



# Corporate Presentation

Helping Minds Heal

March 2026

Nasdaq: HELP  
Cboe CA: HELP

# Cautionary Statement

The information contained in this presentation has been prepared by Cybin Inc. and its affiliates ("Helus" or the "Company"), which operates as Helus Pharma and its respective affiliates. The information contained in this presentation: (a) is provided as at the date hereof, is subject to change without notice, and is based on publicly available information, internally developed data and third party information from other sources; (b) does not purport to contain all the information that may be necessary or desirable to fully and accurately evaluate an investment in the Company; (c) is not to be considered as a recommendation by the Company that any person make an investment in the Company; and (d) is for information purposes only and shall not constitute an offer to buy, sell, issue or subscribe for, or the solicitation of an offer to buy, sell or issue, or subscribe for any securities in any jurisdiction in which such offer, solicitation or sale would be unlawful. Where any opinion or belief is expressed in this presentation, it is based on certain assumptions and limitations and is an expression of present opinion or belief only. The third-party information has not been independently verified. While the Company may not have verified the third-party information, it believes that it obtained the information from reliable sources and has no reason to believe it is not accurate in all material respects. No warranties or representations can be made as to the origin, validity, accuracy, completeness, currency or reliability of the information. Helus disclaims and excludes all liability (to the extent permitted by law), for losses, claims, damages, demands, costs and expenses of whatever nature arising in any way out of or in connection with the information in this presentation, its accuracy, completeness or by reason of reliance by any person on any of it. This presentation should not be construed as legal, financial or tax advice to any individual, as each individual's circumstances are different. Readers should consult with their own professional advisors regarding their particular circumstances. In making an investment decision, investors should not rely solely on the information contained in this presentation. The delivery of this presentation, at any time, will not imply that the information contained in the presentation is correct as of any time subsequent to the date set forth on the cover page of the presentation or the date at which such information is expressed to be stated, as applicable. No securities commission, exchange or similar regulatory authority in Canada or the United States has reviewed or in any way opined on the merits of this presentation, and any representation to the contrary is an offence.

Certain statements in this presentation constitute forward-looking information or forward-looking statements, within the meaning of applicable securities legislation (together, "forward looking statements"). All statements, other than statements of historical fact contained in this presentation, including, without limitation, statements regarding Helus' future, strategy, plans, objectives, goals and targets, and any statements preceded by, followed by or that include the words "believe", "expect", "aim", "intend", "plan", "continue", "will", "may", "would", "anticipate", "estimate", "forecast", "predict", "project", "seek", "should" or similar expressions or the negative thereof, are forward-looking statements. These statements are not historical facts but instead represent only Helus's expectations, estimates and projections regarding future events. These statements are not guaranteeing future performance and they involve assumptions, risks and uncertainties that are difficult to predict. Therefore, actual results may differ materially from what is expressed, implied or forecasted in such forward-looking statements.

Forward-looking statements are based on a number of factors and assumptions made by management and considered reasonable at the time such information is provided, and forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause the actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements. Risk Factors that could cause actual results, performance or achievement to differ materially from those indicated in the forward-looking statements include, but are not limited to the following: regulatory, legislative, legal or other developments with respect to its operations or business; general economic conditions and financial markets; the loss of key management personnel; capital requirements and liquidity; access to capital; the timing and amount of capital expenditures; the impact of disease outbreaks; conflicts of interest; uninsurable risks; and litigation and other factors beyond the Company's control. Readers are cautioned that the foregoing list and the risk factors under the heading "Risk Factors" are not exhaustive. The forward-looking information and forward-looking statements included in this presentation are made as of the date of this presentation. The Company does not undertake any obligation to update such forward-looking statements or forward-looking information to reflect new information, subsequent events or otherwise unless required by applicable securities law. Readers should not place undue importance on forward-looking information and should not rely upon this information as of any other date. Third party information has not been independently verified. No warranties or representations can be made as to the origin, validity, accuracy, completeness, currency or reliability of the information.

## RISK FACTORS

There are a number of risk factors that could cause future results to differ materially from those described herein. A discussion of the principal risk factors relating to the Company's operations and business appear in the Company's most recently filed management's discussion and analysis and the annual information form, which are available under the Company's profile on [www.sedarplus.ca](http://www.sedarplus.ca) and with the United States Securities and Exchange Commission on EDGAR at [www.sec.gov](http://www.sec.gov). Additional risks and uncertainties, including those that the Company is not aware of currently, or that it currently deems immaterial, may also adversely affect the Company's business or any investment therein. All of the forward-looking statements made in this presentation are qualified by these cautionary statements and other cautionary statements or other factors contained herein. Although management believes that the expectations conveyed by forward-looking statements herein are reasonable based on information available on the date such forward-looking statements are made, there can be no assurance that forward-looking statements will prove to be accurate, as actual results and future events could differ materially from those anticipated in such statements. The Company undertakes no obligation to update forward-looking statements if circumstances or management's estimates or opinions should change except as required by applicable securities laws. The forward-looking statements contained herein are presented for the purposes of assisting readers in understanding the Company's plan, objectives and goals and may not be appropriate for other purposes. The reader is cautioned not to place undue reliance on forward-looking statements.

## CAUTIONARY NOTE REGARDING FUTURE-ORIENTED FINANCIAL INFORMATION

To the extent that any forward-looking statement in this presentation constitutes "future-oriented financial information" or "financial outlooks" within the meaning of applicable securities laws, such information is being provided to demonstrate the anticipated market penetration and the reader is cautioned that this information may not be appropriate for any other purpose and the reader should not place undue reliance on such future-oriented financial information and financial outlooks. Future-oriented financial information and financial outlooks, as with forward-looking statements generally, are, without limitation, based on the assumptions and subject to the risks set out above under the heading "Cautionary Statement Regarding Forward-Looking Information". The Company's actual financial position and results of operations may differ materially from management's current expectations and, as a result, the Company's revenue and expenses.

## CAUTIONARY NOTE REGARDING REGULATORY MATTERS

The Company conducts research and development and is focused on developing and commercializing therapeutics are regulated as controlled substances in certain jurisdictions, including Canada, Ireland, The United Kingdom, The United States, and certain of the states and provinces therein. For these reasons, the Company may be (a) subject to heightened scrutiny by regulators, stock exchanges, clearing agencies and other authorities, (b) susceptible to regulatory changes or other changes in law, and (c) subject to risks related to drug development, among other things, including a possibility such scheduling or laws would need to change for the Company to commercialize certain of its proposed products. The Company makes no medical, treatment or health benefit claims about the Company's proposed products, nor have any regulatory authorities approved such proposed products. The efficacy of such products has not been confirmed by approved research. If the Company cannot obtain the approvals or research necessary to commercialize its business, it may have a material adverse effect on the Company's performance and operations.

## DRUG DEVELOPMENT.

Drug development involves long lead times, is very expensive and involves many variables of uncertainty. There is no assurance that any timelines estimated herein will be met. Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to the Company. This presentation contains certain forward-looking statements regarding anticipated or possible drug development timelines. Such statements are informed by, among other things, regulatory guidelines for developing a drug with safety studies, proof of concept studies, and pivotal studies for new drug application submission and approval, and assumes the success of implementation and results of such studies on timelines indicated as possible by such guidelines, other industry examples, and the Company's development efforts to date.

## INDUSTRY INFORMATION

This presentation also contains or references certain market, industry and peer group data which is based upon information from independent industry publications, market research, analyst reports and surveys and other publicly available sources. Although the Company believes these sources to be generally reliable, such information is subject to interpretation and cannot be verified with complete certainty due to limits on the availability and reliability of data, the voluntary nature of the data gathering process and other inherent limitations and uncertainties. The Company has not independently verified any of the data from third party sources referred to in this presentation and accordingly, the accuracy and completeness of such data is not guaranteed.

## US DISCLAIMER

This corporate overview is not a prospectus or an offering memorandum pursuant to applicable United States securities laws. The securities of Helus may not be offered or sold in the "United States", or to, or for the account or benefit of, "U.S. persons" as such terms are defined in Regulation S under the United States Securities Act of 1933, as amended (the "U.S. Securities Act"), unless pursuant to the registration requirements of the U.S. Securities Act and applicable state securities laws or an exemption from such registration requirements. The securities of Helus have not been approved or disapproved by the United States Securities and Exchange Commission, or any other securities commission or regulatory authority in the United States, nor have any of the foregoing authorities passed upon or endorsed the merits of any of the securities of Helus nor have they approved this presentation or confirmed the accuracy or adequacy of the information contained in this presentation. Any representation to the contrary is a criminal offense.

# Leading the Development of Novel Serotonergic Agonists ("NSAs")<sup>1,2</sup>

- 1** **Two proprietary clinical programs, HLP003 and HLP004, targeting major depressive disorder ("MDD") and generalized anxiety disorder ("GAD") with positive Phase 2 safety and efficacy results**
- 2** **Lead program HLP003 has been granted U.S. Food and Drug Administration Breakthrough Therapy Designation and is in Phase 3 studies for the adjunctive treatment of MDD**
- 3** **Differentiated pipeline with potential for expansion into additional mental health indications with high unmet need affecting >200M people in the U.S.<sup>3</sup>**
- 4** **Strong intellectual property portfolio with over 350 filed patents of which >100 are granted which provide patent protection until at least 2041**

Notes:

- 1) NSAs: synthetic molecules designed to activate serotonin pathways that are believed to drive neuroplasticity.
- 2) Forward looking statements are subject to risks and assumptions. See "Cautionary Statement" on page 2 of this presentation. There is no assurance that timelines will be met. Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to Helus. Such statements are informed by, among other things, regulatory guidelines for developing a drug with timeline safety studies, proof of concept studies, and pivotal studies for new drug application submission and approval, and assumes the success of implementation and results of such studies on timelines indicated as possible by such guidelines, other industry examples, and Helus's development efforts to date.
- 3) Addressable market is estimated based on U.S. census population of 337,049,203 as of September 8, 2024, and on U.S. prevalence of indications including depression, anxiety disorders/PTSD, bipolar disorder, substance use/addiction disorders, eating disorders, cluster headaches/migraine, and chronic pain management.

# Executing on Our Innovative Pipeline to Enable a Paradigm Shift in Mental Health

PROGRAM	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
<b>HLP003</b> Deuterated NSA (Oral)	Adjunctive treatment of MDD	Phase 3 study dosing underway Granted FDA Breakthrough Therapy Designation			<ul style="list-style-type: none"> <li><b>Q4 2026:</b> Phase 3 APPROACH topline data<sup>1,2</sup></li> </ul>
<b>HLP004</b> Deuterated NSA (Intramuscular)	GAD	Phase 2 signal-finding study complete			<ul style="list-style-type: none"> <li>✓ <b>Q1 2026:</b> Phase 2 Topline Data</li> </ul>
<b>HLP005</b> Phenethylamines and Tryptamines	Central Nervous System (CNS) Disorders	Preclinical studies			

Notes:

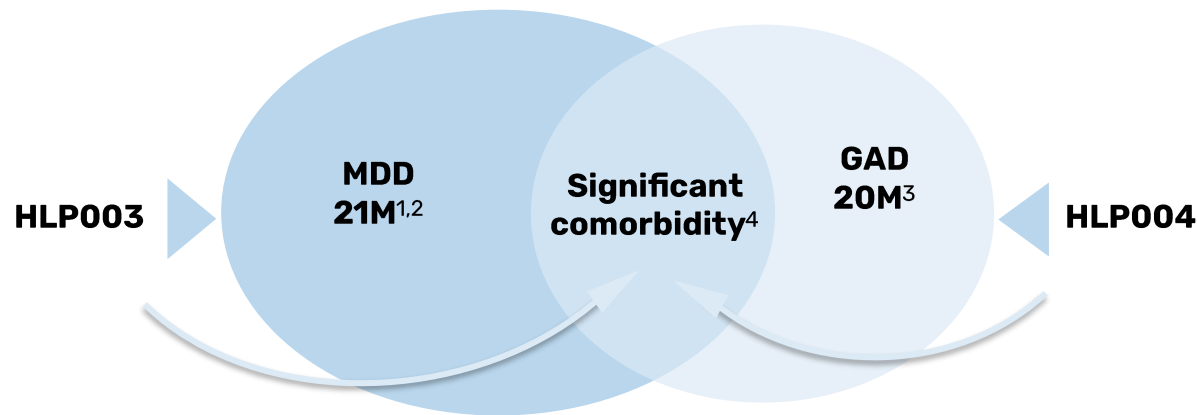
- 1) Forward-looking statements are subject to risks and assumptions. See "Cautionary Statement" on page 2 of this presentation.
- 2) Subject to receipt of all necessary regulatory approvals from all applicable governmental authorities, including, as applicable, the academic and scientific organizations with which Helus is working. There are multiple risk factors regarding the ability to successfully commercially scale a chemically synthesized process to obtain psilocin and other analogues. There is no assurance that timelines will be met. Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to Helus. Such statements are informed by, among other things, regulatory guidelines for developing a drug with timeline safety studies, proof of concept studies, and pivotal studies for new drug application submission and approval and assumes the success of implementation and results of such studies on timelines indicated as possible by such guidelines, other industry examples, and Helus's development efforts to date.

# Portfolio strategy expands addressable market and commercial opportunity<sup>5,6</sup>

**Broaden addressable market & address comorbidities**

**Leverage portfolio and drive commercial synergies**

**Addressing overlapping needs in MDD and GAD**



## **HLP003** Build platform

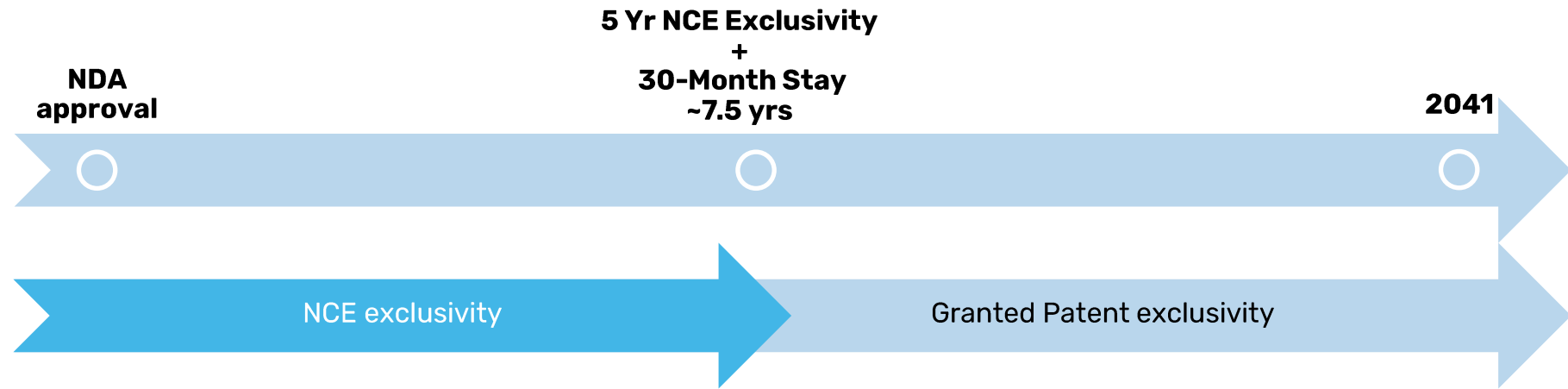
- Salesforce and distribution network
- Reimbursement and contracting framework

## **HLP004** Leverage Economies of Scale

- Contracting
- Salesforce share-of-voice

# Strong IP Portfolio Supporting HLP003 and HLP004<sup>1,2,3</sup>

## U.S. Exclusivity Timeline



### ✓ **Multilayered** IP strategy

- Compositions and:
  - Oral Dosage Forms – HLP003
  - Injectable Formulations – HLP004
- Focused formulations
- Salt / crystalline forms
- Methods of treatment supported by positive clinical data

- ✓ **Issued patents** provide IP protection until at least **2041**
- ✓ Continued focus on patent lifecycle
- ✓ Protection of additional program IP as well as other NSAs

Notes:

- 1) "Granted Patent Exclusivity" dates are based on issued patents and assume maintenance fee payments, with no early termination or invalidation. Patent and exclusivity terms vary by jurisdiction and are subject to change. "NCE Exclusivity" refers to U.S. FDA regulatory exclusivity under the Hatch-Waxman Act and is an estimate only. Data exclusivity is distinct from patent protection and may provide additional market exclusivity. All dates are estimates and subject to legal, regulatory, or commercial developments.
- 2) Subject to receipt of all necessary regulatory approvals from all applicable governmental authorities, including, as applicable, the academic and scientific organizations with which Helus is working. There are multiple risk factors regarding the ability to successfully commercially scale a chemically synthesized process to obtain psilocin and other analogues. There is no assurance that timelines will be met. Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to Helus. Such statements are informed by, among other things, regulatory guidelines for developing a drug with timeline safety studies, proof of concept studies, and pivotal studies for new drug application submission and approval, and assumes the success of implementation and results of such studies on timelines indicated as possible by such guidelines, other industry examples, and Helus's development efforts to date.
- 3) Forward-looking statements are subject to risks and assumptions. See "Cautionary Statement" on page 2 of this presentation.

# Reducing Burden on Clinical Infrastructure

Interventional Psychiatry Clinics have been growing in the U.S.

**Approximately 8,000 existing Interventional Psychiatry clinics with capacity**

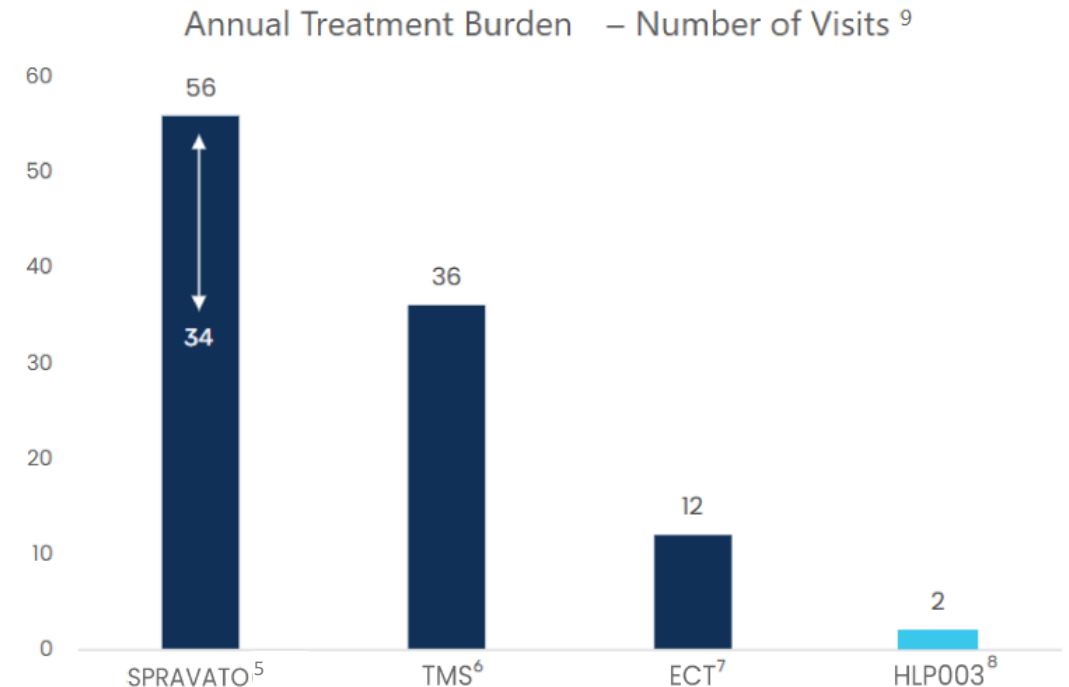
- 5300 SPRAVATO<sup>1</sup> clinics
- 750 ketamine-only clinics<sup>2</sup>
- 2,300 TMS clinics<sup>3</sup>

**Infrastructure to support uptake of HLP003 will exist in all types of Interventional Psychiatry clinics**

**Partnership with osmind<sup>4</sup>:**

- Leverage extensive network of > 800 psychiatry clinics in the U.S
- Strengthen expertise in logistics, clinical workflows and reimbursement pathways

HLP003 offers the opportunity to significantly reduce treatment burden



# HLP003

Deuterated Oral NSA  
Adjunctive Treatment of MDD

# MDD: Leading Contributor to Mental Health Patient Burden

**>300M**

persons worldwide with MDD<sup>1</sup>

**50-75%**

of MDD patients also have anxiety symptoms<sup>4</sup>

**>21M**

persons with MDD in the US<sup>2</sup>

**2 out of 3**

patients do not experience relief with standard of care<sup>5</sup>

**20x**

increased suicide risk for an individual with depression vs. without depression<sup>3</sup>

**Up to 38%**

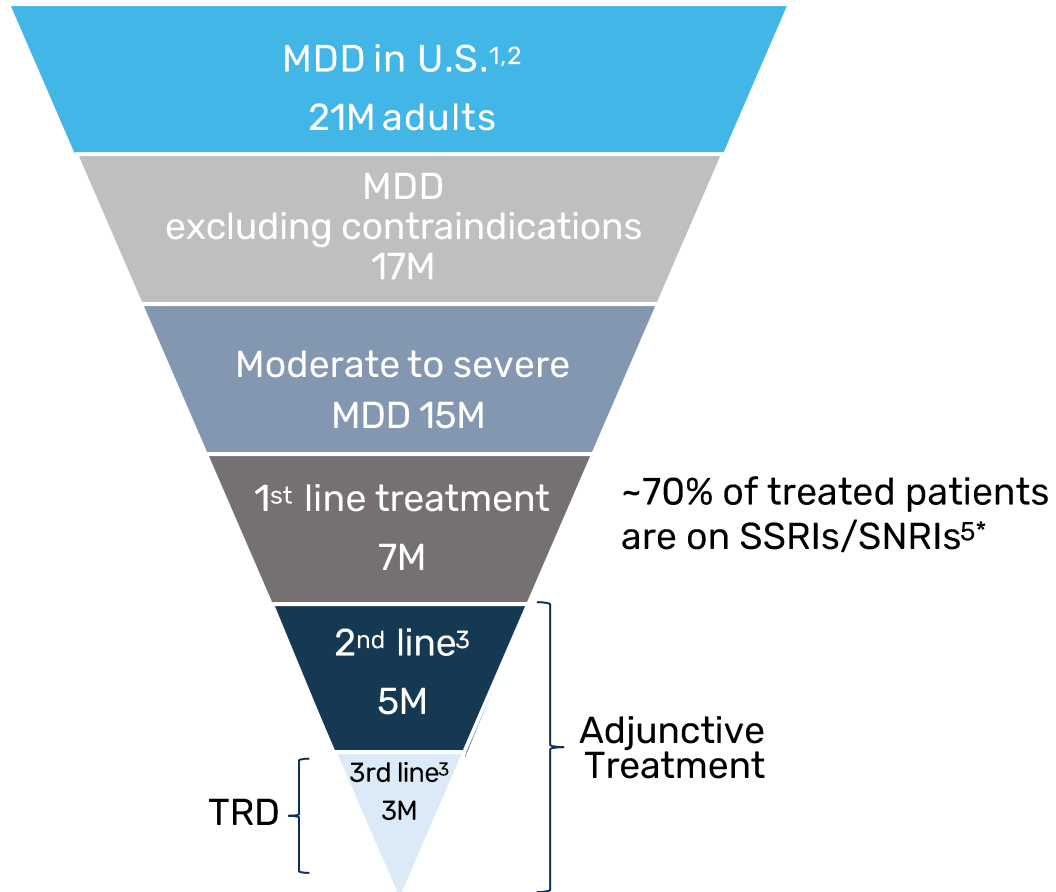
of patients experience at least one side effect with current standard of care (SSRI/SNRI)<sup>\*6</sup>

Notes:

1-6: See references on slide 39.

\*SSRI = Selective serotonin reuptake inhibitor, SNRI = Serotonin-norepinephrine reuptake inhibitor.

# Why Adjunctive Treatment Matters in MDD



## Benefits of adjunctive treatment:

- ✓ Begin treatment immediately
- ✓ Prevent withdrawal symptoms
- ✓ Remove barriers to treatment transition
- ✓ Build on benefits of background medications

## Expansion potential into adjacent behavioral disorders<sup>4</sup>

Indications with early supporting studies	U.S. Prevalence	Estimated Addressable Market
Anxiety Disorders / PTSD	19.1%/ 3.6%	64/12 million
Substance Use / Addiction Disorders	14.5%	48 million
Eating Disorders	0.3-1.2%	1-4 million
<b>Total</b>		<b>~115 million</b>

Notes:

1) <https://www.nimh.nih.gov/health/statistics/major-depression>  
 2) Vasiliadis, H. M., Lesage, A., Adair, C., Wang, P. S., & Kessler, R. C. (2007). Do Canada and the United States differ in prevalence of depression and utilization of services?. *Psychiatric services* (Washington, D.C.), 58(1), 63-71. <https://doi.org/10.1176/ps.2007.58.1.63>  
 3) Sinyor, M., Schaffer, A., & Levitt, A. (2010). The sequenced treatment alternatives to relieve depression (STAR\*D) trial: a review. *Canadian journal of psychiatry*, 55(3), 126-135. <https://doi.org/10.1177/070674371005500303>  
 4) Regier, Darrel J., et. al., DSM-5 Field Trials in the United States and Canada, Part II: Test-Retest Reliability of Selected Categorical Diagnoses October 2012. *American Journal of Psychiatry* 170(1)  
 5) Luo et al. (2020). National Prescription Patterns of Antidepressants in the Treatment of Adults With Major Depression in the U.S. Between 1996 and 2015: A Population Representative Survey Based Analysis. *Frontiers in Psychiatry* 11.  
 \*SSRI = Selective serotonin reuptake inhibitor, SNRI = Serotonin-norepinephrine reuptake inhibitor

# HLP003 Program Overview

Positive 12-month Phase 2 Results in MDD (2 doses – 16 mg)

## Sustained improvements in depression symptoms

- **Mean ~23-point reduction** in Montgomery-Asberg Depression Rating Scale (MADRS) scores from baseline at 12 months (average baseline MADRS was ~32) following 2 doses of HLP003 16 mg

## Durable response and remission rates

- **100%** of 16 mg patients receiving 2 doses were **responders at 12 months**
- **71%** of 16 mg patients receiving 2 doses were in **remission at 12 months**

## Favorable safety and tolerability profile

- All reported adverse events (“AEs”) **mild to moderate; no AEs of suicidality**
- No AEs/serious adverse events (“SAEs”) reported in the 12-month follow up

## Expedited Regulatory Pathway

- **U.S. FDA Breakthrough Therapy Designation** for adjunctive treatment of MDD

## Next Steps

- **Topline efficacy data readout from Phase 3 APPROACH study expected Q4 2026<sup>1,2</sup>**

Notes:

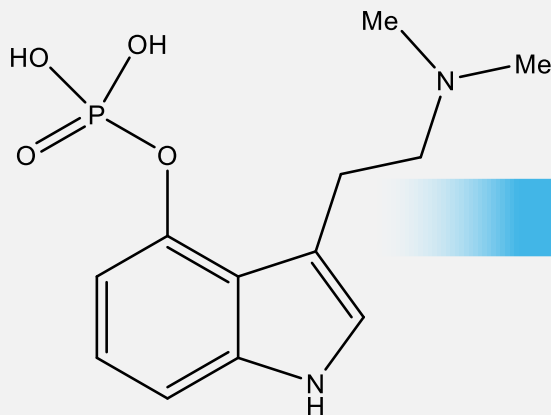
1) Forward-looking statements are subject to risks and assumptions. See “Cautionary Statement” on page 2 of this presentation.

2) Subject to receipt of all necessary regulatory approvals from all applicable governmental authorities, including, as applicable, the academic and scientific organizations with which Helus is working. There are multiple risk factors regarding the ability to successfully commercially scale a chemically synthesized process to obtain psilocin and other analogues. There is no assurance that timelines will be met. Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to Helus. Such statements are informed by, among other things, regulatory guidelines for developing a drug with timeline safety studies, proof of concept studies, and pivotal studies for new drug application submission and approval, and assumes the success of implementation and results of such studies on timelines indicated as possible by such guidelines, other industry examples, and Helus’s development efforts to date.

# Deuterated Psilocin Offers Several Advantages<sup>1</sup>

## Psilocybin

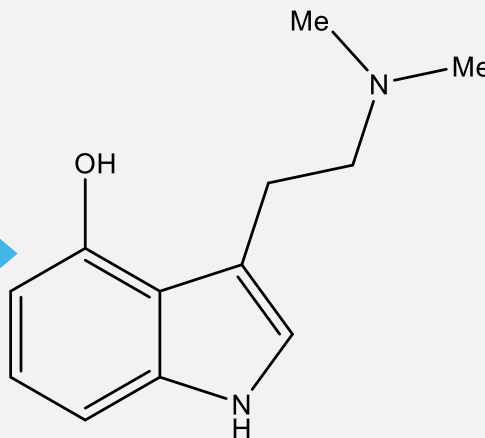
### Inactive Prodrug



- Slow onset
- PK variability

## Psilocin

### Active Metabolite



- Short-lived outside of body
- Unstable - susceptible to oxygen, light, metals, solvents, etc.

## Advantages of Deuterated Psilocin (HLP003)

### Bypasses first metabolic step

- ✓ Increasing efficiency of delivery
- ✓ Decreasing drug load
- ✓ Reducing variability

### Potentially better brain penetration

- ✓ Reduced risk of off target effects

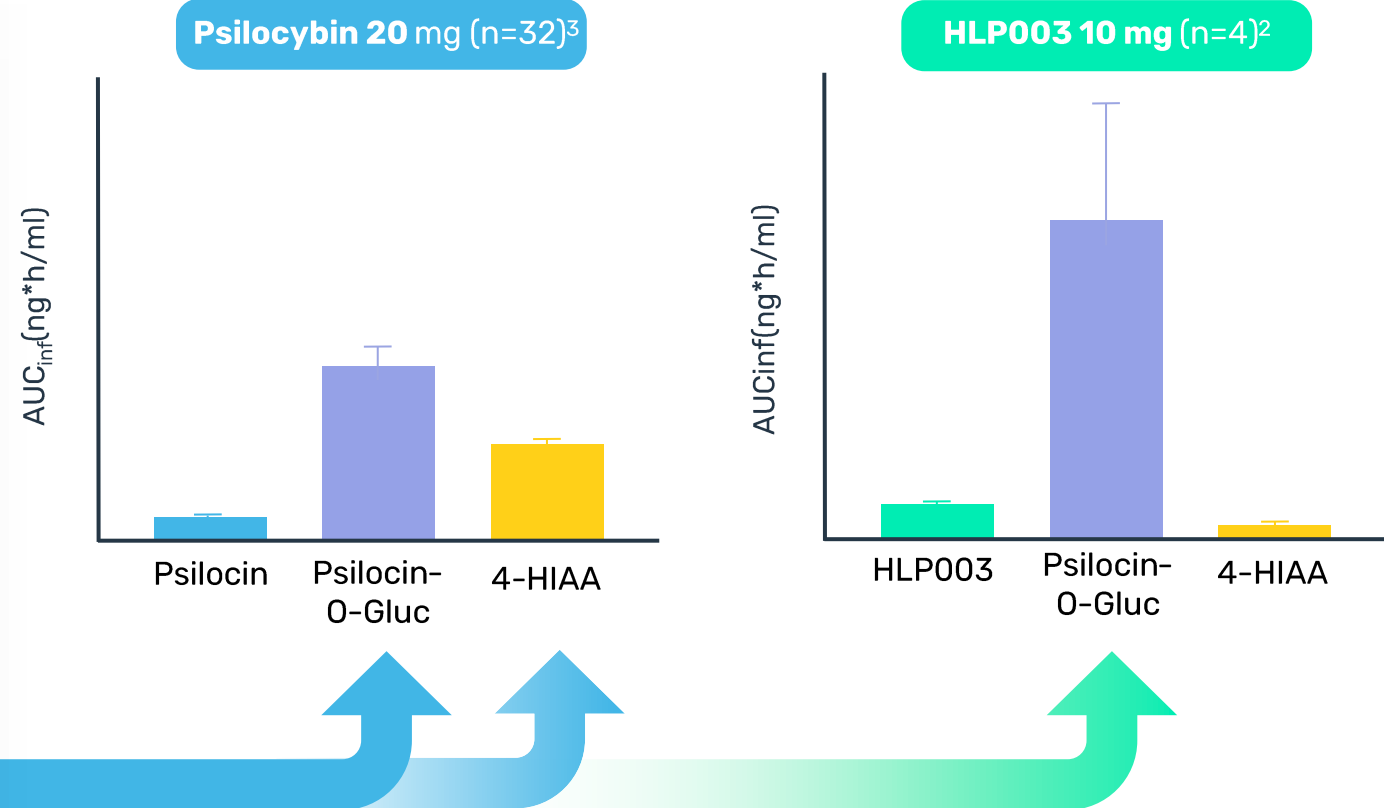
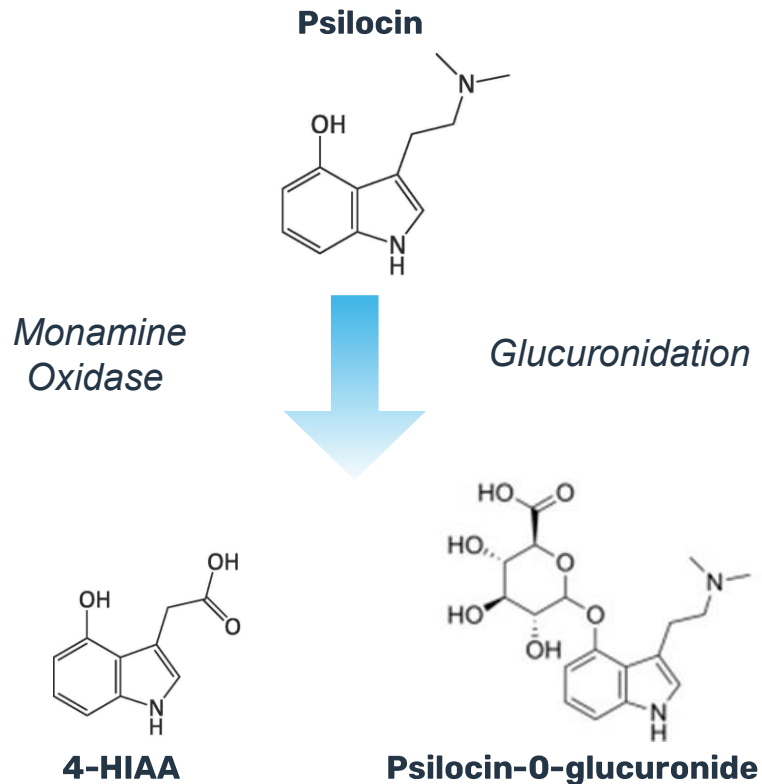
### Alters metabolic route

- ✓ Potentially improving safety of co-administration with other drugs

### Stabilizes active moiety

# Shift in metabolism may reduce drug interaction risk<sup>1</sup>

## Psilocin is Metabolized into Inactive Breakdown Products



*HLP003 shifts metabolism away from monoamine oxidase toward glucuronidation, which may reduce drug interaction risk*

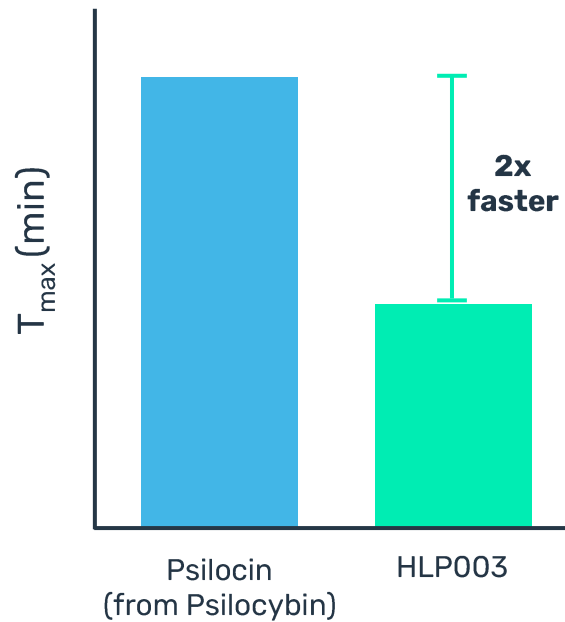
Notes:

- 1) As compared to psilocybin.
  - 2) HLP003 10 mg AUC data from pooled plasma samples obtained from normal healthy volunteers (n=4)
  - 3) Psilocybin 20 mg AUC data (n=32) from Ley et al Neuropsychopharmacology (2023) 48:1659 – 1667
- Psilocin-O-Gluc: Psilocin-O-glucuronide; 4-HIAA: 4-hydroxyindole-3-acetic acid

# Faster and higher brain penetration than psilocybin in rodent studies<sup>1,2,3</sup>

## Potential for faster onset of clinical effects

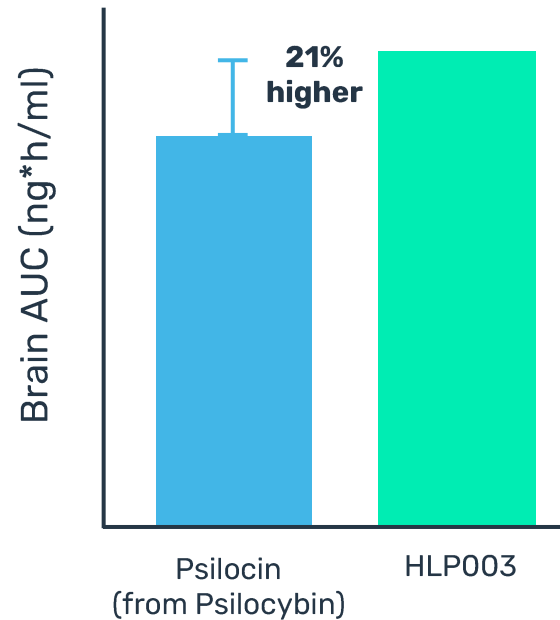
### Brain Concentration (n=15)



HLP003 achieved peak brain concentrations 2x faster vs psilocybin

## Potential for better efficacy

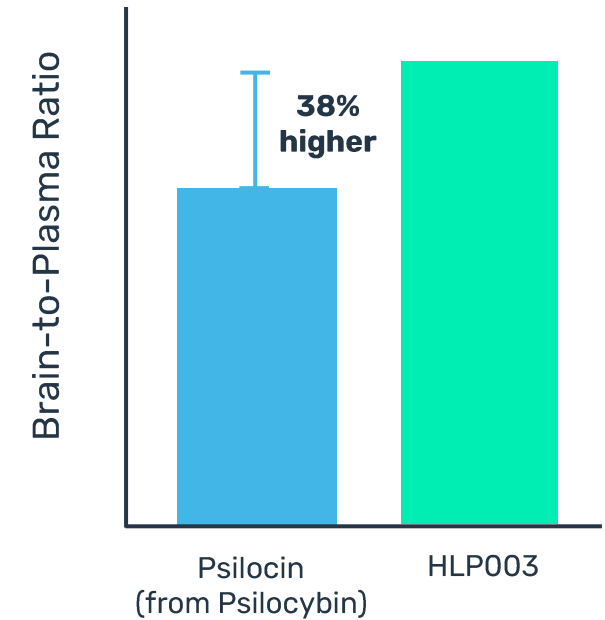
### Brain Exposure (n=15)



HLP003 21% higher brain exposures (AUC) vs. equivalent dose of psilocybin

## Potential to limit off-target AEs in the periphery

### Brain to Plasma Ratio (n=15)

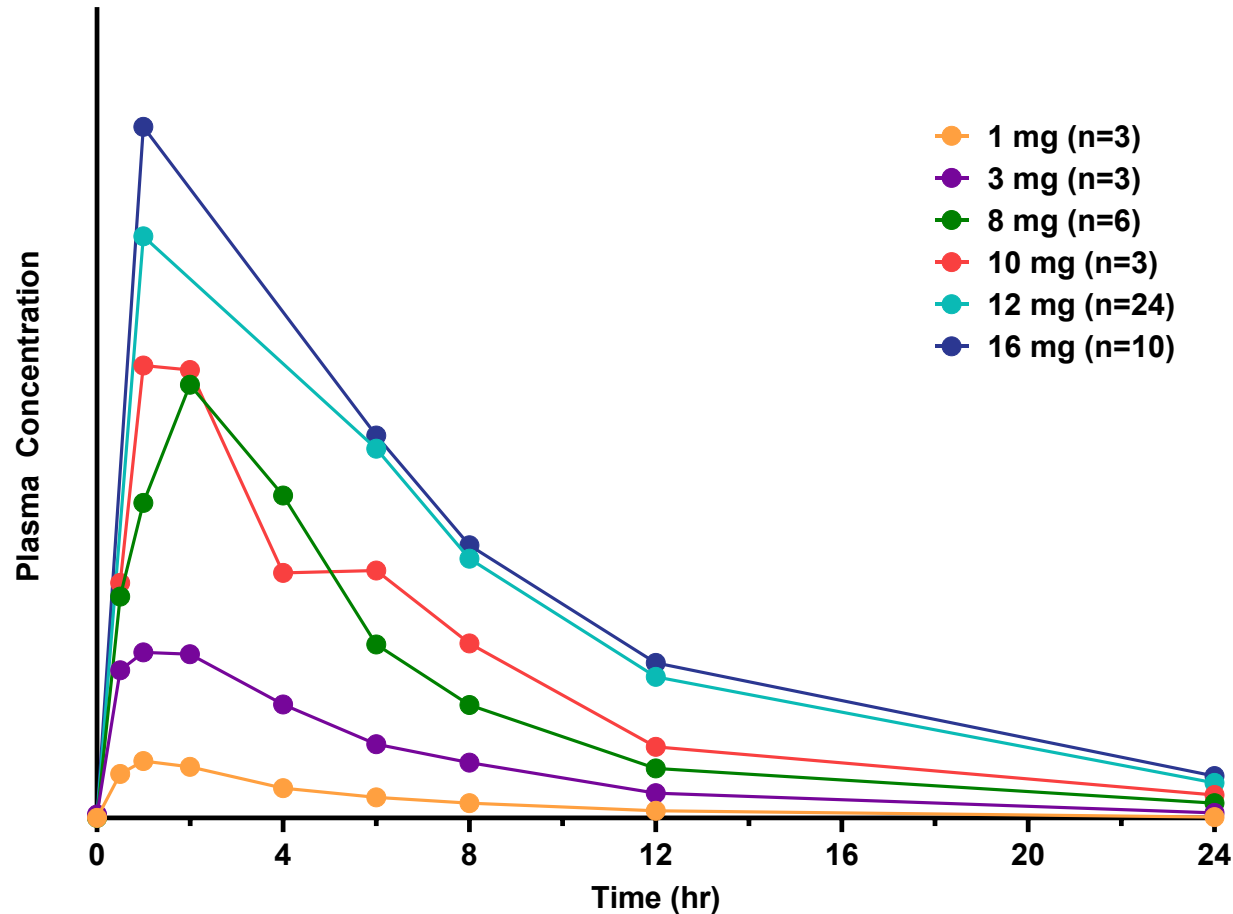


HLP003 38% higher brain to plasma ratio vs psilocin from psilocybin

#### Notes:

- 1) Data from HLP003 preclinical study.
- 2) Compounds were administered via IV bolus injection with plasma and brain collection 0.25, 0.5, 1, 2 and 4 hr after administration (n=3 per time point)
- 3) Brain to plasma ratios were derived as (mean brain AUC<sub>0-4hr</sub>/mean plasma AUC<sub>0-4hr</sub>) resulting in 15 animals contributing to a single composite AUC value.

# Deuteration translates into a desirable PK Profile in Phase 1/2



## PK Benefits of HLP003

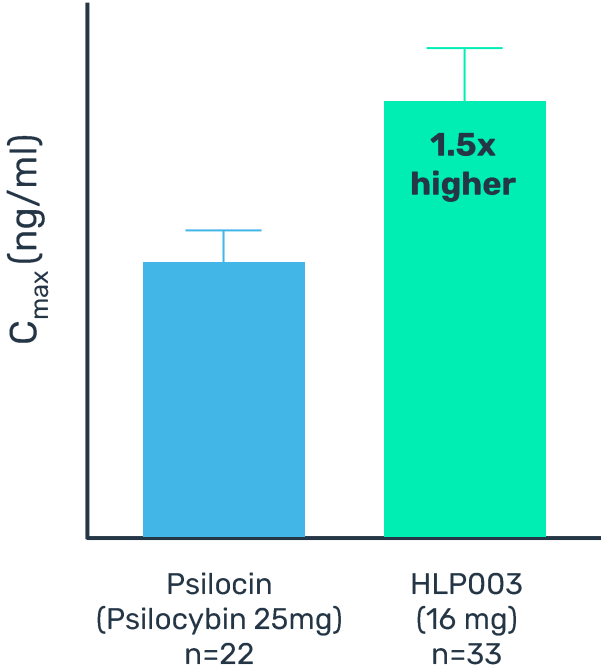
- ✓ Rapid absorption
- ✓ Short half life
- ✓ Good tissue distribution
- ✓ Low variability in PK
- ✓ Dose proportional

increases in  $C_{max}$  and AUC

Note:  
Helus Phase 1/2 data on file.

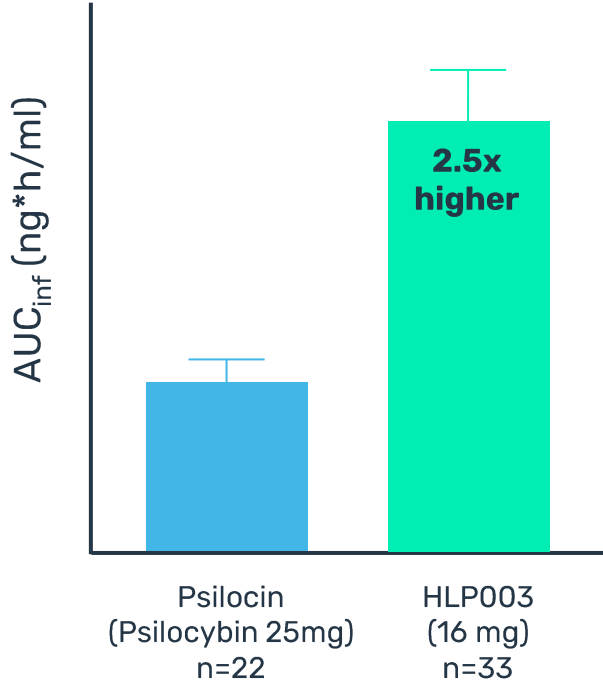
# HLP003 16 mg delivers plasma levels higher than 25 mg of psilocybin in Phase 1/2

## Psilocin vs. HLP003: $C_{max}$



16 mg HLP003 delivers a  $C_{max}^{1,2}$  1.5x higher vs. 25 mg psilocybin – **potentially offering greater opportunity to cross pharmacodynamic effect threshold<sup>2,3</sup>**

## Psilocin vs. HLP003: $AUC_{inf}$



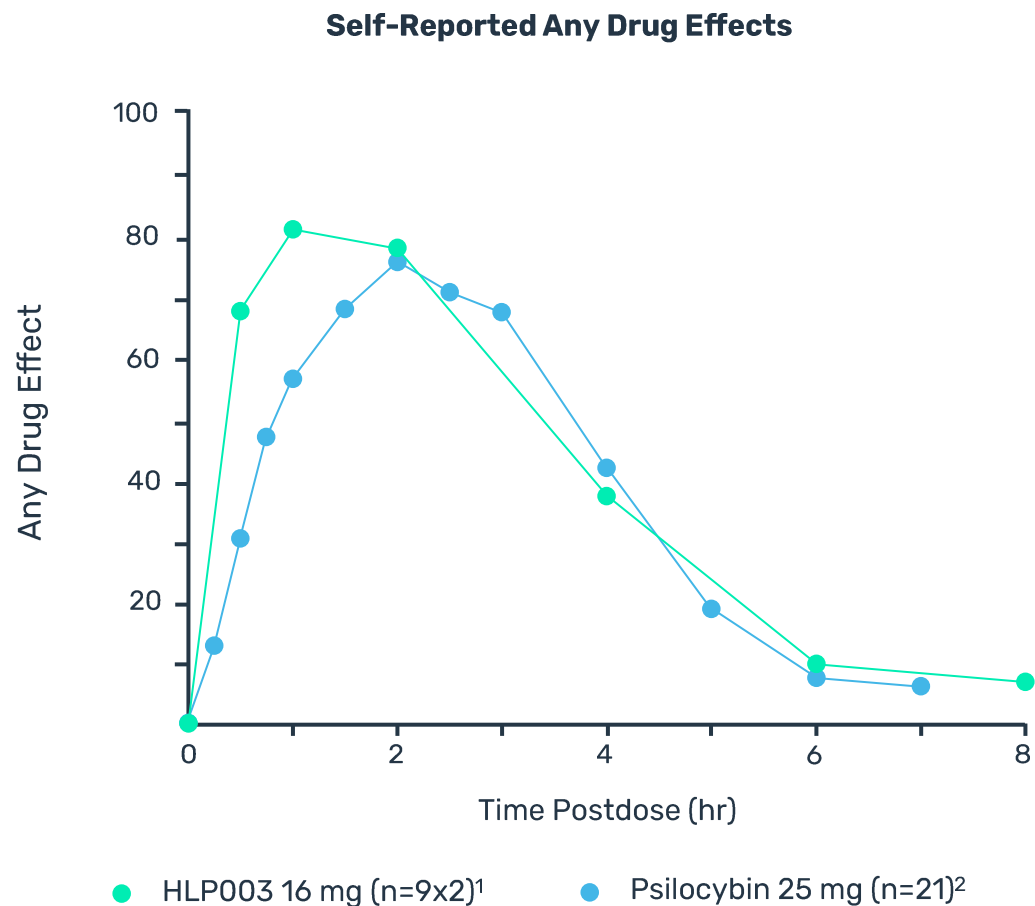
16 mg HLP003 delivers an  $AUC^{1,2}$  2.5x higher vs. 25 mg psilocybin<sup>2,3</sup> – **Higher plasma levels are related to higher intensity, which is correlated with therapeutic benefit<sup>4</sup>**

Notes:  
1) HLP003 PK data on file.  
2) Geometric means (+95% CI) shown for  $AUC_{inf}$   
3) Psilocybin 25 mg PK data from Holze et al, 2022.

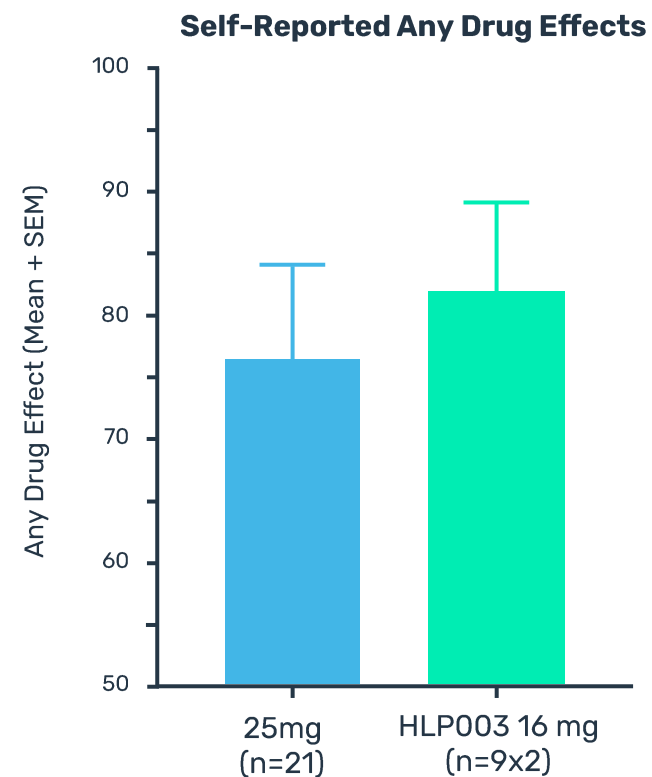
4) Yaden & Griffiths, 2020. <https://dx.doi.org/10.1021/acsptsci.0c00194>

# Favorable pharmacodynamic profile in Phase 1/2

## Potentially Faster Onset of Clinical Effects



## Higher Intensity of Clinical Effects



- Lower dose 16 mg HLP003 delivers **superior** intensity to 25 mg psilocybin
- Higher intensity correlated with therapeutic benefit<sup>3</sup>

Notes: VAS = visual analogue scale, any drug effect

1) VAS data for HLP003 16 mg from Helus phase 2 study in MDD, using HLP003 oral solution pooled over 2 administrations.

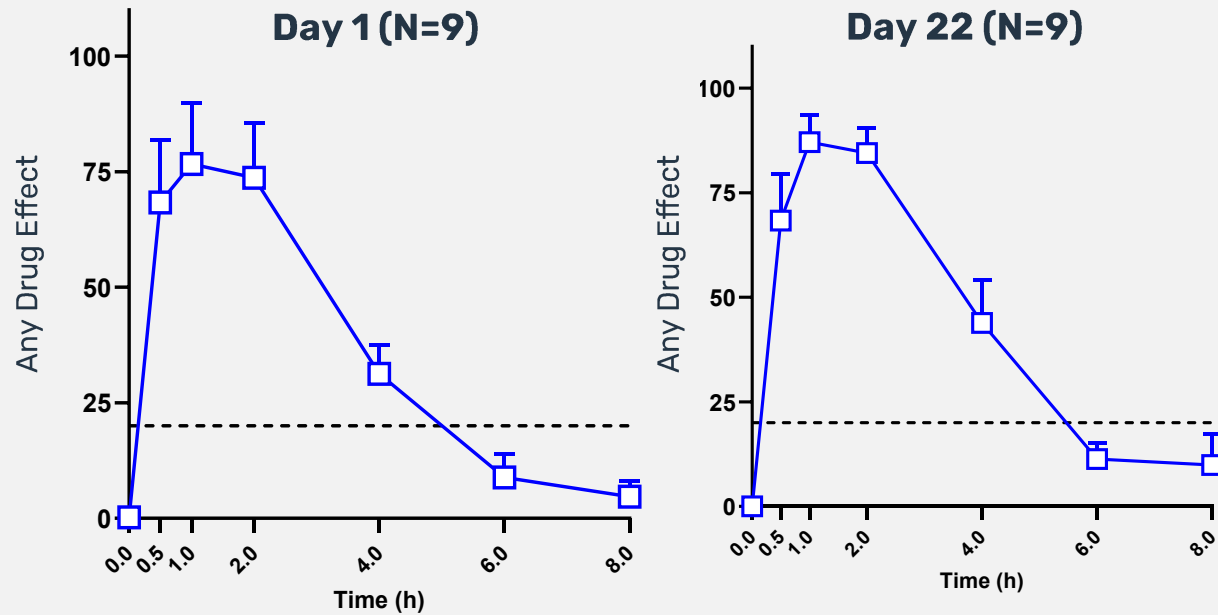
2) VAS data for psilocybin 25 mg from Holze et al, 2022; using psilocybin capsules

3) Yaden & Griffiths, 2020. <https://dx.doi.org/10.1021/acspsci.0c00194>

# Reproducible Pharmacodynamic Effects

Self Reported Any Drug Effect Score (Indicator of Subjective Drug Effect)<sup>1</sup>

## 16 mg cohort in Phase II study<sup>2,3</sup>



## Benefits of HLP003

- ✓ Effects reproducible with repeated dosing
- ✓ Acute subjective effects lasting ~4-6 hrs<sup>3</sup>

Notes:

- 1) Patient reported Visual Analog Scale (VAS).
- 2) Graphs show mean (SEM).
- 3) Horizontal dashed line indicates VAS at 20% to assess onset and offset of effects (adapted from Holze et al. 2022).

# Summary HLP003 Advantages Compared to Psilocybin<sup>1</sup>

## Reduced PK & PD Variability

- Removal of metabolic step and deuteration potentially reduce PK and PD variability

## Improved Drug Delivery

- $C_{max}$  **1.5x higher**; AUC **2.5x higher** vs. 25 mg dose of psilocybin
- Higher plasma levels potentially offer: 1) greater opportunity to cross PD effect threshold 2) higher intensity, which is correlated with therapeutic benefit

## Consistent and Reproducible Effects

- Potentially faster onset of clinical effects
- Pharmacodynamic effects reproducible with repeated dosing

## Rapid Onset with ~4-6 Hour Duration

- Acute subjective effects within 15 min of dosing
- Duration of acute effects fits well into existing interventional day clinic setting

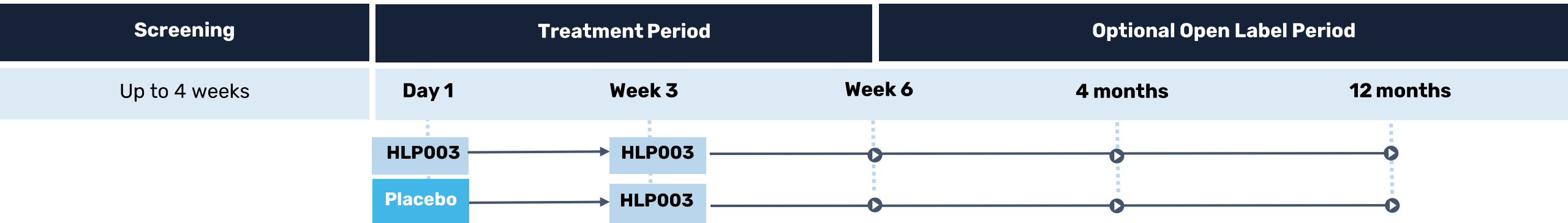
## Safety Profile

- Shifts in metabolism may reduce drug interaction risk
- Greater brain penetration in rodents shows potential to limit off-target AEs in periphery

## Stable Formulation & Convenient Oral Capsule

- Supports product handling & development
- Familiar dosing format and simple administration

# HLP003: Phase 2a Trial Design in MDD<sup>1,2</sup>



**Phase 1:** Single ascending dose study (1-10 mg), n=12

**Phase 2a:** RCT in MDD patients (12 mg, n=24; 16 mg, n=12)

Patients allowed to remain on stable doses of antidepressant medications.

## Key Inclusion Criteria:

- ✓ Moderate to severe MDD (MADRS  $\geq$  21)
- ✓ Inadequate response to antidepressant medication

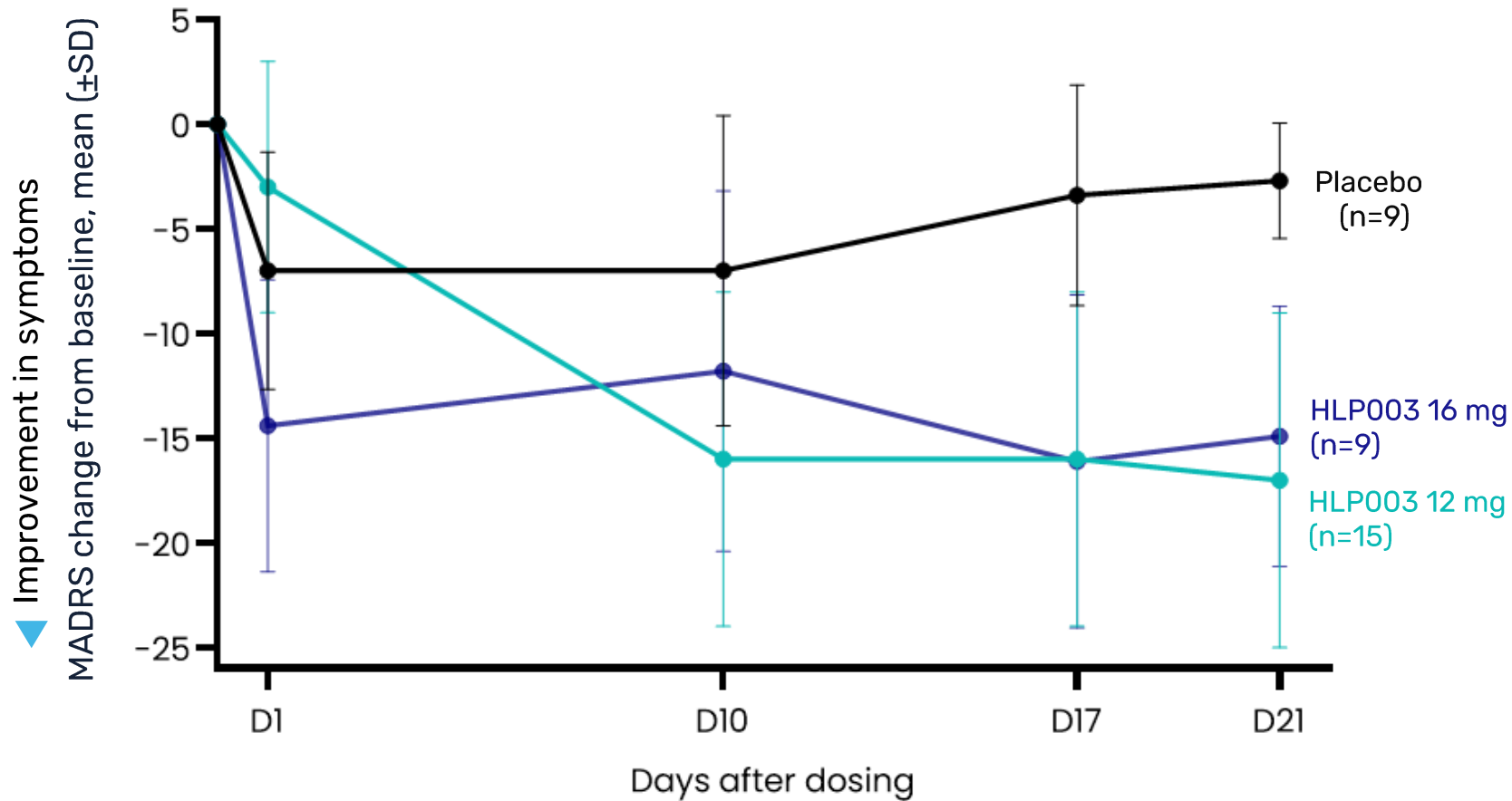
## Primary Endpoint:

- ✓ Reduction in depression symptoms (change in MADRS score) at Week 3 after a single dose vs. placebo

### Notes:

- 1) Primary efficacy assessed at Week 3; Optional 12 week follow up to assess durability of effects.
- 2) Forward looking statements are subject to risks and assumptions. See "Cautionary Statement" on page 2 of this presentation. There is no assurance that timelines will be met. Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to Helus. Such statements are informed by, among other things, regulatory guidelines for developing a drug with timeline safety studies, proof of concept studies, and pivotal studies for new drug application submission and approval, and assumes the success of implementation and results of such studies on timelines indicated as possible by such guidelines, other industry examples, and Helus's development efforts to date.

# Large Improvement in Depression Symptoms After Single Dose of HLP003<sup>1</sup>



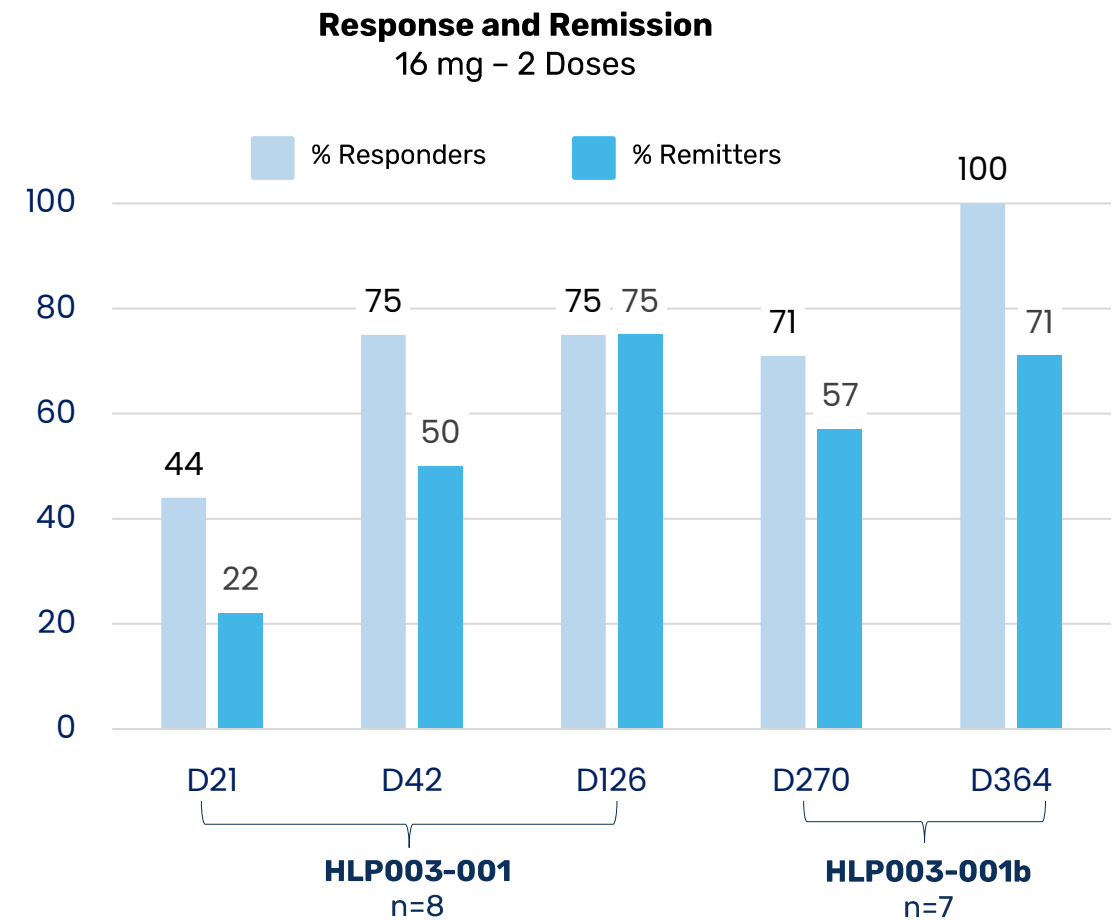
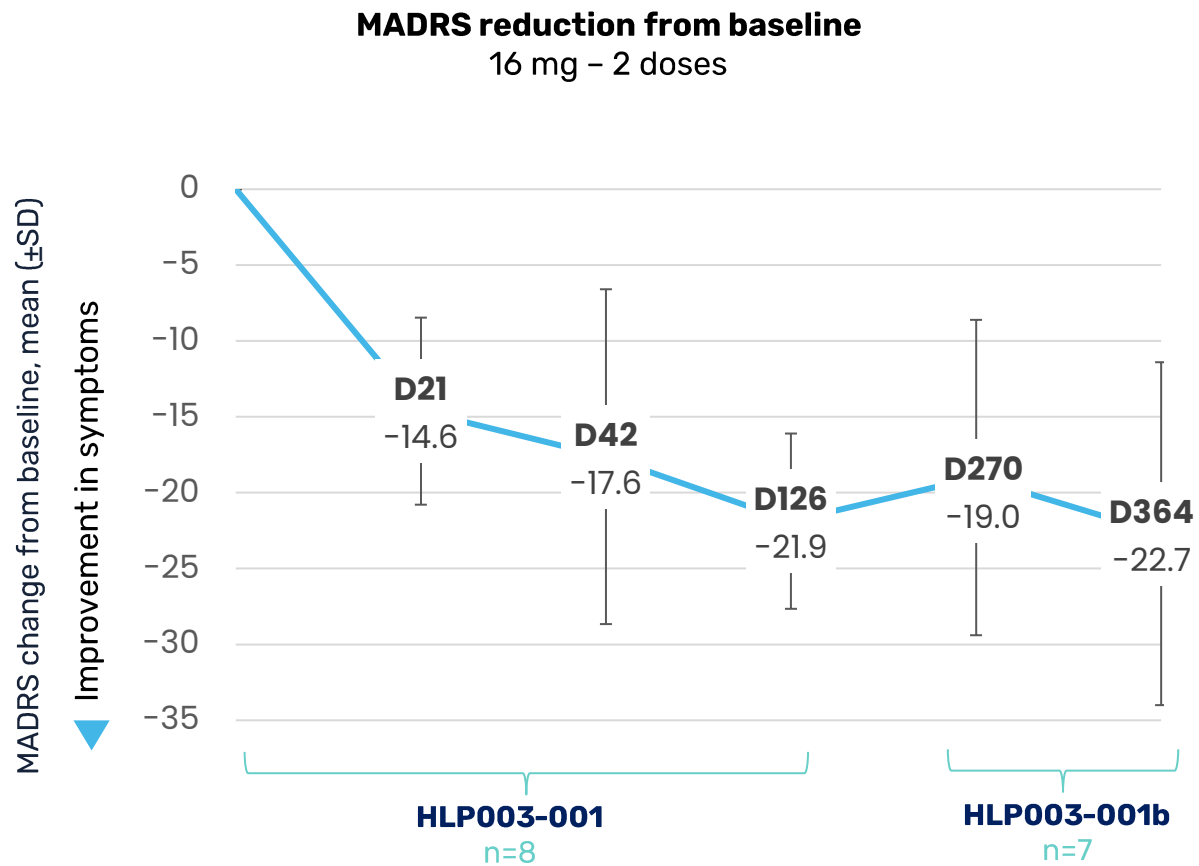
Dose <sup>1</sup>	Primary Endpoint*	Effect size	p-value
12 mg	-14.11	2.31	0.0001
16 mg	-12.99	2.54	0.0080

\*Primary endpoint: LS-means<sup>2</sup> difference in change from baseline in MADRS total score between HLP003 and placebo at 3 weeks

Notes:

- 1) Data based on patients who received at least one dose of HLP003 and have at least one post-baseline MADRS assessment.
- 2) LS-means = Least Squares Means

# HLP003: Sustained Improvements in Depression Symptoms at 12 Months<sup>1</sup>



Note:

1) Data based on post-hoc analysis of patients who received two doses of 16 mg of HLP003 and participated in long-term extension study.

# Phase 3 PARADIGM Program Overview

**Study design aligned with FDA guidance and two meetings with FDA**

**Addressing functional unblinding**

**Phase 3 underway**

The pivotal program will consist of 2 studies plus an extension<sup>1,2,3</sup>:

- APPROACH: Two-arm study of two 16 mg doses of HLP003 vs. placebo
- EMBRACE: Three-arm study with two 16 mg doses, 8 mg doses, and a placebo arm
- EXTEND: Long-term extension study to confirm durability of effect, time to redosing and frequency of redosing for participants who did not respond in the first two studies or relapsed during the extension study
- Use of remote, independent, blinded raters
- Dosing session procedural safeguards designed to prevent functional unblinding
- Long-term efficacy data points up to one year to outlast expectancy bias
- Multinational Phase 3 program will include more than 100 sites across the U.S., Europe and Australia<sup>1,2,3</sup>
- Study sites selected with clinical expertise and training in depression studies
- Clinical supplies manufactured and ready

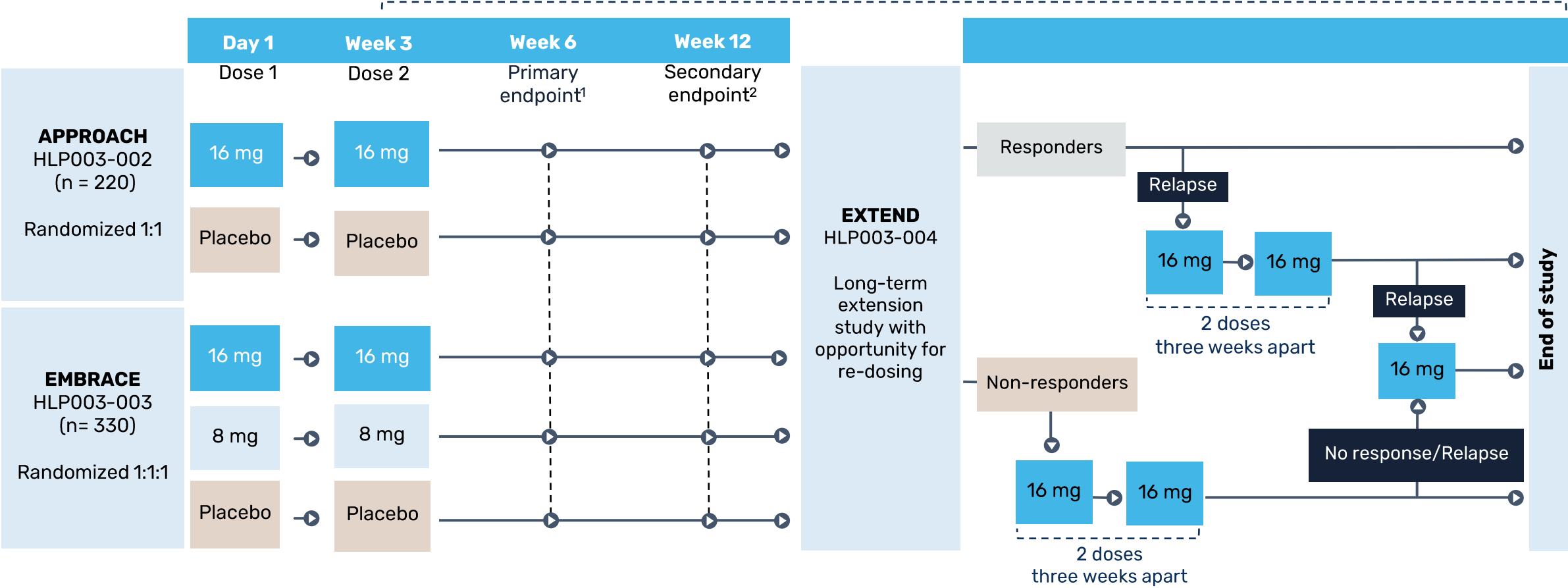
Notes:

1) Forward-looking statements are subject to risks and assumptions. See "Cautionary Statement" on page 2 of this presentation.

2) Subject to receipt of all necessary regulatory approvals from all applicable governmental authorities, including, as applicable, the academic and scientific organizations with which Helus is working. There are multiple risk factors regarding the ability to successfully commercially scale a chemically synthesized process to obtain psilocin and other analogues. There is no assurance that timelines will be met. Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to Helus. Such statements are informed by, among other things, regulatory guidelines for developing a drug with timeline safety studies, proof of concept studies, and pivotal studies for new drug application submission and approval, and assumes the success of implementation and results of such studies on timelines indicated as possible by such guidelines, other industry examples, and Helus's development efforts to date.

3) Helus is prioritizing the progression of its HLP003 program. The advancement of Helus's other clinical programs are contingent on Helus's ability to continue raising capital under its current and future financing arrangements. No assurances can be given that Helus will be able to raise the additional capital that it may require for its anticipated future development.

# PARADIGM: HLP003 Phase 3 Pivotal Program in MDD



Phase 3 APPROACH topline data expected in Q4 2026<sup>3</sup>

Notes:

- 1) Primary endpoint: MADRS change from baseline at 6 weeks.
- 2) Key secondary endpoint: MADRS change from baseline at 12 weeks.
- 3) Forward-looking statements are subject to risks and assumptions. There is no assurance that timelines will be met. Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to the Company. Such statements are informed by, among other things, regulatory guidelines for developing a drug with safety studies, proof of concept studies, and pivotal studies for new drug application submission and approval, and assume the success of implementation and results of such studies on timelines indicated as possible by such guidelines, other industry examples, and the Company's development efforts to date.

# HLP004

Deuterated Intramuscular NSA  
Treatment of GAD

# High Patient Burden and Persistent Treatment Gaps in GAD Create a Clear Opportunity for Innovation

## Significant Unmet Need in GAD

>300M

persons worldwide with anxiety disorders<sup>1</sup>

>20M

persons with GAD in the US<sup>2</sup>

77%

of GAD patients in the US are moderate-to-severe<sup>3</sup>

~\$95B

annual costs of anxiety disorders in the US<sup>4</sup>

Most common

anxiety disorder within primary care<sup>5</sup>

>45%

patients in interventional psychiatric practices suffer from GAD<sup>6</sup>

## Current Treatments Continue to Fail GAD Patients

- **2/3** of GAD patients experience no relief with initial SoC treatment<sup>7</sup>
- **57%** of patients with anxiety do not adhere to SoC due to side effects<sup>8</sup>
- Average time to discontinuation is **<90 days**<sup>9</sup> due to efficacy / safety
- Last approval was in **2007** (Cymbalta<sup>10</sup>); **no approved adjunctive treatment to date**

### Notes:

- 1) Yang, X., et al. Epidemiol Psychiatr Sci, 2021. 30:e36.
- 2) Ringeisen, H., et al. RTI International, 2023.
- 3) Kessler, R.C., et al. Arch Gen Psychiatry, 2005. 62(6):617-27.

- 4) Little, et. al. Medical Economics. 2023. <https://www.medicaleconomics.com/view/not-screening-for-anxiety-costs-and-solutions>.
- 5) Ansara, E.D. Ment Health Clin, 2020. 10(6):326-334.
- 6) Helus, Proprietary quantitative HCP market research (n=60). 2024.

- 7) Little, A. Am Fam Physician, 2009. 80(2):167-72.
- 8) Stein, M.B., et al. Psychiatr Serv, 2006. 57(5):673-80.
- 9) Louie D, et al. Treatment Patterns for Newly Diagnosed Generalized Anxiety Disorder (GAD): Insights from Real-World Evidence. Presentation at ACNP 2026.
- 10) CYMBALTA is a registered trademark of Eli Lilly and Company.

# HLP004's Emerging Best-in-Class Profile

## Positive Phase 1 and Phase 2 Results in Moderate-to-Severe Generalized Anxiety Disorder

### Rapid, Robust Treatment Effect

**Clinically meaningful and statistically significant ~10-point HAM-A reduction** at 6 weeks in both active doses (2 mg and 20 mg) with effects seen as early as **Day 2**

### Effects in Real World Clinical Setting

Effects seen as an **adjunct on top of SOC in moderate-to-severe GAD**

### Superior Durability, Response & Remission

Durable effects from single cycle **through at least 6 months with ~70% responders and ~40% in remission**

### Favorable Safety Profile

**Transient** mild-to-moderate AEs; **no drug-related SAEs or suicidality**

### Scalable Within Practice Paradigm

**In Phase 1 dose-ranging trial, acute effects lasted 90 minutes and time to discharge readiness was ~3 hours** well within existing interventional psychiatry infrastructure

### Franchise Durability

90+ issued patents including **Composition of Matter IP through to 2041**

# Comprehensive Studies Characterizing Dimethyltryptamine (DMT) Pharmacological Properties

Study	Key Findings
Phase 1/2a study with IV DMT in moderate to severe MDD (no SSRIs) <sup>1</sup>	Rapid and durable antidepressant and anxiolytic effects after single administration
Phase 1 IV/IM study <sup>1</sup>	Characterized safe and well-tolerated IM route
Phase 1 SSRI DDI study <sup>1</sup>	Non-deuterated DMT safe and well-tolerated when co-administered with SSRIs with potential additive effects
Phase 1 Study of IV HLP004 and IV DMT	Deuteration extends the duration of effects of DMT
Phase 1 IM/IV dNSA study <sup>2,3</sup>	Established relationship between IV and IM doses and provided safety and pharmacodynamic data
<b>HLP004-002: Phase 2 IM Signal finding in GAD patients</b>	IM administration of HLP004 provides rapid, robust and sustained relief from symptoms of GAD
<b>HLP004-001: Phase 1 IM Dose ranging study</b>	HLP004 IM provides higher exposure, slower clearance, and a prolonged systemic duration, while preserving rapid onset compared to DMT (within 15 minutes) and has dose-dependant pharmacokinetics

**Run in  
Parallel**

Notes:

- 1) Completed with SPL026, a non-deuterated IV DMT
- 2) dNSA = deuterated novel serotonergic agonists
- 3) Study completed with related dNSA, SPL028

# HLP004 Was Designed To Improve Upon IV DMT To Deliver Rapid & Durable Symptom Relief Via Single Treatment Cycle

## Limitations of IV DMT

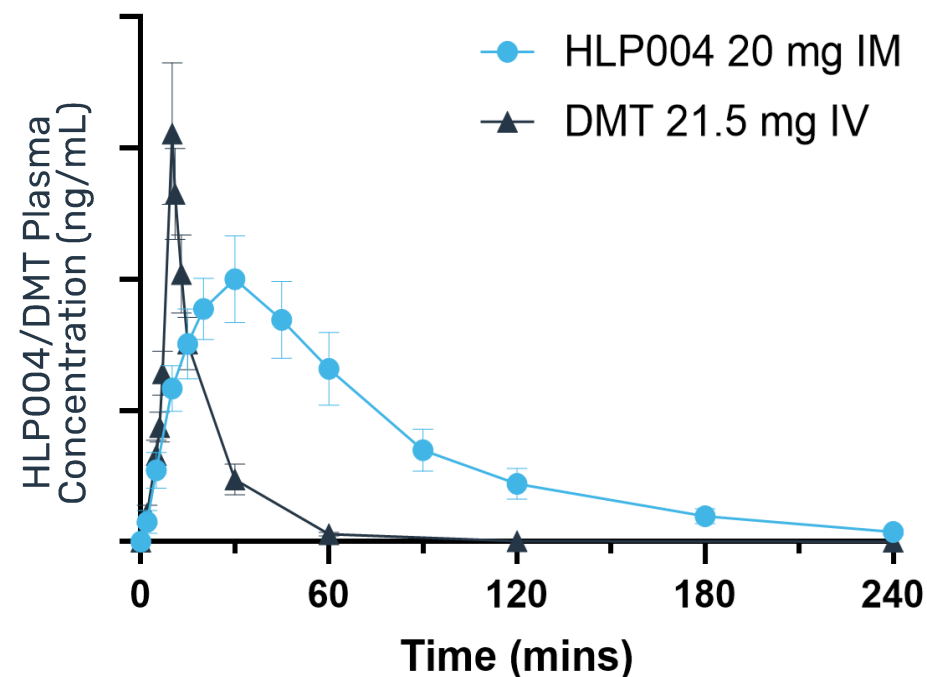
- **Unfavorable pharmacokinetics:** rapid peak, rapid elimination resulting in short-lived, intensive <30 min experience
- **Not scalable:** requires carefully controlled infusions

## HLP004 IM D-DMT

- ✓ **Favorable pharmacokinetics:** rapid peak but lasts 60-90 min; favorable experience, shorter than psilocybin and LSD
- ✓ **Greater scalability:** can be easily administered in clinical setting

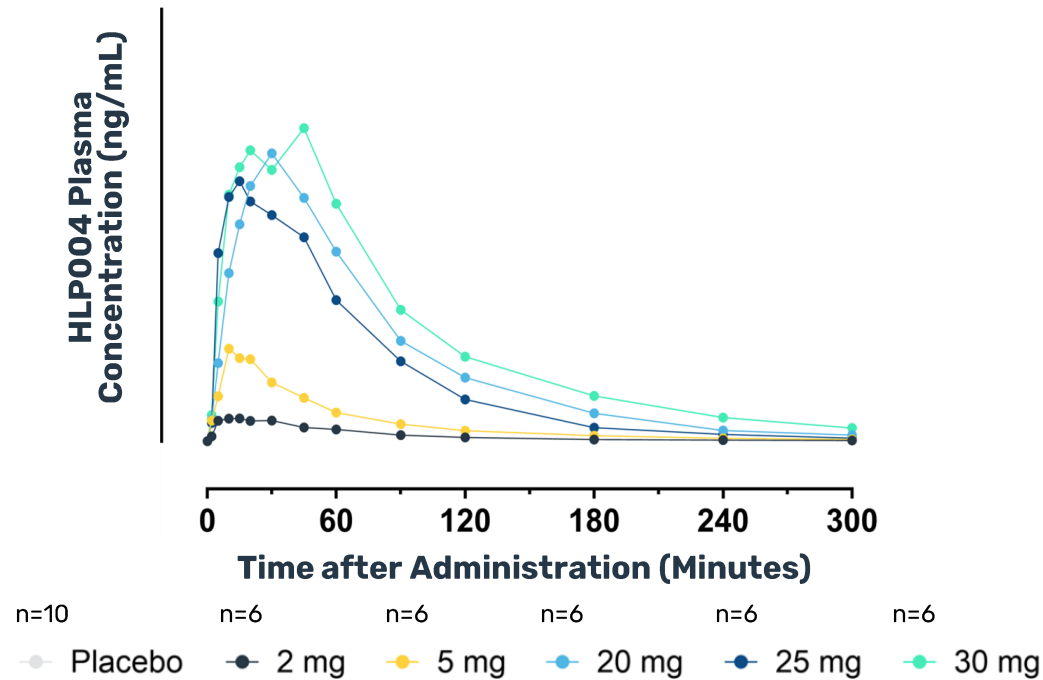
## HLP004

Improved Pharmacokinetic Properties vs. IV DMT



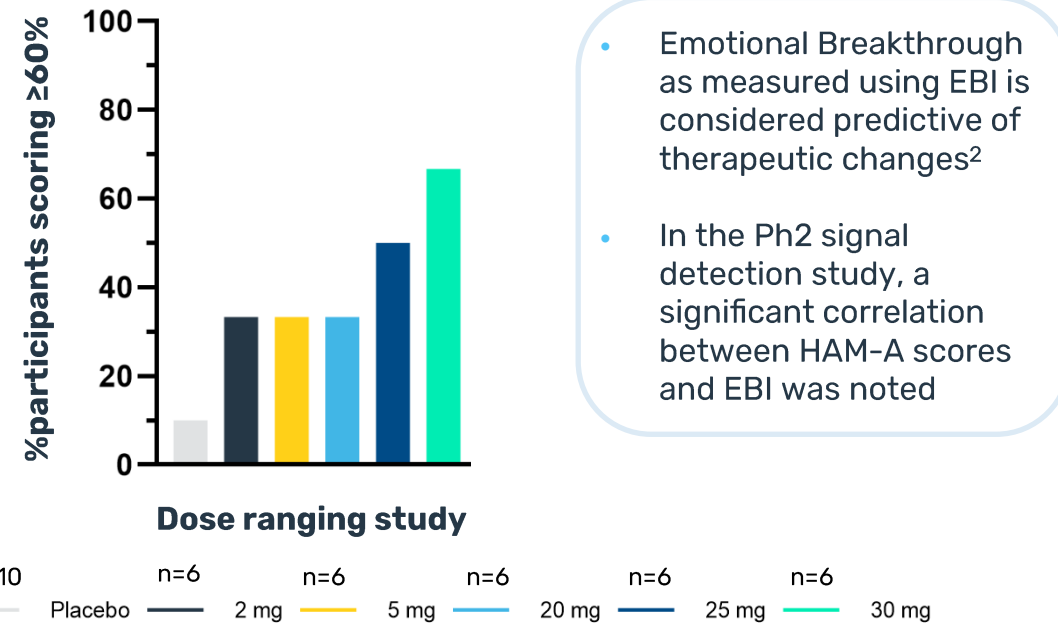
# Linear, Predictable and Reproducible Pharmacokinetics and Robust Pharmacodynamics

## Pharmacokinetics



- **Rapid absorption and onset of response** within 15 min of IM administration
- **Dose-proportional increases in plasma concentrations**
- **Rapid elimination and short duration acute effects** with half-life of 60 minutes across all doses

## Emotional Breakthrough Inventory (EBI)<sup>1</sup>



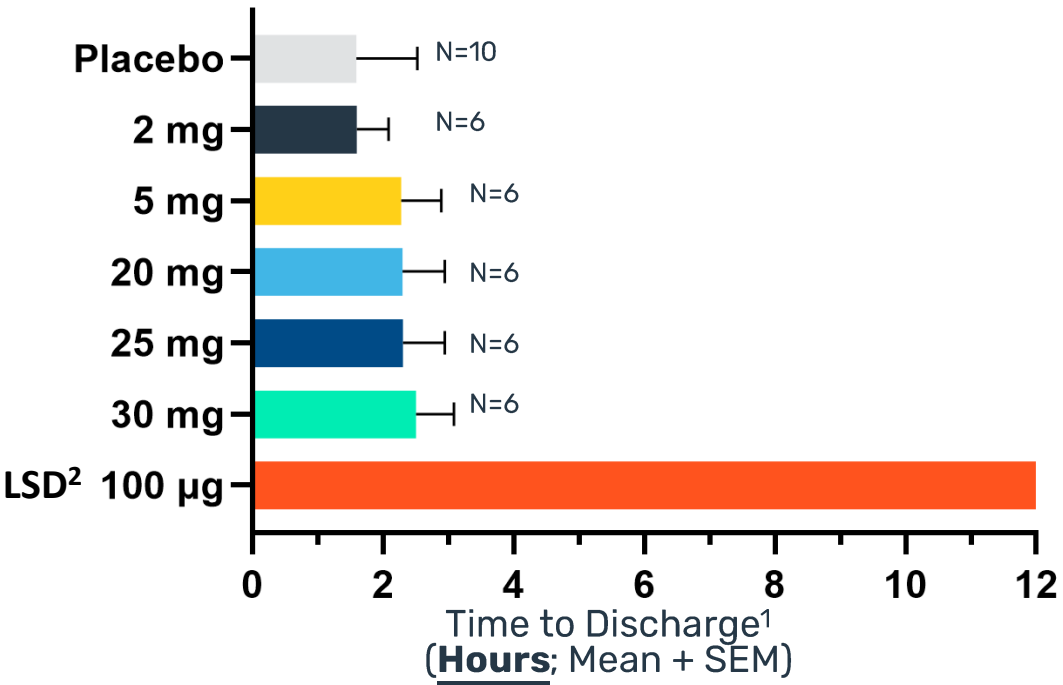
- Emotional Breakthrough as measured using EBI is considered predictive of therapeutic changes<sup>2</sup>
- In the Ph2 signal detection study, a significant correlation between HAM-A scores and EBI was noted

- **Robust pharmacodynamic effects consistent with therapeutic effect** as demonstrated by EBI in both 20 mg and 2 mg
- **In the dose-ranging study, the proportion of participants scoring ≥60% on EBI were similar for the 2 mg and 20 mg groups and lower for the placebo group**

### Notes:

- 1) The Emotional Breakthrough Inventory (EBI) is a validated, 6-item self-report questionnaire designed to measure the intensity of emotional release and therapeutic breakthroughs during a psychedelic experience.
- 2) Roseman L *et al.* Emotional breakthrough and psychedelics: Validation of the Emotional Breakthrough Inventory. *J Psychopharmacol.* 2019;33(9):1076-1087.

# Intramuscular Administration Permits Rapid Discharge Within ~3 Hours



**Acute effects last 90 minutes only<sup>3</sup>**

**Ready for discharge** within ~3 hours allowing for access into existing SPRAVATO<sup>4</sup> treatment paradigm

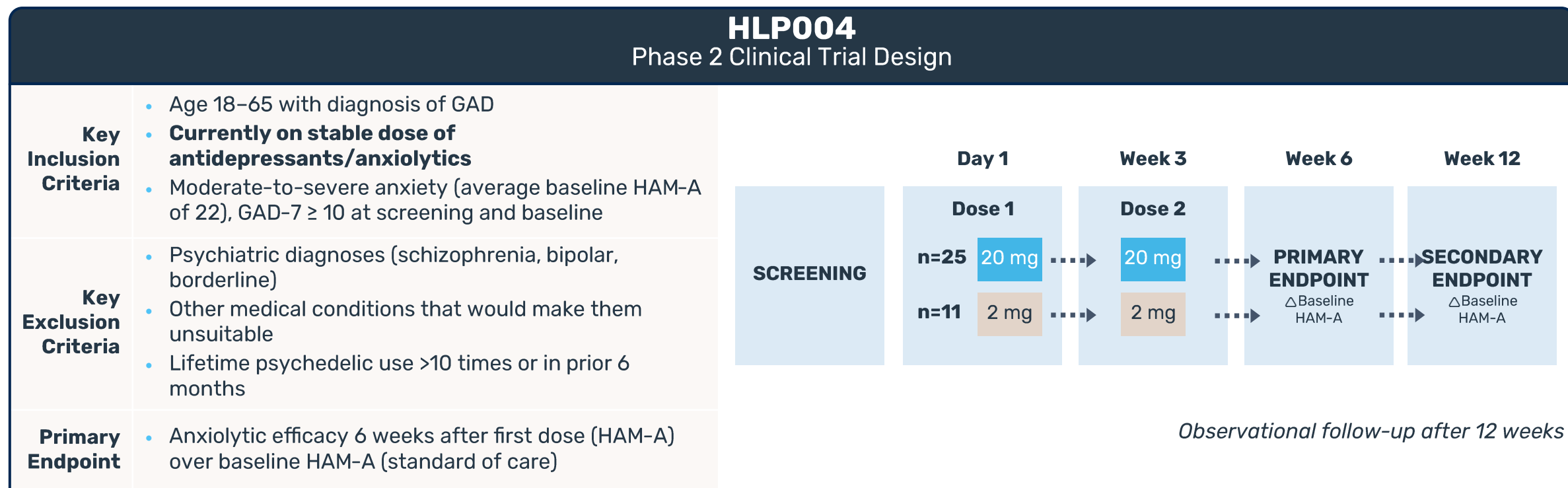
Notes:  
1) Time to first 'Yes', as assessed using the Clinical Global Assessment of Discharge Readiness (CGADR), starting at 60 minutes. Popova, et al. Am J Psychiatry 2019;176:428. Daly, et al. Supplement to JAMA Psychiatry. 2019;76:893.  
2) Robison, et al. JAMA, 2025. 334(15):1358-1372. For the 100 µg dose group, 97.5% resolution of acute affects within 12 hours.  
3) Not statistically different from placebo after 90 mins.  
4) SPRAVATO is a registered trademark of JOHNSON & JOHNSON Corporation, USA

# HLP004

## Phase 2 Topline Data in Generalized Anxiety Disorder

# HLP004 Phase 2 Signal Detection Study in GAD

Double-blinded Phase 2 study of HLP004 as an adjunctive treatment on top of SOC for patients suffering with GAD



- **Designed as a signal detection study to assess within subject changes in two active dose levels**
  - Not powered to show separation between doses
- **Designed to mimic real-world treatment paradigm**

# HLP004 Phase 2 Baseline Characteristics Demonstrate Real World Treatment Paradigm

Characteristic	20 mg (n=25)	2 mg (n=11)	Overall (n=36)
<b>Age (years); Mean (SD)</b>	34.6 (9.92)	42.4 (12.14)	37.0 (11.08)
<b>Female (n; %)</b>	23 (92.0)	7 (63.6)	30 (83.3)
<b>White (n; %)</b>	14 (56.0)	6 (54.5)	20 (55.6)
<b>BMI (kg/m<sup>2</sup>); mean (SD)</b>	28.6 (6.06)	26.2 (5.02)	27.9 (5.80)
<b>Past psychedelic used (n; %)</b>	2 (8.0)	2 (18.2)	4 (11.1)
<b>HAM-A<sup>1</sup> at Baseline; Mean (SD)</b>	22.0 (5.42)	21.0 (5.74)	21.7 (5.46)

## Key Takeaways

- Moderate-to-severe patients (average HAM-A lower than monotherapy trials), consistent with subjects on concomitant SoC
- Inadequately responding patients are a harder to treat population

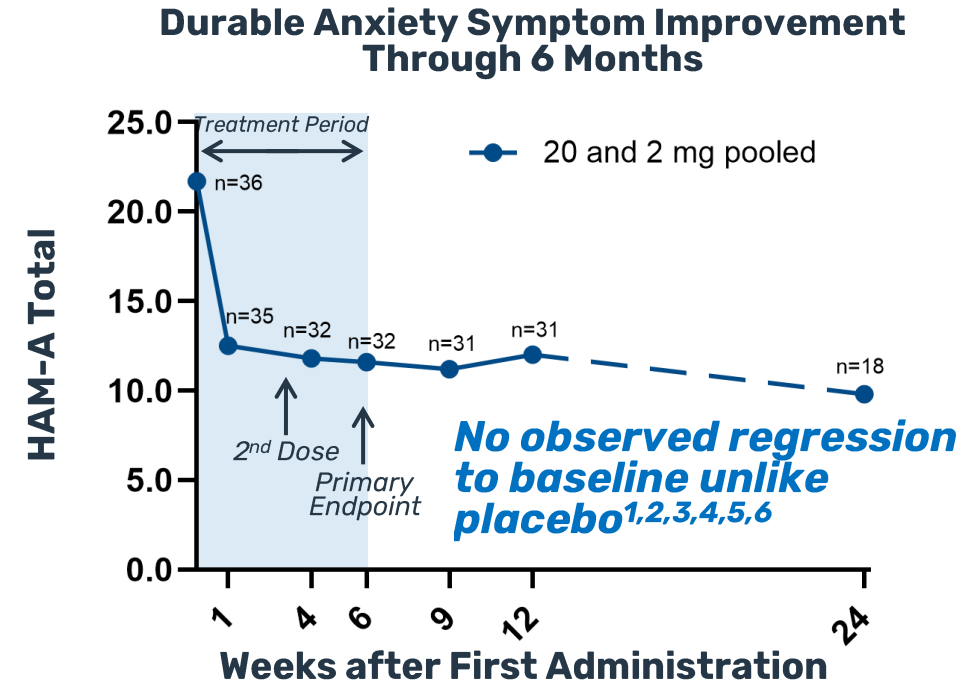
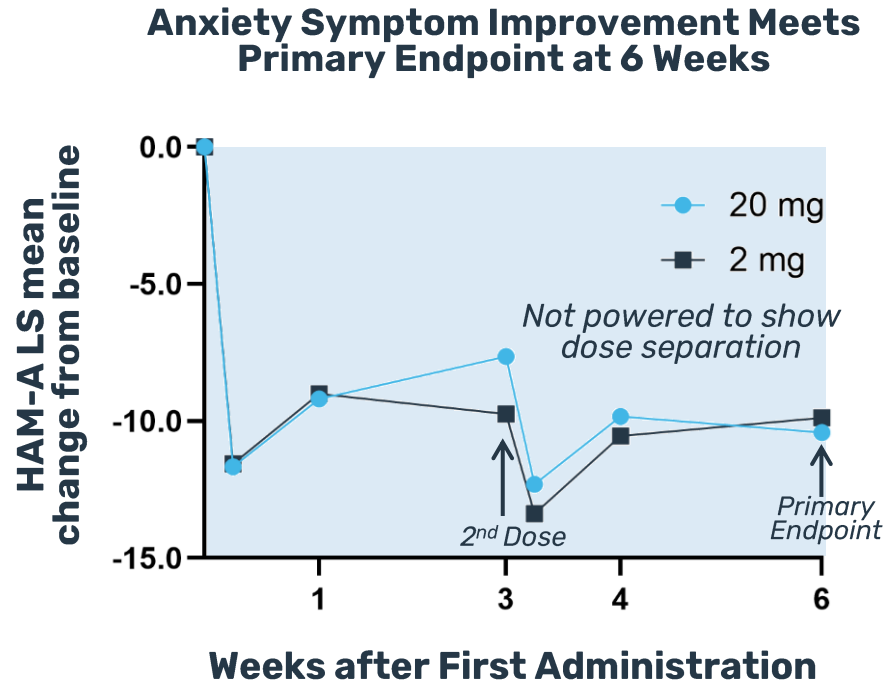
- **Known to be a challenging population to show an effect in adjunct - no approved adjunctive in GAD on top of SOC**

### Notes:

Some values subject to affect of rounding.

1) Hamilton Anxiety Rating Scale (HAM-A) has total score range of 0-56, where ≤17 indicates mild severity, 18-24 moderate and 25-30 severe.

# HLP004 Demonstrated Rapid and Profound Effects over SoC, with Effects Sustained Through at Least 6 Months



- **Rapid, within-subject improvements** from Day 2
- **Both doses show statistically significant improvement:** ~10-point within-subject HAM-A change from baseline ( $p < 0.0001$ )
- **No separation between doses**
- **Durable improvements** for 6 months
- **Placebo effects regress to baseline after stopping treatment in GAD<sup>1,2,3,4,5,6</sup>**
- **Sustained improvements** following second dose

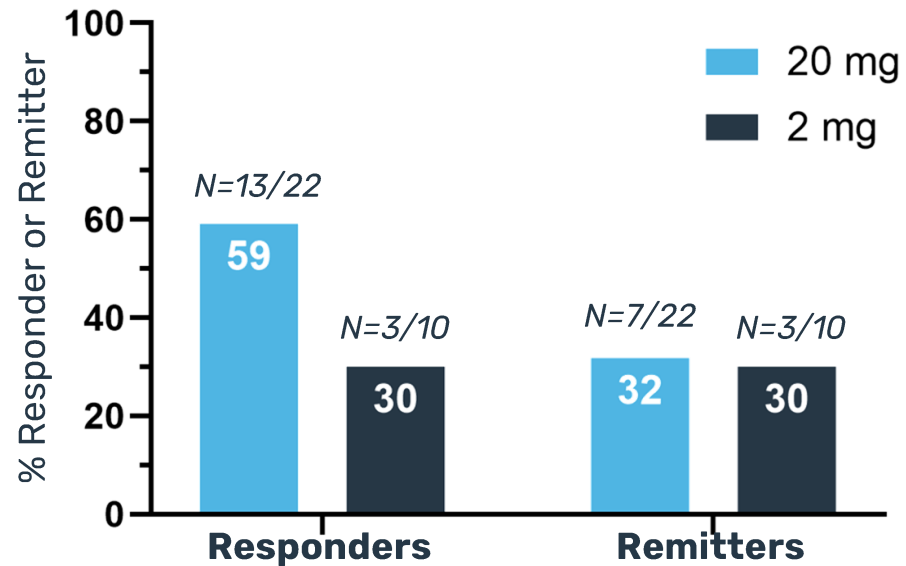
## Notes:

- 1) Gueorguieva, et al. Lancet Psychiatry, 2017. 4(3):230-237.
- 2) Rutherford, et al. Depress Anxiety, 2015. 32(12):944-57.
- 3) Berwian, I.M., et al. Psychol Med, 2017. 47(3):426-437.
- 4) Jones, B.D.M., et al. JAMA Network Open, 2021. 4(9):e2125531-e2125531.

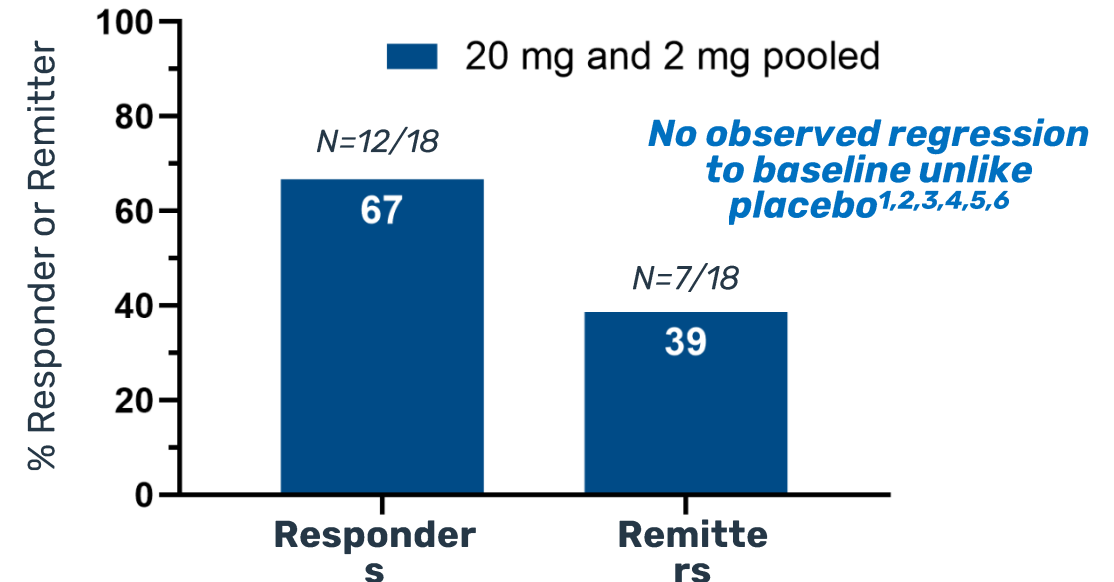
- 5) Davidson, et al. Eur Neuropsychopharmacol, 2008. 18(9):p. 673-81.
- 6) Quitkin, et al. Arch Gen Psychiatry, 1984. 41:p. 782-786.

# Single HLP004 Treatment Cycle Resulted in ~70% Responders and ~40% Remitters at 6 months

## Responders and Remitters at 6 Weeks



## Responders and Remitters at 6 Months



- Up to ~60% responders and ~1/3<sup>rd</sup> remitters at 6 weeks
- ~70% responders and ~40% remitters at 6 months
- Sustained improvements at 1 year
  - 5 participants; 4 of which were remitters
  - Average HAM-A is 4.0

### Notes:

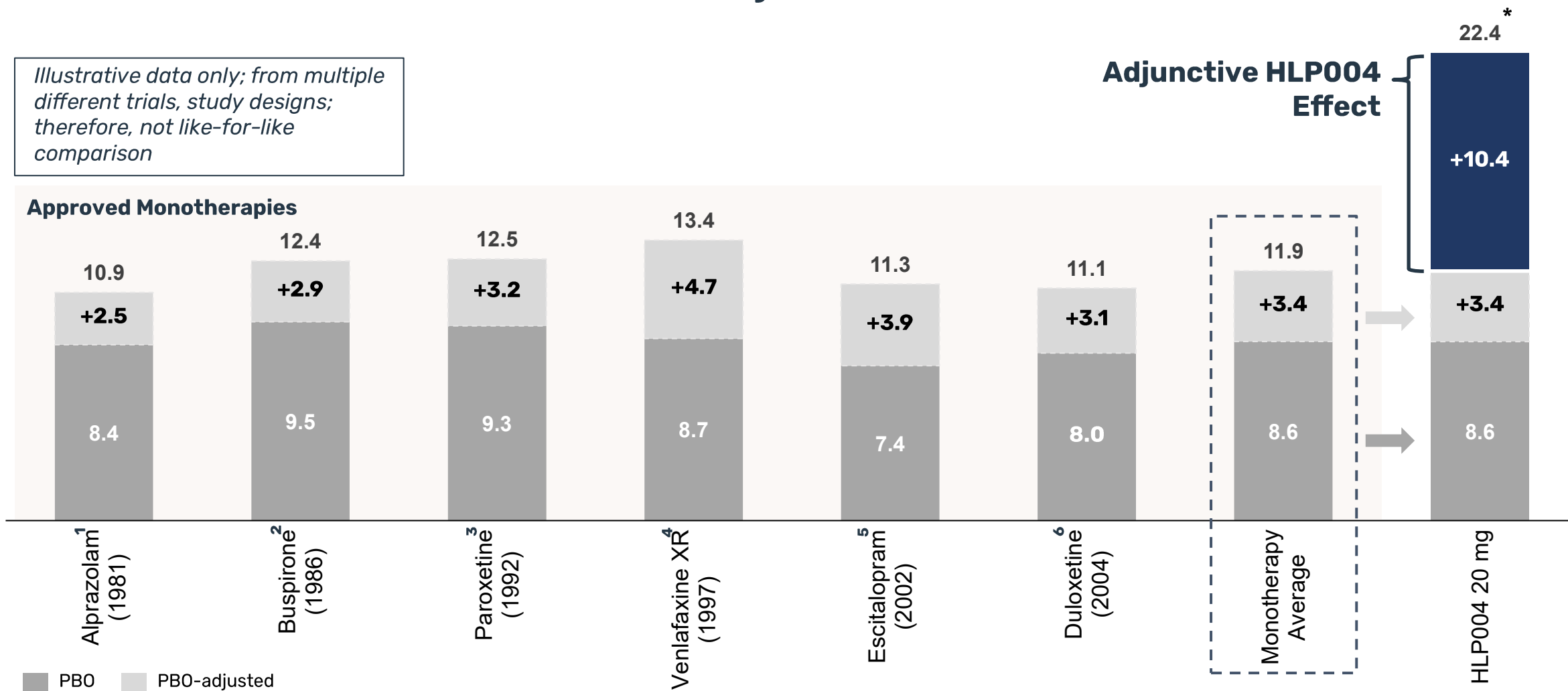
- 1) Gueorguieva, et al. Lancet Psychiatry, 2017. 4(3):230-237.
- 2) Rutherford, et al. Depress Anxiety, 2015. 32(12):944-57.
- 3) Berwian, I.M., et al. Psychol Med, 2017. 47(3):426-437.
- 4) Jones, B.D.M., et al. JAMA Network Open, 2021. 4(9):e2125531-e2125531.

- 5) Davidson, et al. Eur Neuropsychopharmacol, 2008. 18(9):p. 673-81.
- 6) Quitkin, et al. Arch Gen Psychiatry, 1984. 41:p. 782-786.

# Impact of HLP004 in Real World Clinical Setting

## Illustrative Benefit of Adjunctive Treatment in GAD

*Illustrative data only; from multiple different trials, study designs; therefore, not like-for-like comparison*



**Notes:**

Some values subject to affect of rounding.

- 1) Rickels 2005.
- 2) Sramek 1996.
- 3) Rickels 2003.
- 4) Gelenberg, 2007.
- 5) Davidson 2004.
- 6) Allgulander 2008.

*\*Absolute HAM-A response calculated using 10.42 response of HLP004 in adjunctive setting and monotherapy average of 11.93*

# HLP004's Emerging Best-in-Class Profile As a Short Acting Treatment for Psychiatric Conditions

	Acute Subjective Effects	Ready to Discharge	Fits SPRAVATO's <sup>2</sup> Commercial Model	Single Treatment Cycle	Durability with Single Treatment Cycle	Patient Population in Trial	AEs	Intellectual Property
<b>HLP004</b> <i>(D-DMT; GAD)</i>	<b>~90 Minutes</b>	<b>100% within ~3 hours<sup>1</sup></b>	<b>Yes</b>	<b>2 doses</b>	<b>At least 6 months+</b>	<b>Real-world adjunctive</b>	<b>Transient</b>	<b>CoM 2041</b>
<b>SOC</b>	<b>Minimal</b>	<b>-</b>	<b>-</b>	<b>Chronic</b>	<b>Daily Dosing Required</b>	<b>Monotherapy</b>	<b>Sexual Dysfunction, Weight Gain, Insomnia</b>	<b>Generic</b>

**Favorable to HLP004**

**Notes:**

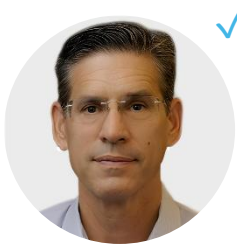
To-date, no head-to-head comparisons of any other products to any of our product candidates in any clinical trial have been completed; results have been obtained from different trials with different designs, endpoints and patient populations; results may not be comparable.

1) For 30 mg dose.

2) SPRAVATO is a registered trademark of JOHNSON & JOHNSON Corporation, USA.

# Leadership Team with Proven Record of Regulatory and Commercial Success

## Leadership



**Michael Cola**  
Chief Executive Officer



**Eric So**  
Executive Chairman &  
Co-Founder



**Amir Inamdar MBBS,  
DNB(Psych), FFPM**  
Chief Medical Officer



**Alex Nivorozhkin, Ph.D.**  
Chief Scientific Officer



**Aaron Bartlone**  
Chief Operating Officer



**George Tzirias**  
Chief Business Officer



**Paul Glavine**  
Co-Founder & Chief  
Growth Officer

## Scientific Advisors



**Dr. Freda Lewis Hall**  
Former Chief Medical Officer &  
Chief Patient Officer, Pfizer



**Dr. Thomas Laughren**  
Former FDA Director for the  
Division of Psychiatry Products



**Dr. Maurizio Fava**  
Chair, Mass General Brigham  
Dept of Psychiatry,  
Massachusetts General Hospital



**Dr. Steve Brannan**  
Former CMO, Karuna  
Therapeutics



**Dr. Robert Langer**  
Co-founder, Moderna



**Andrew J Cutler, MD**  
Psychiatrist, PI,  
Strategic Advisor  
> 400 Clinical Trials

# Leading the Development of NSAs<sup>1,2</sup>

- 1** Two proprietary clinical programs, **HLP003** and **HLP004**, targeting MDD and GAD with **positive Phase 2 safety and efficacy results**
- 2** Lead program HLP003 has been granted **U.S. Food and Drug Administration Breakthrough Therapy Designation** and is in **Phase 3 studies for the adjunctive treatment of MDD**
- 3** **Differentiated pipeline** with potential for expansion into **additional mental health indications with high unmet need affecting >200M people in the U.S.**<sup>3</sup>
- 4** **Strong intellectual property portfolio** with over 350 filed patents of which >100 are granted which provide patent protection until at least 2041

Next Key Milestone: Phase 3 topline data from HLP003 APPROACH study in Q4 2026

Notes:

- 1) Novel serotonergic agonists (NSAs): synthetic molecules designed to activate serotonin pathways that are believed to drive neuroplasticity.
- 2) Forward looking statements are subject to risks and assumptions. See "Cautionary Statement" on page 2 of this presentation. There is no assurance that timelines will be met. Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to Helus. Such statements are informed by, among other things, regulatory guidelines for developing a drug with timeline safety studies, proof of concept studies, and pivotal studies for new drug application submission and approval, and assumes the success of implementation and results of such studies on timelines indicated as possible by such guidelines, other industry examples, and Helus's development efforts to date.
- 3) Addressable market is estimated based on U.S. census population of 337,049,203 as of September 8, 2024 and on U.S. prevalence of indications including depression, anxiety disorders/PTSD, bipolar disorder, substance use/addiction disorders, eating disorders, cluster headaches/migraine, and chronic pain management.

# Thank You

Nasdaq: **HELP** | Cboe CA: **HELP**

Contact: [irteam@helus.com](mailto:irteam@helus.com)

# References

## SLIDE 5

- 1) <https://www.nimh.nih.gov/health/statistics/major-depression>
- 2) Vasiliadis, H. M., Lesage, A., Adair, C., Wang, P. S., & Kessler, R. C. (2007). Do Canada and the United States differ in prevalence of depression and utilization of services?. *Psychiatric services (Washington, D.C.)*, 58(1), 63–71. <https://doi.org/10.1176/ps.2007.58.1.63>
- 3) Ringeisen, H., et. al. (2023). *Mental and Substance Use Disorders Prevalence Study (MDPS): Findings Report*. RTI International.
- 4) Zbozinek TD, et. al. Diagnostic overlap of generalized anxiety disorder and major depressive disorder in a primary care sample. *Depress Anxiety*. 2012 Dec;29(12):1065–71.
- 5) Forward-looking statements are subject to risks and assumptions. See “Cautionary Statement” on page 2 of this presentation.
- 6) Subject to receipt of all necessary regulatory approvals from all applicable governmental authorities, including, as applicable, the academic and scientific organizations with which Helus is working. There are multiple risk factors regarding the ability to successfully commercially scale a chemically synthesized process to obtain psilocin and other analogues. There is no assurance that timelines will be met. Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to Helus. Such statements are informed by, among other things, regulatory guidelines for developing a drug with timeline safety studies, proof of concept studies, and pivotal studies for new drug application submission and approval, and assumes the success of implementation and results of such studies on timelines indicated as possible by such guidelines, other industry examples, and Helus’s development efforts to date.

## SLIDE 7

- 1) SPRAVATO is a registered trademark of JOHNSON & JOHNSON Corporation, USA.
- 2) <https://www.grandviewresearch.com/industry-analysis/us-ketamine-clinics-market-report>
- 3) <https://neurostar.com/hcp/>, <https://www.brainsway.com/find-a-provider/>, <https://magventure.com/>
- 4) OSMIND is a registered trademark of OSMIND INC., USA.
- 5) Esketamine package insert
- 6) Hutton et al. (2023). Dosing transcranial magnetic stimulation in major depressive disorder: Relations between number of treatment sessions and effectiveness in a large patient registry. *Brain stimulation*, 16(5), 1510–1521. <https://doi.org/10.1016/j.brs.2023.10.001>
- 7) Thirthalli, J., Naik, S. S., & Kunigiri, G. (2020). Frequency and Duration of Course of ECT Sessions: An Appraisal of Recent Evidence. *Indian journal of psychological medicine*, 42(3), 207–218. [https://doi.org/10.4103/IJPSYM.IJPSYM\\_410\\_19](https://doi.org/10.4103/IJPSYM.IJPSYM_410_19)
- 8) HLP003 profile is illustrative and is subject to further validation in Phase 3 studies
- 9) No head-to-head comparisons have been made in any clinical trials that have been completed; results have been obtained from different trials with different designs, endpoints and patient populations; results may not be comparable.

## SLIDE 9

1. World Health Organization. (2017). *Depression and other common mental disorders: global health estimates*. World Health Organization. <https://iris.who.int/handle/10665/254610>.
2. <https://www.nimh.nih.gov/health/statistics/major-depression>; Vasiliadis, H. M., Lesage, A., Adair, C., Wang, P. S., & Kessler, R. C. (2007). Do Canada and the United States differ in prevalence of depression and utilization of services?. *Psychiatric services (Washington, D.C.)*, 58(1), 63–71. <https://doi.org/10.1176/ps.2007.58.1.63>
3. American Association of Suicidology, 2014. <https://www.cga.ct.gov/asafersconnecticut/tmy/0129/Some%20Facts%20About%20Suicide%20and%20Depressio n%20-%20Article.pdf>
4. Hopwood M. (2023). Anxiety Symptoms in Patients with Major Depressive Disorder: Commentary on Prevalence and Clinical Implications. *Neurology and therapy*, 12(Suppl 1), 5–12. <https://doi.org/10.1007/s40120-023-00469-6>
5. Little A. Treatment-resistant depression. *Am Fam Physician*. 2009;80:167–72.
6. Cascade E, Kalali AH, Kennedy SH. Real-World Data on SSRI Antidepressant Side Effects. *Psychiatry (Edgmont)*. 2009 Feb;6(2):16–8.

# Appendix

# Favorable Safety Profile of HLP003

- No AEs were reported at the 12-month follow up
- No reports of suicidal ideation or behavior or any long-term adverse sequelae

In the short-term study:

- No SAEs and no participant discontinued the study due to an AE
- Most common AEs were nausea, elevated blood pressure and headache
- Increases in blood pressure were transient and resolved without intervention
- No clinically relevant changes in chemistry, hematology markers or ECG parameters

# HLP004: Generally Well-Tolerated, Adverse Events were Transient, with No Drug Related Serious Adverse Events Recorded

SOC Psychiatric Disorders AEs > 10% across all participants	20 mg N (%)	2 mg N (%)	Total N (%)
Hallucination, visual	11 (44.0)	1 (9.1)	12 (33.3)
Time perception altered	4 (16.0)	1 (9.1)	5 (13.9)
Anxiety	3 (12.0)	1 (9.1)	4 (11.1)
Confusional state	4 (16.0)	0	4 (11.1)
Depersonalization / derealization disorder	3 (12.0)	1 (9.1)	4 (11.1)
Emotional disorder	4 (16.0)	0	4 (11.1)

**All AEs were mild/moderate**

**No severe or serious AEs**

**No suicidality-related safety signal**

- No discontinuations due to AEs
- All related AEs resolved without sequelae
- No AEs required emergent intervention
- All AEs largely confined to the day of dosing