# Axsome Therapeutics Announces FDA Approval of SYMBRAVO® (meloxicam and rizatriptan) for the Acute Treatment of Migraine with or without Aura in Adults

January 30, 2025

*A single oral dose of SYMBRAVO provided rapid migraine pain freedom and return to normal functioning within 2 hours, and sustained efficacy through 24 and 48 hours*

*85% and 77% of patients treated with a single dose of SYMBRAVO did not require migraine rescue medication within 24 hours in two Phase 3 studies*

*SYMBRAVO demonstrated superior efficacy across a broad range of migraine severity (mild, moderate, and severe), and in head-to-head evaluation*

*SYMBRAVO incorporates Axsome's rapid absorption technology and mechanisms that target multiple migraine attack pathways*

*Company to host conference call and webcast Friday, January 31, at 8:00 AM Eastern*

NEW YORK, Jan. 30, 2025 (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 SYMBRAVO® (meloxicam and rizatriptan) for the acute treatment of migraine with or without aura in adults.[1] SYMBRAVO represents a novel multi-mechanistic approach to treating migraine that targets multiple pathways underlying a migraine attack. SYMBRAVO can rapidly eliminate migraine pain and return patients to normal functioning, with efficacy sustained through 24 and 48 hours in some patients after a single dose. The efficacy of SYMBRAVO was demonstrated across a broad range of settings including at the earliest onset of migraine when the pain was mild, in patients with moderate and severe migraine pain, and in those with a history of various responses to prior acute treatments. The Company expects SYMBRAVO to be commercially available in the U.S. in approximately four months.

Richard B. Lipton, MD, Professor of Neurology and Director of the Montefiore Headache Center, Albert Einstein College of Medicine, commented, "A significant proportion of migraine patients experience inadequate efficacy with currently available acute treatments, leading to even greater suffering, and an increased risk of worsening of migraine pain and attack frequency. Results of multiple clinical trials demonstrate that SYMBRAVO can provide rapid and long-lasting freedom from migraine pain, whether treatment is taken early in the attack while the pain is mild, or later in the attack when the pain may be severe. The approval of SYMBRAVO is a long awaited and much welcomed advancement for clinicians and our patients, providing a new, meaningful treatment option."

Stewart Tepper, MD, Clinical Professor of Neurology at the Geisel School of Medicine at Dartmouth and Vice President of the New England Institute for Neurology and Headache, said, "Migraine is a debilitating condition that affects millions of Americans. Unfortunately, many patients still struggle to find an option that effectively treats their attacks and is both safe and well tolerated, which creates a great need for new migraine medicines. SYMBRAVO's approval by the FDA provides a new medicine for physicians and patients that was designed to target key unmet needs in the migraine treatment space. The clinical data supporting its approval validates the additive benefit of SYMBRAVO's multi-mechanistic design and demonstrates its potential to make a meaningful difference for the migraine community."

Susan Doughty, Executive Director of the Coalition for Headache and Migraine Patients (CHAMP), added, "Migraine is one of the most misunderstood and stigmatized neurological diseases, despite the fact that one in four households in the U.S. includes someone living with it. This widespread lack of understanding creates unnecessary barriers for individuals seeking proper diagnosis, care, and treatment. CHAMP, alongside our 20 plus dedicated coalition organizations and patient advocates, is committed to empowering the migraine community by providing education, reducing stigma, and advocating for fair and equitable access to treatment options. The approval of SYMBRAVO as a new acute treatment for migraine is an important step forward, offering a new option for people seeking relief. We also see this moment as an opportunity to continue to shine a bright light on migraine, fostering greater awareness and helping to dismantle the stigma that so often surrounds this disease."

The FDA approval of SYMBRAVO is based on the results of the Phase 3 MOMENTUM trial that treated migraine of moderate and severe pain intensity, the Phase 3 INTERCEPT trial that treated migraine when the initial pain was mild, and the Phase 3 MOVEMENT long-term open label safety trial. In this comprehensive clinical program, over 21,000 migraine attacks were treated with SYMBRAVO.

In the MOMENTUM trial, SYMBRAVO demonstrated a statistically significantly greater percentage of patients achieving pain freedom and freedom from their most bothersome symptom (photophobia, phonophobia, nausea) 2 hours after dosing compared to placebo. SYMBRAVO also demonstrated statistical superiority for pain relief (reduction of moderate or severe pain to no pain or mild pain) and the ability to perform normal daily activities. The benefits of pain freedom at 2 hours were sustained through 24 and 48 hours for many patients. In a head-to-head comparison, SYMBRAVO demonstrated statistically significant superiority compared to rizatriptan on sustained pain freedom from 2 to 24 hours. Notably, these benefits were seen with only a single dose of SYMBRAVO. In the MOMENTUM trial, 77% of patients treated with SYMBRAVO did not require rescue medication within 24 hours post dose.

In the INTERCEPT trial, SYMBRAVO demonstrated a statistically significantly greater percentage of patients achieving pain freedom and freedom from their most bothersome symptom (photophobia, phonophobia, nausea) 2 hours after dosing compared to placebo. The benefits of pain freedom at

2 hours were sustained through 24 and 48 hours for many patients. Notably, these benefits were seen with only a single dose of SYMBRAVO. In the INTERCEPT trial, 85% of patients treated with SYMBRAVO did not require rescue medication within 24 hours post dose.

The most common adverse reactions (≥1% and greater than placebo) in the controlled studies were somnolence and dizziness, being reported each in 2% and 1% of patients in the SYMBRAVO and placebo arms, respectively. The long-term safety of SYMBRAVO was demonstrated in the MOVEMENT trial, which assessed 706 patients dosing intermittently for up to 12 months and treating at least 2 migraines per month with SYMBRAVO.

SYMBRAVO is engineered with Axsome's patented MoSEIC ™ (Molecular Solubility Enhanced Inclusion Complex) rapid absorption technology. MoSEIC results in a five times faster median time to maximum plasma concentration for meloxicam while maintaining a long plasma half-life, enabling meloxicam's use as a new molecular entity for the acute treatment of migraine. SYMBRAVO is protected by a robust patent estate extending out to at least 2040.

Herriot Tabuteau, MD, Chief Executive Officer of Axsome Therapeutics, said, "Today's approval of SYMBRAVO marks an important milestone for the migraine community by providing a rationally designed novel acute treatment for this debilitating condition. Migraine attacks strike without warning, and disrupt the lives of estimated more than 39 million patients in the U.S. alone. SYMBRAVO provides patients and clinicians an important new option which can quickly stop a migraine attack, keep it away, and allow patients to resume their normal activities, with just a single dose. SYMBRAVO demonstrates Axsome's commitment to developing and delivering differentiated new treatments to improve the lives of patients living with difficult to treat central nervous system disorders."

**Conference Call Information**

Axsome will host a conference call and webcast on Friday, January 31, at 8:00 a.m. Eastern Time to discuss the approval of SYMBRAVO. Dr. Stewart Tepper, Clinical Professor of Neurology at the Geisel School of Medicine at Dartmouth and Vice President of the New England Institute for Neurology and Headache, will join the call and will be available to answer questions during the Q&A session. To participate in the live conference call, please dial (877) 405-1239 (toll-free domestic) or +1 (201) 389-0851 (international). A live webcast can 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.

**About Migraine**

Migraine is a serious neurological condition characterized by recurrent attacks of pulsating, often severe and disabling head pain associated with nausea, sensitivity to light, and sensitivity to sound.[2] It is estimated that over 39 million Americans suffer from migraine, and it is the leading cause of disability among neurological disorders in the United States according to the American Migraine Foundation.[3-5] Extensive surveys of migraine sufferers underscore the unmet need for therapies that work faster, more consistently, and result in less symptom recurrence.[6,7] Over 70% of patients report experiencing an inadequate response to their oral, acute migraine treatment.[8]

**About SYMBRAVO**

SYMBRAVO is a novel, oral, single-dose medicine approved for the acute treatment of migraine with or without aura in adults. SYMBRAVO consists of MoSEIC™ meloxicam and rizatriptan. Meloxicam is a new molecular entity for migraine enabled by Axsome's MoSEIC (Molecular Solubility Enhanced Inclusion Complex) technology, which enables the rapid absorption of meloxicam while maintaining a long plasma half-life. Meloxicam is a COX-2 preferential non-steroidal anti-inflammatory drug (NSAID) and rizatriptan is a 5-$HT_{1B/1D}$ agonist. SYMBRAVO is designed to provide rapid, enhanced, and consistent migraine pain relief, and reduced symptom recurrence. The exact mechanism of action of SYMBRAVO in the treatment of acute migraine is unknown.

For more information, visit www.symbravo.com.

**What is SYMBRAVO (sim-BRAH-voh)? SYMBRAVO is a combination of meloxicam (an NSAID) and rizatriptan (a triptan).** SYMBRAVO is an oral prescription medicine used to treat acute migraine headaches with or without aura in adults.

SYMBRAVO is not used to prevent or decrease the number of migraine headaches you have or for treatment of hemiplegic or basilar migraines. SYMBRAVO is not indicated as a treatment for cluster headaches or for use in children.

**WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT SYMBRAVO?**

**SYMBRAVO may increase the risk of a heart attack or stroke that can lead to death.** This risk may happen early in treatment and may increase with increasing doses, and longer use, of NSAIDs.

**Do not take SYMBRAVO right before or after a heart surgery called a "coronary artery bypass graft" (CABG).**

**Avoid taking SYMBRAVO after a recent heart attack unless your healthcare provider (HCP) tells you to. You may have an increased risk of another heart attack if you take NSAIDs after a recent heart attack.**

**Stop taking SYMBRAVO and get emergency help right away if you have any of the following symptoms which can be indicative of a heart attack or stroke:**

- discomfort in your chest that lasts for more than a few minutes, or that goes away and comes back
- severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw
- pain or discomfort in your arms, back, neck, jaw, or stomach
- shortness of breath with or without chest discomfort
- breaking out in a cold sweat
- nausea or vomiting
- feeling lightheaded

- weakness in one part or one side of your body
- slurred speech

**People with risk factors for heart disease should not take SYMBRAVO unless a heart exam is done and shows no problem. You have a higher risk for heart disease if you:**

- have high blood pressure
- have high cholesterol
- smoke
- are overweight
- have diabetes or a family history of diabetes

**SYMBRAVO can increase the risk of potentially life-threatening bleeding, ulcers, and tears (perforation) of the esophagus, stomach, and intestines that can occur anytime during use and without warning symptoms.**

**SYMBRAVO may cause serious allergic or skin reactions which can be life-threatening.** Stop taking SYMBRAVO and get emergency help right away if you develop:

- sudden wheezing or problems breathing or swallowing
- rash or reddening of your skin with blisters or peeling
- blisters or bleeding of your lips, eyelids, mouth, nose, or genitals
- swelling of your lips, tongue, throat, or body
- fainting

**SYMBRAVO already contains an NSAID (meloxicam).** Do not use SYMBRAVO with other medicines to lessen pain or fever or with other medicines for colds or sleeping problems without talking to your HCP first, because they may contain an NSAID also.

**Do not take SYMBRAVO if you:**

- have or had heart problems or right before or after heart bypass surgery
- have or had a stroke or transient ischemic attack (TIA)
- have or had blood vessel problems of your legs and arms, stomach (ischemic bowel disease), or kidneys
- have or had hemiplegic or basilar migraines
- have uncontrolled high blood pressure
- take propranolol-containing medicines
- have taken other triptan or ergot-containing medicines within the last 24 hours
- take an antidepressant medicine called monoamine oxidase inhibitor (MAOI) or have taken a MAOI within the last 2 weeks
- are allergic to meloxicam, rizatriptan, NSAIDs, or any of the ingredients in SYMBRAVO
- have had an asthma attack, hives, or other allergic reaction after taking aspirin or any other NSAIDs
- have moderate to severe kidney problems and are at risk of kidney failure or if you are on dialysis

**SYMBRAVO may cause serious side effects. These serious side effects include:**

- Heartbeats that are too fast or too slow
- New or worse high blood pressure
- Heart failure
- Life-threatening skin reactions
- Liver or kidney problems including organ failure
- Low red blood cell count
- Asthma attacks in people who have asthma

**Medication Overuse Headaches:**Some people who use too many SYMBRAVO tablets may have worse headaches.If your headaches get worse, your HCP may decide to stop your treatment with SYMBRAVO.

**Stop taking SYMBRAVO and get emergency help right away if you have any of the following:**

- **Stomach and intestinal problems.** Symptoms of gastrointestinal and colonic ischemic events may include sudden or severe stomach pains even after meals; sudden weight loss; severe nausea, vomiting, constipation, diarrhea; and bloody diarrhea.
- **Circulation problems to legs and feet.** Symptoms of peripheral vascular ischemia may include cramping and pain in your legs and hips; heaviness or tightness in leg muscles; burning, aching, numbness, tingling, or weakness in your legs, feet, or toes; cold feelings or color changes in one or both legs or feet.
- **Serotonin syndrome.** Can happen when taking SYMBRAVO with antidepressant medicines called SSRIs or SNRIs. Stop taking SYMBRAVO and call your doctor right away if you have any of the following symptoms:
    - mental status changes including agitation, hallucinations, or coma

- fast heartbeat
- changes in your blood pressure
- increased body temperature
- tight muscles
- trouble walking

- **Stop taking SYMBRAVO and call your healthcare provider right away if you have any of the following symptoms:**
  - nausea
  - vomiting blood
  - more tired or weaker than usual
  - blood in your bowel movement or it is black and sticky like tar
  - diarrhea
  - itching, skin rash, or blisters with fever
  - unusual weight gain
  - your skin or eyes look yellow
  - indigestion or stomach pain
  - swelling of the arms, legs, hands, or feet
  - flu-like symptoms
  - tenderness in your right upper side
  - vision problems

**COMMON SIDE EFFECTS**

**The most common side effects of SYMBRAVO include dizziness and tiredness.**

These are not all the possible side effects of SYMBRAVO. 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:**
  - Propranolol containing medicines such as Inderal® LA or Innopran® XL
  - Aspirin or other anti-coagulants (blood thinners)
  - Medicines to help your mood including SSRIs and SNRIs
- If you are unsure if you take any of these medicines, ask your HCP. They can tell you if it is safe to take SYMBRAVO with your other medicines.
- Tell your HCP if you are pregnant or plan to become pregnant. SYMBRAVO is not recommended during pregnancy. Taking NSAIDs, including SYMBRAVO, at about 20 weeks of pregnancy or later may harm your unborn baby. **NSAIDs, including SYMBRAVO, should not be taken after about 30 weeks of pregnancy.**
- Tell your HCP if you are breastfeeding or plan to breastfeed.

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

- have or have had heart problems, high blood pressure, chest pain, or shortness of breath
- have any risk factors for heart or blood vessel problems
- have kidney or liver problems
- have asthma

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

- take daily preventative aspirin
- you are pregnant or plan to become pregnant
- you are breastfeeding or plan to breastfeed

**HOW TO TAKE**

- SYMBRAVO is available by prescription only.
- Take SYMBRAVO exactly as instructed by your HCP.
- The maximum daily dose of SYMBRAVO is 1 tablet. Talk to your HCP about what to do if your headache does not go away or comes back.
- Take SYMBRAVO for the shortest time needed.
- Swallow SYMBRAVO tablets whole. **Do not** crush, chew, or divide the tablets.
- SYMBRAVO can be taken with or without food.
- Do not give SYMBRAVO to other people.
- If you take too much SYMBRAVO 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 SYMBRAVO, call 866-496-2976 or visit SYMBRAVO.com.

This summary provides basic information about SYMBRAVO 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 SYMBRAVO and how to take it. Your HCP is the best person to help you decide if SYMBRAVO is right for you.

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*Please see full Prescribing Information, including Boxed Warning for risk of serious cardiovascular and gastrointestinal adverse events, 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 major depressive disorder and excessive daytime sleepiness associated with narcolepsy and obstructive sleep apnea 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 the Company's website at www.axsome.com.

**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 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 circumstance.

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