Axsome Therapeutics Receives FDA Agreement under Special Protocol Assessment (SPA) for the MOMENTUM Phase 3 Trial of AXS-07 in Migraine

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FDA agreement achieved on Phase 3 trial design, endpoints, and statistical approach

Trial to enroll patients with a history of inadequate response to prior migraine treatments

Trial initiation anticipated 1Q 2019

NEW YORK, Feb. 06, 2019 (GLOBE NEWSWIRE) -- Axsome Therapeutics, Inc. (NASDAQ: AXSM), a clinical-stage biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders, has reached agreement with the U.S. Food and Drug Administration (FDA) under a Special Protocol Assessment (SPA) for the design, endpoints, and statistical approach of the planned MOMENTUM (Maximizing Outcomes in Treating Acute Migraine) Phase 3 trial of AXS-07 (MoSEIC™ meloxicam and rizatriptan) in the acute treatment of migraine. MOMENTUM will enroll only patients with a history of inadequate response to prior migraine treatments. The SPA provides agreement that the MOMENTUM trial design adequately addresses objectives that, if met, will support the regulatory submission for approval of AXS-07 for the indication of acute treatment of migraine in adults with or without aura. Based on FDA feedback during this SPA process, Axsome believes that only one Phase 3 trial may be needed for the approval of AXS-07. Axsome anticipates starting the MOMENTUM trial in the first quarter of 2019, with topline results expected within approximately one year of trial initiation.

"We are pleased to have reached this SPA agreement with the FDA. It reduces the clinical development and regulatory risk for the AXS-07 program as it confirms the FDA's agreement that the Phase 3 MOMENTUM trial is adequately designed to support an NDA filing for marketing approval," said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "Based on its differentiated profile, AXS-07 may result in superior efficacy that would address the major reasons for patient dissatisfaction with current migraine treatments. We look forward to launching the Phase 3 MOMENTUM trial this quarter."

AXS-07 is a novel, oral, rapidly absorbed, investigational medicine consisting of MoSEIC meloxicam and rizatriptan. The distinct mechanism of action and rapid absorption of MoSEIC meloxicam, combined with the known efficacy of rizatriptan, are expected to result in rapid, superior and consistent relief of migraine pain, with lower symptom recurrence, as compared to currently available therapies.

The MOMENTUM study is a Phase 3, randomized, double-blind, multicenter, controlled trial to assess the efficacy and safety of AXS-07 in the acute treatment of migraine. Approximately 875 patients, with a history of inadequate response to prior migraine treatments, will be randomized in a 2:2:2:1 ratio to treatment with AXS-07, rizatriptan, meloxicam, or placebo. The two co-primary endpoints of the trial are the proportion of patients who are free from headache pain two hours after dosing, and the proportion of patients who no longer suffer from their most bothersome migraine-associated symptom (nausea, photophobia, phonophobia) two hours after dosing.

About Special Protocol Assessments

The Special Protocol Assessment (SPA) process is a procedure by which the FDA provides official evaluation and written guidance on the design and size of proposed protocols that are intended to form the basis for a new drug application.

An SPA documents the FDA's agreement that the overall design (e.g., entry criteria, dose selection, endpoints) and planned analysis of a study can adequately address objectives in support of a regulatory submission. However, final determinations for marketing application approval are made after a complete review of a marketing application and are based on the entire data in the application. An SPA may only be modified with the agreement of the FDA and the trial sponsor or if the director of the FDA reviewing division determines that a substantial scientific issue essential to determining the safety or efficacy of the drug was identified after the testing began.

About Migraine

Over 37 million Americans suffer from migraine according to the Centers for Disease Control, and it is the leading cause of disability among neurological disorders in the United States according to the American Migraine Foundation. Migraine is characterized by recurrent attacks of pulsating, often severe and disabling head pain associated with nausea, and sensitivity to light and or sound. It is estimated that migraine accounts for $78 billion in direct (e.g. doctor visits, medications) and indirect (e.g. missed work, lost productivity) costs each year in the United States [1]. Published surveys of migraine sufferers indicate that more than 70% are not fully satisfied with their current treatment, that nearly 80% would try a new therapy, and that they desire treatments that work faster, more consistently, and result in less symptom recurrence [2,3].

About AXS-07

AXS-07 is a novel, oral, investigational medicine under development for the acute treatment of migraine. AXS-07 consists of MoSEIC™ meloxicam and rizatriptan. Meloxicam is a new molecular entity for migraine enabled by Axsome's MoSEIC (Molecular Solubility Enhanced Inclusion Complex)

technology, which results in rapid absorption of meloxicam while maintaining a long plasma half-life. Meloxicam is a COX-2 preferential non-steroidal anti-inflammatory drug and rizatriptan is a 5-$HT1_{B/D}$ agonist. AXS-07 is designed to provide rapid, enhanced and consistent relief of migraine, with reduced symptom recurrence.

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 four clinical-stage candidates, AXS-05, AXS-07, AXS-09, and AXS-12. 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 a Phase 2 trial in smoking cessation. AXS-07 is being developed for the acute treatment of migraine. AXS-12 is currently in a Phase 2 trial in narcolepsy. The Axsome Pain and Primary Care business unit (Axsome PPC) houses Axsome's pain and primary care assets, including AXS-02 and AXS-06, and intellectual property which covers these and related product candidates and molecules being developed by Axsome and others. AXS-02 is being developed for osteoporosis, the pain of knee osteoarthritis, and chronic low back pain. AXS-06 is being developed for osteoarthritis and rheumatoid arthritis. AXS-02, AXS-05, AXS-06, AXS-07, AXS-09, and AXS-12 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 and completion of the trials, futility analyses and receipt of interim results, which are not necessarily indicative of the final results of our ongoing clinical trials; 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 ASCEND clinical trial 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; 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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Source: Axsome Therapeutics, Inc.