Axsome Therapeutics Announces AXS-05 Achieves Primary Endpoint in Phase 2 Trial in Smoking Cessation

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Demonstrated statistically significant reduction in daily smoking compared to active comparator (p=0.0016)

Trial conducted in collaboration with Duke University

NEW YORK, April 15, 2019 (GLOBE NEWSWIRE) -- Axsome Therapeutics, Inc. (NASDAQ: AXSM), a clinical-stage biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders, today announced that Duke University has completed its topline analysis of the Phase 2 trial of AXS-05 for smoking cessation treatment. The analysis showed that AXS-05 met the prespecified primary endpoint and significantly reduced daily smoking as compared to the active comparator bupropion. The trial was conducted at the Duke Center for Smoking Cessation under a research collaboration between Axsome and Duke University. The Phase 2 study was a randomized, double-blind, active-controlled trial, in which 58 adult smokers were treated either with AXS-05 (45 mg dextromethorphan/105 mg bupropion), or the active comparator bupropion (105 mg), twice daily, and assessed over a 3-week period.

Treatment with AXS-05 resulted in a 25% greater reduction in the average number of cigarettes smoked per day over the 3-week period, the prespecified primary endpoint, as compared to bupropion (average reductions of 8.49 and 6.79 cigarettes per day for AXS-05 and bupropion, respectively, p=0.0016). Consistent with this finding, a greater proportion of smokers receiving AXS-05 experienced a more than 50% reduction in expired carbon monoxide levels, a biochemical marker of smoking intensity, as compared to those treated with bupropion (52.0% for AXS-05 versus 30.4% for bupropion, p=0.15). In addition, subjects who took AXS-05 as prescribed on a given day smoked 1.0 fewer cigarette on the day of medication use (p=0.026) and 1.2 fewer cigarettes on the following day (p=0.008) as compared to those who missed one or both doses.

“The findings in this trial are notable because AXS-05 was compared to bupropion, an approved treatment for smoking cessation.” said James Davis, MD, Medical Director of the Duke Center for Smoking Cessation, and principal investigator of the trial. “The improvement of AXS-05 over bupropion observed in this trial is similar in magnitude to the improvement over placebo reported for the approved smoking cessation treatment varenicline in studies with a similar design. Reduction in ad-lib smoking was selected as the primary endpoint in this trial, because it has been shown to correlate with smoking abstinence. I look forward to the continued evaluation of AXS-05 as a smoking cessation treatment.”

Medication adherence was similar between the study arms for both the morning dose (97.1% for AXS-05 and 96.6% for bupropion) and the evening dose (76.3% for AXS-05 and 79.4% for bupropion). In the study, AXS-05 was safe and well tolerated with no serious adverse events. The most commonly reported side effects were headache, dry mouth, and insomnia/vivid dreams, with similar incidences in both treatment arms.

“The topline results of this Phase 2 trial in smoking cessation add to the growing body of clinical data demonstrating biologic activity for AXS-05 in different areas of unmet medical need including major depressive disorder,” said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. “We would like to thank the team at the Duke Center for Smoking Cessation for their collaboration with Axsome and for the execution of this important trial. We look forward to continuing to analyze these results with the team at Duke and to determining the next steps for this program.”

“Smoking is widely recognized as the leading cause of preventable death and affects approximately 40 million adults in the U.S. alone,” said Cedric O’Gorman, MD, Senior Vice President of Clinical Development and Medical Affairs of Axsome. “Unfortunately, the vast majority of smokers who attempt to quit fail to do so highlighting the need for new approaches. We look forward to learning more about the potential of the novel mechanisms of action of AXS-05 to address this condition.”

AXS-05 is a novel, oral, NMDA receptor antagonist, also known as a glutamate receptor modulator, a potentially new mechanism of action for smoking cessation treatment. AXS-05 consists of dextromethorphan and bupropion, and utilizes Axsome’s metabolic inhibition technology to increase the bioavailability of dextromethorphan. Both components of AXS-05 are nicotinic acetylcholine receptor antagonists, a mechanism that is relevant to nicotine dependence.

About the Phase 2 Trial

The trial was a Phase 2, randomized, double-blind, active-controlled study to evaluate the efficacy and safety of AXS-05 for smoking cessation treatment. A total of 58 smokers were randomized in a 1:1 ratio to receive either AXS-05 (45 mg dextromethorphan/105 mg bupropion) (n=31), or bupropion (105 mg) (n=27), twice daily, and assessed over a 3-week period. Enrolled subjects were daily smokers using 10 or more cigarettes per day. The average number of cigarettes smoked per day at baseline was 20 for AXS-05 and 17 for the bupropion treatment groups. The primary outcome measure was the change in smoking intensity, measured using the number of cigarettes smoked per day, assessed via daily smoking diaries. The trial was conducted at the Duke Center for Smoking Cessation.

About Smoking

Nearly 40 million American adults smoke and around 70% report that they want to quit. Tobacco use results in approximately 500,000 premature

deaths each year in the U.S., according to the Centers for Disease Control and Prevention. Smoking is the single largest cause of premature deaths worldwide accounting for an estimated almost 20% of all deaths in developed countries [1]. Direct health care and lost productivity costs as a result of smoking total nearly $300 billion a year in the U.S. alone. It is estimated that only 3 to 5% of cigarette smokers who attempt to quit without assistance are successful for 6 to 12 months, and that relapse rates remain above 80% even with current treatments [2].

About AXS-05

AXS-05 is a novel, oral, investigational NMDA receptor antagonist with multimodal activity under development for the treatment of central nervous system (CNS) disorders. AXS-05 consists of dextromethorphan and bupropion and utilizes Axsome's metabolic inhibition technology. The dextromethorphan component of AXS-05 is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, also known as a glutamate receptor modulator, which is a novel mechanism of action, meaning it works differently than currently available therapies for depression. The dextromethorphan component of AXS-05 is also a sigma-1 receptor agonist, nicotinic acetylcholine receptor antagonist, and inhibitor of the serotonin and norepinephrine transporters. The bupropion component of AXS-05 serves to increase the bioavailability of dextromethorphan, and is a norepinephrine and dopamine reuptake inhibitor, and a nicotinic acetylcholine receptor antagonist. AXS-05 is covered by more than 30 issued U.S. and international patents which provide protection out to 2034. AXS-05 is not approved by the FDA.

About Axsome Therapeutics, Inc.

Axsome Therapeutics, Inc. is a clinical-stage biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders for which there are limited treatment options. Axsome's core CNS product candidate portfolio includes four clinical-stage candidates, AXS-05, AXS-07, AXS-09, and AXS-12. AXS-05 is currently in a Phase 3 trial in treatment resistant depression (TRD), a Phase 2/3 trial in agitation associated with Alzheimer's disease (AD), and a Phase 2 trial in smoking cessation. AXS-05 is also being developed for major depressive disorder (MDD). AXS-07 is currently in a Phase 3 trial for the acute treatment of migraine. AXS-12 is currently in a Phase 2 trial in narcolepsy. The Axsome Pain and Primary Care business unit (Axsome PPC) houses Axsome's pain and primary care assets, including AXS-02 and AXS-06, and intellectual property which covers these and related product candidates and molecules being developed by Axsome and others. AXS-02 is being developed for osteoporosis, the pain of knee osteoarthritis, and chronic low back pain. AXS-06 is being developed for osteoarthritis and rheumatoid arthritis. AXS-02, AXS-05, AXS-06, AXS-07, AXS-09, and AXS-12 are investigational drug products not approved by the FDA. For more information, please visit the Company's website at axsome.com. The Company may occasionally disseminate material, nonpublic information on the company website.

References

1. Dani JA and Heinemann S (1996) Neuron 16:5, pp. 905-8.

2. Hughes JR, et al. (2004) Addiction 99:1, pp. 29-38.

Forward Looking Statements

Certain matters discussed in this press release are "forward-looking statements". We may, in some cases, use terms such as "predicts," "believes," "potential," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. In particular, the Company's statements regarding trends and potential future results are examples of such forward-looking statements. The forward-looking statements include risks and uncertainties, including, but not limited to, the success, timing and cost of our ongoing clinical trials and anticipated clinical trials for our current product candidates, including statements regarding the timing of initiation and completion of the trials, futility analyses and receipt of interim results, which are not necessarily indicative of the final results of our ongoing clinical trials; our ability to fund additional clinical trials to continue the advancement of our product candidates; the timing of and our ability to obtain and maintain U.S. Food and Drug Administration ("FDA") or other regulatory authority approval of, or other action with respect to, our product candidates (including, but not limited to, FDA's agreement with the Company's plan to discontinue the bupropion treatment arm of the ADVANCE-1 study in accordance with the independent data monitoring committee's recommendations); the potential for the ASCEND clinical trial to provide a basis for approval of AXS-05 for the treatment of major depressive disorder and accelerate its development timeline and commercial path to patients; the Company's ability to successfully defend its intellectual property or obtain the necessary licenses at a cost acceptable to the Company, if at all; the successful implementation of the Company's research and development programs and collaborations; the success of the Company's license agreements; the acceptance by the market of the Company's product candidates, if approved; and other factors, including general economic conditions and regulatory developments, not within the Company's control. The factors discussed herein could cause actual results and developments to be materially different from those expressed in or implied by such statements. The forward-looking statements are made only as of the date of this press release and the Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstance.

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