Axsome Therapeutics Announces AXS-05 Achieves Primary and Key Secondary Endpoints in the MERIT Phase 2 Trial in Treatment Resistant Depression

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AXS-05 significantly delayed the time to relapse of depression compared to placebo (p=0.002, primary endpoint)

AXS-05 significantly prevented relapse of depression over at least 6 months compared to placebo (p=0.004, key secondary endpoint)

NEW YORK, Aug. 09, 2021 (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 AXS-05, a novel, oral, investigational NMDA receptor antagonist with multimodal activity, met the primary and key secondary endpoints in the MERIT (Mechanistic Evaluation of Response in TRD) Phase 2 trial, and substantially and statistically significantly prevented relapse of depressive symptoms compared to placebo in patients with treatment resistant depression (TRD). The MERIT study was a randomized, double-blind, placebo-controlled, relapse prevention, multi-center, U.S. trial, which evaluated 44 TRD patients. Patients in stable remission after treatment with AXS-05 were randomized to continue treatment with AXS-05 or to discontinue AXS-05 and switch to placebo.

AXS-05 met the primary endpoint by substantially and statistically significantly delaying the time to relapse of depressive symptoms as compared to placebo (p=0.002), with no relapses observed with AXS-05 over at least 6 months of double-blind treatment. AXS-05 also met the key secondary endpoint of relapse prevention, based on the rates of relapse during the double-blind treatment period (0.0% of AXS-05 patients, 36.4% of patients switched from AXS-05 to placebo, p=0.004).

AXS-05 was well tolerated in the trial. There were no treatment-emergent adverse events reported in >1 patient in the AXS-05 group. One subject in the AXS-05 group experienced two serious adverse events (gout and bacteremia), both of which were deemed not related to the study medication.

A new drug application (NDA) for AXS-05 for the treatment of major depressive disorder is under Priority Review by the U.S. Food and Drug Administration (FDA), with a Prescription Drug User Fee Act (PDUFA) target action date of August 22, 2021.

About the MERIT Study

MERIT was a Phase 2, randomized, double-blind, placebo-controlled, multi-center study to evaluate AXS-05 compared to placebo in preventing relapse of depressive symptoms in patients with treatment resistant depression (TRD). Treatment resistance was defined as ongoing symptoms of depression despite receiving treatment with two or more prior antidepressants during the current major depressive episode. TRD patients were enrolled into MERIT from the long-term, open-label Phase 3 trial of AXS-05, and were required to be in stable remission prior to randomization. Stable remission was defined as at least two consecutive Montgomery-Åsberg Depression Rating Scale (MADRS) scores of ≤12, separated by at least 4 weeks.

A total of 44 TRD patients who experienced a stable remission after up to 12 months of open-label treatment with AXS-05 (45 mg dextromethorphan-105 mg bupropion) tablets twice daily, were randomized 1:1 to continue AXS-05, or to discontinue AXS-05 and switch to placebo, in a double-blind fashion, for at least 26 weeks or until a relapse of depressive symptoms occurred. Relapse was defined in the study by one or more of the following: MADRS total score ≥18 for 2 consecutive assessments; a ≥2-point increase from randomization in the Clinical Global Impression of Severity, with a minimum CGI-S score of 4, for 2 consecutive assessments; hospitalization due to worsening of depression or risk of suicide; investigator determination of relapse or need for additional antidepressant or treatment switch.

The primary endpoint in the study was time from randomization to relapse calculated by the Kaplan-Meier estimates and the hazard ratio. The key secondary endpoint, to assess relapse prevention, was the percentage of patients without relapse.

About Major Depressive Disorder

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% of U.S. adults, or approximately 19 million, experience MDD each year[1]. 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 disease[2]. Nearly two-thirds of diagnosed and treated patients do not experience adequate treatment response with currently available first-line therapy[3], 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 (dextromethorphan-bupropion) 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 oral therapies for major depressive disorder. The dextromethorphan component of AXS-05 is also a sigma-1 receptor agonist. The bupropion component of AXS-05 serves to increase the bioavailability of dextromethorphan, and is a norepinephrine and dopamine reuptake inhibitor. AXS-05 is currently covered by more than 100 issued U.S. and international patents, with expiration dates out to 2040. AXS-05 has been granted U.S. Food and Drug Administration (FDA) Breakthrough Therapy designations for the treatment of MDD and for treatment of Alzheimer's disease agitation. A new drug application (NDA) for AXS-05 for the treatment of major depressive disorder is under Priority Review by the FDA, with a Prescription Drug User Fee Act (PDUFA) target action date of August 22, 2021. AXS-05 is not approved by the FDA.

About Axsome Therapeutics, Inc.

Axsome Therapeutics, Inc. is a biopharmaceutical company developing novel therapies for central nervous system (CNS) conditions that have limited treatment options. Through development of therapeutic options with novel mechanisms of action, we are transforming the approach to treating CNS conditions. At Axsome, we are intensely committed to developing products that meaningfully improve the lives of patients and provide additional therapeutic options for physicians. 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. Substance Abuse and Mental Health Services Administration. (2020). Results from the 2019 National Survey on Drug Use and Health. Retrieved from https://www.samhsa.gov/data/.

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, whether potential filing issues or issues identified by FDA during the substantive review may impact the potential approvability of the Company's NDA submission for AXS-05 in MDD or the timing of such approval, and whether the FDA will agree 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 successful submission of and approval by the FDA of an NDA for AXS-07 for the acute treatment of migraine in adults with or without aura, pursuant to our special protocol assessment for the MOMENTUM clinical trial; 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 amount of capital required for the Company's commercial launch of its product candidates, and the potential impact on 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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