

## PSYCHEDELICS

May 2021

### EXECUTIVE SUMMARY

Psychedelics has seen huge increase in investment focus in the last few years, but for many it remains a misunderstood, much maligned, and extremely niche sector. Here we seek to give you its history, research - past and present, who are the companies involved – established and start-up – big and small – public and private, and who the big investors in this sector are.

Investors are now actively investing in psychedelic medicine. Recent reports indicate that the global market for functional mushrooms, is forecasted to reach \$34.3 billion by 2024 and continues growing at a respectable CAGR of 8%.<sup>1</sup>

Unlike cannabis, which remains federally illegal in the U.S., the work psychedelic companies are doing is legal. This creates a greater opportunity to access growth capital from private investors who may not want to touch cannabis. It also sets the industry apart with it also being a more concentrated space because the barriers to entry are much higher.<sup>2</sup> The U.S. Food and Drug Administration (USFDA) status on the use of psychedelics appears to be quickly evolving, following the breakthrough therapy status for treatment-resistant depression in 2020 which appears poised to receive approvals in 2021. Back in December 2019, a ketamine-like drug – esketamine – was licenced for use in the UK as a rapid onset treatment for major depression, and in December 2020, regulators approved UK's Small Pharma to conduct the world's first clinical trial to explore DMT as a treatment for depression.

With mental health becoming a global problem – which has only been exasperated by the COVID pandemic – there is real urgency to find alternative and new treatments. Untreated mental health problems account for 13% of the total global burden of disease. Currently more than 300 million people suffer from depression worldwide, and around 800,000 people commit suicide every year. Of that 300 million – more than a third of people suffer from treatment-resistant depression, meaning they do not respond to at least 2 or 3 currently available therapies and treatments. In addition, addictions are on the increase and two years ago the NHS reported that 10% of inpatients in hospital were alcohol dependant.

A huge part of this crisis is because currently available treatments have not changed since 1980s and we still don't actually have a cure for any of these mental health problems. Without new drugs and treatments, it is projected that, by 2030, mental health problems (particularly depression) will be the leading cause of mortality and morbidity globally.

However, there is some encouraging news on treatments with numerous clinical trials underway around the world and psychedelic medicines already showing positive results in their Phase II and III trials. Finally, there could be a new approach to treating this growing issue.

There is still some catching up around the world to do – in the most part from drug regulators – where urgent reviews and new evaluations and categorisations of psychedelic chemicals are needed. A campaign to educate and bring awareness of the positive aspects of psychedelics as a credible treatment is also needed. If there are good results, we do not want to have populations who are reluctant to take that treatment due to out of date and misinformed views.

<sup>1</sup> <https://www.globenewswire.com/news-release/2020/11/26/2134221/0/en/Pure-Extracts-Advances-Plans-for-the-Processing-of-Functional-Mushroom-Formulations.html>

<sup>2</sup> <https://www.bloomberg.com/news/articles/2020-02-11/move-over-pot-psychedelic-companies-are-about-to-go-public>

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## INTRODUCTION

Psychedelics originates from the Greek *psyche* (soul) and *delein* (to manifest) which literally means mind manifesting. This term is in reference to their ability to alter the consciousness, inducing perpetual distortions as part of an organic experience. When regulated and guided under psychotherapy these experiences can be used as a tool to revolutionize the treatment of mental illness. Despite the reality that psychedelics are currently our only hope in tackling particular mental illnesses, their history and subsequent tarnished reputation gives rise to a multitude of opinions, preconceptions, confusion and acuties that have hindered their medical development for over fifty years. However, this is changing, and the psychedelic renaissance is well under way. This report will try to deepen your understanding of these useful and safe medical treatments, the potential for their future and how you can be involved in this new booming industry.

These psychoactive experiences and drugs have been a loyal partner in our communal and spiritual evolution from the beginning of man, through western and eastern development: a practise which still takes place in the Amazon to this day. Entheogenic transpired to synthetic in the early 1940s, with research actualising the potential these drugs have by continuing centuries of ancient history with modern science to create a new medication treatment. This was all tragically halted in the 1970s due to psychedelics leaking into recreational use, subsequently being caught in political and spiritual agendas, eventually triggering a 'War on Drugs'. Thereafter Governments moved to make all psychedelics illegal and held within the highest restriction levels and therefore halting scientific exploration entirely.

If it was not for underground academic research and scientific activism, psychedelics may never have been successfully reintroduced to meet their medical potential. Public figures like American scientific journalist Michael Pollan have opened conversations to change stigma and public opinion slowly inducing a backlash on the regulatory restrictions on psychedelics. Now we are at the precipice of psychedelic acceptance from governments and public health authorities alike which is creating tangible opportunities for the investment community to participate in the developing of a true growth industry. This could not have come sooner as mental illness is a crisis that is getting out of control. By 2030 global mental health costs are expected to increase to \$6 trillion with depression growing to be the biggest global disease burden.

The current global pandemic has brought England's suicide rate to historic highs, levels not seen since World War II.<sup>3</sup> This increasing pressure and rapidly rising problem is driving the pressure on the world's regulators to look again at the psychedelic research. The current approach to mental health is arguably not working, having barely changed since the 1980s it is also extremely costly. The world has taken note and so has legislation. Thus, it is looking likely that "This paradigm-shift in the treatment of mental health disorders could be the single best thing to come out of 2020."<sup>4</sup>

The room for growth within this new sector is large, from digital therapeutics, drug development and clinical psychotherapy. Canada has capitalized on the diversity of different ventures with most of the publicly traded companies listed on their exchanges, but the US is catching up and start-ups are seeking to fill the gap in the market. Despite there being fewer European based companies, the ones there have been established for longer with clinical trials in Phase II and soon Phase III. For example, Compass Pathway, a UK biotech company is engaged in Phase IIb clinical trials to show efficacy of their patented synthetic Psilocybin, regarding treatment-resistant depression. Compass Pathway is the first pure play psychedelics company to go public on a major American exchange. On the first day of trading the share price jumped 71% from an open of \$17 to a close of \$29 and the company was able to raise \$127 million to accelerate the efforts in bringing their drug to market. Compass Pathway's 34 million outstanding shares are now valued at almost \$1.5 billion.

Psychedelics are here to stay and will be a part of our future but, as Dr. Srinivas Rao, Chief Scientific Officer of ATAI Life Sciences, in his closing statements at the Mapping the Mind conference in 2019 stated, "Ultimately,

<sup>3</sup> <https://medicalxpress.com/news/2020-08-pandemic-effect-suicide-heightens.html>

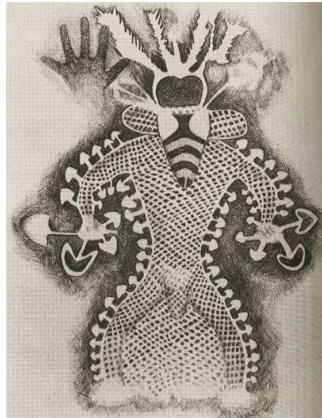
<sup>4</sup> <https://ca.finance.yahoo.com/news/trends-psychedelic-drugs-research-four-110000314.html>

getting psychedelics to patients will take capital, strategy, and creative thinking, particularly regarding the clinical and reimbursement models. However, the benefits to the patient are likely to be enormous.”<sup>5</sup>

## THE HISTORY OF PSYCHEDELICS

### ANCIENT ORIGINS

Archaeologists have provided fossil evidence showing that humans have used psychoactive plants for 10,000 years, playing a part in ritual ceremonies throughout the development of civilisation and society.<sup>6</sup> Cave paintings from Algeria 4713 B.C. even depict images of psychoactive mushrooms.<sup>7</sup> Professor David Nutt, leading neuropsychopharmacologist, argues “There are three things that define humans; one is drug-taking, the others are language and culture”<sup>8</sup> and some scholars even claim they played a part in the evolution of consciousness.<sup>9</sup>



*Line drawing of the 'Mushroom Shaman' figure as depicted in the ancient cave paintings in Tassili N'ajjer.*

The Ancient Greeks and, subsequently, the Romans hosted mystic ceremonies from 1600BC to 396AD, which involved a psychedelic potion called kykeon similar to LSD. Similar ceremonies would contain spells and many have been recorded, indicating the plethora of substances used (rue, hellebore, mushrooms, ephedra, ergot, barley, darnel, nard and cannabis) and how they were experienced and ingested. Participants would experience an altered state of consciousness, hypnotic or narcotic state and vivid dreams.<sup>10</sup> These spells occurred over many sessions until the desired outcome was achieved (usually answers to personal issues) and the individual would be expected to share their experience with the spiritual guides. Similar experiences were recorded in the Near East, Persia and Asia.

Archaeological artifacts from Mexico, as well as the so-called Mayan "mushroom stones" of Guatemala have also been interpreted by some scholars as evidence for ritual and ceremonial usage of psychoactive mushrooms extending as far back as the precultures of Mesoamerica.<sup>11</sup> This coincides with the natural distribution of psychedelic mushrooms.<sup>12</sup> From the Spanish explorers we learn that mushrooms were a vital part of life for the Aztecs. In Nahuatl, the language of the Aztecs, the mushrooms were called teonanácatl, or "God's flesh" and allowed them to understand the world by communicating with it. After the defeat of the Aztecs, the Spanish forbade traditional religious practices and rituals that they considered "pagan idolatry", including ceremonial mushroom use. For the next four centuries, the Indians of Mesoamerica hid their use of entheogens from the Spanish authorities.

In South America, Ayahuasca ceremonies using the Ayahuasca hallucinogenic beverage (containing the psychedelic molecule DMT) traditionally used by indigenous people of the Amazon basin still occurs to this day,

<sup>5</sup> <https://www.atai.life/2020/11/09/atais-chief-scientific-officer-joins-leaders-in-psychedelic-medicine-at-mapping-the-mind-2/>

<sup>6</sup> Meriin, D., 'Archaeological Evidence for the Tradition of Psychoactive Plant Use in the Old World', *Economic Botany*, Vol. 57, No. 3 (2003), 295–323.

<sup>7</sup> McKenna, T., *Food of the Gods: A Radical History of Plants, Psychedelics and Human Evolution*, (London, 1999).

<sup>8</sup> Nutt, D., 'Mind Altering', *RSA Journal*, Vol. 163, No. 4 (2017), 18–22.

<sup>9</sup> Albert, B., *Event Horizons of the Psyche: Synchronicity, Psychedelics, and the Metaphysics of Consciousness* (California, 1993).

<sup>10</sup> Sumler, A., 'Ingesting Magic: Ingredients and Ecstatic Outcomes in the Greek and Demotic Magical Papyri', *Arian: A Journal of Humanities and the Classics*, Vol. 25, No. 1 (2017), 99–126.

<sup>11</sup> Stamets, P., *Psilocybin Mushrooms of the World: An Identification Guide*, (California, 1996).

<sup>12</sup> [https://inecol.repositorioinstitucional.mx/jspui/bitstream/1005/115/1/8330\\_2005-16.pdf](https://inecol.repositorioinstitucional.mx/jspui/bitstream/1005/115/1/8330_2005-16.pdf)

and it has a long and rich history.<sup>13</sup> Today tourists visit the area to experience the ancient shamanistic practices that have been developed over centuries and modern-day companies have taken these practices to inspire therapeutic applications. Indeed, Professor Eduardo Kohn – Professor of Anthropology at McGill University, has spent years studying Ayahuasca in its native setting and condones the investigation of its implementation in the modern world.

## BIRTH OF MODERN PSYCHEDELICS

Despite Christianity painting traditional psychedelics as heretical, they were rediscovered by western science in the last part of the second millennium. Scientific understanding and research began in 1897 when German chemist Arthur Heffter first isolated mescaline (primary psychoactive compound in peyote cactus). Not much happened in terms of discovery until 1943 when Swiss chemist Albert Hofmann discovered the hallucinogenic effects of LSD (lysergic acid diethylamide) derived from the compound of ergot (fungus that grows on wheat). Hofmann was then able to isolate psilocybin and psilocin (psychoactive components of the Mexican ‘magic mushrooms’ *Psilocybe Mexicana*) and published his findings in the 1950s.<sup>14</sup> Inspired by this discovery Hofmann produced LSD under the name Delysid and sent it to fellow scientists, encouraging its research among the medical community. During this ‘stimulating’ period Albert Huxley wrote “this is how one ought to see, how things really are”.<sup>15</sup>

During World War II Hofmann continued worked on Delysid in Switzerland where it was commercially produced by Sandoz in the hope it could be a treatment for psychiatric illnesses. Indeed, before the 1970’s, over 700 studies with 40,000 patients using psychedelic drugs took place. Psychedelic research produced over 1,000 scientific papers and books and was an avid topic of conversation at international conferences (at the peak of its popularity in 1961 Royal Medico-Psychological Association devoted the whole of its three-day meeting to psychedelic drugs). The reports from these studies were revolutionary in many areas, treating recovering alcoholics, soothing anxieties of terminal cancer patients and the ease of symptoms of ‘difficult to treat’ psychiatric illnesses. It was clearly demonstrated that psychedelic drugs affect all mental functions: perception, emotion, cognition, body awareness and one’s sense of self.<sup>16</sup>

Research rapidly evolved and their beneficial results were reported with enormous zeal. However, there was beginning to be rising concern about their safety especially as they had been administered to thousands of people, treating a massive array of conditions, with widely varying restrictions and care being used in the investigations.

## WAR ON DRUGS

The 1960s saw an awkward junction between different methodologies of research and lacking control groups. The medical world started to question results and so started the reduction of psychedelics being given the credit they were potentially due. There were studies completed throughout Canada with extensive control but without therapy which minimised the results quite significantly.<sup>17</sup> Previously scientific study had been conducted with enthusiasm, but now universities and a growing number of scientists thought psychedelic experiments were not being conducted in a responsible manner and marginalised those who associated with it, and some opting for the opposite extreme with scientists wanting to promote negative outcomes.

Professor David Nutt argues that it is possible that the alcoholic drinks industry played a part in fuelling this line of enquiry as they saw the drugs industry as competition, thus waging their own war against it. The alcohol industry sought to get rid of its competition by terrifying people into believing that drugs are harmful to them and unpredictable, yet despite the contradictory nature of this, this narrative seemed to be coming true. Indeed, in the late 1960s there were concerns about the safety of psychedelics (chromosomal damage, carcinogen,

<sup>13</sup> <https://maps.org/articles/5408-the-ayahuasca-phenomenon>

<sup>14</sup> Kupferschmidt, K., ‘High Hopes: Psychedelic Drugs Fell from Grace in the 1960s. Now, Scientists Are Rediscovering Them as Potential Treatments for a Range of Illnesses’, *Science*, Vol. 345, No. 6192 (2014), 18–23.

<sup>15</sup> Hofmann, A., *Meeting with Aldous Huxley* (trans. Ott, J in *LSD: My Problem Child* (1980, London).

<sup>16</sup> Brown, D., ‘Psychedelic Healing?’ *Scientific American Mind*, Vol. 18, No. 6, (2007) 66–71.

<sup>17</sup> Ludwig et al. *LSD And Alcoholism* (1970, Springfield).

teratogenesis) despite these concerns having no real evidential basis and being based on a few studies with high doses of LSD that were conducted on pregnant women.<sup>18</sup> It was, in fact, repeatedly documented that chances of psychosis were deemed very low and only if a patient already has a predisposition to psychoses.

The fears and worries of the scientific community were surfacing at the same time as the explosion of psychedelics as they leaked into the subculture of the 1960s. This attracted widespread negative attention, which became equated with controversy. Various counterculture movements claimed to draw inspiration from psychedelic drugs and were broadly seen as promoting anti-government views or questioning accepted values and precepts of mainstream society. This psychedelic culture coincided with mass protest movements and opposition to middle class establishment values by the younger generations and a backlash to the Vietnam war.<sup>19</sup> The media attention surrounding LSD's association with social disobedience and antiauthoritarian attitudes served further to erode support for its clinical use.<sup>20</sup> This confusion over the abilities and uses of psychedelics even saw the U.S military and intelligence agencies wanting to use it as a psychochemical weapon against their enemies, even developing a truth serum, believing it could also disorient foreign leaders and armies.<sup>21</sup>

Association with these psychedelic drugs became so toxic that the once esteemed academic Timothy Leary was fired from Harvard due to his promotion of psychedelics. This backfired as Leary started to promote chemical experimentation to radically shatter ontological certainties revamping the social and political structures of American society, thus becoming the 'High Priest' of the psychedelic cult. The medical message was altered to one of hedonistic satisfaction giving rise to the phrase "turn on, tune in and drop out".<sup>22</sup> Individuals like Historian David Farber were focusing on the cultural change psychedelics could achieve, creating a spiritualist environment, claiming "LSD use as an agent in the production of cultural reorientation".<sup>23</sup> Religious rhetoric was used to make psychedelic discourse more intelligible to a broader American audience, and due to religion's powerful voice in the United States this also cemented its downfall.

Sadly, for psychedelics "for all its talk of chemical revolution, was not born out of a cultural vacuum; rather it borrowed heavily from the American Dream in an attempt to legitimize the psychedelic experience."<sup>24</sup> Psychedelics were no longer wonder drugs, they were increasingly presented as drugs of abuse and cultural catastrophe. Politicians depicted psychedelics as a threat to society with President Johnson warning they "threaten our nation's health, vitality and self-respect".<sup>25</sup> The moral tide was turning and now media would take charge in their destruction. This psychedelic trend never caught on with quite the same vigour in Europe but the worldwide reputation for their dark side and abuse was becoming impossible to ignore.

## LEGAL RAMIFICATIONS

Despite repeated protest from scientific professionals, psychedelics were criminalised by governments across the world in a rapid domino effect. The U.S. Food and Drug Administration (FDA) at this time was also granted new powers and authority, which combined with the support for increasing regulations of drugs, led them to prohibit direct distribution of psychedelics to physicians.<sup>26</sup> In 1965, the U.S. Drug Abuse Control Amendments further restricted their medical use, by bring in licence requirements for manufacturing chemicals used for research and the FDA ceased many laboratories work. This research halted completed in 1967 as the National Institute of Mental Health ended all psychedelic research. By 1970 psychedelics were now 'publicly' deemed the most dangerous drugs and legally classified in the most restrictive category along with heroin, and above cocaine, in the Controlled Substances Act. This category is almost entirely made up of psychedelic drugs and means that they are considered to have "high abuse potential", "no currently accepted medical use" and that there is a "lack of accepted safety for users under medical supervision".<sup>27</sup> Any psychedelic research was now

<sup>18</sup> Geber, W., 'Congenital Malformations Induced by Mescaline, Lysergic Acid Diethylamide, and Bromolysergic Acid in the Hamster', *Science*, Vol. 158, No. 3798 (1967), 265-267.

<sup>19</sup> Abrahart, D., 'A Critical Review of Theories and Research Concerning Lysergic Acid Diethylamide (LSD) and Mental Health', (Doctoral thesis, University of Portsmouth, 1998).

<sup>20</sup> Dyck, E. 'Hitting Highs at Rock Bottom': LSD Treatment for Alcoholism, 1950-1970', *Social History of Medicine*, Vol. 19, No. 2 (2006), 313-329.

<sup>21</sup> Kupferschmidt, K., 'High Hopes: Psychedelic Drugs Fell from Grace in the 1960s', *Science*, Vol. 345, No. 6192 (2014), 18-23.

<sup>22</sup> Koch, C., 'This Is Your Brain on Drugs', *Scientific American Mind*, Vol. 23, No. 2, (2012), 18-19.

<sup>23</sup> Elcock, C., 'The Fifth Freedom: The Politics of Psychedelic Patriotism', *Journal for the Study of Radicalism*, Vol. 9, No. 2 (2015), 17-40.

<sup>24</sup> *Ibid.*

<sup>25</sup> Doblin, R., *Regulation of The Medical Use of Psychedelics and Marijuana* (Doctoral Dissertation, Harvard University, 2001).

<sup>26</sup> Doblin, R., *Regulation of The Medical Use of Psychedelics and Marijuana* (Doctoral Dissertation, Harvard University, 2001).

<sup>27</sup> Kupferschmidt, K., 'High Hopes: Psychedelic Drugs Fell from Grace in the 1960s', *Science*, Vol. 345, No. 6192 (2014) 18-23.

required to be approved by the Bureau of Narcotic and Dangerous Drugs - predecessor to the Drug Enforcement Administration (DEA).

Between 1973 (last study in the US on LSD in humans was published) and 1990 there were no human studies with psychedelic drugs. Although not illegal to research, it was notoriously difficult to gain permission and could harm reputations therefore causing funding to dry up. This was even despite John Ehrlichman, former assistant to Richard Nixon, notoriously admitting in 1992 that the Nixon administration had lied about the harmful effects of psychedelic drugs and had manipulated media coverage of them for political advantage. The damage had already been done.<sup>28</sup>

The United Kingdom also vastly expanded its drug controls with the Misuse of Drugs Act in 1971. Psychedelics such as LSD, mescaline and psilocybin were considered to be among the most dangerous substances and were made Class A drugs. Schedule 1 in the UK broadly mirrors Schedule 1 of the 1971 United Nations Convention on Psychotropic Substances, adoption of which is a requirement of UN membership.<sup>29</sup> Fifty years later psychedelic drugs remain more legally restricted than heroin and cocaine, which are Schedule 2, Class A in the UK. The same can be said for almost all European countries.

MDMA – ‘Ecstasy’ took a slightly different route, originating as MDA and discovered in 1912. Its hallucinogenic effects were discovered in 1955, leading to its reputation as “The Love Drug”. In the 1960s, psychiatrists Claudio Naranjo and Alexander T. Shulgin conducted initial testing of its therapeutic potential, which consequently led psychotherapist Leo Zeff to adopt MDA in his sessions in the 1960. In 1985, against the backdrop of increased abuse of MDMA, it became a Schedule I controlled substance in the United States and banned in most other countries soon thereafter. This was despite the corrective PR campaign by Rick Doblin – founder of the first non-profit venture Earth Metabolic Design Laboratories. This campaign, however, would go on to inspire Rick Doblin to set up the Multidisciplinary Association for Psychedelic Studies (‘MAPS’) which in turn has driven the birth of the modern psychedelic renaissance.<sup>30</sup>

## PSYCHEDELIC RENAISSANCE

‘The War on Drugs’ was caused by the myriad of contradicting voices and alternative agendas which overshadowed the medical potential of psychedelics. The medical industry needed to ‘reclaim’ the psychedelic drugs, pick up on its research into their effects on mental illness and therefore begin the slow repairing of the harmful damage that had been done to their reputation and those scientists who associated with it.

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## DEBUNKING LIES

In the 1970s and 1980s there was an effort to understand the facts surrounding psychedelics, especially LSD. Examining nearly a hundred papers, leading scientist Norman Dishotsky found that LSD does not cause chromosome damage in human beings at normal doses.<sup>31</sup> He also found no convincing evidence of a raised rate of birth defects in children of LSD users.<sup>32</sup> One of the mostly consistently cited dangers of psychedelic therapy is the possibility that severe psychotic episodes can be induced with vivid traumatising flashbacks. Any other form of deep-probing psychotherapy carries the same risks. However, these risks are severely diminished in the right setting with a therapist’s guidance. All available surveys suggest that, if used correctly, therapeutic use of psychedelic drugs is not dangerous.<sup>33</sup> Psychedelics do not cause life-threatening changes in cardiovascular, renal, or hepatic functions<sup>34</sup> and do not engender drug dependence or addiction.<sup>35</sup> Most clearly, there are methods for minimising risks so that they are within acceptable levels and it is generally agreed that psychedelics potential for harm is very limited.<sup>36</sup>

<sup>28</sup> Baum, D., ‘Truth, lies, and Audiotape’, in (ed.) Smith, L., *The Moment: Wild, Poignant, Life Changing Stories from 125 Writers and Artists*, (New York, 2012).

<sup>29</sup> United Nations. Convention on psychotropic substances, 1971. [www.unodc.org/pdf/convention\\_1971\\_en.pdf](http://www.unodc.org/pdf/convention_1971_en.pdf).

<sup>30</sup> <https://www.atai.life/programs/mdma-derivative/>

<sup>31</sup> Dishotsky, N et al. ‘LSD and Genetic Damage’, *Science*, Vol. 172, No. 3982 (1971), 431-440.

<sup>32</sup> Bastiaans, J., ‘Mental Liberation Facilitated by the Use of Hallucinogenic Drugs’, in (ed.) Grinspoon, L, and Bakalar, J., *Psychedelic Reflections*, (New York, 1983).

<sup>33</sup> *Ibid.*

<sup>34</sup> Nichols, D., ‘Hallucinogens’, *Pharmacology & Therapeutics*, Vol. 101, No. 2 (2004), 131-181.

<sup>35</sup> O’Brien, C., ‘Drug Addiction and Drug Abuse’, in (ed.) Hardman, J., *Goodman and Gilman’s The Pharmacological Basis of Therapeutics*, (New York, 2001).

<sup>36</sup> The Royal Society for the encouragement of Arts, Manufactures & Commerce 2007: 287.



The most serious danger of psychedelic therapy appeared to be suicide.<sup>37</sup> However, many researchers have observed that they see psychedelic drugs as more likely to prevent suicide than to cause it; with the suicide rate in LSD treated patients being lower than in psychiatric patients as a whole.<sup>38</sup> Indeed, a questionnaire given to 2,532 relevant professionals received 617 replies and found only one suicide in individuals treated with psychedelics while twenty-five respondents believed that psychedelics had helped them prevent suicides.<sup>39</sup> The suicide rate fell during the psychedelic boom and even when LSD users did attempt suicide, there was no direct relationship to taking of the drug. Psychiatrist Sidney Cohen conducted a survey which showed that the dangers of psychedelics can be minimized and their use as research tools should be continued. Another survey covered nearly all patients who had been administered LSD in Britain until 1969 and found that there were only two suicides, both of which were unrelated to the drug.<sup>40</sup> The author of these surveys concluded that with adequate psychiatric supervision and appropriate conditions the incidence of adverse reactions is low.<sup>41</sup> Indeed Professor David Nutt argues “Probably more people have died trying to jump from balcony to balcony in Magaluf when drunk than have ever died jumping under the influence of LSD”.<sup>42</sup> Medical Researchers Savage and Stolaroff (Johns Hopkins University) corroborated this line of reasoning and wrote that the risks could be minimised and claimed that “there is substantial evidence that many avenues may be opened up by research with the psychedelics, both in developing new treatment methods and improving the understanding of the human mind”.<sup>43</sup>

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## FUNDING ISSUES

Despite this emerging research, larger clinical studies were almost impossible to instigate throughout the western world because of the practical, financial, and bureaucratic obstacles imposed by Schedule 1 classification or its equivalent.<sup>44</sup> For example, because of the burden of compliance with the UN’s Schedule I, only one manufacturer in the world produced psilocybin at sufficient quantity, quoting a group a prohibitive £100,000 for 1g (50 doses). In the UK, to hold a Schedule 1 drug, institutions require a licence costing about £5,000. Only four UK hospitals carry such licences, which come with regular police inspections and onerous rules on storage and transport. Prescribers of a Schedule 1 substance also must hold a licence, which costs £3,000. These restrictions, and the accompanying bureaucracy, mean that the cost of clinical research using psychedelics is 5-10 times that of research into less restricted drugs such as heroin.

The self-reinforcing cycle of stigma generated by Schedule I classification means that historically almost all grant funders have been uncomfortable funding research into psychedelics, and similar problems are encountered with ethics committees. Legal prohibition of some psychotropic substances continues to be a condition of UN membership.<sup>45</sup> The UN Schedule I creates its own circular argument for psychedelics to remain stringently restricted, even though the original reasons for classifying them as such were largely based on misinformation and not on proven research. However due to the undeniable fact that psychedelics are not harmful in relation to other controlled substances and are not habit forming, and because evidence suggests medical use has potential, it has become harder to sustain the argument against their relaxing of classification.

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## RENEWED RESEARCH

Things really began to change in the 1990’s when “open-minded regulators at the FDA decided to put science before politics when it came to psychedelic and medical marijuana research”, and this spawned a growing number of other country regulators, most recently in Norway, to question the need for such draconian restrictions.<sup>46</sup> The FDA’s ground breaking approval of GW Pharmaceuticals’ Epidiolex in June 2018, a medicine

<sup>37</sup> Geert-Jorgensen et al. ‘LSD Treatment: Experience Gained within a Three-Year Period’, *Acta Psychiatrica Scandinavica*, Vol. 40, No. 180 (1964), 373-382.

<sup>38</sup> Grinspoon, L., and Bakalar, J., *Psychedelic Drugs Reconsidered*, (New York, 1979).

<sup>39</sup> Clark, W., and Funkhouser, G., ‘Physicians and researchers disagree on psychedelic drugs’, *Psychology Today*, Vol. 3, No. 11 (1970), 70-73.

<sup>40</sup> Wilson, J., ‘Foreword’, in (ed.) Cohen, *Drugs of hallucination: The Uses and Misuses of Lysergic Acid Diethylamide* (London, 1964).

<sup>41</sup> Malleson, N., ‘Acute Adverse Reactions to LSD in Clinical and Experimental Use in the United Kingdom’, *British Journal of Psychiatry*, Vol. 118, No. 543 (1971) 229-230.

<sup>42</sup> <https://medium.com/rsa-journal/mind-altering-a-conversation-e7eb812dcbf4>

<sup>43</sup> Savage, C., and Stolaroff, M., ‘Clarifying the Confusion Regarding LSD-25’, *The Journal of Nervous and Mental Disease*, Vol. 140, No. 3 (1965), 218-221.

<sup>44</sup> Nutt, D., & King, L., & Nichols, D., ‘Effects of Schedule I Drug Laws on Neuroscience Research and Treatment Innovation’, *Nat Rev Neurosci*, Vol. 14 (2013), 577-85.

<sup>45</sup> Hari, J., *Chasing the Scream*, (New York, 2015).

<sup>46</sup> Higgins, A., ‘Odd Push in Drug Averse Norway: LSD is OK’ 2015 nytimes.com <http://bit.ly/1FntGeK>.

made from cannabis, to treat two rare and severe forms of epilepsy, has paved the way for making psychedelics into medicines. The clinical development of cannabidiol (CBD) into an FDA-approved therapy is an inspiring example of how traditional medicines can be transformed into modern ones through advanced pharmacological techniques that ensure patient safety.

It was now easier for research institutes and fellows to study them for example in the 1970s and 1980s, Dr Jan Bastiaans, a Dutch psychiatrist treated about 300 patients with psychedelics including many concentration camp survivors suffering from alexithymia (subclinical inability to identify and describe emotions experienced by one's self or others), reporting a success rate of 67%.<sup>47</sup> He claimed to help most of his patients and a small follow-up study showed that all his contactable LSD treated patients were still satisfied with the treatment.<sup>48</sup>

Research has also now been conducted using newer psychedelics such as dipropyltryptamine (DPT). Therapists using DPT have the advantage of a shorter duration of action than LSD as well as the fact that it has not been the object of sensationalistic publicity. DPT assisted therapy was shown to be superior to placebo therapy on both therapist and patient ratings and it increased the depth of self-exploration and helped towards a better psychodynamic resolution.<sup>49</sup> Professor Shulgin is a highly respected chemist and psycho-pharmacologist (dubbed “godfather of psychedelics”) who strongly believes that only human testing illustrates how psychedelics affect sensory perception. He was granted a scheduled drug license in the early 1980s and was able to create and test new psychedelics drugs. He was the first to synthesise many newer psychedelics which have been shown to be useful as adjuncts to therapy. However, Shulgin’s laboratory was raided in 1994 and his licence was revoked for violating the licence’s terms. The DEA stated “Professor Shulgin’s publications, in our opinion, are pretty much cookbooks on how to make illegal drugs”. Continued evidence of research being misunderstood and brought into disrepute.<sup>50</sup>

With the nascent acknowledgement of the research safety of LSD, MDMA truly got a second chance of medical acceptance through Dr Rick Doblin in 1986. He recognised that the most effective means of ensuring access to MDMA lay through established regulatory pathways and he founded the now renowned Multidisciplinary Association for Psychedelic Studies (MAPS) with the primary goal of making MDMA an FDA-approved medicine. This privately funded organization catalysed much of the recent wave of research, including the Heffter Research Institute in 1993, the Beckley Foundation in England and the Russian Psychedelic society. By seeking out interested researchers to assist in developing the experimental design for the studies and help to obtain funding and government approval many clinical trials were being conducted. MAPS is still extremely active today and in 2020 raised more than \$30 million in just a few months via its Capstone Challenge (with several well-known benefactors participating), allowing it to advance its Phase III MDMA clinical trials in the U.S., Canada, and Israel. They have also initiated numerous FDA approved clinical trials in the U.S. Switzerland, Israel and Spain and have raised more than \$100million for their studies since their creation in 1986.<sup>51</sup>

Recent pilot studies performed have shown clinical efficacy in anxiety associated with, inter alia:

- advanced cancer<sup>52</sup>;
- obsessive compulsive disorder<sup>53</sup>;
- tobacco addiction<sup>54</sup>;
- alcohol addiction<sup>55</sup>; and
- cluster headaches<sup>56</sup>.

These trails must pass three clinical milestones before they can be marketed to the public. Once establishing it is a place of interest it must go through three rounds of intensive testing and measure that can take years.

- Phase I (for safety, usually in 20-80 volunteers)

<sup>47</sup> Bastiaans, J., ‘Mental Liberation Facilitated by the Use of Hallucinogenic Drugs’, in (ed.) Grinspoon, L., and Bakalar, J., *Psychedelic Reflections*, (New York, 1983).

<sup>48</sup> Maalste, N., ‘Progress Report Winter 1999: Follow-up study of Bastiaans LSD Therapy’, *MAPS Bulletin*, Vol. 8, No. 4 (1999), 2-3.

<sup>49</sup> Soskin, R., ‘Dipropyltryptamine in psychotherapy’, *Current Psychiatric Therapies*, Vol. 15, (1975), 147-156.

<sup>50</sup> Shulgin, A., ‘The Chemistry Continues’, in *TIHKAL: The Continuation* (New York, 1997), 387-599.

<sup>51</sup> The Multidisciplinary Association for Psychedelic Studies (MAPS) publishes a quarterly bulletin that reports on the status of current scientific research into psychedelic substances: [www.maps.org](http://www.maps.org)

<sup>52</sup> Grob, C., & Danforth, A., & Chopra, G., ‘Pilot Study of Psilocybin Treatment for Anxiety in Patients with Advanced Stage Cancer’, *Arch Gen Psychiatry*, Vol. 68 (2011), 71-8.

<sup>53</sup> Moreno, F., & Wiegand, C., & Taitano, E., & Delgado, P., ‘Safety, Tolerability, and Efficacy of Psilocybin in 9 Patients with Obsessive-Compulsive Disorder’, *J Clin Psychiatry*, Vol. 67 (2006), 1735-40.

<sup>54</sup> Johnson, M., & Garcia-Romeu, A., & Cosimano, M., & Griffiths, R., ‘Pilot Study of the 5-HT2AR Agonist Psilocybin in the Treatment of Tobacco Addiction’, *J Psychopharmacol*, Vol. 28 (2014), 983-92.

<sup>55</sup> Bogenschutz, M., & Forcehimes, A., & Pommy, J., ‘Psilocybin-Assisted Treatment for Alcohol Dependence: A Proof-of-Concept Study’, *J Psychopharmacol*, Vol. 29 (2015), 289-99.

<sup>56</sup> Sewell, R., & Halpern, J., & Pope, H., ‘Response of Cluster Headache to Psilocybin and LSD’, *Neurology*, Vol. 66 (2006), 1920-2.

- Phase II (for efficacy, in several hundred subjects)
- Phase III (more extensive data on safety and efficacy come from testing the drug in up to several thousand people).

This flurry of fundraising also coincided with a gradual easing of the ‘psychedelic drug’ stigma. Interestingly this attitude shift is happening faster in the US than in Europe.

## PUBLIC OPINION

During the 1990s and 2000s activists Terence McKenna and Michael Pollan were moved, after their psychedelic experiences, to dedicate their lives to its rebirth with one of Pollan’s book titled *How to Change Your Mind*. Despite the medical community coming to this conclusion relatively quickly having reversed many of their preconceived notions of psychedelics, public opinion has been slower to reverse, especially as regulations are still tight around the drugs.

Professor David Nutt experienced first-hand how career limiting public support of drugs in a public setting can be. In 2009, Nutt was fired for saying on a television programme that cannabis is less harmful than alcohol based purely on scientific data and expressing his belief that our drugs laws “do not fit with the facts”.<sup>57</sup> Indeed many people have pointed out that psychedelics do not seem to meet the three criteria for being put in the strictest Schedules. Despite frequent calls for a reassessment of drug laws and regulation of research, it is curious but significant to note that no government in the past hundred years has dared to commission a wide-ranging inquiry into drugs and drug policy or reassess the position of psychedelics within the law.<sup>58</sup> We believe this is changing with even the Chairman of the UK Advisory Council on the Misuse of Drugs stating recently that he had “no idea” why psilocybin should be categorised as Class A.<sup>59</sup> Hofmann, interviewed shortly before his hundredth birthday, called LSD “medicine for the soul” and was frustrated by the worldwide prohibition of it. “It was used very successfully for ten years in psychoanalysis,” he said, adding that the drug was misused by the counterculture of the 1960s, and then criticized unfairly by the political establishment of the day. He conceded that it could be dangerous if misused, because a relatively high dose of 500 micrograms will have an extremely powerful psychoactive effect.<sup>60</sup>

This renewed interest has taken off in America where the topic of drugs is in debate; Washington, Denver, Oakland, Santa Cruz, Ann Arbor, and Michigan have all recently decriminalised the possession of psilocybin. In these cities, psychedelics have become the lowest law enforcement priority for the Police Departments. In November 2020 Oregon legalised the use of psilocybin in supervised therapeutic settings (they also decriminalized all drugs, including heroin and cocaine, so possessing small (for personal use) amounts of these substances no longer carries the threat of jail or prison time). “The value of Oregon’s moves, both symbolically and practically, is hard to overstate.” As ballot initiatives can ultimately inspire action beyond state borders; political leaders in New York, which doesn’t have an open-ended process, and surrounding areas started to talk up legalization after Massachusetts and Maine legalized, and they’ve already become more vocal after New Jersey voted to legalize this year.<sup>61</sup>

The Oregon measure creates a state-licensed psilocybin-assisted therapy system. Patients over the age of 21 will be allowed to buy, possess and use psilocybin under the supervision of trained facilitators, while manufacture, delivery and administration of the drug will be allowed at supervised, licensed facilities. “Now there is a new form of hope for all Oregonians and those willing to travel to Oregon rather than having to travel to places like Jamaica where psychedelic retreats are already legal,” said Mike Arnold, Founder and President of Silo Wellness, an Oregon-based company with retreat operations in Jamaica.<sup>62</sup>

<sup>57</sup> Nutt, D., ‘Mind Altering’, *RSA Journal*, Vol. 163, No. 40 (2017). 18–22.

<sup>58</sup> The Royal Society for the encouragement of Arts, Manufactures & Commerce 2007: 327.

<sup>59</sup> House of Commons Science and Technology Committee 2006: 26.

<sup>60</sup> Smith, C., Interview with Hofmann (The New York Times, 2006).

<sup>61</sup> <https://www.vox.com/future-perfect/21552710/oregon-drug-decriminalization-marijuana-legalization>

<sup>62</sup> <https://www.benzinga.com/markets/cannabis/20/11/18251638/psyched-oregon-legalizes-psilocybin-washington-dc-decriminalizes-psychedelics-cybin-and-entheon->

Finally, modern methodologically-sound psychedelic research is beginning not to be as strictly limited by law and approval processes.

## CONCLUSION

Psychedelics have taken a complex path from the enthusiastic explosion of research in the late 1950s to a complete legal lock down and medical abandonment a decade later, to the start of a reopening of new research opportunities in the 1990s/2000s. Never before has any type of drug or treatment shown such promise only to end with such restrictive barriers to research. Scientists worked, and lobbied, hard throughout the 80s and 90s to dispel persisting doubts with the experimental data in the 1970s. Lessons had been learnt from the past and now psychedelics, administered in a safe research environment, where subjects were carefully screened, prepared and supported by therapists are going ahead.

Medical uses of psychedelics were highly regarded in scientific circles long before they gained a reputation for recreational abuse and a huge amount of research was produced describing the benefits of psychedelic drugs in glowing terms. Overenthusiasm and methodological shortcomings damaged the medical reputation of psychedelic drugs as did untrained individuals using powerful psychological tools irresponsibly. Although they were generally considered to be safe, soon the consensus was that almost all of the benefits prescribed to these chemicals were unfounded and premature. Many years later, there is little to remind us that psychedelics were once established as legitimate treatments. The prohibition had ended mainstream psychedelic research along with the possibility of discovering any clinical use for almost forty years.

It appeared that the barriers preventing psychedelic research are not justified by the concerns regarding potential for abuse. It has been shown that most of the hazards encountered when working with psychedelics were exaggerated or are avoidable. There is certainly real clinical potential as evidenced by the cornucopia of research that has been produced. Historically, well managed psychedelic therapy is at least as beneficial as regular analysis. When the benefits are potentially so great, an ethical imperative implores scientists to explore possible alternative treatments using psychedelic drugs. Even if psychedelics are finally proven to be inadequate for clinical use, the only way to achieve a conclusive judgement is through carefully controlled safety-conscious research. Thus, through 2000s onwards we see a slow but powerful renaissance, which is now in full swing. Below is an outline of the uses and functions of each particular drug in development by companies to aid in overall understanding of their particular uses and treatments and areas of potential investment.

## HOW DO THEY WORK AND WHAT DO THEY TREAT?

Some of the criticisms of psychedelic methodology underlie a complete unfamiliarity with the way psychedelics work. There are many erroneous implications of the unfounded relationships between these drugs and dangers which are the result of fundamental misunderstanding.<sup>63</sup>

Hallucinations imply a negative experience characterized by horror and anxiety not euphoria, wonder and revelation reported by most users of the drugs. In the medical use of these drugs, hallucinations are the individual re-perceiving their reality and enabling their brain and body to heal whilst gaining healthier perspectives. Referring to psychedelic chemicals as ‘drugs’ can evoke negative images of ‘drugged up’ socially reprehensible individuals but psychedelics are not like any other restricted drug - heroin, nicotine, morphine and cocaine. Here we outline how psychedelics work and affect the individual, and which specific psychedelics can potentially treat which mental illness.

## OVERVIEW OF PSYCHEDELICS FUNCTION

“Psychedelic drugs affect all mental functions: perception, emotion, cognition, body awareness and one’s sense of self”.<sup>64</sup> Unlike other drugs, the psychedelics’ effect depends heavily on the environment and on the expectations of the subject, which is why combining them with psychotherapy is vital.

Scientists divide classical psychedelic drugs into two basic chemical groups: tryptamines (such as LSD, DMT and psilocybin) and phenethylamines (such as mescaline and MDMA). Lastly there are dissociative anaesthetics considered to have psychedelic effects at low, non-anaesthetic doses (examples: synthetic compounds like Ketamine Phencyclidine). The exact mechanisms differ, but see outline effects set out below:-

- All the tryptamine hallucinogens (which make up the majority of psychedelic drugs) selectively bind to specific serotonin receptors on neurons, mimicking the effects of the nerve-signalling chemical, or neurotransmitter, serotonin on these receptors.<sup>65</sup>
  - Serotonin is responsible for many important functions, including mood, memory, appetite, sexual appetite and sleep. It is such an essential neurochemical that any substance that interferes with its action might be expected to produce dramatic changes in brain function.<sup>66</sup>
- Phenethylamines mimic the chemical structure of another neurotransmitter, dopamine. However, they also bind to many of the same serotonin receptors activated by the tryptamines.
- Dissociative Anaesthetics – PCP is well known for its primary action on the NMDA receptor and consequently impacts the synaptic development and plasticity in the brain. Memory loss, loss of muscular co-ordination and changes to breathing and heart rate occur.

## HOW DO PSYCHEDELICS CREATE PERCEPTUAL CHANGE?

Neuroscientists believe that activation of a particular set of serotonin receptors, the 2A subtype, which are highly expressed (or present) in the cortex, the outermost layer of the brain, interferes with the processing of sensory information. Consciousness is thought to involve a complex interaction among the cortex, the thalamus and the striatum. Disruption of this network by activation of serotonin 2A receptors is now the most popular theory for the mechanism of the pharmacological change that creates the psychological effect.

David Nichol, leading pharmacologist and medicinal chemist, comments that “the psychological effect is harder to define but, in some way, produces changes in the way the subject perceives pain and distress. Psychedelics seem able to produce a profound cognitive change that provides the patient with a new insight, the ability to see the world from a new perspective, somehow reducing anxiety and raising the pain threshold.”<sup>67</sup>

<sup>63</sup> Poole, R., & Brabbin, C., ‘Drug Induced Psychosis’, *British Journal of Psychiatry*, Vol. 168, No. 2 (1996), 135-138.

<sup>64</sup> Brown, D., ‘Psychedelic Healing?’, *Scientific American Mind*, Vol. 18, No. 6 (2007), 66-71.

<sup>65</sup> Nichols, D., ‘Psychedelics’, *Pharmacol Rev*, Vol. 68, No. 2 (2016), 264-355.

<sup>66</sup> *ibid*.

<sup>67</sup> Nichols, D., ‘Hallucinogens’, *Pharmacology & Therapeutics*, Vol. 101, No. 2 (2004), 131-181.

## WHY DO WE NEED PSYCHEDELICS?

The overwhelming statistics and social devastation of mental illness are an immense – and growing - strain on our modern society. Currently controlled “psychedelic” drugs such as psilocybin and MDMA have shown early promise in the treatment of debilitating mental and neurological disorders. “Given the scale of this problem, it’s critical that we develop alternatives to current treatments,” comments Dr. Srinivas Rao.<sup>68</sup> Psychedelics were once seen as a potential answer and this is how desperately we need them now. Furthermore, given many drugs of abuse are used routinely in medicine, it seems that we have an ethical responsibility to pursue psychedelic research if there is any chance they might have a unique therapeutic value for certain conditions we cannot currently treat effectively.<sup>69</sup> These are the issues our society is facing and what impact they have.

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### DEPRESSION

More than 300 million people suffer from depression worldwide. Close to 800,000 people commit suicide every year and suicide is the second leading cause of death among 15- to 29-year-olds. Symptoms of depression often seep into every corner of the lives of those suffering. While mild forms of the disease may impair the ability to focus, feel motivated, and maintain social relationships, more severe forms often leave the patient unable to function normally, and in some cases, lead to the ultimate cost - the patient’s life.<sup>70</sup> Importantly, this pain is not solely limited to those diagnosed. On a micro-level, depression also profoundly impacts the lives of those close to the affected person, from friends and family to co-workers and acquaintances. On a macro-level, with 4.4% (322 million people) of the global population suffering across the world, even if an individual is not being directly affected by a friend or loved one’s illness, he or she is indirectly impacted by society at large.<sup>71</sup>

More than 100 million people suffer from treatment-resistant depression, meaning they don’t respond to currently available therapies.<sup>72</sup> A huge part of this issue is due to the fact that currently available treatments haven’t changed since the 1980s; often limited primarily to psychotherapy and a broad drug class called SSRIs (selective serotonin re-uptake inhibitors). Current antidepressants such as fluoxetine can only treat the symptoms of depression and can bring side effects such as anxiety and low sex drive.<sup>73</sup> On top of that they have variable results and serious habit-forming tendencies.

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### PTSD

PTSD is a chronic condition characterized by recurring and intrusive thoughts or memories and often co-occurring with major depression. A Danish study found that persons with PTSD were 13 times more likely to commit suicide than the general population. In the US alone, an estimated 13 million people meet the criteria for a PTSD diagnosis. At present, the only FDA approved treatments for PTSD are selective serotonin reuptake inhibitors (SSRIs); namely sertraline hydrochloride (Zoloft) and paroxetine hydrochloride (Paxil). Unfortunately, not only does each come with significant side-effects, two-thirds of patients either do not respond or have only a partial response to SSRIs.<sup>74</sup> The prevalence of mental health and central nervous system (CNS) disorders is growing year on year, with roughly 1 in 4 people around the world affected by these conditions in their lifetimes, and with mental health set to become the biggest disease burden globally, almost certainly exacerbated by the current pandemic.<sup>75</sup>

<sup>68</sup> Rao, S., ‘Psychedelics for Depression: The Promise, Risks, & Costs’, *Mapping the Mind 2019* <https://www.youtube.com/watch?v=nvulyZXCm0>

<sup>69</sup> Lewis, J., *The Hallucinogenic Way of Dying: Can Psilocybin Reduce Death Anxiety in End-Stage Cancer Patients?* (LA Weekly, 2004).

<sup>70</sup> <https://mappingthemind.ca/event/mapping-the-mind-2019/>

<sup>71</sup> <https://medium.com/insightnetwork/burdens-of-depression-the-individual-38ee35b892bd>

<sup>72</sup> Rao, S., ‘Psychedelics for Depression: The Promise, Risks, & Costs’, *Mapping the Mind 2019* <https://www.youtube.com/watch?v=nvulyZXCm0>

<sup>73</sup> <https://www.labiotech.eu/brain/atai-compass-pathways-psychedelics/>

<sup>74</sup> <https://www.prnewswire.com/news-releases/atai-life-sciences-launches-empathbio-to-treat-post-traumatic-stress-disorder-with-novel-mdma-product-301117010.html>

<sup>75</sup> <https://www.psychedelicfinance.com/articles/global-investors-back-psychedelic-medicine-start-up-with-3-8m-series-a-round>

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## ADDICTION

When it comes to treating addiction, the rate of success is so low that society has been conditioned to accept and expect failure. There is a need for an alternative approach, that addresses the human cost of addiction for individuals, families and society at large. Strikingly, all alcoholism treatment trials using psychedelics, controlled or not, were shown to help 50% of patients. This figure is far greater than that claimed by any other treatment. When psychedelics offer the chance to help other untreatable conditions there is an argument for their use. The Centres for Disease Control and Prevention estimates that the economic burden of opioid addiction is more than \$78 billion annually and for alcoholism is estimated to be around \$250 billion.<sup>76</sup>

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## OBSESSIVE COMPULSIVE DISORDER (“OCD”)

There are an estimated six million OCD sufferers in the US and effective treatment is limited. A quarter do not respond to conventional therapies at all and, even when medication is effective, a 30%-50% reduction in symptoms is the best that trials show can be achieved.<sup>77</sup> Patients can suffer from a wide range of obsessions and compulsions; some of them showering for hours; others put on their clothes over and over again until they felt right, checking and rechecking appliances, etc.<sup>78</sup>

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## ALZHEIMER’S AND PARKINSON’S

Globally an estimated 50 million people have a diagnosis of dementia and population prevalence continues to increase.<sup>79</sup> Alzheimer’s disease accounts for approximately 50–70% of cases.<sup>80</sup> Alzheimer’s is a complex disease with multiple therapeutic targets, and as single target approaches continue to fail, there is a growing and widespread belief that a successful therapeutic approach will have to hit multiple targets simultaneously. And that’s exactly what a conventional drug developer doesn’t want to hear because that exponentially increases the complexity and cost of drug development.<sup>81</sup>

Many diseases of the body are caused in part by inflammation such as rheumatoid arthritis and other autoimmune diseases with even the creation of immunotherapy for some cancers in the 2010s. The pharmaceutical and biotech industry has invested heavily in testing anti-inflammatory drugs for Alzheimer’s and Parkinson’s disease and whilst there has not been an overtly successful anti-inflammatory an alternative that is being explored is Ketamine. It is believed that by blocking a receptor for glutamate in the brain Ketamine can decrease inflammation (caused by an increased amount of glutamate in the brain). The therapeutic scope of these new insights is potentially bigger than depression or drugs. There is also interest in the role of diet, obesity, stress, gum disease, the gut microbiome and other risk factors in low-grade inflammation that could be controlled without drugs. In addition, there are now dozens of studies measuring the anti-inflammatory effects of psychological interventions, such as meditation or mindfulness, or lifestyle management programmes, diets or exercise regimes.<sup>82</sup>

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## CLUSTER HEADACHES

Migraine and cluster headaches (CH) are prevailing, episodic, often chronic headache disorders that have a considerable impact on the individual and society.<sup>83</sup> Migraine with a prevalence of nearly 15% worldwide is a significant cause of disability and notably burdens medical costs and loss of productivity. Cluster headaches are a rarer but particularly painful and debilitating form of headache disorder with a prevalence around 1 in 1000 individuals.<sup>84</sup> While there are numerous treatment practices for headache disorders, none are ideal and most

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<sup>76</sup> <https://psychedelicinvest.com/10-psychedelic-companies-investors-should-have-on-their-radar/>

<sup>77</sup> Frood, A., ‘Psychedelic drug “Hope for OCD”’, (BBC News, 2006).

<sup>78</sup> Moreno, F., & Wiegand, C., & Taitano, E., & Delgado, P., ‘Safety, Tolerability, and Efficacy of Psilocybin in 9 Patients with Obsessive-Compulsive Disorder’, *J Clin Psychiatry*, Vol. 67 (2006), 1735–40.

<sup>79</sup> Alzheimer’s Society, 2019 and UK Government Web Archive, 2020.

<sup>80</sup> Draper, B., *Understanding Alzheimer’s Disease and Other Dementias*, (London, 2013).

<sup>81</sup> <https://www.forbes.com/sites/abbierosner/2020/02/21/microdosed-lsd-may-finally-be-the-breakthrough-for-alzheimers-disease/?sh=4bc7745053a8>

<sup>82</sup> <https://www.theguardian.com/commentisfree/2020/jan/19/inflammation-depression-mind-body>

<sup>83</sup> Schuster, N., & Vollbracht, S., & Rapoport, A., ‘Emerging treatments for the primary headache disorders’, *Neuro Sci*, Vol. 36 (2015), 109–113.

<sup>84</sup> Robbins, M., & Starling, A., & Pringsheim, T., & Becker, W., & Schwedt, T., ‘Treatment of Cluster Headache’, *The American Headache Society Evidence-based Guidelines*, Vol. 56 (2016), 1093–1106.

exhibit unsatisfactory effectiveness, tolerability, or patient adherence. There are presently no pharmacological treatments available specifically developed for CH. The currently used methods originated as treatments for other indications and were found helpful in CH by chance. CH is known to sometimes be resistant to the conventional therapies (around 20% in chronic cases of CH).<sup>85</sup> Considering that CH is one of the most intense and disabling pain conditions known, the urgency of the circumstances has led care providers and patients to try unusual or experimental remedies.<sup>86</sup> Although there is no cure, patients can sometimes cure the headache by inhaling pure oxygen at the onset of an attack. Other treatments include blocking calcium channels with the drug verapamil, which is used for cardiac arrhythmia, or taking triptans, also used for migraines. A 2006 study showed that participants found psilocybin and LSD to be capable of stopping attacks, ending cluster cycles, and extending the break between cycles.

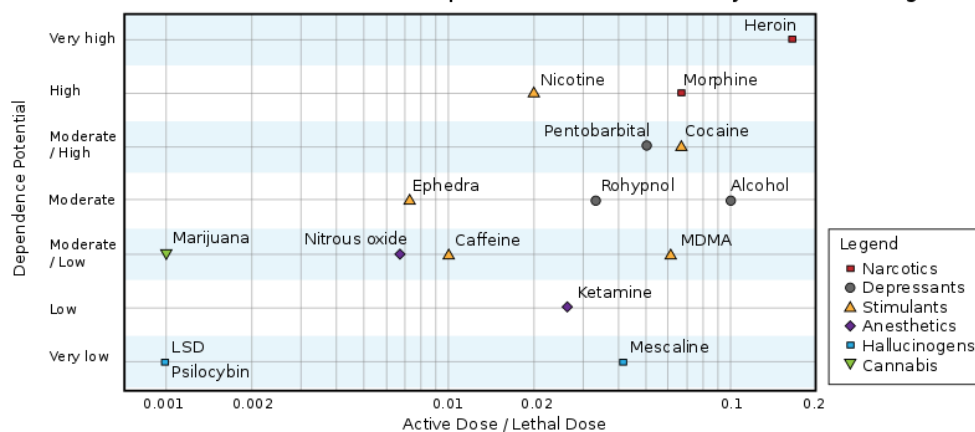
## ANXIETY AND DEPRESSION IN CANCER PATIENTS

A systematic review and meta-analysis show the prevalence of major depression (15%), minor depression (20%), and anxiety (10%) in patients treated for cancer. Two thirds of patients with cancer and depression also have clinically significant anxiety symptoms.<sup>87</sup> One of the largest issues surrounding this is that 73% of these depressed cancer patients do not receive effective psychiatric treatment, and only 5% see a mental health professional.<sup>88</sup> Symptoms of anxiety in patients with cancer more often coexist with clinical depression than present as anxiety alone, and treatment for depression may also resolve anxiety.

## TREATMENT RISKS

Psychedelics are physiologically safe, non-addictive, and do not induce dependence.<sup>89</sup> In the late 1960s there were concerns about safety (chromosomal damage, carcinogen, teratogenesis, psychotic episodes, suicide, flashbacks) inculcated by the politically driven and media led condemnation of LSD in the 1960s.<sup>90</sup> These were mainly based on speculation and a few studies where extremely high doses of LSD were used with individuals that should not have been exposed to it.<sup>91</sup> Nearly all of these previous attempts at suggesting psychedelics posed a high risk were debunked by scientists through the 1980s up to the present day. Psychedelics do not cause life-threatening changes in cardiovascular, renal, or hepatic functions<sup>92</sup> and do not engender drug dependence or addiction.<sup>93</sup> The general consensus seems to be; when administered under the right conditions by trained professionals, they are reasonably safe.

Active/Lethal Dose Ratio and Dependence Potential of Psychoactive Drugs



<sup>85</sup> Goorah, R., & Buture, A., & Ahmed, F., 'Evidence-based Treatments for Cluster Headache', *The Clin Risk Manag*, Vol. 11 (2015), 1687–1696.

<sup>86</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC584001/>

<sup>87</sup> Smith, H., 'Depression in Cancer Patients: Pathogenesis, Implications and Treatment', *Oncol Lett*, Vol. 9, Issue. 4, (2015), 1509-14.

<sup>88</sup> Walker, C., & Hansen, M., 'Prevalence, Associations, and Adequacy of Treatment of Major Depression in Patients with Cancer', *Lancet Psychiatry*, Vol. 1, Issue. 5 (2004), 343-50.

<sup>89</sup> Brunton, L., & Chabner, B., & Knollman, B., *The Pharmacological Basis of Therapeutics*, (London, 2011).

<sup>90</sup> Grinspoon, L., & Bakalar, J., *Psychedelic Drugs Reconsidered*, (New York, 1997).

<sup>91</sup> Geber, W., 'Congenital Malformations Induced by Mescaline, Lysergic Acid Diethylamide, and Bromolysergic Acid in the Hamster', *Science*, Vol. 158, No. 3798 (1967), 265-267.

<sup>92</sup> Nichols, D., 'Hallucinogens', *Pharmacology & Therapeutics*, Vol. 101, No. 2 (2004), 131-181.

<sup>93</sup> O'Brien, C., 'Drug Addiction and Drug Abuse', in (eds.) Hardman, J., *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, (New York, 2001), 621–642.



Numerous recent studies have produced no cause for concern when using psychedelics on human subjects.<sup>94</sup> Furthermore, an FDA meeting claimed that psychedelic drugs have an acceptable risk-benefit ratio and that they are no more dangerous than other drugs routinely used in human research.<sup>95</sup> Reviews of published reports of adverse reactions and negative long-term effects due to psychedelics concluded that the evidence was controversial and, if any negative effects do exist, they are “subtle or nonsignificant”.<sup>96</sup> Overall recent modern science agrees with Cohen (who was cautious about the research conducted over them) but outright argued they were “astonishingly safe”.<sup>97</sup>

A 1984 review of adverse reactions to psychedelics found little evidence of harm in controlled settings.<sup>98</sup> Furthermore, in 2010, an analysis of harms caused to recreational users and to society by a range of psychotropic substances ranked LSD and psilocybin among the safest of all those studied.<sup>99</sup> The therapeutic index (toxic dose as a ratio of standard dose) for LSD and psilocybin is about 1000; for cocaine it is 15, for heroin it is 6, and for alcohol it is 10.<sup>100</sup> A substantial majority of therapists believe that LSD therapy was worth the risks.<sup>101</sup> Indeed the research data currently available seem to indicate that responsible use of psychedelics by experienced professionals should continue.<sup>102</sup>

## THERAPEUTIC POTENTIAL

One of the most important aspects of these drugs is how we harness their potential and how we use them on patients. For thousands of years there have been spiritual guides for the ingestion of this medicine, with years of experience and understanding themselves and this should be a large part of designing the methodology to safely and effectively practice psychedelic medicine. Within the medical community there is an understanding that psychedelics need to be treated with respect not rushed into commercialization.

It is now well established that psychedelics depend greatly on “set and setting”<sup>103</sup>. This refers to the way the experience is overwhelmingly coloured by the individual's mindset during the effects of the drug as well as the surroundings and atmosphere.<sup>104</sup> If psychedelics are administered to anxious or depressed subjects in unfamiliar laboratory conditions while impersonal assistants wander around in lab coats, the strong effects may cause them to believe that they are temporarily insane. Conversely, if the situation is more relaxed and researchers are sympathetic and understanding, the subjects will have an enjoyable and constructive session.<sup>105</sup> The importance of “set and setting” was also missed by some researchers who criticised early positive LSD studies for lacking controls. In investigators' zeal to eliminate outside influences, patients were sometimes physically restrained or put in frightening environments and not reassured if they became anxious.<sup>106</sup> Clearly this was not compatible with the comfortable and positive set and setting required for meaningful and useful outcomes. Many studies were criticised for the way their controls facilitated bad reactions in patients by reducing the comfort level and raising apprehensions about the trial.

Indeed Rick Strassman of the University of New Mexico School of Medicine (1990 to 1995 performed the first human study using psychedelic drugs in about 20 years, investigating the effects of DMT on 60 human subjects) argues “Psychedelics may be therapeutic to the extent that they elicit processes that are known to be useful in a therapeutic context: transference reactions and working through them; enhanced symbolism and imagery; increased suggestibility; increased contact between emotions and ideations; controlled regression; et cetera,”. The caution he implies “all depends, though, on set and setting...These same properties could also be turned to very negative experiences, if the support and expectation for a beneficial experience aren't there.”<sup>107</sup>

<sup>94</sup> Hasler, F., ‘Acute Psychological and Physiological Effects of Psilocybin in Healthy Humans’, *Psychopharmacology*, Vol. 172, No. 2 (2004), 145-156.

<sup>95</sup> Drug Abuse Advisory Committee 1992: 31.

<sup>96</sup> Halpern, J., & Pope, H., ‘Hallucinogens on the Internet: a vast new source of underground drug information’, *American Journal of Psychiatry*, Vol. 158, No. 3 (1999), 481-483.

<sup>97</sup> Cohen, S., ‘Lysergic Acid Diethylamide: Side-effects and Complications’, *Journal of Nervous and Mental Disease*, Vol. 130 (1960), 33-40.

<sup>98</sup> Strassman, R., ‘Adverse Reactions to Psychedelic Drugs’, *J Nerv Ment Dis*, Vol. 172 (1984), 577-95.

<sup>99</sup> Nutt, D., & King, L., & Phillips, L., ‘Drug Harms in the UK: a Multicriteria Decision Analysis’, *Lancet*, Vol. 376 (2010), 1558-65.

<sup>100</sup> Gable, R., ‘Comparison of Acute Lethal Toxicity of Commonly Abused Psychoactive Substances’, *Addiction*, Vol. 9 (2004), 686-96.

<sup>101</sup> Malleon, N., ‘Acute Adverse Reactions to LSD in Clinical and Experimental Use in the United Kingdom’, *British Journal of Psychiatry*, Vol. 118, No. 543 (1971), 229-230.

<sup>102</sup> Horton, R., ‘Reviving Research into Psychedelic Drugs’, *Lancet* Vol. 367, No. 9518 (2006), 1214.

<sup>103</sup> Brown, D., ‘Psychedelic Healing?’, *Scientific American Mind*, Vol. 18, No. 6, (2007), 66-71.

<sup>104</sup> Hoffer, A., ‘Treatment of Alcoholism with Psychedelic Therapy’, in (eds.) Aaronson, B., & Osmond, H., *Psychedelics: The Uses and Implications of Hallucinogenic Drugs* (New York, 1970), 357-365.

<sup>105</sup> Eisner, B., & Cohen, S., ‘Psychotherapy with Lysergic Acid Diethylamide’, *Journal of Nervous and Mental Disease*, Vol. 127, No. 6 (1958), 528-539.

<sup>106</sup> Dyck, E., ‘“Hitting Highs at Rock Bottom”: LSD Treatment for Alcoholism, 1950-1970’, *Social History of Medicine* Vol. 19, No. 2 (2006), 313-329.

<sup>107</sup> Brown, S., ‘Research Explores New Visions for Hallucinogens’, *Chronicle of Higher Education*, Vol. 53, No. 16 (2007) 12.

Some people are unsuitable for psychedelic experiences or obviously would not benefit from psychedelic-assisted therapy. The patient should be carefully screened and extensively prepared for the experience and qualified professionals must be on hand. Many negative consequences of psychedelic use are due to illicit misuse where this preparation has been absent. Furthermore, a good screening process will eliminate the possibility of psychopathologies being confused with the consequences of LSD use.<sup>108</sup>

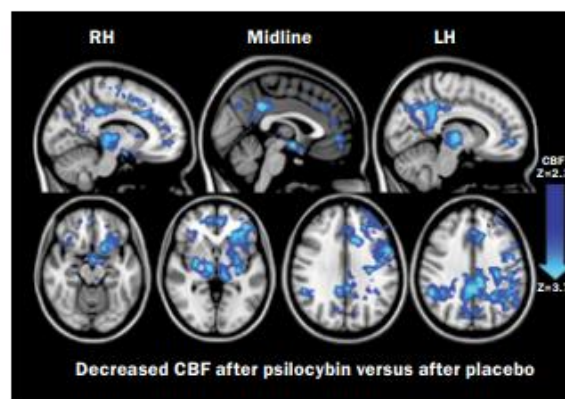
## PSILOCYBIN

Upon ingestion, psilocybin is rapidly converted to psilocin by the liver. Psilocin then acts as a partial agonist for some types of 5-hydroxytryptamine receptors (serotonin receptors), which leads to the profound mood and perceptual changes reported by users. It indirectly raises the concentration of dopamine (neurotransmitter linked to arousal and reward).<sup>109</sup>

British scientists have taken MRI's whilst individuals were experiencing the drug. Brain activity was widely reduced;

- That is, these mind-altering drugs decreased hemodynamic activity, including blood flow, in selected regions, such as the thalamus, the medial prefrontal cortex (mPFC), the ACC and the posterior cingulate cortex (PCC). Activity in these regions dropped by up to 20%, relative to before the injection. Even more striking, the deeper the reduction in activity in the ACC and mPFC, the stronger the subject felt the effects of the hallucinogen. Nowhere did activity show an increase.
- The communication between the PFC and cortical regions in the back of the brain was also disrupted.<sup>110</sup>

Blue areas show where there has been decreased cerebral blood flow (CBF) after psilocybin as compared with after saline (placebo). Remarkably, no significant increase in blood flow was detected in either the left hemisphere (LH) or the right hemisphere (RH).



This reduced activity in those regions allow the content of the limbic systems that process emotion and perhaps sensory cortices to play a relatively more dominant role. What is intriguing is that the regions that show the strongest reduction in activity are among the most heavily interconnected in the brain. They act like traffic circles or hubs that link disparate regions. Thus, the brain on psilocybin becomes more disconnected, more fragmented, which might explain some of the dissociative aspect's patients felt.

- Reducing activity in the brain default mode network, where we create our sense of self and ego (which filters all incoming info according to our personal needs and priorities) means our ego shifts from the foreground to the background and we see this as a part of a large field of awareness. Shift in awareness is important as feel more connected in a world bigger than ourselves becoming altruistic and lose more fear in death.

Psilocybin is generally well tolerated by healthy individuals, with hormone levels, liver function, and blood sugar typically remaining constant throughout an experience. As we have established “bad trips” are relatively rare

<sup>108</sup> Abrahart, D., 'A Critical Review of Theories and Research Concerning Lysergic Acid Diethylamide (LSD) and Mental Health' (Doctoral thesis, University of Portsmouth, 1998).

<sup>109</sup> <https://www.atai.life/programs/psilocybin/>

<sup>110</sup> Carhart-Harris, R., 'Neural Correlates of the LSD Experience Revealed by Multimodal Neuroimaging', *Proceedings of the National Academy of Sciences of the United States of America*, Vol. 113, No. 17 (2016) 4853–4858.

and seem to arise at high doses and in uncontrolled environments for those who are already vulnerable. Overall, psilocybin is approximately 100 times less potent than LSD and its effects persist about half as long.<sup>111</sup>

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## TREATMENTS

### Depressive Disorders (including treatment-resistant depression)

- Patients with depression spend too much time of self-reflection thus psilocybin may loosen this psychological spasm. Leading psychedelic researcher at Imperial College – Robin Carhart-Harris “when this organization collapses the self dissolves” allowing regions that are controlled by the cortex to become autonomous “the emotional centres have been let off the leash”.<sup>112</sup>
- In 2016, researchers at Imperial College London found that psilocybin coupled with psychological support seemed to “markedly reduce” depressive symptoms in twelve patients with unipolar treatment-resistant depression. Participants reported improvements in anxiety symptoms as well as their ability to take pleasure in their lives. Similar effectiveness was found in a randomized double-blind study examining the effects of psilocybin on depressive symptoms in patients with life-threatening cancer. Indeed, Roland Griffiths a psychiatrist leading psilocybin study at Johns Hopkins University argues “completely unique in terms of their pharmacology and alteration in mood”.<sup>113</sup>
- Most recent studies for its effects on depression are under trial in Usona Institute by Compass Pathways who have gone to regulatory agencies, after being granted FDA breakthrough status.

### Substance Abuse Disorders

- Many trials through the 1950s onwards were conducted on alcoholism, the most recent (2014-2020) being NYU trial by Michael Bogenschutz using psilocybin assisted therapy to treat alcoholism. Matt Johnson trial (2014) at Johns Hopkins using psilocybin to treat tobacco addiction. In 2018, University of Alabama, led by Peter Hendriks, studied psilocybin to treat crack cocaine addiction. University of Madison, Wisconsin (2018) trialed using psilocybin to treat opioid addiction.

### Anorexia and Obesity

- Other mental issues like anorexia, which is one of the most fatal psychiatric conditions with no current medication available for treatment, have responded well to psilocybin. At the Johns Hopkins Centre for Psychedelics and Consciousness Research, investigators have launched a clinical trial to determine whether two moderate to high doses of psilocybin can alleviate symptoms of anorexia nervosa when combined with motivational interview-based therapy.<sup>114</sup>

### Personality disorders

- In 2011, Roland Griffiths and colleagues published a study suggesting that, in addition to promoting increases in aesthetic appreciation, creativity, and imagination in users – a single high-dose of psilocybin may result in durable personality changes, with approximately half of healthy participants recording increases in openness (as measured by the NEO Personality Inventory). A follow up study published in 2017 found that doses of 20-30mg total elicited mystical type experiences that brought about lasting changes in altruism, gratitude, and connection to others when combined with spiritual practices like regular meditation.<sup>115</sup>

### OCD

- Psilocybin has also been safely used in the treatment of subjects with obsessive-compulsive disorder (OCD) and was associated with acute reductions in core OCD symptoms in several subjects.<sup>116</sup> In a

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<sup>111</sup> <https://www.atai.life/programs/psilocybin/>

<sup>112</sup> Kupferschmidt, K., ‘High Hopes: Psychedelic Drugs Fell from Grace in the 1960s’, *Science*, Vol. 345, No. 6192 (2014) 18–23.

<sup>113</sup> Ibid.

<sup>114</sup> <https://www.atai.life/programs/psilocybin/>

<sup>115</sup> <https://www.atai.life/programs/psilocybin/>

<sup>116</sup> Moreno, F., & Wiegand, C., & Taitano, E., & Delgado, P., ‘Safety, Tolerability, and Efficacy of Psilocybin in 9 Patients with Obsessive-Compulsive Disorder’, *J Clin Psychiatry*, Vol. 67 (2006), 1735-40.

double-blind study on subjects that had failed to respond to standard antidepressants, psychedelics have been shown to produce quick improvements.<sup>117</sup> These results were repeated in a study that showed 71% of patients felt better the day after treatment. In addition, 35% still felt better a week later and none improved when dosed with a placebo.<sup>118</sup> Other recent studies have shown that psychedelics can increase the sense of personal wellbeing or life satisfaction in 79% of volunteers and they have shown further potential in treating addictions.<sup>119</sup>

- In another 2006 study, researchers at the University of Arizona, led by psychiatrist Francisco Moreno, found that psilocybin relieved the symptoms of a small 'test group' of nine patients with OCD. All nine experienced improvements with at least some of the doses tested. "What we saw was a drastic decrease in symptoms for a period of time," Moreno says. "People would report that it had been years since they had felt so good."<sup>120</sup>

#### Terminal Cancer Distress

- Preliminary results of a current study led by psychiatrist Charles Grob of the Harbour-UCLA Medical Centre suggest that psilocybin may reduce the psychological distress associated with terminal cancer. This research seeks to measure the effectiveness of psilocybin on the reduction of anxiety, depression and physical pain in advanced-stage cancer patients. Grob's study is almost complete; 11 out of 12 subjects have already been treated. Although the formal data analysis has not been completed, "my impression," Grob says, "from just staying in touch with these people and following them is that some do seem to be functioning better psychologically. There seems to be less anxiety, improved mood and an overall improved quality of life. There also seems to be less fear of death."<sup>121</sup>
- Stephen Ross, MD, has been researching psilocybin treatment in cancer patients since 2009, reducing anxiety and fear of death, paving the way for the first ever Phase III trial. In a population study of 230, 152 respondents to the US National Survey on Drug Use and Health (NSDUH) from 2001 to 2004, a history of reported psychedelic use was associated with lower reported levels of serious psychological distress, the need for mental health treatment, and psychiatric medicine.<sup>122</sup>

#### LSD

The mechanism by which LSD works is mainly mediated by activation of serotonin receptors (namely 5HT2A receptors or 5hydroxytryptamine 2A receptor, 5-HT2AR) however like psilocybin the interactions between the receptor activation and the resulting impairment in cognition and induction of hallucinations are still poorly understood.

One study suggests that LSD-induced 5-HT2AR activation leads to a breakdown of inhibitory processes in the hippocampal prefrontal cortex. Specifically, it has demonstrated to reduce brain activity in the right middle temporal gyrus, superior/middle/inferior frontal gyrus, anterior cingulate cortex, and the left superior frontal and postcentral gyrus and cerebellum. Studies also have shown activation of the right hemisphere, altered thalamic functioning, and increased activity in the paralimbic structures and the frontal cortex; this all leads to

<sup>117</sup> Berman, R., 'Antidepressant Effects of Ketamine in Depressed Patients', *Biological Psychiatry*, Vol. 47, No. 4 (2000), 351-354.

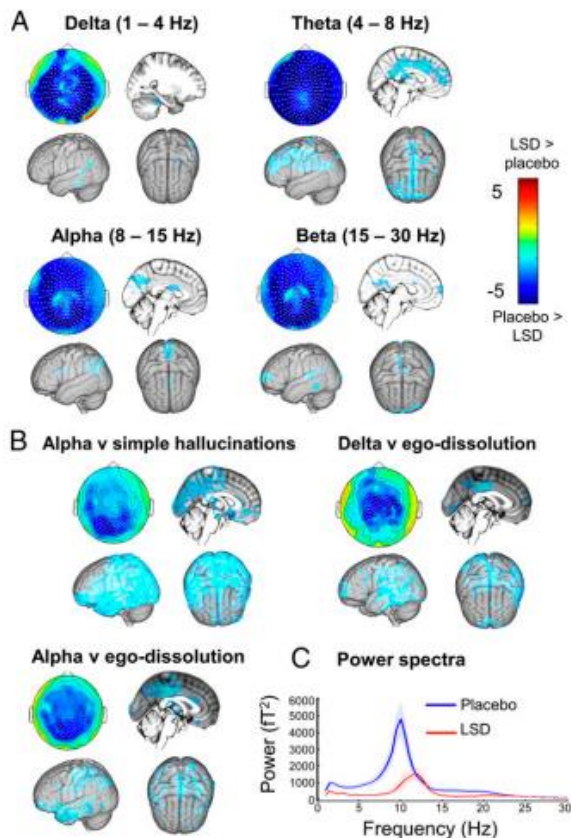
<sup>118</sup> Zarate, C., 'A Randomized Trial of an N-methyl-D-aspartate Antagonist in Treatment-Resistant Major Depression', *Archives of General Psychiatry*, Vol. 63 (2006), 856-864.

<sup>119</sup> Krupitsky, E., 'Single Versus Repeated Sessions of Ketamine-Assisted Psychotherapy for People with Heroin Dependence', *Journal of Psychoactive Drugs*, Vol. 39, No. 1 (2007), 13-19.

<sup>120</sup> Moreno, F., & Wiegand, C., & Taitano, E., & Delgado, P., 'Safety, Tolerability, and Efficacy of Psilocybin in 9 Patients with Obsessive-Compulsive Disorder', *J Clin Psychiatry*, Vol. 67 (2006), 1735-40.

<sup>121</sup> Grob, C., 'The Use of Psilocybin in Patients with Advanced Cancer and Existential Anxiety', in (eds.) Winkelman, M., & Roberts, T., *Psychedelic Medicine: New Evidence for Hallucinogenic Substances as Treatments*, (California, 2007).

<sup>122</sup> Kupferschmidt, K., 'High Hopes: Psychedelic Drugs Fell from Grace in the 1960s', *Science*, Vol. 345, No. 6192 (2014) 18-23.



**Fig. 5.** MEG results. (A) Statistical analysis of planar gradiometer-configured MEG data comparing LSD with placebo in the eyes-closed condition. Blue indicates less power under LSD. Units are t-statistics. Significant sensor clusters are marked such that stars correspond to  $P < 0.01$  and crosses to  $P < 0.05$  (corrected). Source localization results are also displayed. (B) Significant correlations between changes (decreases) in oscillatory power and subjective phenomena. (C) Power spectra for the significant sensor cluster in B (simple hallucinations), with placebo data plotted in blue and LSD in red ( $n = 14$ ).

the formation of induced visual imageries.<sup>123</sup> LSD has a high affinity for a range of different neurotransmitter receptors, but its characteristic psychological effects are thought to rest state functional connectivity (RSFC) in major resting state networks (RSNs) such as the default-mode network (DMN), and the emergence of novel patterns of communication. High-level cortical regions, such as the posterior cingulate cortex (PCC), and some of the principal effects of psilocybin revealed by MRI with studies suggest that an “entropic” effect on cortical activity is a key characteristic of the psychedelic state.<sup>124</sup>

Resting-state functional magnetic resonance studies showed that LSD acutely reduced the integrity of functional brain networks and increased connectivity between networks that normally are more dissociated. LSD increased functional thalamocortical connectivity and functional connectivity of the primary visual cortex with other brain areas. The latter effect was correlated with subjective hallucinations. LSD acutely induced global increases in brain entropy that were associated with greater trait openness 14 days later.<sup>125</sup>

Preliminary Report on the Effects of a Low Dose of LSD on Resting-State Amygdala Functional Connectivity LSD increased amygdala seed-based connectivity with the right angular gyrus, right middle frontal gyrus, and

the cerebellum, and decreased amygdala connectivity with the left and right postcentral gyrus and the superior temporal gyrus. This low dose of LSD had weak and variable effects on mood, but its effects on positive mood were positively correlated with the increase in amygdala–middle frontal gyrus connectivity strength.

LSD’s marked effects on the visual cortex did not significantly correlate with the drug’s other characteristic effects on consciousness, however. Rather, decreased connectivity between the parahippocampus and retrosplenial cortex (RSC) correlated strongly with ratings of “ego-dissolution” and “altered meaning,” implying the importance of this particular circuit for the maintenance of “self” or “ego” and its processing of “meaning.” Strong relationships were also found between the different imaging metrics, enabling firmer inferences to be made about their functional significance.<sup>126</sup>

## TREATMENTS

### Alcoholism

- In 2012 using data from six trials in alcoholism, a meta-analysis that compared treatment with LSD against controls in 536 people found that LSD treatment was favoured in terms of objectively measured improvements in alcohol misuse. They determined a 95% confidence increase of the possibility of change within the patient.<sup>127</sup>

<sup>123</sup> Jalal, B., ‘The Neuropharmacology of Sleep Paralysis Hallucinations: Serotonin 2A Activation and a Novel Therapeutic Drug’, *Psychopharmacology (Berl)*, Vol. 235, No. 11 (2018), 3083-3091.

<sup>124</sup> Carhart-Harris, R., ‘Neural Correlates of the LSD Experience Revealed by Multimodal Neuroimaging’, *Proceedings of the National Academy of Sciences of the United States of America*, Vol. 113, No. 17 (2016) 4853–4858.

<sup>125</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5603820/>

<sup>126</sup> Carhart-Harris, R., ‘Neural Correlates of the LSD Experience Revealed by Multimodal Neuroimaging’, *Proceedings of the National Academy of Sciences of the United States of America*, Vol. 113, No. 17 (2016) 4853–4858.

<sup>127</sup> Krebs, J., ‘Lysergic Acid Diethylamide (LSD) for Alcoholism’, *J Psychopharmacol*, Vol. 26, (2012), 994-1002.

## Anxiety

- In many psychiatric disorders, the brain may be viewed as having become entrenched in pathology, such that core behaviours become automated and rigid. Consistent with their “entropic” effect on cortical activity, psychedelics may work to break down such disorders by dismantling the patterns of activity on which they rest. Future work is required to test this hypothesis and the others that have been presented here as part of a broader initiative to properly utilize these valuable scientific tools.
- In patients with anxiety associated with life-threatening disease, anxiety was reduced for 2 months after two doses of LSD. In medical settings, no complications of LSD administration were observed. These data should contribute to further investigations of the therapeutic potential of LSD in psychiatry.<sup>128</sup>
- In substance abuse, it is well established that anxiety and stress are important triggers for relapse. It is possible that 5HT2A receptor downregulation by hallucinogens could help in stress-induced relapses. LSD may also have effects on the expression of brain-derived neurotrophic factor (BDNF) and glial cell line-derived neurotrophic factor (GDNF). Both play critical roles in neurogenesis, synaptic plasticity, learning, and memory. There is some evidence that LSD can induce neuroplastic changes suggesting a basis for the persistent behavioural changes. LSD also induces remodelling of pyramidal cell dendrites.<sup>129</sup>
- LSD Treatment in patients suffering from anxiety symptoms in severe somatic diseases or in psychiatric anxiety disorders (LSD-assist) is now in Phase II in Switzerland.<sup>130</sup>

## Cluster headaches

- LSD and psilocybin have been linked with relief of cluster headaches which are said to be more painful than giving birth without anaesthetics.<sup>131</sup> Conventional treatments are largely ineffective and have severe side effects.<sup>132</sup> Natural substances similar to LSD are commonly prescribed for migraines and psychedelics appear to be an effective treatment, 52% of sufferers self-medicating with psilocybin reported cluster period termination and 95% claimed that the remission period was extended. With LSD, 88% reported cluster period termination and 80% had an extended remission period.<sup>133</sup>
- Those reports intrigued Torsten Passie, a psychiatrist at the Hanover Medical School in Germany and an expert on LSD. So he, John Halpern, and other colleagues decided to test 2-bromo-LSD (BOL), which was developed by Sandoz, the Swiss company that discovered the psychedelic effects of LSD and marketed it as a drug for some time, as a kind of placebo compound in LSD trials.<sup>134</sup> The results of the Phase II trials in Switzerland showed it induced remission in patients suffering from cluster headache (CH).<sup>135</sup>

## Alzheimer Dementia (“AD”)

- It is a progressive neurological disorder characterized by extracellular amyloid protein deposition and intracellular tau protein aggregates (tangles) that, in accumulation, are associated with a variety of pathological processes including microtubular damage, axonal transport disruption and, ultimately, cell death. The hippocampus, a key structure in the ability to learn and retain information and a site for neurogenesis, is particularly vulnerable to AD pathology and one of the earliest parts of the brain to be affected by the disease.
- Psychedelics induce brain plasticity and modify connectivity between brain regions and there is considerable anecdotal evidence of cognitive benefits from micro-dosing—a dose that does not cause perceptual change or impair functioning.<sup>136</sup> Promoting neuroplasticity and neurogenesis via the 5HT2A-

<sup>128</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5603820/>

<sup>129</sup> Kvam, T., & Stewart, L., & Andreassen, O., ‘Psychedelic Drugs in the Treatment of Anxiety, Depression and Addiction’, *Tidsskr Nor Lægeforen*, Vol. 138, No. 18 (2018).

<sup>130</sup> <https://clinicaltrials.gov/ct2/show/NCT03153579>

<sup>131</sup> Horgan, J., ‘Psychedelic Medicine: Mind bending, Health Giving’, (New Scientist, 2005).

<sup>132</sup> Honigsbaum, M., ‘Headache Sufferers Flout New Drug Law’, (The Guardian, 2005).

<sup>133</sup> Sewell, R., ‘Response of Cluster Headache to Psilocybin and LSD’, *Neurology*, Vol. 27, No. 66 (2006), 1920-1922.

<sup>134</sup> <https://www.sciencemag.org/news/2011/06/lsd-alleviates-suicide-headaches>

<sup>135</sup> <https://clinicaltrials.gov/ct2/show/NCT03781128>

<sup>136</sup> Carhart-Harris, R., ‘The Therapeutic Potential of Psychedelic Drugs: Past, Present, and Future’, *Neuropsychopharmacology*, Vol. 42, No. 11 (2006), 2105-2113.

R in regions such as the hippocampus could theoretically help protect this and other brain structures and may, therefore, hold potential for treating AD.<sup>137</sup>

- Shlomi Raz (CEO of Eleusis Therapeutics) demonstrates that if you look at the symptoms of Alzheimer's and the disease progression, not only is the loss of 2A receptor expression correlated with cognitive impairment and toxic amyloid burden, but you also have a significant increase in the incidence of depression and anxiety, which are psychiatric conditions known to be significantly influenced by serotonin 2A receptor function. LSD, in particular, seemed like an attractive candidate for such a therapeutic approach, as it is capable of potent and prolonged activation of the serotonin and dopamine neurotransmission receptors implicated in Alzheimer's disease, and specifically the serotonin 2A receptor.<sup>138</sup>

## MDMA

MDMA (3,4-methylenedioxy-N-methylamphetamine) is also chemically classified as a phenethylamine, but its action in the brain is substantially different from that of other drugs discussed in this report. In contrast to most psychedelics, MDMA does not directly stimulate serotonin 2A receptors but instead causes dopamine, serotonin and norepinephrine (another neurotransmitter) to be released from their stores in neuron endings.<sup>139</sup> There is some controversy about whether MDMA has neurotoxic effects. Most researchers believe, however, that the occasional moderate use of MDMA at therapeutic doses would not be damaging. There have been no recent studies using mescaline, although MAPS plan to initiate some in the future.

In contrast to the traditional psychedelics, the dissociative anesthetics selectively bind to Nmethyl-D-aspartic acid (NMDA) receptors, blocking the neurotransmitter glutamate from activating these receptors. This is because glutamate is an essential neurotransmitter that activates neurons, this blocking effect seems to prevent the processing of sensory information by the brain.

These effects are thought to result in the anxiolytic, prosocial and empathic responses seen with MDMA administration in humans. As a result, MDMA is often classified as an entactogen rather than a typical psychedelic.<sup>140</sup> Several studies in humans have demonstrated that MDMA increases plasma levels of oxytocin.<sup>141</sup> MDMA's entactogenic effects typically last approximately six hours and are hypothesized to promote a sense of psychological safety which may allow patients to more effectively address their individual traumas during psychotherapy.<sup>142</sup>

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## TREATMENTS

### PTSD

- Psychiatrist Michael Mithoefer in Charleston, S.C., is currently running an MDMA study for treatment-resistant PTSD victims of crime, war or childhood sexual abuse. So far 17 out of 20 such subjects have already undergone the experimental therapy. "At this point the results are very promising," Mithoefer says. "It certainly seems that there's very good reason to go on to larger Phase III trials."<sup>143</sup>
- MAPS recently published results from their Phase II clinical trials, which demonstrated that after MDMA-assisted psychotherapy, 56% of participants no longer met the criteria for PTSD two-months after the final session. Additionally, researchers followed up with 91 participants twelve months later and found that 67% still did not meet PTSD criteria, with many reporting substantial improvements in many areas in their life, including relationships, sleep quality, and general wellbeing. With a Phase III

<sup>137</sup> <https://www.frontiersin.org/articles/10.3389/fnsyn.2020.00034/full#B25>

<sup>138</sup> <https://www.forbes.com/sites/abbierosner/2020/02/21/microdosed-lsd-may-finally-be-the-breakthrough-for-alzheimers-disease/?sh=4bc7745053a8>

<sup>139</sup> Brown, D., "Psychedelic Healing?", *Scientific American Mind*, Vol. 18, No. 6 (2007) 66–71.

<sup>140</sup> <https://www.prnewswire.com/news-releases/atai-life-sciences-launches-empathbio-to-treat-post-traumatic-stress-disorder-with-novel-mdma-product-301117010.html>

<sup>141</sup> <https://www.atai.life/programs/mdma-derivative/>

<sup>142</sup> <https://www.prnewswire.com/news-releases/atai-life-sciences-launches-empathbio-to-treat-post-traumatic-stress-disorder-with-novel-mdma-product-301117010.html>

<sup>143</sup> Mithoefer, M., "MDMA-Assisted Psychotherapy for the Treatment of Post Traumatic Stress Disorder", in (eds.) Winkelman, M., & Roberts T., *Psychedelic Medicine: New Evidence for Hallucinogenic Substances Treatments*, (California, 2007).

trial now underway, many anticipate MDMA to be the first psychedelic-like drug to be approved by the FDA for the treatment of PTSD.

- It is hypothesized that the effects of MDMA allows a person to voluntarily navigate difficult emotions when recalling traumatic memories due to a reduction in activity in the amygdala, a region of the brain activated during fear responses. This reduction in fear allows for a decreased defensiveness about revisiting painful experiences, making room for new perspectives and different responses towards deep-rooted traumatic memories.

#### Cancer Anxiety and Depression

- A study at Harvard, led by John Halpern, will begin shortly to look into MDMA-assisted psychotherapy in subjects with anxiety associated with advanced-stage cancer (similar to Grob's psilocybin study) using measures to evaluate anxiety, pain and overall quality of life.

### DMT

N,N-dimethyltryptamine (DMT), is a psychoactive indole alkaloid present in the South American beverage Ayahuasca, an entheogenic brew that often contains Banisteriopsis caapi vine, the Psychotria viridis shrub, as well as a variety of other ingredients. Critically, in this form, DMT's effects can persist for up to 3-6 hours, due to the presence of monoamine oxidase inhibitors (MAOIs), which prevent oxidization of DMT in the digestive tract and allows it to be absorbed in the stomach and small intestine; without this, the body metabolizes orally ingested DMT too quickly to allow it to have any effect.<sup>144</sup>

Structurally, DMT is similar to psilocybin, closely resembling the neurotransmitter serotonin and the hormone melatonin, associated with feelings of calm and sleep, respectively. Additionally, though DMT is endogenously produced by some mammalian tissues, including the human lungs and brain, its function continues to be debated. Like many psychedelic compounds, DMT acts on a variety of 5-HT receptors: In particular, it is a partial agonist of the 5-HT<sub>1A/2A/2C</sub> receptors, primarily in cortical neurons and the limbic system, where it is believed to increase neuroplasticity and decrease functional connectivity, respectively. This is critical since neural plasticity is especially important for exerting the anti-depressant effects of serotonergic psychedelics.<sup>145</sup>

The experiences reported by both recreational users and clinical trial participants include an altered reality, visualization of geometric patterns with closed eyes, altered sense of time and space, unusual somatic sensations, perception of dream-like situations and presence of external sentient forms, among others. However, unlike most psychedelics, for example psilocybin, DMT exhibits extremely rapid onset and short duration of action.

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## TREATMENTS

### Depression

- Ideal for psychedelics-assisted psychotherapy. Despite similarity to other psychedelics, however, DMT exhibits comparatively more rapid onset and shorter duration of action when not administered alongside the MAOIs present in the 'Ayahuasca brew'. For example, unlike a psilocybin experience, which can last upwards of 6-hours, DMT's hallucinogenic effects can pass in just 15 minutes.
- While there have been few well-controlled clinical studies exploring isolated DMT as a treatment for depression, several recent studies have demonstrated the utility of Ayahuasca in the treatment of major depression.<sup>146</sup> In rat cells, in vitro assays have shown DMT to promote neuroplasticity, as assessed by neuronal growth and increased synaptic connections, both processes correlated with

<sup>144</sup> <https://www.atai.life/programs/n-n-dimethyltryptamine/>

<sup>145</sup> Ibid.

<sup>146</sup> <https://pubmed.ncbi.nlm.nih.gov/25806551/>



improvements in depressive symptoms.<sup>147</sup> Moreover, using multivariate EEG observations of DMT's effects on brainwaves have shown changes hypothesized to be beneficial for depression.

## KETAMINE

Ketamine is an anaesthetic with analgesic, stimulant and psychedelic properties. Chemically related to phencyclidine (PCP), it has been used extensively in human and veterinary medicine. Like PCP, it is a 'dissociative' anaesthetic which means that patients feel detached and remote from their immediate environment. Users say that under its influence they assume a different point of view, outside of body and self.<sup>148</sup>

Ketamine appears to hold particular promise as a psychedelic therapy because it is already among Western medicine's pharmacopoeia. In addition to being part of a different chemical class of drugs than the other psychedelics, ketamine is in a separate legal class as an FDA-approved Schedule III drug. This designation means that any physician can administer it for an off-label use if he or she believes it will help the patient.

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## TREATMENTS

### Depression, Anxiety and Addiction

- The benefits of dissociative anaesthetics such as ketamine may simply be the result of enduring biochemical changes in the brain but they can accomplish dramatic results in many areas of mental health.
- In 2006 Carlos Zarate of the National Institute of Mental Health published a study demonstrating ketamine's unusual antidepressant properties.<sup>149</sup> A single infusion of ketamine relieved symptoms of depression in some patients within a few hours, and that relief persisted for several days. This was the third study that showed ketamine's powerful and enduring antidepressant effects. In an intriguing finding from one of the previous studies, subjects received the ketamine as an anaesthetic for orthopaedic surgery—so they were not even conscious during the mind-altering segment of the drug's action in the brain—and the antidepressant effects occurred postoperatively.<sup>150</sup>
- In other work seeking to help cure addicts, a preliminary ketamine study, in which psychiatrist Evgeny Krupitsky of St. Petersburg, Russia, treated 59 patients with heroin dependency, produced encouraging results. And the Iboga Therapy House in Vancouver, Canada, has recently begun a study that has so far successfully treated three out of 20 opiate-addicted subjects with ibogaine. The experimental procedure substantially reduced the withdrawal symptoms associated with opiate addiction, helping the addicts to recover and break their dependency on the drug.<sup>151</sup>

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<sup>147</sup> [https://www.cell.com/cell-reports/pdf/S2211-1247\(18\)30755-1.pdf](https://www.cell.com/cell-reports/pdf/S2211-1247(18)30755-1.pdf)

<sup>148</sup> <https://www.drugwise.org.uk/ketamine/>

<sup>149</sup> Walter, B., 'Good News about Depression', (Scientific American Mind, 2007)

<sup>150</sup> <https://www.seattletimes.com/seattle-news/health/peoples-pharmacy-surprising-drug-for-severe-depression/>

<sup>151</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5996271/>

## INVESTMENT OPPORTUNITIES IN THE PSYCHEDELIC INDUSTRY

## PSYCHEDELICS AND THE MARKET

Investors are starting to bet big on psychedelic medicine. Recent reports indicate that the global market for functional mushrooms, is forecasted to reach \$34.3 billion USD by 2024 and continues growing at a respectable CAGR of 8%.<sup>152</sup>

Unlike cannabis, which remains federally illegal in the U.S., the work psychedelic companies are doing is legal. This creates a greater opportunity to access growth capital from private investors who may not want to touch cannabis. It also sets the industry apart with it also being a more concentrated space because the barriers to entry are much higher.<sup>153</sup> The U.S. Food and Drug Administration (USFDA) status on the use of psychedelics appears to be evolving, subsequent to breakthrough therapy status for treatment-resistant depression in 2020 which appears poised to receive approvals in 2021.

Ronan Levy (Co-Founder and CEO of Field Trip) says the legal cannabis market, which is expected to hit \$19 billion in annual sales this year, has nothing on the hallucinogenic drugs “Psychedelics as an industry is much larger and more significant than cannabis,” he argues. “The way to frame the psychedelic industry is what chunk of the \$240 billion U.S. mental health market are psychedelics going to take? I think it’ll be most of it.”<sup>154</sup>

Adding further legitimacy to the space, Johnson & Johnson, the pharma giant, puts years of investment into studying into the benefits and potential side effects of esketamine. Its approval by the FDA represented the first new drug for depression in decades and Brad Loncar, a biotech investor who specializes in cancer and rare diseases, argues the FDA’s decision “is the ultimate signal for investors...It shows that there’s a regulatory path forward for this class of drugs, which typically causes a flood of investment in the area.”<sup>155</sup>

Indeed, a few weeks after the U.S. FDA approved the Johnson & Johnson’s ketamine-like nasal spray for depression, a group of European technology investors just got together for the largest-ever private financing round for a psychedelic medicine biotech company, ATAI.<sup>156</sup> While the UK remains the main European hub for psychedelics research, a recent €105M Series C round from the German player ATAI Life Sciences suggests the rest of Europe may start to catch up.<sup>157</sup> After the US and Canada, the UK is one of the big hubs of the field. A large part of this influence comes from the UK firm Compass Pathways, which is partly owned by ATAI. Compass gave a huge jolt to the field in September 2020 with a €108M Nasdaq IPO and its stock price was swiftly driven up by 70%.<sup>158</sup>

MAPS have raised millions to advance clinical trials on MDMA, most recently raising \$30 million to complete a Phase III study in veterans.<sup>159</sup>

Acadia Pharmaceuticals has been adding to its pipeline of late, most recently picking up new Alzheimer’s and dementia candidates in a milestone-heavy deal with Vanderbilt University. Now, in a larger deal, they’ve added a new preclinical and early-stage clinical pipeline of pain drugs, buying out CerSci Therapeutics for \$52.5 million upfront and \$887 million in milestones. The company had been developing for multiple neurological indications but had been focused on non-opioid painkillers for acute and chronic pain. A lead compound, ACP-044, was shown tolerable in Phase I studies. Acadia said a Phase II study is planned for 2021<sup>160</sup> Most recently in Canada seventeen healthcare professionals have been approved to use psilocybin for professional training.<sup>161</sup>

<sup>152</sup> <https://www.globenewswire.com/news-release/2020/11/26/2134221/0/en/Pure-Extracts-Advances-Plans-for-the-Processing-of-Functional-Mushroom-Formulations.html>

<sup>153</sup> <https://www.bloomberg.com/news/articles/2020-02-11/move-over-pot-psychedelic-companies-are-about-to-go-public>

<sup>154</sup> <https://www.forbes.com/sites/willyakowicz/2020/10/07/psychedelic-therapy-company-field-trip-health-goes-public-to-revolutionize-mental-health-treatments/?sh=5a9baef179a5>

<sup>155</sup> <https://www.cnn.com/2019/03/27/psychedelic-medicine-start-ups-vet-ketamine-psilocybin-for-depression.html>

<sup>156</sup> <https://www.cnn.com/2019/03/27/psychedelic-medicine-start-ups-vet-ketamine-psilocybin-for-depression.html>

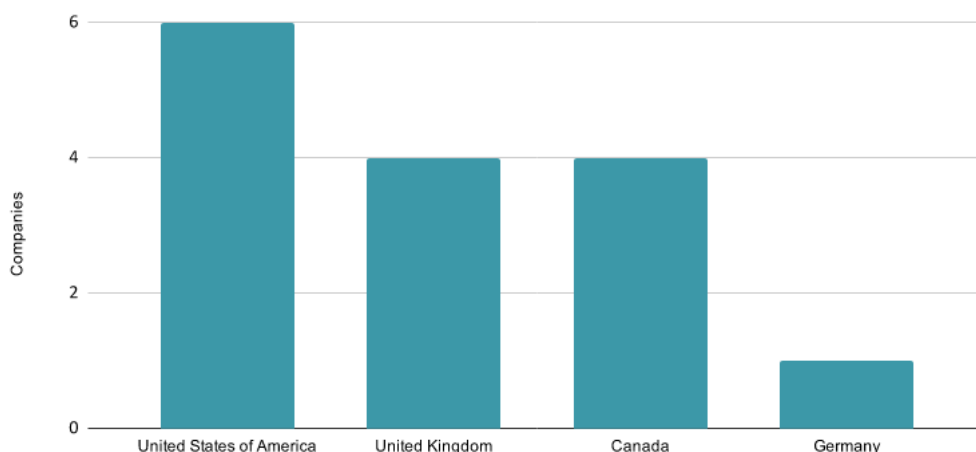
<sup>157</sup> <https://www.labiotech.eu/brain/atai-compass-pathways-psychedelics/>

<sup>158</sup> <https://www.labiotech.eu/brain/atai-compass-pathways-psychedelics/>

<sup>159</sup> <https://endpts.com/atai-adds-mdma-biotech-to-growing-list-of-psychedelic-makers-acadia-adds-52-5m-upfront-pain-buyout/>

<sup>160</sup> <https://endpts.com/atai-adds-mdma-biotech-to-growing-list-of-psychedelic-makers-acadia-adds-52-5m-upfront-pain-buyout/>

<sup>161</sup> <https://therapsil.ca/17-canadian-healthcare-professionals-approved-to-use-psilocybin-for-professional-training/>



*Companies developing psychedelic treatments for mental health disorders grouped by headquarters location. Source: GlobalData.*

George Goldsmith, Co-Founder of Compass Pathways, in a recent interview with The Telegraph comments “This isn’t a place to be fast and loose...It’s a place to do the highest quality science at the biggest and best scale you can. But we need to get it absolutely right. Psychedelic research was out in the cold for 50 years. If we get it wrong, are we going to wait for another 50?”. Cosmo Feilding-Mellen, the CEO of UK psychedelics startup Beckley Psytech added that Compass’ IPO “reflects the fact that psychedelic medicines are no longer a taboo, they are something that mainstream media, business, and healthcare can support.”<sup>162</sup>

Organization	Phase	Indications	Company headquarters
Multidisciplinary Association for Psychedelic Studies	III	Post-traumatic stress disorder	US
Mind Medicine	II	Anxiety disorders; cluster headaches	US
Compass Pathways	II	Clinical depression	UK
Yale University	II	Clinical depression; nicotine addiction	US
DemeRx	I	Opioid addiction	US
Eleusis	I	Alzheimer’s disease	UK

*Organizations developing psychedelic treatments for mental health disorders at the clinical stage. Source: GlobalData.*

## UK AND EUROPEAN COMPANIES

### COMPASS PATHWAYS (“CMPS” – NASDAQ)

[www.compasspathways.com](http://www.compasspathways.com)

In 2016 co-founders George Goldsmith (CEO) and Ekaterina Malievskaia (CIO) created Compass Pathways based in London, UK. The Company is pioneering the development of a new model of psilocybin therapy, where its proprietary formulation of synthetic psilocybin, COMP360, is administered in conjunction with psychological support.

<sup>162</sup> <https://www.labiotech.eu/brain/atai-compass-pathways-psychedelics/>

## About

The FDA Phase IIb clinical trial of psilocybin therapy for treatment resistant depression is expected to have results in 2021.<sup>163</sup> The psychological support is developed alongside the pharmacological aspect as they are training therapists through FDA-approved programmes.<sup>164</sup> They are opening 20 new trial sites across Europe and North America (bringing their trials to 21 sites in 10 countries including Czech Republic, Denmark, Ireland, Portugal and Spain).<sup>165</sup>

- Also strengthened their board and leadership team with appointments of Linda McGoldrick as non-Executive Director; Greg Ryslik as Senior Vice President, Data Science, Machine Learning and Digital Health Research; and Stephen Schultz as Senior Vice President, Investor Relations and established Drug Discovery Center with the University of the Sciences in Philadelphia.<sup>166</sup>

They collaborate with academic institutions and researchers as shown below, providing psilocybin to research free of charge, in exchange for the right to use safety data.<sup>167</sup>



They also have partnerships with

- The Psychiatry Consortium
  - In November 2020 they joined as a member of a strategic collaboration of leading medical research charities and pharmaceutical companies focusing on the challenge of identifying and validating novel drug targets to address the unmet therapeutic needs of the people living with mental health conditions.
- The Grady Trauma Project
  - Compass is supporting the group in research to investigate perceptions of psychedelics in underserved groups, particularly racial and ethnic minorities, to help inform best practices. The project focuses on Post-Traumatic Stress Disorder and the clinical and physiological implications of trauma exposure.
- Mindstrong Health delivers digital biomarkers of brain health.
  - They are working with Mindstrong Health on our treatment-resistant depression clinical trial to assess digital biomarkers as exploratory clinical endpoints.

<sup>163</sup> <https://www.globenewswire.com/news-release/2020/10/15/2109066/0/en/Trends-in-Psychedelic-Drugs-Research-and-Four-Stocks-You-Should-Know-About.html>

<sup>164</sup> <https://compasspathways.com/our-research/psilocybin-therapy/about-psilocybin-therapy/>

<sup>165</sup> <https://www.bloomberg.com/news/articles/2020-02-11/move-over-pot-psychedelic-companies-are-about-to-go-public>

<sup>166</sup> <https://www.globenewswire.com/news-release/2020/11/12/2125453/0/en/COMPASS-Pathways-plc-announces-financial-results-for-third-quarter-2020.html>

<sup>167</sup> <https://compasspathways.com/our-research/psilocybin-therapy/investigator-initiated-studies/#from-subnav>

## Funding

Compass Pathways is the largest and best-funded public psychedelic company so far. €68M Series B round in March<sup>168</sup>, as of November, they announced their financial results for third quarter with the complete upsized initial public offering on Nasdaq raising \$146.6 million. It the first psychedelic company to be listed on a U.S. exchange and has a market cap of \$1.37 billion.<sup>169</sup> On 27<sup>th</sup> April 2021, they announced the launch of a further round of 4,000,000 NASDAQ listed ADS.

## Investors

- ATAI is the largest investor in Compass Pathways. ATAI invested alongside Peter Thiel, the iconoclastic Silicon Valley investor and Facebook board member who is increasingly dabbling in health and biotech. ATAI co-founders Lars Wilde and Florian Brand are both affiliated with Compass; a third founder, Christian Angermayer, is a German entrepreneur and investor.<sup>170</sup>

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## BECKLEY PSYTECH

<https://www.becklepsytech.com/>

In 2019 co-founders Amanda Feilding and Cosmo Feilding-Mellen created Beckley Psytech – a company dedicated to helping patients suffering from neurological and psychiatric disorders by developing a pipeline of psychedelic compounds into licensed pharmaceutical medicines. Their vision is supplemented by their partnership with the Beckley Foundation.<sup>171</sup>

## About

### Beckley Foundation

- In 1998 Amanda set up the Beckley Foundation, a non-profit NGO focused on evidence-based drug policy reform and scientific research into psychedelic medicines. Over the last 20 years the Beckley Foundation has become a world-famous pioneer in psychedelic research. Beckley Psytech will have first opportunity to support the commercialisation of the Foundation’s intellectual property and will allocate a share of its revenues to fund the Foundation’s ongoing research as part of its commitment to corporate social responsibility.
- Highlights of the Beckley Foundation’s work include:
  - 2007 - First Ethics Committee approval of LSD study since prohibition
  - 2009 - Beckley-Imperial Psychedelic Research Program
  - 2012 - First ever brain imaging study on psilocybin
  - 2014 - First ever brain imaging study on LSD
  - 2014 - Psilocybin Tobacco Addiction Study
  - 2016 - Psilocybin Treatment Resistant Depression
  - 2017 - Ayahuasca Neurogenesis study
  - 2018 - LSD Micro-dosing study

They are using their Series A funding to advance its lead programme exploring the use of synthetic 5-MeO-DMT, a unique psychedelic agent with a short duration of action, in the treatment of neuropsychiatric diseases. The funding will help with scaling up resources to develop novel pharmaceutical formulations and delivery methods for synthetic 5-MeO-DMT, as well as to progress preclinical and clinical trials.

The Beckley Psytech team comprises talent from across the psychedelic and drug discovery fields. It boasts an executive team led by Marc Wayne, a pioneer of the Canadian medical cannabis industry, as Chairman of Board and CEO Cosmo Feilding-Mellen, a serial drug development entrepreneur specialising in the science of

<sup>168</sup> <https://www.labiotech.eu/brain/atai-compass-pathways-psychedelics/>

<sup>169</sup> <https://www.forbes.com/sites/willyakowicz/2020/10/07/psychedelic-therapy-company-field-trip-health-goes-public-to-revolutionize-mental-health-treatments/?sh=5a9baef179a5>

<sup>170</sup> <https://www.cnn.com/2019/03/27/psychedelic-medicine-start-ups-vet-ketamine-psilocybin-for-depression.html>

<sup>171</sup> <https://www.psychedelicfinance.com/articles/global-investors-back-psychedelic-medicine-start-up-with-3-8m-series-a-round>

psychoactive drugs. Dr Steve Wooding, the former head of global commercial strategy for Janssen, Johnson and Johnson's pharmaceutical division, is the company's Chief Scientific Officer.<sup>172</sup>

### Funding

#### Investors

- Mediq Ventures
- Berti Investments
- Jam Jar Investments
- Murray Goldman

Prominent global biotech investors including Canadian businessman Greg Bailey, CEO of bio-pharma development company Juvenescence, and Jim Mellon, a renowned international investor and Juvenescence chairman, are supporting a \$3.8m Series A round which will be used to scale the business, build out the team and progress drugs through clinical trials. They join founding investor Chris Schnarr, a former director of world-leading diversified cannabis company Canopy Growth, as shareholders.<sup>173</sup>

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### SMALL PHARMA – (ABOUT TO LIST ON THE TSX)

[www.smallpharma.co.uk](http://www.smallpharma.co.uk)

Small Pharma aims to bring a new paradigm to the treatment of depression and other mental health conditions through psychedelic-assisted therapy. Founded in 2015 by CEO Peter Rands – an Oxford Chemistry graduate, they have a team of leading experts in the field of psychedelic research including their Chief Scientific Officer - Carol Routledge – who has over 30 years in the UK and US pharmaceutical and biotechnology sectors.

In December 2020, Small Pharma announced they had received regulator approval from the UK regulators for a world's first DMT clinical trials to explore use of DMT for depression.

Also in December 2020, it was announced that Unilock Capital Corp (a Special Purpose 'Capital Pool' Vehicle listed on TSX-V) would purchase all the issued and outstanding shares in Small Pharma – as a 'qualifying transaction'. A private placement raise of \$58m closed in March 2021 – run by Canaccord Genuity and Eight Capital with significant institutional investors from UK, US and Canada taking a significant proportion of the placement. The resulting company will be renamed as Small Pharma Inc and start trading in March 2021.

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### ELEUSIS

<https://www.eleusisltd.com/>

Founded in 2013, by CEO Shlomi Raz, Eleusis is a private UK biotechnology company that is demonstrating the benefits of psychedelics on treating Alzheimer's with their studies serving to accelerate their efforts to transform psychedelics into medicines.<sup>174</sup>

#### About

Raz wanted to prioritize the development of a new "not-so-psychedelic psychedelic" drug candidate for use in ophthalmology, for the treatment of retinal disease. The idea is that it will be a much more cost-effective path for demonstrating the anti-inflammatory and neuroprotective effects of this drug class. This approach would also set the foundation, both commercially as well as scientifically, to advance LSD into Phase II trials for Alzheimer's.<sup>175</sup> Having completed Phase I clinical trial results published in Psychopharmacology demonstrating

<sup>172</sup> <https://www.psychedelicfinance.com/articles/global-investors-back-psychedelic-medicine-start-up-with-3-8m-series-a-round>

<sup>173</sup> <https://www.psychedelicfinance.com/articles/global-investors-back-psychedelic-medicine-start-up-with-3-8m-series-a-round>

<sup>174</sup> <https://www.businesswire.com/news/home/20200305005059/en/Elleusis-Announces-Published-Preclinical-Research-Revealing-Long-Lasting-Antidepressant-Like-Effects-of-Psychedelics-When-Compared-to-Ketamine-in-Animals>

<sup>175</sup> <https://www.forbes.com/sites/abbiorosner/2020/02/21/microdosed-lsd-may-finally-be-the-breakthrough-for-alzheimers-disease/?sh=4bc7745053a8>

that LSD is well-tolerated in healthy older adults they intend to look toward a Phase II trial in LSD to research what the scientific research has shown: that LSD may have significant potential in treating Alzheimer's disease.

#### Funding

Series A \$3.5 million and in July 2020 a later stage VC drew in \$12.5M with 4 investors, including San Diego State University Research Foundation, the Government of the UK, a Noetic Psychedelic Fund and Tom Rutledge.<sup>176</sup>

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#### AWAKN LIFE SCIENCES

[www.awaknlifesciences.com](http://www.awaknlifesciences.com)

Founded in 2020, Awakn Life Sciences is a clinical-biotech company researching, developing and delivering evidenced based psychedelic medicine to treat Addiction and other mental health conditions.

They have a dual strategic focus to develop and commercialise psychedelic medicines to treat patients in a UK and EU chain of medical psychedelic clinics. Their first ketamine-assisted therapy clinic opened in March 2021 in Bristol and they have plans to roll out a further 15 to 20 clinics in UK and Europe in the next 2 years.

Their Scientific Advisory Team includes Professor David Nutt, Dr Michael Mithoefer, Professor Celia Morgan and Professor Matthew Johnson – all globally recognised experts in psychedelic medicine research.

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#### ATAI LIFE SCIENCES

<https://www.atai.life/>

In 2018 co-founders Christian Angermayer, Florian Brand and Lars Wilde created ATAI Life Sciences as a global biotech company builder. German-born it has quickly become the most prominent private promoter and driver of psychedelic therapy.<sup>177</sup> With bases in New York, and San Diego they are developing psychedelic and non-psychedelic compounds for various mental health indications. They combine funding, technology, scientific and regulatory expertise with a focus on psychedelic therapy and other drugs with differentiated safety profiles and therapeutic potential.<sup>178</sup> George Petrocheilos, Co-Founder & Managing Partner of Catalio Capital Management argues "Christian and the ATAI team have singlehandedly invented and created an entire sector, and have built with ATAI the leading company in it," said "Their work has the potential to change the lives of hundreds of millions of people, and we are proud to be an investor."<sup>179</sup>

#### About

Their recent financing will be used primarily to fund pre-clinical and clinical development of ATAI's existing mental health programs, to expand its drug candidate pipeline and further advance ATAI's platform technologies. The Company expects the proceeds to provide the necessary runway to accomplish several key clinical milestones including Phase 2 data readouts for arketamine in treatment resistant depression at Perception Neuroscience and ibogaine in opioid use disorder at DemeRx, as well as the completion of Phase 1 and initiation of Phase 2 trials at four other programs.

- GABA Therapeutics and ATAI Life Sciences partner to develop a novel GABA modulator for the treatment of mood disorders.<sup>180</sup>
- ATAI Life Sciences launches EmpathBio to treat post-traumatic stress disorder with novel MDMA product in August.<sup>181</sup>
  - EmpathBio is focused on developing MDMA derivatives with different pharmacological profiles than MDMA. The company believes that such changes may permit the entactogenic effects of MDMA to be separated from some of the known adverse effects. If successful, such

<sup>176</sup> <https://pitchbook.com/profiles/company/154373-05#overview>

<sup>177</sup> <https://endpts.com/atai-adds-mdma-biotech-to-growing-list-of-psychedelic-makers-acadia-adds-52-5m-upfront-pain-buyout/>

<sup>178</sup> <https://www.atai.life/mission/>

<sup>179</sup> [https://www.prnewswire.com/news-releases/atai-life-sciences-announces-closing-of-125-million-series-c-financing-round-301178915.html?tc=eml\\_cleartime](https://www.prnewswire.com/news-releases/atai-life-sciences-announces-closing-of-125-million-series-c-financing-round-301178915.html?tc=eml_cleartime)

<sup>180</sup> <https://www.prnewswire.com/news-releases/gaba-therapeutics-and-atai-life-sciences-partner-to-develop-a-novel-gaba-modulator-for-the-treatment-of-mood-disorders-300922354.html>

<sup>181</sup> <https://www.prnewswire.com/news-releases/atai-life-sciences-launches-empathbio-to-treat-post-traumatic-stress-disorder-with-novel-mdma-product-301117010.html>

an approach could help minimize some of the transient physiological changes caused by MDMA, potentially expanding the pool of PTSD patients who will be medically eligible for the therapy.

- ATAI Life Sciences takes on opioid crisis by acquiring Kures to develop novel therapeutics for opioid abuse in July.<sup>182</sup>
- ATAI launches Viridia Life Sciences to develop novel formulations of DMT in July.<sup>183</sup>
  - Viridia Life Sciences is leveraging ATAI's drug development expertise to generate multiple DMT products based on alternative routes of administration. Importantly, Viridia's DMT product will be paired with a digital therapeutic being developed by ATAI-company Introspect Digital Therapeutics, with the aim of streamlining preparation, integration, and continued patient engagement. Development is underway with clinical trials expected to begin early next year.
- ATAI launches IntroSpect Digital Therapeutics, appoints veteran software engineer David Keene as CEO in June 2020.<sup>184</sup>
- ATAI Life Sciences Announces Joint Venture with DemeRx to Develop Ibogaine For Opioid Use Disorder in January 2020.<sup>185</sup>
- ATAI Life Sciences Partners with Neuronasal Inc. to Develop Novel Treatment for mild Traumatic Brain Injury (mTBI) in January 2020.<sup>186</sup>
- US firm Perception Neuroscience was acquired by ATAI in 2019, and is developing a modified form of ketamine in phase II to treat clinical depression.<sup>187</sup>

ATAI provides operational support to all other companies listed below.

<sup>182</sup> <https://www.prnewswire.com/news-releases/atai-life-sciences-takes-on-opioid-crisis-by-acquiring-kures-to-develop-novel-therapeutics-for-opioid-abuse-301091027.html>

<sup>183</sup> <https://www.prnewswire.com/news-releases/atai-launches-viridia-life-sciences-to-develop-novel-formulations-of-n-n-dimethyltryptamine-dmt-for-a-range-of-mental-health-conditions-301098059.html>









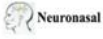









<sup>184</sup> <https://www.prnewswire.com/news-releases/atai-launches-introspect-digital-therapeutics-appoints-veteran-software-engineer-david-keene-as-ceo-301081067.html>

<sup>185</sup> <https://www.prnewswire.com/news-releases/atai-life-sciences-announces-joint-venture-with-demerx-to-develop-ibogaine-for-opioid-use-disorder-300992769.html>

<sup>186</sup> <https://www.prnewswire.com/news-releases/atai-life-sciences-partners-with-neuronasal-inc-to-develop-novel-treatment-for-mild-traumatic-brain-injury-mtbi-300981591.html>

<sup>187</sup> <https://www.labiotech.eu/brain/atai-compass-pathways-psychedelics/>



Company	Lead Compound	Lead Indication	Preclinical	Phase I	Phase II	Phase III
 COMPASS Pathways	Psilocybin <sup>1,2</sup>	Treatment Resistant Depression				
 DemeRx	Ibogaine	Opioid Use Disorder				
 PERCEPTION Neurosciences	Arketamine	Treatment Resistant Depression				
 gaba	Deu-Etifoquine	Generalized Anxiety Disorder				
 Neuronasal	N-acetylcysteine	Mild Traumatic Brain Injury				
 KURES	Deu-Mitragynine	Opioid Use Disorder				
 DemeRx	Noribogaine	Opioid Use Disorder				
 VIRIDIA LIFE SCIENCES	N,N-dimethyltryptamine	Treatment Resistant Depression				
 EmpathBio	MDMA Derivatives	Post Traumatic Stress Disorder				

1. COMP360, a proprietary, synthetic, high-purity, polymorphic formulation of psilocybin.  
 2. ATAI does not provide operational support to COMPASS Pathways

### Funding

In 2019 ATAI’s funding, which totals \$43 million, comes from Michael Auerbach’s New York-based Subversive Capital, but also includes investors ranging from Apeiron Investment Group, which is Angermayer’s family office; Bail Capital, a private equity firm; and Efrem Kamen, founder of the health care fund Pura Vida Investments. Prior investors include billionaire investor Mike Novogratz and the Icelandic businessman Thor Bjorgolfsson.<sup>188</sup> On the 23<sup>rd</sup> of November 2020 they announced the successful closing of its \$125 million Series C financing round, including \$32 million of its 2020 convertible debt that converted in connection with the Series C. The round was co-led by Apeiron Investment Group, the family office of ATAI’s founder Christian Angermayer, Peter Thiel, and Catalio Capital Management; joined by other existing investors including Future Ventures and Galaxy Investment Partners, as well as new investors including Falcon Edge Capital and Pura Vida Pro, LLC. On 21<sup>st</sup> April 2021, ATAI announced a NASDAQ listed IPO – date to be confirmed.

<sup>188</sup> <https://www.cnbc.com/2019/03/27/psychedelic-medicine-start-ups-vet-ketamine-psilocybin-for-depression.html>

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## LOPHORA

<https://www.lophora.com/>

Lophora is a Danish biotech created in 2018, developing a novel (patentable) molecule that targets the serotonin 2a receptor to treat central nervous system diseases including treatment resistant depression.

### About

Company is based on the science that co-founder and CSO Professor Jesper Kristensen and his team from University of Copenhagen have been working on for some 15 years. Their team developed a new chemical entity which has a different molecular scaffold from psilocybin but has the same ability to trigger biological responses via the serotonin 2A receptor with the difference being that the new molecule is selective.<sup>189</sup>

- Next to the patentability of their molecule, it might also be beneficial as it doesn't target the serotonin 2b receptor (tangentially related to cardiovascular side effects). The first human trials are planned early 2022.

### Funding

The company has raised \$2 million (from Bio Innovation Institute) and is building on 15 years of work by the University of Copenhagen (with grants up to \$3 million rewarded for that work).<sup>190</sup>

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## OCTARINE

<https://octarinebio.com/>

Octarine is a Danish company founded in September 2018 by Nethaji Gallage (CEO) and Nick Milne (CSO) based on foundational research conducted at the University of Copenhagen and Technical University of Denmark. It is a synthetic biology company developing biosynthetic platforms for cannabinoids, psychedelics and their novel improved derivatives announced the successful closing of Seed financing led by the Danish State Growth Fund (Vækstfonden) with participation from Enexis AB, Oskare Capital and cannabis and psychedelic industry veteran Bruce Linton.

### About

Using their unique biosynthetic platform, they engineer microorganisms to produce a range of natural and novel cannabinoid and psilocybin derived molecules with improved pharmacokinetic and therapeutic properties. They are developing proprietary enzyme platform technologies to efficiently modify molecules, and fermentation platforms to effectively scale-up production.

- They are entering pre-clinical studies with novel-improved- cannabinoid and psychedelic derivatives.<sup>191</sup>

### Funding

This latest financing comes shortly after the company closed a pre-seed round earlier this year, led by the Danish State Growth Fund (Vækstfonden) with participation from Enexis AB, Oskare Capital and cannabis and psychedelic industry veteran Bruce Linton. Bringing the total amount raised by the company to over \$1.8M USD.<sup>192</sup>

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<sup>189</sup> <https://psychedelicinvest.com/bo-tandrup-lophora-a-new-version-of-psilocybin/>

<sup>190</sup> <https://blossomanalysis.com/companies/lophora/>

<sup>191</sup> [https://www.prweb.com/releases/european\\_synthetic\\_biology\\_company\\_octarine\\_raises\\_1\\_8m\\_usd\\_in\\_funding\\_and\\_enters\\_pre\\_clinical\\_studies\\_with\\_novel\\_improved\\_cannabinoid\\_and Psychedelic\\_derivatives/prweb17533542.htm](https://www.prweb.com/releases/european_synthetic_biology_company_octarine_raises_1_8m_usd_in_funding_and_enters_pre_clinical_studies_with_novel_improved_cannabinoid_and Psychedelic_derivatives/prweb17533542.htm)

<sup>192</sup> <https://www.psychedelicfinance.com/articles/european-synthetic-biology-company-octarine-raises-1-8m-usd-in-funding-and-enters-pre-clinical-studies-with-novel-improved-cannabinoid-and-psychedelic-derivatives>

## CANADIAN COMPANIES

## MIND MEDICINE (“MMEDF” – NEO)

<https://mindmed.co/>

In 2019 Mind Medicine was co-founded by JR Rahn, Leonard Latchman, Scott Freeman and Stephen Hurst as a neuro-pharmaceutical company that discovers, develops, and deploys psychedelic-inspired medicines to improve health, promote wellness, and alleviate suffering. MindMed made history becoming the first psychedelics pharmaceutical firm to go public following the company’s historic IPO on the Canadian NEO Exchange. Since coming public the stock has more than doubled. MindMed applied for an additional listing on the NASDAQ on September 21, 2020, just days after Compass Pathways went public.<sup>193</sup>

### About

They have moved beyond ketamine and psilocybin mushrooms and now looking towards LSD as a treatment compound. MindMed has started clinical trials for LSD to treat anxiety and cluster headaches, as well as clinical trials for MDMA and DMT. The company is planning to address the opioid crisis by developing a non-hallucinogenic version of the psychedelic ibogaine.

- Currently preparing two separate Phase II clinical trials; one focused on ADHD using LSD micro-dosing and the other on opioid addiction via the company’s ibogaine derived molecule 18-MC. MindMed’s 18-MC will utilize a non-hallucinogenic version of the ibogaine compound and is the company’s lead drug development program. They have a collaboration agreement with University Hospital Basel (UHB), licensing the rights to one of the richest libraries of human psychedelics data in the world. MindMed received a plethora of data owing to its exclusive collaboration with Liechti Lab, giving it access to over 10 years of psychedelics research. The company has already advanced five programs—including three Phase II studies for adult ADHD, anxiety disorder, and cluster headaches, respectively.<sup>194</sup>

As of December, based on positive pre-IND meeting with U.S. Food and Drug Administration (FDA), MindMed is now prepared to open an Investigational New Drug (IND) in August 2021 with a Phase 2b clinical trial for LSD assisted therapy in anxiety. MindMed continues dose escalation of 18-MC in Phase I SAD/MAD; Meeting confirmed with FDA.<sup>195</sup> The primary focus is:

- LSD for anxiety ADHD
- 18-MC for OUD
- LSD for adult ADHD
- LSD for cluster headaches

### Funding

The Company raised \$24 Million in a pre-IPO round which included Kevin O’Leary and Bruce Linton, a founder of Canopy Growth Corporation. “Psychedelics have been under-researched and stigmatized by society. As an investor, I am attracted to MindMed because they are solving health problems through federally-authorized clinical trials, and have no interest in recreational use,” claimed O’Leary in Forbes.<sup>196</sup> As of December, MindMed announced \$50 million bought deal public offering<sup>197</sup> and their market cap is around \$328 million. Mind Med was first listed in March 2020 at \$0.50 and moved to a NASDAQ listing in April 2021 – currently trading at \$5.62.

<sup>193</sup> <https://www.globenewswire.com/news-release/2020/10/15/2109066/0/en/Trends-in-Psychedelic-Drugs-Research-and-Four-Stocks-You-Should-Know-About.html>

<sup>194</sup> <https://insiderfinancial.com/compass-pathways-investors-need-to-look-at-mmedf/180479/>

<sup>195</sup> <https://www.psychedelicfinance.com/articles/mindmed-announces-successful-completion-of-pre-ind-meeting-with-the-fda-for-project-lucy>

<sup>196</sup> <https://www.forbes.com/sites/willyakowicz/2020/10/07/psychedelic-therapy-company-field-trip-health-goes-public-to-revolutionize-mental-health-treatments/?sh=5a9baef179a5>

<sup>197</sup> <https://www.psychedelicfinance.com/articles/mindmed-announces-50-million-bought-deal-public-offering>

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**FIELD TRIP HEALTH (“FTRPF” – CANADIAN STOCK EXCHANGE)**

<https://www.fieldtriphealth.com/>

Field Trip Health is based in Toronto and founded in 2019 by Joseph del Moral (CEO), Roman Levy (executive chairman), Hannan Feliman (president) and Ryan Yermus and Mujeeb Jafferri who all except Jafferri previously founded CanvasRx (Canadian cannabis clinic acquired by Aurora Cannabis for \$37 million in 2016).<sup>198</sup> They are a global leader in the development and delivery of psychedelic therapies. Its primary business is the development of its clinic network across the Americas.

### About

The company opened its first ketamine clinic in Toronto while expanding into the US market via locations in New York and Los Angeles.

#### Psilocybin-producing Fungi Research and Cultivation

- Since January 2020, Field Trip has successfully cultivated 24 varieties (from 13 different species) of psilocybin-producing fungi and truffles in a temporary facility at UWI’s Mona Campus, and in October 2020, Field Trip substantially completed construction of a 2,072 sq. ft. custom-built research and cultivation facility situated on UWI’s Mona campus.

FT-104 is a next-generation, synthetic psychedelic molecule whose design is, in part, based on classical serotonin 2A psychedelics.

- Patents are pending on FT-104’s structure, formulation and use in treating a variety of central nervous system disorders. Preliminary results for FT-104 demonstrate that FT-104 is similar in potency to psilocybin but may provide a significantly shorter duration of psychedelic experience relative to psilocybin (in the range of two to four hours, which is approximately half the duration of psilocybin), making it a more convenient and potentially preferable option for psychedelic therapy. FT-104 is concurrently undergoing optimization and GMP scale-up, as well as pre-clinical evaluation, both of which are expected to be completed by June 2021. Field Trip anticipates that FT-104 will enter Phase 1, clinical trials in the second half of calendar year 2021.

#### Field Trip Health Centres

- Currently they have 6 clinical hubs for psychedelic therapies in 2020 but Levy argues they plan to scale up to 75 in the next few years.<sup>199</sup> These centres are primarily dedicated to the treatment of depression and other mental health conditions using proprietary protocols and settings within a framework of ketamine-assisted therapies but will offer therapies using other psychedelic molecules where and when permitted, including in The Netherlands and the State of Oregon.
- During the second fiscal quarter, following the successful opening of its Toronto location in March 2020, Field Trip opened Field Trip Health centres in the United States with locations in New York and Los Angeles. In October 2020, Field Trip completed construction at its Chicago location and expects to begin providing therapies to people in December.
- Field Trip also announced that it has entered into a lease to build a Field Trip Health centre in Amsterdam, Netherlands, which will provide programs utilizing truffles containing psilocybin, which are legal in The Netherlands. Field Trip has also entered into two additional leases in Atlanta, GA and Houston, TX, respectively bringing the total number of Field Trip Health centres to a total of seven, ahead of schedule. The Field Trip Health centre in Atlanta, GA will be a 5,189 sq. ft. facility located at Building 200, 750 Glenwood Avenue and is a part of the redevelopment of GlenCastle, which is Atlanta’s historic city stockade, stables and farm, that is being restored and repurposed into Atlanta’s most unique and creative office campus. The Houston centre is a 4,600 sq. ft. facility

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<sup>198</sup> <https://www.fieldtriphealth.com/>

<sup>199</sup> <https://www.forbes.com/sites/willyakowicz/2020/10/07/psychedelic-therapy-company-field-trip-health-goes-public-to-revolutionize-mental-health-treatments/?sh=5a9baef179a5>

located at Suite 4310 Westheimer Road, Suite 220 in Houston’s River Oaks neighbourhood and will offer seven treatment rooms and a large group therapy room.

#### Digital Teletherapy Tools: Trip and Portal

- During the second fiscal quarter, Field Trip also launched the Trip, a mobile app that provides users with a framework and tools to make the most of self-directed consciousness-expanding activities such as meditation and breathwork. Trip was released to users on Apple and Android platforms and has over 3,600 active users.
- Field Trip also launched Portal, a proprietary digital tool designed to complement its in-person therapeutic experience. Portal provides users with content, information, meditations, and synchronous and asynchronous communication tools for people in its psychedelic therapies and programs.<sup>200</sup>

In December 2020, Field Trip Health touched down in Santa Monica to tackle depression and anxiety with psychedelic Therapies.<sup>201</sup> Field Trip Health and WHOOP announce partnership to measure effect of psychedelic therapies on physiology and mental health.<sup>202</sup>

#### Funding

Field Trip closed a Series A financing round that raised \$8.5 million from a variety of investors including cannabis-focused asset manager Silver Spike Capital and Harris Fricker, the former CEO of GMP Capital Inc., which helped a number of marijuana companies go public. They currently have a market cap of around \$155 million.

In November for the second fiscal quarter, Field Trip reported patient services revenues of \$94,532 from its Toronto and New York Field Trip Health centres, which began continuous operations in June and August, respectively.<sup>203</sup>

In August 2020, Field Trip closed a \$12 million private placement deal, which brought the total amount it has raised since founding to \$20 million. They subsequently launch an IPO in October 2020 on the Canadian Stock Exchange and after the first day of trading Field Trip’s market cap was \$102 million.<sup>204</sup>

In December they announced an increase to bought deal financing to \$17.4 Million.<sup>205</sup>

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#### CHAMPIGNON BRANDS (“SHRMF” – CSE)

<https://champignonbrands.com/>

Founded in 2019 in Vancouver it was one of the first psychedelic companies to go public alongside MindMed in March. Champignon specializes in the formulation of mushroom-infused consumer packaged goods (CPG) and uses a research-driven approach in its quest to promote holistic health and wellness. With a network of ketamine clinics complementing its sharp focus on research and development.

#### About

They own 75% of the Canadian Rapid Treatment Centre of Excellence (CRTCE), a fully operational ketamine clinic in Mississauga, Ontario and the only clinic in the country approved by Health Canada to perform psilocybin doses. Led by CEO Dr Roger McIntyre, a widely recognized expert in the study and treatment of mood disorders, Champignon is blazing a trail in an exciting new industry.<sup>206</sup> Champignon continues to be inspired by sustainability, as its medicinal mushroom-infused SKUs are organic, non- GMO and vegan certified.<sup>207</sup>

<sup>200</sup> <https://www.globenewswire.com/news-release/2020/11/30/2136953/0/en/Field-Trip-Health-Ltd-Reports-Second-Fiscal-Quarter-2021-Financial-Results-Announces-Two-New-Field-Trip-Health-Center-Locations.html>

<sup>201</sup> <https://mlangeleno.com/psychedelic-therapy-company-field-trip-health-santa-monica>

<sup>202</sup> <https://www.globenewswire.com/news-release/2020/11/19/2130016/0/en/Field-Trip-Health-Ltd-and-WHOOP-announce-partnership-to-measure-effect-of-psychedelic-therapies-on-physiology-and-mental-health.html>

<sup>203</sup> <https://www.globenewswire.com/news-release/2020/11/30/2136953/0/en/Field-Trip-Health-Ltd-Reports-Second-Fiscal-Quarter-2021-Financial-Results-Announces-Two-New-Field-Trip-Health-Center-Locations.html>

<sup>204</sup> <https://www.forbes.com/sites/willyakowicz/2020/10/07/psychedelic-therapy-company-field-trip-health-goes-public-to-revolutionize-mental-health-treatments/?sh=5a9baef179a5>

<sup>205</sup> <https://www.psychedelicfinance.com/articles/field-trip-health-ltd-announces-increase-to-bought-deal-financing-to-17-4-million>

<sup>206</sup> <https://www.proactiveinvestors.co.uk/companies/news/922268/champignon-brands-is-making-a-scientific-case-for-psychedelic-medicine-922268.html>

<sup>207</sup> <https://champignonbrands.com/>

- Champignon’s CPG portfolio of premium organic, sustainable and non-genetically modified organism mushroom formulations is highlighted by the company’s flagship brand, Vitality Superteas. Vitality Superteas were formulated to revolutionize conventional organic tea through the infusion of a proprietary blend of artesian mushrooms with medicinal properties.

During the third quarter of 2020, Champignon plans to progress forward in its quest to develop medicinal psychedelics through clinical trials. Champignon intends to develop non-hallucinogenic and hallucinogenic therapies using the following psychedelic substances.<sup>208</sup>

- Hallucinogenic Therapies: High Doses of Psilocybin and LSD.
- Non-Hallucinogenic Therapies: Microdoses of Psilocybin, MDMA and LSD.

Champignon executed a series of game-changing acquisitions earlier this year, including AltMed, which owned ketamine clinic operator the Canadian Rapid Treatment Centre of Excellence (CRTCE) and California-based Wellness Clinic of Orange County.

- AltMed has three trials in the Phase I stage and three trials in the preclinical stage during 2020, as well as seven patents for its ketamine/psilocybin delivery platforms and formulations. The company also has a preferred commercial relationship with InterVivo Solutions, Canada’s largest neuroscience-focused preclinical contract research organization, to collaborate on Phase I testing and novel drug development of psychedelic molecules and delivery systems.<sup>209</sup>

In November the Canadian Rapid Treatment Centre of Excellence (the “CRTCE”) announced the opening of a new clinic in downtown Toronto. Both the existing Mississauga clinic and newly opened Toronto clinic (the “CRTCE Clinics”) address the unmet need of depression and suicide through novel ketamine therapy treatment. “These CRTCE Clinics address the unmet need of depression and suicide,” said Dr. Joshua Rosenblat, Medical Director, CRTCE. “Ketamine therapy is highly effective in treating people with severe depression where other treatments have proven to be ineffective. During the COVID-19 pandemic, the need for effective treatment have become exponentially critical.”<sup>210</sup>

- The first of its kind in Canada, the CRTCE multidisciplinary outpatient clinical research facility has specialized in providing breakthrough rapid onset treatments for depression, including but not limited to intravenous ketamine and intranasal esketamine. These therapies aid patients suffering from several treatment-resistant conditions such as major depressive disorder and/or bipolar disorder.

The company is proposing changing its name to Apotheosis Scientific Ltd.

### Funding

The company closed its \$2.85 million IPO in February, which was led by PI Financial. The company recently closed a C\$15 million in June 2020 financing to fund its ambition to open five ketamine clinics in North America by the end of 2020.<sup>211</sup> Their market cap is around \$73.3 million.

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REVIVE THERAPEUTICS (“RVV” - CSE)

<https://revivethera.com/>

In 2012 Revive Therapeutics was founded with Michael Frank as CEO based in Toronto. It is a life sciences company focused on the research and development of therapeutics for infectious diseases and rare disorders, and it is prioritizing drug development efforts to take advantage of several regulatory incentives awarded by the FDA such as Orphan Drug, Fast Track, Breakthrough Therapy and Rare Paediatric Disease designations.

<sup>208</sup> <https://www.thecannabisinvestor.ca/the-rise-of-psychedelic-stocks-2-new-ipos-go-head-to-head-heres-the-surprising-winner/>

<sup>209</sup> <https://www.proactiveinvestors.co.uk/companies/news/921914/champignon-brands-revamps-its-brand-identity-to-better-reflect-its-scientific-focus-on-psychedelic-medicine-921914.html>

<sup>210</sup> <https://champignonbrands.com/news/canadian-rapid-treatment-center-of-excellence-opens-second-location/>

<sup>211</sup> <https://www.proactiveinvestors.co.uk/companies/news/921914/champignon-brands-revamps-its-brand-identity-to-better-reflect-its-scientific-focus-on-psychedelic-medicine-921914.html>

## About

They are in their Phase I development of psilocybin for methamphetamine use disorder with University of Wisconsin where they hope to deliver through precise dosed formulations, capsules, sublingual spray, gel caps, effervescent tables and oral/transmucosal strips.<sup>212</sup> Only on the pre-clinical stage of development for depression and anxiety with target FDA approval.<sup>213</sup>

- There are approximately 1.1M people aged 12 or older who have a Methamphetamine Use Disorder in the United States. The economic cost in the U.S. is approximately \$23 billion.<sup>214</sup>

In February, Revive announced plans to acquire Psilocin Pharma Corp. for \$2.75 million. As of November, they entered into an exclusive research collaboration agreement with PharmaTher Inc., a wholly-owned subsidiary of Newscope Capital Corporation and a specialty psychedelics pharmaceutical company, to accelerate the development of psilocybin in the treatment of cancer and the discovery of novel uses of undisclosed psychedelic compounds.<sup>215</sup> The collaboration will give Revive the exclusivity to advance the research of psilocybin in the treatment of cancer and leverage PharmaTher's panaceaAI™ psychedelic discovery AI platform to screen, identify and evaluate undisclosed psychedelic compounds directed at pre-specified targets for use with Revive's drug delivery technology.<sup>216</sup>

- PharmaTher repurposes psychedelic pharmaceuticals, such as ketamine and psilocybin, for FDA approval to treat cancer and disorders of the brain and nervous system. Their goal is to advance the commercialization of panaceaAI™, their drug repurposing artificial intelligence platform, and clinical product pipeline with ketamine and psilocybin in the treatment of Parkinson's Disease, depression, pain, traumatic brain injury and stroke.<sup>217</sup>

Revive Therapeutics signs supply agreement with Havn Life Sciences for psychedelic compounds<sup>218</sup> and have also entered into a supply and collaboration agreement with Red Light Holland Financing Inc. an arm's length party.<sup>219</sup>

They are also prevalent in the cannabis market with their cannabinoid pharmaceutical portfolio focusing on rare inflammatory diseases. The company was granted FDA orphan drug status designation for the use of Cannabidiol (CBD) to treat autoimmune hepatitis (liver disease) and to treat ischemia and reperfusion injury from organ transplantation.

## Funding

They are public, currently trading<sup>220</sup> with a market cap of \$127.13 million.<sup>221</sup>

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## CYBIN ("CYBN" – NEO)

<https://www.cybin.com/>

In 2019 Cybin was co-founded by Paul Galvine (COO) and Eric So (President) with Doug Drysdale as CEO.. Cybin is a Toronto-based life sciences company focused on psychedelic pharmaceutical therapies that went public in November<sup>222</sup> after they announced it has completed a reverse take-over with Clarmin Explorations.<sup>223</sup>

## About

<sup>212</sup> <https://revivetherapeutics.com/2020/11/revive-therapeutics-provides-update-on-oral-thin-film-product-with-psilocybin/>

<sup>213</sup> <https://revivetherapeutics.com/investor-relations/>

<sup>214</sup> <https://psychedelinvest.com/10-psychedelic-companies-investors-should-have-on-their-radar/>

<sup>215</sup> <https://www.globenewswire.com/news-release/2020/11/18/2129037/0/en/Revive-Therapeutics-Announces-Research-Collaboration-with-PharmaTher-for-Development-of-Psilocybin-in-Cancer-and-Discovery-of-Novel-Uses-of-Psychedelics.html>

<sup>216</sup> <https://revivetherapeutics.com/2020/11/revive-therapeutics-announces-research-collaboration-with-pharmather-for-development-of-psilocybin-in-cancer-and-discovery-of-novel-uses-of-psychedelics/>

<sup>217</sup> <https://revivetherapeutics.com/2020/11/revive-therapeutics-announces-research-collaboration-with-pharmather-for-development-of-psilocybin-in-cancer-and-discovery-of-novel-uses-of-psychedelics/>

<sup>218</sup> <https://revivetherapeutics.com/2020/10/revive-therapeutics-signs-supply-agreement-with-havn-life-sciences-for-psychedelic-compounds/>

<sup>219</sup> <https://www.globenewswire.com/news-release/2020/02/10/1982221/0/en/Revive-Therapeutics-to-Pursue-the-Psychedelic-Market-With-Agreement-and-Investment-in-Red-Light-Holland-Financing.html>

<sup>220</sup> <https://simplywall.st/stocks/ca/pharmaceuticals-biotech/cse-rvv/revive-therapeutics-shares>

<sup>221</sup> <https://seekingalpha.com/symbol/RVVF/overview>

<sup>222</sup> [https://www.businesswire.com/news/home/20201105006044/en/Cybin-Completes-Reverse-Take-Over-Transaction#:~:text=TORONTO%2D%2D\(BUSINESS%20WIRE\)%2D%2D,takeover%20of%20Clarmin%20Explorations%20Inc.](https://www.businesswire.com/news/home/20201105006044/en/Cybin-Completes-Reverse-Take-Over-Transaction#:~:text=TORONTO%2D%2D(BUSINESS%20WIRE)%2D%2D,takeover%20of%20Clarmin%20Explorations%20Inc.)

<sup>223</sup> [https://aequitasneo.com/en/about/press-releases/cybin-goes-public-on-the-neo-exchange?utm\\_source=ln&utm\\_medium=social&utm\\_campaign=Cybin-launch](https://aequitasneo.com/en/about/press-releases/cybin-goes-public-on-the-neo-exchange?utm_source=ln&utm_medium=social&utm_campaign=Cybin-launch)

Cybin is currently working towards a Phase IIa and IIb clinical trial to study psilocybin use for major depressive disorder. The trial will include 120 patients taking four doses of a sublingual film containing psilocybin over a four-month period.<sup>224</sup>

The company's business model is centred around its two core subsidiaries, Serenity Life Sciences and Natures Journey Inc., which comprise Cybin's two-pronged approach toward delivering fungi-derived psychedelic and medicinal products.

- Serenity Life Sciences is focused on furthering research and development of psilocybin-based medications.
- Natures Journey Inc. operates the Journey brand, which specializes in developing proprietary medicinal mushroom products that target and promote mental wellness, immune boosting detoxification and overall general health and wellbeing.<sup>225</sup>

Cybin's Journey brand is launching a range of supplements comprised of popular fungi-derived ingredients such as Reishi, Lion's Mane and Cordyceps. Purported to aid focus and concentration while promoting neurogenesis, Journey's range of nutraceutical products provides Cybin with a crucial foothold within the non-psychedelic legal supplement market, which is valued at over \$25 billion globally and growing at a 9% year-over-year rate.

As of December, Cybin signs a definitive agreement to acquire Adelia Therapeutics as part of its commitment to strategic growth.<sup>226</sup>

- Adelia is an innovative biopharmaceutical company committed to addressing unmet mental health needs through the development of proprietary psychedelic therapeutics with improved dosing efficacy and therapeutic indices. Adelia's leadership team brings a wealth of clinical development experience and major academic research affiliations, including the Massachusetts Institute of Technology, Harvard, Stanford, Yale, and North-eastern University.
- Newly acquired novel psychedelic molecules diversify Cybin's development portfolio, providing access to multiple future indications. Selective modification, through deuteration of psychedelic parent molecules, allows control of the duration of action of these new chemical entities, enabling the design of both short and long-acting treatments. Adelia brings a range of technologies related to novel therapeutics, delivery methods, and therapeutic regimens, as well as six patent applications.
- Adelia contributes an expanding library of psychedelic derivative drug development candidates. The first lead compounds are expected to enter clinical studies in 2021, subject to receipt of approvals.
- Cybin gains access to new patent-protected active pharmaceutical ingredients obtained by way of selective modification of the parent molecules. Also, proprietary drug delivery platform developed by Adelia to administer psychedelic therapies and bypass liver metabolism. Cybin gains an operating development facility in the epicentre of the Boston biotechnology centre, which broadens its presence in the United States.

### Funding

The Company recently closed a \$45 million subscription receipt financing in relation to its reverse takeover transaction, which marked the largest subscription receipt financing in the Canadian psychedelic sector.<sup>227</sup>

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ENTHEON BIOMEDICAL ("ENBI" – CNSX)

<https://entheonbiomedical.com/>

Entheon was founded in 2019 and based in Vancouver as a biotechnology research and development company committed to developing and commercializing a portfolio of safe and effective DMT based psychedelic

<sup>224</sup> <https://www.greenmarketreport.com/psychedelic-company-cybin-to-begin-trading-next-week/>

<sup>225</sup> <https://www.networknewswire.com/clients/cybin-inc/>

<sup>226</sup> <https://www.cybin.com/cybin-signs-definitive-agreement-to-acquire-adelia-therapeutics-as-part-of-its-commitment-to-strategic-growth/>

<sup>227</sup> [https://aequitasneo.com/en/about/press-releases/cybin-goes-public-on-the-neo-exchange?utm\\_source=ln&utm\\_medium=social&utm\\_campaign=CYBN-launch](https://aequitasneo.com/en/about/press-releases/cybin-goes-public-on-the-neo-exchange?utm_source=ln&utm_medium=social&utm_campaign=CYBN-launch)



therapeutic products for the purposes of treating addiction and substance use disorders. Subject to obtaining all requisite regulatory approvals and permits, Entheon intends to generate revenue through the sale of its DMT products to physicians, clinics and licensed psychiatrists in the United States, certain countries in the European Union and throughout Canada.<sup>228</sup> Entheon Biomedical went public after closing its reverse acquisition with MPV Exploration Inc. in November 2020.

### About

Entheon Biomedical Announced CRO Agreement with CHDR for Phase 1 Clinical Trial; Centre for Human Drug Research Led DMT Study to Start in 2021. CHDR is a Leiden, Netherlands-based contract research organization that specializes in early-stage clinical drug research.<sup>229</sup> In 2022 they're timeline includes

- Phase 1/2a Study – Opioid-Use disorder
- Phase 2b/3 Study – Nicotine-Use Disorder, multicenter,
- Phase 2b Study – Opioid-Use Disorder
- Phase 2b Study – Alcohol-Use Disorder.<sup>230</sup>

As of December, Entheon Biomedical Announced DMT Drug Supply Agreement with Psygen Labs Inc. Completion of Initial DMT Research Drug Batch and Exercise of Warrants. Under the European Medicines Agency (EMA) regulatory framework, Psygen will supply Entheon with DMT for upcoming formulation, preclinical, clinical, and post-approval commercialization phases.<sup>231</sup>

- "We are excited that Psygen has completed its initial research batch of non-GMP DMT. The completion of this batch represents the crucial chemical validation and formulation steps that are a regulatory requirement prior to human administration," said Chief Executive Officer of Entheon, Timothy Ko. "Partnering with Canada's first licensed manufacturer of restricted psychedelic drug products fosters an ecosystem of collaboration and innovation within the Canadian psychedelic space, and we are thrilled by the progress being made."

### About Psygen Labs Inc.

- A Calgary-based company specializing in the synthetic manufacture of psychedelic medicines. The company provides non-exclusive access to psychedelic drug substances and products for clinical research and therapeutic applications. Psygen is well positioned to be a lead supplier for the emerging commercial market. Psygen has sponsored a Licensed Dealer who holds a license for the manufacture, sale, import, export, and analysis of psilocybin, MDMA, DMT, LSD, 2C-B, and mescaline. Psygen's chemists and manufacturing lab currently reside at the University of Alberta. Psygen has applied to Health Canada for a corporate Dealer's License which will allow the company to manufacture, possess, sell, import, export, research, develop, and analyze psychedelic drug substances and products. Psygen is actively developing and constructing a 6000sq/ft lab capable of large-scale synthesis, formulation, and distribution of the above and additional psychedelics. Psygen intends to be the leader in psychedelic supply chain solutions and is committed to supporting the renaissance in research and clinical treatment of a wide variety of mental health issues.<sup>232</sup>

December also saw their investment in Wonder Scientific (University Researchers and Product Development experts create custom, naturally derived, active pharmaceutical ingredients (APIs) to supply the growing global clinical and commercial demand for psychedelics).<sup>233</sup>

### Funding

<sup>228</sup> <https://entheonbiomedical.com/>

<sup>229</sup> <https://www.newsfilecorp.com/release/69242>

<sup>230</sup> [https://entheonbiomedical.com/documents/EntheonBiomedical\\_Intro\\_v3\\_R.pdf](https://entheonbiomedical.com/documents/EntheonBiomedical_Intro_v3_R.pdf)

<sup>231</sup> <https://psychedelicstockwatch.com/psychedelic-stock-news/entheon-biomedical-announces-dmt-drug-supply-agreement-with-psygen-labs-inc-completion-of-initial-dmt-research-drug-batch-and-exercise-of-warrants>

<sup>232</sup> <https://psychedelicstockwatch.com/psychedelic-stock-news/entheon-biomedical-announces-dmt-drug-supply-agreement-with-psygen-labs-inc-completion-of-initial-dmt-research-drug-batch-and-exercise-of-warrants>

<sup>233</sup> <https://www.newsfilecorp.com/release/69518/Entheon-Biomedical-Announces-Corporate-Update-Including-Investment-in-Wonder-Scientific>

Entheon will become public with a market capitalization of just C\$6.46 million, having about C\$3.0 million in working capital upon completion of the amalgamation, which is plenty to move forward with the clinical trial. Potential cash from the exercise of warrants is approximately C\$7.0 million.<sup>234</sup>

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#### PHARMATHER (CSE: PHRM)

<https://www.pharmather.com/>

Founded in 2020 PharmaTher, a wholly-owned subsidiary of Newscope Capital Corporation with Fabio Chianelli as CEO (previously was the Founder and President of Revive Therapeutics Ltd). PharmaTher repurposes psychedelic pharmaceuticals, such as ketamine and psilocybin, for FDA approval to treat disorders of the brain and nervous system. Their goal is to advance the commercialization of panaceaAI™, our drug repurposing artificial intelligence platform, and their ketamine focused product pipeline in the treatment of Parkinson's Disease, depression, and pain.

#### About

- As of December PharmaTher, Granted Pre-IND Meeting with the FDA for Ketamine in Parkinson's Disease and they also expands Research Partnership with University Health Network for Development of Digital Therapeutics Platform<sup>235</sup>
  - Parkinson's Disease is a debilitating disorder that affects over 1 million people in the U.S. and more than 7 million people worldwide. There is currently no cure for Parkinson's Disease, although some drug combinations are used to treat the disease symptoms. The global Parkinson's Disease market is expected to grow from USD \$5 billion in 2019 to USD \$7.5 billion by the end of 2025<sup>6</sup> and it is estimated that the potential market opportunity for LID-PD to be over USD \$3 billion in the U.S. alone.
  - Ketamine is an FDA-approved drug with a known safety profile. PharmaTher entered into an exclusive license agreement with the University of Arizona to develop and commercialize ketamine to treat Parkinson's disease and movement disorders. The Company also has filed with the FDA to receive orphan drug designation for ketamine in the treatment of LID-PD.
  - The Company has assembled a prolific scientific and clinical team experienced in Parkinson's disease and movement disorders, including Dr. Scott Sherman and Dr. Torsten Falk from the University of Arizona, Dr. Alberto Espay from the University of Cincinnati and Dr. Robert Hauser from the University of South Florida.

Company has entered into an exclusive license agreement with BioRAE, for the development and commercialization of a novel biocompatible and biodegradable gelatin methacryloyl microneedle delivery technology developed at the University of California for use with psychedelic pharmaceuticals, including, but not limited to Psilocybin, Ketamine, Ibogaine, LSD, MDMA, DMT, and Cannabinoids.<sup>236</sup>

#### Funding

Pharmather debuted with a market cap of \$13 million.<sup>237</sup>

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#### MYDECINE INNOVATIONS

<https://www.mydecine.com/>

Reinvented in 2020 Mydecine is a public biotechnology life sciences syndicate based in Vancouver dedicated to developing and producing adaptive pathway medicine and natural health products, all stemming from

<sup>234</sup> <https://www.wallstreetinvestorclub.com/optin1605033042562>

<sup>235</sup> <https://www.globenewswire.com/news-release/2020/12/01/2137283/0/en/PharmaTher-Expands-Research-Partnership-with-University-Health-Network-For-Development-of-Digital-Therapeutics-Platform.html>

<sup>236</sup> <https://in.finance.yahoo.com/news/pharmather-secures-exclusive-rights-novel-110000613.html>

<sup>237</sup> <https://theseedinvestor.com/psychedelic-stocks/pharmather-cse-phrm-is-the-latest-psychedelics-ipo>

mushrooms.<sup>238</sup> Mydecine has exclusive access to a full cGMP certified pharmaceutical manufacturing facility with the ability to import/export, cultivate, extract/isolate, and analyse active mushroom compounds with full government approval through Health Canada. Mydecine also operates out of a state-of-the-art mycology lab in Denver, CO to focus on genetic research for scaling commercial cultivation of rare (non-psychedelic) medicinal mushrooms.

### About

Mydecine has three divisions that provide different products and services related to the mushroom-based pharmaceutical business. Two of the three divisions were from acquisitions in the past year.

- In June 2020, Mydecine acquired Mindleap Health, a digital telehealth platform that gives individuals access to mental health professionals online.
- In September 2020, Mydecine completed its acquisition of NeuroPharm for \$6M. The company is responsible for managing clinical trials to develop unique and proprietary pharmaceutical and natural health products addressing mental wellness in vulnerable populations such as veterans and first responders.
- Mydecine also has a 50% stake in Alternative Distribution Company to support nation-wide distribution and manufacturing. Alternative Distribution is a Texas-based distributor with existing relationships with thousands of stores, including market leaders like HEB, Costco (COST), Whole Foods (WFM), Kroger (KR), and more.

Mydecine will operate in both the therapeutic and consumer goods side of the mushroom market. On the consumer side, they will be introducing proprietary fungi infused goods starting with coffee and chocolate product lines in Q4 2020.

Mydecine is working closely with military health agencies in both Australia, Canada, the Netherlands, Great Britain, and the United States to study veterans with Post Traumatic Stress (PTS). Currently, they have seven clinical trials underway studying the relationship between psychedelics and PTS and have another one planned for 2021.<sup>239</sup> In December they were to make the first commercial export of legal psilocybin mushrooms.<sup>240</sup>

Engaging with ProPharma Group proceeding with FDA filings and approval for novel research and multiple phase clinical trials.<sup>241</sup>

### Funding

Mydecine currently has a market cap of C\$70m.

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BETTER PLANT SCIENCES (PLNT: CSE) / NEON MIND BIOSCIENCES (NEON:CSE)

<https://betterplantsciences.com/>

Better Plant offers plant-based products for optimum health and wellness. It is a vertically integrated company with a team whose complementary experience enables acquisition, development, manufacturing, and direct-to-consumer distribution of our products. Its all-natural products vary in use from pain treatment to disease prevention to skin care, all without chemicals or harmful ingredients. It has an extensive catalogue of over 400 proprietary product formulas. Better Plant currently has over 75 plant-based products for sale through eCommerce and/or in retail stores under the brands Jusu, Urban Juve, and Wright & Well. This wellness firm has a substantial investment in the psychedelics market thanks to a majority ownership stake in NeonMind who owns approximately 51%.<sup>242</sup>

### About

<sup>238</sup> <https://psilocybinalpha.com/company/mydecine-innovations-group-mycology>

<sup>239</sup> <https://psychedelicinvest.com/10-psychedelic-companies-investors-should-have-on-their-radar/>

<sup>240</sup> <https://www.globenewswire.com/news-release/2020/12/08/2141227/0/en/Mydecine-Innovations-Group-to-Make-First-Commercial-Export-of-Legal-Psilocybin-Mushrooms.html>

<sup>241</sup> <https://www.mydecine.com/news/mydecine-innovations-group-engages-the-propharma-group-to-proceed-with-fda-filings-and-approval-for-novel-research-and-multiple-phase-clinical-trials>

<sup>242</sup> <https://betterplantsciences.com/press-release/better-plant-subsiary-neonmind-announces-filing-of-final-prospectus-in-connection-with-an-initial-public-offering/>

It has over 200 proprietary wellness formulas at various stages of commercialization, including over 20 products that are now for sale through e-commerce or brick and mortar retail stores. It has 14 patent applications to protect its formulas.<sup>243</sup>

NeonMind, plans to eventually launch branded products, according to its parent company, such as mushroom-infused items designed to “support immune, cognitive, memory and other brain functions.” And as of December became a listed company. No securities in Better Plant were sold as part of the NeonMind IPO offering. The listing of NeonMind on the Exchange will not affect the listing of Better Plant and Better Plant’s common stock will continue to trade.<sup>244</sup>

In October Health Canada granted approval for NeonMind’s preclinical trial to test psilocybin as a treatment for weight loss and food addiction.

- In early November 2020 their Preclinical Trial commenced at the University of British Columbia. Once information from this trail is accessible, they will apply for a planned Phase II Human Clinical Trial in early 2021.<sup>245</sup>
- NeonMind use proprietary formulations to commercialize mushroom-infused functional food products, with revenues projected to begin in late 2020, securing reliable source of psilocybin through an agreement with Psygen Labs.<sup>246</sup>
- Pending patents include the administration of psychedelic compounds to:
  - Aid in weight loss
  - Treat obesity and its complications
  - Reduce food cravings
  - Treat compulsive eating disorder
  - altering the diet of an individual

### Funding

Better Plant Sciences have a market cap of C\$12m.

### HAVN LIFE SCIENCES (“HAVN” - CSE)

Havn Life Sciences is a newcomer to the psychedelics industry, based in Vancouver a biotechnology company pursuing standardized extraction of psychoactive compounds, the development of natural healthcare products, is pleased to announce the first preclinical study to focus on the effects of psilocybin on the immune system. They went public in September 2020.<sup>247</sup>

### About

The company holds a Section 56 exemption from Health Canada, meaning it can research and develop psilocybin for scientific use. Havn sells itself to investors as a company investigating psychoactive compounds to develop natural health products.

As of December, Havn Life Sciences has started one of the first preclinical studies on psilocybin and the immune system. The Havn Life team will begin this preclinical study in Q1 2021. This study is the first step required to file an application for the development of psilocybin delivery methods that could address inflammatory and immune diseases such as arthritis. Although there is discussion related to the possible effects of psilocybin on inflammation, there has been no research on psilocybin's impact on the immune system. This will be the one of the first studies to quantify the effects of psilocybin on the immune system and will also compare the differences in how psilocybin affects the immune system between the sexes.<sup>248</sup>

<sup>243</sup> <https://www.psychedelicfinance.com/company/better-plant-sciences>

<sup>244</sup> <https://betterplantsciences.com/press-release/better-plant-subsiary-neonmind-announces-filing-of-final-prospectus-in-connection-with-an-initial-public-offering/>

<sup>245</sup> <https://neonmindbiosciences.com/psychedelic-research>

<sup>246</sup> <http://bit.ly/NeonMindSignsPsilocybinAgreement>

<sup>247</sup> <https://havnlife.com/havn-life-sciences-granted-section-56-exemption-to-begin-scientific-work-with-psilocybin/>

<sup>248</sup> <https://www.psychedelicfinance.com/articles/havn-life-sciences-undertakes-one-of-the-first-preclinical-studies-on-psilocybin-and-the-immune-system>

## Funding

Havn Life Sciences announces increase in bought deal financing to \$10 Million.<sup>249</sup>

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## PURE EXTRACTS TECHNOLOGIES CORP (PULL:CN)

<https://pureextractscorp.com/>

In 2006 Doug Benville (COO) created Pure Extracts in Vancouver as a plant-based extraction company focused on cannabis, hemp and later the rapidly emerging functional mushroom sectors.<sup>250</sup> Company CEO, Ben Nikolaevsky comments, "Moving into the field of mushroom extractions is an obvious and exciting opportunity to leverage our advanced technology and proven capabilities. We look forward to launching our functional products commercially within the next few months and can't help but see the similarities to the cannabis sector regarding the pathways to both medical and recreational legalization. I believe our ability to immediately begin working in this burgeoning sector will create immense value for our business, our stakeholders, partners and shareholders alike."<sup>251</sup> On September 2020, Pure Extracts was granted its Standard Processing License by Health Canada under the Cannabis Act and the Company's stock began trading on the Canadian Securities Exchange (CSE) on November 5, 2020.<sup>252</sup>

Pure Extracts has commenced the expansion of its business model to include mushroom formulations through the use of extraction processes that have proven compatible with its existing infrastructure. The Company is working closely with its scientific advisor, Dr. Alexander MacGregor, the founder of the Toronto Institute of Pharmaceutical Technology, to develop high bio-available products and novel delivery methodologies including pills, capsules, and edibles. Furthermore, the Company believes that there exists a significant opportunity for it to become an important extraction partner for the commercialization of new functional mushroom products designed with purity and consistency in mind. In that regard, Pure Extracts has signed a Letter of Intent (LOI) with one of Canada's leading functional mushroom wellness brands to co-develop CBD enhanced mushroom products.<sup>253</sup>

- Pure has contracted \$30MM in sales for first year of operations
- With 5 Years' experience of volatile plant molecule extraction
- Purpose-built EU GMP compliant facility, allowing for international distribution<sup>254</sup>

Pure Extracts aims to eventually enter the growing field of psychedelic mushroom processing as an additional aspect of its diverse extraction market penetration strategy. In the interim, three functional products such as lion's mane, turkey tail and reishi are being created under the 'Pure Mushrooms' brand. In herbal medicine, these products are thought to boost memory, support the immune system or reduce stress. Pure Mushrooms products are projected for availability by the end of Q1 2021 via direct-to-consumer sales utilizing the Company's capital efficient, e-Commerce web portal. The creation of these products will validate the Company's processes and capabilities and prepare it as additional strains become available.

Currently the company features an all-new, state-of-the-art processing facility located just 20 minutes north of world-famous Whistler, British Columbia. The bespoke facility has been constructed to European Union GMP standards aiming towards export sales of products and formulations, including those currently restricted in Canada, into European jurisdictions where they are legally available.

## Funding

<sup>249</sup><https://www.globenewswire.com/news-release/2020/12/15/2145555/0/en/Havn-Life-Sciences-announces-increase-in-Bought-Deal-Financing-to-10-Million.html>

<sup>250</sup><https://pureextractscorp.com/about>

<sup>251</sup><https://www.globenewswire.com/news-release/2020/11/26/2134221/0/en/Pure-Extracts-Advances-Plans-for-the-Processing-of-Functional-Mushroom-Formulations.html>

<sup>252</sup><https://www.globenewswire.com/news-release/2020/11/26/2134221/0/en/Pure-Extracts-Advances-Plans-for-the-Processing-of-Functional-Mushroom-Formulations.html>

<sup>253</sup><https://www.streetinsider.com/Globe+Newswire/Pure+Extracts+Advances+Plans+for+the+Processing+of+Functional+Mushroom+Formulations/17653610.html>

<sup>254</sup><https://www.psychedelicfinance.com/company/pure-extracts-corp>

They had a Pre-Money Valuation of \$16M<sup>255</sup> with investors who have financed the company for a total \$9.45M CAD.<sup>256</sup>

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#### CORE ONE LABS (“COOL” – CSE)

Developing a thin-film oral strip, which could become one of the potential novel delivery forms for psychedelic medicines. They are working to develop IP in this space.

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#### PHARMADRUG (“BUZZ” – CSE)

Pharmadrug is an international medical company who acquired Pharmadrug GmbH, a German medical cannabis distributor. They just entered psychedelics through the acquisition of Super Smart, a Netherlands-based retailer with a focus on magic mushrooms.

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#### TRYP THERAPEUTICS (“TRYP” – CSE)

Focusing on rare diseases and conditions which have not been met with any medical solutions yet. Currently looking at the treatment of fibromyalgia, a condition characterized by musculoskeletal pain, fatigue, sleep, memory and mood issues.

### U.S. COMPANIES

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#### SILO WELLNESS

<https://www.silowellness.com/>

Silo was founded in San Francisco by Antonio Bustamante, Ashton Braun, Chia-ying Jackie Lee in 2018. They have been in the psychedelics and functional mushroom space since 2018. In addition to its IP portfolio, SILO is focusing on consumer product and wellness centre/retreat brand development for psychedelic and functional mushrooms.

##### About

In 2019 they formulated and announced a patent-pending psilocybin nasal spray in Jamaica. This metered-dosing delivery modality was created for consumer micro dosing to address some of the primary issues that may prevent many from trying natural psychedelics for the first time, including dose reliability, taste, stomach upset, and stigma. The nasal spray bypasses the digestive system by entering the bloodstream through the nasal membranes.<sup>257</sup>

- Silo Wellness claims to have filed a provisional patent application in July, “to cover metered dosing formulations of plant and fungal compounds for oral, nasal, sublingual, and topical use.” They also intend to develop products around other psychedelic plants, such as peyote and ayahuasca.<sup>258</sup>
  - Essentially to ease new timers into using these drugs and giving them a way in and giving them to the masses. functional mushroom – did some testing in Missouri in 2000 with teachers. Acceptable reliable meter dosing form through natural medicine which others may be afraid of can see a familiar modality and can have a controlled meter.

<sup>255</sup> <https://www.psychedelicfinance.com/articles/pure-extracts-corp-ipo-round>

<sup>256</sup> <https://au.finance.yahoo.com/news/pure-extracts-technologies-corp-commence-170000958.html>

<sup>257</sup> <https://www.silowellness.com/>

<sup>258</sup> <https://psychedelicreview.com/magic-mushroom-microdosing-nasal-spray-announced/>

Its go-to-market revenue strategy includes scaling its United States Silo Reboot brand of functional mushrooms (via [www.SiloReboot.com](http://www.SiloReboot.com)) and its magic mushroom cultivation and psychedelic retreat operations in Jamaica (via [www.SiloRetreats.com](http://www.SiloRetreats.com)). Products from changa for the immune system, Turkey Tail for inflammation.<sup>259</sup>

First of its kind U.S legal psychedelic retreat

- In Jamaica
  - With their military veterans mushroom retreat with the world's first legal magic mushroom growers' certification.
- Oregon Ketamine-Assisted Wellness Retreat<sup>260</sup>
  - Coming in January 16-21, 2021 and will pursue a clinical psilocybin-assisted counselling element with patients using the psilocybin nasal spray prior to sessions through either licensees or through Silo's own branded psilocybin service centres.

#### Funding

In September Silo raised \$9,000,000 / Series A from Andreessen Horowitz VC and 2 other investors<sup>261</sup> which currently totals their funding to \$12 million.

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#### EHAVE (EHVVF: OTC)

<https://www.ehave.com/>

Found in 2012 in Ontario, Ehave is a public healthcare company developing a next generation of digital solutions for stakeholders in the medical cannabis and mental health sectors. Making its mark in the psychedelic medicine space as a provider of digital therapeutics delivering evidence-based therapeutic interventions to patients with a focus on ADHD and ADD.

#### About

Their primary focus is on improving the standard care in therapeutics to prevent or treat brain disorders or diseases through the use of digital therapeutics, independently or together, with medications, devices, and other therapies to optimize patient care and health outcomes.

- Their main product is the Ehave Telemetry Portal, which is a mental health informatics platform that allows clinicians to make objective and intelligent decisions through data insights. The Ehave Infinity Portal offers a powerful machine learning and artificial intelligence platform with a growing set of advanced tools and applications developed by Ehave and its leading partners. This empowers patients, healthcare providers, and payers to address a wide range of conditions through high quality, safe, and effective data-driven involvement with intelligent and accessible tools.<sup>262</sup>
- With an interest in psychedelic research, Ehave's Dashboard offers the medical and research community an opportunity to share information with an emphasis on security. The Ehave Dashboard has been developed through years of testing with mental healthcare professionals at one of Canada's largest hospitals, Toronto's Hospital for Sick Children. In addition to providing better outcomes, the proprietary platform allows individuals to take control of their physical and mental health by enabling them to carry their medical records with them wherever they go.<sup>263</sup>

Ehave, Inc. Announces Psychedelic Retreats Through Its Mycotopia Therapy Subsidiary

- They will utilize their mental health informatics platform to offer psychedelic retreats through its wholly owned subsidiary, Mycotopia Therapy. The psilocybin-guided wellness retreats will be offered in

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<sup>259</sup> <https://siloreboot.com/collections/all>

<sup>260</sup> <https://siloretreats.com/schedule>

<sup>261</sup> <https://www.crunchbase.com/organization/silo-d400>

<sup>262</sup> <https://www.ehave.com/post/ehave-inc-launches-premier-psychedelic-retreat-centers-partnership-and-myifeid-card-giveaway>

<sup>263</sup> <https://www.globenewswire.com/news-release/2020/10/15/2109066/0/en/Trends-in-Psychedelic-Drugs-Research-and-Four-Stocks-You-Should-Know-About.html>

various locations around the world and will be supervised by qualified medical professionals in a safe, legal, and comfortable setting.<sup>264</sup>

- The retreats will be located in Jamaica [www.mycomeditations.com](http://www.mycomeditations.com) and Amsterdam [www.psychedelicsights.com](http://www.psychedelicsights.com). Both of the premier psilocybin-guided wellness retreats will be supervised by highly qualified medical professionals. The primary focus of the retreats will be to serve as a means of improving the mental health of individuals suffering from anxiety, OCD, treatment-resistant depression, addiction, and anxiety and depression related to terminal illness. Ehave's premier psilocybin-guided wellness retreats are not to be confused with recreational drug use. The retreats are a controlled process guided by trained and licensed counsellors using psychedelics as self-exploratory and therapeutic plant medicine. Ehave will be the booking partner and expects to list additional retreats for more consumer options.<sup>265</sup>

Ehave also owns a piece of the PsyTech Summit , which brings together decision makers, investors, clinicians, thought leaders, and advocates for the purpose of advancing psychedelics science, business, and reform.

Funding: Current Market Cap of \$6.51m

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## GABA THERAPEUTICS

<https://gabarx.com/>

GABA Therapeutics is a California based biotechnology company focused on developing its lead compound GRX-917 for anxiety, depression and a broad range of neurological disorders. GRX-917 has the potential to become front-line therapy for anxiety and has composition-of-matter patent protection until 2036. Moreover, preclinical studies using etifoxine have demonstrated efficacy in a broad range of other neurological disorders, including pain, multiple sclerosis, epilepsy and Alzheimer's disease.

- “We are very pleased to partner with the team at ATAI,” said Dr. Ian J. Massey, CEO, GABA. “They are building a world-class portfolio of mental health companies and GRX-917’s potential to address the immense unmet medical need of unmanaged anxiety makes it a natural addition. We are grateful to have the funding and support of ATAI to drive forward this important program.”
- “We are thrilled to partner with GABA and will fully support all efforts to bring GRX-917 to patients as quickly as possible,” added Christian Angermayer, Founder, ATAI Life Sciences.<sup>266</sup>
  - GABA Therapeutics’ lead compound, GRX-917, is a deuterated version of etifoxine, a safe and effective anxiolytic medication approved in approximately 40 countries with rapid onset and efficacy comparable to leading benzodiazepines like alprazolam (Xanax™) and lorazepam (Ativan™). In contrast to these and other benzodiazepines, however, more than 30 years of clinical experience with etifoxine suggest that GRX-917 is unlikely to produce serious side effects like sedation, amnesia, tolerance or physical dependence.

## Funding

The Series A investment of up to \$15.5 million will fund the program through a Phase IIa proof-of-concept study.<sup>267</sup>

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## WAKE NETWORK

<https://wake.net/>

The Wake Network is furthering their research of psychedelic medicine with the help of mycology and fungus-derived therapy for patients fighting mental illnesses such as PTSD, depression, alcoholism, and addictions to

<sup>264</sup> <https://www.globenewswire.com/news-release/2020/08/28/2085438/0/en/Ehave-Inc-Announces-Psychedelic-Retreats-Through-Its-Mycotopia-Therapy-Subsidiary.html>

<sup>265</sup> <https://www.ehave.com/post/ehave-inc-launches-premier-psychedelic-retreat-centers-partnership-and-myifeid-card-giveaway>

<sup>266</sup> <https://www.atai.life/2020/11/09/gaba-therapeutics-and-atai-life-sciences-partner-to-develop-a-novel-gaba-modulator-for-the-treatment-of-mood-disorders-2/>

<sup>267</sup> <https://www.atai.life/2020/11/09/gaba-therapeutics-and-atai-life-sciences-partner-to-develop-a-novel-gaba-modulator-for-the-treatment-of-mood-disorders-2/>



opioids to name a few. The Wake Network says that their approach is to advance the field of fungi & plant medicine. The company states that it is built on three pillars: clinical research, wellness professionals, and technology, to assemble a team of leaders and researchers who plan to lead the future of mental and holistic health. The company aims to implement these goals by integrating with a leading cloud-based data & clinical trial platform.

### About

Earlier this year, Wake Clinics opened a 3,000-acre mountain retreat, private beach and pavilion in Jamaica (soon to include British Virgin Islands, Denver, Netherlands and Brazil)<sup>268</sup>. The facility offers psilocybin-based therapy where licensed professionals assess patients and track biofeedback. Therapists who work at the clinic provide ongoing monitoring to ensure the full integration of the healing process.

- Wake Jamaica is a separate division of the business and is a cultivation-focused joint venture subsidiary that is managed by Pauline Smith and her group of mycologists and farmers.
- The other division of WAKE is focused on the development of a line of premium functional mushroom products.<sup>269</sup>

The company uses AdvancedCare, a leading virtual clinical trial platform, utilized by CROs worldwide for research. AdvancedCare works with a cost-efficient software and hardware platform that provides patient feedback, medication intake, and vitals monitoring all in real-time. As the advance in pharm-tech solutions continues to rise, The Wake Network has made an exclusive agreement with AdvancedCare to further their scientific research, data collection, and communications relating to psilocybin studies.<sup>270</sup>

### Funding

The Wake Network had a seed funding round of \$154,000 in August 2020.

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## GILGAMESH PHARMACEUTICALS

<https://www.gilgameshpharmaceutical.com/>

In 2019 Jonathan Sporn (CEO), Dalibor Sames (CSO), Andrew Kruegel and Mike Cunningham co-founded Gilgamesh a private preclinical biotechnology company based in New York, which aims to produce novel Psychotropic Drugs for the Treatment of Neuropsychiatric conditions including depression, anxiety, substance use, and stress-related disorders. They have a disciplined focus on developing innovative new chemical entities (NCE's) leveraging a unique combination of medicinal chemistry, intellectual property strategy, neuroscience & neurobiology, and drug development expertise. Gilgamesh and/or its Columbia University Partner have filed intellectual property for all of its key programs. Gilgamesh is a Y-Combinator company leveraging the tremendous business expertise and network of Y-Combinator. Gilgamesh has a team of entrepreneurs and experienced drug developers who have exited start-ups and have worked on blockbuster pharmaceutical products in big pharma to insure operational excellence and execution.<sup>271</sup>

### About

With their understanding of chemistry and neurobiology for ketamine analogs and psychedelic-related central nervous system compounds. They have known mechanisms of action, efficacy and demonstrated safety in long-term use in a variety of psychiatric conditions. A high probability of success is ensured by using these proven compounds as the basis for developing a portfolio of novel and patent protected new medicines.

They are developing Arylcyclohexylamine, a "Better Ketamine" that is fast to clinic and exit. Treatment-Resistant Depression (adjunctive) as well as opiate use disorder. Oral formulation, composition of matter patent, robust efficacy, non-dissociative, low abuse potential, rapid onset, anti-suicidal.

<sup>268</sup> <https://wake.net/clinics/>

<sup>269</sup> <https://mushroomstocks.com/cannabis-article/wake-network-is-creating-a-multi-faceted-platform-to-bring-psychedelic-therapies-to-market/>

<sup>270</sup> <https://thedalesreport.com/life-sciences/psychedelic-startup-the-wake-network-backed-up-by-an-all-female-mycologist-team/>

<sup>271</sup> <https://www.psychedelicfinance.com/company/gilgamesh-pharmaceuticals>

- Serotonergic Micro-Dose for ADHD, MDD with Cognitive Impairment, which will be safe home use, low abuse potential, subchronic use, no SSRI/SNRI AEs, rapid onset.
- Novel Ibogaine Analogue for Opioid Use Disorder (reduce relapse, withdrawal) as a single or periodic Tx, reduces withdrawal, reduces need for maintenance therapy, rapid onset.

The expected drug profiles are all in very large multibillion dollar markets that will be of interest to pharma and insurance customers given the high unmet need in psychiatry.

#### Funding

Gilgamesh has raised a pre-seed round of \$2.6M for lead optimization of molecules.<sup>272</sup>

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## TACTOGEN

<https://tactogen.com/>

Tactogen is a pharma tech start-up based in California created in 2020 developing the next generation of empathogen medicines. Founded by Genentech data science leader and PhD neuroscientist Matthew Baggott and deeptech serial entrepreneur Luke Pustejovsky, Tactogen's purpose is to increase the experience of connection between people.

#### About

Gentler, less euphoric compounds within the MDMA family can increase feelings of openness and connection and will be safe and effective for at-home use.

- Using AI, Tactogen has mined the back catalogue of research and discovered hidden gems and novel compounds that were never made illegal but that have clear therapeutic promise. Tactogen's lead candidate compounds are not as 'mind blowing' as psilocybin or MDMA, but they produce emotional openness and grounding and can facilitate psychotherapy, decision-making, and psychological growth.<sup>273</sup>

#### Funding

Although the company has not made any concrete announcements. It has indicated that it is a public benefit corporation.<sup>274</sup>

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<sup>272</sup> <https://www.psychedelificfinance.com/company/gilgamesh-pharmaceuticals>

<sup>273</sup> <https://angel.co/company/tactogen-1>

<sup>274</sup> <https://blossomanalysis.com/companies/tactogen/>