Lykos Therapeutics - News Release Archive

Lykos Therapeutics Statement on FDA Advisory Committee Meeting

Dear Colleagues,

As you know, Lykos is entering the final stages of a multi-year effort to study and apply for approval from the U.S. Food and Drug Administration (FDA) for midomafetamine (MDMA) capsules used in combination with psychological intervention ("MDMA-assisted therapy") for the treatment of post-traumatic stress disorder (PTSD) in adults. Our work takes place against the backdrop of a national PTSD crisis, with an estimated 13 million Americans suffering from this condition, including millions of veterans and survivors of sexual assault and domestic abuse. Effective treatment options are unfortunately limited, and an estimated 40% to 60% of patients with PTSD do not experience remission.[1] No new PTSD treatment has been approved by the FDA in nearly 25 years.

Lykos' guiding compass is to research and develop midomafetamine-assisted therapy as a potential new treatment for PTSD. We have conducted significant scientific research and development, including execution of two Phase 3 trials as required by the FDA for approval of new treatments.

Last week, the FDA Psychopharmacologic Drugs Advisory Committee (PDAC) met to discuss midomafetamine. While we were of course disappointed by the outcome, we were not surprised by the important questions raised. We are advancing a novel treatment and have worked closely with the FDA over the course of years to address these complex issues. Ultimately, the final decision for the potential approval of midomafetamine rests with the FDA, and we are deeply committed to providing any information needed to enable its thorough review. We have full confidence in the rigor and thoughtfulness that the FDA will give our application.

In addition, we acknowledge that several issues raised during the PDAC meeting have now become the focus of public dialogue. This is a new and complex treatment that raises unique and important questions. We feel it is important to share the company's perspectives related to key points which were raised.

- **Evidence of Effectiveness:** We are confident that our application provides evidence of the clinical effectiveness of midomafetamine in treating adults with PTSD. It includes two multi-site, randomized, placebo-controlled, Phase 3 clinical trials, both of which met their primary and secondary endpoints. Participants in the treatment group showed clinically meaningful improvement in their symptoms relative to participants in the control group. This difference was statistically significant with subsequent evidence of durability in a long-term follow-up study.
- **Functional Unblinding:** This was cited as a core concern and a potential source of bias at the PDAC meeting. Functional unblinding is a known research challenge for psychiatric drugs with psychoactive effects.[2] It was discussed extensively with the FDA during the 2017 Special Protocol Assessment (SPA) process to agree on our Phase 3 trial design. While there is no perfect solution to functional unblinding, we took many steps to minimize its potential impact, including the use of independent, blinded third-party clinician raters to assess outcomes. The weight of evidence suggests a very low likelihood that the observed midomafetamine effect can be adequately explained by functional unblinding.
- **Prior MDMA Use:** PDAC members raised questions regarding potential bias of the Phase 3 study population given a subset of participants reported limited pre-study use of illicit MDMA. The data indicates that prior illicit MDMA use had no impact on the results, as there was no meaningful difference in primary outcome measure (change in CAPS-5) or adverse events reported between the subgroup of Phase 3 participants who reported prior illicit MDMA use and the subgroup of participants who did not.
- **Psychological Intervention in Research Protocol:** As agreed in Lykos' SPA, the Phase 3 protocol included psychological intervention delivered alongside midomafetamine or placebo. Significant steps were taken to ensure standardization and consistency in the psychological intervention across therapists, sites, and treatment

groups, and to thus allow for valid comparison between the midomafetamine and placebo groups. This consistency is supported by the lack of variability in treatment outcomes between Phase 3 clinical sites.

- **Regulation of Psychological Intervention if Midomafetamine is Approved:** The PDAC meeting included questions regarding the regulation of psychological intervention delivered with midomafetamine, if approved. The practice of psychotherapy is already a regulated field with mandatory reporting requirements and oversight provided by licensing boards and professional societies. We expect that healthcare professionals providing psychological intervention with midomafetamine, if approved, will utilize their clinical judgment to effectively deliver treatment, with appropriate oversight from these governing bodies. This will be in addition to controls and requirements set forth in the product labeling and the Risk Evaluation and Mitigation Strategy (or REMS) program.
- **Cardiovascular and Hepatotoxicity Risks:** The PDAC raised questions regarding potential cardiovascular issues and hepatoxicity related to the administration of midomafetamine. We will continue to work with the FDA to characterize the data and/or collect new data to address these potential risks, if required. As we stated during the PDAC meeting, we are confident that these can be safely addressed in a post-marketing environment.
- **Sponsor and Investigator Bias:** Several committee members raised questions about recent allegations of sponsor and investigator bias as reported in the media. This included questions about the recruiting and enrollment processes utilized in Lykos' Phase 3 program. Like all research sponsors, Lykos and its clinical sites are subject to regular FDA inspections. We have full confidence in the FDA to continue to assess the integrity of Lykos' research through its inspection process.
- **Therapist Misconduct:** We would like to address a case of therapist misconduct during a 2015 Phase 2 trial that received attention at the PDAC meeting. This was a terrible and harmful instance of malpractice that caused profound suffering to a participant. Lykos reported this violation to Health Canada, the FDA, and the relevant Institutional Review Board and banned the therapist pair associated with this case from all future work. Since then, we carefully developed and implemented new policies and practices aimed to prevent, detect, investigate, encourage reporting of, and thoroughly respond to potential instances of misconduct or unethical behavior. We investigate all allegations and complaints of misconduct. Lykos has implemented independent channels for individuals to report misconduct, and these will be expanded to suit the post-marketing environment if midomafetamine is approved.

Over the coming weeks, we will continue to collaborate with the FDA and will answer all questions they have to help inform their decision-making process. Misinformation has been circulated about our program, and we want to clarify that the FDA has received all data and supporting documentation. It is our hope that this letter provides a useful summary that is responsive to some of the most commonly asked questions.

We continue to deeply appreciate the profound support of all those stakeholders who are committed to improving outcomes for those suffering from PTSD. Unfortunately, effective treatment options remain limited for the millions of people who suffer every day.

Thank you,
Amy Emerson, CEO, Lykos Therapeutics

Midomafetamine (MDMA) capsules have not been approved by any regulatory agency. The safety and efficacy of midomafetamine have not been established for the treatment of PTSD. Investigational midomafetamine is also being studied in other indications.

[1] Steenkamp et al, 2015; Bradely et al, 2005; Brady et al, 2000

[2] Relevant examples of approved products that faced issues of functional unblinding include the trials for clozapine and esketamine.

Full References

Steenkamp MM, Litz BT, Hoge CW, Marmar CR. Psychotherapy for military-related PTSD: a review of randomized clinical trials. JAMA. 2015;314(5):489-500.

Bradley R, Greene J, Russ E, Dutra L, Westen D. A multidimensional meta-analysis of psychotherapy for PTSD. Am J Psychiatry. 2005;162(2):214-227.

Brady K, et al. Efficacy and safety of sertraline treatment of post-traumatic stress disorder: a randomized controlled trial. JAMA. 2000;283(14):1837-1844.

---

https://news.lykospbc.com/2024-06-13-Lykos-Therapeutics-Statement-on-FDA-Advisory-Committee-Meeting