ACADIA Study Links ACP-104 (N-desmethylclozapine) to Improved Cognition in Schizophrenia Patients

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ACADIA's Clinical Development of ACP-104 Supported by The Stanley Medical Research Institute

SAN DIEGO, Aug. 3 /PRNewswire-FirstCall/ -- ACADIA Pharmaceuticals Inc. (Nasdaq: ACAD), a biopharmaceutical company utilizing innovative science to fuel drug discovery and clinical development of novel treatments for central nervous system disorders, today announced publication of research linking the mechanism of ACP-104 (N-desmethylclozapine) to the ability of clozapine to improve cognition in patients with schizophrenia. The research, conducted by scientists at ACADIA and Vanderbilt University and published in 'Psychopharmacology' (July 16, 2004, e-pub), shows that ACP-104, the principal metabolite of clozapine, stimulates m1 muscarinic receptors in brain nerve cells that play an important role in cognition.

ACADIA is developing ACP-104 as a novel therapy for schizophrenia with the added potential for improving cognitive function. The clinical program for ACP-104 is supported in part through a three-year development agreement with The Stanley Medical Research Institute ("SMRI"), the leading nonprofit organization focused on cutting edge research into treatments for schizophrenia.

According to the published article, the muscarinic m1 receptor stimulating properties of ACP-104 are unique among all antipsychotic drugs and may be responsible for the superior clinical effects of clozapine. The researchers observed that ACP-104, but not clozapine itself, is a potent and efficacious m1 muscarinic receptor agonist. This finding resulted from a systematic profiling of a large number of neuropsychiatric drugs and their metabolites against a wide range of drug targets using ACADIA's proprietary functional assays. ACADIA has built functional assays for the majority of the drug targets in the G-protein coupled receptor and nuclear receptor gene families.

"It is widely appreciated that clozapine is unique among antipsychotic drugs in its ability to partially address the cognitive disturbances of schizophrenia," said Mark R. Brann, Ph.D., ACADIA's President and Chief Scientific Officer. "The finding that ACP-104, clozapine's predominant metabolite, is a robust m1 muscarinic receptor agonist, while clozapine itself blocks this target, was an unexpected and truly exciting discovery. By directly administering ACP-104, thereby avoiding the highly variable step of having it metabolized in the body from clozapine, we hope to offer an improved therapy that provides a more consistent cognitive benefit to patients," added Dr. Brann.

The journal article also describes the analysis of drug blood levels relative to clinical response obtained in two clinical trials that included 92 schizophrenia patients treated with clozapine. This analysis showed that high ratios of ACP-104 relative to clozapine resulted in better response by these patients in a wide range of clinical measures reflecting cognitive performance.

"We are very excited by the finding that patients who form high levels of ACP-104 from clozapine show a cognitive improvement," said Dr. Michael Knable, Executive Director of SMRI. "Treatment of cognitive deficits is perhaps the biggest challenge in schizophrenia therapy today. ACP-104 with its unique muscarinic mechanism of action may provide a promising new approach to address cognition and improve the lives of patients with schizophrenia."

About Schizophrenia

Schizophrenia is a debilitating mental illness characterized by disturbances such as hallucinations and delusions as well as a range of negative symptoms, including cognitive disturbances. Cognitive disturbances often prevent schizophrenia patients from readjusting to society and require patients to be under medical care for their entire lives. Despite the availability of a variety of current antipsychotic drugs with worldwide sales exceeding $12 billion, cognitive disturbances are poorly addressed by existing therapies and represent a large unmet medical need in schizophrenia therapy.

About ACADIA Pharmaceuticals

ACADIA Pharmaceuticals is a biopharmaceutical company utilizing innovative science to fuel drug discovery and clinical development of novel treatments for central nervous system disorders. ACADIA currently has five drug programs in clinical and preclinical development directed at large unmet medical needs and major commercial markets, including Parkinson's disease, schizophrenia, chronic pain, and glaucoma. Using its proprietary drug discovery platform, ACADIA has discovered all of the drug candidates in its product pipeline. ACADIA's headquarters and biological research facilities are located in San Diego, California and its chemistry research facilities are located in Copenhagen, Denmark.

About The Stanley Medical Research Institute

The Stanley Medical Research Institute is the largest private source of research funding for severe mental illness and is based in Bethesda, Maryland. SMRI supports research in academic and corporate environments that is directly linked to discovering new treatments for schizophrenia and bipolar disorder. Further information about SMRI can be obtained at www.stanleyresearch.org.

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 efficacy and development of ACP-104. 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 and commercialization. For a discussion of these and other factors, please refer to the company's registration statement on Form S-1 as well as other subsequent filings with the Securities and Exchange Commission.

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