ACADIA Pharmaceuticals Announces Positive Top-line Results from ADVANCE Trial of Pimavanserin as Treatment for Negative Symptoms of Schizophrenia

November 25, 2019

- ACADIA to initiate second pivotal study in the first half of 2020

- Conference call and webcast to be held today at 5:00 p.m. Eastern Time

SAN DIEGO--(BUSINESS WIRE)--Nov. 25, 2019-- ACADIA Pharmaceuticals Inc. (Nasdaq: ACAD), today announced positive top-line results from its ADVANCE study, a 26-week, randomized, double-blind, placebo-controlled study in 403 patients. ADVANCE evaluated the efficacy and safety of adjunctive pimavanserin treatment in patients with predominantly negative symptoms of schizophrenia who have achieved adequate control of positive symptoms with their existing antipsychotic treatment. No drug is approved by the FDA for the treatment of the negative symptoms of schizophrenia.

Pimavanserin demonstrated a statistically significant improvement on the study's primary endpoint, the change from baseline to week 26 on the Negative Symptom Assessment-16 (NSA-16) total score, compared to placebo (-10.4 vs. -8.5; p=0.043; effect size = 0.21). A greater improvement in the NSA-16 total score compared to placebo was observed in the 53.8% of patients (n=107) who received the highest pimavanserin dose of 34 mg (-11.6 vs. -8.5; unadjusted p=0.0065, effect size = 0.34). In this study, pimavanserin did not separate from placebo on the key secondary endpoint, the Personal and Social Performance (PSP) scale.

ACADIA plans to commence a second pivotal study with the 34 mg dose of pimavanserin in the first half of 2020. Additional results from the ADVANCE study will be presented at future scientific meetings.

"The negative symptoms of schizophrenia such as social withdrawal, apathy, anhedonia, loss of motivation, blunted affect, and restricted speech contribute significantly to low function levels, long-term disability, and increased caregiver burden," said Dr. Henry A. Nasrallah, M.D., Professor of Psychiatry, Neurology, & Neuroscience, Director, Neuropsychiatry and Schizophrenia Programs, at the University of Cincinnati College of Medicine. "Historically, it has been a challenge for clinicians to treat and significantly improve the negative symptoms of schizophrenia. There are no FDA-approved treatments indicated for the treatment of the negative symptoms of schizophrenia and there remains a serious and significant unmet need."

"The positive efficacy results and favorable tolerability profile of pimavanserin observed in the ADVANCE study represent an important step forward for patients and their families, given the lack of currently approved treatment options for the negative symptoms of schizophrenia," said Serge Stankovic, M.D., M.S.P.H., ACADIA's President. "We are pleased with the positive efficacy findings in this difficult to treat patient population and identified the 34 mg dose as demonstrating greater efficacy with favorable tolerability. We look forward to initiating a second pivotal study with the 34 mg dose during the first half of 2020."

In the study, pimavanserin was well-tolerated with high completion rates of approximately 86% in both the pimavanserin and placebo treatment groups and similar rates of adverse events between pimavanserin (39.8%) and placebo (35.1%). Additionally, no clinically significant differences in vital signs, weight, metabolic syndrome or extrapyramidal symptoms were observed in the pimavanserin group compared to placebo. Serious adverse events were reported in 2.0% of patients on pimavanserin and 0.5% of patients on placebo and discontinuations due to adverse events were also low, 5.0% for pimavanserin and 3.0% for placebo.

About ADVANCE

The Phase 2 ADVANCE study was a 26-week, randomized, double-blind, placebo-controlled, multi-center, international study designed to examine the efficacy and safety of pimavanserin in patients with schizophrenia who have predominant negative symptoms while on a stable background antipsychotic therapy. 403 patients were randomized to receive once-daily pimavanserin (n=201) or placebo (n=202) as an adjunct treatment to their ongoing antipsychotic in a flexible dosing regimen. The starting daily dose of 20 mg of pimavanserin at baseline could have been adjusted to 34 mg or 10 mg during the first eight weeks of treatment. 53.8% of patients who were randomized to receive pimavanserin completed the trial on 34 mg, 44.7% on 20 mg, and 1.5% on 10 mg. The primary endpoint of the study was the change from baseline to week 26 on the Negative Symptom Assessment-16 (NSA-16) total score.

Baseline characteristics were similar across two treatment arms. The most prevalent background antipsychotics in the study included risperidone (38.5%), aripiprazole (32.5%), and olanzapine (28.0%). The average age of patient in the study was 37.2 years.

Conference Call and Webcast Information

ACADIA will discuss top-line results from its ADVANCE study of pimavanserin for adjunctive treatment for the negative symptoms of schizophrenia via conference call and webcast today at 5:00 p.m. Eastern Time. The conference call can be accessed by dialing 855-638-4820 for participants in the U.S. or Canada and 443-877-4067 for international callers (reference passcode 5696604). A telephone replay of the conference call may be accessed through December 2, 2019 by dialing 855-859-2056 for callers in the U.S. or Canada and 404-537-3406 for international callers (reference passcode 5696604). The conference call will also be webcast live on ACADIA's website, www.acadia-pharm.com, in the investors section and archived until December 25, 2019.

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 Schizophrenia and Negative Symptoms

According to the National Mental Health Institute, approximately one percent of the U.S. population develops schizophrenia during their lifetime[1]. Schizophrenia is a chronic, debilitating and often progressive mental illness characterized by disturbances in thinking, emotional reaction, and behavior. These disturbances may include positive symptoms, such as hallucinations and delusions, and a range of negative symptoms, including loss of interest, emotional withdrawal, and cognitive disturbances.

Studies show that about 40 to 50 percent of schizophrenia patients suffer from predominant negative symptoms[2]. While currently available antipsychotic treatments for schizophrenia target positive symptoms, most patients remain functionally impaired because of negative symptoms, cognitive deficits, and limited social function.

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 the negative symptoms of schizophrenia 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]NAMI, Mental Help, PsyCom, SAMHSA study, NIMH data consolidation.
[2]Patel et al. 2015; Haro et al. 2015; Bobes et al. 2010; Chue and Lalonde, 2014.

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