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

September 14, 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 September 14, 2020, Axsome Therapeutics, Inc. issued a press release announcing new data from the GEMINI Phase 3 trial in major depressive disorder, which was presented at the 33rd Congress of the European College of Neuropsychopharmacology.

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 14, 2020.
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: September 14, 2020

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

Axsome Therapeutics Presents New Data from GEMINI Phase 3 Trial with AXS-05 Demonstrating Rapid and Significant Improvements in Patient-Reported Outcomes in Major Depressive Disorder

Rapid, durable, and statistically significant improvement demonstrated in patient-reported depressive symptoms, as measured by the QIDS-SR-16 total score compared to placebo (p=0.001)

Clinical response on the QIDS-SR-16 demonstrated in 53% of patients with AXS-05 compared to 33% for placebo (p<0.001)

Significant improvement on the PGI-I demonstrated, with 47% of patients reporting their depression being "very much" or "much" improved with AXS-05 versus 31% with placebo (p=0.007)

Statistically significant improvement at week 1 versus placebo in QIDS-SR-16 total score (p=0.016), and PGI-I (p=0.008), compared to placebo

Potentially first-and-only, oral NMDA receptor antagonist with multimodal activity for the treatment of depression

NEW YORK, September 14, 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 AXS-05, a novel, oral, investigational NMDA receptor antagonist with multimodal activity, rapidly and significantly improved patient-reported outcomes of depression in patients with major depressive disorder (MDD) in the GEMINI Phase 3 trial. These findings were presented at the 33rd Congress of the European College of Neuropsychopharmacology (ECNP), being held virtually September 12-15.

The GEMINI study was a randomized, double-blind, placebo-controlled, multi-center, U.S. trial, in which 327 adult patients with confirmed moderate to severe MDD were randomized to treatment with either AXS-05 (dextromethorphan/bupropion modulated delivery tablet) or placebo once daily for the first 3 days and twice daily thereafter for a total of 6 weeks. Two patient-reported outcomes (PROs) for depression were assessed in this trial: the Quick Inventory of Depressive Symptomatology (Self-Report) (QIDS-SR-16), and the Patient Global Impression of Improvement (PGI-I) for depression. The QIDS-SR-16 is a well-established PRO that was the primary outcome measure in the landmark NIH-funded STAR*D trial of antidepressant treatments[3]. A PRO is a report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else. PROs therefore provide a measurement of patients' perception of their own depression status as a result of an intervention. The PROs complement the clinician-rated measures, such as the Montgomery-Åsberg Depression Rating Scale (MADRS), that were also assessed in the GEMINI trial.

AXS-05 demonstrated a highly statistically significant reduction in patient-reported depressive symptoms compared to placebo at Week 6, with mean reductions from baseline in the QIDS-SR-16 total score of 7.8 points for AXS-05 and 5.4 points for placebo, representing 48% and 34% reductions from baseline, respectively (p=0.001). AXS-05 rapidly and durably improved patient-reported depressive symptoms as compared to placebo with statistical significance on the QIDS-SR-16 total score demonstrated at Week 1 (p=0.016), the earliest time point assessed, at Week 2 (p<0.001), and at all time points thereafter. Clinical response on the QIDS-SR-16 (defined as ≥50% improvement) was statistically significantly greater for AXS-05 compared to placebo at Week 1 (p=0.048), at Week 2 (p<0.001), and at every time point thereafter, being achieved by 53.4% of AXS-05 patients compared to 32.9% of placebo patients at Week 6 (p<0.001).

On the patient-reported global measure of depression, the PGI-I, AXS-05 demonstrated highly statistically significant improvements as compared to placebo, with 47.2% of patients treated with AXS-05 reporting that their depression was "very much" or "much" improved compared to 31.3% of placebo patients at Week 6 (p=0.007). Improvement on the PGI-I with AXS-05 as compared to placebo was rapid and durable with statistical significance demonstrated at Week 1 (p=0.008) and at all time points thereafter.

The results on these patient-reported measures are consistent with those observed with the corresponding clinician-rated scales, the MADRS and the Clinical Global Impression of Improvement (CGI-I). As previously reported, AXS-05 met the primary endpoint in the GEMINI trial by demonstrating a highly statistically significant reduction in the MADRS total score compared to placebo at Week 6, with mean reductions from baseline of 16.6 points for AXS-05 and 11.9 points for placebo (p=0.002). AXS-05 also demonstrated statistically significant improvement at Week 6 compared to placebo on the CGI-I (p=0.016). Rapid improvement in depressive symptoms was also demonstrated on these clinician-rated scales, with statistically significant improvements starting at Week 1 and every timepoint thereafter (MADRS p=0.007, CGI-I p=0.035).

"The positive results with AXS-05 on patient-reported outcomes are significant since depression, by its very nature, involves symptoms that may be unobservable and known only to the patient," said Cedric O'Gorman, MD, Senior Vice President of Clinical Development and Medical Affairs of Axsome. "These patient-reported outcomes mirror the results previously reported with clinician-rated scales and confirm the rapid and substantial antidepressant effects of AXS-05. With its novel oral glutamatergic mechanism targeting NMDA, AXS-05 may help to address the needs of the many patients living with depression, about two thirds of whom fail to respond to currently available antidepressants."

AXS-05 was well tolerated in the trial. The most commonly reported adverse events in the AXS-05 arm were dizziness, nausea, headache, diarrhea, somnolence, and dry mouth. Treatment with AXS-05 was not associated with psychotomimetic effects or weight gain.

AXS-05 is a novel, oral, non-competitive NMDA receptor antagonist, also known as a glutamate receptor modulator, a new mechanism of action which is thought to help enhance synaptic connections and improve the communication between brain cells in people with major depressive disorder. In addition, AXS-05 is a sigma-1 receptor agonist; enhances brain levels of serotonin, noradrenaline, and dopamine, which are key neurotransmitters involved in the regulation of mood; and displays anti-inflammatory properties, which may be relevant to treating MDD. The multimodal actions of AXS-05 may be complementary and synergistic for the treatment of this biologically-based condition. AXS-05 is covered by 45 issued U.S. and international patents providing protection out to 2034, and Axsome maintains worldwide rights.

AXS-05 was granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) for the treatment of MDD in March 2019.

About the GEMINI Trial

GEMINI (Glutamatergic and Monoaminergic Modulation in Depression) was a Phase 3, randomized, double-blind, multicenter, placebo-controlled trial of AXS-05 in patients with major depressive disorder (MDD) conducted in the U.S. A total of 327 patients with a confirmed diagnosis of moderate to severe MDD were randomized in a 1:1 ratio to receive AXS-05 (45 mg dextromethorphan/105 mg bupropion) (n=163), or placebo (n=164), twice daily for 6 weeks. The primary endpoint of the study was the change from baseline in the total score of the Montgomery-Åsberg Depression Rating Scale (MADRS), a clinician-rated scale, at Week 6. Two patient-reported outcomes (PROs) for depression were also assessed: the Quick Inventory of Depressive Symptomatology (Self-Report) (QIDS-SR-16), and the Patient Global Impression of Improvement (PGI-I) for depression. The mean MADRS total scores at baseline were 33.6 for the AXS-05 group and 33.2 for the placebo group. The mean QIDS-SR-16 total scores at baseline were 16.2 for the AXS-05 group and 15.8 for the placebo group. P-values were calculated based on least square mean estimates.

About the Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR-16)

The Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR-16) is a well-established, 16-item, validated rating scale used to provide a patient-reported assessment of depression. The scale is used to rate the severity of depression as assessed by the patient across nine question domains comprising sad mood, concentration, self-criticism, suicidal ideation, interest, energy/fatigue, sleep disturbance, changes in appetite or weight, and psychomotor agitation or retardation. The total score ranges from 0 to 27 with higher scores indicating more severe depression.

About Major Depressive Disorder (MDD)

Major depressive disorder (MDD) is a debilitating, chronic, biologically-based disorder characterized by low mood, inability to feel pleasure, feelings of guilt and worthlessness, low energy, and other emotional and physical symptoms, and which impairs social, occupational, educational, or other important functioning. In severe cases, MDD can result in suicide. According to the National Institutes of Health, an estimated 7.1% of U.S. adults, or approximately 17 million, experience MDD each year[1]. According to the World Health Organization (WHO), depression is the leading cause of disability worldwide, and is a major contributor to the overall global burden of disease[2]. Nearly two thirds of diagnosed and treated patients do not experience adequate treatment response with currently available first-line therapy[3], highlighting the need for additional therapies with new mechanisms of action. The majority of initial failures also fail second-line treatment. Patients diagnosed with MDD are defined as having treatment resistant depression (TRD) if they have failed to respond to two or more antidepressant therapies.

About AXS-05

AXS-05 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 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, 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 45 issued U.S. and international patents which provide protection out to 2034. AXS-05 has been granted U.S. Food and Drug Administration (FDA) Breakthrough Therapy designation for the treatment of MDD. AXS-05 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), treatment resistant depression (TRD), 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. National Institute of Mental Health. (2017). Major Depression. Retrieved from https://www.nimh.nih.gov/health/statistics/major-depression.shtml.

2. World Health Organization. Fact Sheets: Depression, accessed October 9, 2018, http://www.who.int/en/news- room/fact-sheets/detail/depression.

3. Rush AJ, et al. (2007) Am J. Psychiatry 163:11, pp. 1905-1917 (STAR*D Study).

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.

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