



Axsome Therapeutics Completes Successful FDA Pre-NDA Meeting for AXS-05 for the Treatment of Major Depressive Disorder

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NDA submission on track for 4Q 2020

NEW YORK, July 13, 2020 (GLOBE NEWSWIRE) -- Axsome Therapeutics, Inc. (NASDAQ: AXSM), a biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders, today announced that it has completed a successful pre-New Drug Application (NDA) meeting with the U.S. Food and Drug Administration (FDA) for AXS-05 for the treatment of major depressive disorder (MDD). AXS-05 is a novel, oral, investigational NMDA receptor antagonist with multimodal activity. The purpose of the meeting was to reach agreement with the FDA on the proposed content and format of the Company's planned NDA submission including the clinical and nonclinical requirements.

Based on the feedback from the FDA, the Company believes its regulatory data package will be sufficient to support an NDA for AXS-05 in MDD, and Axsome remains on track to submit the planned NDA in the fourth quarter of 2020. Acceptance of the final NDA will be subject to the FDA's review of the complete filing. Axsome received Breakthrough Therapy Designation from the FDA for AXS-05 for the treatment of MDD in March 2019.

"Axsome is pleased with the outcome of our recent pre-NDA meeting with the FDA, which confirmed the studies and data to be presented in our planned NDA submission of AXS-05 in major depressive disorder," said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "We remain on track to complete the submission in the fourth quarter. As a Breakthrough Therapy designated program, AXS-05 is eligible for Priority Review, and we look forward to continuing to work with the FDA to bring this new potential therapy to patients living with depression as quickly as possible. If approved, AXS-05 has the potential to be the first oral, NMDA receptor antagonist for the treatment of depression."

Axsome previously announced positive results from two pivotal, randomized, controlled trials of AXS-05 in patients with a confirmed diagnosis of moderate to severe MDD, the GEMINI and ASCEND trials, which demonstrated rapid, substantial, and statistically significant reductions in depressive symptoms with AXS-05 compared to control. In the 327-patient, placebo-controlled GEMINI trial, AXS-05 met the primary endpoint by demonstrating a reduction from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score of 16.6 points at Week 6 compared to 11.9 points for placebo ($p=0.002$). AXS-05 rapidly and durably improved depressive symptoms as compared to placebo with statistical significance on the MADRS total score demonstrated at Week 1 ($p=0.007$), the earliest time point assessed, and at all time points thereafter. Remission was achieved by 39.5% of AXS-05 patients compared to 17.3% of placebo patients at Week 6 ($p<0.001$). In the active-controlled ASCEND trial, which enrolled 80 patients with confirmed moderate to severe MDD, AXS-05 met the primary endpoint, demonstrating a statistically significant average mean reduction from baseline in the MADRS total score over the 6-week treatment period of 13.7 points for AXS-05 compared to 8.8 for bupropion ($p<0.001$). At Week 6, AXS-05 demonstrated a 17.2 point reduction in the MADRS total score compared to a 12.1 point reduction for bupropion ($p=0.013$). AXS-05 was well tolerated in both trials with the most commonly reported adverse events in the AXS-05 arm being dizziness, nausea, headache, diarrhea, somnolence, and dry mouth. Treatment with AXS-05 was not associated with psychotomimetic effects, weight gain, or increased sexual dysfunction.

About Major Depressive Disorder (MDD)

Major depressive disorder (MDD) is a debilitating, chronic, biologically-based disorder characterized by low mood, inability to feel pleasure, feelings of guilt and worthlessness, low energy, and other emotional and physical symptoms, and which impairs social, occupational, educational, or other important functioning. In severe cases, MDD can result in suicide. According to the National Institutes of Health, an estimated 7.1% of U.S. adults, or approximately 17.3 million, experience MDD each year¹. According to the World Health Organization (WHO), depression is the leading cause of disability worldwide, and is a major contributor to the overall global burden of disease². Nearly two-thirds of diagnosed and treated patients do not experience adequate treatment response with currently available first-line therapy³, highlighting the need for additional therapies with new mechanisms of action. The majority of initial failures also fail second-line treatment. Patients diagnosed with MDD are defined as having treatment resistant depression (TRD) if they have failed to respond to two or more antidepressant therapies.

About AXS-05

AXS-05 is a novel, oral, patent-protected, investigational NMDA receptor antagonist with multimodal activity under development for the treatment of Alzheimer's disease agitation, 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, a sigma-1 receptor agonist, an inhibitor of the serotonin and norepinephrine transporters, a nicotinic acetylcholine receptor antagonist, and an inhibitor of microglial activation. 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 42 issued U.S. and international patents which provide protection out to 2034. AXS-05 has been granted U.S. Food and Drug Administration Breakthrough Therapy designation for major depressive disorder, Fast Track designation for treatment resistant depression, and 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), treatment resistant depression (TRD), Alzheimer's disease (AD) agitation, and as 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

1. National Institute of Mental Health. (2017). Major Depression. Retrieved from <https://www.nimh.nih.gov/health/statistics/major-depression.shtml>.
2. World Health Organization. Fact Sheets: Depression.
3. Rush AJ, et al. (2007) Am J. Psychiatry 163:11, pp. 1905-1917 (STAR*D Study).

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-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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