TSND-201 (methylone) for the Treatment for PTSD: Initial Results from an Open-Label Study (IMPACT-1)

Amanda Jones[1], Jennifer Warner-Schmidt[1], Martin Stogniew[1], Blake Mandell[1], Hannah Kwak[1], Paul W Miller[2], Terence HW Ching[3], Lynnette Averill[4], Benjamin Kelmendi[3]

[1]Transcend Therapeutics, [2]Mirabilis Health Institute, [3]Yale University School of Medicine, Department of Psychiatry, [4]Baylor College of Medicine

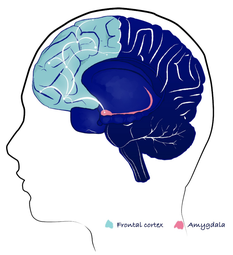
transcend THERAPEUTICS

Introduction

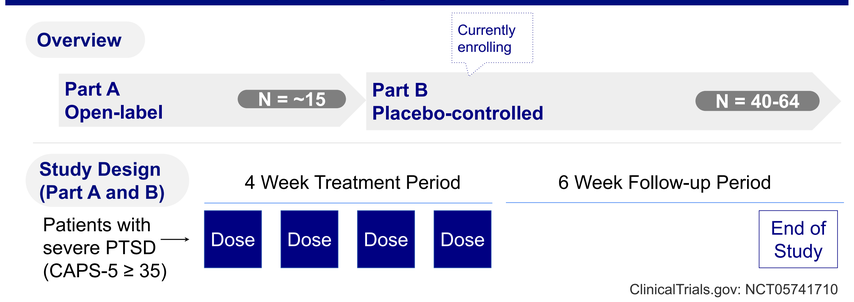
- Post-traumatic stress disorder (PTSD) is a serious debilitating disorder impacting approximately 13M Americans each year[1]
- Suicide risk in PTSD is increased by at least 6-fold compared to the general population[2]
- Approximately half of people diagnosed with PTSD also have a diagnosis of MDD[3]
- Approved pharmacotherapies for the treatment of PTSD (sertraline and paroxetine) have limited effectiveness. Less than 30% of patients treated with first-line pharmacotherapy achieve remission, which often takes many weeks to achieve[4]
- There is an urgent need for rapid-acting, non-hallucinogenic treatments for PTSD

About TSND-201 (Methylone)

- **Methylone is a rapid-acting neuroplastogen**
  - Rapidly induces neuroplasticity gene expression (e.g., BDNF) in brain areas underlying pathophysiology of PTSD, depression, and anxiety[5]
- **Well-characterized primary pharmacology**
  - Monoamine transporters are primary site of action
  - No binding at 5HT2A receptor, not hallucinogenic
  - Rapid, robust serotonin and norepinephrine release in the frontal cortex



IMPACT-1 Study Design



ClinicalTrials.gov: NCT05741710

Key Inclusion	Key Exclusion
• Age 18-65 • DSM-5 diagnosis of PTSD • CAPS-5 ≥ 35 • Failed 1 prior PTSD treatment (therapy or pharmacological)	• Concurrent substance abuse disorder • Use of MDMA or psychedelic within the past 12 months • History of schizophrenia, psychotic disorder, bipolar, personality disorder, etc.

- TSND-201was administered once a week for 4 weeks. Each dose given as an initial dose, followed by a second dose 90 minutes later
- Participants were accompanied by a trained Mentor during the dosing session who provided non-directive support
- After the 4-week treatment period, participants attended follow-up visits at 1, 2, 3, and 6 weeks following the last dose
- Safety was assessed via standard measures including adverse events
- PTSD symptoms were assessed via CAPS-5, depressive symptoms were assessed via MADRS
- Changes from baseline were analyzed using a paired t-test p-values

Results

Demographics

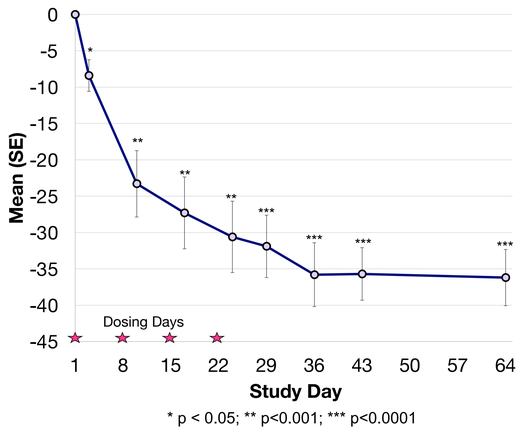
Table 1. Demographic and Baseline Characteristics (Safety Population)

Characteristic	Unit	TSND-201 (N=14)
Age Mean (range)	Years	42.4 (23 – 65)
Sex (n, %)	Female	10 (71.4)
	Male	4 (28.6)
Race (n, %)	White	13 (92.9)
	Not reported	1 (7.1)
Duration of PTSD Mean (SD)	Months	34.0 (32.96)
Baseline Scores Mean (range)	CAPS-5	47.8 (38 - 59)
	MADRS	30.8 (14 - 46)

Baseline scores are presented for the mITT population.

Efficacy

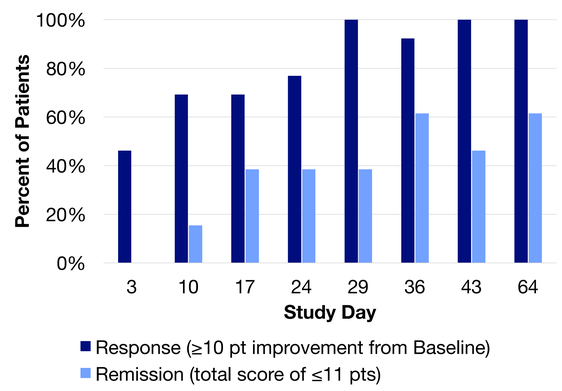
Figure 1. Mean Change from Baseline in CAPS-5 (mITT Population)



* p < 0.05; ** p<0.001; *** p<0.0001

- TSND-201 produced rapid and durable improvements in CAPS-5 scores
- **Rapid:** On Day 3, CAPS-5 scores decreased by 8.4 pts. By Day 10, CAPS-5 scores decreased by 23.3 pts
- **Durable:** 6 weeks after the last dose, CAPS-5 scores decreased by 36.2 pts

Figure 3. Response and Remission on CAPS-5 (mITT Population)



- High rates of response and remission occurred after TSND-201 treatment
- **Rapid:** At Day 10, nearly 40% of participants achieved remission
- **Durable:** Remission was achieved in 61.5% of participants at the end of study

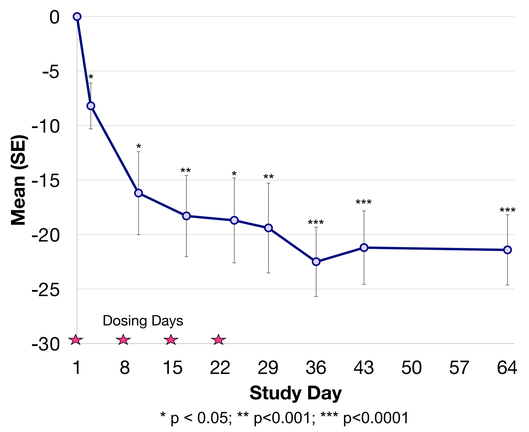
Safety

Table 2. Treatment-Emergent Adverse Events in > 1 Participants (Safety Population)

Adverse Event	TSND-201 (N=14)
Any AE	**78.6%**
Headache	42.9%
Decreased appetite	28.6%
Non-cardiac chest pain	21.4%
Fatigue	21.4%
Bruxism	14.3%
Dizziness	14.3%
Hyperhidrosis	14.3%
Influenza-like illness	14.3%
Insomnia	14.3%
Nasopharyngitis	14.3%

- Majority of TEAEs were transient and of mild severity
- No drug-related SAEs occurred
  - One unrelated SAE occurred (victim of assault) 20 days after the last dose

Figure 2. Mean Change from Baseline in MADRS (mITT Population)



* p < 0.05; ** p<0.001; *** p<0.0001

- Treatment with TSND-201 demonstrated rapid and durable improvements on depressive symptoms
- **Rapid:** On Day 3, MADRS scores decreased by 8.2 pts. By Day 10, MADRS scores decreased by 16.2 pts
- **Durable:** 6 weeks after the last dose, MADRS scores decreased by 21.4 pts

Conclusions

- TSND-201 demonstrated rapid, robust, and durable effects on PTSD symptoms; however, limitations of this study include an open-label design and small sample size.
- PTSD symptom remission and response occurred rapidly after treatment with TSND-201.
- Rapid improvement on depressive symptoms occurred concurrently with PTSD symptom improvement.
- TSND-201 was generally safe and well tolerated, the most common AE was headache.
- This study supports further development of TSND-201 as a treatment for PTSD. Part B of IMPACT-1, a randomized, placebo-controlled study, is currently enrolling.

References

1. NIMH, 2023. 2. Bachynski et al., *Injury Prevention,* 2012. 3. Flory and Yehuda, *Dialogues Clin Neurosci,* 2015. 4. Kelmendi et al, *European Journal of Psychotraumatology,* 2016. 5. Warner-Schmidt et al., *ASCP annual meeting*, 2023

Disclosures

AJ, JW-S, MS, BM, HK are full-time employees with equity in Transcend Therapeutics. BK has equity in Transcend Therapeutics. THWC and LA are consultants to Transcend Therapeutics.