4 August 2026

72 patient multi-indication trial approved to fast track TRP-8803 commercialisation

- **Human Research Ethics Committee (HREC) approval secured for world-first phase 1b/2a 8-indication basket study across in 72-patients of TRP-8803**
- **Study will evaluate TRP-8803 (IV-infused psilocin) across eight major disorders with high unmet treatment needs in a single clinical framework**
- **Study indications include Anorexia Nervosa, Body Dysmorphic Disorder, Obsessive Compulsive Disorder, Generalised Anxiety Disorder, Post Traumatic Stress Disorder, Treatment-Resistant Depression, Fibromyalgia and Irritable Bowel Syndrome**
- **Treatment-Resistant Depression to be evaluated across two distinct patient cohorts with one cohort on antidepressant therapy and another off**
- **All indications selected for their strong scientific rationale and growing clinical evidence supporting the therapeutic potential of TRP-8803**
- **New Clinical Trial Research Agreement executed with Swinburne University to leverage specialist expertise**
- **Multi-indication basket study builds on encouraging Phase 2 Binge Eating Disorder results which delivered 100% response and 50% remission**
- **Patient recruitment to commence shortly across all indications, with first patient dosing expected later this quarter**
- **Dosing in initial cohorts anticipated before the end of CY2026**
- **Study expected to generate a comprehensive clinical dataset for precision-controlled IV-infused psilocin**
- **Trial to expand clinical evidence supporting TRP-8803, while unlocking development, commercial and partnering opportunities**

Melbourne, Australia – Entropy Neurodynamics Limited ('**Entropy Neurodynamics**' or the '**Company**') (**ASX: ENP**), a clinical-stage biotechnology company developing precision-controlled psychedelic therapies, advises that it has received Human Research Ethics Committee approval to commence a Phase 1b/2a multi-indication basket study evaluating TRP-8803 (IV-infused psilocin) across eight significant and widespread disorders. The Company has also entered into a Clinical Trial Research Agreement ('CTRA') with Swinburne University to conduct this world-first trial initiative.

This milestone marks the next phase of the Company's broader clinical strategy to position TRP-8803 as a precision-controlled treatment platform for high-value disorders with large,

undertreated patient populations.

The basket study is designed to assess TRP-8803 across multiple indications within one clinical framework, helping the Company prioritise future development opportunities while strengthening the clinical evidence base for its proprietary intravenous psilocin platform.

Management commentary

CEO, Mr Jason Carroll said: *"Securing HREC approval and executing our expanded Clinical Trial Research Agreement with Swinburne University represents a significant milestone in the evolution of TRP-8803 from a promising lead asset into a scalable precision treatment platform capable of addressing multiple high-value neuropsychiatric disorders."*

"Following the highly encouraging clinical outcomes generated in treatment-resistant Binge Eating Disorder, we now can systematically evaluate TRP-8803 across eight additional disorders that share common underlying mechanisms. Rather than pursuing these indications sequentially, our world-first basket study enables us to evaluate them in parallel, significantly accelerating our understanding of where TRP-8803 has the greatest clinical and commercial potential."

"Importantly, our expanded partnership with Swinburne provides the clinical infrastructure, specialist expertise and operational capacity required to efficiently execute a study of this scale. With first dosing expected later this quarter, we believe Entropy is entering one of the most active and value-generating periods in the Company's history, with the potential to deliver multiple clinical milestones and further establish TRP-8803 as a differentiated precision-controlled psychedelic therapy."

Study overview

The approved Phase 1b/2a open-label study will evaluate the safety, tolerability and preliminary efficacy of TRP-8803 across eight disorders with significant unmet medical need and shared underlying features, including cognitive inflexibility, emotional distress and persistent bodily symptoms.

The study is expected to enrol 72 participants across nine clinical cohorts of eight participants each. The Treatment-Resistant Major Depressive Disorder (TRD) arm includes two separate cohorts: patients receiving stable antidepressant therapy (SSRI or other antidepressant) and patients not receiving antidepressant treatment. This design will allow the Company to assess TRP-8803's safety and clinical activity across distinct TRD treatment settings, while generating indication-specific efficacy signals to guide future development priorities.

The eight indications being evaluated are:

- Anorexia Nervosa
- Fibromyalgia (chronic pain)
- Irritable Bowel Syndrome
- Obsessive Compulsive Disorder
- Body Dysmorphic Disorder
- Generalised Anxiety Disorder
- Post Traumatic Stress Disorder
- Treatment Resistant Major Depressive Disorder

Participants will receive two doses of TRP-8803, administered approximately two weeks apart, alongside a structured psychedelic-assisted psychotherapy program.

The primary endpoint is safety. Secondary and exploratory endpoints will assess changes in anxiety, quality of life, disease-specific symptoms and broader patient-reported outcomes. The protocol also includes advanced biomarker assessments, including MRI, functional MRI, electroencephalography (EEG), speech analysis and qualitative patient interviews, to further characterise TRP-8803's biological and clinical effects across multiple indications.

Unlike traditional single-indication development programs, the basket trial allows Entropy to assess the broader therapeutic potential of its proprietary intravenous psilocin platform across multiple disorders in parallel, providing a capital-efficient way to identify the strongest clinical and commercial opportunities for future development.

Strategic rationale

The basket study marks a world-first initiative in neuropsychiatry and an important strategic milestone in the development of TRP-8803. It is expected to broaden the program from a single lead indication to a systematic assessment of the wider therapeutic potential of Entropy's precision-controlled intravenous psilocin platform.

The study builds on highly encouraging clinical outcomes in Binge Eating Disorder (ASX announcement: 7 July 2026), where the first patient cohort achieved a 100% clinical response, 50% remission and significant improvements in anxiety and depression.

The selected indications represent areas of substantial unmet medical need, with many sharing a common neurobiological mechanism that may respond to precision-controlled psychedelic therapy. They were chosen based on growing scientific and clinical evidence supporting the therapeutic potential of psychedelics across these disorders, providing a strong basis to evaluate TRP-8803 in high-priority development opportunities.

By assessing multiple disorders within one clinical program, Entropy aims to efficiently identify the indications with the strongest clinical and commercial potential, helping the Company prioritise future development and capital allocation. The study will also expand the clinical safety database for TRP-8803 across multiple patient populations and further differentiate Entropy's precision-controlled intravenous platform from oral psychedelic therapies. Together, these outcomes are expected to create future clinical, commercial and partnering opportunities while further validating TRP-8803 as a scalable precision treatment platform.

The concurrent CTRA with Swinburne University also materially strengthens Entropy's clinical development capability by expanding the operational infrastructure available for the basket study and future clinical programs.

Building on the successful collaboration that has supported TRP-8803 to date, the agreement provides access to additional clinical infrastructure, including greater dosing capacity through multiple dedicated treatment rooms, an expanded multidisciplinary team of investigators, psychiatrists, physicians, psychologists and psychedelic therapists,

and enhanced research and operational support to help deliver multiple study cohorts in parallel.

This enhanced capability is expected to improve patient throughput, support faster recruitment and dosing across the basket study, and provide a scalable clinical research platform for future expansion of the Company's development pipeline. The Company believes the strengthened partnership positions Entropy to execute increasingly complex clinical programs efficiently while continuing to build one of Australia's leading psychedelic clinical research collaborations.

Next steps

Following HREC approval, the Company will complete the remaining regulatory and site governance requirements needed to commence the study, including Clinical Trial Notification (CTN) acknowledgement and site-specific governance approvals.

Patient recruitment will commence shortly, reflecting significant preparation ahead of HREC approval and positioning the Company to rapidly advance the study into treatment. First patient dosing is expected to commence during the current quarter and, subject to recruitment and operational timelines, the Company anticipates completing dosing in one or more indication cohorts before the end of CY2026.

Entropy believes the basket study could generate several meaningful clinical milestones over the coming months as recruitment progresses across the eight indications. The Company looks forward to updating shareholders on patient dosing, cohort progression and clinical outcomes as the study advances.

Q&A

What is TRP-8803?

TRP-8803 is Entropy's proprietary intravenously administered psilocin formulation. Psilocin is the active metabolite of psilocybin and the compound responsible for the therapeutic and psychoactive effects traditionally associated with psilocybin. TRP-8803 is administered in conjunction with psychotherapy.

How is TRP-8803 different from oral psilocybin?

TRP-8803 delivers psilocin directly into the bloodstream, avoiding the need for gastrointestinal absorption and conversion of psilocybin into psilocin. This may reduce pharmacokinetic variability, improve dosing precision, shorten treatment duration, and allow clinicians to adjust or cease dosing if required.

Why does IV administration of TRP-8803 matter?

IV administration allows clinicians to rapidly achieve and maintain the desired target psilocin blood level and improve the consistency of exposure and therapeutic intensity between patients. It also enables real-time control over duration and intensity of treatment.

Can the infusion of TRP-8803 be stopped if necessary?

Yes. A key advantage of TRP-8803 is that the infusion can be paused or terminated if clinically required, providing an additional level of control and safety not available with oral administration.

What is the purpose of the basket study?

The basket study is designed to evaluate TRP-8803 across multiple neuropsychiatric indications using a common protocol and biomarker framework. The aim is to identify the most promising future development opportunities while generating efficacy, safety and mechanistic data.

How many clinical indications are being studied?

The study evaluates eight clinical indications across nine cohorts, providing the Company with an opportunity to compare clinical outcomes and biomarker findings using a consistent methodology.

Why use a basket study instead of separate trials?

A basket design is a capital-efficient way to evaluate multiple indications simultaneously. It enables direct comparison of clinical response, quality of life, biomarkers and treatment mechanisms while reducing development timelines and costs.

How much will the basket study cost?

The basket study will cost approximately A$3.2 million, which does not include the Company's pending R&D Tax Incentive refund opportunities.

Why is this a study a good use of shareholder capital?

For approximately A$3.2 million, Entropy can evaluate multiple indications, assess biomarkers, refine patient-selection strategies and identify the strongest future development opportunities. Running independent studies across every indication would require substantially greater investment.

What indications are being evaluated?

The study includes disorders characterised by significant unmet need and evidence of dysfunctional brain network activity and cognitive rigidity, including conditions such as treatment-resistant depression, PTSD, OCD, GAD, anorexia nervosa, body dysmorphic disorder, IBS and fibromyalgia.

Why were these indications selected?

Each indication was selected because scientific evidence suggests that dysfunctional beliefs, rigid cognitive patterns, altered self-processing and large-scale brain network dysfunction could potentially be addressed by TRP-8803-assisted therapy.

What is meant by a "transdiagnostic" approach?

A transdiagnostic approach focuses on shared mechanisms across multiple disorders rather than treating each diagnosis as entirely separate. Entropy is investigating whether common processes such as cognitive rigidity, inflexible beliefs and altered brain network function may respond to TRP-8803 across different conditions.

Does the study only help identify lead indications?

No. The study has dual objectives. It evaluates individual indications while also generating a broader transdiagnostic dataset that may support TRP-8803 as a platform therapy across multiple
disorders.

What is the value of studying multiple indications simultaneously?

The design provides both indication-specific insights and broader platform-level data. It allows Entropy to identify which disorders respond best while also understanding whether common treatment mechanisms operate across conditions.

What does Entropy hope to learn about quality of life?

Quality-of-life measures are being collected across all cohorts. This allows the Company to assess whether TRP-8803 improves overall wellbeing and daily functioning beyond changes in disease-specific symptoms.

Why are quality-of-life outcomes important?

Patients ultimately seek improvements in how they feel and function. Improvements in relationships, daily activities, wellbeing and life satisfaction may be as important as reductions in disease symptoms.

What is cognitive flexibility?

Cognitive flexibility refers to an individual's ability to adapt thinking, reassess beliefs and respond constructively to changing circumstances. Reduced flexibility is thought to contribute to many psychiatric conditions.

Why is cognitive flexibility a key endpoint?

Entropy believes cognitive flexibility may represent a core therapeutic mechanism. If improvements in flexibility correlate with clinical outcomes across multiple disorders, it could support a transdiagnostic mechanism of action for TRP-8803.

What biomarkers are included in the study?

The study includes EEG, MRI/fMRI, speech-related assessments and a range of psychological measures designed to better understand treatment response and mechanisms of action.

Why are EEG biomarkers important?

EEG allows researchers to measure real-time changes in brain activity, including markers related to signal diversity and neural entropy, which are hypothesised to play a role in psychedelic-assisted therapy.

What is neural entropy?

Neural entropy refers to the complexity and diversity of brain activity. Our and our collaborators scientific hypothesis is that increasing neural entropy using treatments like TRP-8803 may enhance flexibility in thinking, learning and emotional processing.

How does the basket study support Entropy's broader scientific model?

The study allows the Company to evaluate whether changes in neural entropy, brain network function and cognitive flexibility are associated with clinical improvements across multiple disorders within a single clinical framework.

What role does psychotherapy play?

Psychotherapy is a critical component of treatment. Preparation supported dosing and integration sessions are designed to help participants process treatment experiences and translate emerging insights into lasting behavioural and emotional change.

How does the study build on the earlier BED results?

The Phase 2 BED study demonstrated encouraging remission and improvement rates, providing early clinical support for the precision controlled IV psilocin approach. The basket study extends this platform into additional indications.

What differentiates Entropy from other psychedelic companies?

Entropy combines a proprietary IV psilocin platform, precision-controlled dosing, biomarker development, EEG-based entropy research and a transdiagnostic development strategy designed to identify both disease-specific and platform-wide opportunities.

How could the basket study reduce development risk?

Rather than depending on a single indication, the Company can evaluate multiple opportunities simultaneously. Positive outcomes in one or more indications may create value even if some indications show limited
response.

Could biomarkers eventually help identify likely responders to treatment?

That is one of our long-term objectives. The basket study may help identify biological and psychological characteristics associated with treatment response, supporting more personalised treatment approaches in future studies.

What would constitute success for the basket study?

Success would include demonstration of acceptable safety, encouraging efficacy signals, meaningful improvements in the quality of life and functioning of participants, and biomarker findings that support future development decisions.

What could happen after positive basket-study results?

The Company could prioritise selected indications for later-stage development, pursue regulatory interactions, expand biomarker programs and explore partnership opportunities based on the data
generated.

What can investors look forward to over the next 12 months?

Key milestones include:

- Recruitment and dosing progress
- Cohort-level outcome data
- Additional BED data
- Biomarker analyses
- Identification of lead indications
- Validation of the broader transdiagnostic platform strategy
- Potential partnering and development opportunities

This announcement has been authorised by the Board of Entropy Neurodynamics Limited.

– ENDS –

INVESTOR & MEDIA CONTACT

Jason Carroll
Chief Executive Officer
Entropy Neurodynamics Limited
jcarroll@tryptherapeutics.com

Henry Jordan
Six Degrees Investor Relations
+61 (0) 431 271 538
henry.jordan@sdir.com.au

About Entropy Neurodynamics Limited

Entropy Neurodynamics is a clinical-stage biotechnology company focused on developing proprietary, novel formulations for the administration of psilocin in combination with psychotherapy to treat diseases with unmet medical needs. The Company's lead program, TRP-8803, is a proprietary formulation of IV-infused psilocin (the active metabolite of psilocybin) with potential to alleviate numerous shortcomings of oral psilocybin including: significantly reducing the time to onset of the psychedelic state, controlling the depth and duration of the psychedelic experience, and reducing the overall duration of the intervention to a commercially feasible timeframe. Development of TRP-8803 follows a number of Phase 2a clinical trials using oral psilocybin for the treatment of Binge Eating Disorder, Irritable Bowel Syndrome and Fibromyalgia. Results from each of these trials demonstrated the clinical benefits of psychedelic therapy and will be used to further enhance the development of TRP-8803.

Register for updates

The Company encourages investors to register their details with Automic Group investor portal. This also provides shareholders with the opportunity to elect communication methods to electronic only. This can be done via the following steps:

- *Go to investor.automic.com.au*
- *If you're an existing user, log in with your username and password*
- *If you're a new user, click 'register', select 'Entropy Neurodynamics Limited'. Enter your Holding Number and postcode of the registered address on your holding. If your address is outside Australia, select the country. Follow the prompts to set up a username and password.*
- *Once you have created your account, you will need to update your communication method by clicking 'my details' under the 'profile' section of the investor portal account, then navigating to 'communication preferences' and select 'electronic only'.*

Risks associated with Psilocin

All medicines carry risks and specialist prescribers, such as registered psychiatrists are best placed to assess the suitability of a new medication against a patient's individual circumstances and medical history before proceeding. Adverse effects of psilocybin and similar compounds, such as psilocin, can include temporary increase in blood pressure and a raised heart rate. There may be some risk of psychosis in predisposed individuals. These effects of psilocybin and its derivatives are unlikely at low doses and in the treatment regimen used in psychedelic-assisted psychotherapy and appropriately managed in a controlled environment with direct medical supervision.

Forward-Looking Information

Certain information in this news release, constitutes forward looking information. In some cases, but not necessarily in all cases, forward-looking information can be identified by the use of forward-looking terminology such as "plans", "targets", "expects" or "does not expect", "is expected", "an opportunity exists", "is positioned", "estimates", "intends", "assumes", "anticipates" or "does not anticipate" or "believes", or variations of such words and phrases or state that certain actions, events or results "may", "could", "would", "might", "will" or "will be taken", "occur" or "be achieved". In addition, any statements

that refer to expectations, projections or other characterizations of future events or circumstances contain forward-looking information. Statements containing forward-looking information are not historical facts but instead represent management's expectations, estimates and projections regarding future events. Forward-looking information is necessarily based on a number of opinions, assumptions and estimates that, while considered reasonable by Entropy Neurodynamics as of the date of this news release, are subject to known and unknown risks, uncertainties, assumptions and other factors that may cause the actual results, level of activity, performance or achievements to be materially different from those expressed or implied by such forward looking information, including but not limited to the factors described in greater detail in the "Risk Factors" section of the Company's Replacement Prospectus available at www.asx.com.au These factors are not intended to represent a complete list of the factors that could affect Entropy Neurodynamics; however, these factors should be considered carefully. There can be no assurance that such estimates and assumptions will prove to be correct. The forward-looking statements contained in this news release are made as of the date of this news release, and the Company expressly disclaims any obligation to update or alter statements containing any forward-looking information, or the factors or assumptions underlying them, whether as a result of new information, future events or otherwise, except as required by law.