ASX Release **16 December 2024**

Results from Phase 1b extension refines dose of TRP-8803 (IV-infused psilocin) in obese subjects

- **<u>Objectives of Phase 1b study met:</u> Pharmacokinetic parameters of TRP-8803 in healthy obese volunteers consistent with non-obese healthy human volunteers**
- **This valuable data enables further optimisation of psilocin dosing to achieve the desired pharmacokinetic profiles in future Phase 2 patient trials using TRP-8803**
- **TRP-8803 is an innovative and commercially 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 obese individuals infused with TRP-8803 achieved an onset of psychedelic state within 20 minutes, consistent with TYP's previous healthy human volunteer studies and considerably faster than the 1-2 hours observed using oral psilocybin**
- **All obese participants infused with TRP-8803 achieved a controlled and consistent psilocin dose within the neuroplastic zone over the infusion period (refer figure one below)**
- **Results considerably strengthen Company's data suite in pursuit of active patient studies - Planning for Phase 2 clinical trials into specific indications, including Binge Eating Disorder is well advanced**

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 the following data from its recently completed low-cost, Phase 1b study into an obese human population (refer ASX announcement: 29 November 2024).

This open-label study was undertaken at CMAX Clinical Research in Adelaide using TRP-8803 to determine if there are any differences in pharmacokinetic ('PK') parameters compared to previously studied non-obese subjects (refer ASX announcement: 11 November 2024). The decision to undertake the study followed exceptional results from the Company's healthy human volunteer study, as well as Tryp's Phase 2a Binge Eating Study in collaboration with the University of Florida using TRP-8802 (oral psilocybin), which highlighted an average reduction in binge eating episodes of over 80% in patients compared with baseline in addition to commensurate reductions in Anxiety and Depression and a durability of effect up to 60 days.

The study commenced on 21 November 2024 and completed on 28 November 2024 (refer ASX announcements: 22 and 29 November 2024). It treated three subjects with TRP-8803 over a period of 140 minutes each. Each subject progressed through the treatment well and were respectively discharged shortly after dosage completion.

During the study, participants were administered an initial loading dose of TRP-8803, followed by a maintenance dose. Subjects were administered the same mid-range dosage utilised in the Company's previously completed Phase 1b study into healthy human volunteers (refer ASX announcement: 19 November 2024).

Results overview:

Based on a review of the study results, all obese subjects achieved onset of the psychedelic state in under 20 minutes.

Pleasingly, the data confirmed the previously observed optimal range of psilocin blood levels are highly similar in non-obese and obese individuals. Furthermore, obese volunteers infused with TRP-8803 achieved and maintained controlled psilocin blood levels within the putative therapeutic zone. Previously reported oral dosing studies were not able to achieve this outcome. This highlights the infusion's ability to deliver considerably greater dosage control and avoid the high variability of oral psilocybin dosing which may maximise neuroplastic treatment benefits for patients with neuropsychiatric conditions (refer figure one below).

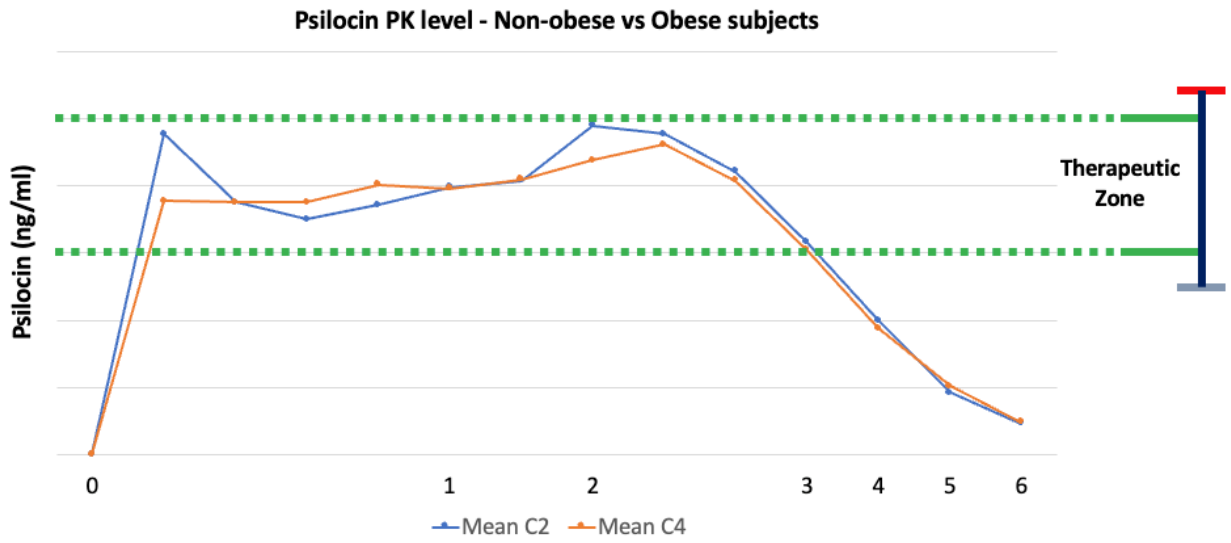

Figure 1: Average psilocin blood concentrations in obese (mean C4) and non-obese subjects (mean C2) infused with TRP-8803

Further exploring the optimal pharmacokinetic profile of TRP-8803 via this low-cost study provides Tryp with valuable human data and outlines a defined pathway for the Company to proceed to Phase 2 clinical studies. These trials are anticipated to commence in CY25 and will include an initiative at treating Binge Eating Disorder.

Management commentary:

Chief Executive Officer, Mr. Jason Carroll said: *"The successful completion of our Phase 1b study into an obese subject population marks another important step in the Company's clinical development pathway for TRP-8803. In particular, the application of the treatment for a cohort of obese subjects has allowed us to obtain very valuable data on accurate dosing levels across diverse patient groups.*

"The results from this study extension clearly demonstrate that the TRP-8803 dose selected for obese subjects will achieve similar pharmacokinetics to the non-obese population. We are confident of the infusion being effective for an obese population without the need for weight-based dosing regimens. The study met the required safety standard, as well as delivery of consistent and accurate psilocin blood levels within the targeted zone when compared to any published results from literature for oral psilocybin dosing regimens.

"The results further support Tryp's stated objective to develop a clinically backed solution for high-precision

neuroplastic treatments to achieve improved health outcomes. The extended Phase 1b results for TRP-8803 will be incorporated into a comprehensive planning program for Phase 2 clinical studies, which are scheduled to commence next year."

TRP-8803 background:

TRP-8803 is the Company's lead asset. It is an innovative and scalable psilocin-based IV-infusion formulation with potential 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.

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.