

**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

Date of Report (Date of earliest event reported): September 08, 2022

Axsome Therapeutics, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction
of Incorporation)

001-37635
(Commission File Number)

45-4241907
(IRS Employer
Identification No.)

22 Cortlandt Street, 16th Floor
New York, New York
(Address of Principal Executive Offices)

10007
(Zip Code)

Registrant's Telephone Number, Including Area Code: (212) 332-3241

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing 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))

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	NASDAQ Global Market

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 September 8, 2022, Axsome Therapeutics, Inc. (the “Company”) issued a press release announcing the enrollment of the first patient in the Company’s ADVANCE-2 (Addressing Dementia via Agitation-Centered Evaluation-2) Phase 3 trial of AXS-05 for the treatment of agitation associated with Alzheimer’s disease.

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 September 8, 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

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 thereunto duly authorized.

Axsome Therapeutics, Inc.

Date: September 8, 2022

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



Axsome Therapeutics Initiates ADVANCE-2 Phase 3 Trial of AXS-05 in Alzheimer's Disease Agitation

NEW YORK, Sept. 08, 2022 (GLOBE NEWSWIRE) -- Axsome Therapeutics, Inc. (NASDAQ: AXSM), a biopharmaceutical company developing and delivering novel therapies for the management of central nervous system (CNS) disorders, announced that it has enrolled the first patient in the ADVANCE-2 trial of AXS-05, an investigational treatment for Alzheimer's disease (AD) agitation.

ADVANCE-2 (Addressing Dementia via Agitation-Centered Evaluation-2) is a Phase 3, randomized, double-blind, placebo-controlled, multicenter, trial to assess the efficacy and safety of AXS-05 for the treatment of agitation associated with AD. Approximately 350 patients will be randomized in a 1:1 ratio to receive AXS-05 or placebo for 5 weeks. The primary efficacy measure is the Cohen-Mansfield Agitation Inventory (CMAI).

AXS-05 has been granted U.S. Food and Drug Administration (FDA) Breakthrough Therapy designation for the treatment of Alzheimer's disease agitation.

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 2050¹. Agitation is reported in up to 70% of patients with AD and is characterized by emotional distress, aggressive behaviors, disruptive irritability, and disinhibition². Agitation in patients with AD has been associated with increased caregiver burden, decreased functioning, accelerated cognitive decline, earlier nursing home placement, and increased mortality²⁻⁴. There are currently no therapies approved by the FDA for the treatment of agitation in patients with AD.

About AXS-05

AXS-05 (dextromethorphan-bupropion) is a novel, oral, patent protected, investigational N-methyl-D-aspartate (NMDA) receptor antagonist with multimodal activity under development for the treatment of Alzheimer's disease (AD) agitation and other central nervous system (CNS) disorders. AXS-05 utilizes a proprietary formulation and dose of dextromethorphan and bupropion, and Axsome's metabolic inhibition technology, to modulate the delivery of the components. The dextromethorphan component of AXS-05 is an uncompetitive NMDA receptor antagonist, also known as a glutamate receptor modulator, and a sigma-1 receptor agonist. The bupropion component of AXS-05 serves to increase the bioavailability of dextromethorphan, and is a norepinephrine and dopamine reuptake inhibitor. AXS-05 is covered by a robust patent estate extending out at least to 2037-2040. AXS-05 has been granted FDA Breakthrough Therapy designation for the treatment of Alzheimer's disease agitation. AXS-05 is not approved by the FDA for the treatment of AD agitation.

About Axsome Therapeutics, Inc.

Axsome Therapeutics, Inc. is a biopharmaceutical company developing and delivering novel therapies for central nervous system (CNS) conditions that have limited treatment options. Through development of therapeutic options with novel mechanisms of action, we are transforming the approach to treating CNS conditions. At Axsome, we are committed to developing products that meaningfully improve the lives of patients and provide new therapeutic options for physicians. 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 continued commercial success of our Sunosi® product and the success of our efforts to obtain any additional indication(s) with respect to Sunosi; the commercial success of our Avelity™ product and the success of our efforts to obtain any additional indication(s) with respect to AXS-05, 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, whether issues identified by FDA in the complete response letter may impact the potential approvability of the Company’s NDA for AXS-07 for the acute treatment of migraine in adults with or without aura, pursuant to our special protocol assessment for the MOMENTUM clinical trial; 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 amount of capital required for the successful commercialization of Sunosi and Avelity and for the Company’s commercial launch of its other product candidates, and the potential impact on 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

References

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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.

