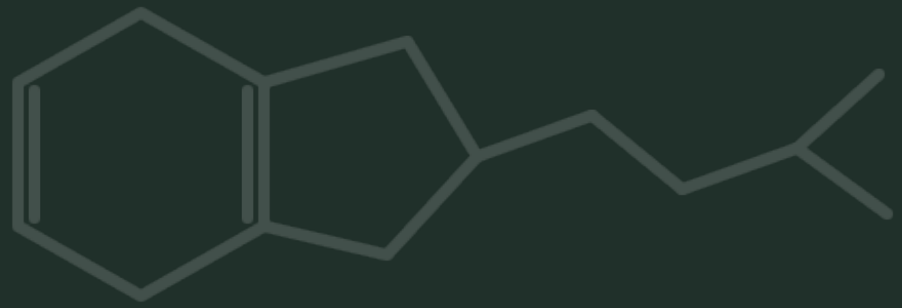
CURRENT RESEARCH & POLICY

Psychedelics as Medicine

Current Research, Regulatory, and Policy Considerations for State Mental Health Systems



National Association of State Mental Health Program Directors

2026 Annual Meeting · Washington, DC · July 2026

Presented at the NASMHPD 2026 Annual Meeting · Washington, DC

THE MOMENT

A field moving faster than most expected

2 of 2

PHASE 3 TRIALS

Psilocybin met its primary endpoint in both pivotal trials for treatment-resistant depression.

Apr 2026

EXECUTIVE ORDER

Priority review vouchers, expanded Right-to-Try for ibogaine, and $50M via ARPA-H.

+37%

PAST-YEAR USE

Hallucinogen use rose from 7.6M to 10.4M adults (2021–2024), led by psilocybin.

4+

STATE PROGRAMS

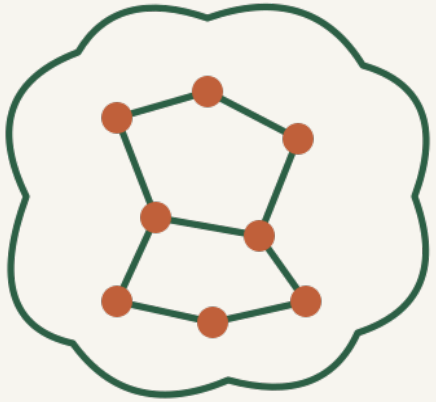
Oregon, Colorado, New Mexico, and Utah have live access frameworks; Texas funds ibogaine.

If the FDA approves psilocybin or another psychedelic, state Medicaid programs face immediate coverage, legal, and budget decisions. The purpose here is preparation — not advocacy.

WHAT THEY ARE

Not a take-home prescription

Psychedelics produce marked changes in perception, mood, thought, and sense of self. In clinical use they are given once or a few times under controlled conditions — fundamentally unlike a daily pill.



Facility-based administration A prepared, monitored treatment setting — not the home.

Trained facilitators present FDA draft guidance: a licensed lead monitor plus an assistant.

Medical monitoring capability Vitals and emergency readiness across the dosing session.

Structured support, before & after Preparation and integration extend across weeks to months.

SET & SETTING

"Set" is the person's mindset — expectations, intentions, mood, history. "Setting" is the physical and social environment. Both shape safety and outcome, and both are actively managed in clinical protocols.

Source: FDA draft guidance on psychedelic drug development (2023).

THE COMPOUNDS

One label, very different drugs

COMPOUND	PRIMARY MECHANISM	DURATION	LEAD INDICATION
Psilocybin	5-HT2A agonist	**4–6 hrs**	TRD, MDD, SUDs, end-of-life
LSD	5-HT2A agonist	**8–12 hrs**	Generalized anxiety
DMT	5-HT2A agonist	**20–30 min**	Depression
4-OH-DiPT prodrug	5-HT2A agonist	**3–4 hrs**	Postpartum depression
MDMA	Monoamine release + oxytocin	**3–5 hrs**	PTSD
Methylone	Monoamine release	**2–4 hrs**	PTSD
5-MeO-DMT	Primarily 5-HT1A agonist	**15–45 min**	TRD, alcohol use
Ibogaine	NMDA / sigma / opioid	**24–36 hrs**	Substance use, PTSD
Ketamine / esketamine	NMDA antagonist	**1–2 hrs**	TRD (esketamine approved)

CLASSIC PSYCHEDELIC ENTACTOGEN ATYPICAL / ADJACENT

Status and designations as of May 2026. Mechanisms and durations abbreviated.

REGULATORY STATUS

Where the pipeline actually stands

BREAKTHROUGH THERAPY

Designation granted

- Psilocybin (TRD, 2018)
- Psilocybin (MDD, 2019)
- MDMA (PTSD, 2017)
- Methylone (PTSD)
- LSD (GAD)
- 4-OH-DiPT prodrug (PPD)

→

PHASE 3 UNDERWAY

Pivotal trials running

- LSD (GAD)
- Deuterated psilocin (MDD)
- 5-MeO-DMT (TRD) — initiating

→

PHASE 3 COMPLETE

Met primary endpoint

- Psilocybin (TRD) — both trials
- MDMA (PTSD) — then CRL, Aug 2024

→

FDA APPROVED

On the market

- Esketamine (TRD; MDD w/ SI)
- No classic psychedelic yet

Priority review vouchers (April 2026) can compress final review from 10–12 months to as little as 1–2 — issued to psilocybin (TRD, MDD) and methylone (PTSD).

Regulatory status as of May 2026. BTD = Breakthrough Therapy designation; CRL = Complete Response Letter.

EVIDENCE · DEPRESSION

The strongest signal — but it often fades

Depression has the deepest evidence base. The recurring pattern: a real, sometimes large antidepressant effect early, which in several trials weakens over the following weeks to months.

Effect met the primary endpoint

−3.6	**Phase 3 TRD · 1** *COMP005 · n=258*	MADRS vs. control, wk 6
−3.8	**Phase 3 TRD · 2** *COMP006 · n=581*	MADRS vs. 1 mg, wk 6
−12.3	**Single-dose MDD** *Raison 2023 · n=104*	MADRS vs. niacin, day 43

Effect faded or missed primary

- **TRD dose-finding** *Goodwin 2022 · n=233*
  Significant at wk 3, no longer significant by wk 12
- **vs. escitalopram** *Carhart-Harris 2021 · n=59*
  No difference on the primary outcome (secondaries favored psilocybin)
- **EPISODE** *Mertens 2026 · n=144*
  Primary endpoint not met; key secondaries did favor psilocybin
- **One-year follow-up** *Yngwe 2026*
  Day-8 benefit faded on clinician-rated depression by 12 months

The early antidepressant signal is genuine; durability and comparator choice remain unresolved — which is exactly why endpoint and trial-design decisions matter so much here.

MADRS differences are placebo-adjusted. Sources: COMPASS Phase 3 (2025–2026); Raison 2023; Goodwin 2022; Carhart-Harris 2021; Mertens 2026; Yngwe 2026.

EVIDENCE · ACROSS CONDITIONS

Promising signals, uneven evidence

PTSD

67% → 71%

No longer met PTSD criteria across two MDMA Phase 3 trials (vs. 32% and 48% on placebo). FDA declined approval in Aug 2024.

End-of-Life Distress

~80%

Sustained clinical response at 6 months in cancer patients; benefits persisted 4–5 years in follow-up. Small samples.

Substance Use

40.5% vs 10%

Smoking abstinence at 6 months (vs. nicotine patch). AUD trials span positive, mixed, and null results.

Anxiety (GAD)

12 weeks

Single LSD dose produced durable anxiety reduction through 12 weeks — under a minimal-support model.

Effect sizes are often substantial and short-term safety in trials is generally good — but samples are small and the strongest data cluster in a few indications.

Sources: Mitchell et al. Nat Med 2021/2023; Griffiths & Ross 2016; Johnson et al. JAMA Netw Open 2026; Robison et al. JAMA 2025.

EVIDENCE · CLOSEST TO YOUR POPULATIONS

The trial that resembles public systems

Most psychedelic trials enroll wealthy, highly educated, predominantly White samples. One psilocybin trial for cocaine use disorder stands apart — and is the most generalizable to the people state systems actually serve.

82.5%

of participants were Black

65%

had incomes at or below $20,000

+29 pts

more cocaine-abstinent days

0

serious adverse events

Psilocybin recipients had ~29 percentage points more cocaine-abstinent days through 180 days, a greater likelihood of complete abstinence (odds ratio 18.4; 30% vs. 0%), and lower lapse risk. *A demographic profile that finally resembles the public mental health population.*

Source: Hendricks et al. JAMA Network Open 2026 (psilocybin for cocaine use disorder, n=40).

READING THE EVIDENCE

What the data does — and does not — show

The data supports

- Encouraging preliminary signals across several conditions
- Effect sizes that are often substantial
- Generally good short-term safety in controlled trials
- A clear warrant for continued, larger research

The data does not yet

- Establish efficacy for complex, real-world populations
- Settle optimal dosing, frequency, or long-term trajectory
- Show durability beyond 6–12 months
- Rule out expectancy: near-total unblinding is unresolved

$100K+

Median income in the two largest US psilocybin trials; 75% held a college degree (vs. 37% nationally).

Sources: Grossman et al. Nature Mental Health 2025; Williams et al. JAMA Psychiatry 2026; NNDC consensus statement 2025.

SAFETY

Generally good in trials — gaps remain

Common & transient

Headache, nausea, anxiety, perceptual distortion, emotional intensity — typically resolving within hours to days. No physiological dependence reported.

Serious — rare, not zero

~4% serious AEs among participants with preexisting neuropsychiatric conditions (worsening depression, suicidal behavior, psychosis, convulsions). None among healthy volunteers.

Psychosis risk rises with vulnerability

Population studies	**0.002%**
Uncontrolled trials	**0.2%**
Randomized trials	**0.6%**
Trials incl. schizophrenia	**3.8%**

Ibogaine is the outlier

QTc prolongation, arrhythmia, and documented fatalities in unregulated settings. Any program requires cardiac screening, continuous monitoring, and emergency access.

Sources: Hinkle et al. JAMA Psychiatry 2024 (214 studies); Sabe et al. Mol Psychiatry 2024. A key finding: only ~24% of post-2005 studies used systematic AE assessment.

THE CORE TENSION

Trials exclude the people you serve

State and territorial systems exist primarily to serve people with serious mental illness, complex trauma, low income, and co-occurring conditions. Nearly all psychedelic trials explicitly exclude exactly these individuals.

- **Psychotic disorders**
- **Bipolar I disorder**
- **Active suicidal ideation**
- **Lithium / MAOIs / some antipsychotics**
- **Unstable medical conditions**
- **Substance use disorders***

** except in trials specifically studying SUDs. The evidence base does not directly apply to many state-system clients — which is itself a case for targeted research.*

Typical exclusion criteria across psychedelic clinical trials.

REALITY ON THE GROUND

Access is already happening

PAST-YEAR HALLUCINOGEN USE

US adults, ages 12+

7.6M *in 2021*

→

10.4M *in 2024*

+37% in three years

Largely driven by psilocybin mushrooms.

Regulated state programs

Oregon alone has served ~16,000 clients since 2023.

Underground networks

298 retreat organizations advertised online as of 2023, with variable oversight.

Risk-context use

A 20,000-person study links use with negative mindset or no support to worsening depression.

Sources: 2024 National Survey on Drug Use and Health; Oregon Psilocybin Services data; Simonsson et al. J Affect Disord 2025.

EMERGING STATE MODELS

Four approaches, already diverging

OREGON

Supported adult-use

- Measure 109 (2020); first in nation
- Facilitators need not be licensed clinicians
- No formal therapy component
- ~1/3 of service centers have closed

NEW MEXICO

Medical model

- Enacted April 2025
- Requires prescriber involvement
- Integrated with the healthcare system
- Contrasts sharply with Oregon

COLORADO / UTAH

Hybrid & pilot

- CO: service centers + personal-use (2022)
- Denver decriminalized first (2019)
- UT: pilot in two licensed health systems
- Prescribing within controlled settings

TEXAS

Ibogaine research

- Up to $50M in matching public funds
- Targets OUD, SUDs, PTSD, TBI
- Veteran-focused
- Largest state ibogaine investment

State program details as of 2026.

THE DELIVERY REALITY

Cost and workforce are the hard part

20–60 *hours*

of professional time per patient across preparation, dosing, and integration.

$11,500 *per patient*

estimated cost of MDMA-assisted therapy for PTSD (two co-therapists, multiple all-day sessions).

$45,000 *per year*

esketamine maintenance can cost this much — a cautionary reimbursement precedent.

A workforce already in shortage

16,940

projected shortage of social workers

8,220

projected shortage of psychologists

6,080

projected shortage of psychiatrists

Sources: Marseille et al. PLoS One 2022; HRSA behavioral health workforce projections.

WHAT TO DO NOW

Five policy considerations

1 **Plan for the fiscal & legal implications now** Model Medicaid coverage obligations and work with the AG's office on authority — before approval, not after.

2 **Invest in research on representative populations** Fund studies in people with serious mental illness, complex trauma, and low income — the generalizability gap.

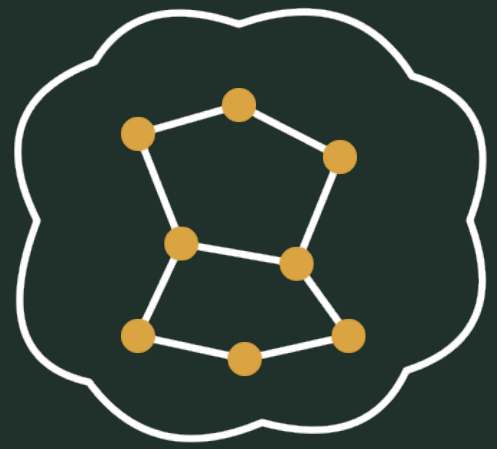
3 **Build oversight frameworks proactively** Credentialing standards, safety protocols, informed consent, and complaint mechanisms — ahead of availability.

4 **Monitor unregulated use and prepare messaging** Track adverse events and give providers and consumers clear information on real risks and benefits.

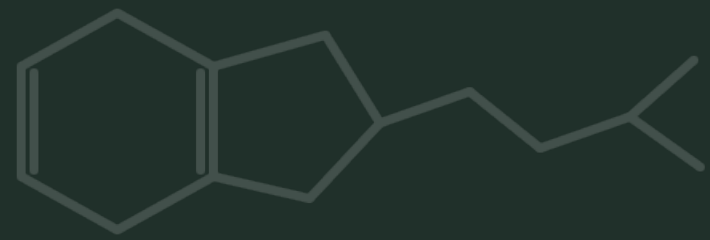
5 **Engage the federal process and coordinate** Keep decision-makers informed and aligned across agencies as psychedelic policy proposals arise.

THE BOTTOM LINE

State directors don’t need to be advocates — but they must be informed.



- The science and regulatory momentum are real; FDA approval could come sooner than expected.
- The evidence base is thinnest exactly where state systems are deepest.
- Access is already happening — regulated or not.
- Preparing in advance is easier than reacting under pressure.



Peter S. Hendricks, PhD *University Professor & Heersink Endowed Chair, UAB*

NASMHPD 2026 Annual Meeting · Washington, DC

APPENDIX · LATEST FEDERAL ACTION

July 2026: coordinated federal implementation

In mid-July 2026, multiple federal agencies announced coordinated actions implementing the April 2026 Executive Order — moving from directive to execution.

CENTERPIECE

HHS–VA partnership

A five-year Memorandum of Understanding (July 13, 2026) to collaborate on research, clinical development, and eventual deployment of rapid-acting psychedelic therapies for veterans, if FDA-approved.

- Increase veteran participation in clinical trials
- Train clinicians to safely administer approved products
- Share real-world safety, effectiveness, and cost data with FDA

FDA Public hearing on future therapeutic use of psychedelics set for Sept 14, 2026, with a comment period.

NIDA $2.3M to academic investigators toward an ibogaine IND for opioid use disorder.

ARPA-H Additional funds made available for ibogaine research.

HRSA Seeking input on the workforce training and care-delivery models needed to implement approved therapies.

Context: *Much of this effort is veteran-focused and advocacy-driven, and officials note FDA approval remains years away — the near-term substance is training, data, and safety protocols, not access.*

Sources: HHS–VA MOU announcement (July 13, 2026); FDA public hearing notice (Federal Register, July 2026); NIDA and ARPA-H statements.