

Psilocybin-Assisted Therapy for TRD

Clinical Evidence Summary • Empax Centre • April 2026

What the Research Shows

Psilocybin-assisted therapy for treatment-resistant depression (TRD) has now been evaluated in two Phase 3 randomised controlled trials, making it one of the most rigorously studied novel psychiatric interventions. These trials enrolled patients who had not responded to at least two adequate courses of antidepressant treatment.

2 of 2

Phase 3 trials achieved
primary endpoint
($p < 0.001$)

839

patients dosed across
both Phase 3 trials

<1%

serious
suicidality-related
adverse events

Source: Compass Pathways COMP005 (2025, n=258) & COMP006 (2026, n=581)

Key Findings

Phase 3 efficacy confirmed: Both COMP005 (single dose, n=258) and COMP006 (two doses, n=581) achieved their primary endpoints with highly statistically significant reductions in depression severity on the MADRS scale versus control (differences of -3.6 and -3.8 points respectively; both $p < 0.001$).^{1,2}

Meaningful response rates: In COMP006, 39% of patients receiving psilocybin 25mg achieved clinically meaningful symptom reduction, with durability data through 26 weeks expected later in 2026.²

Earlier-phase evidence: The Phase 2b trial (NEJM, 2022; n=233) demonstrated significant MADRS score reductions at week 3 with 25mg psilocybin, establishing the dose and therapeutic framework used in Phase 3.³

Independent replication: A separate RCT published in JAMA (2023, n=104) confirmed psilocybin's antidepressant effects with no serious treatment-related adverse events.⁴

Safety profile: Across both Phase 3 trials, serious adverse events related to suicidal ideation occurred in less than 1% of participants. The most common side effects were headache, nausea, and transient emotional distress during sessions.^{1,2}

Meta-analytic support: A BMJ meta-analysis (2024) and multiple systematic reviews confirm a large pooled effect size (Hedge's $g = -0.89$) in favour of psilocybin for depression across all available RCTs.^{5,6}

Regulatory + Government Endorsement

TGA Schedule 8: Since 1 July 2023, psilocybin has been available for therapeutic use in treatment-resistant depression under the Authorised Prescriber pathway.⁷

FDA Breakthrough Therapy: Compass Pathways' COMP360 psilocybin holds FDA Breakthrough Therapy designation, and a New Drug Application is anticipated in Q4 2026.¹

DVA funding: The Australian DVA began funding psychedelic-assisted psychotherapy for eligible veterans in November 2025, following an independent rapid evidence assessment.⁸

Australian pilot data: An Australian open-label pilot trial (2025) demonstrated clinically meaningful depression reductions in treatment-resistant patients, supporting feasibility in the local clinical context.⁹

References

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5. Metaxa AM & Clarke M. BMJ. 2024;385:e077777. (Systematic review & meta-analysis)
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