IND 063384

MEETING MINUTES

Multidisciplinary Association for Psychedelic Studies (MAPS)
Attention: Amy Emerson
Chief Executive Officer
3141 Stevens Creek Blvd #40563
San Jose, CA 95117

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-methylenedioxymethamphetamine (MDMA).

We also refer to the telecon between representatives of your firm and the FDA on January 15, 2021. The purpose of the meeting was to discuss your December 1, 2020 request for formal dispute resolution regarding the partial clinical hold letters dated August 5, 2019, September 27, 2019, and January 30, 2020, signed by Tiffany Farchione, MD, Director, Division of Psychiatry.

A copy of the official minutes of the meeting/telecon is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, please call me at [redacted] or via e-mail at [redacted].

Sincerely,

{See appended electronic signature page}

Paul David
Division Director
Division of Regulatory Operations for Neuroscience
Office of Regulatory Operations
Center for Drug Evaluation and Research

Enclosure:

- Meeting Minutes

U.S. FOOD & DRUG ADMINISTRATION

MEMORANDUM OF MEETING MINUTES

Meeting Type: Type A
Meeting Category: Formal Dispute

Meeting Date and Time: January 15, 2021 12:00 PM – 1:00 PM
Meeting Location: Teleconference

Application Number: IND 063384
Product Name: 3,4-methylenedioxymethamphetamine (MDMA)
Indication: Posttraumatic Stress Disorder
Sponsor Name: Multidisciplinary Association for Psychedelic Studies (MAPS)
Regulatory Pathway: 505(b)(2) of the Federal Food, Drug, and Cosmetic Act

Meeting Chair: Billy Dunn, MD
Meeting Recorder: Paul David, RPh, RAC

FDA ATTENDEES

Office of Neuroscience
Billy Dunn, MD, Director
Eric Bastings, MD, Deputy Director

Office of Neuroscience, Division of Psychiatry
Tiffany R. Farchione, MD, Director
Bernard Fischer, MD, Deputy Director
Javier Muñiz, MD, Associate Director for Therapeutic Review
Jean Kim, MD, Clinical Team Leader
Nancy Dickinson, PharmD, Clinical Reviewer
Juliette Touré, PharmD, BCPP, Senior Policy Advisor

Office of Neuroscience, Division of Anesthesiology, Addiction Medicine, and Pain Medicine
Silvana Borges, MD, Deputy Director (Acting)
Gioia Guerrieri, MD, Clinical Reviewer

Office of Regulatory Operations, Division of Regulatory Operations - Office of Neuroscience
Paul David, RPh, RAC, Division Director
CDR Sarah Seung, PharmD, Regulatory Project Manager

Office of Program Operations
Cathryn Lee, MSN, CRNP, Lead Regulatory Project Manager (detail)

Office of Executive Programs
Melissa Sage, CDER Formal Dispute Resolution Program Manager

SPONSOR ATTENDEES

Multidisciplinary Association for Psychedelic Studies
Rick Doblin, PhD, Executive Director
Amy Emerson, Chief Executive Officer
Berra Yazar-Klosinski, PhD, Deputy Director, Head of Research Development and Regulatory Affairs
Corine de Boer, MD, PhD, Chief Medical Officer, Head of Safety
Michael Mithoefer, MD, Senior Medical Director for Medical Affairs, Training and Supervision
Rebecca Matthews, Director and Head of Clinical Operations
Allison Coker, PhD, Regulatory Affairs Specialist
Joy Sun Cooper, Head of Commercialization
Shannon C. Carlin, MA, AMFT, Director and Head of Training and Supervision

Hyman, Phelps & McNamara, P.C.
Josephine M. Torrente, JD, Counsel to MAPS
Deborah L. Livornese, JD, Counsel to MAPS

1.0 BACKGROUND

On December 1, 2020, Multidisciplinary Association for Psychedelic Studies (MAPS) submitted a Formal Dispute Resolution Request (FDRR) for 3,4-methylenedioxymethamphetamine (MDMA). The FDRR is related to the partial clinical hold letters dated August 5, 2019, September 27, 2019, and January 30, 2020. MAPS requested a meeting with the FDA to discuss their FDRR. The meeting took place on January 15, 2021.

The partial clinical hold was imposed on Protocol MT2, entitled “A Phase 1, Open-Label, Multi-Site Study to Assess Psychological Effects of MDMA-Assisted Psychotherapy when Administered to Healthy Volunteers.” The most recent letter dated January 30, 2020, provided the following reasons to retain the partial clinical hold: 1) Unreasonable and significant risk of illness or injury to human subjects and 2) Unqualified clinical investigators.

MAPS contends that Study MT-2 would not expose the healthy volunteer subjects to an unreasonable or significant risk of illness or injury and the Clinical Investigators and Facilitators conducting the study are qualified by reason of their training and experience, evidenced by licensure by applicable government authorities.

2.0 DISCUSSION

MAPS provided a presentation (see attached), summarizing their dispute resolution request. Please refer to the attached document for additional detail. Highlights of the discussion are as follows:

- Although not part of the FDRR, the Agency inquired about the phase 3 MAPP1 topline results. MAPS stated that there was statistically significant improvement on the CAPS-5 outcome measurement. A meeting to discuss these results with the review division has been requested.

- MAPS has an ongoing phase 1 crossover study, MT-1, similar to the MT-2 study that was placed on a clinical hold. The primary difference is that the MT-2 study has a self-compassion primary endpoint, and MAPS considers this a different focus when compared to the MT-1 study.

- The MT-1 and MT-2 studies have similar patient populations and similar inclusion criteria to exclude subjects with psychiatric disorders.

- The meeting concluded with a discussion of the investigator qualifications (a reason for the clinical hold). MAPS contends that the investigator qualifications and criteria for MT-2 are similar to their ongoing studies that were allowed to proceed.

3.0 DISCLAIMER

This meeting was not conducted with the expectation that decisions would be made or agreements reached at the meeting. The issues discussed were taken into careful consideration by the deciding authority when reaching a decision regarding the formal dispute resolution request.

4.0 ATTACHMENTS

Presentation slides provided by MAPS

FDRR Type A Meeting
IND 063384

3,4-methylendioxymethamphetamine
Posttraumatic Stress Disorder

January 15, 2021

MAPS Public Benefit Corporation

Background

- IND 063384 investigates MDMA-assisted psychotherapy as a treatment for moderate to severe PTSD
  - 2001: IND opened
  - 2017: Breakthrough Therapy Designation (on basis of dose-dependent, durable efficacy in randomized, controlled Phase 2 studies)
  - 2020: First pivotal study (MAPP1) completed under SPA; second study (MAPP2) currently enrolling

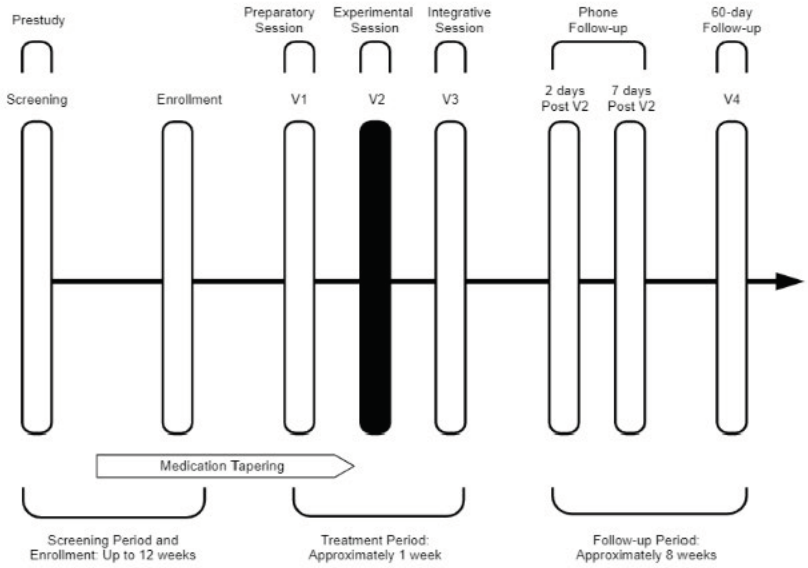
- Study MT-2, a Phase 1 study in healthy volunteers, is on clinical hold
  - Division of Psychiatry asserted deficiencies
    - Unreasonable and significant risk of illness or injury
    - Unqualified clinical investigators

- FDRR Requested Action
  - Removal of the clinical hold

Study MT-2 Design: Phase 1, open-label, single-arm, multi-center

Objective: Explore safety and psychological effects of MDMA and expand knowledge of MDMA-therapy trainees

Study Visits Overview



Dose (at V2 only)	Initial dose: 120 mg Optional supplemental dose: 40 or 60 mg 1.5-2 hours after Initial dose

Study Design Elements

Planned sample	150 healthy normal volunteers

Relevant eligibility criteria	• Education or training in psychotherapy
	• Screening assessments by Independent Rater via the MINI
	• Eligibility determined by site physician and MAPS medical monitor
	• Exclusion of subjects with potential psychiatric disorders or history of mood/anxiety disorder not in remission
	  • No current relevant psychiatric diagnosis
	  • No history of bipolar affective disorder type 1
	  • No history of primary psychotic disorder (MINI)
	  • No 10-year history of suicide attempt
	  • No score ≥ 1 on C-SSRS in past year

Measures of psychological effects	• Self Compassion Scale • Positive and Negative Affect Schedule • Acceptance and Action Questionnaire-II • Professional Quality of Life Scale • Maslach Burnout Inventory – Human Services Survey
Measures of safety	Incidence and severity of various AEs and AESI including suicidal ideation and behavior, cardiac function and abuse liability

"Unreasonable and Significant Risk of Illness or Injury"

- Clinical hold safety concerns based on Phase 1 Study MT-1
  - "Blindness"
    - Single event of blurred peripheral vision (mild) in healthy volunteer taking either MDMA or placebo initially miscoded as "blindness" in electronic CRF
    - Resolved without treatment during Experimental Session (within 4 hours)
    - Total of 2 participants experienced the "expected" (per IB) AE of "Vision Blurred"
  - "Severe suicidality and intentional self-harm"
    - No incidents of suicidal behavior
    - One AESI of suicidal ideation in healthy volunteer taking either MDMA or placebo
      - History of suicidal ideation and lifetime C-SSRS positive for suicidal ideation/behavior
      - SI event during Experimental Session; decreased from active to passive ideation by conclusion of session
      - Fully resolved 3 days following Experimental Session
    - MT-2 conducted in a therapeutic environment where subject is monitored by trained investigators for 8 hours
    - Risk to healthy volunteer subjects is lower than in PTSD subjects who have a higher baseline risk
      - No signal in Phase 2 or Phase 3 studies based on C-SSRS or AEs
      - Phase 2 and 3 studies not on hold
- Risks do not meet regulatory threshold of "unreasonable and significant"

Benefit Inherent in Study MT-2

- Potential for direct benefit to subjects is not required in Phase 1
  - Opportunity to support biomedical research benefits society
  - Ability to gain insights into experience of undergoing MDMA-assisted psychotherapy from participants trained/educated in psychotherapy
  - Opportunity to isolate psychological effects of MDMA from those of PTSD to inform labeling
  - Opportunity to isolate self-compassion effects of MDMA to better understand clinical effects in PTSD and other conditions

- MT-2 does provide potential personal and professional benefit to subjects
  - Multiple psychotherapy sessions (with and without MDMA) offer potential increased emotional regulation and personal understanding
  - Personal experience with treatment modality may be beneficial to treatment providers and their future therapy patients

"Unqualified Clinical Investigators"

- MT-2 investigator requirements
  - Two-person psychotherapy teams
    - At least one licensed psychotherapist
  - Physician
    - Determine subject eligibility at screening
    - Assess subject safety throughout study, including Experimental Session (no on-site requirement))
- Clinical hold seeks to establish unique/novel requirements for Study MT-2
  - Doctoral level therapists
  - Physician on-site during MDMA-assisted session
- Change in requirements is not evidence-based
  - No scientific rationale or literature support provided in clinical hold
- 15 studies, in 366 subjects, have been safely conducted under this IND
  - Includes Phase 1 Study MT-1
  - Includes Phase 3 Study MAPP-1
  - AE profile does not involve AEs of the sort that would require an MD on-site to avoid serious harm

- MT-2 investigators are appropriately qualified

Requested Action/Findings

MAPS requests that the Office of Neuroscience lift the clinical hold on Study MT-2

- Study subjects not exposed to an unreasonable or significant risk of illness or injury
- Clinical investigator qualification requirements reflect appropriate training and experience to conduct the study

MAPS
Public Benefit
Corporation

Questions & Discussion

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/

PAUL A DAVID
02/12/2021 04:01:23 PM