

Axsome Therapeutics, Inc.

AXS-05 R&D Day

CNS Pipeline Overview

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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% ≈ \$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, Olsson 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.

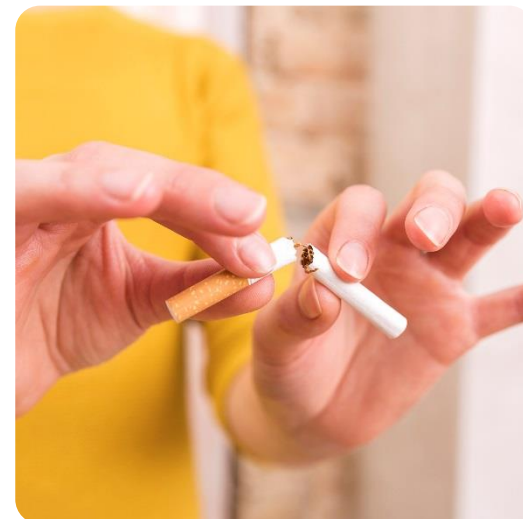
²Hebert, LE, et al. *Neurology*. 2013;80:1778-1783.

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



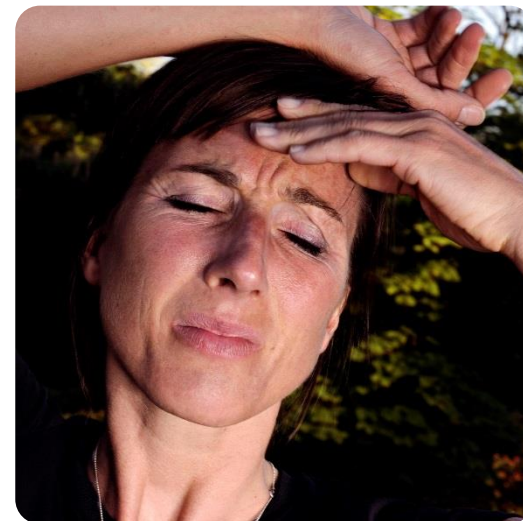
| Product Candidate | Preclinical | Phase 1 | Phase 2 | Phase 3 |
|------------------------|---------------|---------|---------|---------|
| AXS-09 (DM + S-BUP) | CNS Disorders | | | |

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

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

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

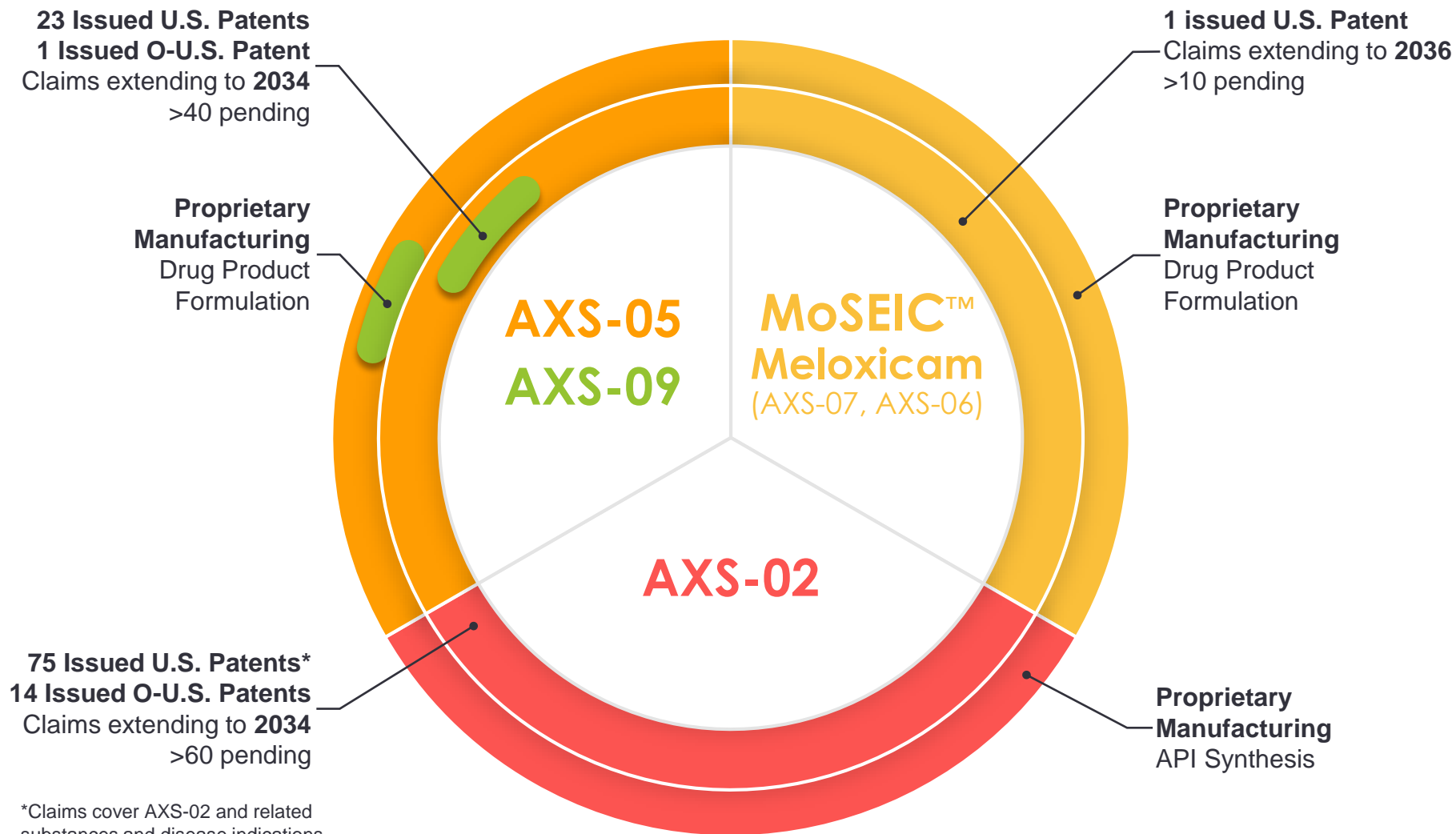
1% ≈ \$100M*



- 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

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