Research News

Treating PTSD with MDMA-Assisted Psychotherapy

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MAPS and MPBC staff and researchers will meet with the FDA on November 29, 2016.

Phase 3 Trials: FDA Grants Request for End of Phase 2 Meeting

On October 3, 2016, the U.S. Food and Drug Administration (FDA) granted our request for an End of Phase 2 Meeting, with the meeting scheduled for November 29, 2016. The goal of this meeting will be to come to an agreement on the design of our upcoming Phase 3 trials, the final stage of research required to make MDMA-assisted psychotherapy a legal prescription treatment for PTSD. Staff and researchers at MAPS and the MAPS Public Benefit Corporation (MPBC) will travel to the FDA's White Oak Campus in Silver Spring, Maryland, for a 90-minute meeting to review the promising data from our six completed Phase 2 studies, and to decide on an efficient and scientifically rigorous design for our Phase 3 trial—with 400 or more additional participants—which we anticipate starting in 2017.

Our submitted meeting materials include a 90-page summary of initial indications of safety and efficacy based on our Phase 2 results, plus what is now known about the toxicology, pharmacology, and abuse liability of MDMA from over 5,000 peer-reviewed scientific papers published on MDMA or Ecstasy. We also had multiple attachments consisting of our Chemistry, Manufacturing, and Control (CMC) proposal for MDMA production under current Good Manufacturing Practice (cGMP) standards for Phase 3 and post-approval formulation, toxicological study proposals, key elements of MDMA-assisted psychotherapy, and references.

"We will receive the FDA's questions on our End of Phase 2 submission package just two days before the meeting, giving our team very little time to prepare our responses for the meeting," says MPBC Executive Director Amy Emerson. "It's both challenging and exciting, since after the meeting we'll have clear direction on the design of our Phase 3 trials." As long as we receive the funding needed to complete the research, we anticipate FDA approval of MDMA-assisted psychotherapy as a treatment for PTSD as early as 2021.

U.S. Veterans Study Officially Completed

Study Completed
Location: Charleston, South Carolina
Principal Investigator: Michael Mithoefer, M.D.
Co-Therapist: Annie Mithoefer, B.S.N.
Estimated study budget: $1,429,000
This study has been fully funded.

On October 27, 2016, MAPS Public Benefit Corporation (MPBC) staff met with investigators in Charleston, South Carolina for the formal closeout of our largest Phase 2 study of MDMA-assisted psychotherapy in 24 U.S. veterans, firefighters, and police officers with chronic, treatment-resistant PTSD. Conducted by Clinical Trial Leaders Rebecca Matthews and Alli Feduccia, Ph.D., the closeout included a thorough review of the study's documentation, database, files, and adherence to regulations. All treatment sessions and long-term follow-up interviews for this study have now been completed. Led by Principal Investigator Michael Mithoefer, M.D., and Co-therapist Annie Mithoefer, B.S.N., in Charleston, South Carolina, the data from this study are now being prepared for analysis and publication in a peer-reviewed scientific journal.

"For us, the end of each of our MDMA/PTSD studies has been a bitter-sweet moment," states Dr. Mithoefer. "It's sad saying goodbye to research participants after the privilege of getting to know them and supporting them in their deep healing journeys. It's a time for celebrating the remarkable results of these journeys, that in so many cases have relieved painful, debilitating symptoms and brought deep healing and fulfilling

reengagement in their lives without the daily burden of PTSD."

Goals for this study included (1) gathering evidence for the safety and effectiveness of MDMA-assisted psychotherapy in people suffering from war-related trauma; (2) comparing the effectiveness of the treatment for people with war-related trauma versus for people with trauma related to sexual abuse, assault, and other causes; (2) comparing different doses of MDMA for therapeutic effectiveness and ability to create a successful double-blind; and (3) increasing awareness and support for our work by assisting a population with mainstream public recognition.

20th Participant Completes 12-Month Follow-Up Interview in Boulder Study *Ongoing study*

Location: Boulder, Colorado
Principal Investigator: Marcela Ot'alora, M.A., L.P.C.
Estimated study budget: $771,000
This study has been fully funded.

On October 17, 2016, the 20th participant completed their 12-month follow-up interview in our Phase 2 study of MDMA-assisted psychotherapy in subjects with chronic, treatment-resistant PTSD in Boulder, Colorado. All subjects have now completed active study participation. 23 subjects will be included in our final analysis, while all 29 subjects, including six who dropped out or were excluded for not meeting study criteria, will be included in our intent-to-treat analysis. Long-term follow-up data will provide additional information to guide the design of our upcoming Phase 3 trials. The final results are being prepared for publication, which is expected in 2017.

Goals for this study include (1) gathering evidence for the safety and effectiveness of MDMA-assisted psychotherapy for subjects with PTSD from a variety of causes, (2) comparing different doses of MDMA for therapeutic effectiveness and ability to create a successful double-blind, (3) exploring whether using intern co-therapists can reduce costs while maintaining treatment effectiveness, and (4) training the next generation of psychedelic psychotherapists.

Fourth Participant Completes 12-Month Follow-Up Interview in Israeli Study *Ongoing study*

Location: Beer Yaakov, Israel
Clinical Investigator: Moshe Kotler, M.D.
Estimated study budget: $509,000
This study has been fully funded.

On October 21, 2016, the fourth of 10 participants completed their 12-month follow-up interview in our Israeli Phase 2 study of MDMA-assisted psychotherapy for PTSD. Led by Principal Investigator Moshe Kotler, M.D., this Phase 2 study has treated 10 subjects with chronic, treatment-resistant PTSD from any cause. Once the final evaluations are complete, we will gather data for inclusion in an international meta-analysis of the safety and efficacy of MDMA-assisted psychotherapy for the treatment of PTSD.

Goals for this study include (1) gathering evidence for the safety and effectiveness of MDMA-assisted psychotherapy for subjects with PTSD mostly related to war and terrorism, (2) comparing different doses of MDMA for therapeutic effectiveness and ability to create a successful double-blind, (3) working in direct association with the Israeli Ministry of Health, and (4) exploring the use of MDMA-assisted psychotherapy in other cultural contexts.

Final Participant Completes 12-Month Follow-Up Interview in Canadian Study *Ongoing study*

Location: Vancouver, British Columbia, Canada
Principal Investigators: Ingrid Pacey, M.D.
Estimated study budget: $470,000
Already raised: $48,000 + $69,000 raised by partners
Needed to complete this study: $353,000

On October 17, 2016, the sixth and final participant completed their 12-month follow-up interview in our Phase 2 pilot study of MDMA-assisted psychotherapy for PTSD in Vancouver, Canada. All participants have completed treatments and 12-month follow-up interviews. This small pilot study gave Canadian therapists experience delivering MDMA-assisted psychotherapy for PTSD, with data collected from three women and three men. The final results are being prepared for publication as a part of a global meta-analysis of MDMA-assisted psychotherapy results.

Goals for this study include (1) gathering evidence for the safety and effectiveness of MDMA-assisted psychotherapy for subjects with PTSD from a highly skilled co-therapist team, (2) comparing different doses of MDMA for therapeutic effectiveness and ability to create a successful double-blind, and (3) initiating the first Canadian research into the potential benefits of psychedelic psychotherapy in over 40 years.

18th Participant Enrolled in Therapist Training Study; Boulder Study Site Initiated *Ongoing study*

Location: Charleston, South Carolina, and Boulder, Colorado
Principal Investigator: Michael Mithoefer, M.D., (Charleston), and Marcela Ot'alora, M.A., L.P.C. (Boulder)
Estimated study budget: $429,000
Already raised: $160,000
Needed to complete this study: $269,000

On September 28, 2016, the 15th participant was enrolled at our study site in Charleston, South Carolina in our ongoing Phase 1 study of the psychological effects of MDMA when used in a therapeutic setting by healthy volunteers. The Charleston site is led by Principal Investigator Michael Mithoefer, M.D. On October 23, the third participant was enrolled at the recently initiated Boulder, Colorado study site. Marcela Ot'alora, M.A., L.P.C., is serving as Principal Investigator of the Boulder site. Enrollment in this study is limited by invitation only to therapists in training to work on MAPS-sponsored clinical trials of MDMA-assisted psychotherapy for PTSD. This study has currently enrolled 18 out of 100 participants across both study sites.

Thirty trainees gathered in Los Angeles, Calif, from September 19–25, 2016, for Part B of the MDMA Therapy Training Program.

MDMA Therapy Training Program: Group Trainings Take Place in Los Angeles and New York *Training Program*

Location: Charleston, South Carolina, and Boulder, Colorado
Principal Investigator: Michael Mithoefer, M.D.
Co-Therapist: Annie Mithoefer, B.S.N.
Estimated study budget: $429,000
Already raised: $160,000
Needed to complete this study: $269,000

From September 19-25, 2016, 30 trainees gathered in Los Angeles, Calif., to participate in Part B of the MDMA Therapy Training Program, and 25 additional trainees participated in the same training from October 16-22, 2016, in Stony Point, New York. The MAPS MDMA Therapy Training Program has enrolled 121 people since December 2014.

The five-part program is preparing therapy teams for upcoming MAPS-sponsored Phase 3 trials of MDMA-assisted psychotherapy for PTSD. All Phase 3 researchers will also complete Parts C-E of the training program, which include an external workshop, a second week-long training, a final evaluation, and clinical supervision.

Part B of the program is a week-long training led by MAPS-sponsored researchers Michael Mithoefer, M.D., Annie Mithoefer, B.S.N., and Marcela Ot'alora, M.A., L.P.C. Trainees learned the techniques of MDMA-assisted psychotherapy as outlined in the Treatment Manual, watched videos of therapy sessions from Phase 2 trials, and dialogued with other therapists in training about the therapeutic approach. The MDMA Therapy Training Program plans to train approximately 300 therapists before 2021, when we anticipate completing Phase 3 clinical trials of MDMA-assisted psychotherapy for chronic, treatment-resistant PTSD.

Conjoint Therapy: First Pair of Participants Receive Treatment *Ongoing study*

Location: Charleston, South Carolina
Principal Investigator: Michael Mithoefer, M.D.,
Sub-Investigator: Candice Monson, Ph.D.
Estimated study budget: $235,000
Already raised: $165,000
Needed to complete this study: $70,000

On August 5, 2016, the first pair of participants was enrolled in our new study of MDMA combined with Cognitive Behavioral Conjoint Therapy (CBCT) for PTSD in Charleston, South Carolina. These participants received their first and second experimental treatment sessions on August 6 and August 23. Final outcome measures for this pair (dyad) were collected during the one-month follow-up interview on October 9, 2016.

Led by Principal Investigator Michael Mithoefer, M.D., and Sub-Investigator Candice Monson, Ph.D., this is a pilot Phase 1/Phase 2 open-label study exploring CBCT integrated with MDMA-assisted psychotherapy for the treatment of chronic posttraumatic stress disorder (PTSD). Dr. Monson is a leading expert on individual and conjoint cognitive therapies to treat PTSD, and was introduced to MAPS by the U.S Department of Veterans Affairs National Center for PTSD.

The study will enroll 10 dyads, with one participant diagnosed with PTSD and one concerned significant other who does not have PTSD but does experience psychosocial distress. The primary goal of this study is to develop a combined method of MDMA with CBCT for PTSD. MDMA will be administered to both participants to help facilitate communication and connection between participants and therapists. We are now screening additional local participants for this study.

MDMA-Assisted Therapy for Social Anxiety in Autistic Adults

Final Participant Treated *Ongoing study*
Location: Los Angeles, California
Principal Investigators: Charles Grob, M.D., and Alicia Danforth, Ph.D.
Estimated study budget: $400,000
Already raised: $13,000 + $15,000 raised by partners
Needed to complete this study: $372,000

On October 29, 2016, the 12th and final participant received their last blinded experimental session in our ongoing study of MDMA-assisted therapy for social anxiety in adults on the autism spectrum. Sponsored by MAPS, this is a collaborative study between MAPS and the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, with blood plasma biomarker analysis conducted by researchers at Stanford University. MAPS-sponsored researcher Alicia Danforth, Ph.D., presented preliminary results on October 8, 2016, at Horizons: Perspectives on Psychedelics in New York City.

Goals for this study include (1) gathering evidence for the safety and effectiveness of MDMA-assisted therapy for autistic adults diagnosed with social anxiety, (2) determining if additional studies in this area are warranted, and (3) initiating a new program of research into a possible beneficial use of MDMA building on collected case accounts.

MDMA-Assisted Psychotherapy for Anxiety Associated with Life-Threatening Illness

12th Participant Treated in Marin Study
Ongoing study
Location: Marin, California
Principal Investigator: Phil Wolfson, M.D.
Estimated study budget: $627,000
Already raised: $248,000
Needed to complete this study: $379,000

On October 24, 2016, the 12th participant was treated in our ongoing study of MDMA-assisted psychotherapy for anxiety associated with life-threatening illness in Marin, Calif. Led by Principal Investigator Phil Wolfson, M.D., with Co-therapist Julane Andries, L.M.F.T., this study is gathering preliminary data about the safety and efficacy of MDMA-assisted psychotherapy for anxiety in 18 subjects diagnosed with a life-threatening illness. We are currently screening additional participants for this study.

We are continuing to make progress on an additional fMRI brain imaging study of the physiological correlates of MDMA-assisted psychotherapy in participants from this study. The brain imaging sub-study is a collaboration between the MAPS-sponsored study and Michael Silver, Ph.D., at the Helen Wills Neuroscience Institute at the University of California, Berkeley.

"Our study is progressing with wonderful experiences and gratifying changes in awareness, reductions of fear, self-worth, and relationships," reports Dr. Wolfson. "As our subjects have life-threatening illnesses, there is the unfortunate possibility of relapse or recurrence. With great sadness, we report the loss of one of our subjects to recurrent cancer. We are privileged to do this work in all its seriousness and great beauty."

Goals for this study include (1) gathering data on the safety and effectiveness of MDMA-assisted psychotherapy for subjects with anxiety associated with life-threatening illness; (2) determining if additional studies are warranted; and (3) initiating MDMA-assisted psychotherapy research for a new clinical indication.

MDMA Research Review Published in *Cell*

On July 14, 2016, the peer-reviewed scientific journal Cell published a new review of current research into the use of MDMA as an adjunct to psychotherapy for a range of neuropsychiatric disorders. Written by Boris Heifets, M.D., Ph.D., and Robert Malenka, M.D., Ph.D., of Stanford University, the article summarizes current knowledge about MDMA's mechanism of action, highlighting its ability to catalyze prosocial, empathogenic effects which may help treat symptoms of medical conditions such as major depressive disorder, social anxiety in autistic adults, posttraumatic stress disorder (PTSD), and schizophrenia. "Elucidating MDMA's mechanisms of actions in the context of treatment trials will pave the way for developing new therapeutic agents that target previously unidentified brain mechanisms," state the authors. "The world's populations need more compassion and empathy for one another. The study of MDMA provides one small but potentially important step toward reaching that goal."

Medical Marijuana Research

DEA Announces Intent to Eliminate Federal Monopoly on Marijuana for Research

On August 11, 2016, the U.S. Drug Enforcement Administration (DEA) announced their intention to grant licenses to additional marijuana growers for research, thereby ending the DEA-imposed 48-year monopoly on federally legal marijuana for research. Since 1968, the University of Mississippi, under contract to the National Institute on Drug Abuse (NIDA), has maintained the only facility in the United States with federal permission to grow marijuana for research.

MAPS has been working to eliminate this marijuana research blockade for over 15 years. NIDA's marijuana can be used for research but not sold as a prescription medicine, making it unacceptable for use in future Phase 3 studies. With

support from MAPS, Lyle Craker, Ph.D., of the University of Massachusetts-Amherst will submit his new application for a DEA license to grow marijuana for research later this year.

"There has been no production monopoly on any other Schedule I substance, like MDMA or LSD—only the cannabis plant," says MAPS Founder and Executive Director Rick Doblin, Ph.D. "Licensing non-government cannabis producers, and thereby creating a path to FDA approval, will finally facilitate the removal of marijuana from Schedule I."

Marijuana for PTSD: NIDA Provides Marijuana for Phoenix Site; Participant Screening Begins

Study in development
Location: Baltimore, Md., and Phoenix, Ariz.
Coordinating Principal Investigator:
Marcel Bonn-Miller, Ph.D. (University of Pennsylvania)
Co-Investigators/Site Principal Investigators:
Sue Sisley, M.D. (private practice) and
Ryan Vandrey, Ph.D. (Johns Hopkins University)
Co-Investigator: Paula Riggs, M.D. (University of Colorado)
Estimated study budget: $2,156,000
Already raised: $2,156,000 grant awarded by the State of Colorado. This study has been fully funded.

On August 10, 2016, the National Institute on Drug Abuse (NIDA) approved the Scottsdale Research Institute's official request to order 6.3kg of marijuana to be used by the Phoenix, Ariz., study site in our upcoming study of medical marijuana for posttraumatic stress disorder (PTSD) in 76 U.S. veterans. Multiple marijuana strains were requested, featuring varying levels of THC and CBD per strain, including high THC/low THC, high CBD/low CBD, balanced THC/CBD, and placebo.

On August 25, 2016, Site Principal Investigator Sue Sisley, M.D., received the first shipment of marijuana from the National Institute on Drug Abuse (NIDA), at the Phoenix, Ariz., site. The marijuana arrived in dried bulk form, and sent to a secondary DEA-licensed laboratory for potency, mold and yeast testing. Researchers at the Phoenix, Ariz., site began screening participants for enrollment on October 3.

The randomized, blinded, placebo-controlled study will test the safety and efficacy of botanical marijuana in 76 U.S. military veterans with treatment-resistant PTSD. The study is funded by a $2.156 million grant from the Colorado Department of Public Health and Environment (CDPHE) to MAPS, which is sponsoring the study. MAPS' study protocol will be replicated using vaporization by the Canadian medical marijuana producer Tilray, and by the University of Sydney using Tilray extracts in orally administered capsules.

The Principal Investigator for this study is Marcel Bonn-Miller, Ph.D., of the University of Pennsylvania. Paula Riggs, M.D., of the University of Colorado, is serving as an additional Co-Investigator to help ensure the study's scientific integrity. The study site in Phoenix, Arizona, will be led by Co-Investigator/Site Principal Investigator (PI) Sue Sisley, M.D. Half of the study's 76 subjects will be treated at the Phoenix site, with the other half treated at Johns Hopkins by Co-Investigator/Site PI Ryan Vandrey, Ph.D.

The first shipment of marijuana from the National Institute on Drug Abuse (NIDA) arrived at the Phoenix, Ariz. site of our upcoming trial of smoked marijuana for symptoms of PTSD in U.S. veterans.

Ayahausca Research

Data Collection Survey Underway *Ongoing study*

Principal Investigator: Jessica Nielson, Ph.D.

As of November 9, 2016, we have received 175 completed responses for our new anonymous questionnaire about the potential risks and benefits associated with taking ayahuasca as a therapy for posttraumatic stress disorder (PTSD). The data collection is being sponsored by the Multidisciplinary Association for Psychedelic Studies (MAPS). Jessica Nielson, Ph.D., is the Principal Investigator for this study.

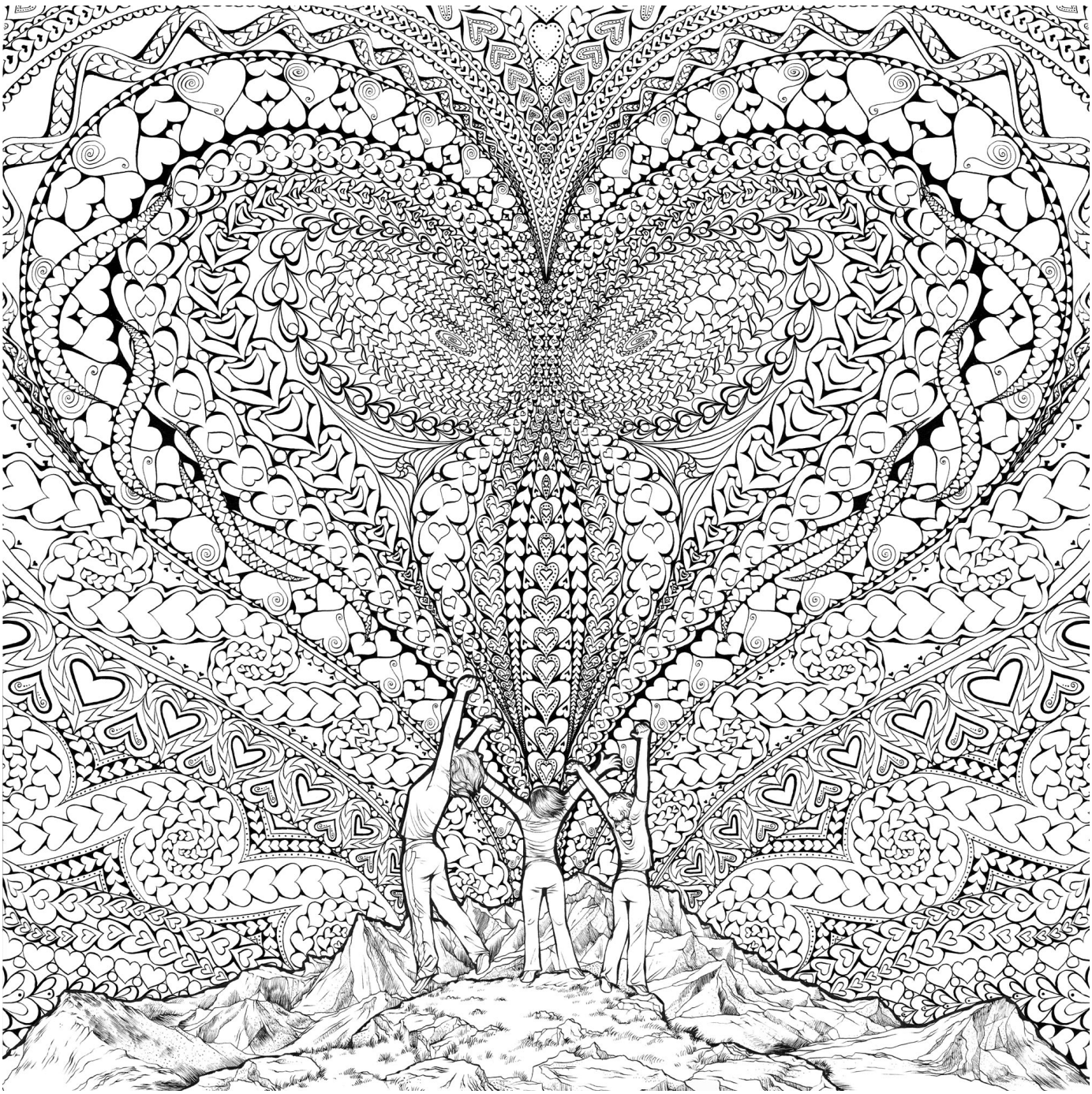
"Initial results show a wide range of responses to ayahuasca from people either with or without a current diagnosis of PTSD," explains Nielson. "An important feature to whether it was healing or harmful suggests the need for experienced facilitators and personal helpers during difficult moments, adherence to dietary and drug interaction recommendations, and some form of post-ceremony integration to help with processing their experiences." To participate, take the survey at **surveymonkey.com/r/AyaPTSD**.

Ibogaine-Assisted Therapy for Drug Addiction

Data Prepared for Publication in Scientific Journals *Ongoing study*

Locations: Mexico and New Zealand
Principal Investigators: Thomas Kingsley Brown, Ph.D. (Mexico), and Geoff Noller, Ph.D. (New Zealand)
Donations are needed to support ibogaine research.

All treatments have been completed in our two observational studies of ibogaine-assisted therapy for drug addiction, which took place at independent treatment centers in Mexico and New Zealand. We anticipate that data from both studies will be published in peer-reviewed scientific journals this year. Both of these studies observed the long-term effects of ibogaine treatment for opioid dependence, and the data from each study will be compared to evaluate how ibogaine treatment varies between different centers. Goals for these study included (1) gathering preliminary evidence about the safety and potential benefits of ibogaine-assisted therapy for opiate addiction, (2) comparing the safety and effectiveness of different ibogaine treatment centers, and (3) initiating and encouraging psychedelic research in New Zealand.



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