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MODERNIZING PSILOCYBIN POLICY TO IMPROVE MENTAL HEALTH OUTCOMES

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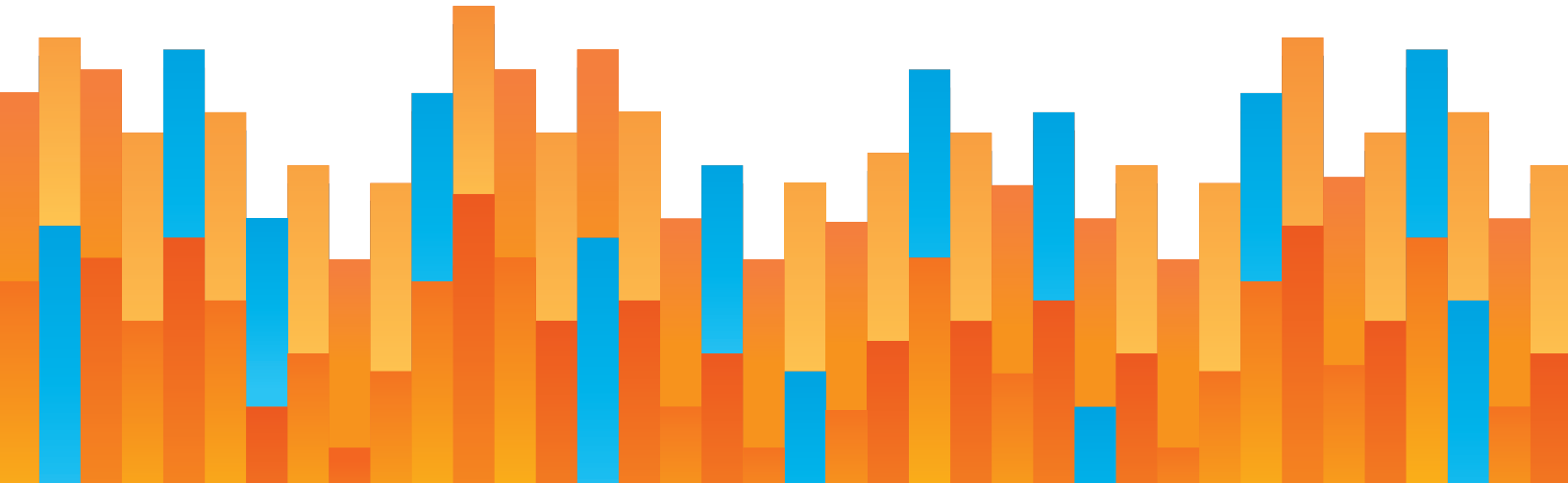

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EXECUTIVE SUMMARY

The COVID-19 pandemic has exacerbated a national mental-health crisis in the United States. Drug overdose deaths have climbed rapidly over the past 20 years, and suicide rates have gradually increased.

Psilocybin and other psychedelics have shown great promise in treating mental-health conditions, but their use is severely limited by legal and social obstacles. Over the past decade, medical and scientific communities have increasingly recognized the potential of psychedelic therapies for the treatment of intractable mental health conditions. Legal and logistical barriers to innovation have remained as the range of potential uses for psychedelic substances has expanded. Accessing a reliable, high-quality supply of experimental drugs for clinical trials has been a major obstacle.

Psychedelics have the potential to be more effective than conventional drugs now being used to treat a range of mental health disorders. Current drug options frequently have efficacy rates in the low teens.[1]

The U.S. Food and Drug Administration (FDA) began expediting psilocybin research and approval by designating it as a "breakthrough therapy" in 2019 after the agency recognized

[1] Jude Sky, "Psychedelic Medicine: A Review of Clinical Research for a Class of Rapidly-Emerging Behavioral Health Interventions," Report Prepared for *BrainFutures*, March 2022. Available at: https://www.brainfutures.org/wp-content/uploads/2022/05/BrainFutures-Psychedelic-Medicine-Report.pdf.

psilocybin-assisted therapy as potentially far more effective than treatments currently available on the market.[2] In 2017, the FDA designated MDMA as a breakthrough therapy for post-traumatic stress disorder.[3]

If research shows SSRIs and psychedelics do not negatively interact when administered together, psychedelic-assisted therapies could transform from stand-alone treatments to complementary treatments, which would expand their markets.

Many of the people who are helped by psychedelic-assisted therapies are also taking other drugs, like selective serotonin reuptake inhibitor (SSRI) antidepressants, for relief. It's important to learn how these common drugs and psychedelics interact with each other. If research shows SSRIs and psychedelics do not negatively interact when administered together, psychedelic-assisted therapies could transform from stand-alone treatments to complementary treatments, which would expand their markets. This could allow participants in the therapy to slowly taper off SSRIs as the longer lasting effectiveness of psychedelic-assisted therapies take hold so that these individuals do not suffer from rapid withdrawal symptoms. Alternatively, there may be some scenarios in which a patient and their doctor wish to continue SSRI usage alongside psychedelic-assisted therapies, although many patients may hope psychedelic therapies can enable them to avoid the need for continual, ongoing medication.

Oregon, Colorado, and Washington, D.C., are already taking strides toward establishing regulatory frameworks that allow licensed professionals to administer psilocybin therapy even without FDA approval of these treatments. Lawmakers in other states have proposed comparable legislation in rapid succession, indicating that state-licensed psychedelic therapies are likely to continue expanding. These regulatory regimes could increase the

[2] Rachel Feltman, "The FDA Is Fast-Tracking a Second Psilocybin Drug to Treat Depression," *Popular Science*, November 26, 2019. Available at: https://www.popsci.com/story/health/psilocybin-magic-mushroom-fda-breakthrough-depression/.

[3] U.S. Food and Drug Administration, "IND 63384: Grant—Breakthrough Therapy Designation," Letter to Multidisciplinary Association for Psychedelic Studies, August 15, 2017, Available at: https://maps.org/wp-content/uploads/2017/08/2017.08.15-IND063384GrantBreakthroughTherapyDesignation1_Redacted.pdf.

accessibility of these therapies because drug makers would not need to recover the costs of FDA trials within their pricing schemes. At the same time, state regulation can ensure the safety of cultivation and manufacturing processes and, where appropriate, restrict access to qualified patients or individuals.

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PART 1

INTRODUCTION AND BACKGROUND

There are a variety of biological ("pharmacotherapy") and psychological ("psychotherapy") treatment options for depression, each of which focuses on a distinct aspect believed to be the primary pathological cause under its own unique theoretical framework.[4] Commonly used pharmaceutical treatments are mostly based on the idea that depression is brought on by a lack of monoamine neurotransmitters, including serotonin (5-HT), dopamine, and norepinephrine and their receptors, which are crucial for controlling mood, arousal, and memory.

Different forms of antidepressants, such as selective serotonin reuptake inhibitors (SSRIs) or monoamine-oxidase inhibitors, are thought to lessen depression symptoms by raising these neurotransmitter levels to differing degrees.[5] Antidepressants,[6] despite helping only a portion of patients diagnosed with severe depression, can have serious side effects,

4 Susan Nolen-Hoeksema, "Mood Disorders and Suicide," In: *Abnormal Psychology*. Boston: McGraw-Hill (2017). p. 172-213.

5 Stephen M. Stahl, "Stahl's Essential Psychopharmacology: Neuroscientific Basis and Practical Applications (Fourth Edition)," Cambridge University Press (2013), 8(1):146-50.

6 Jay C. Fournier et al. "Antidepressant Drug Effects and Depression Severity: A Patient-Level Meta-Analysis." Journal of the American Medical Association, Vol. 303, No. 1 (2010), pp. 47-53. Available at: https://pubmed.ncbi.nlm.nih.gov/20051569/.

including sexual dysfunction and cardiovascular hazards.[7] In addition, there is a considerable risk of relapse after stopping antidepressants, which is why they are frequently taken on a long-term basis.[8]

> *Antidepressants, despite helping only a portion of patients diagnosed with severe depression, can have serious side effects, including sexual dysfunction and cardiovascular hazards.*

Interpersonal therapy and cognitive-behavioral therapy (CBT), both based on many psychosocial theories that aim to change one's behavioral and cognitive biases through regular therapy sessions, are two types of psychotherapy used to address depression. Although there are significant reductions in depression symptoms,[9] recurrence and dropout rates are still rather high.[10] Because of this, typical pharmaco- and psychotherapies for major depressive disorder (MDD) are usually combined, which has been proven to be more successful than either method alone.[11] Even so, a sizable share of MDD patients never fully recover, including roughly 75% after 8 weeks and around 25% after 24 weeks of therapy.[12]

In response to the limitations of traditional pharmacotherapeutic or psychotherapeutic treatments, there has been a rapidly growing interest in the potential use of psychedelic compounds to address depression and various other mental health conditions, and some

7 Glen L. Stimmel and Mary A. Gutierrez, "Sexual Dysfunction and Psychotropic Medications," *CNS Spectrums*, Vol. 8, No. 9 (2006), pp. 24-30. Available at: https://pubmed.ncbi.nlm.nih.gov/16871135/.

8 Michael E. Thase and Timothy Denko, "Pharmacotherapy of Mood Disorders," *Annual Review of Clinical Psychology*, Vol. 4 (2008), pp. 53-92. Available at: https://pubmed.ncbi.nlm.nih.gov/18370614/.

9 Leslie A. Robinson, Jeffrey S. Berman and Robert A. Neimeyer, "Psychotherapy for the Treatment of Depression: A Comprehensive Review of Controlled Outcome Research," *Psychological Bulletin*, Vol. 108, No. 1 (1990), pp.30-49. Available at: https://pubmed.ncbi.nlm.nih.gov/2200072/.

10 Joshua K. Swift and Roger P. Greenberg, "Premature Discontinuation in Adult Psychotherapy: A Meta-Analysis," *Journal of Consulting and Clinical Psychology* ,Vol. 80, No. 4, pp. 547-559. Available at: https://pubmed.ncbi.nlm.nih.gov/22506792/.

11 Pim Cuijpers et al., "Adding Psychotherapy to Pharmacotherapy in the Treatment of Depressive Disorders in Adults: A Meta-Analysis," *Journal of Clinical Psychology*, Vol. 70, No. 9, pp. 1219-1229. Available at: https://pubmed.ncbi.nlm.nih.gov/19818243/.

12 Diego Novick et al., "Recovery in Patients with Major Depressive Disorder (MDD): Results of a 6-Month, Multinational, Observational Study," *Patient Preference and Adherence*, Vol. 11 (2017), pp. 1859-1868. Available at: https://pubmed.ncbi.nlm.nih.gov/29184393/.

have proposed psilocybin as a promising alternative treatment method. Psilocybin is a naturally occurring hallucinogenic substance present in some types of mushrooms. Many cultures throughout history have used it to elicit altered states of consciousness for ceremonial, therapeutic, medical, and spiritual purposes.[13] Psilocybin is currently listed as a Schedule I substance under the Controlled Substance Act and banned under federal law in the United States.[14] Meanwhile, a growing body of data suggests that psilocybin use may have therapeutic advantages.

A 2004 pilot study from the University of California, investigating the possibility of psilocybin treatment in patients with advanced-stage cancer, reignited interest and significantly renewed efforts in psilocybin research, ushering in a new era in the investigation of psychedelic therapy. Since then, much has been discovered about the chemical characteristics of psilocybin as well as its possible therapeutic applications.[15]

Psilocybin has low physiological toxicity, low risk of abuse or addiction, safe psychological reactions, and no linked persistent harmful physiological or psychological effects during or after use.

Generally, psilocybin is said to have the best safety profile of any psychedelic substance. Psilocybin has low physiological toxicity, low risk of abuse or addiction, safe psychological reactions, and no linked persistent harmful physiological or psychological effects during or after use, according to thousands of years of anecdotal data as well as contemporary scientific investigations. Psilocybin overdose is extremely uncommon.[16]

13 Mason Marks and I. Glenn Cohen, "Psychedelic Therapy: A Roadmap for Wider Acceptance and Utilization," *Nature Medicine*, Vol. 27 (2021) pp. 1669-1671. Available at: https://www.nature.com/articles/s41591-021-01530-3.

14 Fenderson, E. (n.d.). *Drug Fact Sheet: Psilocybin*. DEA.gov. Retrieved August 2, 2022, from https://www.dea.gov/sites/default/files/2020-06/Psilocybin-2020_0.pdf

15 Henry Lowe et al., "The Therapeutic Potential of Psilocybin," *Molecules*, Vol. 26, No. 10 (2021), p. 2948. Available at: https://pubmed.ncbi.nlm.nih.gov/34063505/.

16 Bob Yirka, "Phase 1 Clinical Trials for Psilocybin Show No Adverse Effects," *Science X Network*, December 13, 2019, https://medicalxpress.com/news/2019-12-phase-clinical-trials-psilocybin-adverse.html.

The FDA certifies a drug as a breakthrough therapy if preliminary clinical data indicates that it may significantly outperform current treatments. [17] In the space of one year, the FDA designated psilocybin therapy, which is now being evaluated in clinical trials, as a "breakthrough therapy" for the treatment of two different forms of depression. This designation is intended to speed up the customarily drawn-out process of drug development and evaluation. According to the FDA, it is normally requested by a pharmaceutical company and only approved when early research indicates the drug may be a far superior treatment option to those currently on the market.

The FDA's granting of breakthrough status to psilocybin therapy is particularly significant given that psilocybin is a Schedule 1 substance and its manufacture and distribution is expressly forbidden under federal law.

Psilocybin therapy received this designation in 2021 in the ongoing clinical trials being conducted by COMPASS Pathways to examine psilocybin's potential to treat severe depression in patients whose condition has not improved after receiving two antidepressant medications.[18] The FDA's granting of breakthrough status to psilocybin therapy is particularly significant given that psilocybin is a Schedule I substance and its manufacture and distribution is expressly forbidden under federal law.

Dr. Matt Johnson, a prominent scientist at Johns Hopkins University's psychedelics research center and leading expert, claims psilocybin has some abuse potential and risk; however, there isn't much evidence to support it causing physical dependence. Generally, it can be used safely when administered under medical supervision.[19] However, because the

17 U.S. Food and Drug Administration, "Breakthrough Therapy." Webpage published January 4, 2018, https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy.

18 Yasemin Saplakoglu, "FDA Calls Psychedelic Psilocybin a 'Breakthrough Therapy' for Severe Depression," *LiveScience*, November 25, 2019, https://www.livescience.com/psilocybin-depression-breakthrough-therapy.html.

19 Matthew W. Johnson et al., "The Abuse Potential of Medical Psilocybin According to the 8 Factors of the Controlled Substances Act," *Neuropharmacology*, Vol. 142 (2018), pp. 143-166. Available at: https://pubmed.ncbi.nlm.nih.gov/29753748/.

medication tends to intensify the current affective state, unpleasant effects, such as anxiety or psychotic reactions, may happen when psilocybin is delivered in a setting that could trigger negative emotional sentiment.[20] Researchers like Johnson argue it is crucial to provide patients with psychological support and environments that make them feel comfortable and safe in order for psilocybin-assisted therapy to achieve its intended benefits.[21]

Psilocybin offers promise for a range of additional disorders, including anxiety in terminal illness, neurodegenerative disease, obsessive-compulsive disorder, and drug dependency, aside from its potential therapeutic efficacy in treating depression.

Psilocybin initiates long-lasting favorable changes in well-being, attitude, and personality with just one administration if certain measures are taken.[22] Psilocybin offers promise for a range of additional disorders, including anxiety in terminal illness, neurodegenerative disease, obsessive-compulsive disorder, and drug dependency, aside from its potential therapeutic efficacy in treating depression.[23] Although preliminary, these promising findings are mostly based on a limited number of small-scale controlled trials, limiting the widespread acceptance for use in clinical practice.

[20] Frederick S. Barrett et al., "Double-Blind Comparison of the Two Hallucinogens Psilocybin and Dextromethorphan: Effects on Cognition. *Psychopharmacology*, Vol. 235 No. 10 (2018), pp. 2915-2927. Available at: https://pubmed.ncbi.nlm.nih.gov/30062577/.

[21] Matthew W. Johnson, William A. Richards and Roland R. Griffiths, "Human Hallucinogen Research: Guidelines for Safety," *Journal of Psychopharmacology*, Vol. 22, No. 6 (2008), pp. 603-620. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3056407/.

[22] Roland R. Griffiths et al., "Psilocybin Occasioned Mystical-Type Experiences: Immediate and Persisting Dose-Related Effects," *Psychopharmacology* Vol. 218, No. 4 (2011), pp. 649-65, https://pubmed.ncbi.nlm.nih.gov/21674151/.

[23] Stephen Ross et al., "Rapid and Sustained Symptom Reduction Following Psilocybin Treatment for Anxiety and Depression in Patients with Life-Threatening Cancer: A Randomized Controlled Trial," *Journal of Psychopharmacology*, Vol. 30, No. 12 (2016), pp. 1165-1180, https://pubmed.ncbi.nlm.nih.gov/27909164/.

PART 2

REVIEWING RECENT CLINICAL TRIALS

2.1 THE REGULATORY PROCESS FOR DRUG APPROVAL

Many early investors in the psychedelic producer space are aiming to patent psychedelic substances and procedures for making and administering them. But securing patent protection is only one step in pharmaceutical development. Sponsors of potential new drugs must also secure FDA approval before they can market new products by taking proposed new drugs through FDA-supervised clinical trials as part of an investigational new drug application.

The drug development process consists of six stages: discovery, preclinical, phase I, phase II, phase III, and approval:[24]

- **Discovery:** Finding one or more appropriate compounds with the potential to treat particular diseases is the initial step in the drug development process. Researchers screen a large number of compounds in the lab to find those with the desired qualities before choosing the lead candidates and potentially moving forward to preclinical research.

[24] For a review of the drug approval process, see Geoffrey Lawrence, "How to Reform the FDA," Reason Foundation policy brief, August 2022, https://reason.org/policy-brief/how-to-reform-the-fda/.

- **Preclinical Stage:** The preclinical stage involves lab and animal testing of lead compounds to determine if they are safe for human testing. If the drug sponsor determines that a drug may be a viable candidate for further development, the sponsor must submit an investigational new drug application to the FDA documenting the results of preclinical research and request to conduct FDA-supervised clinical trials in humans.
- **Phase I:** Clinical trials in Phase I are meant to confirm basic human safety. A small group of healthy volunteers are administered the medication to screen for any potential negative effects and establish the safe dosage range.
- **Phase II:** The medicine is first tested in Phase II clinical trials on a small number of volunteer patients who suffer from the condition it is intended to treat. Phase II studies evaluate the drug's safety and effectiveness at various doses. Although judgments regarding overall efficacy cannot be formed due to the limited number of patients included, Phase II trials do offer advice on how to best construct larger Phase III trials to verify the drug's safety and efficacy.
- **Phase III:** Phase III trials, commonly referred to as pivotal trials, show a drug's safety and effectiveness in a sizable patient population. Normally, to demonstrate significant efficacy, at least two large-scale clinical trials demonstrating effectiveness beyond a placebo at the 95% confidence level are needed. Phase III trials are frequently multi-center, multinational trials because of the large number of subjects needed.
- **Approval:** The drug sponsor may now submit a new drug application. Regulatory agencies like the FDA examine the data gathered during all study phases (from preclinical to phase III), balance the proposed drug's relative effectiveness versus a placebo and its adverse indications, and then determine whether to approve the product. Following approval, ongoing monitoring and follow-up studies may be required.

In the case of psilocybin and other psychedelics, additional hurdles may impede the development of approved treatments. These substances are classified as Schedule I substances under the federal Controlled Substances Act, which means that their manufacture and distribution are strictly prohibited outside the context of approved clinical research. Even within this context, a drug sponsor must adhere to additional regulatory

procedures to prevent the diversion of inventory, including registration with the Drug Enforcement Administration.

> *Strong evidence favors rescheduling psilocybin. Psilocybin has a low risk of toxicity and a very low potential for dependence or addiction when compared to other Schedule I drugs like heroin and Schedule II drugs like cocaine and fentanyl.*

Strong evidence favors rescheduling psilocybin. Psilocybin has a low risk of toxicity and a very low potential for dependence or addiction when compared to other Schedule I drugs like heroin and Schedule II drugs like cocaine and fentanyl. Moving psilocybin or psilocybin-derived products to Schedules II, III, or IV generally would allow pharmaceutical products to be developed and marketed while restricting access to those receiving a doctor's prescription. A Schedule V designation would allow patients to access psilocybin outside the prescription system as state law may allow, such as administration through a regulated health center, religious organization, or over the counter.

2.2 PSILOCYBIN-RELATED CLINICAL TRIALS UNDERWAY

COMPASS Pathways, Usona Institute, B. More, Clairvoyant Therapeutics, Braxia Scientific, and Incannex Healthcare are all in Phase II of their psilocybin clinical trials. Beckley Psytech and Diamond Therapeutics are also in Phase I. Several of these institutes have combined their research, which aims to provide evidence for FDA approval of psilocybin as a prescription medication.

COMPASS:

COMPASS Pathways is a life sciences company that was started in 2016 to facilitate the process for patients to get evidence-based mental health innovations. In Europe and North

America, the firm is conducting a late-stage clinical trial of psilocybin therapy for people with depression that has failed to respond to other treatments.[25]

COMPASS Pathways published the results of its Phase IIb clinical trial in November 2022 and reported that nearly one-third of patients with treatment-resistant depression (TRD) achieved remission within three weeks of a single dose of psilocybin. This response was sustained through at least twelve weeks after administration.[26] TRD is defined as depression that persists after a person has attempted two different treatments attempting to alleviate depression symptoms.

Following the completion of this clinical trial with 233 enrolled participants the authors were able to show that a single administration of psilocybin (25 mg), despite its high dosage, was capable of lowering the Montgomery-Asberg Depression Rating Scale (MADRS), a clinical parameter used to determine the severity of depression, by 12 points.[27] The MADRS is a standardized questionnaire given to depression patients consisting of 10 questions in which respondents rate their symptoms on a scale of 0 to 6, for a maximum possible score of 60. High scores on the MADRS assessment indicate to mental health professionals that a patient is suffering from severe depressive symptoms based upon their own evaluation of their mental state.

“A high dose of psilocybin works immediately, the day after, for a large number of people, and continues to work," according to COMPASS CEO George Goldsmith's summary of the research.[28] The top-line findings, which revealed that at least twice as many patients in the 25 mg group as opposed to the 1 mg group demonstrated response to the medication and remission from their TRD at weeks 3 and 12, seem to support his claim.

This Phase IIb experiment is the largest randomized control double-blind psilocybin trial ever conducted. COMPASS' psilocybin-assisted therapy protocol appears to be effective in a

25 COMPASS Pathways, “About COMPASS Pathways: Our Values & Mental Health Innovations,” https://compasspathways.com/about-us/.

26 Guy M. Goodwin et al., “Single-Dose Psilocybin for a Treatment-Resistant Episode of Major Depression,” The New England Journal of Medicine,” *New England Journal of Medicine*, Vol. 387, No. 18 (2022), pp. 1637-1648. Available at: https://pubmed.ncbi.nlm.nih.gov/36322843/.

27 Andrea Mastinu et al., “The Bright Side of Psychedelics: Latest Advances and Challenges in Neuropharmacology,” *International Journal of Molecular Sciences*, Vol. 24, Iss. 2 (2023), https://www.mdpi.com/1422-0067/24/2/1329.

28 Cristin Flanagan and Tiffany Kary, “COMPASS Sinks After Depression Therapy Results Fuel Concerns,” *Bloomberg*, November 9, 2021, https://www.bloomberg.com/news/articles/2021-11-09/COMPASSpsilocybin-based-therapy-for-depression-shows-promise#xj4y7vzkg.

significant portion of participants. It's important to keep in mind when analyzing these findings that the population addressed in this were resistant to two other forms of treatment for depression previously. Following conclusion of the Phase IIb trial, COMPASS can submit a proposed design for Phase III trials to the FDA.

> *It's important to keep in mind when analyzing these findings that the population addressed in this were resistant to two other forms of treatment for depression previously.*

Usona Institute

Usona Institute is currently in a Phase II clinical trial investigating how psilocybin could be used to treat people with major depressive disorder (MDD), a condition characterized by significantly depressed mood and loss of interest in activities. More than 3 million cases of MDD per year present within the United States—a much wider population than those with TRD.

This is the first Phase II study of double-blind, placebo-controlled, randomized single-dose psilocybin to treat MDD. Set and setting are given priority in the study's non-directive, supportive psychotherapy framework.[29] Usona is actively analyzing the study's data and anticipates sharing results once available.

B. More

B. More, a non-profit clinical stage biopharmaceutical company, is currently researching psilocybin as a means to treat patients suffering from Alcohol Use Disorder (AUD) who may have been unsuccessful with more traditional drug and treatment programs.[30]

B. More recently announced that it had submitted an investigational new drug application and is planning a Phase IIb trial to examine the effectiveness of synthetic psilocybin for the treatment of AUD over a 24-week period. It will be the second-largest clinical trial of

[29] Usona Institute, "Psilocybin," Retrieved January 6, 2023, from https://www.usonainstitute.org/psilocybin.

[30] B.More Inc., "About Us," Retrieved July 27, 2022, from https://bmoreinc.org/about-us/.

psychedelics ever done, with 226 people taking part. Michael Bogenschutz, Director of the NYU Langone Center for Psychedelic Medicine, will lead the experiment, which is scheduled to begin in the later months of 2023.[31]

Clairvoyant

Clairvoyant is a Canadian drug development company focused on the development of psychedelic drug therapies for addiction. Clairvoyant's lead program is a Phase II trial focused on clinical validation of psilocybin for the treatment of AUD.[32]

Braxia Scientific

In August 2021, Braxia Scientific, based in Canada, announced the initiation of a Phase II trial studying psilocybin for TRD. Braxia and the Usona Institute united together on the project to evaluate the efficacy, viability, and safety of using various doses.[33]

Research institutes in the United States are expected to build upon Braxia's findings. As of December 2022, patients received their first dose in the first-ever Health Canada-approved, multi-dose psilocybin clinical trial conducted at Braxia Scientific's subsidiary Canadian Rapid Treatment Center of Excellence clinic. The trial establishes a psilocybin treatment framework for patients with TRD and opens a new pathway for patients to access psychedelic treatment. More specifically, Braxia has established access to a high-quality source of psilocybin that meets Canadian regulatory requirements for human use in clinical research and has received more than 150 referrals for psilocybin-assisted therapy for TRD at its clinic during the first six weeks of opening recruitment.[34]

31 B. More Inc., "B. More Submits FDA Investigational New Drug Application for Psilocybin Alcohol Use Disorder Program," *PR Newswire*, July 25, 2022, Retrieved July 29, 2022, from https://www.prnewswire.com/news-releases/bmore-submits-fda-investigational-new-drug-application-for-psilocybin-alcohol-use-disorder-program-301591794.html.

32 Clairvoyant Therapeutics, "Psychedelic Medicine Start Up Clairvoyant Therapeutics Welcomes Biotech, Cannabis Veteran Greg Engel as Director, Names Long Trinh as CFO," *PR Newswire*, October 6, 2021, Retrieved July 30, 2022, from https://www.prnewswire.com/news-releases/psychedelic-medicine-start-up-clairvoyant-therapeutics-welcomes-biotech-cannabis-veteran-greg-engel-as-director-names-long-trinh-as-cfo-301393421.html.

33 Michael Haichin, "Psychedelics Drug Development Tracker," *Psychedelic Alpha*, Retrieved December 31, 2022, from https://psychedelicalpha.com/data/psychedelic-drug-development-tracker.

34 Braxia Scientific Corp., "Braxia Scientific Achieves Milestone as Landmark Psilocybin Clinical Trial Commences, Participants Receive First Doses of Psilocybin," *PR Newswire*, January 6, 2023, https://www.prnewswire.com/news-releases/braxia-scientific-achieves-milestone-as-landmark-psilocybin-clinical-trial-commences-participants-receive-first-doses-of-psilocybin-301443725.html.

This study will determine whether psilocybin is safe and well-tolerated by evaluating changes in suicidal ideation and behavior, checking up on any individuals who decide to leave the trial, and quantifying any severe side effects and how long they last. Additionally, this research will examine the effect of psilocybin administration on depression symptoms.[35]

Incannex

Incannex, an Australian pharmaceutical company, is currently partnering with Monash University on a Phase IIa clinical trial evaluating the potential use of a combination of psilocybin administration and a specialized psychotherapy regimen for individuals with severe general anxiety disorder (GAD). The trial's primary goals are to evaluate safety, effectiveness, and tolerability, and its secondary outcomes include evaluations of quality of life, functional disability, and comorbidities. After 30 patients have finished the primary evaluation, an independent data safety monitoring board will perform a preliminary study of results to inform either a second phase of the Phase IIa trial with 42 additional patients or a Phase IIb trial.[36] The FDA has acknowledged that the therapeutic method for developing a psilocybin-assisted therapy for GAD is suitable and expressed interest in its advancement.

“The trial's primary goals are to evaluate safety, effectiveness, and tolerability, and its secondary outcomes include evaluations of quality of life, functional disability, and comorbidities.”

Beckly Psytech

In January 2021, the FDA granted Beckley Psytech authorization to conduct a groundbreaking clinical trial. This trial will be the first to study the effects of psilocybin on patients with transient unilateral neuralgiform headache (SUNHA), a rare form of headache

[35] Brain and Cognition Discovery Foundation, “Psilocybin for Treatment-Resistant Depression,” Retrieved September 8, 2022, from https://clinicaltrials.gov/ct2/show/NCT05029466.

[36] Incannex Healthcare Limited, “INCANNEX Healthcare Quarterly Activities Report and Appendix 4C Cash Flow Statement,” Retrieved September 8, 2022, https://www.prnewswire.com/news-releases/incannex-healthcare-quarterly-activities-report-and-appendix-4c-cash-flow-statement-301594276.html.

characterized by short bursts of intense, burning, piercing or throbbing pain. It will look at how the psychedelic compound might help treat this disabling disease.[37]

MindMedicine Inc.

MindMedicine Inc., also known as MindMed, is a New York-based psychedelic medicine biotech company that develops psychedelic-inspired medicines known as psychoplastogens and therapies to address addiction and mental illness. Their recent study revealed that treatment with escitalopram prior to psilocybin administration "substantially reduced negative drug effects, anxiety, unfavorable cardiovascular effects, and other adverse effects of psilocybin compared with placebo pretreatment" but had "no relevant influence on pleasant mood effects of psilocybin."[38] The study reveals that psilocybin, when co-administered with SSRIs, may be able to reduce the negative side effects of pharmaceutical treatments for mental disorders. Patients and psychedelic firms would benefit if co-administration of SSRI antidepressants and psychedelics was proven to be safe and effective. Co-administration would lower the entry hurdle for patients who might be reluctant to wean themselves off SSRIs (together with their healthcare providers) and would transform psychedelic-assisted therapies from monotherapies to adjunct therapies, considerably extending their markets.[39]

"The study reveals that psilocybin, when co-administered with SSRIs, may be able to reduce the negative side effects of pharmaceutical treatments for mental disorders."

[37] Marks and Cohen, note 13.

[38] Psychedelic Alpha, "MAPS' $70m Investment Vehicle; atai's Increased Stake in COMPASS; SSRI Psilocybin Interaction Study," Psychedelic Bulletin, December 5, 2021, https://psychedelicalpha.com/news/psychedelic-bulletin-maps-70m-investment-vehicle-atais-increased-stake-in-COMPASSpsilocybin-interaction-study.

[39] Psychedelic Alpha, "Psychedelic Research and Clinical Trials in 2021: A Year in Review," Retrieved August 2, 2022, https://psychedelicalpha.com/news/psychedelic-research-and-clinical-trials-in-2021.

PART 3

ACADEMIC RESEARCH INTO PSILOCYBIN

Interest in the potential therapeutic effects of psilocybin and other psychedelic substances extends far beyond those conditions for which psilocybin products are currently undergoing supervised clinical trials. Researchers have been investigating the potential of psilocybin on a smaller scale within academic settings for decades and have identified a wide range of conditions for which psilocybin and other psychedelic substances may prove beneficial.

> *"In a number of 2021 publications, researchers suggested that psychedelic therapies might someday be used to heal brain damage, autism, ADD, ADHD, and Alzheimer's."*

In a number of 2021 publications, researchers suggested that psychedelic therapies might someday be used to heal brain damage, autism, ADD, ADHD, and Alzheimer's. These substances may be used for a far wider range of psychiatric and neurodegenerative therapy indications should the mounting evidence continue to support the hypothesis of

psychedelic-induced neuroplasticity in humans.[40] Neuroplasticity refers to the ability of psychedelics to induce creation of new neural pathways within the brain, which can overcome the deterioration of existing neural pathways.

The promising neurotrophic and anti-inflammatory properties of psilocybin are generating interest as a therapeutic for neurodegenerative diseases based on its ability to promote neuroplasticity. Although preclinical results are consistent, clinical trials are currently scarce and mostly focus on the treatment of depression associated with neurodegenerative diseases like Parkinson's and Alzheimer's.[41]

Psilocybin's effectiveness in reducing alcohol, tobacco, and substance abuse are in line with the results demonstrated by other psychedelic drugs, as the long-lasting improvements were detectable up to six months after psilocybin administration.[42] One study concluded a 67% success rate of smoking cessation that lasted at least 12 months after psilocybin administration.[43] No other known therapy to assist in smoking cessation has even approached this success rate.

> *Another study determined that psilocybin use in isolation may result in a reduction in psychological distress or suicidal tendencies and that other psychedelic treatments are unnecessary to produce these results.*

40 Dölen, J. H. (n.d.). *Psychedelic Research and Clinical Trials in 2021*. Psychedelic Alpha. Retrieved August 2, 2022, from https://psychedelicalpha.com/news/psychedelic-research-and-clinical-trials-in-2021

41 Simon Andrew Vann Jones and Allison O'Kelly, "Psychedelics as a Treatment for Alzheimer's Disease Dementia," *Frontiers in Synaptic Neuroscience*, Vol. 12 (2020) 12, https://www.frontiersin.org/articles/10.3389/fnsyn.2020.00034/full.

42 Elizabeth M. Nielson et al., "The Psychedelic Debriefing in Alcohol Dependence Treatment: Illustrating Key Change Phenomena through Qualitative Content Analysis of Clinical Sessions," *Frontiers in Pharmacology*, Vol. 9 (2018), p. 132. Available at: https://pubmed.ncbi.nlm.nih.gov/29515449/.

43 Matthew M. Johnson, Albert Garcia-Romeu and Roland R. Griffiths, "Long-Term Follow-Up of Psilocybin-Facilitated Smoking Cessation," *American Journal of Drug and Alcohol Abuse*, Vol. 43, No. 1 (2017), pp. 55-60. Available at: https://pubmed.ncbi.nlm.nih.gov/27441452/.

Another study determined that psilocybin use in isolation may result in a reduction in psychological distress or suicidal tendencies and that other psychedelic treatments are unnecessary to produce these results. Its findings suggest use of psilocybin over a lifetime while abstaining from the use of other psychedelic substances, may be especially protective with regard to suicidality and psychological distress. The authors suggest that "psilocybin may have the most favorable safety profile of all classic psychedelic substances."[44]

Medical researchers at Johns Hopkins reported that psilocybin produced large decreases in depression, and that depression severity remained low at one, three, six, and twelve months after treatment.[45]

> *... the early results from the use of psilocybin for depression and other mental health conditions are promising and point to the need for ongoing, carefully designed research protocols.*

The aforementioned studies offer a limited sampling of research findings and share some common methodological shortcomings, including small size, brief pre-treatment periods, and general difficulty establishing blind placebo studies involving psychedelic compounds (because placebos for psychedelic compounds are fairly easy for participants to distinguish upon administration)—make them far from conclusive. These methodological choices make it difficult to generalize findings to a large population. Furthermore, because psilocybin is frequently paired with psychological support, it is difficult to separate the psychotropic from the general care effects.[46] Still, despite such research limitations, the early results

[44] Peter S. Hendricks, Matthew W. Johnson and Roland R. Griffiths, "Psilocybin, Psychological Distress, and Suicidality," *Journal of Psychopharmacology*, Vol. 29, No. 9 (2015), pp. 1041-1043. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4721603/.

[45] Johns Hopkins Medicine Newsroom, "Psilocybin Treatment for Major Depression Effective for Up to a Year for Most Patients, Study Shows," February 15, 2022, https://www.hopkinsmedicine.org/news/newsroom/news-releases/psilocybin-treatment-for-major-depression-effective-for-up-to-a-year-for-most-patients-study-shows.

[46] Joseph M. Barnby and Mitul A. Mehta, "Psilocybin and Mental Health–Don't Lose Control," *Frontiers in Psychiatry*, Vol. 9, No. 293 (2018), pp. 1-3, https://www.frontiersin.org/articles/10.3389/fpsyt.2018.00293/full.

from the use of psilocybin for depression and other mental health conditions are promising and point to the need for ongoing, carefully designed research protocols.

In the U.S., psychedelic research requires DEA authorization, which is neither straightforward nor assured.[47] The DEA restricts the number of scientists who can engage in research and the total mass of psychedelics generated each year, constricting efforts to research and commercialize these substances.[48] These requirements further hinder competition. Many startups in this industry conduct their research abroad, where psychedelic research is easier to accomplish.

47 U.S. Drug Enforcement Administration, "DEA Speeds Up Application Process for Research on Schedule I Drugs," Press Release, January 18, 2018, https://www.dea.gov/press-releases/2018/01/18/dea-speeds-application-process-research-schedule-i-drugs.

48 Mason Marks and I. Glenn Cohen, "Patents on Psychedelics: The Next Legal Battlefront of Drug Development," *Harvard Law Review*, Vol. 135, F. 212 (2022), pp. 212-235, https://harvardlawreview.org/forum/no-volume/patents-on-psychedelics-the-next-legal-battlefront-of-drug-development/.

PART 4

POLICY CONSIDERATIONS

Limitations on research. Several nations, such as Portugal and the Netherlands, do not have laws against using psilocybin, and a study commissioned by the Dutch Ministry of Health concluded that the risks associated with over-the-counter sales to both individuals and the general public were negligible. The Canadian government established compassionate-use regulations to make psilocybin accessible to those with life-threatening illnesses in recognition of its therapeutic effects.

In the U.S., however, federal funding for research is essentially nonexistent as a result of the Schedule I classification of the majority of psychedelics, including psilocybin. A significant barrier is a federal appropriations rider, a clause added to a funding bill that initially passed in 1996, that forbids federal funding from being used to assist any activity that promotes the legalization of any narcotic or other substance classified in Schedule I. Since then, every appropriations process has included a renewal of this rider.

Patents. For roughly 20 years, proprietors of patents have the right to prohibit others from producing or replicating their invention without permission.[49] As a result, drug developers like COMPASS Pathways have applied for patents on psilocybin chemicals and procedures

[49] Kevin J. Hickey, "Patent Law: A Handbook for Congress," Congressional Research Service Report No, R46525, September 16, 2020, https://crsreports.congress.gov/product/details?prodcode=R46525.

for using psychedelics to treat a range of mental health conditions. These businesses contend that patents are required to protect their investments in both drug discovery and commercialization, which involve costly clinical studies and other criteria to win FDA and other regulatory approval as well as support from the medical community. Pharmaceutical companies are incentivized to develop drugs that treat widely held conditions so they can gain the customer base necessary to recover the costs of taking a product through FDA trials, which regularly add up to more than $1 billion.[50] Drug companies have to sell at monopoly prices over a prolonged period to recover these costs and make the risk worthwhile.

> *…drug developers like COMPASS Pathways have applied for patents on psilocybin chemicals and procedures for using psychedelics to treat a range of mental health conditions.*

At the same time, stakeholders, including patient activists, scientists, journalists, attorneys, and indigenous communities have criticized the sudden interest in patenting psychedelics.[51] Some contend that patenting psychedelics constitutes "biopiracy," or the appropriation of indigenous communities' traditions.[52] Others contend that patents turn a select few businesses into the industry's gatekeepers, which might limit innovation, impede research, and prevent access to necessary treatments.

These issues do not apply only to psychedelics. Similar discussions have been sparked by patents on genetic technologies, cancer treatments, and other innovations.[53] However, several characteristics of psychedelics, such as their extended and complex history, create special considerations that might complicate issues with medical product patenting.

50 Lawrence, note 24.

51 Shayla Love, "Is It Possible to Create an Ethical Psychedelics Company?" *Motherboard: Tech by Vice*, April 6, 2021, https://www.vice.com/en/article/m7amw4/is-it-possible-to-create-an-ethical-psychedelics-company.

52 Marks and Cohen, note 13.

53 Lyrissa Lidsky, "Patent Reform Is Needed to Protect Patients' Access to Lifesaving Drugs," *STAT First Opinion*, July 23, 2019, https://www.statnews.com/2019/07/23/patent-reform-protect-access-lifesaving-drugs/.

Two prerequisites for patentability are novelty and non-obviousness. While a mushroom may not be able to be legally patented, due to its natural occurrence and existing availability to the public, extracts of psilocybin or slight variations on its chemical structure may offer novelty. These distinctions undergird the U.S. Patent and Trademark Office's decision to grant some psychedelic patents.[54]

> *The threshold for acquiring a patent is much lower than for gaining FDA approval, which requires clinical trial-based evidence of safety and efficacy.*

The threshold for acquiring a patent is much lower than for gaining FDA approval, which requires clinical trial-based evidence of safety and efficacy. Patent applicants need merely demonstrate that a person with understanding in the relevant technological field may potentially create and use the invention after reading the patent application. The patent office does not require that the approach be fully developed or that its safety and effectiveness be demonstrated.

The medical product patent environment can be described as a thicket: a complex network of interlocking patent rights that prevents rivals from entering. Patent thickets are formed when patent holders pepper the field with multiple patents on the same or nearly related items, discouraging potential researchers and manufacturers from entering the sector entirely for fear of being sued for infringement or having to pay exorbitant license fees to patent holders.[55]

Rules for newness and non-obviousness in U.S. patent law stricter could prevent small changes to existing inventions from being classified as patentable innovations because they are not substantially novel. Giving patents on these small changes adds to the patent thicket and makes people less likely to try new things, which could slow scientific and technological progress.

[54] Shayla Love, "Can LSD Treat Food Allergies? We Don't Know, But It's Already Been Patented," *Motherboard: Tech by Vice,* July 1, 2021, https://www.vice.com/en/article/g5gdzy/can-lsd-treat-food-allergies-we-dont-know-but-its-already-been-patented.

[55] Marks and Cohen, note 48.

Despite criticisms, however, the market is already addressing many of these concerns. Individuals have contributed to nonprofit research organizations like Usona and B. More, whose inventions enter the public domain. Other companies have made or may make "patent pledges" for medical products, essentially waiving their intellectual property claims over those products.[56] These patent pledges sometimes can be confusing in court, considering many parties may attach stipulations to their agreements. However, the market process has already produced a range of outcomes in which psychedelic-assisted therapy would be within the public domain due to private philanthropy and others in which companies seek to fully recoup the costs imposed by pharmaceutical regulation.

Controlled substances. Most psychedelics, excluding ketamine, are Schedule I controlled substances because they have no recognized medical value and a significant misuse potential, according to the DEA.[57] Attempted commercialization of any Schedule I drug includes substantial legal and financial risk, creating market uncertainty and discouraging risk-averse investors. The remaining risk-tolerant investors are likely to coalesce into relatively few research firms, leading to a concentration of patent monopolies. Schedule I classification limits who has distribution and sale access to companies with large funding. Hence, psychedelic market concentration and patent holdings are in the hands of a only few companies.[58] Essentially, firms that can afford to conduct their research and development overseas are the ones that overcome current federal policies on psychedelics.

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[56] See, e.g., Open COVID Pledge: Make the Pledge to Share Your Intellectual Property in the Fight Against COVID-19, https://opencovidpledge.org.

[57] U.S. Drug Enforcement Administration, "Drugs of Abuse: A DEA Resource Guide (2020 Edition)," https://www.dea.gov/sites/default/files/2020-04/Drugs%20of%20Abuse%202020-Web%20Version-508%20compliant-4-24-20_0.pdf.

[58] Mason Marks, "FDA's Kratom Ban Would Harm the Public and Damage the Agency's Credibility," STAT First Opinion, August 23, 2021, https://www.statnews.com/2021/08/23/fdas-kratom-ban-would-harm-the-public-and-damage-the-agencys-credibility.

PART 5

EMERGING LEGAL FRAMEWORKS

Until 2020, the manufacturing and consumption of psilocybin was illegal under federal law and the laws of all 50 states. But in November 2020, Oregon voters enacted the first state-level program designed to authorize professionally facilitated psilocybin services via Measure 109. Measure 109 created a program for administering psilocybin products to individuals aged 21 years or older through a state-regulated program that licenses manufacturers, service centers, and facilitators.[59],[60]

The Oregon Health Authority (OHA) is responsible for setting up the program and making regulations under Measure 109, expected to go live in 2023. The OHA is advised by the Oregon Psilocybin Advisory Board (OPAB). OPAB gives recommendations to OHA based on scientific studies and research about the safety and effectiveness of psilocybin in treating mental health conditions. It also gives recommendations about the requirements, specifications, and guidelines for providing psilocybin services in Oregon. OPAB is crafting a long-term vision to ensure that psilocybin services will gain recognition as a safe,

59 Oregon Secretary of State, "Complete Text of Initiative 34," https://sos.oregon.gov/admin/Documents/irr/2020/034text.pdf.

60 Oregon Department of Justice, Draft Ballot Title for Initiative 34, August 7, 2019, https://sos.oregon.gov/admin/Documents/irr/2020/034dbt.pdf.

accessible, and affordable therapeutic option for adults aged 21 and older in Oregon for whom psilocybin may be appropriate.[61]

> *[Oregon Psilocybin Advisory Board] is crafting a long-term vision to ensure that psilocybin services will gain recognition as a safe, accessible, and affordable therapeutic option for adults aged 21 and older in Oregon for whom psilocybin may be appropriate.*

After participating in a preparatory session to advise a potential consumer and assess his or her suitability—including screening for potentially adverse conditions—consumers would be permitted to schedule an appointment in which psilocybin is administered in a clinical setting at a licensed center under the supervision of a licensed facilitator. In accordance with Measure 109, the Oregon Health Authority (OHA) has recently finalized a rulemaking process to determine many of the program details, including who is qualified to obtain a license as a facilitator, training requirements, a code of conduct for facilitators, and guidelines for packaging, labeling, and product mix.[62] The market is expected to launch in the second half of 2023.

Measure 109 permits cities and counties to put questions on local ballots that would either allow or restrict psilocybin service centers or manufacturing of psilocybin in unincorporated regions under their control. The law forbids the operation of psilocybin service centers inside the boundaries of incorporated cities.

No medical condition is required for patients seeking psilocybin services in Oregon. Psilocybin services could help close the current gap in preventative mental healthcare because clinical-trial participants frequently experience long-lasting sensations of well-being.[63]

61 Oregon Health Authority, Oregon Psilocybin Advisory Board Oregon Health Authority, Meeting Minutes and Working Documents, https://www.oregon.gov/oha/ph/preventionwellness/pages/psilocybin-advisory-board-meetings.aspx.

62 Oregon Health Authority, Public Health Division, "Oregon Psilocybin Services—Administrative Rules," https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/Pages/Psilocybin-Administrative-Rules.aspx.

63 Gabrielle Agin-Liebes et al., "Long-Term Follow-Up of Psilocybin-Assisted Psychotherapy for Psychiatric and Existential Distress in Patients with Life-Threatening Cancer," *Journal of Psychopharmacology*, Vol. 34, No.2 (2020), pp. 155-166. Available at: https://pubmed.ncbi.nlm.nih.gov/31916890/.

Several other jurisdictions are reconsidering new regulatory frameworks for psilocybin use.

Several other jurisdictions are reconsidering new regulatory frameworks for psilocybin use:

- In November 2022, nearly 54% of Colorado voters approved Proposition 122, which will create a regulated market for professionally facilitated psychedelic experiences and decriminalize possession of several common psychedelic substances, starting first with psilocybin and then moving on to mescaline, dimethyltryptamine (DMT), and ibogaine. The law creates a new Regulated Natural Medicine Access Program through which psychedelic professionals would be certified through state-approved training institutes and will conduct psychedelic experiences at approved locations, though consumers would not be able to purchase psychedelic plant medicine directly via retail establishments.[64] The measure gives Colorado's Department of Regulatory Agencies (DORA) broad authority to set up regulatory guidelines for training certification, administration sites, and manufacturing.
- Initiated Ordinance 301 was passed in Denver in 2019 with 50.6 percent of the vote. The law made the possession and use of psilocybin mushrooms by adults the lowest priority for law enforcement in Denver and stopped the city from spending money to enforce penalties related to them.
- Voters in Washington, D.C., approved a ballot measure in November 2020 instructing police to regard the non-commercial distribution, production, possession, and use of entheogenic plants and fungi as one of the lowest priorities for law enforcement.[65] Through local ordinances, psilocybin has also been made legal in three additional cities: Oakland, Santa Cruz, and Ann Arbor.[66]

64 Colorado Secretary of State, Natural Medicine Health Act of 2022, Proposed as Initiative 58, Enrolled as Proposition 122, Full text available at: https://www.sos.state.co.us/pubs/elections/Initiatives/titleBoard/filings/2021-2022/58Final.pdf.

65 Justin Moyer, "D.C. residents to vote on decriminalization of 'magic mushrooms' on November ballot," *The Washington Post*, August 2, 2022, https://www.washingtonpost.com/local/dc-residents-to-vote-on-legalization-of-magic-mushrooms-on-november-ballot/2020/08/05/0e62478c-d720-11ea-b9b2-1ea733b97910_story.html.

66 Ballotpedia, "Oregon Measure 109, Psilocybin Mushroom Services Program Initiative (2020)," Retrieved August 2, 2022, from

A combination of bottom-up grassroots activism and top-down regulatory reform may lead to a reinforcing loop that eventually broadens access to psychedelics in terms of both geography and eligibility requirements.[46] Multiple states are considering legislation in 2023 to decriminalize the possession and use of psilocybin and other psychedelics or to establish legal, regulated markets like Oregon. We expect the current pattern to continue, in which some psychedelics companies openly declare their intentions to enter these regionally legalized markets, while others intend to avoid doing so as long as psychedelics are still illegal at the federal level.[67]

A combination of bottom-up grassroots activism and top-down regulatory reform may lead to a reinforcing loop that eventually broadens access to psychedelics in terms of both geography and eligibility requirements.

https://ballotpedia.org/Oregon_Measure_109,_Psilocybin_Mushroom_Services_Program_Initiative_(2020)#cite_note-Text-1.

67 Kyle Jaeger, "California Bills To Legalize Psychedelics Possession, Allow Interstate Marijuana Commerce And More Teed Up For Key Hurdle Next Week," Marijuana Moment, August 3, 2022, https://www.marijuanamoment.net/california-bills-to-legalize-psychedelics-possession-allow-interstate-marijuana-commerce-and-more-teed-up-for-key-hurdle-next-week/.

PART 6

LOOKING AHEAD

Study into the medical applications of psilocybin and other psychedelic substances is a rapidly emerging field that is quickly changing the landscape of mental health. Within months, results from Phase III clinical trials could begin to emerge. If the clinical data from these trials show that psilocybin is safe and effective, then these products could soon be available with a prescription as treatment for the indicated conditions.[68]

> *"A state-regulated marketplace for psilocybin allows licensed manufacturers of psilocybin products to bypass the billions of dollars in expense that would be necessary to seek FDA approval to market their products, a key advantage."*

States have the authority to remove substances from their own versions of the controlled substances act and allow mental health professionals to recommend these substances for the benefit of their patients. Some states are already embarking on this approach, led by Oregon. A state-regulated marketplace for psilocybin allows licensed manufacturers of

[68] Psychedelic Alpha, "Looking Ahead to a Psychedelic 2022," Retrieved August 4, 2022, from https://psychedelicalpha.com/news/looking-ahead-to-a-psychedelic-2022.

psilocybin products to bypass the billions of dollars in expense that would be necessary to seek FDA approval to market their products, a key advantage. That means naturally occurring psilocybin can be made available to consumers at dramatically lower costs because manufacturers needn't recover this massive regulatory expense over the lifetime of a patent. The downside to this approach is that manufacturers are legally precluded from making any claims about the potential therapeutic benefits of their natural medicines. Further, without FDA approval to market a drug as a recognized treatment for a known health condition, it is unlikely that health insurance providers will reimburse customers for the expense of care.[69]

Even if private insurance companies start providing coverage for psychedelic therapies, however, many patients won't be able to access them because many people who could benefit from them may be on public insurance provided by Medicare or Medicaid. These public programs will not reimburse for treatments using Schedule I substances; therefore, coverage must be at the center of federal and state policy discussions regarding psilocybin services. Given the encouraging results from early clinical trials, policymakers may find that psilocybin services offer a more cost-effective approach to mental health than alternative treatments currently financed through public insurers.[70]

Given the encouraging results from early clinical trials, policymakers may find that psilocybin services offer a more cost-effective approach to mental health than alternative treatments currently financed through public insurers.

Training is required for many doctors who want to use psychedelics in their practices, and developing evidence-based clinical-practice guidelines will be crucial. Standards may

69 U.S. Food and Drug Administration, "Drug Development & Approval Process," Retrieved September 28, 2022, from https://www.fda.gov/drugs/development-approval-process-drugs.

70 Marks and Cohen, note 13.

lessen some healthcare practitioners' concerns about being held liable for medical negligence if patients experience negative effects while receiving these therapies[71]

Which healthcare or paramedical experts will have the authority to assist patients is a final pressing issue. Interest in psychedelics practice extends beyond licensed physicians and psychologists; who else may hold influential positions and what potential licensure systems would entail is not yet known.

One strategy would be to place psychedelics at the center of a prescription-based system that calls for authorized prescribers, usually doctors. Although this strategy has advantages, it could present difficulties in a situation where many patients already use psychedelics, either on their own or with the help of medical experts or spiritual healers. Not everyone will benefit from a prescription model.[72]

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[71] Elizabeth M. Nielson and Jeffrey Guss, "The Influence of Therapists' First-Hand Experience with Psychedelics on Psychedelic-Assisted Psychotherapy Research and Therapist Training," *Journal of Psychedelic Studies*, Vol. 2, Iss. 2 (2018), pp. 64-73. Retrieved Aug 4, 2022, from https://akjournals.com/view/journals/2054/2/2/article-p64.xml.

[72] Matt Lamkin, "Prescription Psychedelics: The Road from FDA Approval to Clinical Practice," *The American Journal of Medicine*, Vol. 135, No. 1 (2022), pp. 15-16, https://www.amjmed.com/article/S0002-9343(21)00521-0/fulltext#seccesectitle0006.

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She previously worked with James Madison Institute (JMI) as a research assistant and grant-writer. During her time at JMI, she promoted education policies that empower Florida parents to choose schools, courses, resources, and programs that fit their child's unique needs, interests, and learning styles. Her research at JMI also emphasized the role of constitutional rights in promoting democracy and freedom.

Aside from research with Reason and JMI, Carlino has developed and conducted a research project that examined the relationship between Cuban enclaves and Cuban wages in Miami, Florida. She has also created a business plan that focused on increasing high school graduation rates via alternative teaching methods and education programs. Through these experiences, she has gained a greater understanding of policy and hopes to use it to advocate for greater economic and social support of disadvantaged Americans.

Carlino recently graduated with a B.S. in economics from Florida State University. She double-majored in economics and media/communication with a minor in business. She plans to continue working in research and hopes to eventually gain employment as a data analyst.

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Through these roles, Lawrence has raised capital, implemented systems for accounting and inventory control, designed internal control processes, managed monthly and quarterly closings and reporting, managed payroll, accounts payable and accounts receivable, managed compliance with state and local regulations, negotiated contracts, and prepared filings with the U.S. Securities and Exchange Commission. Lawrence has also served as senior appointee to the Nevada Controller's Office where he oversaw the state's external financial reporting.

Prior to joining Reason in 2018, Lawrence had also spent a decade as a policy analyst on labor, fiscal, and energy issues between North Carolina's John Locke Foundation and the

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