ACADIA Pharmaceuticals Presents Positive Top-line Results from Pivotal Phase 3 HARMONY Trial of Pimavanserin in Patients with Dementia-Related Psychosis at 12th Clinical Trials on Alzheimer's Disease (CTAD) Meeting

December 5, 2019

- Pimavanserin met the primary endpoint in the study, significantly reducing the risk of relapse of psychosis by 2.8 fold (Hazard Ratio (HR)=0.353, one-sided p=0.0023)

- Pimavanserin met the key secondary endpoint in the study, significantly reducing the risk of discontinuation for any reason by 2.2 fold (HR=0.452, one-sided p=0.0024)

- Currently, there is no FDA-approved drug for the treatment of dementia-related psychosis

- Webcast to be held today at 7:15 p.m. Pacific Time

SAN DIEGO--(BUSINESS WIRE)--Dec. 4, 2019-- ACADIA Pharmaceuticals Inc. (Nasdaq: ACAD) today presented positive top-line results from its Phase 3 HARMONY study at the 12th Clinical Trials on Alzheimer's Disease (CTAD) Meeting, December 4 -7, 2019 in San Diego, California. HARMONY was a double-blind, placebo-controlled, relapse prevention study in 392 patients evaluating pimavanserin for the treatment of dementia-related psychosis.

Pimavanserin met the primary endpoint of the study and was stopped at the pre-planned interim analysis by significantly reducing risk of relapse of psychosis by 2.8 fold compared to placebo (HR = 0.353; one-sided p=0.0023). In addition, pimavanserin met the key secondary endpoint by significantly reducing risk of discontinuation for any reason by 2.2 fold (HR = 0.452; one-sided p=0.0024).

"The results presented today are an important advance for patients and caregivers who struggle with the burden of dementia-related psychosis where no FDA-approved treatment is currently available," said Jeffrey Cummings, M.D., Sc.D., Director Emeritus of Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas. "Reducing the risk of relapse of psychotic symptoms by this magnitude is an important and meaningful outcome as these are serious events which could lead to poor patient outcomes and a significant increase in caregiver burden and distress."

The Phase 3 HARMONY study included a 12-week open-label pimavanserin treatment period prior to the randomization period of the study. In this open-label treatment period, 61.8% of eligible patients met pre-specified criteria for pimavanserin treatment response at both week 8 and week 12 and were subsequently randomized into the double-blind period of the study. For patients in the open-label treatment period, change from baseline to week 8 and week 12 on the Scale for the Assessment of Positive Symptoms-Hallucinations and Delusions (SAPS-H+D) score improved by 63.0% and 75.2% respectively.

"We are extremely pleased to announce the top-line results from this landmark Phase 3 study in dementia-related psychosis," said Serge Stankovic, M.D., M.S.P.H., ACADIA's President. "The HARMONY study was designed to answer three very important questions. First, in the 12-week open-label period, pimavanserin treatment showed a meaningful reduction of the symptoms and stabilization of psychosis across all of the five clinically diagnosed subtypes evaluated. Second, in the 26-week double-blind period, patients on pimavanserin had a nearly three-fold reduction of risk of relapse compared to patients on placebo. And third, pimavanserin was well-tolerated by elderly patients with dementia-related psychosis. We look forward to discussing these results with the FDA in the first half of 2020."

Pimavanserin was well-tolerated over the entire 9-month study duration. Patients receiving pimavanserin treatment had no worsening in cognition, as measured by the Mini-Mental State Examination (MMSE) score, from baseline and no worsening of motor symptoms, as measured by the Extrapyramidal Symptom Rating Scale A-score (ESRS-A), from baseline. In the double-blind period, low rates of adverse events were observed, 41.0% of patients on pimavanserin and 36.6% on placebo. Discontinuations due to adverse events were low, 2.9% for pimavanserin and 3.6% for placebo. Serious adverse events were also low, 4.8% in the pimavanserin group and 3.6% in the placebo group. One death was reported in the open-label period and one death was reported in the pimavanserin group during the double-blind period. Investigators determined neither death was related to the study drug. Additionally, pimavanserin did not result in clinically significant differences in vital signs, weight, or daytime sedation compared to placebo.

ACADIA is planning to meet with the FDA in the first half of 2020 regarding a supplemental NDA submission. The FDA previously granted Breakthrough Therapy Designation for pimavanserin for the treatment of dementia-related psychosis. Currently, no drug is approved by the FDA for the treatment of dementia-related psychosis.

About the HARMONY Study

HARMONY was 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 clinically diagnosed subtypes of dementia including: Alzheimer's disease, dementia with Lewy bodies, Parkinson's disease dementia, vascular dementia, and frontotemporal dementia spectrum disorders.

A total of 392 patients were enrolled in the HARMONY study. The average age of patients in the study was 74.5 years. Patients had an average baseline SAPS-H+D score of 24.4, which is reflective of moderate-to-severe psychosis and an average baseline MMSE score of 16.7, which is consistent with the greatest proportion of enrolled patients having moderate dementia.

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 based on tolerability within the first four weeks. Following the 12-week open-label 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 as represented by the Kaplan-Meier curve and the hazard ratio. Pimavanserin met the primary endpoint of the study by significantly reducing the risk of relapse of psychosis by 2.8 fold compared to placebo (HR = 0.353; one-sided p=0.0023).

Relapse (psychotic exacerbation or 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 worsening of dementia-related psychosis as measured by clinical scales and investigator impression, 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.

Webcast Information

The live webcast will include a presentation of the results by ACADIA management followed by a KOL panel discussion and will begin at 7:15 p.m. Pacific Time. The live webcast will be available on ACADIA's website, www.acadia-pharm.com, under the investors section and will be archived there through January 4, 2020.

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, major depressive disorder, the negative symptoms of schizophrenia, 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 expected timelines with respect to the Company's planned engagement with the FDA. 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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