From the Desk of Rick Doblin, Ph.D.

These days, I increasingly smile at how mainstream psychedelic-assisted psychotherapy is becoming. It's profoundly satisfying to see this occurring, about half a century after the backlash to the psychedelic 1960s and the criminalization, stigmatization, exaggerated risk estimates, and suppression of research into benefits that followed. Over the course of just one week this October, *The Boston Globe* published a favorable article about psychedelic psychotherapy research with one of the more witty headlines in decades: "Lucy in the Sky with Doctors"; *The Wall Street Journal* published a remarkably positive article about our research into MDMA-assisted psychotherapy for posttraumatic stress disorder (PTSD); and the American Psychiatric Association also published an enthusiastic article about the promise of MDMA-assisted psychotherapy for PTSD. The concluding sentence in *The Boston Globe* article summed it all up when it stated that "as the marijuana debate shows, attitude shifts that barely seemed possible can sometimes become inevitable."

MAPS' research is now more consequential, widely recognized, and more extensive than ever before.

We have finally crossed a threshold of legitimacy as the Multidisciplinary Association for Psychedelic Studies (MAPS) progresses from Phase 2 exploratory pilot studies of MDMA-assisted psychotherapy for PTSD to the pivotal Phase 3 studies of safety and efficacy that, if successful, will result in U.S. Food and Drug Administration (FDA) approval for prescription use. MAPS' research is now more consequential, widely recognized, and more extensive than ever before. The primary reasons for this great leap are in large part the result of two developments in MAPS' ongoing relationship with the FDA.

On July 28, 2017, the FDA sent MAPS an Agreement Letter regarding the protocol design for our two pivotal Phase 3 studies of MDMA-assisted psychotherapy for PTSD. The agreement concluded a six-month comprehensive Special Protocol Assessment review process during which MAPS and the FDA discussed, negotiated, and came to an agreement on all the key elements of our study design.

The FDA Agreement Letter was especially important for MAPS since it enabled us to address directly the methodological challenges of conducting successful double-blind clinical trials with psychedelic drugs such as MDMA. Psychedelics are usually, though not always, easy for study volunteers and therapists to distinguish from an inactive placebo (a substitute containing none of the compound being studied). This scientific challenge was made even more difficult when we discovered that what we had thought to be a clever solution of the double-blind problem—using lower doses of MDMA instead of an inactive placebo—completely failed. In our Phase 2 studies, low-dose MDMA did improve the blinding, but to our surprise it came at a cost: Study participants found that the lower doses of MDMA activated their traumatic memories without sufficiently reducing their fearful emotions, thus reducing the effectiveness of the psychotherapy. With this discovery in mind, we proposed to the FDA that our control condition be MAPS' manualized form of psychotherapy (**maps.org/treatmentmanual**) combined with an inactive placebo, compared to the same therapy with full dose (80 or 120 mg) MDMA, a solution which the FDA accepted in the Agreement Letter.

Then, on August 15, 2017, the FDA granted MAPS' application for Breakthrough Therapy Designation (BTD) for MDMA-assisted psychotherapy for PTSD, the FDA's top-priority program to expedite the drug development research process for what the agency considers to be the most promising new treatments. Breakthrough Therapy Designation grants us additional consultations with the FDA about issues related to commercialization earlier in the drug development process, and shortens FDA timelines for meetings and responses. The FDA only grants about one third of all applications from pharmaceutical companies for BTD, and the majority of drugs granted BTD go on to become approved for prescription use.

From a scientific standpoint, the FDA Agreement Letter

is an even more significant milestone for MAPS' research than Breakthrough Therapy Designation, since it commits the FDA to basing its evaluation of our Phase 3 data on the statistical significance of the data and on MDMA's safety profile, accepting the methodological soundness of our protocol design. The FDA's agreement on our Special Protocol Assessment takes the politics out of the scientific equation, so we can all focus on the evidence-based risk/benefit evaluations to be generated by our upcoming Phase 3 studies.

The growing acceptance of MAPS and our psychedelic therapy research has both resulted from and led to unprecedented levels of financial support from many inspiring donors. As of the beginning of November, when I finished writing this letter, MAPS has either raised or received multi-year pledges of more than $18 million of the $26 million we currently estimate we will need for FDA approval of MDMA-assisted psychotherapy for PTSD. That same $26 million may also be sufficient for subsequent approval by the European Medicines Agency (EMA), though we'll know more after our negotiations about Phase 3 requirements with the European regulators, which we're just starting now. Our funding needs will also depend on how many subjects we ultimately need to enroll in our Phase 3 studies in order to obtain statistically significant results.

More than 31 years after I founded MAPS in 1986, we are right now about to start the final stage in the work of making MDMA once again a legal adjunct to psychotherapy. With the continued support of our expanding community, we will move forward together to Phase 3, FDA approval, and beyond.

Psychedelically yours,

Rick Doblin

Rick Doblin, Ph.D.
MAPS Founder & Executive Director

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ARTWORK BY MELISSA WILLIAMS

Melissa Williams

Front cover:
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Back cover:
Masculine / Feminine

Fusing the digital and the organic, the spiritual and the make believe. Painterly hand drawn imagery, photography and digitally created collages, all remaining deeply rooted to nature.

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My name is Melissa Williams, and I am a full time freelance artist and graphic designer from beach side Carrum, a suburb in Melbourne, Australia, with a love for detailed organic illustration and ornamentation.

I have travelled the world for some time, becoming more and more inspired by the amount of beautiful art different countries have to offer.

Textiles and tapestries play a big role in what I do, as well as music, mindfulness and the eternal supply of intricate features found in the botanical.

My designs are all mixed media and use a combination of hand drawn and painted motifs, photography, collage, digital creation, and UV printing on cotton canvas and waterproof vinyl.

Please take the time to look at some of my work, and feel free to contact me for any freelance opportunities or questions.

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Instagram: misprintart

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