ACADIA Pharmaceuticals Announces Late-Breaking Oral Presentation of the Phase 3 HARMONY Study of Pimavanserin in Dementia-Related Psychosis at the Clinical Trials on Alzheimer's Disease (CTAD) 2019 Meeting

October 3, 2019

SAN DIEGO--(BUSINESS WIRE)--Oct. 3, 2019-- ACADIA Pharmaceuticals Inc. (Nasdaq: ACAD) today announced that the presentation of the results from the Phase 3 HARMONY study of pimavanserin in dementia-related psychosis has been accepted for a late-breaking oral communication at the upcoming 12th Clinical Trials on Alzheimer's Disease (CTAD) Meeting, December 4-7, 2019 in San Diego, California.

Late-Breaking Oral Presentation

- Presentation: LB1
- Abstract Title: *HARMONY Relapse-Prevention Study: Pimavanserin Significantly Prolongs Time to Relapse of Dementia-Related Psychosis*
- Presentation Date: Wednesday, December 4, 2019
- Presentation Time: 5:45 p.m. Pacific Time

On September 9, 2019, ACADIA announced that the Phase 3 HARMONY study, a double-blind, placebo-controlled relapse prevention trial evaluating an investigational use of pimavanserin for the treatment of dementia-related psychosis, met its primary endpoint. In the study pimavanserin demonstrated a highly statistically significant longer time to relapse of psychosis compared to placebo. Upon the recommendation of the study's independent data monitoring committee, which met to review the data from the planned interim efficacy analysis, the study was stopped early based on demonstration of efficacy. The pre-specified stopping criteria at the planned interim efficacy analysis required a one-sided p-value less than 0.0033 on the study's primary endpoint.

About the HARMONY Study

HARMONY is a Phase 3 study designed to evaluate the efficacy and safety of pimavanserin for the treatment of delusions and hallucinations associated with dementia-related psychosis across a broad population of patients with the most common subtypes of dementia including: Alzheimer's disease, dementia with Lewy bodies, Parkinson's disease dementia, vascular dementia, and frontotemporal dementia spectrum disorders.

The HARMONY study included a 12-week open-label stabilization period during which patients with dementia-related psychosis were treated with pimavanserin 34 mg once daily. Dose reduction to 20 mg once daily was allowed if clinically justified within the first four weeks. Following the 12-week stabilization period, patients who met pre-specified criteria for treatment response were then randomized into the double-blind period of the study to continue their pimavanserin dose (34 mg or 20 mg per day) or switched to placebo and followed for up to 26 weeks or until a relapse of psychosis occurred. The primary endpoint in the study was time to relapse in the double-blind period.

Relapse (significant worsening of dementia-related psychosis after prior stabilization) was defined in the study by one or more of the following: hospitalization due to dementia-related psychosis, significant deterioration of dementia-related symptoms on clinical scales, withdrawal from the study due to lack of efficacy, or the use of an off-label antipsychotic medication for the treatment of dementia-related delusions and/or hallucinations. All potential relapses and discontinuations in the double-blind portion of the study were adjudicated by an independent adjudication committee to determine if protocol defined relapse criteria were met.

About Dementia-Related Psychosis

Around 8 million people in the United States are living with dementia and studies suggest that approximately 30% of dementia patients, or 2.4 million people, have psychosis, commonly consisting of delusions and hallucinations[1,2]. Dementia-related psychosis includes psychosis in Alzheimer's disease, dementia with Lewy bodies, Parkinson's disease dementia, vascular dementia, and frontotemporal dementia. Serious consequences have been associated with severe or persistent psychosis in patients with dementia such as repeated hospital admissions, increased likelihood of nursing home placement, progression of dementia, and increased risk of morbidity and mortality[3].

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 psychosis, schizophrenia, depression and other neuropsychiatric disorders. In vitro, pimavanserin demonstrated no appreciable binding affinity for dopamine (including D2), histamine, muscarinic, or adrenergic receptors. ACADIA is evaluating pimavanserin in an extensive clinical development program across multiple indications with significant unmet need including dementia-related psychosis, adjunctive major depressive disorder, and the negative symptoms of schizophrenia. 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, schizophrenia or major depressive disorder.

About ACADIA Pharmaceuticals

ACADIA is a biopharmaceutical company focused on the development and commercialization of innovative medicines to address unmet medical needs in central nervous system disorders. ACADIA has developed and commercialized the first and only medicine approved for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis. ACADIA also has ongoing clinical development efforts in additional areas

with significant unmet need, including dementia-related psychosis, schizophrenia, major depressive disorder, and Rett syndrome. This press release and further information about ACADIA can be found at: www.acadia-pharm.com.

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 benefits of pimavanserin as a treatment for dementia-related psychosis or other central nervous system disorders as well as the potential results of clinical trials of pimavanserin in other indications. 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, 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, 2018 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)

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.
- **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 most 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.

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

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 see the full Prescribing Information including **Boxed WARNING** for NUPLAZID.

References

[1] 2017 Alzheimer's Disease Facts and Figures and ACADIA market research

[2]Plassman BL, et al. Prevalence of dementia in the United States: the Aging Demographics, and Memory study. *Neuroepidemiology*. 2007;29(1-2):125-132.

[3]Connors MH et al. *Am J Geriatr Psychiatry* 2018;26(3). Peters ME et al. *Am J Psychiatry* 2015;172(5). Haupt M et al. *Int J Geriatr Psychiatry* 1996;11(11). Naimark D et al. *J Am Geriatr Soc* 1996;44(3). Stern Y et al. *Neurology* 1994;44(12).

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