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PSYCHEDELICS TO LEAD MENTAL HEALTH RENNAISANCE?

A BRIEF HISTORY

Psychedelics have a long history. Indigenous peoples have utilised these substances for millennia, and even Silicon Valley has had its own flirtation with them: tech pioneers like Steve Jobs openly extolled the creative impacts of these mind-altering substances. Many of these individuals went on to achieve some of the greatest feats of modern technology. By 1960, numerous psychedelics were in fact proven clinically as non-addictive, possessing remarkable safety profiles, and potentially able to treat several psychiatric conditions[1].

Yet, despite such a rich and promising past, Nixon's post-sixties war on drugs drew the curtains closed on an era of openness to psychedelics. It saw the end to not only the legality of these drugs amongst countryside raves, but also to a blossoming area of biopharmaceutical research. The ensuing "moral panic" swiftly clouded many drugs within the category, such as LSD, MDMA, Ketamine and Psilocybin (the active compound in "Magic Mushrooms"), all of which were severely criminalised in 1966.

The panic was further fueled by a cacophony of political reporting. In May 1967, Californian newspapers reported on an 'LSD horror-story' involving students who, after a midday 'trip', allegedly started into the sun until it rendered them blind. Similarly, the tale of the 'orange juice man'- who supposedly believed he had become a glass of juice following excessive LSD use became a similarly ubiquitous tale[2]. These stories are emblematic of psychedelic scarelore which, although debunked as hoaxes, nonetheless shaped the conventional narrative around psychedelics for over 60 years, largely eclipsing the significant therapeutic potential these substances hold.

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[1] Sproul, C. (2021) **Explaining the Criminalisation of Psychedelic Drugs**
[2] Mikkelson D (2022) **Fact Check: Did Man Who Used LSD Believe Himself To Be a Glass of Orange Juice?**

However, changing moral attitudes along with recent clinical progress is shifting social perceptions of psychedelics, in a more liberal direction. Such developments could prove crucial for the billion people battling the global mental health crisis that exists today.

RESEARCH LANDSCAPE

Psychedelics, thought to alter brain neuroplasticity, offer a novel approach to treatment.[3] Compounds such as LSD and Psilocybin can be taken as singular high doses, inducing profound and incomprehensible perceptual changes, or rather in 'subperceptual' micro-doses. Despite being illegal, the latter method has recently become common-practice among many Silicon Valley leaders, perhaps hoping to follow in Jobs' footsteps.

While micro-dosing is unfortunately a mixed bag as far as clinical trials are going, contemporary research is, however, increasingly positive on the benefits of higher-dose sessions, which can unlock parts of the mind otherwise unobvious or inaccessible. These induced states often bring about strong emotional release, cathartic insights, and transformational personal (and transpersonal) experience.[4]

A recent psilocybin study at Harvard's John Hopkins School of Medicine revealed that 30% of its participants ranked their psilocybin experience as the single most spiritual of their entire lives. By contrast, an Australian study in the British Medical Journal highlighted the relatively underwhelming impacts of antidepressants which currently line the market: a prescription of exercise alone managed to outperform these conventional drugs to treat depression, which casts a stark light on the reality of current pharmacological treatments, and their inadequacies.

Other trials have also demonstrated the profound impact that high-dose psychedelic experiences can have in transforming the lives of those with conditions such as trauma, depression, anxiety, anorexia nervosa, OCD, alcoholism, and several more. Research at Imperial College London suggests that a single high-dose psychedelic treatment could rival traditional antidepressants, offering faster and more substantial relief, with fewer side effects.

Their most recent study, involving 59 people with moderate-to-severe depression, compared two doses of psilocybin therapy to 43 doses of one of the best performing SSRI antidepressants on the market. Whilst measures of depression were reduced in both categories, remission rates were twice as high in the psilocybin group than those of the conventional antidepressant. Depression reductions also occurred far more quickly in the psilocybin group, and of greater magnitude.[5]

These findings, now published in the **New England Journal of Medicine**, help start to contextualise the potential promise of psychedelics as profound mental-health treatments.

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[3] Huberman, A. (2023) **Psychedelics for Mental Health**
[4] Pollen, M. (2018) **How to Change Your Mind**
[5] O'Hare, R. (2021) **Magic Mushroom Compound Performs As Well As Antidepressant in Small Studies**

These could prove vital for transporting people away from chronic pharmacotherapy, and towards solutions which are empowering and more focused on addressing the root causes of psychological issues.

"Independent research teams and studies are converging on the power of certain kinds of experience, yes with subjective rating scales, but able to predict therapeutic outcomes pretty strongly and very reliably"
Dr. Robin Carhart-Harris

INVESTMENT PROFILE

The emergent psychedelics industry, with over 50 companies now public in the US alone, boasts a combined valuation exceeding $2bn. Some analysts project this to swell to as high as $12 billion by 2030, implying a sectoral compound annual growth rate of over 12%. Nonetheless, this is a market fraught with volatility: pre-revenue biotech companies face high regulatory hurdles, outlandish burn rates, and the scrutiny of a sceptical public culture.

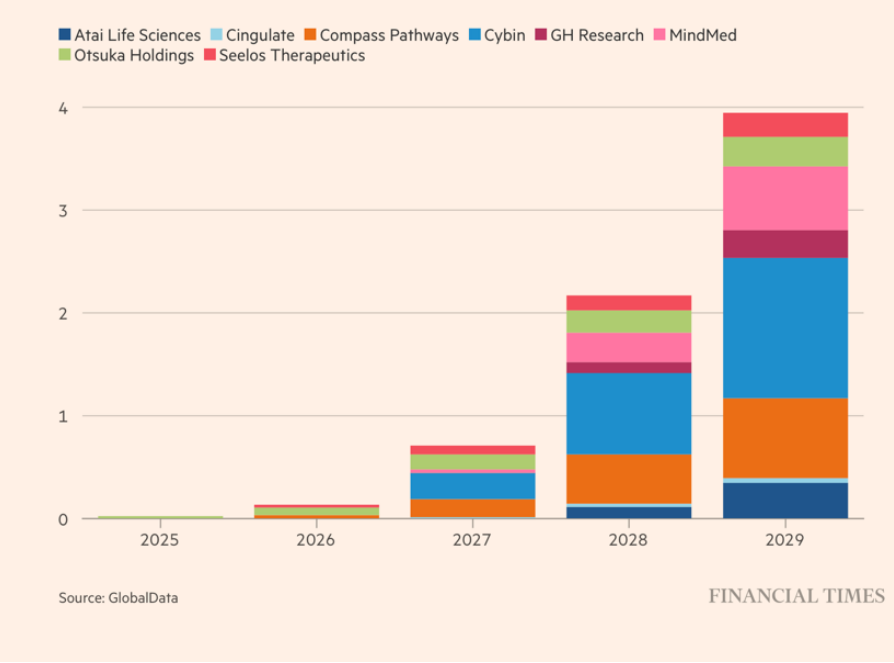

Figure 1: *Annual Projected Revenues for Psychedelic Companies in $bn (2025-2029)*[6]

Mind Medicine is one of the industry's frontrunners, hoping to deliver on the therapeutic potential of psychedelics. It's MM120 (LSD) psychiatry programme is furthest down the pipeline, recently concluding its phase 2B study in March with resounding success in treating patients with Generalised Anxiety Disorder (GAD): The study showed a 65% clinical response rate and a 48% clinical remission rate, both of which sustained until the study's end.

[6] Kinder, T. (2024) **Investors Pile into Psychedelic Drug Start-ups Tackling Mental Health**

Despite competition from drugs already commercialised, such as Johnson & Johnson's ketamine nasal spray 'Spravato' (also treating GAD), MM120 has showcased its potential to deliver superior outcomes and with far fewer patient side effects.

The immense success of the programme so far even led to the FDA's granting of breakthrough therapy designation for MM120, which could accelerate its path to market. The company expects to initiate phase 3 clinical trials towards the year-end. With a market-cap of around $500m, Mind Med ($6.23) has seen its stock surge 72.10% year-to-date, although it remains over 55% down from its April peak of $11.75, following its initial clinical success with MM120. This downward trajectory appears to be in-line with industry-wide trends, as the space lacks regulatory momentum, interest rates remain high, and drug commercialisation appears some time away still.

Another key player is **Atai Life Sciences,** backed by formidable billionaire angel investor Peter Thiel. Headquartered in Berlin, the biotechnology start-up is valued at $211.77m. Atai not only possesses its own intriguing pipeline of psychedelics, but has also been making a series of strategic investments in other psychedelic ventures, most notably the London-based **Compass Pathways**, holding an equity stake of 20.8%. More recently, it invested in private venture 'Beckley Psytech' in the hope to accelerate the clinical development of short-duration psychedelics. These investments perhaps reinforce Atai's position as the biotech with the largest and most diverse portfolio of psychedelic candidates across the space.

Both Atai and Compass are leading research into psychedelic compounds targeting truly severe psychiatric conditions, such as treatment-resistant depression, post-traumatic stress disorder (PTSD), and Schizophrenia. While phase 2 trial data is still forthcoming for Atai, Compass' psilocybin derivative 'COMP360' recently showed promising results in an open-label phase 2 study to treat PTSD, finding 'early and lasting improvements in symptoms' which could provide substantial improvement to patient daily function and quality of life.

Yet despite glimmers of optimism, the sector's setbacks have no doubt suppressed the growth of these stocks. Atai is down over 60% over the last 12 months, and a recent lay-off affecting 30% of its workforce to reduce its burn rate has only further dampened investor sentiment. With $273m in cash and equivalents, management projects a runway until mid-2026, and with access to a term-loan facility worth $160m, it will likely survive until then.

Compass, too, remains rather stagnant. Similarly positioned with a robust $228.6m cash position, it is up slightly from its year-end 2023, albeit recently missing Q2 analyst expectations with EPS -$0.56. Research & Development expenses rose to $29.1m up from $19.8m in Q2 of 2023, largely due to the ongoing phase 3 clinical trials for COMP360. General & Administrative expenses also rose, due to increased headcount.

Until drug commercialisation, Atai (and its close compatriots) will likely continue to issue stock offerings to raise additional funds, which would only dilute existing shareholder value

further. That said, some Wall Street analysts have eye-popping price targets for Atai, with some projections exceeding gains of 500%+ by the year's end.

While the only certainty that these stocks face is unfathomable volatility, this comes in hand with equally incredible opportunity. Many of these psychedelic companies are likely on the frontier of an exciting new frontier within biotech, holding the potential to redefine the psychiatric pharmacology which has all too long dominated the mental-health space, with its resoundingly average impacts for patient quality of life.

Stock performance will likely hinge on success levels in upcoming trials as they progress to later stages, FDA decriminalisation of these substances for medical treatment use, and the speed and ability with which treatments can even be commercialised viably.

This is certainly no safe bet. But, for those with a higher risk tolerance, I would argue that the current market landscape may present a compelling case for investing in this nascent industry. Coupled with the promise of converging international data and yet overwhelming fear and uncertainty, these stocks may be trading at significant discounts to the premiums they would likely demand with a more favourable macro environment. The potential rewards, both financially AND in terms of global mental health impact, could be truly life-changing.