ACADIA Pharmaceuticals Presents Additional Positive Data from the Phase 2 CLARITY Study with Pimavanserin in Adjunctive Major Depressive Disorder at 2019 Psych Congress

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—Pimavanserin as adjunctive treatment to SSRI/SNRI therapies significantly improved sexual dysfunction symptoms compared to placebo in MDD patients

SAN DIEGO--(BUSINESS WIRE)--Oct. 7, 2019-- ACADIA Pharmaceuticals Inc. (Nasdaq: ACAD) today announced that based on secondary analyses from its Phase 2 CLARITY study, adjunctive pimavanserin showed the potential to improve symptoms of sexual dysfunction experienced by patients with major depressive disorder (MDD). These additional data were presented in the poster, "Improvement of Sexual Function Observed During Treatment of Major Depressive Disorder With Adjunctive Pimavanserin" at the 2019 Psych Congress, October 3-6 in San Diego, California.

The CLARITY study was a 10-week, double-blind, placebo-controlled, two-stage sequential parallel comparison design (SPCD) study, which evaluated the efficacy, safety, and tolerability of pimavanserin as an adjunctive treatment for MDD in patients who have had an inadequate response to SSRI or SNRI therapy. In the study, pimavanserin met the overall primary endpoint, the key secondary endpoint, and seven of the eleven pre-specified additional secondary endpoints, including the Massachusetts General Hospital Sexual Functioning Index (MGH-SFI) (nominal p=0.0003)[1]. In addition, in Stage 1, the all-inclusive, parallel design portion of the study (n=207), adjunctive pimavanserin showed significant improvement relative to placebo on mean MGH-SFI scores from baseline after five weeks of treatment (nominal p=0.0002; effect size=0.614).

"Sexual dysfunction occurs in 40%-60% of patients with major depressive disorder, due to either the illness itself and or the effects of antidepressant treatment[2], and is a troublesome side effect for patients who struggle with depression," said Marlene P. Freeman, M.D., Associate Professor of Psychiatry, Harvard Medical School and the Abra Prentice Foundation Chair in Women's Mental Health at Massachusetts General Hospital and co-author of the study. "These results show the potential of adjunctive pimavanserin to not only decrease depressive symptoms, but also address some of the sexual dysfunction observed in MDD patients treated with SSRI/SNRI antidepressant therapy."

"The results of the Phase 2 CLARITY study suggest pimavanserin may represent a novel approach to adjunctive treatment for patients suffering from MDD, including these positive data on sexual dysfunction symptoms observed in pimavanserin patients treated with SSRI/SNRIs. In the study we also observed important additional improvements for patients with MDD, including early and sustained antidepressant response over placebo, decreased daytime sleepiness with overall favorable tolerability," said Serge Stankovic, M.D., M.S.P.H., ACADIA's President. "We look forward to further confirm these findings in our ongoing Phase 3 CLARITY program."

About the Phase 2 CLARITY Study

The study was conducted in collaboration with the MGH Clinical Trials Network & Institute (CTNI) and randomized 207 adult patients with a confirmed inadequate response to existing first-line selective serotonin reuptake inhibitor (SSRI) or serotonin norepinephrine reuptake inhibitor (SNRI) therapy for MDD across 27 U.S. clinical research centers.

Consistent with the SPCD design, the study was conducted in two, five-week sequential stages. Eligible subjects continued receiving their SSRI or SNRI antidepressant at a stable dose for the duration of the study. Patients were randomly assigned (1:3) to pimavanserin 34 mg/day or placebo in Stage 1. Placebo non-responders in Stage 1 (defined as HAMD-17 total score >14 and a percent-reduction from baseline in HAMD-17 total score of <50% at week 5) were re-randomized (1:1) to Stage 2 to receive pimavanserin 34 mg/day or placebo. The primary endpoint of the study was the change in HAMD-17 total score for Stage 1 and Stage 2. Treatment differences from Stage 1 and Stage 2 were combined as weighted averages.

About Major Depressive Disorder

According to the National Institute of Mental Health, MDD affects approximately 16 million adults in the U.S.[3], with approximately 2.5 million adults treated with adjunctive therapy.[4,5] 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.[6]

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,

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 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]Fava M, Dirks B, Freeman MP, et al. A phase 2, randomized, double-blind, placebo-controlled study of adjunctive pimavanserin in patients with major depressive disorder and an inadequate response to therapy (CLARITY). *J Clin Psychiatry*. 2019;80(6):19m12928.
[2]Clayton AH, El Haddad S, Iluonakhamhe J-P, et al. Sexual dysfunction associated with major depressive disorder and antidepressant treatment. *Expert Opin Drug Saf*. 2014;13(10):1361 1374. PubMed CrosRef.
[3]National Institute of Mental Health. (2017). Major Depression. Retrieved from http://www.nimh.nih.gov/health/statistics/major-depression.shtml
[4]IMS NSP, NPA, NDTI MAT-24 month data through Aug 2017.
[5]*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.
[6]Rush AJ, et al. (2007) *Am J. Psychiatry* 163:11, pp. 1905-1917 (STAR*D Study).

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