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

March 7, 2018
Date of report (Date of earliest event reported)

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.)

25 Broadway, 9th Floor **New York, New York** (Address of principal executive offices)	**10004** (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 is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425).
o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12).
o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)).
o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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 x

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. x

Item 2.02. Results of Operations and Financial Condition

On March 7, 2018, Axsome Therapeutics, Inc. (the "Company") issued a press release announcing its financial results for the three months and fiscal year ended December 31, 2017 and an update on the Company's operations. The Company is furnishing a copy of the press release, which is attached hereto as Exhibit 99.1.

In accordance with General Instruction B.2 of Form 8-K, the information included in Item 2.02 of this Current Report on Form 8-K (including Exhibit 99.1 hereto), shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any filing made by the Company under the Exchange Act or Securities Act of 1933, as amended, except as shall be expressly set forth by specific reference in such a filing.

Item 8.01. Other Events

On March 7, 2018, the Company updated its presentation slide deck. Attached as Exhibit 99.2 to this Current Report on Form 8-K is a copy of the presentation slide deck.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Press release dated March 7, 2018.
99.2	Corporate Presentation.

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 hereunto duly authorized.

Axsome Therapeutics, Inc.

Dated: March 7, 2018

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

AXSOME THERAPEUTICS

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

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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NASDAQ: AXSM

AXSOME THERAPEUTICS

March 2018

Forward-Looking Statements & Safe Harbor

Certain information contained in this presentation may include "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. 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 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 and completion of the trials, interim analyses and receipt of interim results; the timing of and our ability to obtain and maintain U.S. Food and Drug Administration or other regulatory authority approval of, or other action with respect to, our product candidates; the Company's ability to obtain additional capital necessary to fund its operations; the Company's ability to generate revenues in the future; 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; the enforceability 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. These factors could cause actual results and developments to be materially different from those expressed in or implied by such statements. Forward-looking statements are not guarantees of future performance, and actual results may differ materially from those projected. The forward-looking statements are made only as of the date of this presentation and the Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstance.

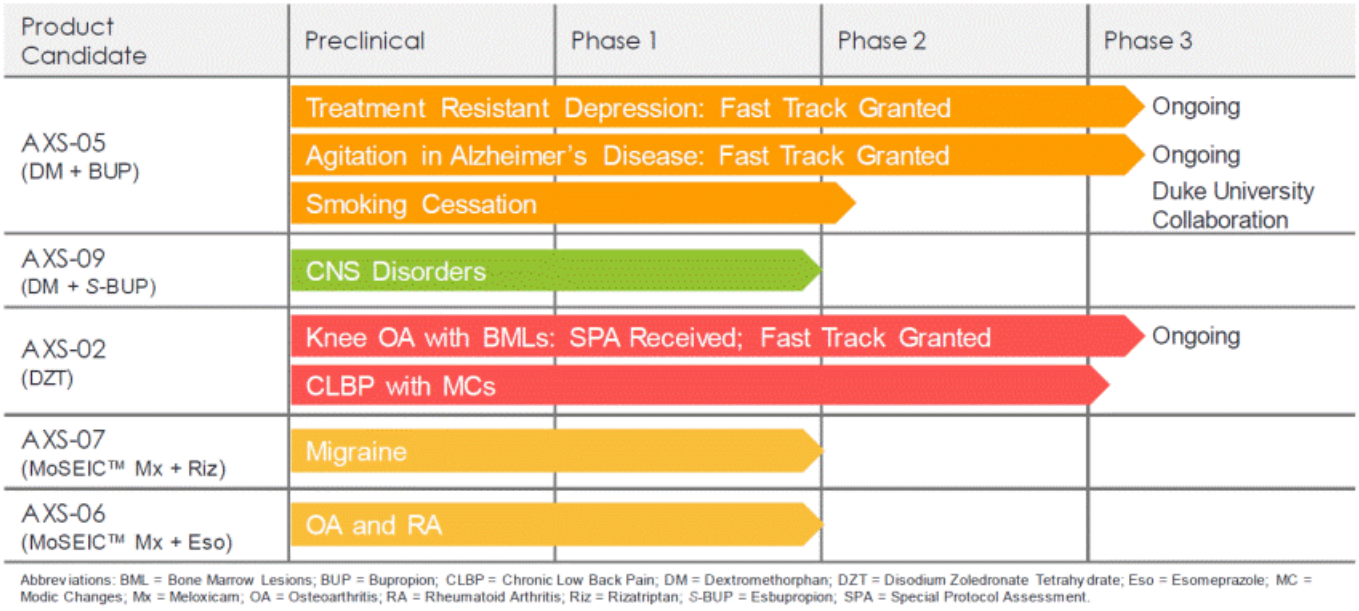
This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation. In addition, these projections, assumptions and estimates are necessarily subject to a high degree of uncertainty and risk.

Developing novel therapies for CNS disorders.

Axsome is addressing growing markets, where current treatment options are limited or inadequate, by leveraging well-characterized compounds to create novel therapeutics to meet unmet medical needs and improve the lives of patients.

Our Candidates and Pipeline

- Five differentiated clinical-stage assets targeting significant and growing markets.
- Patent protection to 2034, Worldwide rights.



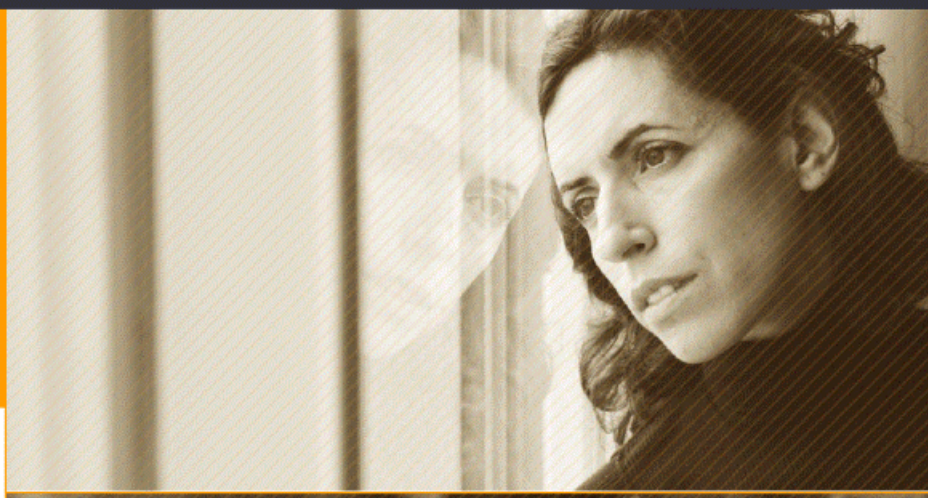
Abbreviations: BML = Bone Marrow Lesions; BUP = Bupropion; CLBP = Chronic Low Back Pain; DM = Dextromethorphan; DZT = Disodium Zoledronate Tetrahydrate; Eso = Esomeprazole; MC = Modic Changes; Mx = Meloxicam; OA = Osteoarthritis; RA = Rheumatoid Arthritis; Riz = Rizatriptan; *S*-BUP = Esbupropion; SPA = Special Protocol Assessment.

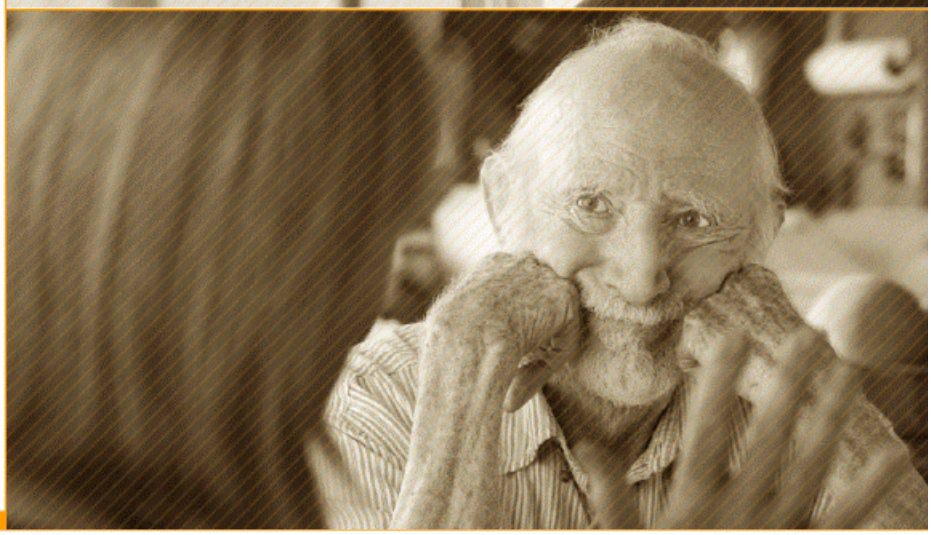
AXS-05

Dextromethorphan (DM) + Bupropion (BUP)

Novel therapy for CNS disorders:

- Treatment Resistant Depression (TRD)
- Agitation in Alzheimer's Disease (AD)





CNS Disorders:
Mechanisms of Action

	Pharmacodynamic Synergy		
Mechanism of Action	DM	BUP	AXS-05 DM+BUP
NMDA Receptor Antagonist	✓		✓
Sigma-1R Agonist	✓		✓
Norepinephrine Reuptake Inhibitor	✓	✓	✓
Serotonin Reuptake Inhibitor	✓		✓
Dopamine Reuptake Inhibitor		✓	✓
Nicotinic ACh Receptor Antagonist		✓	✓

DM = Dextromethorphan; BUP = Bupropion. ✓ Present

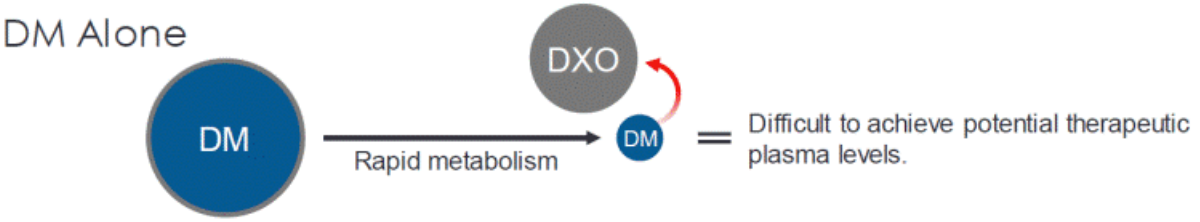
CNS Disorders:
Mechanisms of Action and Relevant Indications

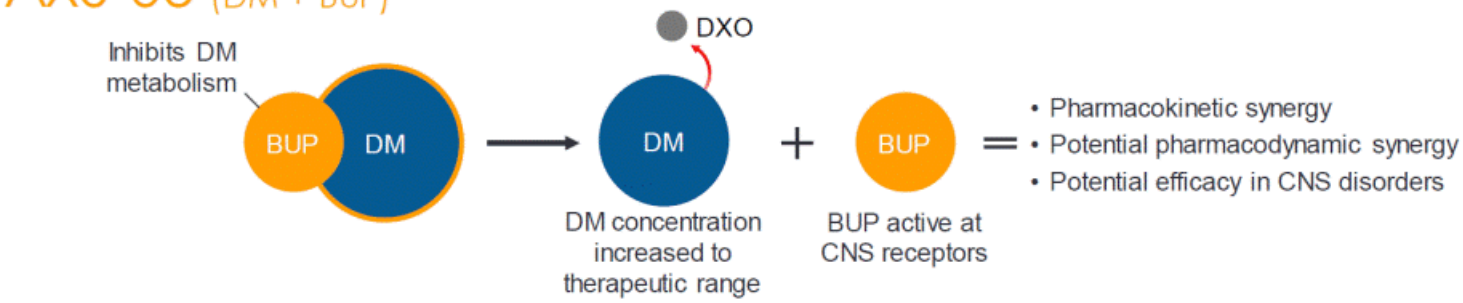
Mechanism of Action	Pharmacodynamic Synergy: DM	BUP	AXS-05 DM+BUP	Relevant Indications[1]: ADHD	Anxiety	Alzheimer's	Depression	Fibromyalgia	OCD	Pain	Smoking cessation	Related Agents[2]
NMDA Receptor Antagonist	✓		✓			▨	▨			▨		• Ketamine • Memantine (Namenda®)
Sigma-1R Agonist	✓		✓			▨	▨		▨			• Fluvoxamine (Luvox®) • Donepezil (Aricept®)
Norepinephrine Reuptake Inhibitor	✓	✓	✓				▨	▨		▨		• Duloxetine (Cymbalta®) • Venlafaxine (Effexor®)
Serotonin Reuptake Inhibitor	✓		✓		▨		▨		▨			• Escitalopram (Lexapro®) • Fluoxetine (Prozac®) • Sertraline (Zoloft®)
Dopamine Reuptake Inhibitor		✓	✓	▨			▨				▨	• Bupropion (Wellbutrin®)
Nicotinic ACh Receptor Antagonist		✓	✓	▨			▨				▨	• Bupropion (Wellbutrin®)

DM = Dextromethorphan; BUP = Bupropion. ✓ Present ▨ Relevant

1. Indications listed are associated with the mechanism of action and are not related to either DM or BUP, unless specifically noted.
2. Agents do not contain DM or BUP, unless specifically noted.

CNS Disorders:
Novel Therapy for CNS Disorders





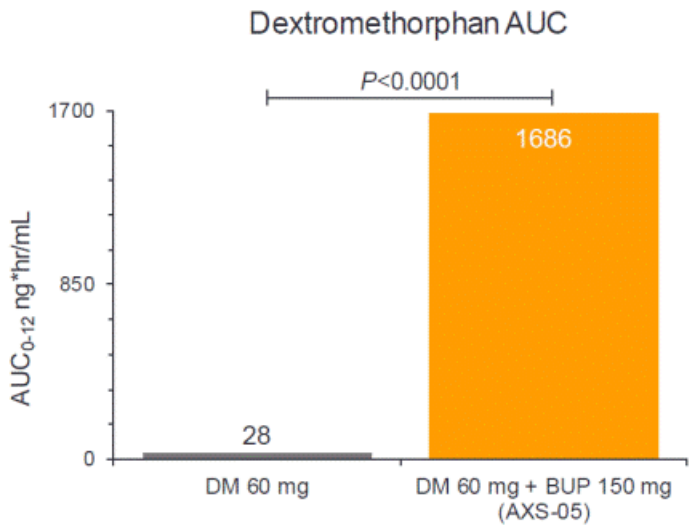
DM = Dextromethorphan; DXO = Dextrorphan; BUP = Bupropion.

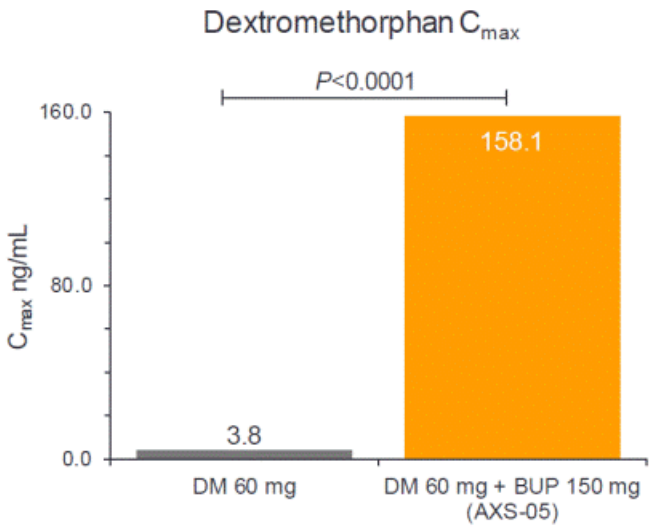
- Phase 1 trials with AXS-05 completed:
  - Significant increase in DM plasma levels.
- Phase 3 trials in TRD and AD Agitation initiated.

IP Overview

- 24 issued patents – protection through 2034.

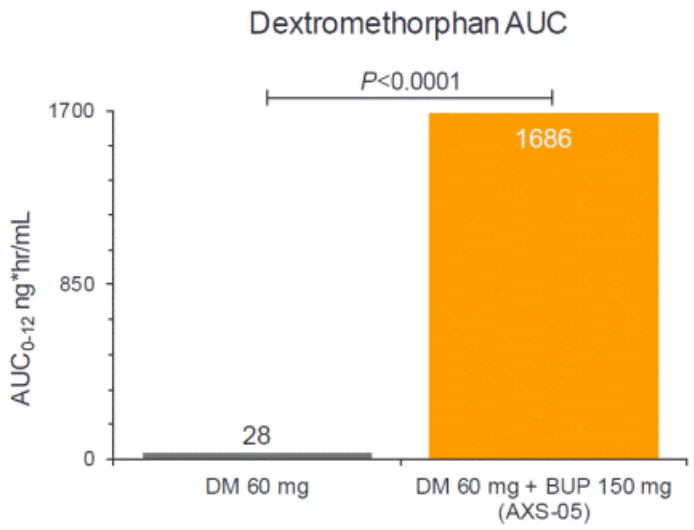
CNS Disorders:
Phase 1 Results

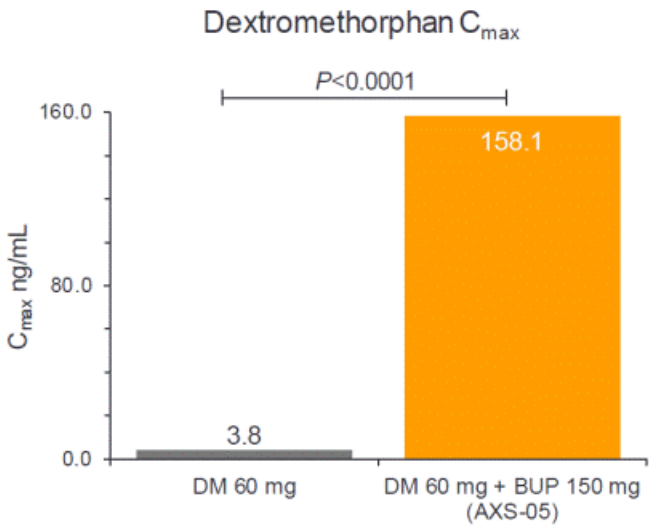




Axsome data on file.
†DM, Dextromethorphan; BUP, Bupropion.

CNS Disorders:
Phase 1 Results





Dose†	AUC_{0-12} ng*hr/mL
DM 20 mg + Q 10 mg	525
DM 30 mg + Q 10 mg	883

Dose†	C_{max} ng/mL
DM 20 mg + Q 10 mg	53
DM 30 mg + Q 10 mg	85

Axsome data on file.
† Nuedexta® NDA 021879, FDA Clinical Pharmacology Review.
DM, Dextromethorphan; Q, Quinidine; BUP, Bupropion.

CNS Disorders:
TRD Overview

- Major Depressive Disorder (MDD) is a leading cause of disease burden in the US.[4]
- 63% and 44% of MDD patients have inadequate response to initial therapy and second line therapy, respectively.[2]
- Only 1 approved drug for TRD = unmet medical need.
- AXS-05 combines the MOA of 4 distinct anti-depressant drug classes into one novel oral therapeutic.
- DM antidepressant effects demonstrated preclinically and clinically.
- Phase 3 ongoing.

3M patients in the U.S.[1-3]

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-05 (DM + BUP)	Treatment Resistant Depression: Fast Track Granted			Initiated

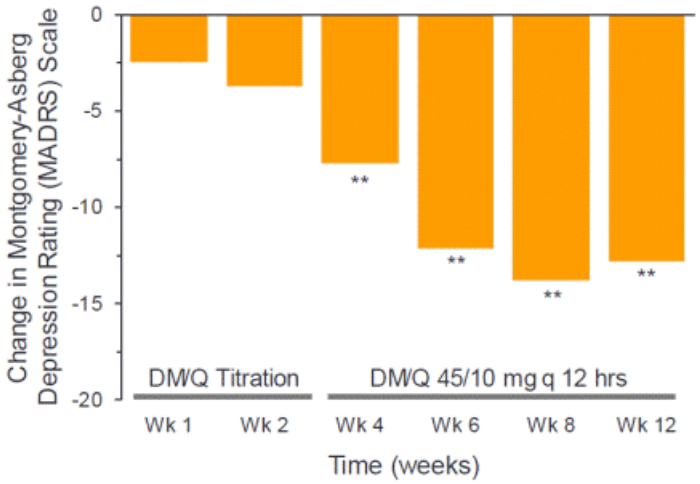
Abbreviations: DM = Dextromethorphan; BUP = Bupropion.

1. Marcus SC, Olfson M. *Arch Gen Psychiatry* 2010;67:1265-1273.
2. Rush AJ, et al. *Am J Psychiatry* 2006;163:1905-1917.
3. U.S. Census Bureau, Population April 1, 2010 to July 1, 2013.
4. Mathers CD, *PLoS Med* 2006; 3(11): e442.

CNS Disorders:
TRD Clinical Rationale

- DM and metabolic inhibitor reduce depressive symptoms in TRD and in AD.

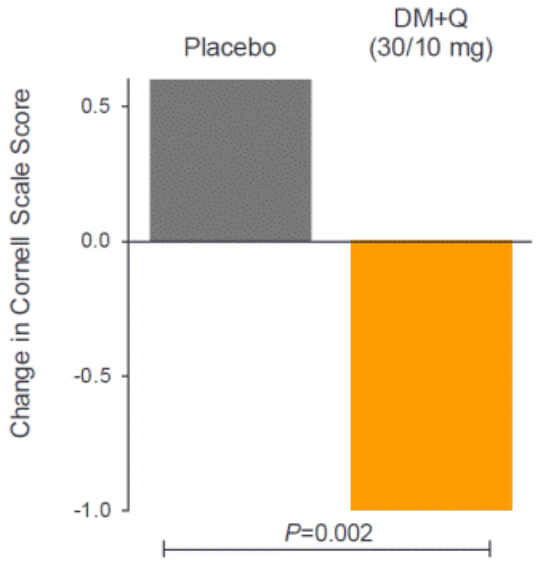
Symptom Reduction in TRD Patients Treated with DM and Metabolic Inhibitor[1]



- Failed 2 to 10 prior treatments
- 45% of patients had ≥ 50% reduction in MADRS

** *P*<0.01 versus baseline

Depressive Symptom Reduction in AD Agitation Patients Treated with DM and Metabolic Inhibitor[2]

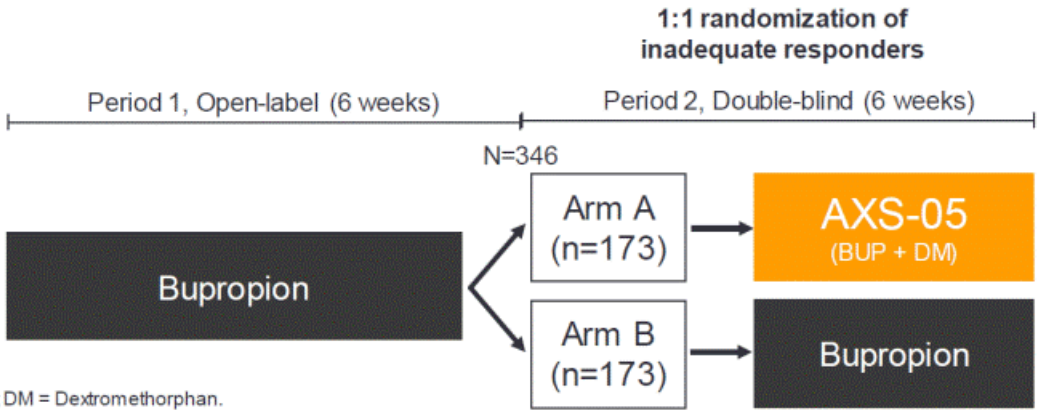


1. Murrough J, et al. *J Affect Disord*. 2017;218:277-283.
2. Cummings J, et al. *JAMA*. 2015;314:1242-1254.

CNS Disorders:
TRD Phase 3 Design

Stride1Study AXS-05

A Phase 3 trial to assess the efficacy and safety of AXS-05 in the treatment of TRD.

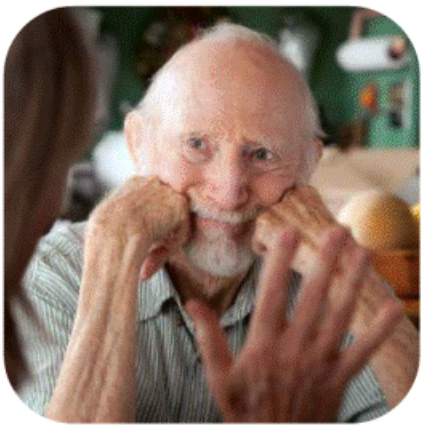


BUP = Bupropion; DM = Dextromethorphan.

- **Primary Endpoint:** Change in depression score from randomization to end of study, measured using the Montgomery-Asberg Depression Rating Scale (MADRS).
- **Key Inclusion Criteria:**
  - Male or female 18-65 years old
  - History of inadequate response to 1 or 2 adequate antidepressant treatments
- Two interim analyses planned.

CNS Disorders:
Agitation in AD Overview

- Agitation and aggression seen in approximately 45% of AD patients during 5-year period.[3]
- Characterized by emotional distress, aggressive behaviors, disruptive irritability, disinhibition, and caregiver burden.[4]
- Associated with[4,5]:
  - Accelerated cognitive decline
  - Earlier nursing home placement
  - Increased mortality
- No approved medication = unmet medical need.
- Proof of concept: DM plus metabolic inhibitor reduced agitation in AD patients.
- Phase 2/3 ongoing.



2M patients in the U.S.[1,2]

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-05 (DM + BUP)	Agitation in Alzheimer's Disease: Fast Track Granted			Initiated

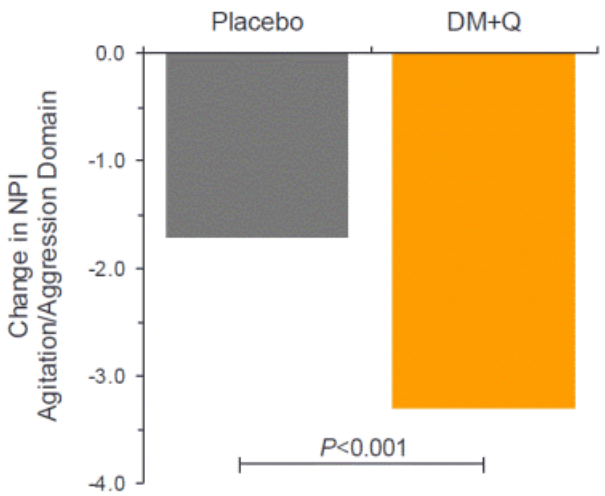
Abbreviations: DM = Dextromethorphan; BUP = Bupropion.

1. Ryu, SH, et al. *Am J Geriatr Psychiatry*. 2005;13:976-983.
2. Hebert, LE, et al. *Neurology*. 2013;80:1778-1783.
3. Steinberg M, et al. *Int J Geriatr Psychiatry*. 2008;2:170-177.
4. Antonsdottir IM, et al. *Expert Opin Pharmacother*. 2015;11:1649-1656.
5. Rabins PV et al. Alzheimers Dement. 2013; 9:204-207.

CNS Disorders:
Agitation in AD Clinical Rationale

- Randomized, double-blind, placebo-controlled, two-stage trial.
  - Placebo (n=125), 30 mg DM + 10 mg quinidine (Q) (n=93), for stage 1.
- DM+Q treatment reduced agitation/ aggression in AD by 46% vs. 24% for placebo (P<0.001)—primary endpoint.
- Statistically significant improvement in multiple secondary endpoints.
- DM plasma levels achieved with AXS-05 in target therapeutic range.
- Potential for additional contribution from bupropion component of AXS-05.

Change in Agitation/Aggression Scores in AD with DM and Metabolic Inhibitor Quinidine (Q)

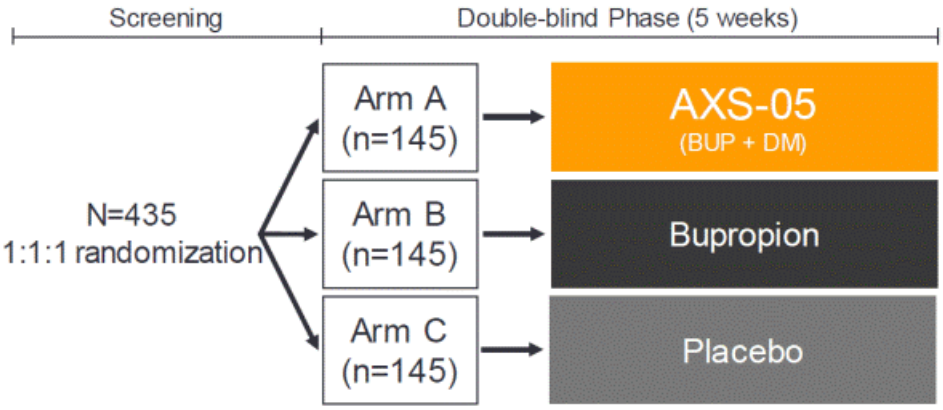


Cummings J, et al. *JAMA*. 2015;314:1242-1254.

CNS Disorders:
Agitation in AD Phase 2/3 Design

ADVANCE STUDY

A Phase 2/3 trial to assess the efficacy and safety of AXS-05 in the treatment of Agitation in AD.

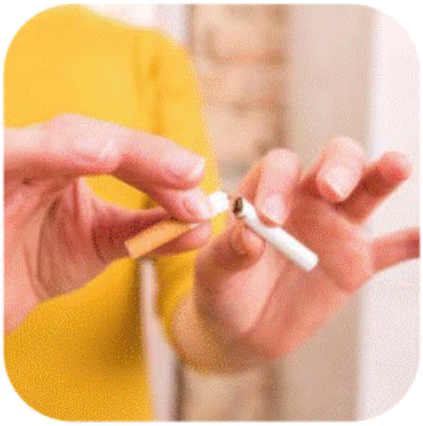


BUP = Bupropion; DM = Dextromethorphan.

- **Primary Endpoint:** Cohen-Mansfield Agitation Inventory (CMAI).
- **Key Inclusion Criteria:**
  - Diagnosis of probable Alzheimer's disease
  - Clinically significant agitation
- Two interim analyses planned.

CNS Disorders:
Smoking Cessation Overview

- Smoking is single largest cause of preventable death in the U.S.[1]
- 70% of smokers want to quit and only 3-5% who attempt to quit without assistance are successful for 6-12 months.[2]
- DM component of AXS-05 significantly reduced nicotine self-administration in nicotine-dependent rats.
- Bupropion component of AXS-05 has been found to be effective for smoking cessation in clinical trials.
- Axsome entered into a research collaboration with Duke University to evaluate AXS-05 in a Phase 2 clinical trial in smokers attempting to quit.
- Phase 2 controlled trial initiation anticipated in 1Q 2018.



40M patients in the U.S.[1]

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-05 (DM + BUP)	Smoking Cessation			Duke University Collaboration

Abbreviations: DM = Dextromethorphan; BUP = Bupropion.

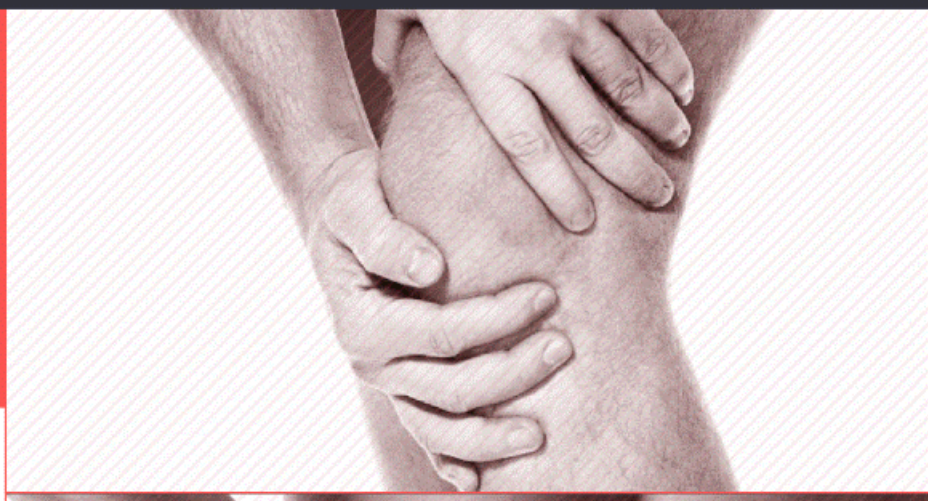
1. U.S. Department of Health and Human Services. The Health Consequences of Smoking: 50 Years of Progress. A Report of the Surgeon General. 2014.
2. Hughes JR, et al. *Addiction*. 2004;99(1):29-38.

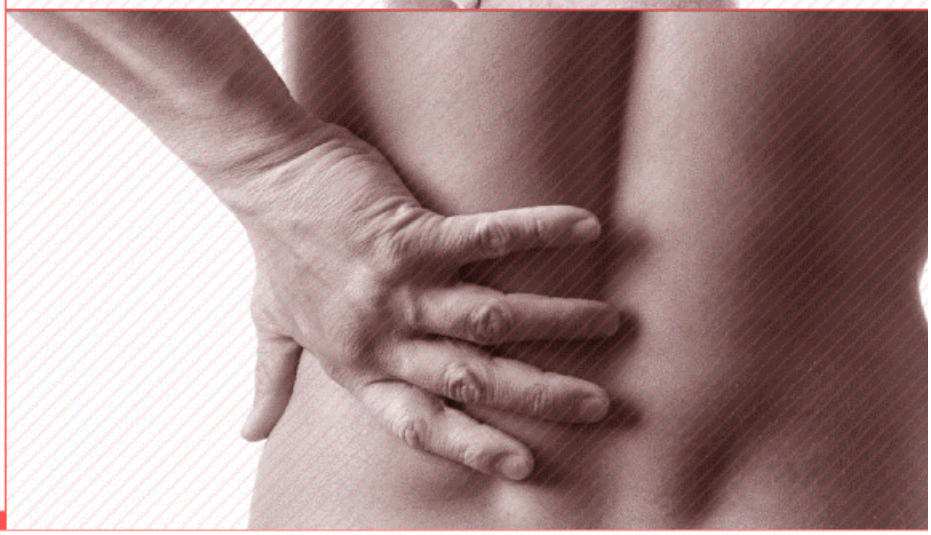
AXS-02

Disodium Zoledronate Tetrahydrate

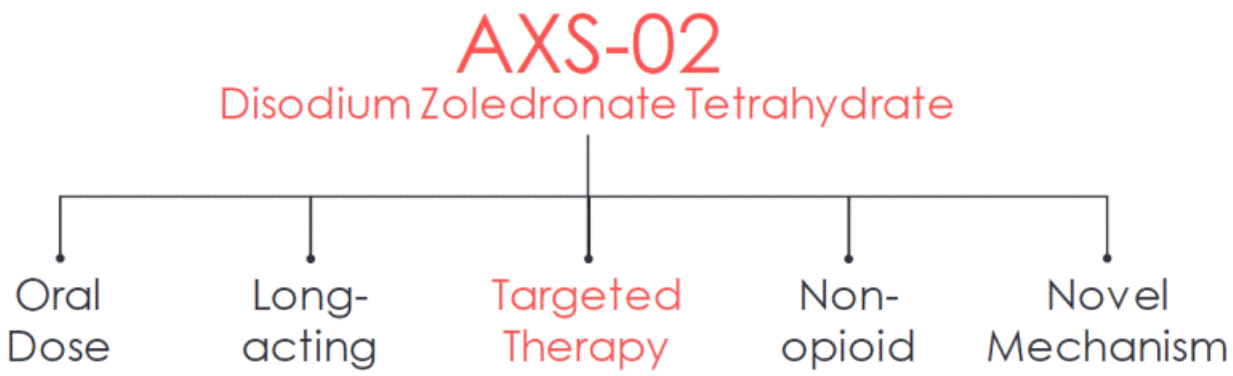
Novel therapy for chronic pain:

- Knee Osteoarthritis (OA) with Bone Marrow Lesions (BMLs)
- Chronic Low Back Pain (CLBP) with Modic Changes (MCs)





Chronic Pain:
Differentiated Therapy



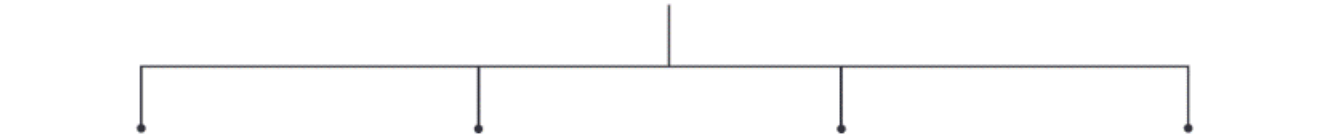
IP Overview

- 75 issued patents* – protection through 2034.
- Drug delivery, pharmacokinetic, composition of matter, and method of use claims.

*Claims cover AXS-02 and related substances and disease indications.

Chronic Pain:
Therapy via Multiple Mechanisms of Action

AXS-02
Disodium Zoledronate Tetrahydrate



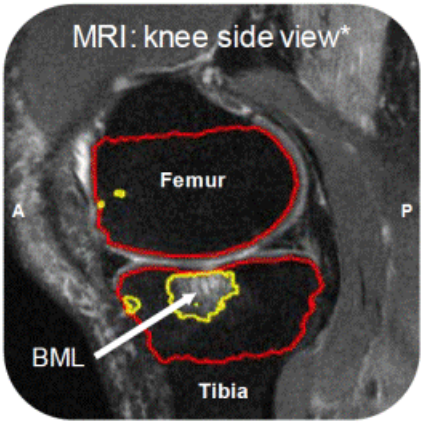
Inhibits bone-resorbing osteoclasts	Downregulates acid-sensing* ion channels	Reduces pro-inflammatory cytokine production	Anti-angiogenic
▼Decreased bone resorption.	▼ASIC1a expression.	▼TNFα production.[4]	▼Angiogenesis.[7]
▼Farnesyl pyrophosphate synthase (FPPS).[1]	▼ASIC activation.[2]	▼IL-6 production.[5]	▼c-FOS expression.[2]
	▼TRPV1 activation.[2,3]	▼IL-8 production.[6]	

* Acid is a well known cause of pain.

1. Green JR, Rogers MJ. *Drug Dev Res*. 2002;55:210-24.
2. Nagae M, et al. *Bone*. 2006;39:1107-15.
3. Abe Y, et al. *J Bone Miner Metab*. 2015;33:125–134.
4. Wolf AM, et al. *Haematologica*. 2006;91:1165-71.
5. Derenne S, et al. *Bone Miner Res*. 1999;14:2048-56.
6. Stathopoulos GT, et al. *Am J Respir Crit Care Med*. 2008;178:50-9.
7. Misso G, et al. *Cancer Biol Ther*. 2012;13:1491-500.

Chronic Pain:
Knee OA with BMLs Overview

- Bone marrow lesions (BMLs) on MRI are associated with pain in knee osteoarthritis (OA).[1]
- BMLs are regions of increased bone turnover, and reduced mineral density.[2,3]
- Zoledronic acid inhibits bone resorption and increases mineral density.
- Phase 3 trial initiated based on positive Phase 2 results with IV zoledronic acid.
- Phase 3 interim analysis: IDMC recommended continuation to full enrollment



7M patients in the U.S.[4-9]

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-02 (DZT)	Knee OA with BMLs: SPA Received; Fast Track Granted			Initiated

Abbreviations: DZT = Disodium Zoledronate Tetrahydrate.

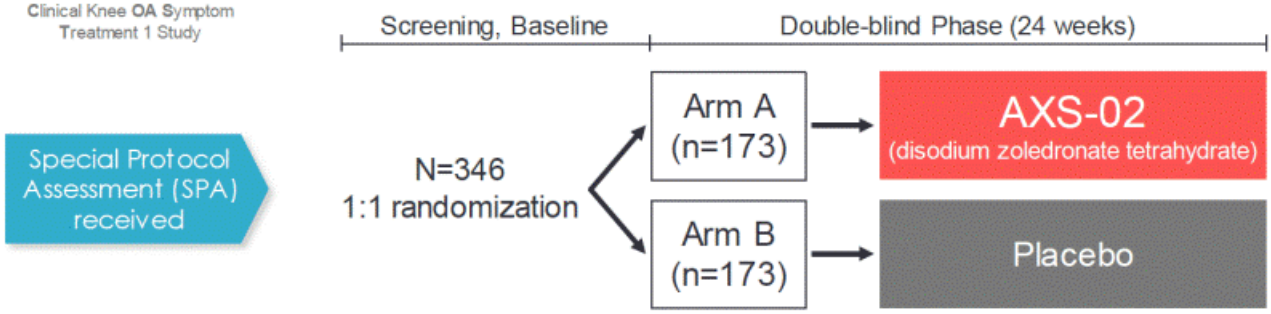
* MRI showing BML in medial tibia from Driban, et al. *Arthritis Res Ther.* 2013;15:R112.
1. Driban JB, et al. *Arthritis Res Ther.* 2013;15:R112.
2. Hunter DJ, et al. *Arthritis Res Ther.* 2009;11:R11.
3. Kazakia GJ, et al. *Osteoarthritis Cartilage.* 2013;21:94-101.
4. Lawrence RC, et al. *Arthritis Rheum.* 2008;58:26-35.
5. Zhang Y, Jordan. *JM Clin Geriatr Med.* 2010;26:355–69.
6. Tanamas SK, et al. *Rheumatology.* 2010;49:2413–19.
7. Guermazi A, et al. *BMJ.* 2012;345:e5339.
8. Jensen OK, et al. *Spine J.* Feb. 14, 2014;pii:S1529-9430(14)00214-9.
9. U.S. Census Bureau, Population April 1, 2010 to July 1, 2013.

AXSOME THERAPEUTICS

Chronic Pain:
Knee OA with BMLs Phase 3 Design

coast-1
Clinical Knee OA Symptom Treatment 1 Study

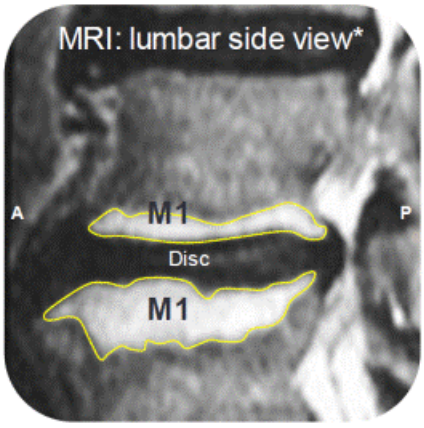
A Phase 3 trial to assess the efficacy and safety of AXS-02 in the treatment of pain of knee OA associated with BMLs.



- **Primary Endpoint:** Change in pain intensity from baseline to week 24, measured using the 0-10 Numerical Rating Scale (NRS).
- **Key Inclusion Criteria:**
  - Male at least 50 years of age or postmenopausal female, with knee OA and BMLs
  - Moderate or worse knee pain
- **Dosage:** Once per week for six weeks; no drug for remainder of double-blind phase.

Chronic Pain:
CLBP with MCs Overview

- Modic changes (MCs) type 1 (M1) on MRI are associated with chronic low back pain (CLBP).[1]
- Increased bone turnover on bone scan is seen in M1 lesions.[2]
- Increased pro-inflammatory cytokines, and vascular density seen in M1 lesions.[3]
- Zoledronic acid reduces bone turnover, suppresses the production of inflammatory mediators, and is anti-angiogenic.
- Phase 2 results: Zoledronic acid reduced pain in patients with CLBP.
- FDA clearance received for IND for Phase 3 trial – initiation planned following readouts from CREATE-1 and STRIDE-1.
- Issued U.S. patents: protection into 2034 – uses of oral zoledronic acid for low back pain.



1.6M patients in the U.S.[4-7]

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-02 (DZT)	CLBP with MCs			

Abbreviations: DZT = Disodium Zoledronate Tetrahydrate.

* MRI showing modic type 1 lesions from Luoma K, et al. *European Congress of Radiology (ECR)*. 2014;Poster B-0458.

1. Zhang Y, et al. *Eur Spine J*. 2008;17:1289-1299.
2. Järvinen J, et al. *Spine: ISSLS Society Meeting Abstracts*. Oct. 2011;Volume Suppl, Abstract GP127.
3. Rahme R, Moussa R. *Am J Neuroradiol*. 2008;29:838–42.
4. Lawrence RC, et al. *Arthritis Rheum*. 2008;58:26-35.
5. Zhang Y, Jordan. *JM Clin Geriatr Med*. 2010;26:355–69.
6. Jensen OK, et al. *Spine J*. Feb. 14, 2014;pii:S1529-9430(14)00214-9. 7. U.S. Census Bureau, Population April 1, 2010 to July 1, 2013.

AXSOME THERAPEUTICS

MoSEIC™ Meloxicam

Novel therapies:

- AXS-07 – Migraine
- AXS-06 – OA and RA

Migraine, OA and RA:
MoSEIC™ Meloxicam Overview

- MoSEIC meloxicam is a potent, oral, rapidly-absorbed, once-daily, non-opioid, COX-2 preferential, pain therapeutic.
- Standard meloxicam has an extended T_{max} (4-6 hours) which delays its onset of action.[1,2]
- Axsome's MoSEIC (Molecular Solubility Enhanced Inclusion Complex) technology substantially increases the rate of absorption of meloxicam while maintaining its approximately 20-hour half-life.
- Phase 1 results: 9 times faster T_{max}, higher C_{max} and similar half-life, compared to Mobic®.
- Potential utility for migraine, and the signs and symptoms of OA and RA.
- AXS-07 is a fixed-dose combination of MoSEIC meloxicam and rizatriptan.
- AXS-06 is a fixed-dose combination of MoSEIC meloxicam and esomeprazole (to reduce risk of NSAID-associated ulcers).

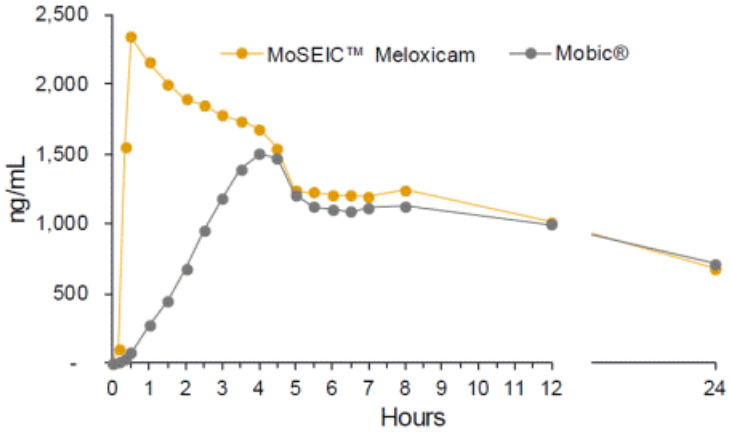
IP Overview

- 1 issued patent – protection through 2036.
- Pharmacokinetic patents
- 14 pending U.S. and international applications.

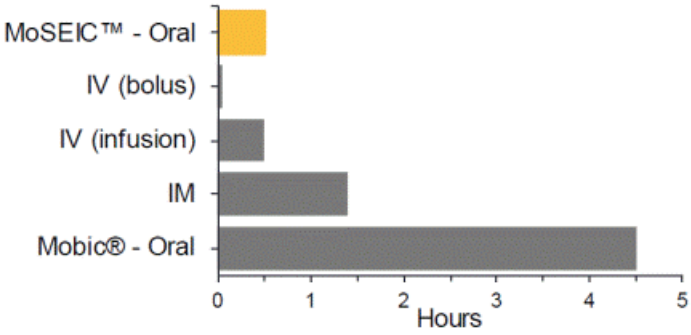
1. Mobic® (meloxicam) FDA Package Insert.
2. Euller-Ziegler et al., *Inflamm Res 50*, Supplement 1 (2001) S5–S9.

Migraine, OA and RA:
MoSEIC™ Meloxicam Phase 1 Results

Mean Meloxicam Concentrations



Meloxicam T_{max} after 15 mg Dose



- MoSEIC meloxicam T_{max} 9 times faster than Mobic® (0.5 hour versus 4.5 hours, respectively, $p<0.0001$).
- Therapeutic plasma levels achieved within 15 minutes of oral dosing of MoSEIC meloxicam.
- MoSEIC meloxicam had higher mean C_{max} ($p=0.0018$), faster time to therapeutic plasma concentration ($p<0.0001$), and time to half-maximal plasma concentration ($p<0.0001$) as compared to Mobic®.
- Terminal half-lives were approximately 20 hours for MoSEIC meloxicam and 22 hours for Mobic®.

Sources: Axsome data on file. IV and IM data from Euller-Ziegler et al., *Inflamm Res 50*, Supplement 1 (2001) S5–S9.

AXS-07:
MoSEIC™ Meloxicam + Rizatriptan for Migraine

- Meloxicam is a new molecule for migraine—not currently approved or used for this indication due to prolonged T_{max}
- MoSEIC delivery enables its use in abortive treatment of migraine
  - Rapid T_{max} of MoSEIC meloxicam is ideal for migraine treatment
  - Extended half-life of MoSEIC meloxicam should lead to lower symptom recurrence
- AXS-07 combines unique PK of MoSEIC meloxicam with proven efficacy of rizatriptan
- FDA Pre-IND written guidance received
- Phase 3 initiation anticipated in 2018

37M patients in the U.S.[1]

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-07 (MoSEIC™ Mx + Riz)	Migraine			

Abbreviations: Mx = Meloxicam; Riz = Rizatriptan.

1. Pleis JR, et al., *Summary health statistics for U.S. adults: National Health Interview Survey, 2009. National Center for Health Statistics. Vital Health Stat 10(249). 2010.*

AXS-07:
Differentiated Clinical Profile for Migraine

- **Rapid absorption and onset of action**
  - Based on rapid absorption of MoSEIC meloxicam and expected additive effect of AXS-07 components
- **Strong and consistent pain relief**
  - Potential for superior efficacy as compared to current treatments based on expected additive effect of AXS-07 components
- **Sustained pain relief**
  - Based on extended MoSEIC meloxicam half-life and expected additive effect of AXS-07 components
- **Pharmacoeconomic benefits**
  - Potentially superior efficacy expected to result in reduced use of medication and medical services, reduced absenteeism and loss of productivity

AXS-06:
MoSEIC™ Meloxicam + Esomeprazole for OA and RA

- AXS-06 is a fixed-dose combination of MoSEIC™ meloxicam and esomeprazole
- Being developed to treat OA and RA, and to reduce the risk of NSAID-associated upper GI ulcers
- Potentially best-in-class NSAID profile:
  - Oral administration with IV-like onset of action
  - Long half-life for sustained effect and once-daily dosing
  - Improved GI safety from esomeprazole component
- Positive Phase 1 results: therapeutic meloxicam concentrations within 15 mins, gastroprotective esomeprazole concentrations
- FDA Pre-IND written guidance received
- AXS-06 is Phase 3-ready

120M NSAID TRx per year in the U.S.

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-06 (MoSEIC™ Mx + Eso)	OA and RA			Phase 3 ready

Abbreviations: Eso = Esomeprazole; Mx = Meloxicam; OA = Osteoarthritis; RA = Rheumatoid Arthritis.

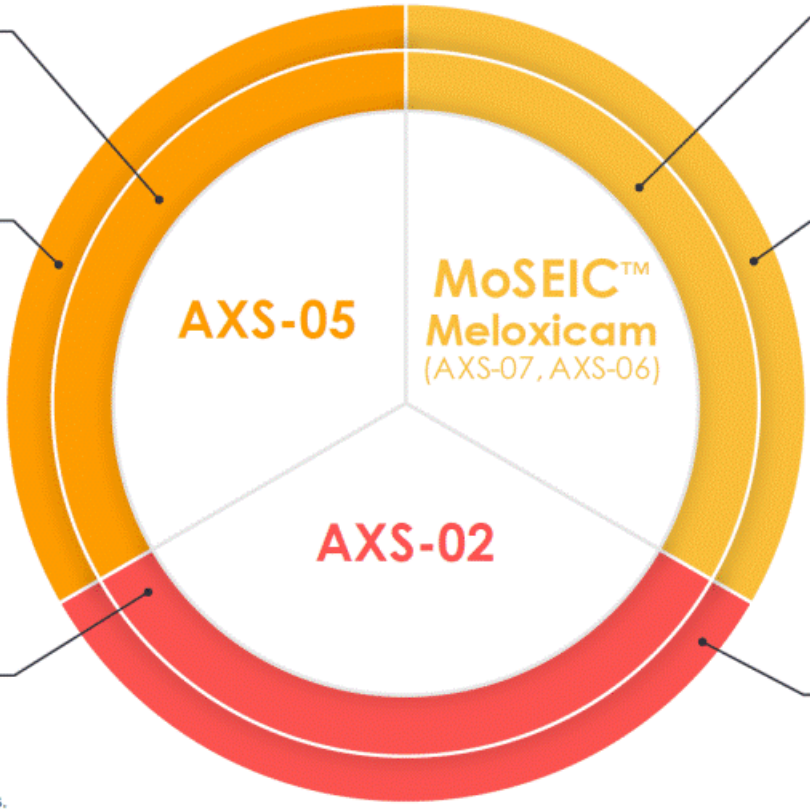
Barriers to Entry

23 Issued U.S. Patents*
1 Issued O-U.S. Patent
Claims extending to **2034**
>40 pending

Proprietary Manufacturing
Drug Product Formulation

1 issued U.S. Patent
Claims extending to **2036**
>10 pending

Proprietary Manufacturing
Drug Product Formulation



66 Issued U.S. Patents*
9 Issued O-U.S. Patents
Claims extending to **2034**
>60 pending

Proprietary Manufacturing
API Synthesis

*Claims cover AXS-02 and related substances and disease indications.

Our Team

Management

Herriot Tabuteau, MD
Founder & CEO

John Golubieski, MBA
CFO

Cedric O'Gorman, MD, MBA
SVP, Clinical Development & Medical Affairs

Mark Jacobson, MA
SVP, Operations

Robert Niecestro, PhD
VP, Clinical & Regulatory

Board of Directors

Roger Jeffs, PhD
Former President, Co-CEO, Director
United Therapeutics Corp.
Prior positions at Amgen and Burroughs Wellcome

Myrtle Potter
Former President, COO
Genentech
Prior positions at Bristol-Myers Squibb and Merck

Mark Saad
Former CFO
Bird Rock Bio, Inc.
Former COO of the Global Healthcare Group at UBS

Mark Coleman, MD
Medical Director
National Spine and Pain Centers
Diplomat of the American Board of Anesthesiology

Herriot Tabuteau, MD
Chairman

AXSOME THERAPEUTICS

Key Financial Information

	As of December 31, 2017
Cash:	$34.0 Million
Debt (Face Value)[1]:	$9.7 Million
Common Shares Outstanding:	25.5 Million
Options and Warrants Outstanding[2]:	4.4 Million

- **Financial guidance**: Cash anticipated to fund operating requirements into the third quarter of 2019.

1. Book value of $9.9 million.
2. Consists of 2.3 million options and 2.1 million warrants.

Clinical Milestones

Product Candidate	Indication	2018	2019
AXS-05 (DM + BUP)	**TRD**	• **STRIDE-1** interim analysis (2Q 2018) • **STRIDE-1** interim efficacy analysis (2H 2018) • **STRIDE-1** top-line results (2H 2018/1H 2019)	
	AD Agitation	• **ADVANCE-1** interim analysis (2H 2018)	• **ADVANCE-1** interim efficacy analysis • **ADVANCE-1** top-line results (2H 2019/1H 2020)
	Smoking Cessation	• **Ph 2** trial start (1H 2018)	• **Ph 2** top-line results
AXS-09 (DM + *S*-BUP)	**CNS Disorders**	✓ **Ph 1** trial results	
AXS-07 (MoSEIC™ Mx + Riz)	**Migraine**	• **Ph 3** trial start	• **Ph 3** top-line results
AXS-02 (DZT)	**Knee OA**	✓ **COAST-1** interim analysis	

Abbreviations: AD = Alzheimer's Disease; BUP = Bupropion; CLBP = Chronic Low Back Pain; DM = Dextromethorphan; DZT = Disodium Zoledronate Tetrahydrate; Eso = Esomeprazole; ; Mx = Meloxicam; OA = Osteoarthritis; RA = Rheumatoid Arthritis; Riz = Rizatriptan; *S*-BUP = Esbupropion; TRD = Treatment Resistant Depression.
✓ Accomplished milestone.
• Upcoming milestone.

AXSOME
THERAPEUTICS

Thank you.

For more information, please contact

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