TSND-201 Demonstrated Rapid, Robust, and Durable Therapeutic Efficacy in a Randomized, Placebo-Controlled Trial (IMPACT-1) for the Treatment of Post-Traumatic Stress Disorder

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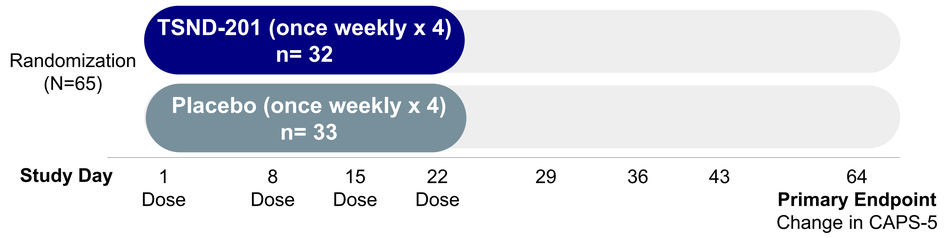
Introduction

- TSND-201 is in clinical development as a potential treatment for PTSD and other CNS conditions
- 13M people in the U.S. live with PTSD
- PTSD causes debilitating symptoms such as nightmares, flashbacks, emotional detachment
- Current treatment options for PTSD (psychotherapy or SSRIs) have limited effectiveness.
- Rapid acting treatments with sustained effects are needed

IMPACT-1 Study Design



Study Design

- Study drug (orally administered) once a week for 4 weeks: 150mg + 100mg (90 min later)
- Patients dosed in-clinic, and remained for 8hrs
- No psychotherapy

Key Eligibility Criteria

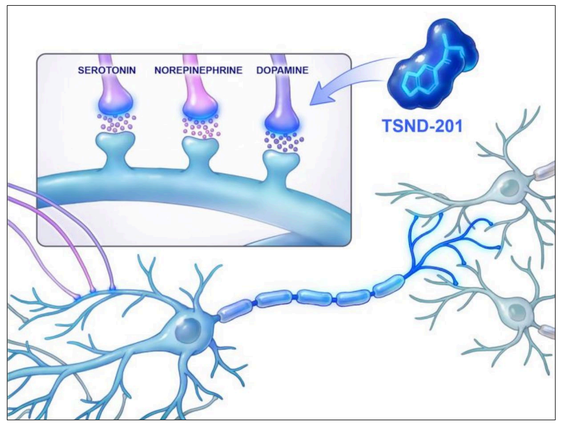
- Adults with severe PTSD (CAPS-5 ≥ 35)
- Tried ≥ 1 prior treatment for PTSD
- No use of antidepressant within 8 weeks
- No use of a psychedelic or MDMA within 12 months

Baseline Characteristics

Characteristic	TSND-201	Placebo
Age, years (mean [SD])	45.1 (10.6)	42.2 (10.4)
Sex, F (n [%])	19 (59.4%)	20 (60.6%)
Race, n (%)		
White	29 (90.6%)	29 (87.9%)
Asian	1 (3.1%)	1 (3.0%)
Black	0	1 (3.3%)
Years (mean [SD]) of PTSD symptoms	20.0 (14.3)	19.5 (13.3)
Prior PTSD Treatments		
Pharmacotherapy	21 (70.0%)	17 (56.7%)
Psychotherapy	28 (93.3%)	28 (93.3%)
CAPS-5 total score (mean [SD])	45.8 (7.11)	46.0 (5.42)
Trauma Type		
Sexual trauma	19 (63.3%)	12 (40.0%)
Military	4 (13.3%)	3 (10.0%)
Other*	7 (23.3%)	15 (50.0%)

* Other includes: non-sexual abuse, exposure to death/violent events, other near-death experiences, etc.

About TSND-201 (Methylone)



- Highly-selective and **rapid releaser** of serotonin, norepinephrine and dopamine[1]
  - No off-target effects, including no affinity for the 5-HT2A receptor[1]
  - No depletion of brain monoamines after repeated doses[2]
- **Rapid and long-lasting neuroplasticity**
  - Increased expression of neuroplasticity factors (e.g., BDNF)[1,3]
  - Increased neurite length (~2x) and branching (~3x)[3]
- **Non-hallucinogenic** in humans[4,5] or animals[6]
- Rapid, robust, and long-lasting effects in multiple behavioral models[3,7,8]

References

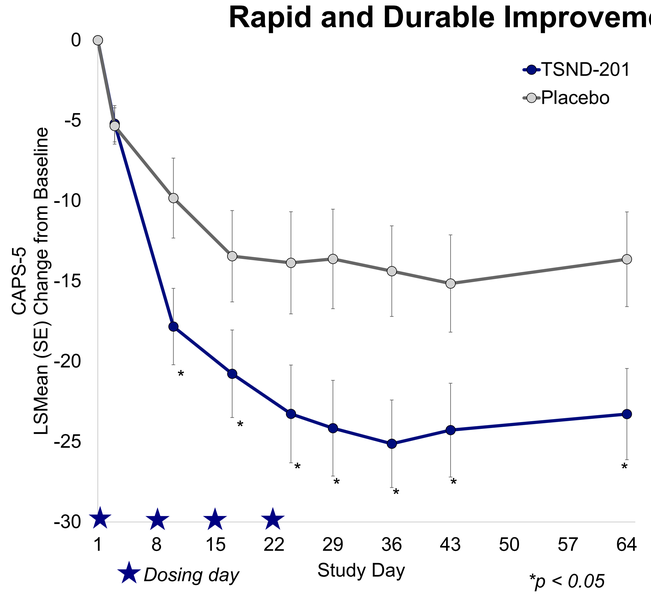
(1) Warner-Schmidt et al., 2024, *Frontiers in Neuroscience,* 18:1353131
(2) Baumann et al., 2012, *Neuropsychopharmacology,* 37(5):1192-203
(3) Warner-Schmidt et al., 2025, *Neuropsychopharmacology*, under review
(4) Poyatos et al., 2023, *Frontiers in Psychiatry*, 14:1122861
(5) Jones et al., 2024, *Neuropsychopharmacology*, 49:418–594
(6) Yu et al., 2025, *Molecular Psychiatry*, under revision
(7) Warner-Schmidt et al., 2023, *Frontiers in Psychiatry*, 13:1041277
(8) Li et al., 2025, *Int J Neuropsychopharmacol,* 28(Suppl 1):i206

DISCLOSURES: JW-S, MS, AJ, HK, BM are full-time employees with equity in Transcend Therapeutics. THWC and BM are consultants with Transcend Therapeutics.

Results

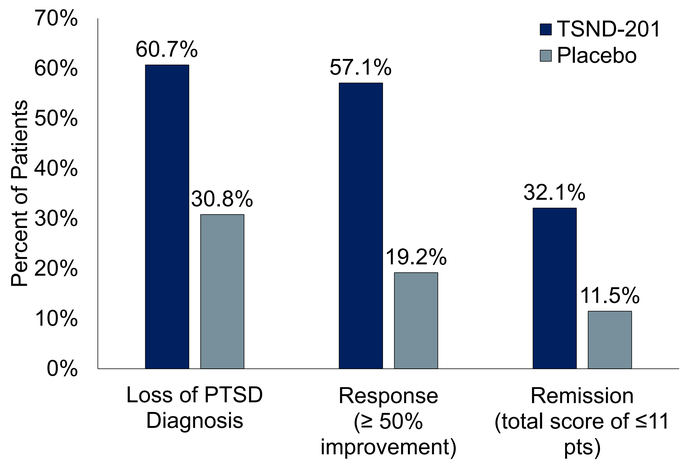
TSND-201 Demonstrated Rapid, Robust, and Durable Effects

Rapid and Durable Improvements on CAPS-5



- **Met primary endpoint**
  - Placebo-adjusted CAPS-5 improvement of -9.64 points on Day 64 (p=0.011)
- **Rapid effects**
  - Placebo-adjusted CAPS-5 improvement of -8.00 points by Day 10 (p=0.012)
- **Durable**:
  - Improvements were sustained for the duration of the trial

Improved Rates of Loss of PTSD Diagnosis, Response and Remission at End of Study



Generally Safe and Well-Tolerated

TEAEs occurring in > 20% of patients

Preferred Term	TSND-201 n (%)		Placebo n (%)	
	Anytime	Started During Dosing Session	Anytime	Started During Dosing Session
At least one TEAE	32 (100.0)	30 (93.8)	24 (72.7)	19 (57.6)
Headache	21 (65.6)	11 (34.4)	14 (42.4)	10 (30.3)
Decreased appetite	16 (50.0)	12 (37.5)	3 (9.1)	2 (6.1)
Nausea	12 (37.5)	7 (21.9)	7 (21.2)	5 (15.2)
Dizziness	11 (34.4)	6 (18.8)	3 (9.1)	3 (9.1)
Blood pressure increased	10 (31.3)	9 (28.1)	0	0
Dry mouth	10 (31.3)	9 (28.1)	1 (3.0)	1 (3.0)
Insomnia	10 (31.3)	1 (3.1)	0	0
Muscle tightness	8 (25.0)	7 (21.9)	1 (3.0)	1 (3.0)
Pre-existing condition improved*	8 (25.0)	8 (25.0)	2 (6.1)	1 (3.0)
Feeling abnormal	7 (21.9)	5 (15.6)	3 (9.1)	3 (9.1)

- No discontinuation due to AEs
- Most AEs occurred on the day of dosing and resolved the same day
- One severe AE of suicidal ideation, unrelated to drug
- SAE of seizure occurred 7 days after the last dose in a participant who had previously experienced a seizure

* "Pre-existing condition improved" includes verbatim terms of positive mood (no euphoria or mania); feeling optimistic; increased focus; emotional openness; clear headed; increased openness; increased confidence; feeling insightful

Conclusions

- TSND-201 is a rapid acting neuroplastogen that increases neurite outgrowth
- Treatment with TSND-201 resulted in rapid and robust improvements in PTSD symptoms
- Durable efficacy following an acute episodic dosing regimen (once per week for 4-weeks)
- TSND-201 was well-tolerated
- Results support the further development of TSND-201 as a treatment for PTSD