Stakes are high ahead of FDA panel vote on ALS drug

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Advocacy groups are pressing U.S. federal regulators to fast-track

approval of an experimental drug treatment for the deadly neurological disease ALS (amyotrophic lateral sclerosis), with a decision expected this week.

The push to approve the drug, so far just called AMX0035, is based on partial data from clinical trials and follows the U.S. Food and Drug Administration's controversial approval last year of the Alzheimer's drug Aduhelm. Many of the FDA's own advisors said the costly Alzheimer's drug was unlikely to help patients.

But advocacy groups for patients with ALS are pushing hard for approval of AMX0035. They say the need is urgent.

Most people with ALS, also known as Lou Gehrig's disease, die of respiratory failure within three to five years, according to the U.S. National Institutes of Health. The disease destroys nerve cells needed to walk, talk, swallow and eventually breathe, steadily robbing patients of movement until they're locked inside their own bodies.

AX0035 is an experimental combination drug that has been shown to extend survival for ALS patients.

An FDA advisory committee is scheduled to meet Wednesday to consider a request from AMX0035's maker, Amylyx Pharmaceuticals, to skip the usually required phase 3 clinical trial and approve its drug based on earlier results.

The drug company's request is supported by the ALS Association, one of the main advocacy and research groups devoted to finding a cure for this disease.

"The community has been asking for a long time that the FDA approve the drug before that [phase 3] trial is complete," said Neil Thakur, chief

mission officer of the ALS Association. "And the reason why is because of a combination of strong clinical benefit and safety data that we've seen for this this drug."

AMX0035 has been shown in early clinical trials to extend ALS patients' lives by about six and a half months, Thakur said.

The drug also slows disease progression in patients by about 25%, said Dr. James Berry, director of the Massachusetts General Hospital's Neurological Clinical Research Institute in Boston and a principal investigator in the AMX0035 trials.

"ALS is a disease that doesn't give us a lot of time to sort of stop and consider," Berry said. "We really need to move when we see something that looks this promising without a safety concern and with a very well-run study that shows us both survival and function benefit."

AMX0035 is a combination of two established drug ingredients—sodium phenylbutyrate and taurursodiol.

Sodium phenylbutyrate is sold under the brand name Buphenyl to treat liver diseases, while taurursodiol is a dietary supplement used in ancient Chinese medicine. Some ALS patients already take both drugs. FDA approval would likely compel insurers to cover the treatment.

The drugs are known to affect different aspects of ALS, Berry said.

"The idea was if we took two drugs that sort of fix two different pathways we know are being affected in ALS, they had a chance of having a synergistic effect—one plus one equals three," Berry said.

Until late last year, the FDA had insisted that Amylyx complete ongoing phase 3 trials before seeking approval for AMX0035.

In December, the agency relented and began a priority review of the drug application, setting June 29 as the target date for a decision.

Phase 2 trials are typically meant to gather safety data and any early signals that would indicate whether a treatment works. Whether a drug actually benefits patients usually isn't established until phase 3 trials. Phase 3 trials involve many more people so the results are more concrete.

The FDA's decision to fast-track consideration of AMX0035 follows its controversial approval of Aduhelm for Alzheimer's patients.

The agency approved Aduhelm under pressure from advocacy groups and the drug's maker, despite mixed clinical trial results and an advisory panel's recommendation against it.

The advisory panel meeting Wednesday is the same group that recommended against Aduhelm. After the FDA overrode its advice, three members resigned in protest.

Some experts are questioning whether the FDA is repeating itself with AMX0035, doing further damage to its scientific credibility by again accepting weaker evidence for a drug touted by disease advocates and drugmakers.

"This is what many people were concerned about in terms of the precedent for FDA approving Aduhelm," Dr. Joseph Ross, a professor of medicine and public health at Yale University, told the *Associated Press*. "They essentially capitulated to both industry and patient advocacy pressure, as opposed to abiding by the science."

Thakur, of the ALS Association, argues that the situations are completely different between AMX0035 and Aduhelm.

"Alzheimer's is a slow acting disease and ALS moves really quickly," he said. "I know people want to compare them because they're all neurology drugs, but the diseases are very different."

In a disease like ALS that takes most lives after a handful of years, six months of extended life is significant, Thakur said.

"What happens if you don't approve the drug and you wait for that phase 3 trial result? You wait a couple of years, and it turns out that the drug works," Thakur said. "Then you would have denied that six and a half months' life extension to all the people who could have been taking the drug. You effectively lose thousands of life years of benefit. And given those two choices, to us, it's a very strong reason to approve the drug as quickly as possible."

The ALS Association invested $2.2 million in Amylyx's research, money raised during the Ice Bucket Challenge campaign that went viral online.

As part of that investment, the ALS Association has what Thakur called a "small royalty stake" that could return up to $3.3 million in proceeds if the drug is approved. He said any money earned from AMX0035 would be plowed back into research.

The ultimate hope is that drug development spurred by Ice Bucket Challenge dollars will lead to medication combinations that extend ALS patients' lives until a cure is found.

"What we're hoping is that drugs like this that have not a life-changing effect but a life-extending effect can work in combination with other drugs, and we can start to transform the experience of ALS to make it a livable disease," Thakur said. "And so a lot of clinical things need to happen, but we also need to transform the treatment space and the drugs that are available, and this could be the start of that process."

More information: The U.S. National Institute of Neurological Disorders and Stroke has more about ALS.