

Axsome Therapeutics, Inc.

AXS-05 R&D Day

CNS Pipeline Overview

Herriot Tabuteau, MD

AXSOME THERAPEUTICS

Chief Executive Officer
Axsome Therapeutics, Inc.
New York City

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Our Candidates and Pipeline

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

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-05 (DM + BUP)	Treatment Resistant Depression: Fast Track Granted			Ongoing
	Agitation in Alzheimer's Disease: Fast Track Granted			Ongoing
	Smoking Cessation			Duke University Collaboration
AXS-09 (DM + S-BUP)	CNS Disorders			
AXS-02 (DZT)	Knee OA with BMLs: SPA Received; Fast Track Granted			Ongoing
	CLBP with MCs			
AXS-07 (MoSEIC™ Mx + Riz)	Migraine			
AXS-06 (MoSEIC™ Mx + Eso)	OA and RA			

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

AXS-05:

Mechanisms of Action and Relevant Indications

Mechanism of Action	Pharmacodynamic Synergy			Relevant Indications ¹							Related Agents ²	
	DM	BUP	AXS-05 DM+BUP	ADHD	Anxiety	Alzheimer's	Depression	Fibromyalgia	OCD	Pain		Smoking cessation
NMDA Receptor Antagonist	✓		✓			■	■			■		<ul style="list-style-type: none"> • Ketamine • Memantine (Namenda®)
Sigma-1R Agonist	✓		✓			■		■				<ul style="list-style-type: none"> • Fluvoxamine (Luvox®) • Donepezil (Aricept®)
Norepinephrine Reuptake Inhibitor	✓	✓	✓			■	■			■		<ul style="list-style-type: none"> • Duloxetine (Cymbalta®) • Venlafaxine (Effexor®)
Serotonin Reuptake Inhibitor	✓		✓		■				■			<ul style="list-style-type: none"> • Escitalopram (Lexapro®) • Fluoxetine (Prozac®) • Sertraline (Zoloft®)
Dopamine Reuptake Inhibitor		✓	✓	■							■	<ul style="list-style-type: none"> • Bupropion (Wellbutrin®)
Nicotinic ACh Receptor Antagonist	✓	✓	✓	■								<ul style="list-style-type: none"> • 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.

AXS-05: Treatment Resistant Depression

3M patients in the U.S.¹⁻³

1% \approx \$150-300M*



- FDA Fast Track Designation
- Phase 3 ongoing
- Interim analysis for futility anticipated 2Q 2018
- Interim analysis for efficacy anticipated 2H 2018
- Full topline results 2H 2018-1H 2019

*Annual estimate for illustrative purposes.

¹Marcus SC, Olfson M. *Arch Gen Psychiatry* 2010;67:1265-1273.

²Rush AJ, et al. *Am J Psychiatry* 2006;163:1905-1917.

³U.S. Census Bureau, Population April 1, 2010 to July 1, 2013.

AXS-05:

Agitation in Alzheimer's Disease

2M patients in the U.S.^{1,2}

1% \approx \$100-200M*



- FDA Fast Track Designation
- Phase 2/3 ongoing
- Interim analysis for futility anticipated 2H 2018
- Interim analysis for efficacy anticipated 2019

*Annual estimate for illustrative purposes.

¹Ryu, SH, et al. *Am J Geriatr Psychiatry*. 2005;13:976-983.

²Hebert, LE, et al. *Neurology*. 2013;80:1778-1783.

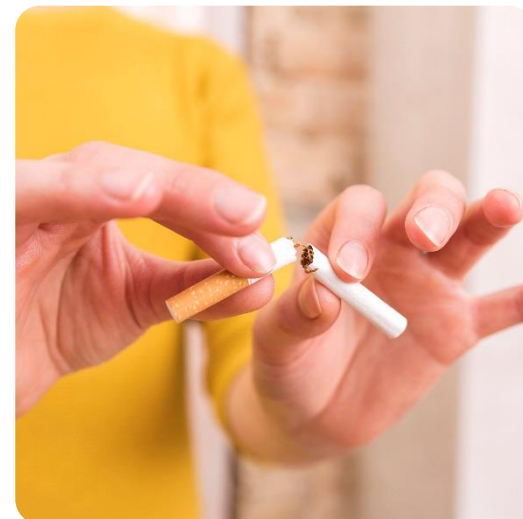
AXS-05:

Agitation in Alzheimer's Disease

40M smokers in the U.S.

28M attempting to quit^{1,2}

1% \approx \$1.3-2.7B*



- Phase 2 initiated in collaboration with Duke University

*Annual estimate for illustrative purposes.

¹U.S. Department of Health and Human Services. The Health Consequences of Smoking: 50 Years of Progress. A Report of the Surgeon General. 2014.

²Hughes JR, et al. *Addiction*. 2004;99(1):29-38.

AXS-09:

Esbupropion + DM

- Esbupropion and DM fixed-dose combination
- Esbupropion is the chirally pure *S*-enantiomer of bupropion.
- Phase 1 trial completed:
 - Pharmacokinetic trial of AXS-09, *R*-bupropion and dextromethorphan, single-entity *S*-bupropion, or single-entity *R*-bupropion
 - Substantial increases in DM plasma concentrations with AXS-09 ($p < 0.0001$ day 1 versus day 8)
 - DM concentrations with AXS-09 comparable to AXS-05
 - AXS-09 was well tolerated
- To be developed in future CNS indications



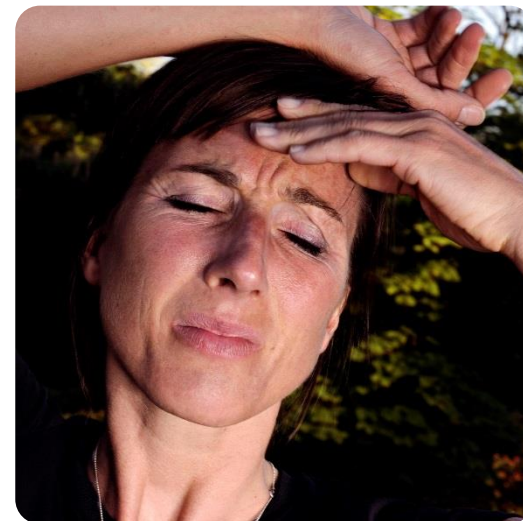
Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-09 (DM + S-BUP)	CNS Disorders			

Abbreviations: DM = Dextromethorphan; S-BUP = Esbupropion.

AXS-07: MoSEIC™ Meloxicam + Rizatriptan for **Migraine**

15M Triptan U.S. Rx's written per year

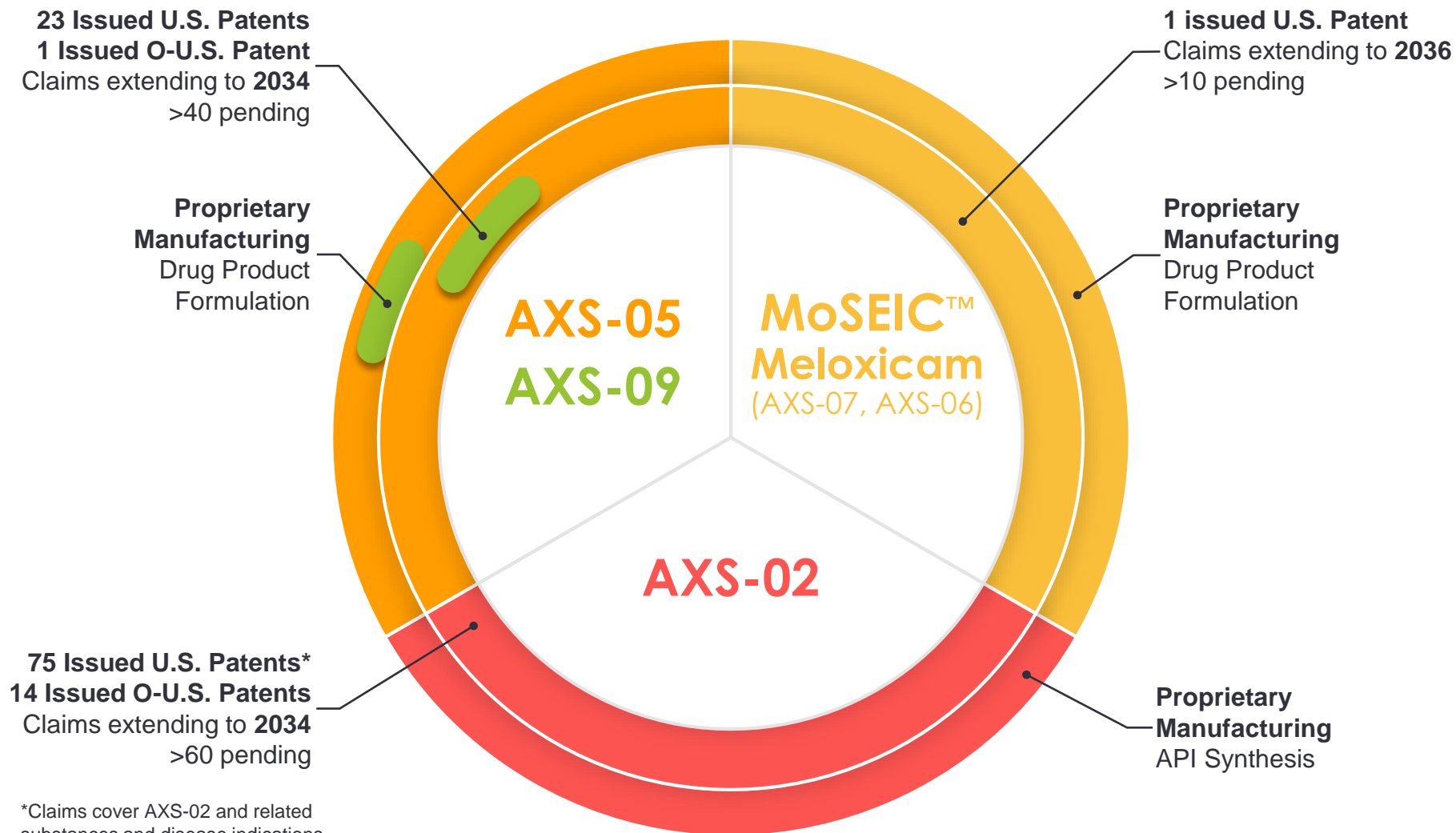
1% ≈ \$100M*



- Phase 3 initiation anticipated in 2018
- MoSEIC meloxicam delivers rapid, IV-like absorption with oral delivery, combined with 20-hour half-life.
- Potential for superior efficacy as compared to current treatments.

*Annual estimate for illustrative purposes.

Broad Intellectual Property



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

Clinical Milestones

Product Candidate	Indication	2018	2019
AXS-05 (DM + BUP)	TRD	<ul style="list-style-type: none"> ● STRIDE-1 interim analysis (2Q 2018) ● STRIDE-1 interim efficacy analysis (2H 2018) ● STRIDE-1 top-line results (2H 2018/1H 2019) 	
	AD Agitation	<ul style="list-style-type: none"> ● ADVANCE-1 interim analysis (2H 2018) 	<ul style="list-style-type: none"> ● ADVANCE-1 interim efficacy analysis ● ADVANCE-1 top-line results (2H 2019/1H 2020)
	Smoking Cessation	✓ Ph 2 trial initiated	<ul style="list-style-type: none"> ● Ph 2 top-line results
AXS-09 (DM + S-BUP)	CNS Disorders	✓ Ph 1 trial results	
AXS-07 (MoSEIC™ Mx + Riz)	Migraine	<ul style="list-style-type: none"> ● Ph 3 trial start 	<ul style="list-style-type: none"> ● Ph 3 top-line results
AXS-02 (DZT)	Knee OA	✓ COAST-1 interim analysis	

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

✓ Accomplished milestone.

● Upcoming milestone.

AXSOME

THERAPEUTICS

Thank you.

For more information, please contact

Mark Jacobson
SVP, Operations

212-332-3243
mjacobson@Axsome.com

axsome.com