# Axsome Therapeutics Announces FDA Approval of AUVELITY® (dextromethorphan HBr and bupropion HCl) for the Treatment of Agitation Associated with Dementia due to Alzheimer's Disease

April 30, 2026

*AUVELITY is a first-in-class treatment, which targets the NMDA and sigma-1 receptors, approved for agitation associated with dementia due to Alzheimer's disease*

*The safety and tolerability profile of AUVELITY in agitation associated with dementia due to Alzheimer's disease has been established across short-term and long-term trials*

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

*Company to host webcast Friday, May 1, at 8:00 AM Eastern Time*

NEW YORK, April 30, 2026 (GLOBE NEWSWIRE) -- Axsome Therapeutics, Inc. (NASDAQ: AXSM), a biopharmaceutical company leading a new era in the treatment of central nervous system (CNS) disorders, today announced that the U.S. Food and Drug Administration (FDA) has approved AUVELITY® (dextromethorphan HBr and bupropion HCl) for the treatment of agitation associated with dementia due to Alzheimer's disease. [1] AUVELITY is a first-in-class treatment for Alzheimer's disease agitation which targets the N-methyl D-aspartate (NMDA) and sigma-1 receptors.

"The approval of our first-in-class medication for agitation associated with Alzheimer's disease marks an important milestone for the millions of patients living with Alzheimer's disease, their families, and their caregivers. We are very pleased to deliver to clinicians and patients a new, effective, FDA-approved treatment option, with a distinct mechanism of action, for this debilitating and critically underserved condition," said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "Alzheimer's disease agitation is the second neuropsychiatric indication for which Auvelity has received FDA Breakthrough Therapy designation, and been granted FDA Priority Review and approval, underscoring Axsome's pioneering work in neuroscience and our dedication to people living with serious brain health conditions."

Alzheimer's disease, a progressive and irreversible brain disorder, is the most common form of dementia, affecting more than 7 million Americans. In addition to cognitive decline, agitation is reported in up to 76% of patients with Alzheimer's disease and can include symptoms ranging from pacing or restlessness to verbal and physical aggression. Agitation is among the most persistent, complex, stressful, and costly aspects of care among patients with behavioral and psychological symptoms of Alzheimer's disease.

Jeffrey Cummings, MD, ScD, Chambers-Grundy Professor of Brain Sciences, UNLV Kirk Kerkorian School of Medicine, commented, "Agitation is highly prevalent in patients with Alzheimer's disease and among the most burdensome aspects of the disease for patients and families. Alzheimer's disease agitation is associated with accelerated cognitive decline, placement in assisted living and long-term care facilities, and increased mortality risk. Treatment for agitation associated with Alzheimer's disease dementia has been a critical unmet medical need. The approval of Auvelity for this condition has the potential to play an important role in patient care for this challenging and impactful symptom of Alzheimer's disease."

George Grossberg, MD, Professor and Director of the Division of Geriatric Psychiatry at the Saint Louis University School of Medicine, said, "Agitation in patients with dementia due to Alzheimer's disease is distressful, consequential, and challenging for patients, their caregivers and healthcare providers. Auvelity is the only FDA-approved product to result in a statistically significantly longer time to relapse of agitation symptoms, compared to placebo, in a long-term study. Importantly, Auvelity showed a compelling safety and tolerability profile, with rates of discontinuation due to adverse events that were low and matched those of placebo. The approval of Auvelity is a significant advancement that provides patients and their caregivers with a much-needed treatment option for this debilitating condition."

The FDA approval of AUVELITY for agitation associated with dementia due to Alzheimer's disease is supported by a comprehensive clinical program which included the Phase 3 ADVANCE-1 and ACCORD-2 studies. ADVANCE-1 was a 5-week, double-blind, parallel-group study in which patients were randomized to treatment with AUVELITY, placebo, or bupropion (the bupropion arm was terminated early for futility). In ADVANCE-1, AUVELITY was statistically significantly superior to placebo in improvement of agitation symptoms as measured by the Cohen-Mansfield Agitation Inventory (CMAI) total score at Week 5, the study's primary endpoint. On the key secondary endpoint of response on the modified Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change (mADCS-CGIC), a statistically significantly greater proportion of patients treated with AUVELITY were rated by clinicians as at least minimally improved compared to placebo. ACCORD-2 was a long-term, double-blind, randomized withdrawal trial in which patients who were known responders to AUVELITY were randomized, in an up to 6-month double-blind phase, to either continue treatment with AUVELITY or switch to placebo. In ACCORD-2, the patients who continued treatment with AUVELITY experienced a statistically significantly longer time to relapse of agitation symptoms, measured by the CMAI, than did patients who switched to placebo.

The safety and tolerability profile of AUVELITY in agitation associated with dementia due to Alzheimer's disease was established across short-term and long-term trials. In the ADVANCE-1 trial, the most common (incidence ≥5% for AUVELITY and more than twice as frequently as placebo) adverse reactions were dizziness and dyspepsia. In the study, 1.3% of patients discontinued AUVELITY due to an adverse event, the same rate as placebo.

The FDA previously granted Breakthrough Therapy designation for AUVELITY for the treatment of agitation associated with dementia due to

Alzheimer's disease. Breakthrough Therapy designation is granted to investigational drugs that show preliminary clinical evidence they may provide substantial improvement over available therapies for a serious or life-threatening condition. The AUVELITY supplemental New Drug Application (sNDA) for the treatment of agitation associated with dementia due to Alzheimer's disease 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 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 inhibiting cytochrome P450 2D6 (CYP2D6), which catalyzes a major biotransformation pathway for dextromethorphan. The exact mechanism of action of AUVELITY in the treatment of agitation associated with dementia due to Alzheimer's disease is unclear.

AUVELITY is also FDA-approved for the treatment of major depressive disorder in adults, an indication which was also developed with FDA Breakthrough Therapy designation and evaluated by the FDA under Priority Review. To date, AUVELITY has been administered to more than 300,000 patients in clinical and real-world settings.

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

**Conference Call Information**

Axsome will host a conference call and webcast on Friday, May 1, at 8:00 a.m. Eastern Time to discuss the approval of AUVELITY. To participate in the live conference call, please dial (877) 405-1239 (toll-free domestic) or +1 (201) 389-0851 (international). A live webcast of the conference call can be accessed on the "Webcasts & Presentations" page of the "Investors" section of the Company's website at axsome.com. A replay of the conference call will be available for approximately 30 days following the live event.

**About Agitation Associated with Dementia Due to Alzheimer's Disease**

Alzheimer's disease is the most common form of dementia affecting more than 7 million people in the U.S.[2] Agitation associated with dementia due to Alzheimer's disease is a neuropsychiatric condition reported in up to 76% of patients with Alzheimer's disease and is characterized by emotional distress, verbal and physical aggressiveness, disruptive irritability, and disinhibition.[2,3] The exact cause of agitation in the brain is not known but it is associated with changes in glutamate and monoamine signaling.[4,5] Agitation has been associated with accelerated cognitive decline, increased caregiver burden, and increased mortality risk, and is a leading cause of assisted living or nursing home placement.[6]

**About AUVELITY**

AUVELITY (dextromethorphan HBr/bupropion HCl) is an oral N-methyl-D-aspartate (NMDA) receptor antagonist, sigma-1 agonist, and aminoketone CYP2D6 inhibitor. AUVELITY is a first-in-class medicine, with a distinct mechanism of action, for the treatment of agitation associated with dementia due to Alzheimer's disease. AUVELITY was initially approved by the U.S. FDA in 2022 for the treatment of major depressive disorder (MDD) in adults, and it 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, for the treatment of MDD. AUVELITY is protected by a robust patent estate extending to at least 2043.

**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) and agitation that may happen with dementia due to Alzheimer's disease (AAD). AUVELITY should not be used as an "as needed" treatment for agitation that may happen with dementia due to Alzheimer's disease.

It is not known if AUVELITY is safe and effective in children with MDD.

**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, or 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

**Hyponatremia.** Low sodium levels in the blood, sometimes severe and causing death, have occurred as a result of treatment with AUVELITY. Elderly patients may be at greater risk. Low sodium levels could be the result of a condition called syndrome of inappropriate antidiuretic hormone secretion (SIADH). Taking AUVELITY with antidepressants called SSRIs may increase the risk. **Stop taking AUVELITY and call your HCP or go to the nearest hospital emergency room right away** if you have any of the following signs or symptoms: headache, difficulty concentrating, memory loss, confusion, weakness and unsteadiness which can lead to falls.

**COMMON SIDE EFFECTS**

**The most common side effects of AUVELITY when treating MDD include** dizziness, headache, diarrhea, feeling sleepy, dry mouth, sexual function problems, and excessive sweating.

**The most common side effects of AUVELITY when treating agitation that may happen with dementia due to Alzheimer's disease include** dizziness and indigestion.

These are not all the possible side effects of AUVELITY. Tell your doctor if you have any side effects. You are encouraged to report side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1–800-FDA-1088.

**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**

- Take AUVELITY exactly as instructed by your HCP.
- **MDD:** Take AUVELITY 45 mg/105 mg once daily in the morning for 3 days. On Day 4, increase to the maximum recommended dosage of AUVELITY 45 mg/105 mg twice a day, taken at least 8 hours apart. Do not take more than 2 AUVELITY tablets in 24 hours.
- **AAD:**
  - Take 1 AUVELITY 30 mg/105 mg tablet once daily in the morning for 7 days.
  - On Day 8, increase to AUVELITY 30 mg/105 mg twice a day, taken at least 8 hours apart. Do not take more than 2 AUVELITY tablets in 24 hours.
  - On Day 15 after starting AUVELITY, increase to the maximum recommended dosage of AUVELITY 45 mg/ 105 mg twice a day, taken at least 8 hours apart, based on tolerability. 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 poison control center at 1-800-222-1222 or go to the nearest hospital emergency room right away.

**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.

AUVELITY is available as 30 mg dextromethorphan/105 mg bupropion and 45 mg dextromethorphan/105 mg bupropion tablets.

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

**About Axsome Therapeutics**

Axsome Therapeutics is a biopharmaceutical company leading a new era in the treatment of central nervous system (CNS) conditions. We deliver scientific breakthroughs by identifying critical gaps in care and develop differentiated products with a focus on novel mechanisms of action that enable meaningful advancements in patient outcomes. Our industry-leading neuroscience portfolio includes FDA-approved treatments for agitation associated with dementia due to Alzheimer's disease, major depressive disorder, excessive daytime sleepiness associated with narcolepsy and obstructive sleep apnea, and migraine, and multiple late-stage development programs addressing a broad range of serious neurological and psychiatric conditions that impact over 150 million people in the United States. Together, we are on a mission to solve some of the brain's biggest problems so patients and their loved ones can flourish. For more information, please visit us at www.axsome.com and follow us on LinkedIn and X.

**Forward Looking Statements**

Certain matters discussed in this press release are "forward-looking statements". The Company 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 commercial success of the Company's SUNOSI ®, AUVELITY®, and SYMBRAVO® products and the success of the Company's efforts to obtain any additional indication(s) with respect to solriamfetol and/or AXS-05; the Company's ability to maintain and expand payer coverage; the success, timing and cost of the Company's ongoing clinical trials and anticipated clinical trials for the Company's current product candidates, including statements regarding the timing of initiation, pace of enrollment and completion of the trials (including the Company's ability to fully fund the Company's disclosed clinical trials, which assumes no material changes to the Company's currently projected revenues or expenses), futility analyses and receipt of interim results, which are not necessarily indicative of the final results of the Company's ongoing clinical trials, and/or data readouts, 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 the Company's current product candidates; the Company's ability to fund additional clinical trials to continue the advancement of the Company's product candidates; the timing of and the Company's ability to obtain and maintain U.S. Food and Drug Administration ("FDA") or other regulatory authority approval of, or other action with respect to, the Company's product candidates, including statements regarding the timing of any NDA submission; 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 Company's ability to successfully resolve any intellectual property litigation, and even if such disputes are settled, whether the applicable federal agencies will approve of such settlements; 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 products and product candidates, if approved; the Company's anticipated capital requirements, including the amount of capital required for the commercialization of SUNOSI, AUVELITY, and SYMBRAVO and for the Company's commercial launch of its other product candidates, if approved, and the potential impact on the Company's anticipated cash runway; the Company's ability to convert sales to recognized revenue and maintain a favorable gross to net sales; unforeseen circumstances or other disruptions to normal business operations arising from or related to domestic political climate, geo-political conflicts or a global pandemic 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 circumstances.

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Source: Axsome Therapeutics, Inc.