Axsome Therapeutics Announces Acceleration of MOMENTUM Phase 3 Trial of AXS-07 in Migraine

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Topline results now anticipated in 2H 2019

Trial enriched with only patients with history of inadequate response to prior migraine treatments

Trial compares AXS-07 to placebo and active comparator

Trial being conducted under FDA Special Protocol Assessment (SPA)

Company to discuss development on the conference call scheduled today at 8:00 AM Eastern

NEW YORK, May 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, today announced the acceleration of the timeline for reporting topline results from the MOMENTUM Phase 3 trial of AXS-07 (MoSEIC™ meloxicam and rizatriptan), Axsome's novel, oral, investigational medicine with distinct dual mechanisms of action for the acute treatment of migraine. The trial is being conducted pursuant to a U.S. Food and Drug Administration (FDA) Special Protocol Assessment (SPA). The first patient was enrolled in the MOMENTUM trial in March 2019, and currently approximately 40% of the target number of patients have been randomized. Based on the faster-than-expected enrollment in this trial, topline results are now expected in the second half of 2019, versus previous guidance of the first quarter of 2020.

The MOMENTUM (Maximizing Outcomes in Treating Acute Migraine) Phase 3 trial is a randomized, double-blind, placebo- and active-controlled study of AXS-07 for the acute treatment of migraine, in which patients are randomized to treatment with AXS-07, rizatriptan, meloxicam, or placebo. Rizatriptan, the active comparator in the trial, is considered to be one of the most efficacious oral medications currently available for the acute treatment of migraine [1].

Patients enrolled in the MOMENTUM trial must have a history of inadequate response to prior acute migraine treatments, assessed using the Migraine Treatment Optimization Questionnaire (mTOQ-4). The mTOQ-4 is a validated questionnaire that assesses efficacy response to prior acute treatments based on four aspects (two-hour pain freedom, efficacy for at least 24 hours with one dose, ability to plan daily activities, and disruption of daily activities) [2]. In addition to having a history of inadequate response, the majority of patients randomized to date in the MOMENTUM trial also report allodynia with their migraine attacks. Allodynia, which is pain from normally non-painful stimuli (such as brushing hair, wearing glasses, taking a shower, etc.), has been shown to be strongly associated with worse outcomes for pain freedom and pain relief after treatment with triptan medications [3,4].

The MOMENTUM trial is being enriched with difficult-to-treat patients because they represent a population for whom superior medicines are urgently needed. The rapid absorption and distinct dual mechanisms of action of AXS-07 provide a scientific rationale for potential success in providing relief for this more treatment resistant population. AXS-07 consists of MoSEIC™ meloxicam and rizatriptan. Meloxicam, a COX-2 preferential non-steroidal anti-inflammatory drug, 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 is a potent 5-$HT_{1B/D}$ agonist.

"The stringent design of the MOMENTUM trial, which is enrolling a difficult-to-treat patient population and utilizing a potent active comparator, sets a high bar for the demonstration of efficacy of AXS-07," said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "Success in this trial would highlight the potentially differentiated efficacy profile of this novel, oral treatment with distinct dual mechanisms of action, designed to address the unmet medical needs in the acute treatment of migraine. We are pleased with the pace of enrollment and look forward to the results of the MOMENTUM trial, anticipated in the second half of 2019, which, if positive, would support the filing of an NDA for AXS-07 potentially as early as 2020."

Elements of the MOMENTUM Trial:

- Eligible patients are randomized in a 2:2:2:1 ratio to treatment with AXS-07, rizatriptan, meloxicam, or placebo. The target number of patients is approximately 875.
- Eligible patients must have a history of inadequate response to prior acute migraine treatments, assessed using the mTOQ-4 questionnaire.
- Co-primary endpoints are freedom from headache pain two hours after dosing, and freedom from the most bothersome migraine-associated symptom (nausea, photophobia, or phonophobia) two hours after dosing, for AXS-07 as compared to placebo.

- Superiority of AXS-07 to the rizatriptan and meloxicam arms (component contribution) will be established based on sustained freedom from headache pain from two to 24 hours after dosing.

The MOMENTUM study is being conducted pursuant to an SPA with the FDA. The SPA provides agreement that the overall MOMENTUM trial design (e.g., entry criteria, dose selection, endpoints) and planned analysis adequately address 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.

Conference Call Information

Axsome will host a conference call and webcast today at 8:00 AM Eastern to discuss the progress of the MOMENTUM Phase 3 trial in the acute treatment of migraine as well as AXS-05 in the treatment of major depressive disorder following a Breakthrough Therapy meeting with the FDA. To participate in the live conference call, please dial (844) 698-4029 (toll-free domestic) or (647) 253-8660 (international), and use the conference ID 3977129. 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 the MOMENTUM Trial

MOMENTUM 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, or phonophobia) two hours after dosing, for AXS-07 as compared to placebo.

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 [5]. 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 [6,7].

About AXS-07

AXS-07 is a novel, oral, investigational medicine with distinct dual mechanisms of action 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-$HT_{1B/D}$ agonist. AXS-07 is designed to provide rapid, enhanced and consistent relief of migraine, with reduced symptom recurrence. AXS-07 is not approved by the FDA.

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) and a Phase 2/3 trial in agitation associated with Alzheimer's disease (AD). AXS-05 is also being developed for major depressive disorder (MDD) and smoking cessation treatment. AXS-07 is currently in a Phase 3 trial 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.

References

1. Ferrari MD, Roon KI, Lipton RB, Goadsby PJ. Oral triptans (serotonin 5-HT(1B/1D) agonists) in acute migraine treatment: a meta-analysis of 53 trials. Lancet. 2001 Nov 17;358(9294):1668-75.

2. Lipton RB, Fanning KM, Serrano D, Reed ML, Cady R, Buse DC. Ineffective acute treatment of episodic migraine is associated with new-onset chronic migraine. Neurology. 2015 Feb 17;84(7):688-95.

3. Lipton RB, Munjal S, Buse DC, Bennett A, Fanning KM, Burstein R, Reed ML. Allodynia Is Associated With Initial and Sustained Response to Acute Migraine Treatment: Results from the American Migraine Prevalence and Prevention Study. Headache. 2017 Jul;57(7):1026-1040.

4. Lipton RB, Munjal S, Buse DC, Fanning KM, Bennett A, Reed ML. Predicting Inadequate Response to Acute Migraine Medication: Results from the American Migraine Prevalence and Prevention (AMPP) Study. Headache. 2016 Nov;56(10):1635-1648.

5. 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.

6. 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.

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

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, pace of enrollment 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, and the number or type of studies or nature of results necessary to support the filing of a new drug application ("NDA") for any of our current product candidates; 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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