Axsome Therapeutics, Inc. Logo

Axsome Therapeutics Announces AXS-07 for the Treatment of Migraine

November 28, 2017

Incorporates new molecular entity for migraine and Axsome's MoSEIC™ technology

Potential for superior efficacy as compared to current treatments

FDA Pre-IND meeting written guidance received

Issued U.S. patent provides protection into 2036

Phase 3 trial anticipated in 2018

NEW YORK, Nov. 28, 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 its next product candidate, AXS-07, which is being developed for the acute treatment of migraine. AXS-07 is an oral, fixed-dose combination 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. Rizatriptan has demonstrated strong efficacy in the treatment of migraine as a single agent. The distinct mechanism of action and rapid absorption of MoSEIC meloxicam, combined with the known efficacy of rizatriptan, is expected to result in rapid, superior and consistent relief of migraine pain, with lower symptom recurrence, as compared to currently available therapies.

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-07 including a planned Phase 3 trial. Based on this feedback, Axsome believes that only one Phase 3 trial may be needed for the approval of AXS-07 for the treatment of migraine. Axsome anticipates starting this trial in 2018 contingent on the availability of resources.

"Migraine attacks are disabling and affect more than 37 million Americans," said Alan M. Rapoport, M.D., Clinical Professor of Neurology at The David Geffen School of Medicine at UCLA, and former President of the International Headache Society. "Patient surveys demonstrate a high level of dissatisfaction with current treatments. Based on its potentially superior clinical profile, AXS-07 may address the major reasons for patient dissatisfaction with current acute care treatments for migraine including less than desired speed of pain relief, failure to successfully treat all patients or all attacks, and recurrence of symptoms within 24 hours after treatment. We look forward to learning more about the potential of AXS-07 as it advances in clinical development."

The U.S. Patent and Trademark Office recently issued patent number 9,821,075 which covers MoSEIC meloxicam and provides protection for AXS-07 into 2036.

"AXS-07 is the second product candidate stemming from our MoSEIC platform which has the potential to generate additional proprietary new medicines," added Dr. Tabuteau. "We are excited about the prospects of AXS-07 to address unmet medical needs in this important neurological condition and look forward to advancing it in late stage clinical trials as early as this coming year."

The rationale for the development of AXS-07 in the treatment of migraine is based on the rapid absorption and long half-life of MoSEIC meloxicam, and the additive and potentially synergistic efficacy resulting from the distinct mechanisms of action of meloxicam and rizatriptan.

The meloxicam component of AXS-07 is a COX-2 preferential non-steroidal anti-inflammatory drug that inhibits the synthesis of prostaglandins, may reduce meningeal inflammation and inhibit central sensitization resulting from the activation of glial cells in the brain stem. Meloxicam is a new molecular entity for migraine and is not currently approved for this indication. Axsome's MoSEIC technology enables meloxicam's use in this indication by significantly increasing the speed of its absorption after oral administration, as demonstrated in a completed Phase 1 clinical trial.

The rizatriptan component of AXS-07 is a 5-$HT1_{B/D}$ agonist that inhibits calcitonin gene-related peptide (CGRP)–mediated vasodilation, has been shown to have central trigeminal antinociceptive activity, and may reduce the release of inflammatory mediators from trigeminal nerves. Rizatriptan is currently approved as a single agent for the acute treatment of migraine.

Clinical Profile of AXS-07

Based on AXS-07's multiple mechanisms of action, the unique pharmacokinetics of the MoSEIC meloxicam component, and results from numerous clinical trials with the rizatriptan component, Axsome believes that AXS-07 may have significant advantages over currently available therapy in the treatment of migraine:

- **Rapid absorption and onset of action.** In a completed Phase 1 trial, therapeutic plasma levels of meloxicam were attained within 15 minutes of oral dosing of MoSEIC meloxicam, with a median time to maximum plasma concentration (T_{max}) that was 9 times faster for MoSEIC meloxicam as compared to standard meloxicam (0.5 hour versus 4.5 hours for MoSEIC and standard meloxicam, respectively, $p<0.0001$). The fast absorption of MoSEIC meloxicam combined with a reported T_{max} for rizatriptan of 1 to 1.5 hours is expected to result in rapid onset of migraine pain relief with AXS-07.

- **Strong and consistent pain relief.** AXS-07 has the potential to provide efficacy that is superior to currently available migraine treatments based on the expected additive effect of MoSEIC meloxicam and rizatriptan. Clinical experience with rizatriptan as a single agent further indicates that AXS-07 may provide more consistent intra-patient efficacy than currently available migraine treatments, as well as efficacy in various stages, severities, and subtypes of migraine including

menstrual migraine.

- **Sustained pain relief.** The approximately 20-hour half-life of MoSEIC meloxicam, combined with the expected additive effect of the rizatriptan component of AXS-07 is expected to result in more sustained efficacy with less recurrence of symptoms with AXS-07 as compared to currently available treatments.

- **Pharmacoeconomic benefits.** The potential superior efficacy of AXS-07 would be expected to result in reduced use of medical services, rescue or repeat medication, absenteeism, and loss of productivity, as compared to currently available treatments.

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 an oral, fixed-dose combination of MoSEIC™ meloxicam and rizatriptan being developed for the acute treatment of migraine. 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's MoSEIC™ Technology

Axsome's MoSEIC (Molecular Solubility Enhanced Inclusion Complex) technology was developed to improve the absorption of drug molecules after oral administration. Using a proprietary process, target drug molecules are combined with solubility enhancers to form inclusion complexes, which are then stabilized using a buffering system, to improve drug release and enhance absorption.

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-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-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; 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

[1] Gooch CL, Pracht E, Borenstein AR. The burden of neurological disease in the United States: A summary report and call to action. Ann Neurol. 2017 Apr; 81(4):479-484.

[2] Smelt AF, Louter MA, Kies DA, Blom JW, Terwindt GM, van der Heijden GJ, De Gucht V, Ferrari MD, Assendelft WJ. What do patients consider to be the most important outcomes for effectiveness studies on migraine treatment? Results of a Delphi study. PLoS One. 2014 Jun 16;9(6):e98933.

[3] Lipton RB, Stewart WF. Acute migraine therapy: do doctors understand what patients with migraine want from therapy? Headache. 1999;39(suppl 2):S20-S26.

AXSOME THERAPEUTICS

Source: Axsome Therapeutics, Inc.