FDA panel backs much-debated ALS drug in rare, 2nd review

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This 2018 photo provided by Amylyx shows the company's co-founders Joshua Cohen, left, and Justin Klee in Cambridge, Mass. on Sept. 2, 2022. A closely watched experimental drug for Lou Gehrig's disease is getting an unusual second look from U.S. regulators on Wednesday, Sept. 7, 2022, amid intense pressure to approve the treatment for patients with the fatal illness. Patients and their families have rallied behind the drug from Amylyx Pharma, launching an aggressive lobbying campaign and enlisting members of Congress to push the Food and Drug Administration to grant approval. Credit: Amylyx via AP, File

A panel of federal health advisers voted Wednesday to recommend approval for an experimental drug to treat Lou Gehrig's disease, a remarkable turnaround for the much-debated medication that was previously rejected by the same group earlier this year.

The Food and Drug Administration advisers voted 7-2 that data from Amylyx Pharma warranted approval, despite hours of debate about the strength and reliability of the company's lone study. The FDA is not required to follow the group's advice, but its positive recommendation suggests an approval is likely later this month.

The FDA has approved only two therapies for the disease, amyotrophic lateral sclerosis, or ALS, which destroys nerve cells needed for basic functions like walking, talking and swallowing.

ALS patients and their families have rallied behind Amylyx's drug, launching an aggressive lobbying campaign and enlisting members of Congress to push the FDA to grant approval.

Despite a negative review published by FDA's internal scientists ahead of the meeting, a majority of the outside panelists said Amylyx had presented enough evidence to suggest the drug is helping patients live longer. The same group of neurology experts narrowly voted against the drug in March, due to concerns about missing data and other issues in the company's study.

"To deprive ALS patients of a drug that might work, it's probably not something I would feel terribly comfortable with," said Dr. Liana Apostolova of Indiana University's School of Medicine, who voted for approval. "At the previous meeting it wasn't that clear and it's still questionable."

Amylyx also appeared to benefit from an unusual exchange in which a company executive—at the FDA's request—committed to pull the drug from the market if its benefits aren't confirmed by a large, ongoing study.

"I'm somewhat assured that if an approval is issued it can be withdrawn in the future," Apostolova noted.

Wednesday's vote concluded a rare second meeting to review several new statistical analyses submitted by Amylyx in support of the treatment's benefit in slowing disease and extending life.

The ALS drug review is being closely watched as an indicator of FDA's flexibility in reviewing experimental medications for the terminally ill and its ability to withstand outside pressure.

Dr. Billy Dunn, FDA's neurology review chief, opened the meeting by detailing the "concerns and limitations" with Amylyx's data, while emphasizing the need for new treatment options.

"We are highly sensitive to the urgent need for the development of new treatments for ALS," Dunn said.

Dunn also noted that a larger Amylyx study being conducted in the U.S. and Europe could provide "more definitive results" by 2024.

In a highly unusual move, Dunn suggested the agency might be more willing to approve the drug if Amylyx would commit to withdrawing its medication if the ongoing 600-patient trial fails to show a benefit. He then called on the company's co-founders to publicly commit to that step, and Amylyx co-CEO Justin Klee said the company would voluntarily withdraw its drug in that scenario.

The FDA has the power to force companies to pull drugs from the market, though it's generally faster if drugmakers voluntarily take that step. In cases where companies resist removal the regulatory process can drag on for years.

"I think the FDA—with all due respect—significantly understates the complexity and likelihood of their pulling the product from the market," said Dr. Caleb Alexander of Johns Hopkins University, one of the two panelists who voted against the drug.

Amylyx conducted one small, mid-stage trial of its drug that showed some benefit in slowing the disease, but it was plagued by missing data and other problems, according to FDA reviewers.

"The final result—for a single study—is borderline and not very statistically persuasive," FDA statistician Tristan Massie told panelists.

The Cambridge, Massachusetts, company says follow-up data gathered after the study concluded showed the drug extended life. Patients who continued taking the drug survived about 10 months longer than patients who never took the drug, according to a new company analysis.

Panelists favoring the drug cited that data, along with the drug's mild side effects, to suggest there would be little downside for patients even if it doesn't ultimately slow ALS.

"The drug is not harmful—it seems like it has a benefit—there's no safety signal here," said Dean Follmann, a biostatistician with the National Institutes of Health.

Earlier Wednesday, more than 20 ALS researchers, patients and family members told the advisers they supported approval. The agency has also received more than 1,200 written comments, largely from ALS patient

advocates.

"I'm asking you to approve it because I know it works. It's extending my life and I want that for others," said Greg Canter, who was diagnosed with ALS in 2018 and participated in Amylyx's study. He credits the drug with improving his lung capacity and slowing his functional decline.

Amylyx's medication comes as a powder that combines two older drugs: one prescription medication for liver disorders and a dietary supplement used in traditional Chinese medicine.

Hanging over the review is FDA's controversial approval of the Alzheimer's drug Aduhelm last year, which was reviewed by the same agency scientists and outside advisers.

In that case, the FDA disregarded the overwhelmingly negative vote by its outside advisers, three of whom resigned over the decision. The agency's approval—which followed irregular meetings with drugmaker Biogen—is under investigation by Congress and federal inspectors.