Pinney Associates

May 31, 2024

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852
Via https://www.regulations.gov

Re: Docket No. FDA-2024-N-1938 for Psychopharmacologic Drugs Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments – Midomafetamine Capsules

Dear Food and Drug Administration and Psychopharmacologic Drugs Advisory Committee,

I am Jack Henningfield, Vice President, Research Health Policy & Abuse Liability at Pinney Associates in Bethesda, Maryland. I am also Adjunct Professor of Behavioral Biology, Part-time, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine.

My work over more than 40 years has involved abuse potential and pharmaceutical development, and over the past decade has included the scientific and regulatory support of the research and development of psychedelic substances and products, including 3,4-Methylenedioxymethamphetamine (MDMA), for sponsors including the Multidisciplinary Association for Psychedelic Studies (MAPS) and Lykos Therapeutics (see more at www.PinneyAssociates.com). My opinions are my own and no pharmaceutical sponsor has had input or has provided financial support for my comment. Additionally, these comments were not vetted with anyone outside of our company, nor did any outside organization compensate us for our time to prepare these comments.

I support the approval of MDMA for the treatment of post-traumatic stress disorder (PTSD). Phase 2 and 3 studies have demonstrated efficacy and, equally importantly, the studies have shown that it can be used safely under various conditions and approaches to therapeutic use that have been employed. These findings provide a foundation for labeling and risk evaluation and mitigation strategies, referred to as REMS, as well as elements to ensure safe use (ETASU) that should be considered in the Food and Drug Administration's (FDA's) benefit-risk evaluation for approval decisions.

See the comment on this docket by my colleague, Dr. Marion Coe, for additional discussion of the need and benefits of a REMS for an approved MDMA product for PTSD.

MDMA is a Schedule I substance under the Controlled Substances Act (CSA) and has remained so during development for medicinal use. Approval of an MDMA drug product for therapeutic use by FDA would necessitate rescheduling to one of the four CSA schedules reserved for drug products that are approved by FDA for therapeutic use or otherwise determined to meet criteria for commonly accepted medical use (CAMU).

Rescheduling of the Lykos Therapeutics drug product would not necessarily apply to MDMA in forms that have not been approved or accepted for CAMU (see discussion of such regulatory issues by Henningfield, Coe, Griffiths et al. 2023).

My team at Pinney Associates has contributed to the Lykos Therapeutics abuse potential assessment and eight factor analysis that is determinative of scheduling with MAPS researchers and has presented these analyses at scientific meetings (Coker, A, Yazar-Klosinski, B., Emerson et al. 2020; Henningfield, 2022).Those analyses and subsequent comments from other abuse potential and CSA scheduling experts suggest that the overall abuse potential and other safety-related risks of MDMA are lower than that of Schedule II stimulants, however, whether it is sufficiently lower as to merit less restrictive scheduling is not universally agreed upon by external experts.

We hope that FDA's rescheduling recommendations will avoid unnecessarily restrictive scheduling and/or burdensome REMS requirements, which could hinder access to those who could benefit from the potentially life-saving benefits of this medication assisted therapy. Such barriers can contribute to exacerbating already existing health disparities related to ethnic/racial factors, geographic location, and economic means.

There is a well-established connection between lower socioeconomic status and higher levels of mental health diagnoses including PTSD. Thus, we urge that FDA's rescheduling recommendation and REMS requirements will take into consideration the importance of not making access to MDMA so restrictive through CSA scheduling and the REMS so as to pose unnecessarily burdensome barriers to use and access to those who could benefit from the potentially life-saving benefits of this medication assisted therapy. This would only serve to worsen existing health care disparities, which again are often related to ethnic/racial factors, geographic location, and economic means.

As I have testified at other FDA meetings, I recommend that all policies, including CSA scheduling and REMS, should take into account the potential impacts on disparities in healthcare access. In this regard, Advisory Committee members, FDA, and other stakeholders might take into consideration the peer reviewed Neuropharmacology commentary in a special issue addressing psychedelics that addressed "policy considerations that support equitable access to responsible, accountable, safe, and ethical uses of psychedelic medicines" (Belouin, Averill, Henningfield, et al., 2023; Also see Yaden, Griffiths & Potash, 2023; Yaden, Yaden & Griffiths, 2021)

We must keep in mind that PTSD contributes to disability, health care costs, and homelessness and appears to likely to contribute to many of our nations approximately 50,000 suicides per year, including nearly 20 suicides per day among veterans and 10 suicides per week among active military personnel in recent years. (Estimates vary but these are from US Vital Statistics and Veterans Affairs [VA] data). We note that Lykos Therapeutics' studies included veterans, and we also note that the National Defense Authorization Act for fiscal year 2024 authorized the study of psychedelic substances, including MDMA, in military populations by the Department of Defense (Veterans News, 2024).

In conclusion, we note that the Lykos Therapeutics' MDMA based drug product administered within the context of behavioral and cognitive therapy has been shown to have unprecedented success in alleviating PTSD, one of the most intractable mental health conditions affecting millions of people in need. Approval of MDMA, with

appropriate CSA scheduling and post-marketing commitments, could substantially advance our nation's efforts to address PTSD.

It is worth reiterating that we must keep in mind that PTSD contributes to disability, health care costs, and homelessness; PTSD also appears likely to contribute to many of our nation's approximately 50,000 suicides per year, which includes nearly 20 suicides per day among veterans and 10 suicides per week among active military personnel in recent years. (Estimates vary but these are from US Vital Statistics and VA data). The approval of MDMA for the treatment of PTSD, with appropriate CSA scheduling and REMS surveillance, could provide tremendous public health benefit for those in our country suffering from this condition.

Thank you very much for the opportunity to provide these comments. Please contact me at jhenning@pinneyassociates.com or 301-718-8440 if you have any questions or need further information.

Sincerely,

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Pinney Associates, Inc.
and
Adjunct Professor of Behavioral Biology, Part-time
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CITATIONS

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Coker, A, Yazar-Klosinski, B., Emerson, A. Doblin, D., Coe, M., and Henningfield, J. Making MDMA a Medicine: Analysis of the 8-factors of the Controlled Substances Act for the Abuse Potential of MDMA. American College of Neuropsychopharmacology Annual Meeting in San Juan, Puerto Rico, December 4-7, 2021.

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