AXS-05: A Mechanistically Novel Oral Therapeutic in Development for Neuropsychiatric Disorders

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Abstract

AXS-05 is a novel, oral, investigational medicine that contains dextromethorphan (DM) and bupropion. The DM component targets the NMDA receptor antagonist, sigma-1 receptor agonist, and an NMDA receptor antagonist. AXS-05 demonstrated efficacy and safety in a Phase 2 trial in smoking cessation and a dose ranging study in depression. Administration of AXS-05 to smokers was associated with a significant reduction in expired carbon monoxide levels, as compared to the active comparator bupropion.

Results

- Subjects Experiencing >50% Reduction in Expired Carbon Monoxide
  - Proportion of Subjects
  - Average Change in Cigarettes per Day over Three Periods

Conclusion

- AXS-05 is a novel, oral, investigational medicine that contains dextromethorphan (DM) and bupropion. AXS-05 resulted in DM plasma concentrations that overlap with the therapeutic range of DM in smoking cessation and depression trials. AXS-05 demonstrated efficacy and safety in a Phase 2 trial in smoking cessation and a dose ranging study in depression. Administration of AXS-05 to smokers was associated with a significant reduction in expired carbon monoxide levels, as compared to the active comparator bupropion.

Results of Phase 2 ASCEND Trial of AXS-05 in Major Depressive Disorder

Methods

- Methodology: ASCEND (Assessing Clinical Episodes in Depression) trial was a 6-week, randomized, double-blind, active-controlled multi-center trial. Eighty adult patients with a confirmed diagnosis of MDD were randomized to 1:1 ratio to treatment with AXS-05 (45 mg DM + 105 mg BUP) or bupropion (150 mg BUP). AXS-05 was dosed twice daily as a novel clinical entity for smoking cessation.

Results

- AXS-05 achieved the primary endpoint demonstrating a statistically significant mean reduction in smoking diaries. Treatment with AXS-05 was not associated with any serious AEs in the trial, and the most commonly reported AEs were nausea, headache, dizziness, dry mouth, insomnia/sleep problems, weight gain, and exacerbation of depression.

Conclusion

- Administration AXS-05 was associated with a rapid and significant reduction in smoking diaries compared to placebo. AXS-05 was well-tolerated and led to a significant reduction in smoking intensity, assessed via daily smoking diaries and smoking diaries at the end of treatment.

Results of Phase 2 Trial of AXS-05 in Smoking Cessation

Methods

- Methodology: A Phase 2, randomized, double-blind, active-controlled trial was conducted to evaluate the efficacy and safety of AXS-05 for smoking cessation treatment. A total of 580 smokers were randomized in a 1:1 ratio to receive AXS-05 (45 mg dextromethorphan [DM] + 105 mg bupropion [BUP]) or BUP (150 mg BUP), twice daily, and assessed over a 3-week interval of non-smoking and smoking cessation. The primary endpoint was the proportion of subjects who abstained from smoking completely for at least 7 days as measured by carbon monoxide readings.

Results

- AXS-05 resulted in a 25% greater reduction in the average number of cigarettes smoked per day over 3-week period, the primary endpoint, as compared to bupropion (average reductions of 8.49 and 6.79 cigarettes per day for AXS-05 and bupropion, respectively, p<0.01). Subjects who received AXS-05 were more likely than those who received bupropion to meet the quit goal (p=0.021) and showed a higher level of confidence in their ability to remain abstinent (p=0.012). AXS-05 did not show an association between daily medication use and smoking.

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