IND 063384

CONTINUE PARTIAL CLINICAL HOLD

Multidisciplinary Association for Psychedelic Studies
Attention: Amy Emerson
Executive Director &
Head of Clinical Development and Regulatory Affairs
1115 Mission Street
Santa Cruz, CA 95060

Dear Ms. Emerson:

Please refer to your investigational new drug application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for 3,4-methyelenedioxy-methamphetamine (MDMA).

We also refer to your amendment dated August 28, 2019, that provides a response to our August 5, 2019, letter which cited the reasons for placing Protocol MT2, titled "A Phase 1, Open-Label, Multi-Site Study to Assess Psychological Effects of MDMA-Assisted Psychotherapy when Administered to Healthy Volunteers", on clinical hold and the information needed to resolve the clinical hold issues.

We have completed the review of your submission and have concluded that removal of the clinical hold from the following proposed study is not warranted. Specifically, the following issues have not been resolved:

1. 21 CFR 312.42(b)(1)(i): Unreasonable and significant risk of illness or injury to human subjects

   You have proposed to expose more non-patients to MDMA in Study MT2 than the total number of patients currently enrolled in your two ongoing phase 3 trials designed to characterize the safety and efficacy of your proposed product for the treatment of PTSD. For example, and as previously noted, we have concerns about an adverse event occurring (i.e., de novo suicidal ideation) in a healthy subject in trial MT1. Your phase 2 data suggest that patients with PTSD have the potential for direct clinical benefit in the context of these ongoing phase 3 trials. However, healthy subjects have no such potential benefit; you have not provided a valid scientific rationale to justify the potentials risks to these individuals.

   Regarding your response citing the Meeting Minutes, dated December 29, 2016, the requirement to establish an adequately-sized safety database should be satisfied by studies in the target population of patients with PTSD and not in healthy individuals.

Information Needed to Resolve Deficiency: You must provide an adequate justification for your assertion that the benefits outweigh the risks for healthy individuals in Study MT2.

2. 21 CFR 312.42(b)(1)(ii): Unqualified clinical investigators

   Your explanation is insufficient. Given that the safety of your proposed product has yet to be adequately characterized, the clinical investigator requirements for conducting research with MDMA-assisted psychotherapy in healthy volunteers must not be less stringent than those required for your ongoing phase 3 studies.

   Information Needed to Resolve Deficiency: The requirements for clinical investigators in Study MT2 must be identical to the requirements for clinical investigators in your phase 3 trials:

   - On-site physician (i.e., not on-call)
   - Lead Facilitator should be a doctoral level PhD/MD-level psychotherapist (or equivalent).
   - Co-Facilitator should have a bachelor's degree *and* be trained in mental health. An example of mental health training is a postgraduate internship-type program at an institute to gain more detailed knowledge of mental health interventions and treatments (e.g., mental health counselor, mental health certification for nursing, etc.).

Therefore, the clinical hold on Protocol MT2 remains in effect until you have submitted the required information and we notify you that you may initiate this clinical study, you may not legally conduct this study under this IND.

Please identify your response to the clinical hold issues as a "**CLINICAL HOLD COMPLETE RESPONSE**."

Following receipt of your complete response to these issues, we will notify you of our decision within 30 days.

If you have any questions, contact CDR Sarah Seung, Regulatory Project Manager, at [redacted] or [redacted].

Sincerely,

{See appended electronic signature page}

Tiffany R. Farchione, MD
Director (Acting)
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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