Corporate Presentation

A Breakthrough Therapy Company

June 2024

NYSE American: CYBN Cboe CA: CYBN



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There are a number of risk factors that could cause future results to differ materially from those described herein. A discussion of the principal risk factors relating to the Company's operations and business appear in the Company's most recently filed managementy discussion and analysis and the annual information form, which are available under the Company's profile on www.sedarplus.ca and with the United states Securities and Exchange Commission on EDGAR at www.sec.gov. Additional risks and uncertainties, including those that the Company is not aware of currently, or that it currently

CAUTIONARY NOTE REGARDING FUTURE-ORIENTED FINANCIAL INFORMATION

To the extent that any forward-looking statement in this presentation constitutes "future-oriented financial information" or "financial outlooks" within the meaning of applicable securities laws, such information is being provided to demonstrate the anticipated market penetration and the reader is cautioned that this information and financial outlooks, as with forward-looking statement and function information and financial outlooks, as with forward-looking statement expertations are without periodical formation. The Company's actual financial position and results of operations managements current expectations are, as a result, the Company's revenue, with the Company's revenue and results of operations managements.

CAUTIONARY NOTE REGARDING REGULATORY MATTERS

The Company conducts research and development and is focused on developing and commercializing psychedelic-inspired regulated medicines. The Canadian, United States and Ireland federal governments regulated trugs. Psilocybin is currently a Schedule I controlled substances act (United States) and a Schedule I controlled substance in Ireland under the Misuse of Drugs Act, 1977, 1984 and 2015, the Misuse of Drugs Regulations 2017 and the Criminal Justice (Psychocated with 1984 and 2016, the Misuse of Drugs Regulations 2017 and the Criminal Justice (Psychocated with 1984 and 2016, the Misuse of Drugs Regulations 2017 and the Criminal Justice (Psychocated with 1984 and 2016, the Misuse of Drugs Regulations 2017 and the Criminal Justice (Psychocated with 1984 and 2016, the Misuse of Drugs Regulations 2017 and the Criminal Justice (Psychocated with 1984 and 2016, the Misuse of Drugs Regulations 2017 and the Criminal Justice (Psychocated with 1984 and 2016, the Misuse of Drugs Regulations 2017 and the Criminal Justice (Psychocated with 1984 and 2016, the Misuse of Drugs Regulations 2017 and the Criminal Justice (Psychocated with 1984 and 2016, the Misuse of Drugs Regulations 2017 and the Criminal Justice (Psychocated with 1984 and 2016, the Misuse of Drugs Regulations 2017, the Misuse of Drugs Regulations 2018, the Misuse of Drugs Regulations 2018, the Misuse of Drugs Regulations 2019, the Misuse of Drugs Regulations 2019, the Misuse 20

RUG DEVELOPMENT

Drug development involves long lead times, is very expensive and involves many variables of uncertainty. Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to the Company. Every patient treated during future studies can change those assumptions either positively (to indicate a faster timeline to new drug applications and other approvals) or negatively (to indicate a slower timeline to new drug applications certain forward-looking statements regarding anticipated or possible drug development timelines. Such statements are informed by, among other things, regulatory guidelines for developing a drug with safety studies, proof of concept studies, and pivotal studies for new drug application submission and assumes the success of implementation and results of such studies on timelines indicated as possible by such guidelines, other industry examples, and the Company's development efforts to date.

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

US DISCLAIME

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Leading the Development of Next-Generation Therapeutics



- ✓ **Leading international, clinical-stage company** developing **next-generation therapeutics** with the potential to transform treatment paradigms for mental health
- ✓ **FDA Breakthrough Therapy Designation** granted to CYB003 for the adjunctive treatment of major depressive disorder (MDD), accelerating the clinical development timeline
- ✓ Well capitalized successfully closed oversubscribed private placement of \$150M USD at a premium to market, with cash position of C\$209 million as of March 31, 2024
- Two proprietary, advanced clinical programs in development for depression and anxiety disorders with demonstrated Phase 2 safety and efficacy
- Robust IP portfolio with more than 60 granted patents and over 200 pending applications
- ✓ Near-term value-driving catalysts across lead clinical programs: (1)(2)
 - Initiate Phase 3 study of CYB003 in MDD in summer of 2024
 - Topline readout from Phase 2 study of CYB004 in generalized anxiety disorder (GAD) expected year-end 2024

Note:

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



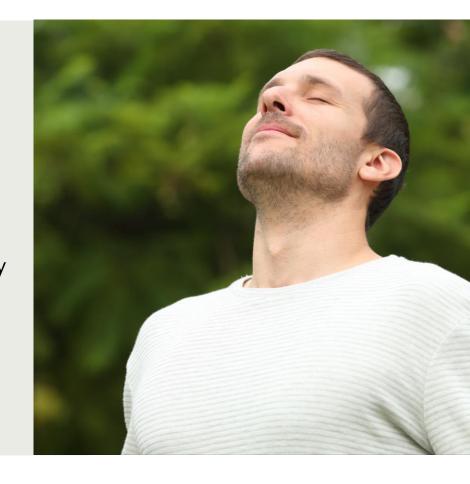
⁽²⁾ Cybin is prioritizing the progression of its CYB003 program. The advancement of Cybin's CYB004 program is contingent on Cybin's ability to continue raising capital under its current and future financing arrangements. No assurances can be given that Cybin will be able to raise the additional capital that it may require for its anticipated future development.

Creating Breakthrough Therapies

We are developing **differentiated**, **next-generation therapeutics** with the potential to **improve clinical outcomes and address key unmet needs** for people with mental health conditions.

Leveraging decades of research with the goal of achieving:

- ✓ Rapid and sustained therapeutic effects with positive safety and tolerability
- ✓ Efficacy with just 1-2 doses vs. existing chronic daily treatments
- ✓ Onset of effects aimed at optimized in-clinic times
- ✓ Convenient dosage forms oral and intramuscular



Note: Forward-looking statements are subject to risks and assumptions. See "Cautionary Statement" on page 2 of this presentation. Certain statements regarding psychedelic-based therapeutics have not been evaluated by the Food and Drug Administration, Health Canada or other similar regulatory authorities, nor has the efficacy of psychedelic-based therapeutics been confirmed by approved research. There is no assurance that any of the Company's compounds will be used to diagnose, treat, cure or prevent any disease or condition and robust scientific research and clinical trials are needed. All such statements are subject to receipt of all necessary regulatory approvals from which all applicable governmental authorities, including, as applicable, the academic and scientific organizations with which Cybin is working. There are multiple risk factors regarding the ability to successfully commercially scale a chemically synthesized process to obtain psilocybin and other analogues.



Experienced Team With Strong Track Record

- Experienced management team with proven track record of bringing multiple drugs to market (60 INDs, 37 exits)
- Developed widely used drugs such as: Allegra, Sabril, Anzemet, Latuda, Vaniga, and esketamine
- 300 combined peer reviewed publications by scientific leadership



Doug Drysdale Chief Executive Officer



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



Aaron Bartlone Chief Operating Officer



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



Allison House-Gecewicz SVP, Clinical Operations



Geoff Varty Ph.D. Head of R&D

Corporate

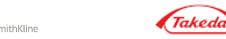






R&D





















Developing Differentiated, Next-Generation Therapeutics for Mental Health Disorders

Two advanced clinical-stage programs with demonstrated Phase 2 safety and efficacy

	PROGRAM (1)(2)(3)	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	REGISTRATION
Deuterated	CYB003-Deuterated Psilocybin Analog Major Depressive Disorder	Phase 2 complete; gra	nted FDA Breakthroug	h Therapy Desiç	gnation		
Psilocybin Program	CYB003-Deuterated Psilocybin Analog Alcohol Use Disorder						
	CYB004-Deuterated Dimethyltryptamine (IM) Generalized Anxiety Disorder	Phase 2 GAD study init	iated				
DMT/dDMT Program	SPL028- Deuterated DMT (IM and IV)	Phase 1 IM & IV comple	ete				
	SPL026 – DMT (IM and IV) Major Depressive Disorder	Completed: Phase 1 (IM	1), Phase 1b SSRI-DDI (I	V), Phase 1/2a in	MDD (IV)		

Notes

³⁾ Cybin is prioritizing the progression of its CYB003 program. The advancement of Cybin's CYB004 and technology programs are all contingent on Cybin's ability to continue raising capital under its current and future financing arrangements. No assurances can be given that Cybin will be able to raise the additional capital that it may require for its anticipated future development.



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Urgent Need to Effectively Treat Mental Health Conditions

>900 million

people globally are affected by a mental health condition⁽¹⁾

1 in 5 U.S. adults experience mental illness each year ⁽²⁾

>700,000

deaths are due to suicide globally every year (3)

Average delay of **11 years** between onset of depression and treatment⁽²⁾ >50% of people will suffer from at least one mental illness at some point in their lifetime⁽⁴⁾

Up to **30%** of people with depression do not respond to traditional antidepressant treatments

Notes



^{(1) 8} countries: US, UK, Germany, France, Japan, Italy, Spain, & Canada

⁽²⁾ https://www.nami.org/mhstats

⁽³⁾ https://www.who.int/news-room/fact-sheets/detail/depression

⁽⁴⁾ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5007565/

⁵⁾ https://www.nami.org/getattachment/Get-Involved/NAMI-National-Convention/Convention-Program-Schedule/Hill-Day-2017/FINAL-Hill-Day-17-Leave-Behind-all-(1).pdf

CYB003: Opportunity to Address Key Unmet Needs in MDD

Depression is a chronic illness that affects people everywhere.

- ~280m people suffer worldwide¹
- Suicide risk is 20x higher for an individual with vs. without depression²
- #1 leading cause of disability due to mental health/illness³
- Costs global economy \$1 trillion each year in lost productivity¹

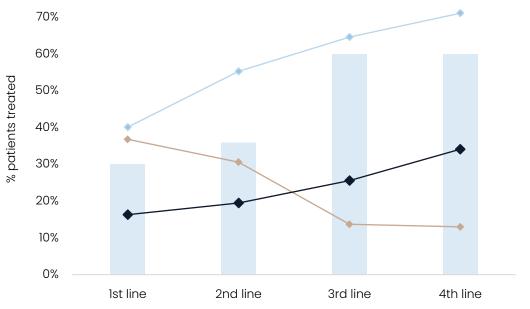
Notes

- 1) WHO (2021), Depression factsheet
- 2) American Association of Suicidology, 2014
- Lancet 2020; 396: 1204–22
- 4) Rush AJ et al. "Acute and longer-term outcomes in depressed outpatient requiring one or several treatment steps: A STAR*D report". The American Journal of Psychiatry. 2006. 163(1):1905-1917. Diagram represents anticipated treatment outcomes as patients cycle through the current depression treatment guidelines
- 5) Sussman et al. J Clin Psychiatry. 2001(Apr);62(4):256-260
- Clayton AH, et al. J Clin Psychiatry. 2002 Apr;63(4):357-66.
- 7) Fava M, et al. J Clin Psychopharmacol. 2002;22(2):137-147.
- *Up to 37% suffer from nausea, diarrhea, constipation, vomiting, dry mouth, and rarely gastrointestinal bleeding (based on a review of package inserts)

Current treatment options leave millions of patients behind.

- 1st line treatments do not work for approximately two-thirds of patients. The treatment success rate decreases at each successive treatment line, as patients try to find one that works for them.
- Antidepressants often have dose-limiting adverse effects, including weight gain (20%)⁵, sexual dysfunction (up to 30%) ⁶, gastrointestinal disturbances* and insomnia (25%) ⁷

Representation of patient outcomes across current treatment lines for depression



Treatment lines per current guidelines⁴

After each line of treatment:

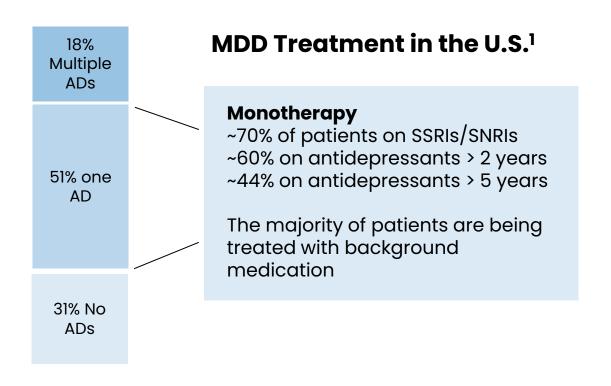
Efficacy decreases

Treatment intolerance increases

Relapse rates increase



Adjunctive MDD Therapy Addresses the Needs of Treating Patients in Clinical Practice



Advantages of Adjunctive Therapy in MDD

- ✓ Allows for immediate treatment without waiting to withdraw from background medications
- Prevents withdrawal symptoms, which could be severe for some patients after years of antidepressant use
- Eliminates logistical hurdles associated with titrating off existing medications
- Background medications could provide some benefit even if inadequate alone

An acute adjunctive therapy with the potential to deliver durable remission could provide a clear clinical benefit

Notes:

1. Luo et al. (2020). National Prescription Patterns of Antidepressants in the Treatment of Adults With Major Depression in the US Between 1996 and 2015: A Population Representative Survey Based Analysis. Frontiers in Psychiatry 11.

*AD = Antidepressant, SSRI = Selective serotonin reuptake inhibitor, SNRI = Serotonin-norepinephrine reuptake inhibitor



FDA Breakthrough Therapy Designation Accelerates Development Pathway for CYB003

- Acknowledges the significant unmet medical need for more effective treatment of MDD
- Provides validation that Phase 2 data for CYB003 shows preliminary evidence of significant clinical improvements over existing therapies

Breakthrough Therapy Designation advantages

- All Fast Track Designation features, including Rolling Review for New Drug Application (NDA)
- More intensive FDA guidance and discussion, including planned clinical trials and plans for expediting manufacturing development strategy
- CYB003 is eligible for Priority Review and Accelerated Approval

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Notes

CYB003: Phase 1/2a Trial Design

Study Design:

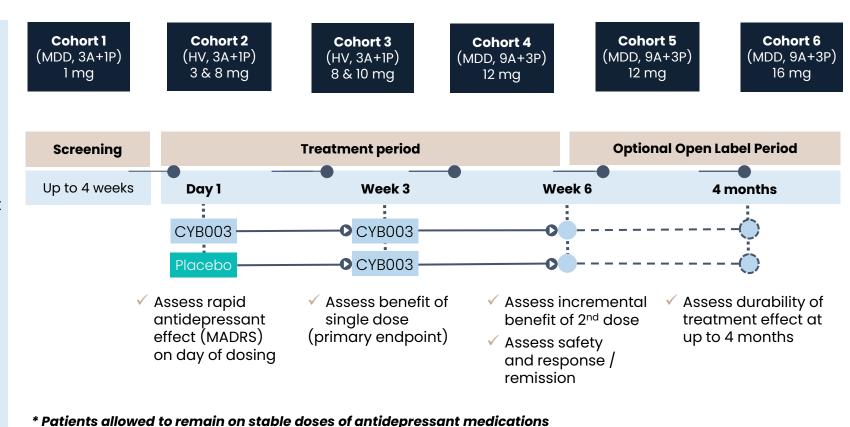
√ Randomized, double-blind, placebo-controlled trial

Key Inclusion Criteria:

- ✓ Men and women, 21 to 65 years old
- ✓ Moderate to severe MDD (MADRS ≥ 21)
- ✓ Inadequate response to antidepressant medication

Endpoints:

- ✓ Reduction in depression symptoms (change in MADRS score) at Week 3 after a single dose*
- ✓ Change in MADRS score at Day 42, after second dose
- ✓ Safety, PK and tolerability



MDD: participants with major depressive disorder; HV: healthy volunteers; Primary efficacy assessed at Week 3; Optional 12 week follow up to assess durability of effects



Demographics and Baseline Characteristics

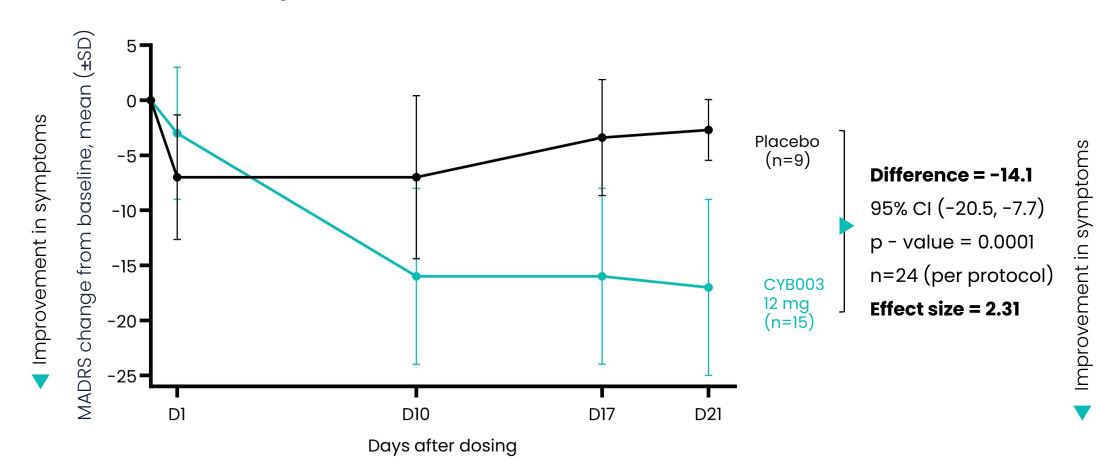
	Cohort 1 (MDD) 1 mg / 1 mg (n=2)	Cohort 2 (NHV) 3 mg / 8 mg (n=3)	Cohort 3 (NHV) 8 mg / 10 mg (n=3)	Cohort 4 (MDD) 12 mg / 12 mg (n=9)	Cohort 5 (MDD) 12 mg / 12 mg (n=9)	Cohort 6 (MDD) 16 mg / 16 mg (n=9)	Placebo- Active (n=13)
Mean age (years)	32.5	23.7	44.0	38.6	42.9	35.6	41.6
Gender							
Male	1	2	2	4	4	6	4
Female	1	1	1	5	5	3	9
Baseline MADRS (SD)#	26.0 (2.83)	NA	NA	31.6 (3.36)	33.7 (3.84)	31.4 (4.03)	30.8 (4.75)

[#] MADRS performed for MDD patients only; MADRS total score ranges 0-60; typical score cut offs are: 0-6 normal; 7-19 mild; 20-34 moderate; and >34 severe depression Note: MADRS: Montgomery-Åsberg Depression Rating Scale, SD: Standard deviation, MDD: Major Depressive Disorder, NHV: Normal Healthy Volunteer



Large Improvement in Symptoms of Depression After a Single Dose

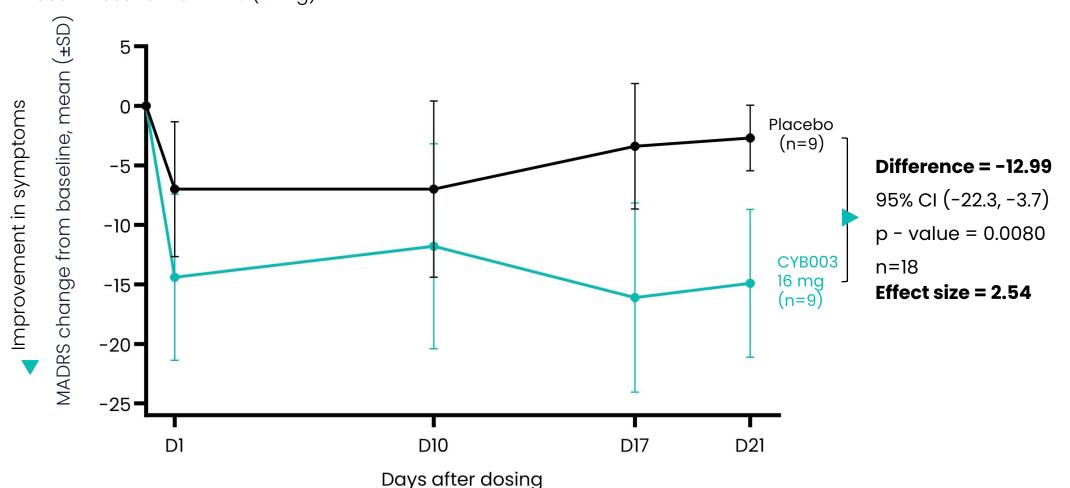
Phase 2 Results - CYB003 (12mg)





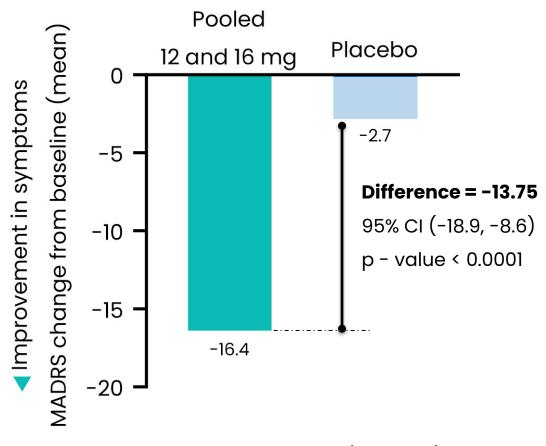
Large Improvement in Symptoms of Depression After a Single Dose

Phase 2 Results - CYB003 (16mg)



Improvement in symptoms

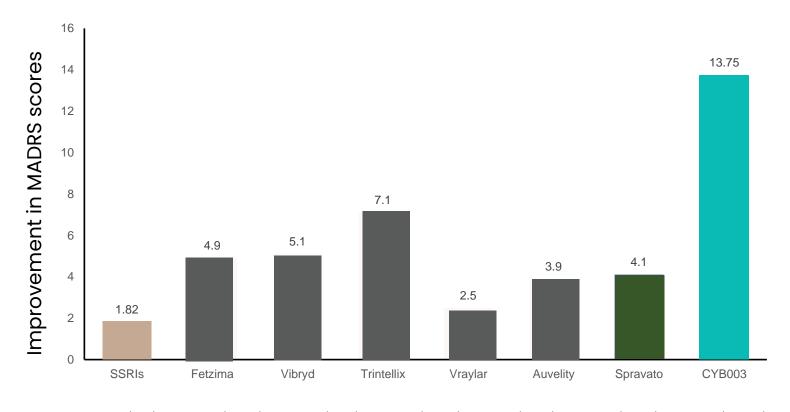
Consistently Large Improvements in Depression Symptoms 3 Weeks After a Single Dose



n=34: n=24 on CYB003; 10 on placebo (per protocol)



CYB003: Significantly Greater Improvements Compared to Existing Therapies⁽¹⁾⁽²⁾⁽³⁾



- Difference from placebo plotted for change from baseline in MADRS scores
- CYB003 effect for 12 and 16 mg pooled after single dose
- Representative effect seen in pivotal studies used for comparators
- Pooled SSRI data from 232 RCTs of antidepressants submitted to FDA (Stone et al, 2022)
- Where MADRS scores were not available, HAMD scores were converted to MADRS scores

References: Stone et al, 2022 (SSRIs), NCT00969709 (Fetzima), NCT01473394 (Vibryd), NCT01153009 (Brintellix), NCT0378215 (Vraylar), NCT04019704 (Auvelity), NCT02417064 (Spravato)

votes.

⁽³⁾ FETZIMA* is a registered trademark of Allergan Sales, LLC, an AbbVie company. VIIBRYD* is a registered trademark of Allergan Sales, LLC, an AbbVie company. TRINTELLIX*, formerly BRINTELLIX*, is a trademark of H. Lundbeck A/S registered with the U.S. Patent and Trademark Office and used under license by Takeda Pharmaceuticals America, Inc. VRAYLAR* is a trademark of Allergan Pharmaceuticals International Limited, an AbbVie company. AUVELITY* is a registered trademark of Assome Therapeutics, Inc. SPRAVATO* is a registered trademark of Johnson & Johnson Corporation. Third party trademarks used herein are trademarks used herein are trademarks of their respective owners.



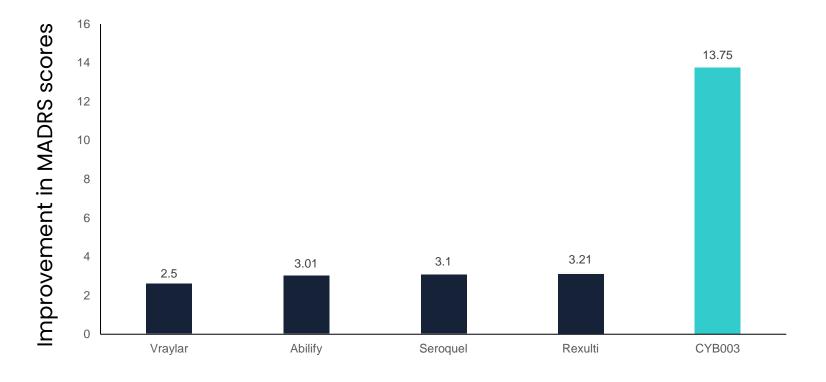
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^{*} Spravato evaluated in TRD; Typical endpoint for MDD studies 6-8 weeks; endpoint is at 4 weeks for Spravato, endpoint for CYB003 is at 3 weeks

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CYB003: Potential for Best-in-Class Status as an Adjunctive Treatment for Depression⁽¹⁾⁽²⁾⁽³⁾



- Difference from placebo plotted for change from baseline in MADRS scores
- CYB003 effect for 12 and 16 mg pooled after single dose
- Maximum effects on MADRS seen in pivotal studies used for comparators

References: Cariprazine (Vraylar) 1.5 mg - NCT03738215; Aripiprazole (Abilify) 5-20 mg - NCT00095823; Quetiapine (Seroquel) 150 mg - D1448C00007; Brexpiprazole (Rexulti) 2 mg - NCT01360645 Endpoints: Vraylar - 6 weeks; Abilify - 14 weeks; Seroquel 6 weeks; Rexulti - 6 weeks; CYB003 - 6 weeks

Notes

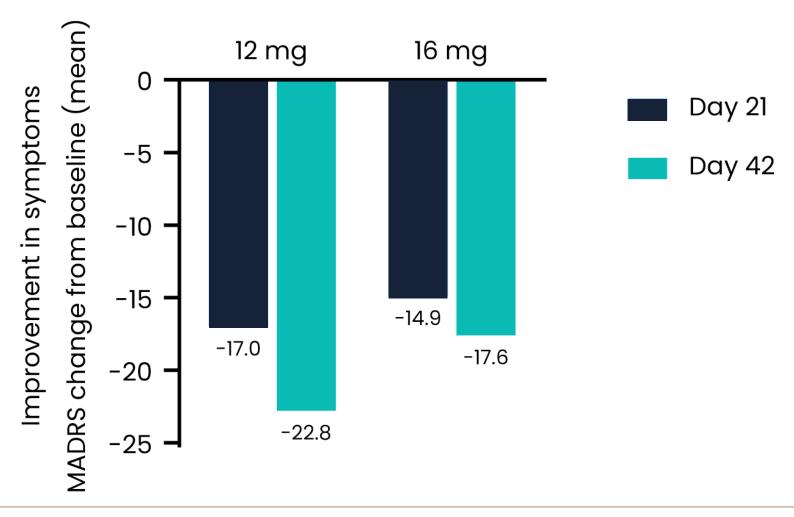
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(3) VRAYLAR® is a 'trademark of Allergan Pharmaceuticals International Limited, an AbbVie company. ABILIFY® is a registered trademark of Otsuka Pharmaceutical Co., LTD. Third party trademarks used herein are trademarks of their respective owners.



Incremental Benefits from a Second Dose

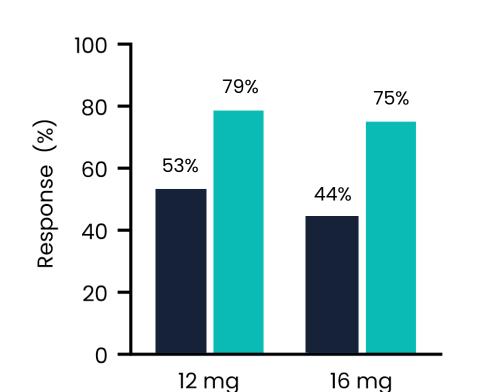


n=24: n=15 (12 mg); n=9 (16 mg) on CYB003 (per protocol)

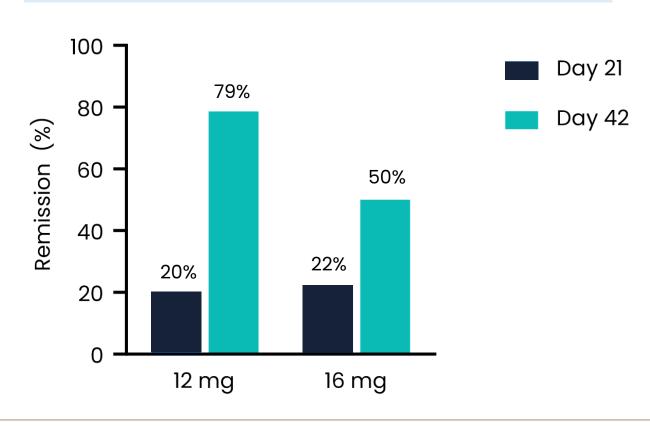


Incremental Response and Remission Rates with a Second Dose

Response: ≥50% reduction in MADRS scores





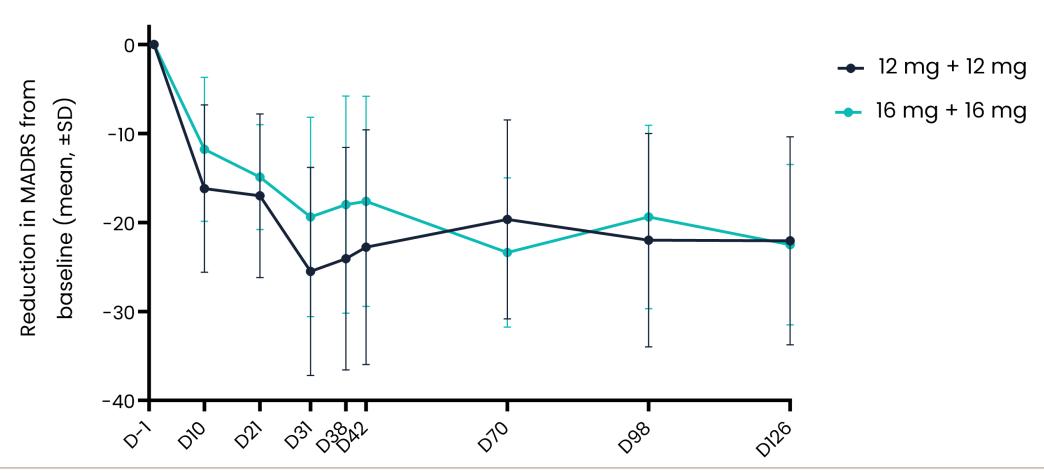


Day 21: n=34, 24 on CYB003, 10 on placebo (ITT)

Day 42: n=32, 22 on CYB003, 10 on placebo (ITT)



Strong and Durable Effects 4 Months After 2 Doses

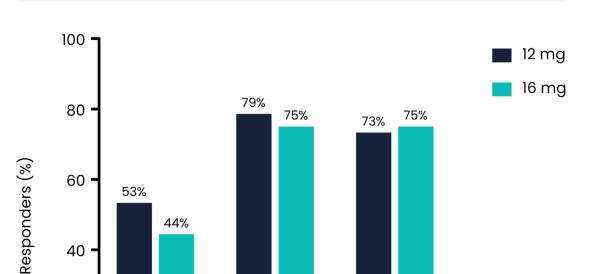


At Day 126: n=15 (12 mg + 12 mg) and n=8 (16 mg +16 mg)



Strong and Durable Effects 4 Months After 2 Doses





D42

D126

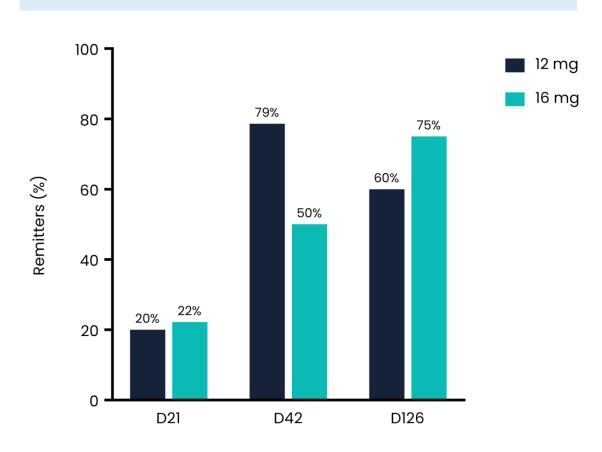
53%

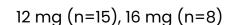
D21

40

20

Remission: MADRS scores ≤10







Favorable Safety Profile Phase 2 CYB003 Results in MDD (1)(2)

- CYB003 well tolerated with no Serious Adverse Events
- No Adverse Events (AEs) of suicidal ideation or behavior
- No participant discontinued the study due to an AE
- Most common AEs were nausea, elevated blood pressure and headache
- · Increases in blood pressure were transient and resolved without intervention
- All AEs were mild or moderate in intensity
- No clinically relevant changes in chemistry, hematology markers or ECG parameters

Notes:

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Positive Phase 2 CYB003 Results in MDD with De-Risked Path to NDA

Rapid onset of effect

Improvement in symptoms after single dose

Large improvements in symptoms

At 3 weeks: 12 mg better than placebo on MADRS by 14.1 points (p=0.0001), Cohen's d=2.31

Incremental benefit of 2nd dose

16 mg better than placebo on MADRS by 13 points (p=0.008), Cohen's d=2.31

Average 5.8 points improvement on the MADRS after 2nd dose (12 mg) >75% response rates and up to 80% remission rates (12 mg) after a 2nd dose

Durable efficacy

Benefit sustained 4 months after 2 doses with 60% of patients on 12 mg and 75% on 16 mg in remission

Favorable safety profile

Excellent safety and tolerability profile – all reported AEs mild to moderate; no AEs of suicidality

Clear path to NDA

Phase 3 plan aligned with FDA at End of Phase 2 meeting

Notes

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Next Steps for Advancing CYB003 Towards NDA⁽¹⁾⁽²⁾

Phase 3 design aligned with FDA guidance



Clinical supplies manufactured and ready



30 study sites selected – with clinical expertise and training in depression studies



Multinational Phase 3 study will include sites across the U.S. and Europe



CYB003 Phase 3 MDD trial expected to initiate in summer of 2024

Notes:

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Deuterated DMT Program⁽¹⁾⁽²⁾⁽³⁾⁽⁴⁾⁽⁵⁾

	PHASE 1	PHASE 2	PHASE 3	UPCOMING MILESTONES
CYB004 (IM) Deuterated DMT	Phase 1 complete	Phase 2 initiated		 Year-end 2024: Topline data from Phase 2 Study of IM CYB004 in Generalized Anxiety Disorder (GAD)
SPL028 Injectable deuterated DMT	Phase 1 IM and IV complete			✓ Completed: Phase 1 IM/IV data in healthy volunteers
SPL026 DMT (IM and IV)	Completed: Phase 1 (IV and IM), Phase 1b SSRI-DDI (IV), Phase 2a in MDD (IV)			 ✓ Completed: Phase 1b SSRI Drug Interaction data readout ✓ Completed: Phase 2a data readout in MDD ✓ Completed: Phase 1 Study (IM and IV)

Notes

- (1) Forward-looking statements are subject to risks and assumptions. See "Cautionary Statement" on page2 of this presentation.
- (2) Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to the Company.

⁽⁵⁾ There is no assurance that the aforementioned will be met. Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to Cybin. Such statements are informed by, among other things, regulatory guidelines for developing a drug with timeline safety studies, proof of concept studies, and pivotal studies for new drug application submission and approval, and assumes the success of implementation and results of such studies on timelines indicated as possible by such guidelines, other industry examples, and Cybin's development efforts to date.



⁽³⁾ Certain statements regarding DMT have not been evaluated by the Food and Drug Administration, Health Canada or other similar regulatory authorities, nor has the efficacy of DMT been confirmed by approved research. There is no assurance that any of the Company's compounds will be used to diagnose, treat, cure or prevent any disease or condition and robust scientific research and clinical trials are needed. All such statements are subject to receipt of all necessary regulatory approvals from which all applicable governmental authorities, including, as applicable, the academic and scientific organizations with which Cybin is working. There are multiple risk factors regarding the ability to successfully commercially synthesized process to obtain DMT and other analogues.

⁽⁴⁾ Cybin is prioritizing the progression of its CYB003 program. The advancement of Cybin's deuterated DMT program is contingent on Cybin's ability to continue raising capital under its current and future financing arrangements. No assurances can be given that Cybin will be able to raise the additional capital that it may require for its anticipated future development.

Significant Unmet Need in GAD: Potential for CYB004 as a New Treatment Modality

High prevalence and burden of anxiety disorders

- Over 300 million people suffer from anxiety disorders worldwide ¹
- GAD is the most common anxiety disorder seen in primary care, with a 12-month prevalence of 2.9% in the U.S.²
- Approximately 77% of adults with GAD experience moderate to severe impairment³
- High comorbidity with depression: 50% of patients with major depression also have an anxiety disorder⁴

Current standard of care is inadequate

- 50% of patients with GAD do not respond to first line treatment with antidepressants such as SSRIs and SNRIs²
- Only 43% of patients with anxiety adhere to SSRI/SNRI treatment, due to side effects⁵

Other treatments have significant limitations:

- Benzodiazepines: risk of dependence, only recommended for short term use²
- Buspirone: delayed onset of effects, adherence challenges with dosing twice daily⁶

CYB004 has the potential to transform the current standard of care, with a new mechanism of action that could offer improved efficacy vs. existing treatments

Notes

-) Yang et al. (2021). Global, regional and national burden of anxiety disorders from 1990 to 2019. results from the Global Burden of Disease Study 2019. Epidemiology and Psychiatric Sciences 30, e36, 1–11. https://doi.org/10.1017/S2045796021000275/2) Ansara E. D. (2020). Management of treatment-resistant generalized anxiety disorder. The mental health clinician, 10(6), 326–334. https://doi.org/10.9740/mhc.2020.11.326
- 2) Anadra 1. (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry, 62(6):617-27.
- Hirschfeld R. M. (2001). The Comorbidity of Major Depression and Anxiety Disorders: Recognition and Management in Primary Care. Primary care companion to the Journal of clinical psychiatry, 3(6), 244-254. https://doi.org/10.4088/pcc.v03n0609 Stein et al. (2006). Antidepressant Adherence and Medical Resource Use Among Managed Care Patients With Anxiety Disorders. Psychiatric Services, 57(5): 673-680.
- Melaragno, A.J. (2021). Pharmacotherapy for Anxiety Disorders: From First-Line Options to Treatment Resistance. Focus, 19(2): 145-160. https://doi.org/10.1176/appi.focus.20200048



Target Product Profile for dDMT optimized with data from 5 clinical studies

	Study	Trial Design	Key findings		
	Phase 1/2a study in MDD	Part A (n=32): SAD study with 4 cohorts (HVs) • IV infusion (~10 min)	✓ IV DMT is well-tolerated and generates breakthrough psychedelic experience (20-30 min)		
SPL026 DMT IV or IM	POC study in moderate to severe MDD (no SSRIs)	 Part B (n=34, 17 active, 17 placebo) First 2 weeks double-blind, placebo-controlled 2 doses 2 weeks apart, all patients received active second dose IV infusion (~10min) 	 ✓ Rapid, robust and durable antidepressant effect ✓ 46% of MDD patients in remission at 3 months ✓ 40% of MDD patients in remission at 6 months ✓ Favorable safety and tolerability in MDD patients ✓ Rapid improvement in anxiety and wellbeing scores 		
17 01 1111	2 Phase 1 IV/IM study	2 HV cohorts, IV crossover, and IM single doseIV infusion (~10 min) and IM injection	 IM DMT is well-tolerated and generates a breakthrough psychedelic experience (~45 min) 		
	Phase 1 SSRI DDI study	 DDI study in moderate to severe MDD patients N=17 (12 on SSRIs, 5 not on SSRIs) Single dose IV infusion (~10 min) 	 ✓ Potential enhanced effect when given as adjunctive to SSRIs: 92% remission rate in SSRI cohort vs. 20% remission (non-SSRI cohort) ✓ DMT safe and well-tolerated when co-administered with SSRIs 		
CYB004	Phase 1 Study of IV CYB004 and IV DMT	 SAD study in healthy volunteers Part A (n=39): IV DMT infusion (90 min) 	 ✓ 90 min infusion was well tolerated with strong psychedelic effects at the highest dose ✓ Bolus + infusion provided sustained psychedelic effects 		
dDMT		 Part B (n=12): IV DMT bolus + infusion Part C (n=24): IV CYB004 bolus (5 min) + infusion (30 min) and IV bolus (5 min) only arms 	over an extende'd period of time ✓ IV dDMT is well-tolerated and generates breakthrough psychedelic experience (~40 min)		
SPL028 dDMT IV or IM	5 Phase 1 IM/IV study	 SAD study with 5 cohorts Part 1 (n=16): IV vs IM cross-over dosing Part 2 (n=22): Single IV or IM doses of SPL028 	✓ IM dDMT dose is well-tolerated and generates breakthrough psychedelic experience (average ~90 min)		



Rapid Onset of Large Treatment Effect in MDD⁽¹⁾⁽²⁾⁽³⁾

Phase 2a trial of IV SPL026 (DMT) in MDD

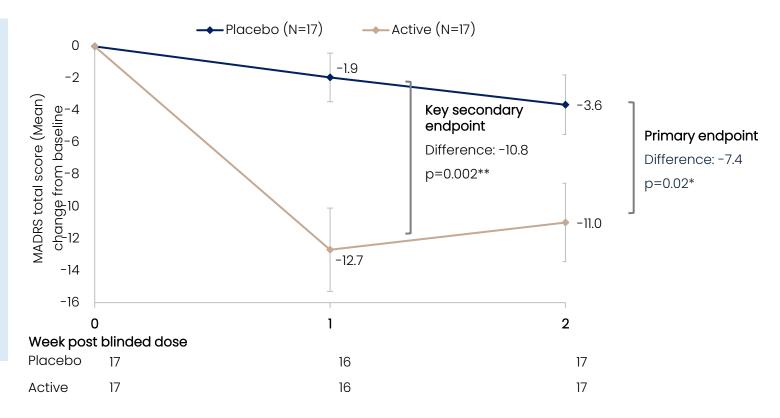
Topline Results

Rapid and robust antidepressant efficacy

- Primary endpoint met with -7.4 point difference between SPL026 (21.5mg IV) and placebo at two-weeks post-dose, as measured by MADRS change from baseline (p=0.02)
- Rapid onset antidepressant effects at one-week post-dose with a difference in MADRS of -10.8 versus placebo (p=0.002)

Favorable safety and tolerability profile

- No drug-related Serious Adverse Events (SAEs)
- All adverse events (AEs) mild or moderate in intensity, and majority resolved during dosing visit



Notes:

Error bars represent Standard Error Mean (SEM); MADRS = Montgomery-Asberg Depression Rating Scale; n = number of datapoints; N = population number; p = p-value; * = p<0.05; ** = p<0.01

n

3) Cybin is prioritizing the progression of its CYB003 program. The advancement of Cybin's deuterated DMT program is contingent on Cybin's ability to continue raising capital under its current and future financing arrangements. No assurances can be given that Cybin will be able to raise the additional capital that it may require for its anticipated future development.

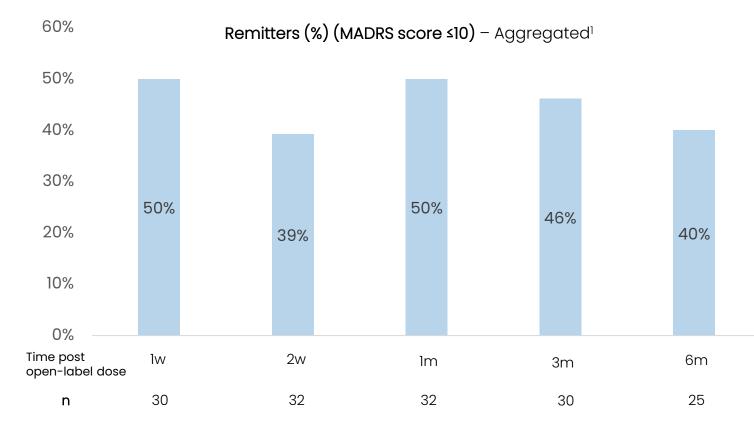


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Sustained Remission Observed at Six Months with DMT Therapy⁽³⁾⁽⁴⁾ Phase 2a trial of IV SPL026 (DMT) in MDD

Key takeaways

- Both remission and response outcomes were consistent in the one and two dose regimens
- Encouraging remission rates
 demonstrated to at least 6 months
- Among the patients who had achieved remission within three months with SPL026, 64% sustained remission to six months²



Notes: MADRS = Montgomery-Asberg Depression Rating Scale; n = number of datapoints

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¹⁾ Refers to mean aggregated outcomes of all patients receiving an active dose in the open label phase; and includes four participants excluded from the formal statistical analysis who received a blinded dose of SPL026 but did not receive a second open label dose.

⁾ Based on data from patients followed up out of study

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Potential Enhanced Efficacy with SSRIs⁽¹⁾⁽²⁾⁽³⁾

Phase 1b SPL026(DMT)-SSRI Drug Interaction Study in MDD

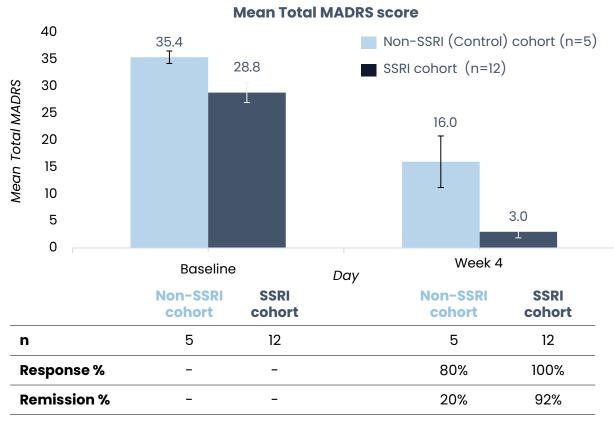
Trial Design

Population: MDD patients (HAM-D ≥14)

Treatment: IV SPL026 (27.5 mg) with support therapy

Topline Results

- ✓ Potentially enhanced antidepressant effects of SPL026 when administered with SSRIs:
 - Week 4 remission rate: 92% (SSRI cohort) vs. 20% (Non-SSRI cohort)
 - Week 4 mean total MADRS: 3.0 (SSRI cohort) vs. 16.0 (Non-SSRI cohort)
- ✓ SPL026 well tolerated by all patients in both the SSRI and non-SSRI cohorts
- ✓ Small number of drug-related adverse events reported, all deemed mild to moderate: SSRI cohort (n=8), Non-SSRI cohort (n=3).



Notes

1) Control (Non-SSRI) cohort N=5: MDD patients not on any pharmacological medication to treat their depression symptoms, Test (SSRI) cohort N=12: MDD patients on stable treatment course of SSRIs

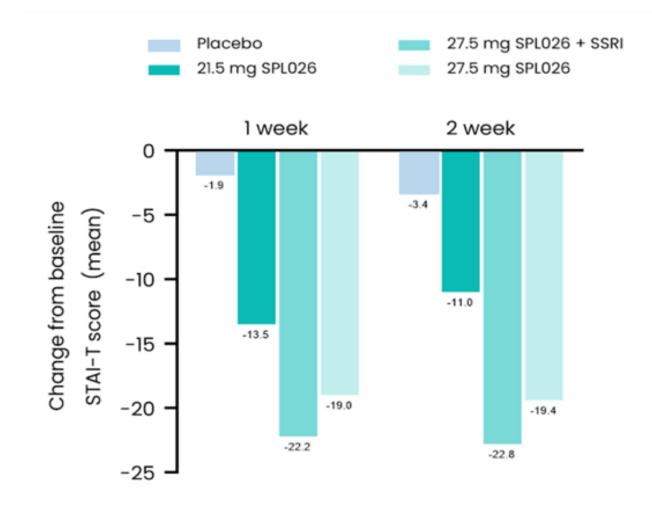
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Strong effects on symptoms of anxiety

- ✓ Efficacy assessed as change from baseline in STAI-T scores
- ✓ Data from the MDD monotherapy (21.5 mg) and SSRI add on studies (27.5 mg)
- ✓ Provides proximal de-risking of development in anxiety



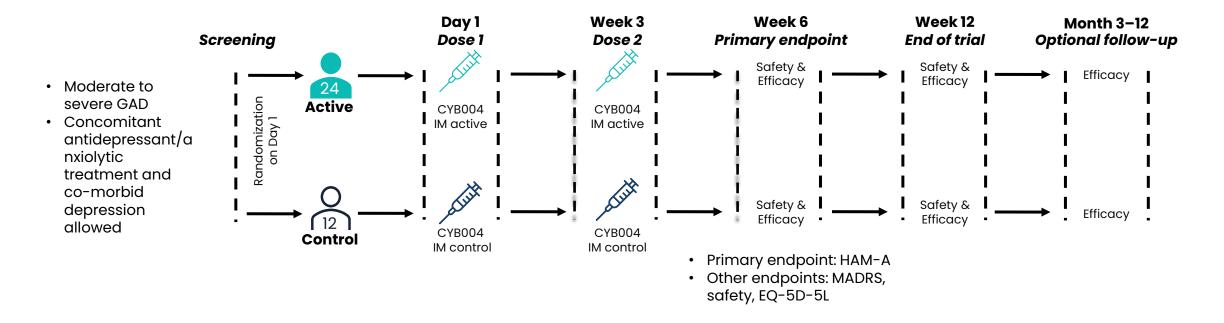
Notes: STAI: State-Trait Anxiety Inventory

Doses: 21.5 mg and 27.5 mg doses administered at different rates 21.5 mg in the Phase 2a MDD study, 27.5 mg in the SSRI DDI study Placebo data reported is from the Phase 2a study in MDD



Phase 2 Proof-of-Concept Study: CYB004 in GAD

The Phase 2 study is designed to evaluate CYB004's efficacy and safety in GAD, time to onset of effects, and durability of effects to 12 months.



Phase 2 study initiated; topline safety and efficacy data expected in Q4 2024

Notes:

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Value-Driving Milestones Across Development Pipeline

Q2 2024 Q3 2024 Q4 2024 Topline efficacy data Initiate Phase 3 ✓ Initiated Phase 2 readout from **CYB004** multisite, multinational trial of CYB004 (IM) in (IM) Phase 2 clinical study of **CYB003** in MDD GAD summer 2024 trial in GAD around year-end 2024

Cybin



Thank You

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Contact: ir@cybin.com

