Newly Published Retrospective Analysis Showed Lower All-Cause Mortality Risk Among Parkinson's Disease Psychosis Patients Treated with NUPLAZID® (pimavanserin) Compared to Those Treated with Other Atypical Antipsychotics

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- Study results consistent across different patient groups, including those in long-term care facilities

SAN DIEGO--(BUSINESS WIRE)--Jan. 3, 2023-- Acadia Pharmaceuticals Inc. (Nasdaq: ACAD) announced today that the journal *Drug Safety* published results from a retrospective analysis finding a lower mortality risk in patients with Parkinson's disease psychosis (PDP) treated with NUPLAZID® (pimavanserin) compared to other atypical antipsychotics over 12 months and across various subgroups. NUPLAZID is the only medication approved by the U.S. FDA for the treatment of hallucinations and delusions associated with PDP.

"We were encouraged by this large, real-world study showing a lower mortality risk in patients with PDP after initiation of NUPLAZID, compared to other atypical antipsychotics. The robust results were achieved across sub-groups and sensitivity analysis using a variety of approaches," said Ponni Subbiah, M.D., M.P.H., Senior Vice President, Global Head of Medical Affairs and Chief Medical Officer, Acadia Pharmaceuticals. "These findings, along with other recently published studies, will help physicians and the patients they treat make decisions about managing Parkinson's disease psychosis symptoms that can be quite troubling and disruptive to patients and their families, significantly impacting their quality of life."[1,2]

The retrospective, real-world, observational study evaluated a cohort of patients identified using 2016-2019 Medicare claims data who were 65 years of age and older in the United States and diagnosed with Parkinson's disease and psychosis, comparing those who newly initiated NUPLAZID (n=2,892) or were prescribed an off-label, comparator atypical antipsychotic (n=19,083; clozapine, quetiapine, risperidone, olanzapine, aripiprazole, brexpiprazole). After matching the two cohorts using propensity scores (PS), there were 2,891 patients in each of the NUPLAZID and comparator cohorts. In the matched cohorts, the hazard ratio (HR) for all-cause mortality for NUPLAZID vs. comparator was 0.78 (95% CI, 0.67-0.91), with the lowest time period-specific HRs in the first 180 days. Researchers also evaluated a sub-cohort of the 30% of patients in long-term care (LTC) or skilled nursing facilities (SNF) [matched n=652 each for NUPLAZID and comparator cohorts]. Similarly, among LTC and SNF residents, the HR was 0.78 (95% CI, 0.60-1.01). Importantly, when mortality was evaluated separately within subgroups, the HR estimates were consistent across all levels of sex, age, and dementia diagnosis.

Non-motor symptoms of Parkinson's disease, including hallucinations and delusions associated with Parkinson's disease psychosis, can be more troublesome than motor symptoms.[3] These symptoms can also worsen over time, making it difficult for patients to know whether or not what they are experiencing is real.[4,5] Psychosis is an important risk factor for mortality in Parkinson's disease. In a retrospective study evaluating the association of death in patients with Parkinson's disease compared to PDP using Medicare data (2007-2015), mortality risk was 34% greater when psychosis was present.[6]

This analysis observed real-world use of NUPLAZID approximately 3.5 years after its FDA approval and subsequent availability in the United States. During this early period, patient characteristics may have differed between NUPLAZID and comparator users, and although matching balanced all measured characteristics, the potential for residual confounding by unmeasured characteristics remains. Additionally, the LTC/SNF sub-cohort analysis was limited by the relatively small sample size.

About Parkinson's Disease and Parkinson's Disease Psychosis

Parkinson's disease is a progressive nervous system disorder that affects about one million people in the United States.[7,8] The signs and symptoms can vary with people experiencing both motor symptoms and non-motor symptoms such as hallucinations (seeing, hearing, or experiencing things that others don't) and delusions (false beliefs). [5,9] Physicians may refer to these Parkinson's-related hallucinations and delusions as Parkinson's disease psychosis.[5] Around 50 percent of people living with Parkinson's may experience hallucinations or delusions during the course of their disease. [9] Non-motor symptoms, as a whole, can be more troublesome than motor symptoms, in terms of quality of life.[3] Parkinson's disease psychosis may add to the burden of caring for a loved one with Parkinson's disease. [10,11]

About NUPLAZID® (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. 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 clinical-stage development efforts are focused on treating the negative symptoms of schizophrenia, Rett syndrome 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 and Indication for NUPLAZID® (pimavanserin)

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 related to the potential opportunity for future growth in sales of NUPLAZID; the timing of ongoing and future clinical studies for pimavanserin; the development and commercialization of trofinetide; and guidance for full-year 2022 NUPLAZID net sales for Parkinson's disease psychosis only and certain expense line items. 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 uncertainty of future commercial sales and related items that would impact net sales during 2022, the risks and uncertainties inherent in drug development, approval and commercialization, and the fact that past results of clinical trials may not be indicative of future trial results. 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.

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