

Mindset Pharma Inc.

Initiating Coverage – The Grateful Meds: Next-Gen Psychedelics, Industry-Leading IP, and a Big Pharma Partner Along for the Trip

MSET-CSE: \$0.33
Speculative Buy
\$1.25 Target

Event – We are initiating coverage on Mindset Pharmaceuticals with a Speculative Buy rating and \$1.25/shr PT, representing 279% upside. Mindset is a differentiated developer of patented psychedelic therapeutics with potentially improved safety and functional profiles that make them better fit for purpose. Importantly, the Company’s patent strength is validated by a bona fide Big Pharma partner that will provide ~US\$30-40M in total development funding, in line with Mindset’s current market cap.

Projected Return: 279%
Discount Rate: 14%

- Psychedelic Drugs Show Promise for the Treatment of Mental Health Conditions** – Psilocybin, DMT (N,N-Dimethyltryptamine), and other first-generation psychedelics are showing promise alongside psychotherapy for treatment-resistant depression (TRD), post-traumatic stress disorder (PTSD), anxiety, and a litany of other mental health indications in active clinical trials conducted by third parties. COMPASS Pathways (CMPS-NASDAQ, NR) leads the psilocybin pack with COMP360, its synthetic psilocybin-assisted treatment for TRD, while Small Pharma’s (DMT-CNSX, NR) SPL026 leads the DMT pipeline with Phase I/II data.
- Despite Clinical Promise, Patents on Classic Psychedelics are Unlikely to Hold** – Even if approved for use by the FDA, patents on first-generation psychedelic compounds will likely prove unenforceable, meaning ‘big pharma’ is less likely to partner with other sector leaders as their business model is not “Pharma-like.”
- Differentiated, Patentable Compounds for Multi-Stage Commercialization** – Mindset is developing four families of drug candidates inspired by psilocybin and DMT but with improved safety profiles and optimized potency and bioavailability. By leveraging the existing data generated in ongoing trials of the classic psychedelic compounds, they may also be among the first second-gen psychedelic drugs to market with robust patent protection.
- First-of-its-Kind Big Pharma Deal Serves as Major IP Validation** – Mindset’s partnership with Otsuka Pharmaceutical (4578-TSE, NR; US\$20B market cap) is one of the first big pharma deals in the space (first and only deal for next-gen drug candidates). In return for single-digit royalties and right of first refusal/negotiation, Otsuka paid US\$5M upfront and agreed to cover all development expenses through the Phase Ib for shorter-acting Family 2 and 4 drug candidates that allow for increased patient throughput (~US\$30-40M total). This unique deal with a global pharma player is a major validation of Mindset’s IP portfolio while providing it with non-dilutive financing.
- Next-Gen Drugs Could Expand Multiple Blockbuster Markets** – While TRD and end-of-life cancer angst are growing, multi-billion-dollar markets, Mindset’s drug candidates could further expand these and other markets by accelerating the onset of action and truncating the hallucinogenic effects, potentially allowing for higher clinical patient throughput.
- Multiple Catalysts on the Horizon** – Upcoming catalysts include lead candidate MSP-1014 moving to Phase I clinical trials as well as Family 2 & 4 lead candidate selection, all by year end. Potential partnerships for Families 1 and 3 may be catalysts over the next 24 months.

Valuation – We value MSET at \$1.25/share using a probability-adjusted DCF (14% discount rate, 5% residual growth, 10% probability of approval of its lead asset for TRD and end-of-life cancer angst). Our Speculative Buy rating reflects anticipated share price volatility as well as the inherent clinical trial risks.

Mindset Pharma Inc.

Market Cap - Basic (\$M)	31
Market Cap - FD (\$M)	45
Net Debt (\$M)	-12
Enterprise Value - FD (\$M)	33
Basic Shares O/S (M)	93
FD Shares O/S (M)	136
Avg. Daily Volume (K)	40
52 Week Range	\$0.30 - \$1.04

Revisions	Old	New
2022E Revenue (\$M)	NA	0.0
2022E EBITDA (\$M)	NA	-0.3
2022E EPS	NA	(\$0.03)

Financial Metrics

FYE - June 30	F2020A	F2021A	F2022E
Revenue (\$M)	0.0	0.0	0.0
Gross Profit (\$M)	0.0	0.0	0.0
Adj. EBITDA (\$M)	(0.0)	(0.0)	(0.3)
EPS	(\$0.03)	(\$0.12)	(\$0.02)

Valuation Data

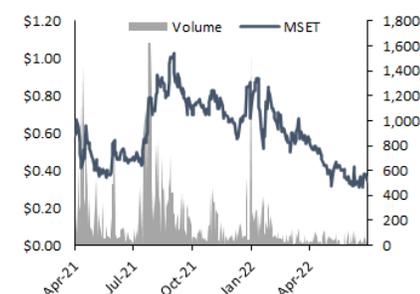
		F2020A	F2021A	F2022E
EV/Sales	MSET	NA	NA	2.2x
	Peers	27.8x	11.5x	2.8x
EV/EBITDA	MSET	NA	NA	NA
	Peers	NA	NA	NA

Quarterly Data

		FQ1	FQ2	FQ3	FQ4
Revenue (\$M)	2021	0.0	0.0	0.0	0.0
	2022	0.0	0.0	2.3	4.3
	2023	4.3	4.3	4.3	4.3
Adj. EBITDA (\$M)	2021	(0.0)	(0.0)	(0.3)	(0.6)
	2022	(1.4)	(2.6)	(0.1)	0.6
	2023	(1.0)	(1.0)	(1.0)	(1.0)
EPS	2021	(\$0.03)	(\$0.12)	(\$0.03)	(\$0.02)
	2022	(\$0.09)	(\$0.08)	(\$0.01)	(\$0.01)
	2023	(\$0.03)	(\$0.03)	(\$0.03)	(\$0.02)

Company Description

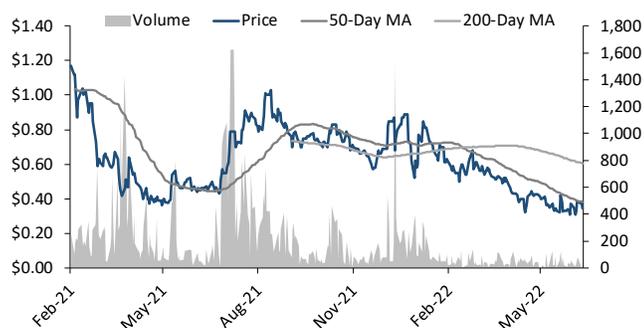
Mindset Pharma Inc. operates as a neuro-pharmaceutical drug discovery and development platform company. It offers psychedelic compounds for treatment-resistant neurological and psychiatric disorders. The company was founded in 2019 and is based in Toronto, Canada.



Source: Consensus Data - CapIQ, Forecasts/Estimates - ECM

Mindset Pharma (CNSX:MSET, \$0.33) - Data Sheet

Speculative Buy | PT: \$1.25



Company Description

Mindset Pharma Inc. operates as a neuro-pharmaceutical drug discovery and development platform company. It offers psychedelic compounds for treatment-resistant neurological and psychiatric disorders. The company was founded in 2019 and is based in Toronto, Canada.

Consensus	3 Mths Ago	Current	Return
Rating:	Outperform	Outperform	
Target:	NA	\$1.25	279%
Median:	NA	\$1.25	279%
High:	NA	\$1.25	279%
Low:	NA	\$1.25	279%

Consensus Ratings Distribution	
Outperform/Buy	2
Perform/Hold	0
Underperform/Sell	0
# Est	2

Key Statistics	Value
52-Week High	\$1.04 215%
52-Week Low	\$0.30 (9%)
Avg Vol (3-Mo)	40
Shares Outstanding	91
Market Cap	45
Net Debt	-12
Enterprise Value	33
Div Yield	0.0%
FYE	Jun

Family / Lead Candidate	Indication	Lead Identification	Lead Optimization	IND-Enabling	Phase I Clinical Trials	Phase II Clinical Trials	Phase III Clinical Trials
Family 1 / MSP-1014	Treatment-Resistant Depression & End of Life Cancer Angst				Expected Q422-Q123		
Family 2	TBD				Expected Q323-Q124		
Family 4	TBD				Expected Q323-Q124		
Family 3	Cognitive/Attentional Impairment				Expected Late 2023		
Undisclosed	TBD						

Key Financial Metrics

Mindset Pharma	F2021A	F2022E	F2023E	F2024E	F2025E	F2026E	F2027E	F2028E	F2029E	F2030E	F2031E	F2032E
Values in C\$M												
Revenue	-	6.6	17.2	20.0	15.0	-	30.0	3.8	60.5	142.4	121.9	198.4
Growth y/y, %	NA	NA	162%	17%	(25%)	(100%)	NA	(87%)	1471%	136%	(14%)	63%
Consensus Revenue		2.3	-	-	-	6.6	52.8	NA	NA	NA	NA	NA
Gross Profit	-	6.6	17.2	20.0	15.0	-	30.0	3.1	57.4	132.9	101.4	165.7
Gross Profit Margin, %	0%	100%	100%	100%	100%	0%	100%	80%	95%	93%	83%	83%
Consensus Gross Profit Margin, %		NA	NA	NA	NA	NA						
Adj. EBITDA	(2.3)	(3.6)	(4.0)	(22.1)	(38.0)	(58.5)	(38.0)	(60.4)	12.4	98.4	69.4	137.2
Adj. EBITDA Margin, %	0%	(55%)	(23%)	(111%)	(253%)	0%	(127%)	(1570%)	20%	69%	57%	69%
Consensus Adj. EBITDA		(19.7)	(18.7)	(27.4)	(44.1)	(61.7)	(43.1)	NA	NA	NA	NA	NA
EPS, \$	\$ (0.20)	\$ (0.19)	\$ (0.11)	\$ (0.21)	\$ (0.28)	\$ (0.31)	\$ (0.16)	\$ (0.21)	\$ 0.01	\$ 0.20	\$ 0.14	\$ 0.29
Consensus EPS, \$		\$ (0.22)	\$ (0.11)	\$ (0.12)	\$ (0.09)	\$ (0.09)	\$ (0.05)	NA	NA	NA	NA	NA

Comparables

Name	MC (US\$M)	EV (US\$M)	Ticker	Price (Local)	1M	3M	YTD	1Y	2020	EV/Sales 2021	2022	2020	2021	2022
Mindset Pharma Inc.	24.8	3.9	MSET	\$0.33	-1%	-38%	-59%	-25%	NA	NA	2.2x	NA	NA	NA
Atai Life Sciences N.V.	591.5	265.7	ATAI	\$3.80	0%	-27%	-52%	-80%	NA	15.4x	3542.1x	NA	NA	NA
Mind Medicine (MindMed) Inc.	279.1	158.6	MNMD	\$0.72	-37%	-38%	-52%	-81%	NA	NA	NA	NA	NA	NA
COMPASS Pathways plc	486.3	245.6	CMPS	\$11.62	24%	-17%	-48%	-69%	NA	NA	NA	NA	NA	NA
Cybin Inc.	96.1	55.1	CYBN	\$0.58	-26%	-29%	-52%	-73%	NA	123.6x	NA	NA	NA	NA
Mydecine Innovations Group Inc.	6.4	10.0	MYCO.F	\$0.71	-20%	-81%	-87%	-96%	5097.5x	194.9x	1.1x	NA	NA	NA
Numinus Wellness Inc.	51.1	18.2	NUMI	\$0.26	-28%	-54%	-50%	-70%	27.8x	11.5x	3.8x	NA	NA	NA
Field Trip Health Ltd.	49.4	11.4	FTRP	\$1.10	7%	-28%	-64%	-84%	NM	16.5x	2.8x	NA	NA	NA
Filament Health Corp.	13.2	11.1	FLHL.F	\$0.08	-26%	-9%	-65%	-71%	NA	NA	NA	NA	NA	NA
Entheon Biomedical Corp.	3.7	3.0	ENBI	\$0.05	-9%	-55%	-85%	-88%	NA	NA	NA	NA	NA	NA
PsyBio Therapeutics Corp.	8.5	6.4	PSYB	\$0.10	43%	25%	-50%	-78%	NA	NA	NA	NA	NA	NA
Average	158.5	78.5			-7%	-31%	-60%	-79%	2562.6x	72.4x	887.5x	NA	NA	NA
Median	50.3	14.8			-15%	-28%	-52%	-79%	2562.6x	16.5x	3.3x	NA	NA	NA

Source: Consensus Data - CapIQ, Historical Data - Company Filings, Forecasts/Estimates - Echelon Capital Markets

Company Overview

Headquartered in Toronto, Ontario, Mindset Pharma is a drug discovery and development company creating novel, differentiated, and patentable psychedelic drug candidates for use primarily in psychedelic-assisted psychotherapy (PAP) settings to treat patients suffering from treatment-resistant neurological and psychiatric disorders. Through its neuro-pharmaceutical drug development platform, Mindset builds upon the known chemical scaffolds of naturally occurring compounds with promising clinical data to create next-generation drug candidates with improved effect sizes, pharmacokinetics, and safety profiles. While the next-gen psychedelics landscape is highly competitive, Mindset has the first-mover advantage with regards to patenting its innovations and arguably has one of the strongest IP positions in the space. Indeed, Mindset’s recent collaboration agreement with Otsuka Pharmaceutical, the first big pharma deal in the space centred around psilocybin- and DMT-like molecules, serves as critical validation of its strong IP position. Mindset has also developed a patent-pending synthesis process that offers cost-effective, large-scale synthesis of cGMP psilocybin to serve the increasing number of ongoing psilocybin studies and human clinical trials.

Exhibit 1 – Overview of Mindset’s Pipeline & Upcoming Catalysts

Family / Lead Candidate	Compound	Indication	Development Stage	Upcoming Catalysts	Estimated Timeline	Comments
Family 1 / MSP-1014	Psilocybin-like	Treatment-Resistant Depression & End of Life Cancer Angst	IND-Enabling	Move to Phase I Clinical Trials Potential Partnership	Q422 - Q223 Late 2022 - 2023	Candidate for Potential Partnership Agreement, Orally-active CNS Penetrant
Family 2	Psilocybin-like	TBD	Lead Optimization	Lead, Indication Selection Move to Phase I Clinical Trials	Q222 - Q322 Q323 - Q124	Otsuka Pharma Partnership Funds Phase I Clinical Trials, Shorter Duration of Effect
Family 4	DMT-like	TBD	Lead Optimization	Lead, Indication Selection Move to Phase I Clinical Trials	Q322 - Q422 Q323 - Q124	Otsuka Pharma Partnership Funds Phase I Clinical Trials, Shorter Duration of Effect
Family 3	Psilocybin-like	Cognitive/Attentional Impairment	Lead Identification	Lead, Indication Selection Move to Phase I Clinical Trials	Late 2022 Late 2023	Microdosing Indications, Longer Duration of Effect
Undisclosed		TBD	Lead Identification	Lead, Indication Selection	TBD	

Source: Company Filings/Press Releases, ECM

Safer, More Potent Drug Candidates Building on Classic Psychedelics’ Promising Initial Data

While classic, first-generation psychedelics such as psilocybin, DMT (N,N-Dimethyltryptamine), MDMA (3-4 methylenedioxymethamphetamine), and ibogaine are showing great clinical promise for the treatment of neuropsychiatric disorders such as TRD, PTSD, anxiety, alcohol use disorder, and end-of-life angst, their market penetration could be hindered by sub-optimal safety profiles and the exceedingly long-lasting hallucinogenic effects (6-8 hours) limiting patient throughput. In addition, it is yet to be seen whether patents on classic psychedelic compounds will provide adequate protection for monetization. Mindset is developing patentable derivatives of psilocybin and DMT with optimized receptor binding profiles that either intensify and truncate the hallucinogenic experience or elongate it to the point that its effects are subperceptual.

Exhibit 2 – Overview of Mindset Pharma’s Drug Portfolio

Macro dosing		Micro dosing	
<p>Family</p> <p>#1</p> <p>PSILOCYBIN-INSPIRED</p> <ul style="list-style-type: none"> • Psilocybin analog – potential 505(b)2 pathway drug. • Similar 5-HT2A receptor binding and functional profile to psilocybin. • CNS penetrant and orally active. 	<p>Family</p> <p>#2</p> <p>PSILOCYBIN-INSPIRED</p> <ul style="list-style-type: none"> • Improved 5-HT2A receptor functional profile. • CNS penetrant and orally active. • Potentially shorter acting. 	<p>Family</p> <p>#4</p> <p>DMT/5-MeO-DMT-INSPIRED</p> <ul style="list-style-type: none"> • Unique serotonergic receptor profile. • Short duration. • Distinct behavioural pattern. 	<p>Family</p> <p>#3</p> <p>PSILOCYBIN-INSPIRED</p> <ul style="list-style-type: none"> • Similar 5-HT2A receptor binding and reduced functional profile to psilocybin. • Long duration of effect.

Source: Company Presentation

Cash Covers Near-Term Burn, MSP-1014 Partnership Could Add Liquidity

Mindset closed the March 2022 quarter (FQ322) with \$11.3M in cash on the balance sheet, no debt, and ~\$28.3M available from currently outstanding warrants and options, including ~\$7M to be exercised by January 2023. While MSR/D/Otsuka will fund the lead candidates from Families 2 and 4 through Phase Ib, a deal or partnership to bring MSP-1014 through human clinical trials and to market would bring in additional upfront cash and/or reduce the cash burn through a cost-sharing agreement. Absent such a deal, we expect the Company to raise ~\$10-15M in equity by the end of F2023 (June 2023) to cover its burn rate.

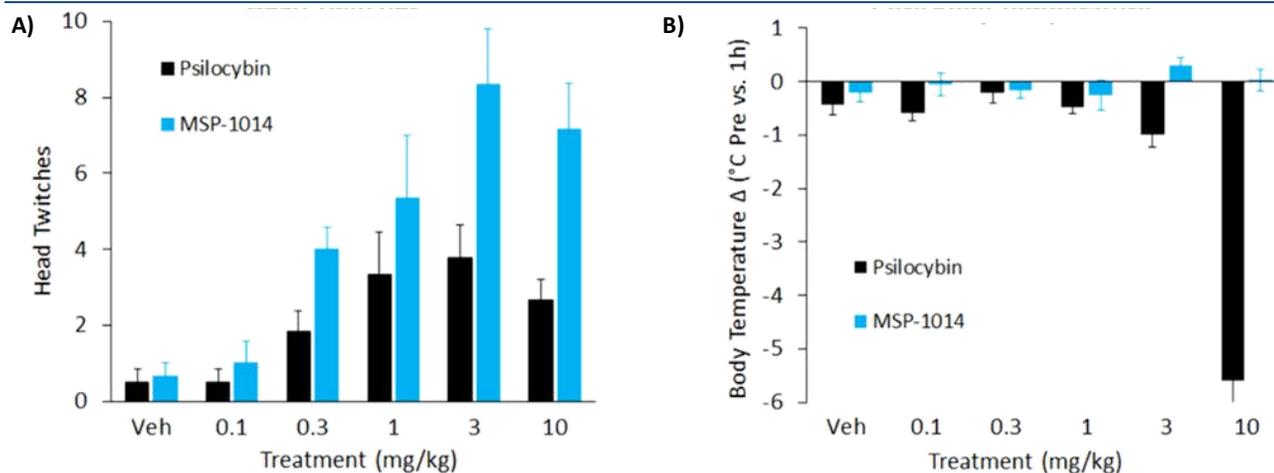
Mindset’s Macro dosing Portfolio

Macro dosing, the consumption of a large enough dose of a psychedelic compound to experience its hallucinogenic effects, is the therapeutic model on which substantively all of the existing clinical data is based. Under the supervision of an administering clinician in a licensed clinic, the patient undergoes a significant psychedelic trip as part of a regimen that involves regular psychotherapy before and after the trip.

Family 1 – Psilocybin Analogs with Improved Bioavailability, Receptor-Binding and Safety Profiles

The lead candidate from this family, MSP-1014, is an orally active, psilocybin-like prodrug that penetrates the central nervous system (CNS) and breaks down into the active major metabolite, psilocin, which binds to the 5-HT_{2A} subtype receptor, a member of the serotonin receptor family (similar to classic psilocybin). Given MSP-1014’s molecular and functional similarities to psilocybin, the Company hopes to utilize aspects of the truncated 505(b)2 regulatory pathway to gain quicker approval by averting the need to repeat some preclinical development work already done by others to assess psilocybin’s safety and clinical efficacy. Management anticipates that MSP-1014 will enter Phase I clinical trials between CQ422 and CQ223.

Exhibit 3 – MSP-1014 vs. Psilocybin Head Twitches (A) and Body Temperature (B)

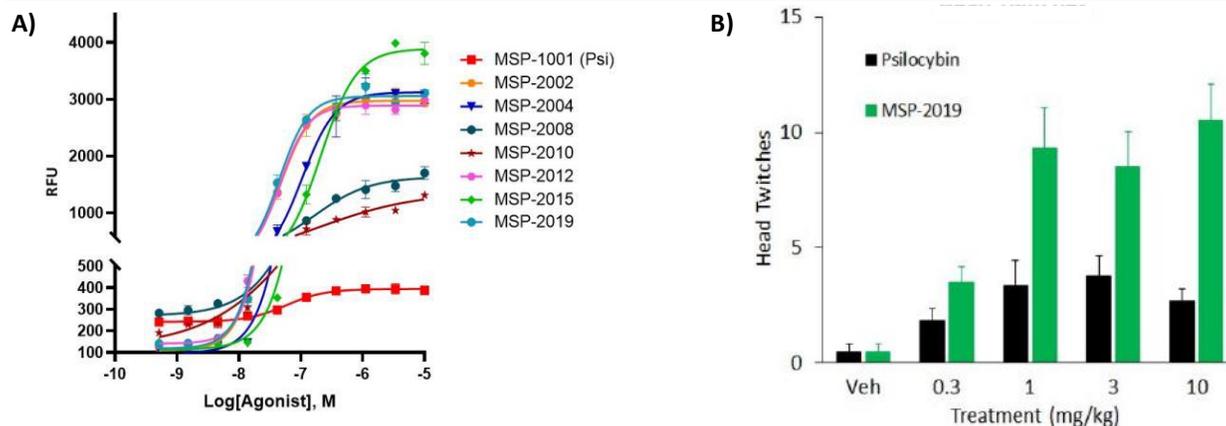


Source: Company Presentation

Family 2 – Shorter-Acting Psilocybin Analogs

Mindset’s Family 2 drug candidates are orally active, third-generation psilocybin analogs that are chemically optimized to have improved receptor binding and function profiles compared to classic psilocybin, leading to a more potent, shorter-acting drug. These drugs may allow for higher throughput of patients in a PAP setting and may be administered at lower doses than classic psilocybin, potentially improving their safety profile. While the lead compound to be advanced from Family 2 and its clinical indication have not yet been specified, its Phase I trials will be funded by the McQuade Center for Strategic Research and Development (MSRD)/Otsuka partnership. The Phase I trial for the lead candidate is expected by management to begin between CQ323 and CQ124.

Exhibit 4 – Family 2 Candidates vs. Psilocybin 5-HT2A Agonism (A) and Head Twitch Count (B)

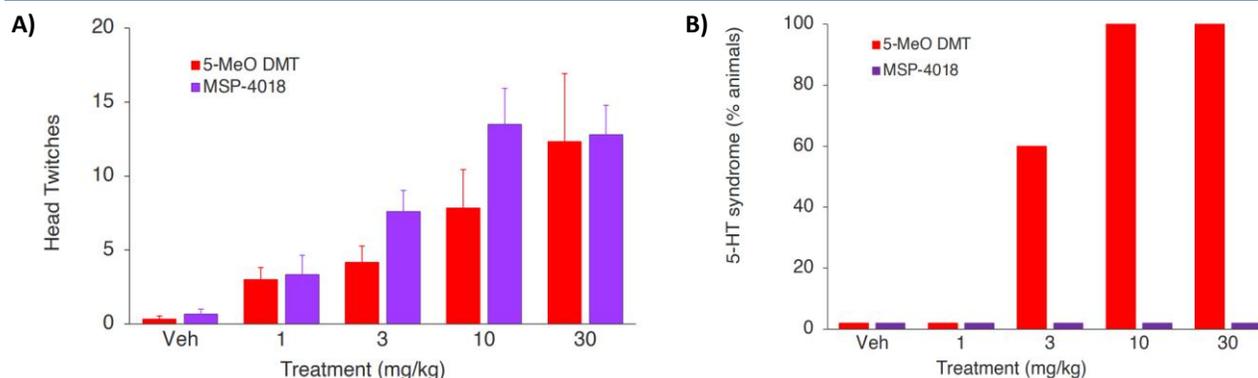


Source: Company Presentation

Family 4 – Potentially Safer DMT/5-MeO-DMT Analogs with a Range of Durations

The Family 4 drug candidates are DMT- and 5-MeO-DMT-inspired drug candidates with unique serotonergic receptor profiles and a range of hallucinogenic effects anticipated to last from minutes to hours. Similar to the Family 2 drugs, the lower dosing and potentially improved safety profile along with the tuned hallucinogenic time make this family of drugs better suited to a PAP setting than classic DMT. More than 25 Family 4 compounds demonstrate similar binding profiles to the 5-HT2A receptor comparable to that of the classic DMT or 5-MeO-DMT, but with a larger effect size. Several of these compounds show heightened activity at the 5-HT1A and 5-HT2C subtype receptors, both of which have been implicated in anti-depressant and substance abuse. As such, the Family 4 compounds' receptor activity signatures differentiate them from Family 2 compounds for potential macrodosing applications. Recent *in vivo* data for certain Family 4 compounds indicate a superior safety profile to 5-MeO-DMT which, despite its [clinical promise for TRD](#), is known to elicit serotonin syndrome effects – a potentially serious drug reaction caused by medications that build up high levels of serotonin in the body. While the lead compound to be advanced from Family 4 and its clinical indication have not yet been specified, its ongoing IND-enabling studies and subsequent human Phase I trials will be funded by the MSRD/Otsuka partnership. Management anticipates that the Family 4 lead candidate compound will enter Phase I clinical trials in late C2023/early C2024.

Exhibit 5 – Family 4 Candidate vs. DMT Head Twitch Count (A) and 5-HT Syndrome Elicitation (B)



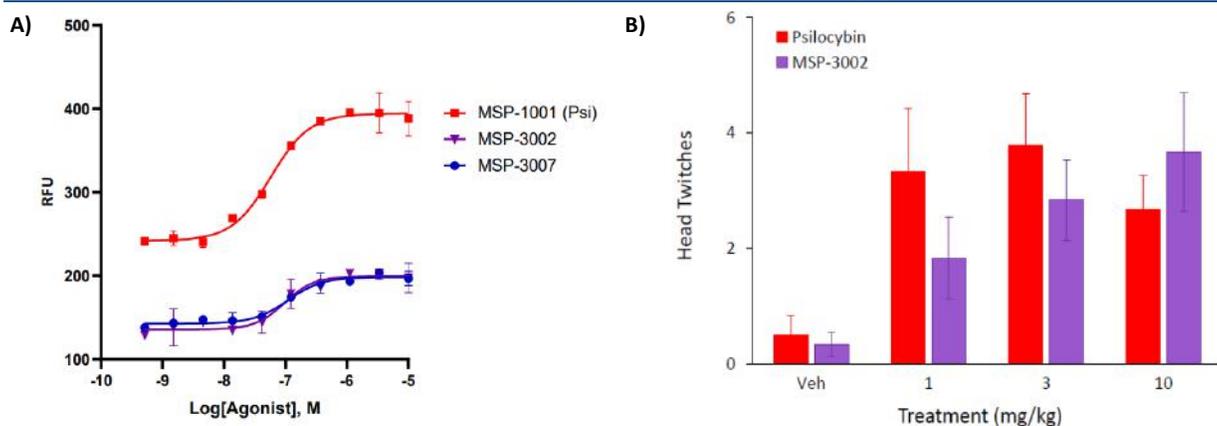
Source: Company Presentation

Mindset’s Microdosing Portfolio

Family 3 – Longer-Acting Psilocybin Analogs for Daily Microdosing

In contrast to Family 2, the Family 3 drug candidates are designed to have a reduced functional profile and a longer duration of effect compared to classic psilocybin, with no hallucinogenic effects at the prescribed dose. These next-generation compounds have the potential to treat specialized indications such as pediatric attention deficit hyperactive disorder (ADHD) and obsessive-compulsive disorder (OCD). Preclinical *in vitro* data in [Exhibit 6A](#) show two microdosing candidates’ reduced 5-HT_{2A} subtype receptor binding profile compared to classic psilocybin. This suggests that, in the event that a patient takes too large a dose, they will not feel the full hallucinogenic effects as if they had taken classic psilocybin. In addition, [Exhibit 6B](#) shows that, at the clinically relevant doses of 1 and 3 mg/kg, MSP-3002 has less of a physical effect on the mice studied in the *in vivo* preclinical trials. Management anticipates that the Family 3 lead candidate compound will enter Phase I clinical trials in C2024.

Exhibit 6 – Family 3 Candidates vs. Psilocybin 5-HT_{2A} Agonism (A) and Head Twitch Count (B)



Source: Company Presentation

There are some indications, such as ADHD, OCD and Alzheimer’s Disease, that could benefit from the pro-cognitive neuroplasticity benefits of psilocybin but over a longer duration without the hallucinogenic effects. Indeed, gentler, non-hallucinogenic drugs would likely be more palatable than classic, hallucinogenic psychedelics for many patients. While the list of potential indications to be addressed by this family of drugs has been narrowed down to those related to cognitive/attentional impairments, the Company will have to clearly define the impaired population in order to begin enrolling for clinical trials.

150+ Second-Generation Psychedelics Covered by 15 US and International Patents

Mindset has screened 150+ new chemical entities (NCEs), resulting in 15 US and international patent filings. Importantly, Mindset was early to recognize the importance of patents’ priority dates (the date on which a patent is filed) and was one of the first companies to begin filing patent applications in early C2020. The Company’s seasoned medicinal chemists noted early that this is of critical importance, as whichever company is first to file a patent on an individual compound gets priority date on that compound, while owners of patents filed later (with overlapping claims) may end up paying royalties on sales of their products to the first mover.

Exhibit 7 – Patent Portfolio Provides Comprehensive Protection of Mindset’s Novel Compounds

Patent	Filing Jurisdiction	Application Number	Priority Date	Compound Family	Status
1	PCT (International)	PCT/CA2021/50125	4/2/2020	Family 1	Patent Pending
2	PCT (International)	PCT/CA2021/50123	4/2/2020	Family 1	Patent Pending
3	PCT (International)	PCT/CA2021/50122	4/2/2020	Family 2	Patent Pending
4	PCT (International)	PCT/CA2021/50755	07/12/2020	Family 3	Patent Pending
5	US	63/122181	7/12/2020	Family 3	Patent Pending
6	PCT (International)	PCT/CA2021/50296	2/3/2021	Family 4	Patent Pending
7	US	63/155634	2/3/2021	Family 4	Patent Pending
8	US	63/260470	21/8/2021	Family 4	Patent Pending
9	US	63/202081	26/5/2021	Combination NCEs	Patent Pending
10	US	62/969934	4/2/2020	Family 1	Incorporated into PCT Patents 1 & 2
11	US	62/969894	4/2/2020	Family 2	Incorporated into PCT Patent 3
12	US	63/056058	24/7/2020	Synthesis Process	Incorporated into PCT Patent 13
13	PCT (International)	PCT/CA2021/51029	24/7/2020	Synthesis Process	Patent Pending
14	US	17/387,845	4/2/2020	Family 1	Patent Pending
15	US	17/387,864	4/2/2020	Family 2	Patent Pending

Source: Company Filings

Otsuka Pharma Deal Validates IP Strength, Funds Families 2 and 4 Through Phase I Trials

In January 2022, Mindset announced a collaboration with MSRD, a division of Otsuka Pharmaceuticals. Headquartered in Tokyo, Japan, Otsuka is a ~¥2.7T (~US\$20B) family of diversified pharmaceutical companies with combined annual revenues of ~¥1.5T (~US\$11B). MSRD focuses on early-stage drug discovery and development, primarily for mental health and renal disorders, is the most active big pharma in psychedelics, and is the only big pharma arm to have invested in the space. MSRD’s first investment was a US\$80M Series B in COMPASS Pathways in early C2020, followed by a collaboration and licensing agreement with Perception Neuroscience, an Atai Life Sciences (ATAI-NASDAQ, NR) subsidiary, for the development of PCN-101 (R-ketamine) for TRD in Japan. Given its involvement with larger, more clinically advanced psychedelics players to date, we surmise that, along with promising medicinal chemistry, Otsuka/MSRD’s decision to partner with Mindset centres around its stronger IP position.

Per the terms of its agreement with Mindset, MSRD has made a US\$5M upfront cash payment and will fund and support the development of the two lead candidates selected from Families 2 and 4, the families of shorter-acting psychedelic analogs, through Phase Ib clinical trials. We estimate that this would cost ~US\$15-20M per candidate. In return, Mindset has granted MSRD a right of first refusal with respect to any asset sale or licensing/collaboration agreements pertaining to the relevant drugs as well as a right of first negotiation with respect to a merger, acquisition, or asset sale. This means that MSRD will have the first right to negotiate a new deal to expand the collaboration and continue co-development after the release of the Phase Ib data. If no right of first refusal is consummated, MSRD will be eligible to receive single-digit percentage royalties on sales of the drugs if ultimately approved by regulators.

Proprietary, Patent-Pending Method for Cost-Effective Psilocybin Synthesis

Mindset has developed a patent-pending synthesis process that offers cost-effective, large-scale synthesis of current good manufacturing practice (cGMP) psilocybin and strategically complements its next-generation drug development program. Management anticipates significant demand for high-quality psilocybin given the increasing number of preclinical studies and clinical trials underway utilizing psilocybin. High-quality psilocybin for clinical research purposes is currently expensive, difficult to procure, and/or uses environmentally toxic components. By contrast, Mindset’s unique synthesis process uses more environmentally friendly, easily obtained, and commercially available reagents under mild reaction conditions for convenient multi-kilogram scale manufacturing.

Exhibit 8 – Advantages of Mindset’s Psilocybin Synthesis Process over Traditional Methods

Mindset Chemical Synthesis	Traditional Chemical Synthesis	Yeast Synthesis	Plant Extraction
Synthesized in GMP Space	Synthesized in GMP Space	Synthesized in GMP Space	Plants Grown on Farms
Environmentally Friendly	Uses Environmentally Toxic Components	Environmentally Friendly	Environmentally Friendly
Pharmaceutical-Grade Consistency	Pharmaceutical-Grade Consistency	Pharmaceutical-Grade Consistency	Tenfold Consistency Variation
Highly Stable	Unstable Intermediaries	Elevated Degradation	High Degradation
< 1 Week Production	1-2 Week Production	1-2 Week Production	Weeks to Months Production

Source: ECM

Lead Candidate: MSP-1014 – A Potentially Safer Psilocybin Prodrug

Mindset’s lead candidate, MSP-1014, is an IP-protected psilocin prodrug (a drug that metabolizes to psilocybin active metabolite, psilocin) that incorporates a conjugated amplifier into a psilocybin-like structure to enhance its 5-HT2A activity (as measured by head twitch count in preclinical studies, which is a gold standard and [validated method](#) of assessing the likelihood of hallucinogenic activity at a given dose using animal models, see [Exhibit 3](#)).

Higher Potency May Allow for Lower Dosing and Fewer Side Effects

MSP-1014 also has no significant effect on core body temperature, which is a common psilocybin side effect that may indicate the disruption of body temperature regulation by serotonin. According to management, the preclinical *in vivo* data show that MSP-1014 has similar or improved preclinical activity in mice models compared to classic psilocybin along with similar or increased 5-HT2A activity when metabolized, meaning clinicians may be able to administer a lower dose of MSP-1014 than psilocybin to minimize side effects while inducing a similar increase in neuroplasticity (see page 28). Mindset will sponsor a preclinical study at the Centre for Addiction and Mental Health (CAMH) to assess how micro and macro doses of MSP-1014 and psilocybin in rats affect the expression of certain neuroplasticity biomarkers that may underlie the long-term behavioral changes associated with psychedelic experiences.

TRD is a Potential Blockbuster Lead Indication, Multiple Others Could Follow

MSP-1014 is being developed for TRD and end-of-life cancer angst and, like all other psychedelic compounds pursuing regulatory approval, is intended for use as a support agent for PAP: professionally supervised use of psychedelics as part of a psychotherapy program. Mindset may be able to leverage collected data to support the use of classic psilocybin to treat other large indications such as major depressive disorder (MDD), postpartum depression, alcohol use disorder, PTSD, and general anxiety – all of which are currently being explored in the clinic – to expand the label of MSP-1014.

Manufacturing Agreement Positions MSP-1014 Well for Potential Partnerships

In January 2022, Mindset announced that it had entered into a manufacturing agreement with a leading contract development and manufacturing organization for the production of pharmaceutical-grade batches of MSP-1014. This manufacturing agreement positions the drug well for a pharma partnership agreement to advance it through human clinical trials. According to management, the drug is also simpler and more cost-effective to manufacture than classic psilocybin, positioning it well for rapid commercialization upon prospective approval.

Lead Indication: Treatment-Resistant Depression

Major Depressive Disorder is One of the Most Common Mental Health Disorders

According to the [World Health Organization](#), depression affects ~380M people worldwide. Major Depressive Disorder (MDD, also known as clinical depression), a subtype of depression, is defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as having at least five of the following eight symptoms for two weeks:

- Depressed mood most of the day nearly every day,
- Increased low interest or pleasure in activities every day or most days,
- Increased weight loss or weight gain when not dieting, or a decrease or increase in appetite most days,
- Slowing down of thoughts and reduction in physical movement,
- Fatigue or loss of energy most days,
- Feelings of worthlessness or increased guilt most days,
- Decreased ability to think or concentrate or indecisiveness most days,
- Having repetitive thoughts of death or suicide.

A C2018 [study](#) found that the 12-month and lifetime prevalences of MDD were 10% and 21%, respectively, and that almost 70% of those diagnosed with MDD received some type of treatment. A C2021 [study](#) found that the economic burden of MDD grew at a 4.1% CAGR from C2018 to C2021 to a total cost of ~US\$326B, including direct treatment costs, the cost of treating comorbidities (such as cardiovascular disease, fibromyalgia and IBS), suicide-related costs, and workplace productivity impacts.

Exhibit 9 – First-Line Depression Treatments

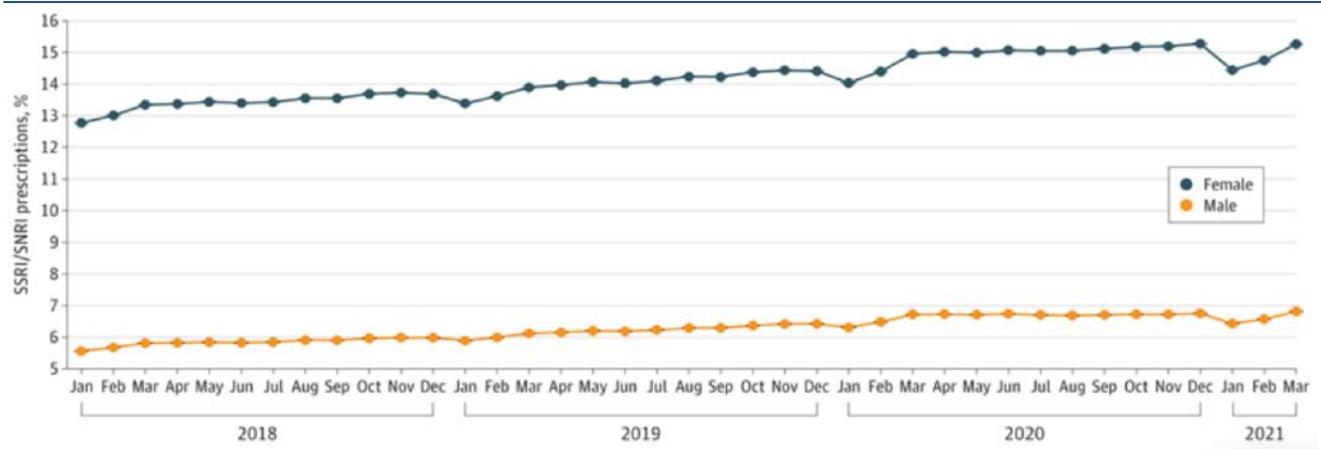
Therapy	Route	Frequency and Duration	Reimbursement	Approximate Annual Cost per Patient (US\$)
Established Common Pharmacotherapies for Depression				
Antidepressants: SSRI/SNRI	Oral	1/day, chronic	Broad	\$500 - 900
Atypical antipsychotics	Oral	1/day, chronic	Broad	\$3,000 - 9,000
Common Psychotherapy for Depression				
CBT	Face-to-face or online	10-20 sessions, 3-4 months	Broad	~\$1,000

Source: COMPASS Pathways Regulatory Filings, ECM

Per Capita SSRI/SNRI Usage is Rising at an ~5% CAGR

Selective serotonin reuptake inhibitors (SSRIs) such as luoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), citalopram (Celexa), and escitalopram (Lexapro) are the most commonly prescribed medications for MDD and work by increasing the circulating levels of the neurotransmitter, serotonin, in the brain by preventing it from being degraded before use. Similarly, serotonin and norepinephrine reuptake inhibitors (SNRIs) such as venlafaxine (Effexor), desvenlafaxine (Pristiq), and duloxetine (Cymbalta) prevent the premature degradation of both serotonin and norepinephrine and are the second-most commonly prescribed class of medications. Between C2018 and C2021, SSRI/SNRI prescriptions per capita increased at a CAGR of ~5% for both males and females (see [Exhibit 10](#)).

Exhibit 10 – Monthly Rates of Serotonergic Drug Prescriptions Among US Adults

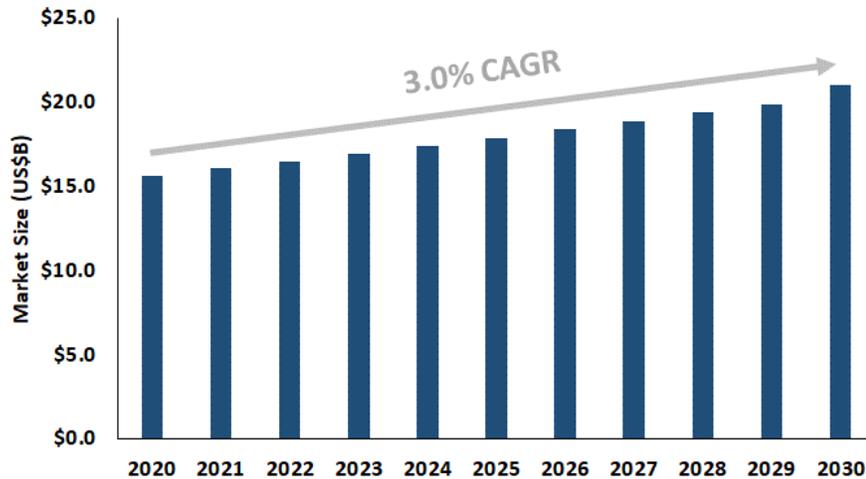


Source: Milani SA, Raji MA, Chen L, Kuo Y. Trends in the Use of Benzodiazepines, Z-Hypnotics, and Serotonergic Drugs Among US Women and Men Before and During the COVID-19 Pandemic. JAMA Netw Open. 2021;4(10): e2131012. doi:10.1001/jamanetworkopen.2021.31012

Low-Cost, Generic Antidepressant Drugs are a Growing, Multi-Billion-Dollar Market

Mental health disorders encompass a wide range of afflictions including, but not limited to, depressive disorders, anxiety and panic disorders, schizophrenia, eating disorders, substance abuse disorders, PTSD, ADHD, and OCD. Over the last two decades, antidepressants have been increasingly prescribed in industrialized countries due to the growing prevalence of depression and anxiety, primary care physicians’ improved ability to recognize these disorders, and an increased willingness to prescribe the medications. While the most common first-line depression treatments are low cost and generic, the global antidepressant drugs market is [projected](#) to grow at a 3.0% CAGR to reach US\$21B by C2030.

Exhibit 11 – Antidepressant Market Size Projection



Source: Research and Markets, Credence Research, ECM

First-Line Therapies are Ineffective for ~30% of Depression Patients

Many commercially available antidepressants intended to treat mental health disorders show limited benefit compared to placebo, can take 6+ weeks to work, and are associated with several side effects including trouble sleeping, drowsiness, fatigue, weakness, changes in blood pressure, memory problems, digestive problems, weight gain, and sexual problems. Indeed, after being prescribed multiple approved antidepressant drugs, [~30%](#) of patients are deemed to be treatment-resistant. This is often due to the drugs’ delayed therapeutic effect, side effects leading to non-compliance, or the patients’ inherent non-responsiveness.

High-Cost Therapies for the Treatment-Resistant are Another Multi-Billion-Dollar Market

A consistently large minority of depression patients do not respond to two or more first-line depression treatments, rendering them treatment-resistant. The market for second-line therapies to treat these patients is comprised of more expensive options such as transcranial magnetic stimulation (TMS), electroconvulsive therapy (ECT), and esketamine (Spravato), with prices in the US\$5-50K per year range in the US (see [Exhibit 12](#)). As such, assuming a total addressable patient population of ~5M in the US, with 50% of patients seeking treatment, we estimate the total addressable TRD market to be ~US\$12.5-125B per year in the US alone. Indeed, TRD is [estimated](#) to have an additional societal cost of ~US\$29-48B per year in the US on top of the societal costs of MDD.

Current TRD Therapies Leave Plenty of Room for Improvement

Besides switching and adding more antidepressants, options for patients suffering from TRD are limited. As outlined in [Exhibit 12](#) below, the various existing second-line treatments are considerably more expensive than the first-line and reimbursement by payors is either limited or non-existent. Esketamine, the most recently approved option, requires up to 56 sessions per year to be effective. ECT has been shown to be somewhat effective in treating depression, however, there are significant side effects. While transcranial magnetic stimulation is considered to be a safer non-invasive option, it appears to be less effective in treating depression.

Exhibit 12 – Comparison of Currently Approved TRD Treatments

Therapy	Route	Frequency and Duration	Reimbursement	Approximate Annual Cost per Patient (US\$)
Novel Pharmacotherapies for Treatment Resistant Depression				
Esketamine	Intranasal	Up to 56 sessions/year, under supervision of a healthcare professional	Limited	\$33,000 - 49,000
Ketamine	Intravenous	Up to 9 injections	No	\$2,500 - 5,000
Somatic Therapies for Treatment Resistant Depression				
Transcranial Magnetic Stimulation (TMS)	Magnetic brain stimulation without anesthesia	5 sessions/week, 4-5 weeks	Limited	\$6,000 - 12,000
Electroconvulsive Therapy (ECT)	Electric brain stimulation under anesthesia	3 sessions/week, 4+ weeks	Limited	\$5,000 - 15,000
Vagus Nerve Stimulation (VNS)	Electric pulses sent to the brain	Duration varies from patient to patient	Limited	\$40,000 - 45,000 for surgical implementation (excl. costs of post-operative device adjustments)
Deep Brain Stimulation (DBS)	Electrical impulses to the brain through implanted electrodes	3-6 hour operations; follow up visits	Limited	\$200,000 - 250,000 for surgical implementation (excl. ~\$95,000 battery replacements costs required every 12-24 months)

Source: ECM

Psychedelics Could be a Safer, More Durable Option for TRD and More

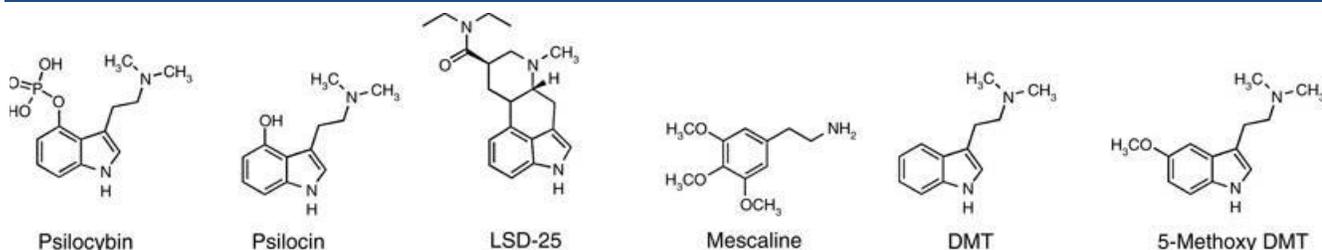
Naturally occurring or “classic” psychedelics are compounds that produce a psychoactive effect by binding to the target serotonin receptors, primarily the 5-HT_{2A} receptor, as well as the 5-HT_{1A} and 5-HT_{2C} receptors. Agonist compounds such as psilocybin and DMT activate receptors to produce a biological response, whereas antagonist compounds such as ibogaine and ketamine produce an effect by blocking the action of agonists.

Classic psychedelics can be categorized into three broad chemical groups:

- **Tryptamines** such as psilocin (the psychoactive metabolite of psilocybin) and DMT,
- **Lysergamines**, a group of tryptamines, including lysergic acid diethylamide (LSD), and
- **Phenethylamines**, a group of serotonergic hallucinogens such as mescaline.

Other adjacent categories include entactogens, such as MDMA, which are structurally similar to both phenethylamines and amphetamines and produce psychedelic-like effects with virtually no hallucinations, and ketamine, which affects a wide range of cellular processes including blockade of NMDA channels. All of Mindset’s putative drug candidates are tryptamines with structures inspired by psilocybin and DMT.

Exhibit 13 – The Chemical Structures of Common Psychedelic Compounds



Source: Nichols D.E. (2009) Hallucinogens. In: Binder M.D., Hirokawa N., Windhorst U. (eds) Encyclopedia of Neuroscience. Springer, Berlin, Heidelberg. https://doi.org/10.1007/978-3-540-29678-2_2131

Psychedelics are generally considered physiologically safe at known doses and have both rapid onset and persisting neurological effects, including changes in mood and brain function. Whereas generic antidepressants allow for increased serotonin for use in transmitting messages between synapses, the long-lasting effects of psychedelics are thought to result from structural changes induced in the neuronal cells and increased neuronal connectivity in the prefrontal cortex, which is known to exert top-down control over a variety of subcortical regions implicated in

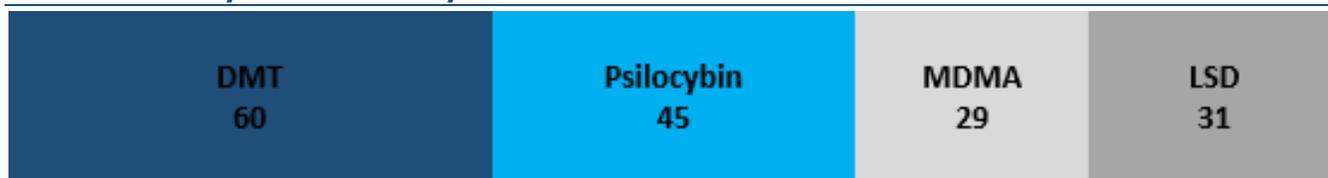
neuropsychiatric disorders such as depression, anxiety, and addiction (see the [Putative Mechanism of Action](#) section). The current Psychedelics R&D landscape for mental health conditions is highlighted in [Exhibit 14](#) below.

Exhibit 14 – Psychedelics R&D Landscape Highlights

Company	Product	Generation	Indication	Compound	Mechanism	Status
Mindset	MSP-1014	Next-Gen	TRD, End of Life Cancer Angst	Psilocybin-like	5-HT2AR agonist	Preclinical
Atai Life Sciences	PCN-101	Next-Gen	TRD	Arketamine	Glutamatergic modulator	Phase II
	DMX-1002	Classic	Opioid Use Disorder	Ibogaine	Kappa agonist, NMDA antagonist	Phase I/II
	VLS-01	Classic	TRD	DMT	5-HT2AR agonist	Phase I
	RLS-01	Classic	TRD	Salvinorin A	Kappa-opioid receptor agonist	Phase I
	EMP-01	Next-Gen	PTSD	MDMA derivative	Serotonergic agonist	Phase I
COMPASS Pathways	COMP360	Classic	TRD, PTSD	Psilocybin	5-HT2AR agonist	Phase IIb
Mind Medicine	LSD	Classic	ADHD, Anxiety Disorders, MDD, Pain	LSD	5-HT2AR agonist	Phase IIb
	18-MC	Next-Gen	Opioid Withdrawal	Ibogaine-like	Kappa agonist, $\alpha\beta4$ nicotinic antagonist	Phase IIa
	LSD (microdosing)	Classic	ADHD	LSD	5-HT2AR agonist	Phase IIa
Cybin	CYB001	Classic	Mental Distress	Psilocybin	5-HT2AR agonist	Phase II
	CYB003	Next-Gen	MDD, Alcohol Use Disorder	Deuterated tryptamine	5-HT2AR agonist	Preclinical
	CYB004	Next-Gen	Anxiety Disorder	Deuterated tryptamine	5-HT2AR agonist	Preclinical
Field Trip Health	Ketamine	Classic	TRD, Anxiety	Ketamine	NMDA antagonist	On market (off-label)
	FT-104	Next-Gen	TRD, Post Partum Depression	Psilocybin-like	5-HT2AR agonist	Preclinical

Source: ECM

Exhibit 15 – Tally of Listed US Psychedelics Clinical Trials



Source: clinicaltrials.gov, ECM

Recent Breakthrough Therapy Designations, FDA Approvals, and Regulatory Updates

On the back of promising initial clinical data, psilocybin has been granted Breakthrough Therapy Designation for both MDD and TRD, while the compound is also being evaluated for smoking cessation, the treatment of regular depression, and terminal cancer angst. This designation expedites the development and review processes for drugs that are intended to treat a serious condition and for which preliminary clinical evidence indicates a substantial improvement over available therapy on clinically significant endpoints. MDMA-assisted psychotherapy has been granted Breakthrough Therapy designation by the FDA for the treatment of PTSD and was approved for Expanded Access in 2019. Expanded access is a pathway for patients with immediately life-threatening conditions to gain access to investigational medical products outside of clinical trials when no alternative therapy options are available (sometimes called “compassionate use”).

Current Pharmacological and Non-Invasive Treatment Options for TRD

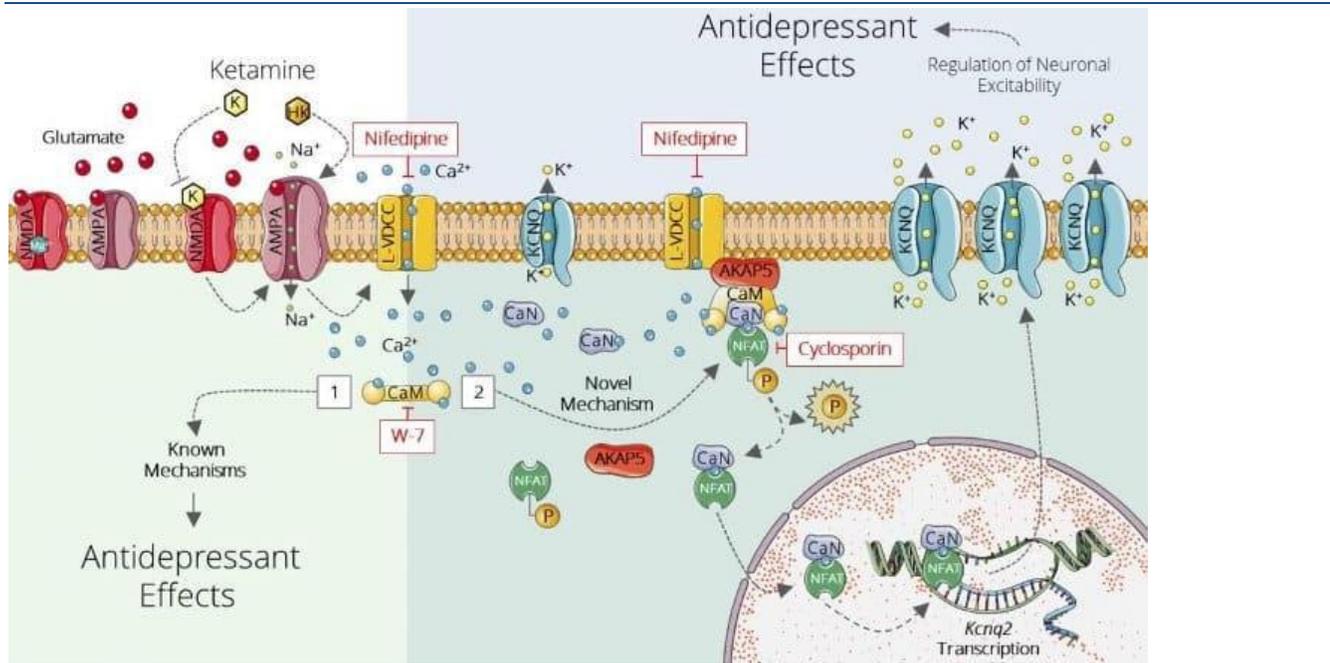
Esketamine (Spravato) – A Ketamine Isomer, the Most Recently Approved TRD Therapy

Differentiated Mechanism of Action May Increase Neuroplasticity in the Prefrontal Cortex

In March 2019, the FDA approved the use of J&J’s (JNJ-NYSE-, NR) Esketamine (Spravato) nasal spray, in conjunction with an oral antidepressant, for the treatment of TRD in adults. Esketamine is a molecular mirror image of ketamine, and it is [postulated](#) that it acts, like ketamine, by blocking the NMDA receptor and release of GABA to allow for the

activation of the AMPA receptor. This may restore synaptic function to improve neuroplasticity and synaptogenesis as well as enhance the production of brain-derived neurotrophic factor (BDNF), which is decreased in the prefrontal cortex and hippocampus in stress and depression.

Exhibit 16 – Esketamine’s Novel Antidepressant Mechanism of Action



Source: Weizmann Institute of Science

Intranasal Administration Allows for Quicker Therapeutic Onset and Lower Dosing

Due to the risk of serious adverse outcomes resulting from sedation and dissociation, and the potential for abuse and misuse of the drug, its availability is highly restricted. The intranasal formulation is less invasive than the IV or injectable versions while circumventing oral-bioavailability issues, allowing for a lower effective dose and resulting in a quicker onset of antidepressant effects as it reaches the brain faster. Fundamentally, esketamine has a different mechanism of action and side effect profile compared to existing antidepressants (ADs) and has fewer drug-drug interactions.

Efficacy Data Justifying Esketamine Approval is Underwhelming

The efficacy of Spravato was evaluated in three short-term (four-week) clinical trials and one longer-term maintenance-of-effect trial. In the three short-term studies, patients were randomized to receive Spravato or a placebo nasal spray, both alongside a new oral AD (due to the gravity of TRD symptoms). The primary efficacy measure was the change from baseline on the Montgomery-Asberg Depression Rating Scale (MADRS) test (see Appendix III). While Spravato demonstrated a statistically significant effect compared to placebo within two days in one of three short-term studies (TRANSFORM-2), the other two (TRANSFORM-1 and 3) showed no statistical significance on the primary endpoint (mean change from placebo at week 4). In the longer-term maintenance-of-effect trial, patients with initial stable response that continued treatment plus oral AD experienced a statistically significant longer time to relapse than those on placebo plus oral AD.

Exhibit 17 – Overview of Esketamine (Spravato) Phase 3 Clinical Trial Efficacy Results

Spravato Phase 3 Study	Treatment	n	Baseline MADRS Score	Mean Δ from Baseline (week 4)	Mean Δ from Placebo (week 4)	One-sided p-Value	Two-sided p-Value
TRANSFORM-1	Esketamine (56 mg) + oral AD	115	37.4	-18.9	-4.1	0.013	0.027
	Esketamine (84 mg) + oral AD	114	37.8	-18.2	-3.2	0.044	0.088
TRANSFORM-2	Esketamine + oral AD	114	37.0	-19.8	-4.0	0.010	0.020
TRANSFORM-3	Esketamine + oral AD	72	35.5	-10.1	-3.6	0.029	0.029

Source: ECM

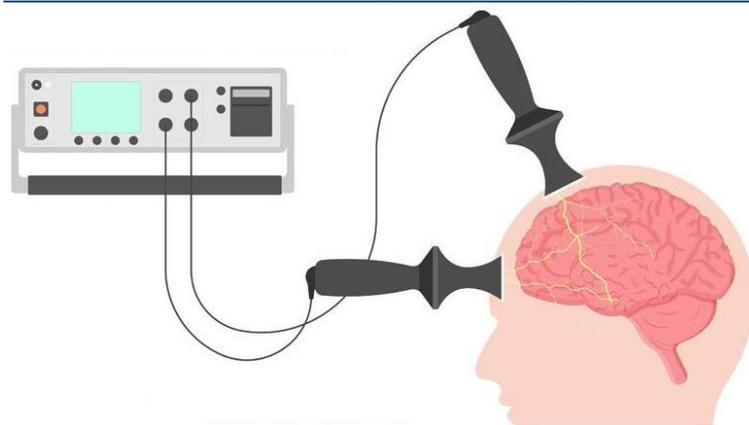
Side Effects and Possible Drug Dependence May be a Barrier to Wider Use

The most common side effects experienced by patients in the clinical trials were disassociation, dizziness, and nausea, while blood pressure also tended to increase transiently with use. According to the FDA, neither the placebo-controlled trials nor long-term, open-label studies showed an increase in risk of interstitial cystitis, liver injury, or impaired cognitive function, all of which are commonly reported complications associated with repeated use of ketamine. A [letter](#) to the editor of the *American Journal of Psychiatry* from Dr. Alan Schatzberg, Stanford professor of psychiatry and behavioural science and president of the American Psychiatric Association, highlighted some serious concerns with the use of esketamine for TRD. First, after about 16 weeks, study participants who were moved from esketamine plus oral AD to placebo plus oral AD experienced a relatively rapid recurrence of depression – faster than was seen in other studies. Second, three suicides occurred shortly after the last dose of esketamine (there were none in the placebo group). Two of the patients who died by suicide showed no previous signs of suicidal activity during the study, either at baseline or at the last visit, possibly reflecting some form of dependence on the drug to maintain a normal mental state. As such, he urged the psychiatric community to proceed with caution with the new drug.

Electroconvulsive Therapy (ECT)

Electroconvulsive Therapy (ECT) or Electroconvulsive Shock Therapy (ECS) is an FDA-approved, nonpharmacologic option that is used in conjunction with an oral AD and is reserved for use only after a patient has been shown not to respond to several other oral ADs. Brief electrical impulses (~5 seconds each) are used to trigger controlled seizures in the brain (~1 minute), and clinical evidence suggests that a series of treatments (usually 6-12 over a few weeks) produce substantial improvements in ~80% of patients with uncomplicated but severe MDD.

Exhibit 18 – ECT: Low-Voltage Shocks Trigger Controlled Seizures in the Brain



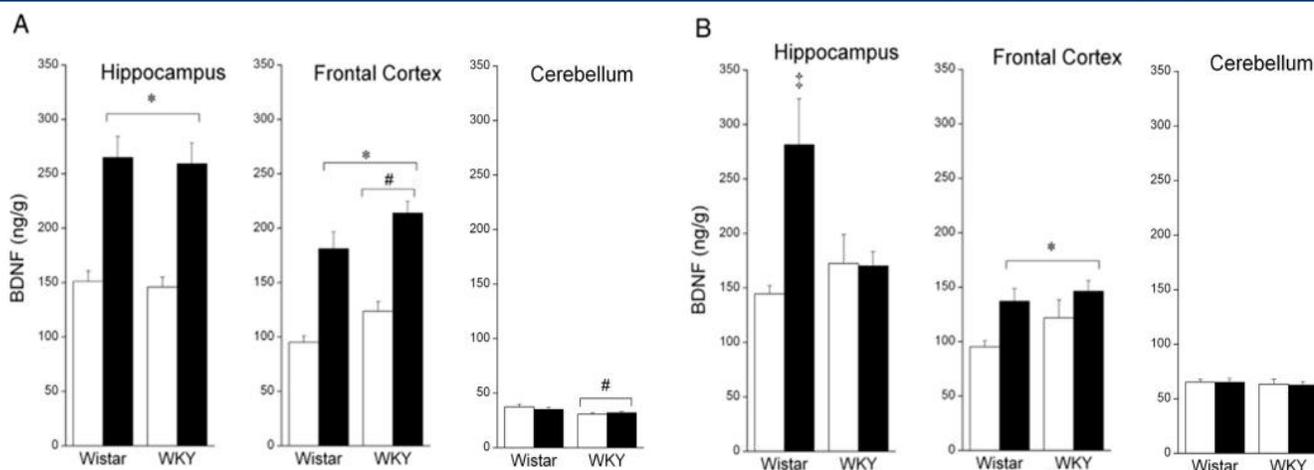
Source: scienceabc.com

All cells, living or dead, produce electromagnetic (EM) fields and all living cells in the body use EM exchanges for communication. Disruption of EM message transmission in cells can cause impaired cell metabolism and may be the underlying cause of many disease processes, including depression.

Similar to Esketamine, ECT Increases Neuroplasticity Via Increased BDNF Production

Much like esketamine use, ECT briefly increases the production of growth factor BDNF, which has been shown to increase neuroplasticity, in the areas of the brain associated with personality and temperament. In a 2014 [study](#), Wistar (normal) and WKY (depressed) rats received 5 days of repeated ECT or sham treatment and were assessed 1 and 7 days later for depression-like behaviour and brain BDNF protein. Both strains showed reduced depression at days 1 and 7. At 1 day after ECT, Wistar and WKY rats showed similar elevations in brain BDNF and CRF (the production of which is dependent on BDNF), however, brain BDNF normalized in WKY rats by 7 days despite sustained elevations of brain CRF. Wistar rats showed sustained elevations of both brain BDNF and CRF at 7 days post-ECT. This effect was most pronounced in the areas of the brain involved in higher-order brain functions and memory – the hippocampus, frontal cortex and neocortex, and brain stem – and less so in the cerebellum, which is responsible for maintaining balance, coordinating movement and vision, and the brain stem, which controls various subconscious body functions.

Exhibit 19 – Brain BDNF Levels Post-ECT in Wistar and WKY Rats at Day 1 (A) and Day 7 (B)



* $p < 0.05$ relative to sham, # $p < 0.05$ relative to Wistar, † $p < 0.0125$ relative to Wistar sham

Source: Kyeremanteng C, et. al. Effects of electroconvulsive seizures on depression-related behavior, memory, and neurochemical changes in Wistar and Wistar-Kyoto rats. *Prog Neuropsychopharmacol Biol Psychiatry*. 2014 Oct 3;54: 170-178. doi: 10.1016/j.pnpbp.2014.05.012

Memory Loss, Difficulty Learning, and General Anesthesia Use Among the Risks of ECT

Continued therapy such as oral ADs or periodic ECT “booster” treatments are usually necessary to prevent relapse and the procedure has been associated with short-term memory loss and difficulty learning. According to the American Psychological Association (APA), some people have trouble remembering events occurring in the weeks immediately before treatment, although these memory problems generally improve within a couple of months post-treatment. In addition, the general anesthesia used in the procedure carries certain rare but serious risks, as it does when used in any procedure. The movie “One Flew over Cuckoo’s Nest”, among many others, portrayed ECT as a very crude and cruel method of treatment. As such, there has been a steady decline in the use of ECT in clinical psychiatry settings, and it remains one of the most underutilized treatments.

Transcranial Magnetic Stimulation (TMS)

Transcranial Magnetic Stimulation (TMS) is an approved TRD therapy that works by non-invasively stimulating the brain. Whereas ECT involves applying electric shocks to the brain while the patient is under general anesthesia, TMS involves delivering MRI-strength electromagnetic pulses from a small pad while the patient is still awake and conscious. The procedure is often also referred to as repetitive TMS, or rTMS, as the practitioner applies these pulses repeatedly over

the 30- to 60-minute session. Indeed, the FDA recommends at least 20 sessions spread over 4 to 6 weeks to treat TRD. The pulses feel like a light tapping and, if performed correctly, the patient generally feels no residual side effects.

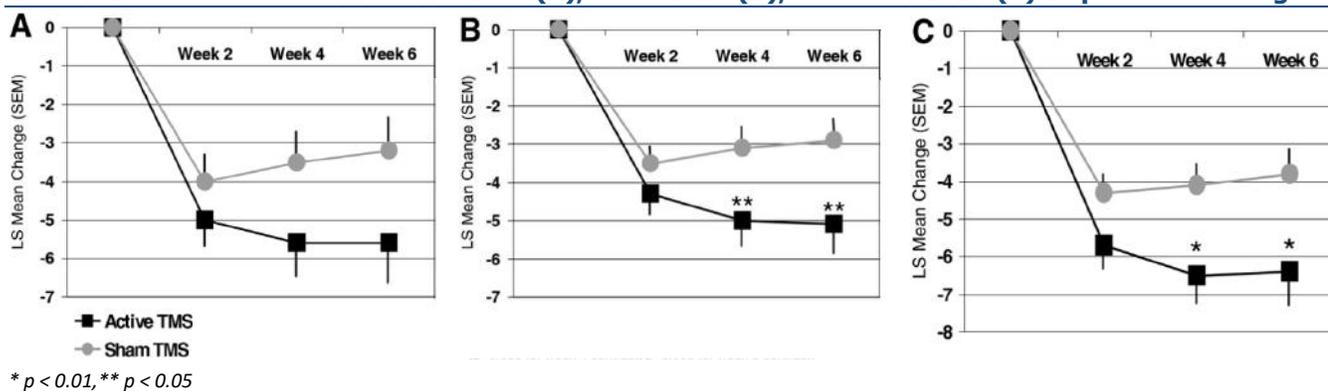
Similar to ECT, Electrical Impulses Generated by TMS Increase Neuroplasticity

TMS takes advantage of two established principles from the field of physics: Faraday’s principle of electromagnetic induction and Ampere’s law. The former states that a perpendicular magnetic field flux generates a voltage across a length of wire, while the latter states that the resultant electric current is proportional to the strength of the magnetic field. In TMS, the magnetic field passes at [right angles](#) to the neurons, which have bent or curved axonal processes that cause them to experience electrical effects. This [induces](#) an electrical field sufficient to activate networks in the superficial layers (outer layers of the brain, associated with personality/mood). However, because of its relatively poor electrical conductivity, there is much less of an effect in the subcortical structures (inner layers of the brain, not associated with personality/mood). Also, depending on the type of coil and intensity of stimulus used, stimulation depth can vary from 2cm to 4cm below the cortical surface, meaning only superficial brain structures are stimulated. In essence, TMS uses EM pulses to generate the same effects as ECT, but without the impedance of the skull and superficial tissues. Therefore, it needs lesser stimulus strength and there is no need for a true seizure or any form of anesthesia.

TMS is Safe and May be Effective (Depending on the Efficacy Measurement Used)

A 2007 [study](#) of 301 TRD patients (155 in the treatment arm, 146 in the control arm) showed that TMS is well tolerated and that adverse events were generally mild and limited to transient scalp discomfort or pain. The same study showed that, at the 4- and 6-week timepoints, the subjects receiving TMS had significantly reduced depression rating scores compared to the placebo arm on the HAM-D 17 and HAM-D 24 scales, but not the MADRS scale (at the 5% significance level). As discussed on page 49, however, the HAM-D tests are often criticized due to their relatively high number of test questions related to sleep and eating. This means that TMS’ effect on mood and depression may be confounded with the effect on sleep and eating parameters. In addition, the TMS subjects had a significantly lower baseline MADRS score at randomization as the protocol does not specify a minimum symptom severity score on the MADRS for study inclusion at screening, whereas a minimum score of 20 on the HAM-D 17 test was required.

Exhibit 20 – TMS Reductions in MADRS (A), HAM-D 17 (B), and HAM-D 24 (C) Depression Ratings



Source: O’Reardon J. P. et. al. Efficacy and Safety of Transcranial Magnetic Stimulation in the Acute Treatment of Major Depression: A Multisite Randomized Controlled Trial. *Biol. Psychiatry* 2007; 62: 1208-1216. doi: 10.1016/j.biopsych.2007.01.018

A 2014 [meta-analysis](#) that pooled data from six randomized controlled trials (RCTs) showed that 46.6% of subjects in the active TMS arms responded to the treatment versus 22.1% in the control arms. On average, the TMS treatment groups achieved a statistically significant 0.86 pooled standard deviation greater reduction in symptoms than the placebo groups. The risk difference translated into a ‘number needed to treat’ (NNT) of 3.4, meaning one patient would get clinical response in every 3.4 patients being treated. Typically, an NNT of less than 5 is considered [clinically relevant](#) in practice. We note that all six RCTs included in this meta-analysis also used HAM-D tests for their outcome assessments.

While these results are encouraging, the effects of TMS are generally somewhat [transient](#). Most TMS patients see improvements for many months after treatment stops, with the average length of response being ~1 year. As is the case for most mood disorders treatments, there is a high recurrence rate. It is also important to note that the studies conducted to assess the efficacy of TMS did not include active psychotherapy alongside the TMS treatment.

COMPASS Pathways Leading the Charge for Psilocybin TRD Trials

Potential for Mindset to Leverage Existing Psilocybin Data for Human Study Go-Ahead

Given that MSP-1014’s active metabolite and thus putative mechanism of action are the same as those of classic psilocybin, management expects to be able to leverage preclinical psilocin/psilocybin safety and efficacy data to expedite the path to the clinic for various indications, starting with TRD. To that end, [Exhibit 21](#) shows an overview of the current ongoing clinical programs involving psilocybin for various mental health and neurological indications.

Exhibit 21 – Clinical Programs Involving Classic and Novel Formulations of Psilocybin

Company / Organization	Compound	Indication	Status
COMPASS	Psilocybin / COMP360	Treatment-resistant depression (TRD)	Entering Phase III
Braxia Scientific	Psilocybin	TRD	Phase II
COMPASS	Psilocybin / COMP360	Post-traumatic stress disorder (PTSD)	Phase II
Usona Institute	Psilocybin	Major depressive disorder (MDD)	Phase II
B.More	Psilocybin	Alcohol use disorder	Phase II
Tryp Therapeutics	Psilocybin / TRP-8802	Overeating disorders	Phase II
Cybin	Psilocybin / CYB001	MDD	Phase II
Incannex	Psilocybin	Generalized anxiety disorder	Phase II
Mydecine	Psilocybin	Smoking cessation, PTSD	Phase II
Beckley Psytech	Psilocybin	Short-lasting unilateral neuralgiform headaches	Phase I
Ceruvia Life Sciences	Psilocybin / SYN-101	Migraine	Phase I
Ceruvia Life Sciences	Psilocybin / SYN-101	Cluster headache	Phase I
Ceruvia Life Sciences	Psilocybin / SYN-101	Obsessive compulsive disorder	Phase I
Diamond Therapeutics	Psilocybin	Anxiety	Phase I
Eleusis	Psilocybin / ELE-Psilo	MDD	Phase I
Filament Health	Psilocybin / PEX010	MDD	Phase I

Source: ECM

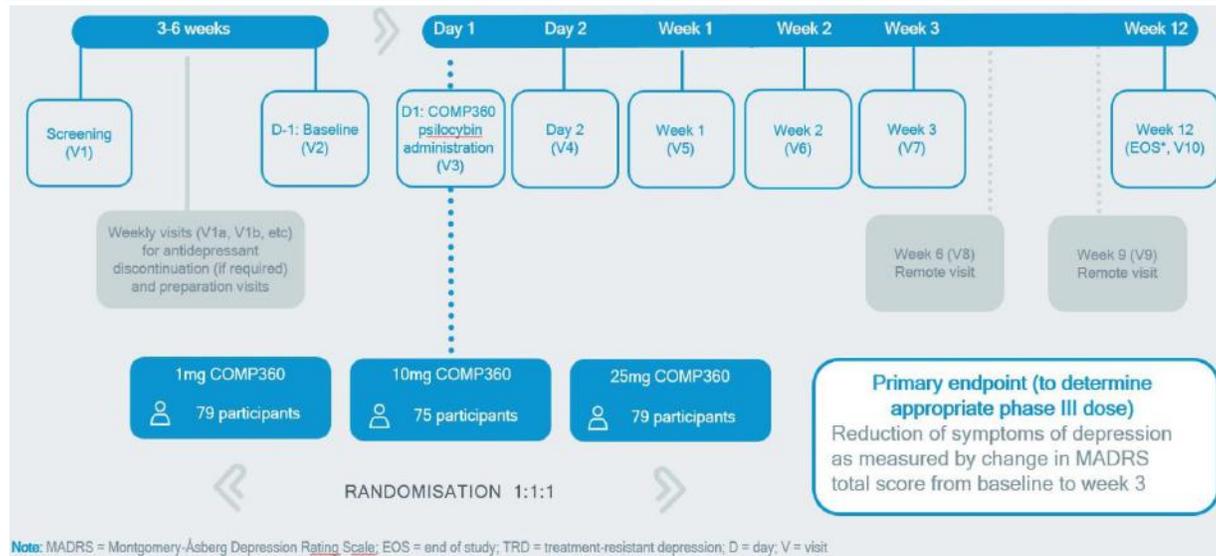
COMP360 – Proprietary Psilocybin Formulation Entering Phase III for TRD

Given the similarities between classic psilocybin and Mindset’s lead candidate, MSP-1014, and that Mindset will look to leverage existing safety and efficacy data from classic psilocybin clinical trials to accelerate the timeline to regulatory approval for clinical trials, the results and reliability of these trials are of significant importance.

Phase I Demonstrated Safety

Between 2017 and 2019, COMPASS conducted a Phase I [study](#) to assess the safety of 10mg and 25mg doses of COMP360, its proprietary pharmaceutical-grade synthetic psilocybin formulation, in 89 healthy participants. The study concluded that the 10mg and 25mg doses of psilocybin were generally well tolerated and did not have any detrimental short- or long-term effects on cognitive functioning or emotional processing. These findings allowed COMPASS to enter Phase II TRD trials in C2020, the design of which is outlined in [Exhibit 22](#) below.

Exhibit 22 – COMPASS Pathways’ Phase IIb COMP360 Study Design and Endpoints



Source: COMPASS Pathways Company Presentation

Phase IIb Primary Endpoint Met: Reduction in Depression Rating at Six Weeks

In November 2021, COMPASS presented the top-line data from its Phase IIb trial of COMP360 plus psychotherapy in 233 participants, with the primary endpoint being a change in the patient’s depression rating on the MADRS scale. At week three of the trial, patients on the higher dose (25mg) saw a 6.6-point greater reduction in MADRS than those on the 1mg dose which is, for all intents and purposes, a placebo. This 38% reduction from the baseline score in the 25mg dose, versus 17% in the 1mg dose, is a [statistically significant](#) change in depression severity and shows clinically meaningful outperformance versus traditional oral ADs. This is similar to the 7.2-point reduction in MADRS observed in a C2021 university-led [study](#) (no industry involvement) in which 59 patients received psychological support along with two doses of either psilocybin or placebo, three weeks apart. For context, a [C2020 meta-analysis](#) showed that the average reduction in MADRS after six weeks of SSRI usage is ~3 points and a C2009 [meta-analysis](#) found that escitalopram, a leading SSRI, outperformed placebo by only 2.3 points on the MADRS scale.

Exhibit 23 – COMP360 Showed a Rapid, Statistically Significant Reduction in MADRS Total Score



Source: COMPASS Pathways Company Presentation

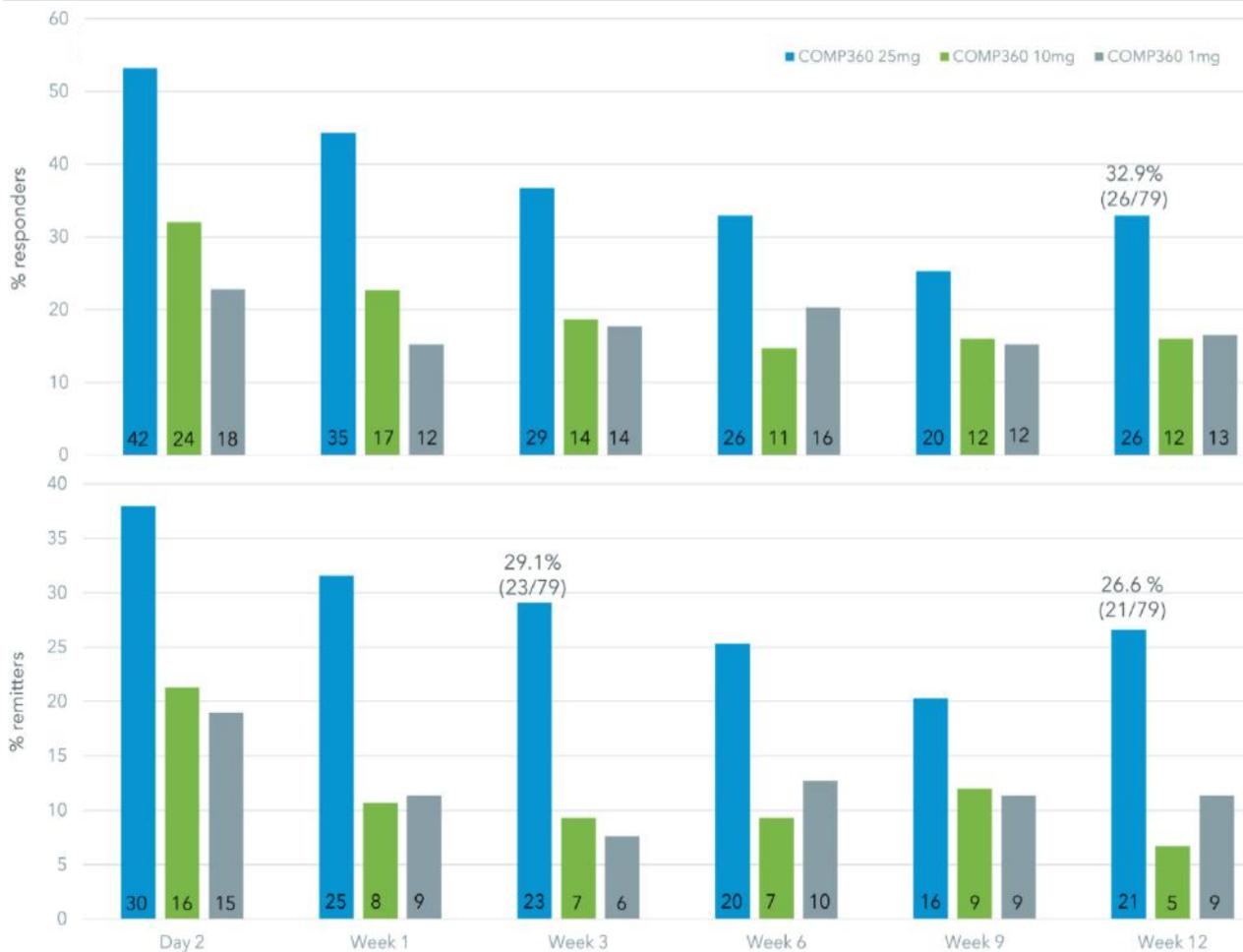
Phase IIb Secondary Endpoint: Very Promising Response and Remission Rates in 25mg Cohort

As shown in [Exhibit 24](#), patients in the 25mg psilocybin dose group had a response rate of 33% ($\geq 50\%$ reduction in MADRS score from baseline) at week 12 of the study compared to 16% in the 1mg placebo group. The remittance rate (MADRS total score ≤ 10) in the 25mg group at week 12 was 27% compared to 11% in the 1mg placebo group. In addition, 24% of the patients in the 25mg group were sustained responders ($\geq 50\%$ MADRS score reduction at weeks 3 and 12, and at least one visit out of weeks 6 and 9, and who did not start any new depression treatments) compared to just 10% in the 1mg placebo group.

Placebo Effect Consistent with Other Psychedelic Trials, 25mg Dose Outperformance is Key

Given that at least two existing antidepressant therapies had previously provided no benefit to the participants in this trial, the fact that 24% of those in the 25mg group were sustained responders after 12 weeks is a significant positive finding. However, it should be noted that 10% of the 1mg placebo group were also sustained responders at week 12, which is consistent with the reduction in PTSD symptoms observed in the placebo group of MAPS' first Phase III [study](#) of MDMA-assisted psychotherapy. Given that the patients in the placebo arm also received psychological support throughout the study period, it is not surprising to see even an idiosyncratic reduction from the baseline MADRS score. The nature of this support is not clear and, while it may have been the main contributor to the improvements observed in the placebo group, the 25mg group's clear outperformance distinctly justifies the commencement of larger trials.

Exhibit 24 – COMP360 Showed a Rapid, Statistically Significant Improvement in Depression



Source: COMPASS Pathways Company Presentation

Concerning Safety Signals in Phase IIb Likely Unrelated to Psilocybin Administration

While the vast majority of the COMP360 psilocybin side effects were mild to moderate in nature (headaches, nausea), a total of 19 treatment-emergent serious adverse events (TESAEs) were reported across 12 patients in the study – 5/12 in the 25mg group and 6/12 in the 10mg group. Concerningly, these TESAEs involved suicidal ideation and behaviour as well as self-injury. COMPASS’ management emphasized that the suicidal behaviour was primarily observed among non-responders to the therapy and that of the 12 patients experiencing TESAEs, only 1 occurred within 24 hours of dosing, with the rest occurring up to 62 days later. As such, it is not clear that there is a direct link between the TESAEs and the drug. In contrast to the placebo effect, inflated expectations among non-responders could potentially lead to outsized despair if it becomes obvious that the patient received a placebo dose or if beneficial effects are not immediately experienced.

Commencement of Phase III Expected by CQ322, Potential for Approval as Early as C2024

While these numbers are small enough for the difference between the treatment and placebo arms to lack statistical significance, the apparent connection between an ‘active’ dose of COMP360 and serious adverse events may lead observers and stakeholders to question COMP360’s safety profile. Pending the outcome of a meeting with the FDA to review the data from the Phase IIb trial, COMPASS anticipates advancing to a larger Phase III clinical trial by CQ322 and may be positioned to seek marketing approval as early as C2024.

Exhibit 25 – Treatment Emergent Serious Adverse Events (TESAEs) Ordered by 25mg Arm

MedDRA preferred term	COMP360 25mg	COMP360 10mg	COMP360 1mg	Overall
	N=79	N=75	N=79	N=233
Number of patients per category (%)				
Patients with a TESAE	5 (6.3)	6 (8.0)	1 (1.3)	12 (5.2)
	Any TESAE			
Suicidal behaviour	3 (3.8)	0	0	3 (1.3)
Intentional self-injury ¹	2 (2.5)	2 (2.7)	1 (1.3)	5 (2.1)
Suicidal ideation	2 (2.5)	2 (2.7)	0	4 (1.7)
Drug withdrawal syndrome ²	1 (1.3)	0	0	1 (0.4)
Adjustment disorder with anxiety	1 (1.3)	0	0	1 (0.4)
Adjustment disorder with mixed anxiety and depressed mood	1 (1.3)	0	0	1 (0.4)
Depression	0	1 (1.3)	0	1 (0.4)
Hospitalisation	0	1 (1.3)	0	1 (0.4)

Source: COMPASS Pathways Company Presentation

End-of-Life Cancer Angst is Another Potential Blockbuster Opportunity

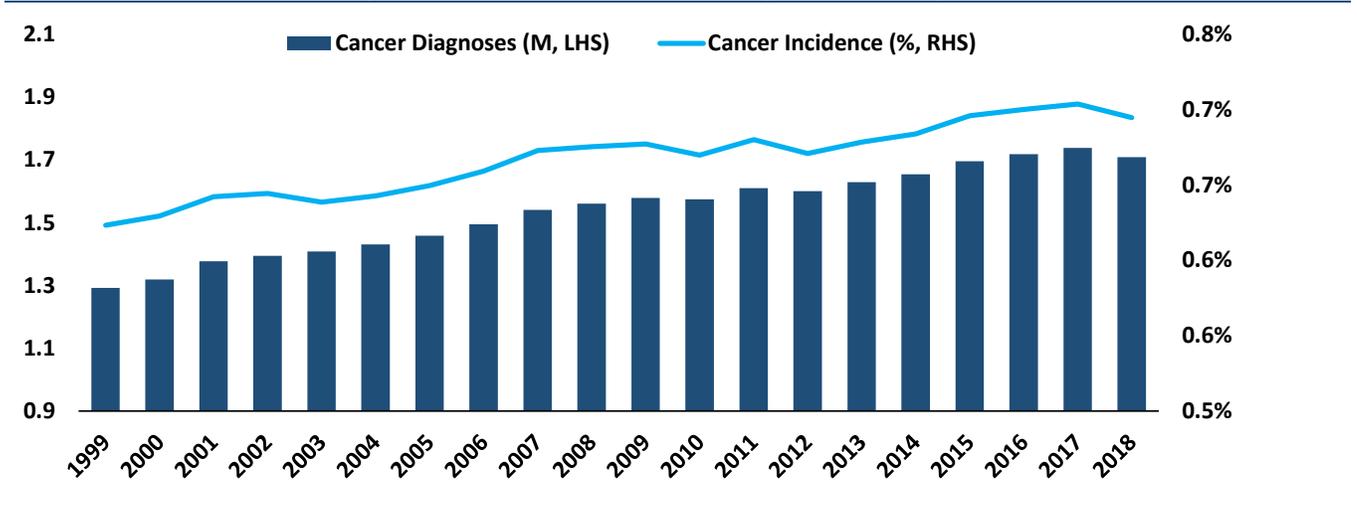
Cancer Diagnoses are Rising Both Nominally and on a Per Capita Basis

According to the US CDC and as outlined in [Exhibit 26](#) below, the number of cancer diagnoses has risen in the US at a CAGR of 1.5% per year between C1999 and C2018. In the same time frame, the incidence per capita has risen at a 0.6% CAGR. While advancements in therapeutics, as well as early screening and detection capabilities, have brought overall five-year cancer survivability to ~70% (C2010-2016), the recent pandemic is presumed to have caused many cancer screenings and potential early diagnoses to be missed, allowing cancers to progress to later stages. This is likely to reduce the overall survivability over the coming years.

Increasing Cancer Diagnoses Lead to Large and Growing End-of-Life Cancer Angst Market

After diagnosis, up to 40% of cancer patients develop chronic, clinically significant anxiety and depression, which meaningfully reduce quality of life. In addition, these secondary diagnoses have been associated with decreased treatment adherence, prolonged hospitalization, decreased quality of life, and increased suicidality – all behaviours that reduce the efficacy of treatment and increase medical system resource use. While antidepressants and benzodiazepines are used to treat patients with end-of-life cancer angst, side effects and limited evidence of efficacy often lead to low adherence and minimal improvement in symptoms. With ~1.5-2.0M new cancer diagnoses per year in the US, an ~30% five-year fatality rate, and up to 40% of patients experiencing end-of-life cancer angst, the addressable population in the US for a psychedelic therapy is between 180-240K people. Assuming a US\$10,000 price for this therapy, the total addressable market is between US\$1.8-2.4B per year.

Exhibit 26 – US Cancer Diagnoses and Incidence Trends (C1999-2018)



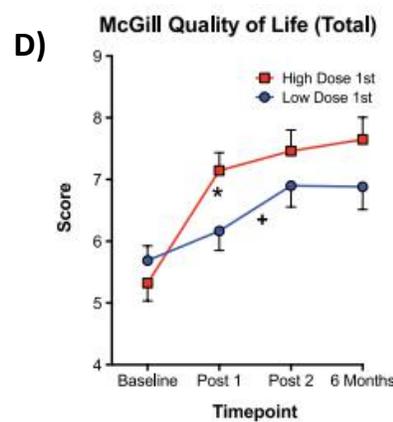
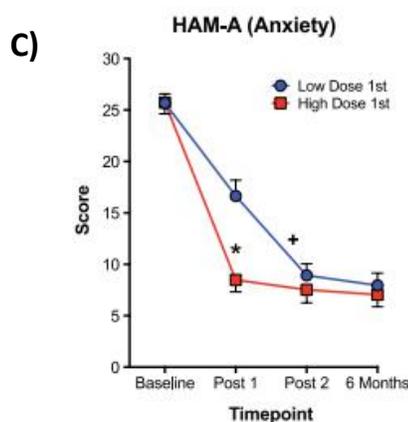
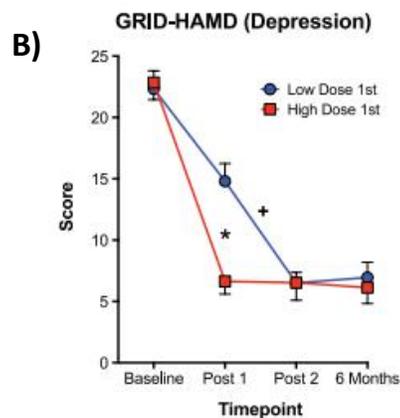
Source: US CDC, ECM

Early Data Suggest Psilocybin Improves End-of-Life Cancer Angst and Quality of Life

A C2016 randomized, double-blind cross-over [trial](#) investigated the effects of psychotherapy alongside a very low (placebo-like) dose (1 or 3 mg/70 kg) or a high dose (22 or 30 mg/70 kg) of psilocybin in 51 cancer patients with life-threatening diagnoses and symptoms of depression and/or anxiety. The results (see [Exhibit 27](#)) show that the high dose conferred a meaningfully large clinical response and induced symptom remission in the majority of patients at the six-month timepoint. These reductions in depression and anxiety symptoms were also shown to be associated with increases in quality of life, as shown in [Exhibit 27D](#).

Exhibit 27 – Effect of Psilocybin on End-of-Life Cancer Depression and Angst at Six Months

A) Measure	Group	Assessment time-point					
		Post-session 1		Post-session 2		6 months ^b	
		Clinical response	Symptom remission	Clinical response	Symptom remission	Clinical response	Symptom remission
GRID-HAMD-17 (Depression)	Low-Dose-1st (High-Dose-2nd)	32%	16%	75%	58%	77%	59%
	High-Dose-1st (Low-Dose-2nd)	92%***	60%**	84%	68%	79%	71%
HAM-A (Anxiety)	Low-Dose-1st (High-Dose-2nd)	24%	12%	83%	42%	82%	50%
	High-Dose-1st (Low-Dose-2nd)	76%***	52%**	80%	60%	83%	63%



*p<0.05, **p<0.01, ***p<0.001

Source: Griffiths RR, Johnson MW, Carducci MA, et al. Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *J Psychopharmacol.* 2016;30(12):1181-1197. doi:10.1177/0269881116675513

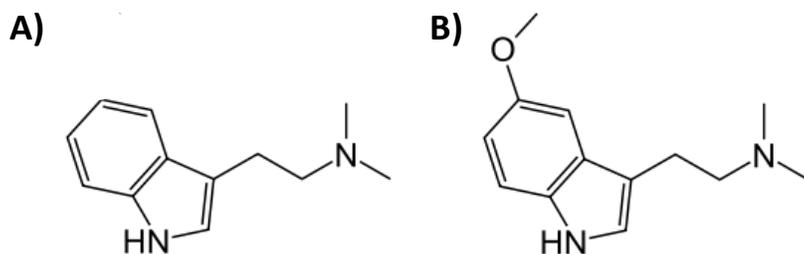
Family 4: DMT and its Use for the Treatment of Neurological Indications

DMT and 5-MeO-DMT are Widely Studied, Naturally Occurring Hallucinogens

Known as the “spirit molecule”, N,N-dimethyltryptamine (DMT) is a compound widely found in nature both in [animals](#) and in a wide variety of [plants](#). While it has been used for healing and spiritual purposes by indigenous populations of the Amazon Basin for centuries due to the brief, episodic visual hallucinations elicited by ingestion of large-enough amounts, it is a Schedule I controlled substance in the US, which means it is illegal to manufacture, purchase, possess, or distribute the drug given its high potential for abuse, a lack of accepted safety parameters, and no recognized medical use. It can be researched, however, under registration and approval from both the DEA and FDA. In the late C1990s, research recommenced after a 20-year embargo with the examination of its [dose-response](#) and [psychopharmacology](#) in humans in carefully controlled settings.

5-Methoxy-N,N-Dimethyltryptamine (5-MeO-DMT), which is chemically similar to DMT, also appears in many plants and animals, including in the venomous secretions of the Sonoran Desert/Colorado River toad. Unlike DMT, however, it has not been found endogenously in humans. Whereas the DMT experience tends to be highly visual, the 5-MeO-DMT experience is often described as a perspective shift, akin to a near-death experience.

Exhibit 28 – The Chemical Structures of DMT (A) and 5-MeO-DMT (B)



Source: ChemSpider, ECM

DMT has More Potent Hallucinogenic Effects, Reduced Duration Compared to Psilocybin

The ED₅₀ (the concentration or dose effective in producing 50% of the maximal response) of DMT is approximately one-tenth of that of psilocybin, while its maximum activation of 5-HT_{2A} receptors is approximately double. This means a much smaller dose of DMT is required for a similar activation of the 5-HT_{2A} receptors, while increased potency is often associated with a shorter half-life. Indeed, DMT's half-life in animals is ~5 minutes versus ~50 minutes for psilocybin. Similar to Mindset's Family 2 candidates, this allows for much shorter PAP session length and thus higher throughput of patients in the clinic.

5-MeO-DMT is inactivated by monoamine oxidase A (MAO-A) and metabolized to produce bufotenine, which binds to the 5-HT_{2A} receptor with much higher affinity than 5-MeO-DMT itself. Concurrent use of 5-MeO-DMT with an MAO inhibitor (MAOi), as is often the case when using plant preparations (e.g., ayahuasca), often leads to an enhanced and prolonged drug effect as well as more severe toxicity. Mechanistically, both MAOi and 5-MeO-DMT act agonistically on serotonergic systems and readily cause hyperserotonergic effects or serotonin toxicity.

Classic DMT and 5-MeO-DMT Have Shown Clinical Promise for Various Neurological Indications

As previously discussed, deficits in adult neurogenesis are associated with the physiopathology of depression, and modulation of neurogenesis is thought to be behind the [action](#) of several antidepressants. Similar to other studied psychedelics, DMT enhances neural plasticity and neurogenesis by increasing dendritic spine density and synapse formation. In addition, DMT has anti-inflammatory and anti-ischemic properties through its sigma-1 receptor activation. For these reasons, DMT and 5-MeO-DMT are being explored as treatments for neurological conditions such as [TRD](#), [PTSD](#), and [substance abuse disorder](#). In observational studies, 5-MeO-DMT demonstrates therapeutic potential across a variety of psychiatric symptoms in veteran populations. In a C2019 [study](#), ~80% of veterans diagnosed with depression (n = 149) or anxiety (n = 173) endorsed improvements in these conditions after receiving 5-MeO-DMT in a group setting.

Classic DMT and 5-MeO-DMT Toxicity Leaves Room for Improvement

5-MeO-DMT toxicity was first [reported](#) as a lethal syndrome in sheep after they grazed on *Phalaris tuberosa*, a plant containing 5-MeO-DMT. Mouse, rat, sheep, and monkey models revealed ataxia, mydriasis, head nodding, tremor, convulsion, and shivering after administration of 5-MeO-DMT. The LD₅₀ (the amount of an ingested substance that kills 50% of a test sample) of 5-MeO-DMT in mice ranged from 48-278 mg/kg for different administration routes. For context, however, the study of 5-MeO-DMT in veterans previously discussed included dosages in the 0.05-0.15 mg/kg range (assuming an average weight of 90kg). DMT is also [reported](#) to have an antagonistic effect at the 5-HT_{2B} receptors, which are [associated](#) with heart valve disease.

Small Pharma Phase I/II DMT Trial in MDD Patients

In October 2021, the UK's Medical and Healthcare Products Regulatory Agency (MHRA) granted Innovative Licensing and Access Pathway (ILAP) status to SLP026, Small Pharma's injectable formulation of DMT and lead candidate for the treatment of MDD. Similar to the US FDA's fast-track designation, ILAP could enable a speedier, more efficient drug development process and provides access to specialist advice throughout. In February 2021, Small Pharma initiated the world's first dose-escalating, placebo-controlled DMT-assisted psychotherapy clinical trial to evaluate the safety, tolerability, and pharmacokinetics/pharmacodynamics of SPL026.

Placebo-Controlled Phase I Study – No Significant Safety Issues Identified

In September 2021, Small Pharma reported Phase I clinical data evaluating the use of its lead candidate, SPL026 (injectable DMT), alongside psychotherapy for the treatment of MDD in 32 healthy, psychedelic-naïve volunteers in London, UK. While there were minimal short-lived adverse events reported on dosing day, no serious drug-related adverse events were reported and no statistically significant negative effects on anxiety or wellbeing were reported during the three months of follow-up.

Phase II Study May Yield Data Mindset can Leverage in Truncated 505(b)2 Regulatory Pathway

The Phase I data has enabled the Company to identify and select a safe and well-tolerated dose of SPL026 to potentially elicit a breakthrough psychedelic experience and treat MDD in the Phase IIa study, which is currently enrolling 68 MDD patients (42 in the treatment arm, 26 in the placebo arm) and is expected to be completed in February 2023. While Mindset's lead candidate from the DMT-inspired Family 3 group of molecules has not yet been selected, a prodrug of DMT may be able to leverage existing safety and efficacy data generated by Small Pharma using the same 505(b)2 regulatory pathway as the Company intends to employ to bring MSP-1014 to market for a similar indication. If Mindset were to decide on a DMT derivative or alternate indication, however, this pathway would likely not be available.

Patentability of Psychedelic Compounds Key for Big Pharma Partnerships

We believe that in order for larger, more established pharmaceutical companies to enter the psychedelics space via a partnership or collaboration agreement, the drugs being developed would have to have strong patent protection such that the eventual revenues would not be undercut by black market or generic versions of the drugs. In the case of undifferentiated psilocybin, for example, administering clinicians could use any supplier of the required dose to treat their TRD patients. Notably, there have been only two deals to date between a big pharma name and a psychedelic company, both for the development of definitively patentable drugs. The first was a collaboration and licensing agreement between Otsuka Pharmaceutical and Perception Neuroscience, an Atai Life Sciences subsidiary, for the development of PCN-101 (arketamine, R-ketamine) for TRD in Japan. The second was the deal between Otsuka and Mindset for the development of lead candidates selected from Families 2 and 4, the shorter-acting drugs inspired by psilocybin and DMT, respectively.

Mindset's Differentiated, Next-Gen Compounds have Strong, Early Patent Protection

While peers such as COMPASS are generating impressive valuable data that we believe will ultimately lead to FDA approval of psilocybin, Mindset's differentiated drug candidates will be able to leverage this data from a stronger IP position and win over time due to their potential improved safety profile and tuned duration of effect. To date, Mindset has filed nine provisional patent applications that cover a broad range of novel, next-generation drug candidates and two covering novel psilocybin synthesis and manufacturing methods (see [Exhibit 7](#)). This includes four Patent Cooperation Treaty (PCT) applications, which make it possible to simultaneously seek patent protection in a large number of countries by filing a single "international" patent application instead of several separate national filings or regional patent applications. Mindset continues to file final PCT applications at the one-year timepoint from the filing of provisional patents.

While Nature Cannot be Patented, Some Exploitable Loopholes May Exist

To [obtain a patent](#) on a psychedelic compound (or any other invention), examiners at the Patent and Trademark Office (PTO) must be convinced that the technology is 1) novel, 2) non-obvious, and 3) useful, while not falling into one of three categories of [excluded subject matter](#): laws of nature, abstract ideas, and natural phenomena. Psilocybin is a known compound isolated from the *Psilocybe mexicana* mushroom in 1957 and thus is not patent-eligible, however, novel derivatives of the compound with meaningfully differentiated pharmacological properties could qualify if not previously publicly disclosed. In addition, synthesis methods or methods of use may be patented. The non-obviousness of a psilocybin derivative is perhaps more nuanced as, for psilocybin derivatives to be patent-eligible, they must not be obvious to an ordinary chemist given all the information available about the topic.

Prior Prohibition Puts Psychedelics in the PTO Examiners’ Blind Spot, Leading to Low-Quality Patents

Patents are [presumed](#) to be valid in the US unless the PTO deems the inventions ineligible and, given the longstanding prohibition on their use and research, the nuances of novel psychedelics’ chemical structures, formulations and non-obviousness may be a blind spot for many application examiners. As such, a lack of experience may lead to lower examination standards and flimsier patent approvals for novel psychedelic compounds, allowing companies to acquire broad but arguably low-quality patent claims across the space. This appears to be beginning already, with COMPASS Pathways acquiring a [patent](#) in C2020 for the “treatment of depression and other various disorders with psilocybin.” There are 162 claims inherent in the application, including methods of administering psilocybin in a room with muted colours and soft furniture, a bed, a couch, a high-resolution sound system, or a therapist holding the patient’s hand.

COMPASS’ Psilocybin Patents May Not Hold Up to Scrutiny

While the aforementioned COMPASS patent application has not yet been granted, it cannot be used in any way to claim ownership or patent infringement. Even so, patent rights are not ironclad and are often challenged (and invalidated) in court for lack of novelty, non-obviousness, and/or patent eligibility. Many of the claims outlined in the COMPASS patent are arguably not novel and have been done throughout the history of psychedelic therapy in prior clinical trials, academic research centres, and at retreats (though not necessarily systematically or defined formally). On July 28, an examiner at the UK IP Office issued a non-binding [opinion](#) on COMPASS’ [UK patent](#) in which 21 claims are made regarding the large-scale production of psilocybin for use in medicine. While the patent remains valid, the examiner concluded that claims 1, 3 and 10-20 are not inventive and are “within the common general knowledge of the person skilled in the art” based on pre-existing research that ought to have been reviewed prior to the patent being granted. This opinion was requested on behalf of a non-profit group and, while this type of request for opinion from a patent examiner is not available in the US, there does exist a more formal post-grant review process.

Other Companies Developing Patentable Second-Generation Psychedelics

Exhibit 29 – Companies Developing Second-Generation Psychedelics

Company	Product	Indication	Compound	Status	Potential Benefits vs. Classic Psychedelic
Mindset	MSP-1014	TRD, End of Life Cancer Angst	Psilocybin Derivative	Preclinical	Shorter duration, improved pharmacokinetic profile, potentially improved toxicity
Cybin	CYB003	MDD, Alcohol Use Disorder	Deuterated Psilocybin	Preclinical	Reduced side effects, faster onset of action, shorter duration
	CYB004	Anxiety Disorder	Deuterated DMT	Preclinical	Longer duration, reduced dose, less negative experiences
	CYB005	Neuroinflammation	Phenethylamine Derivative	Preclinical	Improved CNS activation, long duration of action, improved toxicity
Atai Life Sciences	PCN-101	TRD	Arketamine	Phase II	Longer duration, faster acting, lower abuse potential
	EMP-01	PTSD	MDMA Derivative	Phase I	Improved cardiovascular profile
Mind Medicine	18-MC	Opioid Withdrawal	Ibogaine Derivative	Phase IIa	Non-hallucinogenic, non-cardiotoxic
Field Trip Health	FT-104	TRD, Post Partum Depression	Psilocybin Derivative	Preclinical	Shorter duration
BetterLife Pharma	BETR-001	MDD, TRD, PTSD, cluster headaches	LSD Derivative	Preclinical	Non-hallucinogenic
Delix Therapeutics	TBG		5-MeO-DMT Derivative	Preclinical	Non-hallucinogenic
Mydecine	MYC-004	Smoking Cessation	Patch-delivered Psilocybin	Preclinical	Faster onset of action, reduced side effects, shorter duration

Source: ECM

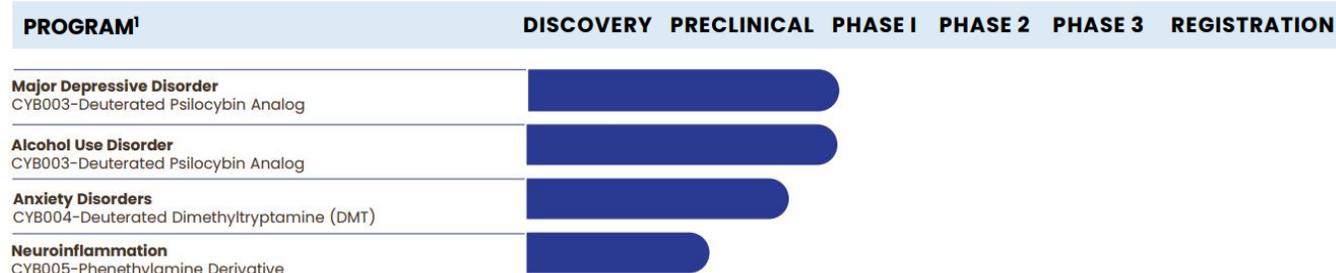
Cybin – The First Psychedelics Company to List on the NYSE

Cybin (CYBN-NYSE, NR) is widely known for being the first psychedelics company to list on the NYSE. Its flagship second-generation psychedelic, CYB003, is a late-preclinical stage asset intended to treat MDD and alcohol abuse disorder. According to Cybin, CYB003 is a “deuterated psilocybin analog designed to achieve less variability in plasma levels, faster onset of action, shorter duration of effect and potentially better tolerability versus oral psilocybin.” That way, an eight-hour therapy session could take just four hours – less demanding for both patient and provider.

Cybin is also developing CYB004, an inhalable, deuterated DMT analog aimed at treating depression, anxiety, and substance abuse disorders. Compared with DMT, its potential benefits include increased strength (reduced dosage) and more sustained duration to alleviate negative experiences. Based on preclinical results, inhaled CYB004 demonstrated ~41% improved bioavailability compared with inhaled DMT, as well as rapid onset of effect, similar low variability, and ~300% longer duration of effect when compared with IV DMT, indicating the potential to extend the therapeutic window.

Cybin expects to apply in CQ322 to begin a pilot study of CYB004 in humans. The company is also conducting a Phase II study to assess the effect of classic psilocybin in treating mental distress in healthcare workers on the front line of the COVID-19 pandemic.

Exhibit 30 – Cybin’s Second-Generation Psychedelic Drug Development Pipeline



1. Subject to receipt of all necessary regulatory approvals from all applicable authorities

Source: Cybin Company Presentation

Atai Life Sciences – Betting on Many Horses in the Psychedelics Race

Atai Life Sciences has launched or acquired a stake in 16 different psychedelics companies since C2019. In addition to developing several first-generation psychedelic medicines, it is developing PCN-101, the R isomer of ketamine and mirror opposite of esketamine, for TRD and EMP-101, an MDMA derivative, for PTSD. Through Perception Neurosciences, Atai is partnered with Otsuka for the development of PCN-101 and has entered Phase II clinical trials. EMP-01 is a preclinical-stage asset from EmpathBio (Private) that is being developed as a combination drug treatment with Bionomics’ (BNO-ASX, NR) BNC210, a Phase II asset with potential to treat PTSD and social anxiety disorder.

Mydecine also has a [virtual healing platform](#) that provides personalized support, content, and education throughout each participant's psychedelic-assisted journey. The platform offers access to one-on-one or group telehealth coaching with certified specialists, on-demand educational content, community engagement, curated meditations, and relaxing sounds, all integrated into a daily health journal to improve mental health.

Enveric Biosciences

Enveric Biosciences (ENVB-NASDAQ, NR) has developed PsyAI, a machine learning drug development tool, that built a catalogue of possible molecule combinations and alterations (the "Psybrary"). From this extensive list of possible psychedelics, Enveric has filed 14 patents for second-generation psychedelics: four of them are mescaline or MDMA derivatives, while ten come from psilocybin and DMT. In March 2022, Enveric announced the publication of four patent applications for novel molecules of the tryptamine family.

MindMed

What other companies might call second-generation psychedelics, MindMed (MNMD-NASDAQ, NR) calls third-generation psychedelics. In fact, it refers to 18-MC as a "structural analogue to classic psychedelics" that "requires a full development program" and has the "strongest available intellectual property." 18-MC is MindMed's flagship substance and is focused on treating opioid abuse disorders, with the added characteristic that this ibogaine-derivative drug is non-hallucinogenic. Earlier this year, MindMed successfully completed Phase 1 clinical trials of the drug. MindMed also recently received FDA clearance to study MM-120, a pharmacologically optimized form of LSD being developed for generalized anxiety disorder.

BetterLife Pharma

Based out of Vancouver, BC, BetterLife Pharma (BETR-CNSX, NR) is a mental health-focused biotechnology company developing second-generation, non-hallucinogenic psychedelics. Its lead candidate, BETR-001 (2-bromo-LSD), is a preclinical, non-hallucinogenic derivative of LSD with the potential to treat MDD, TRD, PTSD, and cluster headaches. 2-bromo-LSD was originally synthesized by Albert Hoffman, the chemist who invented LSD, and it has been shown in human trials in the 1950s-60s to be non-hallucinogenic. While it is not a controlled substance, its manufacture has historically been regulated and restricted due to its use of LSD as a reagent in its synthesis. BetterLife, however, has devised a manufacturing method for BETR-001 that involves no controlled substances at any stage, allowing for the manufacturing and final product to be totally free of controlled substance regulations.

Delix Therapeutics

Delix Therapeutics is a privately held developer of non-hallucinogenic versions of psychedelic compounds intended to treat neuropsychiatric disorders such as TRD, substance use disorder, PTSD, cognitive impairment in schizophrenia, and neurodegeneration. Whereas some argue that the hallucinogenic experience is a key component of psychedelics' therapeutic effect, Delix hypothesises that the same effects can be achieved by solely relying on the compounds' ability to promote structural and functional neuroplasticity in cortical neurons. As such, the company's non-hallucinogenic psychoplastogens may pave the way for take-home prescription drugs that do not require the presence of a clinician for administration of the drug and supervision of the patient while in a hallucinogenic state. Such a drug would be deliverable at a much lower cost using the traditional antidepressant model, would have a lower abuse potential, and would have a meaningfully expanded set of putative addressable markets.

Psychedelics' Putative Mechanism of Action: Increased Neuroplasticity

Neuroplasticity, once thought by neuroscientists to manifest only during childhood, is the ability of the brain to rewire throughout a person's life and is the basis of both learning and brain repair after injury. The putative efficacy of PAP in treating neurological or psychiatric disorders stems from the induction of neuroplasticity in the "personality region" of the brain and resultant increased interconnectivity. Recent advances in brain stimulation and imaging technology, such as magnetic brain stimulation and functional magnetic resonance imaging (fMRI) have revealed that the brain is adaptable and capable of reorganizing itself throughout life and creating new neural pathways to adapt to its needs.

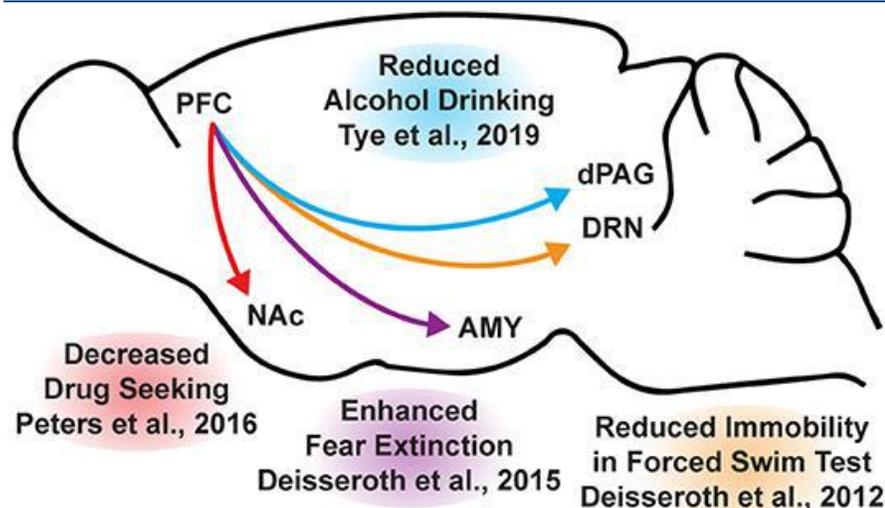
Neuronal Atrophy Leads to Decreased Communication Between Brain Regions

Depression patients often exhibit a negative cognitive bias characterized by pessimism, poor cognitive flexibility, rigid thought patterns, and negative fixations regarding ‘self’ and the future. This rigidity, introspection, and self-referential thinking are associated with the default mode network (DMN), a large-scale brain network comprised of several high-level cognitive areas, including the prefrontal cortex (PFC), which controls mood, cognition, joy, fear, and more. In many psychiatric diseases such as depression, bipolar disorder, PTSD, and addiction, neurons in the PFC atrophy, branches retract and synapses are lost, leading to decreased network integration in the brain. For example, in depressed patients, the DMN interacts more frequently with itself than in healthy patients, while interacting less frequently with other networks such as the executive network (EN) or the salience network (SN), resulting in impaired cognition and disrupted mood, among other symptoms.

Decreased Brain Interconnectivity Leads to Various Neuropsychiatric Disorders

Human imaging, post-mortem studies, and animal models suggest that reduced brain interconnectivity, induced or exacerbated by stress, plays a [key role](#) in the pathophysiology of depression and related disorders. Indeed, the PFC is known to exert top-down control over a variety of subcortical regions, and recent research has identified a number of circuits originating in the PFC that control behaviours relevant to the treatment of depression, anxiety, and addiction.

Exhibit 33 – Stimulation of the Prefrontal Cortex Leads to Improved Neuropsychiatric Symptoms

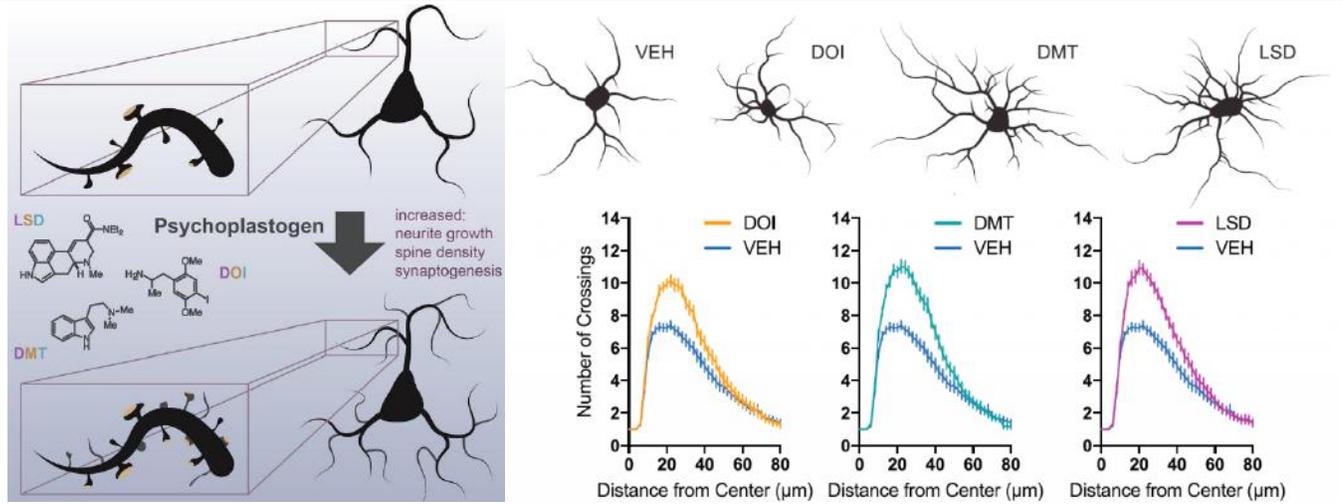


Source: Vargas M V, Meyer R, Avanes A A, Rus M, Olsen D E, Psychedelics and Other Psychoplastogens for Treating Mental Illness. *Front. Psychiatry.* 2021;12, 727117 doi: 10.3389/fpsyt.2021.727117

Psychedelics Restore the Neuronal Complexity Required for Proper Function

To induce the positive effects highlighted in [Exhibit 33](#), psychedelic compounds capable of promoting structural and functional neuroplasticity in the PFC could be used to counteract the neuronal atrophy, elimination of synapses, and associated structural changes that result in impaired function in downstream regions of the brain. Changes to the neuronal network can be structural or functional. Structural plasticity includes neuritogenesis (generation of new neurons), spinogenesis (increased number or complexity of dendritic spines, reflecting more synaptic strength), and synaptogenesis (increased strength of synapses, related to learning and memory formation). A C2018 [study](#) shows that serotonergic psychedelics such as LSD and DMT increase neuritogenesis, spinogenesis, and synaptogenesis to promote plasticity in rats via an evolutionarily conserved mechanism, while a C2021 [study](#) similarly indicates that psilocybin induces neuroplasticity in the PFC in mice.

Exhibit 34 – Psychedelics Increase Neuronal Complexity

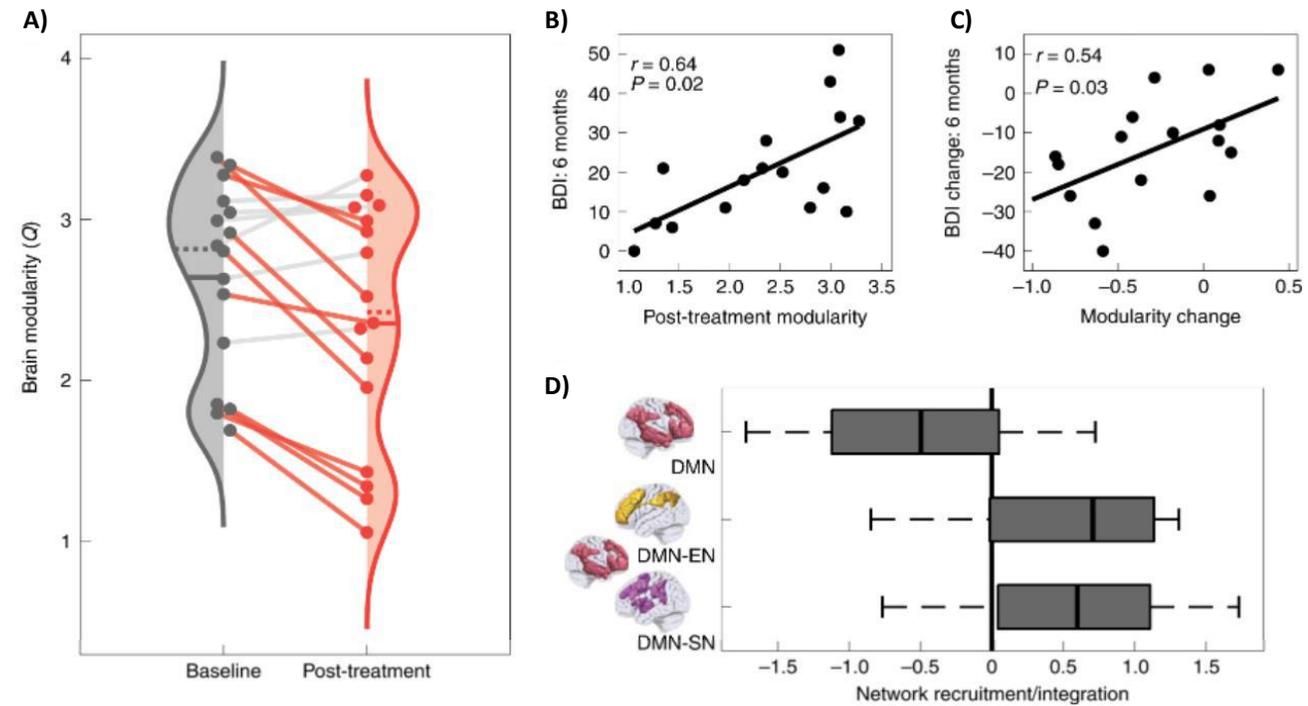


Source: Ly C, Greb A C et al., Psychedelics Promote Structural and Functional Neural Plasticity. Cell. 2018;23 3170-3182. doi: 10.1016/j.celrep.2018.05.022

Psilocybin Restores Neuronal Function to Increase Neuroplasticity, Brain Interconnectivity

A C2022 study showed that increased brain interconnectivity (decreased modularity in Exhibit 35C) as a result of psilocybin therapy in TRD patients was associated with improved depression symptoms (reduced BDI score in Exhibit 35C) up to six months post-dosing. Decreased brain modularity, represented by a flatter profile in Exhibit 35A, indicates a global increase in brain network integration following psilocybin therapy in patients with TRD. Patient data in Exhibit 35A are connected by solid lines and rendered in colour if modularity decreased. The solid and dotted lines show the decrease in the mean and median modularity, respectively. Exhibit 35D shows decreased DMN self-interaction post psilocybin dosing in favour of interaction with other intrinsic networks such as the EN and SN.

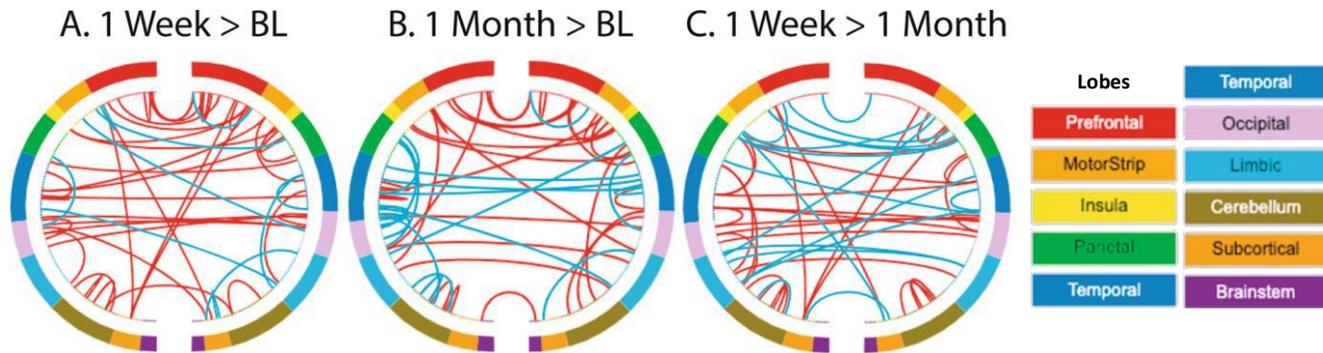
Exhibit 35 – Psilocybin-Associated Reduction in TRD Related to Increased Brain Interconnectivity



Source: Daws, R.E., Timmermann, C., Giribaldi, B. et al. Increased global integration in the brain after psilocybin therapy for depression. Nat Med (2022). <https://doi.org/10.1038/s41591-022-01744-z>

Similarly, functional MRI (fMRI) [studies](#) have found that the psychedelic state is associated with a less constrained and more intercommunicative mode of brain function (see [Exhibit 36](#) below), which is consistent with descriptions of the nature of consciousness in the psychedelic state.

Exhibit 36 – Effects of a Single Dose of Psilocybin on the Strength of Functional Brain Connections



Circle brain plots of functional connections that significantly increase (red lines) or decrease (blue lines) in strength (A) at 1 week compared to baseline, (B) at 1 month compared to baseline, and (C) at 1 week compared to 1 month

Source: Barrett FS, Doss MK, Sepeda ND, Pekar JJ, Griffiths RR. Emotions and brain function are altered up to one month after a single high dose of psilocybin. *Sci Rep.* (2020) 10:2214. doi: 10.1038/s41598-020-59282-y

Increased Neuroplasticity in the Prefrontal Cortex is a “Window of Opportunity” for Psychotherapy

The combined data indicate that psychedelics could be facilitating the positive effects of the psychotherapy received in conjunction with the psychedelics. A C2020 [study](#) found that emotions and brain function are altered for at least one month post a single high dose of psilocybin, indicating that psilocybin increased neuroplasticity is long-lasting enough for the concomitant psychotherapy to direct the new connections and ensure they are strengthened in a targeted way. Without the guidance of the psychotherapist, the increased neuroplasticity induced by psychedelics may lead to transient or untargeted development of the neuronal network and the specific development intended to ameliorate the relevant disorders may not occur. Similarly, guided psychotherapy in the absence of the increased neuroplasticity may not ameliorate the patient’s symptoms as the functional or structural changes are not able to occur.

Epilepsy and Other Seizure Disorders May be Worsened by Increased Neuroplasticity

When a person has an epileptic seizure, the nerve fibres involved in seizing become better insulated by the fatty substance, myelin. While myelin plasticity contributes to many brain functions, including attention, learning and memory, a C2022 [study](#) showed that increased neuroplasticity heightens the risk that further myelination around these specific nerve fibres allows the brain to have seizures more efficiently. Given that seizures are known to beget more seizures and that psychedelics’ putative mechanism of action is based on neuroplasticity, seizure disorders are already an exclusion criterion in COMPASS’ Phase II [trial](#). While the C2022 study suggests new drug targets to interrupt this specific process to prevent seizures from escalating, seizure disorders would likely be a contraindication should psilocybin receive regulatory approval.

Scalability of Psychedelic-Assisted Therapy

Psychedelics’ Delivery to Patients will be Crucial for Successful Roll-out

Upon putative FDA approval, hallucinogenic psychedelic substances will not be for take-home use and will be administered to patients only in designated locations under the supervision of trained clinical staff in a psychedelic-assisted psychotherapy context. As such, their administration will rely on the construction of new infrastructure with designated clinics as well as trained clinicians and other staff.

Ketamine Clinics Lay the Track for Other Psychedelics to Hit the Ground Running

Since the popularization of ketamine-assisted psychotherapy over the last few years and the approval of J&J’s esketamine nasal spray, Spravato, ketamine clinics have been rapidly opening across North America. Indeed, between C2015 and C2018, the number of clinics across the US offering ketamine therapy and ketamine-assisted psychotherapy grew from 60 to ~300, and a handful of publicly traded companies operate small but growing networks of clinics. For example, Delic Holdings Corp. (DELC-CSE, NR) operates 12 clinics with 15 more in development, Wellbeing Digital Sciences One (MEDI-NEO, NR), formerly Ketamine One, operates 11 clinics with 2 more in development, and Numinus Wellness (NUMI-TSX, NR) recently acquired Novamind to grow its network to 13 ketamine clinics. Given the similarities between the infrastructure required for ketamine- and other psychedelic-assisted therapies, we believe the development of ketamine clinic networks and infrastructure will provide a foundation for future psychedelic-assisted therapies, as many clinics will offer more psychedelic-assisted therapies beyond ketamine.

Exhibit 37 – US and Canadian Cities with Ketamine Clinics



Source: Google Maps, bestketamineclinics.com, ECM

~625 Psychedelic-Assisted Therapy Clinics Required to Treat 10% of TRD Patients in the US Alone

Assuming that 10% of the ~4.3M forecast treatment-eligible TRD patients in the US receive psychedelic-assisted therapy per year and that each treatment includes three sessions per treatment, the US will require the infrastructure to conduct ~1.3M sessions per year. This translates to ~25K treatment sessions per week or 5K treatment sessions per workday. Assuming each clinic can conduct an average of eight psilocybin treatment sessions per day (four clinicians, each conducting two 6-hour sessions per day with COMP360, MSP-1014 etc.), the US will require ~625 dedicated clinics and ~2.5K treating clinicians to meet the TRD demand alone. Given that psychedelics could be approved for other neurological indications beyond TRD, the number of clinics required will likely be much larger.

Profitability of Ketamine Clinics Incentivizes Rapid Network Expansion

Nevertheless, the growth of the ketamine clinic infrastructure from 60 clinics to ~300 in three years is highly encouraging and shows how rapidly supply can expand to meet demand, especially when the microeconomics allow the clinics to operate profitably. According to Delic, the owner of the largest chain of psychedelic wellness clinics, the cost of opening a ketamine clinic in the US is ~US\$250K and the clinics are able to break even in roughly six months with ~25-30% operating margins on a revenue base of ~US\$1M per clinic (see [Exhibit 38](#) below).

Exhibit 38 – US and Canadian Cities with Ketamine Clinics

DELIC CORP

BUSINESS MODEL

Delic Corp owns the largest chain of psychedelic wellness clinics in the country and a scalable ecosystem to increase revenue, profit margins and patient base.

CLINIC FINANCIALS | CASE STUDY

Open a Clinic	>	Cost \$250,000 USD	>	Break even in -6 months
Average Clinic Revenue	>	\$1M USD at ~25-30% operating profit		

KETAMINE

Treatment Cost

\$300-750/session

x 6+ monthly boosters

With 12 open today across 9 states, we will add an additional 15 clinics in the next 18 months, bringing access and relief to millions of Americans.

PSILOCYBIN

Treatment Cost

\$10,000/session*

*projected

MDMA

Treatment Cost

\$4,000-\$5,000/session*

*projected

PATIENT ECONOMICS | 10-year average spend: \$62,000

Source: Delic Holdings Corp. Corporate Presentation

Mindset's Capital Structure

Cash Covers Near-Term Burn, MSP-1014 Partnership Could Add Liquidity

Mindset closed the March 2022 quarter (FQ322) with \$11.3M in cash on the balance sheet, no debt, and ~\$28.3M available from the exercise of 43.7M currently outstanding warrants and options (both in- and out-of-the-money) with weighted average exercise prices of \$0.78 and \$0.49, respectively. This includes ~\$7M in outstanding warrants and options to be exercised by January 2023. While MSRD/Otsuka will fund the lead candidates from Families 2 and 4 through Phase Ib, a deal or partnership to bring MSP-1014 through human clinical trials and to market would bring in additional upfront cash and/or reduce the cash burn through a cost-sharing agreement. Absent such a deal, we expect the Company to raise \$10-15M in equity by the end of F2023 (June 2023) to cover its burn rate.

Given that the Company's valuation is driven in large part by its drug candidates' likelihood of regulatory approval, its market capitalization ought to increase with each de-risking event (publication of positive safety/efficacy data, advancement to successive clinical development stages), creating a virtuous cycle in which each de-risking event raises the valuation. This dynamic enables successively large financings at less dilutive prices to fund each stage of development.

Exhibit 39 – Capital Structure Summary

Based on a Share Price of \$0.33	Basic	Effect of Dilutive Securities	Diluted	Expiry Date	Number of Warrants	Weighted Average Exercise Price	Weighted Average Years to Expiry
Shares (M)	92.7	43.7	136.5	24-Jun-22	2,250,000	\$0.15	0.23
Market Cap (M)	\$30.6	\$14.4	\$45.0	15-Dec-22	8,593,238	\$0.60	0.71
Debt (M)	\$0.0		\$0.0	15-Dec-22	446,776	\$0.40	0.71
Leases (M)	\$0.0		\$0.0	16-Dec-22	2,146,187	\$0.60	0.71
Cash (M)	\$11.3	\$28.9	\$40.2	15-Apr-24	10,000,000	\$1.10	2.04
Enterprise Value (M)	\$19.3	(\$14.5)	\$4.9	15-Apr-24	798,252	\$0.75	2.04
				19-Apr-24	1,403,598	\$1.10	2.04
					25,638,051	\$0.78	1.30
Equity as a % of Capital	73.1%		52.9%				
Debt as a % of Capital	0.0%		0.0%				
Cash as a % of Capital	26.9%		47.1%				
Cash as a % of MV of Equity	36.9%		89.2%				
Cash per Share	\$0.12		\$0.29				

Type of Shares	Outstanding	Common Share Equivalents	Exercise/Conversion Proceeds	Notes
Basic Share Count	92,744,280	92,744,280		
Options	18,086,988	18,086,988	\$8,893,372	Weighted average exercise price of \$0.49
Warrants	25,638,051	25,638,051	\$19,997,680	Weighted average exercise price of \$0.78
Fully Dil. Shares Outstanding		136,469,319	\$28,891,052	

Source: Company Filings, ECM

Insiders Own ~11% of the Shares Outstanding

Mindset has a majority retail shareholder base, with plenty of runway for adoption by institutional investors. Management collectively owns ~10.2M shares, representing ~11% of the shares outstanding.

Exhibit 40 – Insider Holdings Summary

Holder	Occupation/Notes	Common Stock Equivalent Held	Position Date
Richard Patricio	Independent Chairman	2,982,875	3.22%
James Passin	Independent Director	2,285,250	2.46%
Philip Williams	Independent Director	1,978,200	2.13%
Malik Slasi	Senior VP of Innovation, Scientific Advisory Board	1,523,500	1.64%
James Lanthier	CEO	1,189,000	1.28%
Jessica Whitton	Insider	152,350	0.16%
Joseph Araujo	CSO, Scientific Advisory Board	64,000	0.07%
Arvin Ramos	CFO	1,000	0.00%
Insider Total		10,176,175	10.97%

Source: CapIQ, ECM

Financial Forecasts

MSRD Contract Income to be Recognized as Revenue

Per its collaboration agreement with MSRD for the development of Families 2 and 4 drug candidates, Mindset received cash payments of \$6.2M (US\$5.0M) upfront for general purposes and \$5.1M (US\$4.0M) for preclinical R&D in FQ322 (CQ122), resulting in a single contract liability on the balance sheet. The cash intended for R&D is recognized as revenue during the quarter in which the R&D costs are incurred along with a proportional amount of the upfront payment until it is fully recognized. We expect the Company to receive a further ~\$12M in R&D-related payments from MSRD over the coming 18 months and for it all to be recognized as revenue within those 18 months as IND-enabling preclinical studies are undertaken to prepare the drug candidates for Phase I clinical trials. We expect the Company to receive and spend ~\$20M over the course of F2024 to conduct Phase I clinical trials for the two drug candidates (see [Exhibit 41](#)).

Exhibit 41 – Projected MSRD Contract Liabilities and Recognition in Revenue

	F2022	F2023	F2024	F2025	F2026	F2027	F2028
Beginning MSRD contract liability, C\$M	-	9.7	-	-	-	-	-
Upfront cash payment from MSRD, C\$M	6.2	-	-	-	-	-	-
Upfront cash payment realized in revenue, C\$M	(1.7)	(4.5)	-	-	-	-	-
Ending upfront cash contract liability, C\$M	4.5	-	-	-	-	-	-
Family 2 & 4 R&D payment from MRSD, C\$M	10.1	7.4	20.0	-	-	-	-
Family 2 & 4 R&D realized in revenue, C\$M	(4.8)	(12.7)	(20.0)	-	-	-	-
Ending Family 2 & 4 R&D contract liability, C\$M	5.2	-	-	-	-	-	-
Ending MSRD contract liability, C\$M	9.7	-	-	-	-	-	-

Source: Company Filings, ECM

Subsequent to completion of the Phase I clinical trials in F2024, our base case expectation for the drug candidates is for them to be partnered out in F2025 (see [Exhibit 49](#))

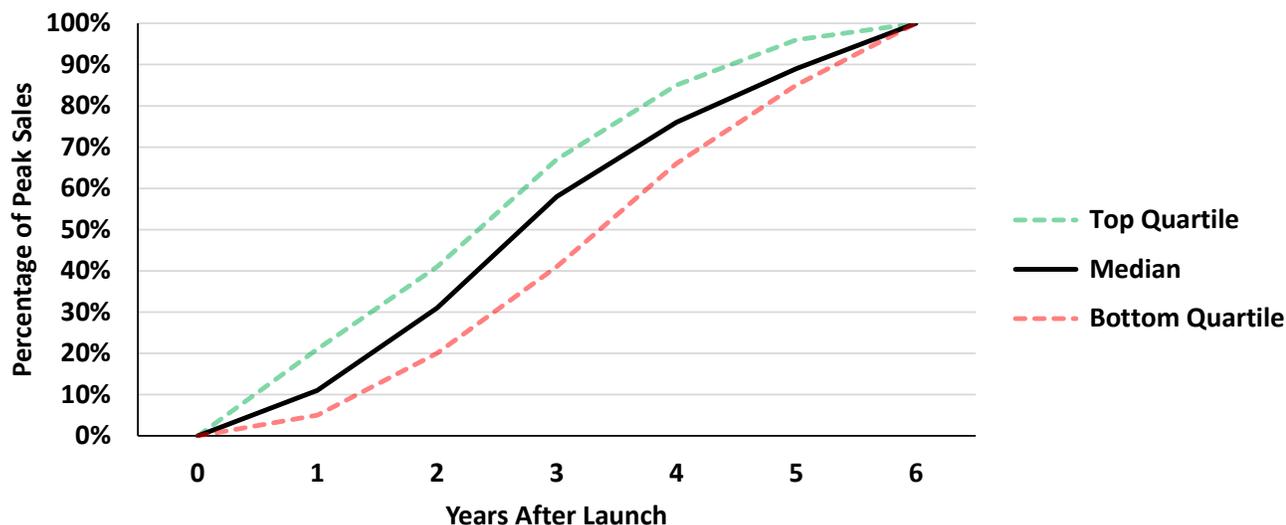
TRD Key Assumptions

MSP-1014 TRD Addressable Market

With a projected population growth of 1% per year in the US, and adults comprising 76% of the population, we estimate that there will be ~270M adults in the US in F2028. Assuming an 11% prevalence of depression in the US, with 70% of patients seeking treatment and a 33% non-response rate, we estimate the total addressable TRD population to be ~6.9M people in F2028. Of these 6.9M people, we assume 75% are eligible for treatment (no history of psychedelic use,

schizophrenia, or other prohibitive risk factors) and that the starting market penetration of psychedelics as a treatment category for TRD is 18%, ramping to 28% by F2034. This translates to ~930K patients receiving psychedelic-assisted psychotherapy as a treatment for TRD in F2028, ramping to ~1.5M in F2034. Our model assumes a typical new drug launch curve, as shown in Exhibit 42, and that MSP-1014 will be the second psychedelic compound to market for TRD. According to a C2015 [study](#), the second entrant to a market typically acquires 20-55% of the market at peak sales, depending on their share of promotional spending.

Exhibit 42 – Typical New Drug Launch Curve



Source: Robey, S., David, F. Drug launch curves in the modern era. *Nat Rev Drug Discov* 16, 13–14 (2017). doi: 10.1038/nrd.2016.236

Our model conservatively assumes that, after launching in F2028, MSP-1014 will acquire a peak market share of 20% in F2034 and that the launch will follow the typical curve shown in Exhibit 42 above. Each patient is expected to require three psychedelics sessions per year, resulting in 30.6K total doses administered in F2028, ramping to ~918K in F2034.

Exhibit 43 – TRD Addressable Market and MSP-1014 Market Penetration Forecasts

	F2028	F2029	F2030	F2031	F2032	F2033	F2034
US Population, M	355.4	359.0	362.5	366.2	369.8	373.5	377.3
<i>US Population Growth, %</i>	1%	1%	1%	1%	1%	1%	1%
<i>US Adult Population, %</i>	76%	76%	76%	76%	76%	76%	76%
<i>US MDD Prevalence, %</i>	11%	11%	11%	11%	11%	11%	11%
<i>US MDD Patients that Seek Treatment, %</i>	70%	70%	70%	70%	70%	70%	70%
<i>US MDD Treatment Non-responders, %</i>	33%	33%	33%	33%	33%	33%	33%
US TRD Prevalence, M	6.9	6.9	7.0	7.1	7.1	7.2	7.3
<i>US TRD Patients Eligible for Treatment, %</i>	75%	75%	75%	75%	75%	75%	75%
US TRD Eligible Treatment Population, M	5.1	5.2	5.3	5.3	5.4	5.4	5.5
<i>US TRD Patients Treated with Psychedelics, %</i>	18%	20%	22%	24%	26%	27%	28%
US TRD Patients Treated with Psychedelics, 000s	926.6	1,039.8	1,155.2	1,272.8	1,392.7	1,460.7	1,530.0
<i>TRD MSP-1014 Penetration Rate, %</i>	1%	2%	6%	12%	15%	18%	20%
<i>TRD Therapy Sessions per Year, #</i>	3	3	3	3	3	3	3
US TRD MSP-1014 Treatments, 000s	30.6	68.6	214.9	442.9	635.1	780.0	918.0

Source: ECM

MSP-1014 TRD Pricing and Unit Economics

In line with the psilocybin session pricing projections by Delic Corp., the largest chain of psychedelics wellness clinics in the US (see Exhibit 38), we assume a price per session of US\$10,000 starting in F2026 that increases with 2% annual inflation from F2026 through F2034. While pricing is yet to be determined for classic psilocybin treatment, US\$10,000 per session may be a somewhat conservative estimate given the US\$33,000-49,000 per year cost of esketamine (see Exhibit 12). We expect that, of this US\$10,000 session price, 90% will accrue to the clinics and administering physicians with Mindset recognizing the remaining 10% (~US\$1,000 per session) as revenue.

Exhibit 44 – MSP-1014 TRD Pricing Assumptions and Unadjusted Revenue Forecast

	F2028	F2029	F2030	F2031	F2032	F2033	F2034
US TRD MSP-1014 Treatments, 000s	30.6	68.6	214.9	442.9	635.1	780.0	918.0
<i>US MSP-1014 Gross Price per Treatment Session, US\$</i>	\$10,404	\$10,612	\$10,824	\$11,041	\$11,262	\$11,487	\$11,717
<i>Inflation Rate, %</i>	2%	2%	2%	2%	2%	2%	2%
<i>Gross-to-Net, %</i>	90%	90%	90%	90%	90%	90%	90%
<i>US MSP-1014 Net Price per Treatment Session, US\$</i>	\$1,040	\$1,061	\$1,082	\$1,104	\$1,126	\$1,149	\$1,172
US TRD MSP-1014 Revenue, US\$M	31.8	72.8	232.6	489.1	715.2	896.0	1,075.6

Source: ECM

MSP-1014 Probability of Clinical Trial Success for TRD

We assume a 10% probability that MSP-1014 will ultimately be approved by the FDA for the TRD indication. While this is slightly above the [historical average](#) of 7.3% for psychiatric drugs between C2011 and C2020 (n = 442), we believe a higher-than-average probability is warranted due to the gravity of the indication as well as COMPASS' encouraging psilocybin safety and efficacy data. Assuming MSP-1014 sales in the ex-US regions (rest of the world, ROW) are 50% of those generated in the US and that the drug is approved in those markets in F2029, we project total MSP-1014 probability-adjusted revenues of ~\$3.8M in F2028, ramping to ~\$195.0M in F2034, for the TRD indication.

Exhibit 45 – MSP-1014 TRD Probability-Adjusted Revenue Forecast

	F2028	F2029	F2030	F2031	F2032	F2033	F2034
US TRD MSP-1014 Revenue, US\$M	31.8	72.8	232.6	489.1	715.2	896.0	1,075.6
<i>TRD MSP-1014 Prob. Of Approval, %</i>	10%	10%	10%	10%	10%	10%	10%
US TRD MSP-1014 Revenue (Prob. Adjusted), US\$M	3.2	7.3	23.3	48.9	71.5	89.6	107.6
<i>USD/CAD</i>	1.21	1.21	1.21	1.21	1.21	1.21	1.21
US TRD MSP-1014 Revenue (Prob. Adjusted), C\$M	3.8	8.8	28.1	59.2	86.5	108.4	130.1
<i>US Revenue Growth, %</i>	NA	128.9%	219.4%	110.3%	46.2%	25.3%	20.0%
<i>ROW TRD MSP-1014 Revenue, % of US</i>	0%	50%	50%	50%	50%	50%	50%
ROW TRD MSP-1014 Revenue (Prob. Adjusted), C\$M	-	4.4	14.1	29.6	43.3	54.2	65.1
Total TRD MSP-1014 Revenue (Prob. Adjusted), C\$M	3.8	13.2	42.2	88.8	129.8	162.6	195.2

Source: ECM

End-of-Life Cancer Angst Key Assumptions

End-of-Life Cancer Angst Addressable Market

With the same assumptions regarding the size of the US adult population outlined above, we assume a 1% incidence rate and a 3% prevalence rate, with a total death rate of 7% in a given year. This leads to a total US adult terminal cancer population of 11.2M people in F2029, when we would expect the drug to be approved. Of these 11.2M people, we assume 75% are eligible for treatment (no history of psychedelic use or other prohibitive risk factors) and that the starting market penetration of psychedelics as a treatment category for end-of-life cancer angst is 14% in F2029, ramping to 27% by F2034. This translates to ~235K patients receiving psychedelic-assisted psychotherapy as a

treatment for end-of-life cancer angst in F2029, ramping to ~477K in F2034. Our model assumes that Mindset will acquire 40% of this market in F2034, following the typical launch curve shown in Exhibit 46, and that each patient will require two psychedelics sessions per year, resulting in 12K sessions in F2029, ramping to ~382K in F2034.

Exhibit 46 – End-of-Life Cancer Angst Addressable Market and MSP-1014 Market Penetration

	F2028	F2029	F2030	F2031	F2032	F2033	F2034
US Population, M	355.4	359.0	362.5	366.2	369.8	373.5	377.3
<i>US Population Growth, %</i>	1%	1%	1%	1%	1%	1%	1%
<i>US Adult Population, %</i>	76%	76%	76%	76%	76%	76%	76%
<i>US Cancer Prevalence, %</i>	3%	3%	3%	3%	3%	3%	3%
<i>US Cancer Incidence, %</i>	1%	1%	1%	1%	1%	1%	1%
<i>US Cancer Death Rate, %</i>	7%	7%	7%	7%	7%	7%	7%
US Total Adult Terminal Cancer Population, M	11.1	11.2	11.3	11.4	11.5	11.7	11.8
<i>US Terminal Cancer Patients with End of Life Angst, %</i>	20%	20%	20%	20%	20%	20%	20%
<i>US Terminal Cancer Patients with End of Life Angst Eligible, %</i>	75%	75%	75%	75%	75%	75%	75%
US End of Life Cancer Angst Eligible Treatment Population, M	1.7	1.7	1.7	1.7	1.7	1.7	1.8
<i>US End of Life Cancer Angst Patients Treated with Psychedelics, %</i>	12.0%	14.0%	16.0%	20.0%	23.0%	25.0%	27.0%
US End of Life Cancer Angst Patients Treated with Psychedelics, 000s	199.6	235.2	271.5	342.8	398.1	437.1	476.8
<i>End of Life Cancer Angst MSP-1014 Penetration Rate, %</i>	-	2%	5%	14%	26%	34%	40%
<i>End of Life Cancer Angst Therapy Sessions per Year, #</i>	2	2	2	2	2	2	2
US End of Life Cancer Angst MSP-1014 Treatments, 000s	-	11.6	26.9	95.6	207.8	299.0	381.9

Source: ECM

MSP-1014 End-of-Life Cancer Angst Pricing and Unit Economics

Similar to the pricing outlined in the case of TRD previously, we assume a price per session of US\$10,000 starting in F2026 that increases with 2% annual inflation from F2028 through F2034. We expect that of this US\$10,000 session price, 90% will accrue to the clinics and administering physicians with Mindset recognizing the remaining 10% (~US\$1,000 per session) as revenue.

Exhibit 47 – MSP-1014 End-of-Life Cancer Angst Pricing Assumptions, Unadjusted Revenue Forecast

	F2028	F2029	F2030	F2031	F2032	F2033	F2034
US End of Life Cancer Angst MSP-1014 Treatments, 000s	-	11.6	26.9	95.6	207.8	299.0	381.9
<i>US MSP-1014 Gross Price per Treatment Session, US\$</i>	\$10,404	\$10,612	\$10,824	\$11,041	\$11,262	\$11,487	\$11,717
<i>Inflation Rate, %</i>	2%	2%	2%	2%	2%	2%	2%
<i>Gross-to-Net, %</i>	90%	90%	90%	90%	90%	90%	90%
<i>US MSP-1014 Net Price per Treatment Session, US\$</i>	\$1,040	\$1,061	\$1,082	\$1,104	\$1,126	\$1,149	\$1,172
US End of Life Cancer Angst MSP-1014 Revenue, US\$M	-	12.4	29.1	105.6	234.0	343.4	447.5

Source: ECM

MSP-1014 Probability of Clinical Trial Success for End-of-Life Cancer Angst

Similar to TRD, we believe a probability of approval of 10% is warranted for MSP-1014 and that sales from the RoW are 50% of that of the US. This leads to ~\$2.2M in probability-adjusted revenues from the US and RoW markets in F2029, ramping to ~\$81M in F2034, for the end-of-life cancer angst indication.

Exhibit 48 – MSP-1014 End-of-Life Cancer Angst Probability-Adjusted Revenue Forecast

	F2028	F2029	F2030	F2031	F2032	F2033	F2034
US End of Life Cancer Angst MSP-1014 Revenue, US\$M	-	12.4	29.1	105.6	234.0	343.4	447.5
<i>End of Life Cancer Angst MSP-1014 Prob. Of Approval, %</i>	10%	10%	10%	10%	10%	10%	10%
US End of Life Cancer Angst MSP-1014 Revenue (Prob. Adjusted), US\$M	-	1.2	2.9	10.6	23.4	34.3	44.7
<i>USD/CAD</i>	1.21	1.21	1.21	1.21	1.21	1.21	1.21
US End of Life Cancer Angst MSP-1014 Revenue (Prob. Adjusted), C\$M	-	1.5	3.5	12.8	28.3	41.6	54.1
<i>US End of Life Cancer Angst Revenue Growth, %</i>	NA	NA	135.5%	262.9%	121.7%	46.7%	30.3%
<i>ROW End of Life Cancer Angst MSP-1014 Revenue, % of US</i>	50%	50%	50%	50%	50%	50%	50%
ROW End of Life Cancer Angst MSP-1014 Revenue (Prob. Adjusted), C\$M	-	0.7	1.8	6.4	14.2	20.8	27.1
Total End of Life Cancer Angst MSP-1014 Revenue (Prob. Adjusted), C\$M	-	2.2	5.3	19.2	42.5	62.3	81.2

Source: ECM

Families 2 and 4 Partnership, Milestones, and Royalty Revenue Assumptions

Given MSR D’s interest and investment in the development of the lead candidates of Families 2 and 4, we expect that these two candidates would be partnered out either to MSR D or another global pharma player. We estimate that in return for a licensing agreement subsequent to the conclusion of Phase Ib human trials in F2025, each asset would be able to garner ~\$25M in upfront payments, ~\$125M in milestone payments for Phase II and Phase III readouts, ~\$150M for FDA approval for a CNS indication with ~\$1,500M in peak sales in F2035, and ~15% in royalties on sales by the partner. We assume a 30% probability that each drug is partnered out and a 10% probability that the drug is ultimately approved.

Recent Otsuka CNS Agreement Guides Partnership Assumptions

We believe these assumptions are reasonable given the deal terms of the September 2021 [agreement](#) between Otsuka and Sunovion Pharmaceuticals, a subsidiary of Sumitomo Dainippon Pharma (DPM-SWB, NR), for the worldwide development and commercialization of four clinical-stage assets with potential CNS indications (two Phase I, one Phase II, and one Phase III). Per the agreement, Sunovian received US\$270M upfront from Otsuka and is eligible for up to US\$620M in development milestone payments as well as shared expenses and profits on the drug sales, if ultimately approved.

Exhibit 49 – Families 2 & 4 Projected Partnership, Milestones, and Royalty Revenues

	F2024	F2025	F2026	F2027	F2028	F2029	F2030	F2031	F2032	F2033	F2034
Family 2 Lead Candidate Partnership Upfront Payment, C\$M	-	25.0	-	-	-	-	-	-	-	-	-
Family 2 Lead Candidate Development Milestones, C\$M	-	-	-	50.0	-	75.0	150.0	-	-	-	-
Family 2 Lead Candidate Development and Milestone Payments, C\$M	-	25.0	-	50.0	-	75.0	150.0	-	-	-	-
<i>Family 2 Probability of Partnership, %</i>	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
Family 2 Partnership & Milestones Revenues (Prob. Adjusted), C\$M	-	7.5	-	15.0	-	22.5	45.0	-	-	-	-
Family 2 Partner Revenues, C\$M	-	-	-	-	-	-	165.0	465.0	870.0	1,140.0	1,335.0
<i>Family 2 Probability of Approval, %</i>	-	-	-	-	-	-	10%	10%	10%	10%	10%
<i>Family 2 Mindset Royalty Rate, %</i>	-	-	-	-	-	-	15%	15%	15%	15%	15%
Family 2 Royalty Payments from Partner (Prob. Adjusted), C\$M	-	-	-	-	-	-	2.5	7.0	13.1	17.1	20.0
Total Family 2 Revenues (Prob. Adjusted), C\$M	-	7.5	-	15.0	-	22.5	47.5	7.0	13.1	17.1	20.0
Family 4 Lead Candidate Partnership Upfront Payment, C\$M	-	25.0	-	-	-	-	-	-	-	-	-
Family 4 Lead Candidate Development Milestones, C\$M	-	-	-	50.0	-	75.0	150.0	-	-	-	-
Family 4 Lead Candidate Development and Milestone Payments, C\$M	-	25.0	-	50.0	-	75.0	150.0	-	-	-	-
<i>Family 4 Probability of Partnership, %</i>	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
Family 4 Partnership & Milestones Revenues (Prob. Adjusted), C\$M	-	7.5	-	15.0	-	22.5	45.0	-	-	-	-
Family 4 Partner Revenues, C\$M	-	-	-	-	-	-	165.0	465.0	870.0	1,140.0	1,335.0
<i>Family 4 Probability of Approval, %</i>	-	-	-	-	-	-	10%	10%	10%	10%	10%
<i>Family 4 Mindset Royalty Rate, %</i>	-	-	-	-	-	-	15%	15%	15%	15%	15%
Family 4 Royalty Payments from Partner (Prob. Adjusted), C\$M	-	-	-	-	-	-	2.5	7.0	13.1	17.1	20.0
Total Family 4 Revenues (Prob. Adjusted), C\$M	-	7.5	-	15.0	-	22.5	47.5	7.0	13.1	17.1	20.0

Source: ECM

Forecasted Income Statement

Given our assumption that the lead candidates from Families 2 and 4 will be partnered out, we do not expect Mindset to incur R&D costs for these assets after the upfront payments in F2025. The low-cost synthesis and production of MSP-1014 are expected to afford Mindset an 80% gross margin in the first year of product sales, which we then expect to ramp to 84% by F2034. In the event of a partnership agreement, however, the model will be adjusted to incorporate any upfront cash payments and royalties to be paid to Mindset to the partner once sales begin. We expect annual R&D expenditures to accelerate from ~\$6.6M in F2022 to ~\$60M in F2027 with the MSP-1014 clinical trials for TRD and end-of-life cancer angst set to commence later this calendar year. The Company's general and administrative (G&A) costs are expected to ramp from ~\$0.5M for F2022 to ~\$4.5M in F2028 and ~\$7.5M by F2034 while MSP-1014 sales and marketing costs are expected to begin in F2027 at ~\$4M, ramp to ~\$10M in F2029, and decline to ~\$6M by F2034.

Exhibit 50 – Financial Summary and Forecast Estimates

Financial Summary (C\$M)	F2022E	F2023E	F2024E	F2025E	F2026E	F2027E	F2028E	F2029E	F2030E	F2031E	F2032E	F2033E	F2034E
US TRD MSP-1014 Revenue (Prob. Adjusted)	-	-	-	-	-	-	3.8	8.8	28.1	59.2	86.5	108.4	130.1
ROW TRD MSP-1014 Revenue (Prob. Adjusted)	-	-	-	-	-	-	-	4.4	14.1	29.6	43.3	54.2	65.1
Total TRD MSP-1014 Revenue (Prob. Adjusted)	-	-	-	-	-	-	3.8	13.2	42.2	88.8	129.8	162.6	195.2
US End of Life Cancer Angst MSP-1014 Revenue (Prob. Adjusted)	-	-	-	-	-	-	-	1.5	3.5	12.8	28.3	41.6	54.1
ROW End of Life Cancer Angst MSP-1014 Revenue (Prob. Adjusted)	-	-	-	-	-	-	-	0.7	1.8	6.4	14.2	20.8	27.1
Total End of Life Cancer Angst MSP-1014 Revenue (Prob. Adjusted)	-	-	-	-	-	-	-	2.2	5.3	19.2	42.5	62.3	81.2
Total MSP-1014 Revenue (Prob. Adj.), C\$M	-	-	-	-	-	-	3.8	15.5	47.5	107.9	172.3	225.0	276.4
Family 2 Partnership & Milestones Revenues (Prob. Adj.), C\$M	-	-	-	7.5	-	15.0	-	22.5	45.0	-	-	-	-
Family 2 Royalty Payments from Partner (Prob. Adj.), C\$M	-	-	-	-	-	-	-	-	2.5	7.0	13.1	17.1	20.0
Family 2 Drug Total Revenue, C\$M	-	-	-	7.5	-	15.0	-	22.5	47.5	7.0	13.1	17.1	20.0
Family 4 Partnership & Milestones Revenues (Prob. Adj.), C\$M	-	-	-	7.5	-	15.0	-	22.5	45.0	-	-	-	-
Family 4 Royalty Payments from Partner (Prob. Adj.), C\$M	-	-	-	-	-	-	-	-	2.5	7.0	13.1	17.1	20.0
Family 4 Drug Total Revenue, C\$M	-	-	-	7.5	-	15.0	-	22.5	47.5	7.0	13.1	17.1	20.0
Psilocybin Synthesis Revenue, C\$M	-	-	-	-	-	-	-	-	-	-	-	-	-
MSRD Collaboration Revenue, C\$M	6.6	17.2	20.0	-	-	-	-	-	-	-	-	-	-
Total Revenue	6.6	17.2	20.0	15.0	-	30.0	3.8	60.5	142.4	121.9	198.4	259.2	316.5
Growth, %	NA	162%	17%	-25%	-100%	NA	-87%	1471%	136%	-14%	63%	31%	22%
Gross Profit	6.6	17.2	20.0	15.0	-	30.0	3.1	57.4	132.9	101.4	165.7	218.7	266.7
MSP-1014 Gross Profit Margin, %	100%	100%	100%	100%	-	100%	80%	95%	93%	83%	83%	84%	84%
G&A	0.5	1.2	1.6	3.0	3.5	4.0	4.5	5.0	5.5	6.0	6.5	7.0	7.5
Sales & Marketing	-	-	-	-	-	4.0	9.0	10.0	9.0	6.0	7.0	6.0	6.0
R&D	9.7	20.0	40.5	50.0	55.0	60.0	50.0	30.0	20.0	20.0	15.0	12.0	10.0
Adj. EBITDA	(3.6)	(4.0)	(22.1)	(38.0)	(58.5)	(38.0)	(60.4)	12.4	98.4	69.4	137.2	193.7	243.2
Adj. EBITDA Margin, %	-55%	-23%	-111%	-253%	0%	-127%	-1570%	20%	69%	57%	69%	75%	77%
EPS - WAD, \$	(\$0.19)	(\$0.11)	(\$0.21)	(\$0.28)	(\$0.32)	(\$0.17)	(\$0.22)	\$0.01	\$0.21	\$0.14	\$0.29	\$0.42	\$0.53

Source: ECM

Valuation

We are initiating coverage of Mindset with a Speculative Buy rating and \$1.25/shr target price that is derived from a probability-adjusted DCF (14% discount rate and 5% residual growth). Our \$1.25/shr target price represents 279% of upside from the current price of \$0.33 (see [Exhibit 51](#) below for DCF inputs and sensitivities). Our target price implies an equity value of ~\$450M, which is at the upper end of the current valuations of peer groups shown in [Exhibit 52](#).

Exhibit 51 – DCF Assumptions (A), Discounted Cashflows (B), and Sensitivity Analysis (C)

A Assumptions		C		Discount Rate		
				13%	14%	15%
Current Stock Price	\$0.33	Residual Growth	7%	\$2.15	\$1.65	\$1.25
WACC (%)	14%		6%	\$1.80	\$1.40	\$1.10
Residual Growth Rate (%)	5%		5%	\$1.60	\$1.25	\$1.00
Tax Rate	21%		4%	\$1.40	\$1.10	\$0.90
PV of CFs	(32.5)		3%	\$1.25	\$1.00	\$0.80
PV of Terminal Value	440.9					
Enterprise Value	408.3					
Pro Forma Net Cash (F2022) *	40.5					
Equity Value	448.8					
Pro Forma Dil. Shares Outstanding (F2034)	357.6					
DCF Target Price	\$1.25					
DCF Target Price % Upside	279%					

B Discounted Cashflows	F2022	F2023	F2024	F2025	F2026	F2027	F2028	F2029	F2030	F2031	F2032	F2033	F2034
Operating Profit (EBIT)	(17.1)	(10.9)	(28.9)	(44.8)	(65.3)	(44.8)	(67.2)	5.6	91.6	62.6	130.3	186.9	236.4
LESS: Income Tax	-	-	-	-	-	-	-	1.2	19.2	13.1	27.4	39.2	49.6
Net Operating CF (NOPAT)	(17.1)	(10.9)	(28.9)	(44.8)	(65.3)	(44.8)	(67.2)	4.4	72.4	49.4	103.0	147.6	186.8
D&A	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Change in WC	3.4	-	-	-	(0.5)	(2.5)	2.2	(4.7)	(6.7)	1.7	(6.2)	(5.0)	(4.7)
Capex	-	-	-	-	-	-	-	-	-	-	-	-	-
FCF	(13.7)	(10.8)	(28.9)	(44.8)	(65.8)	(47.3)	(65.1)	(0.3)	65.7	51.1	96.7	142.6	182.1
Tax Rate %	-	-	-	-	-	-	-	21%	21%	21%	21%	21%	21%
PV of Annual CF	(13.7)	(9.5)	(22.2)	(30.2)	(39.0)	(24.5)	(29.6)	(0.1)	23.0	15.7	26.1	33.7	37.8
Terminal Value													2124.1

* Assuming the exercise of all outstanding dilutive securities

Source: ECM

Comparables

Second-Generation Psilocybin Comparables

There are four groups of comparable companies that encompass the markets and product types that are being worked on by Mindset. The most directly comparable companies are those with second-generation psychedelic drug development programs. While this group includes industry leaders such as COMPASS and Atai, which are also further along in developing classic psychedelics for various indications, the average market capitalization of this group is ~US\$197M.

Classic and Other Psychedelics Comparables

The second group of comparables includes classic psychedelics companies such as Filament Health (FH-NEO, NR) and Revive Therapeutics (RVV-CSE, NR) along with ketamine clinic companies such as Numinus Wellness and Field Trip Health. Given that one of the microdosing indications listed for the lead Family 3 compound is likely to be ADHD, the list also includes Social Capital Suvretta Holdings Corp. I (DNAA-NASDAQ, NR), which is set to merge with digital therapeutics platform Akili Interactive (Private) and launch EndeavorRx, its FDA-cleared and CE-marked prescription digital therapeutic for pediatric ADHD. The transaction values the company at ~US\$1B (post-money).

DMT and Second-Generation DMT Comparables

While Mindset's DMT analog (Family 3) products are in the preclinical stage for now, the third group of comparables, including market leader, GH Research (GHRS-NASDAQ, NR), is comprised of companies developing classic DMT and second-generation DMT for various mental health indications.

Exhibit 52 – Comparables Analysis

Values in US\$ (unless otherwise stated)	Ticker	MC (US\$M) Basic	EV (US\$M)		Returns				EV/Sales	
			FD	1M	3M	YTD	1Y	2020	2021	2022
Mindset Pharma Inc.	MSET	25	4	-1%	-38%	-59%	-25%	NA	NA	2.2x
Second-Generation Psilocybin Comparables										
Atai Life Sciences N.V.	ATAI	591	266	0%	-27%	-52%	-80%	NA	15.4x	3542.1x
Mind Medicine (MindMed) Inc.	MNMD	279	159	-37%	-38%	-52%	-81%	NA	NA	NA
Cybin Inc.	CYBN	96	55	-26%	-29%	-52%	-73%	NA	123.6x	NA
Mydecine Innovations Group Inc.	MYCO.F	6	10	-20%	-81%	-87%	-96%	5097.5x	194.9x	1.1x
Enveric Biosciences, Inc.	ENVB	11	-10	2%	-29%	-77%	-90%	NA	NA	NA
Average		196.9	95.8	-16%	-41%	-64%	-84%	5097.5x	111.3x	1771.6x
Median		96.1	55.1	-20%	-29%	-52%	-81%	5097.5x	123.6x	1771.6x
Classic Psychedelics and Other Comparables										
COMPASS Pathways plc	CMPS	486	246	24%	-17%	-48%	-69%	NA	NA	NA
Filament Health Corp.	FLHL.F	13	11	-26%	-9%	-65%	-71%	NA	NA	NA
PsyBio Therapeutics Corp.	PSYB	9	6	43%	25%	-50%	-78%	NA	NA	NA
Social Capital Suvretta Holdings Corp. I	DNAA	316	316	0%	0%	0%	-1%	NA	NA	NA
Numinus Wellness Inc.	NUMI	51	18	-28%	-54%	-50%	-70%	27.8x	11.5x	3.8x
Field Trip Health Ltd.	FTRP	49	11	7%	-28%	-64%	-84%	15120.2x	16.5x	2.8x
Greenbrook TMS Inc.	GTMS	24	63	-40%	-55%	-68%	-88%	1.5x	1.2x	1.0x
Average		135.4	95.9	-3%	-20%	-49%	-66%	5049.8x	9.8x	2.5x
Median		49.4	18.2	0%	-17%	-50%	-71%	27.8x	11.5x	2.8x
DMT and Second-Generation DMT Comparables										
GH Research PLC	GHRS	568	297	2%	-42%	-53%	-49%	NA	NA	NA
Small Pharma Inc.	DMT	25	-6	-29%	-47%	-69%	-75%	NA	NA	NA
Pharmadrug Inc.	PHRX	8	9	-14%	-40%	-14%	-60%	17.0x	NA	NA
Algernon Pharmaceuticals Inc.	AGN	6	5	-34%	-43%	-13%	-71%	NA	NA	NA
Entheon Biomedical Corp.	ENBI	4	3	-9%	-55%	-85%	-88%	NA	NA	NA
Average		122.2	61.5	-17%	-45%	-47%	-69%	17.0x	NA	NA
Median		8.2	4.9	-14%	-43%	-53%	-71%	17.0x	NA	NA
Partnered, Early-Stage Biotech										
CureVac N.V.	CVAC	2,635	2,003	-22%	-26%	-59%	-78%	35.9x	22.7x	25.4x
Merus N.V.	MRUS	995	614	9%	-22%	-28%	8%	20.5x	13.3x	13.7x
Turning Point Therapeutics, Inc.	TPTX	3,742	2,830	1%	171%	58%	-1%	113.2x	91.5x	424.8x
Janux Therapeutics, Inc.	JANX	517	156	20%	-17%	-37%	-51%	NA	74.8x	38.9x
Gritstone bio, Inc.	GRTS	199	52	28%	-33%	-79%	-69%	12.9x	1.1x	3.1x
Ovid Therapeutics Inc.	OVID	151	-0	10%	-35%	-33%	-47%	NA	NA	NA
Average		1,373.0	942.3	8%	6%	-30%	-40%	45.6x	40.7x	101.2x
Median		755.6	384.7	10%	-24%	-35%	-49%	28.2x	22.7x	25.4x

Source: ECM

Partnered Early-Stage Biotech Comparables

The final group of comparables includes other early-stage (preclinical, Phase I) biotechnology companies with meaningful collaboration agreements with big pharma partners, similar to Mindset's agreement with MSD/Otsuka. The details of these partnerships are outlined in [Exhibit 53](#) below.

Exhibit 53 – Early-Stage Biotechnology Companies with Big Pharma Partnerships

Therapeutic Area	Biotechnology Company	Biotechnology Company Market Cap (US\$M)	Pharma Partner	Upfront Cash (US\$M)	Partnership Description
Epilepsy / seizures	Ovid Therapeutics	150.7	Takeda	196	Takeda secured exclusive, worldwide rights from Ovid to develop and commercialize soticlestat, an oral CH24H-inhibitor for the treatment of Dravet syndrome and Lennox-Gastaut syndrome in children and adults
HIV	Gritstone Bio	198.8	Gilead	30	Partnered to develop an HIV-specific therapeutic vaccine using Gritstone's personalized antigen-based prime-boost vaccine platform
Oncology	Janux Therapeutics	516.6	Merck	NA	Partnered to develop novel T cell engager drug candidates (using Janux' proprietary Tumour Activated T Cell Engager (TRACTr) technology) directed against two cancer targets selected by Merck. Janux will be eligible to earn up to \$500.5M per target in upfront and milestone payments plus royalties on any eventual sales. Merck will fund the R&D
Oncology	Merus	994.7	Eli Lilly	40	Partnered to research and develop up to three CD3-engaging T-cell-redirecting bispecific mAb therapies for the treatment of cancer
Oncology	Turning Point Therapeutics	3,742.2	Zai Lab	25	Partnered to develop and commercialize TPX-0022, a small-molecule multi-tyrosine kinase inhibitor of colony-stimulating factor-1 receptor (CSF1R), MET and SRC in greater China
COVID	CureVac	2,635.3	GSK	90	GSK and CureVac partner to develop next-generation mRNA COVID-19 vaccines

Source: ECM

Appendix I: Management and Board of Directors

Management

James Lanthier, MBA – CEO

A seasoned technology executive with strong expertise in corporate finance, public markets, and M&A. Most recently, Mr. Lanthier was a co-founder and CEO of Future Fertility, an innovative early-stage developer of AI applications for human infertility. As a C-Suite executive, Mr. Lanthier has assisted in the growth and successful exit of numerous technology-enabled businesses through the public markets, including Mood Media, the world's largest in-store media provider, and Fun Technologies, a pioneer in online casual games.

Arvin Ramos – CFO

Mr. Ramos holds a degree in commerce and is a member of the Chartered Professional Accountants of Ontario. Mr. Ramos has over 15 years of business experience, having supported a broad range of industries, including mining, technology, and banking. Mr. Ramos serves as CFO of several junior mining companies.

Joseph Araujo – CSO

A behavioural pharmacologist with extensive experience in facilitating the discovery and development of novel CNS drugs. He has co-founded, held executive level positions, and consulted for Life Sciences companies including CanCog Technologies, Vivocore, Karyopharm Therapeutics, NPM Pharma, Ketogen, and Epione Animal Health. He did his graduate training in pharmacology at the University of Toronto and has done extensive research examining psychoactive drugs.

Malik Slassi, PhD – Senior VP of Innovation

Dr. Slassi was the Founder, President, and Chief Scientific Officer of Fluorinov Pharma Inc., acquired by Trillium Therapeutics in January 2016. He is a seasoned medicinal chemist with a remarkable track record of success in drug discovery & development in the biopharmaceutical industry, spanning over 30 years. He has significant experience in the successful identification and development of drug candidates across multiple therapeutic areas including Neurology, Psychiatry, and Immunology. Dr. Slassi has extensive experience in the areas of intellectual property management, corporate and scientific operations. He is an accomplished inventor with over 130 issued and published patents and patent applications, and author of more than 65 scientific and review articles. Dr. Slassi holds a Ph.D. in chemistry from the University of Claude Bernard, Lyon, France, and completed his postdoctoral training at the Chemistry Department of the University of Montreal, Canada.

Jason Atkinson, MBA, CFA – Corporate Development

A finance professional with experience in private equity, venture capital, investment banking, and corporate finance. He has played a key role in raising capital and providing advisory services to private and publicly listed entities across multiple industries. He holds an MBA from the Degroote School of Business and is a CFA Charterholder.

Fiona Randall, Ph.D – Senior VP of External Alliances and Scientific Strategy

A trained neuroscientist and accomplished scientific, business development and alliance leader who brings both industry drug discovery and development and strategic partnering experience. Dr. Randall has worldwide experience in scientific leadership from academic and industry roles based in the UK, China, Japan, and the USA and has worked for Merck, GSK, Eisai, and Vertex during her career spanning all disease areas and therapeutic modalities. Dr. Randall has spent her research career as an electrophysiologist, building both understanding of the function of neuronal networks and how they are disrupted in diseases, as well as how to address these disruptions therapeutically. In industry, she has worked on a range of neurology programs, predominantly in neurodegenerative diseases, neuro-inflammation, and psychiatry, and has led multi-disciplinary, matrixed teams to deliver decision making data packages for therapeutic programs. Dr. Randall has extensive experience in leading strategic partnerships to deliver cutting edge innovation through the combination of partner technologies under a variety of deal structures.

Board of Directors

Richard Patricio, Chairman

President and CEO of Mega Uranium Ltd., a uranium-focused investment and development company with assets in Canada and Australia. He is a qualified lawyer (Ontario) with over 15 years of experience working with and for public companies. He has built a number of mining companies with global operations and spent 10 years with a TSX-listed investment company focused on the early-stage investment space. Mr. Patricio holds and has held senior officer and director positions in several companies that are listed on the TSX, ASX, NYSE, and AIM exchanges. Mr. Patricio received his law degree from Osgoode Hall and was called to the Ontario bar in 2000.

Joseph Araujo, Director

See above.

Philip Williams, Director

Mr. Williams has more than 20 years of finance industry experience. His diverse experience includes roles as a C-Suite Executive, sell-side research analyst, in fund management, managing director of investment banking, and sits on the boards of several public companies in Canada.

James Passin, Director

A 19-year hedge fund and private equity fund veteran with deep experience in emerging market equities and venture capital. He is a director of BDSec JSC, the largest investment bank in Mongolia, where he was awarded the Friendship Medal by the Mongolian state. Formerly a Principal at New York-based Firebird Management LLC, Mr. Passin has been called a “Daredevil Investor” by the *New York Times* and “the Indiana Jones of Frontier Stock Markets” by the *Financial Times*.

Appendix II: Investment Risks

Share Dilution Risk

It is highly likely that the Company will sell additional equity securities in future offerings, including through the sale of securities that are convertible to equity, to finance its operations, acquisitions, or projects, and issue additional common shares if outstanding warrants, stock options, and/or convertible debenture conversion rights are exercised, which may result in dilution of current investors.

Early-Stage Development and Scientific Uncertainty

Mindset's products are at an early stage of development and significant additional investment in R&D, product validation, production scale-up, manufacturing, and regulatory submissions will be required prior to commercialization. There can be no assurance that any such products will be developed. The development and regulatory processes may require access to raw materials and inputs that may not be available in sufficient amounts or in a timely fashion to allow completion of development or receipt of regulatory approval of any product or process. Furthermore, it is not known whether any of Mindset's drug candidates will meet applicable health regulatory standards and obtain regulatory approvals required for commercialization and distribution.

Patent and IP Risk

Mindset's success will depend in part on its ability to obtain, maintain, and enforce patent rights, maintain trade secret protection, and operate without infringing the proprietary rights of third parties. There can be no assurance that pending patent applications will be allowed, that issued patents will provide it with any competitive advantage or will not be challenged by any third parties, or that patents of others will not have an adverse effect on its ability to conduct its business. Furthermore, there can be no assurance that others will not independently develop similar products or duplicate any of Mindset's patented products.

Changes in Patent Law and its Interpretation Could Impair Mindset's Patents

Obtaining and enforcing patents in the biopharmaceutical industry is costly, time-consuming and inherently uncertain, and involve technological and legal complexity. The Supreme Court of Canada and the US Supreme Court have ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations creating uncertainty with respect to the value of patents, once obtained. Depending on decisions by the federal courts, and international treaties entered into by these nations, the laws and regulations governing patents could change in unpredictable ways that would weaken Mindset's ability to obtain patents or to enforce patents it may obtain in the future.

Product Liability Claims

Although Mindset currently carries what it believes to be adequate product liability and clinical trial insurance, there can be no assurance that it will be able to maintain its current insurance, or obtain other insurance as required, on acceptable terms, with adequate coverage in the future against potential liabilities or at all. If the Company's clinical trial and product liability insurance prove inadequate, product liability claims may harm its business.

Government Regulations

Biotechnology and pharmaceutical companies operate in a high-risk regulatory environment where the manufacture and sale of therapeutic products are governed by numerous statutes and regulations in the countries where Mindset intends to market its products. Such legislation affects the approval of manufacturing facilities, controlled research, and testing procedures, review, and approval of manufacturing, preclinical and clinical data prior to marketing approval, as well as regulation of marketing activities, notably advertising and labelling.

Healthcare Reimbursement

Mindset's ability to successfully market its products may depend in part on the extent to which reimbursement will be available from government health administration authorities, private health insurers, and other organizations.

Uncertainty exists as to whether newly approved healthcare products will qualify for reimbursement and challenges to the price of medical products are becoming more frequent. There can be no assurance that adequate third-party coverage will be available at price levels that would allow the Company to meet our forecasts.

Unfavourable Publicity or Consumer Perception

The psychedelic medicine industry is highly dependent upon consumer perception regarding the safety, efficacy, and quality of synthetic psychedelics as well as products produced or manufactured using natural psychedelics. Consumer perception of psychedelics may be significantly influenced by scientific research or findings, regulatory investigations, litigation, media attention, and other publicity regarding the consumption of products produced or manufactured using natural or synthetic psychedelics. There can be no assurance that future scientific research, findings, regulatory proceedings, litigation, media attention, or other research findings or publicity will be favourable to the medical and/or recreational psychedelics industry or any particular product, or consistent with earlier publicity.

Reliance on Third Parties to Plan and Conduct Preclinical and Clinical Trials

Mindset may rely on third parties to conduct preclinical development activities and clinical development activities. Preclinical activities include in vivo studies providing access to specific disease models, pharmacology and toxicology studies, and assay development. Clinical development activities include trial design, regulatory submissions, clinical patient recruitment, clinical trial monitoring, clinical data management and analysis, safety monitoring, and project management. If there is any dispute or disruption in its relationship with third parties, or if third parties are unable to provide quality services in a timely manner and at a feasible cost, Mindset's active development programs may face delays. Further, if any of these third parties fails to perform as expected or if their work fails to meet regulatory requirements, testing could be delayed, cancelled, or rendered ineffective.

Reliance on Contract Manufacturers

Mindset has limited manufacturing experience and will likely rely on contract manufacturing organizations (CMOs) to manufacture its drug candidates for preclinical studies and clinical trials. The Company may rely on CMOs for manufacturing, formulation, filling, packaging, storing, and shipping of drug product in compliance with current Good Manufacturing Practices (cGMP) regulations. Health Canada, the FDA, and other equivalent regulatory bodies in other jurisdictions ensure the quality of drug products by carefully monitoring drug manufacturers' compliance with cGMP regulations.

There can be no assurances that CMOs will be able to meet the Company's timetable and requirements. Mindset may not contract with alternate suppliers for any drug substance production in the event that a current provider is unable to scale up production, or if it otherwise experiences any other significant problems. If the Company is unable to arrange for alternative third-party manufacturing sources on commercially reasonable terms or in a timely manner, Mindset may be delayed in the development of its product/compound candidates. Further, CMOs must operate in compliance with cGMP and failure to do so could result in, among other things, the disruption of product supplies. The Company's dependence upon third parties for the manufacture of its products/compounds may adversely affect its profit margins and its ability to develop and deliver products in a timely and competitive basis.

Regulatory Risks

Successful execution of the Company's strategy is contingent, in part, upon compliance with regulatory requirements from time to time enacted by governmental authorities and obtaining all regulatory approvals, where necessary, for the sale of psychedelic medicines. The psychedelic medicine industry is a new industry, and the Company cannot predict the impact of the ever-evolving compliance regime in respect of this industry. Similarly, Mindset cannot predict the time required to secure all appropriate regulatory approvals for its future products, or the extent of testing and documentation that may, from time to time, be required by governmental authorities. The impact of compliance regimes, any delays in obtaining or failure to obtain regulatory approvals may significantly delay or impact the development of markets as well as its business and products.

Patient Enrollment in Clinical Trials

As Mindset's product/compound candidates advance from preclinical testing to clinical trials, an increasing number of patients that meet its eligibility criteria will need to be enrolled. There is significant competition for recruiting patients in clinical trials, and there may be delays in enrolling the patients needed to complete clinical trials on a timely basis or at all.

Market Price of Common Shares and Volatility

The market price of Mindset's common shares is affected by many variables not directly related to its success and is, therefore, not within its control. These include other developments that affect the breadth of the public market for the shares, the release or expiration of lock-up, escrow or other transfer restrictions on the shares, and the attractiveness of alternative investments. The effect of these and other factors on the market price of the shares is expected to make the price volatile in the future, which may result in losses to investors.

Dependence on Key Personnel, Employees, and Third-Party Providers

Mindset's success is largely dependent on the performance of its directors and officers and the loss of any of these individuals could have a material detrimental impact on its business. The Company does not intend to acquire any key man insurance policies and there is, therefore, a risk that the death or departure of any key member of management, a director, employee, consultant, or advisor could have a material adverse effect on its business, operations, and financial condition.

Reliance on a Single Facility

Mindset has engaged InterVivo Solutions (Private), a specialty testing facility that is focused on neuropsychological conditions, to deliver initial pharmacokinetics (PK) work to provide the basis for interpreting the dose-related efficacy, safety, and toxicological effects of its drug candidates. A significant portion of the Company's business will be conducted at InterVivo's facility. Accordingly, any adverse changes or developments affecting the facility could have a material adverse effect on its business, financial condition, and results of operations.

Delays in Clinical Testing

Mindset cannot predict whether any clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, or at all. Its development costs will increase if it experiences delays in clinical testing. Significant clinical trial delays could allow Mindset's competitors to bring products to market earlier, impairing its ability to successfully commercialize its drug candidates and harming its financial condition and prospects. Product development costs will increase if it experiences delays in testing or approval or if more or larger clinical trials are required than planned. Additionally, changes in regulatory requirements and policies may occur, necessitating amendments to the study protocols. Delays or increased product development costs may have a material adverse effect on Mindset's business, financial condition, and results of operation.

Appendix III: Depression Diagnosis and Measurement Tools

Unlike many other chronic diseases, there is no serum biomarker that can be measured to provide an objective diagnosis of MDD or to show the effects of a prescribed therapy. Clinicians instead rely on questionnaire-based rating scales that are intended to give a semi-quantitative read-out of the patient’s symptomology, with the Hamilton Depression Rating Scale (HAM-D or HRSD) and MADRS arguably being the best-validated and most widely used in clinical trials. The tools/tests can be conducted by either the clinician (clinician-rated) or the patient (self-rated). An overview of the main MDD assessment tools is shown in Exhibit 54 below.

Exhibit 54 – Validated Assessment Tools for Diagnosis of MDD and Measurement of Severity

Administration	Tool Name (Acronym)	Number of Items/Questions	Question Type	Sensitivity	Specificity
Clinician-rated	Hamilton Depression Rating Scale (HAM-D)	21	Scale (0 - 4, 0 - 2)	88%	89%
	Primary Care Evaluation of Mental Disorders (PRIME)	26	Yes/No, Multiple choice	< 70%	93%
	Montgomery-Asberg Depression Rating Scale (MADRS)	10	Scale (0 - 6)	88%	89%
Self-rated	Beck Depression Inventory (BDI)	21	Scale (0 - 3)	87%	79%
	Center for Epidemiologic Studies Depression Scale (CES-D)	20	Scale (0 - 4)	72%	70%
	Geriatric Depression Scale (GDS)	30	Yes/No	85%	73%
	Patient Health Questionnaire (PHQ-9)	9	Scale (0 - 3)	66%	80%
	Quick Inventory for Depressive Symptomology (QIDS)	16	Scale (0 - 3)	77%	82%

Source: ECM

Hamilton Depression Rating Scale (HAM-D or HRSD)

The HAM-D is a clinician-rated scale and is the oldest and most widely used instrument to rate the severity of depression symptoms. While the scale is widely used to measure the effectiveness of antidepressant medication in clinical trials and has been considered the gold standard, its use began to be questioned in the 1990s, particularly due to the relatively high number of questions related to sleep and eating. Four additional items that are generally not included in calculating a total score have since been added to the original seventeen-item questionnaire. The first nine items rate intensity or severity on a scale of 0 to 4 and the latter eight use a 0 to 2 scale. Despite its limitations, it is still widely used in clinical trials as its sensitivity (true positive rate) and specificity (true negative rate) are among the best in class.

Montgomery-Asberg Depression Rating Scale (MADRS)

MADRS is a clinician-rated test that was developed in 1979 and covers all of the DSM-4 criteria of MDD except psychomotor retardation and agitation. To address some of the perceived limitations of the HAM-D test, each of the 10 depression symptoms, measured on a scale from 0 to 6, is weighted equally and correlates well with the total 60-point score. One C2020 [meta-analysis](#) that included 137 datasets (109 HAM-D, 88 MADRS) and 44,104 subjects (32,399 HAM-D, 11,705 MADRS) showed that there is no statistically significant, clinically meaningful difference between the HAM-D and MADRS rating scales when measuring the reduction of depression symptoms as a result of oral AD use.

Beck Depression Index (BDI)

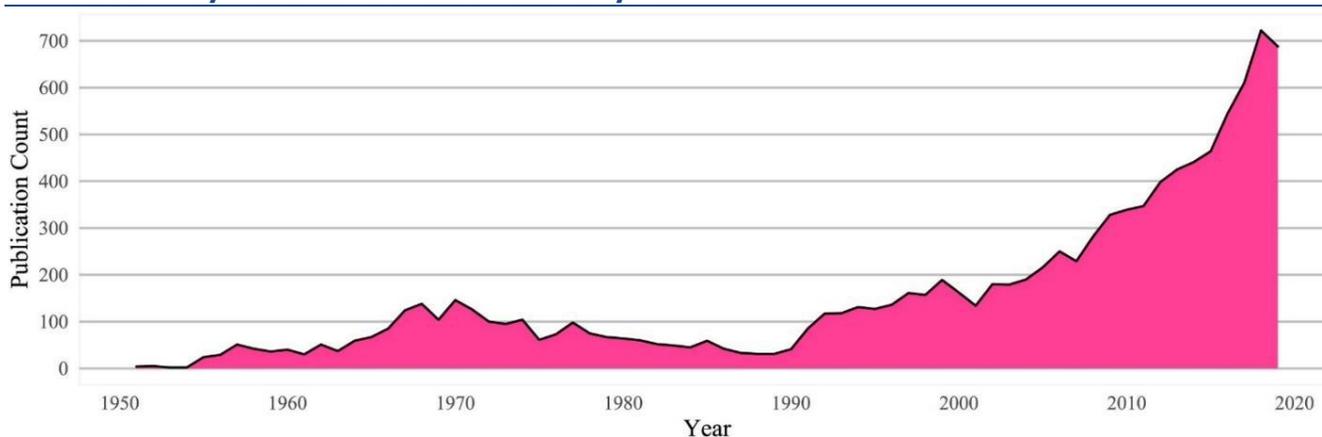
BDI was developed in 1969 and is a 21-item, self-rating depression symptom test. Many clinicians prefer to use patient self-rated scales as they are more scalable, and the results [correlate](#) well with clinician-rated scales. The BDI has high sensitivity and specificity and is valid and reliable in assessing the severity of depressive symptoms. Among its shortcomings are its high item difficulty (requires the patient to be able to read and understand the questions) and poor discriminant validity against anxiety.

Appendix IV: Brief History of Clinical Psychedelics Research

Decades of Clinical Research Came to a Halt in 1970

While the documented use of psychedelic plants such as magic mushrooms (psilocybin) and ayahuasca (DMT) in rituals and ceremonies goes back thousands of years, formal study of their use in treating neurological disorders dates back only to the 1950s. Over a period of ~15 years, psychiatrists treated tens of thousands of people with “psychedelic psychotherapy” after the medical community began seeing positive reports from researchers on the effects of LSD on test subjects. While psychedelics were legal at that time, the counterculture/anti-war movements of the 1960s led President Richard Nixon to sign the 1970 Controlled Substances Act that illegalized LSD and psilocybin, causing the number of psychedelic research papers to decline through the coming decades until the field was revived in 1990.

Exhibit 55 – Psychedelics Publication Count by Year



Source: Petranker Rotem, Anderson Thomas, Farb Norman; *Psychedelic Research and the Need for Transparency: Polishing Alice’s Looking Glass*, *Frontiers in Psychology* (2020) 11:1664-1078, doi: 10.3389/fpsyg.2020.01681

Research Resumed in 1990 with Much Stricter Controls in Place

The current boom in psychedelic research began in 1990 when the FDA allowed Dr. Rick Strassman to study the effects of DMT on human subjects under experimental conditions. This time, the scientific community is enacting strict controls to prevent widespread use outside of the clinics. As such, strict rules are in place to ensure that the doctors and therapists who prescribe and administer the psychedelic treatments are adequately trained. Nowadays, the scientific community understands the importance of the patient’s physical and mental conditions before, during, and after dosing with a psychedelic medicine. At the time of writing, there are 45 active, enrolling, or recruiting clinical trials listed on clinicaltrials.gov exploring the use of psilocybin for various conditions, along with 60 DMT trials, 29 MDMA, and 31 LSD (see [Exhibit 55](#)). Note that these tallies do not include next-generation derivatives of the aforementioned compounds.

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Company: Mindset Pharmaceutical Inc. | MSET-CSE, Stefan Quenneville, hereby certify that the views expressed in this report accurately reflect my personal views about the subject securities or issuers. I also certify that I have not, am not, and will not receive, directly or indirectly, compensation in exchange for expressing the specific recommendations or views in this report.

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