ACADIA Pharmaceuticals Initiates Phase 3 CLARITY Program with Pimavanserin as Adjunctive Treatment for Major Depressive Disorder

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SAN DIEGO--(BUSINESS WIRE)--Apr. 25, 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 (CNS) disorders, today announced the initiation of the Phase 3 CLARITY-2 study and plans to initiate the Phase 3 CLARITY-3 study in the upcoming months. These studies will evaluate the efficacy and safety of pimavanserin as adjunctive treatment in patients with major depressive disorder (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). Pimavanserin is a selective serotonin inverse agonist preferentially targeting 5-HT_{2A} receptors, which may play a role in depression.

“We are pleased to announce the initiation of the Phase 3 CLARITY program. The results observed in the original Phase 2 CLARITY study showed significant promise for patients with MDD, including a significant antidepressant response, improvement in disability, decreased daytime sleepiness, no meaningful weight gain, and improved sexual function,” said Serge Stankovic, M.D., M.S.P.H., ACADIA’s President. “We believe pimavanserin has the potential to be a very important treatment option for the millions of MDD patients where there remains unmet medical need. Based on feedback we received from the U.S. FDA, if we’re successful in the Phase 3 program, we plan to use the Phase 2 CLARITY study and positive study results from at least one of these two Phase 3 studies to support a supplemental NDA submission.”

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 SSRI or a SNRI. CLARITY-2 will enroll approximately 280 patients in the U.S. and CLARITY-3 will enroll approximately 280 patients internationally. Patients in both studies will be 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 complete the CLARITY-2 or CLARITY-3 studies will be eligible to participate in a 52-week open-label extension study to evaluate the long-term safety and tolerability of pimavanserin.

About CLARITY
CLARITY was a Phase 2, 10-week, randomized, double-blind, placebo-controlled, multi-center, 2-stage sequential parallel comparison design 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 MGH Clinical Trials Network & Institute and randomized 207 patients across 28 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).

About Major Depressive Disorder (MDD)
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 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 major depressive disorder. 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 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 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 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, 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.

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).

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 CYP3A4 inducers may reduce NUPLAZID exposure. Monitor patients for reduced efficacy and an increase in NUPLAZID dosage may be needed.

Pediatric Use: Safety and efficacy have not been established in pediatric patients.

Dosage and Administration: Recommended dose: 34 mg taken orally once daily, without titration.

Indication: NUPLAZID is an atypical antipsychotic indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088. You can also call ACADIA Pharmaceuticals Inc. at 1-844-4ACADIA (1-844-422-2342).

NUPLAZID is available as 34 mg capsules and 10 mg tablets.

Please see the full Prescribing Information including Boxed WARNING for NUPLAZID at https://www.nuplazid.com/pdf/NUPLAZID_Prescribing_Information.pdf.

View source version on businesswire.com: https://www.businesswire.com/news/home/20190425005313/en/

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