ACADIA Pharmaceuticals to Combine CLARITY-2 and CLARITY-3 Phase 3 Studies Evaluating Pimavanserin for the Adjunctive Treatment of Major Depressive Disorder

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- Top-line results expected in 3Q20

SAN DIEGO--(BUSINESS WIRE)--May 26, 2020-- ACADIA Pharmaceuticals Inc. (Nasdaq: ACAD) announced today that following positive feedback from the U.S. Food and Drug Administration the company plans to combine its CLARITY-2 and CLARITY-3 Phase 3 studies evaluating pimavanserin for the adjunctive treatment of major depressive disorder (MDD) into one study with a pre-specified statistical analysis plan. As a result, no new patients will be enrolled in the two identically designed Phase 3 studies, each of which will be concluded with slightly more than 50% enrollment. Top-line results from the combined study are expected in the third quarter of 2020.

If positive, the results from the combined study, along with the positive results from the previously announced pivotal CLARITY study, would form the basis for a supplemental new drug application for pimavanserin in the adjunctive treatment of MDD.

About CLARITY-2 and CLARITY-3

CLARITY-2 and CLARITY-3 are both 6-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 selective serotonin reuptake inhibitor (SSRI) or a serotonin norepinephrine reuptake inhibitor (SNRI). Patients in both studies were randomized to receive six weeks of oral treatment with either 34 mg of pimavanserin or placebo, once daily, in addition to their ongoing antidepressant. The primary endpoint in both studies is the change from baseline on the 17-item Hamilton Depression Rating Scale (HAMD-17) total score.

Patients who completed the Phase 3 studies were eligible to participate in the ongoing 52-week open-label extension study to evaluate the long-term safety and tolerability of pimavanserin in MDD. The open-label extension study is continuing as planned.

About CLARITY

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

In the trial, pimavanserin met the overall primary endpoint of the weighted average results of Stage 1 and Stage 2 by significantly reducing the HAMD-17 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 the Karolinska Sleepiness Scale (p=0.0205) and the Massachusetts General Hospital Sexual Functioning Index (p=0.0003).

In the parallel design portion (Stage 1) of this SPCD study, adding pimavanserin to first-line SSRI or SNRI therapy also significantly reduced HAMD-17 scores compared to placebo (p=0.0003). On the key secondary endpoint, pimavanserin also demonstrated statistically significant reductions compared to placebo in the Sheehan Disability Scale score (p=0.004).

About Major Depressive Disorder

According to the National Institute of Mental Health, MDD affects approximately 17 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 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 the potential benefits of pimavanserin as adjunctive treatment for major depressive disorder 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, 2019 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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