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): May 31, 2022

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)

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 May 31, 2022, Axsome Therapeutics, Inc. (the "Company") issued a press release announcing the publication of the results from the Company's pivotal GEMINI Phase 3 clinical trial of AXS-05 in major depressive disorder in The Journal of Clinical Psychiatry.

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 May 31, 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: May 31, 2022

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

Axsome Therapeutics Announces Publication of Pivotal GEMINI Phase 3 Trial of AXS-05 in Major Depressive Disorder in The Journal of Clinical Psychiatry

AXS-05 (dextromethorphan-bupropion) demonstrated rapid, substantial, and statistically significant antidepressant efficacy compared to placebo starting 1 week after treatment

NEW YORK, May 31, 2022 /PRNewswire/ – Axsome Therapeutics, Inc. (NASDAQ: AXSM), a biopharmaceutical company developing and delivering novel therapies for the management of central nervous system (CNS) disorders, today announced the publication on May 30, 2022 of the results from the pivotal GEMINI Phase 3 clinical trial of AXS-05 (dextromethorphan-bupropion) in major depressive disorder (MDD). AXS-05 is a novel, oral, investigational N-methyl-D-aspartate (NMDA) receptor antagonist with multimodal activity. The article, “Efficacy and Safety of AXS-05 (dextromethorphan-bupropion) in Patients with Major Depressive Disorder: A Phase 3 Randomized Clinical Trial (GEMINI),” was published in The Journal of Clinical Psychiatry and is available in full at: https://www.psychiatrist.com/jcp/depression/efficacy-safety-of-axs-05-dextromethorphan-bupropion-mdd/.

“The results published in *The Journal of Clinical Psychiatry* are consistent with strong and rapid antidepressant effects, and with a favorable safety profile with AXS-05,” said Maurizio Fava, MD, Psychiatrist-In-Chief, Department of Psychiatry, Massachusetts General Hospital, Executive Director, Clinical Trials Network & Institute, Associate Dean for Clinical & Translational Research, Slater Family Professor of Psychiatry, Harvard Medical School, and co-author of the publication. “Depression is a difficult-to-treat condition with potentially devastating consequences for patients and their families. Based on these results and its novel oral NMDA antagonist mechanism, AXS-05 may represent an important new treatment option for patients with depression.”

“We are very pleased with the publication of the pivotal GEMINI trial results in *The Journal of Clinical Psychiatry*, a leading scientific journal, less than two weeks after the publication of the pivotal ASCEND trial results in *The American Journal of Psychiatry*,” said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "These studies demonstrate a consistent efficacy profile for AXS-05 and form the basis of our NDA for the treatment of depression. If approved, we look forward to making AXS-05 available to Americans suffering from depression as soon as possible.”

The GEMINI trial assessed the efficacy and safety of AXS-05 versus placebo in patients with MDD. A total of 327 patients with a confirmed diagnosis of moderate to severe MDD were randomized to receive AXS-05 (45 mg dextromethorphan/105 mg bupropion tablet) (n=163), or placebo (n=164), once daily for the first 3 days and twice daily thereafter, for a total of 6 weeks. The primary endpoint was the change on the Montgomery-Åsberg Depression Rating Scale (MADRS) score from baseline to week 6. The key secondary endpoints were the change from baseline in the MADRS total score at week 1, change from baseline in the MADRS total score at week 2, remission on the MADRS at week 2, and clinical response on the MADRS at week 6.

In the trial, AXS-05 demonstrated rapid, substantial, and statistically significant improvement in depressive symptoms and induction of remission compared with placebo. The change from baseline in MADRS score to week 6 was significantly greater with AXS-05 than with placebo (-15.9 points vs. -12.0 points; least-squares mean difference=-3.87; p=0.002). The MADRS score change with AXS-05 was significantly greater than placebo at week 1, the first timepoint, and at every timepoint thereafter (week 1: -7.20 vs. -4.97 points; least-squares mean difference=-2.23; p=0.007). Remission rates were significantly greater with AXS-05 at week 2 and every timepoint thereafter (week 6: 39.5% vs. 17.3%; treatment difference=22.2%; p<0.001). The majority of secondary outcomes favored AXS-05. Results for most other secondary endpoints were significantly better with AXS-05 than with placebo at almost all timepoints.

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

The article was published online in *The Journal of Clinical Psychiatry* in advance of the corresponding upcoming print issue.

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 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 NMDA receptor antagonist, also known as a glutamate receptor modulator, which is a novel mechanism of action, meaning it works differently than currently approved oral therapies for major depressive disorder. The dextromethorphan component of AXS-05 is also 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 currently covered by more than 100 issued U.S. and international patents, with expiration dates out to 2040. AXS-05 has been granted FDA Breakthrough Therapy designations for the treatment of MDD and for the treatment of Alzheimer's disease agitation. A new drug application (NDA) for AXS-05 for the treatment of major depressive disorder is under review by the FDA. AXS-05 is not approved by the FDA.

About Axsome Therapeutics, Inc.

Axsome Therapeutics, Inc. is a biopharmaceutical company developing and delivering novel therapies for 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 newly acquired Sunosi product; 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 potential filing issues or issues identified by FDA during the substantive review may impact the potential approvability of the Company's NDA submission for AXS-05 in MDD or the timing of such approval; 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 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 amount of capital required for the continued commercialization of Sunosi and for the Company's commercial launch of its 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