



Axsome Therapeutics Accelerates Completion of the ADVANCE-1 Phase 2/3 Trial of AXS-05 in Alzheimer's Disease Agitation

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Randomizations concluded and trial participation in process of concluding to ensure patient safety during COVID-19 pandemic

AXS-05 and placebo arms fully enrolled with estimated completion rate of more than 90%

Topline results now expected early 2Q 2020

NEW YORK, March 20, 2020 (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 it is accelerating the completion of the ADVANCE-1 Phase 2/3 trial of AXS-05 in patients with Alzheimer's disease (AD) agitation to ensure the safety of this vulnerable patient population during the COVID-19 pandemic, while maintaining the integrity of the clinical trial. AXS-05 (dextromethorphan/bupropion modulated delivery tablet) is a novel, oral, investigational NMDA receptor antagonist with multimodal activity. Randomizations into the study have concluded and patient participation is concluding. With the acceleration of trial completion, topline results from ADVANCE-1 are now expected in early second quarter of 2020, versus previous guidance of the third quarter of 2020.

The decision to accelerate the completion of this trial was made in light of the newly issued U.S. Food and Drug Administration (FDA) *Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic*, which discusses the potential impact of the pandemic on the conduct of clinical trials and on the resulting need to ensure the safety of trial participants. The ADVANCE-1 trial is enrolling only patients 65 years of age or older, the demographic at highest risk for COVID-19 related fatalities. The conclusion of patient randomization and participation in the ADVANCE-1 trial enables patient compliance with recent and evolving COVID-19 related national, state and local government directives and executive orders that persons 65 years and older isolate at home.

In the original design of the trial, approximately 435 patients were to be randomized in a 1:1:1 ratio to receive AXS-05, bupropion, or placebo for 5 weeks (approximately 145 patients per treatment arm). The AXS-05 and placebo arms are fully enrolled and more than 90% of patients in these arms are estimated to have completed the study. In December 2018, an independent data monitoring committee (IDMC) performed an unblinded, pre-specified interim analysis for futility on the first approximately 30% of the targeted number of patients. The IDMC recommended continuation of the AXS-05 and placebo treatment arms and no further randomization of patients to the bupropion treatment arm. Subsequently, patients were randomized in a 1:1 ratio to receive AXS-05 or placebo.

About the ADVANCE-1 Trial

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. The primary efficacy measure is the Cohen-Mansfield Agitation Inventory (CMAI).

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 approximately 45% 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, 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 consists of a proprietary formulation and dose 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 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 40 issued U.S. and international patents which provide protection out to 2034. AXS-05 has been granted U.S. Food and Drug Administration (FDA) Breakthrough Therapy designation for the treatment of MDD as well as Fast Track designations for the treatment of treatment resistant depression and for the treatment of Alzheimer's disease agitation. 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 five clinical-stage candidates, AXS-05, AXS-07, AXS-09, AXS-12, and AXS-14. 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 is being developed for major depressive disorder (MDD). AXS-05 is also being developed for

smoking cessation treatment. AXS-07 is currently in a Phase 3 trial for the acute treatment of migraine. AXS-12 is being developed for the treatment of narcolepsy. AXS-14 is being developed for the treatment of 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.

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 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 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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