ACADIA Pharmaceuticals Presents Data from the Phase II Study of Pimavanserin in Alzheimer's Disease Psychosis at the Clinical Trials on Alzheimer's Disease (CTAD) 2017 Meeting

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Data Confirmed Significant Improvement in Psychosis in Patients with Alzheimer's Disease with Substantively Greater Benefit in Patients with More Severe Psychotic Symptoms

SAN DIEGO--(BUSINESS WIRE)--Nov. 3, 2017-- ACADIA Pharmaceuticals Inc. (NASDAQ: ACAD), a biopharmaceutical company focused on the development and commercialization of innovative medicines to address unmet medical needs in central nervous system (CNS) disorders, today announced the presentation of data from the Phase II -019 Study of pimavanserin in Alzheimer's disease psychosis at the 10 th Clinical Trials on Alzheimer's Disease (CTAD) meeting in Boston. The -019 Study data are being presented at the symposium titled, "The Importance of Serotonin in Alzheimer's Disease Psychosis and the Role of Pimavanserin."

Pimavanserin met the primary endpoint in the Phase II -019 Study, showing a statistically significant reduction in psychosis versus placebo, as previously reported. Data presented at CTAD showed multiple sensitivity and responder analyses supportive of the primary result and demonstrated substantively greater benefit in those patients with more severe psychosis. Building on these data, ACADIA recently initiated the Phase III HARMONY study of pimavanserin in dementia-related psychosis. Dementia-related psychosis includes psychosis in Alzheimer's disease, dementia with Lewy bodies, Parkinson's disease dementia, vascular dementia, and frontotemporal dementia. There is no drug approved by the FDA for dementia-related psychosis. In October 2017, the FDA granted Breakthrough Therapy Designation for pimavanserin for the treatment of dementia-related psychosis.

"In the Phase II -019 Study, pimavanserin significantly reduced psychosis in patients with Alzheimer's disease without negatively impacting cognition," said Clive Ballard, MBChB, MRCPsych, Pro-Vice-Chancellor and Executive Dean, University of Exeter Medical School. "Pimavanserin also had a favorable tolerability profile compared to known adverse effects of current antipsychotics. With no approved treatment for dementia-related psychosis, there is a significant unmet need. The results of the study indicate that pimavanserin could be an important new treatment option for this elderly and underserved patient population."

Key Findings from the Phase II -019 Study Presented at CTAD Symposium

The Phase II -019 Study data are being presented by Clive Ballard in the presentation titled, "Clinical Trial of Pimavanserin in Alzheimer's Disease Psychosis." The Phase II -019 Study was a double-blind, placebo-controlled trial designed to evaluate the efficacy and safety of pimavanserin in 181 patients with Alzheimer's disease psychosis. Top-line results of the study were previously reported in December 2016.

Pimavanserin met the primary endpoint in the study, showing a statistically significant reduction in psychosis versus placebo as measured by the Neuropsychiatric Inventory-Nursing Home (NPI-NH) Psychosis score at week 6 of dosing (delta = 1.84, p=0.0451, effect size [Cohen's d] = 0.32). The proportion of responders at week 6 that had an NPI-NH Psychosis score improvement of ≥ 30% was 55.2% for pimavanserin-treated patients versus 37.4% for placebo (p=0.0159).

Importantly, in the -019 Study, no detrimental effect was observed on cognition for pimavanserin-treated patients compared to placebo. Atypical antipsychotics have been associated with a statistically significant acceleration of cognitive deterioration in patients with Alzheimer's disease.

The pimavanserin and placebo groups did not separate statistically on the secondary endpoints of the Alzheimer's Disease Cooperative Study - Clinical Global Impression of Change (ADCS-CGIC) or the Cohen-Mansfield Agitation Inventory Short Form (CMAI-SF), nor on the exploratory endpoints of the mean change in NPI-NH Psychosis score at week 12 or the Alzheimer's Disease Cooperative Study - Activities of Daily Living (ADCS-ADL).

Data presented at CTAD from a pre-specified subgroup analysis demonstrated a substantively larger and significant reduction in psychosis in pimavanserin-treated patients with more severe psychosis, further underscoring the effect seen on the primary result. Approximately one-third of patients in the study had more severe psychotic symptoms (NPI-NH Psychosis score ≥12). In this subgroup, pimavanserin demonstrated a statistically significant reduction in psychosis versus placebo on the NPI-NH Psychosis score at week 6 (delta = 4.43, p=0.0114, effect size [Cohen's d] = 0.73). Additionally, the proportion of responders at week 6 that had an NPI-NH Psychosis score improvement of ≥ 30% was 88.9% for pimavanserin-treated patients versus 43.3% for placebo (p=0.0004).

Larger effects were also observed on the NPI-NH Psychosis score in pimavanserin-treated patients with prior antipsychotic use.

As previously reported, pimavanserin was well tolerated in this frail and elderly population and the safety profile was consistent with what has been observed in previous studies.

Other Presentations at CTAD Symposium: "The Importance of Serotonin in Alzheimer's Disease Psychosis and the Role of Pimavanserin"

The -019 Study data are being presented as part of a three-part symposium. The symposium also includes a presentation by Stephen M. Stahl, MD, PhD, Adjunct Professor of Psychiatry, University of California, San Diego, titled, "The Role of 5-HT $_{2A}$ Receptors in the Pharmacology of Alzheimer's Disease Psychosis." Serotonin 2A receptors are highly expressed in brain regions critical for processing sensory information and performing executive functions. Circuitry performing these functions may be deregulated when neurodegeneration has occurred. Selective 5-HT$_{2A}$ inverse agonists/antagonists can be used to restore balance to these deregulated circuits. Pimavanserin is a non-dopaminergic selective serotonin inverse agonist (SSIA) preferentially targeting 5-HT$_{2A}$ receptors.

Furthermore, a presentation by Pierre N. Tariot, MD, Banner Alzheimer's Institute and University of Arizona College of Medicine, titled, "Review of

Pimavanserin Clinical Results in the Context of Historical Alzheimer's Disease Psychosis Trials," reviews the results of the pimavanserin Phase II -019 Study compared to Alzheimer's disease psychosis studies with other antipsychotics. Off-label use of atypical antipsychotics is associated with modest and often equivocal efficacy and significant acceleration in cognitive decline in patients with dementia, as well as other adverse effects.

The symposium's moderator is Jeffrey Cummings, MD, ScD, Director of Cleveland Clinic Lou Ruvo Center for Brain Health, who reviews epidemiology, clinical phenomenology and psycho-social consequences of dementia-related psychosis and the current treatment options and opportunities.

About Dementia-Related Psychosis

Around 8 million people in the United States are living with dementia, of which around 5.5 million people suffer from Alzheimer's disease. Approximately half the people with dementia 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 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.

Phase III HARMONY Study

Pimavanserin is currently being evaluated in a Phase III study, HARMONY, which is designed to evaluate its efficacy and safety 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 FDA has granted Breakthrough Therapy Designation for pimavanserin for the treatment of dementia-related psychosis. No drug is approved by the FDA for dementia-related psychosis.

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®, and is the first and only medicine approved for this indication. NUPLAZID is not approved for the treatment of patients with dementia-related psychosis.

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 pimavanserin could be an important new treatment for elderly and underserved patients with dementia-related psychosis; whether selective 5-HT2A inverse agonists/antagonists, such as pimavanserin, can be used to restore balance to brain regions critical for processing sensory information and performing executive functions; 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 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: 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/20171103005668/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