NASDAQ: AXSM

AXSOME THERAPEUTICS

October 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, pace of enrollment and completion of the trials (including our ability to fully fund our disclosed clinical trials, which assumes no material changes to our currently projected expenses), 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 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 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; the Company’s anticipated capital requirements, including the Company’s anticipated cash runway and the Company’s current expectations regarding its plans for future equity financings prior to the readout from its Phase 3 clinical trials; 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 serious CNS disorders, where current treatment options are limited or inadequate, by creating novel therapeutics to improve the lives of patients.

Our Technologies

Enabling new and innovative medicines to treat CNS conditions

Chiral & Formulation Chemistry

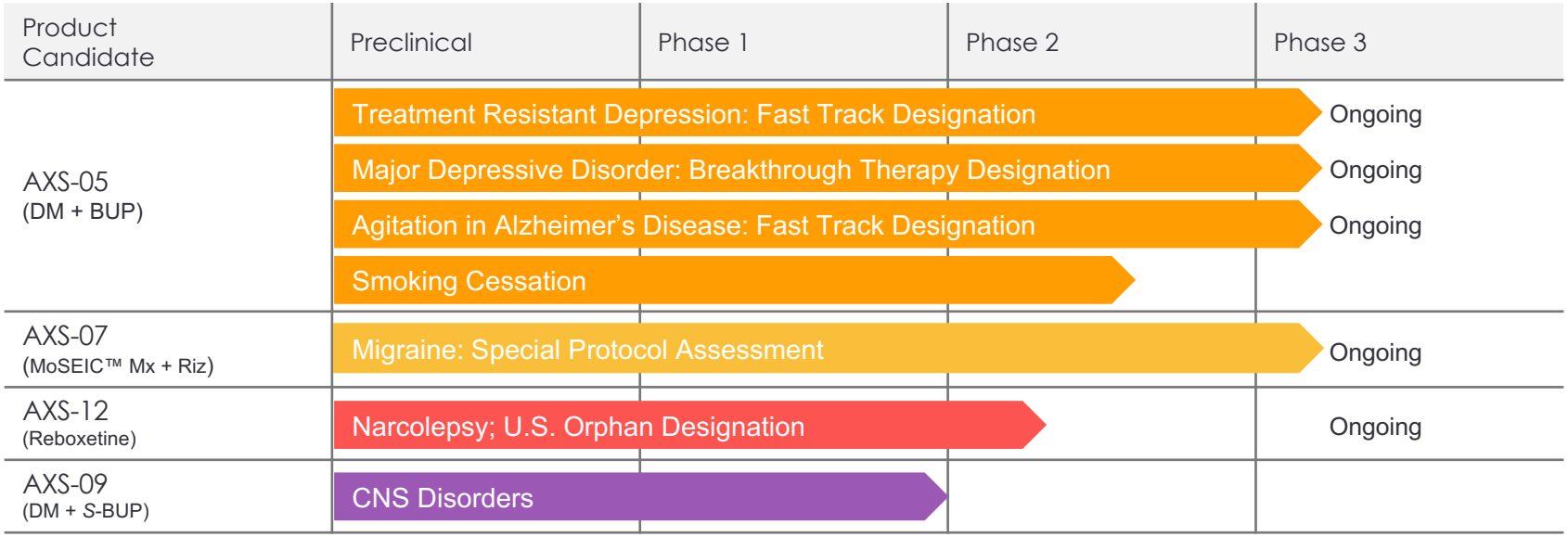
MoSEIC™ Delivery

Metabolic Inhibition

Chemical Synthesis & Analysis

Our CNS Candidates and Pipeline

- Four differentiated clinical-stage product candidates targeting serious CNS conditions.
- 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.

AXS-05

(dextromethorphan/bupropion) modulated delivery tablet

Novel therapy for CNS disorders:

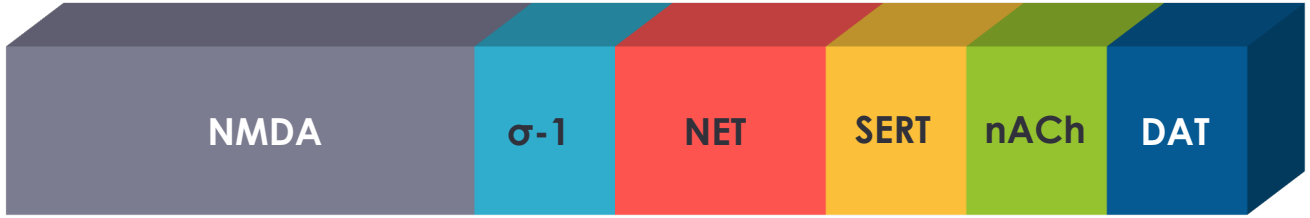
- Treatment Resistant Depression (TRD)
- Major Depressive Disorder (MDD)
- Agitation in Alzheimer's Disease (AD)
- Smoking Cessation

AXS-05:
Novel Multimodal Therapy for CNS Disorders

Single Target

Multimodal

Ketamine



AXS-05
(dextromethorphan/bupropion) modulated delivery tablet

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.

AXS-05:
Mechanisms of Action

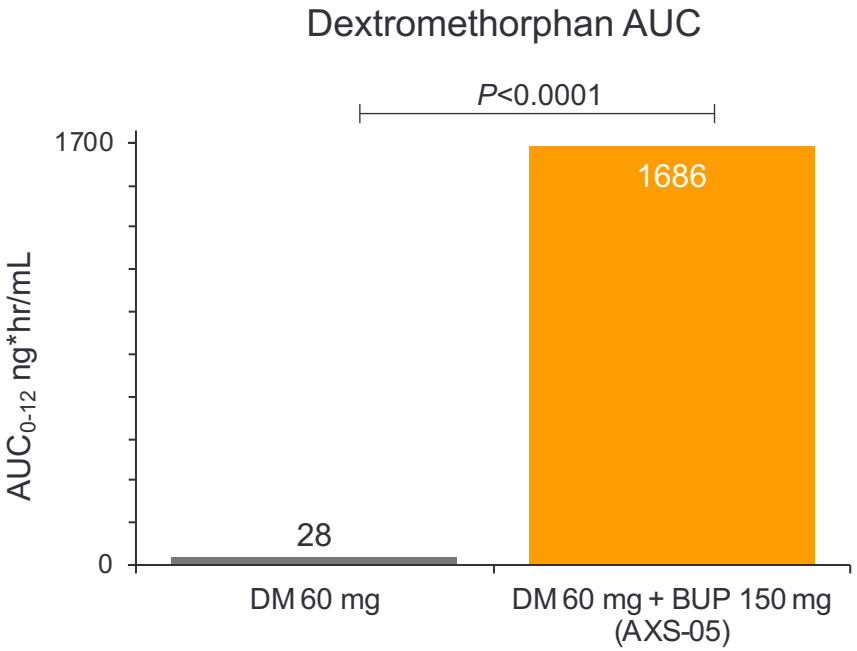
Multimodal Activity **Relevant Indications**

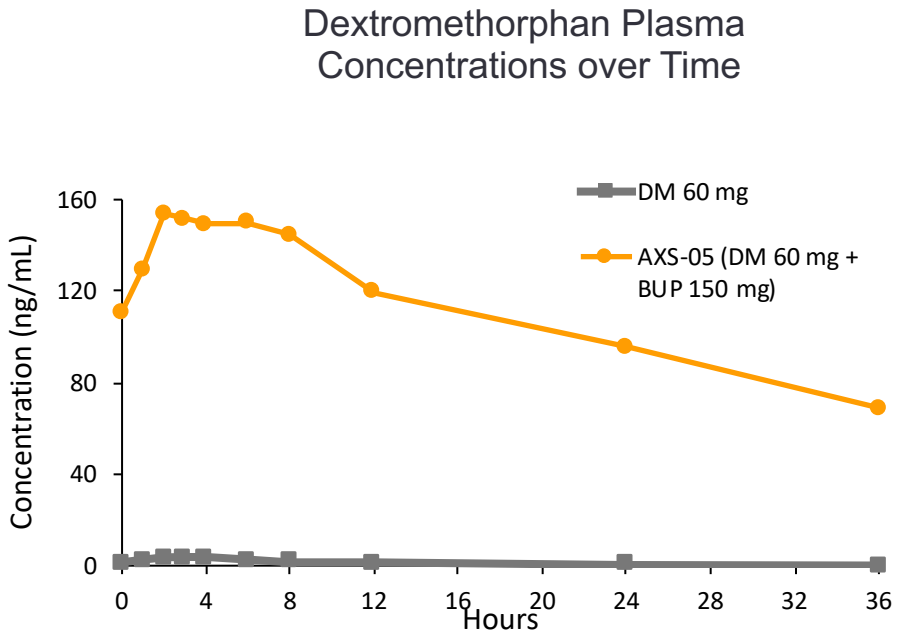
AXS-05 Mechanisms	ADHD	Anxiety	Alzheimer's	Depression	Fibromyalgia	OCD	Pain	Smoking cessation	Related Agents
NMDA Receptor Antagonist			■	■			■		• Ketamine • Memantine (Namenda®)
Sigma-1R Agonist			■	■		■			• Fluvoxamine (Luvox®) • Donepezil (Aricept®)
Norepinephrine Reuptake Inhibitor				■	■		■		• Duloxetine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

■ Relevant

1. Indications listed are associated with the mechanism of action and are not related to AXS-07 components, unless specifically noted.
2. Agents do not contain AXS-07 components, unless specifically noted.

CNS Disorders:
Phase 1 Results





Abbreviations: DM = Dextromethorphan; BUP = Bupropion.
Axsome data on file.

AXSOME THERAPEUTICS

CNS Disorders:
Depression Overview

- 63% and 44% of MDD patients have inadequate response to initial therapy and second line therapy, respectively.[2]
- AXS-05's novel antidepressant MOAs target glutamate and monoamine pathways.
- Substantial, rapid antidepressant effect demonstrated in completed ASCEND trial in patients with MDD.
- FDA Breakthrough Therapy Designation received for MDD.
- GEMINI Phase 3 trial in MDD initiated.

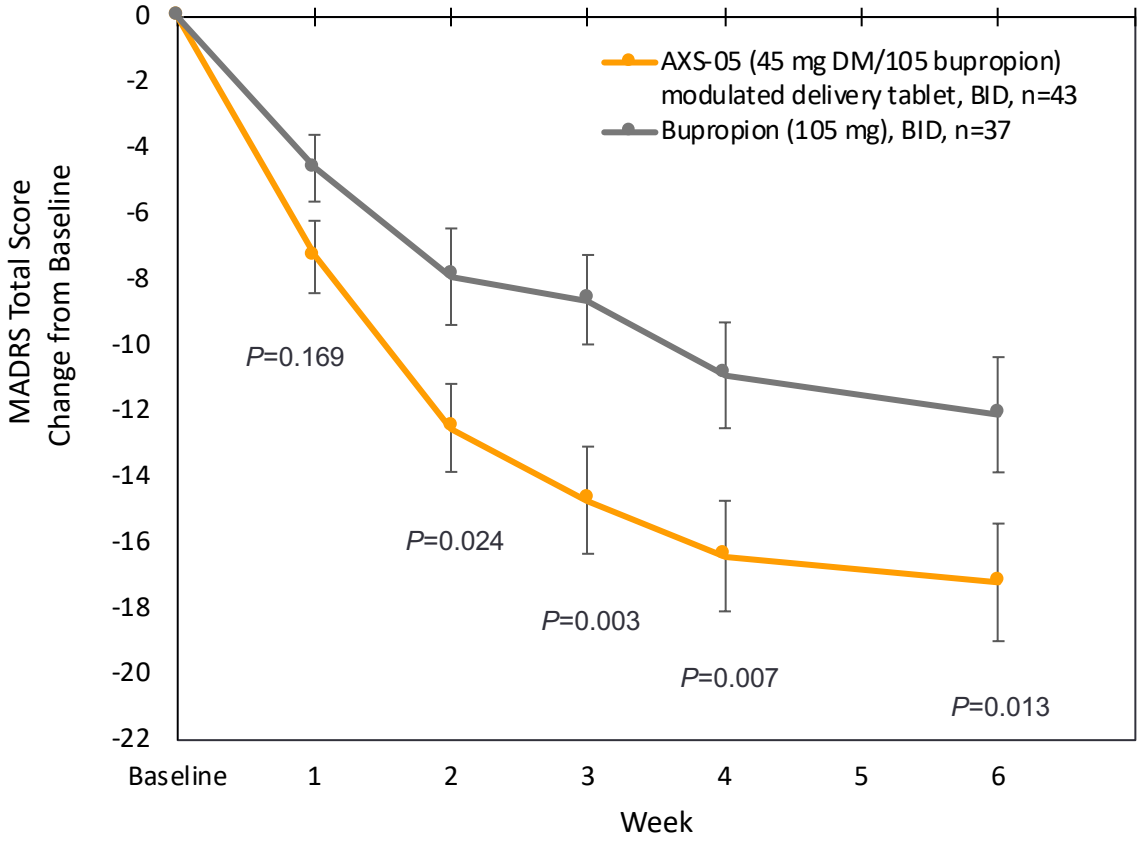
17.3M patients in the U.S.[1]

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				Ongoing

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.

CNS Disorders:
Depression Results of ASCEND Trial in MDD



	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

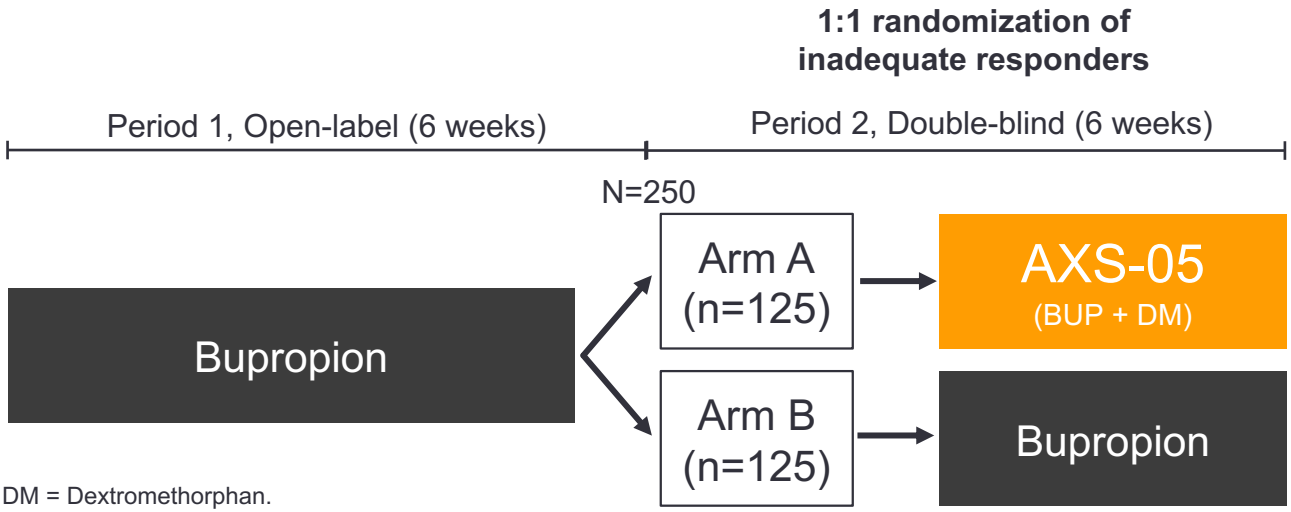
Abbreviations: BID = twice daily; BUP = Bupropion.

AXSOME THERAPEUTICS

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.



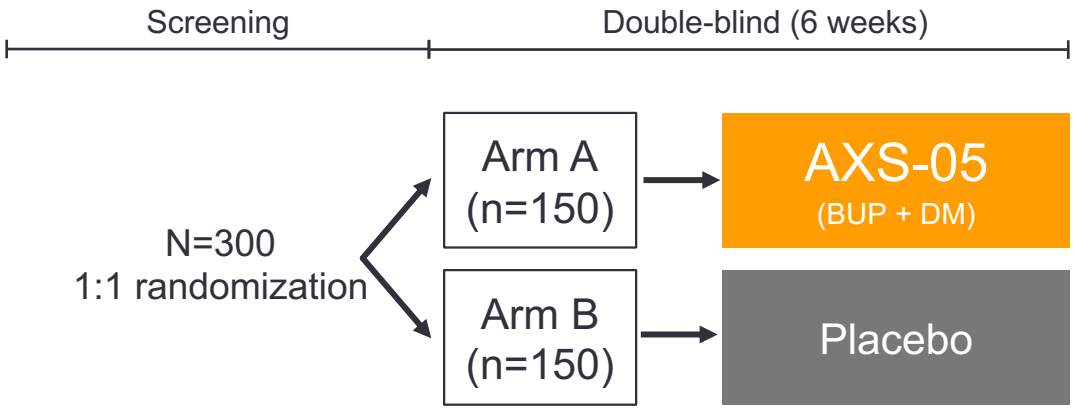
BUP = Bupropion; DM = Dextromethorphan.

- **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:
MDD Phase 3 Design

GEMINI STUDY

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



BUP = Bupropion; DM = Dextromethorphan.

- **Assessments:** Montgomery-Asberg Depression Rating Scale (MADRS), safety parameters, other clinician-rated scales, as well as patient-reported outcome measures.
- **Key Inclusion Criteria:**
  - Male or female 18-65 years old
  - Confirmed diagnosis of moderate to severe MDD

CNS Disorders:
Agitation in AD Overview

- Agitation seen in approximately 70% of AD patients.[2]
  - Emotional distress, aggressive behaviors, disruptive irritability, disinhibition, and increased caregiver burden.[4]
- Associated with[3,4]:
  - Accelerated cognitive decline
  - Earlier nursing home placement
  - Increased mortality
- No approved medication = high unmet medical need.
- Proof of concept: DM plus metabolic inhibitor reduced agitation in AD patients[5].
- 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.

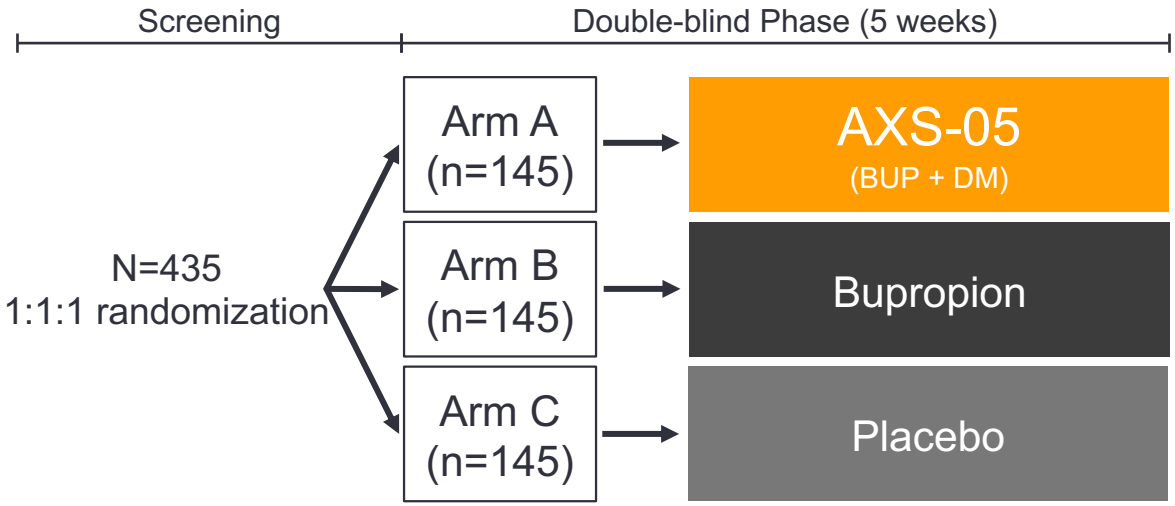
1. Hebert, LE, et al. *Neurology*. 2013;80:1778-1783.
2. Tractenberg R, et al. *J Neuropsychiatry Clin Neurosci*. 2002;14:11-18.
3. Antonsdottir IM, et al. *Expert Opin Pharmacother*. 2015;11:1649-1656.
4. Rabins PV et al. Alzheimers Dement. 2013; 9:204-207.
5. Cummings J, et al. JAMA. 2015;314:1242-1254.

AXSOME THERAPEUTICS

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.

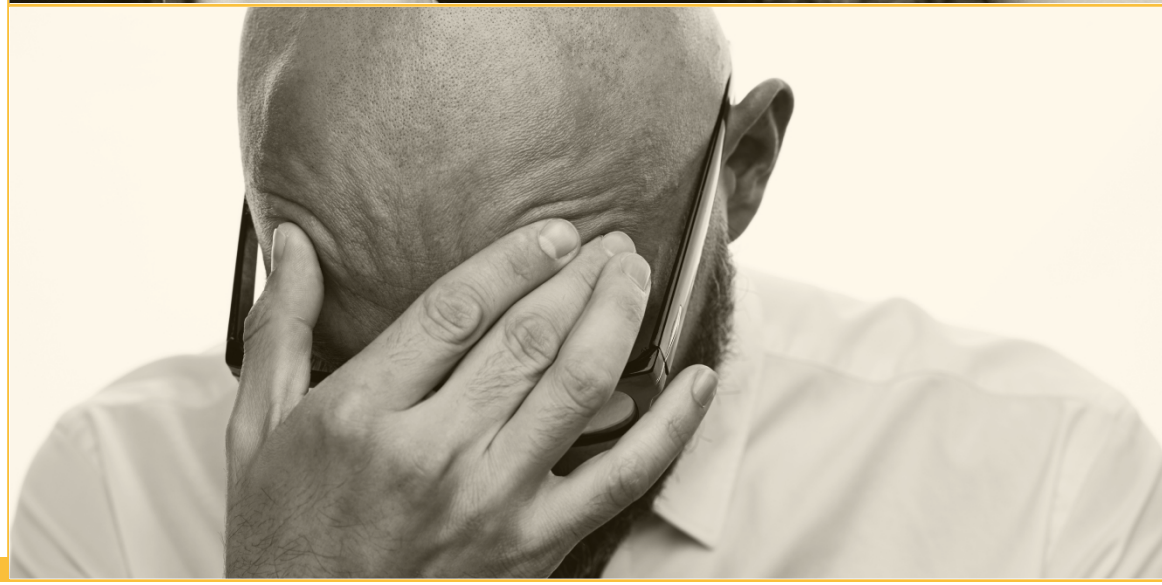
1. U.S. Department of Health and Human Services. The Health Consequences of Smoking: 50 Years of Progress. A Report of the Surgeon General. 2014.
2. Hughes JR, et al. *Addiction*. 2004;99(1):29-38.

AXS-07

(MoSEIC™ meloxicam/rizatriptan)

Novel therapy for:

- Migraine



AXS-07:
MoSEIC™ Meloxicam + Rizatriptan for Migraine

- AXS-07 incorporates dual mechanisms of action, rapid absorption of MoSEIC™ meloxicam, and extended half-life.
  - Meloxicam is a new molecule for migraine enabled by MoSEIC delivery.
  - Rizatriptan is a potent $5HT_{1B/D}$ agonist.
- Potential for enhanced and sustained efficacy in abortive treatment of migraine.
- Ongoing Phase 3 trial in patients with history of inadequate response.
  - Targeting difficult-to-treat migraines
- FDA Special Protocol Assessment.

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

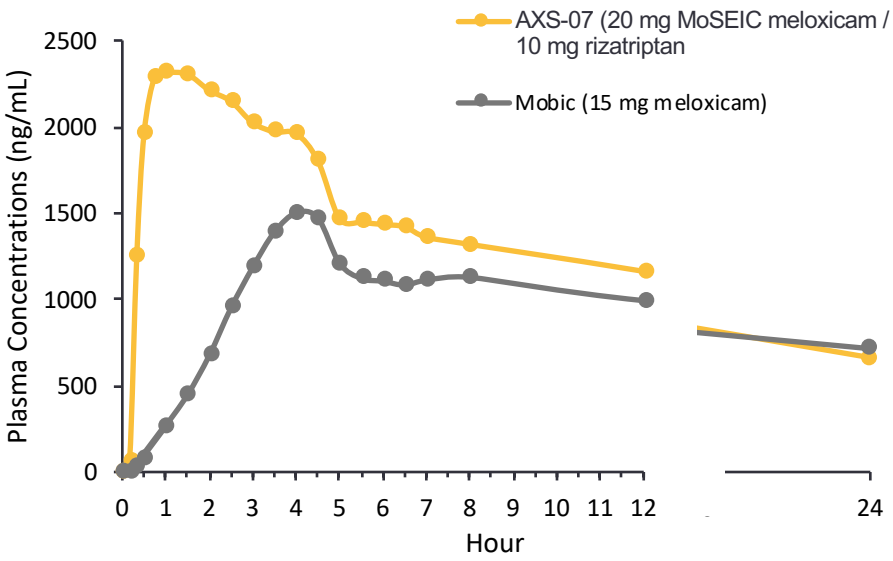
Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-07 (MoSEIC™ Mx + Riz)	Migraine: Special Protocol Assessment → Ongoing			

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

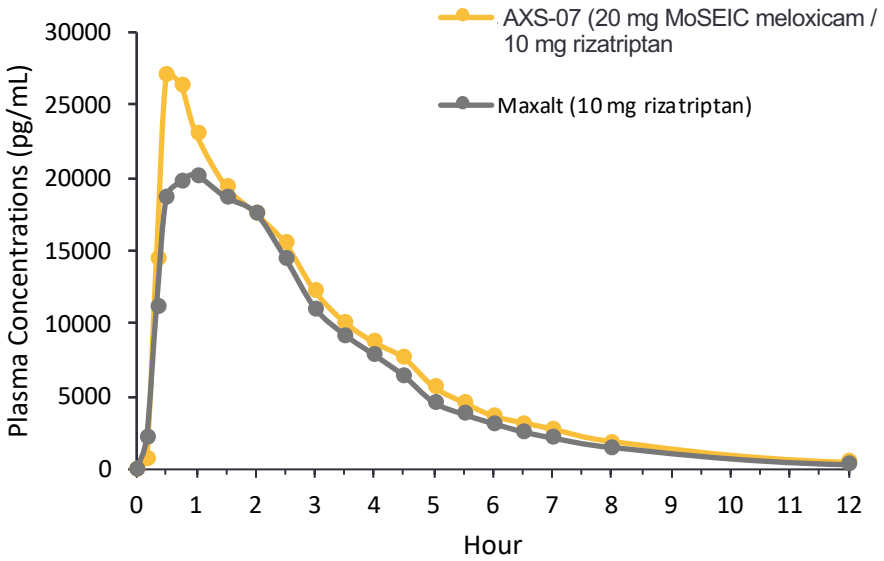
1. Pleis JR, et al., *Summary health statistics for U.S. adults: National Health Interview Survey, 2009. National Center for Health Statistics. Vital Health Stat 10(249). 2010.*

Migraine:
AXS-07 Phase 1 Results

Mean Meloxicam Concentrations



Mean Rizatriptan Concentrations



- Therapeutic AXS-07 MoSEIC™ meloxicam concentrations reached in 17 minutes.
- Maximum concentrations of AXS-07 rizatriptan reached in 38 minutes.
- MoSEIC meloxicam terminal half-life of 18.2 hours.

Sources: Axsome data on file.

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

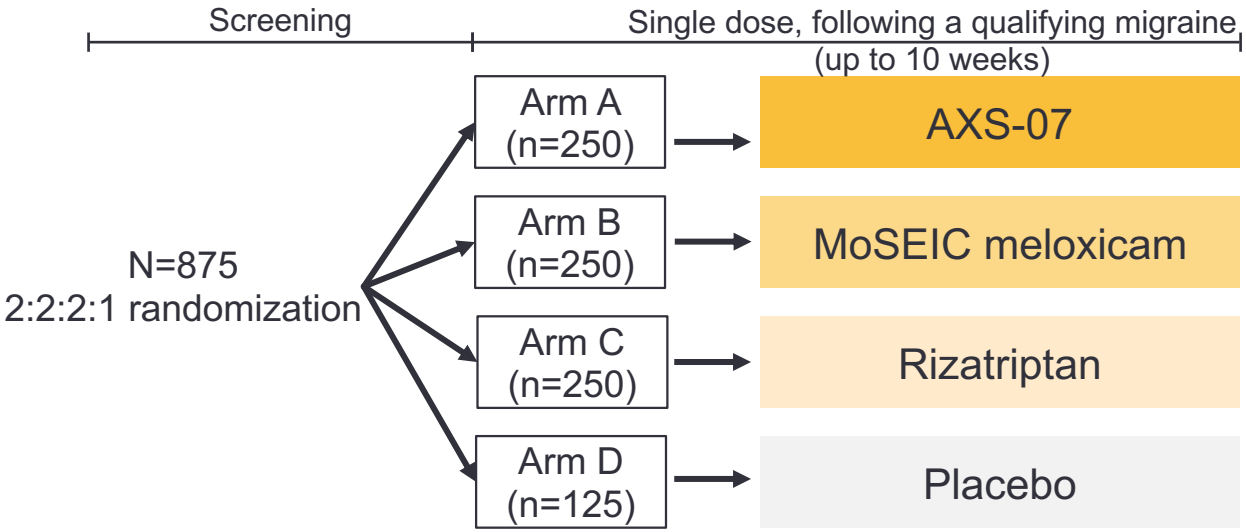
Potentially superior efficacy expected to result in reduced use of medication and medical services, reduced absenteeism and loss of productivity

Migraine:

AXS-07 Phase 3 Trial in Patients with History of Inadequate Response

MOMENTUM STUDY

A Phase 3 trial of AXS-07 for the acute treatment of migraine in adults with a history of inadequate response.



- **Co-primary Endpoints:** Pain freedom and freedom from most bothersome symptom at 2 hours post-dose, AXS-07 vs. placebo
- **Key Secondary Endpoint**: Sustained pain freedom from 2 to 24 hours, AXS-07 vs. active comparators
- **Key Inclusion Criterion:** History of inadequate response to prior acute migraine treatments
- **FDA Special Protocol Assessment (SPA)**

AXS-12

(reboxetine)

Novel therapy for:

- Narcolepsy

CNS Disorders:
Narcolepsy Overview

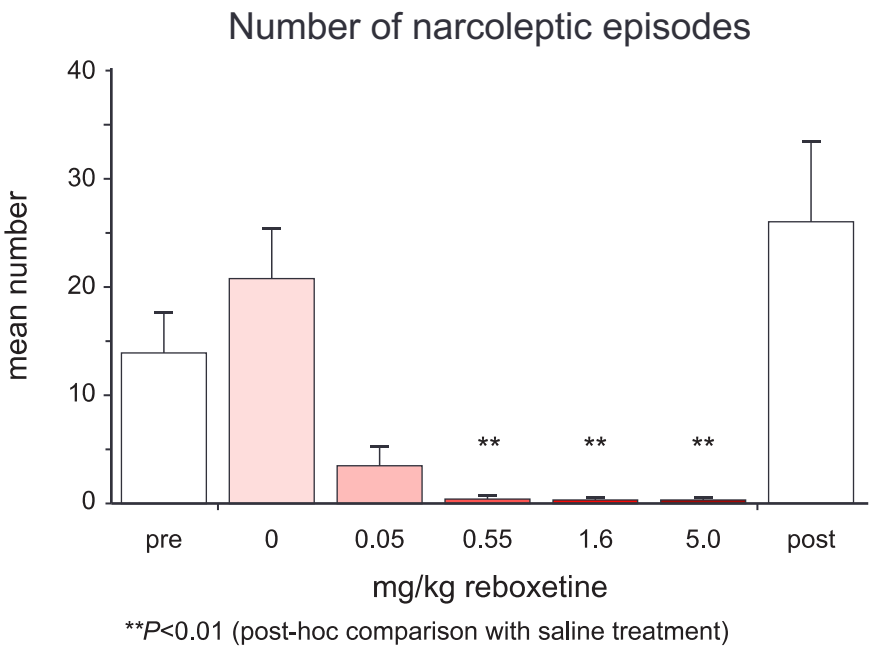
- Debilitating sleep disorder characterized by excessive daytime sleepiness (EDS) and cataplexy.
- Limited treatment options
  - Only one approved agent for cataplexy.
  - Most currently approved drugs are scheduled.
- AXS-12 showed potent activity in genetic mouse model of narcolepsy, and positive effects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

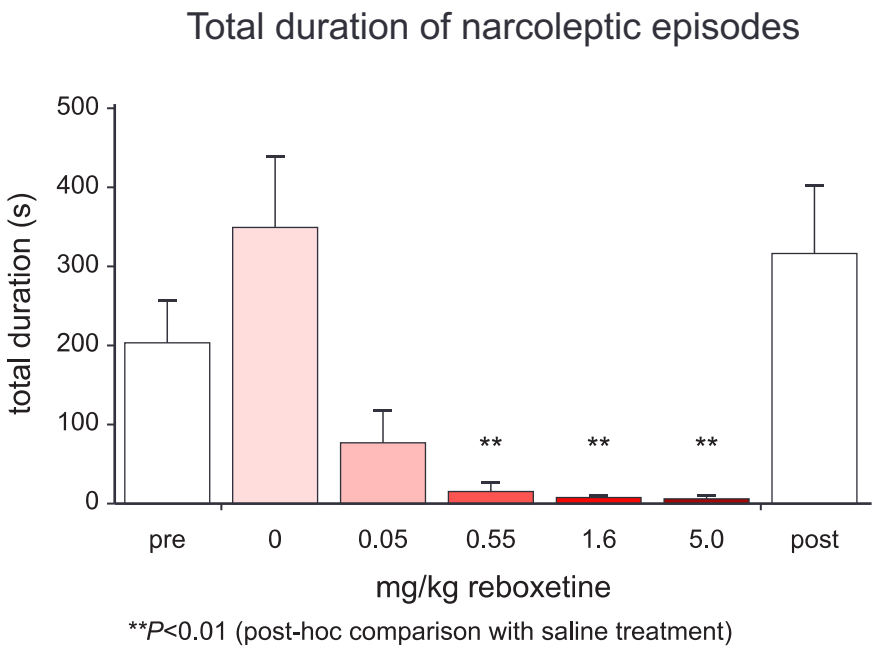
Orphan Disease

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 AXS-12 Effects in Mouse Model





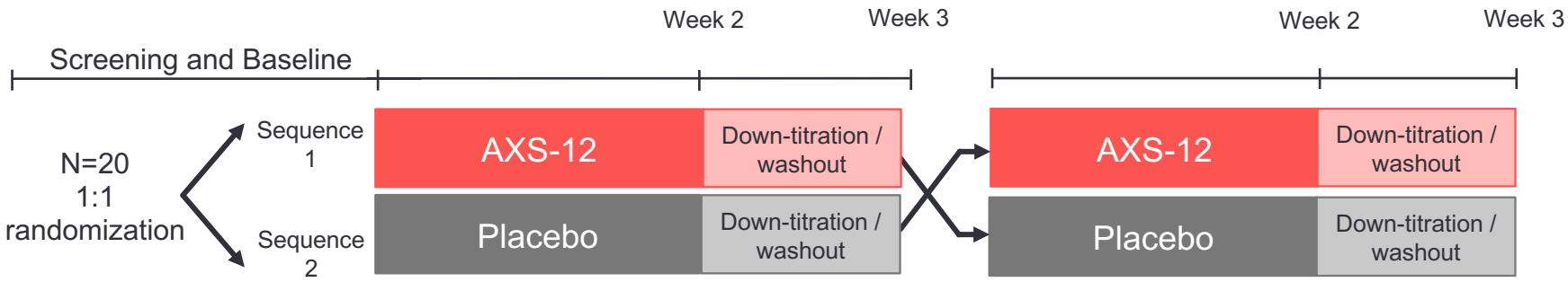
- Reboxetine dose-dependently reduced the number of narcoleptic episodes in hypocretin (orexin)-deficient mice (P<0.0001)

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

CNS Disorders:
Narcolepsy Phase 2 Design

CONCERT STUDY

Multi-center, Randomized, Double-blind, Placebo-controlled, 3-Week Crossover Study to Assess the Efficacy and Safety of AXS-12 in Subjects with Cataplexy and Excessive Daytime Sleepiness in Narcolepsy

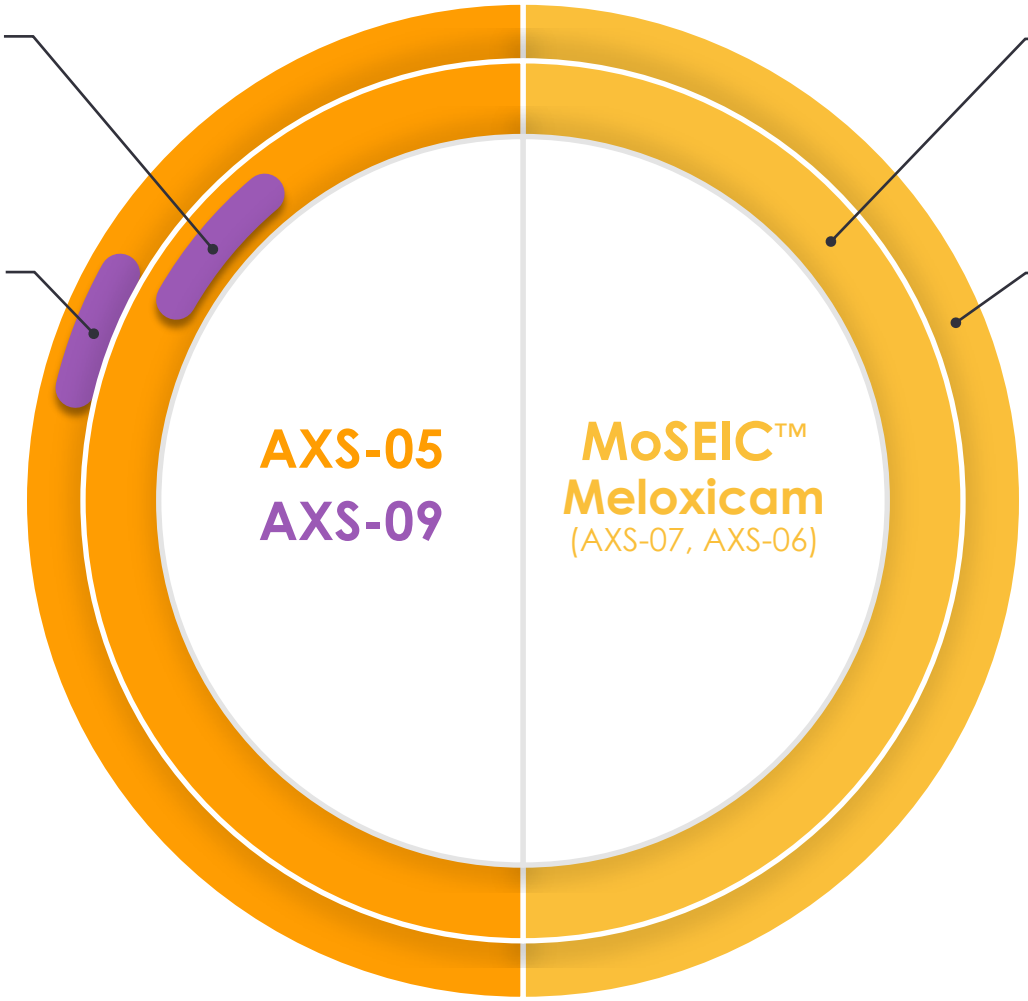


- **Primary Endpoint:** Frequency of cataplexy attacks
- **Other Assessments**: Measures of other symptoms of narcolepsy including excessive daytime sleepiness.
- **Key Inclusion Criteria**:
  - Diagnosis of narcolepsy and cataplexy
  - Male or female 18 – 70 years old

Barriers to Entry

32 Issued U.S. Patents
5 Issued O-U.S. Patents
Claims extending to **2034**
>45 pending

Proprietary Manufacturing
Drug Product Formulation



14 issued U.S. Patents
2 issued O-U.S. Patent
Claims extending to **2036**
>40 pending

Proprietary Manufacturing
Drug Product Formulation

Our Team

Management

Herriot Tabuteau, MD
Founder & CEO

Nick Pizzie, CPA, MBA
Chief Financial Officer

Dave Marek
Chief Commercial Officer

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 June 30, 2019
Cash:	$53.8 Million
Debt (Face Value):	$20.0 Million
Common Shares Outstanding:	34.3 Million
Options and Warrants Outstanding[1]:	3.3 Million

- **Financial guidance**: Cash anticipated to fund operating requirements into the fourth 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 (4Q 2019)	
	AD Agitation		● **ADVANCE-1** topline results (1H 2020)
	MDD	✓ **ASCEND** topline results ✓ **FDA** Breakthrough Therapy Designation ✓ **GEMINI** trial start ● **GEMINI** topline results (4Q 2019)	
	Smoking Cessation	✓ **Ph 2** topline results	
AXS-07 (MoSEIC™ Mx + Riz)	**Migraine**	✓ **FDA SPA** Granted ✓ **MOMENTUM** trial start ● **MOMENTUM** topline results (4Q 2019)	
AXS-12 (Reboxetine)	**Narcolepsy**	✓ **CONCERT** trial start ● **CONCERT** topline results (4Q 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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