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Sector Momentum Builds Ahead of ENP’s Next Clinical Readouts

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Company Snapshot

Company	Entropy Neurodynamics Limited
Lead asset	TRP-8803, a proprietary formulation of intravenously (IV) infused psilocin, the active metabolite of psilocybin.
Lead indications	Binge eating disorder (Phase 2), with treatment-resistant depression entering the clinic through the eight-indication basket study and a planned US trial
Shares on issue	1,633.6m
Share Price (close 30 Sep 2026)	\$0.0395
Market Capitalisation	\$64.5m
Net Cash (30 June 2026)	\$5.6m

Table 1: Sources: ASX announcements Appendix 4E (28 August 2026). Market data as of 30 September 2026

Psychiatry could be getting its first genuinely new class of medicine since the SSRIs arrived in the late 1980s. Psychedelic compounds that spent half a century outside mainstream medicine have now produced five positive Phase 3 trials across depression and anxiety, all reported in the past eighteen months, and the world's largest pharmaceutical companies are paying billions to own them. Entropy Neurodynamics is Australia's entrant: a Melbourne clinical-stage company that delivers psilocin, the active agent of psilocybin, through an intravenous infusion giving clinicians enhanced control.

Entropy spent the past eight weeks assembling its own part of the story. 12 weeks after their second and final infusion, every patient in the company's first binge eating disorder cohort maintained a clinically meaningful improvement, and half remained in full remission. Around that result, the company locked in pharmaceutical-grade manufacturing with BioCina and signed with University of California, San Francisco (UCSF) to run TRP-8803 head-to-head against escitalopram (Lexapro), a widely prescribed antidepressant in the US. The pieces of a US development program are now visibly in place.

The sector kept moving around it. Lilly completed its acquisition of AtaiBeckley on 11 September at up to US\$3.8 billion. Definium reported its second and third positive Phase 3 results for its LSD drug in August and September. Compass Pathways commenced a rolling NDA submission for COMP360 psilocybin in treatment-resistant depression, and on 14 September the FDA held a public hearing on how psychedelic therapy should actually be delivered.

Addressing the Delivery Bottleneck

Whether psilocybin-class therapy works in psychiatric disease is no longer the open question. Compass Pathways has run two positive, well-controlled Phase 3 trials of psilocybin in treatment-resistant depression, COMP005 and COMP006. ENP's own oral pathfinder studies showed an 80% reduction in binge eating episodes, a 75% clinically meaningful response in refractory irritable bowel syndrome and pain improvement in all treated fibromyalgia patients.

The commercial problem is delivery. Oral psilocybin takes 30 to 90 minutes to act and can occupy a supervised treatment room, a psychiatrist and a therapy team for six to eight hours, with variable intensity

along the way. Industry commentary around the Lilly transaction called delivery the biggest remaining barrier to wider use. Developers across the sector are converging on the same bottleneck from different directions including nasal sprays, inhalers and dissolving tablets.

TRP-8803 takes a different route; it's an intravenous infusion the clinician steers in real time. Dosing runs in two phases, and that's what makes the platform unique. A short loading infusion lifts psilocin into the therapeutic range within about 20 minutes, then a separate maintenance infusion holds the patient at the target intensity for as long as the protocol requires. Onset and duration are controlled independently. The clinician sets the depth of the experience, decides when it ends, and can turn the maintenance infusion down or off at any point, after which drug levels fall quickly.

Early clinical signs have been encouraging. In Cohort 1 of the Phase 2 binge eating disorder trial, six out of six patients reached a full psychedelic state on a standard dose under the 140-minute loading-plus-maintenance format, with nine of 12 sessions reaching a full psychedelic state. Cohort 2 tests a 60-minute format. If efficacy holds at 60 minutes, a treatment room that handles one oral patient a day could plausibly handle four to six infusion patients. That's the difference between a boutique service and a scalable product.

The patient pool is large, and big pharma is paying to get in. Around 2.8 million US adults sit in the treatment-resistant depression pool and roughly 3.1 million US adults have binge eating disorder in any year. Large pharmaceutical companies have been buying their way into the category. AbbVie paid US\$1.2 billion for Gilgamesh and its lead asset bretisilocin, a short-acting synthetic psychedelic in Phase 2 for major depressive disorder. Otsuka paid US\$1.2 billion for Transcend Therapeutics and its lead asset TSND-201 (methylone), an MDMA analogue now in Phase 3 for post-traumatic stress disorder. Lilly also paid up to US\$3.8 billion for AtaiBeckley, whose lead asset BPL-003 is an intranasal 5-MeO-DMT for treatment-resistant depression built around a roughly two-hour clinic visit.

US Clinical Development Strategy

The centrepiece of the recent news is the US depression trial. ENP has signed a pre-Clinical Trial Agreement with the University of California, San Francisco for a Phase 2 head-to-head study of TRP-8803 against escitalopram (Lexapro), a widely prescribed antidepressant in the US, in up to 80 young adults with major depressive disorder. Depression severity is assessed at eight weeks and six months, with brain-activity (EEG) measures built in.

The Principal Investigator is Professor Robin Carhart-Harris, the Ralph Metzner Distinguished Professor of Neurology and Psychiatry at UCSF. Carhart-Harris founded the Centre for Psychedelic Research at Imperial College London, the first of its kind, led the brain-imaging studies of psilocybin and LSD that underpin the modern field, and is its most cited researcher, with more than 52,000 citations. He was lead author of the landmark New England Journal of Medicine trial comparing oral psilocybin with escitalopram. He also chairs ENP's Scientific Advisory Board and is the company's exclusive biomarker development partner.

ENP will act as the US FDA sponsor for the trial. The sequence from here is to finalise the protocol and consent documents with UCSF, hold a pre-IND meeting with the FDA, submit the Investigational New Drug application that permits US trials, then sign the binding trial agreement following completion of the FDA regulatory process. The company guides to a first half of CY2027 start, funded from existing cash, option conversions and pending R&D tax refunds.

Strategic Objectives of the US Program

- **Move upstream.** Around 19.7 million US adults experienced a major depressive episode in 2025, with prevalence highest among young adults aged 18 to 25 at 14.2%. Much of psychedelic drug development has focused on treatment-resistant populations, particularly patients who have already failed multiple conventional therapies. This trial tests a limited course of therapy much earlier in the disease.
- **Benchmark against the incumbent.** Escitalopram was prescribed to approximately 9.45 million US patients in 2024, generating 41.8 million prescriptions. A head-to-head result against the standard of care is worth more to partners and payers than another placebo comparison.
- **Open a US regulatory foundation.** Subject to FDA clearance, the IND supports not just this trial but future Phase 2b/3 studies in whichever indications the basket study elevates.
- **Set up the partnering conversation.** Management states the program is designed to open the Company to commercial partnership discussions.

Recent Milestones

- **19 August.** Manufacturing agreement with BioCina, a TGA-licensed, FDA-inspected Australian contract manufacturer with the regulatory framework to handle Schedule 9 APIs including psilocin. A 24-week program produces GMP clinical drug and the stability data required for US and European filings, with ENP retaining all intellectual property.
- **26 August.** UCSF pre-Clinical Trial Agreement covered above.
- **14 September.** 12-week durability data from BED Cohort 1, summarised below.

12-Week Durability: BED Cohort 1

The Phase 2 trial with Swinburne University is treating 12 chronic, treatment-resistant binge eating disorder (BED) patients in two cohorts of six. Each patient receives two TRP-8803 infusions roughly two weeks apart alongside structured psychotherapy. Four-week results for Cohort 1 were released on 7 July, and the 14 September announcement reported how the same six patients looked at the 12-week follow-up. The comparison is below.

Outcome	4 weeks	12 weeks
Clinical remission (no binge episodes)	50% (3 of 6)	50% (3 of 6)
Clinically meaningful improvement (30%+ from baseline)	100%	100%
Weekly binge eating episodes	74% reduction	73% reduction
Anxiety (GAD-7)	58% reduction	50% reduction
Depression (PHQ-9)	57% reduction	42% reduction
Life satisfaction	63% improvement	61% improvement
Clinical Global Impression (clinician-rated)	33% improvement	44% improvement

Table 2: Source: ASX announcements, 7 July and 14 September 2026

Patients received only two infusions, and the response was essentially unchanged 12 weeks later, in a group that had failed prior treatment and carried the disease for a median of fifteen years. The FDA's final psychedelic guidance nominates week 12 as the durability assessment point for chronic psychiatric

conditions. ENP has now generated encouraging durability data at that same regulatory timepoint, albeit in a small, open-label Phase 2 cohort.

Cohort 2 is fully recruited and doses under the shorter 60-minute regimen endorsed by the independent safety board, against 140 minutes in Cohort 1. Topline and the full 12-patient Phase 2 dataset are due in Q4 CY2026.

The 72-Patient Basket Study

Alongside the BED program and the planned US depression trial, ENP is evaluating TRP-8803 in 72 patients across eight disorders in a single basket study. The key benefit is cost: one protocol, run in parallel cohorts, shows where the drug works best for A\$3.2m, far less than running each indication as its own trial.

The eight disorders chosen were treatment-resistant depression, post-traumatic stress disorder, obsessive compulsive disorder, generalised anxiety disorder, anorexia nervosa, body dysmorphic disorder, fibromyalgia and irritable bowel syndrome. Nine cohorts of eight patients each run the same open-label protocol, two TRP-8803 infusions roughly two weeks apart with psychological support, dosing in parallel rather than one after another. One of the depression cohorts doses patients while they remain on their existing antidepressants, a design point that widens the eventual treatable population. First dosing was targeted for the September quarter, and the read-outs expected to arrive on a rolling basis over the next 12 months.

A Proven In-Clinic Treatment Model

Spravato, J&J's esketamine nasal spray for treatment-resistant depression, is the closest commercial precedent for what ENP is building, a supervised, in-clinic psychiatric drug, delivered in repeat short sessions. Its trajectory is the best available evidence for what a reimbursed TRP-8803 could look like. Spravato generated US\$584m in the June 2026 quarter, up 40% operationally year on year. Full-year 2025 sales were roughly US\$1.7 billion, consensus expects about US\$2.3 billion for 2026, J&J now designates the drug a key franchise with peak sales that could exceed US\$5 billion. Around 87% of sales are American. Spravato shows two things, payers will fund short, supervised, in-clinic psychiatric treatment at premium prices, and a national network of certified treatment sites already exists.

Recent Deals, Acquisitions and Regulatory Events in the Space

- **Lilly completed the AtaiBeckley acquisition.** Shareholders approved on 8 September, the deal closed on 11 September at US\$6.75 per share plus contingent rights worth up to US\$2.50, up to US\$3.8 billion in total. Lead asset BPL-003 (intranasal 5-MeO-DMT, a roughly two-hour visit) holds Breakthrough Therapy status and is in Phase 3.
- **Definium (formerly MindMed) went three for three in Phase 3.** Its LSD tablet DT120 met all primary and key secondary endpoints in the Voyage anxiety study (12 August), then again in the 245-patient Panorama study (14 September), following June's positive depression result. FDA Breakthrough Therapy in MDD was granted 27 August. A pre-NDA meeting is set for Q4 2026 with filing planned for H1 2027.
- **Compass files this quarter.** The rolling psilocybin NDA's final submission is on track for Q4 2026 with launch expected in H1 2027. Management flags approval, DEA rescheduling, state action and payer adoption as the gating items.
- **Two more potential acquirers showed their hand.** J&J led an US\$85m Series C in Delix Therapeutics with a right of first negotiation over its lead candidate, and Lundbeck's CEO said the company is pursuing neuroscience bolt-ons of US\$1.5 to 2 billion.

- **Two more Phase 3 programs are lining up.** Helus Pharma's psilocin-analogue Phase 3 in adjunctive depression is fully enrolled with a readout expected in Q4 2026, and GH Research's inhaled 5-MeO-DMT is Phase 3-ready following the lifting of its US clinical hold in January, with pivotal development targeted to commence in 2026.
- **The FDA opened the delivery question to the public.** A 14 September Part 15 hearing on the therapeutic use of psychedelics took four hours of testimony from around 80 commentators across medicine, veterans' groups, pharmacy, industry and patient advocacy, before a panel that included the FDA, the Veterans Health Administration and SAMHSA, with written comments closing 5 October. The recurring themes were calls for national standards on provider training and credentialing, structured patient screening, monitoring and follow-up, and realistic answers on clinic capacity, insurance reimbursement and long-term safety data collection, with witnesses noting that oral sessions of six to 12 hours need qualified staff present throughout. The American Psychiatric Association responded that FDA's determination of safety and effectiveness must remain the foundation for clinical use. Days earlier, the head of the FDA's drug centre co-authored a development framework for the class in the New England Journal of Medicine.
- **At home, one decision is pending.** The TGA's final decision on extending Schedule 8 psilocybin access to palliative care patients is due in the coming months, after a 29 May interim refusal and a consultation that closed 31 July. RANZCP also issued new guidance for Authorised Prescribers in July 2026.

Upcoming Catalysts

Catalyst	Expected timing	Significance
First patient dosed in 72-patient basket study	Was targeted for Sep quarter	Confirms execution of the eight-indication basket program
BED Cohort 2 topline (60-minute regimen)	Q4 CY2026	Tests whether Cohort 1 efficacy can be maintained with a materially shorter treatment window
Full 12-patient Phase 2 BED dataset	Q4 CY2026	Dataset that supports partnering discussions
FDA pre-IND meeting, then IND submission (UCSF trial)	Ahead of targeted H1 CY2027 trial start	Regulatory gateway for ENP's US clinical development strategy
Basket cohort readouts, incl. on-SSRI depression cohort	Rolling, next 12 months	Drives indication selection
Sector: COMP360 NDA filing and decision; Helus Phase 3 readout	Q4 2026 onward	Category approval precedent

Table 3: Sources. Company filings

ASX Comparisons

The table below sets out ASX listed companies with psychedelic medicine exposure.

Company (Ticker)	Lead Asset, Indication and Delivery	Clinical Stage	Market capitalisation (AUD, m)
Entropy Neurodynamics (ASX: ENP)	TRP-8803, psilocin, BED plus eight-indication basket, intravenous	Phase 2 (open label); FDA IND planned	\$64.5m
Emyria (ASX: EMD)	Psychedelic-assisted therapy delivery: MDMA and psilocybin clinic network (Empax), services to drug sponsors	Services and care model; supports third-party trials	\$37.1m

Table 4: Sources. Company filings. Market data from Iress accessed 30 Sep 2026.

Global Comparisons

The table below sets out selected global comparators developing psychedelic or related rapid-acting psychiatric therapies

US\$1.00 = A\$1.43

Company (Ticker)	Lead Asset, Indication and Delivery	Clinical Stage	Market capitalisation (AUD, m)
Definium Therapeutics (Nasdaq: DFTX), formerly MindMed	DT120, LSD, GAD and MDD, dissolving tablet	Three positive Phase 3 trials across 608 patients (Voyage 214, Panorama 245, Emerge 149); 1,000+ Phase 3 dosing sessions; NDA planned H1 2027	\$7,341.9
AtaiBeckley	BPL-003, 5-MeO-DMT, TRD, nasal spray	Phase 3 with Breakthrough Therapy status; Phase 2b treated 193 patients	Acquired by Lilly for up to US\$3.8bn (~A\$5.43bn)
Compass Pathways (Nasdaq: CMPS)	COMP360, psilocybin, TRD, oral	Two positive Phase 3 trials across 839 patients (COMP005 n=258; COMP006 n=581), including 6-month durability; rolling NDA underway with final submission Q4 2026	\$2,566.4
GH Research (Nasdaq: GHRS)	GH001, 5-MeO-DMT, TRD, inhaled	Phase 3-ready, with pivotal program targeted to commence in 2026; Phase 2b treated 81 patients	\$2,421.6
Helus Pharma (Nasdaq: HELP), formerly Cybin	HLP003, psilocin analogue, adjunctive MDD, oral	Phase 3 fully enrolled (first pivotal ~220 patients); readout expected Q4 2026	\$1,880.6
Entropy Neurodynamics (ASX: ENP)	TRP-8803, psilocin, BED plus basket, intravenous	Phase 2 open-label; 6 BED patients treated to date (12-patient trial), plus 14 healthy volunteers in Phase 1b; US IND pathway planned	\$64.5

Table 5: Sources: Company filings. Market data from Iress accessed 30 Sep 2026.

Closing thoughts

The next several readouts should start answering the questions that matter most for ENP: whether the clinical effect seen in the initial BED cohort can be reproduced using a materially shorter 60-minute infusion, and whether TRP-8803 shows meaningful activity across the broader basket study. The first will help determine whether ENP's IV delivery model can offer a practical commercial advantage, while the second should begin to identify which indications have the strongest clinical potential. In parallel, progress through the FDA pre-IND and IND process will show whether the US development program is advancing towards its targeted H1 CY2027 start. From there, the focus should shift towards selecting the strongest indications for larger controlled studies and potential partnering discussions, giving investors a much clearer view of where TRP-8803 ultimately fits within the rapidly developing psychedelic medicines market.

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