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 Dementia-Related Psychosis

April 5, 2021

- Conference call and webcast to be held today at 8:00 a.m. Eastern Time

SAN DIEGO--(BUSINESS WIRE)--Apr. 5, 2021-- 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 dementia-related psychosis (DRP). The FDA issued a CRL to indicate that they have completed their review of the application and has determined that the application cannot be approved in its present form.

Despite prior agreements with the Division of Psychiatry regarding the pivotal Phase 3 HARMONY study design targeting a broad DRP patient population analyzed as a single group, the Division, in the CRL, cited a lack of statistical significance in some of the subgroups of dementia, and insufficient numbers of patients with certain less common dementia subtypes as lack of substantial evidence of effectiveness to support approval.

The DRP pivotal HARMONY study met its prespecified primary and secondary endpoints with robust and persuasive clinical and statistical superiority of pimavanserin over placebo, which was a prospectively agreed prerequisite for the DRP indication. Statistical separation by dementia subgroups and certain minimum numbers of patients with specific subtypes were not among the prespecified requirements.

“Acadia stands behind the robustly positive results from the pivotal Phase 3 HARMONY study and the prospectively agreed trial design and criteria for establishing efficacy in DRP. Over the entire course of the review, the Division did not raise any concerns regarding the agreed upon study design, including the issues raised in the CRL,” said Steve Davis, Chief Executive Officer of Acadia. “We will immediately request a Type A meeting to work with the FDA to address the CRL and determine an expeditious path forward for the approval of pimavanserin in DRP.”

The Division also stated in the CRL that it considers the Phase 2 Alzheimer’s disease psychosis study -019, a supportive study in the sNDA filing, to not be adequate and well controlled, citing that it was a single center study with no type I error control of secondary endpoints in which certain protocol deviations occurred. The Company believes these observations impact neither the positive results on the study’s primary endpoint, nor the study’s overall conclusions of efficacy.

There were no safety issues or concerns raised in the CRL.

sNDA Submission for Dementia-Related Psychosis

The sNDA submission of pimavanserin for the treatment of hallucinations and delusions associated with DRP was supported by results from the pivotal Phase 3 HARMONY study, which met its primary endpoint, demonstrating that pimavanserin significantly reduced the risk of relapse of psychosis by 2.8 fold compared to placebo (hazard ratio = 0.353; one-sided p=0.0023). Pimavanserin also met the key secondary endpoint in the study, significantly reducing the risk of discontinuation for any reason by 2.2 fold compared to placebo (hazard ratio = 0.452, one-sided p=0.0024). The sNDA also included positive efficacy results from two additional placebo-controlled studies, both of which met their respective primary endpoints: the Phase 2 (-019) study in patients with Alzheimer’s disease psychosis and the Phase 3 (-020) study in patients with Parkinson’s disease psychosis. In addition, the sNDA included a large safety database from completed and ongoing studies representing over 1,500 patients with neurodegenerative disease.

Conference Call and Webcast Information

Acadia management will discuss today’s announcement via conference call and webcast at 8:00 a.m. Eastern Time. The conference call may be accessed by dialing 855-638-4820 for participants in the United States or Canada and 443-877-4067 for international callers (reference passcode 6894834). A telephone replay of the conference call may be accessed through April 19, 2021 by dialing 855-859-2056 for callers in the United States or Canada and 404-537-3406 for international callers (reference passcode 6894834). The conference call also will be webcast live on Acadia’s website, www.acadia-pharm.com under the investors section and will be archived there through May 3, 2021.

About Dementia-Related Psychosis

Approximately 8 million people in the United States are living with dementia, a condition with a core feature of declining cognition (changes in memory, decision-making abilities, language, etc.) resulting in functional impairment. Dementia is a manifestation of an underlying condition which is often progressive and neurodegenerative in nature. In addition to cognitive decline, dementing illnesses almost universally lead to neuropsychiatric symptoms, including hallucinations, delusions, and changes in behavior.

It is estimated that 2.4 million Americans (or 30% of people with dementia) experience dementia-related hallucinations and delusions. These symptoms may be frequent and severe and may recur over time. A hallucination is defined as a perception-like experience that occurs without an external stimulus and is sensory (seen, heard, felt, tasted, sensed) in nature. A delusion is defined as a false, fixed belief that is resolutely held despite evidence to the contrary. Dementia-related psychosis occurs in many types of dementia, including Alzheimer’s disease, dementia with Lewy bodies, Parkinson’s disease dementia, vascular dementia, and frontotemporal dementia. Serious consequences have been associated with psychosis in patients with dementia, such as repeated hospital admissions, increased likelihood of nursing home placement, faster progression of dementia, and increased risk of morbidity and mortality.

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 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20210405005229/en/

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