



ACADIA Announces Pimavanserin Meets Primary and Key Secondary Endpoints in Pivotal Phase III Parkinson's Disease Psychosis Trial

November 27, 2012

Pimavanserin Demonstrates Highly Significant Antipsychotic Efficacy and Maintenance of Motor Control in Parkinson's Patients

Significant Improvements Also Observed in All Secondary and Exploratory Measures

Conference Call and Webcast to Be Held Today, November 27, 2012, at 8:00 am Eastern Time

SAN DIEGO--(BUSINESS WIRE)--Nov. 27, 2012-- ACADIA Pharmaceuticals Inc. (NASDAQ: ACAD) today announced successful top-line results from its pivotal Phase III trial evaluating the efficacy, tolerability and safety of pimavanserin in patients with Parkinson's disease psychosis (PDP). Pimavanserin is ACADIA's proprietary, non-dopaminergic product candidate that selectively blocks serotonin 5-HT_{2A} receptors. Pimavanserin met the primary endpoint in the Phase III trial by demonstrating highly significant antipsychotic efficacy as measured using the 9-item SAPS-PD scale (p=0.001). Pimavanserin also met the key secondary endpoint for motoric tolerability as measured using Parts II and III of the Unified Parkinson's Disease Rating Scale, or UPDRS. These results were further supported by a highly significant improvement in the secondary efficacy measure, the Clinical Global Impression Improvement, or CGI-I, scale (p=0.001). In addition, clinical benefits were observed in all exploratory efficacy measures with significant improvements in nighttime sleep, daytime wakefulness and caregiver burden. Consistent with previous studies, pimavanserin was safe and well tolerated in this Phase III trial.

"These data represent an unprecedented advance for Parkinson's patients who suffer from the psychosis frequently associated with this disease," said Jeffrey Cummings, M.D., Sc.D., Director of the Cleveland Clinic Lou Ruvo Center for Brain Health. "Among Parkinson's patients, psychosis is the leading cause of institutionalization and dramatically increases the risk of mortality. Neurologists have limited options to treat this serious disorder, and off-label use of current antipsychotics is linked to increased risk of death and serious adverse events, as well as loss of motor control. The results of this study suggest that a selective, non-dopaminergic-based therapy has the potential to transform the treatment landscape for patients with this debilitating disorder."

Primary Endpoint

The primary endpoint of the trial was antipsychotic efficacy as measured using the SAPS-PD, a 9-item scale adapted from the hallucinations and delusions domains of the Scale for the Assessment of Positive Symptoms, by comparing the mean change from baseline to day 43 for pimavanserin versus placebo. SAPS-PD assessments were performed by blinded, independent centralized raters. The pimavanserin arm demonstrated a robust 5.79 point improvement in psychosis at day 43 compared to a 2.73 point improvement for placebo, representing a highly significant and clinically meaningful treatment difference of 3.06 points on SAPS-PD (p=0.001).

	Baseline Mean		Mean Change at Day 43		P-value
	PBO (n=90)	PIM (n=95)	PBO	PIM	
SAPS-PD	14.73	15.88	-2.73	-5.79	0.001

Note: mixed model repeated measures (MMRM) method was applied in the primary analysis of the intent-to-treat (ITT) population. The significance test was based on least-square mean change from baseline for each arm using a 2-sided beta = 0.05.

Key Secondary Endpoint

The key secondary endpoint of the trial evaluated motoric tolerability and functional outcome using Parts II and III of the UPDRS. The objective of this secondary endpoint was to demonstrate that pimavanserin could achieve its antipsychotic effects without worsening motor function as compared to placebo in PDP patients. A pre-specified, non-inferiority analysis was used to compare the mean change from baseline to day 43 for pimavanserin versus placebo using a two-sided 95 percent confidence interval (CI) for the treatment difference. Motoric improvements were seen in both the pimavanserin and placebo arms and the CI associated with the treatment difference did not exceed a pre-specified margin of 5 points for clinically relevant change, confirming that pimavanserin met this key secondary endpoint and did not worsen motor function in PDP patients.

Secondary and Exploratory Efficacy Measures

The secondary efficacy measure in the trial was an assessment of clinical global improvement by the investigator using the CGI-I scale. Pimavanserin demonstrated a highly significant improvement on this measure (p=0.001), further supporting its antipsychotic efficacy.

In addition, other clinical benefits of pimavanserin were observed in exploratory efficacy measures of sleep and caregiver burden. Sleep was assessed using the SCOPA-sleep scale, which was designed to enable the investigator to evaluate nighttime sleep and daytime wakefulness in Parkinson's patients. Pimavanserin demonstrated significant improvements on both nighttime sleep (p=0.045) and daytime wakefulness (p=0.012) on SCOPA.

Caregiver burden was assessed using the Caregiver Burden Scale. This scale was completed by the caregiver to provide a quantitative assessment of burden associated with the patient's functional/behavioral impairments, the circumstances of at-home care, as well as the caregiver's health, social life

and interpersonal relations. Pimavanserin demonstrated a highly significant improvement on the Caregiver Burden Scale ($p=0.002$).

Safety and Tolerability Profile

Consistent with previous studies, pimavanserin was safe and well tolerated in this trial. Based on a preliminary analysis of safety data, the most common adverse events were urinary tract infection (11.7% PBO vs. 13.5% PIM) and falls (8.5% PBO vs. 10.6% PIM). Adverse events were generally characterized as mild to moderate in nature. The only serious adverse events that occurred in more than one patient were urinary tract infection (1-PBO vs. 3-PIM) and psychotic disorder (0-PBO vs. 2-PIM). Ninety percent of the patients who completed the clinical phase of this trial elected to roll over into the ongoing open-label safety extension study. Patients were only eligible to participate in the extension study if the treating investigator also deemed them to be likely to benefit from continued treatment with pimavanserin.

"We are excited with the results of this study which demonstrate that pimavanserin has the potential to offer PDP patients a new treatment option that, for the first time, can achieve the desired clinical profile by providing an effective, safe and well tolerated antipsychotic therapy," said Uli Hacksell, Ph.D., Chief Executive Officer of ACADIA. "We remain committed to advancing pimavanserin to registration as a first-in-class treatment for this large unmet medical need. These results also suggest that pimavanserin may have the ideal clinical profile to address a broader range of neuropsychiatric disorders that are underserved by currently marketed antipsychotics."

"These significant and consistent top-line results are a strong validation of the optimized study design used in this trial," said Roger G. Mills, M.D., ACADIA's Executive Vice President of Development. "Encouragingly, benefits of pimavanserin were seen by patients, caregivers and investigators, as well as the independent raters. Following the successful outcome of this pivotal Phase III trial, we will continue our ongoing preparations for a confirmatory pivotal Phase III trial, the -021 Study, using the same trial design."

About the Trial Design

The pivotal Phase III trial, referred to as the -020 Study, was a multi-center, double-blind, placebo-controlled study designed to evaluate the efficacy, tolerability and safety of pimavanserin as a treatment for patients with PDP. A total of 199 patients were enrolled in the study and randomized on a one-to-one basis to receive either 40 mg of pimavanserin or placebo once-daily for six weeks, following a two-week screening period including brief psycho-social therapy. Patients also received stable doses of their existing anti-Parkinson's therapy throughout the study. The primary endpoint of the -020 Study was antipsychotic efficacy as measured using the "SAPS-PD" scale, which consists of nine items from the hallucinations and delusions domains of the Scale for the Assessment of Positive Symptoms, or SAPS. These nine items have been shown to be particularly relevant to the expression of psychotic symptoms in patients with Parkinson's disease and to have high inter-rater reliability for assessment of severity. Motoric tolerability was a key secondary endpoint in the study and was measured using Parts II and III of the Unified Parkinson's Disease Rating Scale, or UPDRS.

Conference Call and Webcast Information

ACADIA will host a conference call and webcast with slides today, November 27, 2012 at 8:00 a.m. Eastern Time to present the top-line results from its pivotal Phase III trial with pimavanserin in patients with PDP. The conference call can be accessed by dialing 866-783-2140 for participants in the U.S. and Canada and 857-350-1599 for international callers (reference passcode 26249437). The conference call will be webcast live on ACADIA's website, www.acadia-pharm.com, under the investors section and will be archived there until December 11, 2012. A telephone replay also may be accessed through December 11, 2012 by dialing 888-286-8010 for participants in the U.S. and Canada and 617-801-6888 for international callers (reference passcode 47904115).

About Pimavanserin

Pimavanserin is ACADIA's proprietary small molecule that acts selectively as an antagonist/inverse agonist on serotonin 5-HT_{2A} receptors and is in Phase III development as a potential first-in-class treatment for Parkinson's disease psychosis. Pimavanserin can be taken orally as a tablet once-a-day. ACADIA discovered pimavanserin and holds worldwide rights to this new chemical entity.

About Parkinson's Disease Psychosis

According to the National Parkinson's Foundation, about one million people in the United States and from four to six million people worldwide suffer from Parkinson's disease. Parkinson's disease psychosis, or PDP, is a debilitating disorder that develops in up to 60 percent of patients with Parkinson's disease. Currently, there is no FDA-approved therapy to treat PDP in the United States. PDP, commonly consisting of visual hallucinations and delusions, substantially contributes to the burden of Parkinson's disease and deeply affects the quality of life of patients. PDP is associated with increased caregiver stress and burden, nursing home placement, and increased morbidity and mortality. There is a large unmet medical need for new therapies that will effectively treat PDP without compromising motor control in patients with Parkinson's disease.

About ACADIA Pharmaceuticals

ACADIA is a biopharmaceutical company focused on innovative treatments that address unmet medical needs in neurological and related central nervous system disorders. ACADIA has a pipeline of product candidates led by pimavanserin, which is in Phase III development as a potential first-in-class treatment for Parkinson's disease psychosis. ACADIA also has clinical-stage programs for chronic pain and glaucoma in collaboration with Allergan, Inc. and two advanced preclinical programs directed at Parkinson's disease and other neurological disorders. All product candidates are small molecules that emanate from discoveries made at ACADIA. ACADIA maintains a website at www.acadia-pharm.com to which ACADIA regularly posts copies of its press releases as well as additional information and through which interested parties can subscribe to receive email alerts.

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 progress and timing of ACADIA's drug discovery and development programs, either alone or with a partner, including the commencement or progress of clinical trials and the results of clinical trials, and the clinical benefits to be derived from ACADIA's product candidates, in each case including pimavanserin. In particular, forward-looking statements include statements regarding the potential implications of the results of the -020 study; the potential for selective, non-dopaminergic-based therapy, such as pimavanserin, to transform the treatment landscape for patients with PDP; the potential of pimavanserin as a first-in-class, effective, safe and well tolerated antipsychotic therapy and treatment for PDP; and the

possibility that pimavanserin may have a clinical profile suitable to address a broader range of neuropsychiatric disorders that are underserved by currently marketed antipsychotics. 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, regulatory review and commercialization, and in collaborations with others, 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, 2011 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.

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