MAPS' US MDMA/PTSD Phase II Study:
The 12th and **Final** Progress Report

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On July 18, 2008 we conducted the final all-day experimental session of our MDMA/PTSD study. It was the third MDMA-assisted session for our 21st and last subject, who had previously had two placebo experimental sessions during the double-blind stage of the protocol. After a series of integration sessions with Annie and me, the subject will meet with Mark Wagner, Ph.D. in mid-September for her final symptom measures, at which point this Phase II study will be completed. Our longer-term follow-up study is considered a separate study and will be initiated shortly after the final subject's two-month follow-up is completed. Since the study started treating subjects 4 1/2 years ago, we'll be evaluating subjects from one to 4 1/2 years after treatment.

The study has now included 51 MDMA-assisted experimental sessions, 16 placebo experimental sessions, 337 non-drug therapy sessions for preparation and integration, and 128 psychological testing sessions. During the four and a half years over which these sessions have taken place there have been no serious drug-related adverse events.

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The next step will be statistical analysis of the data and publishing the results in a peer-reviewed journal. Mark Wagner, the neuropsychologist who has done all the screening, symptom measures and neuropsychological testing, has begun work on the data analysis. We will not be prepared to publish the results prior to peer-reviewed publication, however we continue to be very encouraged by the changes we are seeing in PTSD symptoms and the lack of evidence for any adverse neuropsychological effects.

In the meantime, we have been turning our attentions to preparation for the much larger multi-center trials that are required for FDA drug approval. Before MAPS is in a position to apply for approval of these Phase III studies, they will need data from at least one other Phase II study to demonstrate that our results can be replicated. The studies that are ongoing in Switzerland and Israel (and in the design and approval process in Vancouver) will likely produce this data within the next year or two. The preparations that we'll be working on during this time are related to the design of Phase III trials and the training of therapists to work in Phase III.

Design: Data from the present study will allow us to request FDA and IRB permission to streamline the protocol for Phase III trials in various ways, such as eliminating the presence of an ER nurse, not monitoring liver enzymes after experimental sessions, and decreasing the frequency of vital sign measurements. One of the major remaining challenges in Phase III design is to maximize the effectiveness of the double-blind by making it more difficult for investigators and subjects to distinguish full-dose MDMA sessions from placebo sessions. In our study we used an inactive placebo and compared it to 125 milligrams of MDMA (followed by a supplemental dose of 62.5 milligrams in our later subjects).

There is some PTSD research experience with lower doses. In a Spanish study conducted by Jose Carlos Buso and colleagues--which was stopped for political reasons before full doses were reached--six subjects received either an inactive placebo, 50 milligrams of MDMA or 75 milligrams of MDMA. The Swiss, Israeli and Canadian studies mentioned above are all using low-dose MDMA as an "active placebo." We are currently discussing the possibility of doing an additional Phase II study with low, intermediate, and full-dose MDMA in a small group of PTSD patients, in order to help determine the best active placebo dose for Phase III trials.

Training: In order to conduct a valid study at multiple sites, with different therapists, it is necessary to have a standardized approach to therapy, as defined in a treatment manual and also as a means of determining whether or not different therapist teams are in fact using the same approach. June May Ruse, Ph.D. has spent many hours listening to recordings of our study sessions and has taken the lead role in developing drafts of a treatment manual--with contributions from Rick Doblin, Ilsa Jerome, Annie Mithoefer, and me, along with editing assistance from Elizabeth Gibson. June has also written a draft of about ten rating scales, each focusing on one of the central aspects of our therapeutic approach, which will be necessary for an observer to confirm whether or not a therapist team is adhering to the manual.

Along with the manual and adherence scales, we are designing a training program for potential Phase III therapists. In August, June, Annie, and I scheduled a week to intensively review audio and video recordings from the study sessions in order to further refine the Treatment Manual, the adherence scales, and the training program design. We are well aware that our approach to MDMA-assisted therapy does not lend itself to "manualizing" as readily as some other forms of therapy. Our approach is largely non-directive and, except for the introductory sessions, there is not a predetermined structure regarding what is dealt with in a particular session.

Nevertheless, we believe we can describe the essential elements in a manual, and design valid adherence measures for them. Our approach is largely based on what we've learned from the writings of Stanislav and Christina Grof and others, and in our Holotropic Breathwork training with Stan and Christina. We recognize that our experience in this one study does not give us the definitive answer about the best way to conduct MDMA-assisted therapy. What it does provide is evidence that this can be an effective approach, and is a worthwhile model to carry forward into larger studies.

We're delighted to be bringing this study to completion with encouraging therapeutic results and a good safety profile. At the same time the feeling is bittersweet, because we have so enjoyed working with all the people who have volunteered to participate in this study. We feel great respect and appreciation for their courage and willingness to do this deep experiential work, especially in an experimental protocol. We know that doing so often presented considerable logistical as well as emotional challenges. Their determination to heal has inspired us, as has the community of supporters whose generosity and hard work has made it possible to offer this tool to facilitate healing.

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