Axsome Therapeutics Announces AXS-07 Achieves Both Co-Primary Endpoints and Prevents Migraine Pain Progression in the INTERCEPT Phase 3 Trial in the Early Treatment of Migraine

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Achieved freedom from migraine pain in 33% of AXS-07 patients versus 16% for placebo at 2 hours (co-primary endpoint, p=0.002)

Prevented progression of migraine pain beyond mild intensity in 74% of AXS-07 patients versus 47% for placebo from 2 to 24 hours (p<0.001)

Return to normal functioning achieved in 74% of AXS-07 patients versus 47% for placebo at 24 hours (p<0.001)

Significantly reduced rescue medication use, with 15% of AXS-07 patients using rescue versus 42% of placebo over 24 hours (p<0.001)

Achieved freedom from most bothersome symptom in 44% of AXS-07 patients versus 27% for placebo at 2 hours (co-primary endpoint, p=0.003)

Rapidly relieved migraine symptoms with numerical superiority starting 30 minutes after dosing

NDA submission of AXS-07 in the acute treatment of migraine on track for 4Q 2020

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

NEW YORK, April 06, 2020 (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 substantially and significantly eliminated migraine pain, and substantially and significantly prevented progression of migraine pain intensity in the INTERCEPT Phase 3 trial of AXS-07 in the early treatment of migraine. In the trial, AXS-07 met the co-primary endpoints of freedom from migraine pain and freedom from most bothersome symptoms as compared to placebo. AXS-07 is Axsome's novel, oral, multi-mechanistic investigational medicine for the acute treatment of migraine. INTERCEPT was a randomized, double-blind, placebo-controlled trial in which a total of 302 patients were randomized in a 1:1 ratio to treat a single migraine attack with a single dose of AXS-07 (20 mg MoSEIC™ meloxicam/10 mg rizatriptan), or placebo, at the earliest sign of migraine pain, while the pain intensity was mild.

AXS-07 met both of the two co-primary endpoints by demonstrating a statistically significantly greater percentage of patients as compared to placebo achieving pain freedom (32.6% versus 16.3%, p=0.002) and freedom from most bothersome symptom (43.9% versus 26.7%, p=0.003), 2 hours after dosing. AXS-07 durably relieved migraine pain with a statistically significantly greater percentage of patients as compared to placebo achieving sustained pain freedom from 2 to 24 hours after dosing (22.7% versus 12.6%, p=0.030), and from 2 to 48 hours after dosing (20.5% versus 9.6%, p=0.013). AXS-07 rapidly eliminated migraine symptoms, with numerical separation from placebo as early as 30 minutes for migraine pain freedom and most bothersome symptom freedom, achieving statistical significance for migraine pain at 90 minutes (p=0.003) and at every timepoint thereafter.

A single dose of AXS-07 significantly prevented progression of migraine pain beyond mild intensity while significantly reducing the use of rescue medication. Freedom from pain progression from 2 to 24 hours after dosing was achieved by 73.5% of AXS-07 patients versus 47.4% of placebo patients (p<0.001). The effect on pain progression translated to a significant reduction in the use of rescue medication, with only 15.3% of AXS-07 patients requiring rescue medication through 24 hours after dosing, versus 42.2% of placebo patients (p<0.001).

AXS-07 substantially and significantly reduced functional disability, and demonstrated overall disease improvement. AXS-07 treatment resulted in 73.5% of patients able to perform normal activities at 24 hours compared to 47.4% of placebo patients (p<0.001). On the Patient Global Impression of Change (PGI-C) scale, 52.4% of AXS-07 patients were very much or much improved compared to 27.7% of placebo patients (p<0.001).

"The INTERCEPT study demonstrated high rates of freedom from migraine pain with AXS-07 treatment, and utilized an innovative design to evaluate migraine pain progression. It is remarkable that early treatment with AXS-07 prevented migraine pain progression in the vast majority of patients and enabled a similarly high percentage of patients to return to normal functioning," said Dr. Stewart Tepper, Professor of Neurology at the Geisel School of Medicine at Dartmouth. "The multiple mechanisms of AXS-07 address the many disordered physiological processes implicated in migraine attacks. These results, coupled with previous clinical data showing superiority of AXS-07 over an active comparator, provide clinical evidence that this synergistic, multi-mechanistic approach and the rapid absorption of AXS-07 may translate to important benefits for a wide range of patients. As clinicians continue to seek options for their patients with improved efficacy over currently available therapies, AXS-07 may offer an important new treatment for this disabling condition."

AXS-07 was generally safe and well tolerated in the trial. The most commonly reported adverse events with AXS-07 were somnolence, dizziness, and paresthesia, all of which occurred at a rate of less than five percent. There were no serious adverse events in the trial.

"We are very pleased with the strong results of the Phase 3 INTERCEPT trial, which confirm the superior and durable efficacy of AXS-07. The prevention of migraine pain progression, and the substantial increase in the rate of pain freedom demonstrated with early treatment with AXS-07, expand and enhance its differentiated profile for the acute treatment of migraine," said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "With

INTERCEPT and the previously completed MOMENTUM Phase 3 trial in patients with a history of inadequate response to prior acute treatments, AXS-07 has now been evaluated in two positive well-controlled trials. These trials demonstrate the efficacy of AXS-07 against potent active and placebo comparators, across a spectrum of migraine attack settings, regardless of the timing of migraine treatment, disease severity, or baseline pain intensity. INTERCEPT strengthens our planned NDA for AXS-07 in the acute treatment of migraine, which remains on track to be submitted to the FDA in the fourth quarter."

AXS-07 has been evaluated in the completed MOMENTUM Phase 3 trial for which positive results were previously announced. The MOMENTUM trial enrolled only patients with a history of inadequate response to prior acute treatments, with patients waiting to treat their attacks only when the migraine pain had reached moderate or severe intensity. This is in contrast to the INTERCEPT trial, which enrolled all comers and in which patients were instructed to administer AXS-07 at the earliest sign of migraine pain while the pain was mild, before progressing to moderate or severe intensity.

"Migraine is one of the most disabling disorders, incapacitating sufferers and seriously damaging home life, social activity and the ability to work. Published surveys have underscored that patients remain dissatisfied with the efficacy of currently available therapies," said Cedric O'Gorman, MD, Senior Vice President of Clinical Development and Medical Affairs of Axsome. "The results of the INTERCEPT trial demonstrate for the first time that AXS-07 can halt migraine pain progression before reaching moderate or severe intensity. These data grow the body of clinical evidence in support of the potential of AXS-07 to be a multi-mechanistic treatment for migraine with efficacy that is superior to the current standard of care, and which can rapidly, robustly, and durably alleviate symptoms, and return patients to their normal daily activities."

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 more than 30 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.

Summary of Topline Results of the INTERCEPT Trial

Patient Population

- Patients were instructed to administer AXS-07 at the earliest sign of migraine pain, while the pain was mild, before progressing to moderate or severe intensity.
- Enrolled all comers.

Co-Primary Endpoints, Onset, and Durability

- AXS-07 demonstrated statistically significant improvement as compared to placebo on both of the co-primary endpoints of pain freedom (32.6% versus 16.3%, p=0.002), and freedom from most bothersome symptom (43.9% versus 26.7%, p=0.003), 2 hours after dosing.
- AXS-07 was numerically superior to placebo as early as 30 minutes for migraine pain freedom and most bothersome symptom freedom, achieving statistical significance for migraine pain freedom at 90 minutes (p=0.003) and at every time thereafter.
- Sustained pain freedom from 2 to 24 hours after dosing was experienced by 22.7% of patients treated with AXS-07, compared to 12.6% with placebo (p=0.030).
- Sustained pain freedom from 2 to 48 hours after dosing was experienced by 20.5% of patients treated with AXS-07, compared to 9.6% with placebo (p=0.013).

Prevention of Migraine Pain Progression, and Rescue Medication Use

- AXS-07 prevented progression of migraine pain intensity beyond mild in 73.5% of patients versus 47.4% of placebo patients from 2 to 24 hours (p<0.001).
- Rescue medication was used by 15.3% of AXS-07 patients, compared to 42.2% of placebo over 24 hours (p<0.001).

Functional and Global Improvement

- The ability to perform normal activities was achieved by 73.5% of AXS-07 patients compared to 47.4% of placebo patients at 24 hours (p<0.001).
- On the Patient Global Impression of Change (PGI-C) scale, 52.4% of AXS-07 patients were very much or much improved compared to 27.7% of placebo patients (p<0.001).

Safety and Tolerability

- AXS-07 was generally safe and well tolerated in the trial.

- The most commonly reported adverse events with AXS-07 were somnolence, dizziness, and paresthesia, all of which occurred at a rate of less than five percent.

- There were no serious adverse events in the trial.

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 INTERCEPT trial of AXS-07 in the early 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 5960729. 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 INTERCEPT Trial

INTERCEPT (Initiating Early Control of Migraine Pain and Associated Symptoms) is a Phase 3, randomized, double-blind, multicenter, placebo-controlled trial evaluating the early treatment of migraine with AXS-07. A total of 302 patients were randomized in a 1:1 ratio to treatment with AXS-07 or placebo. Patients were instructed to administer AXS-07 at the earliest sign of migraine pain, while the pain was mild. 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.

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 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 $5\text{-HT}_{1B/1D}$ 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 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 for smoking cessation treatment. 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 the treatment of 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.

References

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.

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; 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. 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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