Axsome Therapeutics Initiates Phase 3 Study of AXS-02 for Knee Osteoarthritis Associated with Bone Marrow Lesions

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First Patient Enrolled in the COAST-1 Study
Non-Opioid, Oral, Targeted, Potentially First-in-Class Mechanism for Pain
Novel Biomarker-Based Approach for the Treatment of Knee Osteoarthritis Pain
COAST-1 Study Being Conducted under FDA Special Protocol Assessment

NEW YORK, March 28, 2016 (GLOBE NEWSWIRE) -- Axsome Therapeutics, Inc. (NASDAQ:AXSM), a clinical-stage biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders, enrolled the first patient in the COAST-1 (Clinical Knee Osteoarthritis Symptom Treatment 1) study, a Phase 3 trial evaluating the efficacy and safety of AXS-02 for the treatment of the pain of knee osteoarthritis (OA) associated with bone marrow lesions (BMLs). AXS-02 is a potent osteoclast inhibitor being developed as an oral, targeted, non-opioid, potentially first-in-class therapeutic for chronic pain.

“BMLs, which are visible on MRI, are linked to knee pain and cartilage damage, and are present in a significant percentage of patients with knee OA,” said Graeme Jones, M.D., Professor of Rheumatology and Epidemiology and Head of the Musculoskeletal Unit at the Menzies Research Institute (University of Tasmania), and Head of the Department of Rheumatology at Royal Hobart Hospital. “Unfortunately there is currently no drug approved to treat knee OA pain associated with BMLs. This trial is important because it explores a potential treatment for this unmet need, and because it is the first knee OA trial for regulatory approval to use BMLs for patient selection.”

The COAST-1 study is being conducted pursuant to a U.S. Food and Drug Administration (FDA) Special Protocol Assessment (SPA). An SPA documents the FDA's agreement that the design and planned analysis of a clinical trial adequately address scientific and regulatory objectives that, if met, would support a regulatory submission for approval of a drug.

“Knee OA is a significant source of chronic disability for millions of patients. A hallmark of the condition is joint pain, often associated with bone changes, including osteophytes and BMLs. These processes can lead to loss of normal joint function and may progress to eventual joint failure resulting from progressive cartilage loss,” said Thomas J. Schnitzer, M.D., Ph.D., Professor in the Departments of Physical Medicine and Rehabilitation, and Internal Medicine-Rheumatology, at Northwestern University Feinberg School of Medicine. “The condition substantially decreases day-to-day functioning and quality of life, and may necessitate surgical replacement of the knee joint.”

“We believe that AXS-02 holds promise in the treatment of knee OA due to its unique, non-opioid mechanisms of action for pain,” said Randall Kaye, M.D., Chief Medical Officer of Axsome. “AXS-02 potently inhibits bone turnover and localizes preferentially to regions of increased turnover. BMLs therefore represent an entirely novel biomarker strategy for identifying knee OA patients that may respond to AXS-02 treatment.”

“We are pleased to initiate a Phase 3 trial in this important indication which touches the lives of so many,” said Herriot Tabuteau, M.D., Chief Executive Officer of Axsome. “The initiation of the COAST-1 study represents the achievement of another key milestone for Axsome, following our initial public offering in November 2015. Axsome has now initiated three pivotal trials, in three indications, with two product candidates, in less than one year.”

About the COAST-1 Study

COAST-1 (Clinical Knee Osteoarthritis Symptom Treatment 1) is a randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of AXS-02 administered orally to patients with knee osteoarthritis (OA) associated with bone marrow lesions (BMLs). This trial is anticipated to enroll approximately 346 patients with clinically diagnosed knee OA and at least one confirmed BML in the affected knee on MRI. Eligible patients must be at least 50 years of age, either

male or postmenopausal female, and have at least moderate pain intensity. After a baseline period, patients meeting the entry criteria will be randomized in a 1:1 ratio to receive either (1) AXS-02 tablets once per week or (2) matching placebo tablets once per week, under fasting conditions for 6 weeks. Randomized patients will remain blinded for an additional 18 weeks, totaling 24 weeks for the double-blind phase. The primary endpoint is the change in pain intensity from baseline to week 24, measured using a 0-10 numerical rating scale (NRS). Axsome has reached agreement with the U.S. Food and Drug Administration (FDA) regarding a Special Protocol Assessment (SPA) for the COAST-1 study. The SPA provides agreement that the design and planned analysis of the COAST-1 study adequately address objectives that, if met, would support a regulatory submission for approval of AXS-02 for the treatment of the pain of knee OA associated with BMLs.

About AXS-02

AXS-02 (disodium zoledronate tetrahydrate) is a potent osteoclast inhibitor being developed as an oral, targeted, non-opioid, potentially first-in-class therapeutic for chronic pain. AXS-02 has a high affinity for bone mineral, and reduces osteoclast activity by inhibiting the farnesyl pyrophosphate synthase (FPPS) enzyme. AXS-02 is being developed for the treatment of complex regional pain syndrome (CRPS), the pain of knee osteoarthritis (OA) associated with bone marrow lesions (BMLs), and chronic low back pain (CLBP). Phase 3 trials are underway with AXS-02 in CRPS and knee OA associated with BMLs, and are planned in CLBP. AXS-02 is an investigational medication not approved by the FDA.

About Knee Osteoarthritis (OA) associated with Bone Marrow Lesions (BMLs)

Knee OA is a disorder characterized by periarticular bone changes, progressive loss of articular cartilage, joint space narrowing, and eventual total joint failure. It is clinically manifested by knee pain, significant physical disability, and reduced quality of life. BMLs are regions of increased signal intensity on magnetic resonance imaging (MRI) of the knee in patients with knee OA. BMLs are strongly associated with the presence and severity of knee pain, and predict disease severity and structural progression in patients with knee OA, based on published studies. Results of epidemiological studies suggest that there are approximately 7 million symptomatic patients in the United States, 50 years of age and older, with radiographic knee OA and BMLs.

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, including pain, for which there are limited existing treatment options. Axsome's product candidate portfolio includes two late-stage candidates, AXS-02 and AXS-05. AXS-02 is currently in Phase 3 trials in complex regional pain syndrome (CRPS) and knee osteoarthritis (OA) associated with bone marrow lesions (BMLs) with an additional Phase 3 trial planned in chronic low back pain (CLBP) associated with Modic changes (MCs). AXS-05 is currently in a Phase 3 trial in treatment resistant depression (TRD). AXS-02 and AXS-05 are investigational products not approved by the FDA. For more information, please visit the company website at www.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; the timing of and our ability to obtain and maintain U.S. Food and Drug Administration or other regulatory authority approval of, or other action with respect to, our product candidates; 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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