Clinical Development of AXS-05 for Treatment Resistant Depression and Agitation Associated with Alzheimer’s Disease

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ABSTRACT

Axsome Therapeutics is developing AXS-05, an oral, investigational medicine combining dextromethorphan (DM) and bupropion, in late-stage clinical development for TRD, Alzheimer’s disease (AD) agitation and cognition dependency.

AXS-05 is a novel, oral, investigational medicine combining dextromethorphan (DM) and bupropion, in late-stage clinical development for TRD, Alzheimer’s disease (AD) agitation and cognition dependency. AXS-05 is a fixed-dose combination of bupropion and dextromethorphan. AXS-05 combines the mechanisms of action of bupropion, an SSRI, and a glutamatergic agent.

RESULTS: In the Phase 2/3 studies, AXS-05 was generally well tolerated. There was no difference in the rates of adverse events or serious adverse events between AXS-05 and bupropion or placebo. The most common adverse events reported in the AXS-05 group were nausea, vomiting, and headache. There were no treatment-emergent serious adverse events associated with AXS-05.

Key Inclusion Criteria:
- College-Minority: African-American, Hispanic, Asian, or Native American
- Age ≥ 18 years old
- MDD diagnosis with resistance to at least 2 prior antidepressant treatments
- Full Sample (n=106)
- SSRI monotherapy (n=51)
- SSRI+DM (n=39)
- AXS-05 (n=14)
- Placebo (n=2)

Key Exclusion Criteria:
- History of MDD, bipolar disorder, or schizophrenia
- Active suicidal behavior or intent
- History of substance use disorder in the past year

Overview
- AXS-05 is a novel, oral, investigational medicine combining dextromethorphan (DM) and bupropion (BUP), in late-stage clinical development for TRD, Alzheimer’s disease (AD) agitation and cognition dependency.

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DM Pharmacokinetics with AXS-05

1. Phase 1 Pharmacokinetic Trial of AXS-05: A Phase 1 study was conducted in healthy volunteers to evaluate the pharmacokinetic profile of AXS-05 and to determine the optimal dosing regimen for further clinical development.

2. Phase 3 Clinical Trials: Phase 3 clinical trials are ongoing to evaluate the efficacy and safety of AXS-05 in TRD and Alzheimer’s disease agitation.

Reduction in depresive Symptoms as a Function of DM Plasma Levels

Changes in depressive symptoms were evaluated in subjects who were taking AXS-05 and the combination of bupropion and DM. Increases in depressive symptoms were observed in the subjects taking AXS-05 alone, but not in the combination of bupropion and DM. The combination of bupropion and DM resulted in a significant decrease in depressive symptoms compared to AXS-05 alone.

Conclusion
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