

## **A Phase 1b Study of Potential Safety and Pharmacokinetic Interactions between Cocaine and EMB-001, with Exploratory Efficacy Measures**

M. Detke<sup>1,2</sup>, G. Connor<sup>1</sup>, D. Kelsh<sup>3</sup>, J. Straub<sup>1</sup>, A. Robbins<sup>1</sup>, C. Gloff<sup>1</sup>, N. Goeders<sup>1,4</sup>

<sup>1</sup>Embera NeuroTherapeutics, Inc; <sup>2</sup>Indiana University; <sup>3</sup>Vince & Associates Clinical Research; <sup>4</sup>LSU Health - Shreveport

**The Methodological Question Being Addressed:** This study used a crossover design to address potential safety interactions between EMB-001 and cocaine, and to assess effects of EMB-001 on cocaine PK. In addition, a cross-study meta-analytic approach was used to assess potential effects of cocaine on EMB-001 PK, to optimize drug development efficiency. Furthermore, a biomarker (cortisol) was used to assess the hypothesis that EMB-001 would blunt the stressor response to cocaine infusion, an innovative method to potentially enhance maintenance of abstinence from cocaine use.

**Introduction:** EMB-001 is a combination of metyrapone (MET), a cortisol synthesis inhibitor, and oxazepam (OX), a benzodiazepine. EMB-001 reduced cocaine and nicotine self-administration in rats, reduced cocaine use in a human pilot study, and showed trends of decreased tobacco use, craving and withdrawal symptoms in a small study in humans. The present study was required by the FDA to investigate potential drug-drug interactions between EMB-001 and cocaine prior to planned Phase 2 and 3 studies in cocaine use disorder (CUD).

**Methods:** This was a double-blind, placebo-controlled crossover study of non-treatment-seeking subjects with CUD. Each subject received one week of oral BID dosing of MET/OX 720/24 mg and one week of oral BID placebo, randomized for order and separated by a one-week washout. On the last day of each dosing week, each subject received 40 mg IV cocaine. Primary outcomes were safety and PK. The potential effects of cocaine on EMB-001 PK were assessed with a cross-study meta-analytic approach, leveraging data from a previously completed safety/PK study of EMB-001 at the same dose(s) and without cocaine. Exploratory outcomes included craving and subjective measures, as well as cortisol biomarker response to cocaine infusion.

**Results:** 93% of AEs were mild; all were mild or moderate. There were no SAEs. There were few clinically significant changes in vital signs, ECGs or other safety lab measurements. There were no significant PK interactions, either within study or across studies. Exploratory biomarker measures showed that EMB-001 significantly blunted the cortisol response to cocaine, supporting the mechanistic hypothesis.

**Conclusions:** EMB-001 was well-tolerated and no new safety signals were observed. The crossover design allowed for greater statistical power with fewer subjects, and the meta-analytic approach leveraged data from an already-completed study, instead of exposing more subjects to potential risks and unnecessary procedures. This allowed us to conclude that no clinically significant interactions between EMB-001 and cocaine were observed in PK, safety or exploratory craving/subjective measures. In addition, assessment of a biomarker allowed for an observation that supports the novel mechanistic hypothesis. Overall, these results support future studies of this novel mechanistic approach in CUD and tobacco use disorder, areas of unmet need with few or no approved treatments.

**Disclosures:** The authors are all employees, consultants or vendors of Embera NeuroTherapeutics, Inc., which partially funded the work reported here. Research reported in this poster was also supported by the National Institute on Drug Abuse of the National Institutes of Health under grant number 1U01DA038879-01A1. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.