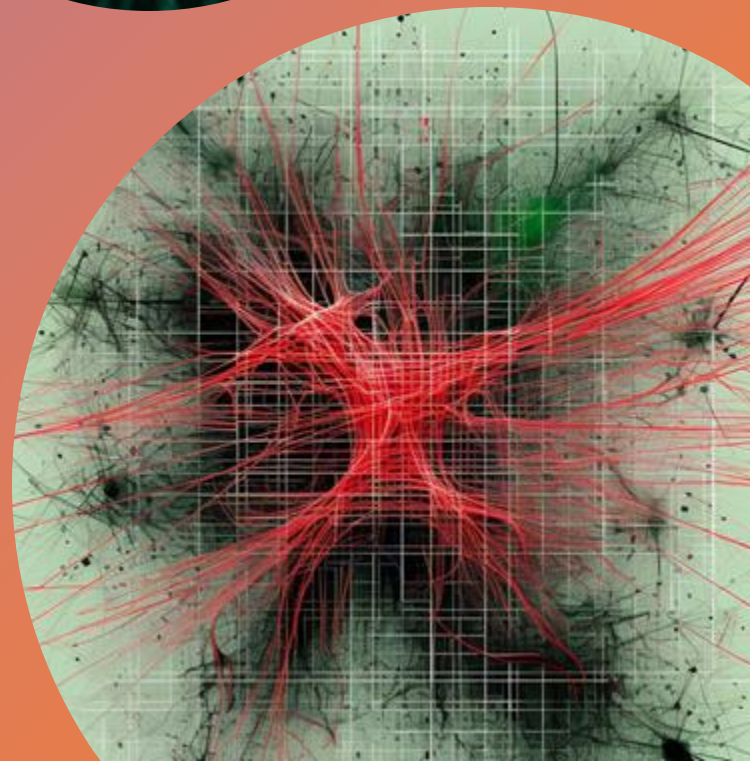
Advancing a non-hallucinogenic psychedelic drug combination

For treatment-resistant depression



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The Team

Yale SCHOOL OF MEDICINE | Yale PSYCHIATRY

Alfred Kaye, MD, Ph.D.

Assistant Professor of Psychiatry, Yale University

- Principle Investigator, expertise in studying the neurocircuitry underlying stress-related disorders and psychedelic treatment

Christopher Pittenger, MD, Ph.D.

Director, Yale Program for Psychedelics Science

- Elizabeth Mears and House Jameson Professor of Psychiatry, Yale University

John Krystal, MD

Co-Founder & Chief Scientific Advisor, Freedom Biosciences

- Department of Psychiatry Chair, Yale University
- Groundbreaking discovery of ketamine's rapid antidepressant effects in clinical populations

Dina Burkitbayeva, MBA

Co-Founder & Chief Executive Officer, Freedom Biosciences

- Co-founder, PsyMed Ventures
- Serial entrepreneur from Harvard Business School with expertise funding cutting-edge mental health treatments

Addressing the Mental Health Crisis

Innovative solutions are urgently needed for treatment-resistant depression

1 We are in a mental health crisis

- ***300M people*** live with major depressive disorder (MDD)
- MDD is a ***leading cause of disability***, reducing life expectancy by 10 years on avg
- ***100M people*** struggle with treatment-resistant depression (TRD)

2 Current treatment options are inadequate

Intensive:

- **Transcranial magnetic stimulation (TMS):** daily 30m sessions for 6-10 weeks
- **Electroconvulsive therapy (ECT):** invasive and requires general anesthesia
- **Ketamine/Esketamine:** requires 2-hour session 2x week

Costly

- TMS $6-15K per patient per course of treatment
- ECT $10K+ per patient per year
- Esketamine $18-45K per patient per year

Ineffective

- Despite options many patients remain non-responsive

Our Promising New Approach:

Guanfacine + Psilocybin

- ✓ ***Effective antidepressant effects***
- ✓ ***No hallucinogenic impact***
- ✓ ***Safe***
- ✓ ***More accessible***

CADTH. Continuous Glucose Monitoring for Type 1 Diabetes: A Health Technology Assessment. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2020

Axis Health. "TMS Therapy Costs." *Axis Health System*, https://www.axismh.com/content/tms-therapy-costs

Ross, E. L., Zivin, K., & Maixner, D. F. (2018). Cost-effectiveness of Electroconvulsive Therapy vs Pharmacotherapy/Psychotherapy for Treatment-Resistant Depression in the United States. JAMA Psychiatry, 75(7), 713-722.

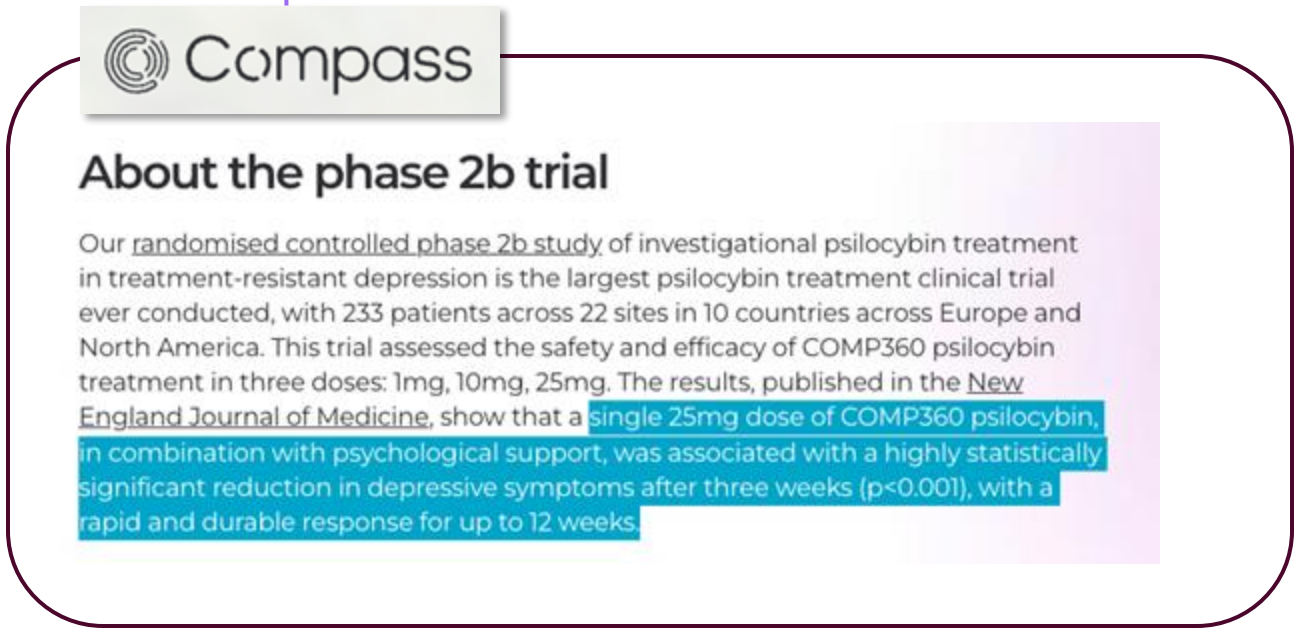
Now is the Time to Develop Psychedelic Therapeutics

Growing and Strong Interest
In 5ht-based psychedelics. 102 psilocybin trials in last 5 years

Strong Therapeutic Results
In MDD/TRD patient populations

Greater Acceptance
By patients and practitioners

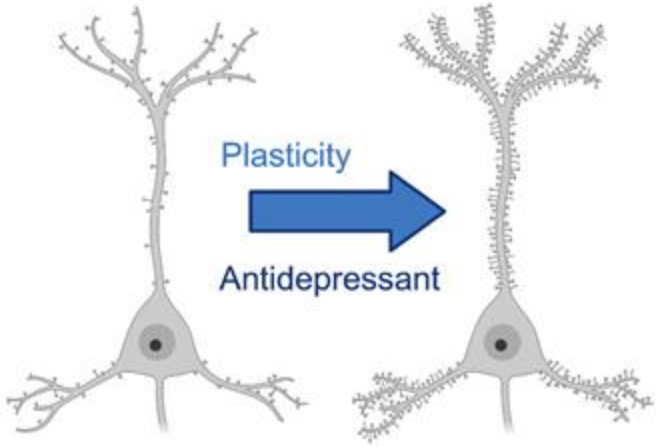
Problem: hallucinogenic effects
Our approach is unique and potentially more effective than competitors (Delix, Gilgamesh, Terran)

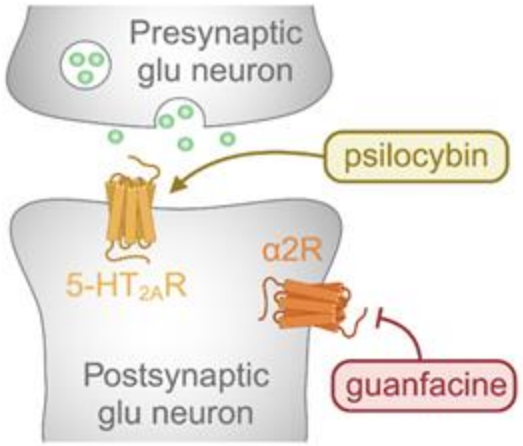


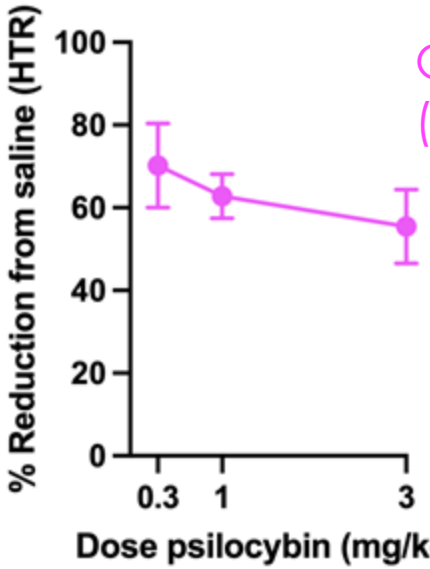
https://www.ncbi.nlm.nih.gov/books/NBK590596/table/ch2.tab2/

Solution: psilocybin + guanfacine

Guanfacine blocks psilocybin's hallucinogenic effects while retaining therapeutic benefits







Guanfacine pretreatment (0.15 mg/kg) reduces HTR

Reduced Side Effects

Diminishes psilocybin's hallucinogenic effects, improving tolerability

Enhanced Accessibility

Allows for safer use in broader, possibly outpatient, clinical settings, reaching a wider patient population

Therapeutic Retention

Maintains psilocybin's antidepressant benefits, shown to be highly effective even in treatment-resistant patients

Composition of Matter:

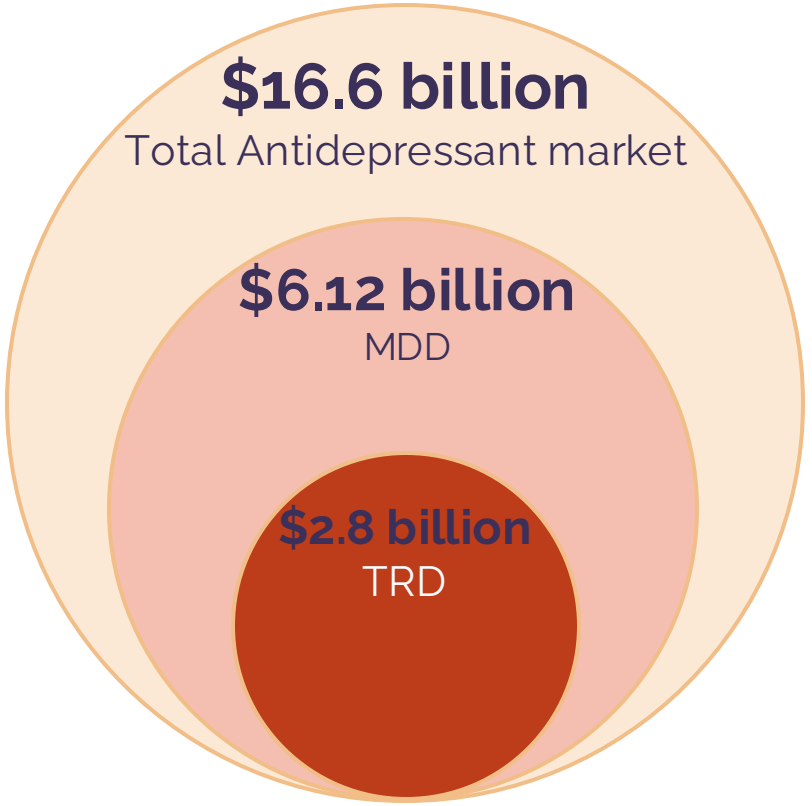
- PCT and Follow-on Provisional patent applications pending

Our proprietary combination drug has blockbuster potential

18M Patients with MDD
11M treated patients

27% of patients have TRD
4.86M patients

$1.7B in projected annual revenue
Assuming 170,000 TRD patients treated, estimated $10,000 annual cost of drug



Global Major Depressive Disorder Market Share. The Business Research Company. https://www.thebusinessresearchcompany.com/market-insights/global-major-depressive-disorder-market-2024
(n.d.). *Treatment Resistant Depression Market*. Market Data Forecast. https://www.marketdataforecast.com/market-reports/treatment-resistant-depression-market

Budget and Milestones

3 months

Hallucinogenic effect blockade
Guanfacine blocks psilocybin's hallucinogenic effects, enhancing safety and control in therapy.

3 months

Preservation of antidepressant efficacy
Guanfacine maintains psilocybin's antidepressant effects, preserving therapeutic potential.

4 months

Optimizing dosage and timing
Refine psilocybin dosage and guanfacine timing to maximize therapeutic impact and clinical relevance.

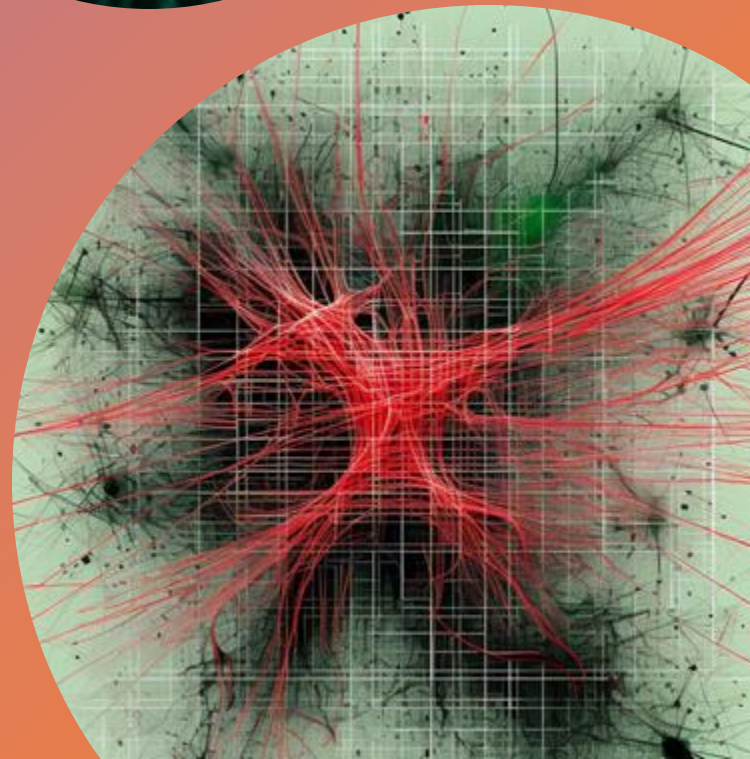
6 months

Alternative candidate drug combinations
Test additional combinations similar to guanfacine-psilocybin to enhance efficacy and identify optimal therapeutic strategies.

5 months

Evaluating short-acting psychedelics
Test DMT and 5-Meo-DMT for comparable therapeutic effects to psilocybin, providing greater treatment flexibility.

Appendix



Projected revenue calculations

Patients with MDD	18,815,000
% Patients on Treatment	62%
MDD Treated Patients	11,665,300
% Receiving Therapy	
MDD - 1L	100%
MDD- 2L	54%
MDD- 3L (TRD)	27%
MDD- 4L (TRD)	13%
% Treated with our drug	
MDD Patients Treated with our drug at Peak Year - 1L	0%
MDD Patients Treated with our drug at Peak Year - 2L	0%
TRD Patients Treated with our drug at Peak Year - 3L (TRD)	3%
TRD Patients Treated with our drug at Peak Year - 4L (TRD)	5%
TRD Patients Treated with our drug - 3L	94,489
TRD Patients Treated with our drug - 4L	75,824
Total TRD Patients Treated with our drug	170,313
Estimated cost of drug (annually) - assume 1/3 of estimated psilocybin treatment	$10,000
Annual Gross Revenue	$1,703,133,800
Gross to Net Discount	20%
Net Revenue	$1,362,507,040

Psychedelic therapeutics companies raised substantial capital and attracted big name investors


THE WALL STREET JOURNAL.

EXCLUSIVE

Wall Street Backs New Class of Psychedelic Drugs

Psychedelic-therapy industry gets a reality trip as investors focus on treatments costing less time and money


FINANCIAL TIMES

Investors pile into psychedelic drug start-ups tackling mental health

Sovereign wealth funds Temasek and Mubadala in talks to fund biotech groups harnessing mind-altering substances

Company	IPO Date & Amount	Total Funding to date	Investors or Partners	Breakthrough Designation
ATAI Life Sciences (NASDAQ: ATAI)	June 18, 2021, at $15 per share, raising $225 million	Approximately $450 million	Peter Thiel's Founders Fund	No
MindMed (NASDAQ: MMED)	April 27, 2021 - $24 million	$200 million	Fidelity Management, Driehaus Capital Management	Yes (for MM120 LSD for GAD)
GH Research (NASDAQ: GHRS)	June 24, 2021 - $16 per share, Approximately $160 million	$315 million	RA Capital Management, RTW Investments	No
COMPASS Pathways (NASDAQ: CMPS)	September 17, 2020 - $146 million	$343 million	ATAI Life Sciences, Founders Fund	Yes
Cybin Inc (NASDAQ: CYBN)	November 2020 - $32.28 million	$130 million	Kernel, Catalent	No

Non-hallucinogenic Psychedelics

Freedom Biosciences

Potential for substantial benefits based on optimization (i.e. no required therapists, shorter or no in clinic dosing sessions and lower intensity of effect)

Treatment	Duration of session	Dosing Session Therapist Required	Supportive and integrative Psychotherapy Required	Cost of treatment	Duration of protection	Frequency of Treatment	Intensity of subjective effect
Non-hallucinogenic Psychedelics	TBD, may be a seamless and at-home treatment	Unlikely	Likely not required	Lower	TBD	TBD	Low
5-MeO-DMT	30-40 mins + recovery time prior to discharge	TBD	TBD	TBD	TBD	Likely 3 sessions	High
DMT	45 mins + recovery time prior to discharge	TBD	TBD	TBD	TBD	Likely 3 sessions	High
Psilocybin	6 hours	Yes (likely 2)	Yes, preparatory and integrative therapy required	High	Up to 6 months?	2-3 sessions	High
MDMA	8 hours	Yes (likely 2)	Yes, 12 sessions: 3 preparatory & 9 integrative sessions	High	6 months+ for PTSD?	3 sessions	Medium

Source: Freedom Biosciences Scientific Team Analysis

There remains a need in the treatment landscape for non-hallucinogenic psychedelics

Our combination follows a unique approach of combining two well-understood and studied drugs vs NCEs with unknown profiles

Competitor	Basis	Status	Pros	Cons	Net	Investors
Guanfacine-Psilocybin Combination	Combination approach with proven psychedelic to reduce hallucinations	Preclinical	Addresses major drawback to use	Clinical POC	Builds on proven therapeutic by improving safety	
Gilgamesh Therapeutics	Non-dissociative, rapid-acting NCE; non-hallucinogenic NCE	Phase 2a; IND enabling	IP; first in class potential	Unknown efficacy	High upside / high risk	Partnership with AbbVie $65m upfront + upto $2b in downstream economics
Delix Therapeutics	Non-hallucinogenic NCEs	Phase 1	IP; first-in-class potential	Unknown efficacy	High upside / high risk	ARTIS Ventures, RA Capital Management, and OMX Ventures
Terran Biosciences	Combinations; non-hallucinogenic NCEs	Preclinical	IP	Potential for loss of efficacy with combination; unknown efficacy of pro-drugs/NCEs	High upside / high risk to NCEs	Catalytic Impact Foundation, Transhuman Capital, and the Noetic Fund
Onsero Therapeutics	GPCR targeted approach to non-hallucinogenic NCEs	Preclinical	IP	Unknown efficacy	High upside / high risk	Route 66 Ventures and the Noetic Fund