Axsome Therapeutics Announces Positive Outcome of Interim Analysis of ADVANCE-1 Phase 2/3 Trial of AXS-05 in Alzheimer's Disease Agitation

December 10, 2018

IDMC recommends continuation of trial evaluating AXS-05 versus placebo in Alzheimer's disease agitation

IDMC recommends no further enrollment to single-agent bupropion arm

NEW YORK, Dec. 10, 2018 (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 a positive outcome of the interim analysis for the ADVANCE-1 Phase 2/3 trial of AXS-05 in agitation associated with Alzheimer's disease (AD). An independent data monitoring committee (IDMC) conducted the unblinded, pre-specified interim analysis for futility. Based on the results of the analysis, the IDMC recommended continuation of the AXS-05 treatment arm. Additionally, the IDMC recommended no further randomization of subjects to the bupropion treatment arm of the study. The IDMC did not indicate that there were any safety concerns in the study. Axsome intends to follow the IDMC's recommendations.

AXS-05 is a novel, oral, investigational medicine consisting of dextromethorphan and bupropion. Patients in the ADVANCE-1 trial were being randomized in a 1:1:1 ratio to treatment with AXS-05, placebo, or bupropion. The primary endpoint of the study is the change in the Cohen Mansfield Agitation Inventory (CMAI) for AXS-05 as compared to placebo. The single-agent bupropion arm of the study was included to compare the efficacy of AXS-05 to the bupropion component, with the goal of demonstrating the superiority of AXS-05, as required by the U.S. Food and Drug Administration's (FDA's) combination product rule. In accordance with the IDMC's recommendation, the study will now continue enrollment in a 1:1 ratio to only the AXS-05 and placebo arms. The ADVANCE-1 interim futility analysis was performed on the first approximately 30% of the target number of subjects.

"The positive recommendation by the IDMC to continue the ADVANCE-1 trial is an important milestone for the Alzheimer's disease agitation program and we look forward to the continued development of AXS-05 for this indication," said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "We are pleased that further enrollment to the bupropion single-agent arm is no longer deemed necessary. Inclusion of that arm was driven by the FDA's guidelines to examine contribution of the individual components of product candidates like AXS-05 that contain two active agents. We anticipate that implementation of the IDMC's recommendations may provide greater flexibility to our operating plans and timelines which we will evaluate in the coming weeks. We will continue to be rigorous with our oversight of the conduct of the study."

AXS-05 combines glutamatergic, monoaminergic and anti-inflammatory mechanisms of action, and Axsome's proprietary metabolic inhibition technology. Pharmacokinetic data from Phase 1 trials of AXS-05 and clinical observations with the dextromethorphan component indicate that AXS-05 increases dextromethorphan concentrations into a potentially therapeutic range. AXS-05 has been granted FDA Fast Track designation for the treatment of AD agitation.

"Agitation is reported in up to 70% of Alzheimer's disease patients, is highly distressing for patients and their caregivers, and is associated with significant negative outcomes, including earlier institutionalization and increased mortality," said Cedric O'Gorman, MD, Senior Vice President of Clinical Development and Medical Affairs of Axsome. "There is currently no approved treatment for Alzheimer's disease agitation. The significant clinical impact of this unmet medical need underscores the importance of the ADVANCE-1 trial in evaluating the potential of AXS-05 to treat this serious indication."

About the ADVANCE-1 Study

ADVANCE-1 (Addressing Dementia Via Agitation-Centered Evaluation 1) is a Phase 2/3 multicenter, randomized, double-blind, controlled trial to evaluate the efficacy and safety of AXS-05 in patients with agitation associated with Alzheimer's disease. Approximately 435 patients were to be randomized in a 1:1:1 ratio to receive AXS-05, bupropion, or placebo for 5 weeks. The primary efficacy measure is the Cohen-Mansfield Agitation Inventory (CMAI). The trial incorporates two interim analyses to be performed by an independent data monitoring committee. The first interim analysis was performed on the first approximately 30% of the target number of subjects to assess futility. The second interim analysis is anticipated to be performed on the first approximately 60% of the target number of subjects to assess efficacy.

About Alzheimer's Disease (AD) Agitation

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that manifests initially as forgetfulness advancing to severe cognitive impairment and memory loss. It afflicts an estimated 5 million individuals in the United States, a number that is anticipated to increase to approximately 14 million by 2050. In addition to cognitive decline, individuals diagnosed with AD frequently experience behavioral and psychological symptoms including agitation which is reported in up to 70% of patients. Agitation is characterized by emotional distress, aggressive behaviors, disruptive irritability, and disinhibition. Agitation in patients with AD has been associated with increased caregiver burden, decreased functioning, earlier nursing home placement, and increased mortality. There are currently no therapies approved by the FDA for the treatment of agitation in patients with AD.

About AXS-05

AXS-05 is a novel, oral, investigational drug product under development for the treatment of central nervous system (CNS) disorders. AXS-05 consists of bupropion and dextromethorphan and utilizes Axsome's metabolic inhibition technology. Dextromethorphan is an NMDA receptor antagonist, sigma-1 receptor agonist, nicotinic acetylcholine receptor antagonist, and inhibitor of the serotonin and norepinephrine transporters. Bupropion serves to increase the bioavailability of dextromethorphan, and is a norepinephrine and dopamine reuptake inhibitor, and a nicotinic acetylcholine receptor antagonist. AXS-05 is an investigational drug product not approved by the FDA. The safety and efficacy of AXS-05 have not yet been established.

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), a Phase 2 trial in Major Depressive Disorder (MDD), and a Phase 2 trial in smoking cessation. AXS-07 is being developed for the acute treatment of migraine. AXS-12 is being developed for the treatment of the symptoms of 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.

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 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.

Axsome Contact:
Mark Jacobson
Senior Vice President, Operations
Axsome Therapeutics, Inc.
25 Broadway, 9th Floor
New York, NY 10004
Tel: 212-332-3243
Email: mjacobson@axsome.com
www.axsome.com

Source: Axsome Therapeutics, Inc.