INDUSTRY REPORT

HEALTHCARE SPECIAL SITUATIONS

Shroom Shmooz

Psychedelics and the Hype Cycle – Where Does It Go in 2024 and Beyond?

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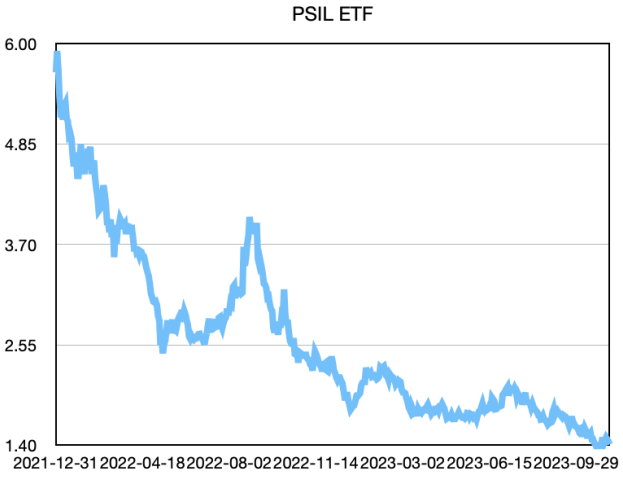
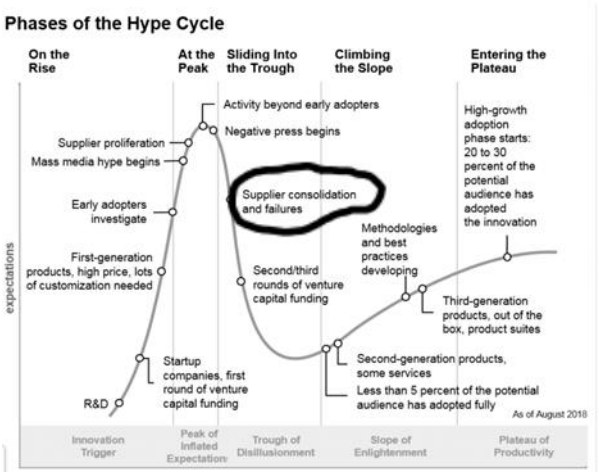
KEY POINTS

- **Psychedelic stocks continue their bad trip despite the psychedelic renaissance.** The headlines flowing out of the psychedelics sector over the past year indicate that the psychedelic renaissance appears to be gaining momentum. Clinical trials at various stages involving psychedelic substances, led by MDMA, psilocybin, ketamine, and DMT, have produced results showing clinical promise in a number of treatment-resistant mental health disorders. At the same time, the momentum toward legalization continues with high expectations that MDMA-AT will become the first Schedule I psychedelic substance to be legalized in the US for the treatment of PTSD in 2024. However, despite these tailwinds, public investors in the psychedelics space have endured negative returns over the last couple of years and shown little signs of reversal.
- **Too early for a public market in psychedelics?** The funding that is fueling the psychedelic renaissance has been largely driven by venture capital, which is not unusual for an emerging industry. VCs have parked more than $1.4 billion in private psychedelic startups since 2017. The buzz around psychedelics brought their early introduction to the public markets in 2020, with most companies seeking funds from a listing on a public exchange being drug development companies that are years away from generating revenue and profit. Following the initial albeit brief enthusiasm for the first round of psychedelic IPOs, hindsight indicates that the psychedelics' embrace of the public markets has been premature. The PSIL ETF, currently the only psychedelics ETF trading in the US, has lost 86% of its value since its launch in September 2021.
- **Psychedelics and the hype cycle.** From a public investor perspective, it's hard to argue against the fact that the past two years have been a slide toward the trough of the disillusionment part of the hype cycle. While all points to the big picture for psychedelics being positive, a deeper look shows that most publicly traded companies in the sector find themselves in financially precarious positions. We are seeing the beginning of a shakeout in the industry, which is not unusual for this part of the hype cycle.
- **Where does it go from here?** A continuing shakeout in the psychedelics sector and a likely significant shrinkage in the universe of publicly traded psychedelic companies are in the cards until the trough of disillusionment in the hype cycle is reached. Moving beyond the trough onto the recovery slope will require multiple triggers, including the advancement of more clinical trials through the approval process, the removal of bottlenecks (i.e., infrastructural and payor reimbursement) that threaten to slow the pace of the rollout of psychedelic-assisted therapies (PATs) once approved, starting with MDMA-AT for PTSD, the emergence of big pharma interest in psychedelics, and a possible MAPS IPO as it looks secure quick access to the substantial funds it will likely need for the rollout of its MDMA therapy once approved.

STATISTICS



Source: WTR



Source: Gartner

Reflecting on the Psychedelic Winter amid the Psychedelic Renaissance

Shunned for decades in a long-lasting backlash against the counterculture era of the 1960s and 1970s, the psychedelic renaissance appears to be in full swing. Interest in the therapeutic value of psychedelics in the treatment of a variety of mental health disorders has never been higher. While mental health disorders were all too common prior to the onset of COVID-19, it is the pandemic that has raised awareness of the severity of the human and economic costs of the mental health crisis. The positive consequence of the pandemic is that it has pushed mental health up the totem pole of healthcare priorities, resulting in unprecedented urgency to seek better solutions than are currently available. While yet to be legalized, the news flow from the psychedelics sector has been mostly positive, with significant momentum evident in key areas.

First, there has been an explosion of medical psychedelics research in recent years. According to the ClinicalTrials.gov database, there are currently 133 active clinical trials at the Phase II stage and three that are conducting or have completed Phase III studies. Many of these studies to date have produced positive outcomes for a variety of psychedelic substances targeting a number of treatment resistant mental health disorders, and none more so than MAPS' Phase III studies of its MDMA-AT candidate for treating PTSD, whose results were very impressive in terms of safety and efficacy.

Second, there has been a noticeable warming by regulators around the world toward psychedelics, particularly since 2017, that has accelerated since the advent of the COVID-19 pandemic. In the US, at the state level, Oregon and Colorado have decriminalized and legalized natural psilocybin, with other states and localities in the process of following suit. Although federally psychedelics remain Schedule I substances, the FDA did grant breakthrough status to MAPS' MDMA-AT in 2017 and a similar designation in 2018 to the ongoing work from COMPASS Pathways' investigations into psilocybin as a therapy for treatment-resistant depression (TRD), and then again in 2019 to Usona Institute's research into the therapeutic effects of psilocybin on major depressive disorder (MDD). Following the completion of MAPS' Phase III studies, which produced excellent results, there is high expectation that its MDMA-AT candidate for treating PTSD will be approved by the FDA by mid-2024. Outside of the US, Health Canada began to grant exemptions for using psilocybin in end-of-life care and research purposes in 2022, while Alberta became the first Canadian province to establish a regulatory framework to oversee psychedelic therapies. In 2023, Australia became the first country to reschedule selected psychedelics, psilocybin and MDMA, to allow psychiatrists to prescribe these substances to patients with depression or PTSD.

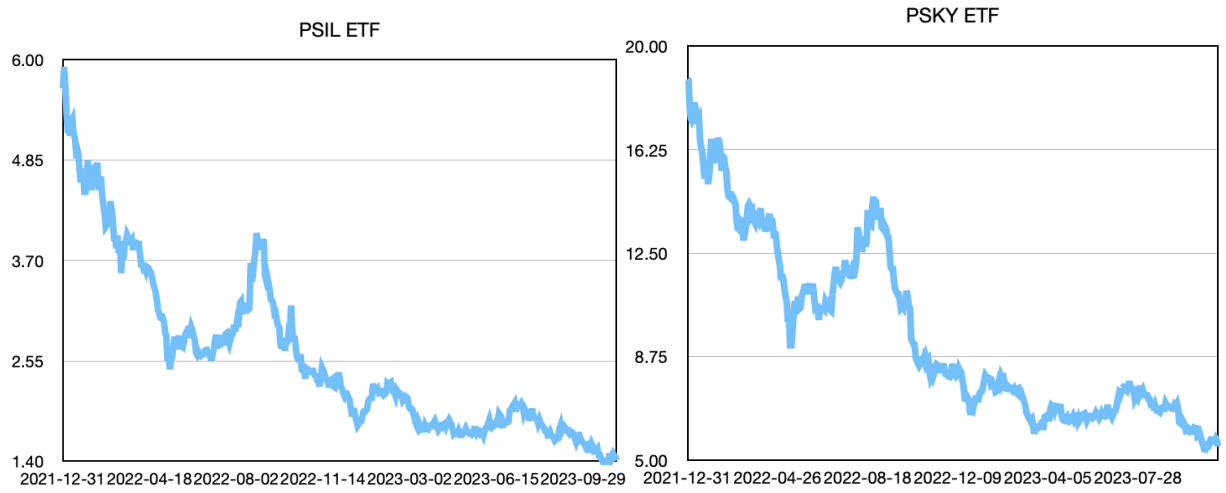
Third, there is tangible evidence of the growing acceptance of psychoactive substances as a viable option for more effective treatment of psychiatric disorders from the end-user, physicians, and payor community. In this respect, JNJ's S-ketamine-based Spravato, the first and currently only FDA-approved psychedelic-like treatment for a mental disorder (TRD) has seen explosive growth in uptake in recent quarters and is on pace to become a $1 billion-plus market in the not-too-distant future. Based on JNJ's 3Q23 quarterly print, the global Spravato market is running at $732 million in annual run-rate sales (of which the US accounts for $616 million) versus $400 million ($352 million in the US) recorded in the year-ago quarter. The FDA granted Spravato marketing authorization in 2019 and the company has seen a recent growth spurt in which Spravato sales have recorded Y/Y increases of more than 80% in each of the past three quarters, driven by ongoing launches, increased physician confidence in the treatment, and strong patient uptake supported by expanded access both in terms of available infrastructure (i.e., clinics) and payor reimbursement.

As we look forward to the expected legalization of MDMA in 2024 and other psychedelics, led by psilocybin, DMT and LSD are expected to follow suit over the next three to five years and progress toward more robust payor coverage giving broader-based accessibility to PATs. They took a major step forward with approval in May by the American Medical Association (AMA) for the assignment of the first-of-its kind current procedural terminology (CPT) code, an insurance billing code for long-form PAT.

Against the positive backdrop described above, it is little wonder that there is currently plenty of excitement and eager anticipation, at least in the real world of psychedelics. Indeed, in a major momentum statement reaffirming the psychedelic renaissance, MAPS' annual psychedelics science conference held in Denver in the summer attracted a record 12,000 attendees, made up predominantly of mental healthcare providers and practitioners.

However, for all these apparent psychedelics headline tailwinds, the past two years have represented very rough territory for public investors in the psychedelics space. This is starkly reflected in the performances of the AdvisorShares Psychedelics ETF (NYSEArca: PSIL), the only pure psychedelics-related ETF currently trading on a US exchange, which has lost more than 85% of its value since its listing in mid-September 2021, and Canada's Horizons Psychedelic Stock Index ETF (NEO: PSYK), the world's first ever psychedelics ETF, which has dropped by a similar degree since it was first listed on the NEO exchange (now Cboe) in January 2021. This has been coined as the *Psychedelic Stocks Winter,* which is showing no signs of abating, raising the question as to whether investors can make money in psychedelics.

Figure 1: PSIL and PSYK ETF Performances



Source: WTR

The Evolution of Investing in Psychedelics

The early funding for psychedelics research emanated from philanthropic gifts from private donors and nonprofit foundations. Nonprofits, such as MAPS, Usona Institute, and Heffter, did much of the heavy lifting in funding psychedelics research in the early days of the psychedelic renaissance whose green shoots started to sprout in the 1990s. However, it was not until 2017 that we started to see for-profit companies emerge in the psychedelics space. It was at that time, just six years ago, that VC funds began to consider psychedelics as a bona fide target for investment. According to data collated from Psychedelics Alpha, five private psychedelics companies raised an aggregate of ~$14 million in funding rounds in 2017. The momentum accelerated with the advent of the COVID-19 pandemic, with VC-backed funding sharply increasing to $643 million in 2021. Although there was a drop in funding in 2022 in line with the broader downturn in funding, last year's ~$336 million worth of financing rounds for private psychedelic startups was the second best on record after 2021.

Figure 2: Investment Flow in Private Psychedelic Startups

YEAR	SEED	SERIES A	SERIES B+	OTHER	TOTAL
2020	28,396,300	29,263,655	215,000,000	27,706,250	300,366,205
% PER ROUND	9%	10%	**72%**	9%	
2021	41,920,000	178,800,000	362,400,000	59,905,000	643,025,000
% PER ROUND	7%	28%	56%	9%	
2022	35,000,000	165,200,000	79,000,000	56,600,000	335,800,000
% PER ROUND	10%	**49%**	24%	17%	

Source: Psychedelics Alpha, New Fund Capital

While there are hundreds of private companies operating in the psychedelics sector, the buzz/hype around psychedelics was sufficient to encourage some psychedelic startups to seek a broader target audience to fund their research and development appetite by 2020. That was the year when psychedelics were introduced to the North American public markets for the first time, starting with a handful of companies via IPOs and reverse takeovers (RTOs). The flow of psychedelic companies seeking listings on the publicly traded markets increased in 2021. Our list incorporates 37 listed companies in North America. In total, there are more than 50 companies involved in psychedelics trading on North American exchanges, but our list only includes those companies whose focus is predominantly on psychedelics and whose market cap is at least $1 million. About 80% of the names on our list are companies involved in drug discovery and development.

The majority of listed psychedelics companies trade on the smaller exchanges, predominantly in Canada, such as the CSE or NEO, with many of them also trading on the OTC markets in the US. These marketplaces are typically characterized by limited liquidity and little institutional investor interest. Only 11 out of the 36 companies on the list are trading on the major exchanges, nine on the NASDAQ, one on the NYSE, and one on Canada's TSX.

Figure 3: Publicly Traded Psychedelics Companies in North America

Drug Discovery/Development	Mkt Cap, USD MN	Compound Manufacurers	Mkt Cap, USD MN	Treatment Clinics/Wellness Centers	Mkt Cap, USD MN
GH Research (NASDAQ: GHRS)	419	Red Light Holland (CSE: TRIP)	17	Numinus Wellness (TSX: NUMI)	26
Compass Pathways (NASDAQ: CMPS)	345	Optimi Health (CSE: OPTI)	11	Braxia Scientific (CSE: BRAX)	2
Atai Life Sciences (NASDAQ: ATAI)	201	Psyched wellness (CSE: PSYC)	9	Universal Ibogaine (TSXV: IBO)	2
Cybin (NYSE: CYBN)	163	Lucy Discovery Scientific (NASDAQ: LSDI)	4	Irwin Naturals (CSE: IWIN)	1
MindMed (NASDAQ: MNMD)	107	PsyBio Therapeutics (TSXV: PSYB)	1	**Aggregate**	**30**
Incannex Health (NASDAQ: IXHL)	71	**Aggregate**	**42**		
Seelos Therapeutics (NASDAQ: SEEL)	26				
Filament Health (NEO: FH)	18				
PharmaTher (CSE: PHRM)	10				
Revive Therapeutics (CSE: RVV)	8				
Core One Labs (CSE: COOL)	6				
Psyence Group (CSE: PSYG)	6				
Awakn Life Sciences (NEO: AWKN)	5				
Silo Pharma (OTC: SILO)	5				
Bright Minds Biosciences (NASDAQ: DRUG)	5				
Mydecine Innovations Group (CSE: MYCO)	5				
BetterLife Pharma (CSE: BETR)	5				
Enveric Biosciences (NASDAQ: ENVB)	4				
Tryp Therapeutics (CSE: TRYP)	3				
Nova Mentis Life Science (CSE: NOVA)	3				
Aion Therapeutics (CSE: AION)	3				
Lobe Sciences (CSE: LOBE)	3				
MindBio Therapeutics (CSE: MBIO)	2				
Clearmind Medicine (NASDAQ: CMND)	2				
PharmaDrug (CSE: PHRX)	2				
Nirvana Life Sciences (CSE: NIRV)	1				
Algernon Pharmaceuticals (CSE: AGN)	1				
Albert Labs (CSE: ABRT)	1				
Aggregate	**1,428**				

Source: WTR

There was undoubtedly an initial appetite by investors in selected high-profile psychedelic-related IPOs. UK-based psilocybin drug developer, Compass Pathways (NASDAQ: CMPS), became the first psychedelic company to go public on a major US exchange on September 18, 2020. Its upsized IPO both in terms of offering and price started at $17 and then more than tripled over the ensuing three months, valuing the company at $2.2 billion. Other psychedelic IPOs on the main exchanges were also well received early on, including Germany-based Atai Life Sciences' (NASDAQ: ATAI) upsized IPO, which started at $15 on June 18, 2021, and surged by one-third on its first couple of days of trading, valuing the company at more than $3 billion, and GH Research (NASDAQ: GHRS), which developed 5-MeO-DMT therapies for the treatment of patients with TRD, IPOed at $16 on June 25, 2021, rising 67% to a high of $26.85 in October 2021, valuing the company at $1.4 billion.

However, despite this initial albeit brief enthusiasm, hindsight clearly indicates that psychedelics' evidently premature embrace of the public markets has been a failed experiment. The majority of listed psychedelics companies have only made it to the smaller exchanges, predominantly in Canada, such as the CSE or NEO, with many of them also trading on the OTC markets in the US. These marketplaces are characterized by less regulation and limited liquidity, which attract little or no institutional investor interest, a recipe for fundraising challenges. Only 12 out of the 37 companies

in our list are trading on the major exchanges, nine on the NASDAQ, one on the NYSE, and one on Canada's TSX. For the most part, the valuations for those on the major boards are higher, but are all currently in small-cap territory, under $420 million. Most of the companies listed in Figure 3 are microcaps. It may therefore be no surprise to learn that retail investors dominate the shareholder base of psychedelic companies. We have seen one study (cf. Psychedelics Alpha) that suggests retail investors make up 69% of the publicly traded psychedelics shareholder base, which compares with ~17% of the biotech sector at large. The study compares the ownership characteristics of nine representative psychedelics stocks with those of nine pre-revenue biotech comps.

While this study involves a small universe of companies, given where most of the psychedelic stocks trade, it would not be surprising to see a high level of retail ownership in these companies. This is an important point as retail investors typically have a much shorter investment horizon than institutional investors or venture capitalists. We would add that there is somewhat of a divide between venture capitalists and public investors (mainly made up of retail investors) in the psychedelics space. Notably, private rounds for similar-stage non-public companies have generally received higher valuations of up to three times compared with the public ones. There has been little diminution in VC enthusiasm for the long-term evolution of psychedelics who are better prepared for the long game.

Institutional investor interest in publicly traded psychedelics has thus far been limited to the selected few. GH Research has the highest level of institutional ownership with 57%. While institutional investors are evidently underexposed to the sector, there are recent indications that some heavyweight institutional investors are beginning to show interest in the sector. In September 2023, Steve Cohen's Point72 hedge fund disclosed that it acquired an 8.1% in Cybin. Interestingly, this disclosure came after Cybin announced that it had agreed to acquire Small Pharma, marking an important consolidation in the emerging psychedelics sector.

Figure 4: Institutional Holdings in Publicly Traded Psychedelic Majors

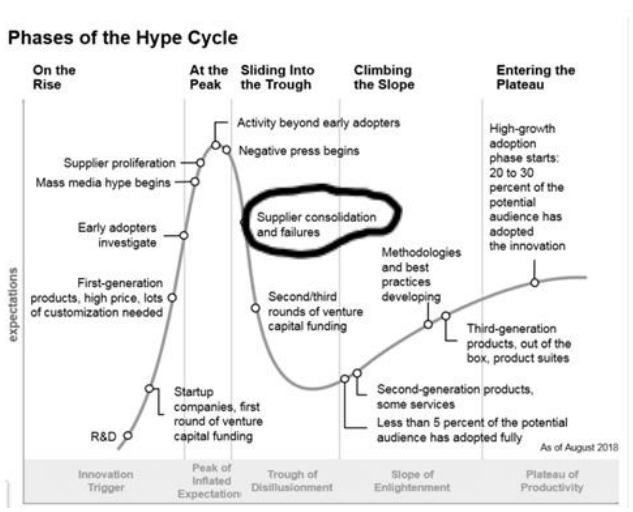
Company	Insider Holding %	Institutional % of Outstanding	Institutional % of Float	Lead Insitutional Investor
GHRS	40.4%	57.0%	95.8%	BVF Inc
CMPS	45.1%	16.1%	29.4%	Ark Investment
MNMD	4.7%	10.5%	11.2%	Alyeska Investment Group
ATAI	9.6%	9.8%	10.9%	Blackrock
CYBN	22.0%	9.5%	12.2%	Point72

Source: Company Filings, WTR

Psychedelics and the Hype Cycle

In the mid-1990s, management consulting firm Gartner developed a model to describe the adoption of new technologies, particularly the adoption life cycle of a new technology. Gartner called its model the hype cycle. Gartner developed the hype cycle model to provide one perspective of technology adoption and educate its clients about the promise of an emerging technology within the context of their industry and individual appetite for risk. Gartner's model has five key phases of an innovation's lifecycle illustrated in Figure 5. Gartner's model has since been applied to other types of innovations, across different sectors including life sciences. That's because the hype cycle is effectively a description of how humans respond to new things that we perceive to benefit us. The hype cycle hypothesis could be applied to the emerging psychedelics sector, even though it may lack a single trigger event, unlike classical technological innovations like the automobile or the internet that had clearly defined innovation triggers.

Figure 5: Gartner's Hype Cycle Model/ Psychedelic Invest Index



Source: Gartner

Source: Psychedelic Invest

The first stages of the hype cycle are the *innovation trigger leading* to the *peak of inflated expectations*. The trigger is anything that sets off a period of rapid development and growing interest. Venture capitalists are usually the first to be attracted to the initial ascent of the hype curve, and this has been the case in psychedelics as described above. For psychedelics, we could point to regulatory milestones seen to be pushing psychedelics along the pathway to decriminalization/legalization such as state-level legislation decriminalizing psychedelics and FDA-granted breakthrough status to some psychedelic drug research, the explosion in the scientific research of medicinal psychedelics and the momentum in investment going into funding the research, the advent of the pandemic that pushed mental health up the totem pole of healthcare priorities resulting in unprecedented urgency to seek alternative solutions to what is available, a longstanding history of use throughout human history, documented evidence of profound personal experiences these compounds potentiate and the rush of media interest that has helped to destigmatize and legitimize the use of psychedelics for therapeutic purposes. We would argue the hype began in 2017 and accelerated with the advent of COVID-19.

The peak of inflated expectations occurs when the expectations for the innovation/new solution rise above the current reality of the capabilities to execute. In psychedelics, this occurred in 2021, coincidentally with the peak of psychedelic financings (both private and public). At that time, most of the drug developers were still in the early stages of their clinical trials (and most still are). Although bolstered by encouraging early results, they were and are still years away from potential legalization and commercialization. On the client-facing side of psychedelics, there has been an exponential growth in ketamine clinics from about 300 at the time of Spravato's launch following its approval in 2019 to more than 2,700, but many of these clinics are struggling financially.

From a public investor perspective, it's hard to argue against the fact that the past two years have been a slide into the trough of the disillusionment part of the hype cycle. A deeper look shows that many companies in the sector are struggling financially despite the positive momentum in the sector's macro environment. Based on the latest financial statements, we have calculated that 19 (68%) out of the 28 psychedelic drug developers included in our list have cash runways of less than 12 months. The majority of these, 17, have cash runways of less than six months. Within our universe of drug developers, seven or one-quarter of the count can claim a cash runway of two years or better. These companies are predominantly at the higher end of the market cap range. Put simply, a significant portion of publicly traded psychedelic drug developers are in a precarious financial position. In this part of the hype cycle, it is not unusual to see a shakeout in the industry through bankruptcies or retrenchment and consolidation.

Shakeout in the Psychedelics Industry is Underway

Ironically, it is within the picks and shovels segment of the psychedelics sector (i.e., clinic networks) that financial troubles seem to be most prominent. This year has been marked by upheaval in that area, with some high-profile clinic network operators in retrenchment mode. Delic Corp's (OTC: DLCFF) Ketamine Wellness Centers, one of the largest ketamine networks in the US, announced that it was shuttering its entire network of 13 clinics due to a lack of funds. Around the same time, Field Trip, which had outlined grandiose expansion plans on its listing on the Canadian Securities Exchange in October 2020, closed five of its nine clinics, laid off most of its staff, and sought

protection from creditors under Canada's Companies Creditors Arrangement Act, before selling its clinics in the US and Canada to third parties resulting in the dissolution of the company. Another casualty in the ketamine clinics space is Irwin Naturals sector, whose expansion strategy with respect to ketamine clinics was set back when it abandoned its attempt to acquire Braxia Scientific (CSE: BRAX). The reason given was somewhat opaque, citing the absence of a clear business rationale to go ahead with the transaction. Subsequently, it was disclosed that Irwin, which received a $40 million credit facility in February 2023, received default notices from its lender resulting from a failure to meet certain covenants. While the lender is for now forbearing its rights related to those notices, if demand for repayment were to occur, Irwin has stated that it would not have the financial resources to repay such obligations.

While we have not yet seen a rush of bankruptcies in the psychedelics sector, that may simply be a question of time. As highlighted earlier in this report, many psychedelic drug developers are struggling for cash to fund their development programs. Their ability to continue to raise dilutive capital via equity offerings is at risk as industry share prices remain depressed. While some programs will be abandoned, as several prominent psychedelic companies have shelved programs to conserve cash, including MindMed (NASDAQ: MNMD), Atai Life Sciences (NASDAQ: ATAI) and Beckley Psytech, what we are seeing is that some of the distressed pipeline assets considered promising are being picked up by others. For example, financially challenged Entheon Biomedical (CSE: ENBI) sold its primary DMT Phase I program to Cybin (NYSE: CYBN) in a fire sale in 2022. This acquisition has helped accelerate Cybin's own DMT program targeting anxiety disorders (CBY004) by about nine months. The program is targeted to initiate a proof-of-concept Phase II study in 1Q24.

We have also been seeing full-scale M&A across the psychedelics space. In 2022, these deals included Beckley Psytech's purchase for an undisclosed value of Eleusis in the drug development space, and Numinus' $28 million acquisition of Novamind in the clinics space. M&A activity in the sector has moved up a notch in 2023.

In August, struggling Field Trip's psychedelics biotech division, *Reunion Neurosciences*, which was spun out as an independent publicly traded entity in August 2022, was acquired by MPM BioImpact for $13 million. MPM, a biotech-focused investment firm, is dedicated to "investing in breakthrough science and innovative products that can address the world's greatest unmet medical needs".

The buyout of Reunion was followed by the two largest acquisitions in the psychedelics sector to date. In late August, Cybin announced that it had entered into a definitive agreement to acquire UK-based Small Pharma for $50 million. The acquisition was completed in October creating the psychedelic industry's largest deuterated DMT-focused drug development program. As a result, Cybin now has five clinical DMT programs underway, out of the total of eight drugs in its pipeline. Moreover, this acquisition makes Cybin's IP portfolio the largest in the industry, with 28 patents granted and another 158 pending.

Just days after the Cybin/Small Pharma transaction announcement, Japanese global pharmaceutical company, Otsuka Pharmaceutical, announced that it had agreed to acquire Mindset Pharma for $59 million. While this acquisition, also completed in October, ostensibly marks the first relatively significant transaction by big pharma in the psychedelics space, it should be noted that Otsuka does have some history with psychedelics with one of its main focuses being the creation of new mental health treatments, and a history with Mindset. In 2022, Otsuka made a strategic investment to support the development of two families of Mindset's candidates through Phase I trials and provided Mindset with a $5 million upfront cash payment. Additionally, Otsuka has collaborated with Atai in the development of a ketamine candidate targeting depression. The other Otsuka link with psychedelics is that its Senior Managing Director of global pharmaceuticals, Kabir Nath, is currently the CEO of Compass Pathways.

In the biotech space at large, it is commonplace for big pharma, typically driven by a patent cliff and the prospect of a competition surge from generics to its established and highly lucrative established drugs, to acquire or enter into partnerships with clinical stage biotech companies that have successfully developed drug candidates through the initial clinical stages. Big pharma is usually willing to pay a hefty premium for such acquisitions to fill up its development pipeline in order to avoid the costs in terms of time and expense associated with discovery and early failed trials. Outside of Otsuka and arguably JNJ, which developed and commercialized Spravato, the first and only FDA-approved psychoactive drug to treat a mental health disorder, big pharma has largely been conspicuous by its absence in the psychedelics space.

What Next? Probably Too Early for Public Investors; Catalysts on the Horizon

Given the financial constraints described above and the plethora of small companies that dominate the biotech-heavy publicly traded psychedelics landscape, a continuing shakeout in the psychedelics sector and a likely significant shrinkage in the universe of publicly traded psychedelic companies are in the cards until the trough of disillusionment in the hype cycle is reached. Only those with robust IP will have the greatest prospects of survival. We expect venture capitalists will remain the main financial water carriers for the sector. It is probably too early for public investors without taking on significant risk and/or a long-term perspective. Psychedelic companies are unprofitable, and but for a few exceptions, remain years away from potential revenue generation let alone profitability.

Moving beyond the trough onto the recovery slope will, in our view, require multiple triggers including:

The advancement of more clinical trials through the approval process: Thus far, only MAPS has completed a Phase III trial of its MDMA-AT candidate for the treatment for which its two-part study produced very positive outcomes. MAPS has indicated that it is compiling data from 18 MAPS-sponsored Phase II and Phase III studies to form the basis of the New Drug Application, expected to be filed with the FDA later this year. Should that timeline be met, FDA approval for marketing could be granted around mid-2024.

There are currently two other programs set for Phase III trials: Compass Pathways' COMP360 psilocybin-based assisted therapy for TRD and Awakn Life Sciences' ketamine-assisted therapy candidate AWKN-P001 for the treatment of alcohol use disorder. Compass is currently recruiting for its Phase III trial comprising two pivotal studies (COMP005 and COMP006). Initial top-line data on COMP 005 is expected by mid-2024, with COMP 006 top-line data to follow in mid-2025. Both trials are said to be on track, which means COMP360 is unlikely to be available before 2026.

The AWKN-P001 Phase III trial is currently in the planning stage, with its first participant expected to be enrolled in 1Q24. While still in the very early stages, the company's forecast timeline for the trial to be completed is 2026, with trial results expected to be released in the first half of 2027, and possible FDA approval in the second half of 2027.

Both of these projects are still more than two years away from possible approval and commercialization, which for public market participants is a long waiting period with no guarantees of success along the way. There is, however, an encouraging backlog of more than 100 active Phase II trials involving a variety of psychedelics targeting multiple mental health disorders. The laws of probability suggest there could be rush of approvals and therapeutic psychedelics on the market on a four- to six-year time horizon.

Overcoming infrastructure bottlenecks: There is much anticipation for approval of MAPS' MDMA therapy for PTSD in 2024. But it's one thing for the therapy to be approved, it is quite another thing to make the treatment as accessible as possible to the many people who require it. Spravato's experience highlights the potential challenges to the rollout of MAPS' MDMA therapy. While Spravato has become a $730 million market and is on pace to become a blockbuster drug for JNJ, it has taken some four years since FDA approval for TRD in 2019 for it to start registering meaningful revenue. Spravato's belated growth spurt evident in recent quarters reflects the build out of clinic infrastructure since 2019.

Accommodating broad-based access to MDMA-AT is potentially more challenging than for Spravato given the more onerous protocols (longer treatment duration, more preparation time and integration support) involved and infrastructure (larger rooms, more therapists) required to administer the therapy. Many of the existing ketamine clinics simply do not have the necessary capabilities to administer a more complex treatment. One of the potential bottlenecks in the rollout of MDMA-AT, once approved, is the availability of trained administering practitioners. MAPS anticipates that for the PTSD market in North America, it would need as many as 50K trained therapists.

All eyes will be on how quickly MDMA-AT can be rolled out once approved. Once all of that infrastructure is put in place, those that potentially follow MAPS' MDMA rollout such as Compass' psilocybin therapy should have a much lighter lift in their rollouts.

Broader payor coverage: Another critical trigger is the expansion of payor reimbursement for PATs. These, at least initially, will not be inexpensive. Based on available information, ketamine-assisted therapy sessions can run from $200 to $1,500 per session. With patients usually requiring four to six sessions to complete a treatment cycle, the patient outlay could go up to $9K. It's no secret that traditional payors have been slow to embrace Spravato given its expense. MDMA-AT, which is expected to cost the patient up to $15K per treatment cycle, potentially faces the same challenge. The good news is that JNJ has alluded to the fact that payors are warming to reimbursing Spravato on the back of increased physician confidence and patient demand. However, where coverage is offered, it is typically contingent on some demonstration that standard-of-care mental health pathways (i.e., SSRIs) have been exhausted. There are other catalysts that could accelerate the development of more robust payor coverage such as the rise in self-funded employers (the largest payor segment in the US) many of whom have prioritized the mental health of

employees in the post-pandemic world, and the emergence of psychedelic-focused disruptors in the health insurance market, led by third-party benefits administrator Enthea. Moreover, an assigned CPT code effective from the start 2024 is a progressive step toward making reimbursement for PATs a more manageable process for physicians.

Emergence of big pharma interest: As we highlighted earlier, with a rare exception (Otsuka Pharmaceutical), big pharma has been reticent about targeting psychedelics as a pipeline fill opportunity. The legal framework for psychedelics, IP issues, and the protection of a lucrative SSRI market have been among the obstacles to big pharma participation. However, the genericization of most SSRIs, the expected commercialization of MDMA in 2024, and growing body of evidence of the safety and efficacy of psychedelics relative to SSRIs could well trigger a reassessment by big pharma of the psychedelics market. Given the long, expensive, and complex road of clinical trials with vulnerable patient populations, greater interest from big pharma in psychedelics just as it is in the broader biotech world will be a positive signal for investors.

MAPS IPO?: For the MAPS, MDMA-AT has been a more than 30-year clinical project, which is now on the cusp of commercialization. MAPS became a public benefit corporation in 2014 to help fund its clinical studies of MDMA-AT for the treatment of PTSD. For much of the three-decade period, MAPS has relied on philanthropic donations to fund its clinical studies. MAPS donors have given about $140 million in gifts and grants throughout its history. As the clinical trial process entered its final stages, MAPS' research and administrative expenses soared and in 2022 MAPS sourced its first non-philanthropic funding of $70 million in a collaboration agreement with VC Vine Ventures by agreeing to a limited-term revenue share arrangement (6.1% of North America MDMA revenue for eight years of initial drug sales on commercialization of MDMA). It was reported that MAPS considered and rejected the idea of an IPO early this year in part to ensure new shareholders' interests would be aligned with those of the nonprofit. Instead, MAPS chose to go down the Series A financing route raising $215 million through a private share sale to investors with conditions aligned with its principles.

However, there will be significant costs ahead for MAPS once its MDMA-AT candidate for PTSD is granted marketing authorization by the FDA. Commercialization of most mass-market pharmaceuticals typically costs $500 million to $1 billion. MAPS will in all probability need to raise significant additional funds to support the rollout of its therapy in North America, expansion into international markets, and getting approvals for use of the therapy to treat additional mental health indications. Despite its reluctance to the idea of an IPO thus far, an IPO would give MAPS quick access to capital. We suspect that once MDMA is approved, it would be well received by traditional biotech/biopharma investors. A MAPS IPO would very likely be the largest to date in the psychedelics sector and a major boost to the publicly traded psychedelics market. Alternatively, MAPS post FDA MDMA approval might be a sufficient carrot for a big pharma company to get its feet wet in psychedelics.

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Robert Sassoon has been an equity analyst for more than three decades, focusing primarily on global special situations. During his career, Robert has worked for several sell-side institutions in London, Hong Kong, and New York, including Credit Suisse, NatWest Capital Markets, and Societe Generale. In 2017, Robert founded AlphaSituations, an independent idea-generating event driven/special situations investment research service, which produced comprehensive research on early stage/emerging publicly traded and privately owned companies with the goal of telling an underappreciated or unknown story to relevant investors.

Robert has developed a uniquely broad and deep knowledge base in multiple industries from a global perspective and has achieved top five rankings in various analyst surveys, including the Extel and Greenwich surveys. Robert holds an MSc in Economics from the London School of Economics and Political Science, and has held FINRA licenses Series 7, 63, 86, 87, and 24.

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