



Axsome Therapeutics Announces AXS-02 Independent Data Monitoring Committee Recommends Continuation of COAST-1 Trial and Discontinuation of CREATE-1 Trial

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COAST-1 is a Phase 3 trial of AXS-02 in knee osteoarthritis associated with bone marrow lesions

CREATE-1 is a Phase 3 trial of AXS-02 in complex regional pain syndrome

Significant reduction in bone resorption confirms potent pharmacologic activity

Company to host conference call today at 8:00 AM Eastern

NEW YORK, Jan. 09, 2018 (GLOBE NEWSWIRE) -- Axsome Therapeutics, Inc. (NASDAQ:AXSM), a clinical-stage biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders, today announced that an independent data monitoring committee (IDMC) has conducted an interim analysis of the CREATE-1 trial of AXS-02 in complex regional pain syndrome (CRPS), and of the COAST-1 trial of AXS-02 in knee osteoarthritis (OA) associated with bone marrow lesions (BMLs). The IDMC has recommended that the COAST-1 trial be continued to full enrollment, and that the CREATE-1 trial be stopped for futility. In the CREATE-1 trial, AXS-02 treatment resulted in a significant reduction of serum CTx, a marker of bone resorption, as compared to placebo ($p < 0.0001$). Further analysis of the data from the CREATE-1 trial will continue in order to better understand the basis for the outcome of that trial and to inform the ongoing clinical development of AXS-02. The IDMC also reviewed the available safety information in both studies and confirmed that AXS-02 was safe and generally well-tolerated. AXS-02 is a potent osteoclast inhibitor being developed as an oral, targeted, non-opioid, potentially first-in-class therapeutic for chronic pain.

"We are encouraged by the IDMC's recommendation for continuation of the COAST-1 trial, by the favorable overall clinical safety profile of AXS-02, and by the confirmation of pharmacologic activity of orally administered AXS-02 as demonstrated by its effects on serum CTx in the CREATE-1 trial," said Cedric O'Gorman, M.D., Senior Vice President of Clinical Development and Medical Affairs of Axsome. "Knee osteoarthritis associated with bone marrow lesions is a serious and potentially disabling condition with limited treatment options. The demonstrated pharmacologic activity of AXS-02 on bone resorption is relevant not only to knee osteoarthritis but to other potential indications for AXS-02."

"The outcome of the CREATE-1 interim analysis is disappointing, especially in light of its implication for patients living with complex regional pain syndrome," said Dr. Herriot Tabuteau, M.D., Chief Executive Officer of Axsome. "We would like to thank the patients and the investigators who participated in the CREATE-1 trial for joining us in our efforts to address this difficult-to-treat condition. We look forward to assessing next steps in the COAST-1 trial and to continuing to advance our broad, late-stage pipeline which includes three other product candidates, being developed across six different indications, in several either ongoing or soon to be initiated registration trials."

In addition to AXS-02, Axsome's pipeline includes AXS-05, AXS-07, and AXS-06. AXS-05 is a combination of dextromethorphan (an NMDA receptor antagonist, sigma-1 receptor agonist, and serotonin and norepinephrine reuptake inhibitor) and bupropion (a norepinephrine and dopamine reuptake inhibitor, which also increases the bioavailability of dextromethorphan). It is in a Phase 3 trial for treatment resistant depression, a Phase 2/3 trial for agitation associated with Alzheimer's disease, with a Phase 2 trial in smoking cessation anticipated to be initiated this quarter. AXS-07 is an oral, rapidly absorbed, fixed-dose combination of MoSEIC™ meloxicam and rizatriptan being developed for the acute treatment of migraine, with a Phase 3 trial in this indication anticipated to start this year. AXS-06 is a Phase 3-ready, oral, rapidly absorbed, non-opioid, fixed-dose combination of MoSEIC™ meloxicam and esomeprazole which is being developed for the treatment of osteoarthritis and rheumatoid arthritis and for the reduction of the risk of NSAID-associated gastric ulcers.

The COAST-1 trial is a randomized, double-blind, placebo-controlled, Phase 3 trial in patients with knee OA associated with BMLs. Subjects in the COAST-1 trial are randomized in a 1:1 ratio to receive either AXS-02 or placebo once a week for six weeks. The primary endpoint of the trial is the change in weekly average daily pain intensity, using the 0-10 numerical rating scale, at 24 weeks. The COAST-1 interim analysis included 77 subjects and was conducted to assess the assumptions used to determine the sample size of the study, as well as safety. This study is being conducted pursuant to a U.S. Food and Drug Administration (FDA) Special Protocol Assessment. AXS-02 has received Fast Track designation from the FDA for the treatment of the pain of knee OA associated with BMLs. The company will assess next steps for this program.

The CREATE-1 trial was a randomized, double-blind, placebo-controlled Phase 3 trial in patients with CRPS. Subjects in the CREATE-1 trial were randomized in a 1:1 ratio to receive either AXS-02 or placebo once a week for six weeks. The primary endpoint of the trial was the change in weekly average daily pain intensity, using the 0-10 numerical rating scale, at 12 weeks. Secondary outcome measures include assessments of the change in the Patients' Global Impression of Change, Clinicians' Global Impression of Change, and bone turnover measured using serum carboxy terminal telopeptide of collagen type I (CTx) and serum procollagen type I N terminal propeptide. The CREATE-1 interim analysis included 81 subjects and was conducted to assess efficacy and safety. AXS-02 has received Fast Track designation from the U.S. Food and Drug Administration (FDA), and orphan drug designation from the FDA and European Medicines Agency (EMA) for the treatment of CRPS.

Conference Call Information

Axsome will host a conference call and webcast today at 8:00 AM Eastern to discuss the results of the interim analyses as well as to provide a corporate update. To participate in the live conference call, please dial (844) 698-4029 (toll-free domestic) or (647) 253-8660 (international), and use the passcode 2093356. The live webcast can be accessed on the "Webcasts & Presentations" page of the "Investors" section of the Company's website at axsome.com. A replay of the webcast will be available for approximately 30 days following the live event.

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 Complex Regional Pain Syndrome (CRPS)

CRPS is a debilitating condition characterized by severe, continuous, burning or throbbing pain in a limb. The excessive pain is accompanied by changes in skin color, temperature and/or swelling. It is considered to be one of the most painful conditions, results in loss of physical function, and can lead to significant and sometimes permanent disability. There is currently no medication approved for the treatment of CRPS.

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 is dosed once per week for 6 weeks and thereafter may have a duration of effect measured in months. AXS-02 has a high affinity for bone mineral, and reduces osteoclast activity by inhibiting the farnesyl pyrophosphate synthase (FPPS) enzyme. AXS-02 is an investigational product candidate not approved by the FDA. The safety and efficacy of AXS-02 have not yet been established.

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 product candidate portfolio includes four clinical-stage candidates, AXS-02, AXS-05, AXS-06, and AXS-07. AXS-05 is currently in a Phase 3 trial in treatment resistant depression (TRD) and a Phase 2/3 trial in agitation in patients with Alzheimer's disease (AD). AXS-05 is also being developed for smoking cessation. AXS-02 is currently in a Phase 3 trial in 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-07 is being developed for the acute treatment of migraine. AXS-06 is being developed for the treatment of osteoarthritis and rheumatoid arthritis and for the reduction of the risk of NSAID-associated gastric ulcers. AXS-02, AXS-05, AXS-06, and AXS-07 are investigational drug 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, 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 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.

Axsome Contact:

Mark Jacobson
Senior Vice President, Operations
Axsome Therapeutics, Inc.
25 Broadway, 9th Floor
New York, NY 10004
Tel: 212-332-3243
Email: mjacobson@axsome.com
www.axsome.com

