atai
LIFE SCIENCES

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

**Company Overview – January 2023**

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Note: Unless otherwise stated, this presentation is as of January 6th, 2023

# 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, most recently exacerbated by COVID-19; global market size in mental health was $380Bn in 2020 and is expected to grow to $540Bn by 2030[1]

2. atai's objective is to achieve clinically meaningful and sustained behavioral change in mental health patients by developing rapid-acting and patient-centric pharmaceutical and digital treatment solutions

3. atai has 8 clinical stage drug development programs with a focus on compound classes with prior evidence in humans; portfolio approach to avoid binary risk and to optimize likelihood of success

4. Validation of atai's 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. Strong cash position of approx. $304M (as of September 30th, 2022) and access to up to an additional $160m from term loan facility with Hercules[2] lead to anticipated cash runway into 2025

1. THE COVID STATES PROJECT report (May 21, 2021) and https://www.alliedmarketresearch.com/mental-health-market-A11770
2. Total facility size is up to $175M, with $15M drawn to-date (in Q3 2022)

Note: Unless otherwise stated, this presentation is updated as of January 6th, 2023

# Achieving sustained behavioural change in patients through the combination of rapid acting intervention, psychological support and precision mental health

Our Objective

**Achieve clinically meaningful and sustained behavioural change in patients diagnosed with mental health disorders**

Key Strategic Pillars

| Rapid acting intervention (Focus: Rx) | + | Ongoing psychological support (Focus: DTx) | + | Precision mental health (Focus: Biomarkers) |
|---|---|---|---|---|
| 1st, 2nd and 3rd generation compounds with the potential to show strong behavioural plasticity, rapid onset and more durable effect | | Additional ongoing psychological care provided to patients before, during and/or after initial treatment interventions | | The identification of patient sub-types using biological and digital biomarkers |

Note: Rx = Prescription Therapeutics; DTx = Digital Therapeutics

# Our strategy will be delivered through a robust pipeline of drug development programs across several mental health indications with large unmet need

| Program | Indication | Preclinical | Phase 1 | Phase 2 | Phase 3 | Affiliate Company[1] |
|---|---|---|---|---|---|---|
| RL-007 / Compound[2] | Cognitive Impairment Associated With Schizophrenia | | | | | Recognify Life Sciences |
| PCN-101 / R-ketamine | Treatment-Resistant Depression | | | | | Perception Neuroscience |
| GRX-917 / Deuterated etifoxine | Generalized Anxiety Disorder | | | | | GABA Therapeutics |
| KUR-101 / Deuterated mitragynine | Opioid Use Disorder | | | | | Kures |
| VLS-01 / DMT | Treatment-Resistant Depression | | | | | Viridia Life Sciences |
| DMX-1002 / Ibogaine | Opioid Use Disorder | | | | | DemeRx IB |
| EMP-01 / MDMA derivative | Post-Traumatic Stress Disorder | | | | | EmpathBio |
| **LIMITED TO EQUITY INTEREST** | | | | | | |
| COMP360 / Psilocybin[3] | Treatment-Resistant Depression | | | | | COMPASS Pathways |
| COMP360 / Psilocybin[3] | Post-Traumatic Stress Disorder | | | | | COMPASS Pathways |
| COMP360 / Psilocybin[3] | Anorexia Nervosa | | | | | COMPASS Pathways |

Note: Information as of November, 2022, unless otherwise stated. DMT = N,N-dimethyltryptamine; MDMA = 3,4-Methylenedioxymethamphetamine

1. Perception, Recognify, DemeRx IB, and Kures are all variable interest entities; GABA is a non-consolidated VIE with operational involvement through Master Service Agreement (MSA) model; EmpathBio and Viridia are wholly-owned subsidiaries; COMPASS Pathways is a non-controlling equity interests
2. RL-007 compound is (2R, 3S)-2-amino-3-hydroxy-3-pyridin-4-yl-1-pyrrolidin-1-yl-propan-1-one(L)-(+) tartrate salts
3. Developing COMP360, a formulation of psilocybin, administered with psychological support from specially trained therapists

**Chart updated as of 1/6/2023**

# We expect to deliver several meaningful R&D milestones anticipated across our key programs through 2024[1] with cash runway into 2025

**Achieved and expected milestones**

**Key achievements to date**

- ✓ Initiation of 8 clinical programs
- ✓ COMP360 Phase 2b results
- ✓ RL-007 Phase 2a results
- ✓ GRX-917 Phase 1 results

**H1'23**

- VLS-01 Phase 1 results
- DMX-1002 Phase 1 results
- RL-007 Phase 2b first subject dosed
- GRX-917 Efficacy study first subject dosed

**H2'23**

- EMP-01 Phase 1 results
- COMP360 Phase 2 results (PTSD)
- COMP360 Phase 2 results (Anorexia)

**2024**

- RL-007 Phase 2b PoC results (H1)
- VLS-01 Phase 2a PoC results (H1)
- GRX-917 Efficacy study results

**$304M in cash as of September 30, 2022, plus access to up to an additional $160M from Hercules term loan facility[2], provides runway expected into 2025**

Note: PoC = Proof of Concept
1. Based on current expectations and projections as of the date of this presentation, and subject to change
2. Total facility size is up to $175M, with $15M drawn to-date (in Q3 2022)
Unless otherwise stated, this presentation is updated as of January 6th, 2023

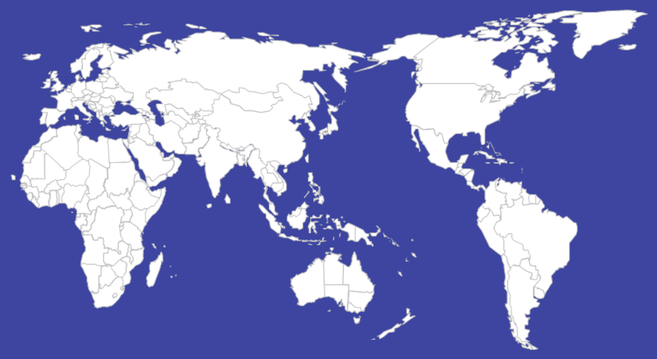
# Cognitive Impairment Associated with Schizophrenia

# CIAS & Schizophrenia

## Disease Overview

Cognitive impairment associated with Schizophrenia (CIAS) & Schizophrenia often lead to individuals making choices they feel are out of their control


## CIAS & Schizophrenia in numbers



**~24m**

**Global sufferers of Schizophrenia[1]**

**15th**

**Leading cause of disability worldwide (2016)[2]**

**~$155bn**

**U.S. economic burden from adults with CIAS or Schizophrenia (direct + indirect costs)[3]**

## HUGE NEED FOR DEVELOPMENT

**~20 yrs**

### Lost life expectancy[4]

Schizophrenia results in a life expectancy of approximately 20 years below that of the general population

**~30%**

### Low treatment rate[5]

Only ~30% of people with psychosis receive specialist mental health care

**~80%**

### Cognitive impairment is very common[6]

Cognitive impairment is a common and major cause of disability in schizophrenia, with more than 80% of patients showing significant impairment

**0**

### FDA approvals for CIAS

Currently there are no FDA approved treatments for CIAS[7]

1. World Health Organization
2. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016
3. Cloutier et al, The economic burden of schizophrenia in the United States in 2013. J Clin Psychiatry 2016;77(6):764-771
4. Bora et al, Cognitive Impairment in Schizophrenia and Affective Psychoses: Implications for DSM-V Criteria and Beyond
5. World Health Organization
6. Bora et al, Cognitive Impairment in Schizophrenia and Affective Psychoses: Implications for DSM-V Criteria and Beyond
7. GlobalData (as of 11/15/2022)

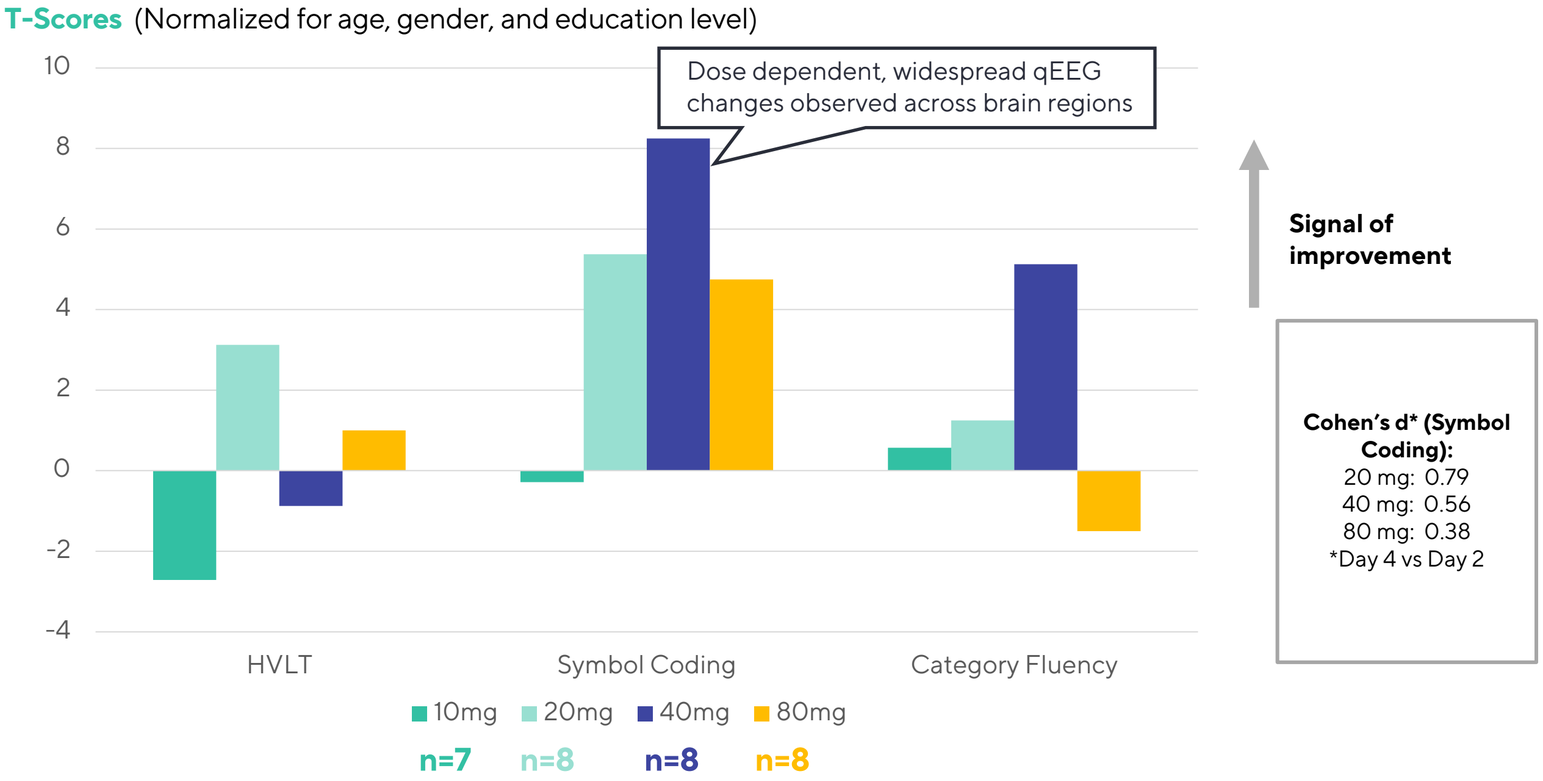
# SUMMARY

| | |
|---|---|
| OWNERSHIP | 51.9%[1] |
| PRODUCT | (2R, 3S)-2-amino-3-hydroxy-3-pyridin-4-yl-1-pyrrolidin-1-yl-propan-1-one(L)-(+) tartrate salt oral capsules (RL-007) |
| PHARMA-COLOGY | GABA/nicotinic modulator |
| PRODUCT FEATURES | Pro-cognitive effects demonstrated in two Phase 1 and two Phase 2 trials<br>No drug-related serious adverse events in over 500 study subject exposures |
| INDICATIONS | Primary: Cognitive Impairment Associated with Schizophrenia (CIAS)<br>Potential: Autism, Alzheimer's dementia |
| CURRENT STATUS | Phase 2a biomarker trial completed in H2'21<br>Phase 2b PoC results expected H1'24 |
| INTELLECTUAL PROPERTY | Issued composition of matter, formulation and method of use patents |
| HIGHLIGHT | Previous Phase 2 showed pro-cognitive potential of RL-007 in 180 patients with diabetic peripheral neuropathic pain |

# RL-007 has previously shown pro-cognitive effects in human clinical studies

***"Symbol coding response is at a level that would correlate with better work/school performance"***
***– Keith Nuechterlein, Ph.D. (Semel Institute for Neuroscience and Human Behavior)***

**PHASE 2 PoM TRIAL - EFFICACY DATA**



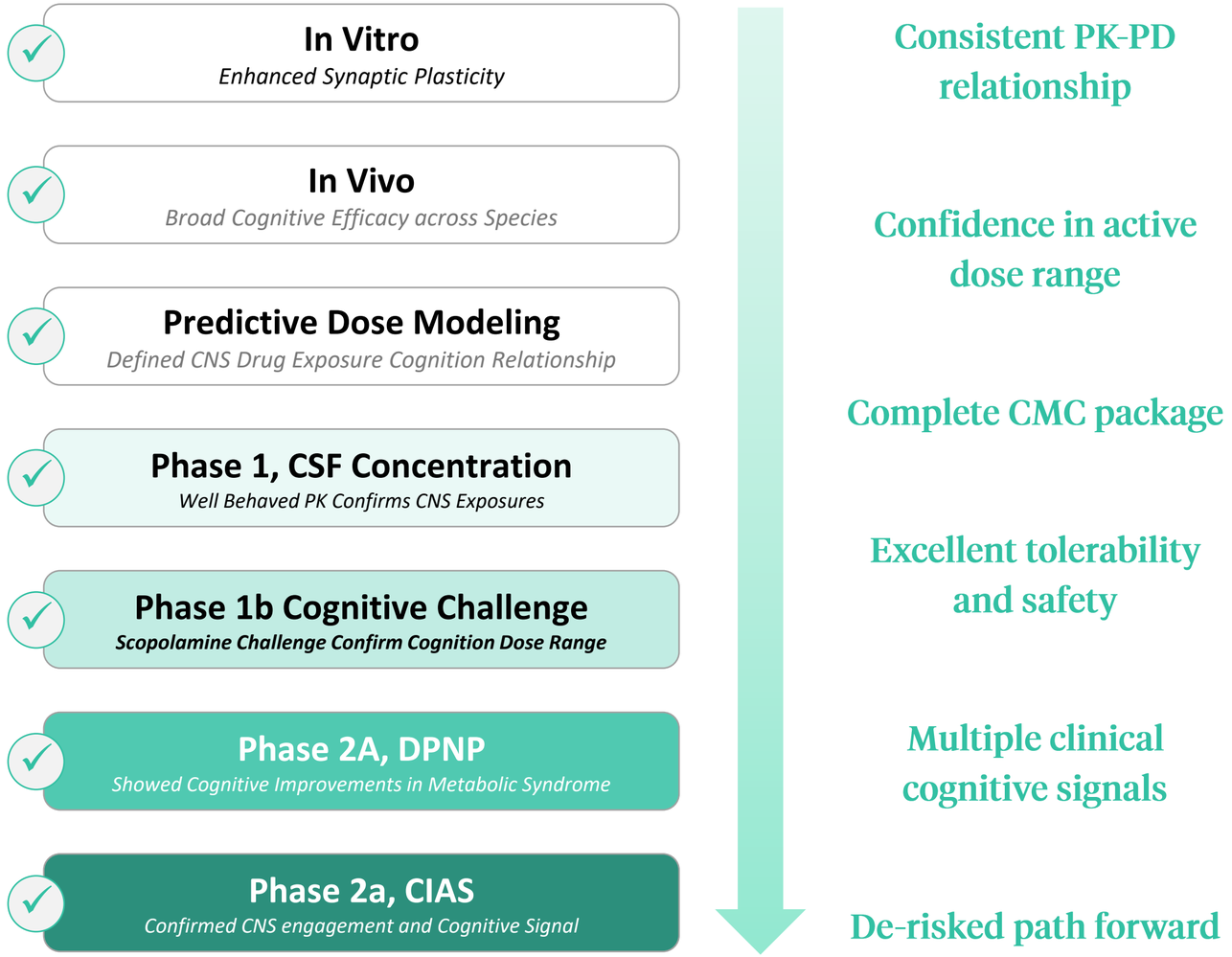

Note: CIAS = Cognitive impairment associated with schizophrenia; HVLT = Hopkins Verbal Learning Test; TID = 3x/day dosing; PoC = Proof of Concept, PoM = Proof of Mechanism

1. Unless otherwise indicated herein, ownership percentage based on ownership of securities with voting rights as of September 30th, 2022.

# RL-007: a de-risked pro-cognitive neuromodulator investigated in >500 subjects with excellent tolerability in humans

## RL-007: demonstrated pro-cognitive treatment for CIAS

1. Pharma developed product in-licensed with extensive pre-clinical & clinical data package
2. Human Phase 1 + 2 data show replicated, clinically significant learning and memory effects, consistent with broad pre-clinical pro-cognitive data
3. Well tolerated ( >500 subjects dosed), centrally acting oral drug
4. Initial indication: cognitive impairment associated with schizophrenia (CIAS) is characterized by episodic learning & memory deficits – no approved treatment

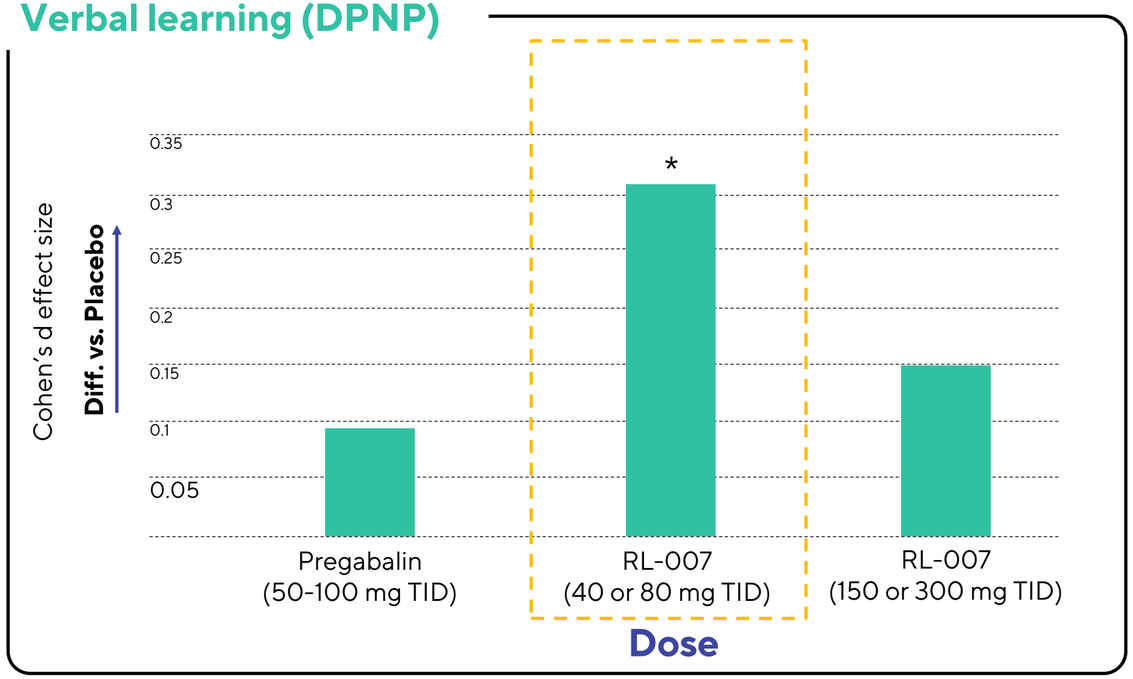



Note: CSF = Cerebrospinal Fluid, DPNP = Diabetic Peripheral Neuropathic Pain, PK = Pharmacokinetics, PD = Pharmacodynamics, CNS = Central Nervous System, CMC = Chemistry, Manufacturing, and Controls

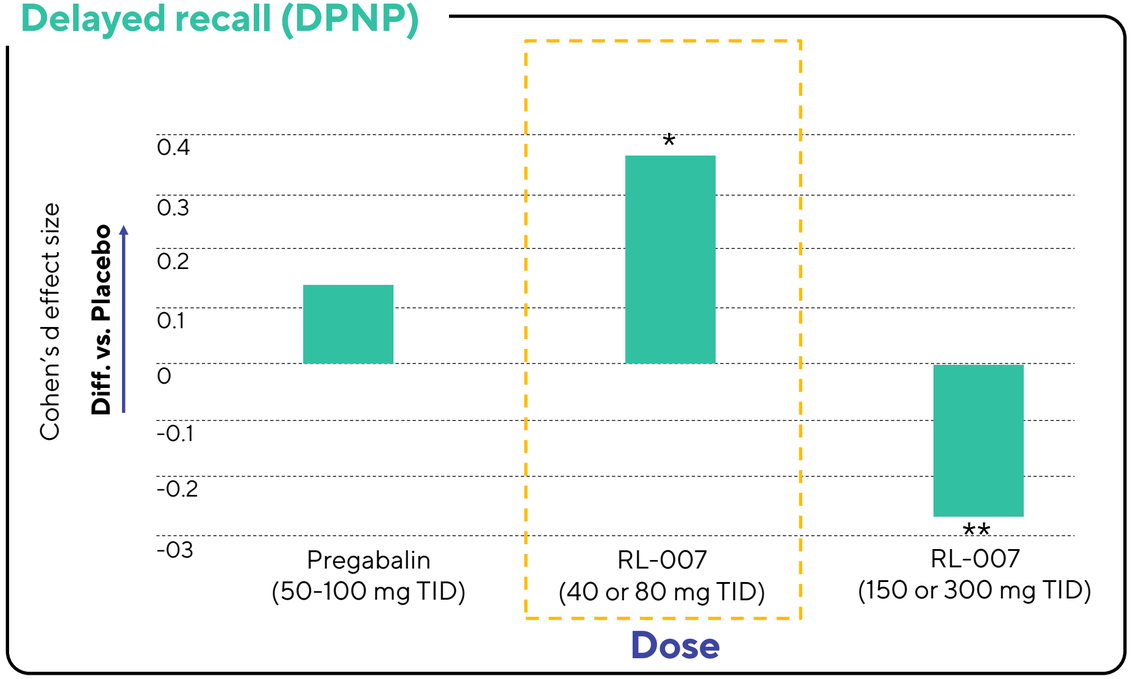
# Additionally, a third-party Phase 2 study in DPNP of RL-007 also showed statistically significant positive cognitive signals

## RL-007 low doses enhanced learning and memory

### Verbal learning (DPNP)




### Delayed recall (DPNP)




(Phase 2 exploratory endpoints – 180 patients[1])

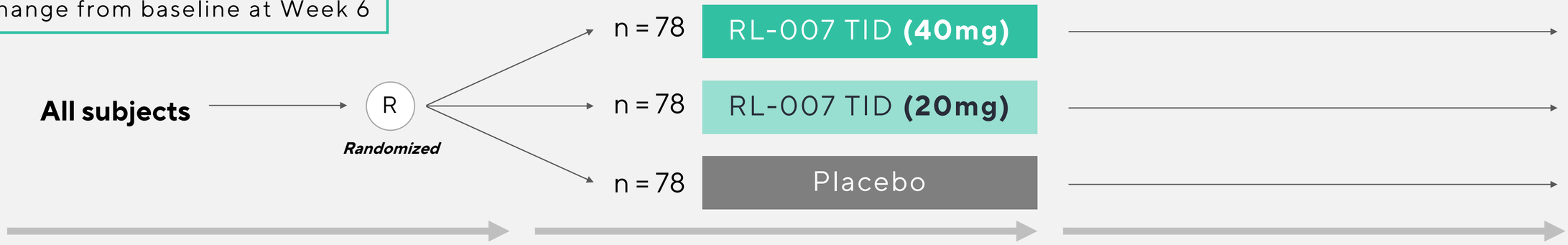
↑ **Indicates direction of improvement**

Note: * = P< 0.05 vs Placebo; **missed significance (P=0.075); Diabetic Peripheral Neuropathic Pain (DPNP);
1. N=60 patients/treatment group; dosed TID = 3x/day dosing; randomized, cross-over design

# RL-007 Phase 2b trial design: randomized 6-week study of RL-007 20mg and 40mg vs placebo in 234 patients with CIAS

## Phase 2b Proof-of-Concept Trial Design

**Primary Endpoint**: MCCB change from baseline at Week 6




| Day -15 to Day -2 | | Day -1 to Week 5 | Week 6 | Week 8 |
|---|---|---|---|---|
| **Screening** | **Randomizing** | **Treatment** | **End of trial** | **Exit** |
| *Visit 1* | *Visit 2* | *Visit 3-7* | *Visit 8* | *Phone call* |
| **Data points collected** | | | | |
| MCCB (efficacy) & VRFCAT (function) | MCCB & VRFCAT | Safety and tolerability, ConMeds, Compliance | MCCB & VRFCAT | Safety and tolerability, ConMeds, Compliance |

**Trial status:** Recruitment ongoing, results anticipated H1'24

Note: MCCB = MATRICS Consensus Cognitive Battery; VRFCAT = Virtual Reality Capacity Assessment Tool; TID = 3x/day dosing

# CIAS & Schizophrenia landscape: RL-007's unique pharmacology, acute cognitive benefit and excellent tolerability differentiate it from pipeline competitors

| | atai company | Therapies in late-stage development focused on treating CIAS | | | Therapies in late-stage development for schizophrenia | |
|---|---|---|---|---|---|---|
| | Recognify Life Sciences | Boehringer Ingelheim | Karuna Therapeutics | Takeda | Minerva Neurosciences | Sunovion |
| **Compound** | RL – 007[1] | BI – 425809 (iclepertin) | KarXT (xanomeline-trospium) | NBI – 1065844 (luvadaxistat) | MIN-101 (roluperidone) | SEP – 363856 (ulotaront) |
| **Development stage** | Phase 2 | Phase 3 | Phase 3 *(in Ph2 for CIAS)* | Phase 2 | Pre-registration | Phase 3 |
| **Mechanism of action** | GABA/nicotinic modulator | GlyT1 inhibitor | Muscarinic M1 / M4 receptor agonist | GPR139 agonist | 5-HT2a / Sigma 2 receptor antagonist | TAAR1 agonist |
| **Focused on treating cognitive impairment associated with schizophrenia** | ✓ | ✓ | ✓ *Also targeting positive & negative symptoms* | ✓ | ✗ *Targeting negative symptoms* | ✗ *Targeting positive & negative symptoms* |
| **Potential for complimentary use with other therapies** | ✓ | | | | | |
| **Targets multiple receptor pathways** | ✓ | | | | | |

Source: Publicly available information, including company websites and clinicaltrials.gov
Note: GABA = gamma-aminobutyric acid; GlyT1 = Glycine transporter type-1; GPR139 = G Protein-Coupled Receptor 139; 5-HT2a = Serotonin 2A receptor; TAAR1 =Trace Amine-Associated Receptor 1
1. RL-007 compound is (2R, 3S)-2-amino-3-hydroxy-3-pyridin-4-yl-1-pyrrolidin-1-yl-propan-1-one(L)-(+) tartrate salts

# Depression

# Depression

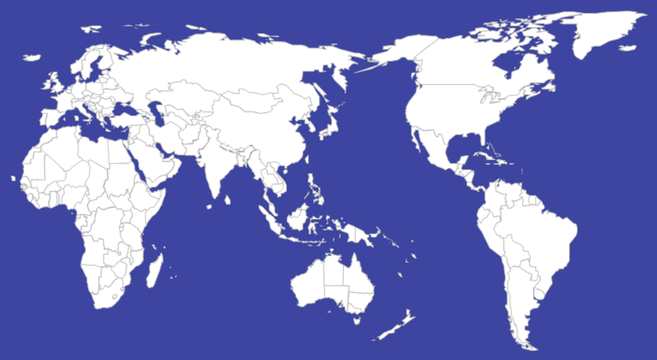
## Disease Overview

Depression is a mood disorder that affects the thoughts and behavior of an individual, leading to psychological, physical, and social problems

**First onset depression (MDD)** → **Persistent depression (MDD)** → **Treatment resistant depression (TRD)**

Treatment resistant depression (TRD) is diagnosed after **two failed courses of antidepressants**

## Depression in numbers



**~300m**

**Global sufferers of depression[1]**

**2nd**

**Leading cause of disability worldwide (2019)[2]**

**~$300Bn**

**U.S. economic burden from adults with MDD (direct + indirect costs)[3]**

## URGENT NEED FOR INNOVATION

**~33%**

### Inadequate response rate

A third of patients with depression respond inadequately or relapse with current treatments[4]

**4-12 weeks**

### Slow onset of treatment effect

Frontline SSRI treatments for depression have slow onset (4-12w)[5]

**~38%**

### Long-term side effects

Over a third of patients experience one or more side effects as a result of SSRI antidepressants[6]

**4**

### Novel therapies approved by FDA in last decade

Only 4 new molecular entities (NMEs) approved by the FDA for depression (MDD or TRD) since 2012, less than 3% relative to oncology (N=138)[7]

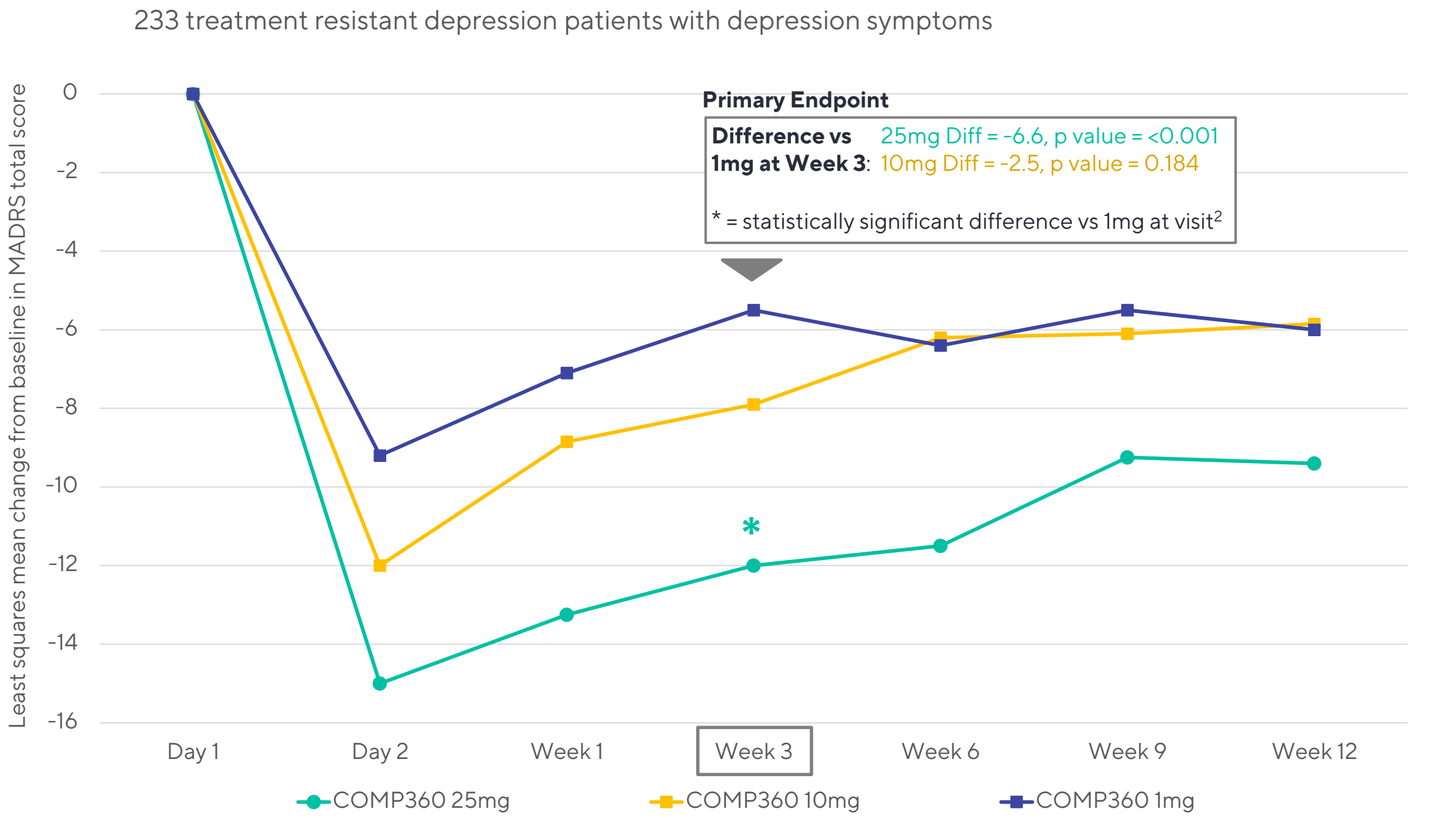
1. World Health Organization (2020)
2. World Health Organization – Disease Burden 2000-2019 (2020)
3. Greenberg et al., "The Economic Burden of Adults with Major Depressive Disorder in the United States (2010 and 2018)" (2021)
4. Salzer, "National Estimates of Recovery-Remission From Serious Mental Illness", Psychiatry Online (2018)
5. Tew et al., "Impact of prior treatment exposure on response to antidepressant treatment in late life" Am J Geriatr Psychiatry (2006)
6. Cascade et al., "Real-World Data on SSRI Antidepressant Side Effects" Psychiatry MMC (2009)
7. GlobalData (as of 15.11.2022). NME approvals include Trintellix, Rexulti, Spravato and Auvelity. Excludes generics, reformulations and biosimilars

# SUMMARY

| | |
|---|---|
| OWNERSHIP | 22.5%[1] |
| 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<br>Potential: Major Depressive Disorder, Autism, Bipolar Disorder, Chronic Cluster Headache |
| CURRENT STATUS | COMP360 Phase 3 (TRD) program expected to commence by end of 2022 |
| 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)

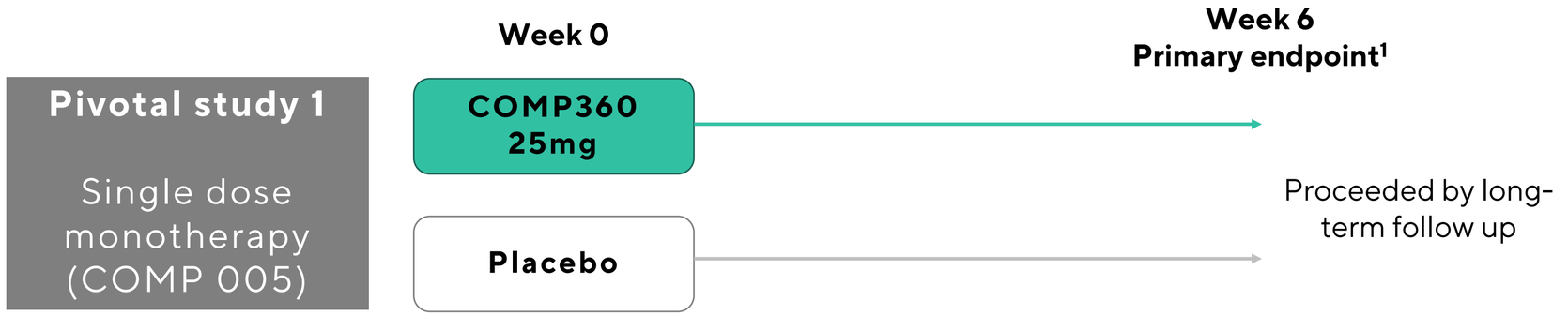



Source: Schedule 13D filed with the SEC as of November 29th, 2021, as amended
Note: MADRS = Montgomery-Åsberg Depression Rating Scale;; COMP360 = a proprietary high-purity, polymorphic crystalline formulation of psilocybin; In COMPASS's model of psilocybin therapy, COMP360 is administered in conjunction with psychological support from specially trained therapists.

1. Ownership percentage as of Sept. 30th, 2022
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.

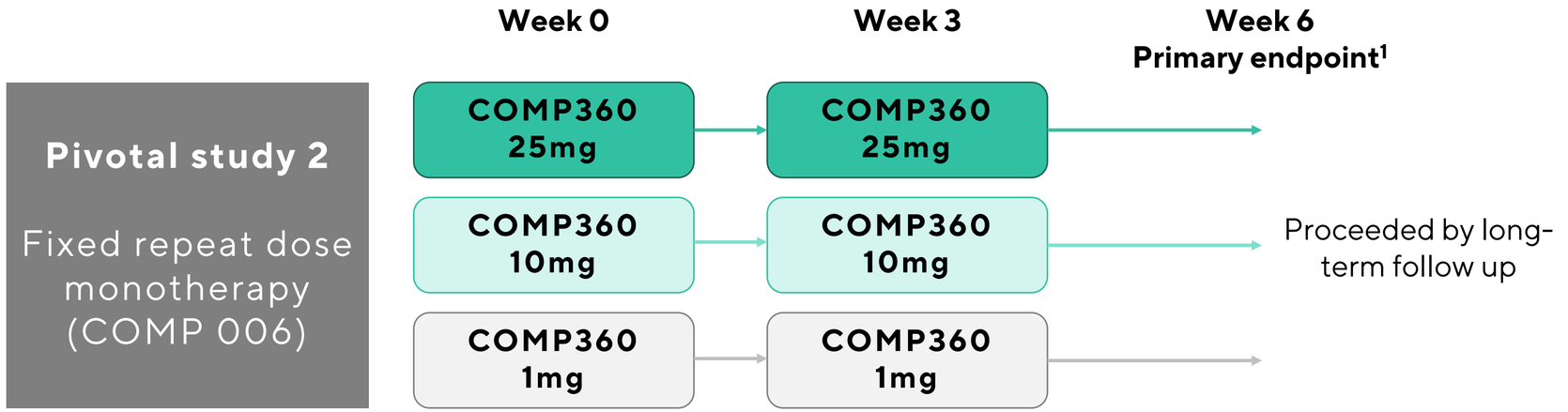
# COMPASS Pathways pivotal phase 3 studies are expected to deliver topline data by 2024 and 2025

## Pivotal Phase 3 Trial Designs




Randomization = 2:1
Target N[2] = 378

**Topline data expected: end of 2024**




Randomization = 2:1:1
Target N[2] = 568

**Topline data expected: mid-2025**

Source: Compass Pathways Capital Markets Day presentation as of October 12, 2022

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

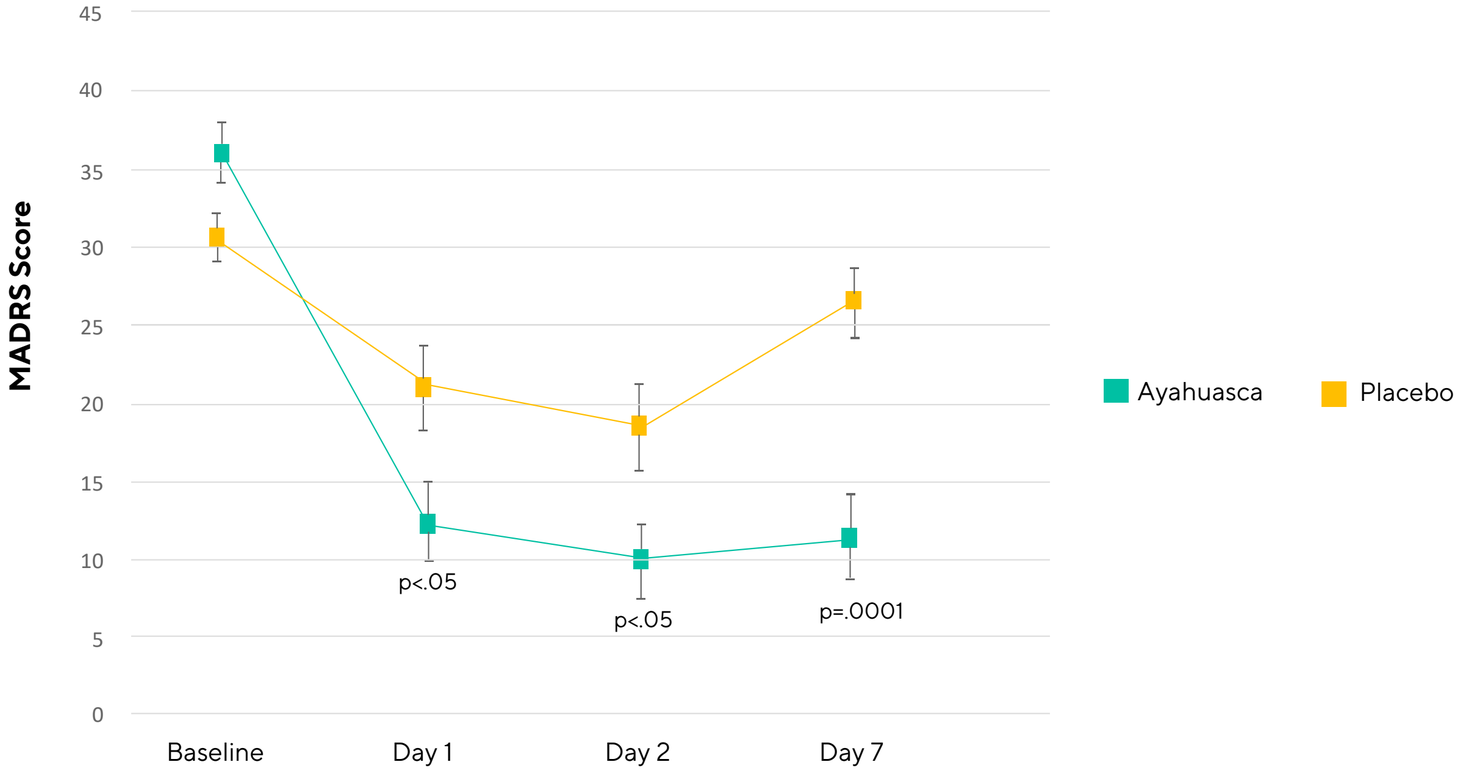
# SUMMARY

| | |
|---|---|
| OWNERSHIP | 100%[1] |
| PRODUCT | Dimethyltryptamine (DMT) in a buccal transmucosal film (VLS-01), DMT is the active psychedelic moiety in Ayahuasca |
| PHARMA-COLOGY | 5-HT2A-R agonist |
| PRODUCT FEATURES | Rapid onset, sustained efficacy after single dose, short duration of psychedelic effect (~30 to 45 minutes) |
| INDICATIONS | Primary: Treatment Resistant Depression<br>Potential: Eating Disorders, Substance Use Disorders |
| CURRENT STATUS | Phase 1 clinical trial initiated in H2'22<br>Phase 1 results expected H1'23 |
| INTELLECTUAL PROPERTY | Filed provisionals on formulations of DMT |
| HIGHLIGHT | VLS-01 is designed to have an improved duration of psychedelic effect whilst improving tolerability |

# VLS-01 may increase patient accessibility by reducing patient and clinic time commitment

**PRIOR EVIDENCE IN HUMANS** (THIRD PARTY STUDY[2])

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




Note: MADRS = Montgomery-Asberg Depression Rate Scale, DMT = Dimethyltryptamine

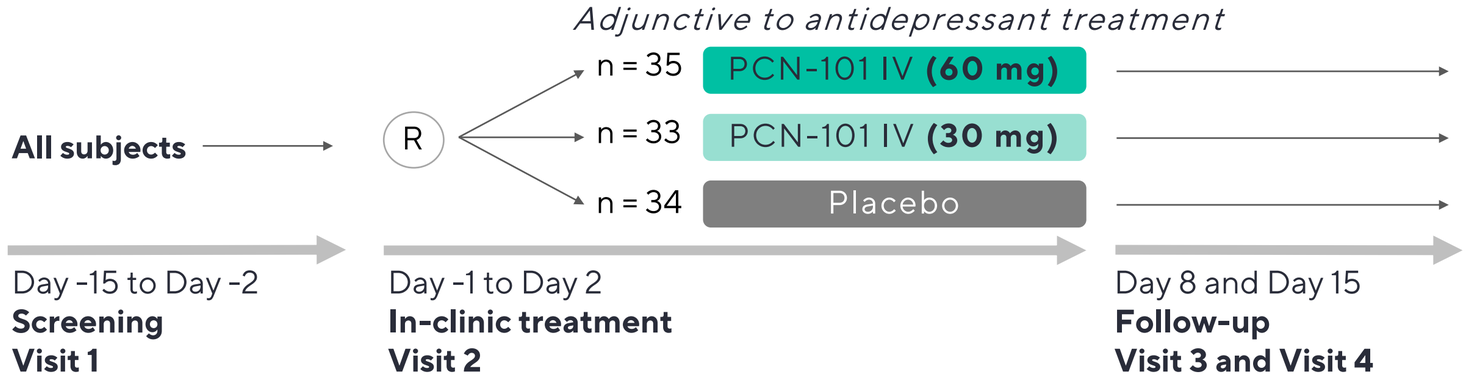
1. Unless otherwise indicated herein, ownership percentage based on ownership of securities with voting rights as of September 30th, 2022
2. Palhano-Fontes et al. "Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression", Psychol Med (2019)

# SUMMARY

| | |
|---|---|
| OWNERSHIP | 58.9%[1] |
| PRODUCT | Subcutaneous R-ketamine (PCN-101) |
| PHARMA-COLOGY | Glutamatergic modulator |
| PRODUCT FEATURES | Rapid-acting, non-dissociative antidepressant with potential for at home use |
| INDICATIONS | Primary: Treatment Resistant Depression<br>Potential: Substance Use Disorder |
| CURRENT STATUS | Phase 2a results announced January 2023 |
| INTELLECTUAL PROPERTY | Issued methods of use of R-ketamine for treatment of depressive symptoms |
| HIGHLIGHT | Third party study: Single IV dose (0.5 mg/kg) of R-ketamine led to a rapid and sustained decrease in MADRS in patients with TRD; dissociation was nearly absent[2] |

# We've completed a Phase 2a study for PCN-101 and are evaluating next steps for the program

**PCN-101 PHASE 2A STUDY[3] IN PATIENTS WITH TREATMENT RESISTANT DEPRESSION (N=102)**




## SUMMARY OF RESULTS *(Preliminary analysis, subject to change)*

1. Study **did not meet its primary endpoint** of a statistically significant change from baseline in participants' MADRS score at 24 hours compared to placebo
2. The mean change on MADRS from baseline at 24 hours was -15.3 for PCN-101 60mg compared to -13.7 for placebo (-1.6 placebo-adjusted; p-value 0.5)
3. PCN-101 demonstrated **encouraging signals of efficacy across all timepoints** despite not achieving statistical significance on the primary endpoint
4. The drug was **generally well-tolerated** with rates of sedation and dissociation comparable to placebo

Note: MADRS = Montgomery-Asberg Depression Rate Scale, CADSS = Clinician-administered dissociative states scale, IV = Intravenous, PBO = Placebo.

1. Unless otherwise indicated herein, ownership percentage based on ownership of securities with voting rights as of September 30th, 2022. Perception does not give effect to the shares of common stock issuable after giving full effect to the anti-dilution feature of the Stock Purchase Agreement, which would not impact our majority position in Perception.
2. Leal et al., "Intravenous arketamine for treatment-resistant depression: open-label pilot study" (2020)
3. NCT05414422

# Anxiety

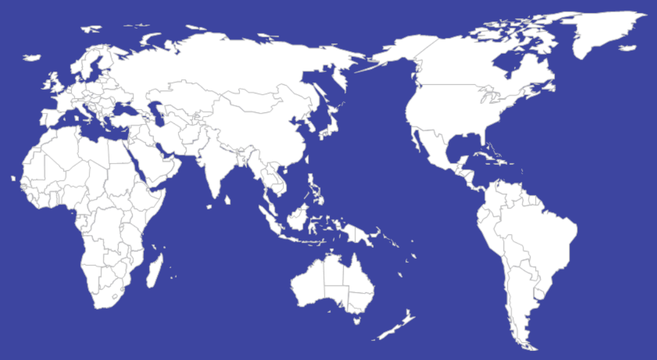
# Anxiety

## Disease Overview

Anxiety disorders develop when feelings of apprehension and unease persist over an extended period and potentially worsen over time

- Generalized Anxiety Disorder (GAD)
- Panic Disorder
- Social Anxiety Disorder (SAD)
- Post-Traumatic Stress Disorder (PTSD)
- Obsessive-Compulsive Disorder (OCD)

## Anxiety in numbers



**~40m**

**Anxiety disorder sufferers in the US[1]**

**#1**

**Most common mental health disorder in the US[2]**

**~$42bn**

**Annual societal cost of anxiety disorders in the US[3]**

## MASSIVE UNADDRESSED NEED

**~7m**

### GAD patients in the US

Approximately 7 million individuals suffer from GAD in the US on an annual basis[1]

**<50%**

### Low treatment rate

Less than half of patients with anxiety disorder in the US receive treatment[1]

**~45%**

### Anxiety and depression are comorbid[3]

A worldwide survey estimated 46% of respondents with lifetime MDD had one of more lifetime anxiety disorders[4]

**0**

### Novel molecules approved in over a decade

All recent approvals by the FDA have been reformulations of long-standing antidepressant and benzodiazepine options[5]


1. Anxiety and Depression Association of America (2021)
2. National Alliance on Mental Illness (2021)
3. DeVane et al., "Anxiety Disorders in the 21st Century: Status, Challenges, Opportunities, and Comorbidity With Depression", AJMC (2005)
4. Kessler et al., "Anxious and non-anxious major depressive disorder in the World Health Organization World Mental Health Surveys", Epidemiol Psychiatry Sci (2015)
5. GlobalData (as of 09.27.2022).

# SUMMARY

| | |
|---|---|
| OWNERSHIP | 54.7%[1] |
| PRODUCT | Deuterated etifoxine HCl oral dosage form (GRX-917) |
| PHARMA-COLOGY | Etifoxine facilitates endogenous production of neurosteroids through agonist activity at the mitochondrial translocator protein (TSPO) |
| PRODUCT FEATURES | GRX-917 is designed to have rapid onset activity of anxiolytic activity like benzodiazepines but without the sedating, addicting, or cognitive impairing properties |
| INDICATIONS | Primary: Generalized Anxiety Disorder<br>Potential: Social Anxiety Disorder, Postpartum Depression |
| CURRENT STATUS | Phase 1 trial completed in H2'22<br>Efficacy study first subjected dosed in H1'23 |
| INTELLECTUAL PROPERTY | Issued composition of matter on deuterated etifoxine (GRX-917) and corresponding methods of use |
| HIGHLIGHT | Preliminary Phase 1 data demonstrated dose-dependent and time-dependent pharmacodynamic effect along with low incidence and severity of adverse events |

# GRX-917 has the potential for benzodiazepine-like rapid-onset efficacy with improved safety and tolerability

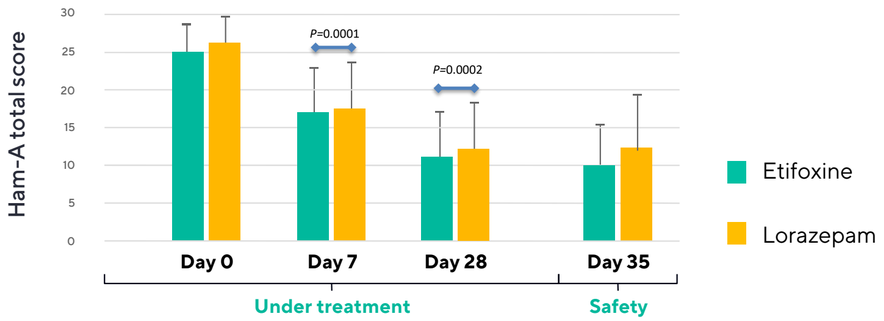
## ETIFOXINE HAS BEEN APPROVED FOR ANXIETY DISORDER SINCE 1979 WITH 14M+ PRESCRIPTIONS

**Etifoxine works as rapidly as lorazepam**, with etifoxine continuing its effects beyond treatment, while lorazepam shows rebound

**Etifoxine** has a **strong safety** record: a review of over **14m prescriptions** in France found no cases of abuse, misuse or dependence[3]

### THIRD PARTY STUDY[2]

Non Inferiority Test




## COMPLETED PHASE 1 TRIAL

**Part 1: Single Ascending Dose**

TREATMENT | SAFETY/PK/PD

**Up to 40 healthy subjects:**
Up to 5 cohorts
25mg to 500mg

**PD Endpoint:**
qEEG

**Part 2: Multiple Ascending Dose**

TREATMENT | SAFETY/PK/PD

**Up to 36 healthy subjects:**
Up to 3 cohorts
100mg to 300mg

**PD Endpoint:**
qEEG

Note: HAM-A = Hamilton Anxiety Rating Scale, SD = standard deviation, qEEG = Quantitative electroencephalography, PK = Pharmacokinetics. PD = Pharmacodynamics, PoC = Proof of Concept;

1. Unless otherwise indicated herein, ownership percentage based on ownership of securities with voting rights as of September 30th, 2022.
2. Nguyen et al., "Efficacy of etifoxine compared to lorazepam monotherapy" (2006)
3. Cottin et al., "Safety profile of etifoxine: A French pharmacovigilance survey" (2016)

# GRX-917 Phase 1 data: no severe or serious adverse events, with minimal sedation or dizziness, confirms favourable safety profile

1. Given every 12 hours for 7 days, GRX-917 was **well-tolerated** with no dose-limiting toxicities identified **up to the highest dose of 300mg**
2. There were **no serious adverse events reported** nor dose-related discontinuations due to adverse events
3. Adverse events in both single- and multiple-ascending dose (SAD and MAD) regimens were **comparable to placebo-treated subjects**
4. **No significant evidence of sedation or other benzodiazepine-like side effects[4]** at any doses tested

## GRX-917 Phase 1 MAD study safety data[1]

| | Placebo N = 15 | GRX-917 100 mg N=9 | GRX-917 150 mg N=9 | GRX-917 200 mg N=9 | GRX-917 300 mg N=8 | GRX-917 All doses N=43 | Total N=58 |
|---|---|---|---|---|---|---|---|
| Any TEAE[2] | 9 (60%) | 7 (78%) | 4 (44%) | 11 (69%) | 4 (44%) | 26 (61%) | 35 (60%) |
| Mild | 9 (60%) | 7 (78%) | 4 (44%) | 11 (69%) | 4 (44%) | 26 (60%) | 35 (60%) |
| Moderate | 2 (13%) | 1 (11%) | 1 (11%) | 1 (6%) | 0 | 3 (7%) | 5 (9%) |
| Severe | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Serious TEAE | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TEAEs leading to discontinuation | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Most common TEAEs[3]** | | | | | | | |
| Headache | 2 (13%) | 4 (44%) | 1 (11%) | 3 (19%) | 1 (11%) | 9 (21%) | 11 (19%) |
| Ventricular tachycardia | 1 (7%) | 0 | 1 (7%) | 2 (13%) | 0 | 3 (7%) | 4 (7%) |
| Nausea | 1 (7%) | 1 (11%) | 1 (11%) | 0 | 0 | 2 (5%) | 3 (5%) |
| Dizziness | 0 | 0 | 0 | 2 (13%) | 0 | 2 (5%) | 2 (3%) |
| Lethargy | 0 | 0 | 1 (11%) | 0 | 1 (11%) | 2 (5%) | 2 (3%) |

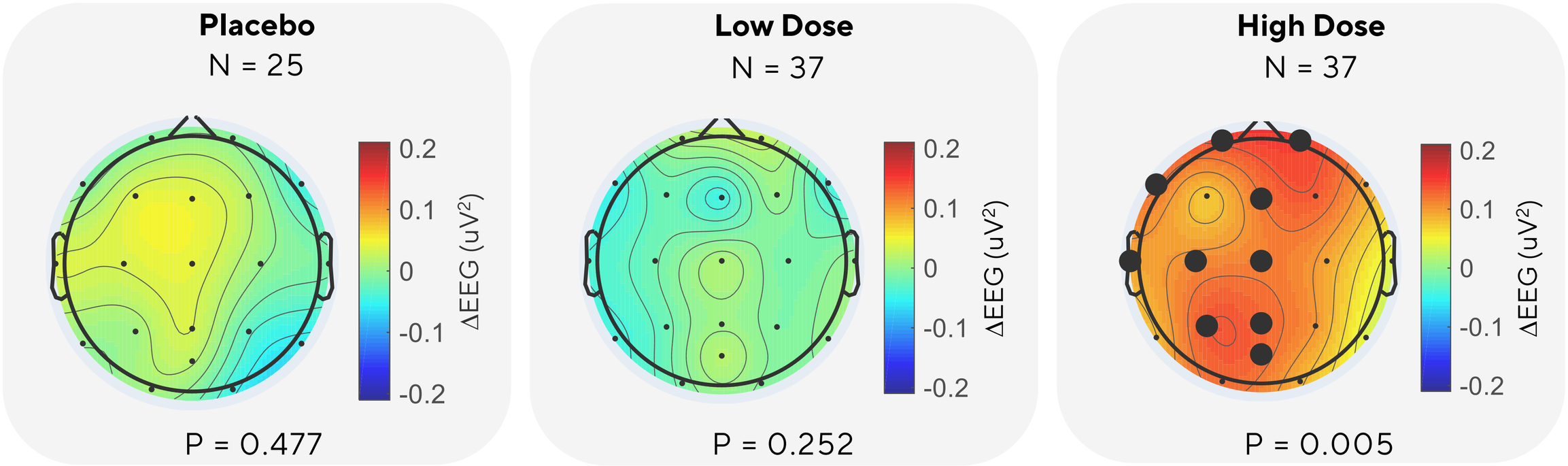
Note: TEAE = Treatment-emergent Adverse Event, SAD = Single Ascending Dose, MAD = Multiple Ascending Dose

1. n = number of subjects reporting at least one TEAE in that category, % - proportion of cohort total
2. Defined as an adverse event that began after the start of trial medication treatment
3. Non-exhaustive. Other recorded TEAEs included Upper respiratory tract infection (3%), Rash erythematous (3%), Dysmenorrhoea (3%), Catheter site pain (3%)
4. Of the 565 patients given XANAX in Ph.3 placebo-controlled trials for anxiety disorders, 41% reported drowsiness versus 22% of those administered placebo (as reported in XANAX FDA label)

**Preliminary data, subject to change**

# GRX-917 Phase 1 data: Dose-dependent increase in frontal beta power was demonstrated, providing evidence of target engagement and mechanism of action

**Changes in Beta power from pre-dose to 3-hour post-dose[1]**




Channels with significant differences (paired t-test; p<0.05, after FDR correction for multiple comparison) are marked with black circles. Topographical maps show distribution of beta power (13-30 Hz) across the scalp.

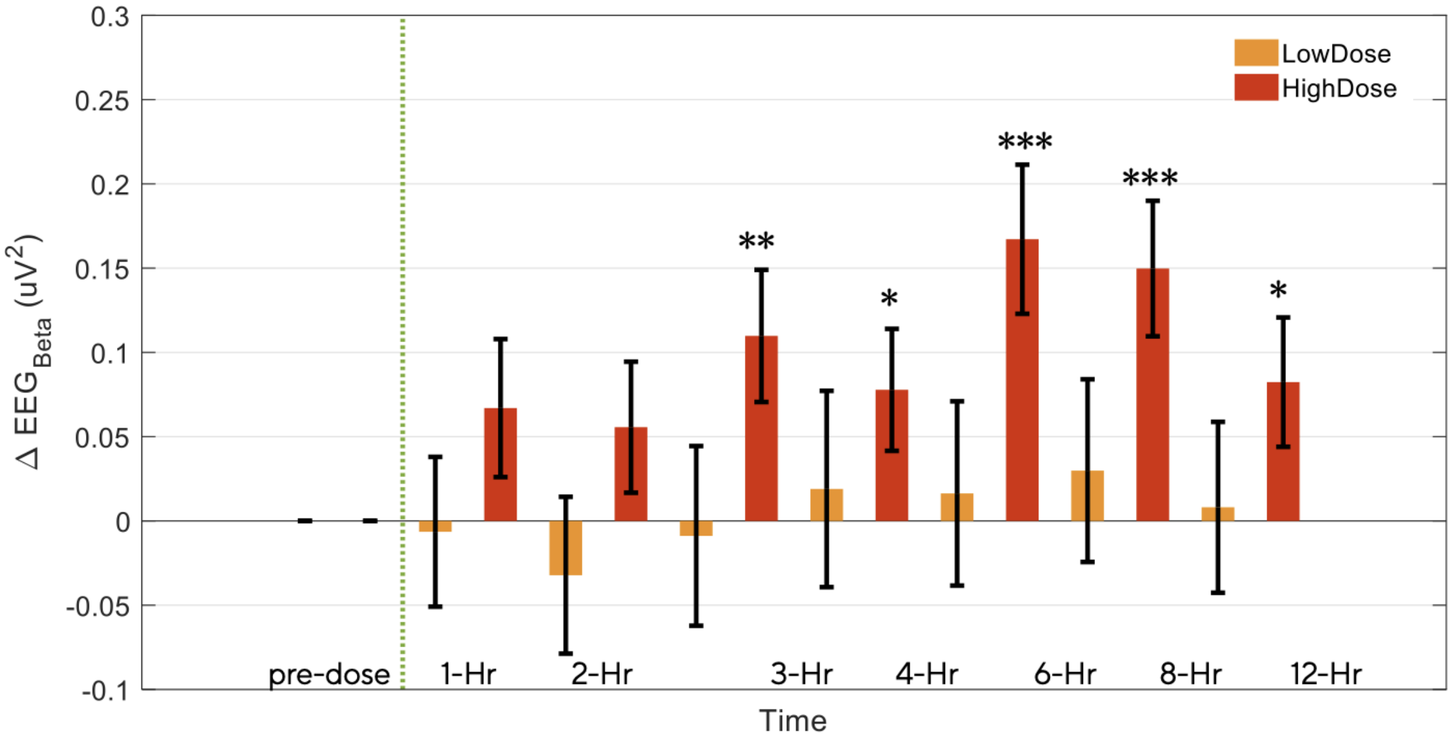
Note: FDR = False Discovery Rate, EEG = Electroencephalogram

1. Power is NOT in log scale and the unit of measurement is $uV^2$
2. Given twice daily every 12 hours

**Preliminary data, subject to change**

# GRX-917 Phase 1 data: The EEG beta effect was also time-dependent, showing a rapid onset of effect with a delayed pharmacodynamic curve

**Group average changes in Beta power for low dose and high dose groups per time point[1]**




- Average differences in each time point is compared to zero and time points with significant changes (t-test, p<.05) were marked with asterisk

  * p<.05 ** p<.01 *** p<.001

Note: EEG = Electroencephalogram

1. Changes in beta power averaged over each channel from pre-dose to each time point (pre-dose power subtracted from post dose at each point)

**Preliminary data, subject to change**

SUMMARY

**There is an unmet need in GAD for therapies with rapid onset, high efficacy, and minimal side effects**

**SSRI/SNRI's are current standard of care for GAD but require 4-6 weeks for onset of effect and have several disadvantages[1]:**

1. SSRI/SNRI-specific inadequacy
2. Lack of tolerability
3. Patient nonadherence to medications that fail to relieve symptoms of anxiety quickly

**Benzodiazepines are second-line treatment, offering fast and effective relief, but carrying significant risk of:**

1. Sedation
2. Impaired cognition
3. Dependence/addiction

# GRX-917 is developed to address unmet need in Generalized Anxiety Disorder (GAD) with rapid onset and favorable safety

Overview of Current Therapeutic Options for Generalized Anxiety Disorder

| Class | Examples | Mechanism of action | Favorable safety profile | Rapid onset | Minimal side effects | Non-addictive |
|---|---|---|---|---|---|---|
| **Benzoxazine** | Deuterated etifoxine (GRX-917) | $GABA_A$ Channel and TSPO Potentiation | ✓ | ✓ | ✓ | ✓ |
| **Selective Serotonin Reuptake Inhibitor (SSRI)** | Escitalopram | SERT blockade | ✓ | | | ✓ |
| **Serotonin and Norepinephrine Reuptake Inhibitor (SNRI)** | Venlafaxine | SERT AND NET blockade | ✓ | | | ✓ |
| **Benzodiazepines** | Lorazepam / Alprazolam | $GABA_A$ Potentiation | | ✓ | | |
| **Tricyclic Antidepressant (TCA)** | Imipramine | Mixed MoA | | | | ✓ |
| **Azapirones** | Buspirone | partial 5-HT1A agonist | ✓ | | | ✓ |
| **Gabapentinoid** | Pregablin | VDCC inhibition | ✓ | | | ✓ |

**Anticipated pharmacological profile based on etifoxine and GRX-197 Phase 1 data**

Note: GABA = Gamma aminobutyric acid, SERT = serotonin transporter , NET = serotonin transporter; MoA = Mechanism of Action; 5HT1a = serotonin 1A receptor; VDCC = voltage dependent calcium channel; TSPO = mitochondrial translocator protein

Source: Publicly available information, including company websites and clinicaltrials.gov, GlobalData, Evaluate Pharma (both as of 2022)

1. DeMartini et al., "Generalized Anxiety Disorder" (2019)

# Substance Use Disorder

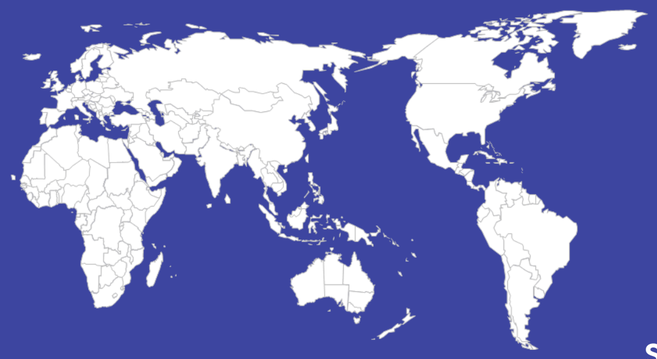
# Substance Use Disorder (SUD)

**Disease Overview**

Substance use disorders are highly prevalent disorders characterized by an inability to control the use of a legal or illegal drugs, alcohol, or medications (e.g., prescription opioids)

**Substance Use Disorder (SUD)** & **Opioid Use Disorder (OUD)**

## SUD in numbers



**~20m+**

**US sufferers of SUD in 2019[1]**

**~70k**

**US deaths from opioid drug overdose in 2020[3]**

**$787bn**

**Societal cost associated with Opioid Use Disorder in the US[4]**

## AN ONGOING PANDEMIC

**~3m**

### Number of OUD sufferers in US

Approximately 3 million individuals in the US suffered from Opioid Use Disorder (OUD) in 2020[2]

**~75%**

### High relapse rates

Approximately ~75% of patients undergoing OUD therapy experience relapse within one year[5]

**~93,000**

### Drug overdose deaths increase ~30%

COVID-19 severely exacerbated the crisis for those with a SUD; drug overdose deaths increase ~30% with ~93,000 deaths in 2020, nearly 70,000 of which involved opioids[6]

**2**

### Limited treatment options for OUD

The current standard of care for OUD consists only of synthetic full and partial opioid receptor agonists (methadone & buprenorphine) and opioid antagonists (naltrexone); withdrawal agents do not treat the opioid addiction and only manage symptoms of withdrawal

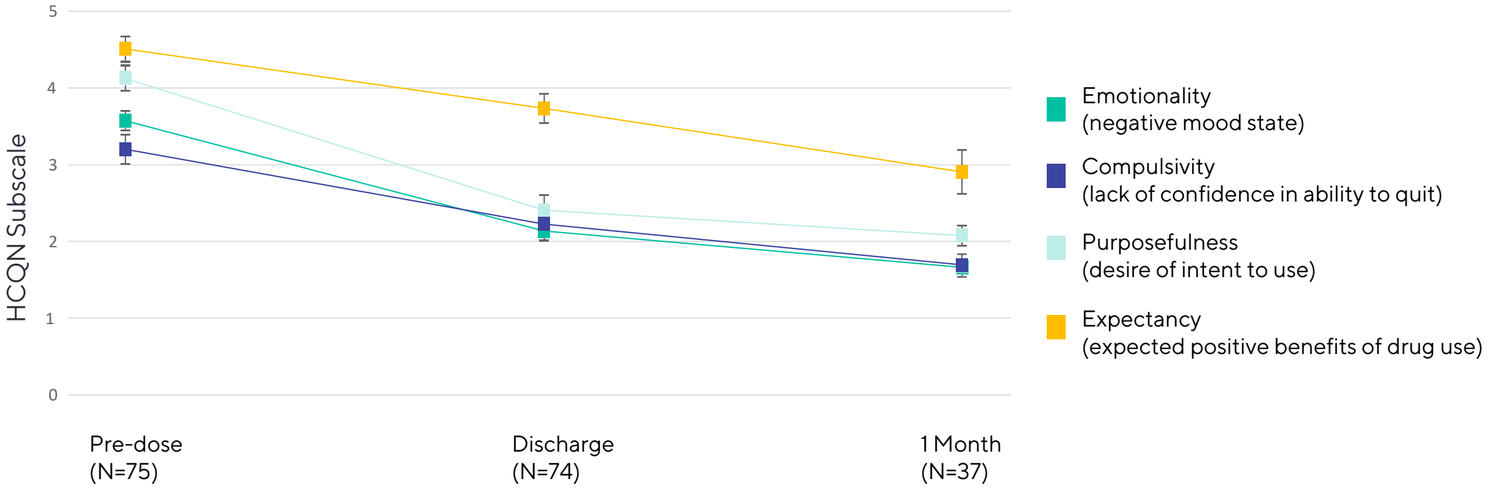
1. SAMSHA - Key Substance Use and Mental Health Indicators in the United States: Results from the 2019 National Survey on Drug Use and Health)
2. Azadfard et al., "Opioid Addiction" (2020)
3. Ahmad FB, Rossen LM, Sutton P. "Provisional drug overdose death counts". National Center for Health Statistics (2021)
4. Murphy, "The cost of opioid use disorder and the value of aversion" (2020)
5. Sinha, "New Findings on Biological Factors Predicting Addiction Relapse Vulnerability" (2011)
6. National Center for Health Statistics – Provisional Drug Overdose Death Counts

# SUMMARY

| | |
|---|---|
| OWNERSHIP | 59.5%[1] |
| PRODUCT | Ibogaine HCl capsules (DMX-1002), ibogaine is a naturally occurring psychedelic compound isolated from a West African shrub, iboga |
| PHARMA-COLOGY | Cholinergic, glutamatergic and monoaminergic receptor modulator |
| PRODUCT FEATURES | A single dose of ibogaine may precipitate rapid withdrawal and long-term abstinence in Opioid Use Disorder patients |
| INDICATIONS | Primary: Opioid Use Disorder<br>Potential: Substance Use Disorder, Post-Traumatic Stress Disorder, Traumatic Brain Injury |
| CURRENT STATUS | Phase 1/2 trial initiated in H2'21<br>Phase 1 results expected H1'23 |
| INTELLECTUAL PROPERTY | Pending method of treatment claims for Opioid Use Disorder for ibogaine |
| HIGHLIGHT | Potential sustained reduction in opioid craving with DMX-1002 single administration |

# A single-dose of ibogaine showed potential for sustained reductions in opioid cravings in 75 opioid-dependent patients

## PRIOR EVIDENCE IN HUMANS (THIRD PARTY STUDY[2])




## ONGOING PHASE 1/2 TRIAL

**Stage 1: Maximum Tolerated Dose**

TREATMENT (MULTIPLE DOSES) | SAFETY/PK

**Subject cohort:**
Recreational opioid users
(up to 24 subjects)

**Objective:**
Dose finding

**Stage 2: Proof of Concept**

TREATMENT VS PLACEBO | SAFETY/EFFICACY

**Patient cohort:**
Opioid dependent patients
(approximately 80 subjects)

**Endpoints:**
Acute withdrawal,
abstinence over 90 days

Note: HCQN = Heroin Craving Questionnaire, PK = Pharmacokinetics.

1. Unless otherwise indicated herein, ownership percentage based on ownership of securities with voting rights as of September 30th, 2022. Refers to ownership in DemeRx IB. DemeRx NB ownership is 6.3%, which does not give effect to option to acquire further shares which may increase the ownership to up to 57.1%
2. Mash et al., "Ibogaine Detoxification Transitions Opioid and Cocaine Abusers Between Dependence and Abstinence: Clinical Observations and Treatment Outcomes" (2018)

## 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 |
|---|---|---|---|---|---|---|
| **Sustained relapse prevention**<br>Single dose administered in monitored setting, providing both withdrawal support and oneiric experience driving sustained remission | Ibogaine (DMX-1002)<br>**DemeRx** | Cholinergic, glutamatergic and monoaminergic receptor modulator | ✓ | ✓ | ✓ | ✓ |
| **Medication Assisted Therapy[1]**<br>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 | | ✓ | ✓ | |
| **Withdrawal Support[2]**<br>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

# Enabling Tech

# Enabling technologies: Our formulation & biomarker stratification companies provide an additional avenue of growth & innovation to the atai platform

## Introspect

*Digital therapeutics platform enabling personalized care*

- Developing digital tools and devices to provide personalized clinical psychotherapy to patients
- Digital therapeutics (DTx) will deliver scalable treatment to those who might not otherwise have access to high-quality psychological care

**Recent milestones**

- Introspect's DTx, IDEA-01, incorporated into clinical development plans for various atai pipeline products, incl. Viridia Life Sciences and EmpathBio

## EntheogeniX

*AI-enabled computational biophysics drug discovery platform*

- Developing new chemical entities (NCEs) by selecting for desirable pharmacological targets of psychedelics while avoiding undesirable anti-targets
- Discovered two novel chemical series with potent 5-HT2A receptor agonism and optimal CNS drug-like properties

**Recent milestones**

- Novel chemical series' have lower hallucinogenic potency than psilocin, whilst maintaining antidepressant-like activity *(data presented at Society of Neuroscience 2022 conference)*

## InnarisBio

*Sol-gel based, nose-to-brain, drug delivery platform*

- Developing a non-invasive, nose-to-brain delivery technology that avoids systemic circulation and first-pass metabolism
- INB-01 is sol-gel based, designed to deliver the drug as a liquid at room temperature, then becoming a gel instantaneously in the nasal cavity

**Recent milestones**

- Initiated Ph.1 proof-of-concept study to demonstrate tolerability, safety and effective brain delivery of intranasal INB-01 *(results expected H1'23)*

## IntelGenx

*Oral Thin Film (OTF) manufacturer licensed to develop re-formulations of scheduled compounds*

- Developing an OTF formulation of Viridia's VLS-01, enabling buccal administration of DMT and avoiding first-pass metabolism
- Utilizes VersaFilm techology that resembles a Listerine breath strip, (already approved in schizophrenia)

**Recent milestones**

- Initiated first-in-human clinical study of an OTF psychedelic drug candidate with buccal VLS-01 Phase 1 study *(results expected H1'23)*

Note: HTR = Head Twitch Response, DTx = Digital Therapeutics, CNS = Central Nervous System, OTF = Oral Thin Film, DMT = Dimethyltryptamine

“Watching my best friend and business partner suffer, being let down by existing treatments and finally finding comfort in psychedelic therapies, was all the inspiration I needed to commit my life to this cause.”

**Florian Brand** | CEO | atai life sciences