

# TSND-201 (methydone) for the Treatment of PTSD, MDD, and Other CNS Disorders

Jennifer Warner-Schmidt<sup>1</sup>, Amanda Jones<sup>1</sup>, Martin Stogniew<sup>1</sup>, Blake Mandell<sup>1</sup>, Benjamin Kelmendi<sup>2</sup>

<sup>1</sup>Transcend Therapeutics, <sup>2</sup>Yale University School of Medicine, Department of Psychiatry

**transcend**  
THERAPEUTICS

For all \*p<0.05, \*\*p<0.01, \*\*\*p<0.001, \*\*\*\*p<0.0001

## Introduction

- Post-traumatic stress disorder (PTSD) is a serious debilitating disorder impacting approximately 13M Americans each year<sup>1</sup>
- Suicide risk in PTSD is increased by at least 6-fold compared to the general population<sup>2</sup>
- Approximately half of people diagnosed with PTSD also have a diagnosis of major depressive disorder (MDD)<sup>3</sup>
- 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<sup>4</sup>
- There is an urgent need for rapid-acting, non-hallucinogenic treatments for PTSD and depression

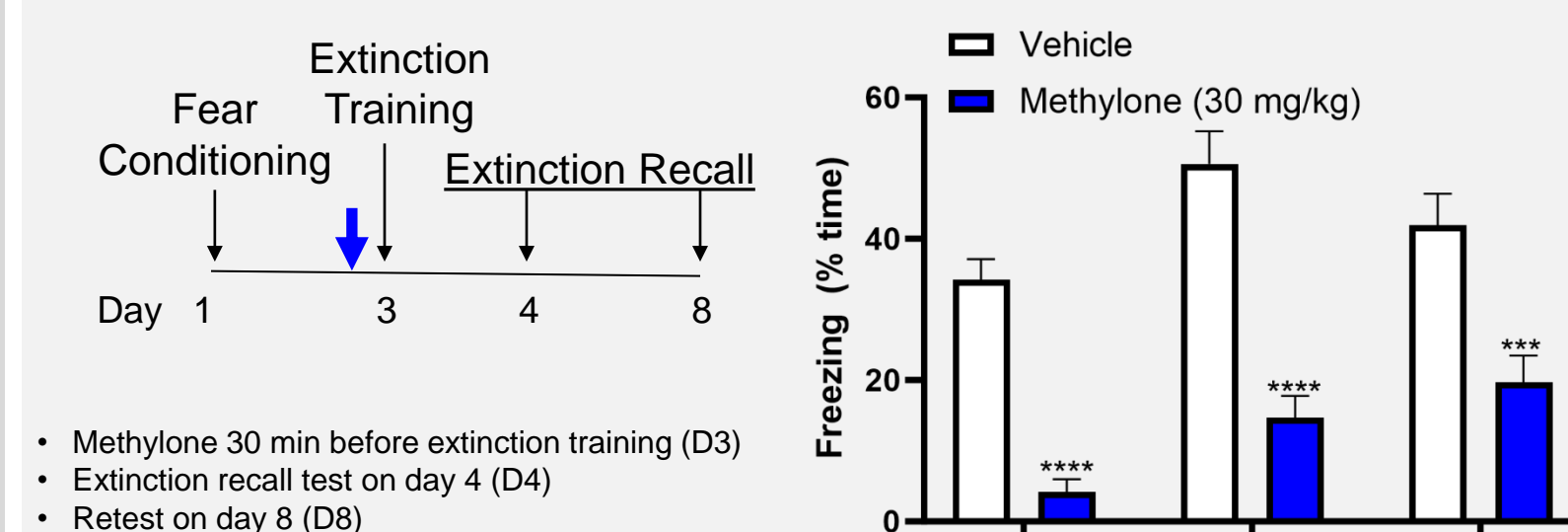
## Results

Preclinical

### PTSD

#### Rapid and Long-Lasting Improvement in Fear Extinction Learning

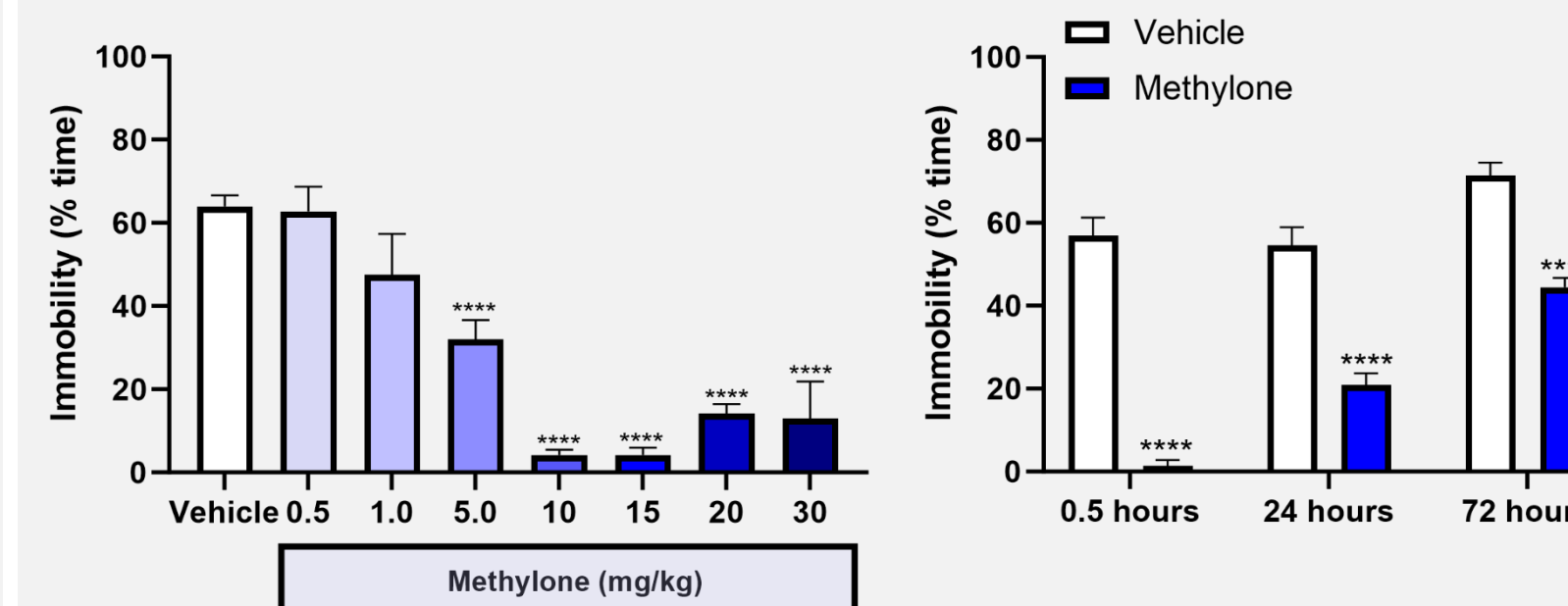
Less time freezing = More beneficial effect



### Depression

#### Rapid and Long-Lasting Antidepressant-Like Activity in the Forced Swim Test

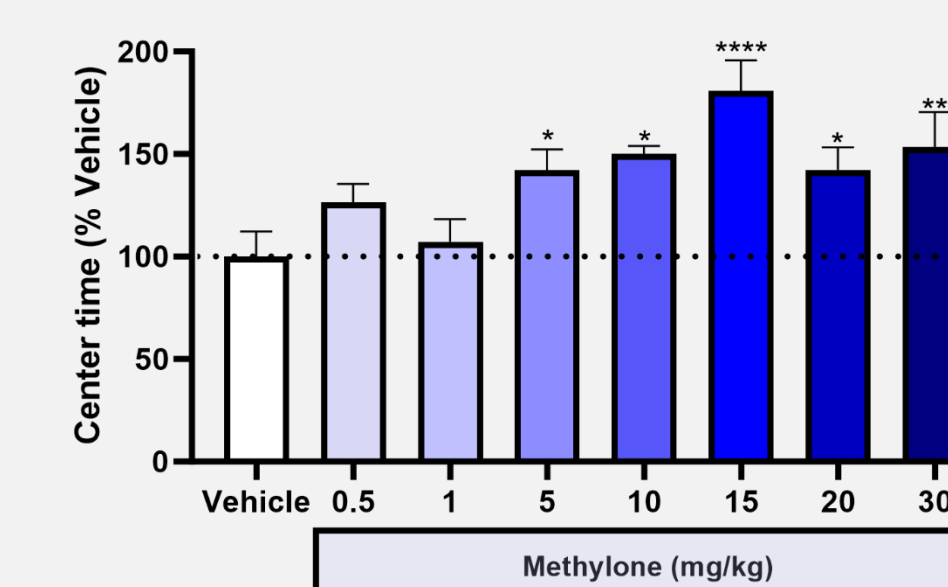
Less immobility = Stronger antidepressant-like responses



### Anxiety

#### Rapid and Robust Anti-Anxiety Activity in the Open Field Test

More center time = Less anxious

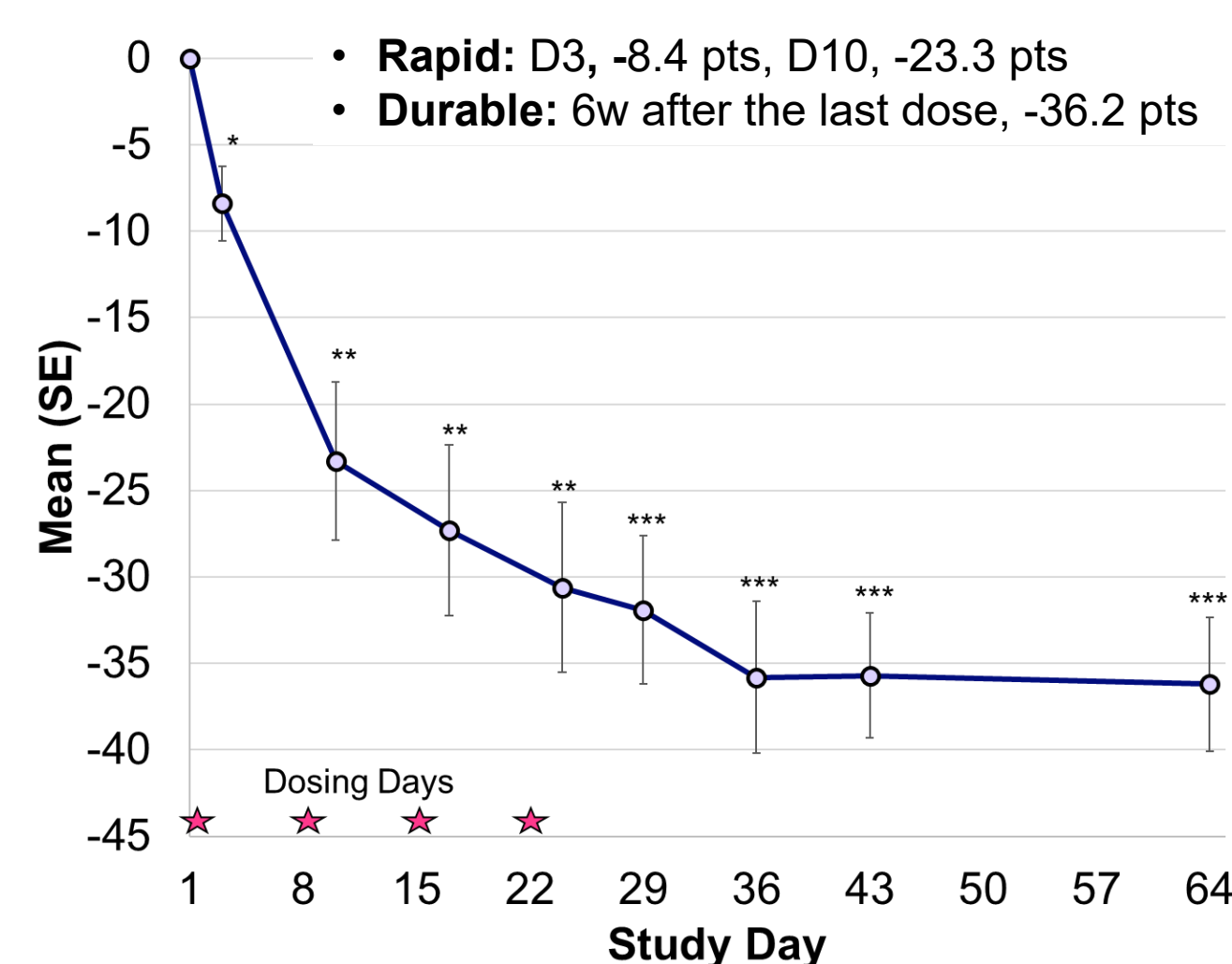


## About TSND-201 (methydone)

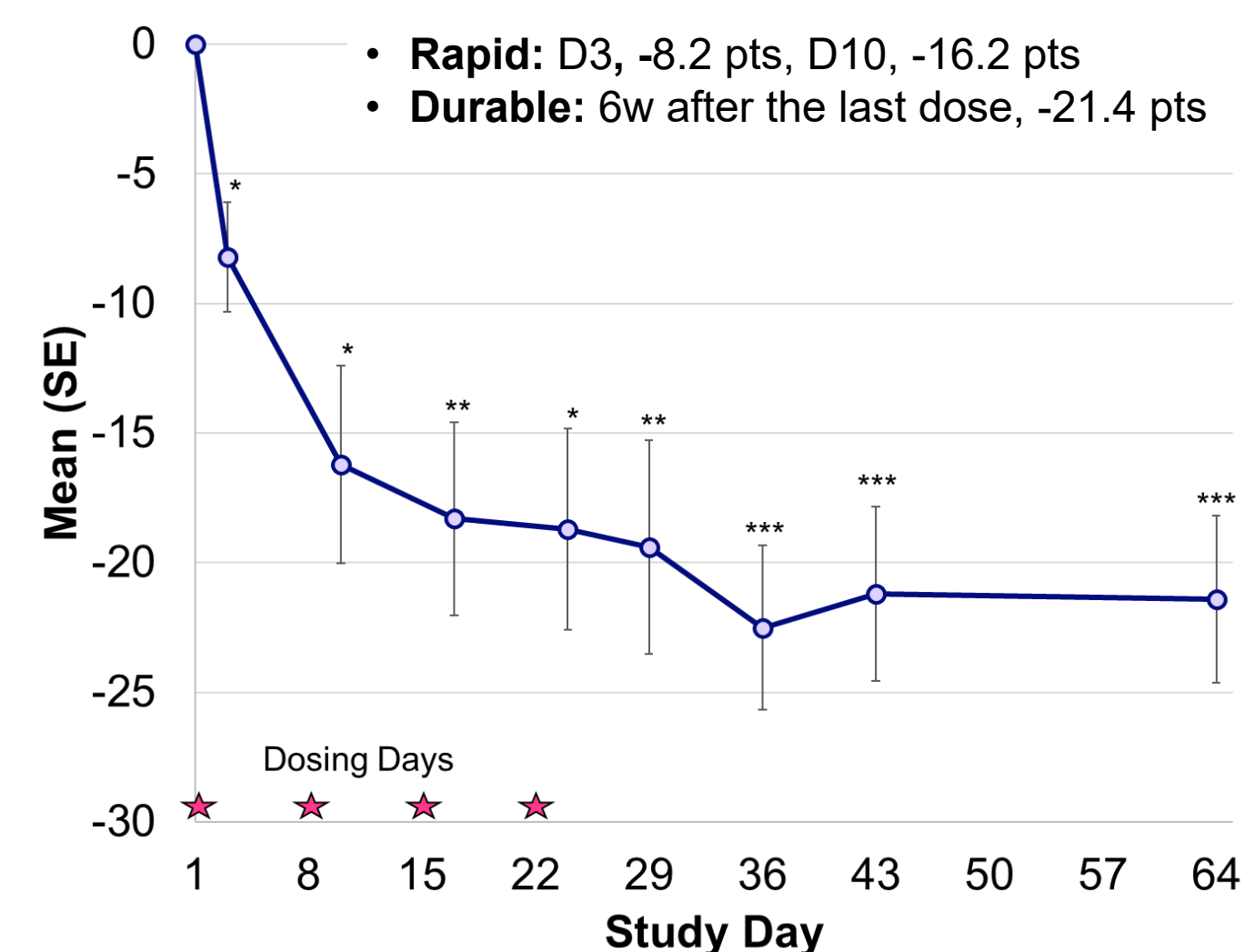
- **Methydone is a rapid-acting neuroplastogen**
- Rapid induction of neuroplasticity gene expression (e.g., BDNF) in brain areas underlying pathophysiology of PTSD, depression and anxiety<sup>5</sup>
- **Well-characterized primary pharmacology**
- Monoamine transporters are primary site of action
- No binding to 5HT2A receptors, not hallucinogenic
- Rapid, robust serotonin and norepinephrine release in the frontal cortex

Clinical

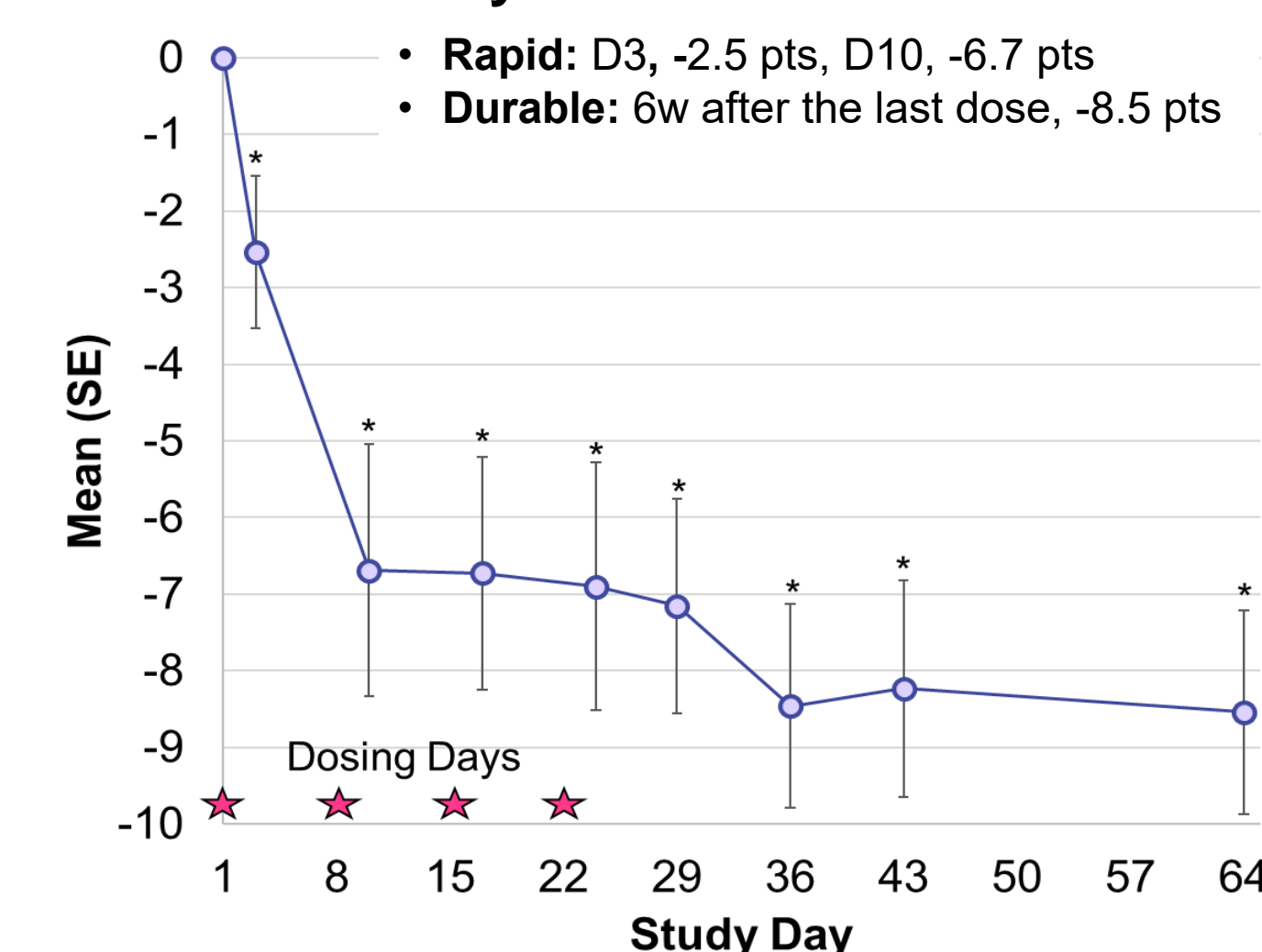
#### Mean Change from Baseline in CAPS-5



#### Mean Change from Baseline in MADRS



#### Mean Change from Baseline in Anxiety Sub-Scale of MADRS



## Methods

**Preclinical Studies:** All studies were performed using standard protocols. FST and OFT were performed in male SD rats. Results and methods have been published<sup>6</sup>. Fear extinction was performed in male C57BL/6J mice based on published methods<sup>7</sup>. Methydone was given intraperitoneally 30 min prior to all tests.

### IMPACT-1A Study Design

- TSND-201 was administered once a week for 4-weeks. Each dose was given as an initial dose followed by a second dose 90 min 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. The primary endpoint was CAPS-5. Data shown also include MADRS and an anxiety subscale of MADRS (i.e., 4 items: inner tension; reduced sleep; reduced appetite; concentration difficulties).
- Safety was assessed via standard measures including adverse events (AE).

## Conclusions

- In preclinical studies, TSND-201 demonstrated rapid, robust, and long-lasting beneficial effects on PTSD-like, depression-like, and anxiety-like behaviors.
- In humans, TSND-201 demonstrated rapid, robust and durable effects on PTSD, depression and anxiety symptoms; however, limitations of this study include an open-label design and small sample size. TSND-201 was generally safe and well-tolerated, the most common AE was headache.
- Together, this work supports further development of TSND-201 as a treatment for PTSD, MDD, and anxiety. A randomized, placebo-controlled study in PTSD patients 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., *Frontiers in Neuroscience*, 2024. 6. Warner-Schmidt et al., *Frontiers in Psychiatry*, 2023. 7. Young et al., *Transl Psychiatry*, 2015.

## Disclosures

JW-S, AJ, MS, BM are full-time employees with equity in Transcend Therapeutics. BK has equity in Transcend Therapeutics.

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