NUPLAZID® (pimavanserin) Efficacy Data from Open-Label Extension (OLE) Study Published in Parkinsonism and Related Disorders

June 3, 2021

- Patients previously treated with 34 mg showed sustained response

- Patients on investigational doses and placebo demonstrated symptom improvement when switched to 34 mg dose during OLE

SAN DIEGO--(BUSINESS WIRE)--Jun. 3, 2021-- Acadia Pharmaceuticals Inc. (Nasdaq: ACAD) today announced publication of open-label extension (OLE) data from patients experiencing hallucinations and delusions associated with Parkinson's disease psychosis (PDP) who had previously completed one of three, six-week, double-blind, placebo-controlled studies.

The OLE efficacy analysis showed that patients previously on NUPLAZID 34 mg had a sustained efficacy response from Week 6 through Week 10, and that patients who had been treated with investigational doses of 8.5 mg and 17 mg or placebo also showed an improvement in the symptoms of psychosis when switched to NUPLAZID 34 mg over the 4 weeks of the OLE. The completed study was published online and in the June issue of *Parkinsonism and Related Disorders*. Full text of the paper can be found at: https://www.prdjournal.com/article/S1353-8020(21)00145-0/fulltext.

"Results from a multi-center OLE study, across 14 countries, demonstrate the extended durability of efficacy of NUPLAZID for treating hallucinations and delusions associated with PDP, in addition to reinforcing the efficacy seen in the original pivotal trial using the 34 mg dose," said Stuart Isaacson, M.D., Director, Parkinson's Disease and Movement Disorders Center of Boca Raton. "As a physician, having NUPLAZID, an FDA-approved and proven therapy to treat these debilitating symptoms without impairing motor function, represents a major step forward. NUPLAZID is a critical first-line therapy for our patients living with PDP, and their caregivers."

Importantly, non-motor symptoms of Parkinson's disease, including hallucinations and delusions, can be more troublesome than motor symptoms. [1] Hallucinations and delusions can also worsen over time, making it difficult for patients to know whether or not what they are experiencing is real.[2,3]

"We're pleased to have additional published data supporting the efficacy of NUPLAZID, as approximately 50 percent of people living with Parkinson's may experience hallucinations and delusions during the course of their disease," said Ponni Subbiah, M.D., M.P.H., Senior Vice President, Global Head of Medical Affairs and Chief Medical Officer at Acadia. "These symptoms can have a significant impact on both patients and their families, negatively impacting their quality of life and causing severe emotional distress."

About the Open-Label Extension (OLE) Study

The OLE study was designed to evaluate the long-term safety of NUPLAZID. The publication includes an analysis of the efficacy results from the initial four weeks of the OLE study and included patients who had previously completed one of three, six-week, double-blind, placebo-controlled studies. All patients in the OLE were treated with NUPLAZID 34 mg. Changes in PDP symptoms were evaluated according to the Scale for the Assessment of Positive Symptoms (SAPS): the SAPS-PD and the Hallucinations + Delusions domains, Clinical Global Impression (CGI) Improvement and Severity scales and Caregiver Burden Scale (CBS).

Of 459 patients enrolled in the OLE, 424 (92.4%) had a Week 4 efficacy assessment. Overall, the response to NUPLAZID 34 mg that was observed in the SAPS-PD scores during the initial six weeks persisted through Week 4 of the OLE (mean change from OLE baseline (standard deviation) to OLE Week 4 for the SAPS-PD of -0.8 (5.6)), while scores among patients switched from placebo to NUPLAZID 34 mg improved (with a mean change from OLE baseline to OLE Week 4 in the SAPS-PD of -2.9 (5.6)). For patients treated with pimavanserin 8.5 mg or 17 mg investigational doses in the previous studies, further improvement was observed during the OLE with NUPLAZID 34 mg.

During the initial four weeks of the OLE study, adverse events (AEs) were reported by 215 (46.8%) patients. Twenty-seven (5.9%) patients had an AE that resulted in discontinuation of the study or study drug. The majority of AEs were of mild or moderate intensity; seven (1.5%) patients had serious AEs. The most common AEs were fall (5.9%), hallucination (3.7%), urinary tract infection (2.8%), insomnia (2.4%), and peripheral edema (2.2%). Complete safety findings from the OLE study over 9 years of study follow-up were previously published by Ballard CG, et al.[4]

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.[5,6] 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). [3,7] Physicians may refer to these Parkinson's-related hallucinations and delusions as Parkinson's disease psychosis (PDP).[3] Around 50 percent of people living with Parkinson's may experience hallucinations or delusions during the course of their disease.[7] Non-motor symptoms, as a whole, can be more troublesome than motor symptoms, in terms of quality of life.[1] PDP may add to the burden of caring for a loved one with Parkinson's disease. [8,9]

About NUPLAZID® (pimavanserin)

NUPLAZID 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 dementia-related psychosis. In addition, Acadia is developing pimavanserin in other neuropsychiatric conditions.

About Acadia Pharmaceuticals

Acadia is trailblazing 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 dementia-related psychosis, negative symptoms of schizophrenia and Rett syndrome, and in early-stage clinical research we are exploring novel approaches to pain management, and cognition and neuropsychiatric symptoms in central nervous system disorders. For more information, visit us at www.acadia-pharm.com and follow us on LinkedIn.

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, 2020 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.

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.**

[1] Martinez-Martin P, Rodriguez-Blazquez C, et al. The Impact of Non-Motor Symptoms on Health Related Quality of Life of Patients with Parkinson's Disease. *Mov Disord*. 2011;26(3):399-406.

[2] Goetz, CG, Fan, W, Leurgans, S, et al. The malignant course of "benign hallucinations" in Parkinson disease. *Archives of neurology*. 2006;63(5), 713–716

[3] Ravina B, Marder K, Fernandez HH, et al. Diagnostic criteria for psychosis in Parkinson's disease: report of an NINDS, NIMH work group. *Mov*

Disord. 2007 Jun 15;22(8):1061-8.

[4] Ballard CG, Kreitzman DL, Isaacson S, et al. Long-term evaluation of open-label pimavanserin safety and tolerability in Parkinson's disease psychosis. *Parkinsonism Relat Disord.* 2020;77:100-106.

[5] Parkinson's Disease Foundation. What is Parkinson's disease? Retrieved from https://www.pdf.org/en/about_pd. Accessed November 2014.

[6] Postuma, RB, et al. MDS Clinical Diagnostic Criteria for Parkinson's Disease. *Mov Disorders*. 2015; 30(12): 1591-1599

[7] Forsaa EB, Larsen JP, Wentzel-Larsen T, et al. A 12-year population-based study of psychosis in Parkinson's disease. *Arch Neurol*. 2010;67:996-1001.

[8] Schrag A, Hovris A, et al. Caregiver-burden in parkinson's disease is closely associated with psychiatric symptoms, falls, and disability. *Parkonism and Related Disorders*. 2006;12:35-41

[9] Aarsland D, Bronnick K, Ehrt U. et al. Neuropsychiatric symptoms in patients with Parkinson's disease and dementia: frequency, profile and associated care giver stress. *J Neurol Neurosurg Psychiatry*. 2007;78:36-42.

View source version on businesswire.com: https://www.businesswire.com/news/home/20210603005317/en/

Media Contact:
Acadia Pharmaceuticals Inc.
Deb Kazenelson
(818) 395-3043
media@acadia-pharm.com

Investor Contact:
Acadia Pharmaceuticals Inc.
Mark Johnson, CFA
(858) 261-2771
ir@acadia-pharm.com

Source: Acadia Pharmaceuticals Inc.