# Axsome Therapeutics Presents Positive Pivotal Phase 3 Results of the ACCORD-2 Trial of AXS-05 in Alzheimer's Disease Agitation and the SYMPHONY Trial of AXS-12 in Narcolepsy at the 2025 American Academy of Neurology (AAN) Annual Meeting

April 4, 2025

*Late-breaking oral presentation of results from the positive pivotal ACCORD-2 Phase 3 trial of AXS-05 in Alzheimer's disease agitation*

*Presentation featuring network meta-analysis of SYMBRAVO® versus oral CGRPs*

NEW YORK, April 04, 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 multiple presentations spanning its innovative, industry-leading psychiatry and neurology portfolio at the 2025 American Academy of Neurology (AAN) Annual Meeting, being held April 5-9 in San Diego, California.

Oral and poster presentations include data from the positive pivotal ACCORD-2 Phase 3 trial of AXS-05 in Alzheimer's disease (AD) agitation, accepted as a late-breaking abstract, and from the positive pivotal SYMPHONY Phase 3 trial of AXS-12 in narcolepsy. Additional data being presented includes a network meta-analysis comparing the efficacy of SYMBRAVO® (AXS-07) to oral CGRPs in the acute treatment of migraine.

Details for the presentations are as follows:

***Alzheimer's Disease Agitation***

**Title**: Efficacy and Safety of AXS-05 in Alzheimer's Disease Agitation: A Phase 3 Randomized Withdrawal Double-Blind Placebo-Controlled Study
**Oral Presentation Date and Time:** Monday, April 7, 11:27 - 11:33 a.m. PT
**Poster Presentation Date and Time:** Monday, April 7, 12:09 - 12:45 p.m. PT
**Session Name:** Late-breaking Science 1
**Poster Number:** 3
**Abstract:** 246

***Narcolepsy***

**Title:** AXS-12 for the Treatment of Narcolepsy: Topline Results from the Phase 3 SYMPHONY Trial
**Oral Presentation Date and Time:** Tuesday, April 8, 10:45 - 11 a.m. PT
**Lead Author:** Michael J. Thorpy, MD, Director of the Sleep-Wake Disorders Center at the Montefiore Medical Center and Professor of Neurology at Albert Einstein College of Medicine, New York, NY
**Session Name:** Clinical Trials Plenary Session
**Program Number:** PL5

**Title:** CRESCENDO: Results from a Survey of Symptom Burden and Quality of Life in Patients with Narcolepsy Type 1
**Poster Presentation Date and Time:** Tuesday, April 8, 8 - 9 a.m. PT
**Lead Author:** Michael J. Thorpy, MD, Director of the Sleep-Wake Disorders Center at the Montefiore Medical Center and Professor of Neurology at Albert Einstein College of Medicine, New York, NY
**Session Name:** Sleep 2
**Program Number:** P8:001

***Migraine***

**Title:** Comparative Efficacy of AXS-07 vs. Gepants for Acute Treatment of Migraine: A Network Meta-Analysis
**Poster Presentation Date and Time:** Tuesday, April 8, 5 - 6 p.m. PT
**Lead Author:** Stephanie Nahas, MD, Associate Professor of Neurology at the Thomas Jefferson University Hospitals-Jefferson Health Center, Philadelphia, PA
**Session Name:** Headache: Advances in CGRP Inhibitors and Migraine 3
**Program Number:** P10.006

**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.

**INDICATION AND IMPORTANT SAFETY INFORMATION**

**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 higher risk for heart disease if you:**

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

**SYMBRAVO can increase the risk of potentially life-threatening bleeding, ulcers, and tears (perforation) of the esophagus (tube leading from the mouth to the stomach), 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, eye lids, 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 (arrhythmias)
- new or worse high blood pressure
- heart failure
- life-threatening skin reactions
- liver or kidney problems including organ failure
- low red blood cell count (anemia)
- 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 AXS-05**

AXS-05 (dextromethorphan-bupropion) is a novel, oral, investigational N-methyl-D-aspartate (NMDA) receptor antagonist, sigma-1 agonist, and aminoketone CYP2D6 inhibitor under development for the treatment of Alzheimer's disease (AD) agitation and smoking cessation. 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, and 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 covered by a robust patent estate extending out to at least 2043. AXS-05 was granted U.S. FDA Breakthrough Therapy designation for the treatment of Alzheimer's disease agitation in June 2020.

**About AXS-12**

AXS-12 (reboxetine) is a highly selective and potent norepinephrine reuptake inhibitor and cortical dopamine modulator under development for the treatment of narcolepsy. AXS-12 is thought to modulate noradrenergic activity to promote maintain tone during wakefulness, and noradrenergic and cortical dopamine signaling to promote wakefulness and enhance cognition. AXS-12 has been granted U.S. Food and Drug Administration (FDA) Orphan Drug Designation for the treatment of narcolepsy. AXS-12 is covered by issued patents providing protection to at least 2039. AXS-12 is an investigational drug product not approved by the FDA.

**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, 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 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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