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 14, 2019
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:

oWritten communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425).

oSoliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12).

oPre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)).

oPre-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 14, 2019, Axsome Therapeutics, Inc. (the "Company") issued a press release announcing its financial results for the three months and fiscal year ended December 31, 2018 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 14, 2019, 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 14, 2019.
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 14, 2019

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 2018 Financial Results and Provides Business Update

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

NEW YORK, March 14, 2019 (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, 2018.

"In 2018, we advanced our clinical programs and significantly expanded our CNS pipeline through the addition of new internally generated product candidates, and the launch of clinical trials in new indications," said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. "We have continued this momentum into 2019, reporting positive results from the Phase 2 ASCEND trial of AXS-05 in major depressive disorder, and initiating the Phase 3 MOMENTUM trial of AXS-07 in migraine and the Phase 2 CONCERT trial of AXS-12 in narcolepsy. All in all, we are currently conducting registration or mid-stage clinical trials with our potentially first- or best-in-class product candidates in five different important CNS indications. In addition, our recently completed financings allow us to advance our deep pipeline well beyond data readouts for all ongoing clinical trials. Over the next several quarters, we look forward to topline results from the Phase 3 STRIDE-1 trial of AXS-05 in treatment resistant depression, the Phase 2 trial of AXS-05 in smoking cessation, the Phase 2 CONCERT trial of AXS-12 in narcolepsy, the Phase 3 MOMENTUM trial of AXS-07 in migraine, and the Phase 2/3 ADVANCE-1 trial of AXS-05 in Alzheimer's disease agitation."

CNS Pipeline Update

Axsome is developing a portfolio of differentiated, patent-protected, central nervous system (CNS) product candidates. CNS disorders are distressing for patients, difficult to treat, and often underserved, with many having no approved or satisfactory treatment options. Axsome accelerates the development of new CNS medicines by utilizing proprietary medicinal chemistry and formulation technologies, and novel mechanisms of action, combined with human proof-of-concept data and innovative clinical trial designs. Axsome's technologies include metabolic inhibition, MoSEIC™ delivery, chiral chemistry and formulation, and proprietary chemical synthesis and analysis. Our CNS pipeline includes three differentiated product candidates in active clinical development.

- **AXS-05:** AXS-05 is a novel, oral, investigational NMDA receptor antagonist with multimodal activity, which is being evaluated in four separate indications: treatment resistant depression (TRD), Alzheimer's disease (AD) agitation, major depressive disorder (MDD), and smoking cessation. AXS-05 consists 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). 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 AD agitation.

  Depression: Axsome is enrolling a Phase 3 trial in TRD (the STRIDE-1 study), and has completed a Phase 2 trial in MDD (the ASCEND study). The Phase 3 STRIDE-1 study is a randomized, double-blind, active-controlled, multicenter 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. To date, approximately 95% of the target number of subjects have been randomized. Topline results are anticipated in the second quarter of 2019.

  In January 2019, Axsome announced positive results from the Phase 2 ASCEND study, a randomized, double-blind, active-controlled, multicenter, U.S. trial, in patients with confirmed moderate to severe MDD. In this study, AXS-05 met the prespecified primary endpoint by rapidly, substantially, and statistically significantly reducing depressive symptoms, measured using the Montgomery-Åsberg Depression Rating Scale (MADRS) total score, as compared to the active comparator bupropion. Further details of the study results are expected to be presented at upcoming scientific meetings. Axsome anticipates meeting with the FDA in the second quarter of 2019 to discuss the potential regulatory path for developing AXS-05 for the broader MDD indication.

AD Agitation: Axsome is enrolling the ADVANCE-1 study, a Phase 2/3, randomized, double-blind, controlled, multicenter, trial to evaluate the efficacy and safety of AXS-05 in patients with agitation associated with AD. In December 2018, Axsome announced positive results of an interim futility analysis for the ADVANCE-1 trial. The interim analysis was conducted by an independent data monitoring committee (IDMC) which recommended continuation of the AXS-05 treatment arm and no further randomization of subjects to the bupropion treatment arm. The IDMC did not indicate that there were any safety concerns in the study. Axsome has followed the IDMC's recommendation. The previously planned second interim analysis will no longer be performed in order to preserve statistical power for the final analysis. To date, just over 40% of the target number of subjects have been randomized in this trial. Topline results are anticipated in the first half of 2020.

Smoking Cessation: AXS-05 is being evaluated in a Phase 2, randomized, double-blind, active-controlled trial for smoking cessation treatment in smokers interested in quitting. The change in smoking intensity will be measured using behavioral and biochemical assessments. The trial is being conducted under a research collaboration between Duke University and Axsome. To date, approximately 95% of the target number of subjects have been randomized in this trial. Topline results are anticipated in the second quarter of 2019.

- **AXS-07:** Axsome is developing AXS-07 for the acute treatment of migraine. AXS-07 is a novel, oral, rapidly absorbed, investigational medicine consisting of MoSEIC meloxicam and rizatriptan. The distinct mechanism of action and rapid absorption of MoSEIC meloxicam, combined with the known efficacy of rizatriptan, are designed to enable rapid, superior, and consistent relief of migraine pain, with lower symptom recurrence, as compared to currently available therapies.

Migraine: In February 2019, Axsome reached agreement with the FDA under a Special Protocol Assessment (SPA) for the design, endpoints, and statistical approach of the MOMENTUM study, a Phase 3, randomized, double-blind, controlled, multicenter trial assessing the efficacy and safety of AXS-07 in the acute treatment of migraine. In March 2019, Axsome enrolled the first patient in this trial. The study will include approximately 875 patients, with a history of inadequate response to prior migraine treatments, who will be randomized in a 2:2:2:1 ratio to treatment with AXS-07, rizatriptan, meloxicam, or placebo. The two co-primary endpoints of the trial are the proportion of patients who are free from headache pain two hours after dosing, and the proportion of patients who no longer suffer from their most bothersome migraine-associated symptom (nausea, photophobia, phonophobia) two hours after dosing. Topline results from this trial are expected in the first quarter of 2020.

- **AXS-12:** Axsome is developing AXS-12 for treatment of the symptoms of narcolepsy. AXS-12 (reboxetine) is a novel, oral, highly selective and potent norepinephrine reuptake inhibitor. AXS-12 has been granted Orphan Drug Designation by the FDA for the treatment of narcolepsy.

Narcolepsy: In January 2019, Axsome initiated the CONCERT study, a Phase 2, randomized, double-blind, placebo-controlled, crossover, multicenter trial of AXS-12 in patients with narcolepsy. The study will enroll approximately 20 patients, all of whom will be treated with AXS-12 for three weeks and with placebo for three weeks. Eligible patients will be randomized to receive either AXS-12 followed by placebo, or placebo followed by AXS-12. Efficacy assessments will include the frequency of cataplexy attacks, and measures of other symptoms of narcolepsy. Topline results from this trial are expected in the second quarter of 2019.

Corporate Update

- In January 2019, Axsome raised gross proceeds of approximately $25.8 million from the sale of shares of its common stock under its at-the-market facility with SVB Leerink, fully utilizing the facility.

- In March 2019, Axsome entered into a $24 million growth capital term loan facility with Silicon Valley Bank (SVB) and WestRiver Innovation Lending Fund. Axsome received $20 million at closing, and can draw the remaining $4 million tranche, at its option, subject to the achievement of positive results from the Company's ongoing Phase 2 trial of AXS-12 in narcolepsy.

Anticipated Clinical Milestones

- **Clinical Trial Readouts:**
  - Phase 3 STRIDE-1 trial of AXS-05 in TRD, topline data (2Q 2019)
  - Phase 2 trial of AXS-05 in smoking cessation, topline data (2Q 2019)
  - Phase 2 CONCERT trial of AXS-12 in narcolepsy, topline data (2Q 2019)
  - Phase 3 MOMENTUM trial of AXS-07 in migraine, topline data (1Q 2020)
  - Phase 2/3 ADVANCE-1 trial of AXS-05 in AD agitation, topline data (1H 2020)

Fourth Quarter 2018 Financial Results

- **Research and development (R&D) expenses:** R&D expenses were $7.2 million for the quarter ended December 31, 2018 and $23.5 million for the year ended December 31, 2018, compared to $4.5 million and $20.0 million for the comparable periods in 2017. The increase was primarily due to increased costs for our STRIDE-1 and ADVANCE-1 studies, initiation and completion of our ASCEND study, and AXS-07 and AXS-12 study startup and manufacturing costs, which was partially offset by a reduction in the costs of our clinical trials for AXS-02 and AXS-06, and nonclinical work on AXS-05.

- **General and administrative (G&A) expenses:** G&A expenses were $2.3 million for the quarter ended December 31, 2018 and $9.4 million for the year ended December 31, 2018 and $2.0 million and $7.2 million for the comparable periods in 2017. The increase in G&A expenses was primarily due to higher intellectual property costs and legal expenses, external fees associated with operating as a public company as well as an increase in personnel costs.

- **Net loss:** Net loss was $9.6 million, or $(0.32) per share for the quarter ended December 31, 2018, compared to a net loss of $7.4 million, or $(0.31) per share for the comparable period in 2017. Net loss for the year ended December 31, 2018 was $31.0 million, or $(1.15) per share, compared to a net loss of $28.9 million, or $(1.27) per share for the comparable period in 2017.

- **Cash:** At December 31, 2018, Axsome had $14.0 million of cash. Including proceeds from the recently completed at-the-market equity financings and new growth capital term loan, Axsome's pro forma cash balance was $52.6 million, which compares to $34.0 million of cash at December 31, 2017.

- **Shares outstanding:** At December 31, 2018, Axsome had 30,087,213 shares of common stock outstanding.

- **Financial guidance:** Axsome anticipates that its current cash, including proceeds from the January 2019 equity financings and March 2019 term loan, will be sufficient to fund its anticipated operations, based on its current operating plans, into at least the fourth quarter of 2021.

Conference Call Information

Axsome will host a conference call and webcast today at 8:00 AM Eastern to discuss fourth quarter and full year 2018 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 conference ID 9087075. 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 core CNS product candidate portfolio includes four clinical-stage candidates, AXS-05, AXS-07, AXS-09, and AXS-12. AXS-05 is currently in a Phase 3 trial in treatment resistant depression (TRD), a Phase 2/3 trial in agitation associated with Alzheimer's disease (AD), and a Phase 2 trial in smoking cessation. AXS-07 is currently in a Phase 3 trial for the acute treatment of migraine. AXS-12 is currently in a Phase 2 trial in narcolepsy. The Axsome Pain and Primary Care business unit (Axsome PPC) houses Axsome's pain and primary care assets, including AXS-02

and AXS-06, and intellectual property which covers these and related product candidates and molecules being developed by Axsome and others. AXS-02 is being developed for osteoporosis, the pain of knee osteoarthritis, and chronic low back pain. AXS-06 is being developed for osteoarthritis and rheumatoid arthritis. AXS-02, AXS-05, AXS-06, AXS-07, AXS-09, and AXS-12 are investigational drug products not approved by the FDA. 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 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, futility analyses and receipt of interim results, which are not necessarily indicative of the final results of our ongoing clinical trials; 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, FDA's agreement with the Company's plan to discontinue the bupropion treatment arm of the ADVANCE-1 study in accordance with the independent data monitoring committee's recommendations); the potential for the ASCEND clinical trial to provide a basis for approval of AXS-05 for the treatment of major depressive disorder and accelerate its development timeline and commercial path to patients; 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,	
	2018	2017	2018	2017
Operating expenses:				
Research and development	$ 7,151,232	$ 4,493,910	$ 23,495,055	$ 19,957,616
General and administrative	2,299,083	1,950,210	9,351,522	7,206,691
Total operating expenses	9,450,315	6,444,120	32,846,577	27,164,307
Loss from operations	(9,450,315)	(6,444,120)	(32,846,577)	(27,164,307)
Interest and amortization of debt discount/premium (expense) income	(248,700)	(340,381)	(1,127,305)	(1,340,199)
Tax credit	0	0	217,418	207,114
Change in fair value of warrant liability	102,000	(646,000)	2.791,000	(646,000)
Net loss	$ (9,597,015)	$ (7,430,501)	$ (30,965,464)	$ (28,943,392)
Net loss per common share — basic and diluted	$ (0.32)	$ (0.31)	$ (1.15)	$ (1.27)
Weighted average common shares outstanding — basic and diluted	29,874,410	24,229,652	26,883,656	22,764,606

Balance Sheet Information:

	December 31, 2018	December 31, 2017
Cash	$ 13,968,742	$ 34,021,123
Total assets	15,379,279	35,555,564
Loan payable, current and long-term	6,910,814	9,932,351
Accumulated deficit	(107,550,307)	(76,584,843)
Stockholders' equity	$ 937,921	$ 16,717,223

Axsome Contact:

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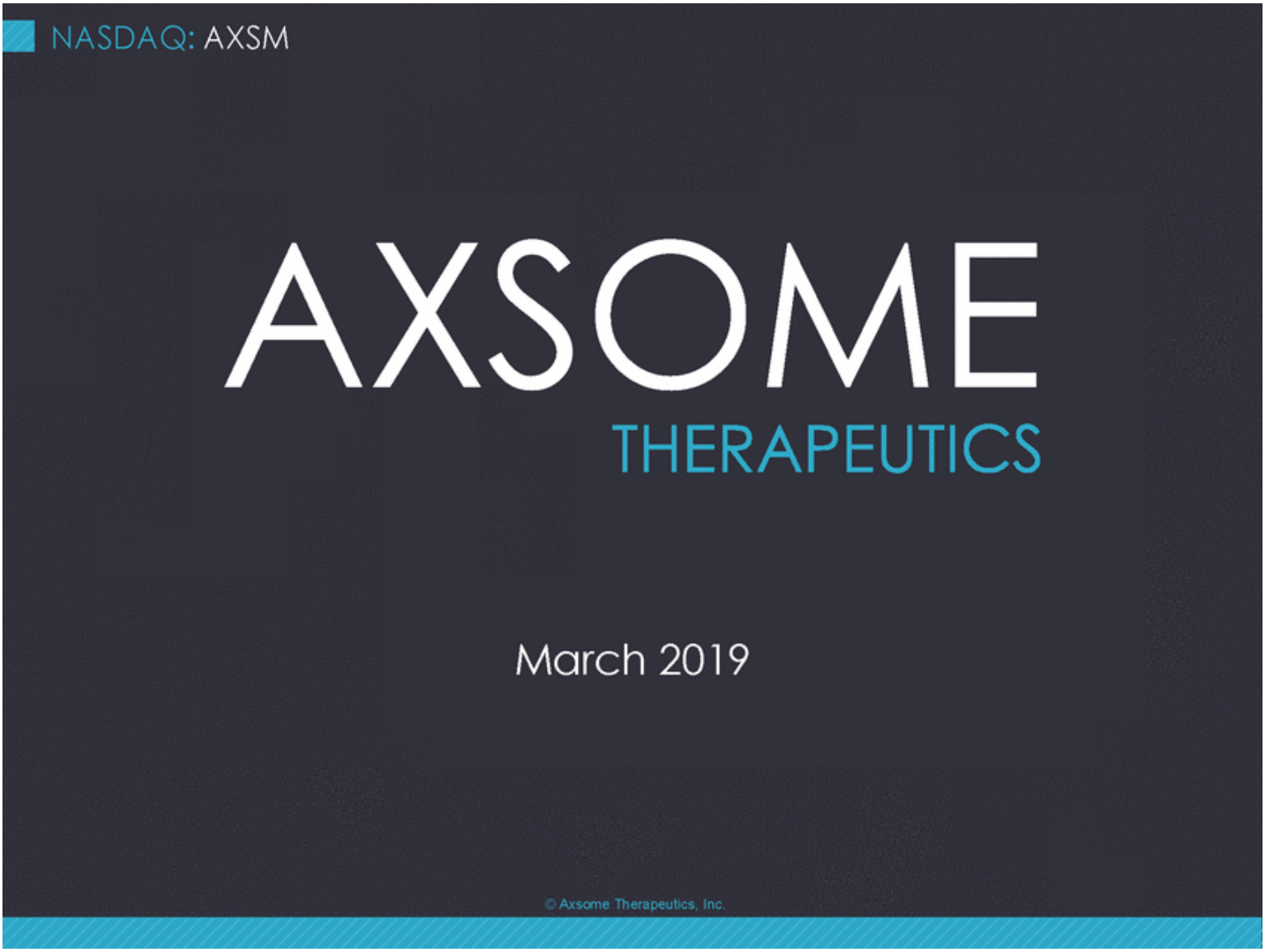
NASDAQ: AXSM
AXSOME
THERAPEUTICS
March 2019
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Forward-Looking Statements & Safe Harbor

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, which are not necessarily indicative of the final results of our ongoing clinical trials; 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, FDA's agreement with the Company's plan to discontinue the bupropion treatment arm of the ADVANCE-1 study in accordance with the independent data monitoring committee's recommendations); the Company's ability to obtain additional capital necessary to fund its operations; the Company's ability to generate revenues in the future; the potential for the ASCEND clinical trial to provide a basis for approval of AXS-05 for the treatment of major depressive disorder and accelerate its development timeline and commercial path to patients; 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 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 Technologies

Enabling new and innovative medicines to treat CNS conditions

Chiral & Formulation Chemistry

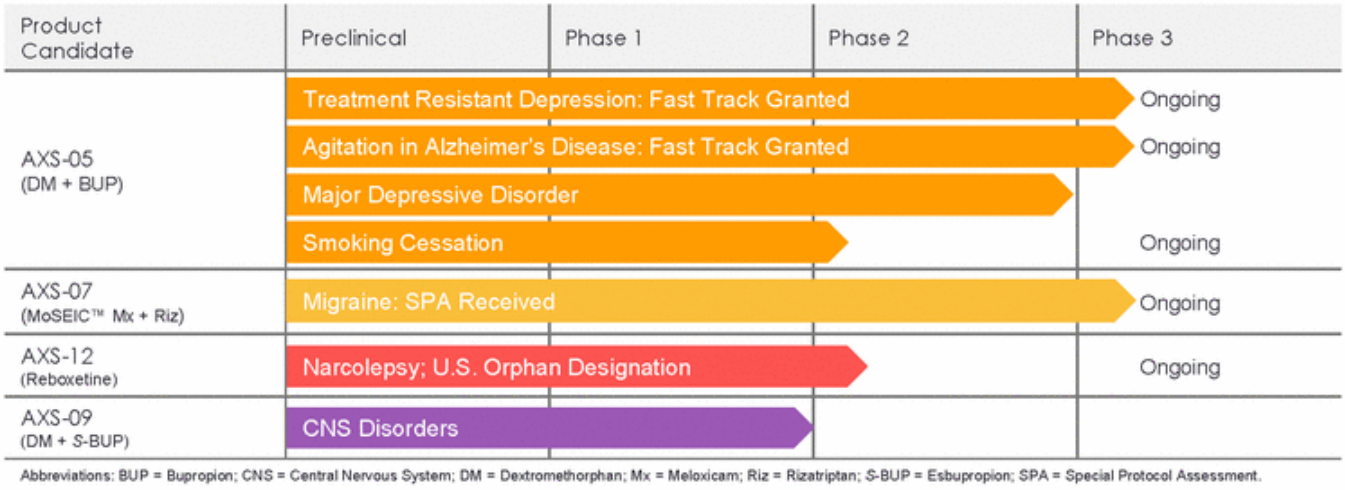
MoSEIC™ Delivery

Metabolic Inhibition

Chemical Synthesis & Analysis

Our CNS Candidates and Pipeline

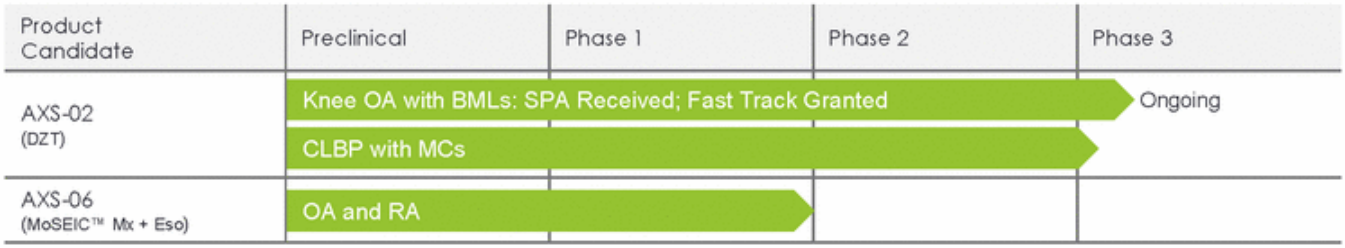
- Four differentiated clinical-stage CNS assets targeting significant and growing markets.
- Patent protection to 2034-2036, worldwide rights.



Abbreviations: BUP = Bupropion; CNS = Central Nervous System; DM = Dextromethorphan; Mx = Meloxicam; Riz = Rizatriptan; *S*-BUP = Esbupropion; SPA = Special Protocol Assessment.

Axsome PPC Candidates and Pipeline

- Two differentiated clinical-stage pain and primary care assets targeting significant and growing markets.
- Patent protection to 2034, worldwide rights.



Abbreviations: BML = Bone Marrow Lesions; CLBP = Chronic Low Back Pain; DZT = Disodium Zoledronate Tetrahydrate; Eso = Esomeprazole; MC = Modic Changes; Mx = Meloxicam; OA = Osteoarthritis; RA = Rheumatoid Arthritis; SPA = Special Protocol Assessment

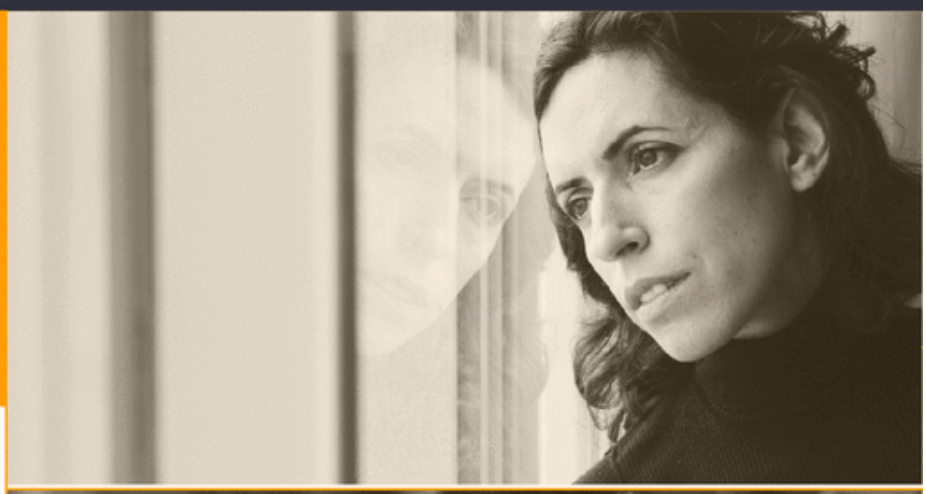
AXSOME THERAPEUTICS

AXS-05

Dextromethorphan (DM) + Bupropion (BUP)

Novel therapy for CNS disorders:

- Treatment Resistant Depression (TRD)
- Agitation in Alzheimer's Disease (AD)
- Major Depressive Disorder (MDD)
- Smoking Cessation

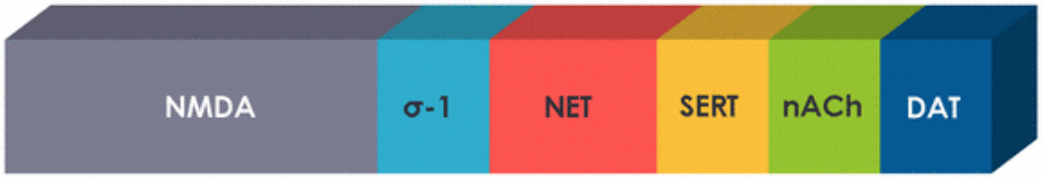


AXS-05:
Novel Multimodal Therapy for CNS Disorders

Single Target

Multimodal

Ketamine



AXS-05
(Dextromethorphan/ Bupropion)

Abbreviations: σ-1 = Sigma-1; DAT = Dopamine Reuptake Transporter; nACh = Nicotinic Acetylcholine Receptor; NMDA = N-methyl-D-aspartate; NET = Norepinephrine Reuptake Transporter; SERT = Serotonin Reuptake Transporter.

CNS Disorders:
Mechanisms of Action

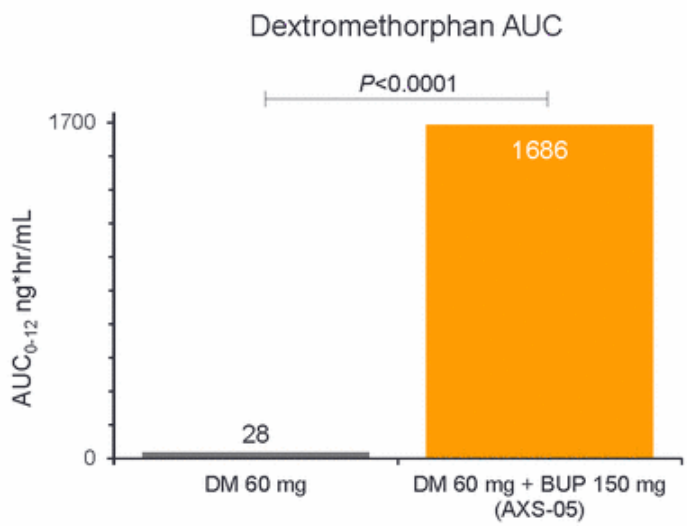
Multimodal Activity | **Relevant Indications**

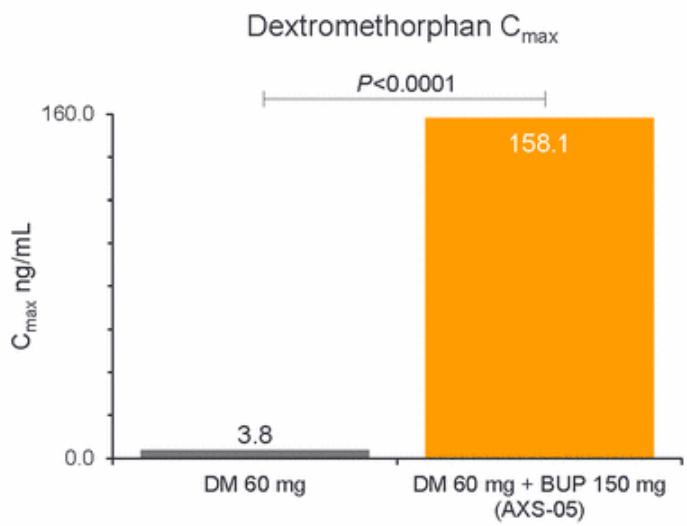
Mechanism of Action	AXS-05	ADHD	Anxiety	Alzheimer's	Depression	Fibromyalgia	OCD	Pain	Smoking cessation	Related Agents
NMDA Receptor Antagonist	✓			▒	▒			▒		• Ketamine • Memantine (Namenda®)
Sigma-1R Agonist	✓			▒	▒		▒			• Fluvoxamine (Luvox®) • Donepezil (Aricept®)
Norepinephrine Reuptake Inhibitor	✓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

✓ 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:
Phase 1 Results





Axsome data on file.

CNS Disorders:
Depression Overview

- 63% and 44% of MDD patients have inadequate response to initial therapy and second line therapy, respectively.[2]
- 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 interim futility analysis: IDMC recommended trial continuation.
- Phase 2 MDD trial completed.

8M patients in the U.S.[1]

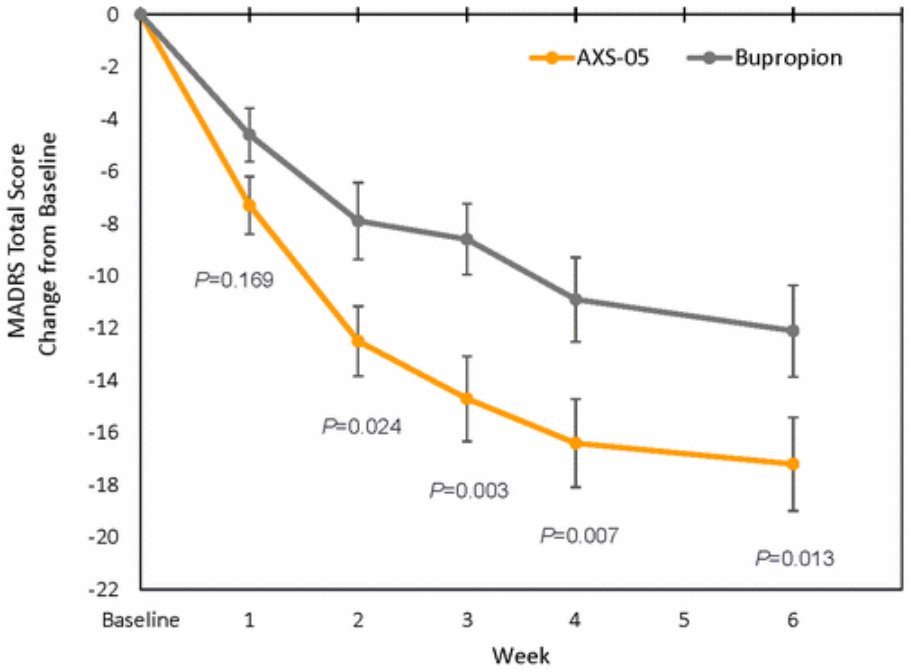
Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-05 (DM + BUP)	Treatment Resistant Depression: Fast Track Granted			Ongoing
	Major Depressive Disorder			

Abbreviations: DM = Dextromethorphan; BUP = Bupropion.

1. Center for Behavioral Health Statistics and Quality. (2017).
2. Rush AJ, et al. *Am J Psychiatry* 2006;163:1905-1917.

AXSOME THERAPEUTICS

CNS Disorders:
Depression Phase 2 Results

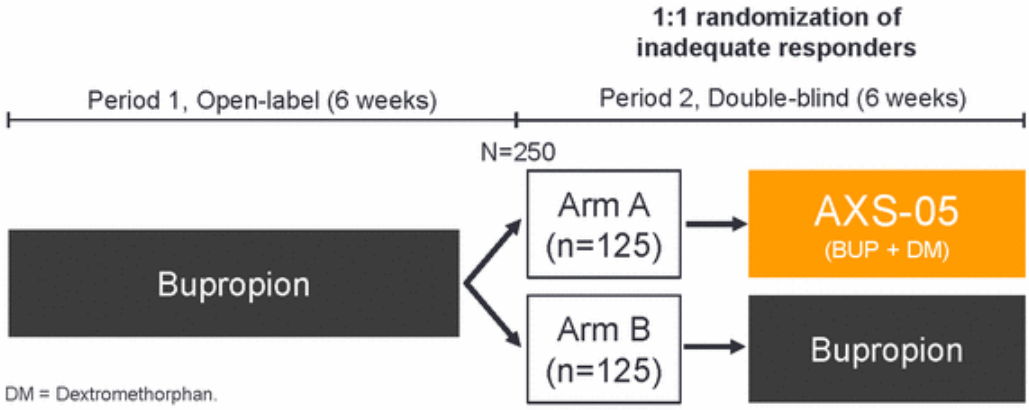


	AXS-05	Bupropion	P-Value
Primary Endpoint			
Change in MADRS Total Score over 6-Week Period (averaged)	-13.7	-8.8	< 0.001
Change in MADRS Total Score at Week 6	-17.2	-12.1	0.013

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.

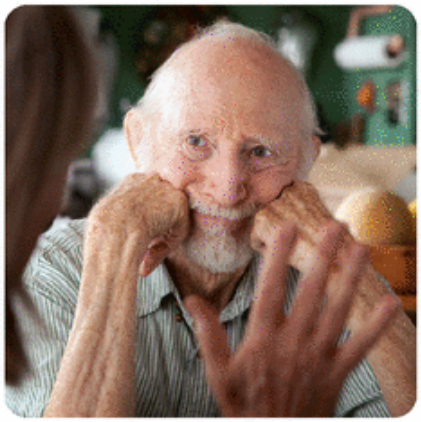


BUP = Bupropion; DM = Dextromethorphan.

- **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
- Interim futility analysis: Conducted in April 2018. IDMC recommended trial continuation.

CNS Disorders:
Agitation in AD Overview

- Agitation seen in approximately 70% of AD patients.[2]
- Characterized by emotional distress, aggressive behaviors, disruptive irritability, disinhibition, and caregiver burden.[4]
- Associated with[3,4]:
  - 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 interim futility analysis: IDMC recommended continuation of AXS-05 arm, no further enrollment to bupropion arm.
- Phase 2/3 ongoing.



3.5M 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			Ongoing

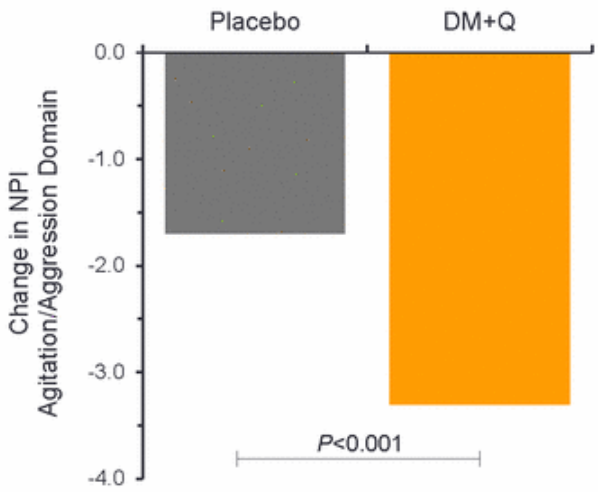
Abbreviations: DM = Dextromethorphan; BUP = Bupropion.

1. Hebert, LE, et al. *Neurology*. 2013;80:1778-1783.
2. Tractenberg R, et al. *J Neuropsychiatry Clin Neurosci*. 2002;14:11-18.
3. Antonsdottir IM, et al. *Expert Opin Pharmacother*. 2015;11:1649-1656.
4. 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)

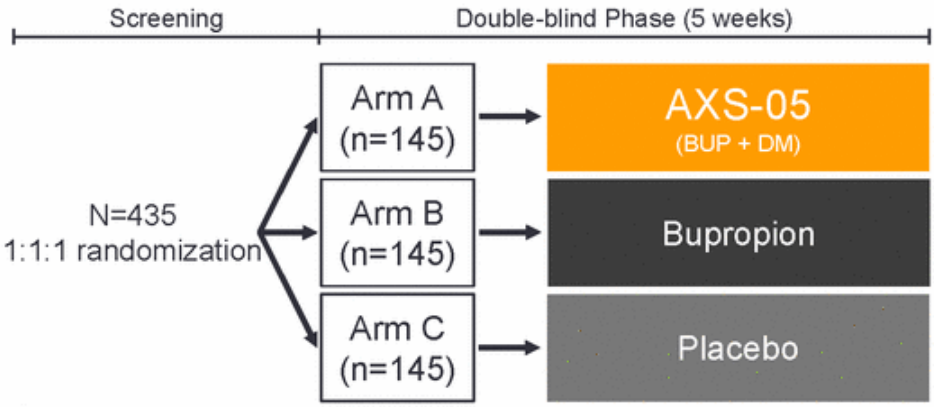


Cummings J, et al. *JAMA*. 2015;314:1242-1254.

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
- Interim futility analysis: Conducted in December 2018. IDMC recommended continuation of AXS-05 arm, no further enrollment into bupropion arm.

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 trial ongoing.

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

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

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-07

MoSEIC™ Meloxicam + Rizatriptan

Novel therapy for:

- Migraine

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
- Phase 3 trial is ongoing.

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

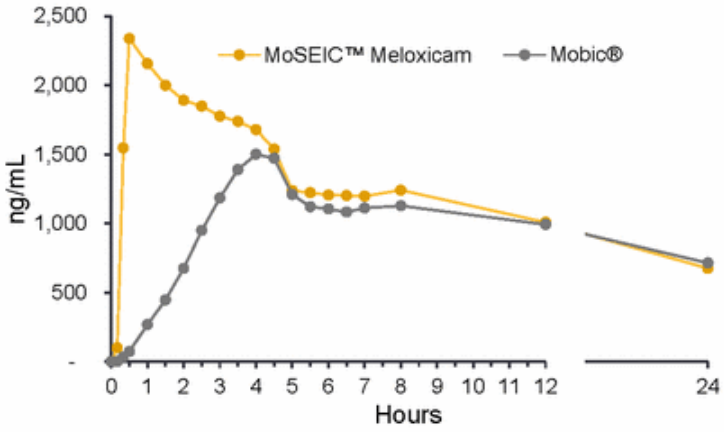
Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-07 (MoSEIC™ Mx + Riz)	Migraine: SPA Received			Ongoing

Abbreviations: Mx = Meloxicam; Riz = Rizatriptan; SPA = Special Protocol Assessment.

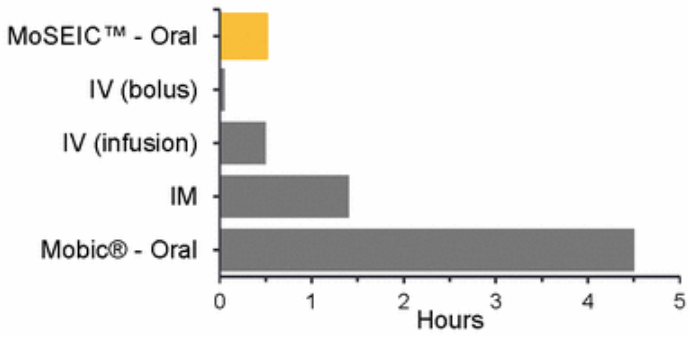
1. Pleis JR, et al., *Summary health statistics for U.S. adults: National Health Interview Survey, 2009. National Center for Health Statistics. Vital Health Stat 10(249). 2010.*

Migraine:
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:
Differentiated Clinical Profile for Migraine

Rapid absorption & onset of action

Based on rapid absorption of MoSEIC meloxicam and expected additive effect of AXS-07 components

Strong & 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

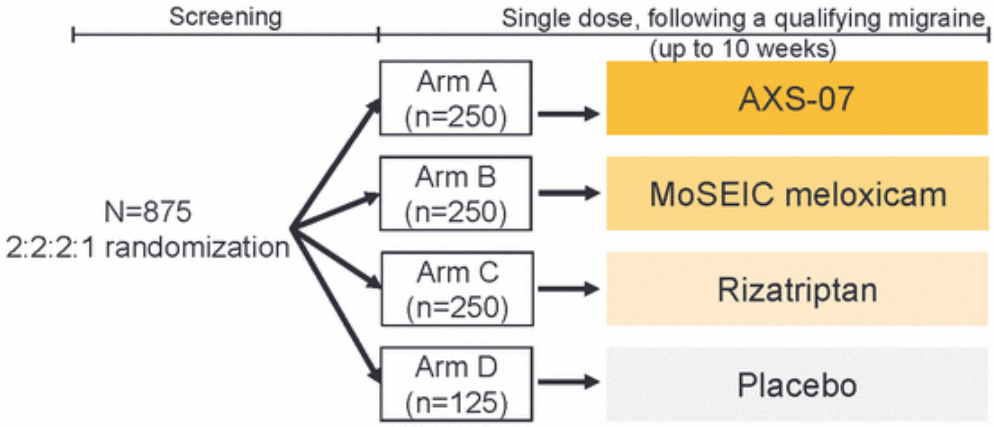
Pharmaco-economic benefits

Potentially superior efficacy expected to result in reduced use of medication and medical services, reduced absenteeism and loss of productivity

CNS Disorders:
Migraine Phase 3 Design

MOMENTUM STUDY

A Phase 3 trial to assess the efficacy and safety of AXS-07 for the acute treatment of Migraine in adults.



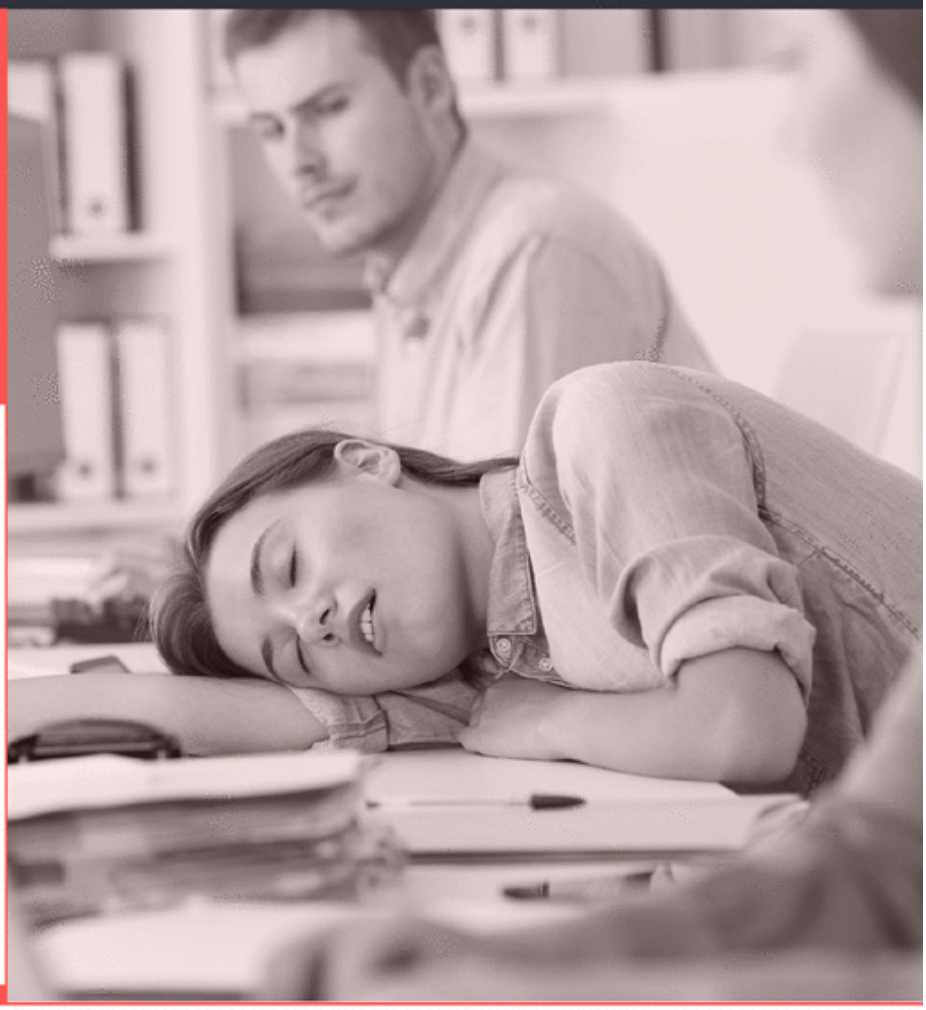
- **Primary Endpoint:**
  - Pain freedom at 2 hours post-dose
  - Freedom from most bothersome symptom at 2 hours post-dose
- **Key Inclusion Criteria:**
  - Inadequate response to prior migraine therapy

AXS-12

Reboxetine

Novel therapy for:

- Narcolepsy



CNS Disorders:
Narcolepsy Overview

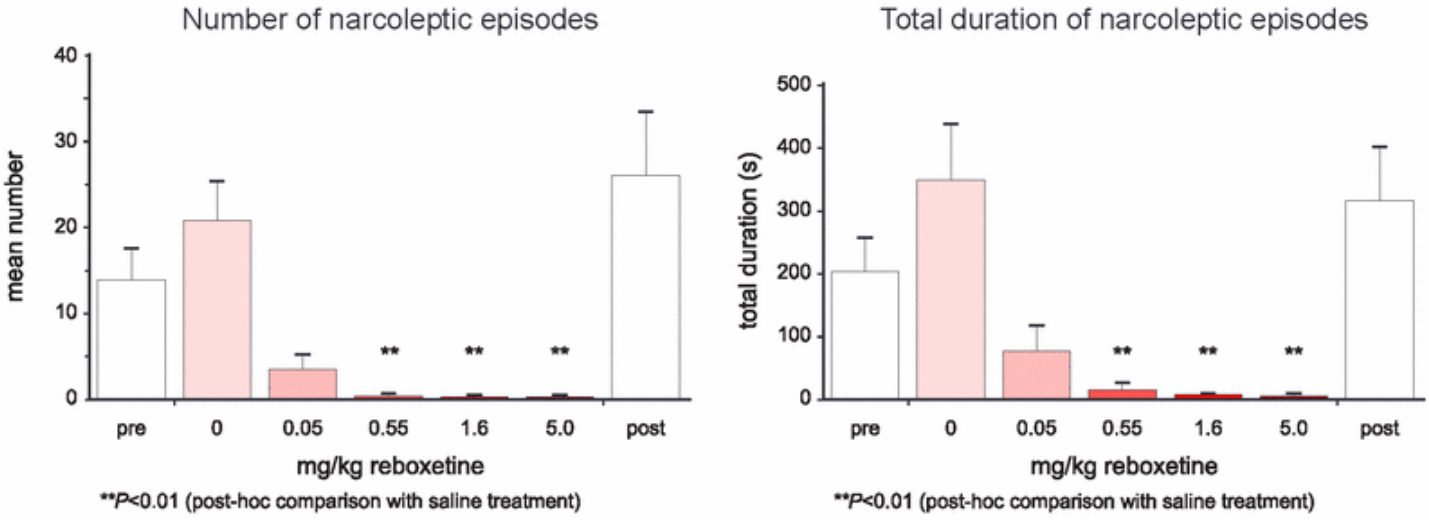
- Debilitating sleep disorder characterized by excessive daytime sleepiness (EDS) and cataplexy.
- Limited treatment options
  - All current approved drugs are scheduled
  - Only one approved agent for cataplexy.
- AXS-12 showed potent activity in genetic mouse model of narcolepsy, and positive effects in human pilot trial in narcolepsy patients.
- Phase 2 trial is ongoing.
- U.S. Orphan Drug Designation.

Orphan Disease

185,000 patients in the U.S.

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-12 (Reboxetine)	Narcolepsy; U.S. Orphan Designation			Ongoing

CNS Disorders:
Narcolepsy Scientific Rationale



- Reboxetine dose-dependently reduced the number of narcoleptic episodes in hypocretin (orexin)-deficient mice (P<0.0001)

Adapted from Schmidt et al. *Behav Brain Res.* 2016 Jul 15;308:205-10.

Barriers to Entry

31 Issued U.S. Patents
2 Issued O-U.S. Patents
Claims extending to **2034**
>45 pending

Proprietary
Manufacturing
Drug Product
Formulation

4 issued U.S. Patents
2 issued O-U.S. Patent
Claims extending to **2036**
>25 pending

Proprietary
Manufacturing
Drug Product
Formulation

97 Issued U.S. Patents
52 Issued O-U.S. Patents
Claims extending to **2034**
>65 pending

Proprietary
Manufacturing
API Synthesis

Our Team

Management

Herriot Tabuteau, MD
Founder & CEO

Nick Pizzie, CPA, MBA
CFO

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

Mark Jacobson, MA
SVP, Operations

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

Key Financial Information

	As of December 31, 2018
Cash (Pro-Forma)[1]:	$52.6 Million
Debt (Face Value):	$20.0 Million
Common Shares Outstanding (Pro-Forma)[1]:	33.3 Million
Options and Warrants Outstanding[2]:	2.5 Million

- **Financial guidance**: Cash anticipated to fund operating requirements into at least the fourth quarter of 2021.

1. Includes the effect of the common stock offering that closed in January 2019 and the growth capital term loan facility that closed in March 2019.
2. Consists of 2.3 million options and 0.2 million warrants; approximate amounts as of March 13, 2019.

Clinical Milestones

Product Candidate	Indication	2019	2020
AXS-05 (DM + BUP)	**TRD**	• **STRIDE-1** topline results (2Q 2019)	
	AD Agitation		• **ADVANCE-1** topline results (1H 2020)
	MDD	✓ **ASCEND** topline results	
	Smoking Cessation	• **Ph 2** topline results (2Q 2019)	
AXS-07 (MoSEIC™ Mx + Riz)	**Migraine**	✓ **FDA SPA** Granted ✓ **MOMENTUM** trial start	• **MOMENTUM** topline results (1Q 2020)
AXS-12 (Reboxetine)	**Narcolepsy**	✓ **CONCERT** trial start • **CONCERT** topline results (2Q 2019)	

Abbreviations: AD = Alzheimer's Disease; BUP = Bupropion; DM = Dextromethorphan; MDD = Major Depressive Disorder; Mx = Meloxicam; Riz = Rizatriptan; SPA = Special Protocol Assessment; TRD = Treatment Resistant Depression.

✓ Accomplished milestone.

• Upcoming milestone.

AXSOME

THERAPEUTICS

Thank you.

For more information, please contact

Mark Jacobson
SVP, Operations

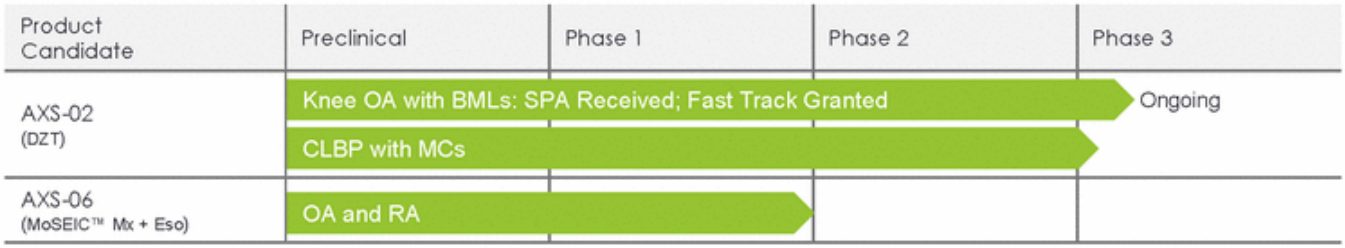
212-332-3243
mjacobson@Axsome.com

axsome.com

APPENDIX – AXSOME PPC

Axsome PPC Candidates and Pipeline

- Two differentiated clinical-stage pain and primary care assets targeting significant and growing markets.
- Patent protection to 2034, worldwide rights.



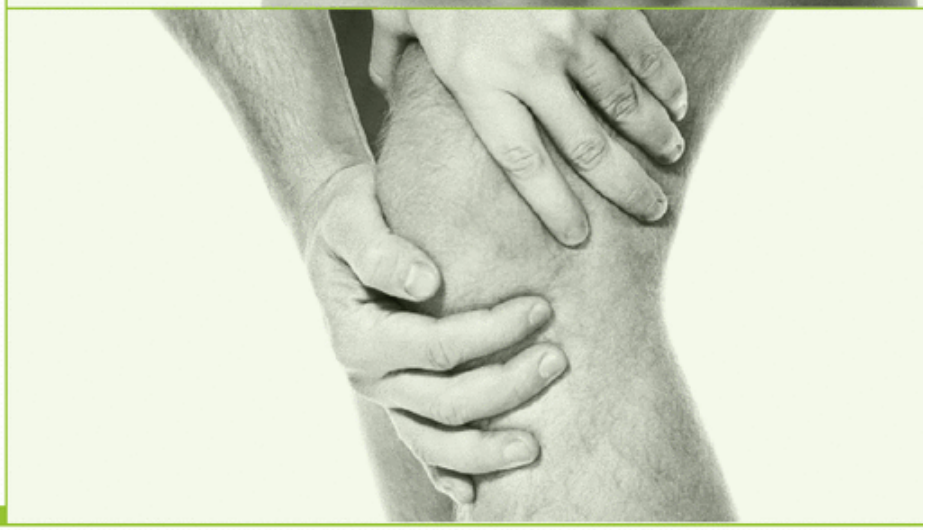
Abbreviations: BML = Bone Marrow Lesions; CLBP = Chronic Low Back Pain; DZT = Disodium Zoledronate Tetrahydrate; Eso = Esomeprazole; MC = Modic Changes; Mx = Meloxicam; OA = Osteoarthritis; RA = Rheumatoid Arthritis; SPA = Special Protocol Assessment

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

AXS-02
Disodium Zoledronate Tetrahydrate

- Oral Dose
- Long-acting
- Targeted Therapy
- Non-opioid
- Novel Mechanism

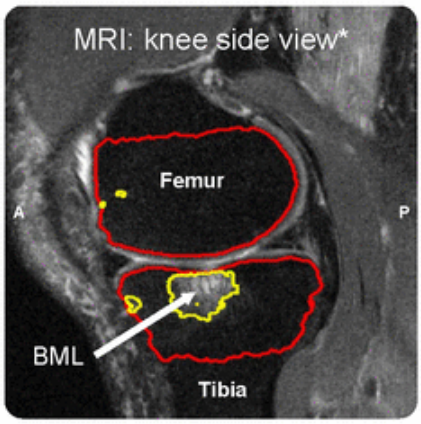
Mechanisms of Action

- Inhibits bone-resorbing osteoclasts
- Downregulates acid-sensing† ion channels
- Reduces pro-inflammatory cytokine production
- Anti-angiogenic

†Acid is a well known cause of pain.

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.

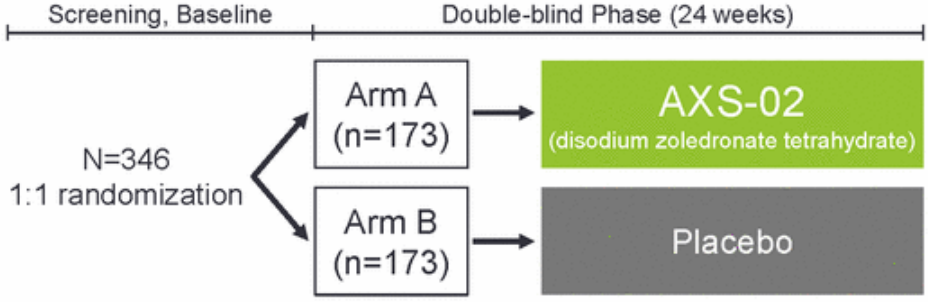
* MRI showing BML in medial tibia from Driban, et al. *Arthritis Res Ther*. 2013;15:R112.
1. Driban JB, et al. *Arthritis Res Ther*. 2013;15:R112.
2. Hunter DJ, et al. *Arthritis Res Ther*. 2009;11:R11.
3. Kazakia GJ, et al. *Osteoarthritis Cartilage*. 2013;21:94-101.
4. Lawrence RC, et al. *Arthritis 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.

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.

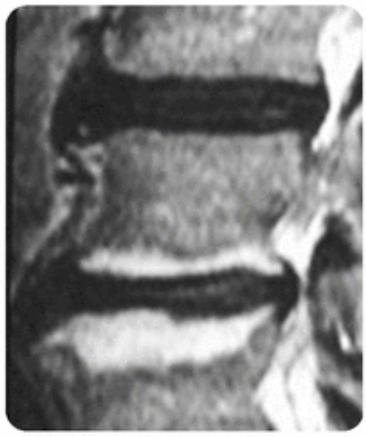
Special Protocol Assessment (SPA) received



- **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.

AXS-06

MoSEIC™ Meloxicam + Esomeprazole

Novel therapy:

- Osteoarthritis
- Rheumatoid arthritis

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-06 is a fixed-dose combination of MoSEIC meloxicam and esomeprazole (to reduce risk of NSAID-associated ulcers).

IP Overview

- 6 issued patents – protection through 2036.
- Pharmacokinetic patents
- More than 25 U.S. and international applications.

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

AXS-06:
MoSEIC™ Meloxicam + Esomeprazole for OA & 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.

AXSOME

THERAPEUTICS

Thank you.

axsome.com