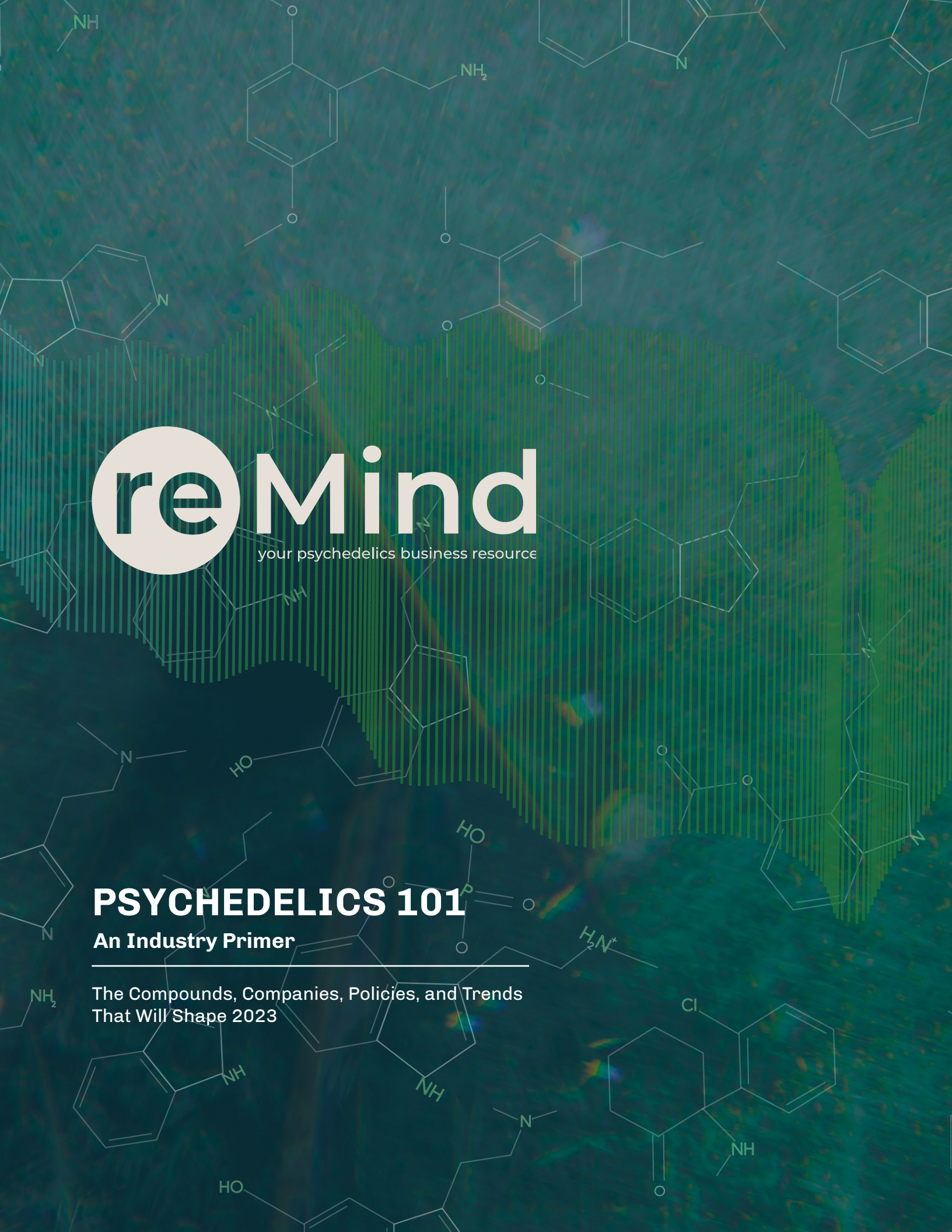

PSYCHEDELICS 101

An Industry Primer

The Compounds, Companies, Policies, and Trends That Will Shape 2023

reMind

your psychedelics business resource

WELCOME TO reMIND

We're building a new kind of community in the rapidly expanding psychedelics industry, one that embraces the wisdom of the old and the innovations of the new, one that welcomes diverse viewpoints and open dialog, and above all, one whose aim is to advance psychedelics in a safe, responsible and ethical manner.

We're dedicating our first annual report to all the newcomers out there. The ones, like us, who are inspired by promise of psychedelics, who see them as a powerful tool in personal development, as well as a beacon of hope in the global mental health crisis. The ones who know there's still much work to be done, research to conduct, policies to hone, marketplaces to develop — but who wish to join in the effort.

Before launching our brand, we consulted with dozens of industry executives, insiders and thought leaders to identify the most salient trends that will shape the future of psychedelics, as well as to understand the historical context that led to this moment and the rapid emergence of this industry. We teamed up with Josh Hardman, editor of *Psychedelic Alpha*, to produce this report. As one of the most discerning analysts covering the industry, Josh is uniquely positioned to distill these insights into an essential industry primer.

We hope you find this report useful, whatever your background, training or discipline is. And we invite you join us and help us deliver on our mission to propel the business of psychedelics forward.

Sara Vaughn
reMind - VP Brand Leader

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A very brief history...

FLESH OF THE GODS

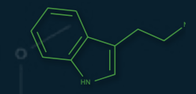
Psychedelics have a remarkably long and rich history of use by humans, which is thought to date back thousands of years. Some indigenous communities in Central and South America consumed (and in some cases continue to consume) psilocybin-containing mushrooms, occasionally referring to them as teonanacatl, or “flesh of the gods.” Across the Atlantic in ancient Greece, some believe that an ergot-infused drink served as a sacrament at the secretive rituals undertaken as part of the Eleusinian Mysteries.

WHAT DO WE MEAN BY ‘PSYCHEDELICS’?

The ‘classical’ psychedelics can be separated into multiple groups based on their chemical structures

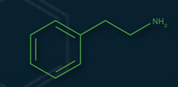
TRYPTAMINES

e.g., psilocybin, 5-MeO-DMT, DMT



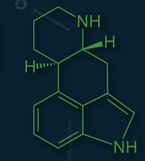
PHENETHYLAMINES

e.g., mescaline, DOI



ERGOLINES

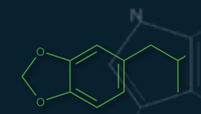
e.g., LSD, LSA



There are also other drugs that are often considered ‘psychedelics,’ including:

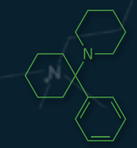
ENTACTOGENS OR EMPATHOGENS

e.g. Notably, MDMA



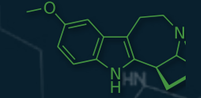
DISSOCIATIVE ANAESTHETICS

e.g. Ketamine, PCP



ATYPICAL PSYCHEDELICS

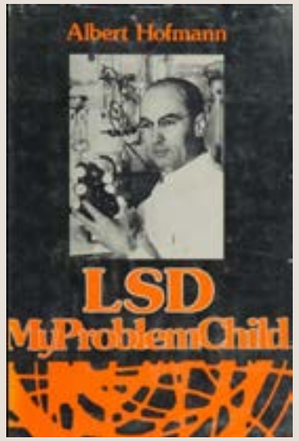
e.g., Ibogaine, Salvinorin A

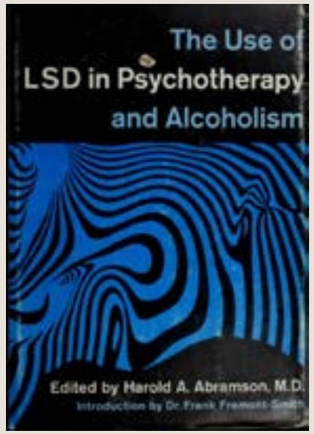


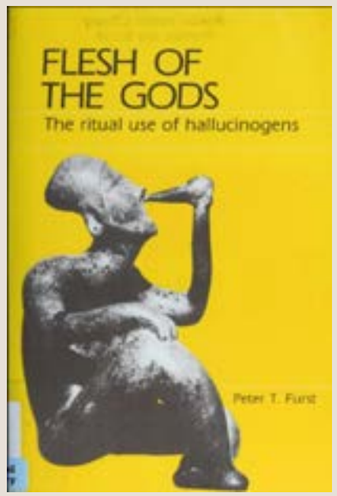
WESTERN ‘DISCOVERY’

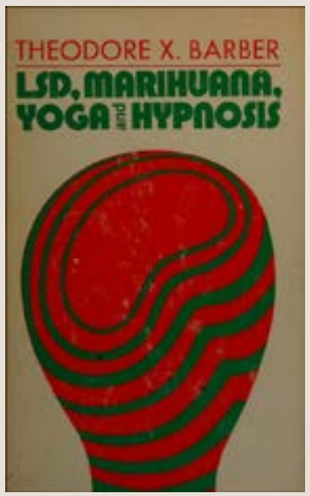
Western folk were late in their ‘discovery’ of psychedelics, then. While an 1896 publication in the British Medical Journal describes the distinctive effects of the mescaline-containing peyote cactus, and at the turn of the 20th century French explorers brought Iboga from Western Africa to France, it wasn’t until the 1940s that psychedelics were substantially explored in the labs of Europe and North America.

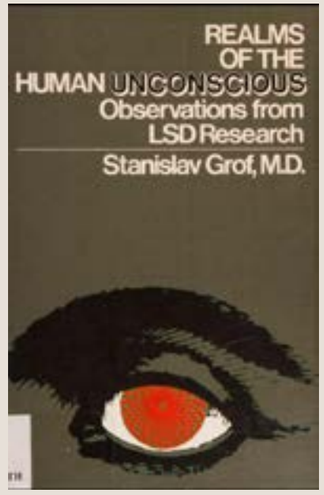
On April 19th, 1943—a half-decade after his initial synthesis of LSD—Swiss chemist Albert Hofmann infamously ingested the substance and documented the first acid trip in the world. This inaugural trip, which involved a mind-bending cycle home from the lab, is commemorated annually as Bicycle Day.











MID-CENTURY EXPERIMENTATION

Researchers and clinicians became very interested in these substances, with Swiss pharmaceutical giant Sandoz (now part of Novartis) providing LSD under the trade name Delysid to researchers, in the hopes of finding a use for this peculiar substance.

More than 40,000 patients had taken LSD by the mid-1960s, with over a thousand scientific publications on the topic. Importantly, LSD was generally administered in the form of LSD-assisted therapy, whereby the drug is used as a catalyst for more conventional talking therapy (see Page 10 for more). This ‘research’ wasn’t exactly controlled, however, with much of the experimentation taking place in the ‘real world.’ The practice of LSD therapy was so prolific in Hollywood, for example, that even folks like the actor Cary Grant took part.

It wasn’t only researchers and therapists that were interested in the curious nature of psychedelics, however. J.P. Morgan VP-cum-ethnomycologist R. Gordon Wasson travelled to a town in Mexico where he came across psilocybin mushrooms, subsequently popularizing the ‘magic mushroom’ in a 1957 Life Magazine dispatch that coined the term. Since then, the popularity of psilocybin-containing mushrooms in the West has, well, mushroomed.

Of course, there’s a side to the history of psychedelics that many will be familiar with: their associations with the counterculture and, ultimately, prohibition. Indeed, a California law that criminalized the possession and manufacture of LSD in 1966 ultimately snowballed into a U.S. and international ban on psychedelics writ large in 1970. Contemporaneously, the thalidomide tragedy prompted countries like the U.S. to strengthen clinical trial and drug development regimes, which—when combined with psychedelics’ newfound Schedule I status—made research into psychedelics almost entirely ground to a halt.

TODAY: A PSYCHEDELIC RENAISSANCE

Throughout a half-century of prohibition, a committed coterie of psychedelic researchers, tinkerers and nonprofits—both underground and above board—have continued their work despite a financial and regulatory quagmire. The last time psychedelics entered the zeitgeist was the flower power groundswell of the mid-century. The present 'psychedelic renaissance,' meanwhile, is based on clinical research, not cultural revolution: less "Sgt. Pepper," more "study protocols."

These researchers brought new legitimacy to claims that psychedelics may be harnessed in the treatment of mental health issues, codifying anecdotal evidence through rigorous, accepted forms of study. Such hope comes at a time of enormous and growing unmet need, with conventional pharma's psychiatric pipelines almost entirely stagnant.

Two decades after Nixon's War on Drugs put psychedelic research on ice, Dr. Rick Strassman began the thaw when he received government funding and approval to study DMT in humans in 1990. Over the course of 5 years, Strassman's research delivered around 400 doses of the powerful, short-acting psychedelics to nearly 60 participants at University of New Mexico's School of Medicine, breaking a 20-year hiatus in legal psychedelic research in humans.

And so, the 'psychedelic renaissance' began.

What are we talking about when we say: 'psychedelic therapy'?

Psychedelic-assisted psychotherapy (PAP) is a term used to broadly describe the administering of psychedelic drugs as part of a broader therapy program. Following patient screening, the sequence often looks something like this, with the potential for multiple repetitions:

Patients discuss with their therapist what they hope to get out of the treatment, ways they can prepare for it, and cover any questions or concerns.

A therapist or facilitator provides guidance and support during the patient's psychedelic experience.

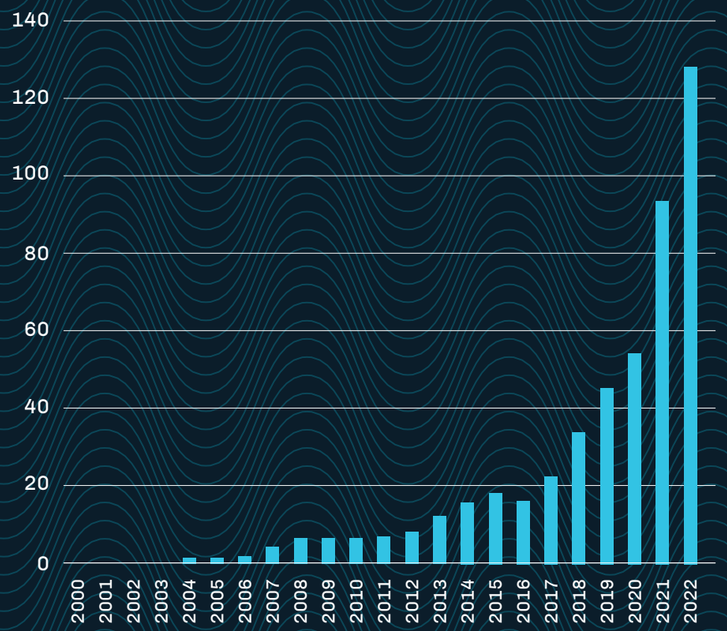
Patients explore the experience afterward with their therapist and identify ways to integrate its meaning and impact into their lives.

This modality is different to the standard of care, which generally involves take-home drugs like SSRI antidepressants that are sometimes given alongside a course of psychotherapy like cognitive behavioural therapy (CBT).

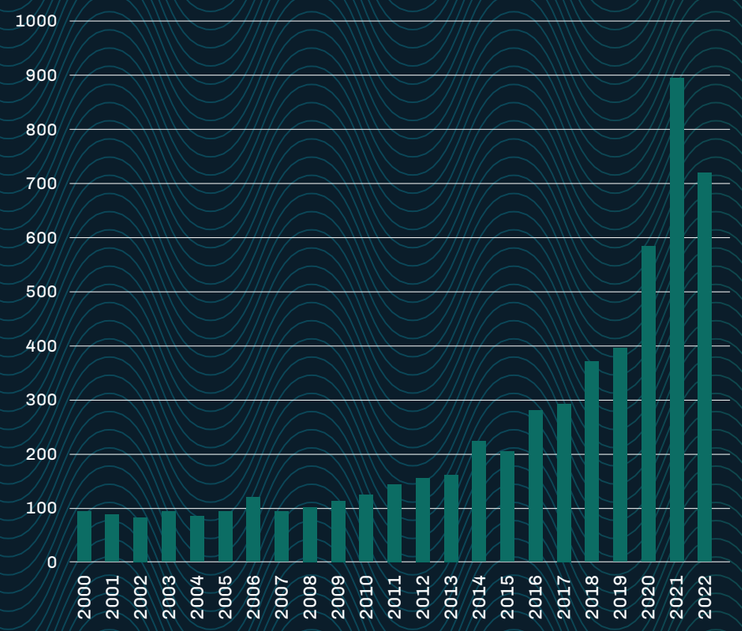
BY THE NUMBERS

An explosion in psychedelic research

RESEARCH AND CLINICAL TRIALS OVER THE PAST HALF-CENTURY



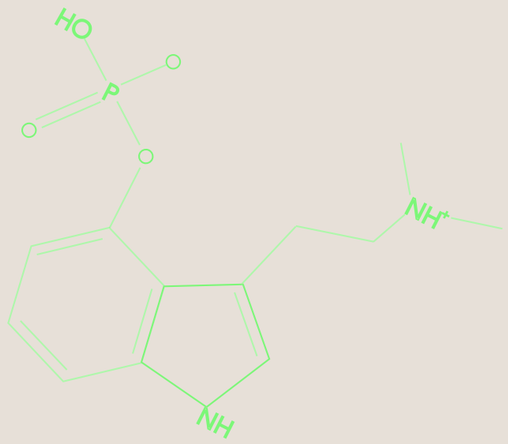
ACTIVE PHYCHEDELICS CLINICAL TRIALS

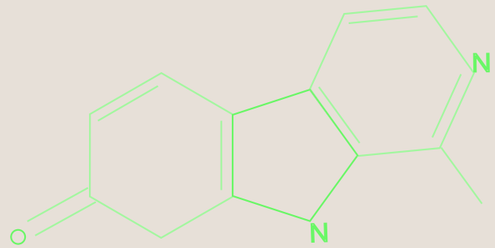


NUMBER OF PSYCHEDELIC PUBLICATIONS BY YEAR

KEY RESEARCH INSTITUTES ACROSS THE WORLD

1. Johns Hopkins Center for Psychedelic and Consciousness Research (2019)
2. Imperial College London Centre for Psychedelic Research (2019)
3. Icahn School of Medicine at Mount Sinai Center for Psychedelic Psychotherapy and Trauma Research (2021)
4. University of California, San Francisco Translational Psychedelic Research Program (TrPR) (2021)
5. Mass. General Hospital Center for the Neuroscience of Psychedelics (2021)
6. UC Berkeley Center for the Science of Psychedelics
7. Yale Psychedelic Science Group (2016)
8. University of Wisconsin-Madison Transdisciplinary Center for Research in Psychoactive Substances (2021)
9. Toronto University Health Network - Nikean Psychedelic Psychotherapy Research Centre (2021)
10. Stanford Psychedelic Science Group
11. University Hospital Basel

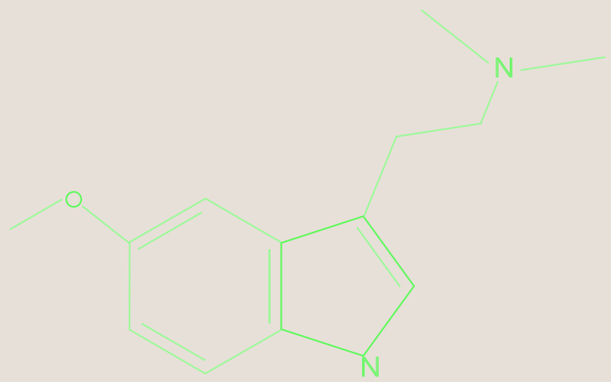




The business of psychedelics

Based on this research, and the unmet need that psychedelics might begin to address, a bevy of business interests have entered the psychedelics space in recent years. Today, they are largely responsible (with the glaring exception of MAPS, and other nonprofits like the Usona Institute) for the development of psychedelics as therapeutics, at least within the conventional biotech model.

These companies are, generally, looking to bring psychedelics to market within the medical model via the formal regulatory drug approval process; setting them apart from many cannabis companies that some might expect to be analogs. Agencies like the FDA evaluate scheduled drugs like psychedelics as they would any other: So long as the benefits of the intervention outweigh the risks, they are suitable for approval.



PSYCHEDELICS VS. CANNABIS

While many investors and onlookers assume that the cannabis market might be a useful comp for nascent psychedelics ventures, it's distinct for several reasons:

1.
Manufacturers and consumer packaged goods companies represent a very small share of psychedelic companies and investors' portfolios. The most significant focus, by far, is on drug discovery and development; i.e., achieving federal-level approval of regulated psychedelic therapeutics.

2.
As such, the health of the nascent psychedelic market is not so reliant on state-by-state decriminalization or legalization efforts, as seen in cannabis.

3.
Operating within this 'medical model' brings a significantly higher cost of entry, a longer path to market, and other business and risk dynamics that more closely resemble those of biopharma.

*Note: None of this is to say there isn't going to be a consumer or retreats market — there already is. But, it's largely a grey market, and not suitable for the average investor due to its murky legal status. Operators in such markets will also have difficulties where they interact with federal agencies, such as the IRS.

THE BIRTH OF PSYCHEDELIC STOCKS

Over the past few years, the pace of psychedelic company formation and activity has rapidly accelerated. Psychedelic drug development was introduced to the public markets in 2020, starting in earnest with MindMed's March IPO.

Over the course of that summer, a number of new competitors came to market through a series of RTO's and program acquisitions.

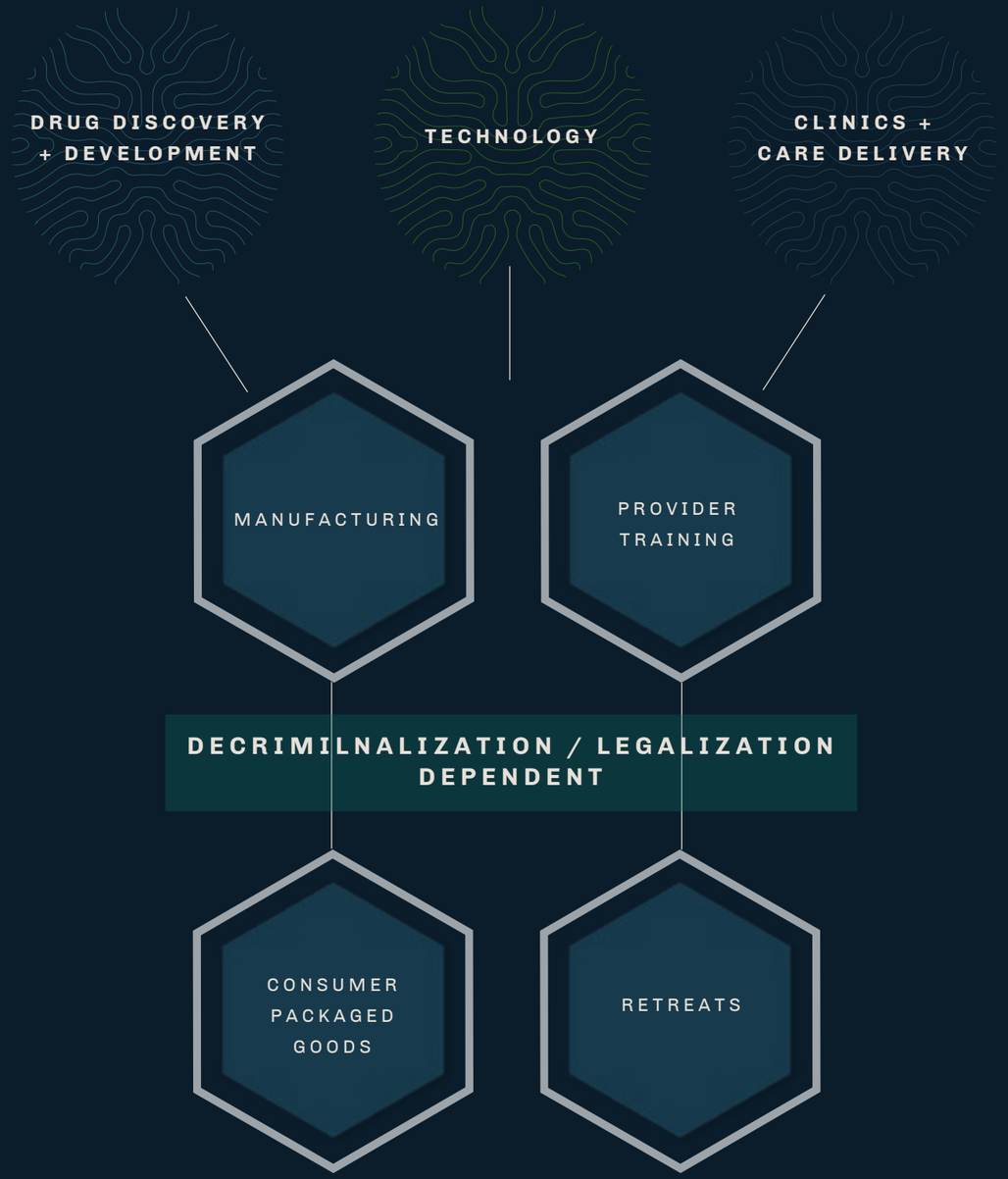
However, the investor frenzy wouldn't begin until after COMPASS Pathways' September 18th NASDAQ listing. What followed were months of rapid and perhaps unsustainable share price appreciation, dozens of new market entrants, and a hype-fueled cycle that has more recently tempered.

Today, most of the clinical research into psychedelics is being undertaken as part of corporate drug discovery and development efforts, which are distributed across around 50 public companies and hundreds of private organizations.

PUBLICLY TRADED COMPANIES	
Atai Life Sciences (NASDAQ: ATAI)	Reunion Neuroscience (NASDAQ: REUN)
Compass Pathways (NASDAQ: CMPS)	Clearmind Medicine (CSE: CMND)
GH Research (NASDAQ: GHRS)	MYND Life Science (CSE: MYND)
MindMed (NASDAQ: MNMD)	Wesana Health (CSE: WESA)
Cybin (NYSE: CYBN)	Psyched Wellness (CSE: PSYC)
Field Trip Health & Wellness (TSXV: FTHW)	HAVN Life Sciences (CSE: HAVN)
Seelos Therapeutics (NASDAQ: SEEL)	PharmaTher (CSE: PHRM)
Small Pharma (TSXV: DMT)	BetterLife Pharma (CSE: BETR)
Numinus Wellness (TSXV: NUMI)	Braxia Scientific (CSE: BRAX)
Bright Minds Biosciences (NASDAQ: DRUG)	Tryp Therapeutics (CSE: TRYP)
Incannex Health (ASX: IHL.AX)	Psyence Group (CSE: PSYG)
Revive Therapeutics (CSE: RVV)	Silo Pharma (OTC: SILO)
Red Light Holland (CSE: TRIP)	Core One Labs (CSE: COOL)
Awakn Life Sciences (NEO: AWKN)	M2BIO (OTC: WUHN)
Mindset Pharma (CSE: MSET)	Neonmind Biosciences (CSE: NEON)
Mydecine Innovations Group (NEO: MYCO)	PharmaDrug (CSE: PHRX)
Filament Health (NEO: FH)	Lobe Sciences (CSE: LOBE)
Enveric Biosciences (NASDAQ: ENVB)	Delic Corp (CSE: DELC)
PsyBio Therapeutics (TSXV: PSYB)	Nova Mentis Life Science (CSE: NOVA)
Optimi Health (CSE: OPTI)	Algernon Pharmaceuticals (CSE: AGN)
Universal Ibogaine (TSXV: IBO)	Silo Wellness (CSE: SILO)
Levitee Labs (CSE: LVT)	Albert Labs (CSE: ABRT)
Entheon Biomedical (CSE: ENBI)	Aion Therapeutics (CSE: AION)
Ehave (OTC: EHVVF)	

PRIVATE COMPANIES	
Beckley Psytech	Fluence
Delix Therapeutics	Maya Health
Diamond Therapeutics	Clairvoyant Therapeutics
Enthea	Terran Biosciences
Gilgamesh Pharmaceutical	Mycrodose Therapeutics
Tactogen	MiKHAL GmbH
Psygen	Psy Therapeutics
Bexson Biomedical	Return Health
Freedom Biosciences	Ceruvia Lifesciences
Psilera	Journey Colab
Octarine Bio	Sacred Medicines
Earth Resonance	Lophora
CaaMTech	Alvarius Pharmaceuticals
CB Therapeutics	Reset Pharma
Heading Health	Mindstate Design
Wake Network	Osmind
MAPS Public Benefit Corporation (PBC)	Mindleap
Aphrodite Health	Journey Clinical
Synthesis Institute	Clerkenwell Health
ATMA Journey Centers	Psylo

THE PSYCHEDELIC VALUE CHAIN



Note: While drug discovery and development is seeing the vast majority of investment, there are many ancillary areas that will become increasingly interesting as we move closer to commercialization.

A PATH TO MARKET

PHASE 1
(typically several months)

To establish an initial safe dose in humans. Small number of participants (n), healthy volunteers.

PHASE 2
(typically several months to 2 years)

To establish safety in the target patient population and attempt to gauge the efficacy of a drug in a variety of doses. Small n, informs larger Phase 3 trials, and adds to safety data.

PHASE 3
(typically 1 - 4 years)

Intended to demonstrate safety and efficacy of a drug. Large n, typically two Phase 3 trials are needed to seek approval.

This later-stage work has been catalyzed by positive signals from regulators in the U.S. and beyond — in particular, the FDA's Breakthrough Therapy Designation ...

COMPASS PATHWAYS PHASE 2B: PSILOCYBIN FOR TRD (EXPECTED TO ENTER PHASE 3 THIS YEAR)

MAPS PHASE 3: MDMA-AT FOR PTSD

FDA BREAKTHROUGH THERAPY DESIGNATIONS (BTDS) FOR PSYCHEDELICS

The FDA grants Breakthrough Therapy Designations to drugs that, in preliminary clinical investigations, show promise in substantially improving the treatment of serious conditions. The designation accelerates development and review timelines.

- MAPS' MDMA-AT for PTSD (2017)
- Compass Pathways' psilocybin for TRD (2018)
- Janssen's Spra vato (esketamine) for TRD (FDA Approved 2019, after receiving BTD earlier)
- Usona Institute's psilocybin for MDD (2019)

The addressable market of these therapies is, theoretically, enormous. A recent estimate from ARK Invest pegged the 2022 aggregate US pharmaceutical sales opportunity for major depressive disorder (MDD), PTSD, and opioid use disorder (OUD) treatments at $44 billion. And that's just if we take into account their potential to address a handful of mental health issues and substance use disorders. Today, a growing number of companies are exploring psychedelics—including their 'next generation' derivatives and analogs—for an increasingly broad range of conditions, from chronic pain to neurodegeneration.

That potential isn't lost on forward-thinking investors, who poured nearly $2 billion into the psychedelics sector last year. It's a diverse investor base: from psychedelic-specific VCs and individuals right through to pharmaceutical giant Otsuka and ARK.

But, it hasn't been an easy ride for those who placed their chips more recently.

THE HYPE CYCLE

The psychedelic sector witnessed a period of overexuberance last year, with valuations of a number of companies disconnecting from fundamentals as investors struggled to grapple with the quirks of the psychedelic sector—early comparisons to cannabis proved misleading (see Page 14 for more) and many investors weren't looking through a biotech lens. This year, many of these valuations have come back down toward reality, to the point where today a number of companies and programs are perhaps even undervalued.

What's more, now that the sector has cooled off we're seeing companies focus on their sustainability and cash flow optimization. In practice, this looks like drug pipeline management and refocusing, with even the largest public psychedelics companies like atai Life Sciences and MindMed putting programs on the backburner.

We're also likely to see consolidation within and between companies, as cheap capital dries up due to macro and industry-specific trends. More on that later in our Trends and Tensions section.

PSYCHEDELIC STOCK PERFORMANCE VS. BIOTECH

Comparative 2022 ETF Growth YTD (%)

Society and the state

Amid a strengthening evidence base and a deepening mental health crisis, governments and regulators have become increasingly interested in psychedelics, and that interest is largely a positive force despite the backdrop of their Schedule I status.

FEDERAL AGENCIES LOOSEN UP

While research into Schedule I substances is cumbersome, government agencies have made some nascent efforts to reduce the burden on psychedelic research in the United States:

- **FDA Breakthrough Therapy Designations (page 19),** which accelerate the review of new drugs, have been granted for a number of psychedelic drug development programs.

- **Federal grant** support for research into the potential therapeutic effects of psychedelics returned in November 2021, when a Johns Hopkins study to investigate psilocybin therapy for smoking cessation received nearly $4m.

- **DEA has increased production quotas** for psychedelics intended to be used in research, removing a hard ceiling on the volume of research and trials (TABLE below).

DEA PRODUCTION QUOTAS FOR PSYCHEDELICS

SUBSTANCE	2021 FINAL	2022 FINAL	% INCREASE
Psilocybin	6,000 grams	8,000 grams	+33.33%
LSD	40 grams	500 grams	+11,1150%
MDMA	3,200 grams	8,200 grams	+156.25%
5-MeO-DMT	35 grams	2,550 grams	+7,185.71%

Given that the research and clinical development of psychedelic therapies is largely happening within the regulated arena of clinical trials, it's easy to think that policy changes might not matter. In fact, a few years ago the executives of many psychedelics companies openly opposed efforts to decriminalize or legalize access to psychedelics. What's more, too much positive attention from popular media and the public may jeopardize the rigor of clinical studies, injecting expectancy and bias.

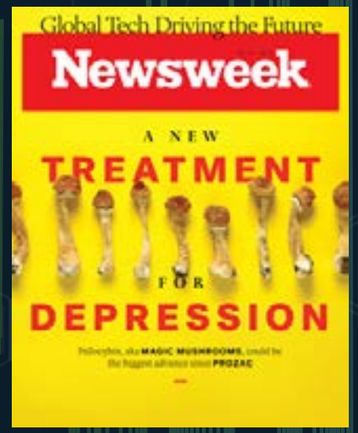
Regardless, the fact that psychedelics are once again tripping into the mainstream is undeniable.

Public perception and policy

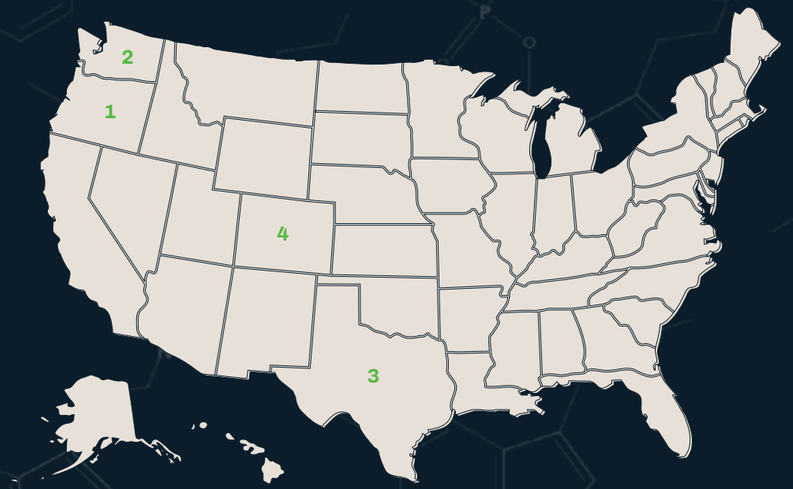
In the most salient example of the interplay between these different arenas of the psychedelic renaissance, society and public opinion is both driving the appetite for research, policy changes, etc.; and is also shaped by it.

Psychedelics are undergoing unequivocal mainstreaming, thanks in part to high-profile podcasts, documentaries, and news stories. This poses some challenges for researchers in the medical model (expectancy effects, for example) but it also makes a more propitious milieu for psychedelic research and development, and eventual commercialization: after all, practitioners, payers and potential patients are not isolated from society and its ever-changing zeitgeist.

Some of this increased public support for psychedelics, and their apparent therapeutic potential, has manifested in pushes to decriminalize or legalize them at state or local levels in the U.S.



KEY PSYCHEDELIC DRUG POLICY REFORMS IN THE U.S.



1

Oregon: Measure 109 = Oregon Psilocybin Services Act (legal psilocybin therapy), Measure 110 = Drug Addiction Treatment and Recovery Act (broad drug decrim.)

2

DC: Initiative 81 = Entheogenic Plant and Fungus Policy Act of 2020 (decrim. of entheogenic plants and fungi)

3

Texas: Even more conservative states are exploring the potential of psychedelics. Last summer a working group was established to study the potential therapeutic applications of a number of psychedelics.

4

Colorado: The passage of Proposition 122 in November decriminalized the possession and use of psychedelic mushrooms and, if approved by the regulating state agency, additional plant-based psychedelic substances for people 21 and older.

PSYCHEDELIC DRUG USE IN THE U.S.

More than 5.5 million U.S. adults use psychedelics

An estimated 5.5+ million people in the U.S. used hallucinogens in the past year, in 2019, which represents an increase from 1.7 percent of the population aged 12 and over, in 2002, to 2.2 percent in 2019

An estimated 4% of the population age 18-25 used them in 2019

The perception of considerable risk for regular LSD use decreased significantly overall for the years 2002-2014, among all age groups

This represents a second path to usage of psychedelics, but is generally not within the remit of psychedelics companies (aside from some clinics and service delivery companies), given the grey area it occupies. Even in situations like that seen in Oregon where psilocybin services will be legal from 2023, there are issues of federal tax codes, limits on the scale of business operations, etc.

It's also worth noting that in legalized and decriminalized settings, access to psychedelic therapy will almost always be out-of-pocket: i.e., it won't be covered by insurance, at least in the first instance. This represents a major cost barrier to entry.

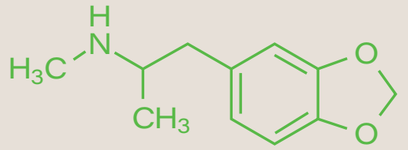
Key milestones and catalysts on the horizon

There are a number of important milestones and potential catalysts on the near-term horizon for psychedelic investors to be aware of. Here are three key ones to watch:

MAPS' MDMA-assisted therapy moves towards potential approval

The second Phase 3 trial of MDMA-assisted therapy for PTSD is expected to provide a read-out by the end of 2022.

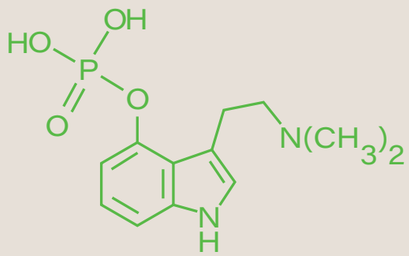
MDMA-assisted therapy could be FDA-approved as early as late 2023.



MDMA

Oregon rolls out psilocybin services

Next year, Oregon begins the roll-out of its Psilocybin Services, which will allow adults to access psilocybin at licensed service centers.

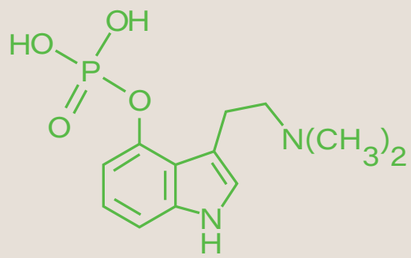


Psilocybin

COMPASS Pathways' psilocybin moves to Phase 3

COMPASS Pathways is expected to initiate its Phase 3 trial of its psilocybin product for treatment-resistant depression (TRD) in the coming months.

We also expect to see long-term follow-up data from its earlier trials, which may provide hints at the durability of the therapy.



Psilocybin

SALIENT TRENDS AND TENSIONS

Key trends and tensions for psychedelic investors to be aware of...

TENSION

THE PSYCHEDELIC PATENT WARS

Intellectual property rights such as patents represent important moats that justify the enormous investments required in drug development efforts; but low-quality patents—such as those that are overbroad, or that do not cover genuinely novel or non-obvious inventions—can stifle the field by posing real or perceived barriers to entry.

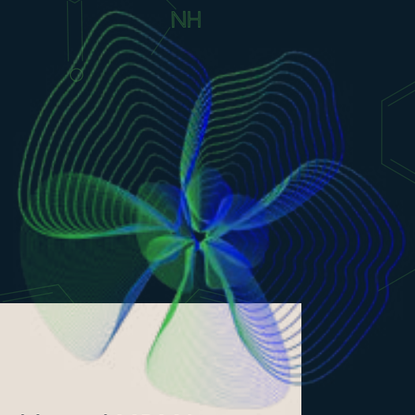
Given that psychedelics have existed for millennia, in some cases, how can they be patented? Those seeking psychedelics-related intellectual property (IP) generally seek to identify derivatives, analogs, and other 'tweaked' forms of known psychedelics which may be patentable. Patents may also be sought on treatment methods, patient populations, and ancillary technologies, among other things.

Concerns around shoddy IP aren't unique to the psychedelics space: Practices like patent trolling, thicketing, and evergreening plague the IP system writ large. But, a confluence of factors have made psychedelics-related patents all-the-more susceptible to being low-quality and controversial.

Navigating these tensions is especially difficult when it comes to 'classic psychedelics' like psilocybin. One option, then, is to go beyond the 'known' compound and explore tweaked versions...

TREND

NEXT-GEN PSYCHEDELICS



While ‘first generation’ psychedelics like psilocybin and MDMA are showing great promise in addressing mental health conditions like depression and PTSD, they’re not necessarily the most optimal.

Companies are now looking to tweak known psychedelics to develop a ‘next generation’ of molecules that may have favorable safety, efficacy and efficiency profiles compared to the first generation of psychedelics under development.

Cynics might say that this is a purely patent-minded pursuit, with new chemical entities in a much better position to clear the standards of novelty and non-obviousness. Proponents, meanwhile, argue that these new chemical entities might provide better safety, efficacy and efficiency profiles.

Some of these next-generation psychedelics merely tweak their first-generation predecessors by adjusting a trip’s length or intensity, but others might remove the trip entirely…

TREND + TENSION

SKIPPING THE TRIP + EXPLORING NONHALLUCINOGENIC PSYCHEDELICS

A growing crop of researchers and companies are exploring next-generation psychedelics that claim to remove the ‘trip’ entirely, while maintaining therapeutic effects. Neuroplasticity is hypothesized as a mechanism that drives at least some part of psychedelics’ apparent therapeutic effects, leading some to describe their non-trippy drugs as psychoplastogens.

If they prove to be efficacious, these molecules may be more scalable, appropriate for certain patients and conditions (such as non-psychiatric ones), and in turn could be much easier to integrate into the prevailing medical system. But, this work is still in its early stages and some researchers are skeptical, arguing that the subjective effects of a psychedelic trip are integral to their apparent therapeutic benefits. Others argue that the ‘trip’ is the ‘whole point’ of psychedelics, opposing these so-called non-hallucinogenic psychedelics on a more fundamental or ethical level.

We should have data on their safety and efficacy in humans in the coming years, as certain ‘psychoplastogens’ enter human trials in the coming months.

These next-generation psychedelics, in particular, might be suited to conditions beyond neuropsychiatry…

TREND

LOOKING BEYOND NEUROPSYCHIATRIC INDICATIONS

While mental health conditions represented the beachhead for psychedelic research, investigators and sponsors are increasingly interested in ailments like neurodegenerative and pain-related disorders.

Early-stage research has shown promise for the potential of addressing headache and pain disorders with psychedelics, for example. More speculative research has suggested that employing psychedelics in the management of Parkinson's and traumatic brain injury is worthy of further exploration.

It is conceivable that low-dose or non-hallucinogenic psychedelics may be more suitable for these conditions, especially where they are to be taken chronically.

This excitement of (re-)exploring a whole class of drugs has led to plenty of excitement, and arguably a shotgun approach in which some companies overextended themselves…

TREND

SLIMMING DOWN DRUG DEVELOPMENT PIPELINES

Many psychedelics companies, especially public ones, are running out of cash as the macro and sector-specific economy chills. Investors are increasingly sensitive to this, especially given the long time to market for biotech (often around a decade).

Companies are now re-evaluating their pipeline programs and refocusing their bets. Sector leaders like atai Life Sciences and MindMed have scaled back some development efforts while doubling-down on lead candidates.

However, slimming down pipelines means shelving drugs that many believe have great potential.

This overexuberance has been tempered by the realization that many fundamental questions remain…

TENSION

QUESTIONS & METHODOLOGICAL ISSUES REMAIN

Despite great progress in evaluating the potential therapeutic benefits of psychedelic therapies, the manner in which these benefits manifest and are modulated remains something of a black box.

This lack of concrete understanding of psychedelics' mechanism of action, for example, has led to a number of schools of thought emerging, and they don't all see eye to eye. Perhaps the most obvious tension is between those who believe the subjective effects of a trip are necessary to the apparent benefits of psychedelics versus those who do not, alluded to above.

This shouldn't be an impediment to drug developers seeking and obtaining approvals for psychedelic therapeutics, as the FDA does not require mechanisms of action to be understood or proven. But, given that industry is largely driving the research agenda today, these fundamental questions about psychedelics' method(s) of action may remain unanswered for some time yet.

What's more, psychedelic trials are strewn with methodological complexities. For example, clinical trials are usually placebo-controlled, but how does one achieve meaningful placebo control when the effects of a psychedelic are so noticeable?

Other fundamental questions remain, such as the durability of psychedelics' therapeutic effects, the optimal dosing, whether 'microdosing' is anything more than a placebo, and many others.

The answers to these questions will inform payer's decisions about whether to cover psychedelic therapeutics...

TENSION + TREND

AN INCREASING FOCUS PAYER COVERAGE, COST-EFFECTIVENESS ASSESSMENTS

In order for any approved psychedelic therapies to reach a meaningful number of people, they must be covered by insurance companies and state healthcare providers.

Unfortunately, psychedelic therapies are significantly more expensive than the standard of care for many mental health illnesses, due primarily to the need for numerous preparatory, dosing, and integrative sessions with multiple facilitators.

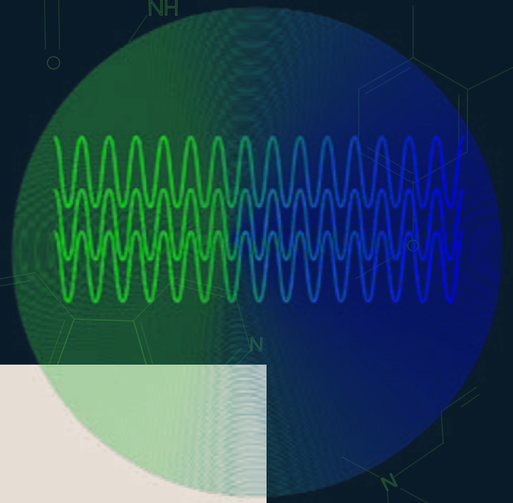
Demonstrating cost-effectiveness is a key hurdle for psychedelic drug developers to clear in order for their therapies to be accepted and covered by insurance payers. Janssen's esketamine nasal spray, Spravato, is not covered by the UK's National Health Service due to regulators' opinion that available data does not justify its cost. This should serve as a warning to psychedelic drug developers.

Today, there's a greater focus on the cost-benefit analysis of such treatments, with drug developers attentive to the health economics of their proposed therapeutics. Other drug developers are looking to make psychedelic therapies more amenable to conventional healthcare settings, such as by exploring shorter-acting drugs.

What's more, the current clinical evidence base for psychedelic therapies is quite short-term. Insurers will be interested in the durability of psychedelics' apparent therapeutic effects, which might be evidenced via data from outside the clinical trials realm...

TREND

AUGMENTING PSYCHEDELIC THERAPY WITH TECHNOLOGY



While the majority of funding is going to psychedelic drug discovery and development companies, digital technologies are becoming an increasingly popular segment for psychedelic investors.

Psychedelic-assisted therapy (PAT) is a labor-intensive process, with therapists administering tens of hours of therapy across the protocol. Companies are increasingly exploring whether digital tools may be used to help to reduce the labor costs associated with PATs while increasing convenience for patients.

Technology may be used to identify potential responders (and non-responders) to PAT; monitor patients during their sessions; monitor patients long-term to predict relapse; etc. Some of these applications are more speculative than others.

Some of these psychedelic technology startups have already been the subject of another trend...

TREND

HARNESSING REAL-WORLD DATA AND EVIDENCE

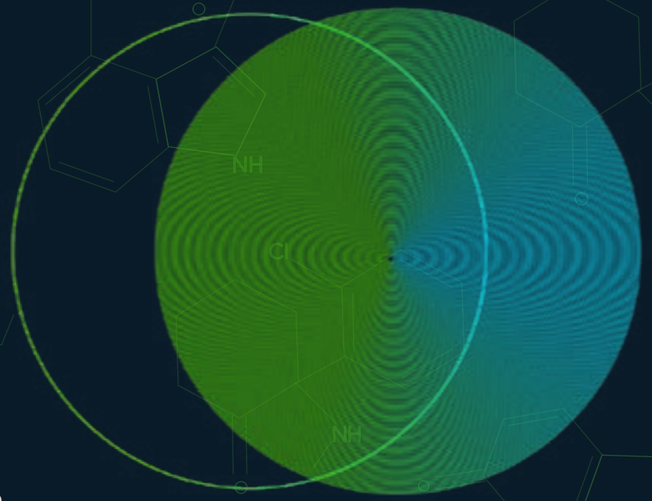
The amount of variables that can be modulated via clinical trials is limited, given that they're expensive and require some level of intra-trial consistency. They also provide a limited timeframe for evaluating psychedelics' effects, often just weeks or months, and involve carefully curated patient populations. These factors limit the inferences that can be made by payers and providers.

In the 'real world,' meanwhile, patient populations and protocol adherence are likely to be far more heterogeneous than in clinical trials, so payers and providers might be interested in seeing real-world, longer-term data on the safety and efficacy of psychedelic therapies.

The collection of real-world data and evidence may strengthen the health economics justification for covering a therapy, and may even provide naturalistic evidence of efficacy in an off-label condition. A growing number of psychedelic drug developers are exploring real-world evidence for these reasons. In fact, there are even psychedelic-specific real-world data and evidence startups, which provide solutions for psychedelic drug developers and practitioners.

Such data can be collected via electronic health records, consumer wearable devices, data relating to insurance claims, and other means.

Many real-world data and evidence collection and analysis solutions are part of the adjunct tech market/value chain segments...



TREND

INCREASED M&A AND LICENSING ON THE HORIZON

Larger psychedelics companies have cash on hand to weather the storm and potentially scoop up programs, trials and IP and development programs at a discount.

Companies like atai Life Sciences have scooped up a large portion of their pipeline through this process, funding drug development efforts and adjunct technology startups which then become atai platform programs and technologies, respectively. Another of the larger psychedelics companies, Cybin, acquired a Phase 1 study from its smaller peer, Entheon Biomedical, for just ~$1M, which it believes will propel it through the clinical trial process 9 months faster.

As more companies approach the end of their cash runways, we can expect to see even more shopping around of assets within the psychedelics sector.

That's to say nothing of conventional biotech and pharma companies...

TREND

SPECULATION AROUND BIG PHARMA'S INTEREST (OR LACK THEREOF)

Psychedelic therapies represent a significant break from the standard of care for mental health disorders, with the current pharmacopoeia largely resembling a subscription model characterized by the chronic administration of antidepressants, for example. Psychedelic-assisted psychotherapy's more interventional style could be incredibly disruptive to conventional pharma's business model.

Perhaps this is why 'big pharma' companies have been largely absent from the psychedelic renaissance. But, some incumbents have shown an interest.

Japan's Otsuka Pharmaceutical was an early investor in COMPASS Pathways (via its Series B), has partnered with atai-owned Perception Neuroscience to acquire exclusive rights to develop and commercialize its r-ketamine product in Japan, and is funding the early-stage development of one of Mindset Pharma's next-generation psychedelics.

If MAPS' MDMA-assisted therapy gains approval for PTSD, and COMPASS Pathways' psilocybin therapy for treatment-resistant depression shows promising results in its first Phase 3 trial, for example, we might see larger players view this as a de-risking and legitimization of the broader class of drugs in general.

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