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

June 7, 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.)

200 Broadway, 3rd Floor **New York, New York**	**10038**
(Address of Principal Executive Offices)	(Zip Code)

(212) 332-3241
Registrant's telephone number, including area code

(Former name or former address if changed since last report,)

Securities registered pursuant to Section 12 (b) of the Act:

Title of each class:	**Trading Symbol(s)**	**Name of each exchange on which registered:**
Common Stock, par value $0.0001 per share	AXSM	The Nasdaq Global Market

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

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 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 5.07. Submission of Matters to a Vote of Security Holders.

At the 2019 annual meeting of stockholders (the "Annual Meeting") of Axsome Therapeutics, Inc. (the "Company") held on June 7, 2019, the following proposals were submitted to the stockholders of the Company:

Proposal 1: The election of one director to serve as a Class I director until the Company's 2022 annual meeting of stockholders and until his successor is duly elected and qualified.

Proposal 2: The ratification of the appointment of Ernst & Young LLP as the Company's independent registered public accounting firm for the fiscal year ending December 31, 2019.

For more information about the foregoing proposals, see the Company's definitive proxy statement on Schedule 14A filed with the United States Securities and Exchange Commission on April 26, 2019 (the "Proxy Statement"). Of the 33,305,310 shares of the Company's common stock entitled to vote at the Annual Meeting, 28,207,298 shares, or approximately 84.69%, were represented at the meeting in person or by proxy, constituting a quorum. The number of votes cast for, against or withheld, as well as abstentions and broker non-votes, if applicable, in respect of each such proposal is set forth below:

Proposal 1: Election of Class I Director.

The Company's stockholders elected the following director to serve as a Class I director until the 2022 annual meeting of stockholders and until his successor is duly elected and qualified. The votes regarding the election of the director were as follows:

Director	Votes For	Votes Withheld	Broker Non-Votes
Roger Jeffs, Ph.D.	15,944,132	1,627,219	10,635,947

Proposal 2: Ratification of Appointment of Ernst & Young LLP.

The Company's stockholders ratified the appointment of Ernst & Young LLP as the Company's independent registered public accounting firm for the fiscal year ending December 31, 2019. The votes regarding this proposal were as follows:

Votes For	Votes Against	Votes Abstaining	Broker Non-Votes
28,179,414	8,252	19,632	0

Item 8.01. Other Events.

On June 7, 2019, the Company issued a press release providing an update on the status of its clinical product candidates, AXS-05, AXS-07, and AXS-12. The full text of the press release is filed as Exhibit 99.1 hereto and incorporated herein by reference.

Additionally, on June 7, 2019, the Company updated its presentation slide deck. A copy of the presentation slide deck is attached hereto as Exhibit 99.2 and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Press release dated June 7, 2019.
99.2	Corporate Presentation.

SIGNATURE

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.

Date: June 7, 2019

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

AXSOME THERAPEUTICS

Axsome Therapeutics Provides Update on Continued Progress at Annual Stockholders' Meeting

Placebo-controlled Phase 3 trial of AXS-05 in MDD on track to start in 2Q 2019

Topline results from both STRIDE-1 Phase 3 trial in TRD and planned placebo-controlled Phase 3 trial in MDD for AXS-05 still anticipated in 2H 2019

Phase 3 MOMENTUM trial of AXS-07 in migraine on track for readout of topline results in 2H 2019

Phase 2 CONCERT trial results of AXS-12 in narcolepsy now anticipated in 2H 2019

Current cash sufficient to fund anticipated operations beyond all clinical trial readouts

NEW YORK, June 07, 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, is providing the following update on the Company's continued progress at its Annual Meeting of Stockholders being held today:

AXS-05

AXS-05 (dextromethorphan/bupropion) is Axsome's novel, oral, investigational NMDA receptor antagonist with multimodal activity being developed for the following indications: treatment resistant depression (TRD), major depressive disorder (MDD), Alzheimer's disease (AD) agitation, and smoking cessation. AXS-05 has been granted U.S. Food and Drug Administration (FDA) Breakthrough Therapy designation for the treatment of MDD and Fast Track designations for the treatment of TRD and for the treatment of AD agitation.

Depression

- Axsome continues to expect topline results from the ongoing Phase 3 STRIDE-1 trial of AXS-05 in TRD in the second half of 2019.
- Axsome is on track to initiate its planned placebo-controlled Phase 3 trial of AXS-05 in MDD this quarter with topline results anticipated in the second half of 2019.
- An NDA filing for AXS-05 in the treatment of MDD is targeted for 2020.

Alzheimer's Disease Agitation

- Axsome remains on track to report topline results from the ongoing Phase 2/3 ADVANCE-1 trial of AXS-05 in agitation associated with Alzheimer's disease in the first half of 2020.

AXS-07

AXS-07 (MoSEIC™ meloxicam/rizatriptan) is Axsome's novel, oral, investigational medicine with distinct dual mechanisms of action being developed for the acute treatment of migraine.

- Based on the continued faster-than-expected enrollment in the MOMENTUM Phase 3 trial of AXS-07 in the acute treatment of migraine, Axsome continues to anticipate topline results from this trial in the second half of 2019. MOMENTUM is being conducted pursuant to an FDA Special Protocol Assessment (SPA).

AXS-12

AXS-12 (reboxetine) is Axsome's novel, oral, potent and highly selective norepinephrine reuptake inhibitor being developed for the treatment of narcolepsy. AXS-12 has been granted Orphan Drug Designation by the FDA for the treatment of narcolepsy.

- Based on current enrollment trends, Axsome now anticipates topline results from the CONCERT Phase 2 trial of AXS-12 in narcolepsy in the second half of 2019 versus previous guidance of the second quarter of 2019.

Financial Update

- Axsome believes that its current cash will be sufficient to fund the Company's anticipated operations, based on its current operating plans, into at least the first quarter of 2021, or approximately 1 year beyond the readout of all of the above ongoing and planned clinical trials.
- Axsome currently does not anticipate future equity financings prior to the readout from its Phase 3 trials.

Anticipated Clinical Trial Readouts

- Phase 3 STRIDE-1 trial of AXS-05 in TRD, topline data (2H 2019)
- Phase 3 placebo-controlled trial of AXS-05 in MDD, topline data (2H 2019)

- Phase 3 trial of AXS-07 in the acute treatment of migraine, topline data (2H 2019)
- Phase 2 trial of AXS-12 in narcolepsy, topline data (2H 2019)
- Phase 2/3 ADVANCE-1 trial of AXS-05 in AD agitation, topline data (1H 2020)

About AXS-05

AXS-05 is a novel, oral, patent-protected, investigational NMDA receptor antagonist with multimodal activity under development for the treatment of major depressive disorder and other central nervous system (CNS) disorders. AXS-05 consists of a proprietary formulation and doses of dextromethorphan and bupropion and utilizes Axsome's metabolic inhibition technology. The dextromethorphan component of AXS-05 is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, also known as a glutamate receptor modulator, which is a novel mechanism of action, meaning it works differently than currently available therapies for depression. The dextromethorphan component of AXS-05 is also a sigma-1 receptor agonist, nicotinic acetylcholine receptor antagonist, and inhibitor of the serotonin and norepinephrine transporters. The bupropion component of AXS-05 serves to increase the bioavailability of dextromethorphan, and is a norepinephrine and dopamine reuptake inhibitor, and a nicotinic acetylcholine receptor antagonist. AXS-05 is covered by more than 30 issued U.S. and international patents which provide protection out to 2034. AXS-05 is not approved by the FDA.

About AXS-07

AXS-07 is a novel, oral, investigational medicine with distinct dual mechanisms of action under development for the acute treatment of migraine. AXS-07 consists of MoSEIC™ meloxicam and rizatriptan. Meloxicam is a new molecular entity for migraine enabled by Axsome's MoSEIC (Molecular Solubility Enhanced Inclusion Complex) technology, which results in rapid absorption of meloxicam while maintaining a long plasma half-life. Meloxicam is a COX-2 preferential non-steroidal anti-inflammatory drug and rizatriptan is a 5-HT1B/D agonist. AXS-07 is designed to provide rapid, enhanced and consistent relief of migraine, with reduced symptom recurrence. AXS-07 is not approved by the FDA.

About AXS-12

AXS-12 (reboxetine) is a novel, oral, investigational medicine in development for the treatment of the symptoms of narcolepsy. AXS-12 is a highly selective and potent norepinephrine reuptake inhibitor. AXS-12 is an investigational drug product not approved by the FDA.

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), and a Phase 2/3 trial in agitation associated with Alzheimer's disease (AD). AXS-05 is also being developed for major depressive disorder (MDD) and smoking cessation treatment. 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, pace of enrollment 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, and the number or type of studies or nature of results necessary to support the filing of a new drug application ("NDA") for any of our current product candidates; our ability to fund additional clinical trials to continue the advancement of our product candidates; the timing of and our ability to obtain and maintain U.S. Food and Drug Administration ("FDA") or other regulatory authority approval of, or other action with respect to, our product candidates (including, but not limited to, 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; the Company's anticipated capital requirements; 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

June 2019

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

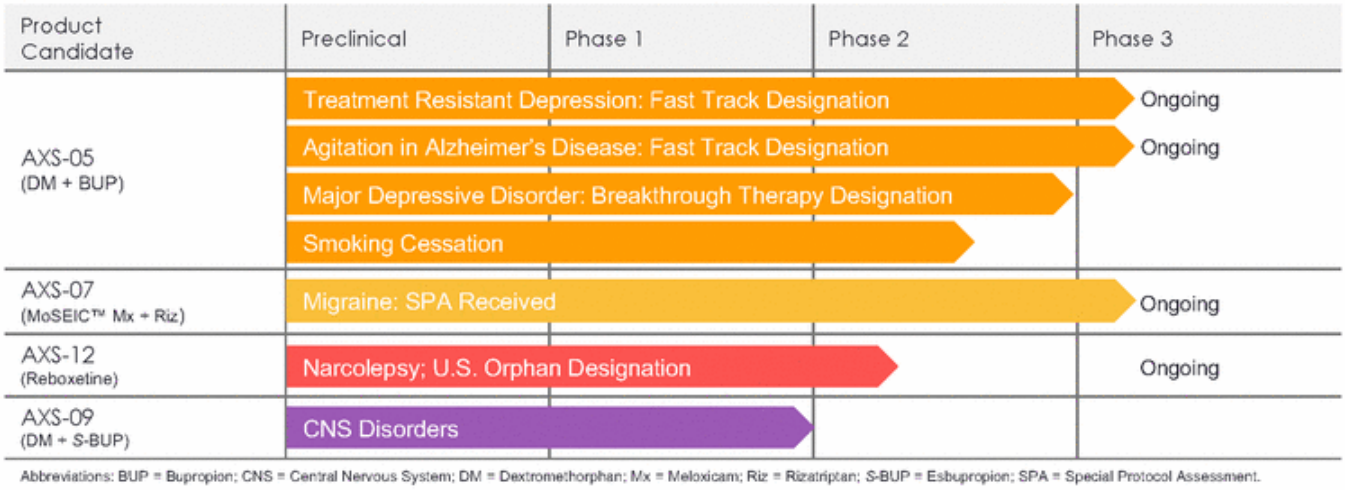
MoSEIC™ Delivery

Metabolic Inhibition

Chemical Synthesis & Analysis

Our CNS Candidates and Pipeline

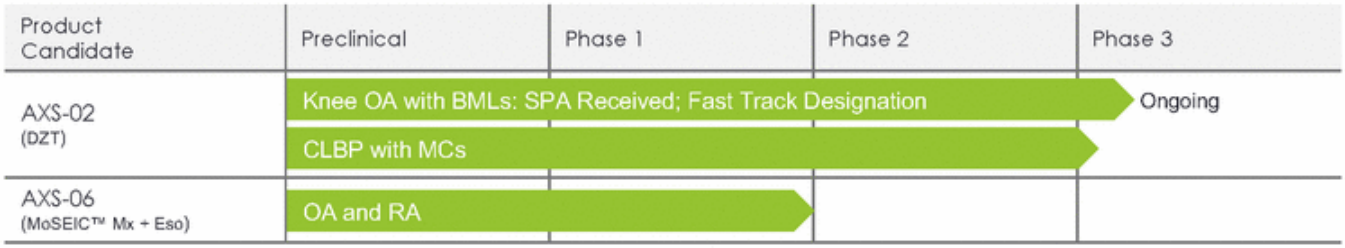
- Four differentiated clinical-stage CNS assets targeting significant and growing markets.
- Patent protection to 2034-2036, worldwide rights.



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.



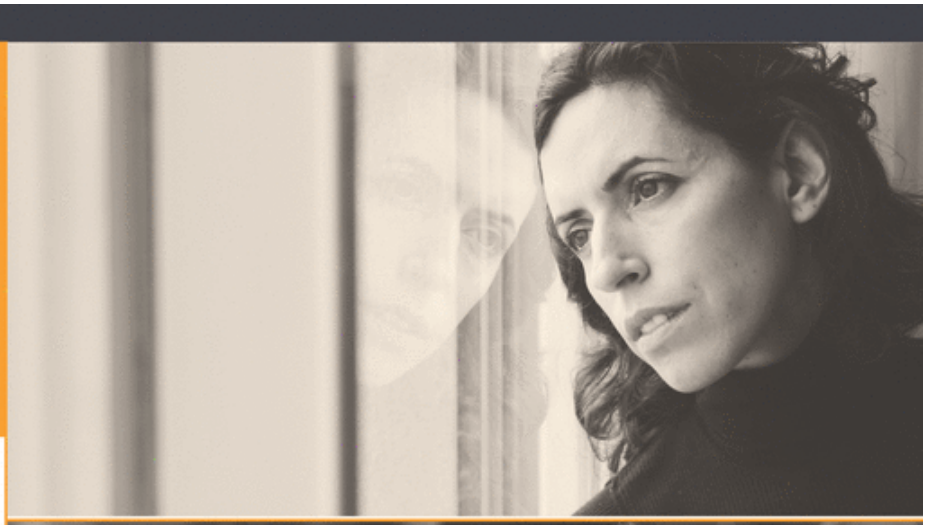
Abbreviations: BML = Bone Marrow Lesions; CLBP = Chronic Low Back Pain; DZT = Disodium Zoledronate Tetrahydrate; Eso = Esomeprazole; MC = Modic Changes; Mx = Meloxicam; OA = Osteoarthritis; RA = Rheumatoid Arthritis; SPA = Special Protocol Assessment

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

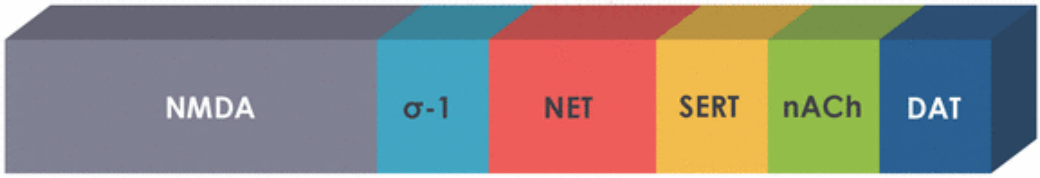


AXS-05:
Novel Multimodal Therapy for CNS Disorders

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

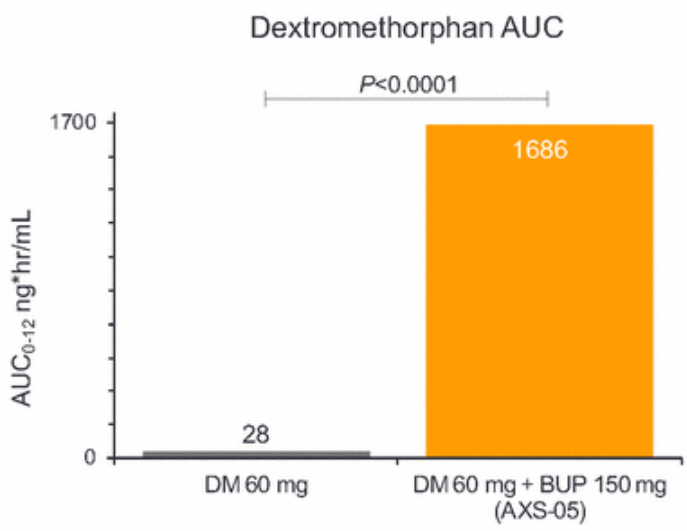
Multimodal Activity | **Relevant Indications**

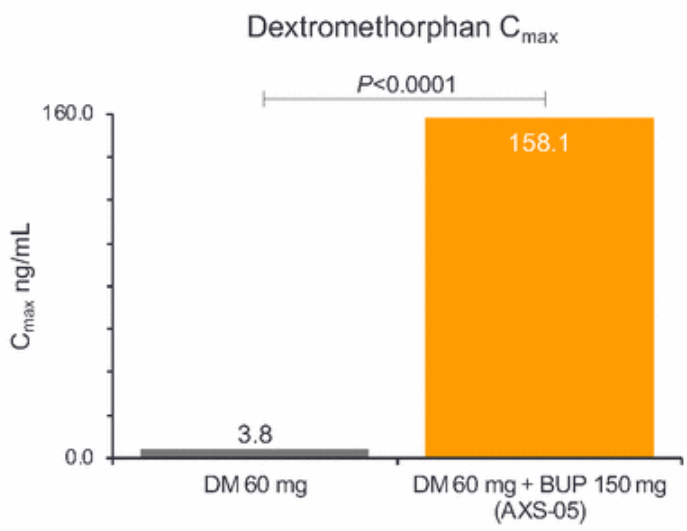
Mechanism of Action	AXS-05	ADHD	Anxiety	Alzheimer's	Depression	Fibromyalgia	OCD	Pain	Smoking cessation	Related Agents
NMDA Receptor Antagonist	✓			■	■			■		• Ketamine • Memantine (Namenda®)
Sigma-1R Agonist	✓			■	■		■			• Fluvoxamine (Luvox®) • Donepezil (Aricept®)
Norepinephrine Reuptake Inhibitor	✓				■	■		■		• 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 Dextromethorphan or Bupropion, unless specifically noted.
2. Agents do not contain Dextromethorphan or Bupropion, 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.
- FDA Breakthrough Therapy Designation received for MDD.
- Phase 2 MDD trial completed.

17.3M patients in the U.S.[1]

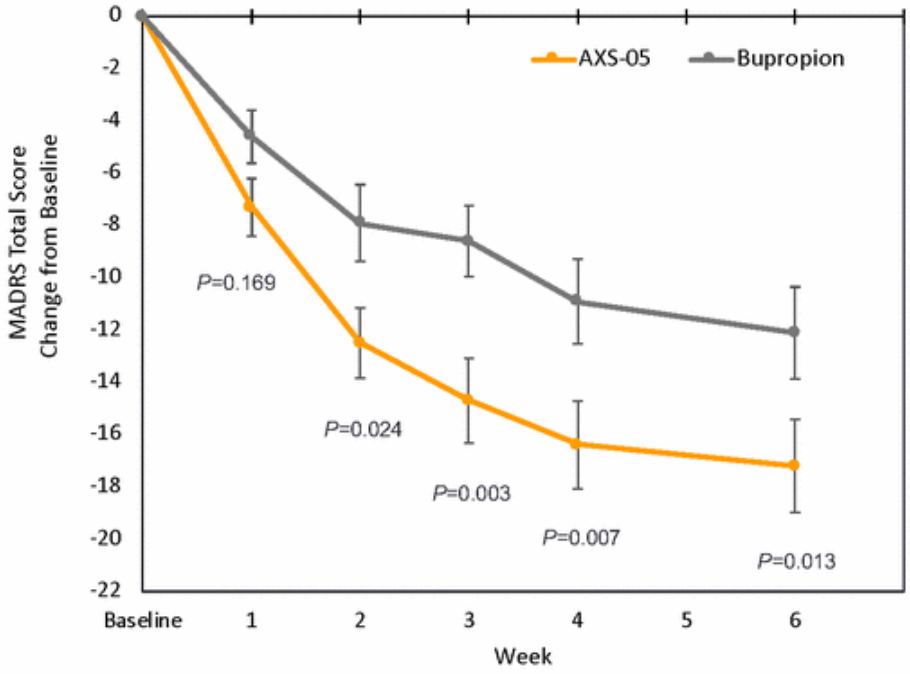
Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-05 (DM + BUP)	Treatment Resistant Depression: Fast Track Designation			Ongoing
	Major Depressive Disorder: Breakthrough Therapy Designation			

Abbreviations: DM = Dextromethorphan; BUP = Bupropion.

1. National Survey on Drug Use and Health (NSDUH). (2017).
2. Rush AJ, et al. *Am J Psychiatry* 2006;163:1905-1917.

AXSOME THERAPEUTICS

CNS Disorders:
Depression Phase 2 Results

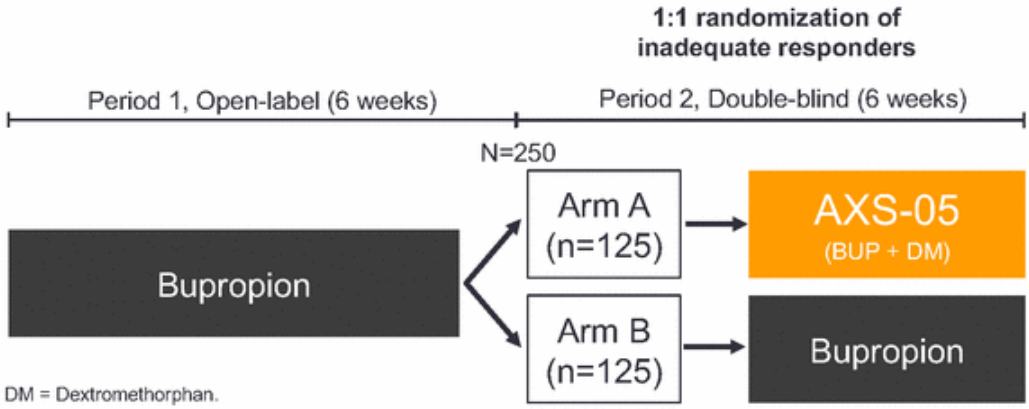


	AXS-05	Bupropion	P-Value
Primary Endpoint			
Change in MADRS Total Score over 6-Week Period (averaged)	-13.7	-8.8	< 0.001
Change in MADRS Total Score at Week 6	-17.2	-12.1	0.013

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.

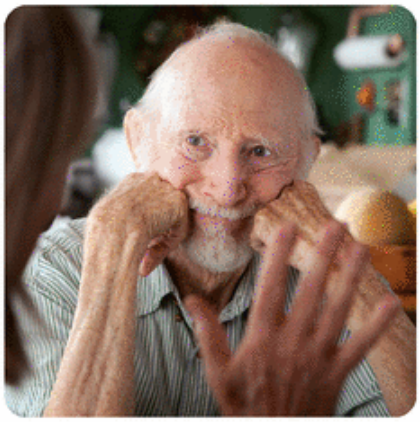


BUP = Bupropion; DM = Dextromethorphan.

- **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 Designation			Ongoing

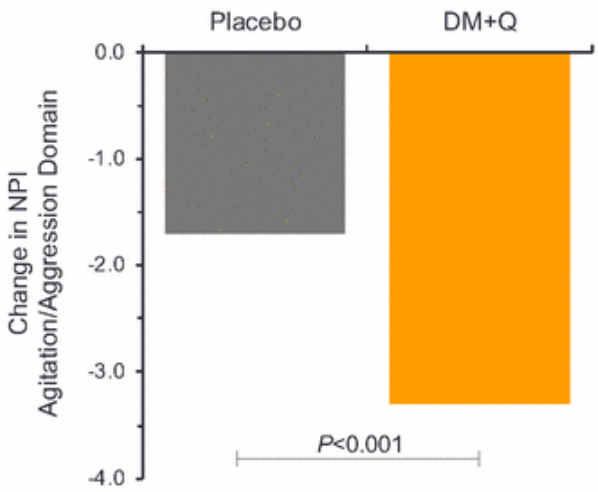
Abbreviations: DM = Dextromethorphan; BUP = Bupropion.

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)

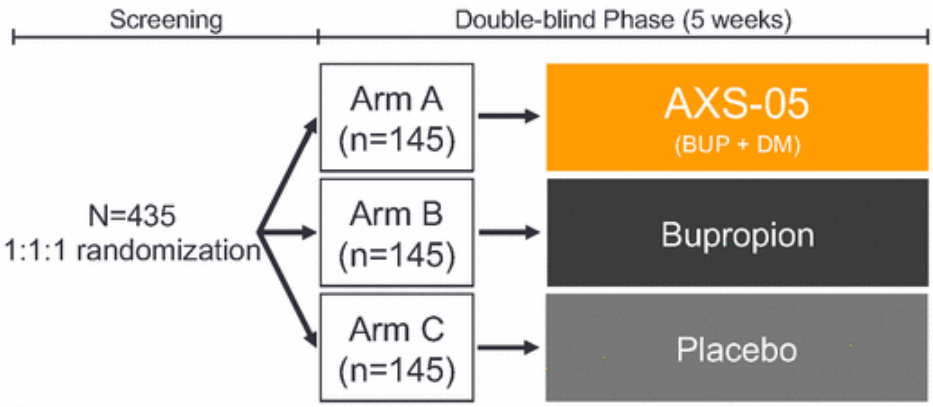


Cummings J, et al. *JAMA*. 2015;314:1242-1254.

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]
- Positive Phase 2 trial results (Duke University collaboration):
  - 25% greater reduction in average cigarettes per day for AXS-05 versus bupropion (p=0.0016)
  - Greater percentage of smokers experiencing >50% reduction in expired carbon monoxide (52.0% for AXS-05 versus 30.4% for bupropion, p=0.15).
- AXS-05 represents a potentially new mechanism of action for smoking cessation.

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

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

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.

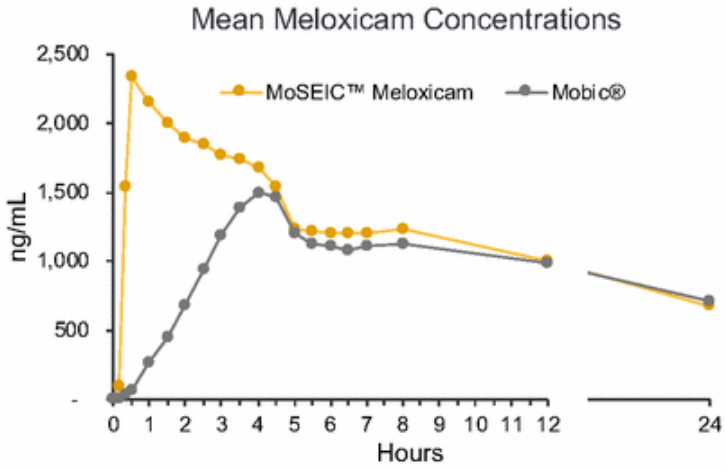
37M patients in the U.S.[1]

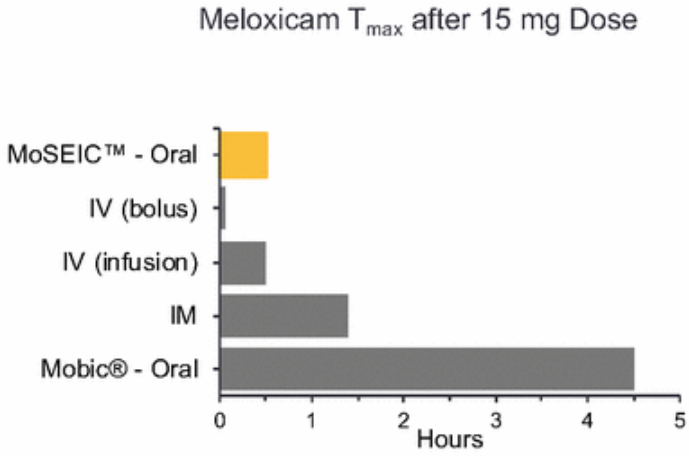
Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-07 (MoSEIC™ Mx + Riz)	Migraine: SPA Received			Ongoing

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





- 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

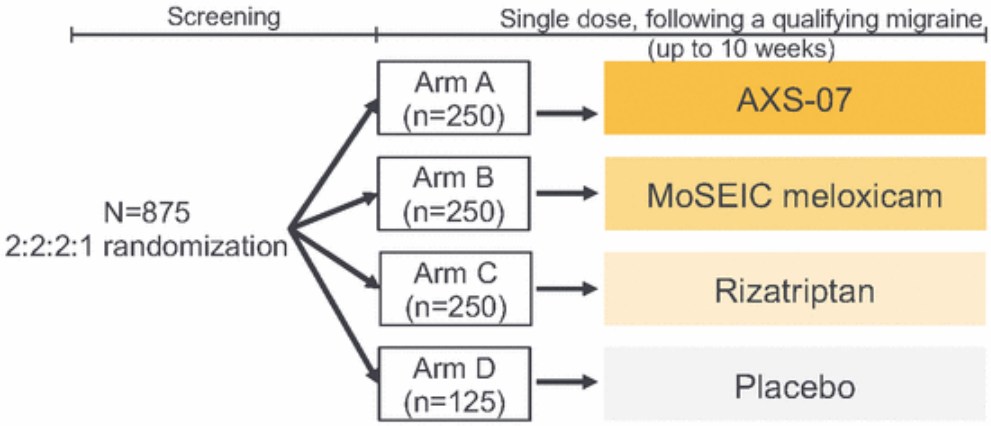
Pharmaco-economic benefits

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.



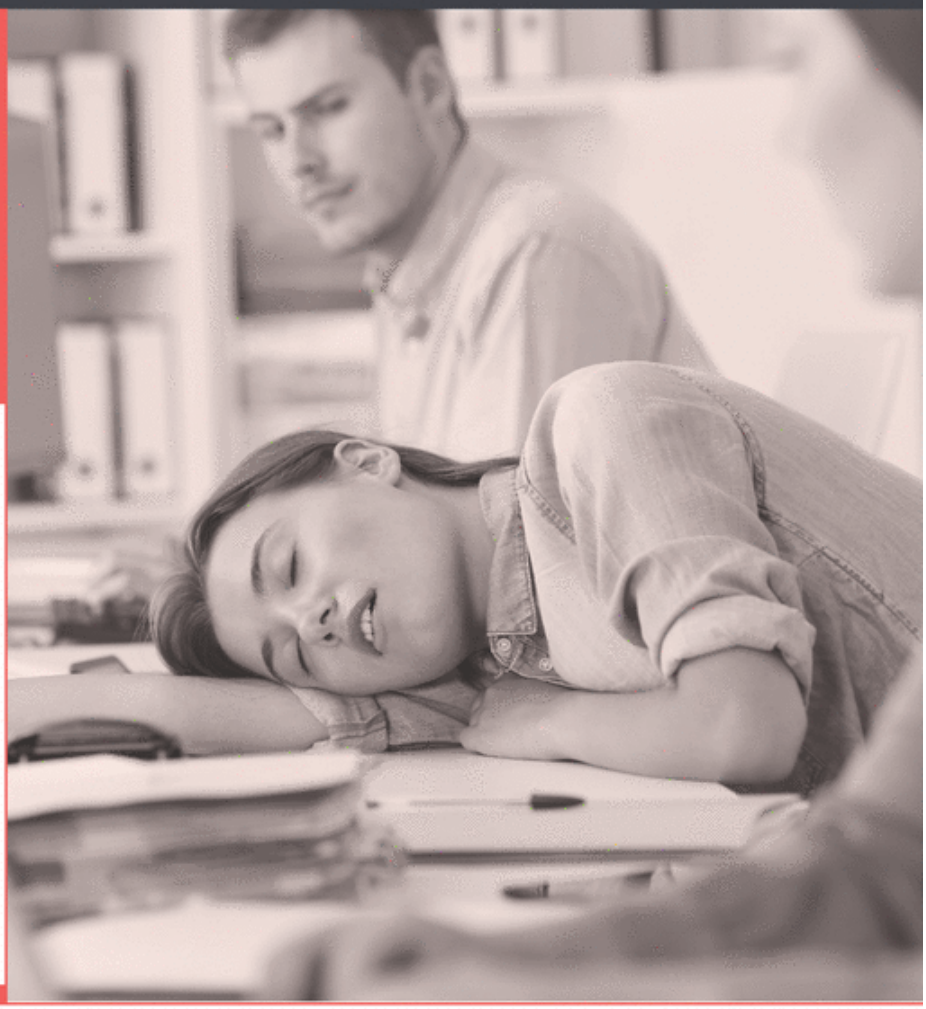
- **Primary Endpoint:**
  - Pain freedom at 2 hours post-dose
  - Freedom from most bothersome symptom at 2 hours post-dose
- **Key Inclusion Criteria:**
  - Inadequate response to prior migraine therapy

AXS-12

Reboxetine

Novel therapy for:

- Narcolepsy



CNS Disorders:
Narcolepsy Overview

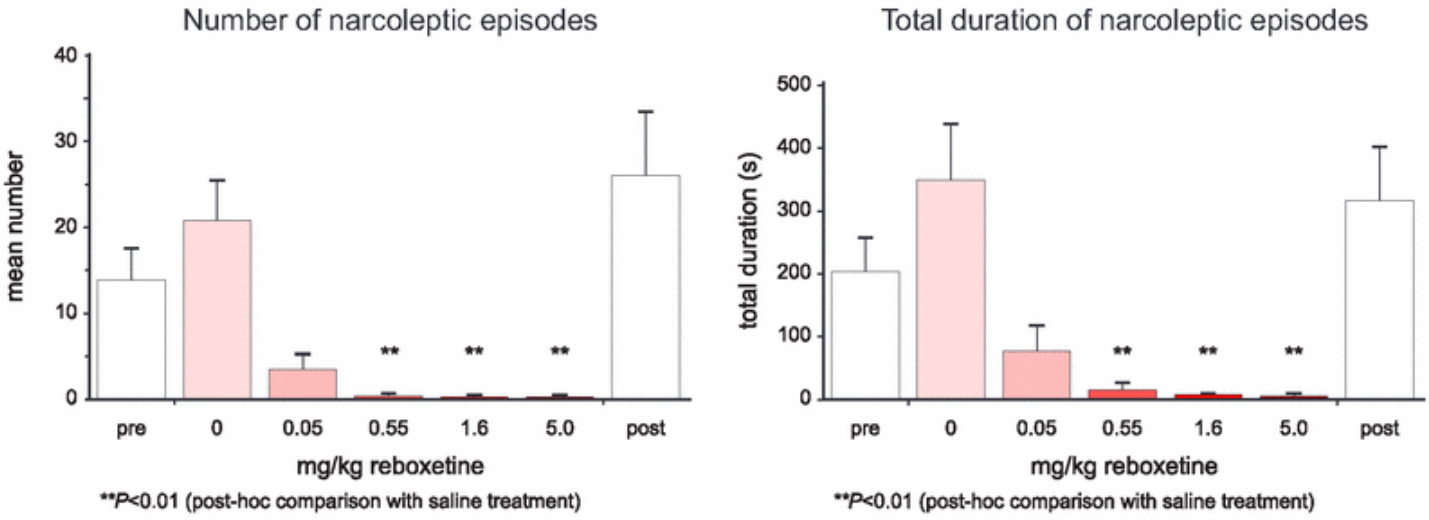
- Debilitating sleep disorder characterized by excessive daytime sleepiness (EDS) and cataplexy.
- Limited treatment options
  - All current approved drugs are scheduled
  - Only one approved agent for cataplexy.
- AXS-12 showed potent activity in genetic mouse model of narcolepsy, and positive effects 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

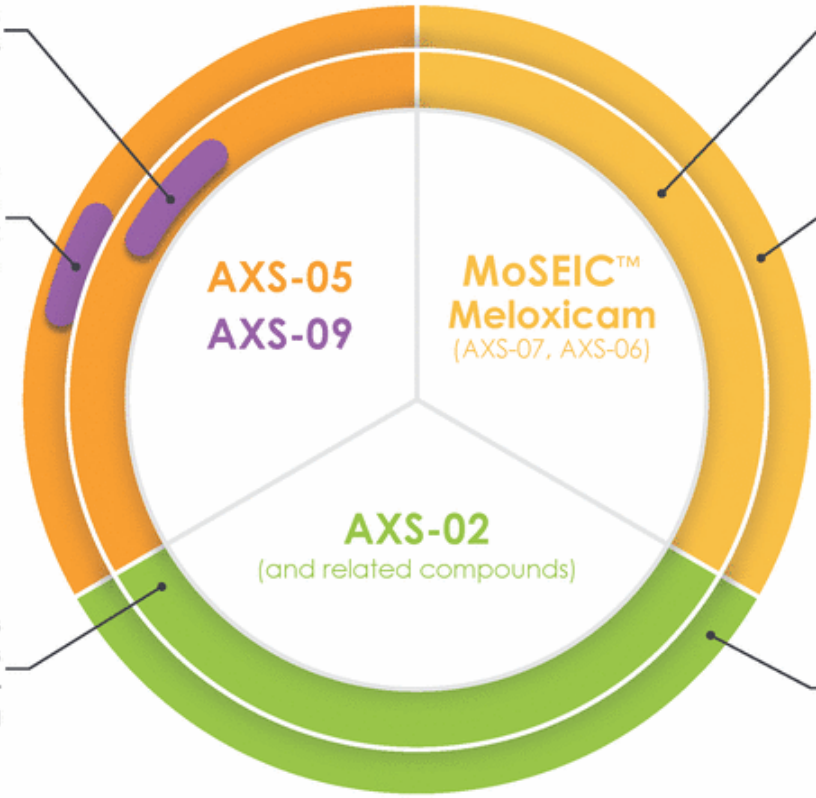
CNS Disorders:
Narcolepsy Scientific Rationale



- 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



32 Issued U.S. Patents
4 Issued O-U.S. Patents
Claims extending to **2034**
>40 pending

Proprietary Manufacturing
Drug Product Formulation

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

Proprietary Manufacturing
Drug Product Formulation

99 Issued U.S. Patents
55 Issued O-U.S. Patents
Claims extending to **2034**
>50 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 March 31, 2019
Cash:	$42.6 Million
Debt (Face Value):	$20.0 Million
Common Shares Outstanding (Pro-Forma)[1]:	33.3 Million
Options and Warrants Outstanding1:	3.3 Million

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

1. Consists of 3.1 million options and 0.2 million warrants.

Clinical Milestones

Product Candidate	Indication	2019	2020
AXS-05 (DM + BUP)	**TRD**	• **STRIDE-1** topline results (2H 2019)	
	AD Agitation		• **ADVANCE-1** topline results (1H 2020)
	MDD	✓ **ASCEND** topline results ✓ **FDA** Breakthrough Therapy Designation • **Ph 3** trial start (2Q 2019) • **Ph 3** topline results (2H 2019)	
	Smoking Cessation	✓ **Ph 2** topline results	
AXS-07 (MoSEIC™ Mx + Riz)	**Migraine**	✓ **FDA SPA** Granted ✓ **MOMENTUM** trial start • **MOMENTUM** topline results (2H 2019)	
AXS-12 (Reboxetine)	**Narcolepsy**	✓ **CONCERT** trial start • **CONCERT** topline results (2H 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

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SVP, Operations

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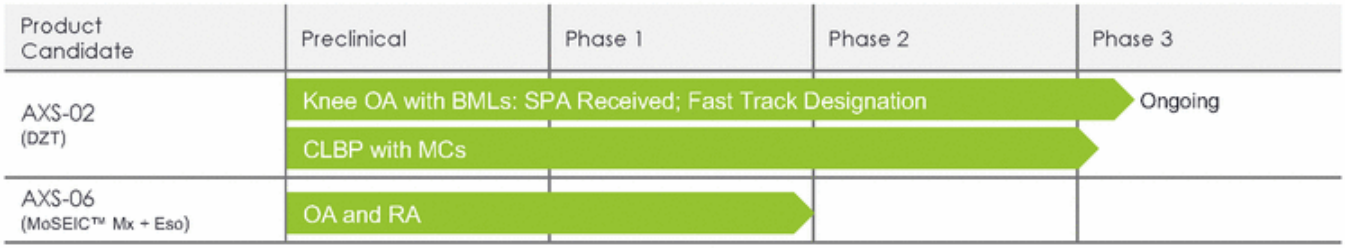
APPENDIX – AXSOME PPC

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.



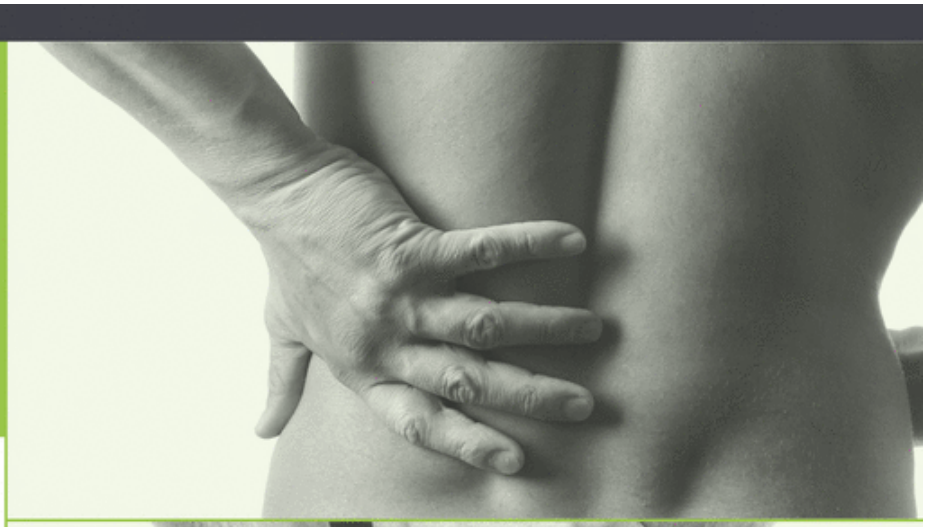
Abbreviations: BML = Bone Marrow Lesions; CLBP = Chronic Low Back Pain; DZT = Disodium Zoledronate Tetrahydrate; Eso = Esomeprazole; MC = Modic Changes; Mx = Meloxicam; OA = Osteoarthritis; RA = Rheumatoid Arthritis; SPA = Special Protocol Assessment

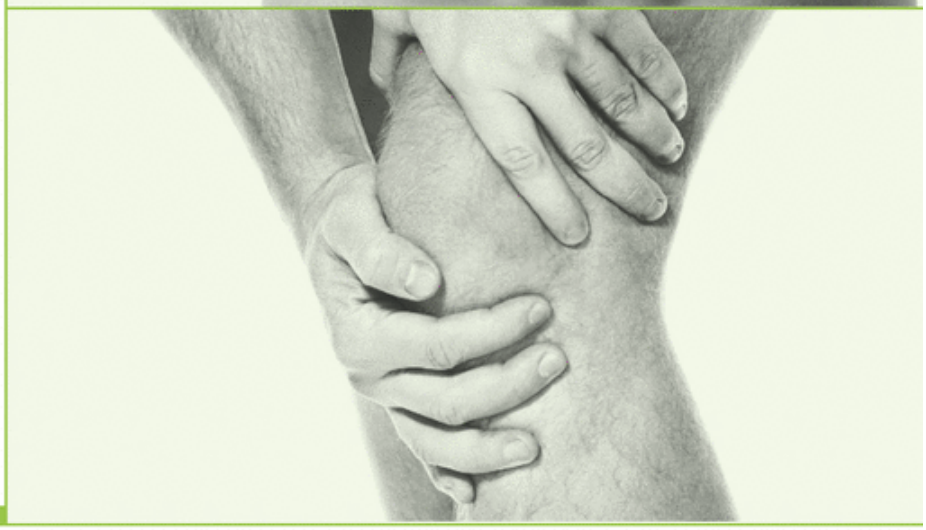
AXS-02

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

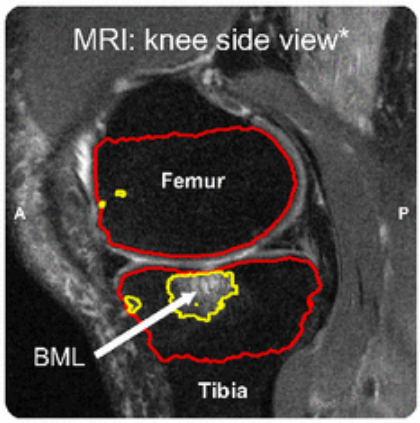
Mechanisms of Action

- 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.

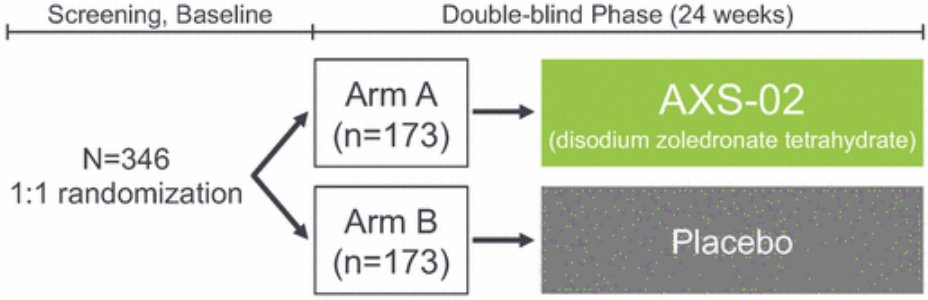
AXSOME THERAPEUTICS

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.

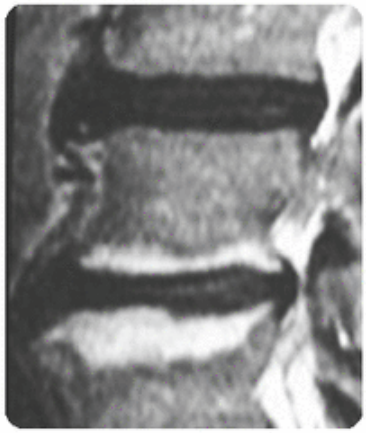
Special Protocol Assessment (SPA) received



- **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.

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