ASX Release **19 November 2024**

Phase 1b determines optimal use of TRP-8803 (IV-infused psilocin)

- **<u>All objectives of the Phase 1b study met</u> including:**
  - **TRP-8803 safe at low, mid and upper dose levels**
  - **Optimal doses and infusion rates of psilocin that achieved target psilocin blood levels were identified**
  - **Greater control of psilocin blood levels achieved compared to oral psilocybin formulations**

- **Data enables optimised psilocin dosing and desired pharmacokinetic profiles for future Phase 2 patient trials utilising TRP-8803**

- **TRP-8803 is an innovative and scalable psilocin-based IV-infusion with potential neuroplastic benefits. Pharmaceuticals that achieve a change in neuroplasticity are known to cause adaptive structural and functional changes within the brain that are thought to be responsible for clinical improvements**

- **TRP-8803 has multiple advantages over oral psilocybin dosing including faster onset (under 20 minutes) with precise control of the depth and duration to the psychedelic state in a commercially feasible timeframe**

- **All trial participants achieved rapid onset of the psychedelic state, compared to one to two hours observed in oral psilocybin trials**

- **Participants infused with TRP-8803 received a controlled and consistent blood level of psilocin within the proposed therapeutic or neuroplastic zone over the infusion period (see figure 1)**

- **Rapid reversibility of TRP-8803 demonstrated when one subject encountered an elevated heart rate outside of study criteria. The IV infusion was able to be quickly halted which resulted in the subject's heart rate returning to normal**

- **Tryp now has all data necessary to proceed to active patient studies. Planning for additional clinical trials utilising TRP-8803 into specific indications is underway**

- **Additional Phase 1b study into obese subject population is set to commence this week with the results designed to confirm TRP-8803 safety in obese patients and provide valuable and cost-effective data on dose selection criteria for a Phase 2 trial aimed at treating Binge Eating Disorder**

Melbourne, Australia – Tryptamine Therapeutics Limited ('**Tryp**' or the '**Company**') (**ASX: TYP**), a clinical-stage biopharmaceutical company focused on the development of TRP-8803 (a proprietary psilocin-based, IV-infused formulation with neuroplastic benefits), is pleased to provide further data from the Company's recently completed Phase 1b study (refer ASX announcement: 18 October 2024). The study successfully met all key objectives enabling advancement to Phase 2 clinical trials utilising the innovative and scalable formulation, TRP-8803 for specific therapeutic indications.

The study has established key safety parameters for TRP-8803 across a range of dosing levels, demonstrated the ability to achieve desired pharmacokinetic (PK) profiles, and refined loading and maintenance doses to achieve target psilocin blood levels and treatment times in volunteers. This additional proprietary data set further strengthens the Company's IP portfolio.

Phase 1b background and TRP-8803 overview:

The new findings follow completion of the Phase 1b study, as well as determination from the Safety Review Council that TRP-8803 was generally safe and well-tolerated in healthy volunteers.

During the study, 11 participants were administered TRP-8803 via IV-infusion at varying dose levels for up to 150 minutes. The study was designed to refine and optimise the dose and infusion rate of TRP-8803 to achieve the precise, desired blood levels of psilocin with an acceptable pharmacokinetic profile.

TRP-8803 is Tryp's lead asset. It is an innovative and scalable psilocin-based IV-infusion formulation with neuroplastic benefits. Neuroplasticity is the ability of neural networks in the brain to change through growth and reorganisation. Treatments which improve neuroplasticity are known to cause adaptive structural and functional changes within the brain.

TRP-8803 offers multiple potential benefits over oral psilocybin, including a faster time to onset with more precise control of the depth and duration of the psychedelic state, while also offering significant overall reductions in the duration of treatment to a commercially feasible timeframe.

Importantly, TRP-8803's major advantage is inherent reversibility, allowing for treatment to be halted quickly if patients experience adverse events. This critical safety benefit cannot be achieved using oral dosing.

Additional study results and outcomes:

Following review the Phase 1b study, the Company has determined several key findings that build a robust foundation for additional Phase 2 clinical trials using TRP-8803.

Trial participants were administered an initial loading dose of TRP-8803, followed by a maintenance dose, across a lower, mid and upper dosing regimen. Following loading of therapeutic dose levels, all participants in the study achieved onset of the psychedelic state in under 20 minutes.

This study established relevant safety parameters for TRP-8803 across the three escalating dose levels at low, mid and high dose levels. This data provides a proprietary operational range of psilocin blood levels and enable the pharmacokinetic profile to be achieved that maximises neuroplastic treatment outcomes.

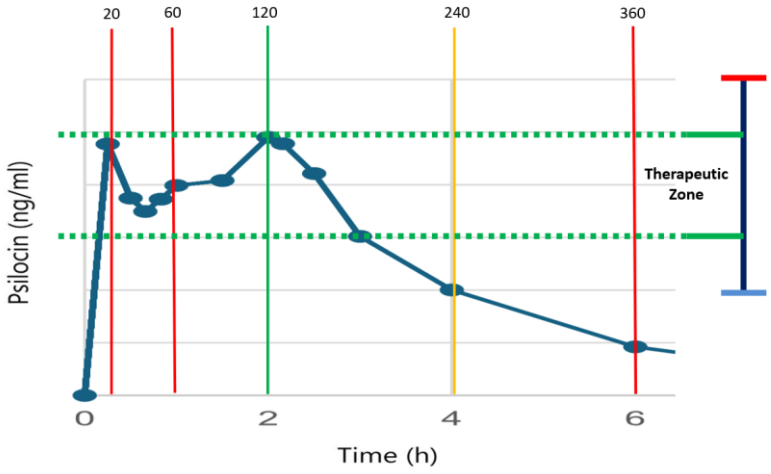

Figure 1: TRP-8803 achieving steady and controlled blood levels of psilocin consistently within the therapeutic zone

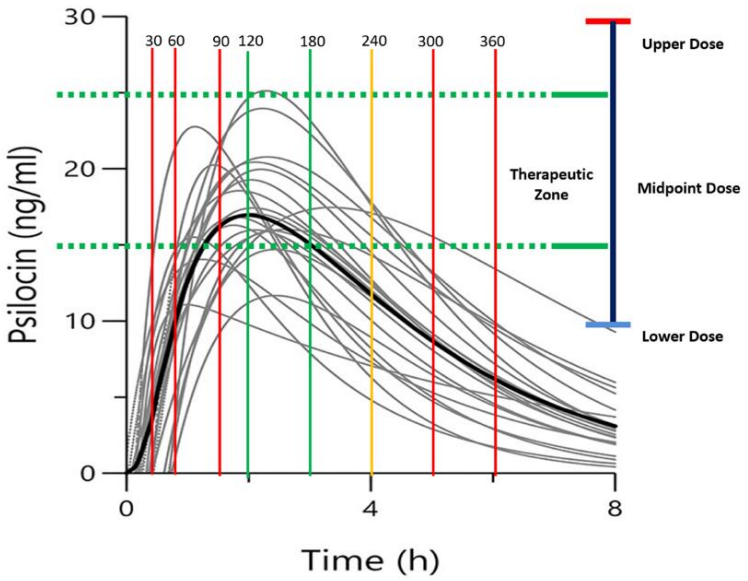

Figure 2: Observed high variability of oral psilocybin dosing (adapted from Holze et. al., *Pharmacokinetics and Pharmacodynamics of Oral Psilocybin Administration in Healthy Participants.* Clin. Pharmacol. Ther. 2023 Apr;113(4):822-831. doi:10.1002/cpt.2821)

Patients infused with TRP-8803 achieved consistent blood levels of psilocin consistently within the therapeutic zone reported previously in the literature for oral psilocybin (Figure 1). This delivery method is anticipated to provide considerably greater dose control avoiding the high variability provided by oral psilocybin dosing (Figure 2). Furthermore, the escalating dosing regimen has confirmed a strong correlation between psilocin blood levels and psychedelic intensity.

During the study, the Company also had the opportunity to demonstrate the reversible nature of TRP-8803 infusion. Within the highest dose cohort, one participant experienced a heart rate increase outside of the tightly designed study criteria of 100 beats per minute. Once the infusion was paused, the participant's heart rate decreased to acceptable levels. This reversibility would not have been possible with oral psilocybin dosing.

Tryp now has all data necessary to proceed to Phase 2 clinical studies. Planning for additional clinical trials utilising TRP-8803 is underway. Tryp's existing Phase 2a studies with TRP-8802 (synthetic oral psilocybin) are continuing which are anticipated to considerably fortify Tryp's intellectual property portfolio and clinical program.

Additional Phase 1b study to further refine dosing rates in an obese subject population:

The Company has made the strategic decision to undertake an additional small, low-cost Phase 1b study in obese subjects. The study is being undertaken at CMAX Clinical Research in Adelaide as an open-label study using TRP-8803 at the mid-range dose to determine if there are any differences in PK parameters within an obese population.

The approved study will add three obese participants to Tryp's existing study protocol, with first participant dosing to be undertaken on 21 November 2024 and the additional two subjects shortly thereafter. The results are anticipated to confirm TRP-8803's dosing within obese patients and to provide valuable and cost-effective data to support dose selection for the Phase 2 clinical program aimed at treating patients with Binge Eating Disorder.

The decision follows the exceptional results delivered from Tryp's Phase 2a study, undertaken in collaboration with the University of Florida, in patients with Binge Eating Disorder. This study utilised TRP-8802 (oral psilocybin) in

conjunction with psychotherapy. Following TRP-8802 administration patients achieved an average reduction in binge eating episodes of over 80% compared with baseline in addition to commensurate reductions in Anxiety and Depression and a durability of effect up to 60 days.

Management commentary:

Chief Executive Officer, Mr. Jason Carroll said: *"To have achieved these positive results from our Phase 1b for TRP-8803 study so quickly has exceeded all expectations and allows the Company to advance its clinical trial pipeline immediately. We are very pleased to have achieved all of the key objectives from the Phase 1b, including safety and optimised blood psilocin levels, all of which further highlight the potential of the treatment to achieve improved health outcomes at scale.*

"More broadly, the Company's goal at the outset of the Phase 1b trial program was to build a comprehensive dataset that could establish a sound framework for the next phase of our planned clinical development pathway. In that respect, the completion of the study has provided Tryp with a valuable proprietary data set that will inform the design of extensive Phase 2 trials, along with the application of TRP-8803 across the Company's broader trial program.

"From a research perspective, Tryp has now established the strong foundations that is essential to advance our world-first trials for IV-infused psilocin to the highest standards of safety, quality and integrity. This diligent approach is what is required to unlock the potential that is inherent in clinically backed psychedelic medicine solutions. We look forward with excitement to ongoing collaboration with our best-in-class research partners and bringing our investors along for the journey in this rapidly emerging field."

This announcement has been authorised for release by the Board of Tryptamine Therapeutics Limited.

-ENDS-

About Tryptamine Therapeutics Limited

Tryp Therapeutics is a clinical-stage biopharmaceutical company focused on developing proprietary, novel formulations for the administration of psilocin in combination with psychotherapy to treat diseases with unmet medical needs. Tryp's lead asset, TRP-8803, is a proprietary, scalable and innovative formulation of IV-infused psilocin (the active metabolite of psilocybin) with neuroplastic benefits. It has the potential to alleviate numerous shortcomings of oral psilocybin including: significantly reducing the time to onset of the neuroplastic state, controlling the depth and duration of the neuroplastic experience, and reducing the overall duration of the intervention to a commercially feasible timeframe. The Company has completed a Phase 2a clinical trial for the treatment of binge eating disorder at the University of Florida, which demonstrated an average reduction in binge eating episodes of greater than 80%.

The Company also has also just completed a Phase 2a successful clinical trial for the treatment of fibromyalgia in collaboration with the University of Michigan and has initiated a Phase 2a clinical trial in collaboration with Massachusetts General Hospital for the treatment of abdominal pain and visceral tenderness in patients suffering from irritable bowel syndrome. Each of the studies is utilising TRP-8802 (synthetic, oral psilocybin) to demonstrate clinical benefit in these indications. Where a positive clinical response is demonstrated, subsequent studies are expected to utilise TRP-8803 (IV-infused psilocin), that has the potential to further improve efficacy, safety, and patient experience.

For more information, please visit www.tryptherapeutics.com.

Investor & media enquiries:

Jason Carroll
Chief Executive Officer
Tryptamine Therapeutics Limited
jcarroll@tryptherapeutics.com

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

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 regimens 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 Tryp 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 Tryp'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 Tryp; 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 Tryp 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.