Axsome Therapeutics Presents New Data from the GEMINI Trial Demonstrating Efficacy of AXS-05 on Anhedonia in Patients with Major Depressive Disorder

June 2, 2022

AXS-05 rapidly and significantly improved anhedonic symptoms, measured by the MADRS anhedonia subscale, starting 1 week after treatment

Data being presented at the American Society of Clinical Psychopharmacology (ASCP) 2022 Annual Meeting

NEW YORK, June 02, 2022 (GLOBE NEWSWIRE) -- Axsome Therapeutics, Inc. (NASDAQ: AXSM), a biopharmaceutical company developing and delivering novel therapies for the management of central nervous system (CNS) disorders, today announced that treatment with AXS-05 (dextromethorphan-bupropion) rapidly and significantly reduced anhedonic symptoms in the GEMINI Phase 3 trial in major depressive disorder (MDD). These new data are being presented today at the American Society of Clinical Psychopharmacology (ASCP) 2022 Annual Meeting, being held in Scottsdale, Arizona and virtually.

"Anhedonia is a disabling, common, and persistent feature of depression that substantially impairs patient functioning," said Roger McIntyre, MD, Professor of Psychiatry and Pharmacology, University of Toronto, Canada and Executive Director of the Brain and Cognition Discovery Foundation in Toronto, Canada. "These results with AXS-05 demonstrate rapid reductions in anhedonic symptoms, and are consistent with observed improvements in patient functioning and quality of life associated with treatment with AXS-05 in clinical trials."

Anhedonia is an impaired capacity to experience or anticipate pleasure. It is present in up to 75% of individuals with MDD[1] and is ranked among the most bothersome symptoms of depression. Anhedonia is associated with suboptimal antidepressant treatment response and poor functional outcomes[2,3].

The GEMINI trial assessed the efficacy and safety of AXS-05 versus placebo in patients with MDD. A total of 327 patients with a confirmed diagnosis of moderate to severe MDD were randomized to receive AXS-05 (45 mg dextromethorphan/105 mg bupropion tablet) (n=163), or placebo (n=164), once daily for the first 3 days and twice daily thereafter, for a total of 6 weeks. The primary endpoint was the treatment effect on the Montgomery-Åsberg Depression Rating Scale (MADRS) score from baseline to week 6. In this secondary, *post-hoc*, analysis of the trial, improvements in anhedonic symptoms in MDD were assessed by the MADRS anhedonia subscale.

In the trial, AXS-05 demonstrated rapid, substantial, and statistically significant improvement in symptoms of anhedonia compared with placebo. The change from baseline to week 6 on the MADRS anhedonia subscale was significantly greater with AXS-05 than with placebo (-9.70 points vs. -7.22 points; p=0.001). The improvement was rapid with the change on the MADRS anhedonia subscale from baseline to week 1, the first timepoint assessed, being significantly greater with AXS-05 than with placebo (-4.44 points vs. -2.69 points; p<0.001). Response, defined as at least a 50% improvement on the anhedonia subscale, was achieved by a statistically significantly greater proportion of patients treated with AXS-05 than with placebo at week 1 (p<0.001) and at every timepoint thereafter. At week 6, response on the anhedonia subscale was achieved by 54% of patients treated with AXS-05 compared to 36% of patients treated with placebo (p=0.002).

"We are pleased to present these new data on AXS-05 at the 2022 annual meeting of the American Society of Clinical Psychopharmacology," said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "These data support the efficacy of AXS-05 in patients with depression with a broad range of symptomatology, and further define its differentiated clinical profile."

Details of the poster presentation are as follows:

Title: Impact of AXS-05, an Oral NMDA Receptor Antagonist, on Anhedonic Symptoms in Major Depressive Disorder
Presentation Number: Th22
Session: Poster Session II
Date: Thursday, June 2, 2022
Time: 12:30 PM – 2 PM MST
Location: Palomino Ballroom 4-10, Fairmont Scottsdale Princess, Scottsdale, AZ

About AXS-05

AXS-05 (dextromethorphan-bupropion) is a novel, oral, patent protected, investigational N-methyl-D-aspartate (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 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 FDA Breakthrough Therapy designations for the treatment of MDD and for the treatment of Alzheimer's disease agitation. A new drug application (NDA) for AXS-05 for the treatment of major depressive disorder is under review by the FDA. AXS-05 is not approved by the FDA.

About Axsome Therapeutics, Inc.

Axsome Therapeutics, Inc. is a biopharmaceutical company developing and delivering novel therapies for 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 committed to developing products that meaningfully improve the lives of patients and provide new 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.

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 continued commercial success of our newly acquired Sunosi product; 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; whether issues identified by FDA in the complete response letter may impact the potential approvability of the Company's 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 continued commercialization of Sunosi and 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.

Axsome Contact:
Mark Jacobson
Chief Operating Officer
Axsome Therapeutics, Inc.
22 Cortlandt Street, 16th Floor
New York, NY 10007
Tel: 212-332-3243
Email: mjacobson@axsome.com
www.axsome.com

References

1. Franken IH, et al. J Affect Disord 2007;99:83 9.
2. Baune BT, et al. Neuropsychiatr Dis Treat 2021;17:2995 3006.
3. Wardenaar KJ, et al. J. Affect. Disord 2012; 136:1198 1203.

Source: Axsome Therapeutics, Inc.