Axsome Therapeutics Announces Further Progress in AXS-05 Depression Clinical Program

August 10, 2020

Enrollment complete in the COMET Phase 3 long-term safety trial of AXS-05 in MDD; NDA filing on track for 4Q 2020

Results from three Phase 2 open-label efficacy trials of AXS-05 in TRD, antidepressant unresponsive MDD, and suicidal ideation, expected in 4Q 2020

MERIT Phase 2 placebo-controlled trial in TRD initiated; topline results expected in 1H 2021

NEW YORK, Aug. 10, 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, announces continued progress toward NDA filing of AXS-05 in the treatment of major depressive disorder (MDD), and the generation of new clinical data to further characterize the antidepressant profile of AXS-05 across a broad spectrum of patients with MDD.

Enrollment has been completed in the COMET (Clinical Outcomes with NMDA-based Depression Treatment) Phase 3 open-label, long-term safety trial to support the planned NDA filing of AXS-05 in MDD. In addition, the required number of patients treated for 6 months has been reached. Filing of the NDA remains on track for the fourth quarter of 2020.

Axsome is also conducting three Phase 2 open-label efficacy sub-studies of the COMET trial which will evaluate the efficacy and safety of AXS-05 in three clinically pertinent MDD patient populations: the COMET-TRD trial in treatment resistant MDD (TRD), the COMET-AU trial in antidepressant unresponsive MDD, and the COMET-SI trial in MDD with suicidal ideation. Efficacy results from these studies are expected in the fourth quarter of 2020.

Further, Axsome has initiated the MERIT (Mechanistic Evaluation of Response in TRD) trial, a Phase 2, double-blind, placebo-controlled, randomized withdrawal study in patients with TRD. Results from the MERIT trial, which are expected in the first half of 2021, along with results from the COMET-TRD trial, which are expected in the fourth quarter of 2020, will provide clinically useful information with AXS-05 in this treatment resistant MDD population.

Depression Clinical Program Update

Major Depressive Disorder (MDD) NDA

- Enrollment has been completed in the COMET Phase 3, open-label, long-term safety trial of AXS-05 to support the New Drug Application (NDA) filing in MDD. Nearly 900 patients have been enrolled, of whom more than 500 have been treated for at least 6 months to date. At least 300 patients treated for 6 months and 100 patients treated for one year are required for the NDA filing. Axsome remains on track to achieve the required number of patients treated for one year in the fourth quarter.

- Axsome previously announced that it had completed a pre-NDA meeting for AXS-05 in MDD with the U.S. Food and Drug Administration (FDA) to reach agreement 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.

Treatment Resistant MDD (TRD)

- COMET-TRD Trial – Axsome is conducting the COMET-TRD trial, a Phase 2 open-label sub-study evaluating the efficacy and safety of AXS-05 in TRD patients. The trial will include approximately 70 patients who have had ongoing symptoms of depression despite receiving treatment with two or more prior antidepressants during the current major depressive episode. The trial endpoints will include the change from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score, clinical response, and remission. Topline results from the COMET-TRD trial are expected in the fourth quarter of 2020.

- MERIT Trial – Axsome is conducting the MERIT trial, a Phase 2, double-blind, placebo-controlled, randomized withdrawal study of AXS-05 in patients with TRD. The trial will include approximately 50 patients who have had ongoing symptoms of depression despite receiving treatment with two or more prior antidepressants during the current major depressive episode. In this trial, patients who experience a sustained remission of depressive symptoms after treatment with open-label AXS-05 will be randomized to continued treatment with AXS-05 or to placebo in a double-blind fashion. The primary endpoint of the trial is the time to relapse of depressive symptoms. Topline results from the MERIT trial are expected in the first half of 2021.

- The MERIT and COMET-TRD trials are being conducted in lieu of the previously planned Phase 3 trial in TRD. This approach will more quickly generate clinically useful information with AXS-05 in this treatment resistant MDD population, starting as early as the fourth quarter of 2020.

Antidepressant Unresponsive MDD

- COMET-AU Trial – Axsome is conducting the COMET-AU trial, a Phase 2 open-label sub-study evaluating the efficacy and safety of AXS-05 in patients with antidepressant unresponsive (AU) MDD. The trial will include approximately 150 patients with ongoing symptoms of depression despite receiving one standard antidepressant pharmacotherapy. The trial endpoints will include the change from baseline in the MADRS total score, clinical response, and remission. Topline results from the COMET-AU trial are expected in the fourth quarter of 2020.

MDD with Suicidal Ideation

- COMET-SI Trial – Axsome is conducting the COMET-SI trial, a Phase 2 open-label sub-study evaluating the efficacy and safety of AXS-05 in MDD patients with suicidal ideation (SI). The trial will include approximately 30 patients. The trial endpoints will include the resolution of suicidal ideation. Topline results from the COMET-SI trial are expected in the fourth quarter of 2020.

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 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 is a novel, oral, patent-protected, investigational NMDA receptor antagonist with multimodal activity under development for the treatment of major depressive disorder, Alzheimer's disease agitation, 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, accessed October 9, 2018, http://www.who.int/en/news-room/fact-sheets/detail/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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