**VIA ELECTRONIC DELIVERY**

August 13, 2024

Robert M. Califf, MD
Commissioner
U.S. Food and Drug Administration
5630 Fishers Lane
Rockville, MD 20852

**RE: Docket No. FDA-2024-N-1809 for "Listening Session: Optimizing FDA's Use of and Processes for Advisory Committees"**

Dear Dr. Califf:

On behalf of Lykos Therapeutics (Lykos), a development stage pharmaceutical company, we appreciate the opportunity to provide comments to the Food and Drug Administration (FDA) in support of its ongoing efforts to optimize the use and processes for Advisory Committees.

The use of advisory committees aims to provide FDA with independent expert advice and nonbinding recommendations on complex scientific, technical, and policy issues. Among other things, concerns about the adequacy of expert qualifications under the existing conflict of interest rules and public misconceptions about the role of the advisory committees in the drug approval process have prompted FDA to evaluate them. As part of these efforts, FDA opened Docket No. FDA-2024-N-1809 to solicit feedback from stakeholders on the use of and processes for advisory committees during a public listening session, held on June 13, 2024, and through written comments to the docket. Lykos appreciates the FDA's efforts to address the issues identified with the advisory committee system.

On June 4, 2024, Lykos had the opportunity to participate in an advisory committee as the sponsor of the new drug application (NDA) for midomafetamine capsules in combination with psychological intervention for the treatment of post-traumatic stress disorder in adults. The comments below are informed by our experience with the June 4, 2024, advisory committee meeting. We provide these written comments with the shared goal of improving public perception of the role of voting and purpose of these meetings and ensuring the utility of the advice received by re-evaluating the procedures around committee composition and roles.

Committee Member Qualifications and Representation

- The agency should ensure the advisory committee members, whether sitting or temporary, include individuals who are qualified in the disease/condition and other issue areas under review, *e.g.*, real world experience implementing REMS (Risk Evaluation and Mitigation Strategy) programs (if appropriate), prescribing controlled substances, treating the relevant patient population, etc. Committee members should be able to provide advice based on experience with the issue areas where the FDA is seeking guidance, so that the advice is effective and meaningful to the agency.

- A patient or caregiver representative from the specific disease/condition should be included on each advisory committee panel for each meeting. The patient or caregiver representative should have lived experience with the disease/condition under review to

adequately speak to the risk/benefits for the specific patient population. This representation should be considered separate from the consumer representative that currently exists as a committee position.

- The distinction between consumer and patient representatives should be made clear. The standards for recruitment, expectations for participation, and voting privileges should also be made clear between the two types of representatives. Currently, there seem to be more restrictions on participation for patient representatives than consumer representatives.

- FDA should reevaluate conflict of interest procedures for identifying advisory committee members. Current no-conflict requirements prevent participation by most leading experts. This becomes increasingly challenging when the subject matter has a small pool of expert physicians and researchers. Full transparency, along with eliminating the non-binding vote, could enable relevant experts to participate on the advisory committee notwithstanding their other relationships.
- To augment the panel representation, FDA should ensure the inclusion of patient experience data (PED), if available, in the agency's background materials and presentation, in accordance with the 21st Century Cures Act and the FDA Reauthorization Act of 2017 (FDARA) Title I. When possible, the agency should prioritize convening of Patient Listening Sessions (or Patient-Focused Drug Development Meetings) for disease areas under review prior to the scheduled advisory committee meeting to assure the findings are included in the background materials and presentation by the agency.
- All members should be required to read all briefing documents and have a command of the information.

Role of the Committee Chair

- The advisory committee chair or designated meeting facilitator should be a neutral, independent position filled by agency employees or Reagan-Udall Foundation employees with experience facilitating effective large meetings with external participants. The agency and its affiliated Foundation have experienced facilitators who have effectively facilitated productive workshops on complex issue areas like the June 27, 2024, hybrid workshop, "Understanding Current use of Ketamine for Emerging Areas of Therapeutic Interest".[1] The facilitator should be able to conduct the meeting with the necessary balance to keep the focus on the available scientific evidence/data and the disease/condition area under review.

- Unintended consequences can occur when the discussion moves away from review of the evidence, as seen during the June 4, 2024, Psychopharmacologic Drugs Advisory Committee meeting for Lykos Therapeutics' NDA for midomafetamine capsules in combination with psychological intervention for the treatment of post-traumatic stress disorder in adults. The FDA/committee chair should emphasize that speakers

[1] https://reaganudall.org/news-and-events/events/understanding-current-use-ketamine-emerging-areas-therapeutic-interest

participating in the Open Public Hearing (OPH) shall disclose their affiliations with all relevant organizations. Unsubstantiated claims and unfounded accusations, unrelated to the data in Lykos' New Drug Application, were made during the OPH and persisted during the Committee discussion.[2] The final discussion and subsequent advice from the committee were in part guided by issues unrelated to the data in Lykos' NDA and likely outside the advisory committee's remit.[3]

Role of Voting

- The advisory committee is a mechanism for the FDA to gain expert advice to support the complex review process and evaluation of a drug, biologic, or medical device. A final vote may not be the most effective way to gather expert advice for the agency's/department's consideration. The agency could consider alternative measurement tools, like a Likert scale[4], be used in place of a vote to enable committee members to effectively assess the briefing submissions.

- As the FDA has noted publicly, it is important to reevaluate the voting component of the advisory committee or at least eliminate voting on questions that are the agency's responsibility for weighing benefit/risk of proposed products and their indications. Non-binding voting at the end of a meeting gives a sense that the advisory committee is deciding with binding power and finality by the committee, which is not the case. An advisory committee's perceived ability to make a final decision creates confusion for the public and especially patients waiting for much needed treatment options. The public should understand that the committee is an external entity, not part of the FDA, nor the ultimate deciding body for approval.

- There is little public awareness or understanding of the role of FDA advisory committees for those not involved in pharmaceutical development. Many perceive the advisory committee to be a functional decision-making body within the agency versus a truly neutral body of outside experts providing advice, with limited access to the primary data.

Thank you for the opportunity to share our recommendations, perspectives, and experiences with you on ways to optimize FDA advisory committees to support the advancement of safe and effective treatment development for patients and communities in need.

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[2] See FDA, June 4, 2024 Meeting of the Psychopharmacologic Drugs Advisory Committee (PDAC), YouTube (June 4, 2024) at 2:00:49, https://www.youtube.com/live/JqQKP8gcY1E (referencing a "high-profile" report from ICER and asking "When was Lykos made aware of the allegations of sexual misconduct noted in the ICER Report, and what steps did Lykos take to investigate?") (hereinafter PDAC Meeting Video); see also ICER, Draft Report, 3,4-Methylenedioxymethamphetamine Assisted Psychotherapy for Post-Traumatic Stress Disorder (PTSD) (March 26, 2024), https://icer.org/wp-content/uploads/2024/03/PTSD_Draft-Report_For-Publication_03262024.pdf (hereinafter ICER Draft Report).

[3] See, e.g., PDAC Meeting Video at 2:06:32 (asking if the therapeutic model is proprietary to Lykos); id. at 2:02:51, 2:03:20, and 4:24:55 (raising allegations that Lykos had discouraged participants from enrolling in the long-term followup study). Other remarks made clear that committee members had read and were relying on the ICER report. Compare PDAC Meeting Video at 8:15:52 ("There's a movement, there's a lot of hype") and at 2:06:53 ("There's a pro-movement, a lot of emphasis on the psychedelic") with ICER Draft Report at 6 ("We heard from various people that feelings around psychedelics lead the community to engage with them more like a religious movement than like pharmaceutical products, that these feelings were common in those participating in the MAPP trials, and that these feelings were sometimes inculcated in patients participating in the trials.").

[4] Likert, R., (1932). The method of constructing an attitude scale. Archives of Psychology, 140, 44-53.

Sincerely,

*Electronically signed by: amy Emerson*
*Reason: I am the approver of this document*
*Date: Aug 13, 2024 15:42 PDT*

Amy Emerson
Chief Executive Officer
Lykos Therapeutics