TSND-201 (Methylone) as a Treatment for PTSD: Rapid, Robust, and Long-Lasting Activity in Phase 2

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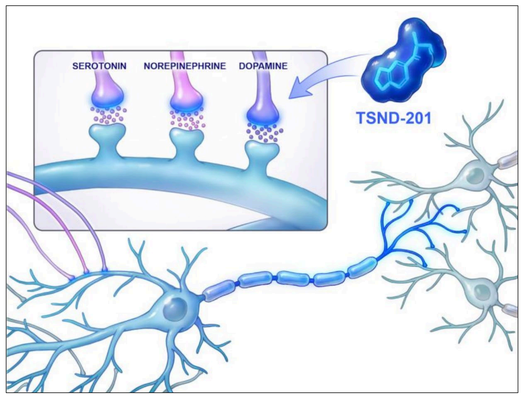
Introduction

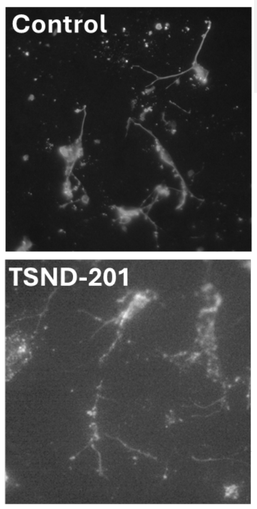
TSND-201 is in clinical development as a potential treatment for post-traumatic stress disorder (PTSD). PTSD is a debilitating psychiatric illness affecting 13 million adults in the United States. Current treatment options for PTSD, psychotherapy or SSRIs, have limited effectiveness. Non-hallucinogenic compounds with rapid and sustained therapeutic benefits may be clinically useful as they may be more accessible to patients, compared to classical psychedelics.

About TSND-201 (Methylone)

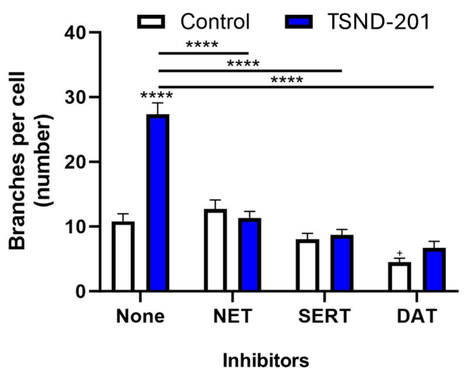


- **Primary pharmacology:** Highly-selective and rapid releaser of serotonin, norepinephrine and dopamine[1]
  - No agonist/antagonist activity at 168 G-protein coupled receptors, including 5HT2A[1]
  - No depletion of brain monoamines after repeated doses[2]
- **Pharmacodynamics**: Rapid and long-lasting neuroplasticity
  - Increased expression of neuroplasticity factors (e.g., BDNF)[1,3]
  - Increased neurite length (~2x) and branching (~3x)[3]
- **No hallucinogenic activity** in humans[4,5] or animals[6]
- Rapid, robust, and long-lasting effects in multiple behavioral models[3,7,8]

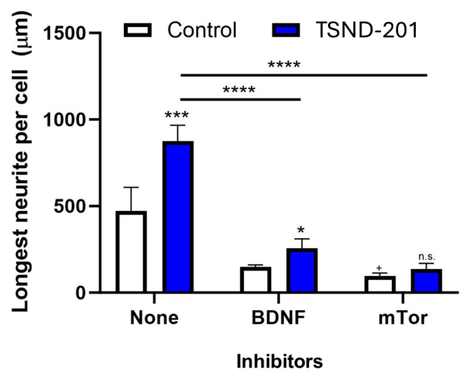
Results



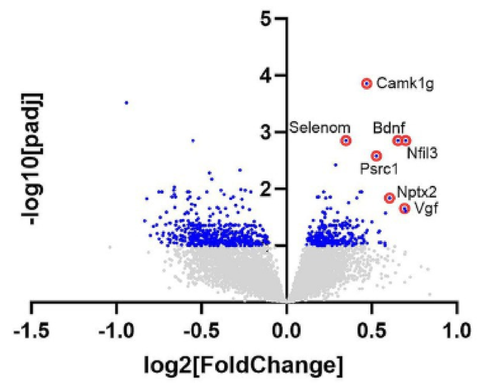
Branching increased ~3x compared with controls
Mediated by activity at NET, SERT, and DAT



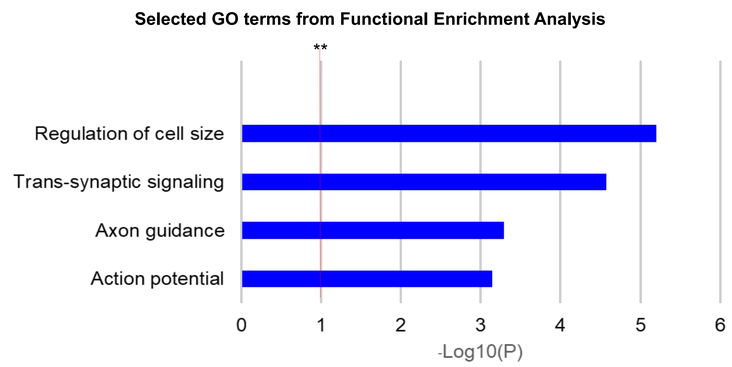
Longest neurite per cell increased ~2X compared with controls
Mediated by neurotrophic factor signaling



Synaptic plasticity, neurotrophic factor gene expression increases *within hours*

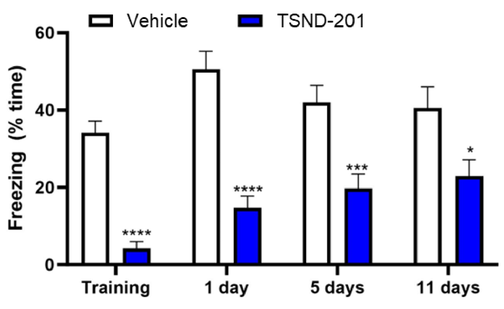


Increased synaptic plasticity and axon guidance markers persist *1-week after dosing*



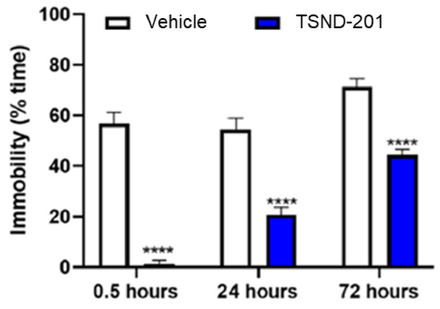
Facilitates fear extinction in a model of PTSD

Less freezing = More extinction



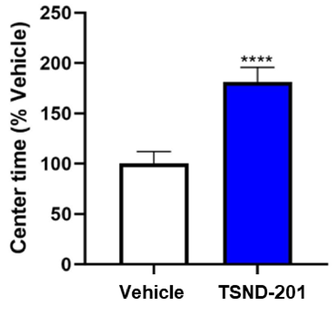
Rapid and long-lasting antidepressant-like activity in the Forced Swim Test

Less immobility = Stronger antidepressant-like effect



Non-sedating anxiolytic activity in the Open Field Test

More center time = less anxiety



Conclusions

- TSND-201 is a non-hallucinogenic, rapid acting neuroplastogen that increases neurite outgrowth
- Preclinical results demonstrate rapid, robust, and long-lasting benefit tests of PTSD, anxiety, depression
- Rapid, robust, and durable clinical efficacy was achieved in a Phase 2 study of PTSD patients following an acute episodic dosing regimen (once per week for 4-weeks)

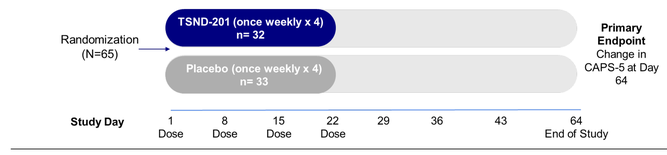
Results support the further development of TSND-201 as a treatment for PTSD, and potentially other CNS disorders

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, BM are full-time employees with equity in Transcend Therapeutics; BK is a consultant with equity in Transcend Therapeutics.

IMPACT-1 Phase 2 Clinical Trial

IMPACT-1 (TSND-201 Phase 2 in PTSD): Study Design



Study Design
- Treatment regimen: 150mg PO followed by 100mg given orally (90 minutes later) once a week for 4 weeks
- Patients observed in-clinic for 8 hours following the dose
- No psychotherapy

Key Eligibility Criteria
- Adults aged 18 to 65 years, with severe PTSD (CAPS-5 ≥ 35)
- Tried at least 1 prior treatment for PTSD (pharmacotherapy or psychotherapy)
- No use of a psychedelic or MDMA within 12 months of screening
- No use of an SSRI or other antidepressant within 8 weeks of screening

IMPACT-1: TSND-201 Met Primary Endpoint and Demonstrated Rapid, Robust, and Durable Effects