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): October 03, 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	**10007**
(Address of Principal Executive Offices)	**(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 October 3, 2022, Axsome Therapeutics, Inc. (the "Company") issued a press release regarding the results of its SHARP trial of Sunosi® (solriamfetol) in cognitively impaired patients with excessive daytime sleepiness (EDS) associated with obstructive sleep apnea (OSA) (the "SHARP Trial"). The SHARP Trial met its primary endpoint by demonstrating a statistically significant improvement in cognitive function with Sunosi as compared to placebo.

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 October 3, 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: October 3, 2022

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

Axsome Therapeutics Announces Sunosi® (Solriamfetol) Meets Primary Endpoint Demonstrating Improvement in Cognitive Function in the SHARP Trial in Cognitively Impaired Patients with Excessive Daytime Sleepiness Associated with Obstructive Sleep Apnea

Statistically significant improvement in cognitive function, as measured by the DSST RBANS compared to placebo (p=0.009, primary endpoint)

Statistically significant patient-reported improvement in cognitive function, as measured by the BC-CCI compared to placebo (p=0.002)

Reduced excessive daytime sleepiness compared to placebo (p=0.004 on ESS)

Activation of human TAAR1 by solriamfetol demonstrated in new pharmacology studies

NEW YORK, October 3, 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, announced that Sunosi met the primary endpoint in the SHARP study and significantly improved cognitive function, measured using the Digit Symbol Substitution Test subtest of the Repeatable Battery for the Assessment of Neuropsychological Status (DSST RBANS), as compared to placebo in cognitively impaired patients with excessive daytime sleepiness (EDS) associated with obstructive sleep apnea (OSA). Superiority of Sunosi as compared to placebo was further demonstrated using patient-reported measures of cognitive function. In the study, Sunosi replicated previous findings by significantly reducing EDS symptoms as compared to placebo.

SHARP (Solriamfetol's Effect on Cognitive Health in Apnea Participants During a Randomized Placebo-controlled Study) was a randomized, double-blind, placebo-controlled, crossover, multicenter, trial in 59 patients with EDS associated with OSA, and impaired cognitive function. Patients were all treated with Sunosi for 2 weeks, and with placebo for 2 weeks, with the treatment periods separated by 1 week of down-titration and washout.

On the study’s primary endpoint, Sunosi demonstrated statistically significant improvement in cognitive function compared to placebo as assessed by the change from baseline on the DSST RBANS (6.49 vs. 4.75, p=0.009), with an effect size of 0.36. The DSST RBANS is an objective neuropsychological test that assesses executive function, processing speed and attention. Statistically significant improvement in cognitive function with Sunosi treatment was also demonstrated using the British Columbia Cognitive Complaints Inventory (BC-CCI) overall score compared to placebo (p=0.002), with an effect size of 0.43. The BC-CCI is a patient-reported test that assesses domains of memory, concentration, trouble expressing thoughts, word finding, and problem solving.

Sunosi significantly improved EDS symptoms compared to placebo, as measured by the Epworth Sleepiness Scale (ESS). The improvement on the ESS with Sunosi treatment was approximately twice that observed with placebo (p=0.004), with an effect size of 0.50.

The most commonly reported adverse events with Sunosi treatment (incidence ≥3%) were nausea (6.9%) and anxiety (3.4%). The study completion rate was 96.7% for patients randomized to each treatment sequence (Sunosi followed by placebo, or placebo followed by Sunosi).

“Cognitive impairment in patients with EDS associated with OSA is extremely common and one of the most burdensome symptoms for patients,” said Richard Bogan, MD, FCCP, Associate Clinical Professor at the University of South Carolina School of Medicine, Associate Clinical Professor at Medical University of South Carolina, and Principal of Bogan Sleep Consultants. “The results of the SHARP study demonstrate a clinically important improvement in cognitive function with Sunosi treatment in cognitively impaired patients with EDS and OSA. Of importance, the results from the patient-reported outcomes are consistent with the objective measures, meaning that patients themselves were able to perceive improvements in their cognitive performance with Sunosi treatment. The ability to address cognitive symptoms would represent an important advancement in the treatment of EDS associated with OSA.”

"We are excited by the demonstrated effect of Sunosi on cognition, using both objective and patient-reported outcomes in the SHARP trial in patients with EDS and OSA experiencing cognitive impairment at baseline," said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "We plan to discuss these results with the FDA as soon as possible. In addition, we recently presented new data demonstrating that solriamfetol has activity at TAAR1, a previously unrecognized target for this molecule which further supports its exploration in cognition."

Detailed study results will be submitted for presentation at upcoming medical meetings and for publication.

New Data Demonstrating Activation of TAAR1 by Solriamfetol Presented at 2022 Psych Congress

New preclinical pharmacology studies have identified agonist activity at the trace amine-associated receptor 1 (TAAR1) and lower potency agonist activity at 5-HT_{1A}receptors for solriamfetol, in addition to its activity as a dopamine and norepinephrine reuptake inhibitor (DNRI). TAAR1 is a G-protein coupled receptor with affinity for the trace amines, and TAAR1 agonists have demonstrated pro-cognitive and wake-promoting effects in rodents and primates[1,2].

Results of the studies demonstrated that solriamfetol activates human TAAR1 *in vitro* at potencies that are within the clinically relevant plasma concentration range and overlap with observed dopamine and norepinephrine transporter inhibitory potencies[3]. No human TAAR1 activity was observed for the wake promoting agent (WPA) modafinil or the DNRI bupropion. In addition, similar to known TAAR1 agonists, solriamfetol reduced the firing frequency of mouse VTA dopamine neurons in a D2-sensitive manner.

These findings were recently presented at the 2022 Psych Congress on September 18, 2022.

The mechanism of action of solriamfetol to improve wakefulness in patients with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea, and to potentially affect cognition, is unclear.

About the SHARP Trial

SHARP (Solriamfetol's Effect on Cognitive Health in Apnea Participants During a Randomized Placebo-controlled Study) was a randomized, double-blind, placebo-controlled, crossover, multicenter, trial in which 59 patients with EDS and OSA, who were experiencing cognitive impairment, were all treated with Sunosi (solriamfetol) for 2 weeks, and with placebo for 2 weeks, with the treatment periods separated by 1 week of down-titration and washout. Patients were randomized in a 1:1 ratio either to treatment with Sunosi followed by placebo (sequence 1), or to treatment with placebo followed by Sunosi (sequence 2). Sunosi was administered orally once daily, starting at 75 mg per day for the first three days and 150 mg per day for the remainder of the 2-week treatment period. The primary outcome measure was the Digit Symbol Substitution Test subtest of the Repeatable Battery for the Assessment of Neuropsychological Status (DSST RBANS). The Digit Symbol Substitution subtest is also referred to as "Coding." The prespecified primary endpoint was the change from baseline in cognitive function as measured by the DSST RBANS after 2 weeks of treatment (average of the 2-, 4-, 6-, and 8-hour post-dose DSST RBANS scores). Secondary endpoints included patient reported measures of cognition including the British Columbia Cognitive Complaints Inventory (BC-CCI) and the Patient Global Impression of Severity (PGI-S) for cognitive symptoms; and the Epworth Sleepiness Scale (ESS) to measure wakefulness. The secondary endpoints were analyzed in a pre-specified testing sequence. All analyses were conducted on an intent-to-treat basis.

About Sunosi® (solriamfetol)

Sunosi is a dual-acting dopamine and norepinephrine reuptake inhibitor indicated to improve wakefulness in adult patients with excessive daytime sleepiness (EDS) associated with narcolepsy or obstructive sleep apnea (OSA). Sunosi received U.S. Food and Drug Administration approval on March 20, 2019 to improve wakefulness in adult patients with EDS associated with narcolepsy or OSA and was designated a Schedule IV medicine by the U.S. Drug Enforcement Agency on June 17, 2019. SK Biopharmaceuticals Co., Ltd., the discoverer of the compound, maintains rights in 12 Asian markets, including Korea, China and Japan. Sunosi has orphan drug designation for narcolepsy in the United States. Sunosi is protected by a robust patent estate with expiries out to 2040. Sunosi is not approved by the FDA for improving cognitive function in patients with EDS due to OSA.

More information about Sunosi, including Full Prescribing Information and Medication Guide, is available here: https://sunosihcp.com/assets/files/sunosi-medication-guide.pdf.

Important Safety Information

SUNOSI (solriamfetol) is available in 75 mg and 150 mg tablets and is a federally controlled substance (CIV) because it contains solriamfetol that can be a target for people who abuse prescription medicines or street drugs. Keep SUNOSI in a safe place to protect it from theft. Never give or sell your SUNOSI to anyone else because it may cause death or harm them and it is against the law. Tell your doctor if you have ever abused or been dependent on alcohol, prescription medicines, or street drugs.

Before taking SUNOSI, tell your doctor about all of your medical conditions, including if you:

- have heart problems, high blood pressure, kidney problems, diabetes, or high cholesterol.
- have had a heart attack or a stroke.
- have a history of mental health problems (including psychosis and bipolar disorders), or of drug or alcohol abuse or addiction.
- are pregnant or planning to become pregnant. It is not known if SUNOSI will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if SUNOSI passes into your breast milk. Talk to your doctor about the best way to feed your baby if you take SUNOSI.

What are the possible side effects of SUNOSI?

SUNOSI may cause serious side effects, including:

- **Increased blood pressure and heart rate.** SUNOSI can cause blood pressure and heart rate increases that can increase the risk of heart attack, stroke, heart failure, and death. Your doctor should check your blood pressure before, and during, treatment with SUNOSI. Your doctor may decrease your dose or tell you to stop taking SUNOSI if you develop high blood pressure that does not go away during treatment with SUNOSI.
- **Mental (psychiatric) symptoms including anxiety, problems sleeping (insomnia), irritability, and agitation.** Tell your doctor if you develop any of these symptoms. Your doctor may change your dose or tell you to stop taking SUNOSI if you develop side effects during treatment with SUNOSI.

The most common side effects of SUNOSI include:

- headache
- decreased appetite
- problems sleeping
- nausea
- anxiety

These are not all the possible side effects of SUNOSI. Call your doctor for advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please find full Prescribing Information here: https://sunosihcp.com/assets/files/sunosi-pi.pdf

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About Obstructive Sleep Apnea, Excessive Daytime Sleepiness, and Associated Cognitive Impairment

Obstructive sleep apnea, commonly referred to as sleep apnea, is a highly prevalent disease (as high as 14% in men and 5% in women) in which excessive daytime sleepiness is a major presenting complaint in many cases. Positive Airway Pressure (PAP) therapy, with its most common form being Continuous Positive Airway Pressure (CPAP), has been shown to be an effective therapy for sleep apnea that frequently results in improvement in excessive daytime sleepiness in many patients; however, not all patients tolerate CPAP therapy and among those who tolerate CPAP, usage is highly variable. Excessive daytime sleepiness may persist in people with sleep apnea despite using CPAP. Cognitive impairment is a common and disruptive symptom in patients with EDS associated with OSA, that may be experienced in the vast majority of patients[4].

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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References

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