The Faces of Phase 2: Principal Investigators in MAPS' Clinical Trials of MDMA-Assisted Psychotherapy for PTSD in Europe

BY MARTA MAZUR

We are thrilled to inclide the energy of newer psychedelic therapists alongside more experienced colleagues. In this edition of the MAPS Bulletin, we present personal statements from a selection of our Europe-based PIs, a highly regarded group with whom we are fortunate to collaborate. Other European sites and PIs will be introduced in future issues.

MAPS Europe as well as MAPS Public Benefit Corporation (MAPS PBC) are wholly-owned subsidiaries of the non-profit Multidisciplinary Association for Psychedelic Studies (MAPS). The MAPS Europe subsidiary was formed at the beginning of 2018 and our primary goal is completing Phase 2 and Phase 3 clinical trials required to develop MDMA-assisted psychotherapy into an approved treatment for PTSD in Europe through the European Medicines Agency (EMA).

We are pleased to announce that MAPS Europe team has grown substantially over the last year. Currently we have five team members fully dedicated to support European operations. Please meet our team by visiting MAPS Europe website at mapseurope.eu/team.

On June 12, 2018, MAPS met in London with the Scientific Advice Working Party of the EMA. On June 28, MAPS received written scientific advice about its Phase 3 protocol and overall drug development plans, with approval to proceed to a Phase 3 trial in Europe. The preparatory Phase 2 studies are expected to start in October 2019. The EMA Phase 3 trial is anticipated to start in 2020, pending funding and regulatory approval by individual European countries.

PHASE 2 STUDY

The formal title of the Phase 2 European trials is an Open-Label, Phase 2, Multicenter Feasibility Study of Manualized MDMA-Assisted Psychotherapy with an Optional fMRI sub-study Assessing Changes in Brain Activity in Subjects with Post-Traumatic Stress Disorder.

The Phase 2 study will serve as the lead-in to the planned Phase 3 study in Europe and will aim to validate assumptions made for statistical power calculations supporting the Phase 3 study. The Phase 2 study will also provide cross-cultural validation data on the updated version of the Primary Outcome measure, the Clinician Administered PTSD Scale for DSM-5 (CAPS-5), which will be used in Phase 3. In addition, the study will gather supportive data on the safety and effectiveness of manualized MDMA-assisted psychotherapy while providing an opportunity for clinical supervision for planned Phase 3 therapy teams. This Phase 2 study will be the first multi-site study of MDMA-assisted psychotherapy for PTSD in Europe, and will explore reproducibility of findings from MAPS' completed FDA-regulated Phase 2 trials in a multi-site format in Europe to confirm the Phase 3 study design.

The Phase 2 study will be conducted in up to 40 participants in 7 countries in Europe, in the Netherlands, Czech Republic, Norway, United Kingdom, Portugal, Finland and Germany. Four sites in total—two in the Netherlands, one in the United Kingdom, and one in the Czech Republic—will participate in the brain imaging sub-study which includes functional Magnetic Resonance Imaging (fMRI) scanning to explore the neurobiological effects of two experimental sessions.

So far, clinical trial applications were submitted to the Dutch, Czech and Norwegian ethics committees and the regulatory authorities. We received a number of questions from the regulatory bodies and despite all the questions and challenges our responses were accepted granting approval to start Phase 2 in the Czech Republic. We anticipate approval from the Netherlands authorities followed by the Norwegian approval in October 2019. We expect that the first participants could be invited for screening visits in the Czech Republic and in the Netherlands in October 2019.

In parallel, the MAPS Europe team is working on the regulatory submission activities in United Kingdom, Portugal, Finland, and Germany. We expect that the clinical trial applications in these countries will be submitted to the country-specific approving bodies between October and December 2019, with approval anticipated between February and April 2020. In clinical trials, Principal Investigators (PIs) are ultimately responsible for ensuring the accuracy and integrity of all data generated by their site, overseeing all site staff, reporting adverse events, retaining study records, among many other duties. Running a clinical research site is no easy task! Our investigators have varied backgrounds, but all have spent their careers preparing for this challenge. Each has assembled excellent teams to accomplish this research.

THE NETHERLANDS, MAASTRICHT UNIVERSITY

PRINCIPAL INVESTIGATOR: DR. KIM KUYPERS

Kim obtained her PhD at Maastricht University where she studied the effects of MDMA on cognition and driving performance in healthy volunteers. Later on, she started focusing on the positive effects of MDMA on social behaviour and since a couple of years she also studies the acute, sub-acute and persisting effects of other psychedelics like psilocybin, LSD, and ayahuasca. Her main goal is to understand the mechanism of action of these substances on the behavioural and biological level.

Dr. Kim Kuypers, Principal Investigator, The Netherlands

Maastricht is in a geographically interesting location, near the border with Belgium, where one of the three national languages is Dutch. We will welcome potential participants from both countries, especially participants who are fluent in speaking and reading Dutch, since this is the language of the study site. We are happy that

Treatment room at Maastricht University in the South of the Netherlands.

with the number of growing EU sites, MDMA-assisted psychotherapy will get more and more attention in Europe. We trust that this will help in the acceptability and normalization of the MDMA-assisted psychotherapy in society. We are very eager to start this special journey and grateful that we can be part of this historical project which will change the face of psychiatric therapy forever.

CZECH REPUBLIC, NATIONAL INSTITUTE OF MENTAL HEALTH, KLECANY

PRINCIPAL INVESTIGATOR: DR. TOMÁŠ PÁLENÍČEK

The National Institute of Mental Health (NUDZ) in Klecany, on the outskirts of Prague, originated as the Prague Psychiatric Center where Stanislav Grof began his first LSD experiments in the early 1960s. Nowadays, NUDZ is not only a psychiatric clinic but also a research center focusing on several areas of both preclinical and clinical research with neuroimaging methods. After a long ban on psychedelic research, in 2015 we managed to get approval for the first human clinical trial in the Czech Republic studying the effects of psilocybin in healthy volunteers. We are delighted to move forward not only with our neuroscientific studies but also be a part of a global community that recognizes the need for delivering psychedelic treatments to patients and are very much looking forward to taking part in the Phase 2 clinical trial of MDMA-assisted psychotherapy for PTSD.

Tomáš Páleníček, PhD, is a licensed psychiatrist and senior researcher at NUDZ. He began his career in preclinical research focusing on neurobiology of psychedelics and new synthetic drugs. At the same time he was trained in clinical psychiatry and specialized in electrophysiology. Over the past five years he has been Principal Investigator of the first projects in Czech Republic studying the acute effects of cannabis and psilocybin in healthy volunteers, and co-investigator of ketamine's fast antidepressant potential in patients with depression.

Dr. Tomáš Páleníček, Principal Investigator, Czech Republic

Research Team, Norway

NORWAY, SYKEHUSET ØSTFOLD, OSLO

PRINCIPAL INVESTIGATOR: PROF. OLE A. ANDREASSEN

The Norwegian Phase 2 study team is located close to the capital Oslo in a hospital outpatient clinic, Sykehuset Østfold. The team is staffed with head of department Ingmar Clausen, study coordinator Inger-Tove van de Vooren, two psychiatrists Stina Fasting Risbråthe and Tor-Morten Kvam, two psychologists Susanne Lund-Høie and Ivar W. Goksøyr, and a special MD advisor Lowan Stewart. Three of the therapists have now received training provided by MAPS, and the whole team is ready and committed to investigating the potential of MDMA-assisted psychotherapy in the treatment of PTSD patients.

Prof. Ole A. Andreassen, Principal Investigator, Norway

Prof. Ole A. Andreassen is psychiatrist and head of the psychiatric Center of Excellence NORMENT/Oslo funded by the Research Council of Norway. Ole A. Andreassen's scientific interests are the causes and mechanisms of severe mental disorders. He has contributed to the development of biobanks and databases, is an experienced PhD and post doc supervisor, publishes regularly in highly ranked journals and is one of the most cited researchers in Norway.

Quotation Tor-Morten Kvam:«There is a huge need for psychiatric treatment innovation, and we believe that MDMA assisted psychotherapy has the potential to relieve suffering from PTSD and possibly other conditions associated with processing of memories and emotions. We are grateful and honored to be a part of this important and cutting edge research. »

Quotation psychologist Ivar Goksøyr :"We are certainly at a very interesting point in time when it comes to this research, with so many unanswered questions. We owe it to ourselves as scientists to try and answer them as quickly as possible, so people in need can get access to new treatments. Our commitment to contribute is unconditional."

UNITED KINGDOM, CARDIFF UNIVERSITY

PRINCIPAL INVESTIGATOR: DR. MAT HOSKINS

Dr. Mat Hoskins is a Consultant Psychiatrist and trauma psychotherapist working for the National Health Service (NHS) in Cardiff, the capital city of Wales. He has also been a Clinical Lecturer for six years, training undergraduate medical students in Adult Psychiatry with Cardiff University.

Dr. Hoskins has been a member of the Cardiff University Traumatic Stress Research Group, under Professor Jonathan I. Bisson, for nearly a decade, publishing work on the efficacy of pharmacological treatments in post-traumatic stress disorder and contributing to treatment guidelines developed by the World Health Organisation and the International Society for Traumatic Stress Studies (ISTSS). Dr Hoskins has been interested in the potential for MDMA-assisted psychotherapy for many years and has worked closely with colleagues in MAPS on bringing this approach to the UK, which is now finally coming to fruition. He will serve as the PI for the Cardiff Phase 2 site in the UK, working alongside counselling and clinical therapist colleagues Chrissie Wilson, Dr. Neil Kitchener and Dr. Julie Dorey.

Dr. Mat Hoskins, Principal Investigator, UK

Dr. Hoskins: "We urgently need new treatments for our patients with PTSD, especially those who haven't responded to conventional approaches with trauma-focused therapy and medication. For my money, this is one of the cruellest and most debilitating illnesses someone can have, and we have a moral obligation to our patients to seek out and develop safe and effective new therapies. The evidence I've seen so far for MDMA-assisted therapy is truly impressive and fills me with hope. Having my own clinical MDMA therapy session a few years ago with Annie and Michael Mithoefer, as part of our therapist training, was a wonderful experience, and helped me integrate what I'd already learned from MAPS in their comprehensive training. My passion is ultimately the NHS, and making sure that, if the evidence continues to support MDMA-assisted therapy, this treatment will be available free at the point of use for those who would benefit from it in the UK. I'm very grateful to MAPS and my colleagues for their support".

This is an amazing journey and we are very grateful for all the support that we are receiving from all the site personnel, study coordinators, therapists, physicians, cardiologists, and technicians involved. Of course, none of this would be possible without the help, support, and engagement of our Principal Investigators, ethics committees and regulatory bodies who challenge us but at the same time are open to a new treatment modalities. Also big thank you to all donors and people who trust that MDMA assisted psychotherapy can improve life's of those suffering from PTSD. Together we are making a change!

If you would like to be involved please note that MAPS Europe team is searching for experienced Clinical Research Associates in Portugal, Finland and Germany, and Independent Raters in Portugal, Finland, Germany and Norway. Lastly, a position for Video Systems Support specialist is also currently open. Please see the MAPS Europe website for additional info: **https://mapseurope.eu/careers**

Marta Mazur, M.Sc. *earned a master's and engineer degree in Biomedical Engineering from the Wroclaw University of Technology in Poland and a master's degree in Natural Medical Sciences from the Free University in Amsterdam, The Netherlands. Marta brings more than 16 years of experience advising on the clinical strategy, developing and managing all phases of clinical research studies in Europe, Asia Pacific, USA and the rest of the world. During her career Marta worked with different pharmaceutical (Novartis, GSK) and biotechnological companies (Genzyme, Sanofi-Aventis) and in Clinical Research Organizations (Parexel and Quintiles) overseeing immunology, oncology, cardiology and rare metabolic diseases studies from the protocol writing stage to the product licensure. In addition, Marta is a certified yoga and meditation teacher and is passionate about the human body and its healing abilities. In her free time, she can be found in nature, gardening, picking herbs and studying naturopathy. Marta is currently serving as the Clinical Program Lead for MAPS Europe, leading the clinical operations team in Europe. Marta is passionate about psychedelic research and is confident that MAPS' work will transform the lives of those suffering from PTSD.*