Axsome Therapeutics, Inc. Logo

# Axsome Therapeutics Reports Fourth Quarter and Full Year 2017 Financial Results and Provides Business Update

March 7, 2018

*Interim analyses of STRIDE-1 and ADVANCE-1 trials of AXS-05 anticipated in 2018*

*Company to host conference call today at 8:00 AM Eastern*

NEW YORK, March 07, 2018 (GLOBE NEWSWIRE) -- Axsome Therapeutics, Inc. (NASDAQ:AXSM), a clinical-stage biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders, today reported financial results for the fourth quarter and year ended December 31, 2017.

"In 2017 we significantly expanded our pipeline and now have five CNS product candidates which are in or are about to enter late-stage clinical trials in five different indications. We continued this momentum into 2018 with the recent announcement of our AXS-09 product candidate, which incorporates chirally pure esbupropion and dextromethorphan," said Herriot Tabuteau, M.D., Chief Executive Officer of Axsome. "In 2018 we are focused on the advancement of our ongoing registration trials of AXS-05, STRIDE-1 for treatment resistant depression and ADVANCE-1 for agitation associated with Alzheimer's disease, and on the launch of our planned Phase 3 trial of AXS-07 for migraine. Importantly, we have now incorporated two interim analyses into both the STRIDE-1 and ADVANCE-1 trials. In each trial, the first interim analysis will be to assess futility and the second will be to assess efficacy. Because these analyses could result in stopping the trials early for efficacy or futility, they provide the possibility for accelerated value creation and represent continued prudent capital resource management. We anticipate both STRIDE-1 interim analyses and the first ADVANCE-1 interim analysis this year."

**Pipeline Update**

Axsome is developing a portfolio of differentiated, patent-protected, central nervous system (CNS) product candidates. CNS disorders are underserved, difficult-to-treat, distressing to patients and caregivers, with many having no approved or satisfactory treatment options. Axsome accelerates the development of new CNS medicines in a cost-efficient manner, by utilizing novel mechanisms of action and novel delivery approaches of well-characterized molecules, combined with human proof-of-concept data and innovative clinical trial designs. Our pipeline currently includes five clinical-stage product candidates.

- **AXS-05:** Axsome is evaluating AXS-05 (bupropion and dextromethorphan) in three separate indications: treatment resistant depression (TRD), agitation associated with Alzheimer's disease (AD), and smoking cessation. AXS-05 is a novel, oral, fixed-dose combination of dextromethorphan (an NMDA receptor antagonist, sigma-1 receptor agonist, and serotonin and norepinephrine reuptake inhibitor) and bupropion (a norepinephrine and dopamine reuptake inhibitor, which also increases the bioavailability of dextromethorphan), under development for the treatment of CNS disorders. AXS-05 has been granted U.S. Food and Drug Administration (FDA) Fast Track designations for the treatment of TRD and for the treatment of agitation associated with AD.

  **TRD:** Axsome is actively enrolling the STRIDE-1 study, a Phase 3, multicenter, randomized, double-blind, active-controlled trial to assess the efficacy and safety of AXS-05 in TRD, defined as major depressive disorder which has failed to respond to two or more antidepressant treatments.

  Two interim analyses, to be conducted by an independent data monitoring committee (IDMC), are now planned for the STRIDE-1 study. The first interim analysis will be performed on the first approximately 40% of the target number of subjects to assess futility. The second interim analysis will be performed on the first approximately 60% of the target number of subjects to assess efficacy. To date over 40% of the target number of subjects have been randomized. Therefore the results of the first interim analysis are expected in the second quarter of 2018.

  **Agitation associated with AD:** Axsome is actively enrolling the ADVANCE-1 study, a Phase 2/3, multicenter, randomized, double-blind, controlled trial to evaluate the efficacy and safety of AXS-05 in patients with agitation associated with AD.

  ADVANCE-1 incorporates two interim analyses to be performed by an IDMC. The first interim analysis will be performed on the first approximately 30% of the target number of subjects to assess futility. The second interim analysis will be performed on the first approximately 60% of the target number of subjects to assess efficacy. Results of the first interim analysis are expected in the second half of 2018.

  **Smoking Cessation:** In December 2017, Axsome entered into a research collaboration with Duke University to evaluate AXS-05 in a Phase 2 clinical trial in smokers attempting to quit. The planned study will be a randomized, double-blind, controlled trial evaluating the impact of AXS-05 on smoking behavior, and will be conducted at the Duke Center for Smoking Cessation. Initiation of this trial is anticipated in the first half of 2018.

- **AXS-09:** In February 2018, Axsome announced positive topline results from a Phase 1 pharmacokinetic study of AXS-09 (esbupropion and dextromethorphan), which is being developed for the treatment of CNS disorders. AXS-09 contains the

chirally pure *S*-enantiomer of bupropion, as compared to Axsome's first generation product candidate AXS-05 (bupropion and dextromethorphan), which contains racemic bupropion (equal amounts of the *S*- and *R*-enantiomers). AXS-09 resulted in substantial increases in dextromethorphan plasma concentrations, the trial's primary endpoint, into a potentially therapeutic range with repeated dosing ($p<0.0001$ day 1 versus day 8). The increased plasma concentrations of dextromethorphan after dosing with AXS-09 were comparable to those achieved with AXS-05 (bupropion and dextromethorphan). Results of this Phase 1 trial coupled with preclinical data also indicate the potential for enhanced absorption and therapeutic effect of the *S*-enantiomer as compared to the *R*-enantiomer. AXS-09 was well tolerated with no serious adverse events reported in the trial. AXS-09 provides Axsome with another attractive product candidate that warrants evaluation in future CNS indications.

- **AXS-07:** Axsome is developing AXS-07 for the acute treatment of migraine. AXS-07 is an oral, fixed-dose combination 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 results in rapid absorption of meloxicam while maintaining a long plasma half-life. Rizatriptan has demonstrated strong efficacy in the treatment of migraine as a single agent. The distinct mechanism of action and rapid absorption of MoSEIC meloxicam, combined with the known efficacy of rizatriptan, is expected to result in rapid, superior and consistent relief of migraine pain, with lower symptom recurrence, as compared to currently available therapies.

  Axsome has received Pre-Investigational New Drug Application (Pre-IND) written guidance from the FDA on a proposed clinical developmental program for AXS-07 including a planned Phase 3 trial. Based on this guidance, Axsome believes that only one Phase 3 trial may be needed for the approval of AXS-07 for the treatment of migraine. Axsome anticipates starting this trial in 2018.

- **AXS-02:** Axsome is developing AXS-02 (disodium zoledronate tetrahydrate) in two separate indications: knee osteoarthritis (OA) associated with bone marrow lesions (BMLs), and chronic low back pain (CLBP) associated with Modic changes (MCs). AXS-02 was also being developed in complex regional pain syndrome (CRPS). AXS-02 is a potent osteoclast inhibitor being developed as an oral, non-opioid, targeted, potentially first-in-class therapeutic for chronic pain. AXS-02 has been granted FDA Fast Track designation for the treatment of knee OA associated with BMLs.

  **Knee OA associated with BMLs:** In January 2018, an interim analysis for efficacy in the Phase 3 COAST-1 trial of AXS-02 for the treatment of the pain of knee OA associated with BMLS was conducted by an IDMC. The IDMC recommended that the trial be continued to full enrollment. The IDMC also reviewed the available safety information in the study and confirmed that AXS-02 was safe and generally well tolerated. Screening in the trial was paused pending the results of the interim analysis and is anticipated to resume after the final readout from the STRIDE-1 trial, as previously disclosed.

  **CRPS:** In January 2018, an interim analysis for efficacy in the Phase 3 CREATE-1 trial of AXS-02 in patients for CRPS was conducted by an IDMC. The IDMC recommended that the trial be stopped for futility. In the trial, AXS-02 treatment resulted in a significant reduction of serum CTx, a marker of bone resorption, as compared to placebo ($p<0.0001$). Further analysis of the data from the CREATE-1 trial will continue in order to better understand the basis for the outcome of that trial and to inform the ongoing clinical development of AXS-02. The IDMC also reviewed the available safety information in the study and confirmed that AXS-02 was safe and generally well tolerated.

- **AXS-06:** Axsome is developing AXS-06 (MoSEIC meloxicam and esomeprazole) for the relief of the signs and symptoms of OA and Rheumatoid Arthritis (RA), and the reduction in the risk of developing upper gastrointestinal ulcers in patients at risk of developing nonsteroidal anti-inflammatory drug (NSAID) associated upper gastrointestinal ulcers. AXS-06 is an oral, non-opioid, rapidly-absorbed, once-daily, COX-2 preferential pain therapeutic with a gastroprotectant. Axsome received Pre-IND written guidance from the FDA on a proposed clinical developmental program for AXS-06. Based on this guidance, Axsome believes that AXS-06 is Phase 3-ready.

**Corporate Update**

- In December 2017, Axsome completed a registered direct offering of common stock and warrants exercisable for shares of its common stock, raising gross proceeds of approximately $9.5 million.

**Anticipated Clinical Milestones**

- **Clinical Trial Initiations:**
  - Phase 2 clinical trial of AXS-05 in smoking cessation, Duke University collaboration (1H 2018)
  - Phase 3 clinical trial of AXS-07 in migraine (2018)

- **Clinical Trial Readouts:**
    - Phase 3 STRIDE-1 trial of AXS-05 in TRD, interim analysis (2Q 2018)
    - Phase 3 STRIDE-1 trial of AXS-05 in TRD, interim efficacy analysis (2H 2018)
    - Phase 2/3 ADVANCE-1 trial of AXS-05 in AD agitation, interim analysis (2H 2018)
    - Phase 3 STRIDE-1 trial of AXS-05 in TRD, top-line data (2H 2018 – 1H 2019)
    - Phase 2/3 ADVANCE-1 trial of AXS-05 in AD agitation, interim efficacy analysis (2019)
    - Phase 2/3 ADVANCE-1 trial of AXS-05 in AD agitation, top-line data (2H 2019 – 1H 2020)

**Fourth Quarter 2017 Financial Results**

- **Research and development (R&D) expenses:** R&D expenses were $4.5 million for the quarter ended December 31, 2017 and $20.0 million for the year ended December 31, 2017 compared to $5.8 million and $21.2 million for the comparable periods in 2016. The decrease in R&D expenses was primarily due to lower costs of previously initiated clinical trials, offset by the initiation of the ADVANCE-1 study as well as an increase in personnel and stock compensation costs.
- **General and administrative (G&A) expenses:** G&A expenses were $2.0 million for the quarter ended December 31, 2017 and $7.2 million for the year ended December 31, 2017 compared to $1.8 million and $6.3 million for the comparable periods in 2016. The increase in G&A expenses was primarily due to higher intellectual property costs, stock compensation expense and placement agent expenses associated with the December 2017 registered direct offering.
- **Net loss:** Net loss was $7.4 million, or $(0.31) per share for the quarter ended December 31, 2017, compared to a net loss of $7.3 million, or $(0.38) per share for the comparable period in 2016. Net loss for the year ended December 31, 2017 was $28.9 million, or $(1.27) per share, compared to a net loss of $27.2 million, or $(1.42) per share for the comparable period in 2016.
- **Cash:** At December 31, 2017, Axsome had $34.0 million of cash compared to $36.6 million of cash at December 31, 2016.
- **Shares outstanding:** At December 31, 2017, Axsome had 25,492,992 shares of common stock outstanding.
- **Financial guidance:** Axsome believes that its cash at December 31, 2017 will be sufficient to fund the company's anticipated operations, based on its current operating plans, into the third quarter of 2019.

**Conference Call Information**

Axsome will host a conference call and webcast today at 8:00 AM Eastern to discuss fourth quarter and full year 2017 financial results as well as to provide a corporate update. To participate in the live conference call, please dial (844) 698-4029 (toll-free domestic) or (647) 253-8660 (international), and use the passcode 8787609. The 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 Axsome Therapeutics, Inc.**

Axsome Therapeutics, Inc. is a clinical-stage biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders for which there are limited treatment options. Axsome's product candidate portfolio includes five clinical-stage candidates, AXS-02, AXS-05, AXS-06, AXS-07, and AXS-09. AXS-05 is currently in a Phase 3 trial in treatment resistant depression (TRD) and a Phase 2/3 trial in agitation associated with Alzheimer's disease (AD). AXS-05 is also being developed for smoking cessation. AXS-02 is currently in a Phase 3 trial in knee osteoarthritis (OA) associated with bone marrow lesions (BMLs) with an additional Phase 3 trial planned in chronic low back pain (CLBP) associated with Modic changes (MCs). AXS-07 is being developed for the acute treatment of migraine. AXS-06 is being developed for the treatment of osteoarthritis and rheumatoid arthritis and for the reduction of the risk of NSAID-associated gastric ulcers. AXS-02, AXS-05, AXS-06, AXS-07, and AXS-09 are investigational drug products not approved by the FDA. For more information, please visit the company website at www.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". 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 success, timing and cost of the Company's ongoing clinical trials and anticipated clinical trials for its current product candidates, including statements regarding the timing of initiation, interim analyses and completion of the trials; the timing of and the Company's ability to obtain and maintain U.S. Food and Drug Administration or other regulatory authority approval of, or other action with respect to, its product candidates; 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; 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.

**Axsome Therapeutics, Inc.**
**Selected Consolidated Financial Data**

**Statements of Operations Information:**

| | Three Months Ended December 31, | | Twelve Months Ended December 31, | |
|---|---|---|---|---|
| | **2017** | **2016** | **2017** | **2016** |
| Operating expenses: | | | | |
| Research and development | $ 4,493,910 | $ 5,806,771 | $ 19,957,616 | $ 21,199,860 |
| General and administrative | 1,950,210 | 1,818,789 | 7,206,691 | 6,343,648 |
| Total operating expenses | 6,444,120 | 7,625,560 | 27,164,307 | 27,543,508 |
| Loss from operations | (6,444,120) | (7,625,560) | (27,164,307) | (27,543,508) |
| Interest and amortization of debt discount/premium (expense) income | (340,381) | (177,657) | (1,340,199) | (132,424) |
| Tax credit | 0 | 474,279 | 207,114 | 474,279 |
| Change in fair value of warrant liability | (646,000) | 0 | (646,000) | 0 |
| Net loss | $ (7,430,501) | $ (7,328,938) | $ (28,943,392) | $ (27,201,653) |
| Net loss per common share – basic and diluted | $ (0.31) | $ (0.38) | $ (1.27) | $ (1.42) |
| Weighted average common shares outstanding – basic and diluted | 24,229,652 | 19,153,993 | 22,764,606 | 19,150,690 |

**Balance Sheet Information:**

| | **December 31, 2017** | **December 31, 2016** |
|---|---|---|
| Cash | $ 34,021,123 | $ 36,618,497 |
| Total assets | 35,555,564 | 38,212,608 |
| Loan payable, current and long-term | 9,932,351 | 9,739,607 |
| Accumulated deficit | (76,584,843) | (47,641,451) |
| Stockholders' equity | $ 16,717,223 | $ 21,571,451 |

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