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

January 9, 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 8.01. Other Events.

On January 9, 2018, Axsome Therapeutics, Inc. (the "Company") issued a press release announcing the conduct, by an independent data monitoring committee, of interim analyses of the Phase 3 CREATE-1 trial of AXS-02 in complex regional pain syndrome and of the Phase 3 COAST-1 trial of AXS-02 in knee osteoarthritis associated with bone marrow lesions, as well as the recommendations of the committee. The full text of the press release is filed as Exhibit 99.1 hereto and is incorporated herein by reference.

On January 9, 2018, Herriot Tabuteau, M.D., the Company's Chief Executive Officer, will present at the 10th Annual Biotech Showcase to provide an overview of the Company's business and late-stage clinical product candidates. The materials to be used in connection with this presentation are filed as Exhibit 99.2 hereto and are incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Press release dated January 9, 2018.
99.2	Corporate Presentation.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Axsome Therapeutics, Inc.

Dated: January 9, 2018

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

AXSOME THERAPEUTICS

Axsome Therapeutics Announces AXS-02 Independent Data Monitoring Committee Recommends Continuation of COAST-1 Trial and Discontinuation of CREATE-1 Trial

COAST-1 is a Phase 3 trial of AXS-02 in knee osteoarthritis associated with bone marrow lesions

CREATE-1 is a Phase 3 trial of AXS-02 in complex regional pain syndrome

Significant reduction in bone resorption confirms potent pharmacologic activity

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

NEW YORK, January 9, 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 announced that an independent data monitoring committee (IDMC) has conducted an interim analysis of the CREATE-1 trial of AXS-02 in complex regional pain syndrome (CRPS), and of the COAST-1 trial of AXS-02 in knee osteoarthritis (OA) associated with bone marrow lesions (BMLs). The IDMC has recommended that the COAST-1 trial be continued to full enrollment, and that the CREATE-1 trial be stopped for futility. In the CREATE-1 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 both studies and confirmed that AXS-02 was safe and generally well-tolerated. AXS-02 is a potent osteoclast inhibitor being developed as an oral, targeted, non-opioid, potentially first-in-class therapeutic for chronic pain.

“We are encouraged by the IDMC’s recommendation for continuation of the COAST-1 trial, by the favorable overall clinical safety profile of AXS-02, and by the confirmation of pharmacologic activity of orally administered AXS-02 as demonstrated by its effects on serum CTx in the CREATE-1 trial,” said Cedric O’Gorman, M.D., Senior Vice President of Clinical Development and Medical Affairs of Axsome. “Knee osteoarthritis associated with bone marrow lesions is a serious and potentially disabling condition with limited treatment options. The demonstrated pharmacologic activity of AXS-02 on bone resorption is relevant not only to knee osteoarthritis but to other potential indications for AXS-02.”

“The outcome of the CREATE-1 interim analysis is disappointing, especially in light of its implication for patients living with complex regional pain syndrome,” said Dr. Herriot Tabuteau, M.D., Chief Executive Officer of Axsome. “We would like to thank the patients and the investigators who participated in the CREATE-1 trial for joining us in our efforts to address this difficult-to-treat condition. We look forward to assessing next steps in the COAST-1 trial and to continuing to advance our broad, late-stage pipeline which includes three other product candidates, being developed across six different indications, in several either ongoing or soon to be initiated registration trials.”

In addition to AXS-02, Axsome’s pipeline includes AXS-05, AXS-07, and AXS-06. AXS-05 is a 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). It is in a Phase 3 trial for treatment resistant depression, a Phase 2/3 trial for agitation associated with Alzheimer’s disease, with a Phase 2 trial in smoking cessation anticipated to be initiated this quarter. AXS-07 is an oral, rapidly absorbed, fixed-dose combination of MoSEIC™ meloxicam and rizatriptan being developed for the acute treatment of migraine, with a Phase 3 trial in this indication anticipated to start this year. AXS-06 is a Phase 3-ready, oral, rapidly absorbed, non-opioid, fixed-dose combination of MoSEIC™ meloxicam and esomeprazole which is being developed for the treatment of osteoarthritis and rheumatoid arthritis and for the reduction of the risk of NSAID-associated gastric ulcers.

The COAST-1 trial is a randomized, double-blind, placebo-controlled, Phase 3 trial in patients with knee OA associated with BMLs. Subjects in the COAST-1 trial are randomized in a 1:1 ratio to receive either AXS-02 or placebo once a week for six weeks. The primary endpoint of the trial is the change in weekly average daily pain intensity, using the 0-10 numerical rating scale, at 24 weeks. The COAST-1 interim analysis included 77 subjects and was conducted to assess the assumptions used to determine the sample size of the study, as well as safety. This study is being conducted pursuant to a U.S. Food and Drug Administration (FDA) Special Protocol

Assessment. AXS-02 has received Fast Track designation from the FDA for the treatment of the pain of knee OA associated with BMLs. The company will assess next steps for this program.

The CREATE-1 trial was a randomized, double-blind, placebo-controlled Phase 3 trial in patients with CRPS. Subjects in the CREATE-1 trial were randomized in a 1:1 ratio to receive either AXS-02 or placebo once a week for six weeks. The primary endpoint of the trial was the change in weekly average daily pain intensity, using the 0-10 numerical rating scale, at 12 weeks. Secondary outcome measures include assessments of the change in the Patients’ Global Impression of Change, Clinicians’ Global Impression of Change, and bone turnover measured using serum carboxy terminal telopeptide of collagen type I (CTx) and serum procollagen type I N terminal propeptide. The CREATE-1 interim analysis included 81 subjects and was conducted to assess efficacy and safety. AXS-02 has received Fast Track designation from the U.S. Food and Drug Administration (FDA), and orphan drug designation from the FDA and European Medicines Agency (EMA) for the treatment of CRPS.

Conference Call Information

Axsome will host a conference call and webcast today at 8:00 AM Eastern to discuss the results of the interim analyses 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 2093356. 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 Knee Osteoarthritis (OA) associated with Bone Marrow Lesions (BMLs)

Knee OA is a disorder characterized by periarticular bone changes, progressive loss of articular cartilage, joint space narrowing, and eventual total joint failure. It is clinically manifested by knee pain, significant physical disability, and reduced quality of life. BMLs are regions of increased signal intensity on magnetic resonance imaging (MRI) of the knee in patients with knee OA. BMLs are strongly associated with the presence and severity of knee pain, and predict disease severity and structural progression in patients with knee OA, based on published studies. Results of epidemiological studies suggest that there are approximately 7 million symptomatic patients in the United States, 50 years of age and older, with radiographic knee OA and BMLs.

About Complex Regional Pain Syndrome (CRPS)

CRPS is a debilitating condition characterized by severe, continuous, burning or throbbing pain in a limb. The excessive pain is accompanied by changes in skin color, temperature and/or swelling. It is considered to be one of the most painful conditions, results in loss of physical function, and can lead to significant and sometimes permanent disability. There is currently no medication approved for the treatment of CRPS.

About AXS-02

AXS-02 (disodium zoledronate tetrahydrate) is a potent osteoclast inhibitor being developed as an oral, targeted, non-opioid, potentially first-in-class therapeutic for chronic pain. AXS-02 is dosed once per week for 6 weeks and thereafter may have a duration of effect measured in months. AXS-02 has a high affinity for bone mineral, and reduces osteoclast activity by inhibiting the farnesyl pyrophosphate synthase (FPPS) enzyme. AXS-02 is an investigational product candidate not approved by the FDA. The safety and efficacy of AXS-02 have not yet been established.

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 four clinical-stage candidates, AXS-02, AXS-05, AXS-06, and AXS-07. AXS-05 is currently in a Phase 3 trial in treatment resistant depression (TRD) and a Phase 2/3 trial in agitation in patients 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, and AXS-

07 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". 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 or other regulatory authority approval of, or other action with respect to, our 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.

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NASDAQ: AXSM

AXSOME THERAPEUTICS

January 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.

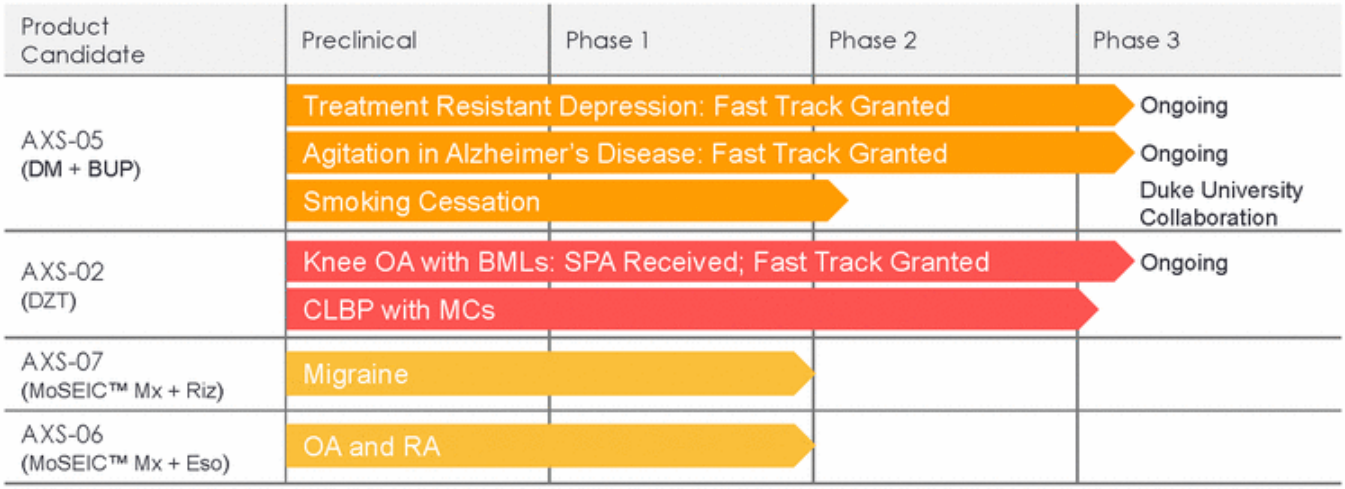
This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Neither we 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

- Four differentiated clinical-stage assets targeting significant and growing markets:
  - AXS-05: novel, oral, fixed-dose combination for multiple CNS indications
  - AXS-02: oral, non-opioid, long-acting, potentially first-in-class therapeutic for chronic pain
  - AXS-07: rapidly-absorbed, new molecular entity for migraine combined with triptan
  - AXS-06: rapidly-absorbed, once-daily, non-opioid, pain therapeutic with a gastroprotectant
- 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; 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

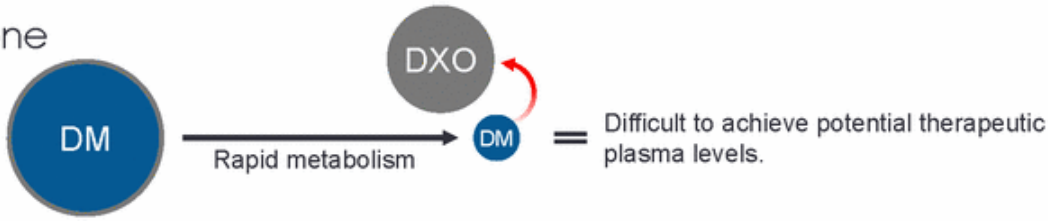
Mechanism of Action	Pharmacodynamic Synergy: DM	BUP	AXS-05 DM+BUP	Relevant Indications[1]: ADHD	Anxiety	Alzheimer's	Depression	Fibromyalgia	OCD	Pain	Smoking cessation	Related Agents[2]
NMDA Receptor Antagonist	✓		✓			■	■			■		• Ketamine • Memantine (Namenda®)
Sigma-1R Agonist	✓		✓			■	■		■			• Fluvoxamine (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

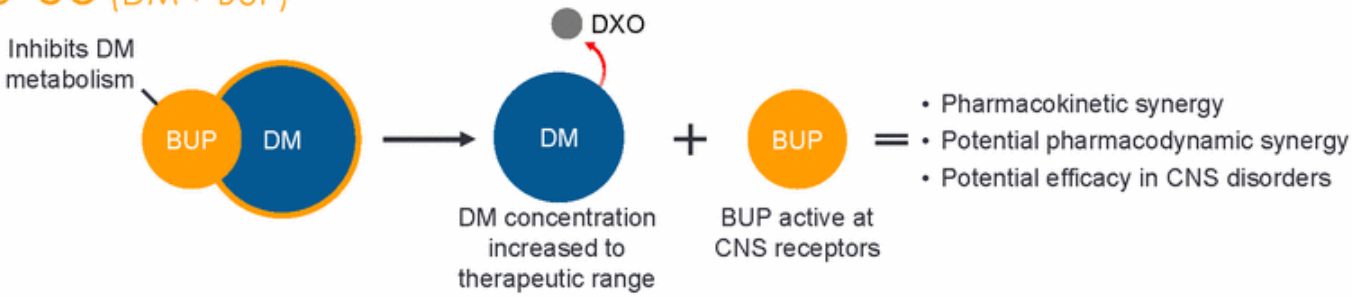
1. Indications listed are associated with the mechanism of action and are not related to either DM or BUP, unless specifically noted.
2. Agents do not contain DM or BUP, unless specifically noted.

CNS Disorders:
Novel Therapy for CNS Disorders

DM Alone



AXS-05 (DM + BUP)



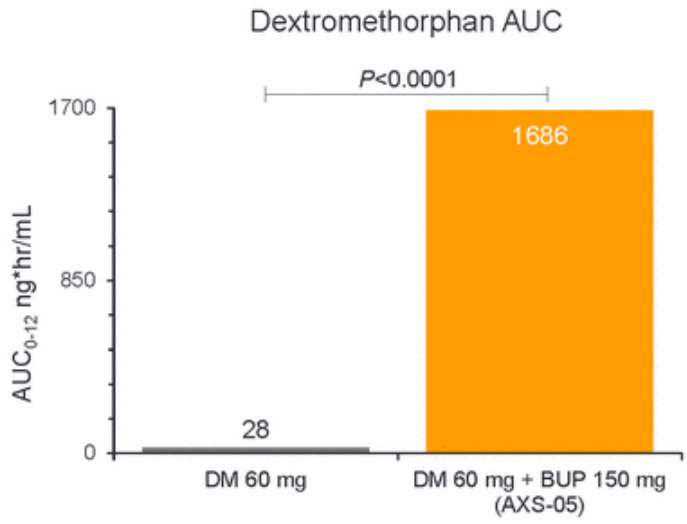
DM = Dextromethorphan; DXO = Dextrorphan; BUP = Bupropion.

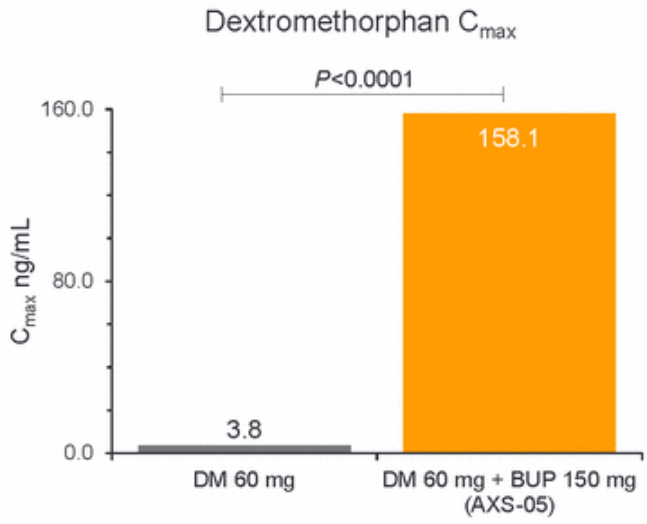
- Phase 1 trials with AXS-05 completed:
  - Significant increase in DM plasma levels.
- Phase 3 trials in TRD and AD Agitation initiated.

IP Overview

- 22 issued patents – protection through 2034.

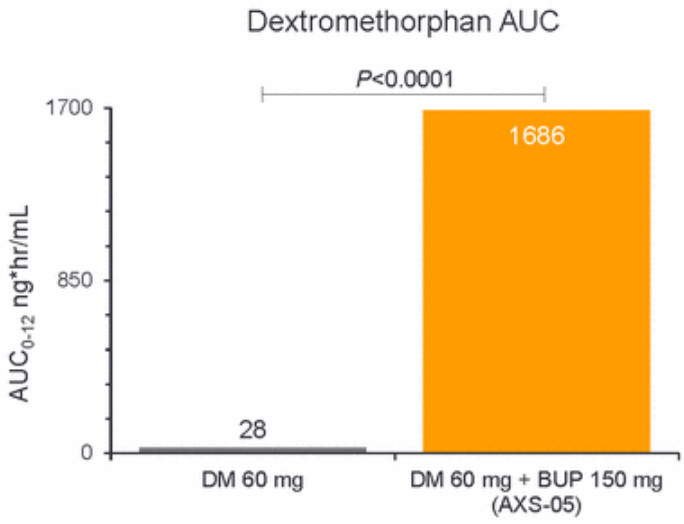
CNS Disorders:
Phase 1 Results

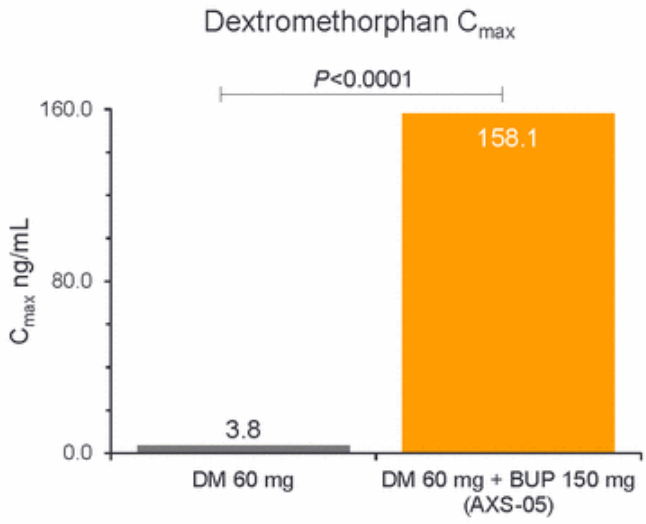




Axsome data on file.
†DM, Dextromethorphan; BUP, Bupropion.

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

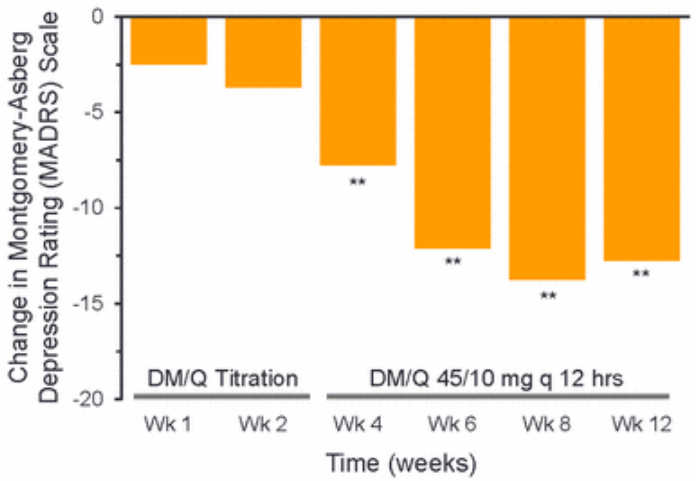
Abbreviations: DM = Dextromethorphan; BUP = Bupropion.

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.

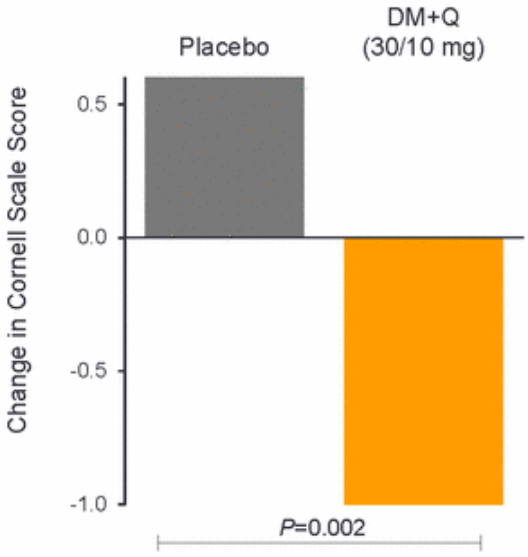
Symptom Reduction in TRD Patients Treated with DM and Metabolic Inhibitor[1]



- 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]

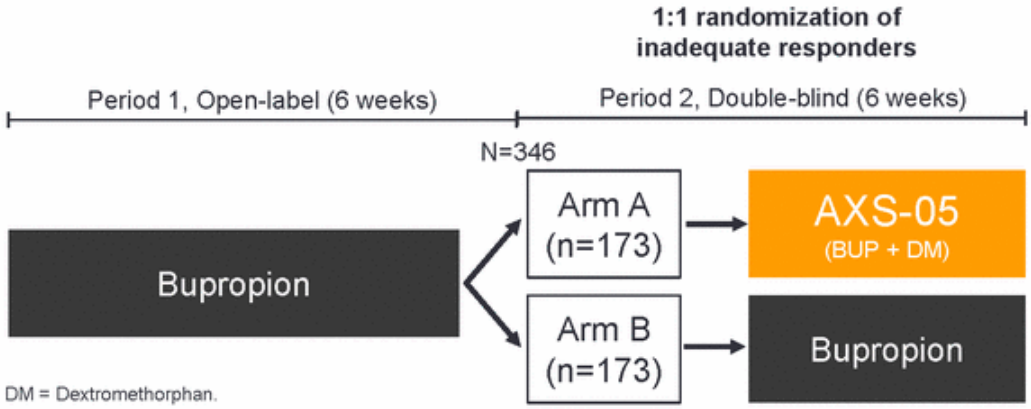


1. Murrough J, et al. *J Affect Disord*. 2017;218:277-283.
2. Cummings J, et al. *JAMA*. 2015;314:1242-1254.

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.

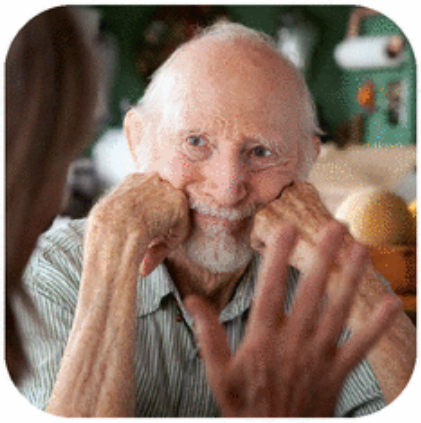


BUP = Bupropion; DM = Dextromethorphan.

- **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

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

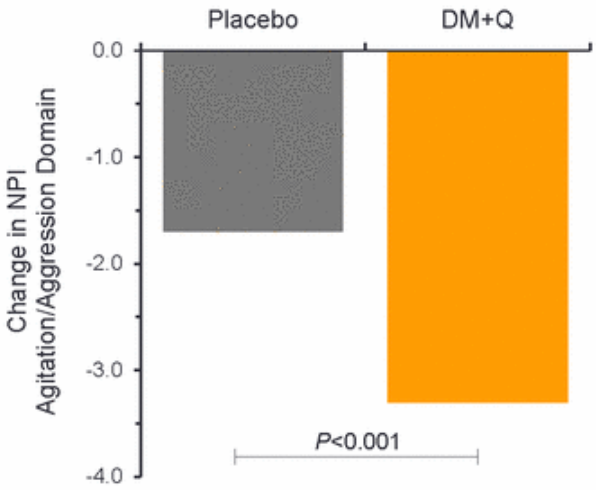
Abbreviations: DM = Dextromethorphan; BUP = Bupropion.

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)

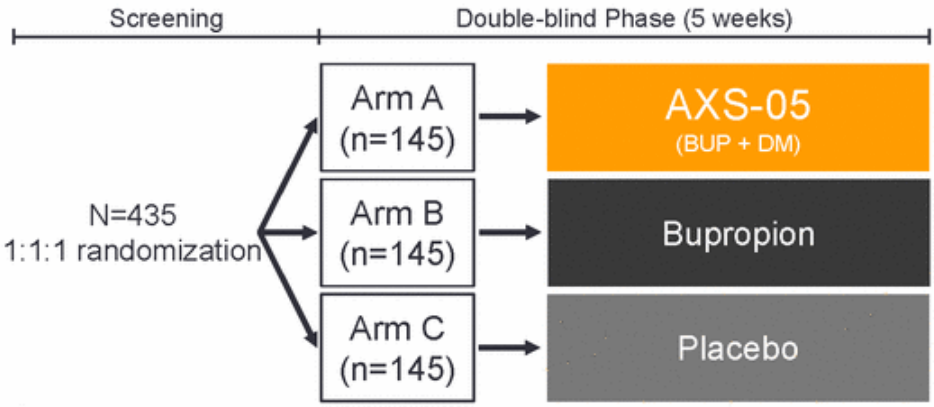


Cummings J, et al. *JAMA*. 2015;314:1242-1254.

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
- Interim analysis 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.

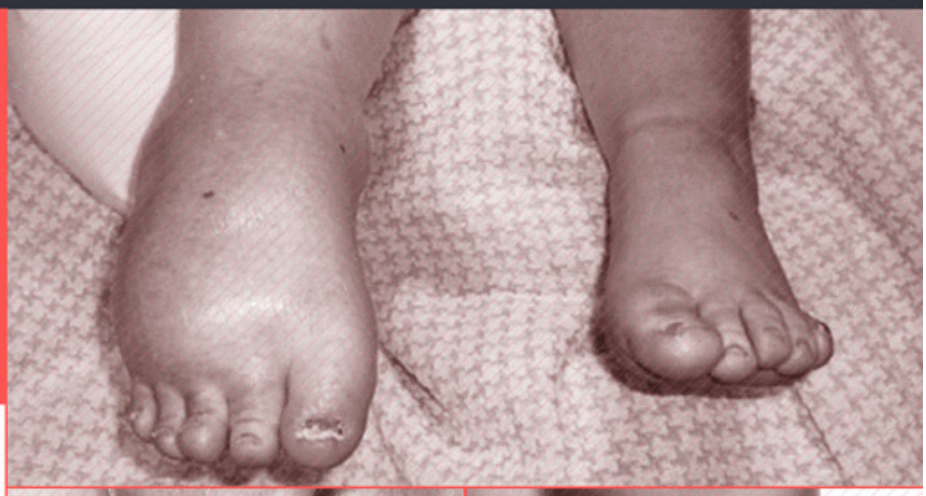
1. U.S. Department of Health and Human Services. The Health Consequences of Smoking: 50 Years of Progress. A Report of the Surgeon General. 2014.
2. Hughes JR, et al. *Addiction*. 2004;99(1):29-38.

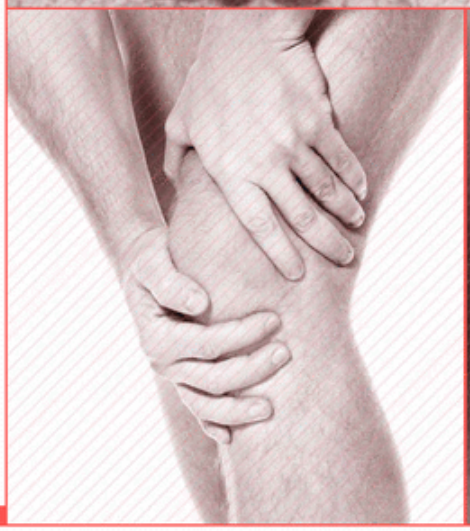
AXS-02

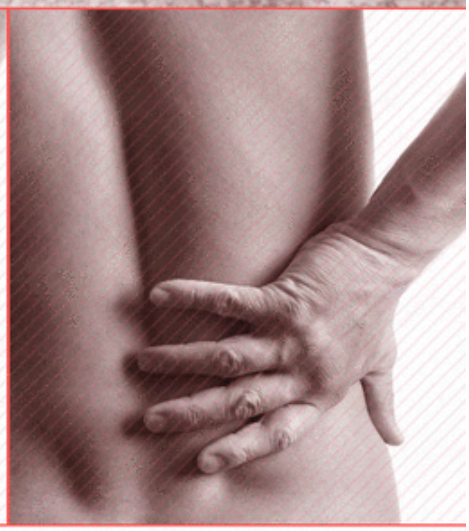
Disodium Zoledronate Tetrahydrate

Novel therapy for chronic pain:

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

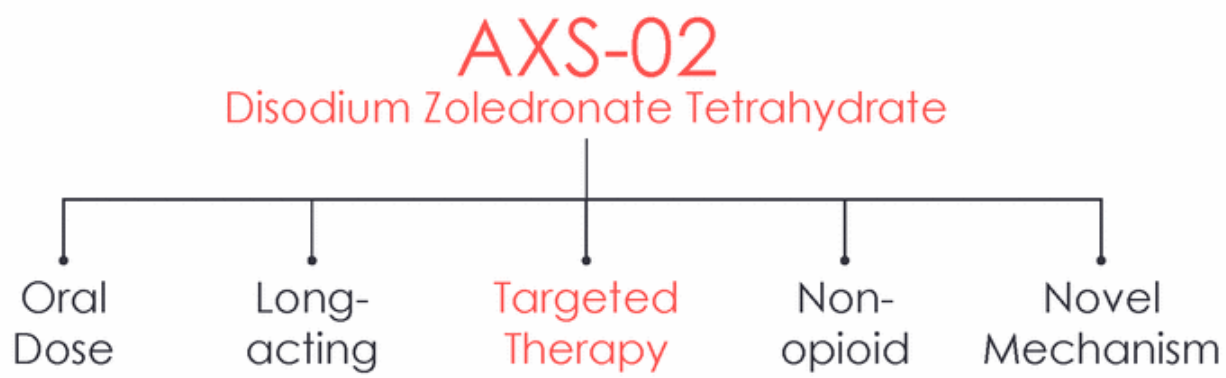






CRPS image source: Voet C, et al. *F1000Reseach.* 2014;3:97.

Chronic Pain:
Differentiated Therapy



IP Overview

- 61 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

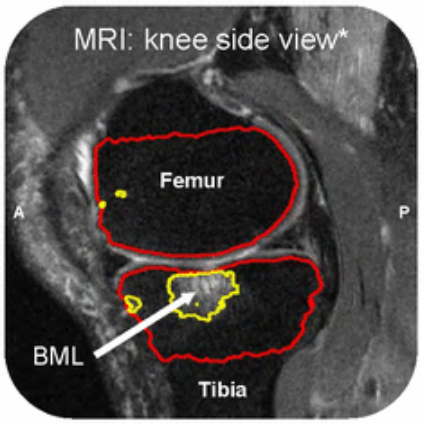
Inhibits bone-resorbing osteoclasts	Downregulates acid-sensing* ion channels	Reduces pro-inflammatory cytokine production	Anti-angiogenic
▼Decreased bone resorption. ▼Farnesyl pyrophosphate synthase (FPPS).[1]	▼ASIC1a expression. ▼ASIC activation.[2] ▼TRPV1 activation.[2,3]	▼TNFα production.[4] ▼IL-6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

* 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.

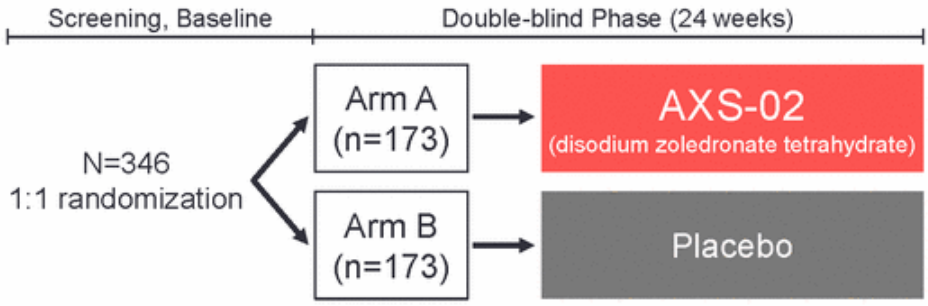
AXSOME THERAPEUTICS

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.

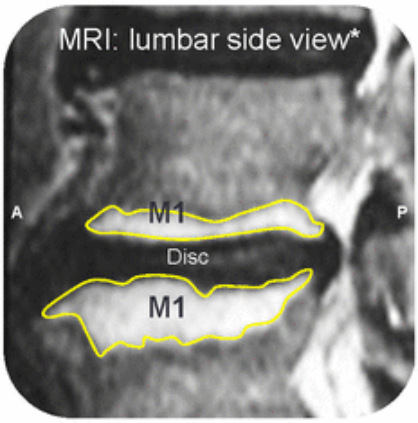
Special Protocol Assessment (SPA) received



- **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.

MoSEIC™ Meloxicam

Novel therapies:

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

Migraine, OA and RA:
MoSEIC™ Meloxicam Overview

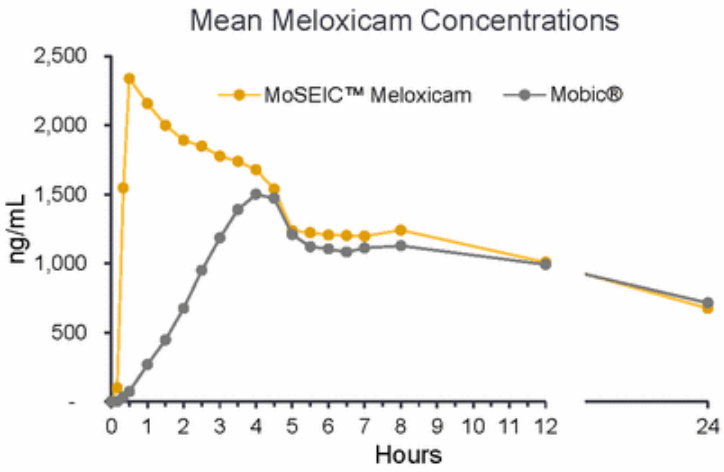
- MoSEIC meloxicam is a potent, oral, rapidly-absorbed, once-daily, non-opioid, COX-2 preferential, pain therapeutic.
- Standard meloxicam has an extended T_{max} (4-6 hours) which delays its onset of action.[1,2]
- Axsome's MoSEIC (Molecular Solubility Enhanced Inclusion Complex) technology substantially 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).

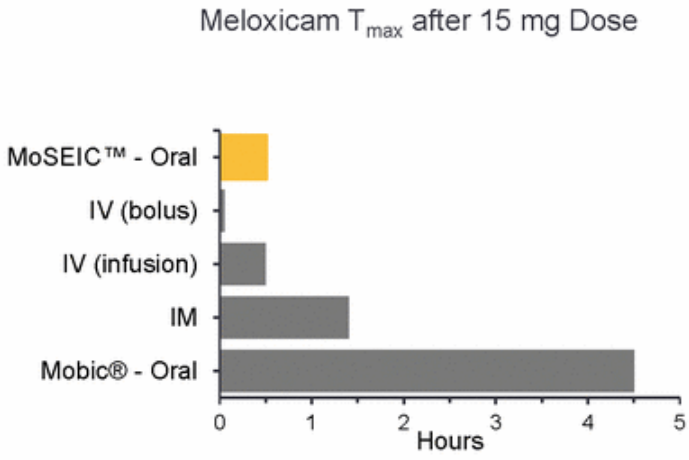
IP Overview

- 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





- 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

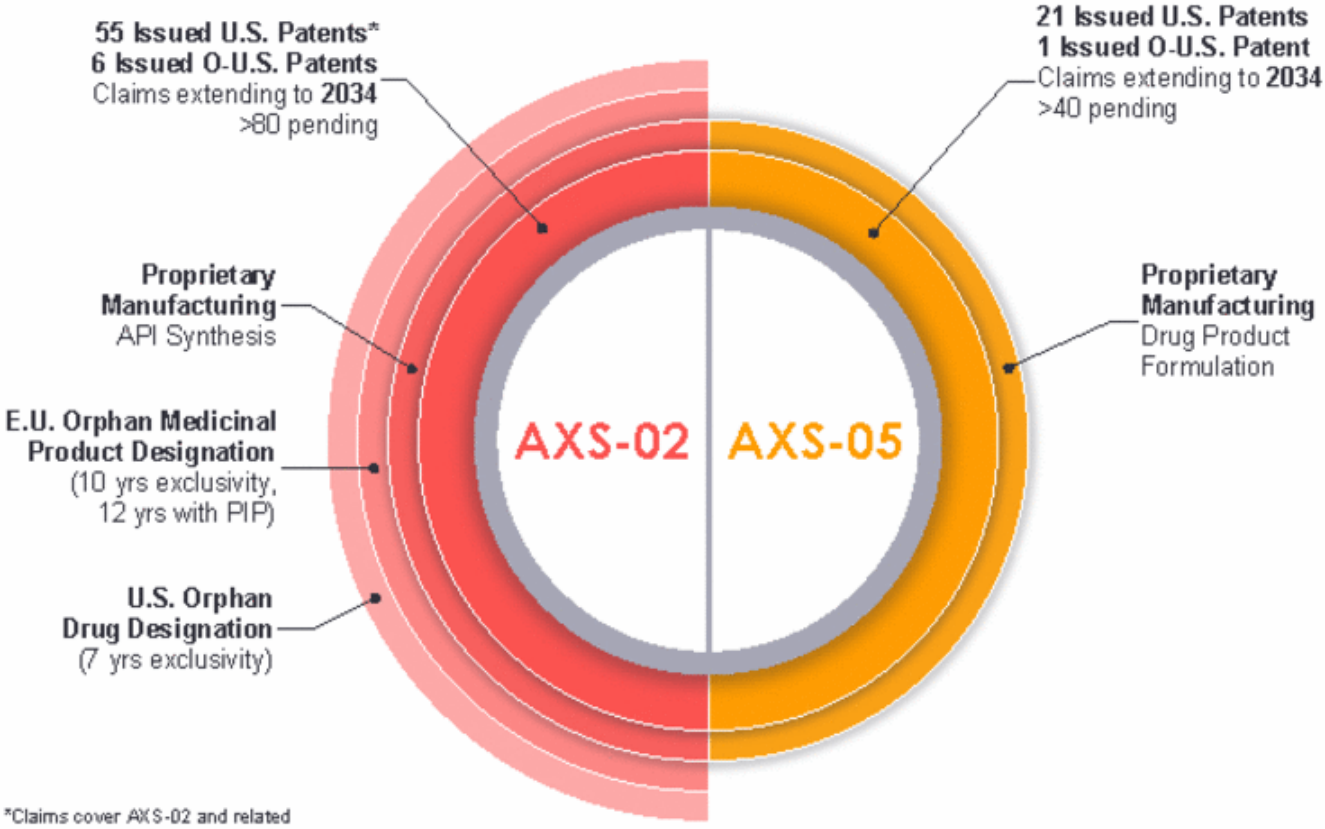
- AXS-06 is a fixed-dose combination of MoSEIC™ meloxicam and esomeprazole
- Being developed to treat OA and RA, and to reduce the risk of NSAID-associated upper GI ulcers
- Potentially best-in-class NSAID profile:
  - Oral administration with IV-like onset of action
  - Long half-life for sustained 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



*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 September 30, 2017[1]
Cash:	$40.7 Million
Debt (Face Value)[2]:	$10.0 Million
Common Shares Outstanding:	25.5 Million
Options and Warrants Outstanding[3]:	4.5 Million

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

1. Pro-Forma to include the effect of the equity capital financings completed in 4th Quarter 2017.
2. Book value of $10.1 million.
3. Consists of 2.4 million options and 2.1 million warrants.

Clinical Milestones

Product Candidate	Indication	2017	2018	2019
AXS-05 (DM + BUP)	**TRD**	✓ **Fast Track** designation	• **STRIDE-1** top-line results (2H 2018/1H 2019)	
	AD Agitation	✓ **Fast Track** designation ✓ **Ph 2/3** trial start		• **ADVANCE-1** top-line results (2H 2019/1H 2020)
	Smoking Cessation	✓ **Duke University** collaboration	• **Ph 2** trial start (1H 2019)	
AXS-02 (DZT)	**Knee OA**		✓ **COAST-1** interim analysis	
	CLBP	✓ **Ph 3 IND** FDA clearance		
AXS-07 (MoSEIC™ Mx + Riz)	**Migraine**	✓ **Ph 3** FDA written guidance	• **Ph 3** trial start	• **Ph 3** top-line results
AXS-06 (MoSEIC™ Mx + Eso)	**OA and RA**	✓ **Ph 1** trial results ✓ **Ph 3** FDA written guidance		

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; TRD = Treatment Resistant Depression.
✓ Accomplished milestone.
• Upcoming milestone.

AXSOME
THERAPEUTICS

Thank you.

For more information, please contact

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