Pfizer Logo

Axsome Therapeutics Enters into Exclusive License Agreement with Pfizer Inc. for Pfizer's Reboxetine Clinical and Nonclinical Data and for New Phase 3 Esreboxetine Product Candidate

Monday, January 13, 2020 - 08:00am

Agreement accelerates ongoing clinical development of AXS-12 (reboxetine) in narcolepsy

Expands Axsome's pipeline with new Phase 3-stage esreboxetine product candidate for fibromyalgia

Esreboxetine met primary endpoints in completed Pfizer Phase 3 and Phase 2 placebo-controlled clinical trials in fibromyalgia ($p<0.001$, and $p<0.001$)

Pfizer to receive $11 million in Axsome stock and upfront cash, and up to $323 million in regulatory and sales milestones

Company to host conference call today at 8:30 AM ET

NEW YORK, January 13, 2020 (Globe Newswire) – Axsome Therapeutics, Inc. (NASDAQ: AXSM), a clinicalstage biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders, has entered into an agreement with Pfizer Inc. (NYSE: PFE) for an exclusive U.S. license to Pfizer's clinical and nonclinical data, and intellectual property for reboxetine, the active pharmaceutical ingredient in AXS-12 which Axsome is developing for the treatment of narcolepsy. The agreement also provides Axsome exclusive rights to develop and commercialize esreboxetine, a new late-stage product candidate now referred to as AXS-14, in the U.S. for the treatment of fibromyalgia.

Under the terms of the agreement, Axsome will receive from Pfizer an exclusive U.S. license to Pfizer data for reboxetine and esreboxetine encompassing a full range of nonclinical studies, and short-term and long-term clinical trials involving more than five thousand patients. The licensed data includes results from a positive Phase 3 and a positive Phase 2 trial of esreboxetine in the treatment of fibromyalgia. Axsome will have the exclusive right and sole responsibility of developing AXS-14 (esreboxetine) in the U.S. for the treatment of fibromyalgia and for other indications.

Pfizer will receive shares of Axsome common stock having a value of $8 million, based on the average closing price of Axsome's common stock for the 10 prior trading days, in consideration for the license and rights. Pfizer will also receive an upfront cash payment of $3 million, up to $323 million in regulatory and sales milestones, and tiered mid-single to low double-digit royalties on future sales. Pfizer will also have a right of first negotiation on any potential future strategic transactions involving AXS-12 and AXS-14.

Axsome recently completed and announced positive results for a Phase 2 trial of AXS-12 in the treatment of narcolepsy and is preparing to advance AXS-12 into Phase 3 trials for the treatment of narcolepsy, as previously disclosed.

“We are very pleased to announce this agreement with Pfizer to help advance the development of AXS-12 for the treatment of narcolepsy and of AXS-14 for the treatment of fibromyalgia, two serious CNS disorders which currently have limited treatment options,” said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. “The valuable clinical and nonclinical data under this exclusive license will enable us to potentially significantly accelerate our AXS-12 clinical program while reducing development risk and costs. Furthermore, we are able to expand our CNS pipeline with AXS-14, which has demonstrated efficacy in completed Phase 3 and Phase 2 trials in fibromyalgia. With the recently announced Phase 2 success of AXS-12 resulting in its planned advancement to Phase 3 this year, and with the addition of AXS-14, our pipeline will now contain four differentiated Phase 3-stage product candidates with the potential to positively affect many of the millions of people living with distressing CNS disorders.”

Summary of the Agreement
Reboxetine (AXS-12)

• Axsome will receive from Pfizer an exclusive U.S. license to data from a full range of nonclinical studies with reboxetine, to data from numerous short-term and long-term clinical trials of patients treated with reboxetine, Page 2 of 4 and to other reboxetine intellectual property. Reboxetine is not approved in the U.S. for any indication and is marketed by Pfizer outside of the U.S. for the treatment of depression.

• Reboxetine is the active pharmaceutical ingredient in AXS-12 which is being developed for the treatment of narcolepsy. Axsome recently completed and announced positive results for a Phase 2 trial of AXS-12 in the treatment of narcolepsy, demonstrating statistically significant improvements in cataplexy, excessive daytime sleepiness, as well as cognitive function compared to placebo. Axsome is preparing to initiate Phase 3 trials of AXS-12 in the treatment of narcolepsy in 2020, as previously disclosed.

• The licensed nonclinical and clinical data are expected to reduce or eliminate the need for Axsome to conduct certain studies thereby mitigating risk and associated costs, and potentially significantly accelerating the clinical development and commercialization timelines of AXS-12.

Esreboxetine (AXS-14)

• Axsome will receive from Pfizer an exclusive license to develop and commercialize esreboxetine, now referred to as AXS-14, in the U.S. for fibromyalgia and all other indications. The license encompasses nonclinical and clinical data for reboxetine including results from a positive Phase 3 and a positive Phase 2 trial of esreboxetine in the treatment of fibromyalgia conducted by Pfizer.

• Esreboxetine, the SS-enantiomer of racemic reboxetine, is the more selective and potent enantiomer, which has been evaluated for the treatment of fibromyalgia. Fibromyalgia is a chronic disorder characterized by widespread pain, fatigue, disturbed sleep, depression, and cognitive impairment. The condition affects approximately 4 million Americans approximately 90% of whom are women. It is considered to be mediated mainly in the CNS. Treatment options for fibromyalgia are limited with only three pharmacologic treatments currently approved by the FDA.

• In a Phase 3 trial conducted by Pfizer in 1,122 patients with fibromyalgia treated with esreboxetine or placebo for 14 weeks, the study met the two primary endpoints demonstrating statistically significant improvements compared to placebo in the weekly mean pain score ($p<0.001$, $p<0.001$, and $p=0.025$, for 4 mg, 8 mg and 10 mg

daily doses, respectively), and the Fibromyalgia Impact Questionnaire (FIQ) total score ($p<0.001$, $p<0.001$, and $p=0.023$, for 4 mg, 8 mg and 10 mg doses, respectively). Esreboxetine also resulted in statistically significant improvements as compared to placebo on the Patient's Global Impression of Change (PGI-C) scale ($p=0.002$, $p=0.001$, and $p=0.007$, for 4 mg, 8 mg and 10 mg doses, respectively), and in fatigue as measured using the Global Fatigue Index ($p=0.001$ and $p=0.001$, for 4 mg and 8 mg daily doses, respectively). 1

• In a Phase 2 trial conducted by Pfizer in 267 patients with fibromyalgia treated with esreboxetine (dose escalated to 8 mg/day) or placebo for 8 weeks, the study met its primary endpoint demonstrating statistically significant improvements compared to placebo in the weekly mean pain score ($p=0.006$,). The study also demonstrated statistically significant additional efficacy outcomes in the FIQ total score ($p<0.001$), the PGIC scale ($p<0.001$), and in fatigue as measured using the Multidimensional Assessment of Fatigue scale ($p<0.001$). 2

• AXS-14 expands Axsome's late-stage pipeline of product candidates for difficult-to-treat CNS disorders.

Financial Terms

• Pfizer will receive shares of Axsome common stock having a value of $8 million, based on the average closing price of Axsome's common stock for the 10 prior trading days. Pfizer will also receive an upfront cash payment of $3 million.

• Pfizer will receive up to $323 million in regulatory and sales milestones, and tiered mid-single to low doubledigit royalties on future sales.

1 Arnold et al., Arthritis Rheum. 2012 Jul;64(7):2387-97
2 Arnold et al., Clin Ther. 2010 Aug;32(9):1618-32

• Pfizer will have a right of first negotiation on any potential future strategic transactions involving AXS-12 or AXS-14.

Conference Call Information
Axsome will host a conference call and webcast with slides today at 8:30 AM Eastern to discuss the agreement with Pfizer. To participate in the live conference call, please dial (844) 698-4029 (toll-free domestic) or (647) 253- 8660 (international), and use the passcode 4656867. 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 Narcolepsy
Narcolepsy can be 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 workand driving-related accidents, and is associated with a 1.5 fold higher mortality rate. Depression is reported in up to 57% of patients.

About Fibromyalgia
Fibromyalgia is a chronic disorder often characterized by widespread pain, fatigue, disturbed sleep, depression,

and cognitive impairment. Other symptoms of this disorder can include tingling in the hands and feet and headaches. Fibromyalgia is considered to be mediated mainly in the central nervous system. Approximately 4 million Americans, 90% of whom are women, suffer from fibromyalgia according to the Centers for Disease Control. Treatment options for fibromyalgia are limited with only three pharmacologic treatments currently approved by the FDA.

About AXS-12
AXS-12 (reboxetine) is a highly selective and potent norepinephrine reuptake inhibitor for the treatment of narcolepsy. AXS-12 modulates noradrenergic activity to promote wakefulness, maintain muscle tone and enhance cognition. AXS-12 has been granted Orphan Drug Designation by the U.S. FDA for the treatment of narcolepsy. AXS-12 is an investigational drug product not approved by the FDA.

About AXS-14
AXS-14 (esreboxetine) is a highly selective and potent norepinephrine reuptake inhibitor for the treatment of fibromyalgia and other conditions. Esreboxetine, the SS-enantiomer of reboxetine, is more potent and selective than racemic reboxetine. AXS-14 is an investigational drug product 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 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 a Phase 3 trial 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.

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, including the potential for the clinical and nonclinical data available under the Company's exclusive license agreement with Pfizer to significantly accelerate development of AXS-12 for the treatment of narcolepsy while reducing development risk and costs, and the potential future development or commercialization of AXS-14 for the treatment of fibromyalgia and other indications; 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.

Axsome Contact:
Mark Jacobson
Senior Vice President, Operations
Axsome Therapeutics, Inc.
200 Broadway, 3 rd Floor New York, NY 10038
Tel: 212-332-3243
Email: mjacobson@axsome.com
www.axsome.co