

May 24, 2022

Patrizia Cavazzoni, MD
Director, Center for Drug Evaluation and Research
U.S. Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Dear Dr. Cavazzoni:

As prescribers specializing in treating people with ALS, we call on the Food and Drug Administration (FDA) to swiftly approve AMX0035 to treat ALS. After reviewing the peer reviewed publications around the CENTAUR trial (DOI: 10.1056/NEJMoa1916945, DOI: 10.1002/mus.27091, DOI:10.1002/mus.27569, DOI:10.1002/ana.26371), we find sufficient evidence that AMX0035 is safe, well-tolerated, and provides a clinically meaningful benefit. As clinicians, we ask FDA to grant approval so we can work with our patients to determine if AMX0035 is right for them.

There is no cure for ALS, and most people with the disease die within 2-5 years of diagnosis. The unmet need is critical and pressing. That means that therapies that provide benefit, even if the effect is incremental, need to be available to ALS specialists and neurologists who are in the front lines providing care and treatment to people with ALS.

AMX0035 showed a significant 2.3 points slowing of ALSFRS-R progression (or 35%) longer retention of function and several months of increase in survival. It is the first time an ALS clinical trial has showed such promise in both function and survival in a phase 2 trial. While these effects may seem incremental, they are meaningful to us as ALS specialists and to our patients. It can mean a difference between walking up the stairs or being restricted to a floor of your home. It can mean being able to feed yourself versus needing help to just cut your food. This means more time for our patients with the people they love.

While we recognize FDA typically relies on two adequate and well-controlled trials and would prefer to see smaller p-values, we implore the Agency to exercise the flexibility described in the FDA's 2019 guidance on ALS drug development. We understand that a single trial with modest p-values may provide uncertainty in the knowledge and firmness of scientific data. But ALS moves too fast to wait for certainty. People with ALS have stated their willingness repeatedly to accept significant risk both of safety and uncertainty of benefit.

The FDA has a choice to make. FDA could choose to not approve AMX0035 now and wait for the confirmatory phase 3 trial, which is already underway. This would mean that if the second trial confirms the positive findings, thousands of people with ALS would have been deprived of this life-changing therapy and pass away due to this fatal disease. If the FDA does the right thing and approves now, and the phase 3 trial fails to replicate, people with ALS may have been treated with an ineffective but a safe drug which would not have caused any substantive harm.

With the peer-reviewed evidence available today we see no substantive safety concerns, and the potential, but not certainty, of benefit. Under these circumstances, and in the case of a rapidly progressing and fatal disease, we can ethically prescribe this treatment, and should be allowed to offer this option to our patients.

Signed,

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