind, placebo-controlled.

GH001 Key Milestones Achieved and Next Steps

Phase 2b Trial

Unprecedented Efficacy in TRD

Positioning GH001 as potentially practice-changing

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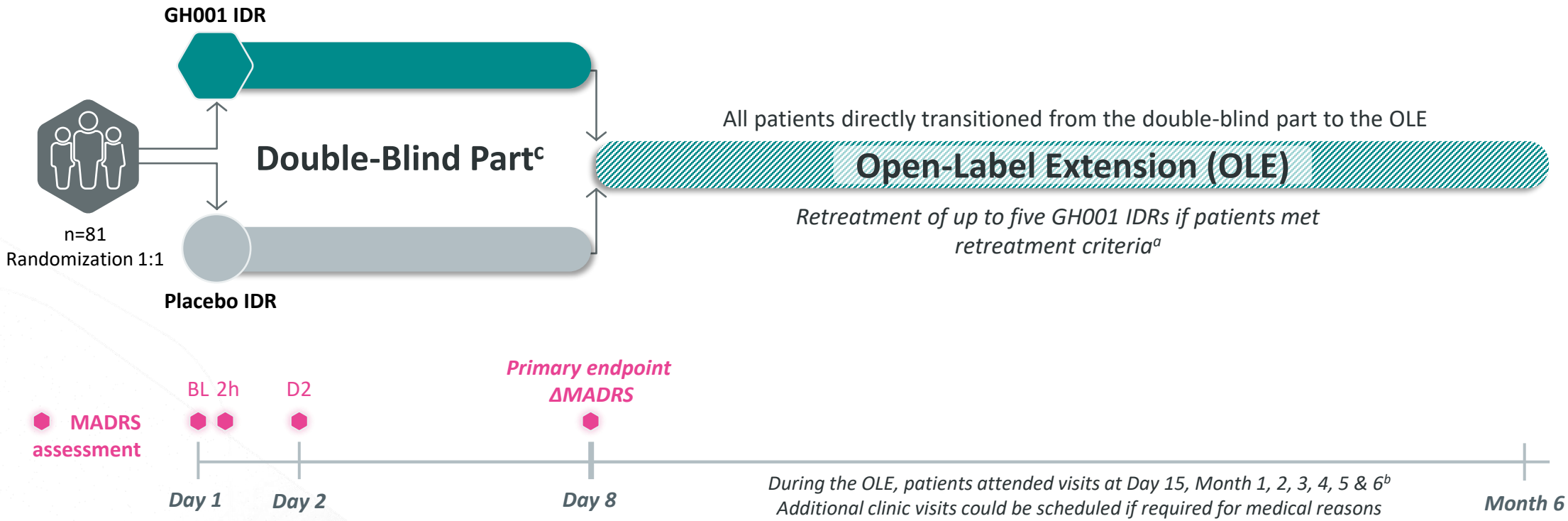
Pivotal Phase 3 Program

Designed in line with the FDA Guidelines and to replicate the Phase 2b data

Global Phase 3 start in 2026

Abbreviations: TRD = Treatment Resistant Depression; IND = Investigational New Drug; FDA = Food and Drug Administration

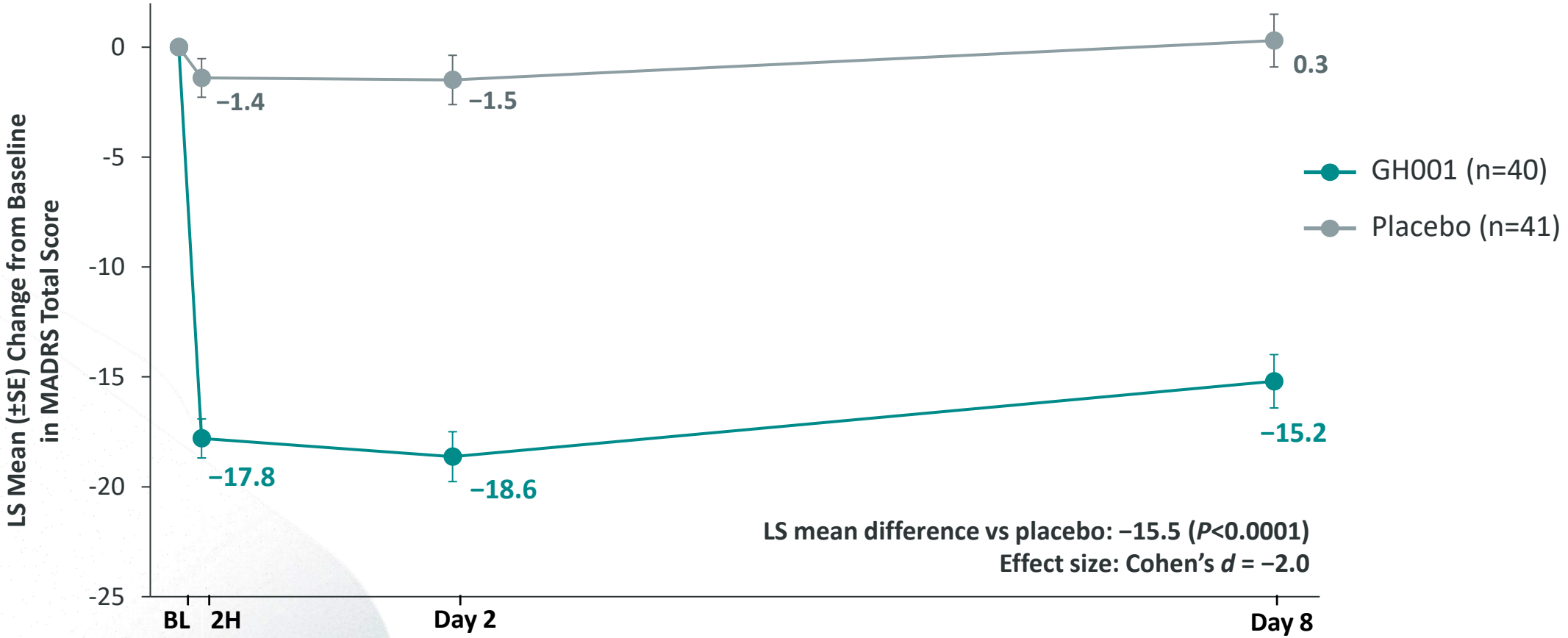
GH001-TRD-201: A Randomized, Double-Blind, Placebo-Controlled, Phase 2b Trial with an Open-Label Extension



This trial was conducted under the supervision of qualified healthcare professionals, providing psychological support per standard of care, but without any planned psychotherapeutic intervention before, during, or after dosing

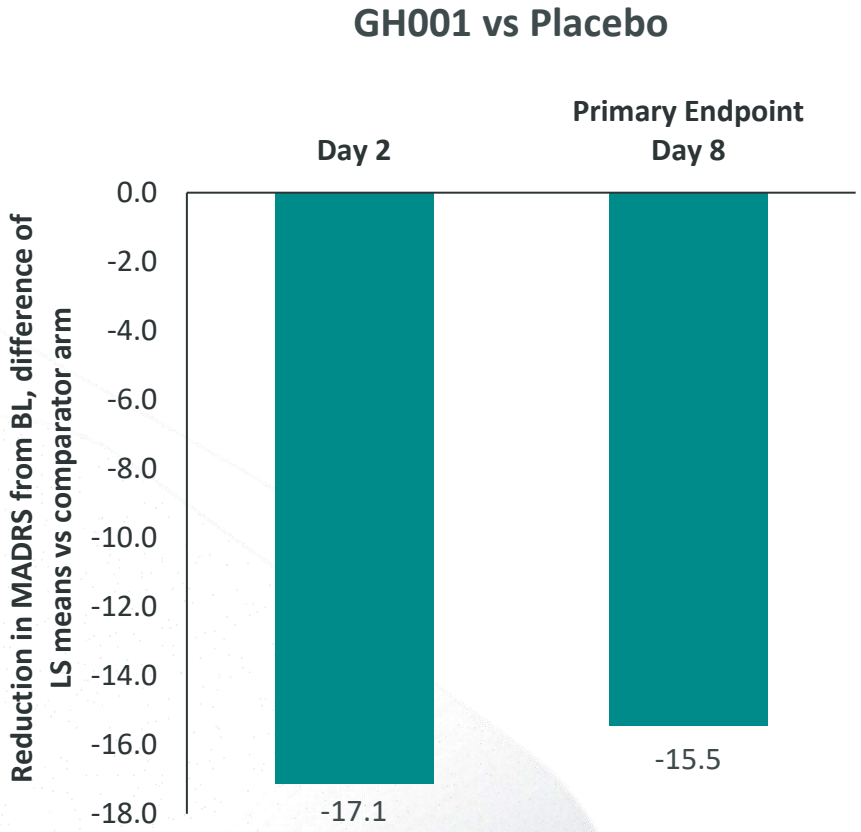
[a]Retreatment criteria: MADRS score >18, or MADRS score >10 and ≤18 and MADRS score ≤10 not observed at Day 8 of the prior treatment or at any visit since, or MADRS score >10 and ≤18 and MADRS score >18 observed since the most recent observation of MADRS score ≤10. [b]Patients also attended assessment visits on Day 2 (phone call) and Day 8 after each retreatment. [c]Efficacy assessments were carried out by independent blinded raters in the double-blind part.
Abbreviations: BL = Baseline; D = Day; h = Hour; IDR = Individualized dosing regimen; MADRS = Montgomery–Åsberg Depression Rating Scale.
ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT05800860, Accessed March 13, 2025.

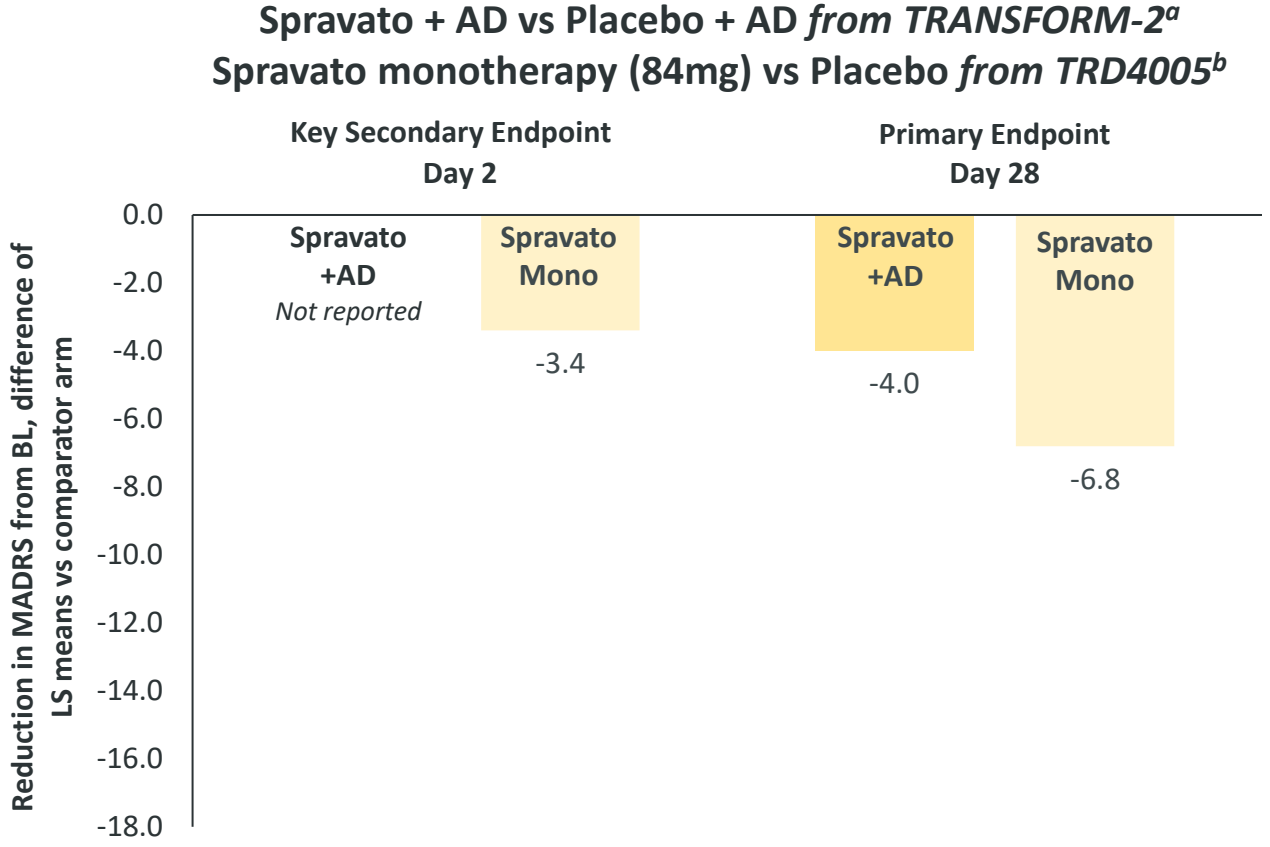
Primary Endpoint: GH001 Led to Mean MADRS Reduction from Baseline of -15.5 on Day 8[a] vs Placebo (*P*<0.0001)



[a]FDA Guidance notes that efficacy with rapid-acting antidepressants generally should be demonstrated within 1 week, supporting a primary efficacy endpoint within this timeframe.
Abbreviations: BL = Baseline; FDA = Food and Drug Administration; H = Hours; LS = Least squares; MADRS = Montgomery-Åsberg Depression Rating Scale; SE = Standard error.
FDA Guidance: Major Depressive Disorder: Developing Drugs for Treatment. https://www.fda.gov/media/113988/download. Accessed on 26 June 2025.

MADRS Total Score Change from Baseline: GH001 and Spravato at Day 2 and Primary Endpoint (Difference from Comparator Arm)



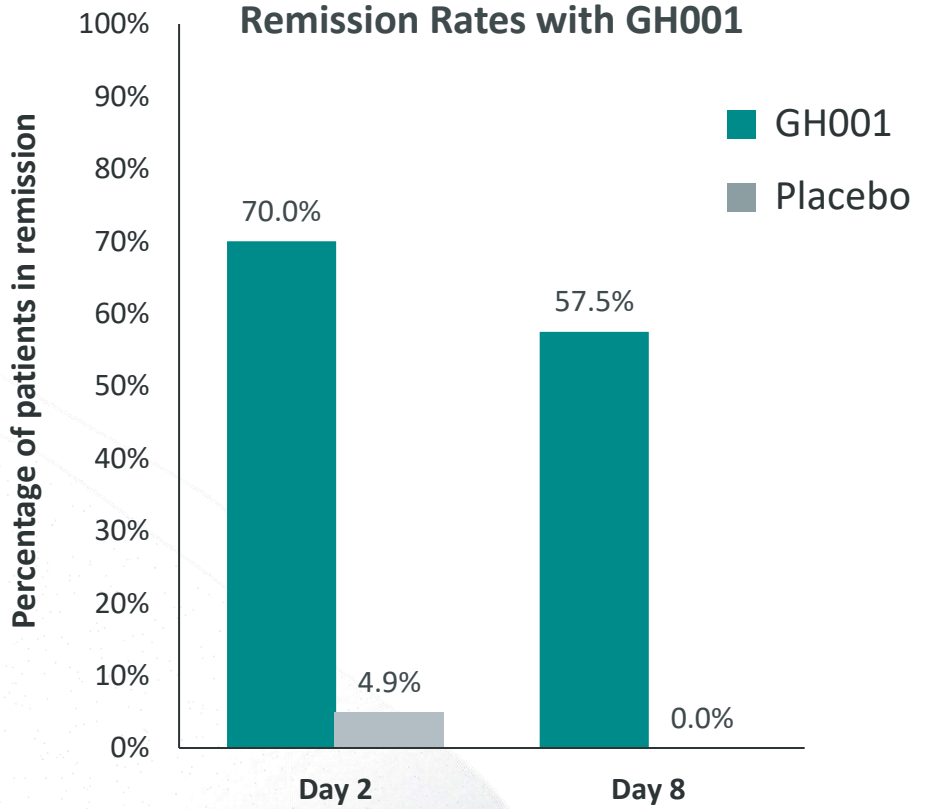


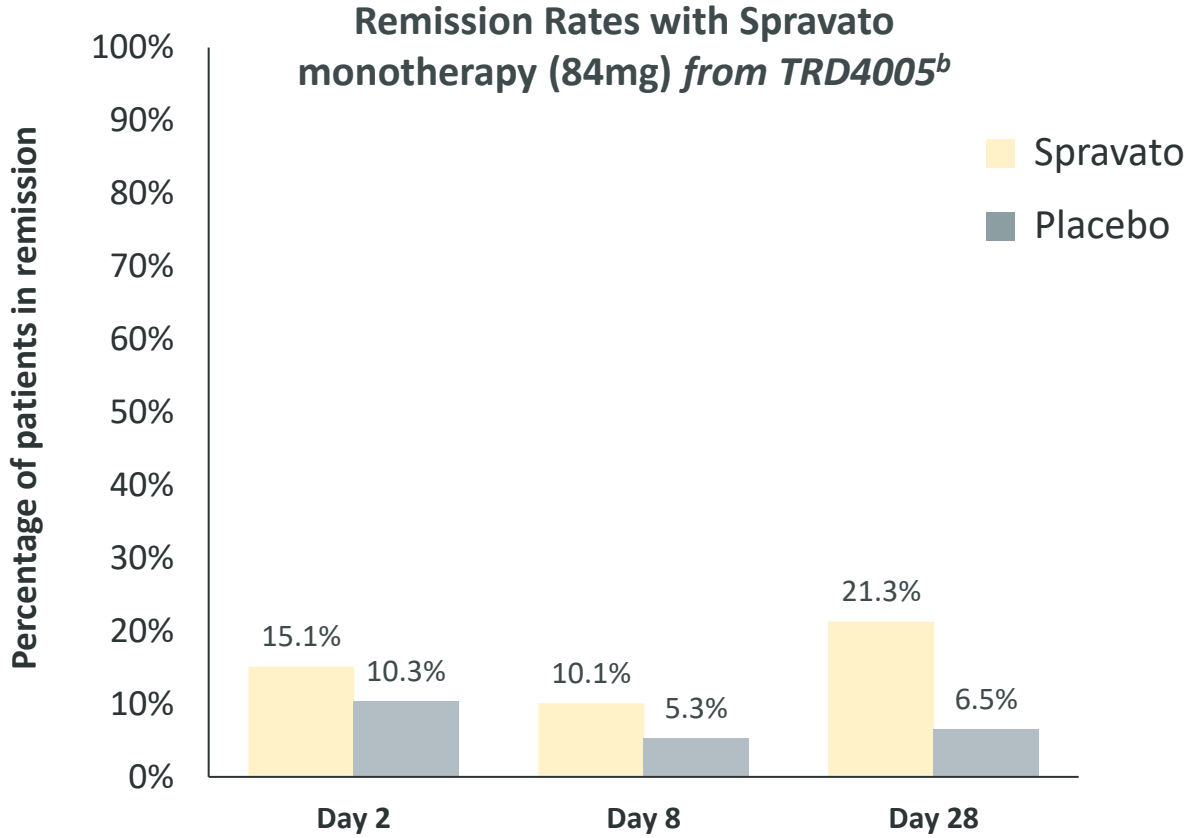
Note: To-date, no head-to-head comparisons of any other products to any of our product candidates in any clinical trial have been completed; results have been obtained from different trials with different designs, endpoints and patient populations; results may not be comparable.

[a]Spravato + AD data from TRANSFORM-2, Popova et al., 2019; [b]Spravato monotherapy data for 84mg dose from TRD4005 trial, Janik et al., 2025; Spravato 56mg MADRS total score change from baseline difference of LS means from PBO was -5.1 at Day 28 and -3.8 at Day 2

Abbreviations: AD = Antidepressant; BL = Baseline; D = Day; LS = Least Squares; MADRS = Montgomery-Åsberg Depression Rating Scale; Mono = Monotherapy.

Secondary Endpoints: Remissions[a] GH001 Day 2 and Day 8 and Spravato Monotherapy (84 mg) Day 2, Day 8 and Day 28



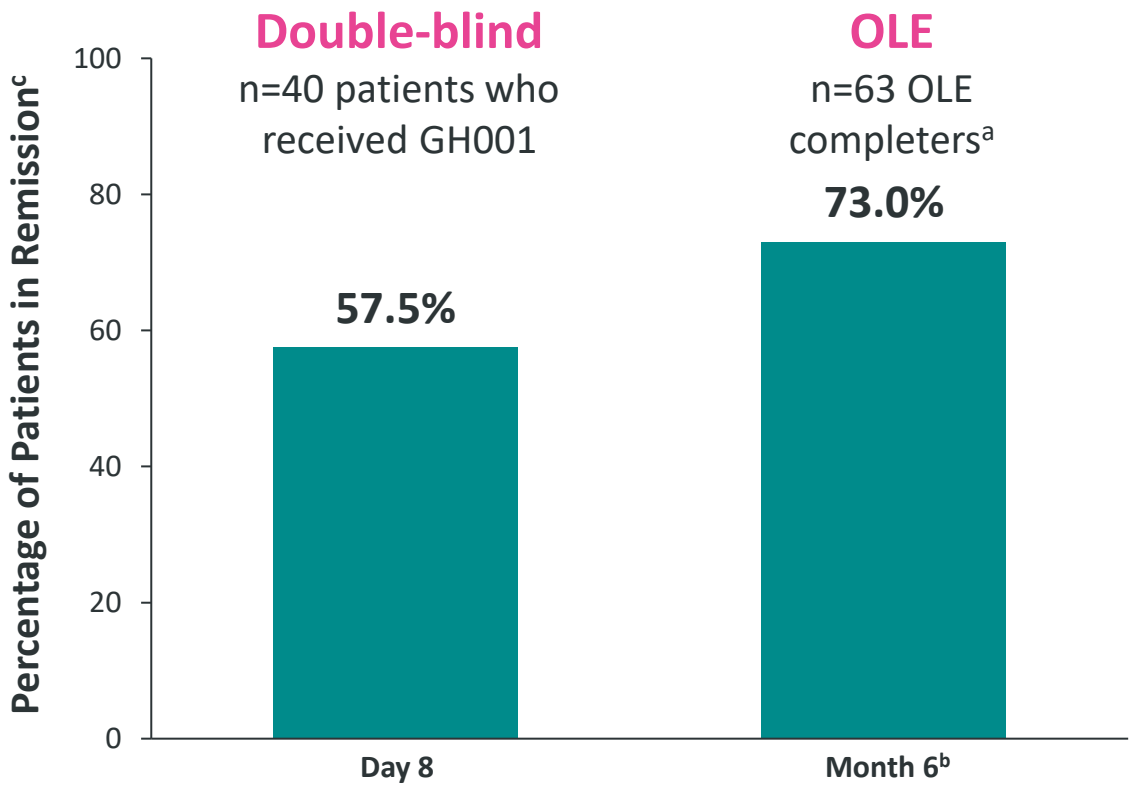


Note: To-date, no head-to-head comparisons of any other products to any of our product candidates in any clinical trial have been completed; results have been obtained from different trials with different designs, endpoints and patient populations; results may not be comparable.

[a]Remission defined as MADRS total score ≤10 for both GH001 and Spravato. [b]Source: Spravato monotherapy data for 84mg dose from TRD4005 trial, Janik et al. 2025; Spravato 56mg participants in the TRD4005 trial achieved remission rates of 13.1% at Day 2, 7.1% at Day 8 and 14.6% at Day 28 (MADRS ≤10)

Abbreviations: MADRS = Montgomery-Åsberg Depression Rating Scale

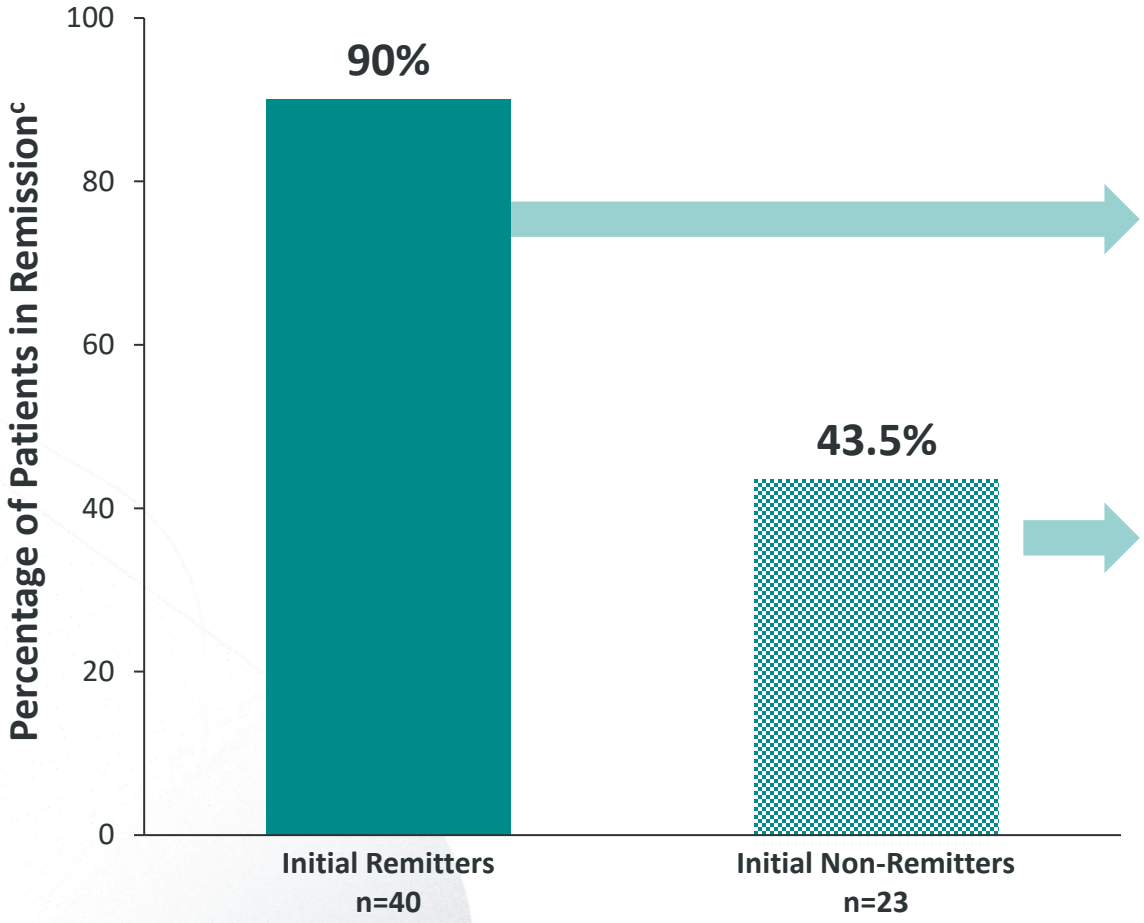
73% Remission Rate at 6 Months in OLE Completers



Patients who completed the OLE received a **mean of four treatments**, with 63.5% (40/63) requiring one to four treatments during the **6 months**

[a]Includes 63 patients who completed the 6-month OLE per protocol (18 patients terminated early are excluded). [b]Approximately 6 months post-study start (median 168 days from Day 1 of double-blind part). [c]Remission defined as MADRS total score ≤10.
Abbreviations: MADRS = Montgomery-Åsberg Depression Rating Scale; OLE = Open-label extension.

Remission Rate at 6 Months[a] in OLE Completers[b]

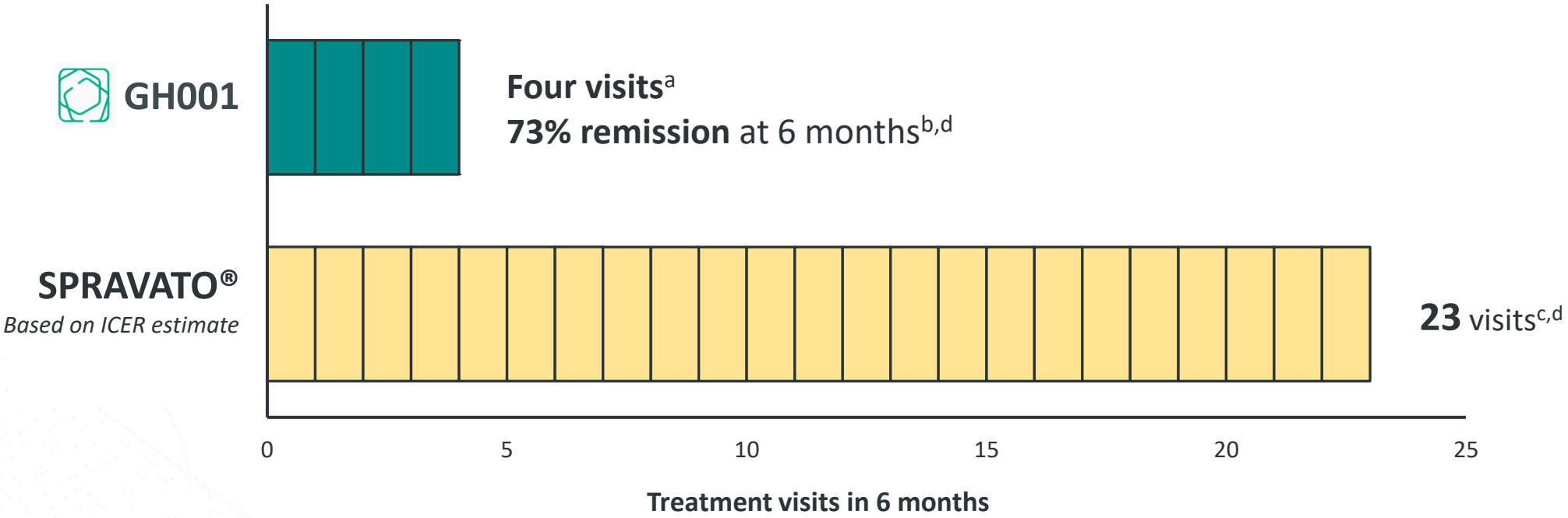


Patients in remission on Day 8 after their first active treatment had a 90% remission rate at 6 Months.

43.5% of the patients not in remission on Day 8 after first active treatment were in remission at 6 Months.

[a]'6 Months' or 'Month 6' (end of trial) was at approximately 6 months post-study start (median 168 days from Day 1 of double-blind part). [b]Includes 63 patients who completed the 6-month OLE per protocol (18 patients terminated early are excluded). [c]Remission defined as a MADRS total score ≤10.
Abbreviations: MADRS = Montgomery-Åsberg Depression Rating Scale; OLE = Open-label extension.

83% Fewer Treatment Visits with GH001 than with Spravato®



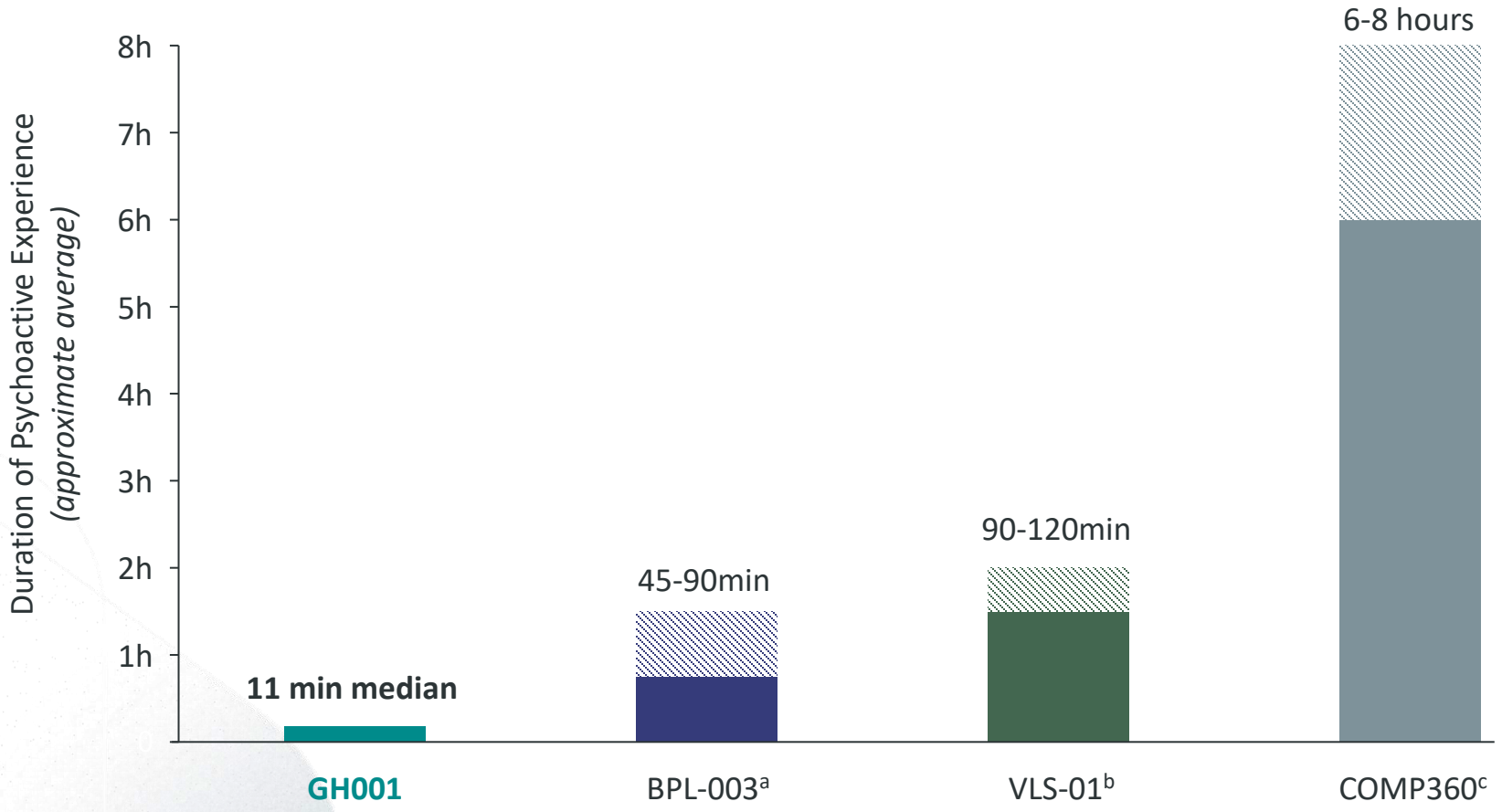
Note: To-date, no head-to-head comparisons of any other products to any of our product candidates have been completed in any clinical trial; results have been obtained from different trials with different designs, endpoints, and patient populations; results may not be comparable.

[a]Four GH001 visits deduced from the mean total number of treatments received by patients who completed the OLE and were in remission at 6-months of the GH001-TRD-201 trial. [b]'6 months' (end of trial) was at approximately 6 months post-study start (median 168 days from Day 1 of double-blind part). [c]SPRAVATO® Assumes 23 treatment visits, as per standard initiation protocol of eight and four sessions in Months 1 and 2, respectively, and ICER assumed maintenance treatment frequency of 2.86 treatments per month for Months 3-6.[1,2,3] [d]Remission defined as MADRS ≤10; Spravato® 32-Week remission rates from ESCAPE-TRD trial were 49.1% remission at 32 weeks (55.0% with LOCF method)[4].

Abbreviations: ICER = Institute for Clinical and Economic Review; LOCF = Last observation carried forward; MADRS = Montgomery-Åsberg Depression Rating Scale; OLE = Open-label extension; TRD = Treatment-resistant depression.

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. 4. Reif et al. New Engl J Med 2023.

Median Duration of the Psychoactive Experience of 11 minutes (Double-Blind & OLE treatments)



Note: To-date, no head-to-head comparisons of any other products to any of our product candidates have been completed in any clinical trial; results have been obtained from different trials with different designs, endpoints, and patient populations; results may not be comparable.

[a]Assumption of BPL-003 duration of ~90min psychoactive phase from Phase 1 SDI results as reported in Rucker et al., 2024. [b]VLS-01 duration of 90-120 minutes psychoactive experience from Phase 1b results, mean SIRS scores graph, (atai Life Sciences Corporate Presentation, October 2025). [c]COMP360 duration of ~6h from Compass Pathways website, which states "The psilocybin experience typically lasts 6 to 8 hours".

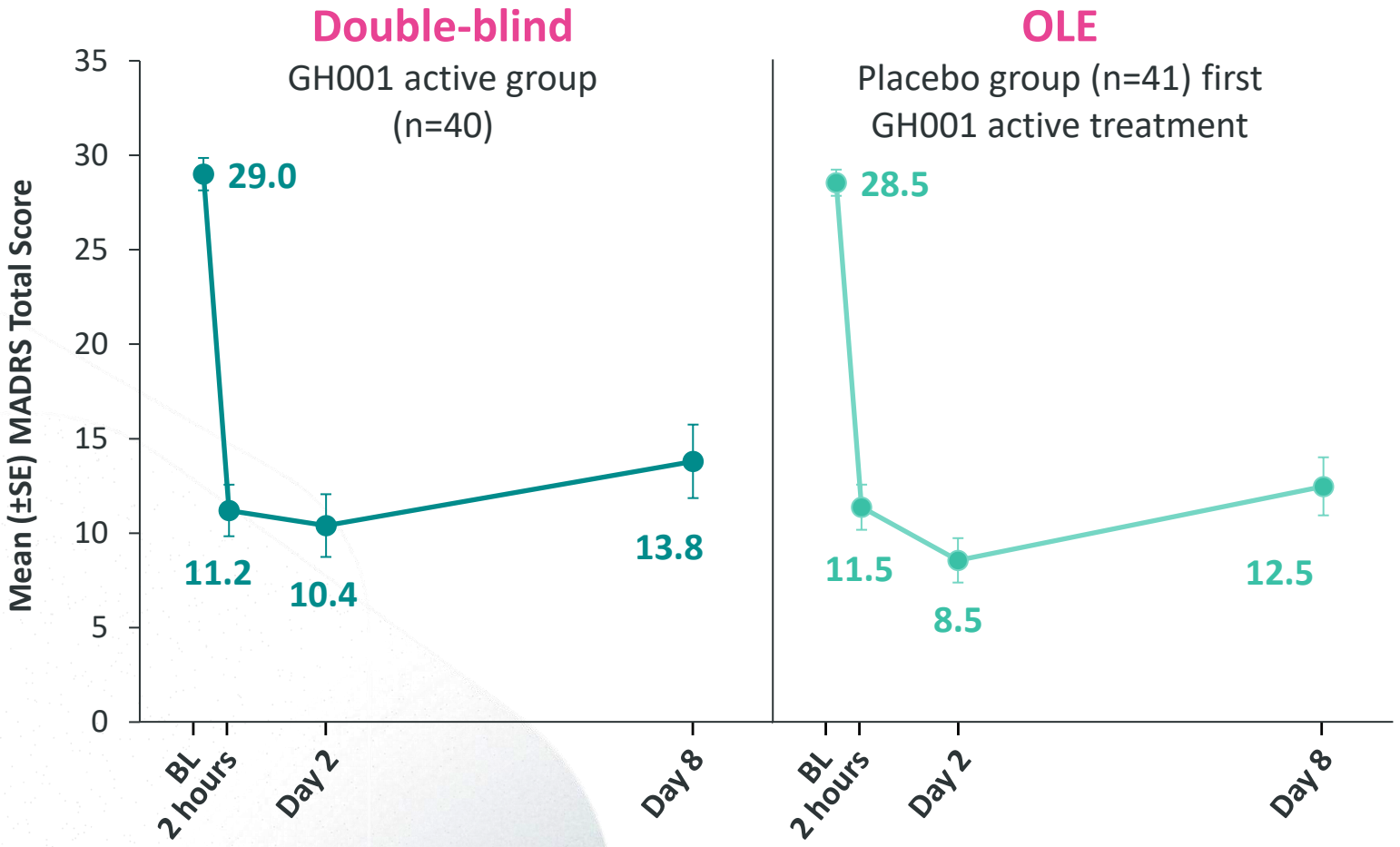
Abbreviations: h = Hours; min = Minutes; OLE = Open-label extension; SDI = Subjective drug intensity; SIRS = Subjective Intensity Rating Scale; TRD = Treatment-resistant depression.

Safety in Double-Blind and Open-Label Extension

- **There were no treatment-related SAEs during the 6-month duration of the trial.**
- All patients completed the double-blind part and automatically transitioned to the OLE
- No TEAEs of suicidal intent or suicidal behavior occurred
- Across the double-blind and OLE, patients were deemed discharge ready by 1 hour from dose administration at 99% of treatment visits (>250 GH001 treatments in 81 patients)

Abbreviations: OLE = Open-label extension; SAE = Serious adverse event; TEAE = Treatment-emergent adverse event.

Reproducibility of MADRS Reduction Demonstrated in Phase 2b Trial



- MADRS reduction in the Placebo group following first active treatment[a] after entering the OLE, was comparable to the results observed in the GH001 group in the DB part, showing **reproducibility of effects.**
- OLE data shows GH001 leads to a **consistent and rapid reduction in MADRS after each GH001 treatment**, as in the DB part

[a]An active treatment refers to treatment with GH001.

Abbreviations: BL = Baseline; DB = Double-blind; MADRS = Montgomery-Åsberg Depression Rating Scale; OLE = Open-label extension; PBO = Placebo; SE = Standard error; SEM = Standard error of mean.

- All patients enrolled in the DB part of the trial directly transitioned into the OLE at the end of the DB period.
- Once a patient completed the Day 8 visit of the DB part, if re-treatment criteria were met, a GH001 treatment could be administered.
- All patients allocated placebo in the DB part received at least one treatment with GH001 in the OLE.

Potential Value-Add for GH001 in TRD

Best in **Therapeutic Category (TRD)**

- **Efficacy:** Pbo-adj MADRS Δ of **-15.5** with GH001 vs **-6.8** with Spravato monotherapy[a] vs **~-4** with oral AD[b]
- **Length of PsE:** Median of **11 mins** with GH001 vs **~1.5 hours** with Spravato[c]
- No additional psychotherapy/therapist visits with GH001; **83% fewer treatment visits** with GH001 than with Spravato[d]

Best in **Class (Psychedelics)**

- **Efficacy:** Pbo-adj MADRS Δ of **-15.5** with GH001 vs **-3.6** with COMP360 (Phase 3 data)[e]
- **Length of PsE:** Median of **11 mins** with GH001 vs **6-8 hours** for COMP360[g] vs **45-90 mins** for BPL-003[f]
- No additional psychotherapy/therapists visits with GH001

Best in **Molecule (Mebufotenin; 5-MeO-DMT)**

- **Efficacy:** Day 8 remission rate of **57.5%** with GH001 vs **26%** with BPL-003 8 mg dose[h]
- **Length of PsE:** Median of **11 mins** with GH001 vs **45-90 mins** for BPL-003[f]
- No additional psychotherapy/therapists visits with GH001

Note: To-date, no head-to-head comparisons of any other products to any of our product candidates have been completed in any clinical trial; results have been obtained from different trials with different designs, endpoints, and patient populations; results may not be comparable. While Spravato has been approved by the FDA, GH001 has not been approved by the FDA or any other regulatory authority.

[a]Spravato® monotherapy data for 84mg dose from TRD4005 trial, presented at ECNP 2024. [b]Auvelity, data at Week 6 GEMINI trial, Iosifescu et al., 2022. [c]Dissociative effects/perceptual disturbances, Popova et al., Am J Psychiatry 2019. [d]Assumes 23 treatment visits, as per standard initiation protocol of 8 & 4 sessions in Months 1 and 2, respectively, and ICER assumed maintenance treatment frequency of 2.86 treatments per month for Months 3-6. See slide 11. [e]Compass Pathways press release June 23, 2025. [f]BPL-003 duration assumption from Phase 1 SDI results as reported in Rucker et al., 2024. [g]COMP360 duration assumption from Compass Pathways website, which states "The psilocybin experience typically lasts 6 to 8 hours". [h]Atai Corporate Deck, July 2025.

Abbreviations: ICER = Institute for Clinical and Economic Review; MADRS = Montgomery-Åsberg Depression Rating Scale; PsE = Psychoactive effect; SDI = Subjective drug intensity; TRD = Treatment-resistant depression; AD = antidepressant; Pbo-adj = placebo-adjusted.

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: EMA = European Medicines Agency; FDA = Food and Drug Administration; i.v. = Intravenous; i.m. = Intramuscular; s.c. = Subcutaneous.

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