



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

**Company Overview** \_\_\_\_\_



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This presentation may include forward-looking statements. All statements other than statements of historical facts contained in this presentation, including statements regarding our future results of operations and financial position, industry dynamics, business strategy and plans and our objectives for future operations, are forward-looking statements. These statements represent our opinions, expectations, beliefs, intentions, estimates or strategies regarding the future, which may not be realized. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expects,” “plans,” “anticipates,” “could,” “intends,” “targets,” “projects,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions that are intended to identify forward-looking statements. Forward-looking statements are based largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy, short term and long-term business operations and objectives and financial needs. These forward-looking statements involve known and unknown risks, uncertainties, changes in circumstances that are difficult to predict and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statement. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and

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The forward-looking statements included in this presentation are made only as of the date hereof. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Moreover, neither we nor our advisors nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. Neither we nor our advisors undertake any obligation to update any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations, except as may be required by law. You should read this presentation with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

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This presentation contains excerpts of testimonials from individuals who have been treated with compounds or derivatives of the compounds underlying our product candidates in the context of third-party studies or otherwise that are solely intended to be illustrative and not representative of the potential for beneficial results of such compounds. Our product candidates are in preclinical or clinical stages of development and none of our product candidates have been approved by the FDA or any other regulatory agency.

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# We are a founder-led team **aiming to develop differentiated treatments** for patients suffering from **mental health disorders**



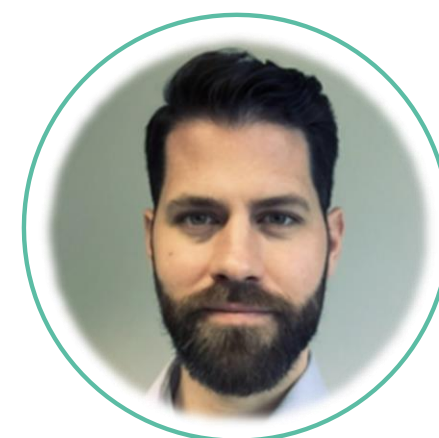
**Christian Angermayer**  
Founder & Chairman



**Florian Brand**  
Co-Founder & CEO



**Srinivas Rao, MD, PhD**  
Co-Founder & CSO



**Lars Wilde**  
Co-Founder



**Greg Weaver**  
CFO



**Rolando Gutierrez, MD**  
CMO



The atai team has collectively led



13

**NDA**s through  
regulatory approval



50+

**IND**  
applications

# Executive Summary and Key Investment Highlights

1

Mental health disorders have become one of largest global health burdens, exacerbated by the COVID-19 pandemic. Despite the unmet patient need, innovations remain limited, with only 7 new neuropsychiatric drugs approved since 2015.

2

As a response to lack of innovation, atai focuses on compounds with prior clinical evidence, including psychedelics whose therapeutic potential has become evident in recent academic studies and which have benefited from recent regulatory momentum.

3

Our platform consists of 11 drug development programs and 6 enabling technologies, focusing on differentiated and potentially disease-modifying mental health treatments. We intend to continue to grow our platform through acquisitions and incubations.

4

Our platform approach: Decentralized drug development process, leveraging the atai team and our enabling technologies such as digital therapeutics to aim for improved safety, efficacy and probability of clinical success across our pipeline.

5

Validation of atai's operating model: IPO of COMPASS Pathways and Otsuka partnership with Perception (first drug development partnership between big pharma and a biopharmaceutical company developing psychedelics).

6

Our pipeline is rich in R&D catalysts over the next 18 months, and we have a team of more than 200 highly experienced FTEs / consultants across our platform, and a strong cash position of approx. \$453M<sup>1</sup>.

# Meaningful R&D catalysts over the next 18 months lead to a unique density of news flow, excluding potential for additional business development opportunities

## Recent Milestones

2021

- ✓ DemeRx doses first subject in Phase 1/2a study of DMX-1002
- ✓ Recognify started Phase 2a study in CIAS with RL-007
- ✓ Perception closed licensing deal with Otsuka for Japan
- ✓ atai entered strategic partnership with IntelGenx
- ✓ DemeRx received approval to start DMX-1002 Phase 1/2 in UK
- ✓ atai announced successful closing of Series D, raising \$157m
- ✓ Perception announced positive Phase 1 results with PCN-101
- ✓ Empath partnered with Bionomics on PTSD drug development
- ✓ atai acquired majority stake in Recognify to develop RL-007 for CIAS
- ✓ Launch of Revixia Life Sciences to develop RLS-01
- ✓ COMPASS successfully IPO-ed on NASDAQ
- ✓ atai launched EmpathBio to develop EMP-01 for PTSD

## Anticipated Milestones next 18 months

- PCN-101 Phase 2a FSI
- RL-007 Phase 2a results
- PCN-101 Phase 2a results
- RL-007 Phase 2b FSI
- GRX-917 Phase 2 FSI
- NN-101 Phase 1 FSI
- DMX-1002 Phase 1 results
- GRX-917 Phase 1 results
- NN-101 Phase 1 results
- KUR-101 Phase 1 results
- EMP-01 Phase 1 results
- VLS-01 Phase 1 results
- PCN-101 (SQ vs. IV BA) results
- IntroSpect app deployment
- EntheogeniX lead candidate
- Psyber prototype deployment
- InnarisBio pilot Phase 1 results

**Legend** ○ Preclinical ○ Phase 1 ○ Phase 2 ● Enabling Technology

## Founded in 2018

As a response to the **significant unmet need and lack of innovation** in the mental health treatment landscape, as well as the **emergence of therapies that previously may have been overlooked or underused**, including psychedelic compounds and digital therapeutics.

# Although mental health has become one of the largest global healthcare challenges, there has been little innovation for patients<sup>7</sup>

## SIGNIFICANT BURDEN

~1bn

### Affected people

Global population with mental health disorders<sup>1</sup>

>50%

### Of US population impacted

Expected that more than half of US population will have a mental health disorder at some point in their lifetime<sup>2</sup>

~\$16tn

### Global economic impact

Estimated global economic costs of mental health disorders by 2030<sup>3</sup>

~4x

### Recent impact of COVID-19

Percentage of US adults experiencing symptoms of depression and anxiety rose from 11% in 2019 to 42% end of 2020<sup>4</sup>

## URGENT NEED FOR INNOVATION

~33%

### Respond inadequately

A third of patients with depression respond inadequately or relapse with current treatments within certain indications<sup>5</sup>

Up to 12 wks

### Slow onset of treatment effect

Frontline treatments for depression and anxiety have slow onset (4-12w)<sup>6</sup>

~75%

### Relapse rate

Most of the patients treated for opioid use disorder (OUD) relapse<sup>7</sup>

7

### Psychiatry approvals since 2015

Only 7 new drugs approved by the FDA for psychiatry disorders since 2015 – less than 10% relative to oncology (N=83)<sup>8</sup>

1. Ritchie, "Global mental health: five key insights which emerge from the data", Our World In Data (2018).  
 2. Kapil, "5 Surprising Mental Health Statistics", National Council for Behavioral Health (2019).  
 3. Patel et al., "The Lancet Commission on global mental health and sustainable development", The Lancet (2018).  
 4. Abbott, "COVID's mental-health toll: how scientists are tracking a surge in depression, Nature (2021)

5. Salzer, "National Estimates of Recovery-Remission From Serious Mental Illness", Psychiatry Online (2018).  
 6. Tew et al., "Impact of prior treatment exposure on response to antidepressant treatment in late life" Am J Geriatr Psychiatry (2006)  
 7. Sinha, "New Findings on Biological Factors Predicting Addiction Relapse Vulnerability" (2011)  
 8. EvaluatePharma (as of 19.03.2021). New drugs include new molecular entities or new active ingredients.

# A resurgence in psychedelic therapies is emerging as promising **disease-modifying drug candidates** progress with **regulatory momentum**



LSD synthesized by Dr. Albert Hofmann at Sandoz research labs<sup>1</sup>



CHARLES UNIVERSITY

Dr. Stan Grof uses LSD to treat heroin addiction in Prague<sup>3</sup>



JOHNS HOPKINS Center for Psychedelic & Consciousness Research

Psilocybin shows sustained decreases in depression and anxiety in cancer patients<sup>5</sup>



COMPASSION Navigating Mental Health Pathways

FDA Breakthrough therapy designations for psilocybin for treatment of TRD.<sup>7</sup>

1938

1953

1960s

1965

Psychedelic therapy developed by Dr. Abram Hoffer and Dr. Humphry Osmond, efficacious in treating alcoholics<sup>2</sup>

Drug Control Amendments forbid the manufacture and sale of psychedelic drugs (scheduling)<sup>4</sup>

“America’s public enemy number one is drug abuse.”

PRESIDENT NIXON, 1971

2016

2017

2018

2019



MAPS

FDA Breakthrough designation for MDMA-Assisted Psychotherapy and announcement of Phase 3 in PTSD<sup>6</sup>

Johnson & Johnson

FDA approval of intranasal S-ketamine for TRD<sup>8</sup>

Early research suggested efficacy in mental health

Novel results and regulatory support underscore therapeutic value

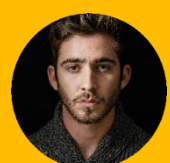
Note: LSD = Lysergic acid diethylamide; TRD = Treatment-resistant depression; MDD = Major depressive disorder; PTSD = Post-traumatic stress disorder.

- Hofmann, MAPS (1996)
- Dyck, “Hitting Highs at Rock Bottom: LSD Treatment for Alcoholism” (2006)
- Williams, “Human Psychedelic Research: A Historical and Sociological Analysis” (1999)
- FDA, Drug Law History (2018)
- Griffiths et al., “Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer” (2016)
- MAPS, announcement breakthrough designation Phase 3 (2017)
- COMPASS, COMPASS Pathways Receives FDA Breakthrough Therapy Designation for Psilocybin Therapy for Treatment-resistant Depression (2018)
- FDA, FDA Approves New Nasal Spray (2019)



# Patient reports: In a study, more than half of the patients ranked **psilocybin therapy** among the top five most meaningful experiences of their lives<sup>1</sup>

“When I had a craving, something in my head quickly thought about the good part, the taste, the feeling, the high, right? But if I think of the drug now... I quickly think about the downside. It changed the perception I have regarding the drug.”<sup>2</sup>



**Male, 25**  
**Ibogaine**

“It sort of relieved a lot of stress, a lot of negative thoughts within my body... opened my eyes to see where my stress and conflict is coming from... It is hard to explain but... it just brought a lot of grief up that I had inside me, it brought it out and I got rid of a lot of grief.”<sup>3</sup>



**Male, 55**  
**Psilocybin**

“I felt like, just like a whole new reborn person... I had not felt that happy in a long, long time. I felt way better about myself.”<sup>4</sup>



**Female, 19**  
**Ayahuasca**

1. Griffiths et al., “Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance” (2006)  
 2. Schenberg et al., “Treating drug dependence with the aid of ibogaine: A qualitative study” (2017)  
 3. Watts et al., “Patients’ Accounts of Increased ‘Connectedness’ and ‘Acceptance’ After Psilocybin for Treatment-Resistant Depression” (2017)  
 4. Argento et al., “Exploring ayahuasca-assisted therapy for addiction: A qualitative analysis of preliminary findings among an Indigenous community in Canada” (2019)

# The atai platform: Decentralized drug development process that leverages our team and enabling technologies to aim for improved probability of clinical success



**People**

- Small teams with entrepreneurial autonomy develop our compounds
- Operational involvement of interdisciplinary atai team
- Access to experienced group of strategic advisors and KOLs

bridgebio ROIVANT SCIENCES

**Process**

- Disciplined selection criteria (including prior evidence in humans)
- Impactful capital allocation to acquired and incubated companies
- Strategic value capturing and high degree of optionality

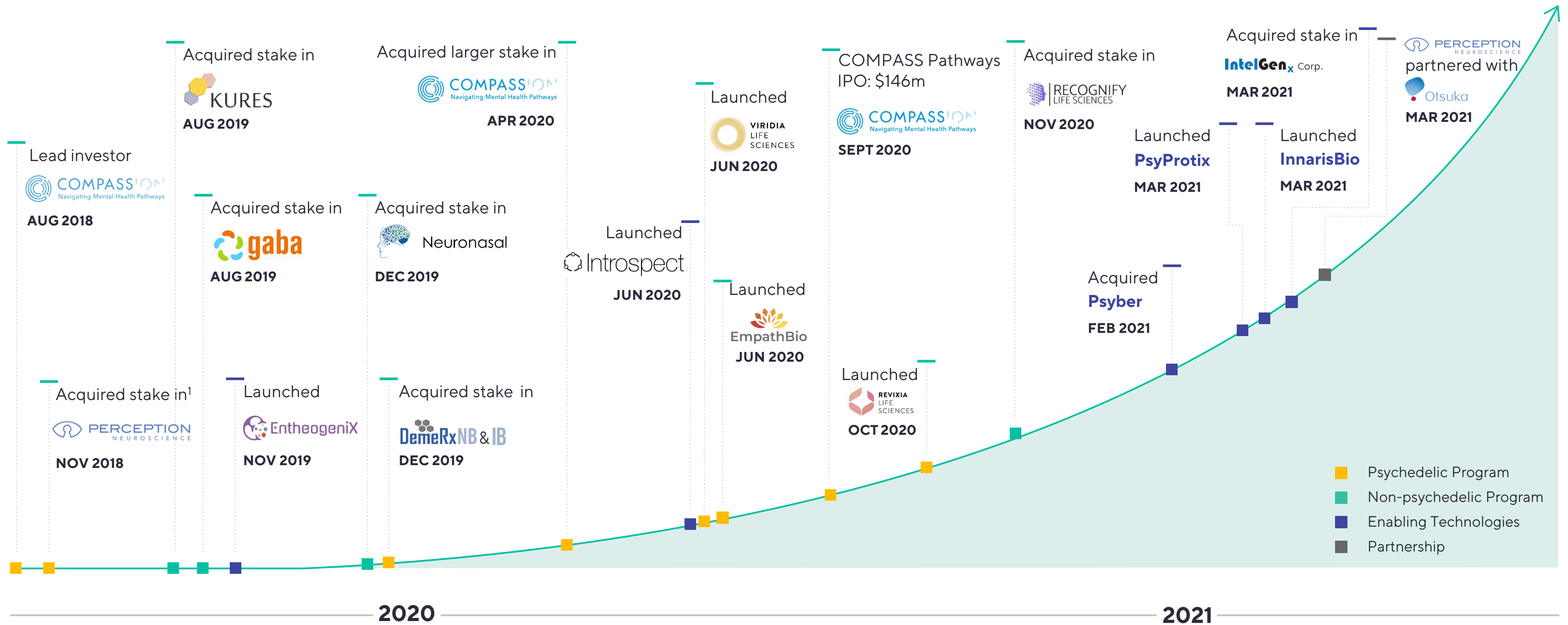
COMPASSION Navigating Mental Health Pathways Otsuka

**Enabling Technologies**

- Digital Therapeutics
- Formulation and biomarkers
- AI-enabled drug discovery

Introspect EntheogeniX

# Rapid Growth via incubations and acquisitions: 6 psychedelic programs, 5 non-psychedelic programs and 6 enabling technologies



1. Ketamine and S-ketamine are psychedelic/dissociative at therapeutic doses, while R-ketamine (the enantiomer that Perception Neuroscience is developing) is assumed to be nonpsychedelic at effective doses.

# Development program overview: Lead compounds, lead indications and stage of development

Lead Compound	Lead Indication	Preclinical	Phase 1	Phase 2	Phase 3	Affiliate Company <sup>1</sup>
PCN-101 / R-ketamine	Treatment-Resistant Depression					Perception Neuroscience
RL-007 / Compound <sup>2</sup>	Cognitive Impairment Associated With Schizophrenia					Recognify Life Sciences
DMX-1002 / Ibogaine	Opioid Use Disorder					DemeRx IB
GRX-917 / Deuterated etifoxine	Generalized Anxiety Disorder					GABA Therapeutics
NN-101 / N-acetylcysteine	Mild Traumatic Brain Injury					Neuronasal
KUR-101 / Deuterated mitragynine	Opioid Use Disorder					Kures
EMP-01 / MDMA derivative	Post-Traumatic Stress Disorder					EmpathBio
RLS-01 / Salvinorin A	Treatment-Resistant Depression					Revixia Life Sciences
VLS-01 / DMT	Treatment-Resistant Depression					Viridia Life Sciences

## LIMITED TO EQUITY INTEREST

Developing COMP360 therapy, with psychological support from specially trained therapists, for treatment-resistant depression. Phase 2b topline data expected in Q4 '21.

COMPASS Pathways

Developing DMX-1001, a formulation of noribogaine, as a potential at-home maintenance therapy for OUD. Preclinical stage.

DemeRx NB

Note: DMT = N,N-dimethyltryptamine; MDMA = 3,4-Methylenedioxymethamphetamine.

(1) Perception, Recognify, DemeRx IB and Neuronasal are all variable interest entities; GABA is a non-consolidated VIE with operational involvement through MSA model, including Srinivas Rao serving as CMO; EmpathBio, Revixia and Viridia are wholly-owned subsidiaries; COMPASS Pathways and DemeRx NB are 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 salt.

## SUMMARY

OWNERSHIP 19.4%<sup>1</sup>

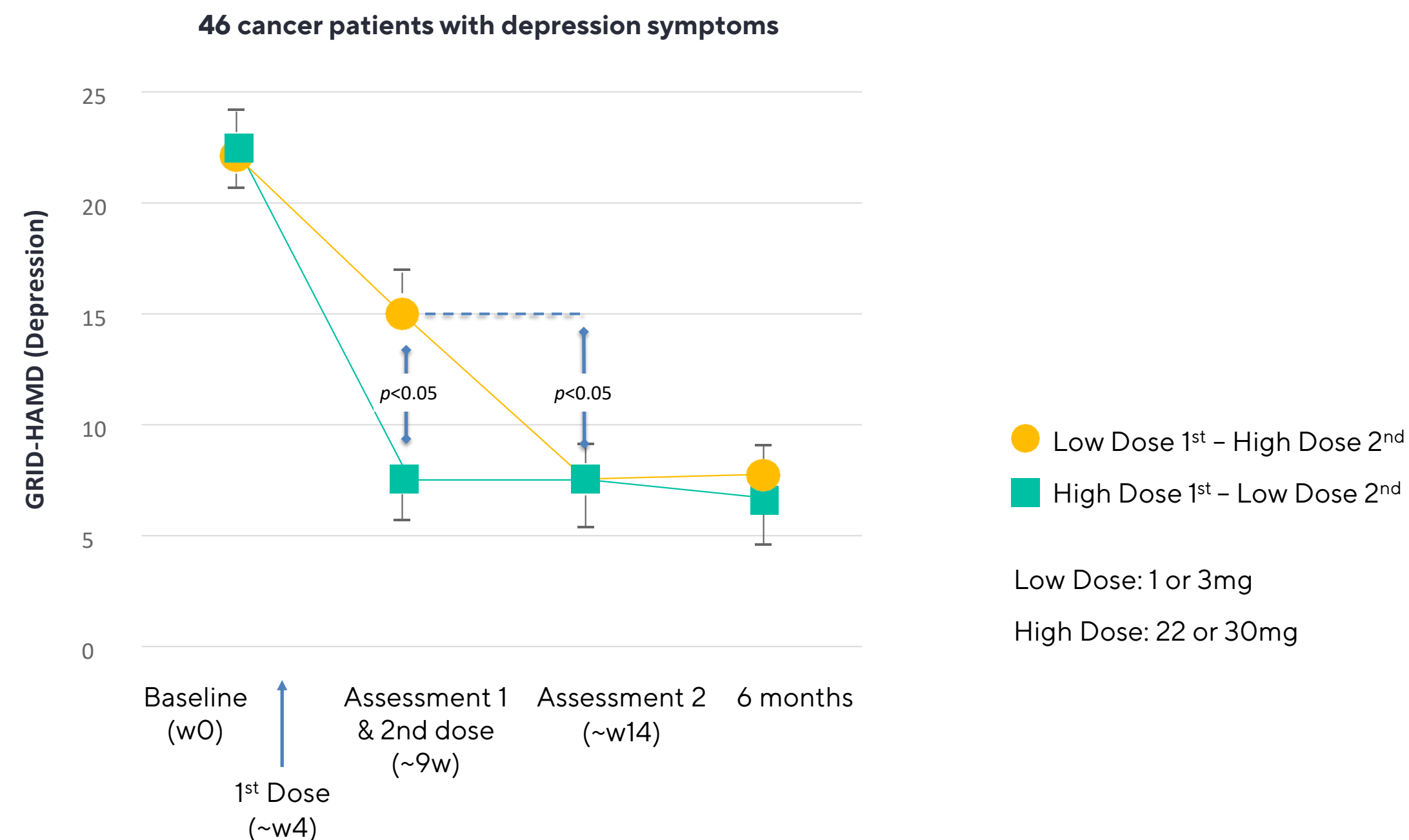
PRODUCT Oral Psilocybin (COMP360)

PHARMA-  
COLOGY 5-HT<sub>2A</sub>-R agonistPRODUCT  
FEATURES Rapid onset, potential for sustained efficacy after single doseINDICATIONS Primary: Treatment Resistant Depression  
Potential: Major Depressive Disorder, Anorexia, Autism, Bipolar Disorder, Chronic Cluster Headache, Body Dysmorphic DisorderCURRENT  
STATUS COMP360 Phase 1 trial completed and results publicly available, Phase 2b trial results expected end of 2021INTELLECTUAL  
PROPERTY Proprietary formulation of synthetic psilocybin, COMP360

HIGHLIGHT Psilocybin demonstrated efficacy in reducing depressive symptoms in humans in an academic, third-party study

# Early clinical signals have shown psilocybin therapy leads to rapid and sustained reduction in depressive symptoms

## PRIOR EVIDENCE IN HUMANS (THIRD PARTY STUDY<sup>2</sup>)



Note: GRID-HAMD = GRID Hamilton 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. Unless otherwise indicated herein, ownership percentage based on ownership of securities with voting rights as of June 30<sup>th</sup>, 2021.

2. Griffiths et al., "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer" (2016)

## SUMMARY

OWNERSHIP 58.9%<sup>1</sup>

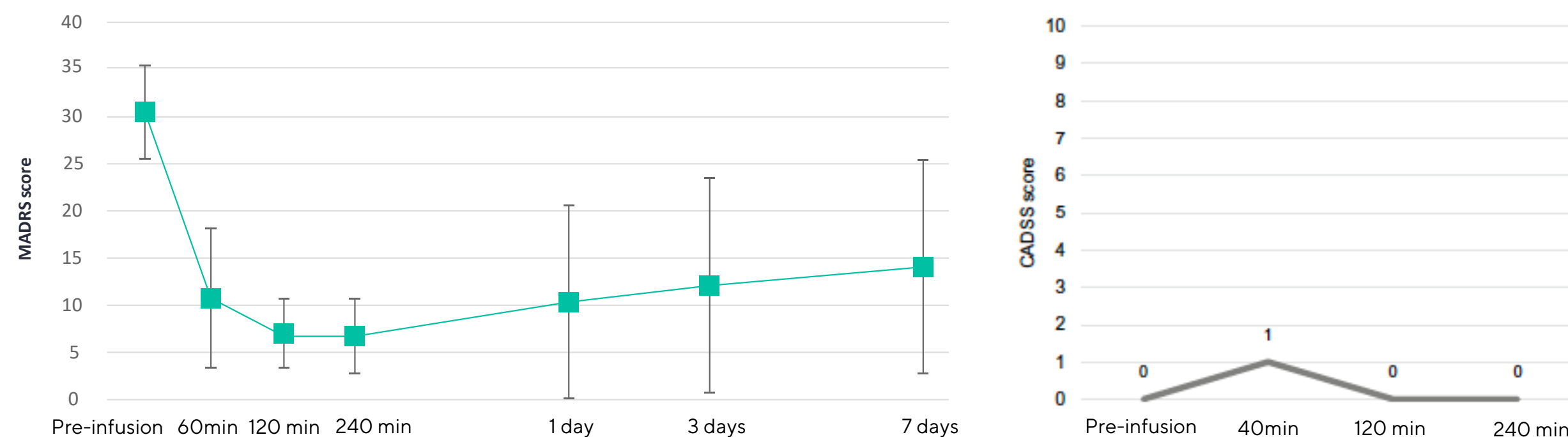
PRODUCT Subcutaneous R-ketamine (PCN-101)

PHARMA-  
COLOGY Glutamatergic modulatorPRODUCT  
FEATURES Rapid-acting, nonpsychedelic antidepressant with potential for at home useINDICATIONS Primary: Treatment Resistant Depression  
Potential: Substance Use DisorderCURRENT  
STATUS Phase 1 trial showed safety and tolerability of R-ketamine at doses of up to 150mg, Phase 2 trial initiated in Q3 '21INTELLECTUAL  
PROPERTY Issued methods of use of R-ketamine for treatment of depressive symptomsHIGHLIGHT 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<sup>1</sup>

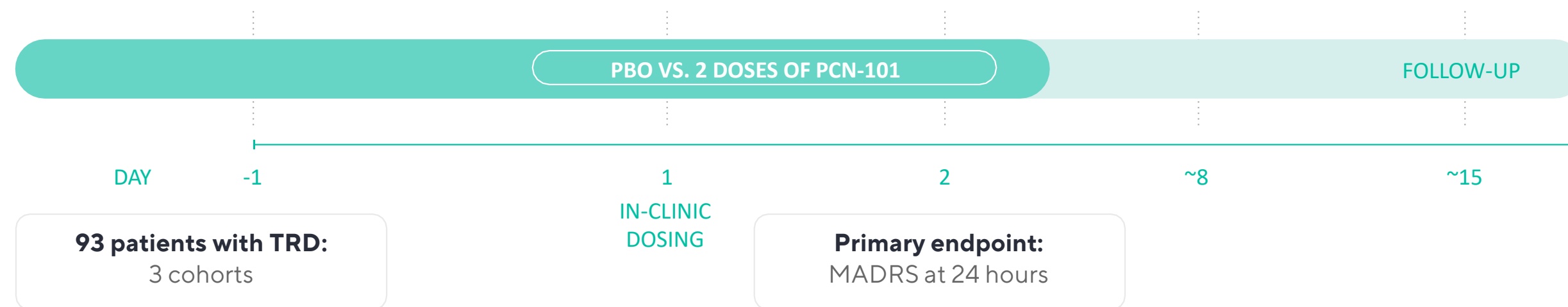
# We aim to develop PCN-101 as a rapid acting antidepressant with potential for at-home use

## PRIOR EVIDENCE IN HUMANS (THIRD PARTY STUDY<sup>2</sup>)

Mean MADRS over 7 days and median CADSS scores of TRD patients after single IV dose (0.5mg/kg) of R-ketamine (n=7)<sup>1</sup>



## PLANNED PCN-101 PHASE 2 TRIAL: Randomized, double blind, placebo-controlled (n=93)

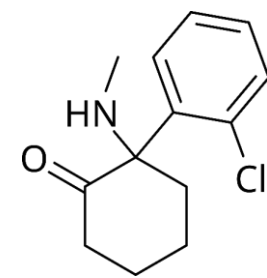


Note: MADRS = Montgomery-Asberg Depression Rate Scale, CADSS = Clinician-administered dissociative states scale, IV = Intravenous, PBO = Placebo.

1. Unless otherwise indicated herein, ownership percentage based on ownership of securities with voting rights as of June 30th, 2021. 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)

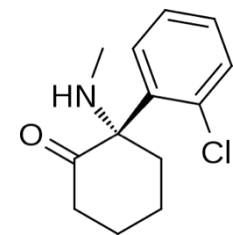
# Deep-dive R-ketamine vs. S-ketamine: Higher-potency, longer lasting antidepressant effect and lower potential for abuse in preclinical models

## Profile of R- vs. S-ketamine

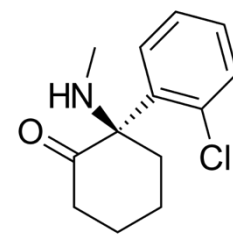


**Ketamine (racemate)**

**S-ketamine**



**R-ketamine**



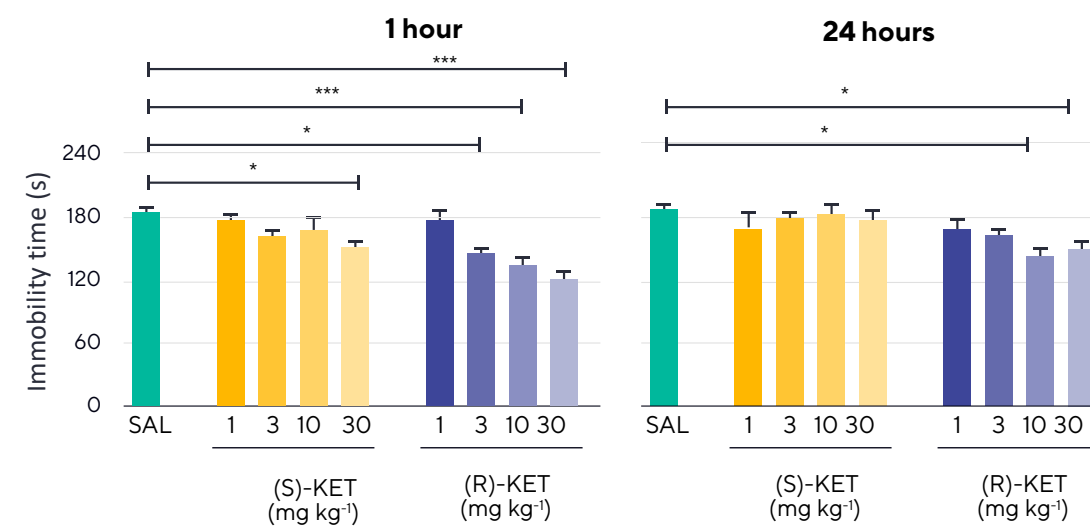
R-ketamine lacks the psychotomimetic and abuse potential of S-ketamine at therapeutic doses in preclinical models.

Like S-ketamine, R-ketamine's mechanism involves increased neuroplasticity through glutamatergic modulation, with potency differences putatively arising from:

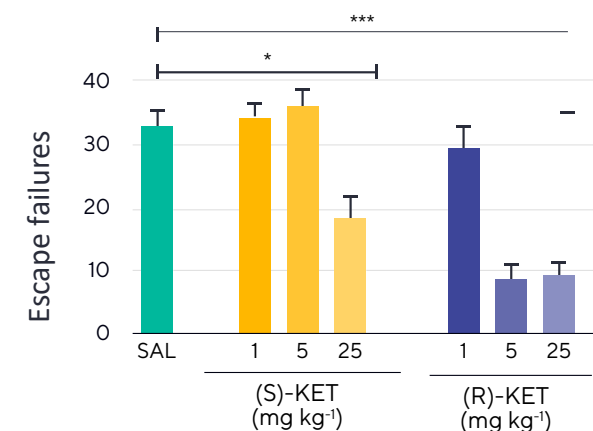
- Different active metabolite profiles
- Different pre- and post-synaptic sites of action
- Involvement of different intracellular pathways (mTORC1 vs. ERK)

## Superior and more durable

### Forced swim test<sup>1</sup> (third party study)



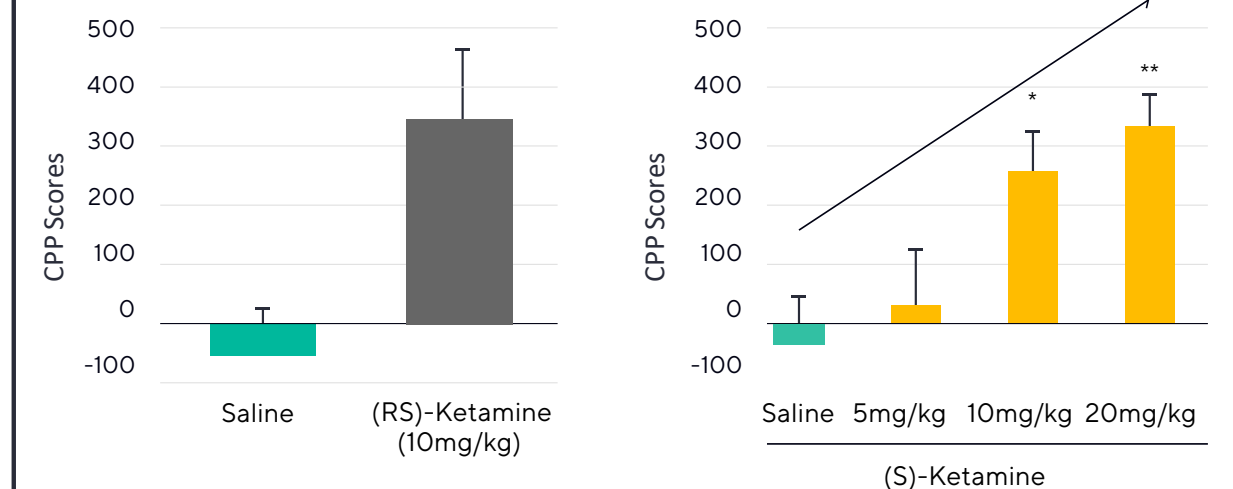
### Learned helplessness test



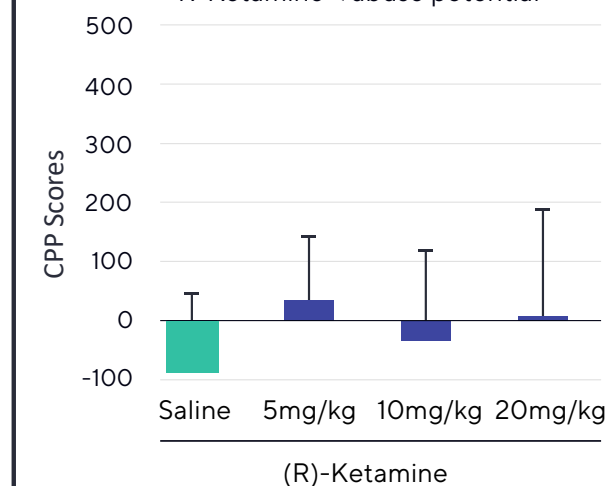
**R-ketamine outperformed and outlasted S-ketamine** in mice; confirmed in multiple other animal models in different labs

## Lower potential for abuse

### Conditioned place preference score test<sup>2</sup> (third party study)



R-Ketamine < abuse potential



**R-ketamine showed less potential for abuse** in mice models, while racemic and S-ketamine have significant risk

Note: mTORC1 = Mechanistic target of rapamycin complex 1, ERK = Extracellular signal-regulated kinases.

Sources: Wei et al., "A historical review of antidepressant effects of ketamine and its enantiomers" (2020); Chang et al., "Comparison of antidepressant and side effects in mice after intranasal administration of (R,S)-ketamine, (R)-ketamine, and (S)-ketamine" *Pharmacology Biochemistry and Behavior* (2019);

1. Zanos et al., "NDMAR inhibition-independent antidepressant actions of ketamine metabolites" (2016);

2. Yang et al., "R-ketamine: a rapid-onset and sustained antidepressant without psychotomimetic side effects" (2015).

# SUMMARY



OWNERSHIP 100%<sup>1</sup>

PRODUCT

Dimethyltryptamine (DMT) in a buccal transmucosal film (VLS-01), DMT is the active psychedelic moiety in Ayahuasca

PHARMA-  
COLOGY

5-HT<sub>2A</sub>-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  
Potential: Eating Disorders, Substance Use Disorders

CURRENT  
STATUS

Pre-clinical: Formulation work and safety testing in progress; Phase 1 clinical trial anticipated to initiate in mid-'22

INTELLECTUAL  
PROPERTY

Filed provisional on formulations of DMT

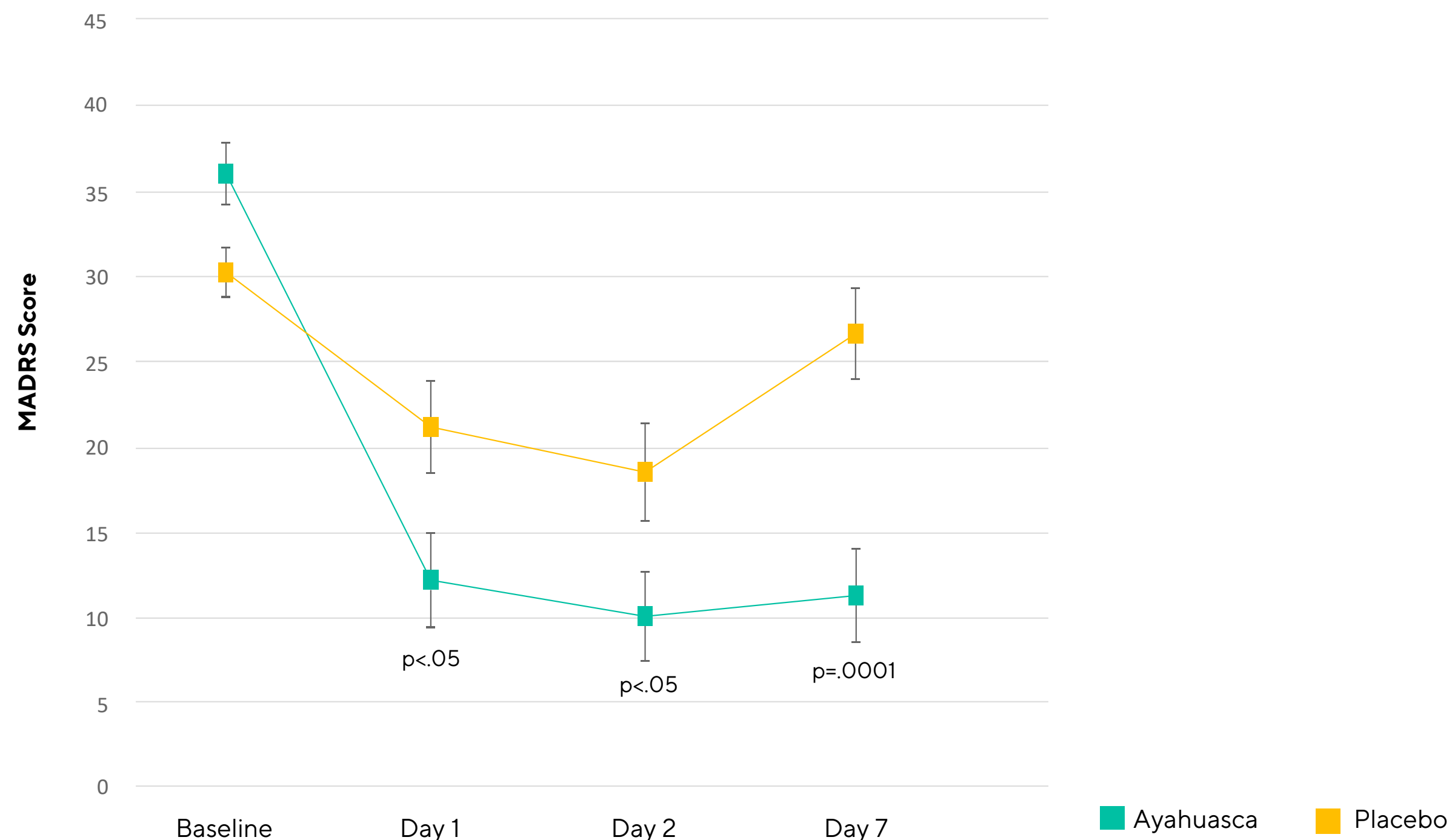
HIGHLIGHT

VLS-01 is designed to have an improved duration of psychedelic effect while improving tolerability

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

### PRIOR EVIDENCE IN HUMANS (THIRD PARTY STUDY<sup>2</sup>)

#### Double-blind, randomized placebo-controlled trial with Ayahuasca in 29 patients with TRD



Note: MADRS: Montgomery-Asberg Depression Rate Scale.

1. Unless otherwise indicated herein, ownership percentage based on ownership of securities with voting rights as of June 30th, 2021.
2. Palhano-Fontes et al. "Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression", Psychol Med (2019)



# SUMMARY



OWNERSHIP 100%<sup>1</sup>

PRODUCT

RLS-01 is a buccal formulation of Salvinorin A (SalA), a naturally occurring psychedelic compound derived from the *Salvia divinorum* plant

PHARMA-  
COLOGY

Non-orally bioavailable, non-nitrogenous agonist of the kappa-opioid receptor (KOR), no interaction with serotonergic mechanisms

PRODUCT  
FEATURES

Rapid-acting hallucinogenic compound, no wash-out of SSRIs required

INDICATIONS

Primary: Treatment Resistant Depression  
Potential: Substance Use Disorder, Pain

CURRENT  
STATUS

Phase 1 clinical trial anticipated to initiate in H2 '22

INTELLECTUAL  
PROPERTY

Filed provisional on formulation of SalA

HIGHLIGHT

Hallucinogenic experiences demonstrated by all six significantly elevated HRS clusters on an active dose, and no significant adverse events (third party study).<sup>2</sup>

# Salvinorin A's subjective effects were demonstrated to be similar to classical psychedelics

## PRIOR EVIDENCE IN HUMANS (THIRD PARTY STUDY<sup>2</sup>)

### Participant ratings on Hallucinogen Rating Scale (HRS) completed 1h after drug administration (n=30)

Cluster	Placebo	Active	P value
Affect	0.75 (0.47)	1.50 (0.58)	<0.001*
Cognition	0.37 (0.41)	1.61 (0.81)	<0.001*
Intensity	0.38 <sup>3</sup> (0.76)	3.00 <sup>2</sup> (0.77)	<0.001*
Perception	0.33 (0.36)	1.71 (0.73)	<0.001*
Somaesthesia	0.31 (0.33)	1.27 (0.54)	<0.001*
Volition	0.94 (0.53)	1.85 (0.46)	<0.001*

Study showed ability of *S. divinorum* leaf to **reach hallucinogenic states of consciousness beyond serotonergic mechanisms.**

All six **Hallucinogen Rating Scale (HRS) clusters were significantly elevated** for participants given the active *S. divinorum* leaf.

**No significant adverse events** were observed or reported by the participants.

Five patients reported **positive changes in relationships** with living family members.










Note: Data are mean ratings with one standard deviation shown in parentheses (\*P < 0.05).

1. Unless otherwise indicated herein, ownership percentage based on ownership of securities with voting rights as of June 30th, 2021.

2. Addy, "Acute and post-acute behavioral and psychological effects of salvinorin A in humans" (2011)

3. Median used instead of mean for nonparametric data

# Depression positioning and landscape: atai's programs are designed to be differentiated from one another and from competitors

	TRD treatments being developed by atai companies				Marketed therapies		Phase II and III competitors		
	Compass	Perception	Viridia	Revixia	J&J	e.g. Lilly, Pfizer	Various	GH Research	Sage / Praxis
Company									
Compound	COMP360	R-ketamine	DMT	Salvinorin A	S-ketamine	SSRI/SNRI	MIJ-821, NRX-102, JNJ-5515, AXS-05	5-MeO-DMT	SAGE-217, PRAX-114
Potential for at home use		✓				✓	✓		✓
Potential for sustained efficacy	✓	✓	✓	✓	✓		tbd	✓	tbd
Rapid onset of treatment effect <sup>1</sup>	✓	✓	✓	✓	✓		tbd	✓	✓
Mechanism of Action	5-HT2A-R agonist	Glutamatergic modulator	5-HT2A-R agonist	KOR agonist	NMDA-R antagonist	SERT / NET blockade	NMDA-R / mGluR2 antagonists	5-HT1A- and 5-HT2A-agonist	GABA <sub>A</sub> positive allosteric modulator

Note: 5HT2A-R = Serotonin 2A receptor, KOR = kappa-opioid receptor, NMDA-R = N-methyl-D-aspartate receptor, NET = Norepinephrine transporter, SERT = Serotonin Transporter, mGluR2 = Metabotropic glutamate receptor 2, GABA = Gamma-aminobutyric acid, DMT = Dimethyltryptamine, 5-MeO-DMT = 5-methoxy-N,N-dimethyltryptamine, SSRI = Selective Serotonin Reuptake Inhibitor, SNRI = Selective serotonin-norepinephrine reuptake Inhibitor., 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.

Sources: GlobalData, Evaluate Pharma (both as of 2021), Uthaug, M. V. et al. Prospective examination of synthetic 5-methoxy-N,N-dimethyltryptamine inhalation: effects on salivary IL-6, cortisol levels, affect, and non-judgment. *Psychopharmacology* 237, 773-785 (2019). company websites  
1. Rapid onset of treatment effect versus standard of care.



# SUMMARY

OWNERSHIP 59.5%<sup>1</sup>

PRODUCT Ibogaine HCl capsules (DMX-1002), ibogaine is a naturally occurring psychedelic compound isolated from a West African shrub, iboga

PHARMA-COLOGY Opioid mediated, cholinergic, glutamatergic and monoaminergic receptor modulator

PRODUCT FEATURES A single dose of ibogaine may precipitate a rapid withdrawal and long-term abstinence in OUD patients

INDICATIONS Primary: Opioid Use Disorder  
Potential: Substance Use Disorder, Post-Traumatic Stress Disorder, Traumatic Brain Injury

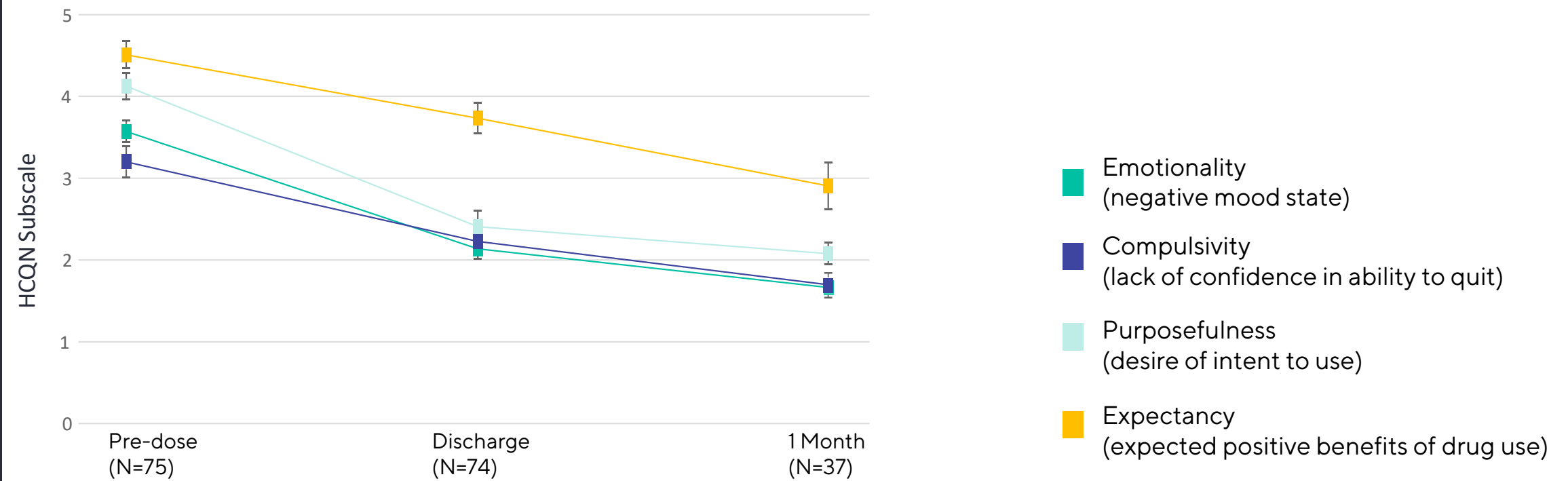
CURRENT STATUS Phase 1/2 trial initiated in Q3 '21

INTELLECTUAL PROPERTY Pending method of treatment claims for OUD for ibogaine, issued method of treatment claims for OUD patients on methadone for noribogaine<sup>3</sup>

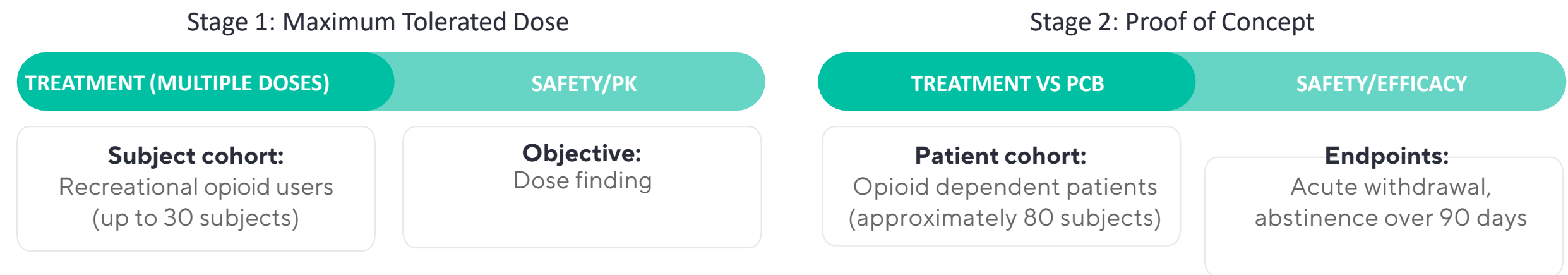
HIGHLIGHT Potential sustained reduction in opioid craving with DMX-1002 single administration

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

## PRIOR EVIDENCE IN HUMANS (THIRD PARTY STUDY<sup>2</sup>)



## ONGOING PHASE 1/2 TRIAL



Note: HCQN = Heroin Craving Questionnaire, PTSD = Post-traumatic stress disorder, OUD = Opioid use disorder, PCB = Placebo, PK = Pharmacokinetics.  
 1. Unless otherwise indicated herein, ownership percentage based on ownership of securities with voting rights as of June 30th, 2021. 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)  
 3. Noribogaine Intellectual property resides in DemeRx NB

# SUMMARY



OWNERSHIP 51.9%<sup>1</sup>

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 Cholinergic, glutamatergic and GABA-B receptor modulator

PRODUCT FEATURES No drug-related serious adverse events in over 500 study subject exposures, pro-cognitive effects demonstrated in two Phase 1 and one Phase 2 trials

INDICATIONS Primary: Cognitive Impairment Associated with Schizophrenia  
Potential: Autism, Alzheimer's dementia

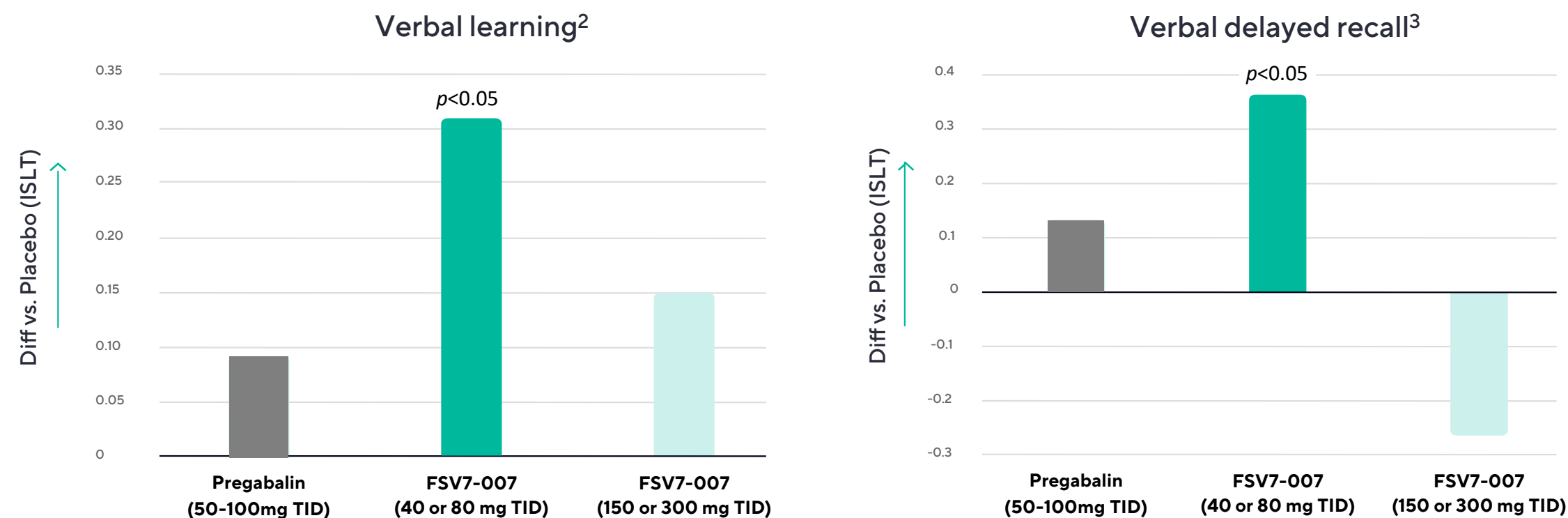
CURRENT STATUS Phase 2a trial initiated in H1'21

INTELLECTUAL PROPERTY Issued composition of matter patent

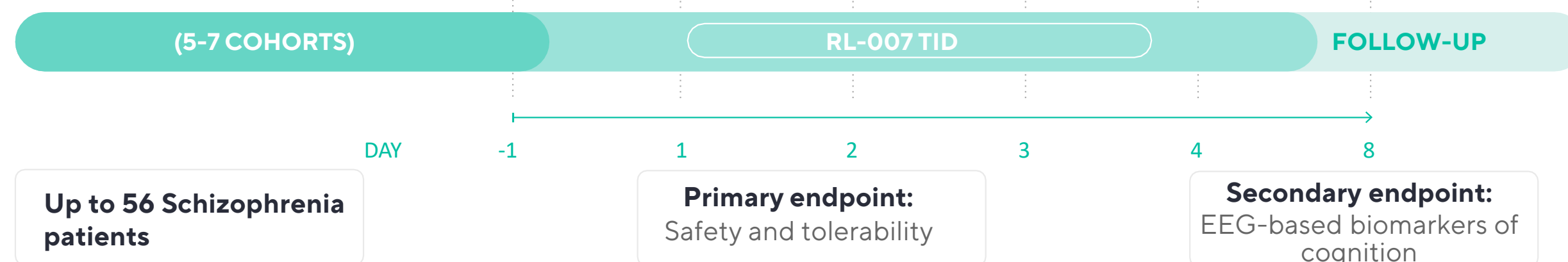
HIGHLIGHT Previous Phase 2 showed pro-cognitive potential of RL-007 in 180 patients with diabetic peripheral neuropathic pain

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

### PRIOR EVIDENCE IN HUMANS



**ONGOING PHASE 2 TRIAL:** Single-arm, single-blind dose-ranging clinical trial



Note: CIAS = Cognitive impairment associated with schizophrenia; RL-007 is (2R, 3S)-2-amino-3-hydroxy-3-pyridin-4-yl-1-pyrrolidin-1-yl-propan-1-one(L)-(+)-tartrate salt; TID denotes 3x/day dosing

1. Unless otherwise indicated herein, ownership percentage based on ownership of securities with voting rights as of June 30th, 2021.

2. Verbal learning was assessed by the "International Shopping List Task" (ISLT)

3. Verbal delayed recall was assessed by ISLT with a delayed recall, as a parameter for short-term memory

# SUMMARY



OWNERSHIP 53.8%<sup>1</sup>

PRODUCT Deuterated etifoxine HCl oral dosage form (GRX-917)

PHARMA-COLOGY Etifoxine facilitates endogenous production of neurosteroids like allopregnanolone 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  
Potential: Social Anxiety Disorder, Postpartum Depression

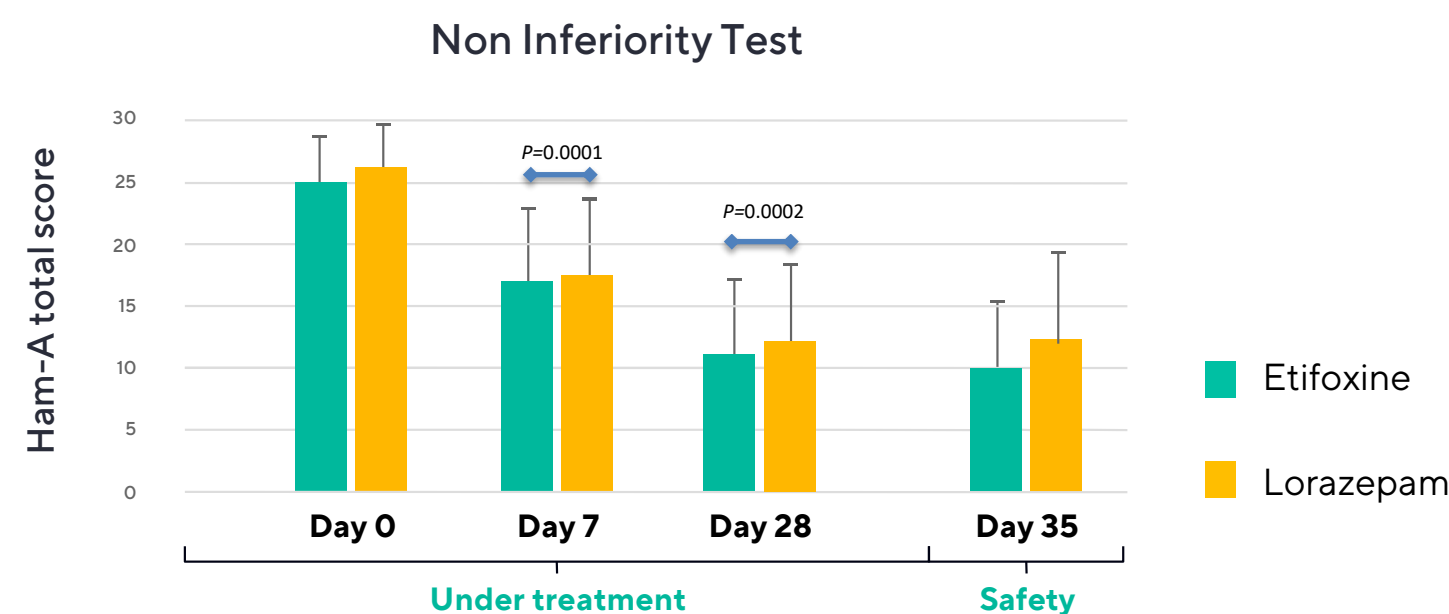
CURRENT STATUS Phase 1 trial initiated in H1'21

INTELLECTUAL PROPERTY Issued composition of matter on deuterated etifoxine (GRX-917) and corresponding methods of use

HIGHLIGHT GRX-917 is aimed to be an improved version of Etifoxine, which already showed promising results

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

## PRIOR EVIDENCE IN HUMANS (THIRD PARTY STUDY<sup>2</sup>)



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<sup>3</sup>

## ONGOING PHASE 1 TRIAL

### Part 1: Single Ascending Dose

TREATMENT

SAFETY/PK/PD

Up to 40 healthy subjects:  
Up to 5 cohorts

PD Endpoint:  
qEEG

### Part 2: Multiple Ascending Dose

TREATMENT

SAFETY/PK/PD

Up to 36 healthy subjects:  
Up to 3 cohorts

PD Endpoint:  
qEEG

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

1. Unless otherwise indicated herein, ownership percentage based on ownership of securities with voting rights as of June 30th, 2021.

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)



# SUMMARY

OWNERSHIP 100%<sup>1</sup>

PRODUCT

EMP-01 is an oral formulation of an MDMA derivative being developed for the treatment of PTSD

PHARMA-  
COLOGY

A monoamine releaser and reuptake inhibitor with prominent effects on serotonin (5-HT)

PRODUCT  
FEATURES

An entactogen; a compound class that increases feelings of empathy and closeness-- with a potentially improved cardiovascular profile compared to MDMA

INDICATIONS

Primary: Post-traumatic Stress Disorder  
Potential: General Anxiety Disorder

CURRENT  
STATUS

Phase 1 trial anticipated to initiate in mid '22

INTELLECTUAL  
PROPERTY

Filed provisional on formulation, combination approach

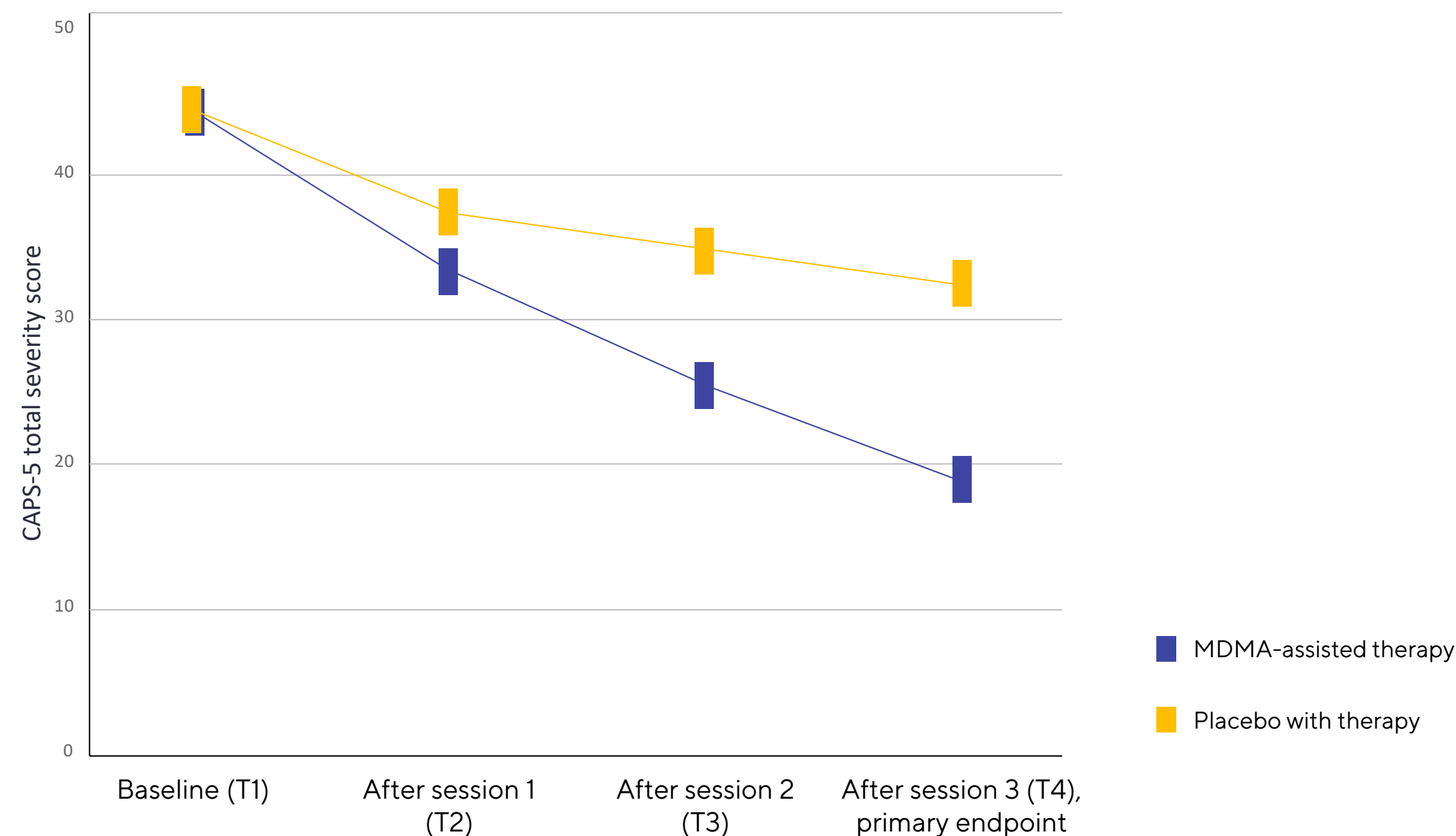
HIGHLIGHT

EMP-01 is aimed to be an improved version of MDMA to treat PTSD symptoms, through an improved cardiovascular profile and potential digital therapeutic support

## MDMA-assisted psychotherapy significantly reduced PTSD symptoms in 90 severe PTSD patients

### PRIOR EVIDENCE IN HUMANS (THIRD PARTY STUDY<sup>2</sup>)

MDMA-assisted therapy significantly reduced CAPS-V scores in PTSD patients (primary endpoint), (n=90)



Note: Change in CAPS-V total severity score from T1 to T4 ( $P < 0.0001$ ,  $d = 0.91$ ,  $n = 89$  (MDMA  $n = 46$ )), as a measure of the primary outcome. Primary analysis was completed using least square means from a mixed model repeated measure (MMRM) analysis model; ( $n=90$ )

1. Unless otherwise indicated herein, ownership percentage based on ownership of securities with voting rights as of June 30th, 2021.
2. Mitchell et al., "MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study" (2021)

# Deep dive Introspect: Powerful digital therapeutics strategies across the pipeline with goal to improve treatment outcomes

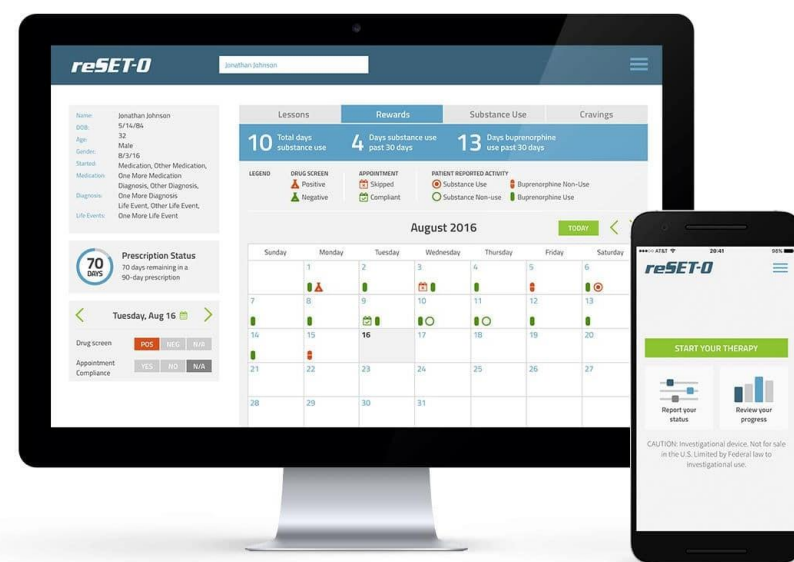


Pear Tx created a precedent

Positive regulatory sentiment

atai's opportunity

reSET-O © from Pear Therapeutics is the first prescription digital therapeutic that obtained FDA approval for treatment of patients with OUD (2018)



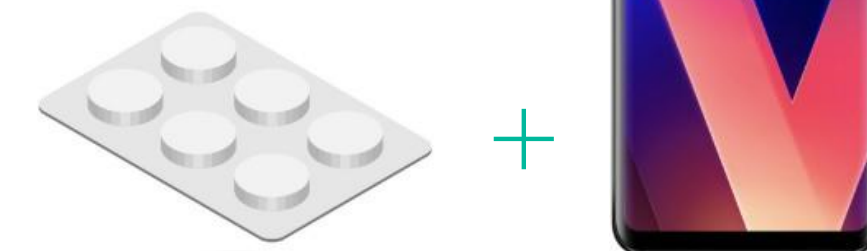
FDA is supporting and stimulating Digital Health initiatives<sup>1</sup>:



Aimed at improved therapeutic outcomes

Regulatory exclusivity possible through development of combination product (i.e., digital app + drug)

Combination also provides opportunity for IP scope expansion



1. FDA, "Digital Health Innovation Action Plan" (2018)

# Financial Position

<b>Issuer (ticker)</b>	ATAI Life Sciences N.V. (NASDAQ: ATAI)
<b>Market capitalization</b>	~\$2.2B <sup>(1)</sup>
<b>Outstanding shares</b>	154.8M <sup>(1)</sup>
<b>Cash &amp; cash equivalents</b>	<ul style="list-style-type: none"> <li>• \$453.6 million as of June 30, 2021</li> <li>• atai is well financed to fund planned operations through 2023</li> </ul>

**APEIRON**<sup>®</sup>  
INVESTMENT GROUP

  
NOVATOR

**CATALIO**  
CAPITAL MANAGEMENT

**THIEL**

  
**GALAXY**  
INVESTMENT PARTNERS, LLC

  
**WOODLINE**  
PARTNERS

  
**FUTURE**  
VENTURES

SUBVERSIVE  
CAPITAL

  
FALCON EDGE CAPITAL

MOORE CAPITAL MANAGEMENT, LP 

**puravida**  
INVESTMENTS 

(1) Market capitalization as of close on October 20<sup>th</sup>, 2021

(2) Shares outstanding as of June 30<sup>th</sup>, 2021







**Investor Contact:**

Greg Weaver

Chief Financial Officer

Email: [greg.weaver@atai.life](mailto:greg.weaver@atai.life)



# Appendix

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## ATAI PLATFORM

### INDICATION DEEP DIVES:

- Overview
- Depression
- CIAS
- SUD
- Anxiety
- mTBI
- MoA



**The atai approach:**  
We are leveraging a  
platform approach to  
to aim for improved  
**probability of clinical  
success**



**Process**



**People**



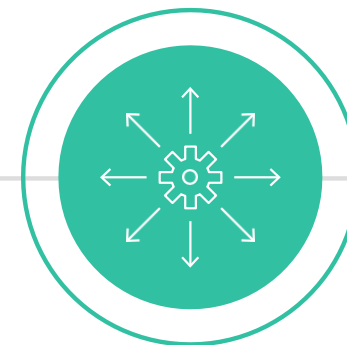
**Enabling Technologies**

# Our process is designed to aim for effective program selection, drug development and value capturing



## Disciplined New Program Selection

- ✓ Prior evidence in humans to increase probability of success
- ✓ Differentiated treatment effect to address unmet patient needs
- ✓ Significant commercial potential and complementary to drug candidates already in pipeline



## Capital Allocation and Decentralized Operations

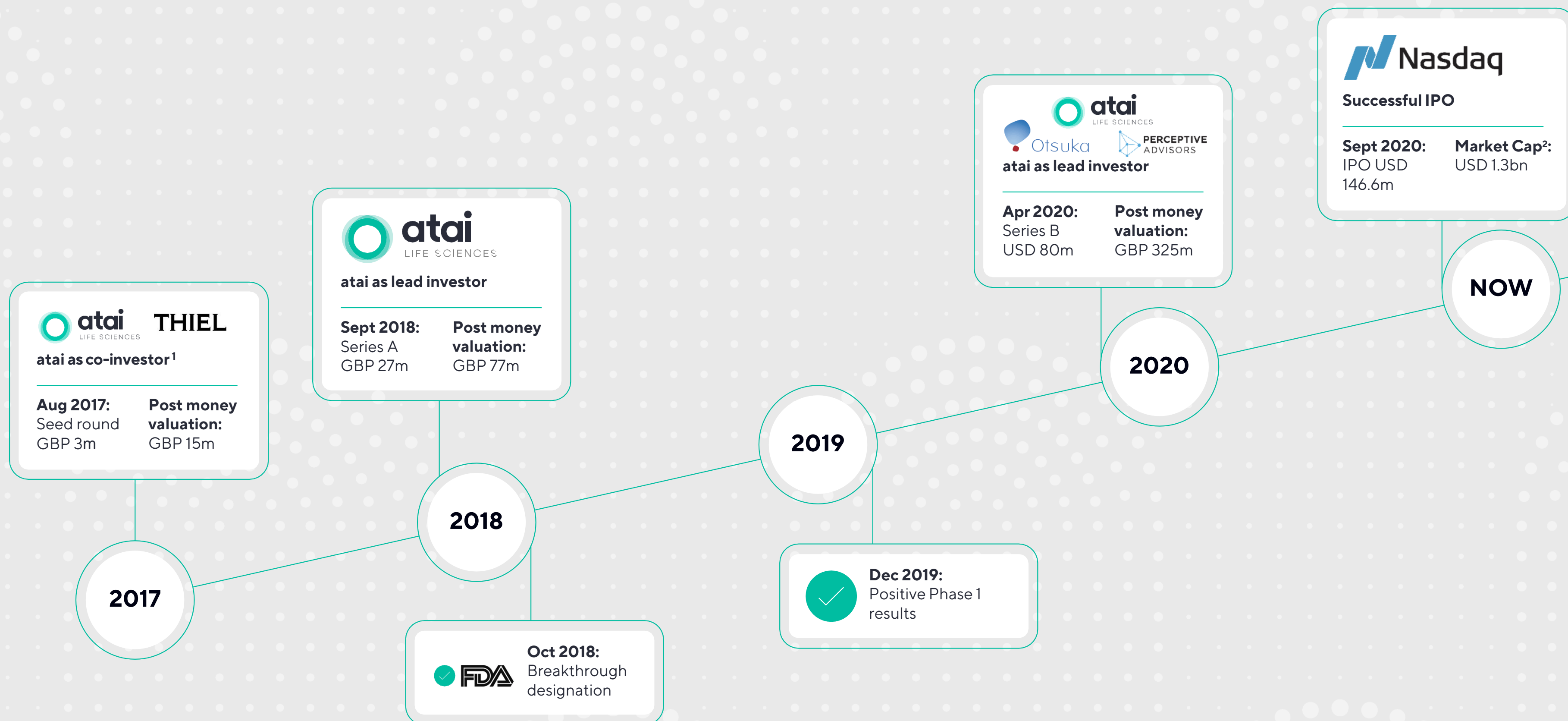
- ✓ Small teams with entrepreneurial autonomy develop our drugs
- ✓ Access to milestone-based funding, shared services and enabling tech
- ✓ Economies of scope and cross-fertilization across our development programs



## Optionality and Strategic Value Capture

- ✓ Internal Development 
- ✓ Strategic Partnerships 
- ✓ IPO 

# Case study: COMPASS Pathways creates a precedent for atai's companies: From **foundation** in 2017 to **public company** today



1. atai co-founder, Christian Angermayer (though his family office, Apeiron) was initial investor into Compass which shareholding was contributed to atai upon atai's incorporation  
2. Market Cap as of October 3, 2021

# Our People: Over 50 atai professionals with strong track record and a group of experienced advisors support the CEOs of our companies with the execution of our trials



**Ryan Barrett**  
GC & Lead of  
Corporate Development



**Greg Bates**  
VP, Regulatory Affairs



**Roman Dahl**  
VP, Operations &  
Innovation



**Majed Fawaz, PhD**  
VP, CMC



**Kasia Frankfort**  
VP, FP&A



**Iqbal Husain**  
VP, Project Direction



**Anne Johnson**  
VP, Global Controller



**David Keene**  
VP, Digital Therapeutics



**Georgina Kilfoil, PMP**  
VP, Clinical Operations



**Glenn Short, PhD**  
VP, Early Development



**Frank Stegert**  
VP, Operations and  
Investment



**Arvind Tewari**  
VP, Digital Strategy and  
Operations



**Vicki Klutzaritz**  
Sr Director, Development  
Operations



**Sanjeev Kumar**  
Sr Director, Technical  
Accounting



**Edmund Neuhaus, PhD**  
Senior Director,  
Psychology



**Carrie Bowen, PhD**  
Director, Neuroscience



**Josh Elliott**  
Director,  
Communications



**Sebastian Giraldo**  
Director, Treasury



**Sarah McEwen, PhD**  
Director, Clinical Science



**Galyna Pidpruzhnykova, PhD**  
Director, Innovation Strategy



**Anna Richardson**  
Chief of Staff, Director  
Stakeholder Engagement



**Nicki Shah**  
Director, Talent  
Acquisition



**Paul Simboli**  
Director, IP Counsel



**Danny Talati**  
Director, Business  
Development



**Michael Auerbach**  
Supervisory Board



**Jason Camm**  
Supervisory Board



**Andrea Heslin Smiley**  
Supervisory Board



**Amir Kalali, MD**  
Supervisory Board



**Sabrina Martucci Johnson**  
Supervisory Board



**Alexis de Rosnay**  
Supervisory Board



**Terence A. Kelly, PhD**  
CEO Perception  
Neuroscience



**Ian Massey**  
CEO GABA  
Therapeutics



**Deborah Mash, PhD**  
CEO DemeRx



**Tom Bradshaw**  
CEO Neuronasal



**Matthew Pando, PhD**  
CEO Recognify



**Pralahad Krishnan**  
CEO Psyber



# Our enabling technologies are designed to drive efficient drug discovery and improved treatment outcomes

## Digital Therapeutics



- ✓ Wholly owned digital therapeutics platform dedicated to providing more comprehensive, personalized care management with potential to secure stronger IP protection

## Psyber

- ✓ Utilizes digital combination tools to empower atai's programs, such as remote monitoring and remote counseling

## AI Enabled Drug Discovery



- ✓ Joint venture with **Cyclica**, with atai currently owning 80%
- ✓ AI-enabled computational biophysics platform designed to optimize and accelerate drug discovery
- ✓ Potential to be a product engine for atai supporting the next generation of novel programs

## Formulation & Biomarker Stratification

### PsyProtix

- ✓ Metabolomics based biomarker approach to develop precision psychiatry

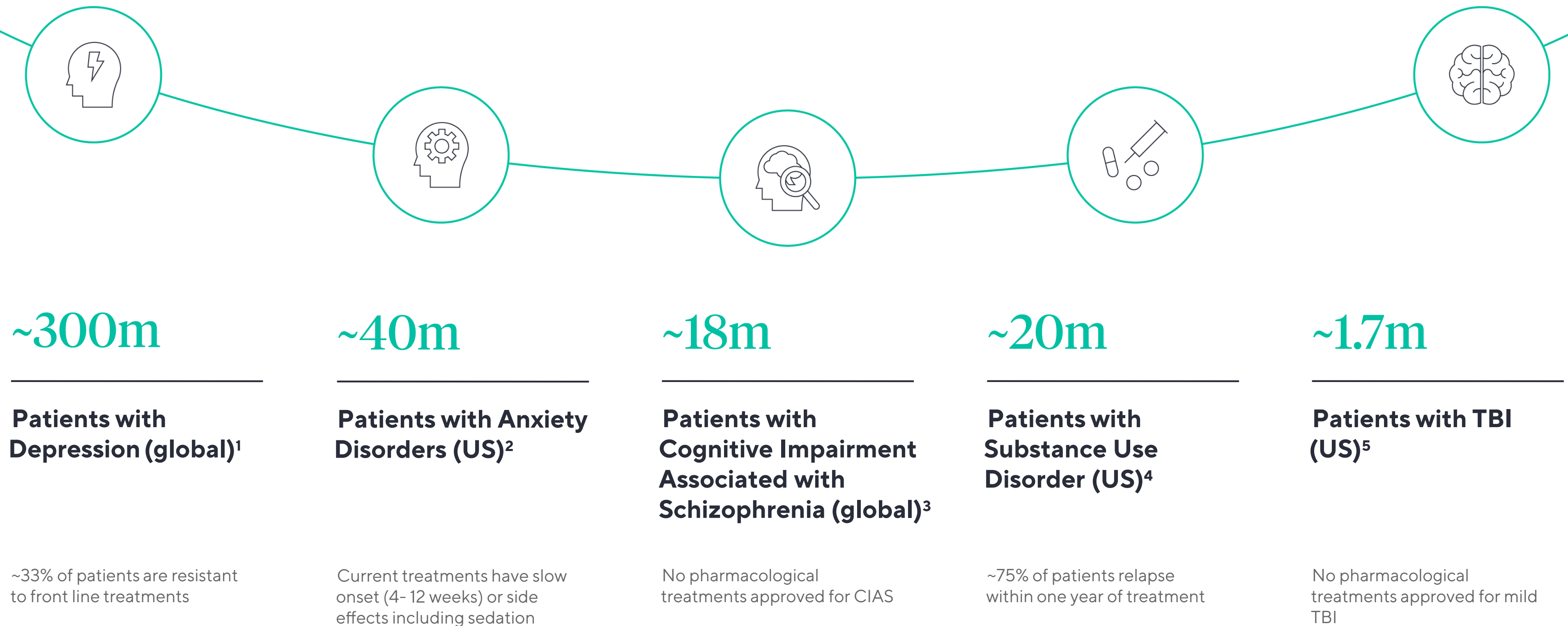
### InnarisBio

- ✓ Joint venture with **Uniquet** to advance direct-to-brain drug delivery technology

### IntelGen<sub>x</sub> Corp.

- ✓ Partnership with **IntelGenx** to develop innovative transmucosal formulations

# We are initially focused on **mental health disorders (DSM-V)** with current **unmet patient need** and **significant market opportunities**



1. World Health Organization (2020)

2. Anxiety and Depression Association of America (2020)

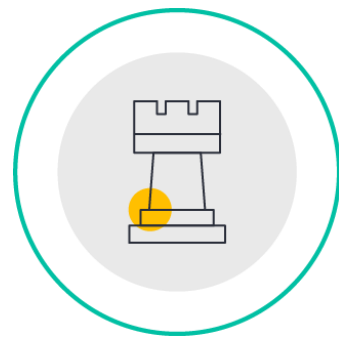
3. Using CSCI Criterion; Reichenberg et al., "Neuropsychological Function and Dysfunction in Schizophrenia and Psychotic Affective Disorders" (2009)

4. SAMSHA - National Survey on Drug Use and Health (2017)

5. Georges et al, "Traumatic Brain Injury", NCBI (2020)



# Robust Ability to Block Strategy: IP, regulatory and restrictive covenants create framework for excluding would-be competitors



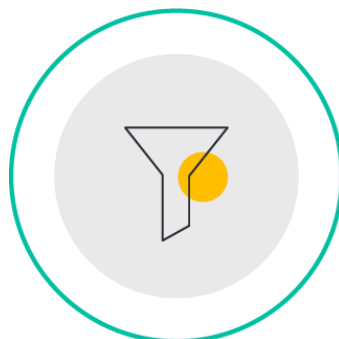
**Robust Specialty  
Pharma IP Strategy**



**Drug & Digital  
Combo  
Therapeutics  
Exclusivity  
Strategy**



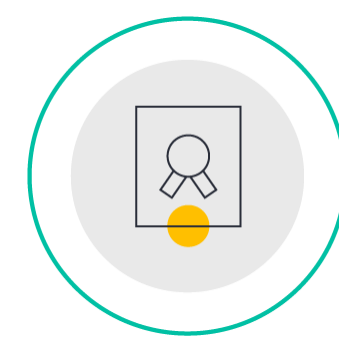
**New Chemical  
Entity Engine**



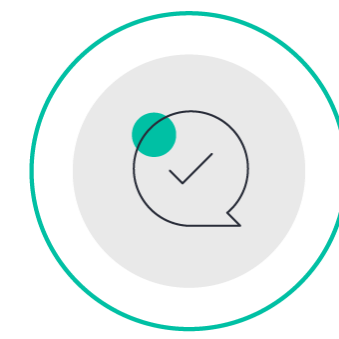
**Differential  
De-scheduling**



**Strategic  
Restrictive  
Covenants**



**Pursuit of  
Extensions of  
Patent Scope**



**Leading IP and  
Regulatory  
Advisors**

# Depression

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# Depression

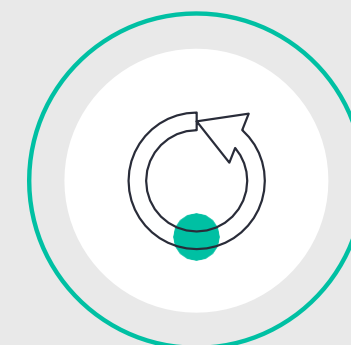
## Opportunity Overview

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



**~300m**

**Global sufferers of depression<sup>3</sup>**



**~60-70%**

**Likelihood of relapse from current SoC<sup>4</sup>**



**~100m**

**Global TRD patients<sup>5</sup>**

## Treatment options for TRD



Antidepressants

Augmentation therapy<sup>1</sup>

S-ketamine

Somatic therapy<sup>2</sup>

High-intensity psychological interventions



**2**

**Approved drugs for TRD (Spravato, Symbyax)**



**\$8bn+**

**Relative market opportunity (antidepressant sales by 2025)<sup>6</sup>**

1. Includes mood stabilizers, atypical antipsychotics, and esketamine.

2. Includes rTMS (repetitive transcranial magnetic stimulation), tDCS (transcranial direct current stimulation), ECT (electroconvulsive therapy), and DBS (deep-brain stimulation).

3. World Health Organization (2020)

4. Hasler et al., Acute psychological and physiological effects of psilocybin in healthy humans: a double-blind, placebo-controlled dose effect study (2004)

5. Pandarakalam, 2018; Sussman et al., 2018; Gaynes et al., 2019

6. Evaluate Pharma (as of 19.03.2021)

# atai is targeting depression via **multiple complementary approaches**

		Depression			
		COMPASSION Navigating Mental Health Pathways	VIRIDIA LIFE SCIENCES	PERCEPTION NEUROSCIENCE	REVIXIA LIFE SCIENCES
	<b>Company</b>				
	<b>Compound</b>	COMP360	DMT	R-ketamine	Salvinorin A
<b>Population / Drug class</b>	<b>Indication</b>	TRD	TRD	TRD	TRD
	<b>MoA Target / Drug Class</b>	5-HT <sub>2A</sub> -R agonist	5-HT <sub>2A</sub> -R agonist	Glutamatergic modulator	Kappa opioid agonist
<b>Convenience / Use</b>	<b>Potential for at home use</b>	⊗	⊗	⊙	⊗
	<b>Potential for concomitant use with SSRIs</b>	⊗	⊗	⊙	⊙
	<b>In-clinic duration</b>	6-8 hours	~2 hours	N/A	~2 hours
<b>Commercial</b>	<b>Distribution channels</b>	New clinics infrastructure	S-ketamine/ psilocybin clinics	Pharmacies	S-ketamine/ psilocybin clinics

# Cognitive Impairment Associated with Schizophrenia

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# Cognitive Impairment Associated with Schizophrenia (CIAS)

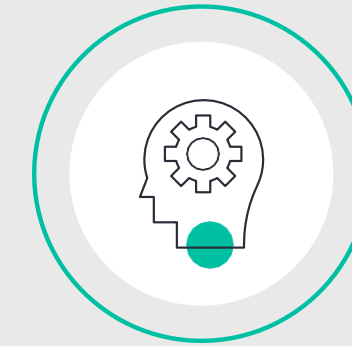
## Opportunity Overview

Schizophrenia is a chronic, psychiatric disorder characterized by a heterogeneous combination of symptoms, including psychosis, social withdrawal, flat emotional affect and cognitive impairment. Nearly all schizophrenia patients are affected by CIAS, limiting both social and non-social cognitive functions.



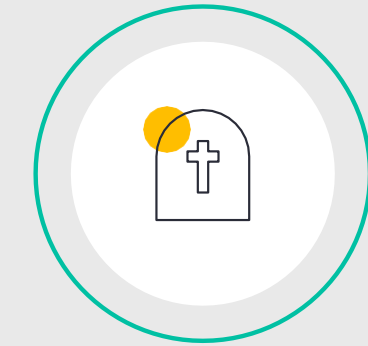
~21m

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



~84%

of schizophrenia patients suffer from significant cognitive impairment<sup>2</sup>



~20 yrs

Lost life expectancy compared to general population (schizophrenia patients)<sup>3</sup>



~\$155bn+

Estimated annual US economic burden due to schizophrenia<sup>4</sup>



\$13bn+

Relative market opportunity (antipsychotic sales by 2025)<sup>5</sup>



To date, there are no pharmacological treatments approved for CIAS

1. Charlson et al., "Global Epidemiology and Burden of Schizophrenia: Findings From the Global Burden of Disease Study" (2016)  
2. Using CSCI Criterion; Reichenberg et al., "Neuropsychological Function and Dysfunction in Schizophrenia and Psychotic Affective Disorders" (2009)

3. Laursen, Nordentoft & Mortensen, "Excess early mortality in schizophrenia" (2014)  
4. Cloutier et al., "The Economic Burden of Schizophrenia in the United States in 2013" (2016)  
5. EvaluatePharma (as of 19.03.2021)

# RL-007 is well positioned, combining a **history of safety** with a **signal of pro-cognitive** effects in humans








## PIPELINE SUMMARY

### 9 Clinical Stage Therapies in Development for CIAS

### 12 Pre-Clinical Stage Therapies in Development

### 17 Different Mechanisms of Action

Overview of Leading Clinical Stage Competitors for Cognitive Impairment Associated with Schizophrenia (CIAS)

							
<b>Therapy</b>	<b>RL-007</b>	BI-425809	PF-03463275	BIIB-104	NBI-1065844	SEP-363856	CVL-231
<b>Primary Indication</b>	<b>CIAS</b>	CIAS	CIAS	CIAS	Schizophrenia	Schizophrenia	Schizophrenia
<b>MoA</b>	<b>GABA / nicotinic modulator</b>	GlyT1 inhibitor	GlyT1 inhibitor	AMPA agonist	DAAO inhibitor	TAAR1 agonist	M4 PAM
<b>Current Phase</b>	<b>II</b>	II	II	II	II	III	I
<b>Notes</b>	<b>Previously assessed in over 500 subjects for other indications with no serious adverse events observed</b>	Completed Phase II with positive results; recruiting for Ph III	Ongoing Phase II	Ongoing Phase II, US and Japan Only	Failed to achieve primary endpoint of easing the negative symptoms of schizophrenia, but met secondary endpoints of cognitive improvement	Breakthrough therapy designation, being developed for schizophrenia but recently demonstrated small improvements in cognitive measures	Recently completed Phase Ib in patients with schizophrenia with positive results; progressing to Phase II

Note: GABA = Gamma aminobutyric acid; TAAR1 = trace amine-associated receptor; GlyT1 = Glycine Transporter 1; AAO = D Amino Acid Oxidase; AMPA =  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; M4 = muscarinic acetylcholine 4; PAM = positive allosteric modulator  
Sources: GlobalData, Evaluate Pharma (both as of 2021)

# Substance Use Disorder

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# Substance Use Disorder (SUD)

## Opportunity Overview

Substance use disorders are highly prevalent disorders characterized by an inability to control the use of a legal or illegal drug, medication or other psychoactive compound

## Treatment options for Opioid Use Disorder (OUD)



Synthetic opioid receptor agonists (methadone and buprenorphine)

Opioid antagonists (naltrexone and naloxone)



~20m+

US sufferers of SUD in 2019<sup>1</sup>



~3m

US sufferers of OUD in 2020<sup>2</sup>



~70k

US deaths from opioid drug overdose in 2020<sup>3</sup>



\$787bn

Societal cost associated with OUD in US<sup>4</sup>



~75%

of patients undergoing OUD therapy experience relapse within one year<sup>5</sup>

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
















# DMX-1002 has the potential to become the first disease-modifying treatment for OUD, minimizing risk of relapse

## SUMMARY

**DMX-1002 could potentially become a paradigm-shifting therapy for Opioid Use Disorder**

**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**

	Therapy	Mechanism of Action	Single Therapeutic Episode	No Opioid Side Effects	Minimal Abuse Potential	High Adherence / Low Risk of Relapse
<p><b>Disease Modification</b></p> <p>Single dose administered in monitored setting, providing both withdrawal support and oneiric experience with goal of complete remission</p>	Ibogaine (DMX-1002) 	Mixed MoA				
<p><b>Withdrawal Support<sup>2</sup></b></p> <p>Therapies given for symptomatic management during supervised withdrawal (detoxification)</p>	Clonidine	Alpha-2 agonist				
	Lofexidine	Alpha-2 agonist				
<p><b>Medication Assisted Therapy<sup>1</sup></b></p> <p>Daily therapy given in substitution of opioid in outpatient setting in attempt to wean off from opioid</p>	Methadone	Mu-agonist				
	Buprenorphine	Partial Mu-agonist				
	Naltrexone	Mu-antagonist				

Source: GlobalData, Evaluate Pharma (both as of 2021)

1. Current Standard of Care

2. Rarely used given high rates of relapse. Used primarily in institutional or penitentiary settings

# Anxiety

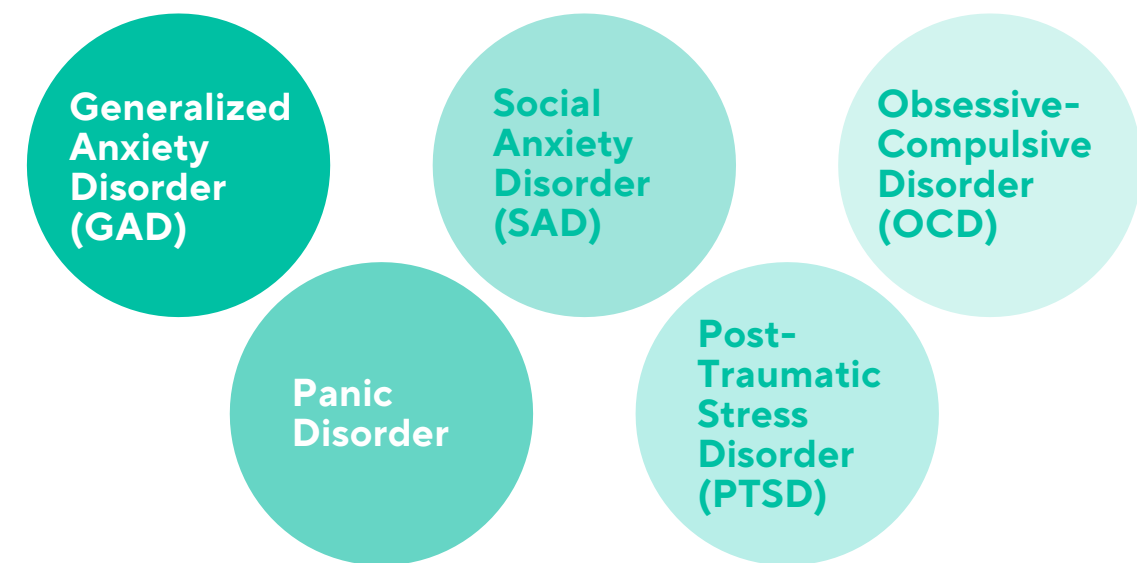
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# Anxiety

## Opportunity Overview

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



## Treatment options for anxiety disorders



- Antidepressants (SSRIs)
- Benzodiazepines
- Psychotherapy



**~40m**  
Anxiety disorder sufferers in the US<sup>1</sup>



**#1**  
Most common mental health disorder in the US<sup>1</sup>



**~7m**  
GAD sufferers in the US<sup>2</sup>



**<50%**  
Less than half of patients with Anxiety disorder in the US receive treatment<sup>2</sup>



**\$42bn+**  
Annual societal cost of anxiety disorders in the US<sup>3</sup>

1. National Alliance on Mental Illness (2021)  
 2. Anxiety and Depression Association of America (2021)  
 3. DeVane et al., "Anxiety Disorders in the 21st Century: Status, Challenges, Opportunities, and Comorbidity With Depression", AJMC (2005)

## SUMMARY



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

SSRI's are current standard of care for GAD but require 4-6 weeks for onset of effect and have several disadvantages<sup>1</sup>:


















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 can fill unmet need in Generalized Anxiety Disorder (GAD) with rapid onset and favorable safety profile

Overview of Current Therapeutic Options for Generalized Anxiety Disorder

Class	Examples	Mechanism of action	Favorable safety profile	Rapid Onset	High Efficacy	Minimal Side Effects	Non-addictive
<b>Benzoxazine</b>	deu-etifoxine (GRX-917) 	GABA <sub>A</sub> Channel and TSPO Potentiation					
Anticipated pharmacological profile based on etifoxine							
<b>Selective Serotonin Reuptake Inhibitor (SSRI)</b>	Escitalopram	SERT blockade					
<b>Serotonin and Norepinephrine Reuptake Inhibitor (SNRI)</b>	Venlafaxine	SERT AND NET blockade					
<b>Benzodiazepines</b>	Alprazolam	GABA <sub>A</sub> Potentiation					
<b>Tricyclic Antidepressant (TCA)</b>	Imipramine	Mixed MoA					
<b>Azapirones</b>	Buspirone	partial 5-HT <sub>1A</sub> agonist					
<b>Gabapentinoid</b>	Pregablin	VDCC inhibition					

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

Source: GlobalData, Evaluate Pharma (both as of 19.03.2021)

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

# Traumatic Brain Injury

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# Traumatic Brain Injury (TBI)

## Opportunity Overview

Traumatic brain injury typically occurs when a sudden force impacts the head or body, resulting in damage and functional impairment of the brain. atai initially focuses on mild traumatic brain injuries.



**~1.7m**

**People sustain TBI each year in US<sup>1</sup>**



**~57k**

**Annual TBI-related deaths in US<sup>2</sup>**



**70-80%**

**Mild TBI accounts for 70 - 80% of all reported TBIs**



**5.3m**

**Americans live with TBI related disabilities<sup>3</sup>**



**70-90%**

**of patients continue to exhibit prolonged neurocognitive dysfunctions<sup>4</sup>**



**To date, there are no pharmacological treatments approved for Traumatic Brain Injury**

1. Georges et al, "Traumatic Brain Injury", NCBI (2020)

2. CDC, "Surveillance Report of Traumatic Brain Injury-related Emergency Department Visits, Hospitalizations, and Deaths" (2014)

3. Thurman et al, "Report to Congress: Traumatic Brain Injury in the United States", CDC (1999)

4. Hoffer et al., "Repositioning drugs for traumatic brain injury", Journal of Biomedical Science (2017)

# Selected CNS indications of interest for psychedelic therapeutics

While **mental health is the initial focus**, adjacent indications may allow for **significant expansion**

**Anti-inflammatory** properties make psychedelics potentially interesting for a variety of therapeutic indications<sup>1</sup>

Indication	Estimated 2026 Market Size (\$BN)	Academic Publications
<b>Eating disorders</b>	7.4*	Positive effects of psychedelics on depression and wellbeing scores in individuals reporting an eating disorder <sup>2</sup>
<b>Obsessive-Compulsive Disorder</b>	3.7*	Safety, tolerability, and efficacy of psilocybin in 9 patients with obsessive-compulsive disorder <sup>5</sup>
<b>Attention Deficit Hyperactivity Disorder</b>	3.3	Perceived outcomes of psychedelic microdosing as self-managed therapies for mental and substance use disorders <sup>3</sup>
<b>Autism Spectrum Disorders</b>	1.4*	Lysergic acid diethylamide (LSD) promotes social behavior through mTORC1 in the excitatory neurotransmission <sup>4</sup>
<b>Multiple Sclerosis</b>	21.1	Psychedelics and immunomodulation: novel approaches and therapeutic opportunities <sup>10</sup>
<b>Ischemic/ Hypoxic Brain Injury</b>	20.0	The Endogenous Hallucinogen and Trace Amine N,N-Dimethyltryptamine (DMT) Displays Potent Protective Effects against Hypoxia via Sigma-1 Receptor Activation in Human Primary iPSC-Derived Cortical Neurons and Microglia-Like Immune Cells <sup>6</sup>
<b>Alzheimer's Disease</b>	10.6	Psychedelics as a Treatment for Alzheimer's Disease Dementia <sup>7</sup>
<b>Migraine Headache</b>	9.6	Exploratory Controlled Study of the Migraine-Suppressing Effects of Psilocybin <sup>11</sup>
<b>Parkinson's Disease</b>	2.4	Neuroprotective potential of Ayahuasca and untargeted metabolomics analyses: applicability to Parkinson's disease <sup>8</sup>
<b>Amyotrophic lateral sclerosis</b>	1.0	Psychedelics as a novel approach to treating autoimmune conditions <sup>9</sup>
<b>Cluster Headache</b>	0.3	Response of cluster headache to psilocybin and LSD <sup>12</sup>

80

\* Company estimate based on worldwide incidence

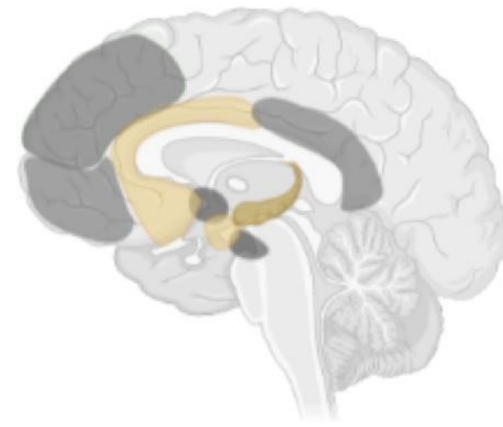
Source: EvaluatePharma for all indications with exception of Eating disorders, Autism spectrum disorder, and obsessive-compulsive disorder, for which there are no currently marketed therapies. Market size was calculated based on estimated worldwide incidence and current yearly average cost of antidepressant therapy

1. Flanagan & Nichols, "Psychedelics as anti-inflammatory agents" (2018). 2. Spriggs et al., "Positive effects of psychedelics on depression and wellbeing scores in individuals reporting an eating disorder" (2020). 3. Lea et al., "Perceived outcomes of psychedelic microdosing as self-managed therapies for mental and substance use disorders" (2020). 4. De Gregorio et al., "Lysergic acid diethylamide (LSD) promotes social behavior through mTORC1 in the excitatory neurotransmission" (2021). 5. Moreno et al., "Safety, tolerability, and efficacy of psilocybin in 9 patients with obsessive-compulsive disorder" (2006). 6. Szabo et al., "The Endogenous Hallucinogen and Trace Amine N,N-Dimethyltryptamine (DMT) Displays Potent Protective Effects against Hypoxia via Sigma-1 Receptor Activation in Human Primary iPSC-Derived Cortical Neurons and Microglia-Like Immune Cells" (2016). 7. Vann Jones & O'Kelly, "Psychedelics as a Treatment for Alzheimer's Disease Dementia" (2020). 8. Katchborian-Neto et al., "Neuroprotective potential of Ayahuasca and untargeted metabolomics analyses: applicability to Parkinson's disease" (2020). 9. Thompson et al., "Psychedelics as a novel approach to treating autoimmune conditions" (2020). 10. Szabo A., "Psychedelics and immunomodulation: novel approaches and therapeutic opportunities" (2015). 11. Schindler et al., "Exploratory Controlled Study of the Migraine-Suppressing Effects of Psilocybin" (2020). 12. Sewell et al., "Response of cluster headache to psilocybin and LSD" (2006)

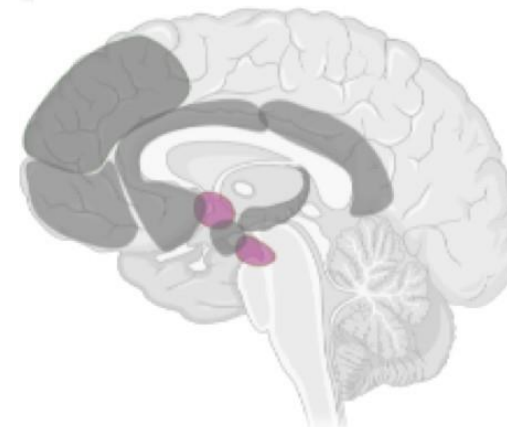


# atai aims to develop novel **disease-modifying strategies** to restore mental health by focusing on neuroplasticity

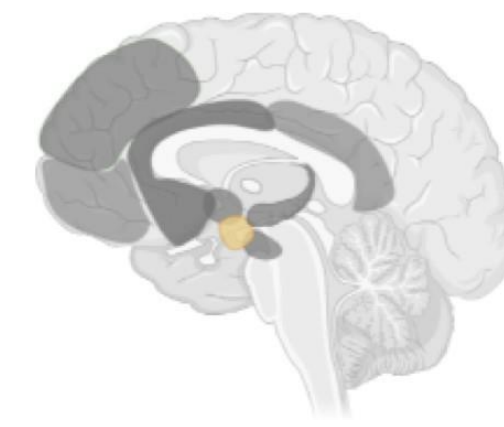
## Standard of Care



- 1 **SSRIs** localized to serotonergic pathways with slow onset, mainly  
↓ **AN**: reduced stress, emotional blunting.

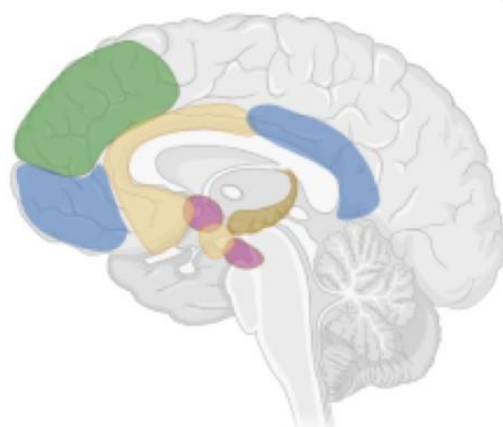


- 2 **Buprenorphine**  
↓ **RN** Opioid receptor agonists for maintenance; drawbacks: respiratory depression and maintained dependency.



- 3 **Benzodiazepines**  
↓ **AN**: sedation, amnesia, impaired motor performance; withdrawal

## atai LIFE SCIENCES

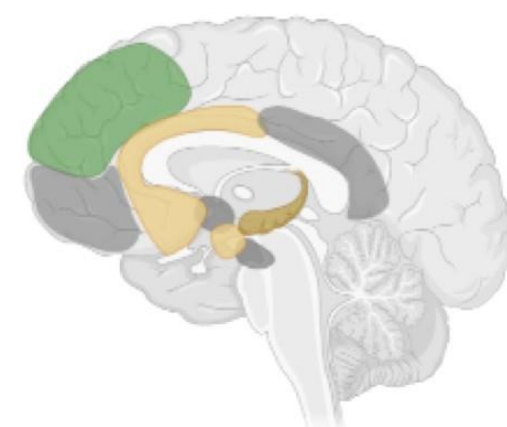


PERCEPTION  
NEUROSCIENCE

DemeRxIB

VIRIDIA  
LIFE  
SCIENCES

- 1 **Pleiotropic re-set of DMN & AN.**  
Increased neuroplasticity combined with psychedelic experience facilitates **regaining control of CC and RN** and “unlearning” negative behaviors.
- 2



gaba  
THERAPEUTICS

- 3 **Modulatory (+/-) effect on AN.**  
Restoration of top-down control of emotions from **CC**.

- Default Mode Network (**DMN**):  
Self awareness
- Cognitive Control (**CC**): Decision making, executive functions
- Reward Network (**RN**): Pleasure
- Affective Network (**AN**): Fear response, social interaction, learning, processing emotions

“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.”