ACADIA Pharmaceuticals Initiates Phase III Study of Pimavanserin in Dementia-Related Psychosis

October 4, 2017

- **Dementia-Related Psychosis Includes Psychosis in Patients with Alzheimer's Disease, Dementia with Lewy Bodies, Parkinson's Disease Dementia, Vascular Dementia, and Frontotemporal Dementia**

- **FDA Grants Breakthrough Therapy Designation to Pimavanserin for Dementia-Related Psychosis**
- **Conference Call to Be Held Today at 5:00 pm ET to Discuss Phase III Development Program**

SAN DIEGO--(BUSINESS WIRE)--Oct. 4, 2017-- ACADIA Pharmaceuticals Inc. (NASDAQ: ACAD) today announced the initiation of HARMONY, a Phase III study to evaluate pimavanserin for the treatment of hallucinations and delusions associated with dementia-related psychosis, a serious medical condition for which there is no therapy approved by the U.S. Food and Drug Administration (FDA). The company also announced that the FDA has granted Breakthrough Therapy Designation to pimavanserin for dementia-related psychosis. Dementia-related psychosis includes psychosis in patients with Alzheimer's disease, dementia with Lewy bodies, Parkinson's disease dementia, vascular dementia, and frontotemporal dementia.

If the clinical development program is successful, and pimavanserin is ultimately approved by the FDA for the treatment of dementia-related psychosis, it would represent a significant expansion of the approved use of pimavanserin. Currently, pimavanserin is the only drug approved by the FDA for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis. It is marketed under the trade name NUPLAZID®.

"We are pleased the FDA has agreed to an efficient development path for pimavanserin in this broad indication and granted Breakthrough Therapy Designation in recognition of this serious unmet need," said Serge Stankovic, M.D., M.S.P.H., ACADIA's Executive Vice President, Head of Research and Development. "Initiation of our Phase III study is supported by clinical and preclinical evidence of pimavanserin's antipsychotic activity without detrimental effects on cognitive function or other side effects associated with antipsychotics currently used off-label for this indication."

Around 8 million people in the United States are living with dementia and approximately half are diagnosed with the disease. Studies suggest that approximately 30% of patients with dementia have psychosis, commonly consisting of hallucinations and delusions. Serious consequences have been associated with severe or persistent psychosis in patients with dementia such as repeated hospital admissions, earlier progression to nursing home care, more rapid progression of dementia, and increased risk of morbidity and mortality.

"With receipt of FDA's Breakthrough Therapy Designation for pimavanserin, we are able to accelerate this important program," said Steve Davis, President and Chief Executive Officer of ACADIA. "Pimavanserin has a unique biological mechanism that distinguishes it from any other antipsychotic. We believe the profile we observed in our Phase II -019 Study in Alzheimer's disease psychosis could be particularly beneficial in this elderly underserved population. In that study, pimavanserin demonstrated antipsychotic effect without impairing cognition and we also observed a very favorable tolerability profile. We were very excited to be the first and only FDA approved drug for the treatment of Parkinson's disease psychosis and are equally excited about the potential to help many more patients suffering from dementia-related psychosis."

The initiation of the pivotal study in dementia-related psychosis, referred to as HARMONY, follows an End-of-Phase II Meeting and agreement with the FDA on the clinical development plan and the design of the Phase III study. ACADIA believes that robust positive results from one Phase III study together with supportive data from prior studies with pimavanserin could serve as the basis of a supplementary New Drug Application (sNDA) for the treatment of hallucinations and delusions associated with dementia-related psychosis.

Breakthrough Therapy Designation serves to expedite the development and review by the FDA of drugs that are intended to treat a serious or life-threatening disease or condition. The Breakthrough Therapy Designation for dementia-related psychosis was granted, in part, based on results of ACADIA's Phase II -019 Study with pimavanserin in Alzheimer's disease psychosis and results of the company's Phase III -020 Study with pimavanserin in Parkinson's disease psychosis. This is the second Breakthrough Therapy Designation for pimavanserin.

About the Phase III HARMONY Study

HARMONY is a Phase III, randomized, double-blind, placebo-controlled study, evaluating the efficacy and safety of pimavanserin for the treatment of hallucinations and delusions associated with dementia-related psychosis. The objective of the study is to evaluate the ability of pimavanserin to prevent relapse of psychotic symptoms in a broad population of patients with the most common subtypes of dementia: Alzheimer's disease, dementia with Lewy bodies, Parkinson's disease dementia, vascular dementia and frontotemporal dementia. The study will be conducted globally and is expected to enroll approximately 360 patients.

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

Clinical Data Supporting Phase III Trial Design

The Phase III development plan is supported by data from two completed clinical studies. As previously announced, in the completed Phase II -019 Study of pimavanserin in Alzheimer's disease psychosis, pimavanserin demonstrated clinically meaningful and statistically significant efficacy of pimavanserin 34 mg over placebo on the primary endpoint as measured by the Neuropsychiatric Inventory-Nursing Home (NPI-NH) psychosis score

at week 6 of dosing (p=0.0451). Results from this Phase II study in Alzheimer's disease psychosis will be presented at the 10 th Clinical Trials on Alzheimer's Disease (CTAD) Meeting on November 3, 2017 in Boston.

Additional clinical evidence for efficacy of pimavanserin in dementia-related psychosis was observed in the Phase III -020 Study in patients with Parkinson's disease psychosis. Approximately a quarter of the patients enrolled in the -020 Study also suffered from mild dementia. In a pre-specified subgroup analysis of these patients, those treated with pimavanserin observed a significant improvement in psychosis compared to placebo. This effect was larger than the overall average effect observed in the study.

Other

ACADIA also announced that due to the potential overlap of clinical sites and study participants between its Phase III HARMONY dementia-related psychosis study and the Company's ongoing Phase II SERENE study of pimavanserin in Alzheimer's disease agitation, it has decided to discontinue enrollment of new patients in the SERENE study. Patients already enrolled will complete the study as planned. Discontinuation of enrollment in the SERENE study will avoid potential interference between the two studies and enable ACADIA to focus external and internal resources on the Phase III dementia-related psychosis program.

Conference Call and Webcast Information

ACADIA management will hold a conference call and webcast today at 5:00 p.m. Eastern Time. The conference call may be accessed by dialing 844-821-1109 for participants in the U.S. or Canada and 830-865-2550 for international callers (reference passcode 94813084). A telephone replay of the conference call may be accessed through October 18, 2017 by dialing 855-859-2056 for callers in the U.S. or Canada and 404-537-3406 for international callers (reference passcode 94813084). 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 October 18, 2017.

About Pimavanserin

Pimavanserin is a selective serotonin inverse agonist (SSIA) preferentially targeting 5-HT_{2A} receptors. These receptors are thought to play an important role in dementia-related psychosis. Pimavanserin is being evaluated in an extensive clinical development program by ACADIA across multiple indications. Pimavanserin (34 mg) was approved for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis by the FDA in 2016 under the trade name NUPLAZID®. NUPLAZID is not approved for the treatment of patients with dementia-related psychosis.

About Dementia-Related Psychosis

Around 8 million people in the United States are living with dementia and approximately half are diagnosed with the disease. Studies suggest that approximately 30% of patients with dementia have psychosis, commonly consisting of hallucinations and delusions. Dementia-related psychosis is a serious medical condition for which there is currently no FDA-approved therapy. 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, earlier progression to nursing home care, more rapid progression of dementia, and increased risk of morbidity and mortality.

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 maintains a website at www.acadia-pharm.com to which we regularly post copies of our press releases as well as additional information and through which interested parties can subscribe to receive e-mail alerts.

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 benefits to be derived from NUPLAZID (pimavanserin); the utility of pimavanserin in indications other than hallucinations and delusions associated with Parkinson's disease psychosis, including indications falling within dementia-related psychosis; whether the profile observed in the Phase II -019 Study in Alzheimer's disease psychosis will be beneficial to elderly patients with dementia-related psychosis; whether the development path for dementia-related psychosis will be efficient; whether NUPLAZID will receive a broad indication for dementia-related psychosis; whether the approved use of NUPLAZID will be significantly expanded; whether positive results from one Phase III study of pimavanserin in dementia-related psychosis will be sufficient basis for the filing or approval of an sNDA for that indication; the timing of presentation of clinical data and results; and the timing or results of future studies involving pimavanserin. 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 discovery, 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, 2016 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) tablets
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.

NUPLAZID is an atypical antipsychotic indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis.

Contraindication: NUPLAZID is contraindicated in patients with a history of hypersensitivity reaction to pimavanserin or any of its components.

Reactions have included rash, urticaria, tongue swelling, circumoral edema, and throat tightness.

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: Strong CYP3A4 inhibitors (eg, ketoconazole) increase NUPLAZID concentrations. Reduce the NUPLAZID dose by one-half. Strong CYP3A4 inducers may reduce NUPLAZID exposure, monitor for reduced efficacy. Increase in NUPLAZID dosage may be needed.

Renal Impairment: No dosage adjustment for NUPLAZID is needed in patients with mild to moderate renal impairment. Use of NUPLAZID is not recommended in patients with severe renal impairment.

Hepatic Impairment: Use of NUPLAZID is not recommended in patients with hepatic impairment. NUPLAZID has not been evaluated in this patient population.

Pregnancy: Use of NUPLAZID in pregnant women has not been evaluated and should therefore be used in pregnancy only if the potential benefit justifies the potential risk to the mother and fetus.

Pediatric Use: Safety and efficacy have not been established in pediatric patients.

Dosage and Administration: Recommended dose: 34 mg per day, taken orally as two 17-mg tablets once daily, without titration.

For additional Important Safety Information, including boxed warning, please see the full Prescribing Information for NUPLAZID at https://www.nuplazid.com/pdf/NUPLAZID_Prescribing_Information.pdf.

View source version on businesswire.com: http://www.businesswire.com/news/home/20171004006297/en/

Source: ACADIA Pharmaceuticals Inc.

Investor Contact:
ACADIA Pharmaceuticals Inc.
Lisa Barthelemy
(858) 558-2871
ir@acadia-pharm.com
or
Media Contact:
Taft Communications
Bob Laverty
(609) 558-5570
bob@taftcommunications.com