



**Healing mental health disorders so that everyone everywhere can live a more fulfilled life.**

**Company Overview – January 2024**



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# atai Life Sciences: **Healing mental health disorders** so that everyone everywhere can live a more fulfilled life

- 1** Mental health disorders are one of the largest global health burdens; in 2019, 1 in every 8 people, or 970 million people, around the world were living with a mental disorder<sup>1</sup>
- 2** atai's objective is to achieve clinically meaningful and sustained behavioral change in mental health patients by developing rapid-acting and durable therapeutics
- 3** Eight clinical-stage drug development programs and strategic investments, each with a robust package of prior clinical evidence
- 4** Validated operating model and ability to capture value: IPO of COMPASS Pathways in 2020 and licensing deal between Otsuka and atai subsidiary Perception Neuroscience in 2021
- 5** Cash, marketable securities, and committed term loan funding are expected to provide runway into 2026<sup>2</sup>

1. World Health Organization

2. Committed term loan funding includes \$45M of additional capital that can be drawn not subject to milestones under the facility with Hercules Capital; marketable securities includes money market funds, U.S. Treasury securities, commercial paper, corporate notes/bonds, U.S. government agencies securities, and public equities

# Our strategy will be delivered through a robust portfolio of psychedelic and non-psychedelic drug development programs and strategic investments

Programs / Investments	Primary Indication	Preclin	Phase 1	Phase 2	Phase 3
PSYCHEDELIC PROGRAMS & STRATEGIC INVESTMENTS					
COMP360 <sup>1</sup> / Psilocybin	Treatment-Resistant Depression				
BPL-003 <sup>2</sup> / 5-MEO-DMT	Treatment-Resistant Depression				
DMX-1002 / Ibogaine	Opioid Use Disorder				
VLS-01 / DMT	Treatment-Resistant Depression				
ELE-101 <sup>2</sup> / Psilocin	Major Depressive Disorder				
EMP-01 / R-MDMA	Post-Traumatic Stress Disorder & others				
EGX-A & EGX-B / Novel 5-HT2A Receptor Agonists	Undisclosed				
NON-PSYCHEDELIC PROGRAMS					
RL-007 / Pro-cognitive neuromodulator <sup>3</sup>	Cognitive Impairment Associated with Schizophrenia				
GRX-917 / Deuterated etifoxine	Generalized Anxiety Disorder				

<sup>1</sup> Strategic Investment in Compass Pathways

<sup>2</sup> Strategic Investment in Beckley PsyTech

<sup>3</sup> RL-007 compound is (2R, 3S)-2-amino-3-hydroxy-3-pyridin-4-yl-1-pyrrolidin-1-yl-propan-1-one(L)-(+)-tartrate salts

Strategic Investment

# atai Life Sciences: Operational Focus & Program Guidance

*We expect to deliver several meaningful R&D milestones across our key programs over next 18 months<sup>3</sup>*

PSYCHEDELIC PROGRAMS & STRATEGIC INVESTMENTS						NON-PSYCHEDELIC PROGRAMS	
COMP360 <sup>1</sup> (Psilocybin)	BPL-003 <sup>2</sup> (5-MEO-DMT)	VLS-01 (DMT)	DMX-1002 (Ibogaine)	ELE-101 <sup>2</sup> (Psilocin)	EMP-01 (R-MDMA)	RL-007 (Pro-Cognitive Neuromodulator)	GRX-917 (Deuterated etifoxine)
<div><div><input checked="" type="checkbox"/> Successful outcome of Ph 2b trial in TRD</div><div><input type="checkbox"/> Ph 2 (PTSD) – data Spring ‘24</div><div><input type="checkbox"/> Ph 3 (TRD) – Pivotal Trial 1 topline data summer ‘24</div><div><input type="checkbox"/> Ph 3 (TRD) – Pivotal Trial 2 topline data mid-‘25</div></div>	<div><div><input checked="" type="checkbox"/> Successful outcome of Ph 1 trial</div><div><input type="checkbox"/> Ph 2a OL (TRD) data in 1H’24</div><div><input type="checkbox"/> Ph 2a OL (AUD) data in mid-‘24</div><div><input type="checkbox"/> Ph 2b (TRD) data in 2H’24</div></div>	<div><div><input checked="" type="checkbox"/> Initial Ph 1 results in 2Q’23</div><div><input checked="" type="checkbox"/> Additional Ph 1 data in 3Q’23</div><div><input type="checkbox"/> Ph 1b first participant dosed in 1H’24</div></div>	<div><div><input checked="" type="checkbox"/> Initial Phase 1 results in 3Q ’23</div><div><input type="checkbox"/> Submit FDA meeting request in 1H’24</div></div>	<div><div><input type="checkbox"/> Ph 1/2a OL (MDD) – data in 1H’24</div></div>	<div><div><input checked="" type="checkbox"/> Ph 1 trial initiated in 3Q’22</div><div><input checked="" type="checkbox"/> Ph 1 results in 4Q ‘23</div></div>	<div><div><input checked="" type="checkbox"/> Successful outcome of Ph 2a trial in CIAS</div><div><input checked="" type="checkbox"/> Ph 2b first patient dosed in 1Q’23</div><div><input type="checkbox"/> Topline Ph 2b data mid-‘25</div></div>	<div><div><input checked="" type="checkbox"/> Ph 1 topline results in 1Q’23</div><div><input checked="" type="checkbox"/> Late breaking presentation at 2023 SOBP annual meeting</div></div>

1. Strategic Investment in Compass Pathways

2. Strategic Investment in Beckley PsyTech

3. All dates provided are as estimated

Abbreviations: PTSD = Post-Traumatic Stress Disorder; CIAS = Cognitive Impairment Associated with Schizophrenia;

TRD = Treatment Resistant Depression; AUD = Alcohol Use Disorder; MDD = Major Depressive Disorder

# BPL-003

(5-MeO-DMT)  
for TRD & Alcohol  
Use Disorder

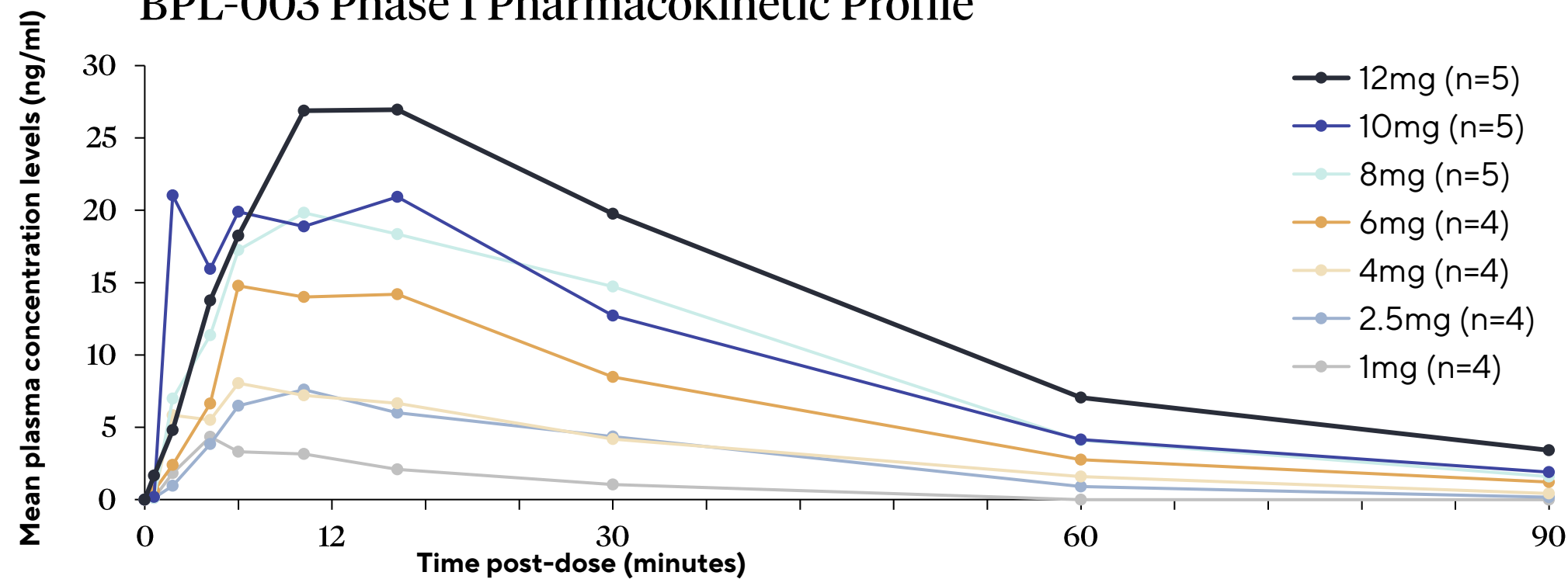
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## BPL-003: Intranasal 5-MeO-DMT

Results from completed Phase 1 SAD study showed BPL-003 had a favorable safety profile and was well tolerated whilst demonstrating dose proportionate PK/PD profile

BPL-003 Phase 1 Pharmacokinetic Profile



### Key Findings

#### Safety

- » All adverse events (AEs) were mild (89.5%) or moderate (10.5%); no Serious AEs occurred
- » Most common AEs (>10%) : nasal discomfort, nausea, vomiting, and headache

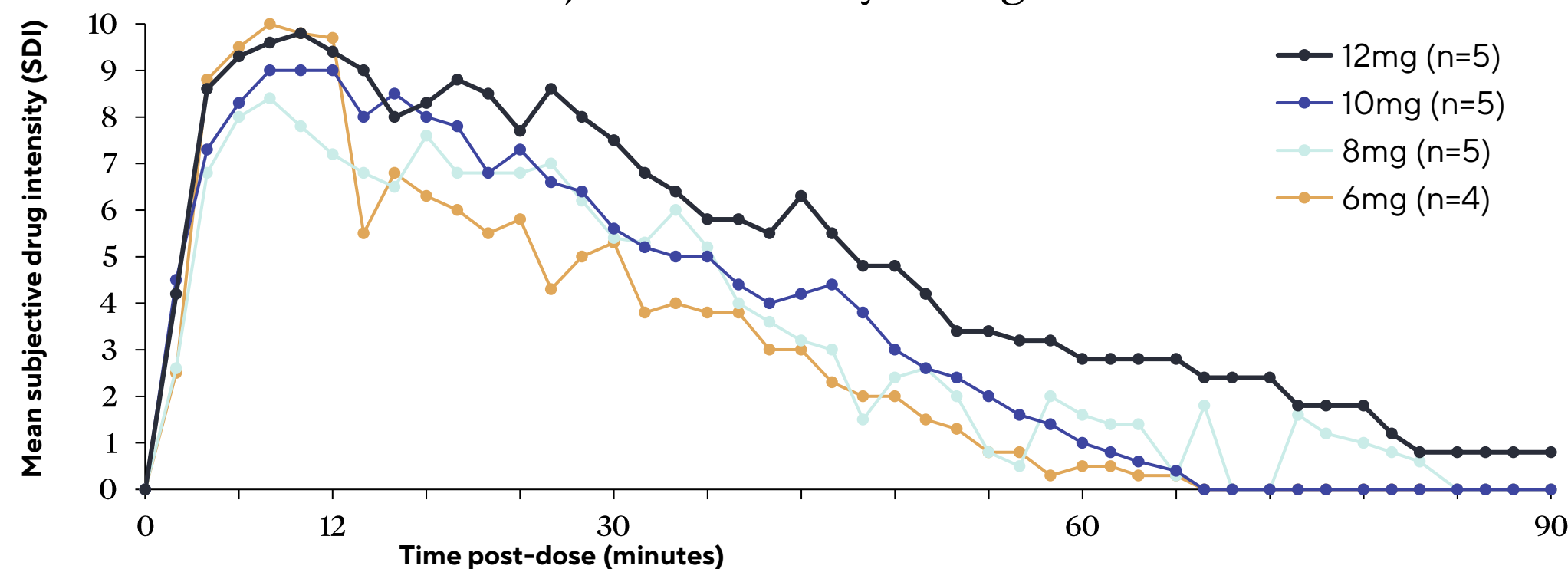
#### Pharmacokinetics (PK)

- » Exposure was dose-proportionate
- » Rapid onset: mean Tmax of 6-17 min
- » Short duration: mean t1/2 of 15-30 min

#### Pharmacodynamics (PD)

- » Subjects were psychedelic naive
- » All subjects on doses  $\geq 6$ mg achieved intensity scores  $\geq 7$
- » Perceptual effects generally fully resolved within 60 - 90 mins

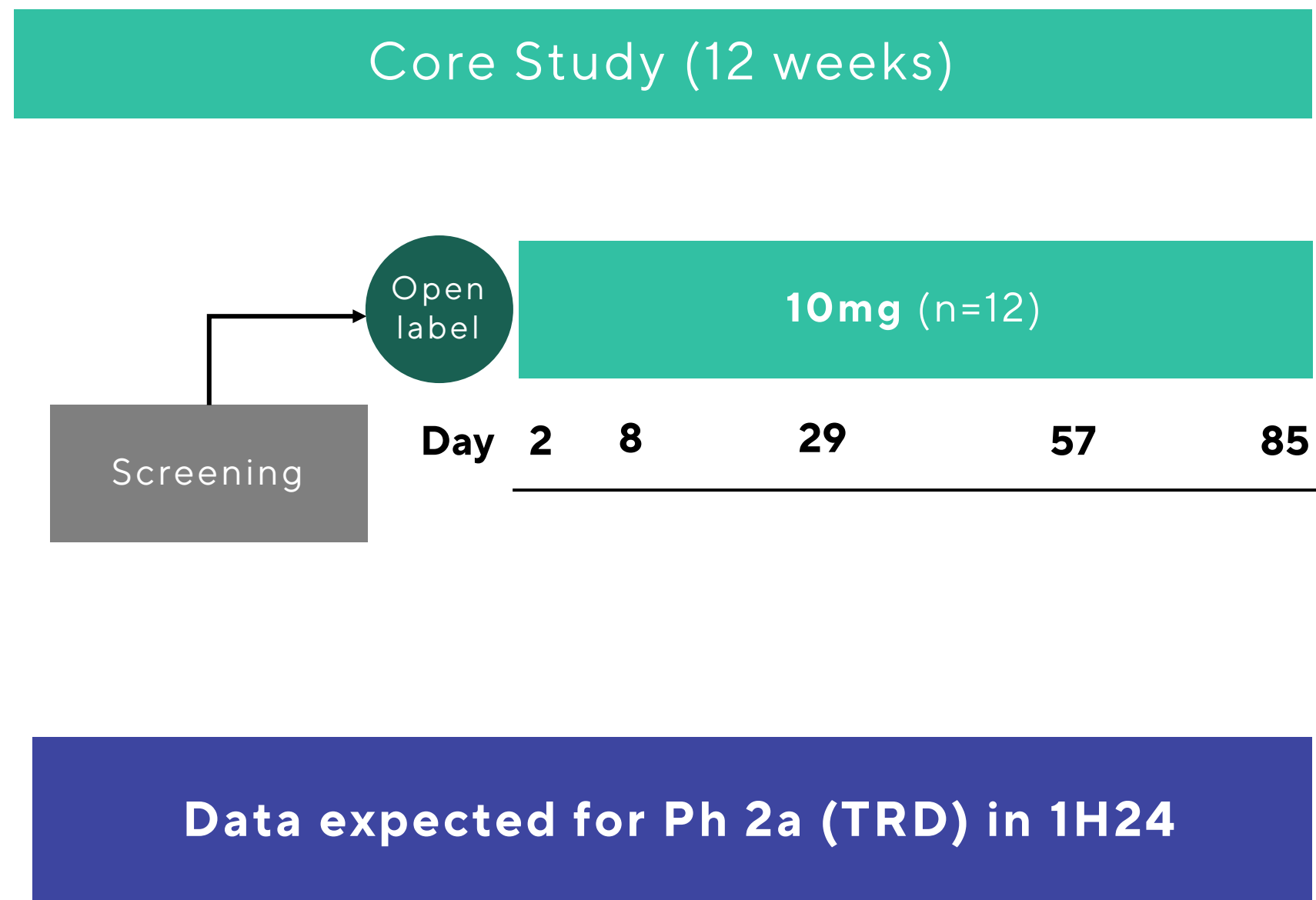
BPL-003 Phase 1 Subjective Intensity Ratings





## BPL-003 Phase 2a Clinical Trial Design

BPL-003 Phase 2a is an open-label monotherapy study in TRD patients



### Key Inclusion Criteria

- » Patients with moderate-severe treatment resistant depression
- » Montgomery-Asberg Depression Rating Scale (MADRS) score  $\geq 24$
- » Willing and able to discontinue current antidepressants

### Key Objectives:

#### Primary Endpoint:

- » Safety and tolerability of BPL-003 monotherapy

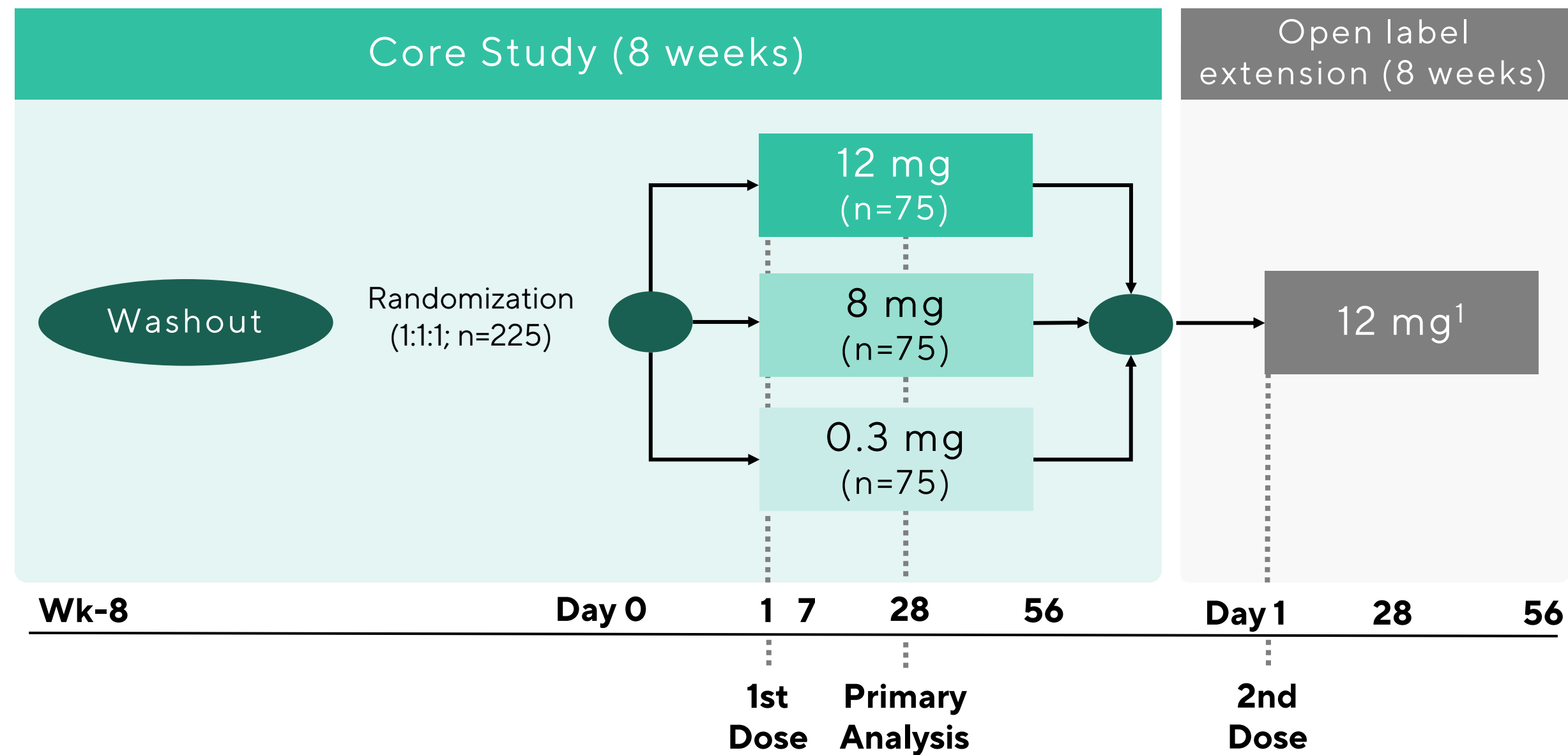
#### Key Secondary Endpoints:

- » MADRS change at Day 2, 8, 29, 57 and 85
- » CGI-S, PGIC, EQ-5D



## BPL-003 Phase 2b Clinical Trial Design

BPL-003 Phase 2b is a randomized, double-blind, single-dose monotherapy study in moderate to severe TRD patients



**Data expected for Ph 2b (TRD) in 2H24**  
*(first patient dosed Oct 2023)*

### Key Inclusion Criteria

- » Patients with treatment-resistant depression
- » Hamilton Depression Scale (HAM-D)  $\geq 19$
- » Willing and able to discontinue current antidepressants

### Key Objectives:

#### Primary Endpoint:

- » MADRS change from baseline at day 28

#### Key Secondary Endpoints:

- » MADRS change at Day 1, 7 and 56
- » CGI-S, PGIC, EQ-5D

<sup>1</sup> Patients entering the open-label extension are randomized 1:1 to receive either a single 12mg dose or a biphasic 4mg and 8mg dose approximately 10 minutes apart  
 Abbreviations: MADRS = Montgomery-Åsberg Depression Rating Scale; CGI-S = Clinical Global Impressions-Severity; PGIC = Patient's Global Impression of Change; EQ-5D = EuroQol-5D

# VLS-01 (DMT) for TRD

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# Product Overview: VLS-01 for Depression

*Designed for a potential rapid, sustained reduction in depressive symptoms from a single dose*

PRODUCT	DMT (N,N-Dimethyltryptamine) in an oral transmucosal film (OTF)
INDICATIONS	<i>Lead:</i> Treatment Resistant Depression <i>Potential expansions:</i> Eating Disorders, Substance Use Disorders
INTELLECTUAL PROPERTY	Granted U.S. patent covering OTF administration of DMT, supported by several pending U.S. and PCT patent applications
CURRENT STATUS	Final Phase 1 data reported in 3Q '23 Phase 1b first participant expected in 1H '24 <sup>3</sup>

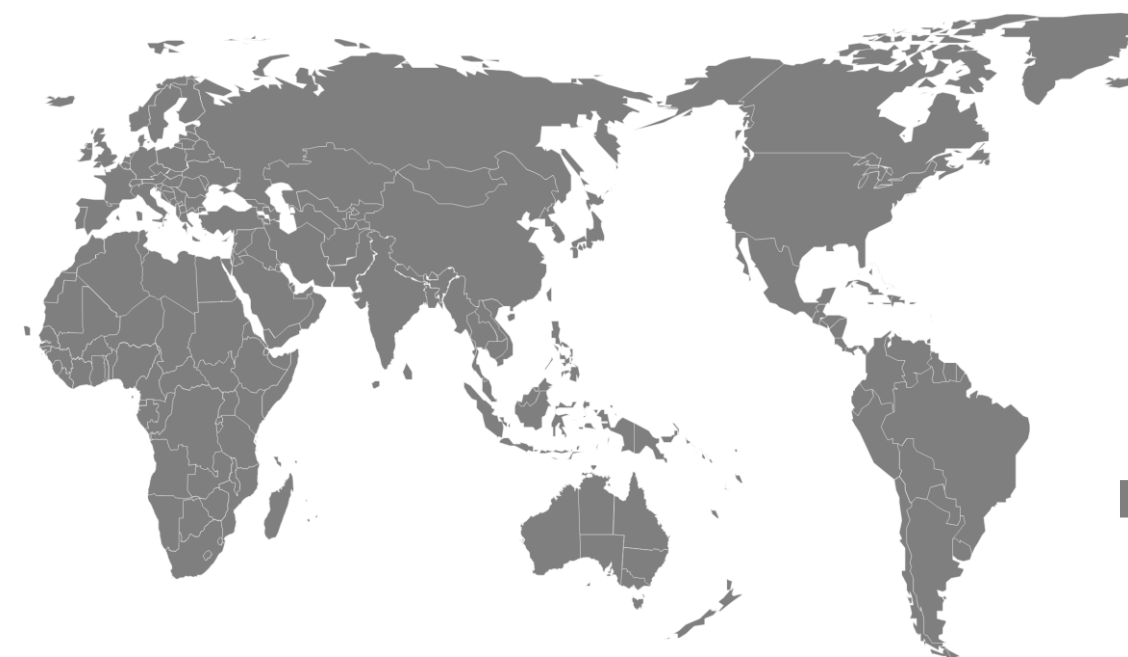
## VLS-01 Key Product Features

- Designed for rapid onset and sustained efficacy after single dose
- Short duration of psychedelic effect (~30 to 45 minutes) with improved tolerability and convenience from OTF delivery relative to other psychedelics in development for depression

## Lead indication overview

- Depression is a mood disorder that affects the thoughts and behavior of an individual, leading to psychological, physical, and social problems
- Treatment resistant depression (TRD) is diagnosed after two failed courses of antidepressants
- FDA approved depression treatments can be characterized by a slow onset, long-term side effects and inadequate response rate

## Global disease burden



**~300m**

Global sufferers of depression in 2019<sup>1</sup>

**33%**

Patients who have inadequate response or relapse after current treatments<sup>2</sup>

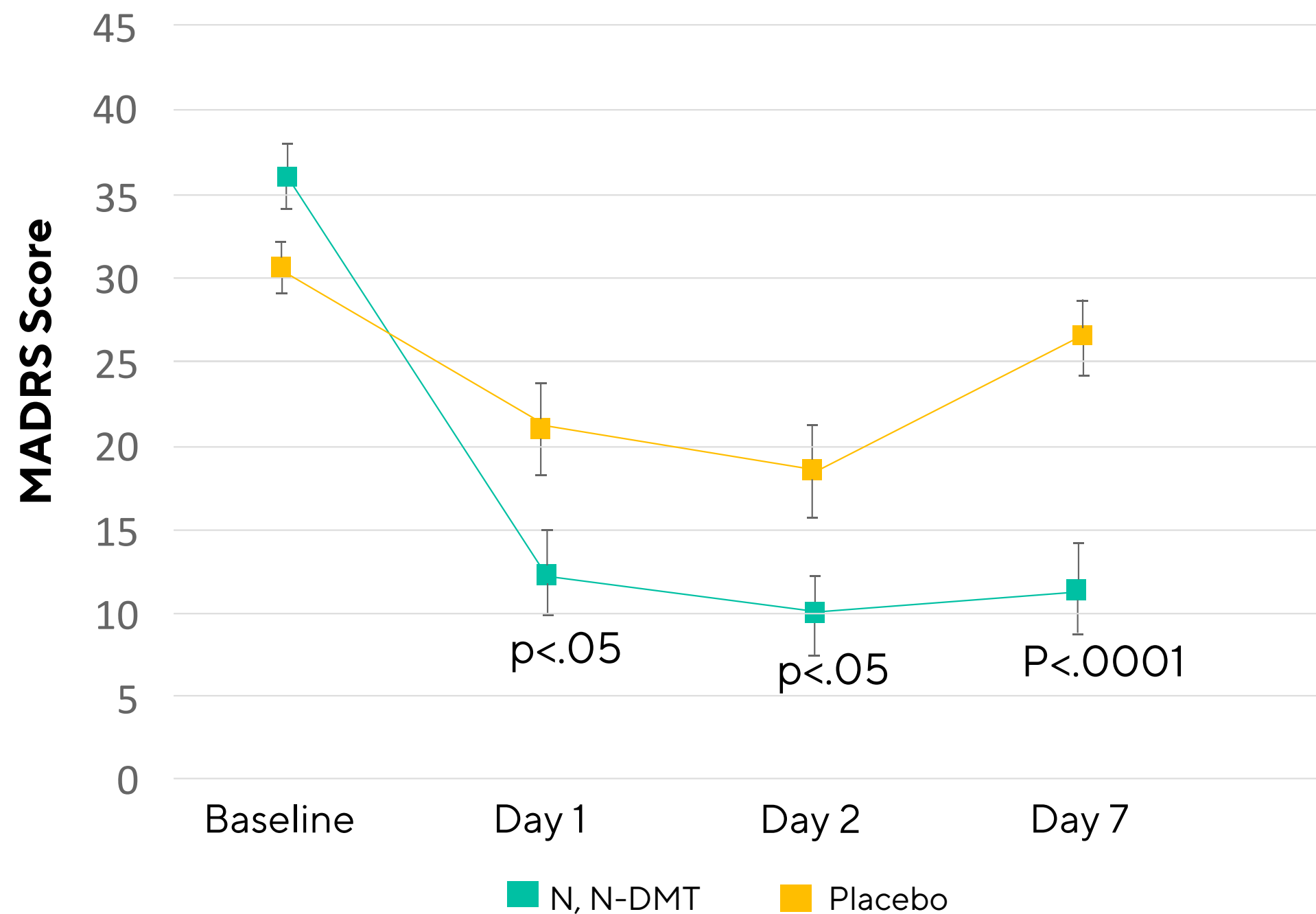
1. World Health Organization  
2. Salzer, "National Estimates of Recovery-Remission From Serious Mental Illness", Psychiatry Online (2018)  
3. Health Volunteer Study

# Clinical Evidence: Efficacy in Randomized Control Trial of DMT in TRD

*Double-blind, randomized placebo-controlled trial with DMT in 29 patients with treatment-resistant-depression*

## PRIOR CLINICAL EVIDENCE (THIRD PARTY STUDY<sup>1</sup>)

**Double-blind, randomized placebo-controlled trial of Ayahuasca (DMT is major active ingredient) in 29 patients with TRD**



## Key Takeaways

1

**Summary:** A single administration of .36 mg/kg met both primary and key secondary efficacy endpoints by demonstrating rapid and statistically significant changes on depression severity measures of HAM-D & MADRS

2

**Primary endpoint (HAM-D - not shown):** N,N-DMT arm achieved the primary endpoint of a statistically significant difference in depression severity relative to placebo ( $p < .05$ ).

3

**Key secondary endpoint (MADRS – see left):** rapid and statistically significant differences were observed at all timepoints assessed, including as early as Day 1 and through Day 7. MADRS is a potential registrational endpoint.

4

There were **no serious adverse events reported**.

Note: TRD = Treatment Resistant Depression; DMT = N,N-Dimethyltryptamine

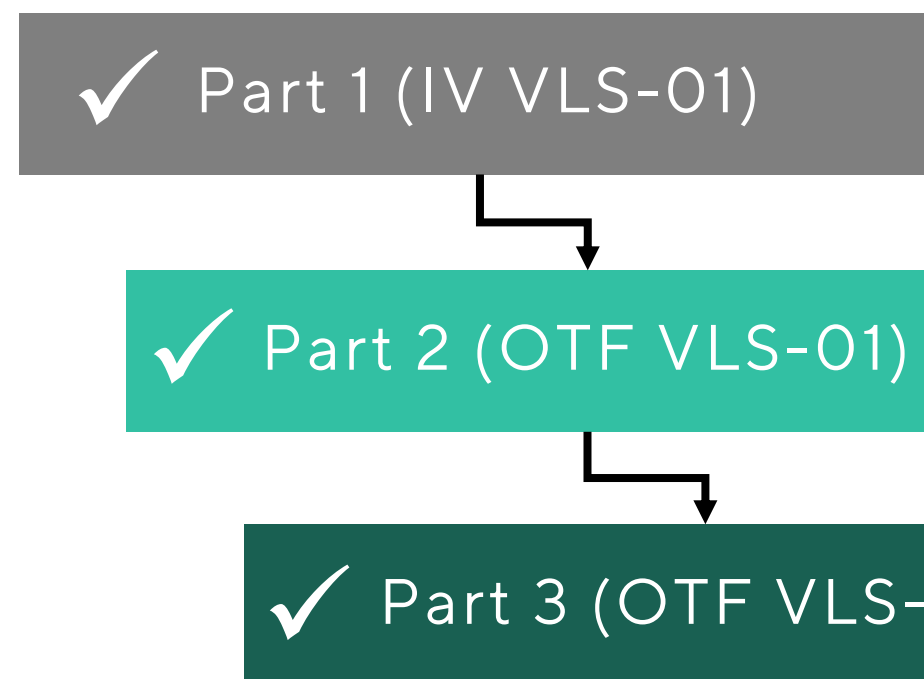
1. Palhano-Fontes et al. "Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression", Psychol Med (2019)



# VLS-01 Phase 1: Clinical Trial Design & Results

*VLS-01 was well-tolerated with a favorable safety profile, with dose-dependent increases in exposure confirmed*

## STUDY DESIGN:



## Phase 1 PK / PD RESULTS:

- **IV VLS-01:** PK / PD results were consistent with the known pharmacological profile of DMT, producing robust exposure-dependent increases in the subject intensity of psychedelic experience.
- **OTF VLS-01:** Produced generally dose-dependent increases in exposure, approaching that seen with IV administration, alongside subjective psychedelic experiences in the majority of patients.
- **OTF VLS-01:** 160mg with a backing layer via buccal administration experienced the most robust and consistent increases in exposure and subjective effects compared to the other OTF cohorts, with results comparable to the 30 mg IV cohort of DMT.

**Program status:** Phase 1b FSI expected in 1H '24

# COMP 360

(psilocybin) for TRD,  
PTSD and Anorexia

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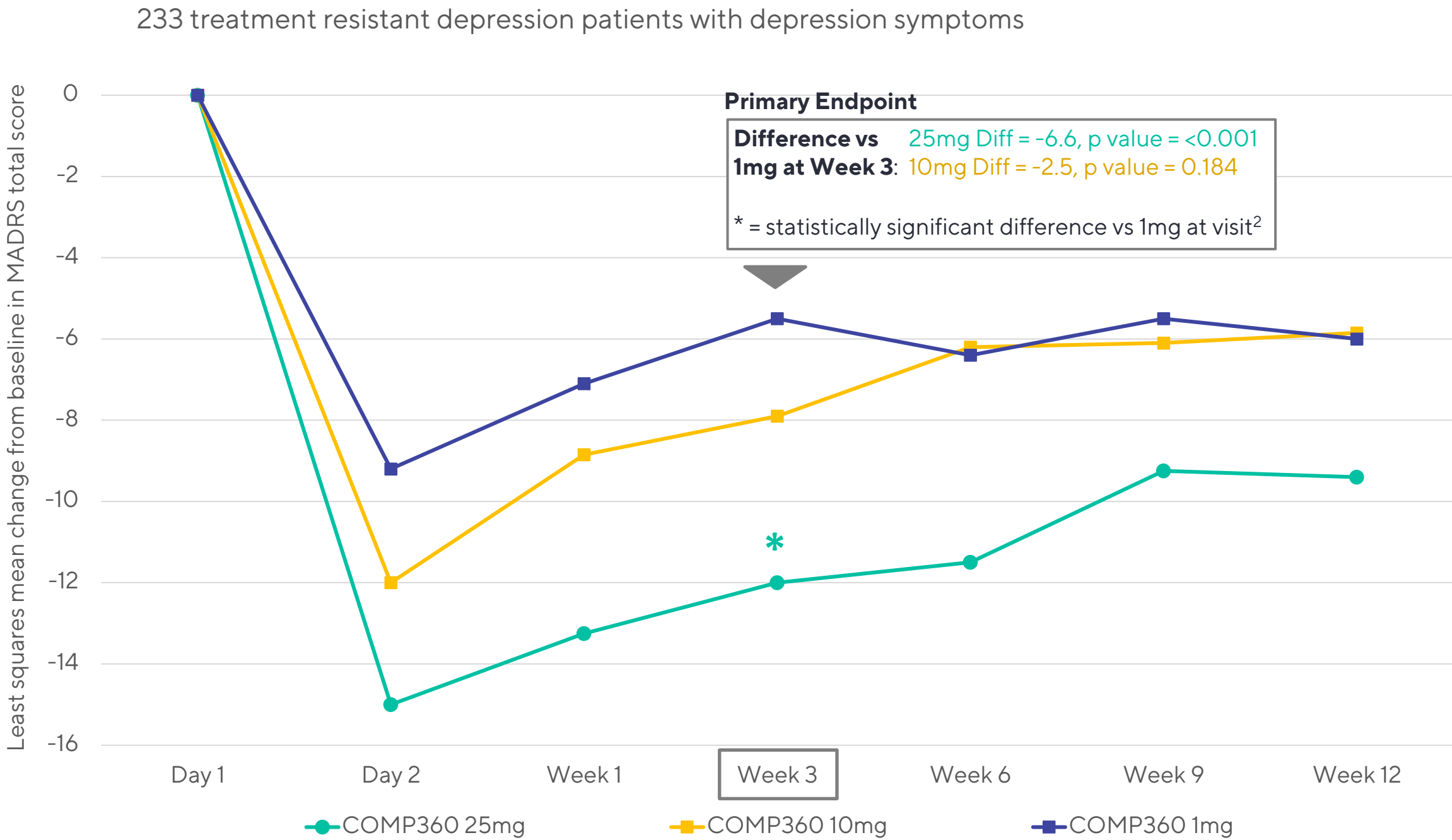


SUMMARY: COMP360

OWNERSHIP	15.5% <sup>1</sup>
PRODUCT	Oral Psilocybin (COMP360)
PHARMA-COLOGY	5-HT2A-R agonist
PRODUCT FEATURES	Rapid onset, potential for sustained efficacy after single dose
INDICATIONS	Primary: Treatment Resistant Depression, Anorexia Nervosa, PTSD Potential: Major Depressive Disorder, Autism, Bipolar Disorder, Chronic Cluster Headache
CURRENT STATUS	Phase 3 pivotal trial 1 data expected summer-24 Phase 3 pivotal trial 2 data expected mid-25
INTELLECTUAL PROPERTY	Proprietary formulation of synthetic psilocybin, COMP360
HIGHLIGHT	COMP360 demonstrated efficacy in reducing depressive symptom severity with rapid and durable response in Phase 2b study

COMP360 Phase 2b trial showed a rapid, sustained reduction in depressive symptoms

PRIOR EVIDENCE IN HUMANS (COMP360 PHASE 2b)



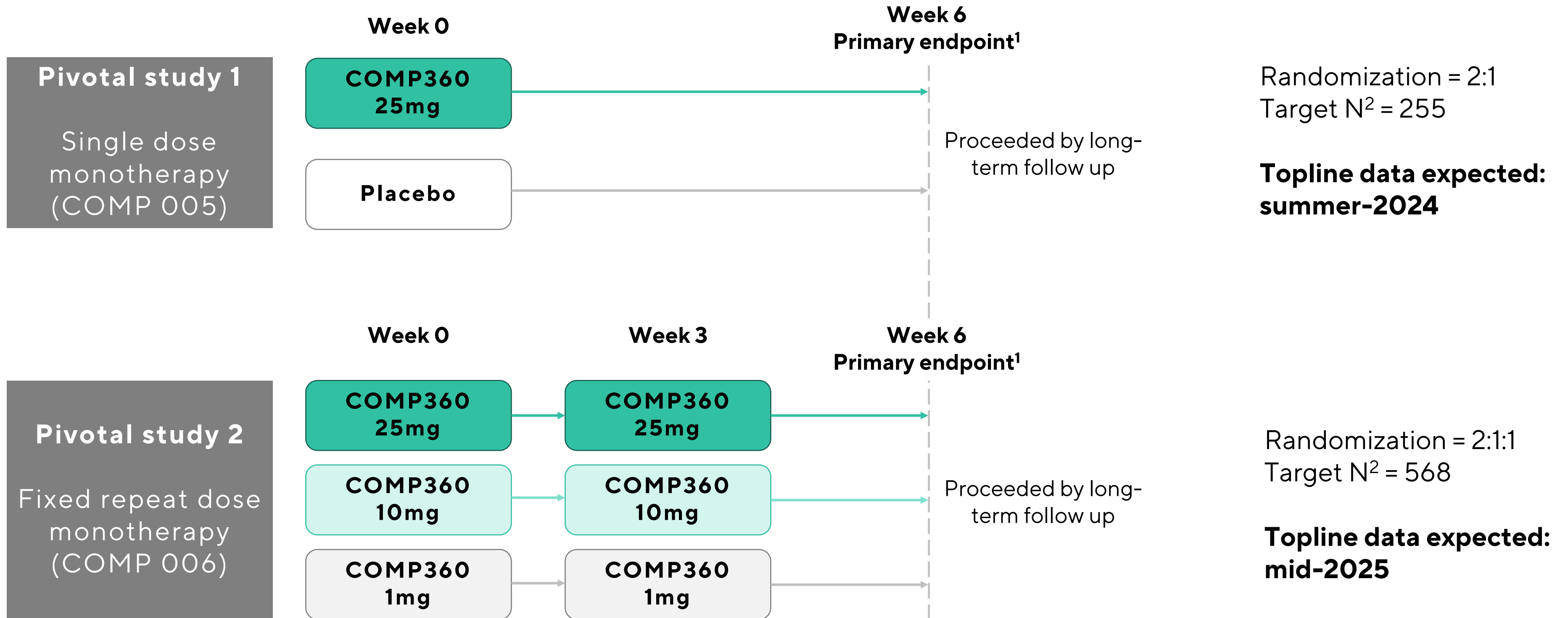
Note: MADRS = Montgomery-Åsberg Depression Rating Scale; COMP360 = a proprietary high-purity, polymorphic crystalline formulation of psilocybin; In COMPASS's model of psilocybin therapy, COMP360 is administered in conjunction with psychological support from specially trained therapists.

1. Ownership percentage as of Sep 30<sup>th</sup>, 2023

2. Post-hoc analysis showed results were also positive at the other time points listed for 25mg dose, however, the nonsignificant finding for the comparison between the 10mg group and the 1mg group terminated significance testing based on the prespecified hierarchical test procedure for all subsequent key secondary efficacy end points.

# COMPASS Pathways is currently conducting a Phase 3 pivotal program, with topline data expected in summer-2024 and mid-2025

## Pivotal Phase 3 Trial Designs



Source: Compass Pathways Capital Markets Day presentation as of May 11<sup>th</sup>, 2023

1. Primary endpoint = Change from baseline in MADRS total score at week 6

2. The participant population (TRD definition and core inclusion / exclusion criteria) remains unchanged compared to Phase 2b



# ELE-101

(psilocin)  
for MDD

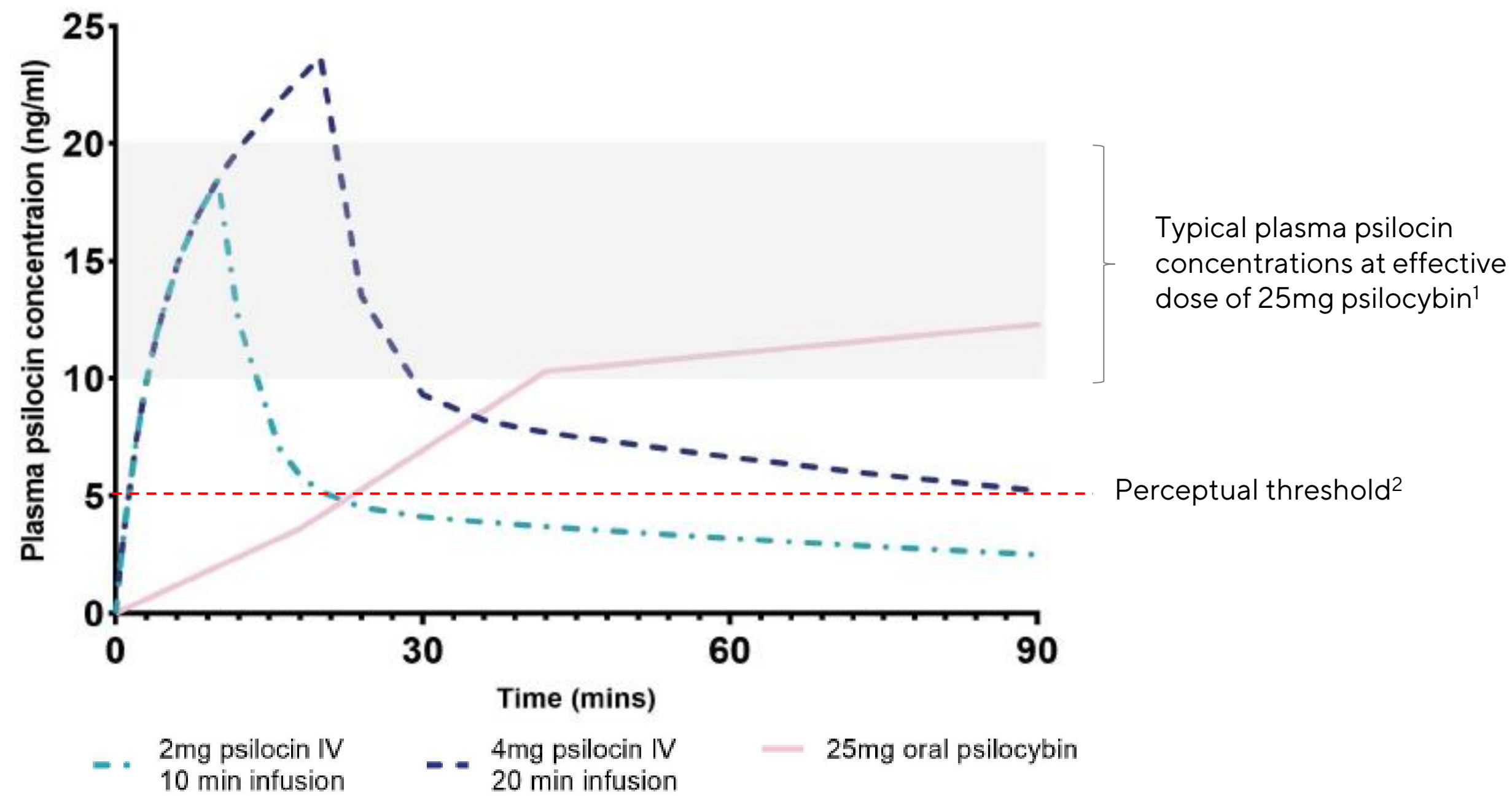
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## ELE-01: IV Psilocin

# Potential benefits of psilocybin's active moiety in an optimized delivery and treatment model

Psilocin pharmacokinetics for  
IV psilocin (simulated) vs. oral psilocybin<sup>1</sup>



## Expected benefits of IV psilocin vs oral psilocybin:

- » Reduced variability
- » Shorter-half life = shorter duration of psychedelic effect, anticipated to be <2 hours

<sup>1</sup> Psilocin simulations based on primary data from Brown et al. 2017, Madsen et al. 2019, Hasler et al. 1997, and Carhart-Harris et al. 2011.

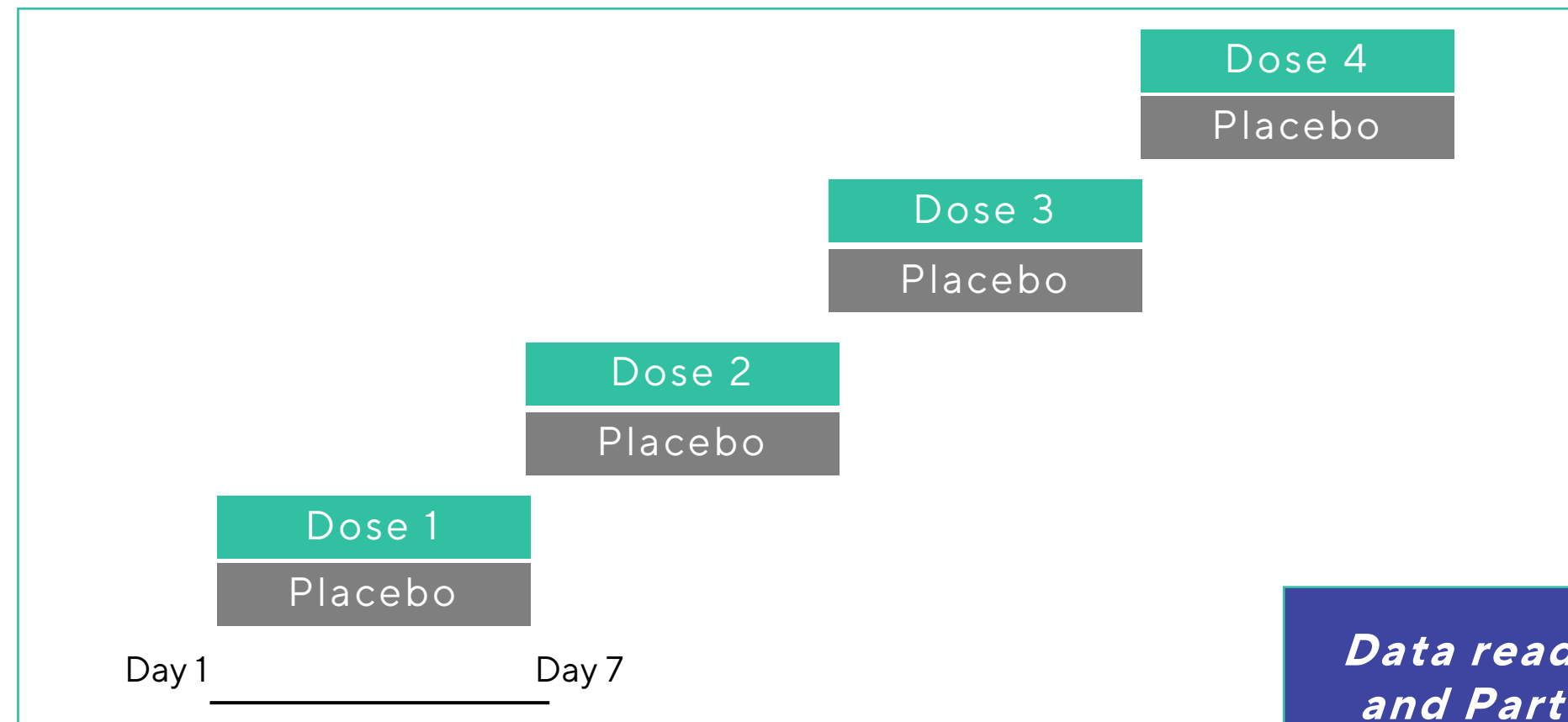
<sup>2</sup> Holze F. et al (2023). Pharmacokinetics and Pharmacodynamics of Oral Psilocybin Administration in Healthy Participants. Clin Pharmacol Ther.

## ELE-101 Phase 1/2a Clinical Trial Design

# Randomized, Phase 1 dose-escalation study in healthy volunteers followed by Phase 2a open-label study in MDD

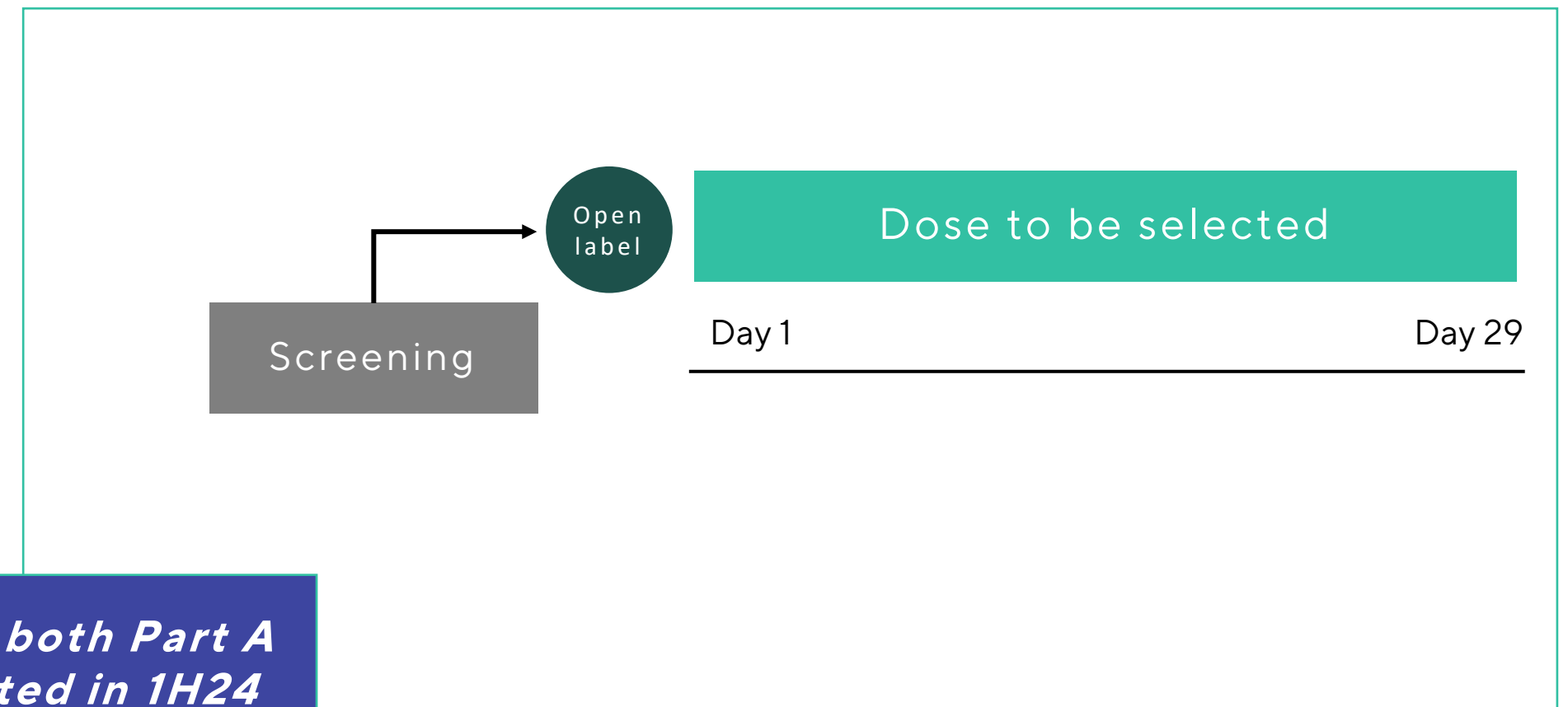
### ELE-101 Phase 1/2a – Part A

Single Ascending Dose



### ELE-101 Phase 1/2a – Part B

Open-label MDD cohort



#### Key Objectives:

- » Safety and tolerability
- » Assessment of PK & PD
  - » Target concentration of psilocin in <2 minutes
  - » Consistency of subjective intensity

#### Key Objectives:

- » Safety and tolerability of ELE-101 in patients with moderate to severe MDD
- » Key Secondary Endpoints:
  - » Assessment of MADRS change (Day 2, 4, 6, 15, 29)
  - » CGI-S, PGIC

# DMX-1002

(ibogaine) for  
Substance Use  
Disorder

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# Product Overview: DMX-1002 for Opioid Use Disorder

*Designed to have a rapid, sustained reduction in depressive symptoms through psychedelic effects*

PRODUCT	DMX-1002 is an oral formulation of ibogaine, which is an indole alkaloid with potential for clinical benefit through oneirophrenic effects
INDICATIONS	<i>Lead:</i> Opioid Use Disorder ("OUD") <i>Potential expansions:</i> Add'l Substance Use Disorders, PTSD, TBI <sup>1</sup>
INTELLECTUAL PROPERTY	Issued and pending method of treatment claims for OUD
CURRENT STATUS	Phase 1 results reported in Q3'23 Expect to submit FDA meeting request in 1H'24

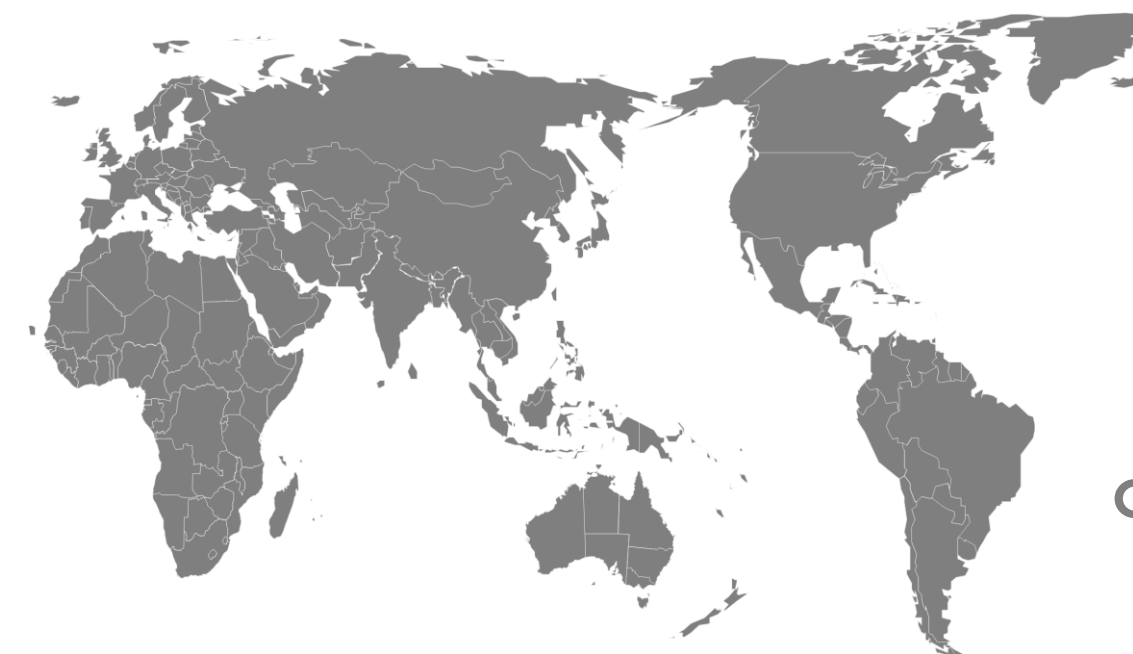
## DMX-1002 Key Product Features

- A single dose of ibogaine delivered in a monitored setting may support withdrawal and long-term relapse prevention in Opioid Use Disorder patients
- *Prior clinical evidence:*
  - In third-party open label studies, ibogaine was associated with significantly reduced opioid cravings, both at discharge and at one month post treatment, as well as improved mood in patients with OUD
  - In addition, a double-blind, placebo-controlled study in subjects with cocaine use disorder demonstrated a statistically significant benefit on urine confirmed relapse of a single administration of ibogaine compared to placebo

## Lead indication overview

- Substance use disorders are highly prevalent and characterized by an inability to control the use of a legal or illegal drugs, such as opioids (including prescription opioids) or alcohol.
- Current standard of care for OUD primarily consists of psychosocial support and synthetic full and partial opioid receptor agonists (methadone & buprenorphine), where approximately 30% of patients achieve treatment success (defined as >80% illicit opioid free weeks). In addition, long-acting opioid antagonists (naltrexone) lead to a proportion of patients achieving treatment success.

## Global disease burden



~3m

US OUD Incidence in 2020<sup>2</sup>

>100k

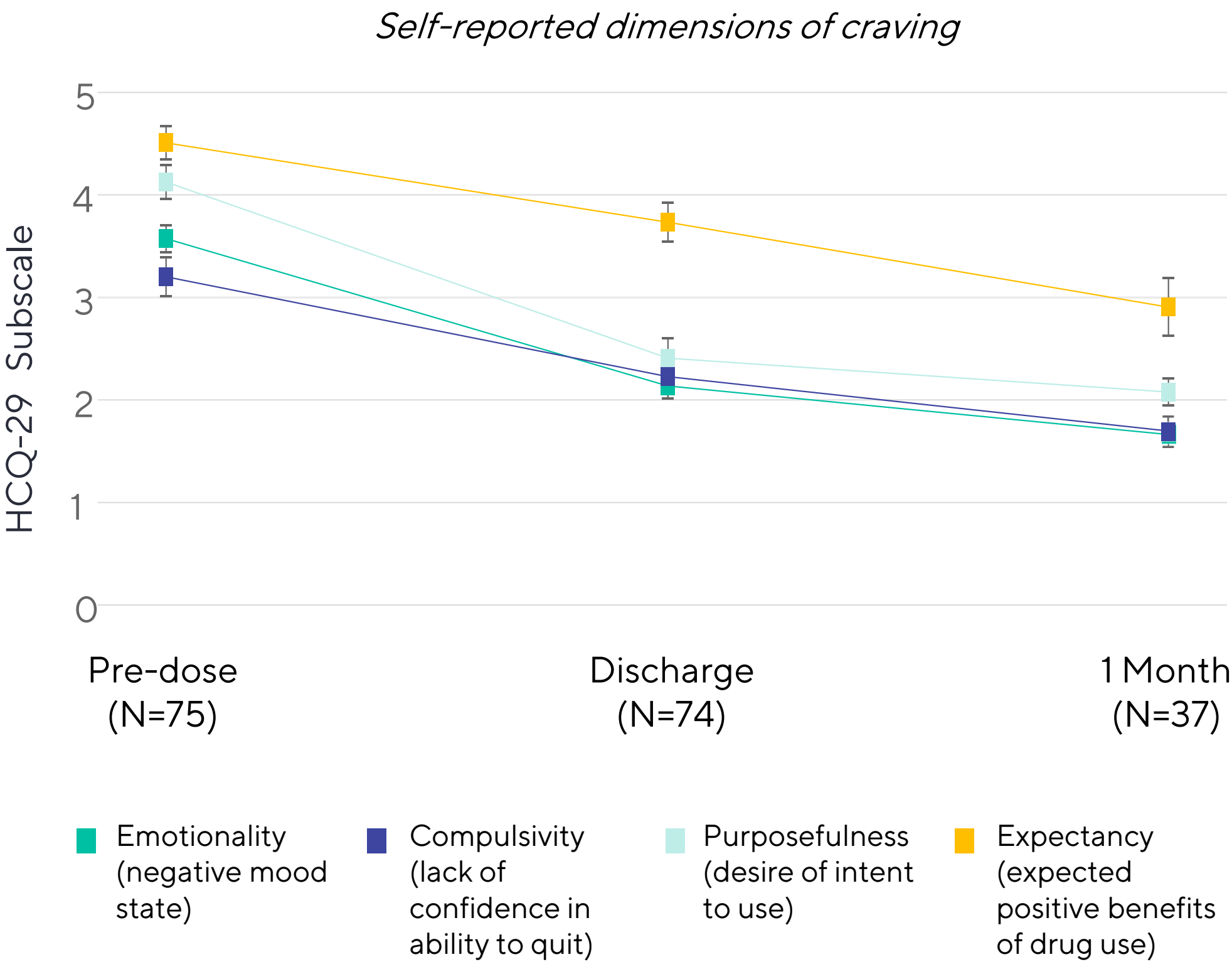
Opioid-related deaths in US in 2022

1. Post traumatic stress disorder and traumatic brain injury, respectively  
 2. World Health Organization  
 3. Salzer, "National Estimates of Recovery-Remission From Serious Mental Illness", Psychiatry Online (2018)

# Clinical Evidence: Efficacy of ibogaine in Open-Label Safety and Efficacy Study<sup>22</sup>

Results from an open-label study of 8-12 mg/kg of ibogaine in patients seeking detoxification from opioids and cocaine

## PRIOR CLINICAL EVIDENCE (THIRD PARTY STUDY<sup>1</sup>)



## Key Takeaways

1

**Summary:** A single-dose of ibogaine showed reductions in self-reported opioid cravings in 74 opioid dependent patients.

2

**Efficacy – Relapse Prevention (shown left):** Opioid dependent patients had significant reductions in the mean scores of four HCQ-29 domains of craving measured at program discharge and out to 1 month for patients continuing through study completion. Cravings are an important mediator of relapse.

3

**Efficacy – Post-Acute Withdrawal Syndrome:** signs and symptoms at post dose assessments were reduced compared to pre-dose baseline withdrawal severity measures. Objective signs of opioid withdrawal were mild and none were exacerbated at later time points.

4

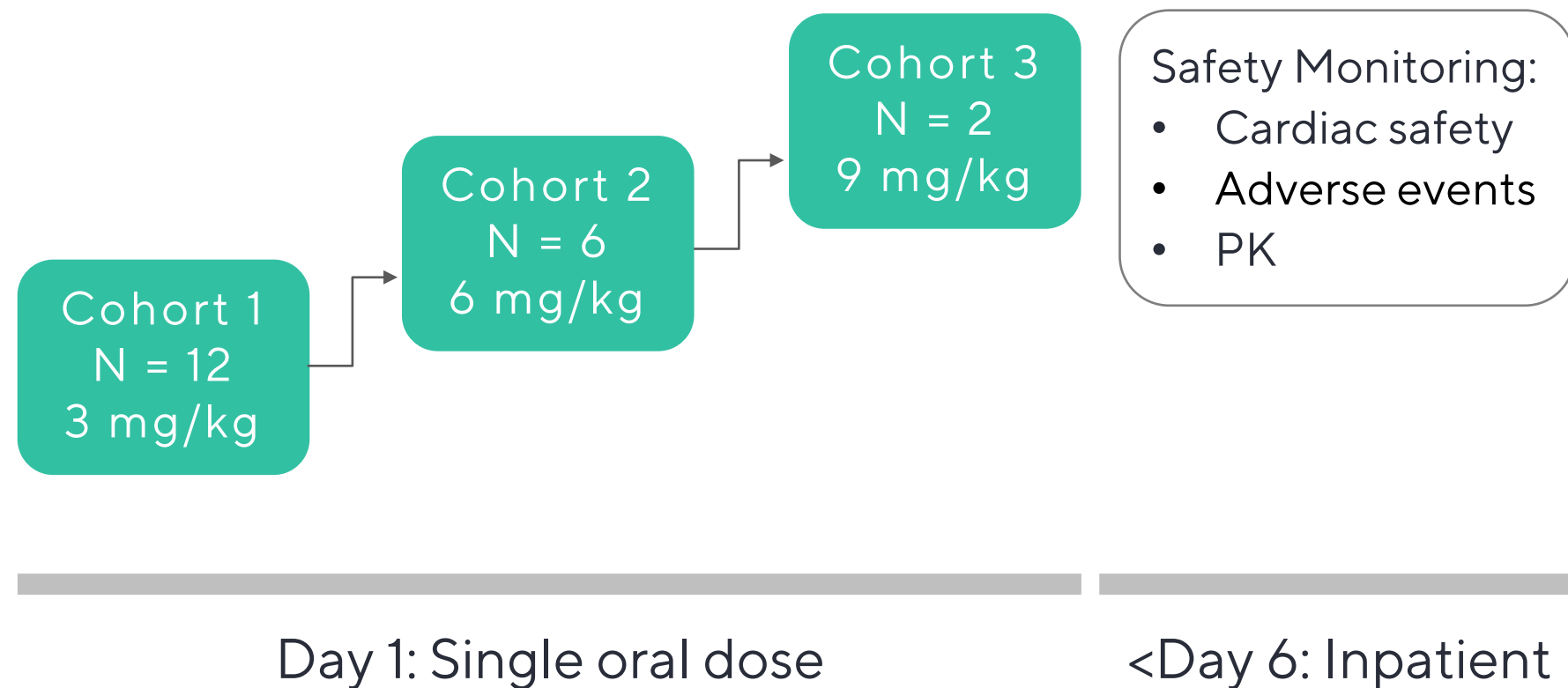
**Safety:** Ibogaine was reported to be well tolerated with no serious adverse events.

Note: TRD = Treatment Resistant Depression; DMT = N,N-Dimethyltryptamine  
1 Mash et al., "Ibogaine Detoxification Transitions Opioid and Cocaine Abusers Between Dependence and Abstinence: Clinical Observations and Treatment Outcomes" (2018)

# Phase 1 Study: DMX-1002 Trial Design & Results Summary

*Demonstrated safety level and plasma concentrations of DMX-1002 in line with previous trials*

## COMPLETED PHASE 1 TRIAL: SINGLE ASCENDING DOSE



**Population:** Healthy male participants

**Design:** Single-blinded, cross-over study. All participants received placebo first, followed by DMX-1002 at a second visit

## SUMMARY OF PHASE 1 RESULTS

### Potential therapeutic plasma levels

- DMX-1002's 9 mg/kg achieved plasma concentrations in line with those described in previous studies where therapeutic effects were observed

### No serious adverse events reported

- Nearly all adverse events were mild-to-moderate (>94%), consistent with prior trials of ibogaine

### Asymptomatic QTc Prolongation

- One of two participants in cohort 3, asymptomatic QTc prolongation was observed, with no cardiac arrhythmias. The QTcF change of 90-94ms resolved without intervention or sequelae

SUMMARY

DMX-1002 could potentially become a paradigm-shifting therapy for Opioid Use Disorder (OUD)

Current standard of care for OUD is medication therapy, requiring opioid substitutes that carry significant side effects

Current strategies for withdrawal support have high rates of relapse

DMX-1002 has the potential to become the first & best in-class treatment for OUD, minimizing risk of relapse

	Therapy	Mechanism of Action	Single Therapeutic Episode	No Opioid Side Effects	Minimal Abuse Potential	High Adherence / Low Risk of Relapse
<b>Sustained relapse prevention</b> Single dose administered in monitored setting, providing both withdrawal support and oneiric experience driving sustained remission	Ibogaine (DMX-1002) <b>DemeRx</b>	Cholinergic, glutamatergic and monoaminergic receptor modulator	✓	✓	✓	✓
<b>Medication Assisted Therapy<sup>1</sup></b> Daily therapy given in substitution of opioid in outpatient setting in attempt to wean off from opioid	Methadone	Mu-agonist				✓
	Buprenorphine	Partial Mu-agonist				✓
	Naltrexone	Mu-antagonist		✓	✓	
<b>Withdrawal Support<sup>2</sup></b> Therapies given for symptomatic management during supervised withdrawal (detoxification)	Clonidine	Alpha-2 agonist	✓	✓	✓	
	Lofexidine	Alpha-2 agonist	✓	✓	✓	

Note: OUD = Opioid Use Disorder  
Source: Publicly available information, including company websites and clinicaltrials.gov, GlobalData, Evaluate Pharma (both as of 2022)  
1. Current Standard of Care  
2. Rarely used given high rates of relapse. Used primarily in institutional or penitentiary settings



# RL-007 for Cognitive Impairment

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# Product Overview: RL-007 for Cognitive Impairment

*Demonstrated consistent pro-cognitive effects in prior clinical trials, with a favorable safety profile in >500 subjects*

PRODUCT	Oral, pro-cognitive neuromodulator
INDICATIONS	<i>Lead:</i> Cognitive impairment associated with schizophrenia <i>Potential expansions:</i> Cognitive disorders including Alzheimer's dementia and/or Autism
INTELLECTUAL PROPERTY	Issued composition of matter, formulation and method of use IP
CURRENT STATUS	Phase 2a CIAS trial completed in H2'21 Phase 2b first patient dosed in 1Q'23 Phase 2b data expected in mid'25

## RL-007 Key Potential Product Features

- Pro-cognitive effects demonstrated across four prior clinical studies, including two Phase 1 and two Phase 2 trials
- Consistent “inverted-U” dose response across clinical & preclinical studies
- Demonstrated safety & tolerability with no evidence of sedative side effects across the 10 clinical studies in >500 subjects

## Lead indication overview

- Cognitive impairment associated with schizophrenia (CIAS) is characterized by attention, learning, memory, and exec function deficits
- Such deficits result in cognitive function around 2.5 standard deviations below the mean of the general population<sup>4</sup>
- CIAS is a common and major cause of disability in schizophrenia, with more than 80% of patients showing significant impairment<sup>2</sup>
- **No FDA approved treatments<sup>3</sup>**

## Global disease burden



~24m

Global sufferers of Schizophrenia<sup>1</sup>

>80%

Patients with Schizophrenia experiencing significant cognitive impairment<sup>2</sup>

1. World Health Organization  
 2. Bora et al, Cognitive Impairment in Schizophrenia and Affective Psychoses: Implications for DSM-V Criteria and Beyond  
 3. GlobalData (as of 6/1/2023)  
 4. Schaffer et al., 2013

# Clinical Evidence: Efficacy on Cognitive Endpoints in a Phase 2 Study

27

*Third-Party Phase 2 study in DPNP showed statistically significant positive cognitive signals (exploratory endpoints)*

## Background

- Phase II, randomized, placebo-controlled, crossover clinical study in subjects with diabetic peripheral neuropathic pain (DPNP) that assessed improvements in verbal learning and memory as an exploratory endpoint
- 4-week placebo periods were compared to 4-week RL-007 periods
  - “Intermediate-dose escalation” RL-007 40mg (first week) to 80mg (n=60)
  - “High-dose escalation” RL-007 150mg (first week) to 300mg (n=60)

## Key Takeaways

1

RL-007 showed statistically significant pro-cognitive effects on learning and memory within the “Intermediate-Dose escalation” 40mg to 80mg arm.

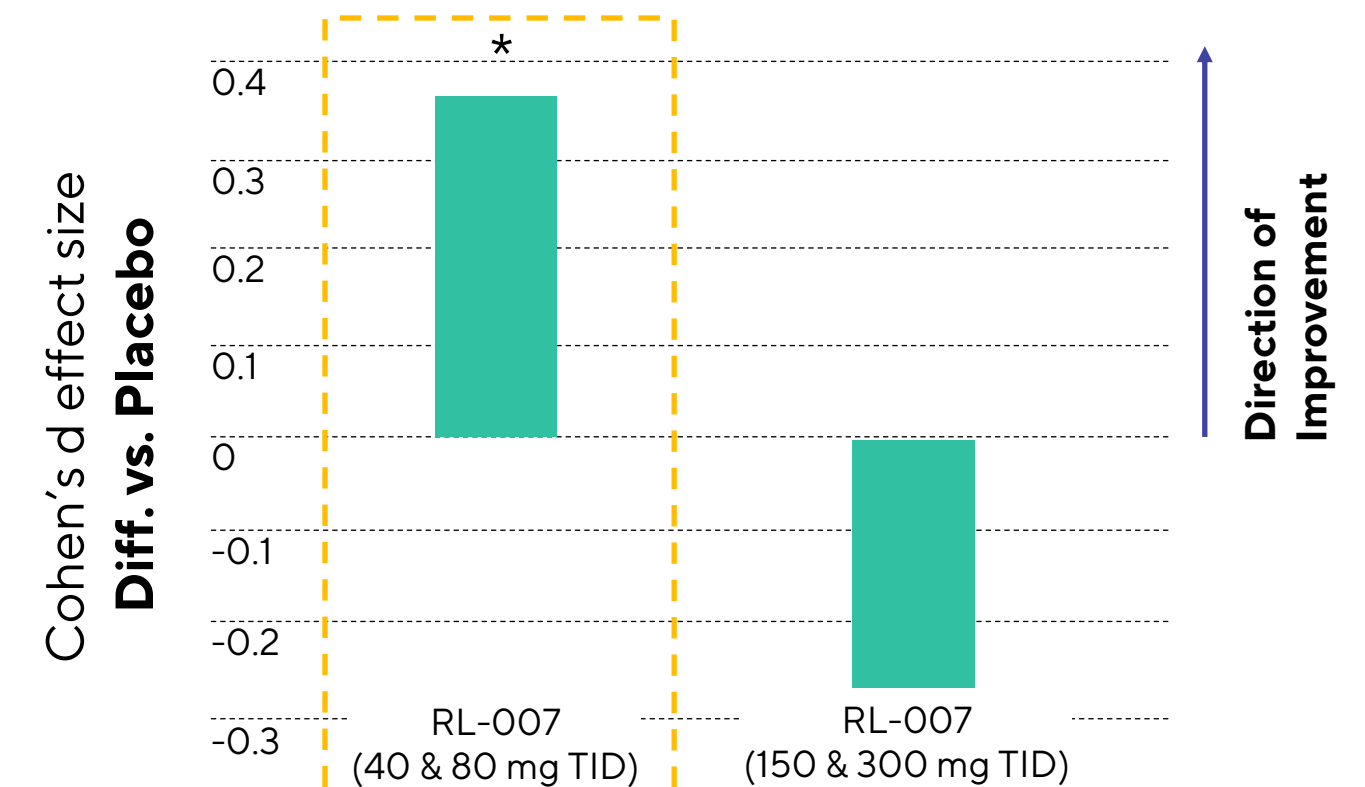
2

The 40 to 80mg arm patients also reported a statistically significant improvement on the Cognitive and Physical Function Questionnaire (p = 0.021)

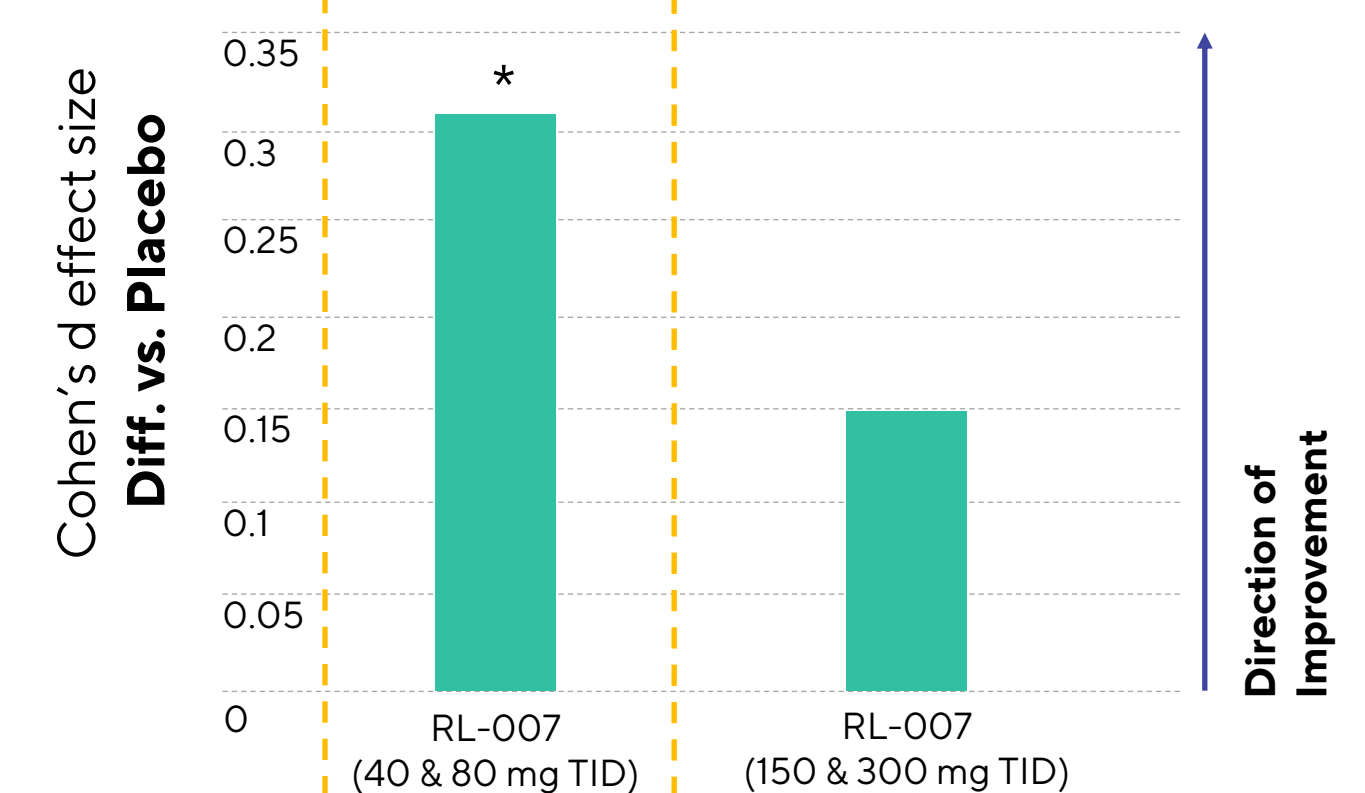
3

Inverted U-shaped dose response whereby intermediate doses yield greater clinical activity is replicated and consistent with from prior clinical and preclinical studies

## Delayed recall



## Verbal learning





# Clinical Evidence: Efficacy Signals Reproduced in Phase 2a Study in CIAS

*atai's Phase 2a study in CIAS demonstrated positive cognitive signals on a subset of MCCB neurocognitive endpoints*

## Background

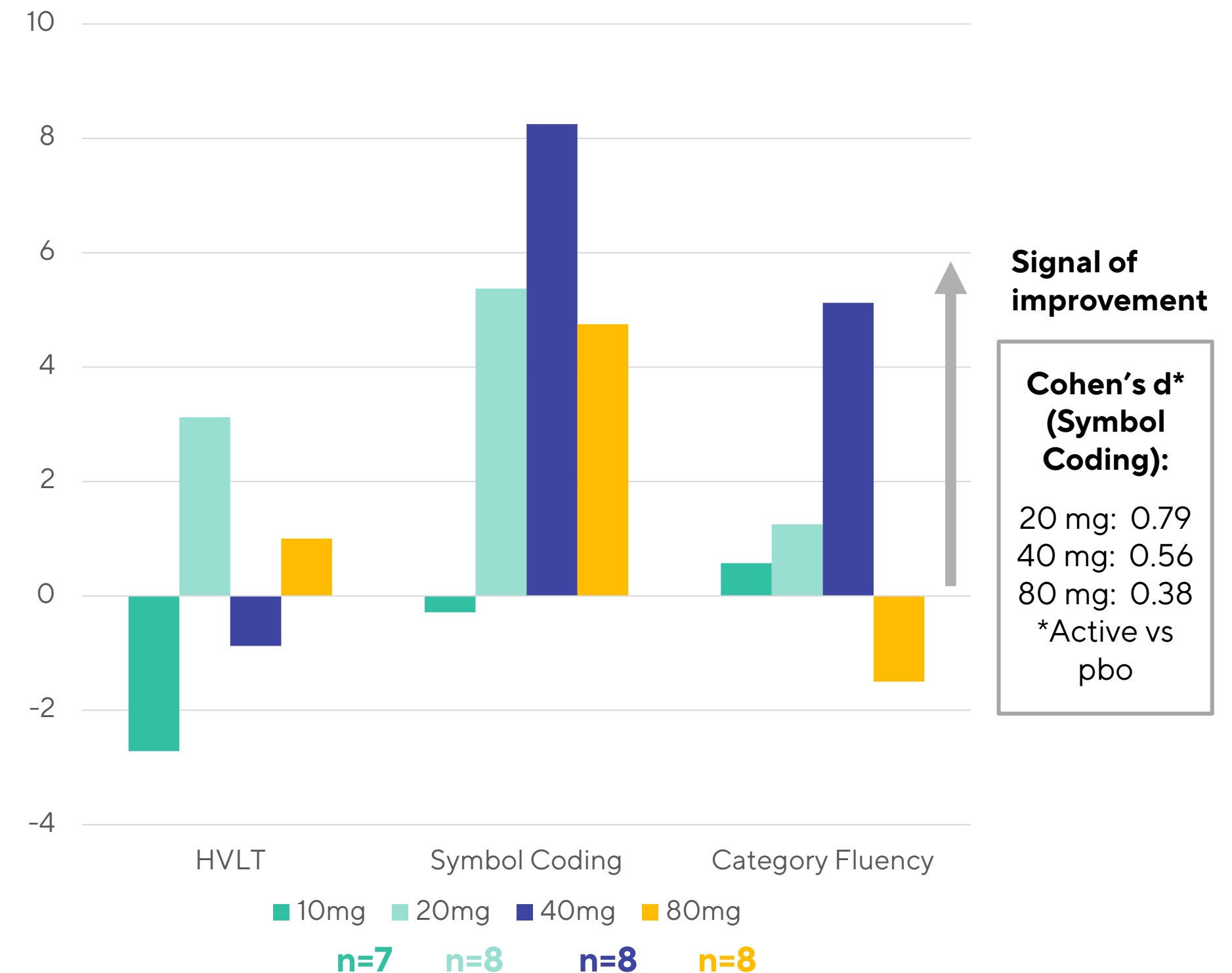
- Cognitive function was assessed in 31 patients with CIAS across four RL-007 cohorts (10, 20, 40 & 80mg). Patients received four doses of placebo followed by six doses of RL-007 over 4-days. Day 2 "pre-RL-007" was compared to Day 4 "post-RL-007".
- The primary objectives of the single-blinded study was to confirm safety on-top of SOC and to identify signals of cognitive benefit in patients with CIAS, including on three MCCB sub-component neurocognitive tests, HVLT<sup>1</sup>, BACS Symbol Coding & Category Fluency

## Key Takeaways

- Study demonstrated dose-related trends for improvements on each MCCB neurocognitive endpoints, including a Cohen's d effect size of 0.79, 0.56 and 0.38 at the 20mg, 40mg, and 80mg, respectively, on the BACS Symbol Coding test.
- Importantly, Symbol Coding is the most sensitive subcomponent and correlates with overall performance on the MCCB neurocognitive composite, the latter being a registrational endpoint and the primary endpoint for the on-going Phase 2b study of RL-007.
- In addition, qEEG data was consistent with the prior clinical evidence and demonstrated increases in amplitude in the alpha band and in the alpha-slow wave index, markers of alertness believed to correlate with aspects of cognition.

## PHASE 2a TRIAL - EFFICACY DATA ON COMPONENTS MCCB COMPOSITE

**T-Scores** (Normalized for age, gender, and education level)

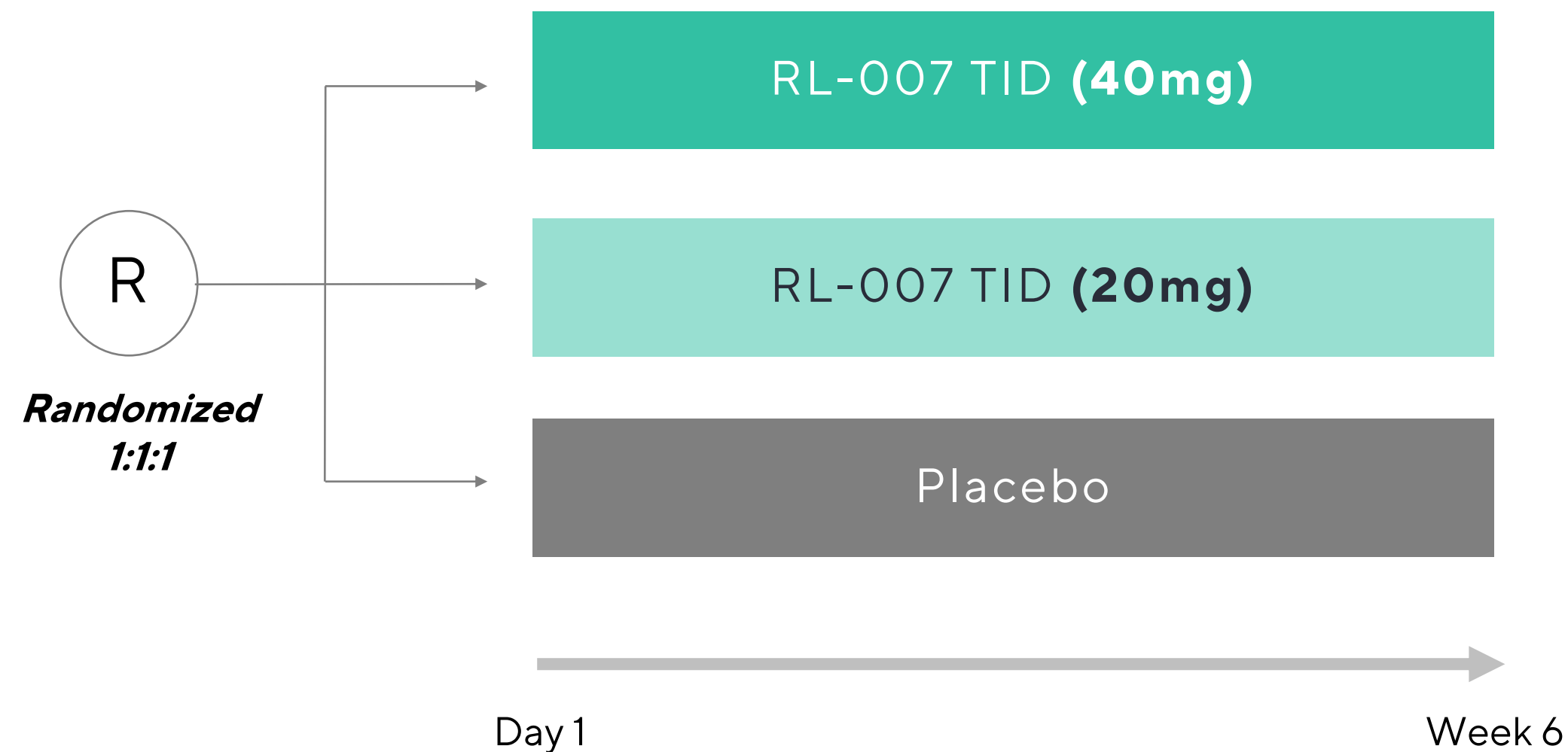


1. Hopkins Verbal Learning Test



# Clinical Trial Design: RL-007 Phase 2b Study

*Randomized, placebo-controlled study of RL-007 in ~234 patients with CIAS*



## **Primary Endpoint:**

- MCCB neurocognitive composite score at Week 6

## **Key Secondary Endpoints:**

- Select Individual Components of MCCB, including BACS Symbol Coding
- Clinical Global Impression Score

**Trial status:** First patient dosed in 1Q'23,  
Topline data anticipated mid'25

# GRX-917 for Anxiety Disorders

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# Product Overview: GRX-917 for Anxiety Disorders

*Designed to have rapid onset of anxiolytic activity but without the negative side effects seen with benzodiazepines*

PRODUCT	Deuterated etifoxine HCl oral dosage form (GRX-917)
INDICATIONS	Lead: Anxiety Disorders (e.g., GAD, SAD, PTSD, etc.)
INTELLECTUAL PROPERTY	Issued composition of matter on deuterated etifoxine (GRX-917) and corresponding methods of use
CURRENT STATUS	Phase 1 trial completed in H2'22 Exploring partnership and external funding opportunities

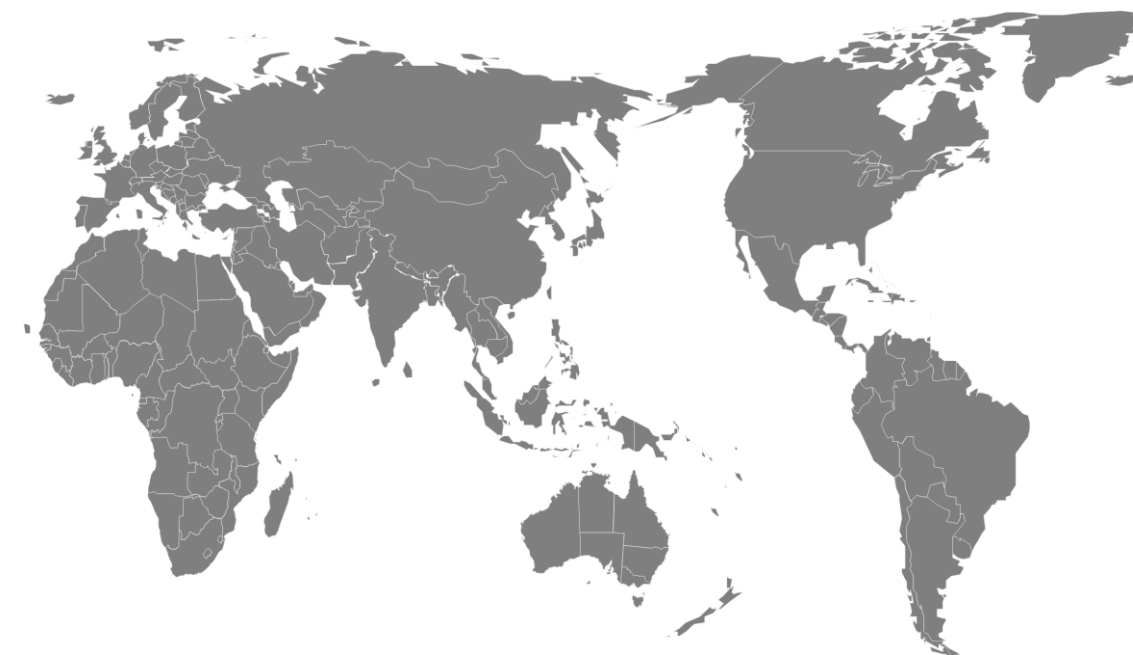
## GRX-917 Key Product Features

- Demonstrated rapid onset activity of anxiolytic activity (non-deuterated etifoxine approved in France)
- Review of ~14m prescriptions in France underscores the strong safety track record for etifoxine
- Differentiated tolerability profile, with limited sedative, addictive and/or cognitive impairing properties, unlike benzodiazepines

## Lead indication overview

- Anxiety disorders develop when feelings of apprehension and unease persist over an extended period and potentially worsen over time
- 50% of US patients go untreated as a result of sub-optimal treatment options<sup>2</sup>
- **No** FDA approved novel treatments over the past decade<sup>3</sup>

## Global disease burden



**~300m**

Anxiety disorder sufferers in 2019<sup>1</sup>

**#1**

Most common mental health disorder<sup>1</sup>

1. World Health Organization

2. Anxiety and Depression Association of America (2021)

3. GlobalData (as of 6/1/2023) - All recent approvals by the FDA have been reformulations of long-standing antidepressant and benzodiazepine options

# Phase 1 Study: GRX-917 Trial Design & Results Summary

*Demonstrated a rapid and dose-dependent PK/PD effect along with a favourable safety profile*

## COMPLETED PHASE 1 TRIAL

### Part 1: Single Ascending Dose

TREATMENT	SAFETY/PK/PD
<b>42 healthy subjects:</b> 5 cohorts 25mg to 500mg	<b>PD Endpoint:</b> qEEG

### Part 2: Multiple Ascending Dose

TREATMENT	SAFETY/PK/PD
<b>60 healthy subjects:</b> 5 cohorts 100mg to 300mg BID	<b>PD Endpoint:</b> qEEG

## SUMMARY OF PHASE 1 RESULTS

### Target engagement demonstrated

- Dose-dependent increases in qEEG beta power

### Safe & well-tolerated

- Well-tolerated with no dose limiting toxicities, with adverse effects comparable to that of placebo

### Sedation comparable to placebo

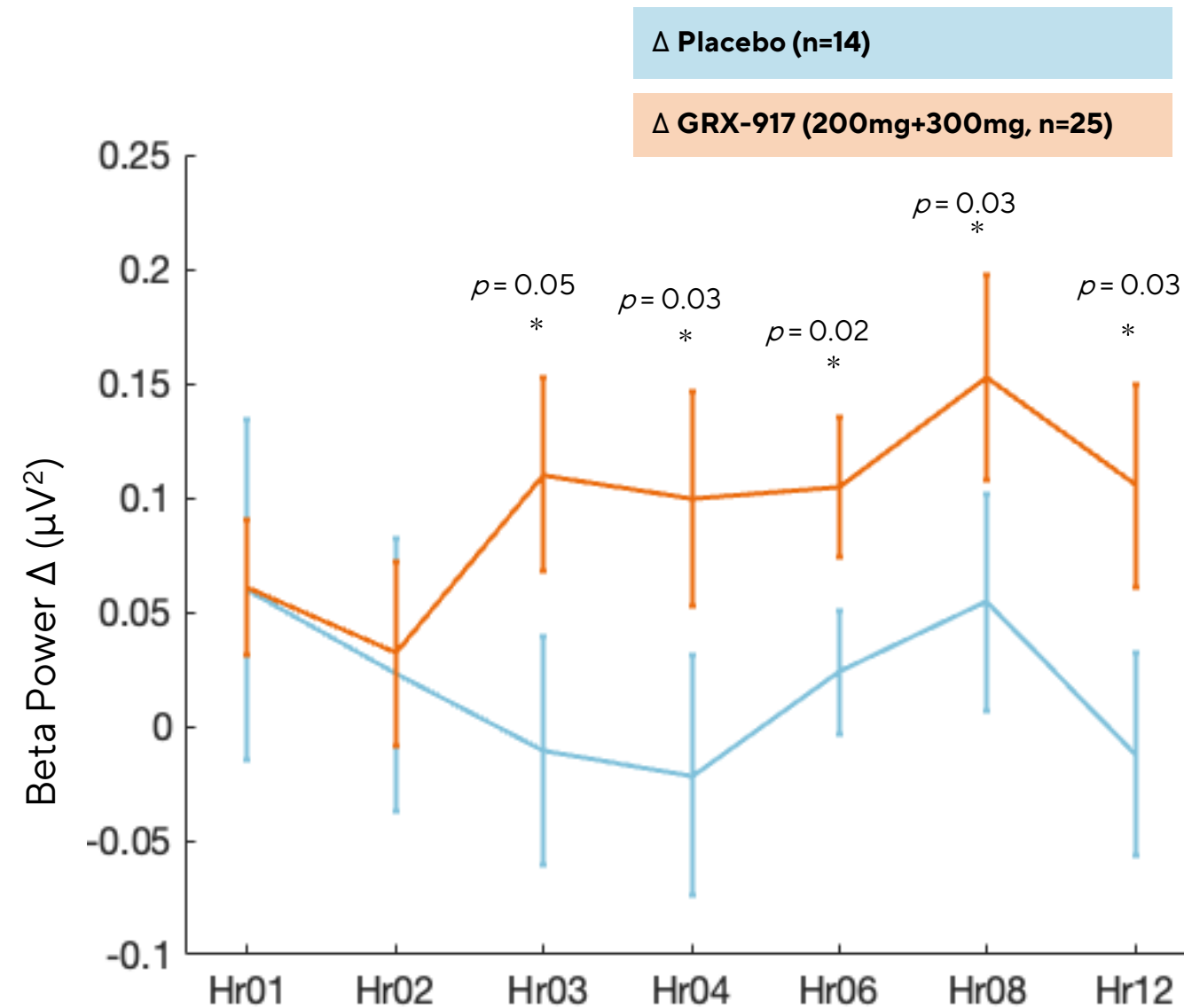
- Sedation in-line with placebo, which was consistent with EEG results and which did not show decreases in qEEG alpha power



# Phase 1 Study: GRX-917 Pharmacodynamic Evidence of Target Engagement

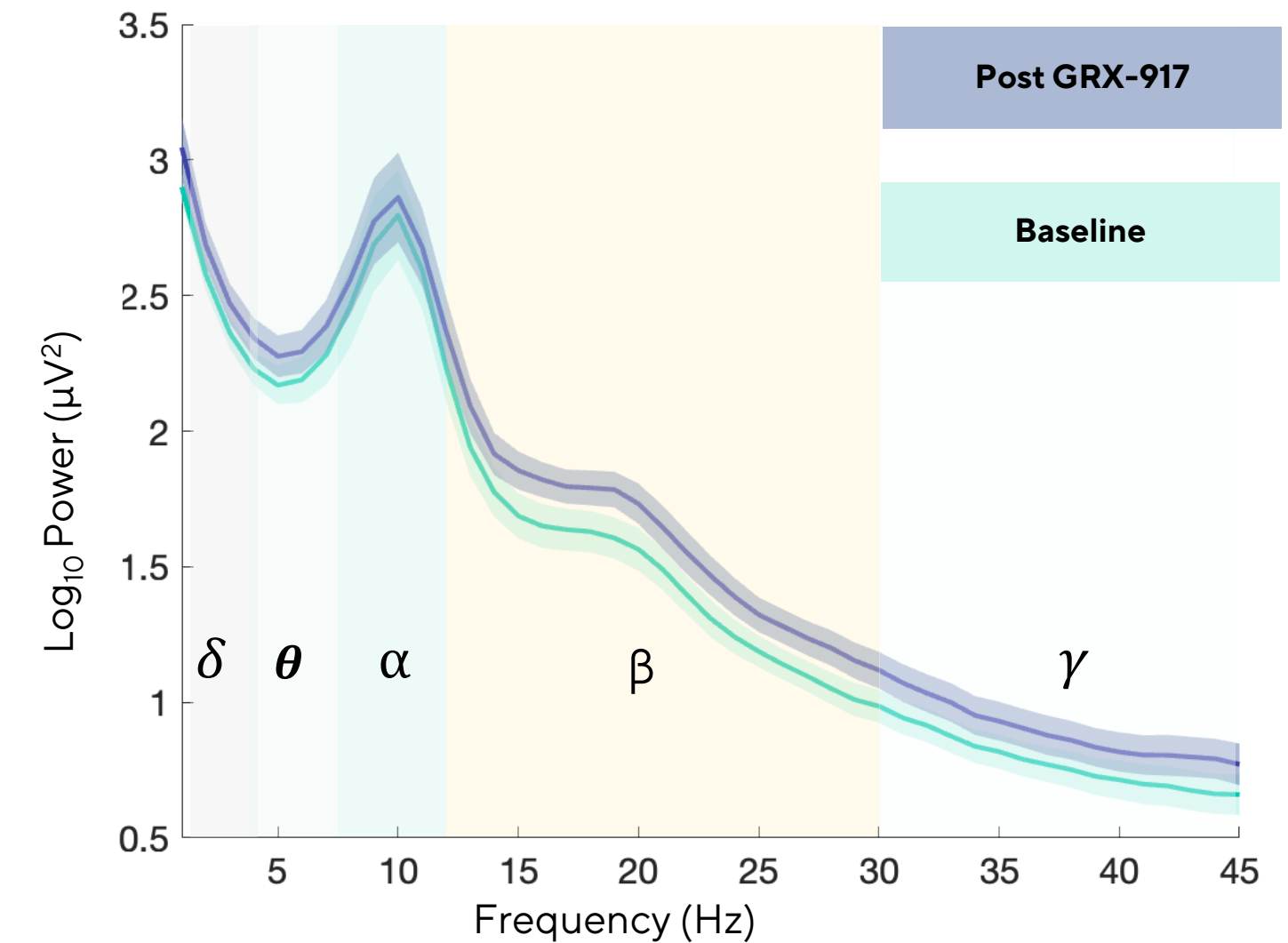
*Beta power increase is in line with pharmacodynamic efficacy of exogenous neurosteroids and benzodiazepines*

## Beta Power Increase



**Sensitivity Analysis:** Line plot showing Beta power  $\Delta$  (mean $\pm$ SEM) at each hour for placebo and GRX-917 (combined 200mg and 300mg cohorts).

## Beta Power Increase + No Alpha Decrease



**Calculation of Difference Wave:** Difference Waves ( $\Delta$  = post minus pre) were compared between GRX-917 and Placebo at each hour and frequency of interest.

**Beta power increase indicates potential for anxiolytic activity, while absence of Alpha power reduction suggests basis for less sedation than with benzodiazepines**





Nasdaq: ATAI

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