

TSND-201 (Methylone) for the Treatment of PTSD: Improvements across each CAPS-5 Cluster and Anxiety Symptoms from the Open-Label Portion of the IMPACT-1 Study

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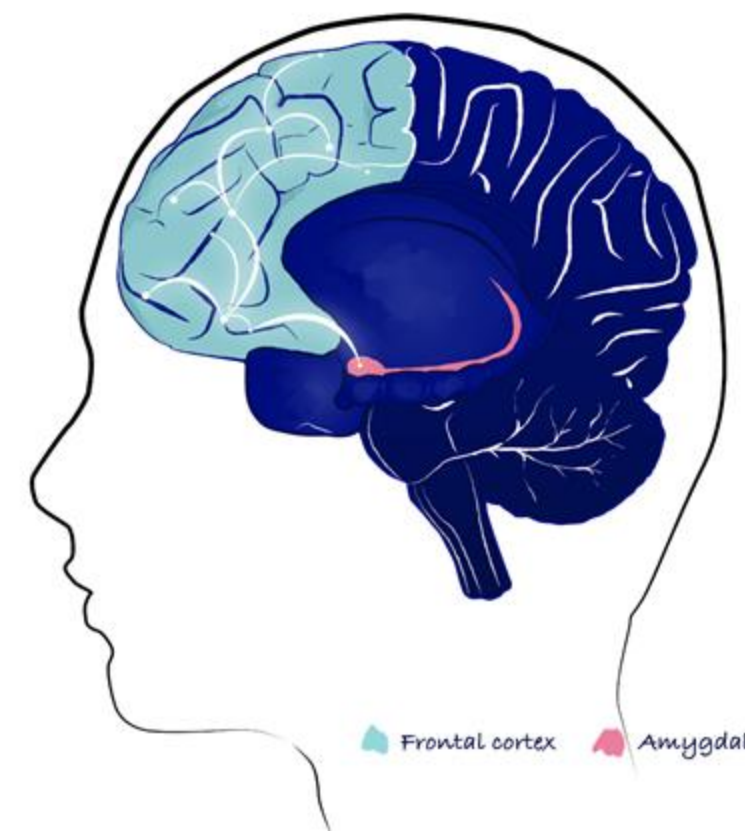
Introduction

- Post-traumatic stress disorder (PTSD) is a serious debilitating disorder impacting approximately 13M Americans each year¹
- Suicide risk in PTSD is increased by at least 6-fold compared to the general population²
- Over 60% of people diagnosed with PTSD also experience significant anxiety symptoms³
- 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 achieve⁴
- 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 anxiety⁵

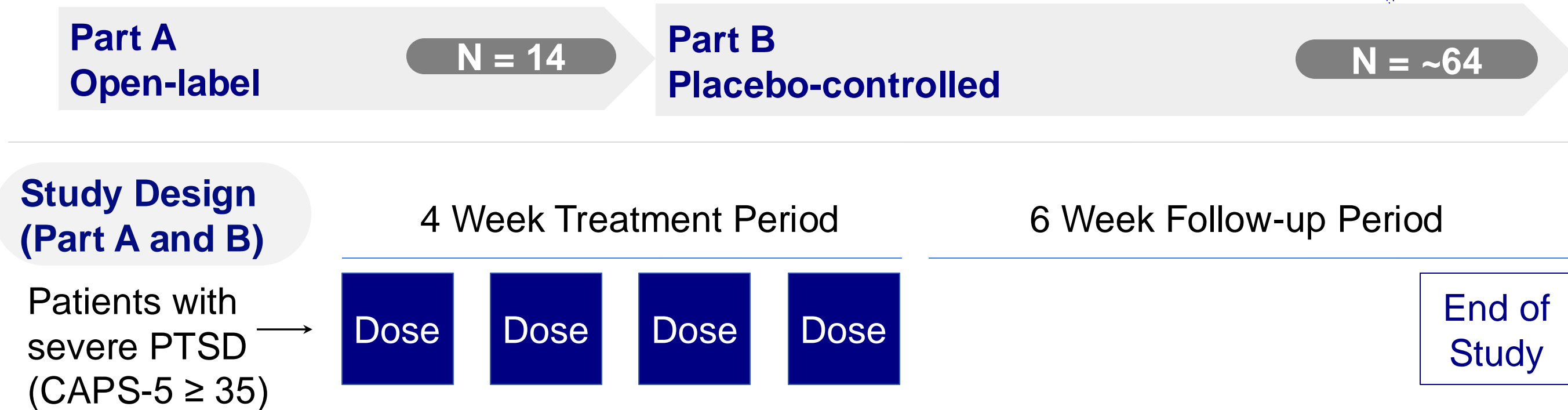


Well-characterized primary pharmacology

- 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

Overview



Key Inclusion

- Age 18-65
- DSM-5 diagnosis of PTSD
- CAPS-5 ≥ 35
- Failed 1 prior PTSD treatment (therapy or pharmacological)

Key Exclusion

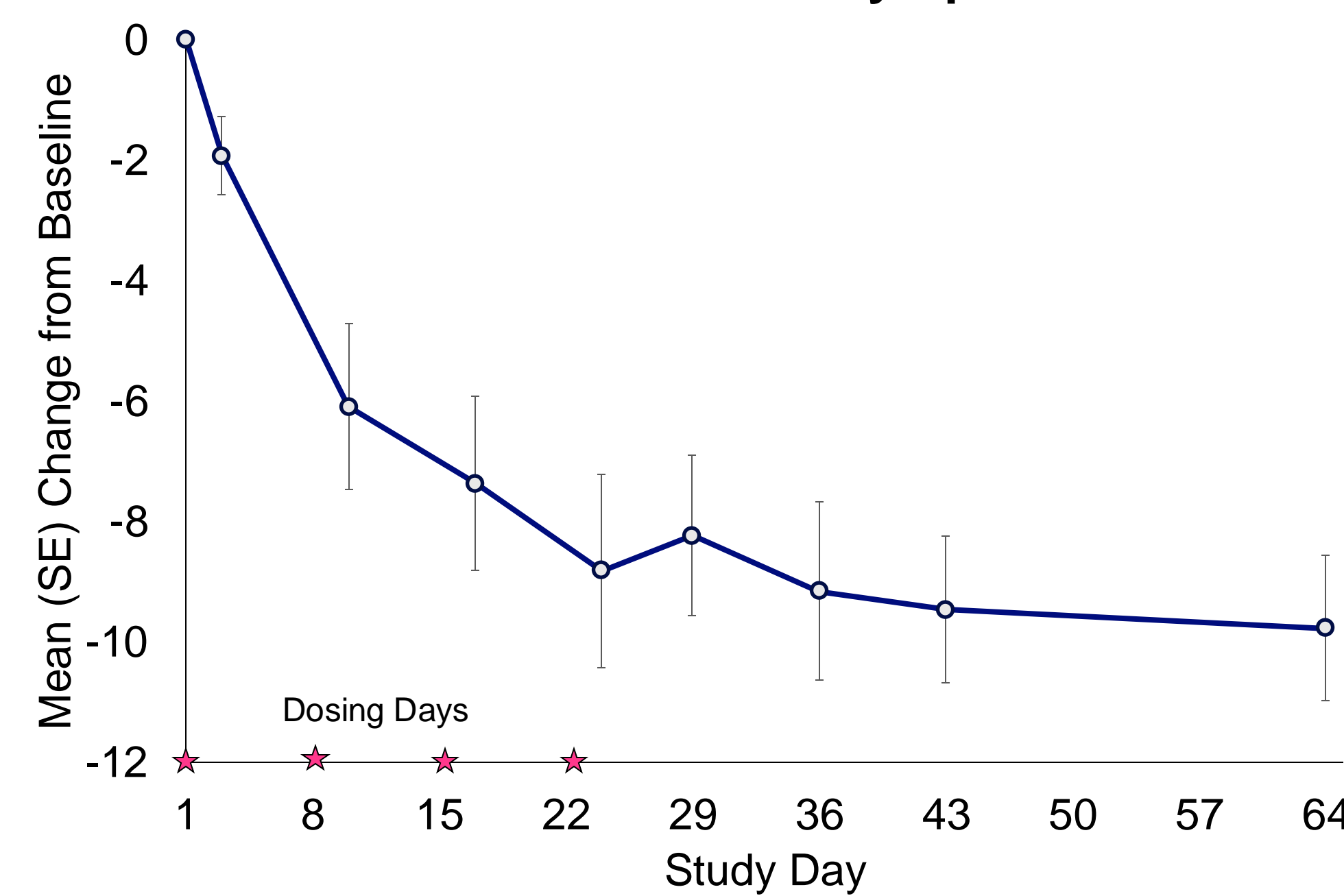
- Concurrent substance abuse disorder
- Use of MDMA or psychedelic within the past 12 months
- History of schizophrenia, psychotic disorder, bipolar, personality disorder, etc.

- TSND-201 was 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, including symptom clusters: Intrusion, Avoidance, Cognition and Mood, Arousal and Reactivity.
- Anxiety symptoms were assessed via 4-items of the MADRS (inner tension, reduced sleep, reduced appetite, and concentration difficulties)

Results

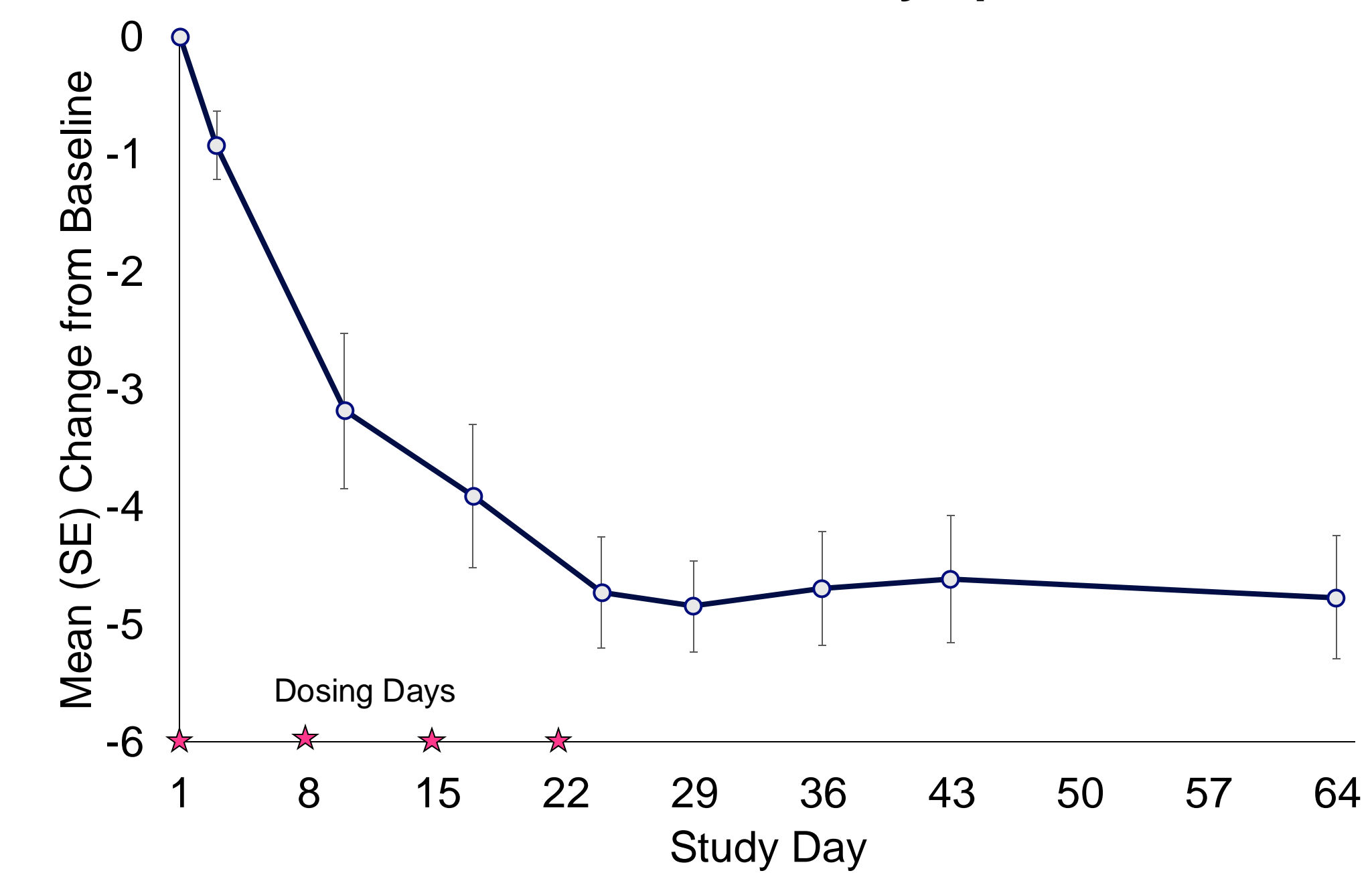
Treatment with TSND-201 Demonstrated Consistent Improvements Across Each CAPS-5 Cluster

Criterion B. Intrusion Symptoms



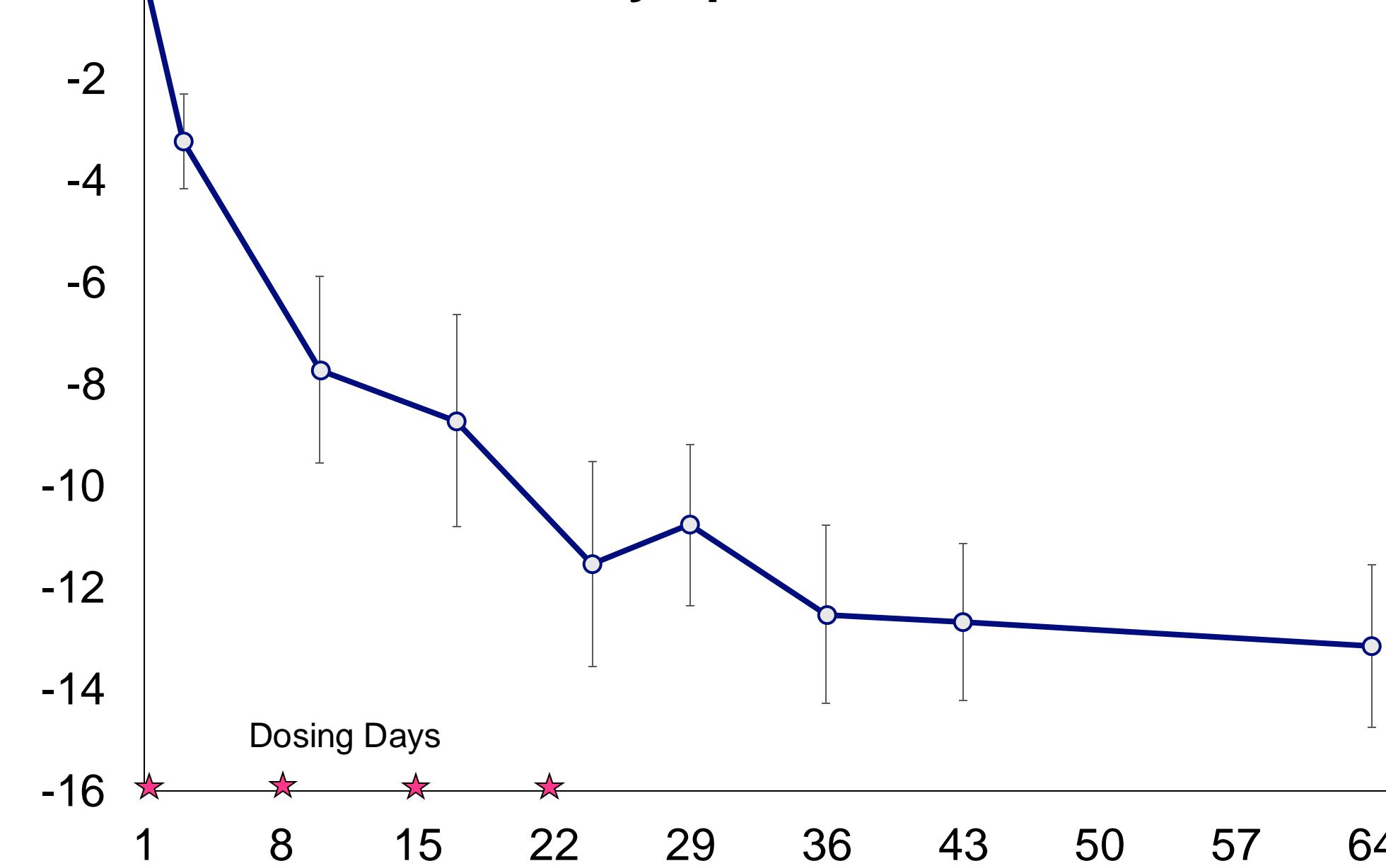
- Intrusion cluster scores can range from 0 to 20
- Mean (range) baseline score was 12.3 (8-18) pts
- At Week 10, scores were decreased by 9.8 pts

Criterion C. Avoidance Symptoms



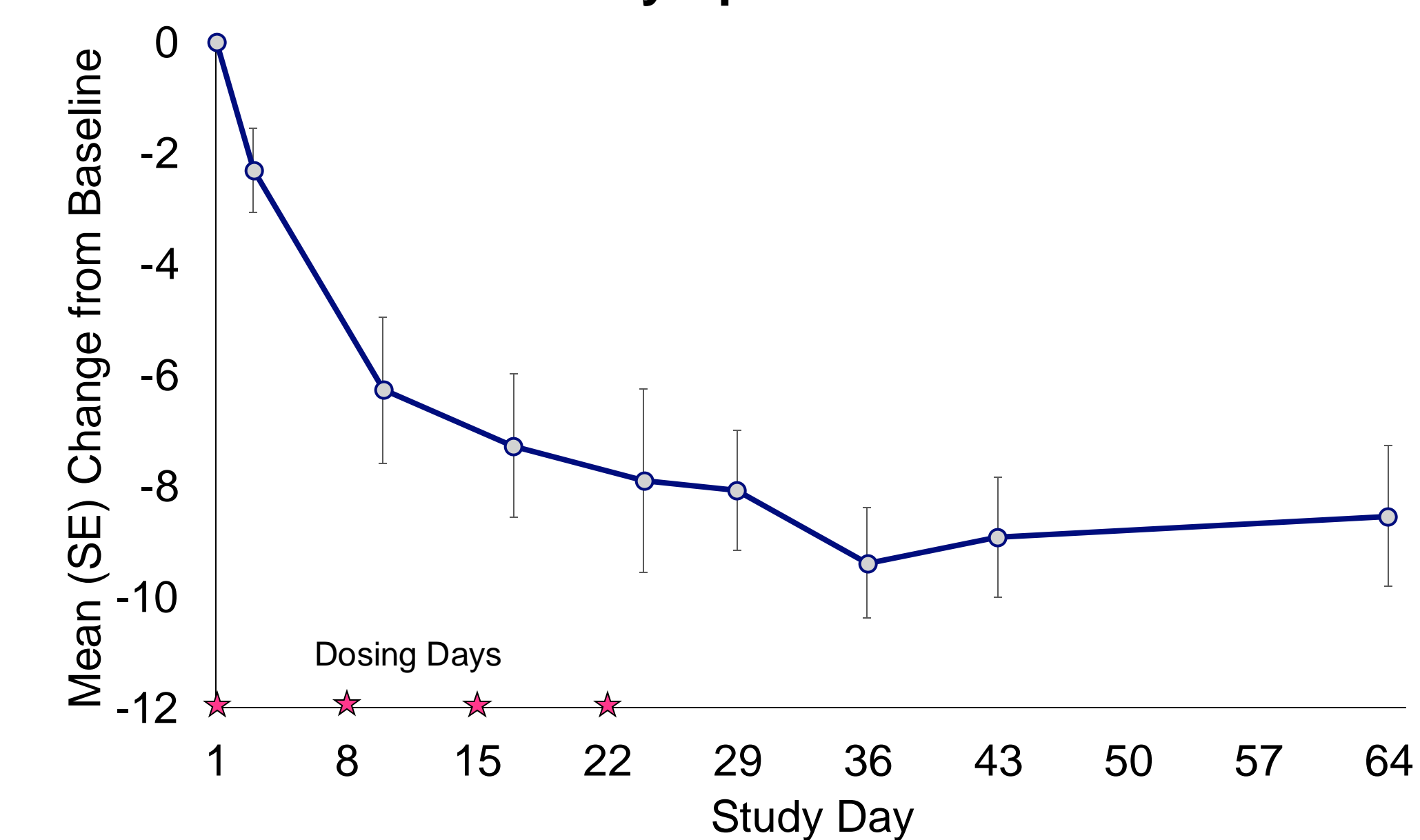
- Avoidance symptom cluster scores can range from 0 to 8
- Mean (range) baseline score was 6.1 (5-7) pts
- At Week 10, scores were decreased by 4.8 pts

Criterion D. Cognition and Mood Symptoms



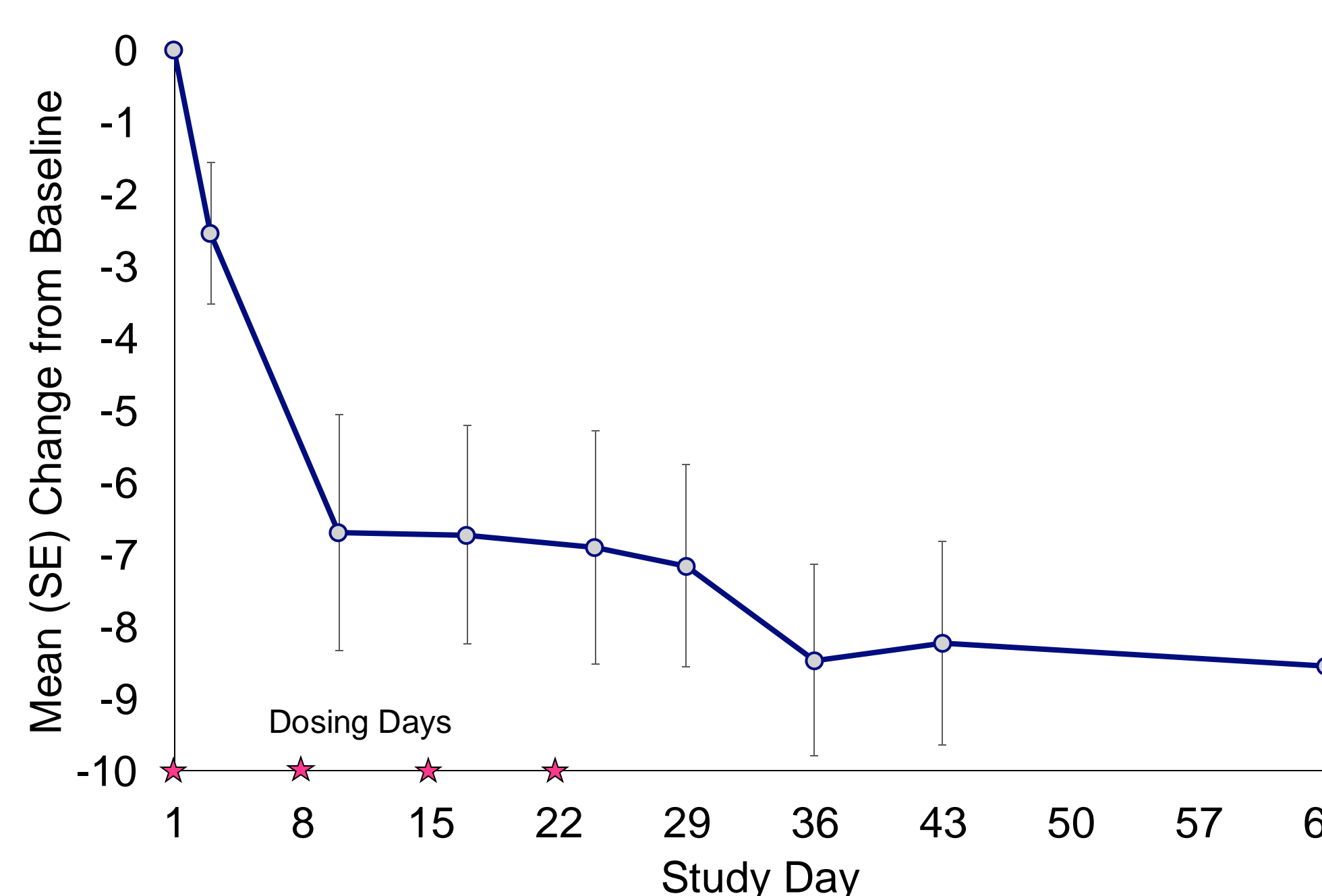
- Cognition and Mood symptom cluster scores can range from 0 to 28
- Mean (range) baseline score was 16.5 (12-21) pts
- At Week 10, scores were decreased by 13.2 pts

Criterion E. Arousal and Reactivity symptoms



- Arousal and Reactivity symptom cluster scores can range from 0 to 24
- Mean (range) baseline score was 12.9 (10-16) pts
- At Week 10, scores were decreased by 8.5 pts

Robust Improvements on Anxiety Items of MADRS



- Four anxiety items on MADRS can range from 0 to 24
- Mean (range) baseline score was 12.9 (6-21) pts
- At Week 10, scores were decreased by 6.7 pts

Conclusions

- TSND-201 demonstrated consistent improvements across each PTSD symptom domain.
- Mean end of study improvements from baseline were 79.4% for Intrusion, 79.9% for Avoidance, 66.1% for Cognition and Mood, and 75% for Arousal and Reactivity.
- Rapid and durable improvement on anxiety symptoms occurred concurrently with PTSD symptom improvement.
- TSND-201 was generally safe and well tolerated, the most common AEs were headache and decreased appetite.
- 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

- NIMH, 2023.
- Bachynski et al., *Injury Prevention*, 2012.
- Wenjie et al., *Medicine*, 2017.
- Kelmendi et al., *European Journal of Psychotraumatology*, 2016.
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Disclosures

AJ, JW-S, MS, BM, HK are full-time employees with equity in Transcend Therapeutics. BK has equity in Transcend Therapeutics. THWC is a consultant to Transcend Therapeutics.