

VIEWPOINT

The Rapid Rise in Investment in Psychedelics— Cart Before the Horse

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jamapsychiatry.com

Anticipating a renaissance, many psychedelic medicine companies have conducted initial public offerings, wherein private companies first issue new shares of stock for sale to the public, making the companies publicly traded entities.¹ As of this writing, there are more than 50 publicly traded companies related to the development or administration of psychedeliclike drugs in the US, with at least 3 valued at more than \$1 billion. The market for psychedelic substances is projected to grow from \$2 billion in 2020 to \$10.75 billion by 2027, a growth rate that may even outpace the legal US cannabis market.²

In the **Table**, we summarize the largest publicly traded psychedelic companies, all of which filed their initial public offerings in 2020 or 2021.^{4,5} In this Viewpoint, we examined key issues to better understand whether this wave of industry-sponsored drug development is being conducted in a manner that can reliably assess the effectiveness of psychedelic drugs.

How Did We Get Here?

The resurgence of interest in psychedelic medicine has been fueled by the popular desire for access and by commercial investment in the hope that psychedelics will be the next blockbuster class of medications. This trend has extended to policy and legislation. Efforts to decriminalize psychedelic substances at the local level have succeeded in Denver, Colorado; Washington, DC; Oakland, California; and other locations. Oregon passed legislation that legalizes access to psilocybin for mental health treatment despite insufficient evidence to support this practice. These regulatory changes may adversely affect the quality and rigor of biomedical research that are usually associated with the development of a new class of drugs.

Several factors attest to this concern. To our knowledge, there is very little research in psychedelics supported by the National Institutes of Mental Health (NIMH) or major pharmaceutical or biotechnology companies, and the pharmaceutical industry has, in many cases, been decreasing or even withdrawing funding from psychotropic research in recent years.⁶ At the same time, interest has been spurred by an expanding body of research demonstrating promising results for psychedeliclike drugs in a range of conditions, including end-of-life anxiety, treatment-refractory depression, post-traumatic stress disorder, and substance use disorder.⁷ In 2018, the US Food and Drug Administration designated psilocybin a breakthrough therapy, after which the pharmaceutical company COMPASS Pathways PLC began phase 2B clinical trials evaluating use of the substance for treatment-refractory depression.⁸ This commercial momentum, coupled with the lack of activity on the part of established pharmaceutical firms, created

a gap in the market now eagerly being filled by a cadre of entrepreneurs promising new, effective treatments for an array of mental health concerns.

Reliance on Intellectual Property

For-profit psychedelic companies are under pressure to generate large financial returns to their investors, and the most straightforward path to doing so is by obtaining patents for unique substances or delivery systems. Psilocybin, mescaline, and dimethyltryptamine are all naturally occurring compounds; therefore, they cannot be patented. To generate patents, these firms strive to generate a unique angle in their treatment paradigm, such as a unique indication, delivery platform (eg, sublingual, aerosolized, oral dissolving tablet), proprietary synthetic compound (eg, COMP360, COMPASS Pathway's proprietary psilocybin), or combination drug (eg, Mind Medicine Inc's 3,4-methylenedioxymethamphetamine [MDMA]-lysergic acid diethylamide [LSD] combination medication). This approach will help for-profit companies satisfy investors, but it will simultaneously limit the generalizability of any clinical outcomes discovered.

The Role of Academic Medical Centers

As the activities undertaken by these companies expand, we must acknowledge that their influence will only increase. These companies are so large that they are funding their own research, which is often conducted at academic medical centers. This is effectively a new iteration of industry-sponsored research, which could introduce bias at the earliest stages of study development, including even influencing the questions that are asked and answered in a given trial.

That said, academic medical centers are not in a position to conduct fully independent research. Funding from private foundations is orders of magnitude less than that available for this sort of industry-sponsored research. For example, the Johns Hopkins Center for Psychedelic and Consciousness Research was started with roughly \$17 million in private funding, whereas the market cap for ATAI Life Sciences is currently around \$1.9 billion.³

These effects have been exacerbated by the lack of investment in this area on the part of the NIMH, and the NIMH has not proactively initiated the research needed to establish the requisite body of knowledge regarding the mechanisms of action and clinical effectiveness of this unique and potentially valuable class of drugs. This contrasts with the extensive research conducted on cannabis and the numerous ketamine studies sponsored by leading federal agencies, including the NIMH.

Table. Largest Public Psychedelic Drug Companies by Market Capitalization^{a,b}

Company	Market cap	Business model	Medications
ATAI Life Sciences, Berlin, Germany	\$1.9 Billion as of November 2021	Decentralized hub-and-spoke model, an incubator for platform companies, providing access to the infrastructure at ATAI Life Sciences with frequent retention of equity by original founder	R-ketamine, ibogaine, etifoxine, N-acetylcysteine, DMT, and more in pipeline
COMPASS Pathways, London, UK	\$1.3 Billion as of November 2021	Developing psilocybin therapy through late-stage clinical trials in Europe and North America for people with treatment-resistant depression; also engaged in therapist training	COMP360 (proprietary, synthetic, high-purity psilocybin)
GH Research, Dublin, Ireland	\$1.3 Billion as of November 2021	Clinical-stage biopharmaceutical company developing proprietary DMT derivative compounds for treatment-resistant depression	5-MeO-DMT (proprietary inhalable and proprietary injectable formulations)
Mind Medicine Inc, New York, New York, US	\$924 Million as of November 2021	Research and development of pharmaceuticals that are experiential therapies or psychedelic-inspired medications	Psilocybin, LSD, MDMA, DMT, 18-MC (ibogaine derivative)
Cybin, Toronto, Ontario, Canada	\$278 Million as of November 2021	Development of novel proprietary compounds derived from psilocybin, DMT, and ketamine	Sublingual psilocybin (CYB001), deuterated tryptamine ODT formulation (based on Zydys [olanzapine] as drug delivery platform) and inhalable formulation
Field Trip Health, Toronto, Ontario, Canada	\$253 Million as of November 2021	Providing psychedelic and ketamine-assisted psychotherapy onsite, and pipeline development of FT-104, a synthetic 5HT _{2A} receptor agonist	Ketamine (sublingual in Canada, intramuscular in US), FT-104 (high-potency psilocybinlike substance)

Abbreviations: DMT, *N*-dimethyltryptamine; LSD, lysergic acid diethylamide; MDMA, 3,4-methylenedioxymethamphetamine; ODT, oral dissolving tablet; 5HT_{2A}, 5-hydroxy-tryptamine 2A; 5-MeO-DMT, 5-methoxy-*N,N*-dimethyltryptamine; 18-MC, 18-methoxycoronaridine.

^a Publicly available financial data including market capitalizations for each

company taken from Yahoo! Finance.³ Information on business models and medications under development taken from individual company websites.

^b Market capitalization is determined mathematically as the price per share of a company's stock multiplied by the number of shares outstanding.

Conclusions

Although popular excitement, policy momentum, and financial investment in psychedelics continue to increase, it is imperative that research maintains scientific rigor and dispassion to outcomes in the pursuit of improved therapeutics and new insights into the mind, brain, and consciousness that this class of molecules may well afford in the coming years. The presence of large-scale, newly established public companies as an unprecedented category of stakeholder may help to further understanding of these molecules and their possible clinical applications, but these firms also have a unique set of self-interests that must be understood and considered. Re-

search enabled by these firms must still meet the same rigorous standards that are expected elsewhere, even if breakthrough status is warranted.

There may be tension between avid advocates of this class of compounds and the deliberately slower pace of adoption encouraged by the scientific method, but rigorous research is necessary to more fully understand the risks and benefits involved in any presumptive clinical application. The first wave of psychedelic research was disrupted by conflict between cultural and political forces. The current wave of psychedelic research could be susceptible to an emerging conflict between entrepreneurial enthusiasm and scientific deliberation.

ARTICLE INFORMATION

Published Online: January 19, 2022.

doi:10.1001/jamapsychiatry.2021.3972

Conflict of Interest Disclosures: Dr Shah reported equity and consulting fees from his role as cofounder of Mantra Health and equity from Two Chairs Clinic, Groupwell, Tempest, and Legion Health. No other disclosures were reported.

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