White Paper on Psilocybin

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Introduction

Psychedelic substances increasingly hold promise for treating various mental health conditions. Enthusiasm about the substances and their potential therapeutic value have been growing during the past decade, and clinical research continues to increase quickly. These factors have led to a rapidly evolving landscape of potential psychedelic therapies.

Recognizing both the promising research and the many New Mexicans with mental health and substance use disorders, there has been significant legislative and executive interest in studying and evaluating the following themes:

1. The efficacy of psilocybin-based therapeutic treatments.
2. The establishment of a program allowing the use of psilocybin mushrooms for therapeutic medical treatments.
3. The need for statutory or regulatory framework for developing such a program.

* Please note that some of the information contained in this document may have changed since its creation.

Psilocybin Mushrooms

Psilocybin is a naturally occurring psychedelic compound produced by more than 200 species of mushrooms, collectively known as psilocybin mushrooms (or "magic mushrooms"). After intake, the pharmacologically inactive psilocybin (prodrug) is quickly converted by the body into the pharmacologically active psilocin, which has mind-altering effects similar to those of LSD and mescaline. The effects generally include hallucinations, changes in perception, a distorted sense of time, and self-reported spiritual experiences, and can include possible adverse reactions such as nausea and panic attacks.[1-4] Effects appear within 15-45 minutes, usually last for four to six hours, and can vary from person to person.[5]

The strength of psilocybin mushrooms can vary greatly. These mushrooms have differing concentrations of the active ingredients, and, consequently, the effects can depend on the dose and type of mushroom used. There is little evidence that people can become physically or psychologically dependent on psilocybin mushrooms.[6] However, it is possible to become tolerant to the drug's effects with regular use (e.g., after several days of continued use), at which time even high amounts of the drug will no longer produce the desired effect.

Natural psilocybin mushrooms are easy to grow and can be grown in a number of environments including an individual's home. While useful for developing ample supply, this raises regulatory and safety considerations.

Synthetic Psilocybin

Several companies, such as Compass Pathways, Usona Institute, ATAI Life sciences, and Psygen Labs, are now producing synthetic psilocybin. Current research on the therapeutic effects of psilocybin is conducted using synthetic psilocybin which ensures supply while controlling for potency, chemical consistency, and dose.

Some companies, like Compass Pathways, are seeking patents for their psilocybin products in an effort to protect their competitive position. Patents may drive up the costs of psilocybin, making the drug less accessible.[7] Synthetic psilocybin is produced according to Good Manufacturing Practices (GMP). GMP is a system of processes, procedures, and documentation that are designed to ensure that a drug is consistently produced and is of high quality.

MDMA

Another psychedelic that has been studied is MDMA (known also as ecstasy). On August 10, 2024, the FDA decided against approving the application citing need for an additional phase 3 study.

Safety Considerations

Adverse Events

Psilocybin ingestion may result in emotionally challenging experiences, which may include paranoia, loss of boundaries, and a distorted sense of self. When such experiences occur in an uncontrolled or unsafe environment, impaired judgement could lead to risk-taking behavior, which may then lead to traumatic injuries or even death.[8] Conversely, when these difficult psychedelic "journeys" occur in the safety of a therapeutic session with a skilled facilitator, they can be associated with positive mental health outcomes.[9,10]

Psilocybin mushrooms may contain phenylethylamines, which are structural relatives to amphetamines and may induce tachycardia, nausea, and anxiety.[11] For individuals with cardiac disease, these effects could be potentially harmful. Another rare adverse event is the development of "persistent hallucinogenic perception disorder," which may be experienced as mild to moderate sensory disturbances or "flashbacks" of the original psychedelic session. Lastly, adverse reactions have also been described when combining psilocybin mushrooms with other substances such as alcohol, cannabis, cocaine, and MDMA.[12]

There are important safety considerations for both natural and synthetic psilocybin production. While synthetic psilocybin production is regulated by GMP (noted above), there are no national standards for regulating mushroom production. Agricultural workers are protected under general OSHA standards, but none are specific to the regular mushroom industry. Mushroom workers lung, a hypersensitivity pneumonitis, is a known occupational risk.[13]

Jurisdictions wanting to establish psychedelic mushroom production will need to address occupational safety. Under Proposition 122, Colorado recently created a framework for

regulating the growth, distribution, and sale of certain psychedelics. It addresses worker safety, including safety around agricultural products (fertilizers, etc.) and prevention of mushroom workers lung.[13]

Risk Mitigation

Most of the risks described above may be minimized through appropriate patient screening and use in a controlled, supportive setting with trained facilitators. Psilocybin has not been studied in patients who are pregnant, breastfeeding or under the age of 21 years. There would be no upper age limit for exclusion as psychedelic-assisted therapy can be safe and well tolerated in older adults without pre-existing conditions.[14] Importantly, there is little evidence that people can become physically or psychologically dependent on psilocybin mushrooms.[7] This is partly explained by the tolerance to their effects, which quickly occurs after several days of continued use.

In addition to the risks of the chemical itself, there can be some risk with the setting of the therapy. Patients will be in a medically induced vulnerable state for a prolonged period of time. In many studies patients are in a clinical setting with two facilitators. Ensuring the design and structure of these facilities promotes an environment that maximizes patient safety is warranted.

Summary of Current Research

Research demonstrates psilocybin to be a promising treatment for some behavioral health conditions, including substance use disorders (SUD), major depressive disorder (MDD), treatment resistant depression (TRD), and end-of-life anxiety and psychological distress. Based on existing evidence, psilocybin has been granted “breakthrough-therapy” status for MDD and TRD from the FDA. (TRD is generally considered to be an inadequate response to at least two antidepressants.)[15]

Phase 3 studies may lead to a rescheduling of psilocybin by the FDA, but this is unlikely to happen before 2027. Phase 3 trials are often conducted at multiple sites and usually have larger samples (1,000 – 3,000) than Phase 2 (100 – 300) or Phase 1 (20 – 80) trials. Phase 3 trials are typically the final step before an application is made to the FDA for clinical use and could result in rescheduling. Despite its "breakthrough-therapy" designation, much remains to be understood about the effectiveness of psilocybin assisted therapies, including who may benefit and who may be at risk of experiencing adverse effects from psilocybin use. The major studies are summarized here:

Depression

In the phase 2 studies using synthesized psilocybin in the context of psychedelic-assisted therapy (PAT) for depression, the limited evidence of small studies with short term outcomes supports effectiveness. Results from four randomized controlled phase 2 trials (RCTs) offer preliminary support for psilocybin-assisted therapy (administered over 1-2 sessions) as a treatment for moderate to severe MDD and TRD.[15-18] Although promising, these trials had some limitations related to study design and the number and relative homogeneity of participants.

Carhart-Harris et al. compared 2 sessions of psilocybin-assisted therapy with daily treatment with the antidepressant escitalopram.[16] Although they saw significant improvements in many outcome measures, their stated primary outcome measure (one of several depression scores), although trending toward improvement was just short of statistical significance.[16] In addition, all of these trials may have had "functional unblinding," which is common to all studies investigating the effects of agents that may induce psychedelic experiences.[19]

During the four phase 2 trials, most adverse events associated with psilocybin were transient, typically occurring on the day of psilocybin dosing.[15-18] Headaches and nausea were common but tended to be mild to moderate and generally did not require intervention.[15,17] Serious adverse events were not observed in the two smaller trials (24 and 59 participants).[16,17] In the largest of the three trials (233 participants), serious adverse events, including instances of severe suicidal ideation and/or suicidal behaviors were seen more frequently among those receiving larger doses of psilocybin.[15] However, this should be understood in the context of treatment-resistant depression, which carries a heavy burden of suicidality generally.

Phase 3 studies are now occurring for TRD and MDD, including at the University of New Mexico (clinicaltrials.gov/study/NCT06308653, clinicaltrials.gov/study/NCT05624268, clinicaltrials.gov/study/NCT05711940). The two phase 3 trials conducted by Compass involve either one or two administrations of 25 mg of psilocybin for TRD, while the Usona uAspire study has a protocol that permits a variable number of 25 mg doses over a year long period. All the phase 3 studies include comparison with inert placebo, and two of the studies also include a lower dose of psilocybin (5 or 10 mg) for comparison.

Substance Use Disorder

Much of the modern research on psilocybin-assisted therapies has focused on depression, which is associated with huge burdens for individuals and societies. But other difficult-to-treat conditions, such as tobacco, alcohol, and other substance use disorders are similarly associated with enormous costs (financial and otherwise) to individuals, families, healthcare systems, and society at large. There is growing interest in understanding how psilocybin and other psychedelic-assisted therapies might affect these and other potentially debilitating conditions (e.g. end of life anxiety and distress).

Data from 2021 show that excessive use of alcohol accounts for more than 178,000 deaths annually in the United States, making it the fifth leading cause of preventable death.[20, 21] Unfortunately, those numbers have continued to increase over the past several years.[22,23] Binge drinking alone costs the US nearly $200 billion annually, including health care and criminal justice expenses as well as decreased workplace productivity.[24] The state of New Mexico is disproportionately affected by alcohol-associated morbidity and mortality, with the highest age-adjusted rates of liver disease and cirrhosis of all the states.[25]

The use of psilocybin-assisted therapy seems to hold promise in the treatment of these debilitating conditions, though further research is needed. A landmark study, partly conducted at the University of New Mexico, showed that 12 weeks of manualized psychotherapy plus two sessions of psilocybin resulted in robust decreases in alcohol intake (based on percentage of heavy drinking days) over and above those produced by active placebo and psychotherapy.[26] The promising results of this study have encouraged other groups to pursue clinical trials of psilocybin-assisted therapy as an intervention for alcohol use disorder (AUD)[27]; as well as animal studies, which attempt to elucidate some of the underlying mechanisms. In fact, there are currently at least 10 active trials of psilocybin treatment for AUD listed on clinicaltrials.gov. Similarly, there is growing interest in research related to other substance use disorders (e.g. opioid use disorder), and emerging data suggest benefit for tobacco cessation.[28]

End Of Life

Another area of research is end-of-life anxiety and distress. In fact, there are several phase 2 multicenter randomized clinical trial studies of psilocybin assisted therapy for palliative or end of life care.[29-32] Given the need for phase 2 and phase 3 studies it will be at least 4-5 years before the FDA could consider approving psilocybin for this indication. However, it is possible that if psilocybin is approved for major depression by 2027 it could be used for depression in the setting of end-of-life care.

Current Research Activities in New Mexico

The UNM Health Sciences Center (HSC) began psychedelic research with Rick Strassman's studies of N,N -dimethyltryptamine-(DMT) and psilocybin from 1990 to 1995.[33] These studies were the first human research of psychedelic compounds since psychedelic research was halted in the early 1970s. UNM remains actively engaged on the national research front with ongoing research plans and proposals in the following areas:

- MDMA assisted therapy for co-occurring post-traumatic stress disorder and opioid use disorder
- Psilocybin for major depression
- Re104, a synthetic serotonergic compound with effects similar to psilocybin, for postpartum depression
- Ketamine for methamphetamine use disorder

Specific studies

Completed:

- Psilocybin Assisted Psychotherapy for Alcohol Use Disorder - In this double-blind randomized clinical trial with 93 participants, the percentage of heavy drinking days during 32 weeks of follow-up was significantly lower in the psilocybin group than in the placebo group. [1]

[1] Bogenschutz MP, Ross S, Bhatt S, Baron T, Forcehimes AA, Laska E, Mennenga SE, O'Donnell K, Owens LT, Podrebarac S, Rotrosen J, Tonigan JS, Worth L. Percentage of Heavy Drinking Days Following Psilocybin-Assisted Psychotherapy vs Placebo in the Treatment of Adult Patients with Alcohol Use Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2022 Oct 1;79(10):953-962.

In Progress:

- uAspire – A phase 3, randomized, Double-Blind, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Psilocybin in Adults with Major Depressive Disorder (MDD). [2]

- MAT-POD Study – MDMA-Assisted Therapy 6 to 12 months After Childbirth for People with Co-occurring Opioid Use and Post Traumatic Stress Disorders. [3]

- RECONNECT - A Multicenter, Randomized, Double-Blind, Parallel-Group Dose-Controlled Study Evaluating the Safety and Efficacy of RE104 for Injection in the Treatment of Patients with Postpartum Depression (PPD). [4]

Starting in 2024:

- Ketamine for Methamphetamine Dependence – A Multicenter, Safety and Efficacy Study sponsored by the National Institute on Drug Abuse (NIDA) Clinical Trials Network beginning at UNM later this year.[5]

*Importantly, the University of New Mexico Health Sciences Interdisciplinary Substance Use and Brain Injury (ISUBI) under the direction of the UNM Research Program for Psychedelic Therapies has DEA approved licenses for MDMA and psilocybin and an FDA Investigational New Drug (IND) for using MDMA for co-occurring PTSD and Opioid Disorder.)

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Further Research Needs

Additional studies are needed to determine if psilocybin is an appropriate first-line medication or should be reserved for people with TRD or MDD who did not respond to an initial course of medication or psychotherapy. An advantage of psilocybin-assisted therapy (PAT) is that it does not require daily administration, as do the currently available oral antidepressants. Results of the phase 3 studies are awaited to determine effectiveness and, if effective, to guide the development of treatment protocols and ensure accessibility. Studies of psilocybin looking at the use of whole mushrooms in a state regulated plan have the potential to accelerate access to PAT if shown to be effective and studies that explore group models of PAT can potentially increase access and affordability.

Summary of Legal Considerations

Several psychedelic drugs, including psilocybin, are designated as Schedule I controlled substances by the Drug Enforcement Administration (DEA). Schedule I substances are illegal, have no approved medical use, and are considered to have the highest potential for abuse. Despite this designation, the FDA has awarded "breakthrough therapy" status to psilocybin, indicating that the drug shows promise for treating certain conditions, and psilocybin is generally agreed to have a low potential for dependence or misuse. In addition, a number of jurisdictions have decided to provide legal protections for psilocybin under state and local laws. These decisions fall roughly into 3 categories: decriminalize possession; legalize in limited settings; and support research.

Schedule I substances are subject to strict regulations, and their possession, distribution, or manufacturing is prohibited. Growing psilocybin mushrooms is not considered illegal drug "manufacturing" under New Mexico state law following a State Court of Appeals decision

from 2005. In State of New Mexico v. Pratt, 2005-NMCA-099, the NM Court of Appeals reversed a drug trafficking conviction, holding that "the act of growing mushrooms" alone did not constitute the "manufacture" of a controlled substance, because growing the mushrooms did not involve "extraction" of psilocybin, whether from a substance of natural origin or through chemical synthesis. However, the possession and distribution of psilocybin mushrooms, as well as possession of drug paraphernalia, are still felonies under both NM law and federal law, and federal law (unlike NM law) further prohibits the Mushroom's "production" (defined at 21 U.S.C. § 802 to include "planting, cultivation, growing, or harvesting of a controlled substance.").

Decriminalization

Many municipalities, including Denver, Ann Arbor, Santa Cruz, Oakland, and the District of Columbia, have enacted legislation to decriminalize the possession and use of psilocybin or have made it the lowest law enforcement priority. It is important to note that these steps are being taken despite state laws being subject to federal preemption and enforcement. In November 2022, Colorado voters approved Proposition 122 creating the Natural Medicine Health Act which has been the most relaxed approach to psychedelic use. As of 2023, it is no longer a crime in Colorado for adults 21 and older to possess, consume, and share psilocybin mushrooms, psilocin, Dimethyltryptamine (DMT), ibogaine, and mescaline - not extracted from peyote. People 21 and older may also grow psilocybin mushrooms in a private residence, but selling these substances is illegal. Additionally, this legislation allows for the use of psilocybin mushroom at licensed facilities, but the state does not plan to issue any licenses until 2025.

Research

In May 2021, Texas legislators passed a bill that directed the Health and Human Services Commission to collaborate with Baylor College of Medicine to conduct a clinical trial on the therapeutic efficacy of using psilocybin in the treatment of treatment resistant post-

traumatic stress disorder (PTSD). The state of Texas committed approximately $1.3 million for this research over a three-year period.

In October 2021, a group of bipartisan legislators in Pennsylvania' introduced a bill called the "Public Health Benefits of Psilocybin Act" that gave the state's Department of Health greater authority to support psilocybin research. The bill authorizes the Department of Health to license two or more growers of "natural psilocybin mushrooms" to cultivate the mushrooms for research into therapeutic purposes. The bill outlines that the manufacturers must certify that they can meet consistent quality and dosages of psilocybin compounds specified by clinical studies. It also directs the Department of Health to prioritize funding for clinical studies regarding psilocybin-assisted treatment of veterans, retired first responders, and their family members.

In January 2023, Arizona enacted budget legislation allowing its Department of Health Services to create an advisory council tasked with establishing criteria to distribute $5 million (fiscal year 2023-2024) for "whole mushroom" clinical trials for the treatment of 13 specific medical conditions much like the Pennsylvania effort. The bill did not legalize psilocybin, but recipients of the grant money who work on the clinical trials will be explicitly protected from prosecution under the bill.

Supervised Use

As of July 2024, Oregon is the only state that has legalized the adult use of psilocybin provided it is administered in a Psilocybin Services Center. Ballot measure 111 legalized adult use (over 21 years of age) of psilocybin if it was provided in a state-approved Psilocybin Services Center. One interesting aspect of the Oregon legislation is that it is not tied to specific medical conditions and adults are free to use the drug for non-medical purposes. Because Oregon moved forward without FDA approval, the state underwent a two-year

development period to address crucial implementation areas including training, products, licensing, research, and equity.

In May 2024, Utah enacted a bill that allows providers at two large health systems the option to treat patients with psilocybin or MDMA. Healthcare providers creating psychedelic treatment programs must only use psilocybin or MDMA in a medical facility and must report the results of treatment to the legislature by July 2026. The pilot program will end in three years, allowing the legislature to choose whether or not to continue it.

Costs

There are two broad categories of cost to consider: regulatory and direct clinical costs.

Regulatory Costs

State costs to regulate psilocybin mushroom businesses and psilocybin treatment providers would depend on (1) the specific regulatory structure that the state ultimately implements (2) the extent to which the federal government exercises its discretion to enforce federal prohibitions on psilocybin-related activities, and (3) how people and businesses respond to these two factors. Accordingly, costs could range from minimal to tens of millions of dollars annually. A potential method to partially or fully offset potential costs would be the collection of regulatory fees and taxes.

For reference, Oregon and Colorado have adopted laws that legalize and regulate the use of psilocybin. Prior to implementation, the Oregon Secretary of State estimated the state would incur $7 million in new expenses over the mandatory two-year development period of the law. Once a program is established, annual costs are estimated at $3.1 million, with fees and taxes assessed under the law expected to cover these costs.[34] Fiscal estimates for the Colorado policy indicate that annual State spending would increase by up to $4.0 million to

develop a regulatory framework for the law, while annual revenue collected once the program is implemented would be approximately $3.0 million. As implementation in Oregon began in January 2023 and the Colorado law is still in development, actual costs are unknown.[34] These examples do not provide any fiscal impact for decriminalizing, and expunging past offenses involving psilocybin production, possession, use, and distribution.

Direct Clinical Costs

In addition to the costs of regulation there are the costs of the psilocybin product and cost of the assisted therapy. The current therapeutic model used in studies typically involves:

1. 6 to 8 hours of preparatory sessions with 2 facilitators between the initial assessment and the day of dosing
2. A 7-to-10-hour dosing session conducted in a comfortable room under the supervision of the same facilitators, and
3. 4 hours of post-dose integration sessions.[18]

While this model is very safe, it is also very costly and will not be widely accessible. To prevent exacerbating existing inequities in access to treatment in NM, it is critical to explore options for subsidizing these therapies for low-income individuals and other populations. Until psilocybin is FDA approved, this therapy won't be covered by Medicaid, Medicare, or private insurance. Even with insurance coverage, there are likely to be issues with access in many parts of NM given the level of resources needed for the current therapy model.

Considerations for mitigating cost include developing a group therapy approach and using natural rather than pharmaceutical psilocybin. The UNM research team is interested in studying a more cost-effective group therapy model. Group psilocybin therapy may potentially be more effective for substance use disorders when a facilitator with lived experience is included in the groups. In addition, group therapy models will need to include facilitators who represent the diverse populations they serve. Currently, some states such as Arizona are exploring the use of whole psilocybin mushrooms grown in an FDA/DEA

approved setting in order to lower costs and increase availability due to the high price of commercially synthesized psilocybin. However, it is unclear if this approach would be supported if the FDA makes psilocybin a Schedule II and there is commercially available product.

New Mexico Medicaid

Medicaid cannot cover the cost of MDMA or psilocybin under the federal match unless the medications are FDA approved. Medicaid currently covers "therapy" but not the two-provider model used for PAT. New Mexico could decide to cover psychedelics with state funds, but this could be costly. To reduce costs, the use of a group therapy model has the potential to decrease the expense of psilocybin assisted therapy by up to 66%. Additionally, the use of whole mushroom products in a state regulated model has the potential to be significantly less expensive than the use of synthesized psilocybin marketed by pharmaceutical companies.

Ethical Considerations

Permitting the compassionate or palliative use of drug-assisted psychotherapy would likely significantly improve the quality of life for persons who have severe and treatment-refractory symptoms that persist despite attempts to control them with therapy, whether these are due to a physical illness, a mental illness, or represent existential distress related to incurable cancer, neurologic disorders such as amyotrophic lateral sclerosis, or other severely disabling and life-limiting conditions. Although the evidence base supporting use for such conditions may be very limited, the utilization of treatments that suggest some promise of benefit for conditions that cause severe suffering, and which have not responded to all standard treatments is generally regarded as ethically permissible and may even be an ethical obligation for appropriately trained providers.

Entheogenic Use – Tribal and Religious Considerations

As policy makers consider next steps, it is essential to engage with Tribes, Pueblos and Nations to ensure that Native American rights and traditions are protected. While specific rituals and beliefs vary, the common thread is the use of natural substances, such as the sacred cactus peyote (Lophophora williamsii), to alter consciousness for spiritual and healing purposes.[35] Tribes and advocacy groups have won legal protections for the use of native plants for ceremonial purposes, such as the 1994 amendment to the American Indian Religious Freedom Act which legalized the use of peyote for religious purposes. In 1967, the Navajo Tribal Council passed amendments to the Navajo Bill of Rights declaring the Freedom of Religion as a fundamental human right, and through Resolution No. CO-65-67 made an exception to the criminal code to allow Azeé (Peyote) to be used for religious purposes within the Navajo Nation. All states except Idaho, Utah, and Texas allow ceremonial use of peyote within the Native American Church, recognizing its cultural and spiritual significance to Indigenous communities, despite its DEA designation as a Schedule 1 controlled substance.

The current interest in psychedelics by modern medical institutions can negatively impact Indigenous cultural use. Increased global demand for psychedelics may place economic pressure on vulnerable groups and lead to harmful cultural appropriation, undermining traditional practices.[36] In addition, demand for naturally grown psychedelics (peyote, psilocybin mushrooms) could disrupt natural environments and traditional harvesting practices. The relationship with land and plants is a common sacred relationship most tribes value in ceremonial practices. For Indigenous People, mushrooms are not to be considered a drug or psychoactive substance but rather as sacred beings or entities with whom a reciprocal relationship is established.[37] Further policy development should be guided by the

principles of respect for Indigenous sovereignty, cultural traditions, and knowledge systems including tribal consultation.[36]

Equity

Psychedelic therapy shows promise for treating both substance use disorders (SUD) and mental health conditions. However, without a deliberate focus on health equity, its benefits may disproportionately favor those with greater financial resources. Ensuring that the workforce of therapists, facilitators, and administrators is culturally competent and diverse is crucial. This workforce must be equipped to meet the unique needs of communities by creating comprehensive, culturally sensitive, and health equity-informed training tools. When considering increasing access to psychedelic treatment, considerations should be given to whether the approach will reinforce existing inequities or minimize them. This is especially true for supervision models that may be prohibitively expensive for many potential patients.

To achieve health equity, it is essential to ensure fair and equitable access to beneficial medical treatments. This includes provisions to support access to drug-assisted psychotherapy for those unable to afford out-of-pocket costs. Strategies might include encouraging private insurers to cover approved uses, providing state subsidies for drug-assisted psychotherapy, or incorporating coverage into state Medicaid guidelines. Additionally, regulatory mechanisms should allow and promote the adoption of innovative therapy approaches that could lower the costs of drug-assisted psychotherapy or broaden access if supported by scientific evidence.

Program Considerations

Broadly, there are four approaches that could be taken in order to develop a State Psilocybin Program. These approaches do not all necessarily address the issues related to psilocybin. For example, funding research is not a means to promote access to the medications in the short-term. Determination of the state's goals regarding psilocybin therapy is warranted.

In addition, any policy development should include Tribal Consultation under the State Tribal Collaboration Act Section 3 C which requires state agencies to make a reasonable effort to collaborate with Indian nations, tribes or pueblos in the development and implementation of policies, agreements and programs of the state agency that directly affect American Indians or Alaska Natives.

Approach 1: Wait for FDA Approval

Psilocybin has a "fast-track" New Drug Approval (NDA) application before the FDA. If the FDA approves this application, regulations regarding manufacturing standards, administration, storage, and safety standards will be created at a federal level. As part of the approval process, the FDA will likely require a Risk Evaluation Management Strategies (REMS) which would fall to the drug manufacturer to develop and implement. The State's role in this scenario would be limited.

Additionally, if psilocybin is FDA approved, then health insurance will potentially cover some of the cost of psilocybin assisted therapy. Given that the costs associated with implementing psychedelic-assisted psychotherapy (PAT) ahead of FDA approval could be significant, the most cost-effective approach to ensuring safe access to PAT may be to wait for the FDA to rule on the NDA applications. Because psilocybin is currently illegal and not regulated by the FDA, neither Medicaid nor Medicare will cover psilocybin at this time. By

waiting for FDA approval and rescheduling, the cost of psilocybin therapy could be covered by insurance (including Medicaid and Medicare) making access more equitable.

Phase 3 studies may lead to a rescheduling of psilocybin by the FDA for major depressive disorder or treatment resistant depression, but this is unlikely to happen before 2027. FDA approval for other indications including substance use disorder or end of life care is quite distant due to the likely reduced interest from industry to study these indications for a compound that may be effective with one to three doses rather than the daily use common to more remunerative pharmaceutical products.

Approach 2: Approve for use in Therapy Centers

In this approach, guidelines for psilocybin assisted therapy based on research protocols would need to be developed. The guidelines would include careful screening practices, close supervision of study participants, specially trained health and mental health professionals, and a carefully delineated therapeutic process designed to administer psilocybin safely. This model is recommended to minimize risk and should include the following steps before psilocybin dosing can begin:

- Extensive screening practices are used to exclude people at risk for adverse effects of psilocybin.
- Stabilization of medical conditions, such as hypertension.
- Preparatory visit to educate patients, set goals, introduce cognitive-behavioral tools, and build rapport between patients and therapists.
- Identification of support personnel to help ensure safety and follow-up.

On the day of psilocybin administration, additional safety checks will be performed. The session may last between 6-8 hours and requires two facilitators who remain involved throughout the process. To optimize outcomes, follow-up visits are recommended. This is known as the integration phase, during which a variety of supportive therapeutic modalities may be incorporated.

Adhering to the therapeutic process for psilocybin-assisted therapy is very important and requires facilitators who are specially trained and certified. Prior to delivering PAT, the state would need to begin recruiting and training facilitators from diverse backgrounds, lived experiences, and communities to ensure equity and access.

Implementing such an approach would likely take 2 to 3 years. Psychedelic training programs typically take one year. Additionally, securing a consistent and viable source for the psilocybin, along with safe and legal distribution channels for psilocybin to be used in therapy sessions, will take a significant amount of time.

Approach 3: Decriminalize and Commercialize

Limited data from observational studies suggest that the majority of people using unsupervised psilocybin mushrooms experience subjective benefits and minimal risks. Retrospective studies suggest that individuals who have consumed psilocybin in the community rarely experience long-term adverse consequences. A review of 6000 psilocybin exposures reported to the National Poison Center between 2000 and 2016 indicated that most calls were from adolescents and young men and were mostly associated with mild and moderate adverse events.[38] A thorough literature review spanning many decades identified rare case reports of severe morbidity or mortality associated with unmonitored psilocybin use in the community.[39,40] Retrospective studies note few fatalities in which psilocybin was believed to be the only drug used; the rare deaths reported typically resulted from events such as drowning or motor vehicle crashes rather than toxicity, although circumstances in most cases were poorly characterized. [38]

Observational studies that have attempted to assess risks of unsupervised use generally had high risk of bias due to lack of comparison groups or population-based estimates, and cross-sectional study designs. In 346 self-reported psilocybin “bad trips”, many of the episodes were associated with thought disorders such as schizophrenia.[41] Factors that

seem to increase risk for serious adverse events include the use of very high doses of psilocybin and combining it with other substances.[41] In a web-based survey of almost 2000 people using psilocybin mushrooms, participants who reported challenging experiences (i.e., "bad trips") were more likely to exhibit traits of neuroticism based on the Ten-Item Personality Inventory.[42]

Implementing such an approach will require legislation that provides sufficient regulatory framework to ensure product (psilocybin) safety and legal protections to those who cultivate, possess, sell, distribute, administer or personally consume psilocybin. Based on other states' experiences, it appears that this approach would take a number of years.

Approach 4: Funding Research

The State could establish a therapeutic psilocybin research fund, administered by the Department of Health, to provide grants to New Mexico research institutions studying psilocybin. Institutions would apply for funding to support research into the risks and benefits of psychedelic-assisted therapy.

Research should focus on areas of public health impact including the following:

1. Opioid use disorder and polysubstance use
2. PTSD focused on first responders and veterans
3. Group therapy models focused on cost effectiveness, increasing equity and access
4. End of life care to address anxiety and demoralization common in terminal illness

Major depressive disorder (MDD) and treatment resistant depression (TRD) have major public health impacts, however with phase 3 studies in process for these indications, depression may not be a priority for state supported psilocybin research. Research focused on developing approaches that are cost effective and improve access to care might include utilizing "whole psilocybin mushrooms", Group Therapy models and accessing Medicaid to cover the therapy component of treatment. Group therapy research would need to be

formatted in a culturally sensitive manner, taking into account differences in areas such as language, accommodations, religious practices, cultures, beliefs and experiences.

After a research institution that receives a grant completes and finalizes a study, the research institution should prepare and submit a report summarizing the results of the study. Finally, the Department of Health could help grant recipients maintain intellectual property rights for what the research produces.

Implementation of such an approach could happen quickly as numerous research studies are already underway in the state of New Mexico. In fact, UNM researchers have already initiated a collaboration with the nonprofit Psychedelic Health Equity Initiative (PHEI). The research will focus on community engagement and models that support equitable access. There is the potential for expanded collaboration among the State of New Mexico, the UNM research program for Psychedelic Assisted Therapies, and PHEI to examine the use of group therapy for the indication of substance use, end of life care, and first responder trauma.

Additional Considerations

Efforts to support community engagement and the creation of a diverse interested partner group must be undertaken. This collaboration will be key to forming a plan for therapeutic use that addresses a wide range of issues specific to New Mexico Communities. Initial input should prioritize the training of facilitators, obtaining a safe supply of psilocybin mushrooms, and addressing potential liability issues before any program course can be implemented. Any legislative authorization to conduct this type of research with psilocybin mushrooms, should carry some level of immunity under both the New Mexico Tort Claims Act and under the New Mexico Civil Rights Act, assuming an adequate informed consent approved by an FDA-approved, AAAHRP-accredited IRB, such as the UNM Health Science Center's Human Research Review Committees.

Appendix A

State Policy Reforms Related to Psychedelics in the United States since 2019[43]

Jurisdiction	Date Enacted	Policy Change	Legal Mechanism	Activity	Substances
Oregon	January 2021	Legalization of supervised consumption	Ballot initiative (109)	Created a license and regulatory framework for production, transportation, delivery, sale, and purchase of psilocybin, and facilitation of psilocybin services, for adults (21 and older); created a Psilocybin Advisory Board	Psilocybin
Oregon	February 2021 (significantly amended in April 2024)	Decriminalization	Ballot initiative (110)	Reclassified personal possession of controlled substances as a civil offense or misdemeanor, based on the quantity; incentivized and funded treatment services; criminal drug activities and possession of larger amounts are still criminal offenses	Most controlled substances, including psychedelics
New Jersey	February 2021	Defelonization	State legislation	Changed possession of 1 ounce or less of psilocybin to a disorderly offense from a third-degree indictable offense (i.e., felony)	Psilocybin
Connecticut	June 2021	Research	Included in a bill revising public health statutes	Assembled a working group to study the health benefits of psilocybin	Psilocybin
Texas	June 2021	Research	State legislation	Initiated a study of alternative therapies to treat PTSD in veterans	MDMA, psilocybin, and ketamine

Jurisdiction	Date Enacted	Policy Change	Legal Mechanism	Activity	Substances
Utah	March 2022	Research	State legislation	Established a Mental Illness Psychotherapy Drug Task Force to study psychotherapy drugs not currently legal	Controlled substances not currently available for legal use that may be used to treat mental illness
Washington	March 2022	Research	Included in state budget bill	Allocated funds to establish a stakeholder group to generate a report on psilocybin services and opportunities	Psilocybin
Connecticut	May 2022	Research	Included in state budget bill	Allocated $1 million in funding over two years and set guidelines for a psychedelic assisted therapy pilot program for veterans, first responders, and direct health care workers to be administered by an in-state medical school; established a Psychedelic Treatment Advisory Board	Psilocybin, MDMA
Maryland	May 2022	Research	State legislation	Established a fund to study alternative therapies to treat PTSD and traumatic brain injuries in veterans	Psychedelics including MDMA, psilocybin, ketamine
Colorado	June 2022	Legalization of supervised consumption (trigger law dependent on federal re-scheduling)	State legislation	If MDMA as part of a prescription drug is moved from the federal Schedule I list, then prescribing, dispensing, transporting, possessing, and using that prescription drug would be legal in Colorado	MDMA

Jurisdiction	Date Enacted	Policy Change	Legal Mechanism	Activity	Substances
Colorado	November 2022	Legalization of cultivation and sharing Legalization of supervised consumption	Ballot initiative	Legalized all five substances for possession, growing, sharing, and use but not retail sale for adults ages 21 or older (the grow-and-give model); established supervised use of psilocybin mushrooms at licensed facilities by adults (21 or older) with the possibility of adding other substances in the future	Psilocybin, psilocin, DMT, ibogaine, and mescaline (excluding peyote)
Arizona	January 2023	Research	Included in state budget bill	Established an advisory council and allocated funds for competitive research grants for clinical trials using psilocybin mushrooms with veterans, first responders, frontline health care workers, and people from underserved communities as research subjects to treat a wide variety of physical and mental health conditions	Whole mushroom psilocybin
Washington	January 2023	Research	State legislation	Established a psilocybin treatment pilot program with populations including first responders and veterans; established a psilocybin advisory board and task force to develop guidance for a regulatory framework for therapeutic use	Psilocybin
Minnesota	February 2023	Research	Included in state health budget bill	Established a Psychedelic Medicine Task Force to report on the use of psychedelic medicines to treat mental health conditions	MDMA, psilocybin, and LSD
Nevada	June 2023	Research	State legislation	Established a Psychedelic Medicines Working Group to develop a plan for therapeutic use	Entheogens, including psilocybin and psilocin

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