FDA rejects MDMA-assisted therapy for PTSD treatment—a researcher explains the challenges psychedelics face

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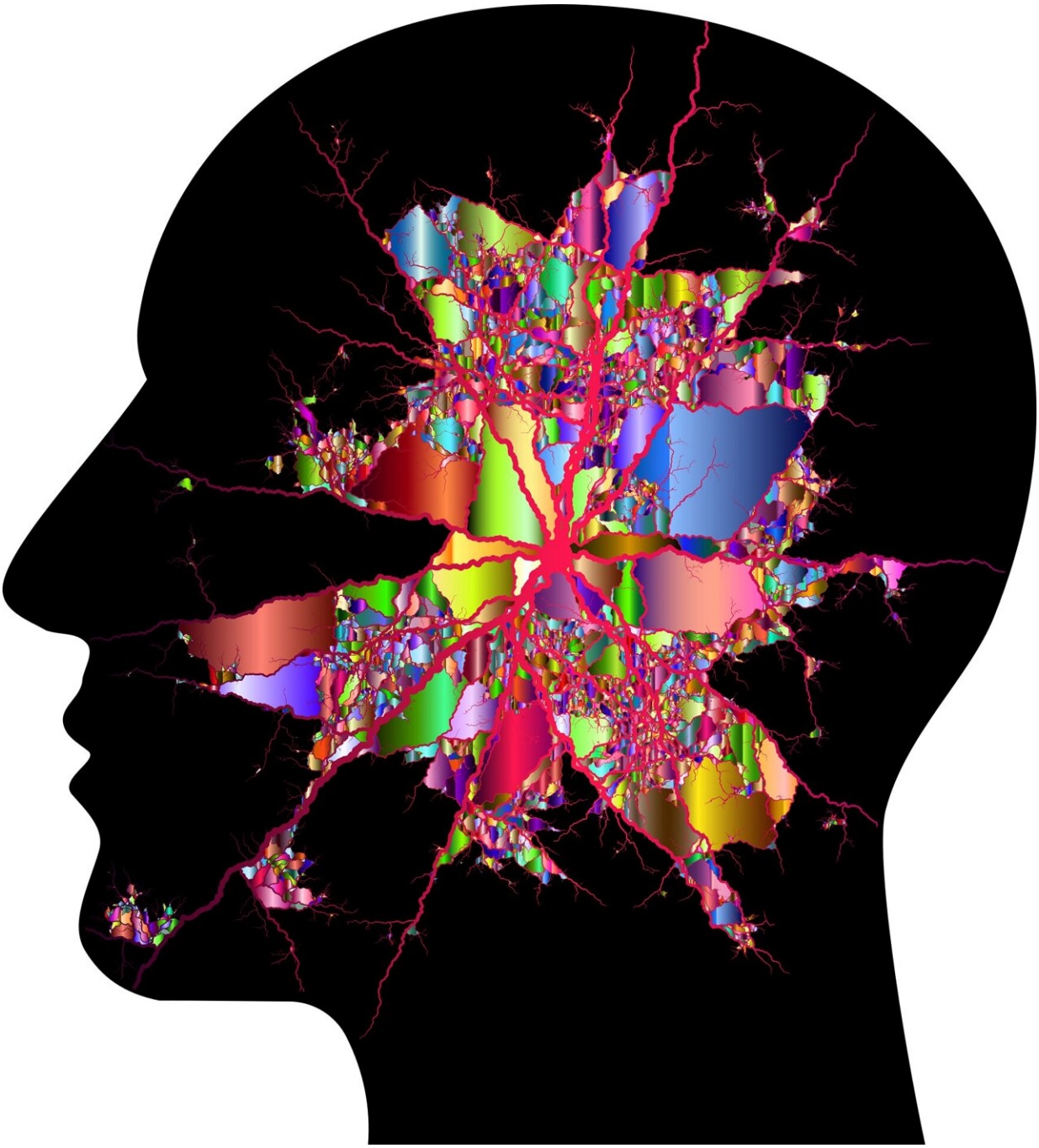

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Drugmaker Lykos Therapeutics announced on Aug. 9, 2024, that the

Food and Drug Administration declined to approve the company's application for the use of MDMA-assisted therapy in the treatment of post-traumatic stress disorder. It is the first such decision issued on a psychedelic drug application.

Many investors and researchers have been predicting a psychedelics boom, with MDMA being just the first of a number of psychedelics in the drug development pipeline.

The FDA's decision has disappointed psychedelic therapy advocates, and the stock prices of psychedelic industry leaders tumbled with the announcement. But the FDA did make recommendations as to how the application could be improved in such a way that MDMA might receive future approval.

Yet another setback came days later when the journal *Psychopharmacology* retracted three papers related to MDMA-assisted therapy, citing "protocol violations amounting to unethical conduct," particularly in one clinical trial.

The Conversation asked drug researcher Benjamin Y. Fong from Arizona State University about what the FDA's decision entails and what it means for the future of psychedelic medications.

What is MDMA, and what types of conditions could it treat?

MDMA, or midomafetamine, is known colloquially as "molly" or "ecstasy." It is technically an amphetamine—like the drug in the attention-deficit/hyperactivity disorder medication Adderall—but MDMA is often categorized as a psychedelic. It is considered to be more pleasure-inducing than other amphetamines, and for this reason, it has

been a popular party drug. Some researchers call MDMA an "empathogen," or a "feeling enhancer."

While MDMA is currently a Schedule I drug—meaning that the Drug Enforcement Administration considers it to be highly dangerous with no accepted medical use—a number of clinical trials point to the benefits of using MDMA in combination with talk therapy for patients suffering from PTSD. The FDA granted "breakthrough therapy" status to MDMA-assisted therapy in 2017, which sped along its development and review.

PTSD affects between 9 million to 13 million people annually in the U.S., and no novel treatments for the condition have been developed in the past 20 years.

Lykos Therapeutics filed an application for FDA approval of its version of MDMA-assisted therapy for PTSD in February 2024. In it, the drug is paired with a type of psychotherapy intended to bring out a patient's "inner healing intelligence," which Lykos defines as "a person's innate capacity to heal the wounds of trauma."

Why did the FDA decline approval of Lykos' MDMA-assisted therapy?

In June 2024, an FDA advisory committee voted overwhelmingly against the idea that the relevant clinical trials had proved the efficacy of MDMA for the treatment of PTSD. Just as decisively, the panel also voted against the idea that the benefits had been shown to outweigh the risks, such as increased blood pressure and abuse potential.

At that time, the advisory committee took issue with several aspects of Lykos' application. First, it noted the problem of "functional unblinding," which is the fact that most people participating in the trial

would know if they are on a powerful psychoactive substance or not, biasing the results. This is a problem for any psychoactive medication, and Lykos critics believe the company should have followed FDA guidance that it use an "active placebo"—a placebo that also has psychoactive effects—for comparison in its previous clinical trials.

The panel also raised questions about the form of psychotherapy used alongside MDMA, as well as ethical concerns about various forms of misconduct in Lykos' trials. In one of the company's studies, a participant reported sexual misconduct by the therapists involved.

The FDA is not bound by the votes of such advisory bodies, but it typically follows their guidance. So the decision on Friday was no great surprise.

What does the FDA's decision mean for the future of MDMA?

The FDA requested an additional phase 3 study, the stage of clinical trials that rigorously demonstrates the safety and efficacy of a particular treatment in comparison to standard treatment.

Lykos stated that it will request a reconsideration of the decision and discuss the FDA's recommendations with the agency to ensure that the company is on the right path forward.

Lykos CEO Amy Emerson, who called the decision "deeply disappointing," says she believes it will take "several years" to conduct the new trial.

But with the journal Psychopharmacology's retraction of three papers related to this work, Lykos has a difficult road ahead of it.

How might this decision affect other psychedelic drugs' approval?

One prominent psychedelics company, Compass Pathways, is generally considered next in line for FDA approval of a psychedelic drug, with phase 3 clinical trials for its synthetic psilocybin well underway. There are other companies preparing for phase 3 trials of their own proprietary compounds.

In the wake of the advisory panel judgment in June, Compass noted that it is not pairing its drug with therapy in the way Lykos has. Another company claimed that it has a "better trial design that is more in line with FDA guidance."

Other psychedelics companies clearly believe they can still succeed where Lykos has not.

Do psychedelics face unique challenges?

The FDA's decision was more about Lykos' specific approach than an outright rejection of psychedelics for therapeutic use.

But psychedelic drug development is a fraught process by nature. The drugs involved induce a severely altered state that puts people in a vulnerable position. Some people in the industry that I have spoken to believe it's nearly impossible to avoid accusations of impropriety, given the nature of the experience.

Most research also pairs psychedelic drugs with some form of therapy or facilitation, and as the FDA has made clear, its role is to assess drugs, not the psychotherapies that might go along with them.

The interaction between the drugs and the human element involved in the treatment is the subject of some debate. Lykos' missteps in its application to shine a light on some of the ways that companies involved in psychedelic drug development face unique obstacles on the way to FDA approval.

Provided by The Conversation