ACADIA Pharmaceuticals to Present Phase 2 CLARITY Results for Pimavanserin as an Adjunctive Treatment in Major Depressive Disorder at the 2019 American Psychiatric Association Annual Meeting

May 18, 2019

SAN DIEGO--(BUSINESS WIRE)--May 18, 2019-- 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 disorders, today announced it will present data from its Phase 2 CLARITY study, which evaluated the efficacy, safety, and tolerability of pimavanserin as an adjunctive treatment for major depressive disorder (MDD) at the 2019 American Psychiatric Association Annual Meeting in San Francisco, May 18 – 22, 2019.

Poster Presentation
Poster: #P8-049
Date/Time: Tuesday, May 21, 2:00 p.m. – 4:00 p.m. Pacific Time
Title: CLARITY: A Phase 2 Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Adjunctive Pimavanserin in Major Depressive Disorder

The Phase 2 CLARITY study was a 10-week, randomized, double-blind, placebo-controlled, multi-center, two-stage sequential parallel comparison design study that evaluated the efficacy, safety, and tolerability of pimavanserin (34 mg once daily). Pimavanserin was administered as an adjunctive treatment in patients with MDD who had an inadequate response to a stable dose of standard antidepressant therapy with either a selective serotonin reuptake inhibitor (SSRI) or a serotonin norepinephrine reuptake inhibitor (SNRI). The study randomized 207 patients across 27 clinical research centers in the U.S. and was conducted in collaboration with the Massachusetts General Hospital (MGH) Clinical Trials Network and Institute.

“There is a significant need for new therapies for the majority of patients suffering from major depressive disorder who do not respond to initial antidepressant therapy,” said Professor Maurizio Fava, M.D., Executive Vice Chair, Department of Psychiatry, MGH, Director of the Division of Clinical Research of the MGH Research Institute, and Associate Dean for Clinical & Translational Research, Harvard Medical School. “The results observed in the Phase 2 CLARITY study combined with a favorable tolerability profile provides evidence that adjunctive treatment with pimavanserin may provide meaningful benefit to those MDD patients who have an inadequate response to either a SSRI or a SNRI therapy.”

In the trial, pimavanserin met the overall primary endpoint of the weighted average results of Stage 1 and Stage 2 by significantly reducing the 17-item Hamilton Depression Rating Scale total score compared to placebo (p=0.039). On the key secondary endpoint, pimavanserin demonstrated statistically significant reductions compared to placebo in the Sheehan Disability Scale score (p=0.004). Positive results were also observed for seven other secondary endpoints, including improvement in daytime sleepiness as measured by the Karolinska Sleepiness Scale and improvement in sexual function as measured by the Massachusetts General Hospital Sexual Functioning Index.

“In this Phase 2 study of pimavanserin as an adjunctive treatment for MDD, we found patients treated with pimavanserin experienced significant reduction in their depression symptoms in addition to improvement in daytime sleepiness and sexual function when compared to placebo,” said Serge Stankovic, M.D., M.S.P.H., ACADIA’s President. “These results are encouraging for patients with MDD who may experience challenges with their current treatment options. We look forward to further evaluating pimavanserin as an adjunctive treatment in our ongoing Phase 3 CLARITY program.”

On April 25, ACADIA announced it had initiated its Phase 3 CLARITY program for pimavanserin as an adjunctive treatment for MDD. The CLARITY-2 study will be based in the U.S. and has already initiated enrollment and the CLARITY-3 study will be based outside the U.S. and will initiate enrollment in the upcoming months. Both studies are six-week, parallel-designed, randomized, double-blind, placebo-controlled, multi-center studies designed to evaluate the efficacy and safety of pimavanserin as adjunctive treatment in patients with MDD who have an inadequate response to standard antidepressant therapy with either a SSRI or a SNRI.

About Major Depressive Disorder
According to the National Institute of Mental Health, MDD affects approximately 16 million adults in the U.S.[1], with approximately 2.5 million adults treated with adjunctive therapy.[2,3] MDD is a condition characterized by depressive symptoms such as a depressed mood or a loss of interest or pleasure in daily activities for more than two weeks, as well as impaired social, occupational, or other important functioning. The majority of people who suffer from MDD do not respond adequately to initial antidepressant therapy.[4]

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 depression, psychosis, and other neuropsychiatric disorders. ACADIA is evaluating pimavanserin in an extensive clinical development program across multiple indications with significant unmet need including dementia-related psychosis, schizophrenia inadequate response, schizophrenia-negative symptoms, and MDD. 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 the adjunctive treatment of patients with MDD.

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 inadequate response, schizophrenia-negative symptoms, 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 adjunctive treatment for MDD 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]National Institute of Mental Health. (2017). Major Depression. Retrieved from http://www.nimh.nih.gov/health/statistics/major-depression.shtml.

[2]IMS NSP, NPA, NDTI MAT-24 month data through Aug-2017.

[3]PLOS One, Characterization of Treatment Resistant Depression Episodes in a Cohort of Patients from a US Commercial Claims Database, Oct 2013, Vol 8, Issue 10.

[4]Rush AJ, et al. (2007) Am J. Psychiatry 163:11, pp. 1905-1917 (STAR*D Study).

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Source: ACADIA Pharmaceuticals Inc.

Investor Contact:
ACADIA Pharmaceuticals Inc.
Mark Johnson, CFA
(858) 261-2771

ir@acadia-pharm.com

Media Contact:
ACADIA Pharmaceuticals Inc.
Maurissa Messier
(858) 768-6068
media@acadia-pharm.com