# Axsome Therapeutics Initiates ACCORD Phase 3 Trial of AXS-05 in Alzheimer's Disease Agitation

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*ACCORD is the second pivotal trial of AXS-05 in Alzheimer's disease agitation*

*No treatments are currently approved for Alzheimer's disease agitation*

NEW YORK, Dec. 31, 2020 (GLOBE NEWSWIRE) -- Axsome Therapeutics, Inc. (NASDAQ: AXSM), a biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders, announced the initiation of the ACCORD (Assessing Clinical Outcomes in Alzheimer's Disease Agitation) study, a Phase 3, randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of AXS-05 in the treatment of Alzheimer's disease (AD) agitation. AXS-05 (45 mg dextromethorphan-105 mg bupropion modulated delivery tablet) is a novel, oral, investigational NMDA receptor antagonist with multimodal activity. There is currently no approved treatment for AD agitation.

ACCORD is being conducted using a randomized-withdrawal design, in which all patients are first treated with open-label AXS-05, with the patients experiencing a treatment response being subsequently randomized in a double-blind fashion to continued treatment with AXS-05 or to switch to placebo. Patients completing the ACCORD trial will be eligible to enter an open-label safety extension trial. Initiation of the safety extension trial is expected imminently. Topline results from the ACCORD trial are anticipated in the second half of 2022.

"Initiation of the ACCORD Phase 3 trial in Alzheimer's disease agitation continues the expedited clinical development of AXS-05 for this serious condition. The potential for AXS-05, with its unique pharmacological profile, in this indication is supported by the positive results in our completed pivotal ADVANCE trial," said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "Alzheimer's disease agitation is a prevalent and debilitating condition that is associated with earlier nursing home placement, accelerated progression to severe dementia, and increased risk of death. There are currently no approved treatments for Alzheimer's disease agitation. If successfully developed, AXS-05 has the potential to address this high unmet need and significantly improve the lives of patients and their caregivers."

Initiation of the ACCORD Phase 3 trial follows a Breakthrough Therapy meeting with the U.S. Food and Drug Administration (FDA), announced in August, to discuss the development plan for AXS-05 in AD agitation. Results of the meeting confirmed the pivotal status of the previously completed ADVANCE trial of AXS-05 in AD agitation. The meeting followed the receipt in June of Breakthrough Therapy designation from the FDA for AXS-05 for the treatment of AD agitation, the second Breakthrough Therapy designation received by Axsome for AXS-05. The designation was supported by the positive results of the ADVANCE trial. A Breakthrough Therapy designation is granted to potentially expedite development and review timelines for a promising investigational medicine when preliminary clinical evidence indicates it may demonstrate substantial improvement on one or more clinically significant endpoints over available therapies for a serious or life-threatening condition.

**About the ACCORD Trial**

ACCORD (Assessing Clinical Outcomes in Alzheimer's Disease Agitation) is a Phase 3, randomized, double-blind, multicenter, placebo-controlled, trial to evaluate the efficacy and safety of AXS-05 in patients with Alzheimer's disease (AD) agitation. Enrolled patients will first enter a 9-week, open-label stabilization period, during which they will be treated with AXS-05 and monitored for a treatment response based on the Cohen-Mansfield Agitation Inventory (CMAI). Patients who experience a treatment response during the stabilization period will then be randomized into the double-blind treatment period, in a 1:1 ratio, to continue treatment with AXS-05 or to switch to placebo, for up to 26 weeks or until a relapse of agitation occurs. The primary endpoint will be the time from randomization to relapse. Assessments will include the CMAI, clinician- and caregiver-rated scales, and safety parameters.

**About Alzheimer's Disease (AD) Agitation**

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, and behavioral and psychological symptoms including agitation. AD is the most common form of dementia and afflicts an estimated 6 million individuals in the United States, a number that is anticipated to increase to approximately 14 million by 2050 [1]. Agitation is reported in up to 70% of patients with AD and is characterized by emotional distress, aggressive behaviors, disruptive irritability, and disinhibition [2]. Agitation in patients with AD has been associated with increased caregiver burden, decreased functioning, accelerated cognitive decline, earlier nursing home placement, and increased mortality [2-4]. There are currently no therapies approved by the FDA for the treatment of agitation in patients with AD.

**About AXS-05**

AXS-05 (dextromethorphan-bupropion modulated delivery tablet) is a novel, oral, patent-protected, investigational NMDA receptor antagonist with multimodal activity under development for the treatment of major depressive disorder and other central nervous system (CNS) disorders. AXS-05 utilizes a proprietary formulation and dose of dextromethorphan and bupropion, and Axsome's metabolic inhibition technology, to modulate the delivery of the components. The dextromethorphan component of AXS-05 is an uncompetitive 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 approved therapies for major depressive disorder. 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 93 issued U.S. and international patents which provide protection out to 2040. AXS-05 has been granted U.S. Food and Drug Administration Breakthrough Therapy and Fast Track designations for Alzheimer's disease agitation. AXS-05 is not approved by the FDA.

**About Axsome Therapeutics, Inc.**

Axsome Therapeutics, Inc. is a biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders for which there are limited treatment options. For the many people facing unsatisfactory treatments for CNS disorders, Axsome accelerates

the invention and adoption of life-changing medicines. Axsome's core CNS product candidate portfolio includes five clinical-stage candidates, AXS-05, AXS-07, AXS-09, AXS-12, and AXS-14. AXS-05 is being developed for major depressive disorder (MDD), Alzheimer's disease (AD) agitation, and as a treatment for smoking cessation. AXS-07 is being developed for the acute treatment of migraine. AXS-12 is being developed for the treatment of narcolepsy. AXS-14 is being developed for fibromyalgia. AXS-05, AXS-07, AXS-09, AXS-12, and AXS-14 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**


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**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, pace of enrollment and completion of the trials (including our ability to fully fund our disclosed clinical trials, which assumes no material changes to our currently projected expenses), futility analyses and receipt of interim results, which are not necessarily indicative of the final results of our ongoing clinical trials, and the number or type of studies or nature of results necessary to support the filing of a new drug application ("NDA") for any of our current product candidates; 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 discontinuation of the bupropion treatment arm of the ADVANCE study in accordance with the independent data monitoring committee's recommendations); the potential for the MOMENTUM clinical trial to provide a basis for approval of AXS-07 for the acute treatment of migraine in adults with or without aura, pursuant to our special protocol assessment; the potential for the ASCEND clinical trial, combined with the GEMINI clinical trial results, 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; the Company's anticipated capital requirements, including the Company's anticipated cash runway; unforeseen circumstances or other disruptions to normal business operations arising from or related to COVID-19; 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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