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ACADIA Pharmaceuticals announces results from Phase II study of antipsychotic in Alzheimer's disease psychosis

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ACADIA Pharmaceuticals Inc., 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 presentation of data from the Phase II -019 Study of pimavanserin in Alzheimer's disease psychosis at the 10th Clinical Trials on Alzheimer's Disease (CTAD) meeting in Boston. The -019 Study data are being presented at the symposium titled, "The Importance of Serotonin in Alzheimer's Disease Psychosis and the Role of Pimavanserin."

Pimavanserin met the primary endpoint in the Phase II -019 Study, showing a statistically significant reduction in psychosis versus placebo, as previously reported. Data presented at CTAD showed multiple sensitivity and responder analyses supportive of the primary result and demonstrated substantively greater benefit in those patients with more severe psychosis. Building on these data, ACADIA recently initiated the Phase III HARMONY study of pimavanserin in dementia-related psychosis. Dementia-related psychosis includes psychosis in Alzheimer's disease, dementia with Lewy bodies, Parkinson's disease dementia, vascular dementia, and frontotemporal dementia. There is no drug approved by the FDA for dementia-related psychosis. In October 2017, the FDA granted Breakthrough Therapy Designation for pimavanserin for the treatment of dementia-related psychosis.

"In the Phase II -019 Study, pimavanserin significantly reduced psychosis in patients with Alzheimer's disease without negatively impacting cognition," said Clive Ballard, MBChB, MRCPsych, Pro-Vice-Chancellor and Executive Dean, University of Exeter Medical School. "Pimavanserin also had a favorable tolerability profile compared to known adverse effects of current antipsychotics. With no approved treatment for dementia-related psychosis, there is a significant unmet need. The results of the study indicate that pimavanserin could be an important new treatment option for this elderly and underserved patient population."

Key Findings from the Phase II -019 Study Presented at CTAD Symposium

The Phase II -019 Study data are being presented by Clive Ballard in the presentation titled, "Clinical Trial of Pimavanserin in Alzheimer's Disease Psychosis." The Phase II -019 Study was a double-blind, placebo-controlled trial designed to evaluate the efficacy and safety of pimavanserin in 181 patients with Alzheimer's disease psychosis. Top-line results of the study were previously reported in December 2016.

Pimavanserin met the primary endpoint in the study, showing a statistically significant reduction in psychosis versus placebo as measured by the Neuropsychiatric Inventory-Nursing Home (NPI-NH) Psychosis score at week 6 of dosing (delta = 1.84, p=0.0451, effect size [Cohen's d] = 0.32). The proportion of responders at week 6 that had an NPI-NH Psychosis score improvement of ≥ 30% was 55.2% for pimavanserin-treated patients versus 37.4% for placebo (p=0.0159).

Importantly, in the -019 Study, no detrimental effect was observed on cognition for pimavanserin-treated patients compared to placebo. Atypical antipsychotics have been associated with a statistically significant acceleration of cognitive deterioration in patients with Alzheimer's disease.

The pimavanserin and placebo groups did not separate statistically on the secondary endpoints of the Alzheimer's Disease Cooperative Study - Clinical Global Impression of Change (ADCS-CGIC) or the Cohen-Mansfield Agitation Inventory Short Form (CMAI-SF), nor on the exploratory endpoints of the mean change in NPI-NH Psychosis score at week 12 or the Alzheimer's Disease Cooperative Study - Activities of Daily Living (ADCS-ADL).

Data presented at CTAD from a pre-specified subgroup analysis demonstrated a substantively larger and significant reduction in psychosis in pimavanserin-treated patients with more severe psychosis, further underscoring the effect seen on the primary result. Approximately one-third of patients in the study had more severe psychotic symptoms (NPI-NH Psychosis score ≥12). In this subgroup, pimavanserin demonstrated a statistically significant reduction in psychosis versus placebo on the NPI-NH Psychosis score at week 6 (delta = 4.43, p=0.0114, effect size [Cohen's d] = 0.73). Additionally, the proportion of responders at week 6 that had an NPI-NH Psychosis score improvement of

≥ 30% was 88.9% for pimavanserin-treated patients versus 43.3% for placebo (p=0.0004).

Larger effects were also observed on the NPI-NH Psychosis score in pimavanserin-treated patients with prior antipsychotic use.

As previously reported, pimavanserin was well tolerated in this frail and elderly population and the safety profile was consistent with what has been observed in previous studies.

Other Presentations at CTAD Symposium: "The Importance of Serotonin in Alzheimer's Disease Psychosis and the Role of Pimavanserin"

The -019 Study data are being presented as part of a three-part symposium. The symposium also includes a presentation by Stephen M. Stahl, MD, PhD, Adjunct Professor of Psychiatry, University of California, San Diego, titled, "The Role of 5-HT_{2A} Receptors in the Pharmacology of Alzheimer's Disease Psychosis." Serotonin 2A receptors are highly expressed in brain regions critical for processing sensory information and performing executive functions. Circuitry performing these functions may be deregulated when neurodegeneration has occurred. Selective 5-HT_{2A} inverse agonists/antagonists can be used to restore balance to these deregulated circuits. Pimavanserin is a non-dopaminergic selective serotonin inverse agonist (SSIA) preferentially targeting 5-HT_{2A} receptors.

Furthermore, a presentation by Pierre N. Tariot, MD, Banner Alzheimer's Institute and University of Arizona College of Medicine, titled, "Review of Pimavanserin Clinical Results in the Context of Historical Alzheimer's Disease Psychosis Trials," reviews the results of the pimavanserin Phase II -019 Study compared to Alzheimer's disease psychosis studies with other antipsychotics. Off-label use of atypical antipsychotics is associated with modest and often equivocal efficacy and significant acceleration in cognitive decline in patients with dementia, as well as other adverse effects.

The symposium’s moderator is Jeffrey Cummings, MD, ScD, Director of Cleveland Clinic Lou Ruvo Center for Brain Health, who reviews epidemiology, clinical phenomenology and psycho-social consequences of dementia-related psychosis and the current treatment options and opportunities.

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