Axsome Therapeutics Presents New Data from MOMENTUM Phase 3 Trial with AXS-07 Demonstrating Rapid Onset of Action and Reduced Symptom Recurrence in the Acute Treatment of Migraine

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Significantly faster time to pain relief as compared to rizatriptan (p<0.001)

Significantly less relapse of migraine pain as compared to rizatriptan (p=0.001)

Benefits demonstrated in patients with a history of inadequate response to prior acute treatments

NEW YORK, Sept. 24, 2020 (GLOBE NEWSWIRE) -- Axsome Therapeutics, Inc. (NASDAQ: AXSM), a biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders, today announced that AXS-07, the Company's novel, oral, multi-mechanistic investigational medicine for the acute treatment of migraine, rapidly relieved and substantially reduced relapse of migraine pain, as compared to the potent active comparator rizatriptan, in the MOMENTUM Phase 3 trial. These findings were presented at the live sessions of the 2020 American Academy of Neurology (AAN) Science Highlights platform held virtually September 23-24.

The MOMENTUM study was a randomized, double-blind, placebo- and active-controlled trial which enrolled only patients with a history of inadequate response to prior acute migraine treatments. A total of 1,594 patients were randomized in a 2:2:2:1 ratio to AXS-07 (20 mg MoSEIC™ meloxicam/10 mg rizatriptan), rizatriptan (10 mg), MoSEIC™ meloxicam (20 mg), or placebo, to treat a single migraine attack of moderate or severe intensity. Rizatriptan, an active comparator in the trial, is considered to be the fastest acting oral triptan and one of the most effective medications currently available for the acute treatment of migraine [1-3].

AXS-07 demonstrated faster and more durable relief of migraine pain as compared to rizatriptan. The probability of achieving pain relief with AXS-07 was greater than with rizatriptan within 30 minutes after dosing and at every time point thereafter, with a median time to migraine pain relief that was nearly 3x faster for AXS-07 compared to rizatriptan (1.5 vs. 4.0 hours, p<0.001). AXS-07 substantially and significantly reduced relapse of migraine pain as compared to rizatriptan, with 45.2% of rizatriptan-treated patients experiencing relapse compared to 21.2% of AXS-07 patients over 48 hours after dosing (p=0.001).

The results on time to migraine pain relief and relapse are consistent with the superiority of AXS-07 over rizatriptan on several other efficacy measures, as previously reported, including rescue medication use (p<0.001), sustained pain relief over 24 hours (p=0.006) and 48 hours (p=0.003), sustained pain freedom over 24 hours (p=0.038) and 48 hours (p=0.003), Patient Global Impression of Change (p=0.022) at 2 hours, and return to normal functioning at 24 hours (p=0.027). Also as previously reported, AXS-07 met both co-primary endpoints of the trial by demonstrating a greater percentage of patients achieving pain freedom (p<0.001) and absence of most bothersome symptom (p=0.002), 2 hours after dosing, as compared to placebo.

"The strong efficacy of AXS-07 in patients with a history of inadequate response is especially notable since it was demonstrated over one of the most effective triptans," said Cedric O'Gorman, MD, Senior Vice President of Clinical Development and Medical Affairs of Axsome. "With its demonstrated rapid, superior, and durable effects in the acute treatment of migraine, AXS-07 may help address the need for more efficacious treatments for this debilitating neurological condition."

AXS-07 was safe and well tolerated in the trial. The most commonly reported adverse events with AXS-07 were nausea, dizziness and somnolence, none of which occurred at a rate greater than placebo or greater than 3%.

AXS-07 is a novel, oral, rapidly absorbed, multi-mechanistic investigational medicine for the acute treatment of migraine, consisting of MoSEIC™ meloxicam and rizatriptan. AXS-07 is thought to act by inhibiting CGRP release, reversing CGRP-mediated vasodilation, and inhibiting neuro-inflammation, pain signal transmission, and central sensitization. Axsome's MoSEIC™ technology significantly increases the speed of absorption of the meloxicam component after oral administration while maintaining a long plasma half-life. AXS-07 is covered by 44 issued U.S. and international patents providing protection out to 2036, and Axsome maintains worldwide rights.

About the MOMENTUM Trial

MOMENTUM (Maximizing Outcomes in Treating Acute Migraine) was a Phase 3, randomized, double-blind, multicenter, controlled trial to assess the efficacy and safety of AXS-07 in the acute treatment of moderate and severe migraine. Eligible patients must have had a history of inadequate response to prior acute migraine treatments, assessed using the Migraine Treatment Optimization Questionnaire (mTOQ-4). A total of 1,594 patients were randomized in a 2:2:2:1 ratio to treatment with AXS-07, rizatriptan, MoSEIC™ meloxicam, or placebo. The two co-primary endpoints of the trial were the proportion of patients who are free from headache pain two hours after dosing, and the proportion of patients who no longer suffered from their 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 MoSEIC™ meloxicam arms (component contribution) was to be established based on sustained freedom from headache pain from two to 24 hours after dosing (key secondary endpoint). The MOMENTUM study was conducted pursuant to an FDA Special Protocol Assessment (SPA).

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 [4]. 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 [5,6].

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-$HT_{1B/1D}$ agonist. AXS-07 is designed to provide rapid, enhanced and consistent relief of migraine, with reduced symptom recurrence. AXS-07 is covered by more than 44 issued U.S. and international patents which provide protection out to 2036. AXS-07 is not approved by the FDA.

About Axsome Therapeutics, Inc.

Axsome Therapeutics, Inc. is a biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders for which there are limited treatment options. For the many people facing unsatisfactory treatments for CNS disorders, Axsome accelerates the invention and adoption of life-changing medicines. Axsome's core CNS product candidate portfolio includes five clinical-stage candidates, AXS-05, AXS-07, AXS-09, AXS-12, and AXS-14. AXS-05 is being developed for major depressive disorder (MDD), treatment resistant depression (TRD), Alzheimer's disease (AD) agitation, and as a treatment for smoking cessation. AXS-07 is being developed for the acute treatment of migraine. AXS-12 is being developed for the treatment of narcolepsy. AXS-14 is being developed for fibromyalgia. AXS-05, AXS-07, AXS-09, AXS-12, and AXS-14 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.

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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 (including our ability to fully fund our disclosed clinical trials, which assumes no material changes to our currently projected expenses), 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, with or without a special protocol assessment); the potential for our clinical trials to provide a basis for accelerated approval of our product candidates for the treatment of several indications and accelerate their development timelines and commercial paths to patients (including, but not limited to, with or without a breakthrough therapy designation); 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; the Company's anticipated capital requirements, including the Company's anticipated cash runway; unforeseen circumstances or other disruptions to normal business operations arising from or related to COVID-19; 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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