Axsome Therapeutics Announces AXS-07 Achieves Co-Primary and Key Secondary Endpoints in MOMENTUM Phase 3 Migraine Trial in Patients with History of Inadequate Response

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Demonstrated statistical significance on regulatory co-primary endpoints of pain freedom (p<0.001) and freedom from most bothersome symptom (p=0.002) at 2 hours, compared to placebo

Demonstrated superiority to rizatriptan active comparator on key secondary endpoint of sustained pain freedom 2-24 hours after dosing (p=0.038)

Demonstrated greater and more sustained migraine pain relief than rizatriptan (p=0.006)

Rapidly relieved migraine pain; significantly reduced use of rescue medication compared to rizatriptan (p<0.001)

Positive results support NDA filing of AXS-07 in the acute treatment of migraine, anticipated in 2H 2020

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

NEW YORK, Dec. 30, 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 that AXS-07, Axsome's novel, oral, multi-mechanistic investigational medicine for the acute treatment of migraine, met the two regulatory co-primary endpoints and significantly improved migraine pain and most bothersome symptoms as compared to placebo in the MOMENTUM Phase 3 trial. AXS-07 also met the key secondary endpoint, demonstrating statistically significant superiority to the active comparator rizatriptan on sustained freedom from migraine pain.

MOMENTUM 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, 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 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. In addition to a history of inadequate response, enrolled patients exhibited a high rate of characteristics that are strongly associated with poor treatment outcomes including cutaneous allodynia (75.4%), severe migraine pain intensity (41.2%), obesity (43.7%), and morning migraine (36.6%). The study was conducted pursuant to a U.S. Food and Drug Administration (FDA) Special Protocol Assessment (SPA). 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].

AXS-07 met the two regulatory co-primary endpoints by demonstrating, with high statistical significance, a greater percentage of patients as compared to placebo achieving pain freedom (19.9% versus 6.7%, p<0.001) and absence of most bothersome symptom (36.9% versus 24.4%, p=0.002), 2 hours after dosing. Superiority of AXS-07 to rizatriptan and MoSEIC™ meloxicam (component contribution) was established as specified in the SPA, by demonstration of a greater percentage of AXS-07 patients achieving sustained pain freedom from 2 to 24 hours after dosing, compared to rizatriptan and MoSEIC™ meloxicam, as well as to placebo (16.1%, 11.2%, 8.8% and 5.3%, respectively; p=0.038, p=0.001, and p<0.001, respectively versus AXS-07). The positive results on both co-primary endpoints along with the demonstration of component contribution support the filing of an NDA for AXS-07 in the acute treatment of migraine.

AXS-07 provided substantially greater and more sustained migraine pain relief compared to placebo and rizatriptan, which translated to a significant reduction in rescue medication use for AXS-07 compared to placebo and rizatriptan. The percentage of patients experiencing sustained pain relief from 2 to 24 hours after dosing was 53.3% for AXS-07, compared to 33.5% for placebo and 43.9% for rizatriptan (p<0.001, p=0.006, respectively versus AXS-07). Sustained pain relief from 2 to 48 hours was also experienced by a statistically significantly greater proportion of AXS-07 patients (46.5%), compared to placebo (31.1%) and rizatriptan (36.5%) patients (p<0.001, p=0.003, respectively versus AXS-07). Rescue medication was used by 23.0% of AXS-07 patients, compared to 43.5% of placebo and 34.7% of rizatriptan patients (p<0.001 for each group versus AXS-07).

AXS-07 provided rapid relief of migraine pain with the percentage of patients achieving pain relief with AXS-07 being numerically greater than with rizatriptan at every time point measured starting at 15 minutes, and statistically significantly greater than with rizatriptan by 60 minutes (p=0.04). The proportions of patients experiencing pain relief 1.5 hours after dosing were 60.5% for AXS-07 compared to 52.5% for rizatriptan and 48.3% for placebo (p=0.019, p=0.004, respectively versus AXS-07). AXS-07 was statistically significantly superior to rizatriptan on several other secondary endpoints including Patient Global Impression of Change (PGI-C) (p=0.022), and return to normal functioning at 24 hours (p=0.027).

"In the MOMENTUM trial, AXS-07 provided greater and more lasting migraine pain relief than rizatriptan. Given that rizatriptan is one of the most effective triptans and that the study enrolled patients with difficult-to-treat migraine, this finding is impressive," said Richard B. Lipton, M.D., Professor and Vice Chair of Neurology, and Director of the Montefiore Headache Center, at the Albert Einstein College of Medicine. "Many patients experience a suboptimal response to their current acute migraine treatments, placing them at increased risk of headache related disability and progression to chronic migraine, factors associated with increased healthcare costs. The results of this study suggest that AXS-07 may provide an important treatment option for people with difficult-to-treat migraine."

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%. There was one serious adverse event in the AXS-07 arm which was deemed by the investigator not to be related to study drug.

“The results of MOMENTUM demonstrate the ability of AXS-07 to provide unique benefits to migraine patients, with fast, strong, and durable relief of migraine pain as compared to a potent active comparator in a stringently designed trial enriched with patients with difficult-to-treat migraine,” said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. “These data have potentially important implications for patient care based on the high rate of inadequate response to and patient dissatisfaction with current treatments. With these positive results, we look forward to filing an NDA for AXS-07 in the acute treatment of migraine in 2020.”

The MOMENTUM study was 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. Based on FDA feedback, Axsome believes that MOMENTUM will be the only efficacy trial required to support an NDA filing for AXS-07 for the acute treatment of migraine. Axsome plans to file the NDA in the second half of 2020.

“The World Health Organization categorizes the disability from severe migraine attacks on the same level as that from quadriplegia, dementia, and acute psychosis. The debilitating pain of migraine damages family life, social life and employment,” said Cedric O’Gorman, MD, Senior Vice President of Clinical Development and Medical Affairs of Axsome. “AXS-07 incorporates multiple mechanisms of action to address various migraine processes with the goal of providing enhanced effectiveness. The results of the MOMENTUM trial validate this approach, demonstrating that AXS-07 can provide significant benefit that is greater than that of currently available treatment, even in patients with difficult-to-treat migraine.”

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 21 issued U.S. and international patents providing protection out to 2036, and Axsome maintains worldwide rights.

Detailed study results, including additional secondary endpoints, will be submitted for presentation at upcoming medical meetings and for publication. AXS-07 is also being evaluated in the INTERCEPT Phase 3 trial which is a randomized, double-blind, placebo-controlled study evaluating the early treatment of migraine with AXS-07. In contrast to the ongoing MOMENTUM trial in which patients with a history of inadequate response treated migraine attacks once they have become of moderate or severe intensity, in the INTERCEPT trial, patients are to administer AXS-07 at the earliest sign of migraine pain.

Summary of Topline Results of the MOMENTUM Trial

Patient Population

- All enrolled patients had a history of inadequate response to prior acute migraine treatments, assessed using the Migraine Treatment Optimization Questionnaire (mTOQ-4), with an average score of 3.6, corresponding to poor response to prior acute treatments.
- Enrolled patients exhibited a high rate of characteristics that are strongly associated with poor treatment outcomes including [2-4]: presence of cutaneous allodynia (pain from normally non-painful stimuli such as brushing hair, wearing glasses, taking a shower) in 75.4%, severe migraine pain intensity in 41.2%, obesity in 43.7%, and morning migraine in 36.6%.

Regulatory Endpoints

- AXS-07 demonstrated a greater percentage of patients as compared to placebo achieving pain freedom (19.9% versus 6.7%, $p<0.001$) and absence of most bothersome symptom (36.9% versus 24.4%, $p=0.002$), 2 hours after dosing, the two regulatory co-primary endpoints.
- AXS-07 demonstrated superiority to rizatriptan and MoSEIC™ meloxicam on the percentage of patients achieving sustained pain freedom from 2 to 24 hours after dosing (16.1%, 11.2%, and 8.8%, respectively; $p=0.038$, $p=0.001$, respectively versus AXS-07), the pre-specified key secondary endpoint to demonstrate component contribution.

Relief of Migraine Pain and Rescue Medication Use

- Sustained pain relief from 2 to 24 hours after dosing was experienced by 53.3% of patients treated with AXS-07, compared to 33.5% with placebo and 43.9% with rizatriptan ($p<0.001$, $p=0.006$, respectively versus AXS-07).
- Sustained pain relief from 2 to 48 hours after dosing was experienced by 46.5% of patients treated with AXS-07, compared to 31.1% with placebo and 36.5% with rizatriptan ($p<0.001$, $p=0.003$, respectively versus AXS-07).
- Rescue medication was used by 23.0% of AXS-07 patients, compared to 43.5% of placebo and 34.7% of rizatriptan patients ($p<0.001$ for each group versus AXS-07).

Effects of AXS-07 versus Rizatriptan

- AXS-07 rapidly relieved migraine pain with the percentage of patients achieving pain relief with AXS-07 being numerically greater than with rizatriptan at every time point measured starting at 15 minutes, and statistically significantly greater than with rizatriptan by 60 minutes (p=0.04).
- AXS-07 was statistically superior to rizatriptan on sustained pain relief from 2 to 24 hours (p=0.006) and from 2 to 48 hours (p=0.003).
- AXS-07 resulted in significantly less rescue medication use than rizatriptan (p<0.001).
- AXS-07 was superior to rizatriptan on the Patient Global Impression of Change (PGI-C) scale (p=0.022) and return to normal functioning at 24 hours (p=0.027).

Safety and Tolerability

- 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%. There was one serious adverse event in the AXS-07 arm which was deemed by the investigator not to be related to study drug.

Conference Call Information

Axsome will host a conference call and webcast with slides today at 8:00 AM Eastern to discuss the topline results of the MOMENTUM trial of AXS-07 in the acute treatment of migraine. To participate in the live conference call, please dial (844) 698-4029 (toll-free domestic) or (647) 253-8660 (international), and use the passcode 3483715. 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 (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 [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-$HT_{1B/1D}$ 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), a Phase 2/3 trial in agitation associated with Alzheimer's disease (AD), and is being developed for major depressive disorder (MDD). AXS-05 is also being developed for smoking cessation treatment. AXS-07 is currently in two Phase 3 trials for the acute treatment of migraine. AXS-12 is being developed for the treatment of narcolepsy. AXS-05, 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

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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, 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 MOMENTUM clinical trial to provide a basis for approval of AXS-07 for the acute treatment of migraine in adults with or without aura, pursuant to our special protocol assessment; the potential for the ASCEND clinical trial, combined with the GEMINI clinical trial results, 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; the Company’s anticipated capital requirements, including the Company’s anticipated cash runway; 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. The data disclosed in this press release are considered topline data and subject to further statistical review and the final results may vary.

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