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

December 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** (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)

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 December 31, 2020, Axsome Therapeutics, Inc. (the "Company") issued a press release announcing the efficacy and safety results from the Company's MOVEMENT trial of AXS-07 in the acute treatment of migraine (the "MOVEMENT Press Release"). The full text of the MOVEMENT press release is filed as Exhibit 99.1 hereto, and is incorporated herein by reference.

Additionally, on December 31, 2020, the Company issued a press release announcing the initiation of the Company's ACCORD (Assessing Clinical Outcomes in Alzheimer's Disease Agitation) Phase 3 trial of AXS-05 (dextromethorphan- bupropion modulated delivery tablet) in Alzheimer's disease agitation (the "ACCORD Press Release"). The full text of the ACCORD press release is filed as Exhibit 99.2 hereto, and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	MOVEMENT Press Release.
99.2	ACCORD Press Release.
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 hereunto duly authorized.

Axsome Therapeutics, Inc.

Dated: December 31, 2020

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

AXSOME THERAPEUTICS

Axsome Therapeutics Announces Positive Efficacy and Safety Results from the Phase 3 MOVEMENT Long-Term Trial of AXS-07 in the Acute Treatment of Migraine

Over 21,000 migraine attacks treated with AXS-07

Achieved migraine pain relief in approximately 70% of patients, and pain freedom in approximately 40% of patients, at 2 hours

Achieved durable relief, with approximately 85% of patients free from rescue medication use over 48 hours

Long-term safety profile consistent with previously completed controlled trials

NDA on track for submission in 1Q 2021

NEW YORK, December 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 positive results from the long-term, open-label Phase 3 MOVEMENT trial of AXS-07, Axsome's novel, oral, multi-mechanistic investigational medicine in the acute treatment of migraine. Treatment with AXS-07, rapidly, substantially, and durably relieved migraine pain and associated symptoms in this trial. AXS-07 was well tolerated over long-term treatment with a safety profile consistent with that observed in the previously reported controlled trials. Axsome remains on track to submit an NDA for AXS-07 in the acute treatment of migraine in the first quarter of 2021.

"The results of the open-label, Phase 3 MOVEMENT trial confirm in a real-world setting the strong efficacy of AXS-07 observed in our previous controlled trials, and demonstrate a favorable long-term safety profile," said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "The rapid and substantial efficacy of AXS-07 now observed in three separate trials indicates that AXS-07 may provide unique benefits to patients with migraine and help address the current unmet need for more effective treatments. These data further support our planned NDA filing of AXS-07 in the acute treatment of migraine in the first quarter."

The MOVEMENT (Multimechanistic Treatment over Time of Migraine Symptoms) trial evaluated the long-term safety of AXS-07 (20 mg MoSEIC™ meloxicam/10 mg rizatriptan), dosed for up to 12 months, in patients with migraine attacks. The study enrolled patients who had completed the previous pivotal studies of AXS-07: the MOMENTUM and INTERCEPT trials. Enrolled patients were allowed to treat up to 10 migraine attacks per month during the up to 12-month period, with one dose of AXS-07 for each migraine that occurred. The safety and efficacy of AXS-07 was assessed during the trial. A total of 706 patients were enrolled. The trial was concluded once at least 300 patients had treated at least 2 migraines a month for 6 months, and approximately 100 patients had treated at least 2 migraines a month for 12 months, as pre-specified. At the time of study conclusion, 515 patients had reached at least 6 months, and 155 patients had reached at least 12 months of treatment. Over 21,000 migraine attacks were treated with AXS-07 during the trial.

In the MOVEMENT trial, administration of AXS-07 resulted in rapid, and substantial relief of migraine pain and associated symptoms. Within 1 hour after dosing, 39% (range: 37-41%) of patients achieved relief of migraine pain, demonstrating the rapid onset of AXS-07. Two hours after administration of AXS-07, relief of migraine pain was achieved by 68% (range: 65-71%) of patients and pain freedom by 38% (range: 37-40%) of patients. Freedom from most bothersome symptom (photophobia, phonophobia, nausea) was achieved by 47% (range: 46-49%) of patients within 2 hours after dosing.

AXS-07 durably relieved migraine pain with 85% (range: 84-86%) of patients free from rescue medication use through 24 hours, and 83% (range: 82-85%) of patients free from rescue medication use through 48 hours after a single administration of AXS-07. Rates of sustained pain relief from 2 to 24 hours and from 2 to 48 hours were 60% (range: 59-62%) and 59% (58-60%), respectively. Rates of sustained pain freedom from 2 to 24 hours and from 2 to 48 hours were 33% (range: 33-35%) and 32% (range: 32-34%), respectively.

AXS-07 was well tolerated with long-term dosing. The safety profile of AXS-07 over the 12-month treatment period was consistent with that previously reported in short-term controlled trials. The most commonly reported adverse events (≥3%) were nausea, dizziness, and vomiting. During the 12-month trial, 1.6% of patients discontinued due to adverse events.

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 80 issued U.S. and international patents providing protection out to 2036, and Axsome maintains worldwide rights.

About the MOVEMENT Trial

MOVEMENT (Multimechanistic Treatment over Time of Migraine Symptoms) was a Phase 3, open-label trial to evaluate the long-term safety of AXS-07 (20 mg MoSEIC™ meloxicam/10 mg rizatriptan), dosed for up to 12 months, in patients with migraine attacks. The study enrolled patients who had completed the previous pivotal studies of AXS-07: the MOMENTUM and INTERCEPT trials. Enrolled patients were allowed to treat up to 10 migraine attacks per month during the up to 12-month period, with one dose of AXS-07 for each migraine that occurred. The safety and efficacy of AXS-07 was assessed during the trial. Efficacy measures included relief of migraine pain and most bothersome symptom (photophobia, phonophobia, nausea), and use of rescue medication.

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, rapidly absorbed, multi-mechanistic investigational medicine for the acute treatment of migraine, consisting 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-HT1B/1D agonist. AXS-07 is designed to provide rapid, enhanced and consistent relief of migraine, with reduced symptom recurrence. AXS-07 is covered by more than 80 issued U.S. and international patents which provide protection out to 2036. AXS-07 is 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.

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 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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AXSOME THERAPEUTICS

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

ACCORD is the second pivotal trial of AXS-05 in Alzheimer's disease agitation

No treatments are currently approved for Alzheimer's disease agitation

NEW YORK, December 31, 2020 (Globe Newswire) – Axsome Therapeutics, Inc. (NASDAQ: AXSM), a biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders, announced the initiation of the ACCORD (Assessing Clinical Outcomes in Alzheimer's Disease Agitation) study, a Phase 3, randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of AXS-05 in the treatment of Alzheimer's disease (AD) agitation. AXS-05 (45 mg dextromethorphan-105 mg bupropion modulated delivery tablet) is a novel, oral, investigational NMDA receptor antagonist with multimodal activity. There is currently no approved treatment for AD agitation.

ACCORD is being 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. Patients completing the ACCORD trial will be eligible to enter an open-label safety extension trial. Initiation of the safety extension trial is expected imminently. Topline results from the ACCORD trial are anticipated in the second half of 2022.

"Initiation of the ACCORD Phase 3 trial in Alzheimer's disease agitation continues the expedited clinical development of AXS-05 for this serious condition. The potential for AXS-05, with its unique pharmacological profile, in this indication is supported by the positive results in our completed pivotal ADVANCE trial," said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "Alzheimer's disease agitation is a prevalent and debilitating condition that is associated with earlier nursing home placement, accelerated progression to severe dementia, and increased risk of death. There are currently no approved treatments for Alzheimer's disease agitation. If successfully developed, AXS-05 has the potential to address this high unmet need and significantly improve the lives of patients and their caregivers."

Initiation of the ACCORD Phase 3 trial follows a Breakthrough Therapy meeting with the U.S. Food and Drug Administration (FDA), announced in August, to discuss the development plan for AXS-05 in AD agitation. Results of the meeting confirmed the pivotal status of the previously completed ADVANCE trial of AXS-05 in AD agitation. The meeting followed the receipt in June of 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. The designation was supported by the positive results of the ADVANCE trial. 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.

About the ACCORD Trial

ACCORD (Assessing Clinical Outcomes in Alzheimer's Disease Agitation) is a Phase 3, randomized, double-blind, multicenter, placebo-controlled, trial to evaluate the efficacy and safety of AXS-05 in patients with Alzheimer's disease (AD) agitation. Enrolled patients will first enter a 9-week, open-label stabilization period, during which they will be treated with AXS-05 and monitored for a treatment response based on the Cohen-Mansfield Agitation Inventory (CMAI). Patients who experience a treatment response during the stabilization period will then be randomized into the double-blind treatment period, in a 1:1 ratio, to continue treatment with AXS-05 or to switch to placebo, for up to 26 weeks or until a relapse of agitation occurs. The primary endpoint will be the time from randomization to relapse. Assessments will include the CMAI, clinician- and caregiver-rated scales, and safety parameters.

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 (dextromethorphan-bupropion modulated delivery tablet) is a novel, oral, patent-protected, investigational NMDA receptor antagonist with multimodal activity under development for the treatment of major depressive disorder 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 N-methyl-D-aspartate (NMDA) receptor antagonist, also known as a glutamate receptor modulator, which is a novel mechanism of action, meaning it works differently than currently approved therapies for major depressive disorder. The dextromethorphan component of AXS-05 is also a sigma-1 receptor agonist, nicotinic acetylcholine receptor antagonist, and inhibitor of the serotonin and norepinephrine transporters. 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 93 issued U.S. and international patents which provide protection out to 2040. AXS-05 has been granted U.S. Food and Drug Administration Breakthrough Therapy and Fast Track designations for Alzheimer's disease agitation. AXS-05 is not approved by the FDA.

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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.

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