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 2, 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 December 2, 2020, Axsome Therapeutics, Inc. (the "Company") issued a press release announcing the results from the Company's open-label, Phase 2, COMET-TRD trial of AXS-05 in patients with treatment resistant depression.

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 December 2, 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: December 2, 2020

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

AXSOME THERAPEUTICS

Axsome Therapeutics Announces Positive Results from the COMET-TRD Trial of AXS-05 in Patients with Treatment Resistant Depression

Rapid and substantial improvement in depressive symptoms achieved by 44% of patients at 2 weeks, 67% at 6 weeks (MADRS response), and sustained with long-term treatment

Rapid and substantial improvement in functioning achieved by 53% of patients at 2 weeks, 64% of patients at 6 weeks (Sheehan Disability Scale), and sustained with long-term treatment

Marked or moderate improvement in depression achieved by 49% of patients at 2 weeks, 78% of patients at 6 weeks (Clinical Global Impression), and sustained with long-term treatment

NEW YORK, December 2, 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 open-label Phase 2 COMET-TRD trial of AXS-05 in patients with treatment resistant depression (TRD). Patients treated with AXS-05 experienced rapid, substantial, and durable improvements in depressive symptoms and functional impairment that was sustained with long-term treatment. The COMET-TRD trial evaluated 70 patients who had ongoing symptoms of depression despite receiving treatment with two or more prior antidepressants during the current major depressive episode. Patients were treated with AXS-05 (45 mg dextromethorphan-105 mg bupropion modulated delivery tablet) twice daily for up to 12 months. AXS-05 is a novel, oral, investigational NMDA receptor antagonist with multimodal activity.

AXS-05 treatment resulted in rapid, substantial, and durable improvement in depressive symptoms, measured using the Montgomery-Åsberg Depression Rating Scale (MADRS). Patients experienced a mean reduction from baseline in the MADRS total score of 10.4 points at Week 1, 14.7 points at Week 2, and 20.6 points at Week 6 (primary timepoint), with AXS-05 treatment. Clinical response on the MADRS (defined as ≥50% reduction in total score from baseline) after treatment with AXS-05 was achieved by 21.4% of patients at Week 1, 44.1% of patients at Week 2, and 67.2% of patients at Week 6. Remission from depression (defined as MADRS ≤10) after treatment with AXS-05 was achieved by 14.3% of patients at Week 1, 19.1% of patients at Week 2, and 43.8% of patients at Week 6. The improvement in depressive symptoms was sustained or increased with long-term treatment with AXS-05.

Patients experienced rapid, substantial, and durable improvement in functional impairment, as measured by the Sheehan Disability Scale (SDS), with AXS-05 treatment. The SDS is a patient-rated scale that was designed to assess functioning in work, social life, and family life, and is among the most commonly used functional impairment scales in depression clinical trials. Clinical response on the SDS (defined as a total score of ≤12) after treatment with AXS-05 was achieved by 37.1% of patients at Week 1, 52.9% of patients at Week 2, and 64.1% of patients at Week 6. This improvement in functioning was maintained or increased with long-term treatment with AXS-05.

Clinicians reported rapid, substantial, and durable global improvement in depressive symptoms, measured by the Clinical Global Impression of Improvement (CGI-I) scale, in patients treated with AXS-05. Marked or moderate improvement in depressive symptoms was achieved after treatment with AXS-05 by 24.6% of patients at Week 1, 48.5% of patients at Week 2, and 78.1% of patients at Week 6. This improvement on the CGI-I was sustained or increased with long-term treatment.

“The data from the open-label COMET-TRD trial demonstrate substantial benefit in patients with depression who had failed to respond to two or more prior antidepressant treatments, a population that is known to be difficult to treat,” said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. “Importantly, the rapid and sustained improvement in depressive symptoms with AXS-05 was accompanied by rapid and clinically meaningful improvement in functioning in this patient population. These results support the differentiated clinical profile of AXS-05, resulting from its novel glutamatergic mechanism of action, in the treatment of depression.”

AXS-05 was well tolerated in the COMET trial. The safety profile observed was consistent with what was previously reported in controlled trials of AXS-05 in MDD, with the most commonly reported adverse events being dizziness, nausea, headache, dry mouth, and decreased appetite.

Separately, results of the Phase 2 COMET-SI trial of major depressive disorder patients with suicidal ideation are still expected before year end.

COMET-TRD Results Summary

A total of 70 treatment resistant depression (TRD) patients, defined as those who had ongoing symptoms of depression despite receiving treatment with two or more prior antidepressants during the current major depressive episode, were enrolled and treated with AXS-05 (45 mg dextromethorphan-105 mg bupropion modulated delivery tablet) twice daily for up to 12 months. Topline results are summarized below:

- The mean MADRS total score was 33.1 at baseline. The mean Sheehan Disability Scale (SDS) score was 19.0 at baseline.

- Treatment with AXS-05 was associated with a mean reduction from baseline in the MADRS total score of 10.4 points at Week 1, 14.7 points at Week 2, and 20.6 points at Week 6. Mean MADRS total score reduction from baseline after 6 and 12 months of treatment with AXS-05 was 22.9 points and 26.3 points, respectively.

- Clinical response on the MADRS (defined as ≥50% reduction from baseline) after treatment with AXS-05 was achieved by 21.4% of patients at Week 1, 44.1% of patients at Week 2, and 67.2% of patients at Week 6. Clinical response on the MADRS total score after 6 and 12 months of treatment with AXS-05 was achieved by 71.7% and 90.9% of patients, respectively.

- Remission from depression (defined as MADRS ≤10) after treatment with AXS-05 was achieved by 14.3% of patients at Week 1, 19.1% of patients at Week 2, and 43.8% of patients at Week 6. Remission from depression after 6 and 12 months of treatment with AXS-05 was achieved by 62.3% and 72.7% of patients, respectively.

- Marked or moderate improvement in depressive symptoms after treatment with AXS-05, assessed by the Clinical Global Impression of Improvement (CGI-I) scale, was achieved by 24.6% of patients at Week 1, 48.5% of patients at Week 2, and 78.1% of patients at Week 6. Marked or moderate improvement after 6 and 12 months of treatment with AXS-05 was achieved by 79.2% and 75.0% of patients, respectively.

- Clinical response on the SDS (defined as a total score of ≤12) after treatment with AXS-05, was achieved by 37.1% of patients at Week 1, 52.9% of patients at Week 2, and 64.1% of patients at Week 6. Clinical response on the SDS after 6 and 12 months of treatment with AXS-05 was achieved by 69.8% and 91.7% of patients, respectively.

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 depression. AXS-05 is also 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 depression. AXS-05 is covered by more than 93 issued U.S. and international patents providing protection out to 2040, 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 COMET-TRD Trial

The COMET-TRD trial was a Phase 2, open-label study evaluating the efficacy and safety of AXS-05 in treatment resistant depression (TRD) patients, defined as those who had ongoing symptoms of depression despite receiving treatment with two or more prior antidepressants during the current major depressive episode. Enrolled patients were treated with AXS-05 (45 mg dextromethorphan-105 mg bupropion modulated delivery tablet) twice daily for up to 12 months. Efficacy measures included the Montgomery-Åsberg Depression Rating Scale (MADRS), Clinical Global Impression of Improvement (CGI-I), and the Sheehan Disability Scale (SDS).

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 7.8% of U.S. adults, or approximately 19.4 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 (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 (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), 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. (2020). Major Depression. Retrieved from https://www.nimh.nih.gov/health/statistics/major-depression.shtml.

2. World Health Organization. Fact Sheets: Depression, accessed November 23, 2020, 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