ASX Release **12 August 2024**

Positive Phase 2a fibromyalgia results deliver pain reduction in 100% of patients, strengthening IP position and clinical trial strategy

- **Phase 2a fibromyalgia trial undertaken with University of Michigan ("UOM') with results presented at the IASP 2024 World Congress on Pain 9 August 2024 in the Netherlands**
- **<u>All patients</u> dosed with TRP-8802 (TYP's oral psilocybin formulation), and administered psychotherapy reported an improvement in fibromyalgia pain severity, sleep, pain interference and at least 3 other endpoints measured one month after dosing**
- **Fibromyalgia is a condition associated with widespread pain – 1m people in Australia[i] and ~10m people in the US[ii] suffer from it and there are currently limited treatment options**
- **Results highlighted that there was a clinically meaningful reduction in pain, pain interference and fatigue**
- **Patients also reported a number of other improvements including clinically meaningful improvements in quality-of-life measures such as sleep, physical activity, and the ability to participate in daily social activities**
- **Clinically meaningful reduction in anxiety and improved cognitive abilities were also reported in 4 out of 5 patients dosed**
- **In addition, one patient reported during follow-up that their sense of smell had returned following a COVID-19 diagnosis in 2021**
- **Results highlight the significant potential for psychedelic-assisted therapy as a compelling treatment pathway for fibromyalgia when compared to the inadequacies of incumbent treatments**
- **Results considerably strengthen Tryp's IP position and lay a strong foundation for a future trial using TRP-8803 (IV-infused psilocin) – Phase 2 trial planning now underway and expected to commence H1 2025**
- **Additional clinical trials progressing well at MGH for patients with IBS, and the beginning of Cohort 3 in the TRP-8803 Healthy Volunteer Study expected to begin soon – updates to be provided in due course**

Melbourne, Australia – Tryptamine Therapeutics Limited ('**Tryp**' or the '**Company**') (**ASX: TYP**), a clinical-stage biotechnology company is pleased to advise it has received highly encouraging, positive results from its recently completed Phase 2a clinical trial conducted in collaboration with the University of Michigan ('UOM') (refer ASX announcement: 10 July 2024). The results are both significant and clinically meaningful, and were presented by UOM researchers at the International Association for the Study of Pain ('IASP') 2024 World Congress in the Netherlands on 9 August 2024.

The trial was designed to evaluate TRP-8802 (oral psilocybin) in conjunction with psychotherapy in patients with fibromyalgia, a condition associated with widespread pain and comorbidities that significantly impact daily living and patient well-being. The trial was undertaken by the UOM, a top-ranked public university in the US in collaboration with Tryp.

Results highlighted that 100% of patients experienced reductions in fibromyalgia pain, sleep disturbance and pain

interference (refer figures one and two below).

Whilst appreciating the limitations of the small number of patients and the open label nature of the 'signal' style study, the results are highly encouraging and considerably strengthen TYP's intellectual property position. Further, the results validate Tryp's clinical trial approach targeting nociplastic pain with an initial focus on fibromyalgia and will inform an additional clinical study utilising TRP-8803 (IV-infused psilocin), which is expected to commence H1 2025.

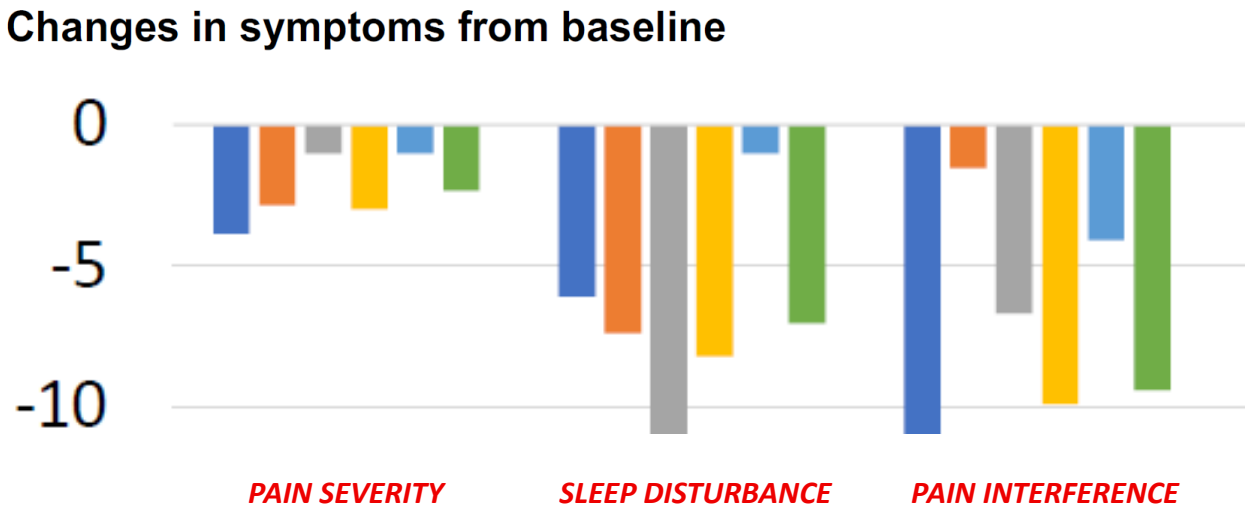


Figure one: Individual patient (001-005) and pooled results highlighting improvements in fibromyalgia domains as presented by University of Michigan 9 August 2024 (adapted)

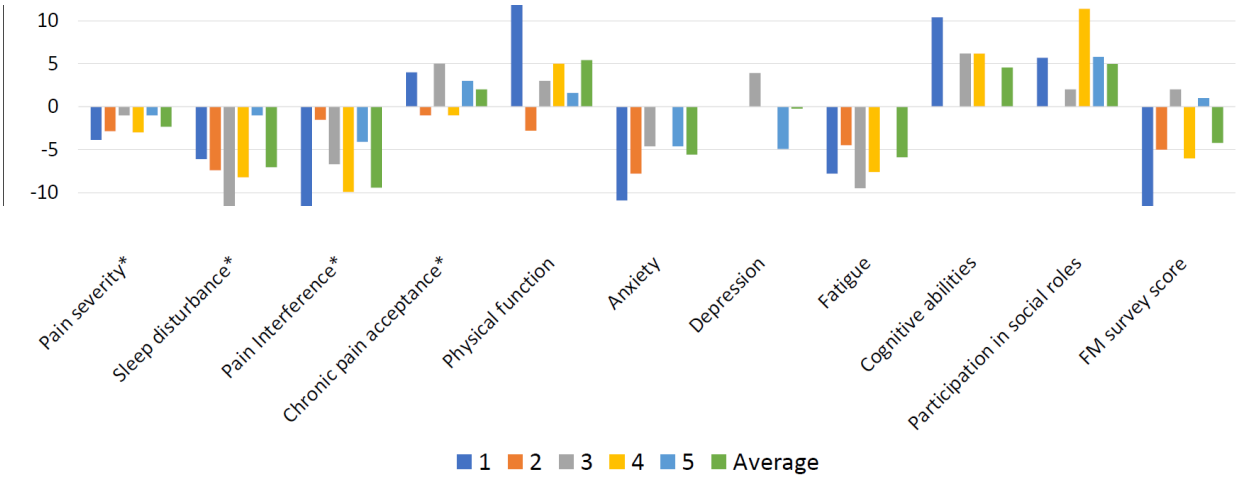


Figure 2. *Indicates secondary Outcome. CPAQ: Chronic Pain Acceptance Questionnaire. Pain Severity reported as change in aggregate pain score from the 7 days prior to the intervention to the end of the intervention. Sleep disturbance, pain interference, physical function, anxiety, depression, fatigue, participation in social activities, and cognitive abilities are all reported as T-scores per PROMIS scoring. Negative change scores indicate improvement for pain severity, pain interference, sleep disturbance, FM score, anxiety, depression, and fatigue. Positive change scores indicate improvement for CPAQ, physical function, participation in social activities, and cognitive abilities.

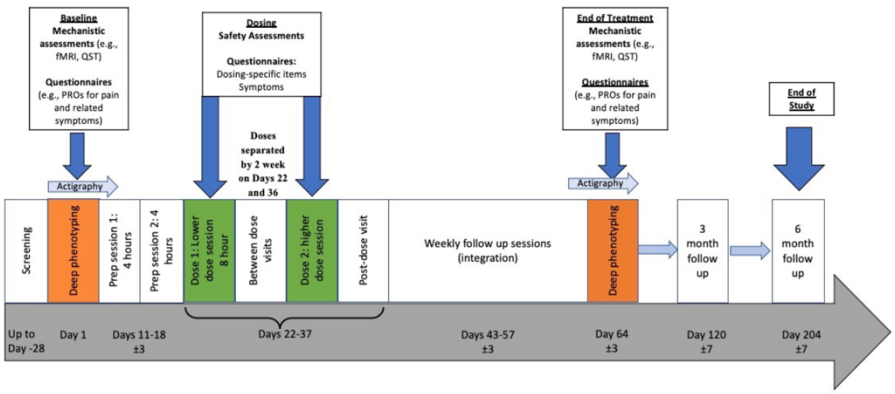
Figure two: Individual patient and pooled results as presented by University of Michigan 9 August 2024 (adapted)

Trial background:

The study was an open-label clinical trial with psychotherapy, seeking to evaluate TRP-8802 (oral psilocybin) in conjunction with psychotherapy in patients with fibromyalgia. A total of five patients were recruited and were administered two doses of TRP-8802 in 15mg initial dose and 25mg second dose formats, two weeks apart. Patients were administered psychotherapy in concert with TRP-8802 and results were compared to baseline values one month following the completion of the second dose.

Materials, Methods, Study Design

Study drug: Two doses of psilocybin (15mg, 25mg), from Usona Institute.
Primary outcome: Safety (AEs, blood pressure and heart rate during dosing)
Secondary Outcomes: Patient Reported Outcome Measurement Information System (PROMIS) Pain Interference, Sleep Disturbance 8b, Patient Global impression of Change, Chronic Pain Acceptance,
Other Outcomes: PROMIS 29+2, 2016 Fibromyalgia survey criteria



Management commentary:

Chief Executive Officer, Mr. Jason Carroll said: *"We are very excited about the results from the Phase 2a clinical trial in collaboration with the University of Michigan. Fibromyalgia is a complex and widespread condition, impacting one million Australians, and imposes a large emotional, physical and economic burden on every sufferer. Despite this, fibromyalgia sufferers have very limited success with current treatments, often resort to the use of opioids and many of these have highly limiting and wide-ranging side effects associated with their use."*

"While still early, these results highlight that psychedelic-assisted therapy may achieve an improved patient outcome through treating the cause of fibromyalgia rather than the limited relief to select symptoms provided from the treatment choices presently open to them. Through this trial we have demonstrated that psychedelic-assisted-therapy may offer an improved future for fibromyalgia patients across Australia and globally."

"On behalf of the Board and management, I would like to take this opportunity to thank the research team at the University of Michigan for their ongoing involvement and their presentation at the prestigious IASP 2024 World Congress on Pain. The presentation of these Phase 2a study results at such an event provides important exposure for Tryp's TRP-8802 and TRP-8803 programs with key industry participants. Looking ahead, the Company will undertake further analysis of these results in partnership with UOM researchers. These findings will be incorporated into planning now underway for an additional trial utilising TRP-8803, Tryp's innovative and scalable IV-infused psilocin formulation. We look forward to providing further updates on trial planning in due course."

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 biotechnology 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 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. 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 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. TRP-8803 is currently being evaluated in a Phase 1 Healthy Volunteer Study in Adelaide, Australia.

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

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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.

[i] https://fibromyalgiaaustralia.org.au/patients/what-is-fibromyalgia/#:~:text=Estimates%20are%20that%20as%20many,(IBS)%20and%20chronic%20headaches
[ii] https://www.fmaware.org/fibromyalgia-prevalence/