Axsome Therapeutics Announces AXS-06 (MoSEIC™ Meloxicam and Esomeprazole) Meets Primary Endpoint in Phase 1 Clinical Trial

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AXS-06 is an oral, rapidly-absorbed, once-daily, non-opioid, COX-2 preferential pain therapeutic with a gastroprotectant

Primary endpoint met with 9 times faster time to maximum plasma concentration (T_{max}) of meloxicam versus Mobic® ($p<0.0001$)

Therapeutic plasma levels of meloxicam achieved within 15 minutes of oral dosing of AXS-06

Gastroprotective concentrations of esomeprazole achieved

Phase 3-ready based on FDA Pre-IND guidance

AXS-06 utilizes Axsome's MoSEIC™ delivery technology

AXS-06 to complement commercialization of AXS-02 in development for complex regional pain syndrome

NEW YORK, July 25, 2017 (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 positive topline clinical trial results from a Phase 1 pharmacokinetic study of AXS-06, a novel, oral, non-opioid, fixed-dose combination of meloxicam and esomeprazole being developed for the treatment of osteoarthritis and rheumatoid arthritis. Axsome has received, from the U.S. Food and Drug Administration (FDA), Pre-Investigational New Drug Application (Pre-IND) written guidance on a proposed clinical developmental plan for AXS-06. Based on this guidance, Axsome believes that AXS-06 is Phase 3-ready. AXS-06 is now Axsome's third product candidate in clinical development and its second differentiated oral, non-opioid product candidate for the management of chronic pain.

The clinical trial results demonstrated, for the first time, rapid achievement of peak plasma levels of meloxicam after oral administration. Meloxicam is a long-acting nonsteroidal anti-inflammatory drug (NSAID) with COX-2 preferential inhibition and potent pain relieving efficacy. However standard meloxicam has an extended time to maximum plasma concentration (T_{max}) which delays its onset of action. AXS-06 utilizes Axsome's proprietary MoSEIC™ (Molecular Solubility Enhanced Inclusion Complex) technology to substantially increase the solubility and speed the absorption of meloxicam while maintaining durability of action. AXS-06 also incorporates esomeprazole, a proton pump inhibitor, to reduce the risk of NSAID-associated gastrointestinal ulcers which can occur with chronic NSAID use.

"AXS-06 provides the benefits of oral administration and demonstrates a more rapid meloxicam T_{max} than that reported with intramuscular administration, highlighting the potential for faster pain relief. In addition, AXS-06 maintains the long half-life of meloxicam which enables once-daily dosing and sustained effect," said Herriot Tabuteau, M.D., Chief Executive Officer of Axsome. "These results indicate that AXS-06 has a potentially best-in-class NSAID profile based on the differentiated pharmacokinetic profile of MoSEIC™ meloxicam and the potentially enhanced gastrointestinal safety from the esomeprazole component. The potential efficacy and safety advantages of AXS-06 as compared to currently available NSAIDs could provide significant benefit to patients."

The study compared the pharmacokinetics of meloxicam and esomeprazole after oral administration of AXS-06 tablets (meloxicam 15 mg, esomeprazole 40 mg), and commercially available Mobic® tablets (15 mg meloxicam) and Nexium® capsules (40 mg esomeprazole) in healthy volunteers. The median T_{max} for meloxicam, the trial's primary endpoint, was 9 times faster for AXS-06 as compared to Mobic® (0.5 hour versus 4.5 hours for AXS-06 and Mobic, respectively, $p<0.0001$). AXS-06 also demonstrated higher mean maximum plasma concentration (C_{max}) ($p=0.0018$), faster time to therapeutic plasma concentration ($p<0.0001$), and time to half-maximal plasma concentration ($p<0.0001$) as compared to Mobic®. Terminal half-lives for meloxicam were similar for AXS-06 and Mobic® at approximately 20 and 22 hours, respectively. Plasma concentrations and terminal half-lives of esomeprazole after AXS-06 and Nexium® administration were comparable. AXS-06 was well tolerated with reported adverse events being similar across the three treatment arms. There were no serious adverse events in the study.

"With its differentiated profile and Phase 3-ready status, AXS-06 complements AXS-02 which is currently in Phase 3 trials in complex regional pain syndrome and knee osteoarthritis," continued Dr. Tabuteau. "The overlapping patient and physician audiences for AXS-02 and AXS-06 should allow Axsome to leverage our commercialization efforts. We look forward to the further development of AXS-06 and to a data readout for AXS-02 in complex regional pain syndrome anticipated in the fourth quarter."

Phase 1 Trial Design

The study was a randomized, parallel group trial to evaluate the pharmacokinetics and safety of meloxicam and esomeprazole after single and multiple dose administration of AXS-06 in healthy volunteers. A total of 30 subjects were randomly assigned in a 1:1:1 ratio to treatment with AXS-06 tablets (15 mg meloxicam, 40 mg esomeprazole), Mobic® tablets (15 mg meloxicam), or Nexium® capsules (40 mg esomeprazole), once daily for 6

days under fasting conditions. The primary endpoint was the T_{max} of meloxicam. Secondary endpoints included C_{max}, time to half maximum concentration, and time to therapeutic concentration.

About the NSAID Market

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used for the treatment of pain and arthritis. Approximately 120 million prescriptions were written for NSAIDs overall in the U.S. in 2016, of which approximately 25% were written for meloxicam. Chronic use of NSAIDs has been reported to be associated with the development of gastrointestinal ulcers in as many as 25% of patients.

About AXS-06

AXS-06 is an oral, non-opioid, fixed-dose combination of MoSEIC™ meloxicam and esomeprazole which is being developed for the treatment of chronic pain. Meloxicam is a long-acting nonsteroidal anti-inflammatory drug (NSAID) with COX-2 preferential inhibition and potent pain-relieving efficacy. AXS-06 utilizes Axsome's proprietary MoSEIC™ (Molecular Solubility Enhanced Inclusion Complex) technology to substantially increase the solubility and speed the absorption of meloxicam while maintaining durability of action. Esomeprazole is a proton pump inhibitor which lowers stomach acidity and which has been shown to reduce the occurrence of NSAID-induced gastrointestinal ulcers. AXS-06 is designed to provide rapid, effective pain relief, and to reduce the risk of NSAID-induced ulcers, with convenient once-daily dosing.

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 three clinical-stage candidates, AXS-02, AXS-05, and AXS-06. 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-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). A Phase 1 trial of AXS-06 has been completed. AXS-02, AXS-05, and AXS-06 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; 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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