# Psychedelics

- Show promising therapeutic effects for treatment of neuropsychiatric, substance abuse disorders and potentially branching out to pain management, migraines, or Autism
- Promote neuroplasticity and potential positive neural adaptions
- Challenging to meet gold standard of double blinded, placebo clinical trials due to the inability to control or mirror subjective effects
- Hallucinogenic and subjective effects vary by substance and by person due to multiple factors
- Experiences can last minutes to hours depending on substance and dose
- Currently no recognized credentialling requirements for therapeutic administration

# Mechanisms of Psychedelic Administration

- **Clinical Trial:** medical research to determine if treatment, prevention, and behavior approaches are safe and effective. Trials follow specific protocols carefully designed to balance the potential benefits and risks to participants and answer specific research questions. Regulated by the FDA.
- **Expanded Access:** also called compassionate use, is the use of an experimental drug outside of clinical trials to treat people with serious or life-threatening diseases. Regulated by the FDA.
- **Right to Try:** use of an experimental drug outside of a clinical trial or expanded access if patient meets criteria (life-threatening illness, no standard treatments available, not eligible for clinical trial) and drug meets certain criteria. NOT regulated by the FDA.
- **Therapeutic Administration:** unregulated administration of medication outside of a clinical trial or expanded access protocol, may be part of an established medical or religious program with supportive care, counseling, and integration components.
- **Recreational Use:** administration or consumption of psychedelic substances outside of a structured therapeutic program or intent.

# Psychedelic Background

- 1970 - Controlled Substances Act ceased research efforts in the US
  - Characterized psychedelics as Schedule I substances with high potential for abuse and/or no accepted medical use
- Expanding clinical and legislative support at national and state levels
  - FDA granted **MDMA-Assisted Therapy** Expanded Access in 2022 for “compassionate use” for PTSD, expected to be approved for use in 2024
  - FDA granted Psilocybin Breakthrough Therapy designation for depression in 2018
- Ongoing research in developing non-hallucinogenic psychedelic analogs

# Clinical Trial Basic Information

- **Phase I trials:** Researchers test a drug or treatment in a small group of people (20–80) for the first time. The purpose is to study the drug or treatment to learn about safety and identify side effects.
- **Phase II trials:** The new drug or treatment is given to a larger group of people (100–300) to determine its effectiveness and to further study its safety.
- **Phase III trials:** The new drug or treatment is given to large groups of people (1,000–3,000) to confirm its effectiveness, monitor side effects, compare it with standard or similar treatments, and collect information that will allow the new drug or treatment to be used safely.
- **Phase IV trials:** After a drug is approved by the FDA and made available to the public, researchers track its safety in the general population, seeking more information about a drug or treatment's benefits, and optimal use.

# Psychedelic Studies

| Medication | Potential Treatment Options Based on Ongoing Clinical Trials | | | | FDA Approval | Notes |
|---|---|---|---|---|---|---|
| | PTSD | Depression | Pain | TBI | | |
| Ketamine | ✓ | ✓ | ✓✓ | - | 1970 (Analgesia) | Used off-label for depression |
| Esketamine | - | ✓✓ | ✓ | - | 2019 (Depression) | |
| MDMA | ✓✓ | ✓ | ✓ | - | 2024 (PTSD) | |
| Psilocybin | - | ✓ | ✓ | - | ~2026 (Depression) | Potential use for headaches |
| LSD | - | | ✓ | - | ~2030 (Anxiety) | Potential use for alcohol use disorder in historic studies |
| DMT (ayahuasca) | - | ✓ | - | - | ~2030+ | |
| Ibogaine | - | - | - | - | ~2030+ | PTSD data from uncontrolled trials |
| 5-MeO-DMT | - | - | - | - | ~2030+ | Undergoing Phase 1 safety studies |
| Cannabinoids (var) | ✓ | - | ✓ | - | 1985 (nausea, vomiting)<br>2018 (seizures) | Not strong evidence for PTSD or pain |

✓✓ Phase 3 RCT (+) ✓ Strongest Phase 2 RCT (+) ✓ Strongest Phase 2 RCT null - No RCT