February 28, 2025

Congressional Psychedelics Advancing Therapies (PATH) Caucus
Representative Jack Bergman (R-MI-01)
Representative Lou Correa (D-CA-46)
United States House of Representatives
Washington, D.C. 20515

Dear Representatives Bergman and Correa:

On behalf of the Association for Prescription Psychedelics (APP), we appreciate the opportunity to provide input on the implementation of psychedelic and entactogenic therapeutics, and we share your commitment to advancing safe, effective, and accessible treatments. The unfortunate reality is the United States is experiencing an unprecedented mental health crisis exacerbated by a lack of innovation in mental health therapies.

APP was formed to: 1) educate policymakers and the public on the potential of patient-centered prescription psychedelic medicine development, 2) advocate for government-sponsored research, and 3) address legislative and regulatory hurdles to advancing this promising area of mental health treatment. APP brings together industry leaders, scientific advisors, and patient advocates to promote the safe and effective introduction of prescription psychedelic medicine into the American healthcare system. **APP, the leading voice for prescription psychedelic medicine, believes that the U.S. Food and Drug Administration's (FDA) New Drug Application (NDA) approval pathway is the only appropriate mechanism that ensures American patients can safely and effectively access these treatments.**

Rigorous, peer-reviewed scientific research and clinical trials demonstrate that these treatments hold the potential to help tens of millions of Americans who suffer from serious health conditions. We appreciate the PATH Caucus's thoughtful approach to these complex issues and look forward to working with you to help address our nation's mental health crisis and make these treatments accessible to patients across the country.

In addition to the comments presented in this response, please don't hesitate to reach out to APP as a trusted resource and partner in the PATH Caucus's critical mission and priorities.

Sincerely,

Jon Kostas
Executive Director
Association for Prescription Psychedelics

State of Play: Mental Health Crisis and Prescription Psychedelic Medicine

More than 50 million patients in the United States are diagnosed with significant mental health conditions — including post-traumatic stress disorder (PTSD), treatment-resistant depression (TRD), generalized anxiety disorder (GAD), and substance use disorder (SUD), among many others.[1] Yet, new treatments and therapies have not kept pace with the growing crisis.

Historically, the limited number of pharmacological innovations available to address difficult-to-treat mental health conditions have adversely inhibited patient outcomes. For example:

- Only two FDA-approved products for the treatment of adults with PTSD are available — sertraline, which received FDA approval in 1991, and paroxetine, which received FDA approval in 1992.[2,3,4] They are categorized as selective serotonin reuptake inhibitors (SSRIs).[5]

- TRD is similarly limited to two FDA-approved products — Olanzapine / Fluoxetine (Symbyax) was approved by the FDA in 2009 and esketamine (Spravato) was approved in 2019.[6,7]

- GAD has not seen an approved medication since 2007, when duloxetine, a selective serotonin and norepinephrine reuptake inhibitor (SNRI), received FDA approval.[8,9]

The innovation in prescription psychedelic medicine is a bright spot in an otherwise bleak mental health treatment horizon. Amid a national mental health emergency where one in five adults experience symptoms of anxiety and depression and where an estimated 17 veterans die by

[1] **National Alliance on Mental Illness**. "Mental Health by the Numbers." April 2023.
[2] **U.S. Department of Veterans Affairs**. "PTSD: National Center for PTSD." January 25, 2024.
[3] **American Chemical Society**. "Molecule of the Week Archive: Sertraline." June 27, 2022.
[4] **National Library of Medicine**. "Paroxetine." April 8, 2020.
[5] **National Library of Medicine**. "Pharmacotherapy for Post-traumatic Stress Disorder In Combat Veterans." January 2012.
[6] **Lilly.** "FDA Approves Symbyax(R) as First Medication for Treatment-Resistant Depression." March 23, 2009.
[7] **Cleveland Clinic**. "Treatment-Resistant Depression."
[8] **Mayo Clinic**. "Duloxetine (oral route)."
[9] **National Library of Medicine**. "Duloxetine for the treatment of generalized anxiety disorder: a review." April 8, 2009.

suicide each day, our nation must explore and advance novel treatments to help patients struggling with PTSD, TRD, GAD, SUD, and other mental health conditions. [10,11,12,13]

To that end, a number of psychedelic and entactogenic compounds have received Breakthrough Therapy Designation (BTD) from the FDA: MDMA for PTSD in 2017,[14] psilocybin for TRD 2018,[15] psilocybin for MDD in 2019,[16] LSD for GAD in 2024,[17] and psilocybin for MDD in 2024. [18] This designation expedites the development and review of drugs intended to treat serious conditions where preliminary clinical evidence indicates the drug may demonstrate substantial improvement over available therapies. The PATH Caucus should encourage the FDA to prioritize the evaluation of promising psychedelic compounds for BTD.

Psychedelics and Potential Treatment Indications

Psychedelic medicines have a rich history of use spanning millennia across various cultures. Some also have a history of abuse which has led to harm, particularly among vulnerable individuals in unsafe settings. Unfortunately, the stigma associated with psychedelics hindered research and development of these promising compounds for decades.

Modern research has identified several distinct compounds that, in popular parlance and public discourse, comprise the prescription psychedelic medicine sphere. Psychedelic compounds can be categorized based on their pharmacological mechanisms and effects. Classic psychedelics primarily act as serotonin 2A receptor agonists, inducing profound changes in perception, mood, and cognition. Entactogens, such as MDMA, enhance emotional openness and connectivity, while dissociatives like ketamine modulate glutamate signaling to produce antidepressant effects.

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[10] **Centers for Disease Control and Prevention**. "Protecting the Nation's Mental Health." August 8, 2024.
[11] **U.S. Department of Veterans Affairs.** "National Veteran Suicide Prevention ANNUAL REPORT, Part 1 of 2: In-Depth Reviews." December 2024.
[12] **U.S. Department of Veterans Affairs.** "National Veteran Suicide Prevention ANNUAL REPORT, Part 2 of 2: Report Findings." December 2024.
[13] **National Library of Medicine**. "Addressing Suicide in the Veteran Population: Engaging a Public Health Approach." November 23, 2020.
[14] **Multidisciplinary Association for Psychedelic Studies.** "FDA Grants Breakthrough Therapy Designation for MDMA-Assisted Therapy for PTSD, Agrees on Special Protocol Assessment for Phase 3 Trials." August 26, 2017.
[15] **Compass Pathways.** "COMPASS Pathways receives FDA Breakthrough Therapy designation for psilocybin therapy for treatment-resistant depression." October 23, 2018.
[16] **Usona**. "FDA grants Breakthrough Therapy Designation to Usona Institute's psilocybin program for major depressive disorder." November 22, 2019.
[17] **MindMed.** "MindMed Receives FDA Breakthrough Therapy Designation and Announces Positive 12-Week Durability Data From Phase 2B Study of MM120 for Generalized Anxiety Disorder." March 07, 2024.
[18] **Cybin**. "Cybin Receives FDA Breakthrough Therapy Designation for its Novel Psychedelic Molecule CYB003 and Announces Positive Four-Month Durability Data in Major Depressive Disorder." March 13, 2024.

Classic Psychedelics

- **Psilocybin** — A serotonin 2A receptor agonist that produces self-transcendent subjective experiences characterized by feelings of awe and wonder, connectedness, psychological insight, and emotional breakthrough or catharsis.[19]
    - *Potential indications for treatment include: TRD, MDD, PTSD, GAD, SUD, chronic pain conditions, and end-of-life distress and demoralization*.

- **Lysergic Acid Diethylamide (LSD)** — LSD is a synthetic ergotamine belonging to the group of classic, or serotonergic, psychedelics, which activates serotonin 2A receptors to increase connectivity in regions of the brain. LSD has distinctive transient, perceptual, and emotional effects which can alter perception, behavior, and mood, as well as produce durable anxiolytic effects and neurogenesis.
    - *Potential indications for treatment include: GAD, PTSD, SUD, depressive disorders, chronic pain conditions, end-of-life distress and demoralization.*

- **Mescaline** — A serotonin 2A receptor agonist that produces self-transcendent subjective experiences characterized by feelings of awe and wonder, connectedness, psychological insight, and emotional breakthrough or catharsis.
    - *Potential indications for treatment include: PTSD, GAD, SUD, depressive disorders, chronic pain conditions, and end-of-life distress and demoralization*.

- **Dimethyltryptamine (DMT)** — A hallucinogen with an unclear receptor target that alters the senses, including sights, sounds, and the perception of time.
    - *Potential indications for treatment include: TRD and MDD.*

Entactogens

- **Methylenedioxymethamphetamine (MDMA)** — An entactogenic or empathogen compound that generally promotes feelings of openness and compassion toward self and others and introspective self-awareness.
    - *Potential indications for treatment include: PTSD, SUD, depression and eating disorders.*

Dissociatives

- **Ketamine**, including esketamine (Spravato®) — A dissociative substance that can produce transcendent experiences characterized by insight and catharsis, though perhaps to a lesser degree than classic psychedelics.
    - *Potential indications for treatment include: SUD, chronic pain conditions, and depressive disorders.*

- **Dextromethorphan** — A dissociative substance that can produce transcendent experiences characterized by insight and catharsis, though perhaps to a lesser degree than classic psychedelics.

[19] **Nature**. "Psilocybin desynchronizes the human brain." July 17, 2024.

- *Potential indications for treatment include: SUD, chronic pain conditions, and depressive disorders.*

Federal Action in Prescription Psychedelic Medicine

With several promising psychedelic compounds already in Phase 3 clinical trials, the immediate priority is ensuring efficient utilization of existing regulatory pathways and improved FDA/DEA communication to bring these treatments to patients.

Concurrently, federal agencies that directly provide healthcare (VA, IHS, DOD) require implementation funding to assess needs, develop protocols, train personnel, and prepare their clinical settings for these novel therapies.

Looking forward, APP encourages the PATH Caucus to prioritize dedicated research funding at scale for additional promising compounds, as the current level of investment from agencies like FDA, VA, and NIH remains disproportionate to both the mental health crisis and the potential of prescription psychedelic medicine to address it.

The Way Forward: A Level Playing Field to FDA Approval

FDA approval can integrate prescription psychedelic medicine into America's healthcare system in a manner that ensures patients can safely access these potentially transformative treatments for four key reasons:[20]

1) **Prescription Information**: The FDA requires labeling for all approved prescription medicines.[21] Labeling for prescription medicines is the FDA's primary tool for communicating drug information to healthcare professionals, patients, and their caregivers. For healthcare professionals, the FDA provides prescribing information that contains a summary of the essential scientific information needed for the safe and effective use of the specific medicine for its approved uses.

2) **Risk Evaluation and Mitigation Strategy (REMS)**: REMS is a drug safety program that the FDA can require for certain medications.[22] REMS includes a risk mitigation goal and is comprised of information communicated to, and/or required activities to be undertaken by, one or more participants (e.g., healthcare providers, pharmacists, patients) who prescribe, dispense, or take the medication. Together, the goal, communications, and/or activities make up the risk mitigation strategy.

[20] **The Regulatory Review**. "A Roadmap to Reimbursement for Psychedelics." April 16, 2024.
[21] **U.S. Food and Drug Administration**. "FDA's Labeling Resources for Human Prescription Drugs For Industry." April 4, 2024.
[22] **U.S. Food and Drug Administration**. "Risk Evaluation and Mitigation Strategies | REMS." May 16, 2023.

3) **Manufacturing Standards**: Products and their specific formulations under clinical trial investigation and/or approved by the FDA are required to adhere to Current Good Manufacturing Practice (CGMP) standards to ensure their stability, purity, and consistency from dose to dose.[23]

4) **Healthcare System Integration**: FDA-approved products have a higher likelihood of adoption by health systems and coverage by insurance companies. Broad and safe access to these innovative treatments can only be achieved if they are FDA-approved and reimbursed through a patient's health insurance carrier. This pathway ensures that as many Americans as possible can access these treatments.

As FDA approval is key to safe patient access, prescription psychedelic medicines should be held to — and follow — the same clinical development standards and approval processes as any other pharmacological intervention. These fair and consistent standards help build trust across the entire healthcare ecosystem and enable patients across the country to safely access potential treatment options.

Implementation Recommendations

APP encourages the PATH Caucus and Members of Congress to consider three key policy improvements to help expand access to safe and effective prescription psychedelic medicine:

1) **Streamline FDA/DEA Coordination:** To ensure safe and effective access, the DEA and FDA should begin communication at the time of an NDA submission. This is particularly critical for products that have received BTD, highlighting the urgency to get these potentially life-saving medicines to patients in need. Regarding investigational psychedelic therapies, we believe establishing early dialogue with the DEA would enable developers to address potential concerns identified in the DEA's review of the FDA rescheduling recommendation following the FDA's Eight-Factor Analysis before they become roadblocks. We urge the PATH Caucus to explore frameworks that facilitate ongoing communication between therapy developers and the DEA throughout the period between NDA filing and potential approval. Given the significant unmet needs these therapies may address, we propose the FDA and DEA could collaborate on the Eight-Factor Analysis concurrent with NDA review period rather than waiting until after FDA approval. Additionally, efficiency could be greatly improved by allowing the FDA to begin its mandatory Eight-Factor Analysis while simultaneously engaging in cross-agency labeling discussions alongside the DEA's evaluation. The current sequential approach creates unnecessary delays that ultimately restrict timely patient access to potentially beneficial treatments.

[23] **U.S. Food and Drug Administration**. "Facts About the Current Good Manufacturing Practice (CGMP)." January 21, 2025.

2) **Coordinated Review Processes**: The creation of a coordinated review process between the FDA and the DEA would improve efficiency and organization in the approval process, benefiting both the patients awaiting treatment and the agencies reviewing them.

3) **Application Enhancements**: Reducing redundancies in application requirements will remove unnecessary red tape and create a more productive environment for treatments. Eliminating the need for sponsors to resubmit identical safety and efficacy data to both the FDA and DEA would significantly streamline the process. Currently, companies must prepare and submit largely overlapping documentation packages to both agencies, despite the FDA already conducting comprehensive reviews that the DEA could leverage in their assessment.

FDA Advisory Committee Improvements

The FDA relies on many advisory committees to provide critical guidance based on the best available science, give the public a voice in important decision-making discussions, and help make thoughtful decisions.[24] Several actions can be taken to improve FDA advisory committees that oversee the consideration of prescription psychedelic medicine. This includes:

- Ensuring committee membership is comprised of experts in psychedelic medicine, such as scientists, clinicians, and industry leaders.

- Establishing clear and consistent guidelines for evaluating psychedelic therapeutics to ensure that prescription psychedelic medicines are not held to higher standards not used in the evaluation of other medications. For example, functional unblinding (patients determining if they are in the active or placebo arms) is possible for a wide variety of psychiatric and other medications.

- Implementing standardized assessment criteria for novel treatment modalities.

Medical Society Engagement

As research on psychedelics continues to advance, it is essential that medical societies begin working closely with the prescription psychedelic medicine industry now to develop clear guidance that can evolve as these treatments advance in their clinical development.

APP believes the *"Guidance on the Safe Use of Ketamine Outside of Acute Pain Management and Procedural Sedation"* developed by the American Society of Anesthesiologists provides an excellent starting framework. [25]

While comprehensive guidelines typically mature after FDA approval as real-world evidence accumulates, preliminary guidance should be established proactively. The PATH Caucus should encourage medical and mental health societies to prepare for the integration of prescription

[24] **U.S. Food and Drug Administration**. "Advisory Committees Give FDA Critical Advice and the Public a Voice." June 13, 2024.
[25] **American Society of Anesthesiologists**. "Guidance on the Safe Use of Ketamine Outside of Acute Pain Management and Procedural Sedation." February 7, 2025.

psychedelic medicine into standard practice through an adaptive approach that recognizes the continuum of care and evolving treatment protocols that naturally develop as these medicines scale within the healthcare system.

Conclusion

The development and implementation of prescription psychedelic medicine presents a historic opportunity to address our nation's mental health crisis with innovative treatments. As research advances and clinical trials demonstrate promising results, it is essential that our regulatory framework evolves to facilitate the safe, effective, and timely delivery of these therapies to patients in need.

We thank Representatives Bergman and Correa and the entire Congressional Psychedelics Advancing Therapies (PATH) Caucus for your leadership and commitment to addressing these critical issues. Your willingness to engage with stakeholders and explore evidence-based approaches to mental healthcare is commendable. We look forward to continuing this important dialogue and serving as a resource as you advance policies that support the responsible development and implementation of prescription psychedelic medicine.