Axsome Therapeutics Announces Expedited Development of AXS-12 for the Treatment of Narcolepsy Based on FDA Breakthrough Therapy Meeting

September 21, 2020

Single Phase 3 trial to be conducted to support an NDA filing of AXS-12 in the treatment of narcolepsy; trial initiation anticipated 1Q 2021

Extensive patient safety database, previously obtained through Pfizer exclusive license, to support NDA filing

Extensive array of completed nonclinical studies sufficient to support NDA filing

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

NEW YORK, Sept. 21, 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 the development plan for AXS-12 for the treatment of narcolepsy has been expedited following a Breakthrough Therapy meeting with the U.S. Food and Drug Administration (FDA). AXS-12 is a novel, oral, highly selective and potent norepinephrine reuptake inhibitor for the treatment of narcolepsy.

The expedited development plan includes one Phase 3 efficacy trial, which, along with the previously completed Phase 2 CONCERT trial, will be used to support the filing of an NDA (New Drug Application) for approval of AXS-12 for the treatment of cataplexy in narcolepsy. The planned Phase 3 trial will be a randomized, double-blind, placebo-controlled, parallel-group study. Axsome intends to initiate this trial in 1Q 2021. Patients completing this trial will be eligible to enroll in an open-label safety extension study.

Also, as part of the expedited development plan, it was established that the data from numerous short-term and long-term clinical trials of patients treated with reboxetine, and the data from a full range of completed nonclinical studies with reboxetine, previously obtained through an exclusive license from Pfizer, can be used to support the filing of an NDA for AXS-12.

“Axsome is very pleased with the FDA feedback from our recent Breakthrough Therapy meeting, which resulted in an expedited path to a potential NDA filing for AXS-12 in the treatment of cataplexy in narcolepsy,” said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. “Narcolepsy is a debilitating condition that interferes with almost every aspect of a patient’s life. Our approach to the development of AXS-12 for narcolepsy reflects our commitment to accelerating the innovation of potentially life-changing medicines for the many patients living with serious CNS disorders.”

Breakthrough Therapy Meeting Outcomes

- One Phase 3 trial of AXS-12 in patients with narcolepsy will be conducted to support, along with the completed Phase 2 CONCERT trial, an NDA filing for AXS-12 in the treatment of cataplexy in narcolepsy.
- The existing short-term and long-term safety database of more than 2,500 patients treated with reboxetine, previously obtained through an exclusive license from Pfizer, along with the safety data from the completed and planned studies of AXS-12 in patients with narcolepsy, would be sufficient to support an NDA filing for AXS-12.
- Certain existing, completed clinical pharmacology (e.g. human pharmacokinetic) studies of reboxetine, previously obtained through an exclusive license from Pfizer, are considered sufficient to support an NDA filing for AXS-12.
- The extensive package of completed nonclinical studies of reboxetine, previously obtained through an exclusive license from Pfizer, are considered sufficient to support an NDA filing for AXS-12.

In August 2020, Axsome received Breakthrough Therapy designation from the FDA for AXS-12 for the treatment of cataplexy in narcolepsy. A Breakthrough Therapy designation is granted to potentially expedite development and review timelines for a promising investigational medicine when preliminary clinical evidence indicates it may demonstrate substantial improvement on one or more clinically significant endpoints over available therapies for a serious or life-threatening condition. The Breakthrough Therapy designation for AXS-12 for the treatment of cataplexy in narcolepsy was supported by the positive results from the Phase 2 CONCERT study, a randomized, double-blind, placebo-controlled, crossover, multicenter U.S. trial. In the trial, 21 patients with a diagnosis of narcolepsy with cataplexy were treated for 2 weeks with AXS-12 or with placebo, followed by a crossover to the other treatment after a 1-week down-titration and washout period. AXS-12 met the primary endpoint demonstrating a highly statistically significant reduction from baseline in the mean weekly number of cataplexy attacks, averaged for the 2-week treatment period (overall treatment effect), as compared to placebo ($p<0.001$), and at the end of the 2-week treatment period ($p=0.002$). AXS-12 also significantly improved excessive daytime sleepiness compared to placebo, as measured by the Epworth Sleepiness Scale and by the frequency of inadvertent naps ($p=0.003$ and $p<0.001$, respectively). In addition, AXS-12 significantly improved cognitive function compared to placebo over the 2-week treatment period as measured by the Ability to Concentrate item of the Narcolepsy Symptom Assessment Questionnaire ($p<0.001$). AXS-12 was well tolerated in this trial with the most commonly reported adverse events being anxiety, constipation, and insomnia.

Conference Call Information

Axsome will host a conference call and webcast with slides today at 8:00 AM Eastern to discuss the expedited development plan for AXS-12 for the treatment of narcolepsy 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 passcode 9584742. 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 FDA Breakthrough Therapy Designation

Breakthrough Therapy designation is granted by the FDA in order to expedite the development and review of drugs for serious or life-threatening conditions. In order to receive Breakthrough Therapy designation, a drug must demonstrate preliminary clinical evidence that the drug may have substantial improvement on at least one clinically significant endpoint over available therapy. Breakthrough Therapy designation provides an organizational commitment involving senior managers from the FDA, more intensive FDA guidance on an efficient drug development program, and greater access to and more frequent communication with the FDA throughout the entire drug development and review process. It also provides the opportunity to submit sections of a New Drug Application (NDA) on a rolling basis, where the FDA may review portions of the NDA as they are received instead of waiting for the entire NDA submission. In addition, Breakthrough Therapy designated products are eligible for Priority Review, where the FDA has a goal to take action on an application within six months, as opposed to ten months under standard review. Breakthrough Therapy designation does not change the standards for approval.

About Narcolepsy

Narcolepsy is a serious and debilitating neurological condition that causes dysregulation of the sleep-wake cycle and is characterized clinically by excessive daytime sleepiness, cataplexy, hypnagogic hallucinations, sleep paralysis, and disrupted nocturnal sleep. Narcolepsy afflicts an estimated 185,000 individuals in the U.S. Cataplexy is seen in an estimated 70% of narcolepsy patients and is a sudden reduction or loss of muscle tone while a patient is awake, typically triggered by strong emotions such as laughter, fear, anger, stress, or excitement. Narcolepsy interferes with cognitive, psychological, and social functioning, increases the risk of work- and driving-related accidents, and is associated with a 1.5-fold higher mortality rate.

About AXS-12

AXS-12 (reboxetine) is a highly selective and potent norepinephrine reuptake inhibitor under development for the treatment of narcolepsy. AXS-12 modulates noradrenergic activity to promote wakefulness, maintain muscle tone and enhance cognition. AXS-12 has been granted U.S. Food and Drug Administration (FDA) Breakthrough Therapy designation and Orphan Drug Designation for the treatment of narcolepsy. AXS-12 is an investigational drug product 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), 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.

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.

Axsome Contact:
Mark Jacobson
Chief Operating Officer
Axsome Therapeutics, Inc.
22 Cortlandt Street, 16th Floor
New York, NY 10007
Tel: 212-332-3243
Email: mjacobson@axsome.com
www.axsome.com

Source: Axsome Therapeutics, Inc.