UsAgainstAlzheimer's
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May 3, 2021

Janet Woodcock, MD
Acting Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Patrizia Cavazzoni, MD
Director, Center for Drug Evaluation and Research
U.S. Food and Drug Administration
10903 New Hampshire Avenue
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Peter Stein, MD
Director, Office of New Drugs
U.S. Food and Drug Administration
10903 New Hampshire Avenue
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Billy Dunn, MD
Director, Office of Neuroscience
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Drs. Woodcock, Cavazzoni, Stein, and Dunn:

We are disappointed that FDA's decision to not approve pimavanserin leaves people with dementia who are living with hallucinations and delusions with no safe and effective therapeutic options. This is a huge, unmet medical need and the lack of safe and effective treatments results in crushing morbidity, premature mortality and institutionalization.

It has been publicly reported that pimavanserin met its prespecified endpoints in a trial design agreed to by the Food and Drug Administration (FDA). UsAgainstAlzheimer's urges Acadia and the FDA to meet as soon as possible to find a path forward for this drug's expeditious approval.

If it is true that the Division of Psychiatry had agreed to a clinical trial design, and that the trial was terminated early because the drug had demonstrated overwhelming evidence of efficacy based on pre-specified endpoints, the decision not to approve this treatment is confusing, frustrating and dismaying.

The determination in the FDA's Complete Response Letter that the application cannot be approved in its present form means a projected 2.4 million patients with the targeted symptoms

now must wait even longer for a treatment. The dementia patients who volunteered for the clinical trial also deserve a clear explanation of why the positive outcome of the trial in which they invested their time, energy and safety was disregarded.

These dementia-related delusions and hallucinations take a severe emotional, financial and social toll on patients and their families– especially on caregivers who are challenged to deal with a loved one whose symptoms prevent them from understanding or dealing with their reality. Dementia-related psychosis is one of the most frequent causes for families' decisions to place their loved ones in institutional care settings, with the additional consequences of family separation and financial burden.

Adding to the urgency for action is the fact that there are no existing good options for treatment of dementia-related psychosis. Anti-psychotic drugs now being used off-label as treatments for these delusions and hallucinations have limited effectiveness and carry black-box warnings for severe side effects – including higher rates of death in older patients with dementia-related psychosis.

The unmet need felt by patients and caregivers led to high hopes that this treatment would soon be available, but the FDA's refusal to approve this treatment means they must wait even longer for a treatment.

We urge the FDA to meet expeditiously with Acadia and seek to identify a path forward for this important therapy.

Respectfully,

George Vradenburg
Executive Chairman and Co-Founder

Russ Paulsen
Chief Operating Officer

Disclosures: The work that UsAgainstAlzheimer's has been doing over the past decade on behalf of patients and caregivers to end Alzheimer's disease has earned financial support from thousands of individuals, institutions, and companies, including Acadia.

The UsAgainstAlzheimer's A-LIST®, Acadia and the Lewy Body Dementia Association jointly conducted a qualitative and quantitative study of people who have a diagnosis of dementia with psychotic symptoms or their care partners. The survey results show that many patients with dementia-related psychosis – who have symptoms such as visual hallucinations, auditory hallucinations, and persecutory delusions – are unaware of what's happening or how to communicate what they are experiencing. This increases stress and anxiety and affects the daily lives of both patients and their caregivers. Two research posters reporting on this dementia-related psychosis research (links here and here) were presented at the 2020 AAIC conference.