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): August 19, 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 August 19, 2022, Axsome Therapeutics, Inc. (the "Company") issued a press release announcing that the U.S. Food and Drug Administration (FDA) has approved AUVELITY™ for the treatment of major depressive disorder (MDD) in adults.

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 August 19, 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: August 19, 2022

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

Axsome Therapeutics Announces FDA Approval of AUVELITY™, the First and Only Oral NMDA Receptor Antagonist for the Treatment of Major Depressive Disorder in Adults

AUVELITY is the first and only rapid-acting oral treatment approved with labeling of statistically significant improvement in depressive symptoms compared to placebo starting at one week[1-4]

AUVELITY uses the first new oral mechanism of action approved for major depressive disorder in over 60 years[1-4]

AUVELITY was developed with FDA Breakthrough Therapy designation and evaluated by the FDA under Priority Review

Company to host webcast today at 8:00 AM ET

NEW YORK, August 19, 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, today announced that the U.S. Food and Drug Administration (FDA) has approved AUVELITY™ (dextromethorphan HBr -bupropion HCl) extended-release tablets for the treatment of major depressive disorder (MDD) in adults.[1] AUVELITY is the first and only rapid-acting oral medicine approved for the treatment of MDD with labeling of statistically significant antidepressant efficacy compared to placebo starting at one week.[1-4] The rapid antidepressant effects of AUVELITY were sustained at all subsequent timepoints.[1] AUVELITY is the first and only oral *N*-methyl *D*-aspartate (NMDA) receptor antagonist approved for the treatment of MDD.[3] Axsome anticipates AUVELITY to be commercially available in the U.S. in the fourth quarter of 2022.

Experience the interactive Multimedia News Release here:

https://www.multivu.com/players/English/9034852-axsome-therapeutics-announces-fda-approval-auvelity/

Maurizio Fava, MD, Psychiatrist-In-Chief, Department of Psychiatry, Massachusetts General Hospital, Executive Director, Clinical Trials Network & Institute, Associate Dean for Clinical & Translational Research, and Slater Family Professor of Psychiatry, Harvard Medical School said, “The approval of Auvelity represents a milestone in depression treatment based on its novel oral NMDA antagonist mechanism, its rapid antidepressant efficacy demonstrated in controlled trials, and a relatively favorable safety profile. Auvelity, which was granted Breakthrough Therapy designation by the FDA, represents the first new oral non-monoamine-based mechanism of action approved to treat major depressive disorder in over sixty years. Nearly two thirds of patients treated with currently available antidepressants do not adequately respond, and those that do may not achieve clinically meaningful responses for up to six to eight weeks. Given the debilitating nature of depression, the efficacy of Auvelity observed at one week and sustained thereafter may have a significant impact on the current treatment paradigm for this condition.”

Michael Pollock, Chief Executive Officer of the Depression and Bipolar Support Alliance (DBSA), a leading national patient advocacy organization focusing on depression and bipolar disorder said, “The mental health crisis in the United States is one of the most pressing health issues facing our country today. Over 20 million American adults experienced major depressive disorder each year prior to the COVID-19 pandemic. These numbers increased dramatically during the pandemic with approximately thirty percent of adults in the U.S. or more than 80 million Americans experiencing elevated symptoms of depression. The need for new treatment options, particularly those with new mechanisms of action, could not be clearer and more urgent for those living with, or impacted by, major depressive disorder.”

Dan V. Iosifescu, MD, Professor of Psychiatry at the New York University School of Medicine, and Director of the Clinical Research Division at the Nathan Kline Institute for Psychiatric Research said, “Major depressive disorder is disabling and potentially life-threatening, causes profound distress for patients and their families, and leads to substantial healthcare resource utilization. Auvelity’s oral NMDA receptor antagonist and sigma-1 receptor agonist activity, which targets glutamatergic neurotransmission, provides clinicians a long sought after new mechanistic approach which may benefit the millions of patients living with this serious condition. In clinical trials, Auvelity has demonstrated rapid and statistically significant improvement in depressive symptoms as early as Week 1, and increased rates of remission at Week 2 compared with placebo. This early benefit with Auvelity was maintained and increased with continued treatment, and was accompanied by a favorable safety and tolerability profile.”

AUVELITY was studied in a comprehensive clinical program which included more than 1,100 patients with depression. The efficacy of AUVELITY in the treatment of MDD was demonstrated in the GEMINI placebo-controlled study, and confirmatory evidence which included the ASCEND study comparing AUVELITY to bupropion sustained-release tablets. In the GEMENI study, AUVELITY was statistically significantly superior to placebo in improvement of depressive symptoms as measured by the change in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score at Week 6, the study's primary endpoint. To evaluate speed of onset of action, the change in MADRS total score from baseline to Week 1 and from baseline to Week 2 were pre-specified secondary efficacy endpoints. The difference between AUVELITY and placebo in change from baseline in MADRS total score was statistically significant at Week 1 and at Week 2.[1] In the ASCEND study, AUVELITY was statistically significantly superior to bupropion sustained-release tablets 105 mg twice daily on the primary outcome measure.[5] The primary outcome measure of the ASCEND study was calculated by assessing the change from baseline in MADRS total scores from Week 1 to Week 6 and then taking the average of those scores.[1] In the placebo-controlled clinical study, the most common (incidence ≥5% for AUVELITY and more than twice as frequently as placebo) adverse reactions were dizziness, headache, diarrhea, somnolence, dry mouth, sexual dysfunction, and hyperhidrosis.[1]

The FDA granted Breakthrough Therapy designation for AUVELITY for the treatment of MDD in March 2019. This designation is granted to candidate drugs that show potential for benefit above that of available therapies based on preliminary clinical data, and it provides the sponsor with added focus from and greater interactions with FDA staff during the development of the candidate drug.[6] The AUVELITY New Drug Application (NDA) was evaluated by the FDA under Priority Review, which is granted by the FDA to applications for medicines that, if approved, would provide significant improvements in the effectiveness or safety of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications.

AUVELITY uses the first new oral mechanism of action in more than 60 years for MDD.[1-4] AUVELITY works on the NMDA receptor, an ionotropic glutamate receptor, and on the sigma-1 receptor in the brain via its dextromethorphan component. The bupropion component of AUVELITY is an aminoketone which increases blood levels of dextromethorphan by competitively inhibiting cytochrome P450 2D6 (CYP2D6), which catalyzes a major biotransformation pathway for dextromethorphan.[1] The exact mechanism of action of AUVELITY in the treatment of MDD is unclear.[1] The blood levels of AUVELITY are determined by the distinct pharmacokinetic interaction between its components which has been found to be non-linear at steady state[1]. AUVELITY is protected by a robust patent estate extending out at least to 2037-2040.

Herriot Tabuteau, MD, Chief Executive Officer of Axsome said, "The approval of Auvelity is the culmination of the tremendous and focused research and development activities conducted by the Axsome team and our collaborators. We are extremely proud to deliver this Breakthrough Therapy-designated new treatment to the millions of patients living with depression at a time when it is most needed, given the recent sharp increase in depression prevalence. We are thrilled to contribute to potentially fundamental advances in neuropsychiatry by providing clinicians the first rapid-acting oral antidepressant demonstrated with FDA labeling, and the first oral glutamatergic medicine approved for depression. Auvelity and the rest of the Axsome neuroscience portfolio reflect our steadfast commitment to developing and delivering potentially life-changing medicines to people living with serious central nervous system disorders."

For patients who need help getting started on AUVELITY, the *Auvelity On My Side* patient support program will offer comprehensive patient support services, including the *Auvelity On My Side* Savings Card to help make treatment more affordable for eligible commercially-insured patients. Additionally, *Auvelity On My Side* will include a samples program, prior authorization support, as well as other patient support tools. All programs will be available immediately upon launch.

Antidepressants increase the risk of suicidal thoughts and behaviors in pediatric and young adult patients. Auvelity is not approved for use in children.

Webcast Information

Axsome will host a webcast and conference call today at 8:00 AM Eastern to discuss the approval of AUVELITY. To access the live webcast please access the following link:

https://event.choruscall.com/mediaframe/webcast.html?webcastid=0E8qLA5v

The live webcast can also be accessed on the "Webcasts & Presentations" page of the "Investors" section of the Company's website at axsome.com. A replay of the webcast will be available for approximately 30 days following the live event. To participate in the live conference call, please dial (877) 405-1239 or for international toll-free access numbers, please click here.

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 U.S. Department of Health and Human Services, an estimated 21 million U.S. adults experienced MDD each year.[7] 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.[8] Nearly two-thirds of diagnosed and treated patients do not experience adequate treatment response with available first-line treatment,[9] highlighting the need for new therapies.

About AUVELITY

AUVELITY is a novel, oral, NMDA receptor antagonist with multimodal activity approved for the treatment of MDD in adults. AUVELITY is a proprietary extended-release oral tablet containing dextromethorphan HBr (45 mg) and bupropion HCl (105 mg). The dextromethorphan component of AUVELITY is an antagonist of the NMDA receptor (an ionotropic glutamate receptor) and a sigma-1 receptor agonist. These actions are thought to modulate glutamatergic neurotransmission. The bupropion component of AUVELITY is an aminoketone and CYP2D6 inhibitor which serves to increase the increase and prolong the blood levels of dextromethorphan. The exact mechanism of action of Auvelity in the treatment of depression is unclear. AUVELITY received Breakthrough Therapy designation from the FDA for the treatment of MDD.

INDICATION AND IMPORTANT SAFETY INFORMATION

WHAT IS AUVELITY (aw-VEHL-ah-tee)? It is a prescription oral medicine used to treat adults with major depressive disorder (MDD). It is not known if Auvelity is safe and effective in children.

Auvelity is not approved for uses other than the treatment of MDD. The ingredients in Auvelity, bupropion and dextromethorphan, are the same ingredients found in some other medicines approved for other uses.

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT AUVELITY?

Auvelity and other antidepressant medicines may increase suicidal thoughts and actions in some children, adolescents, and young adults, especially within the first few months of treatment or when the dose is changed. Auvelity is not for use in children.

You should pay close attention to any new or sudden changes in mood, behavior, thoughts, or feelings or if you develop suicidal thoughts or actions. This is very important when starting or changing the dose of an antidepressant medicine.

Call your healthcare provider (HCP) or get emergency help right away if you or your loved one have any of the following symptoms, especially if they are new, worse, or worry you:

- suicidal thoughts or actions
- new or worsening depression or anxiety
- agitation or restlessness
- trouble sleeping (insomnia)
- acting aggressive, being angry violent
- an extreme increase in activity and talking (mania)
- panic attacks
- new or worsening irritability
- acting on dangerous impulses
- other unusual changes in behavior or mood

Do not take Auvelity if you:

- have or had a seizure disorder.
- have or had an eating disorder like anorexia or bulimia.
- have recently and suddenly stopped drinking alcohol or use medicines called benzodiazepines, barbiturates, or anti-seizure medicines, and you have recently suddenly stopped taking them.
- are taking a monoamine oxidase inhibitor (MAOI), have stopped taking an MAOI in the last 14 days, or are being treated with the antibiotic linezolid or intravenous methylene blue. Ask your HCP or pharmacist if you are unsure whether you take an MAOI. Do not start taking an MAOI until you have stopped taking Auvelity for at least 14 days.
- are allergic to dextromethorphan, bupropion, or any other ingredients in Auvelity.

Auvelity may cause serious side effects. Ask your HCP how to recognize the serious side effects below and what to do if you think you have one:

Seizures. There is a risk of seizures during treatment with Auvelity. The risk is higher if you take higher doses of Auvelity, have certain medical problems, or take Auvelity with certain other medicines. **Do not** take Auvelity with other medicines unless your healthcare provider tells you to.

If you have a seizure during treatment with Auvelity, stop taking Auvelity and call your HCP right away. **Do not** take Auvelity again if you have a seizure.

Increases in blood pressure (hypertension). Some people may get high blood pressure during treatment with Auvelity. Your HCP should check your blood pressure before you start taking and during treatment with Auvelity.

Manic episodes. Manic episodes may happen in people with bipolar disorder who take Auvelity. Symptoms may include:

- greatly increased energy
- racing thoughts
- unusually grand ideas
- talking more or faster than usual
- severe trouble sleeping
- reckless behavior
- excessive happiness or irritability

Unusual thoughts or behaviors. One of the ingredients in Auvelity (bupropion) can cause unusual thoughts or behaviors, including delusions (believing you are someone else), hallucinations (seeing or hearing things that are not there), paranoia (feeling that people are against you), or feeling confused. If this happens to you, call your HCP.

Eye problems (angle-closure glaucoma). Auvelity may cause a type of eye problem called angle-closure glaucoma in people with certain other eye conditions. You may want to undergo an eye examination to see if you are at risk and receive preventative treatment if you are. Call your HCP if you have eye pain, changes in your vision, or swelling or redness in or around the eye.

Dizziness. Auvelity may cause dizziness which may increase your risk for falls.

Serotonin syndrome. A potentially life-threatening problem called serotonin syndrome can happen when you take Auvelity with certain other medicines. **Call your HCP or go to the nearest hospital emergency room right away** if you have any of the following signs and symptoms:

- agitation
- hallucinations
- confusion
- coma
- fast heartbeat
- blood pressure changes
- dizziness
- sweating
- flushing
- high body temperature (hyperthermia)
- shaking (tremors), stiff muscles, or muscle twitching
- loss of coordination
- seizures
- nausea, vomiting, diarrhea

COMMON SIDE EFFECTS

The most common side effects of Auvelity include dizziness, headache, diarrhea, feeling sleepy, dry mouth, sexual function problems, and excessive sweating.

These are not all the side effects of Auvelity. Tell your doctor if you have any side effects. **You can report side effects at 1-800-FDA-1088 or** www.fda.gov/medwatch**.**

BEFORE USING

- **Tell your HCP about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.
- It is important to tell your HCP if you are taking:
  - other medicines containing bupropion or dextromethorphan
  - medicines to treat depression, anxiety, psychotic or thought disorders, including selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants
  - theophylline
  - corticosteroids
  - oral diabetes medicines or use insulin to control your blood sugar
  - medicines to control appetite (anorectic)
  - nicotine medicines to help you stop smoking
  - street (illicit) drugs
  - benzodiazepines, sedative-hypnotic (sleep medicines), or opiates

- If you are unsure if you take any of these medicines, ask your HCP. They can tell you if it is safe to take Auvelity with your other medicines.
- Tell your HCP if you are pregnant or plan to become pregnant. Auvelity may harm your unborn baby if you take it during pregnancy. Auvelity is not recommended during pregnancy. Your HCP will prescribe another treatment for females who plan to become pregnant.
- One of the ingredients in Auvelity passes into your breast milk. Do not breastfeed during treatment with Auvelity and for 5 days after the final dose.

Tell your HCP about all your medical conditions, including if you:

- have problems with your liver or kidneys.
- have diabetes, heart disease, or high blood pressure.
- have a history of seizure, stroke, eating disorder, head injury, or have a tumor in your brain or spinal cord.
- have a history of alcohol or drug abuse.
- have a history of seizure, eating disorder, or abuse alcohol or drugs.
- have low blood sugar, low blood sodium levels, or a history of falls.
- you take certain other medicines that could interact with Auvelity.
- have or had a condition known as bipolar disorder, a family history of bipolar disorder, suicide, or depression.
- have high pressure in the eye (glaucoma).

Review the list below with your HCP. Auvelity may not be right for you if:

- you drink a lot of alcohol.
- you abuse prescription or street drugs.
- you are pregnant or plan to become pregnant.
- you are breastfeeding or plan to breastfeed.

HOW TO TAKE

- Auvelity is available by prescription only.
- Take Auvelity exactly as instructed by your HCP.
- Take Auvelity 1 time a day for 3 days, then increase your dose to 2 times a day (taken at least 8 hours apart). Do not take more than 2 Auvelity tablets in 24 hours.
- If you miss a dose, do not take an extra dose. Wait and take your next dose at the regular time. **Do not** take more than 1 dose of Auvelity at a time.
- Do not change your dose or stop taking Auvelity without talking to your HCP.
- Swallow Auvelity tablets whole. Do not crush, chew, or divide the tablets.
- Do not give Auvelity to other people.
- If you take too much Auvelity call your HCP or seek medical advice promptly.

LEARN MORE

For more information about Auvelity, call 866-496-2976 or visit Auvelity.com.

This summary provides basic information about Auvelity but does not include all information known about this medicine. Read the information that comes with your prescription each time your prescription is filled. This information does not take the place of talking with your doctor. Be sure to talk to your doctor or other HCP about Auvelity and how to take it. Your HCP is the best person to help you decide if Auvelity is right for you.

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Please see full Prescribing Information, including **Boxed Warning** for suicidal thoughts and behaviors, and Medication Guide.

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 Auvelity™ 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 Auvelity 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.

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