UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(D)
of the Securities Exchange Act of 1934

August 31, 2020
Date of report (Date of earliest event reported)

Axsome Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-37635**	**45-4241907**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

22 Cortlandt Street, 16th Floor New York, New York	**10007**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code **(212) 332-3241**

(Former name or former address, if changed since last report)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class:	**Trading Symbol(s)**	**Name of each exchange on which registered:**
Common Stock, Par Value $0.0001 Per Share	AXSM	The Nasdaq Global Market

Check the appropriate box below if the Form 8-K is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425).

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12).

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)).

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Item 8.01. Other Events.

On August 31, 2020, Axsome Therapeutics, Inc. issued a press release confirming the pivotal status and advancement of AXS-05 for the treatment of Alzheimer's disease agitation following a Breakthrough Therapy meeting with the U.S. Food and Drug Administration.

The full text of the press release is filed as Exhibit 99.1 hereto, and is incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release dated August 31, 2020.
104	The cover page from this Current Report on Form 8-K, formatted in Inline XBRL

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Axsome Therapeutics, Inc.

Dated: August 31, 2020

By: /s/ Herriot Tabuteau, M.D.
Name: Herriot Tabuteau, M.D.
Title: President and Chief Executive Officer

Axsome Therapeutics Confirms Pivotal Status and Advancement of AXS-05 for the Treatment of Alzheimer's Disease Agitation Based on Successful FDA Breakthrough Therapy Meeting

Previously completed positive, pivotal ADVANCE-1 trial sufficient with single additional Phase 3 efficacy trial for NDA in Alzheimer's disease agitation

Initiation of Phase 3, placebo-controlled, randomized-withdrawal efficacy trial on track for 4Q 2020

Initiation of long-term safety trial in patients with Alzheimer's disease agitation expected in 4Q 2020

No treatments are currently approved for the treatment of Alzheimer's disease agitation

NEW YORK, August 31, 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 confirmation of the pivotal development status and plan for AXS-05 in the treatment of Alzheimer's disease (AD) agitation following a successful Breakthrough Therapy meeting with the U.S. Food and Drug Administration (FDA). AXS-05 (dextromethorphan/bupropion modulated delivery tablet) is a novel, oral, investigational NMDA receptor antagonist and sigma-1 receptor agonist. There is currently no approved treatment for AD agitation.

Results of the meeting confirm the pivotal status of the previously completed positive ADVANCE-1 trial, and the establishment of the superiority of AXS-05 over its components (component contribution) in the treatment of AD agitation. Consequently, only one additional Phase 3 efficacy trial will be needed to support the filing of an NDA (New Drug Application) for approval of AXS-05 in this indication, and only a placebo control will be required for this trial. This additional Phase 3 efficacy trial will be conducted using a randomized-withdrawal design, in which all patients are first treated with open-label AXS-05, with the patients experiencing a treatment response being subsequently randomized in a double-blind fashion to continued treatment with AXS-05 or to switch to placebo. Axsome is on track to initiate this efficacy trial in the fourth quarter of 2020. Axsome also intends to initiate in the fourth quarter an open-label safety extension trial of AXS-05 in AD agitation patients to supplement the existing AXS-05 long-term safety database.

"Axsome is very pleased with the FDA feedback from our recent Breakthrough Therapy meeting, which confirms a streamlined path to NDA submission for AXS-05 in Alzheimer's disease agitation, including the pivotal status of our completed ADVANCE-1 trial and the need for only one additional placebo-controlled efficacy trial," said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "The randomized-withdrawal design of this additional Phase 3 trial may simultaneously improve signal detection and mitigate placebo response. We remain on track to initiate this trial before year end. Alzheimer's disease agitation is very distressing to patients and their families, and is associated with earlier nursing home placement, accelerated progression to severe dementia, and increased risk of death. If successfully developed, AXS-05 has the potential to address this serious, prevalent, and debilitating condition, for which there is currently no approved treatment."

In June 2020, Axsome received Breakthrough Therapy designation from the FDA for AXS-05 for the treatment of AD agitation, the second Breakthrough Therapy designation received by Axsome for AXS-05. 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-05 in AD agitation was supported by the recent positive results from the pivotal Phase 2/3 ADVANCE-1 study, a randomized, double-blind, controlled, multicenter U.S. trial in which 366 Alzheimer's disease patients were treated with AXS-05, bupropion, or placebo. In this trial, treatment with AXS-05 resulted in a rapid, substantial, and statistically significant improvement in agitation as compared to placebo. On the primary endpoint, AXS-05 demonstrated a statistically significant mean reduction from baseline in the Cohen Mansfield Agitation Inventory (CMAI) total score compared to placebo at Week 5, with mean reductions of 15.4 points for AXS-05 and 11.5 points for placebo ($p=0.010$). AXS-05 was also superior to bupropion on the CMAI total score ($p<0.001$), establishing component contribution. AXS-05 was well tolerated and not associated with cognitive impairment or sedation. The most commonly reported adverse events in the AXS-05 arm were somnolence (8.2% for AXS-05 versus 4.1% for bupropion and 3.2% for placebo), dizziness (6.3%, 10.2%, 3.2%, respectively), and diarrhea (4.4%, 6.1%, 4.4%, respectively).

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 Alzheimer's Disease (AD) Agitation

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, and behavioral and psychological symptoms including agitation. AD is the most common form of dementia and afflicts an estimated 6 million individuals in the United States, a number that is anticipated to increase to approximately 14 million by 2050 [1]. Agitation is reported in up to 70% of patients with AD and is characterized by emotional distress, aggressive behaviors, disruptive irritability, and disinhibition [2]. Agitation in patients with AD has been associated with increased caregiver burden, decreased functioning, accelerated cognitive decline, earlier nursing home placement, and increased mortality [2-4]. There are currently no therapies approved by the FDA for the treatment of agitation in patients with AD.

About AXS-05

AXS-05 is a novel, oral, patent-protected, investigational NMDA receptor antagonist with multimodal activity under development for the treatment of Alzheimer's disease agitation, major depressive disorder, and other central nervous system (CNS) disorders. AXS-05 consists of a proprietary formulation and dose of dextromethorphan and bupropion and utilizes Axsome's metabolic inhibition technology. The dextromethorphan component of AXS-05 is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, also known as a glutamate receptor modulator, a sigma-1 receptor agonist, an inhibitor of the serotonin and norepinephrine transporters, a nicotinic acetylcholine receptor antagonist, and an inhibitor of microglial activation. The bupropion component of AXS-05 serves to increase the bioavailability of dextromethorphan, and is a norepinephrine and dopamine reuptake inhibitor, and a nicotinic acetylcholine receptor antagonist. AXS-05 is covered by more than 42 issued U.S. and international patents which provide protection out to 2034. AXS-05 has been granted U.S. Food and Drug Administration Breakthrough Therapy designation for major depressive disorder, Fast Track designation for treatment resistant depression, and Breakthrough Therapy and Fast Track designations for Alzheimer's disease agitation. AXS-05 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. 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 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.

References

1. Alzheimer’s Association. 2020 Alzheimer’s Disease Facts and Figures. Alzheimers Dement 2020;16(3):391+.

2. Tractenberg RE, Weiner MF, Thal LJ. Estimating the prevalence of agitation in community-dwelling persons with Alzheimer’s disease. J Neuropsychiatry Clin Neurosci. 2002;14:11-18.

3. Porsteinsson AP, Antonsdottir IM. An update on the advancements in the treatment of agitation in Alzheimer’s disease. Expert Opin Pharmacother. 2017;18:611-620.

4. Rabins PV, Schwartz S, Black BS, Corcoran C, Fauth E, Mielke M, Christensen J, Lyketsos C, Tschanz J. Predictors of progression to severe Alzheimer's disease in an incidence sample. Alzheimers Dement. 2013;9:204-207.

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 discontinuation of 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.

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