Acadia Pharmaceuticals Receives Complete Response Letter from U.S. FDA for Supplemental New Drug Application for Pimavanserin for the Treatment of Hallucinations and Delusions Associated with Alzheimer's Disease Psychosis

August 5, 2022

SAN DIEGO--(BUSINESS WIRE)--Aug. 4, 2022-- Acadia Pharmaceuticals Inc. (Nasdaq: ACAD) today announced that the Company has received a Complete Response Letter (CRL) from the U.S. Food and Drug Administration (FDA) regarding its supplemental New Drug Application (sNDA) for NUPLAZID® (pimavanserin) for the treatment of hallucinations and delusions associated with Alzheimer's disease psychosis (ADP).

The CRL indicated that the FDA has completed review of the application, determining that it could not approve the sNDA in its present form, and recommended that Acadia conduct an additional trial in ADP. While the FDA stated that Study 019 demonstrated a statistically significant treatment effect on its primary endpoint, they concluded that there are limitations in the interpretability of the 019 results. The FDA also stated that the positive treatment effect of pimavanserin on dementia-related psychosis in Study 045 (HARMONY) appeared to be driven by the robustly positive results in the Parkinson's disease dementia subgroup, a condition they stated is subsumed within the currently approved NUPLAZID Parkinson's disease psychosis (PDP) indication. Up to 50 percent of PDP patients have dementia.[1]

"We are disappointed with this outcome. The treatment of Alzheimer's disease psychosis continues to be an area of high unmet need, for which there is no approved therapy," said Steve Davis, Chief Executive Officer. "We want to express our gratitude to all of the patients, their families and investigators who have participated in our clinical trials."

NUPLAZID was approved in the U.S. in 2016 and is the first and only treatment for hallucinations and delusions associated with PDP.

About Alzheimer's Disease Psychosis

According to the Alzheimer's Association, approximately six million people in the United States are living with Alzheimer's disease (AD).[2-3] Approximately 30% of patients with AD experience psychosis, commonly consisting of hallucinations and delusions.[4] These symptoms may be frequent and severe and may recur over time.[5] A hallucination is defined as a perception-like experience that occurs without an external stimulus and is sensory (seen, heard, felt, tasted, sensed, smelled) in nature. A delusion is defined as a false, fixed belief despite evidence to the contrary. Serious consequences have been associated with psychosis in patients with dementia, such as increased likelihood of nursing home placement, more severe dementia, and increased risk of morbidity and mortality.[6-7] There is no FDA approved drug for the treatment of Alzheimer's disease psychosis.

About Pimavanserin

Pimavanserin is a selective serotonin inverse agonist and antagonist preferentially targeting 5-HT_{2A} receptors. These receptors are thought to play an important role in neuropsychiatric disorders. In vitro, pimavanserin demonstrated no appreciable binding affinity for dopamine (including D2), histamine, muscarinic, or adrenergic receptors. Pimavanserin was approved for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis by the U.S. Food and Drug Administration in April 2016 under the trade name NUPLAZID®. NUPLAZID is not approved for Alzheimer's disease psychosis. In addition, Acadia is developing pimavanserin in other neuropsychiatric conditions.

About Acadia Pharmaceuticals

Acadia is advancing breakthroughs in neuroscience to elevate life. For more than 25 years we have been working at the forefront of healthcare to bring vital solutions to people who need them most. We developed and commercialized the first and only approved therapy for hallucinations and delusions associated with Parkinson's disease psychosis. Our late-stage development efforts are focused on the negative symptoms of schizophrenia and Rett syndrome. Our early-stage development efforts are focused on novel approaches to pain management, cognition and neuropsychiatric symptoms in central nervous system disorders. For more information, visit us at www.acadia.com and follow us on LinkedIn and Twitter.

Important Safety Information

Indication

NUPLAZID is indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis.

Important Safety Information

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

- **Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.**
- **NUPLAZID is not approved for the treatment of patients with dementia-related psychosis unrelated to the hallucinations and delusions associated with Parkinson's disease psychosis.**

Contraindication: NUPLAZID is contraindicated in patients with a history of a hypersensitivity reaction to pimavanserin or any of its components. Rash, urticaria, and reactions consistent with angioedema (e.g., tongue swelling, circumoral edema, throat tightness, and dyspnea) have been reported.

Warnings and Precautions: QT Interval Prolongation

- NUPLAZID prolongs the QT interval. The use of NUPLAZID should be avoided in patients with known QT prolongation or in combination with other drugs known to prolong QT interval including Class 1A antiarrhythmics or Class 3 antiarrhythmics, certain antipsychotic medications, and certain antibiotics.
- NUPLAZID should also be avoided in patients with a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of torsade de pointes and/or sudden death, including symptomatic bradycardia, hypokalemia or hypomagnesemia, and presence of congenital prolongation of the QT interval.

Adverse Reactions: The common adverse reactions (≥2% for NUPLAZID and greater than placebo) were peripheral edema (7% vs 2%), nausea (7% vs 4%), confusional state (6% vs 3%), hallucination (5% vs 3%), constipation (4% vs 3%), and gait disturbance (2% vs <1%).

Drug Interactions:

- Coadministration with strong CYP3A4 inhibitors (e.g., ketoconazole) increases NUPLAZID exposure. Reduce NUPLAZID dose to 10 mg taken orally as one tablet once daily.
- Coadministration with strong or moderate CYP3A4 inducers reduces NUPLAZID exposure. Avoid concomitant use of strong or moderate CYP3A4 inducers with NUPLAZID.

Dosage and Administration

Recommended dose: 34 mg capsule taken orally once daily, without titration.

NUPLAZID is available as 34 mg capsules and 10 mg tablets.

Please read the full Prescribing Information including **Boxed WARNING.**

Forward-Looking Statements

Statements in this press release that are not strictly historical in nature are forward-looking statements. These statements include but are not limited to statements regarding the timing of future events. These statements are only predictions based on current information and expectations and involve a number of risks and uncertainties. Actual events or results may differ materially from those projected in any of such statements due to various factors, including the risks and uncertainties inherent in drug development, approval and commercialization. For a discussion of these and other factors, please refer to Acadia's annual report on Form 10-K for the year ended December 31, 2021 as well as Acadia's subsequent filings with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All forward-looking statements are qualified in their entirety by this cautionary statement and Acadia undertakes no obligation to revise or update this press release to reflect events or circumstances after the date hereof, except as required by law.

References

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[4] Cummings J et al. Criteria for Psychosis in Major and Mild Neurocognitive Disorders: International Psychogeriatric Associations (IPA) Consensus Clinical and Research Definition. *Am J of Geriatric Psychiatry*. 2020; 28(12): 1256-1269.

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