NASDAQ: AXSM

AXSOME THERAPEUTICS

Corporate Presentation

UBS Global Healthcare Conference

May 24, 2021

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, whether potential filing issues or issues identified by FDA during the substantive review may impact the potential approvability of the Company's NDA submission for AXS-05 in MDD or the timing of such approval, and whether the FDA will agree with the Company's discontinuation of 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 MOMENTUM clinical trial to provide a basis for approval of AXS-07 for the acute treatment of migraine in adults with or without aura, pursuant to our special protocol assessment; the potential for the ASCEND clinical trial, combined with the GEMINI clinical trial results, 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 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.

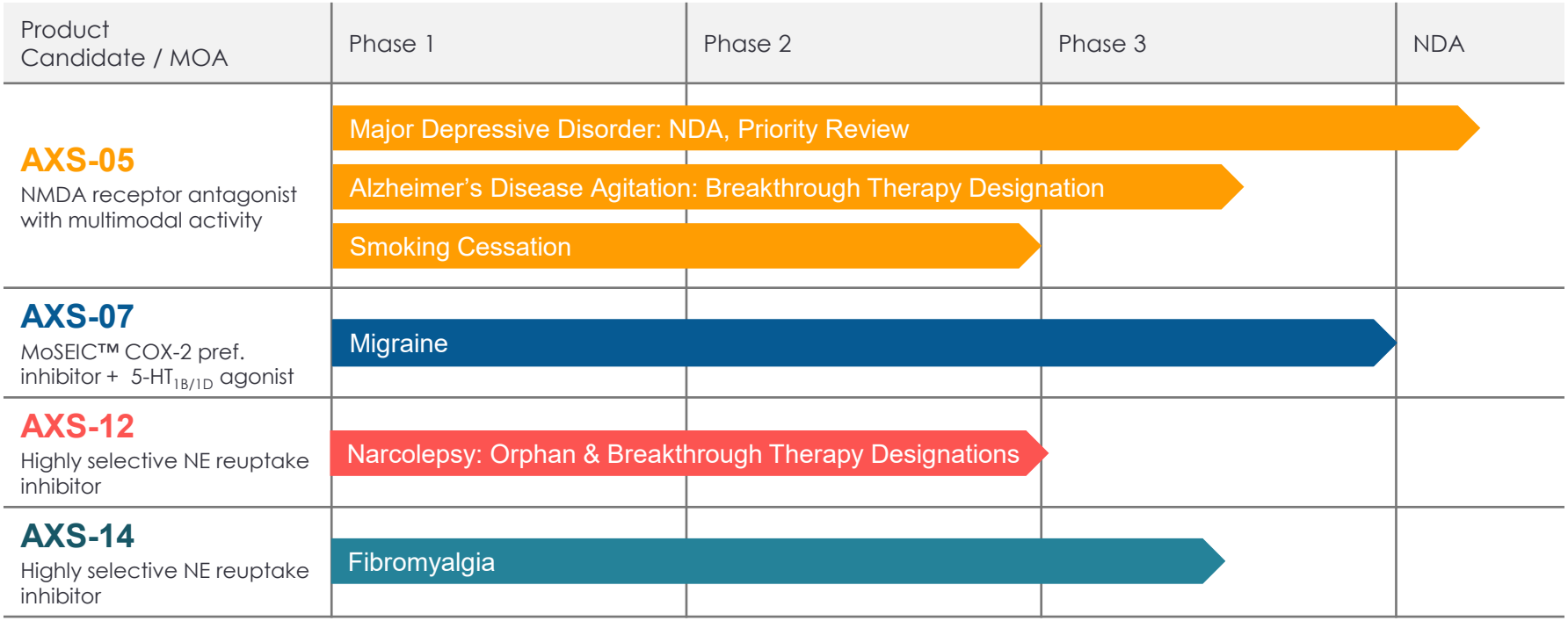
This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Neither we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

For the many people facing unsatisfactory treatments for CNS disorders, Axsome accelerates the invention and adoption of life-changing medicines.

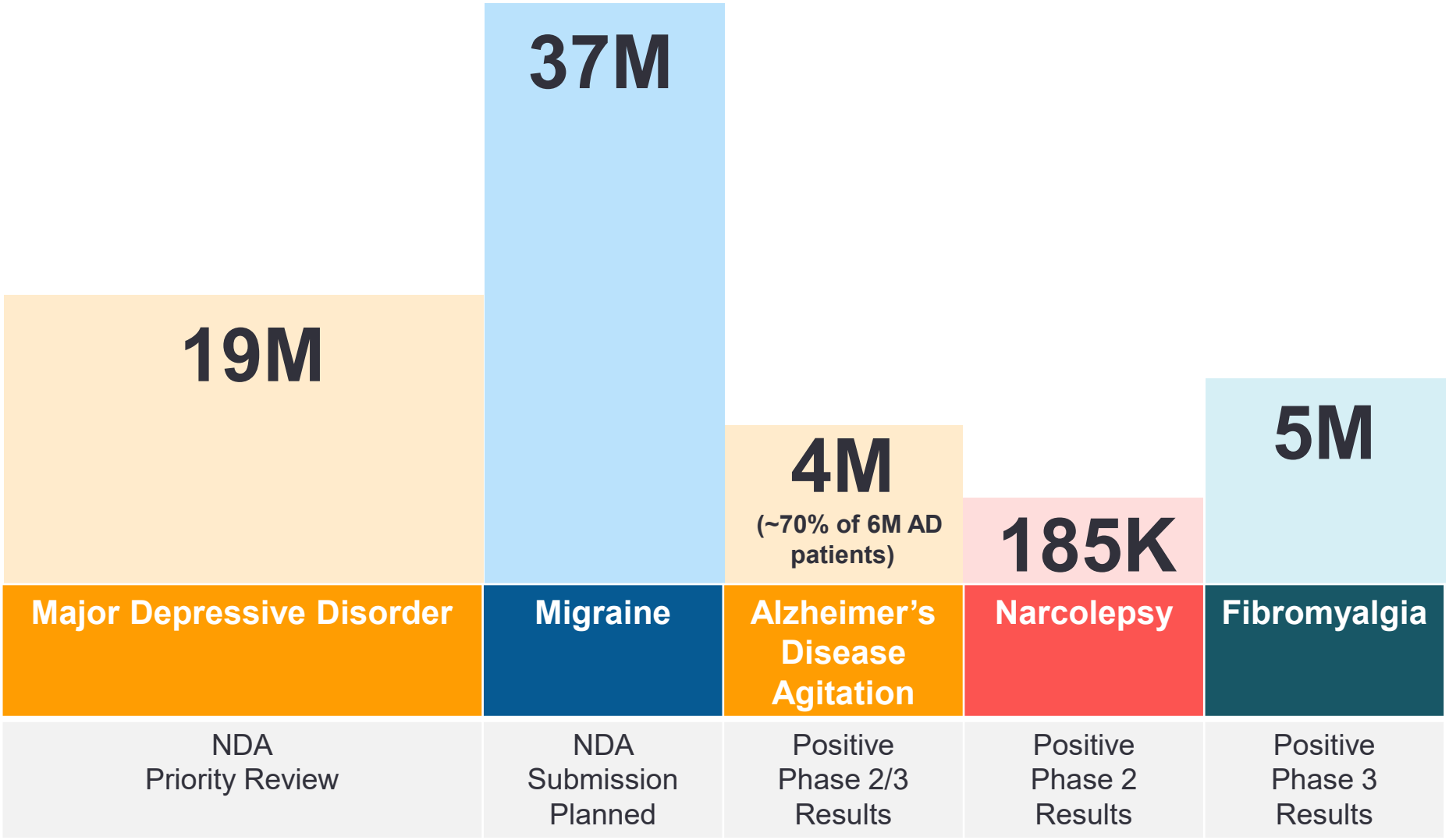
Our CNS Candidates and Pipeline

- Four differentiated clinical-stage CNS assets targeting significant and growing markets
- Patent expirations to 2034-2040, worldwide rights for most product candidates



Abbreviations: CNS = Central Nervous System; NE = Norepinephrine.

Our late-stage portfolio has generated positive data in conditions that affect >60M U.S. patients



AXSOME THERAPEUTICS

AXS-05

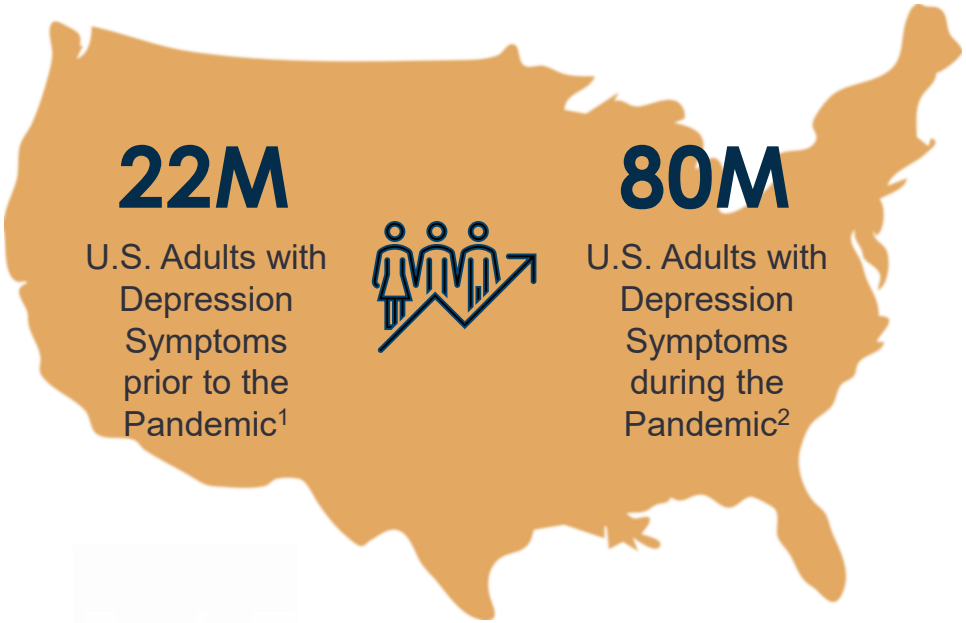
(dextromethorphan/bupropion) modulated delivery tablet

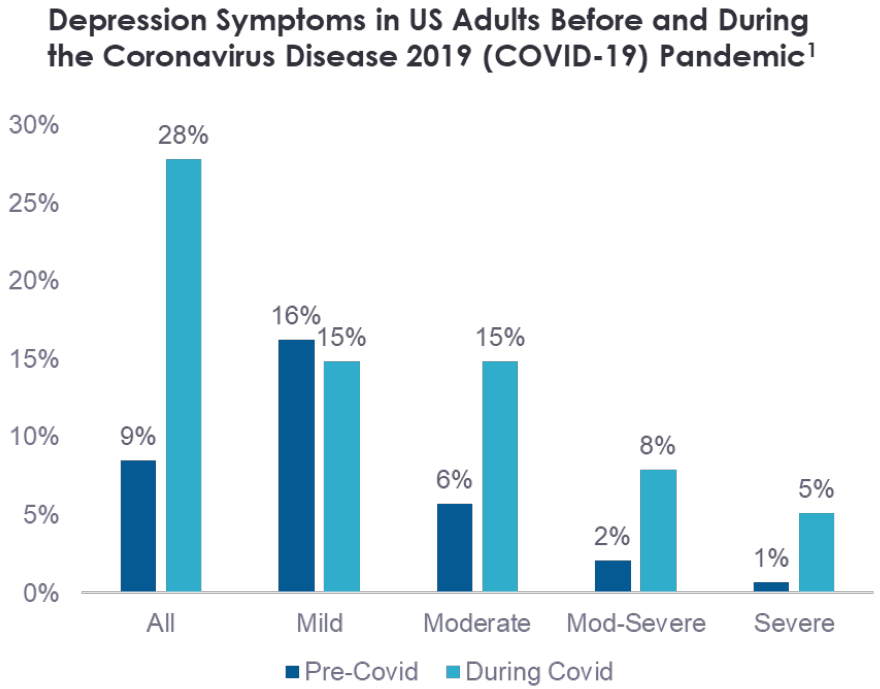
Novel therapy for CNS disorders:

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

Prevalence of Depression Symptoms Before and During Pandemic

- Depression increased more than 3 fold due to pandemic and skewed toward those with more severe symptoms



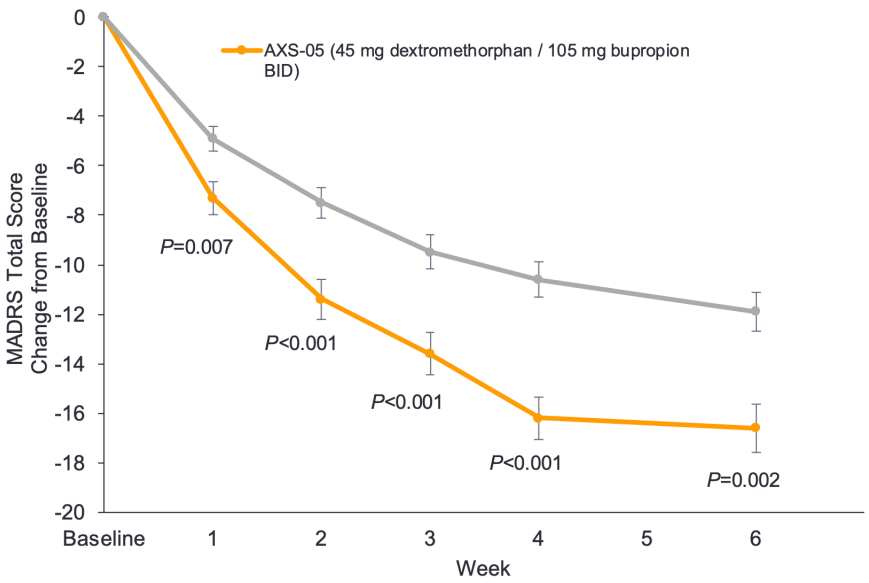


JAMA
The Journal of the American Medical Association

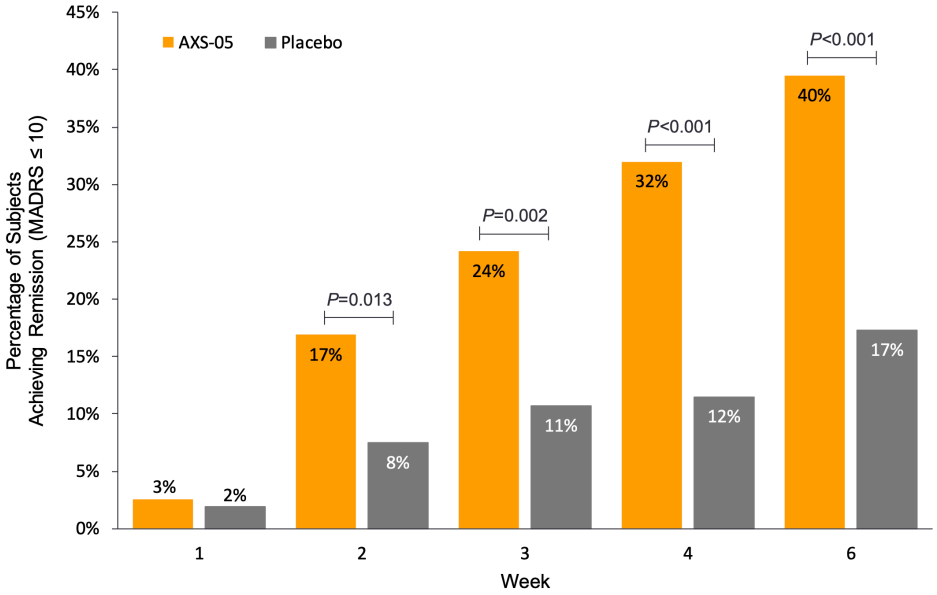
1) Ettman CK, Abdalla SM, Cohen GH, Sampson L, Vivier PM, Galea S. Prevalence of Depression Symptoms in US Adults Before and During the COVID-19 Pandemic. *JAMA Netw Open.* 2020;3(9):e2019686. doi:10.1001/jamanetworkopen.2020.19686
2) US Census Bureau Household Pulse Survey 2020-2021. Retrieved from https://www.cdc.gov/nchs/covid19/pulse/mental-health.htm

GEMINI Study of AXS-05 in MDD: MADRS Change and Remission

Change in MADRS Total Score



Achievement of Remission

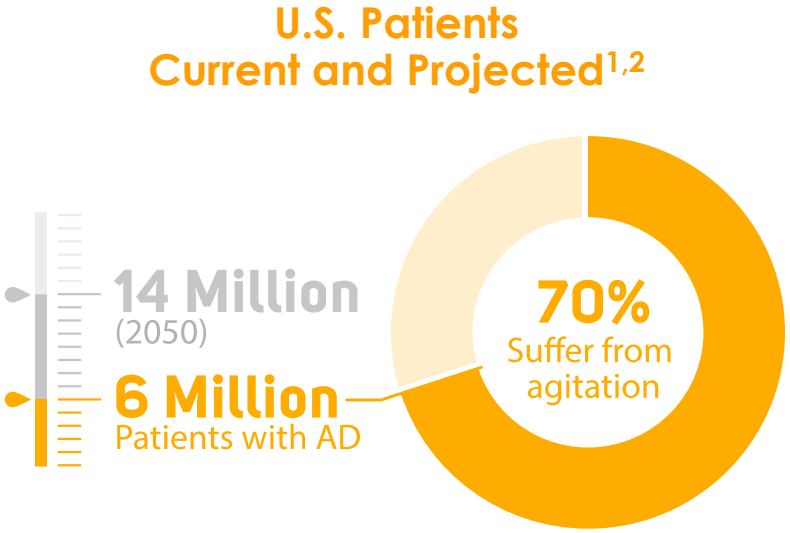


Product Candidate	Phase 1	Phase 2	Phase 3	NDA
AXS-05 (DM + BUP)	Major Depressive Disorder: NDA, Priority Review			

Abbreviations: DM = Dextromethorphan; BUP = Bupropion.

Alzheimer's Disease Agitation: High Unmet Medical Need

- Agitation is seen in up to 70% of Alzheimer's Disease (AD) patients[2]:
  - Emotional distress, aggressive behaviors, disruptive irritability, and disinhibition
- Managing agitation is a major priority in AD[3,4]:
  - Associated with accelerated cognitive decline, earlier nursing home placement, and increased mortality risk
- No approved medication = high unmet medical need:

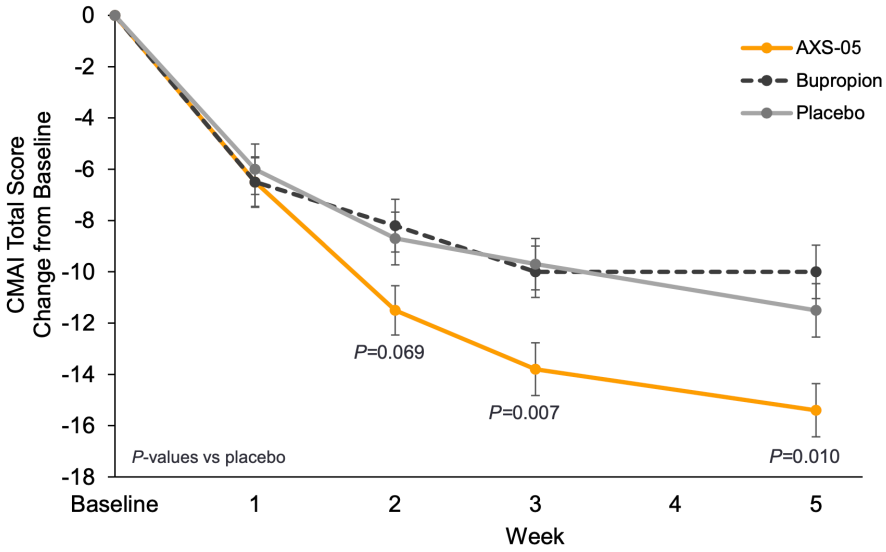


[1]Alzheimer's Association. *Alzheimers Dement.* 2020;16(3):391+. [2]Tractenberg R, et al. *J Neuropsychiatry Clin Neurosci*. 2002;14:11-18.
[3]Porsteinsson AP, et al. *Expert Opin Pharmacother*. 2017; 18:6, 611-620. [4]Rabins PV et al. *Alzheimers Dement*. 2013; 9:204-207.

AXS-05: Alzheimer's Disease Agitation

- Primary endpoint met in ADVANCE-1 pivotal Phase 2/3 trial
- Second pivotal trial initiated – ACCORD Phase 3, placebo-controlled, randomized withdrawal trial
- FDA Breakthrough Therapy Designation received

ADVANCE-1 Study: Change in CMAI Total Score



Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-05 (DM + BUP)	Agitation in Alzheimer's Disease: Breakthrough Therapy Designation			

Abbreviations: DM = Dextromethorphan; BUP = Bupropion.

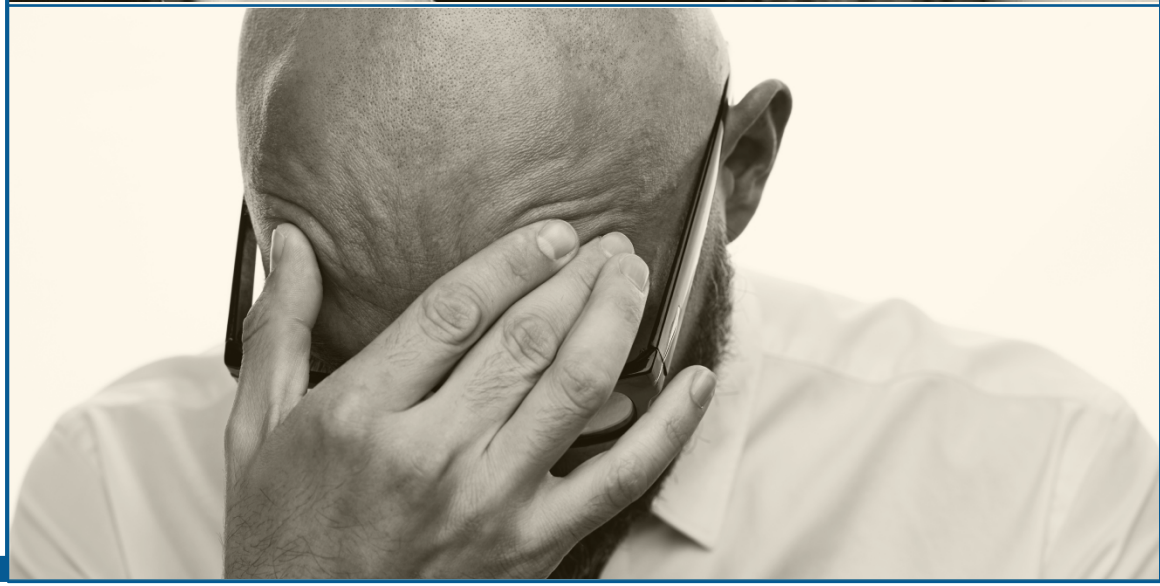
[1]Alzheimer's Association. *Alzheimers Dement.* 2020;16(3):391+. [2]Tractenberg R, et al. *J Neuropsychiatry Clin Neurosci*. 2002;14:11-18. [3]Porsteinsson AP, et al. *Expert Opin Pharmacother*. 2017; 18:6, 611-620. [4]Rabins PV et al. *Alzheimers Dement*. 2013; 9:204-207.

AXS-07

(MoSEIC™ meloxicam/rizatriptan)

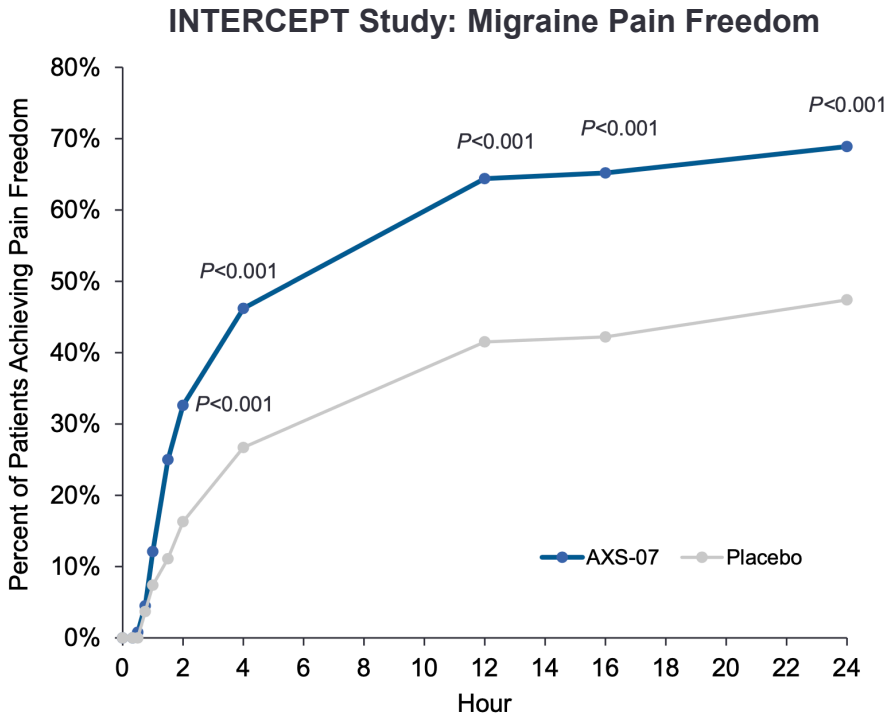
Novel therapy for:

- Migraine



AXS-07:
MoSEIC™ Meloxicam + Rizatriptan for Migraine

- Unmet need for improved efficacy in migraine: disability on par with dementia, quadriplegia, active psychosis[1,2]
- AXS-07: novel, oral, rapidly absorbed, multi-mechanistic
- Rapid and sustained efficacy as compared to placebo and active comparator rizatriptan, in three positive Phase 3 trials:
  - MOMENTUM, in patients with history of inadequate response, vs. placebo and rizatriptan
  - INTERCEPT, in early treatment, vs. placebo
  - MOVEMENT, long-term open-label treatment, up to 12 months
- NDA submission planned 2Q 2021



Product Candidate	Phase 1	Phase 2	Phase 3	NDA
AXS-07 (MoSEIC™ Mx + Riz)	Migraine			NDA Submission Planned

[1]Menken et al. *Arch Neurol*. 2000;57:418-420. [2]Shapiro and Goadsby. *Cephalalgia*. 2007;27:991-4.

AXS-12

(reboxetine)

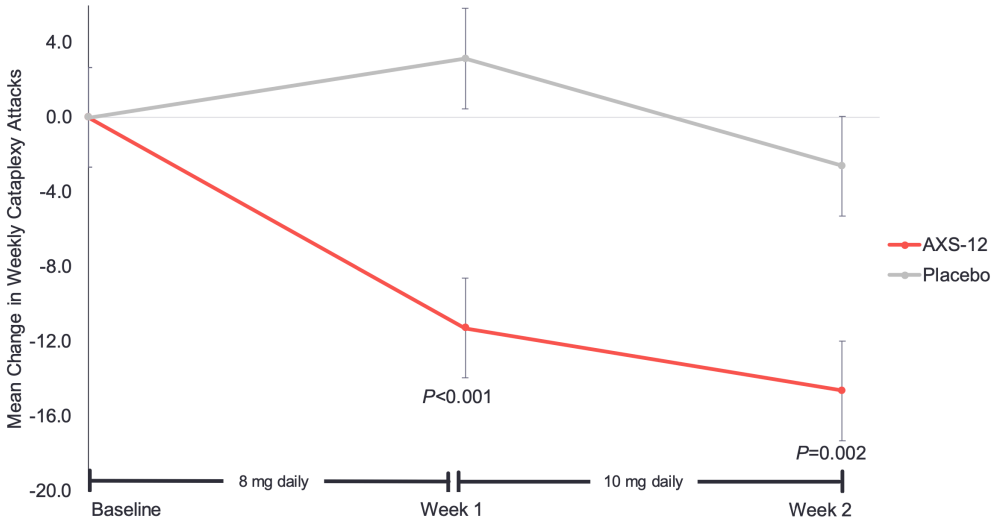
Novel therapy for:

- Narcolepsy

AXS-12 (reboxetine): Narcolepsy

- Debilitating sleep disorder characterized by excessive daytime sleepiness and cataplexy
- Limited treatment options
- Positive Phase 2 results with AXS-12
  - Significant reduction in cataplexy attacks and EDS
  - Significant improvement in cognitive function
- Phase 3 trial initiation anticipated in 3Q 2021

CONCERT Study: Change in Weekly Cataplexy Attacks



Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-12 (Reboxetine)	Narcolepsy; Orphan & Breakthrough Therapy Designation			Phase 3 Planned

AXSOME THERAPEUTICS

AXS-14

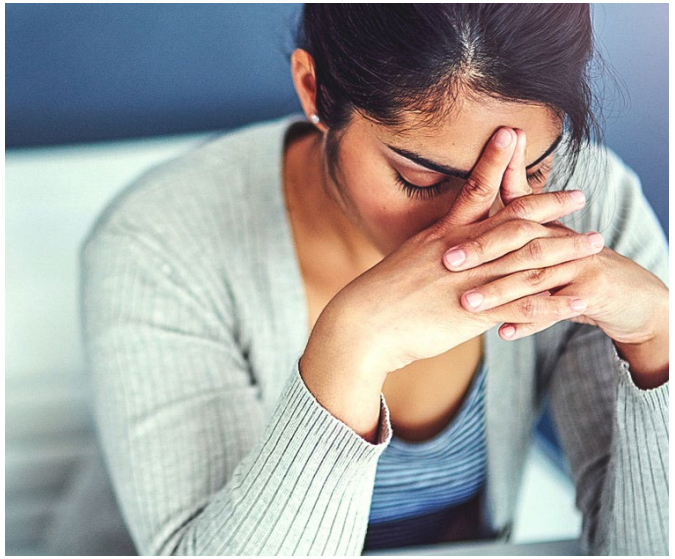
esreboxetine

Novel therapy for:

- Fibromyalgia

AXS-14 (esreboxetine): Fibromyalgia Overview

- Debilitating, chronic, CNS disorder characterized by widespread pain, fatigue, disturbed sleep, depression, and cognitive impairment; ~90% affected are women
- Limited treatment options—only 3 approved agents:
  - Current treatments has variable efficacy and do not address all symptoms
- AXS-14 (esreboxetine) is the SS-enantiomer of racemic reboxetine
- Positive Phase 3 and Phase 2 efficacy results with AXS-14 in fibromyalgia
- FDA meeting held 2Q 2021



5M patients in the U.S.[1]

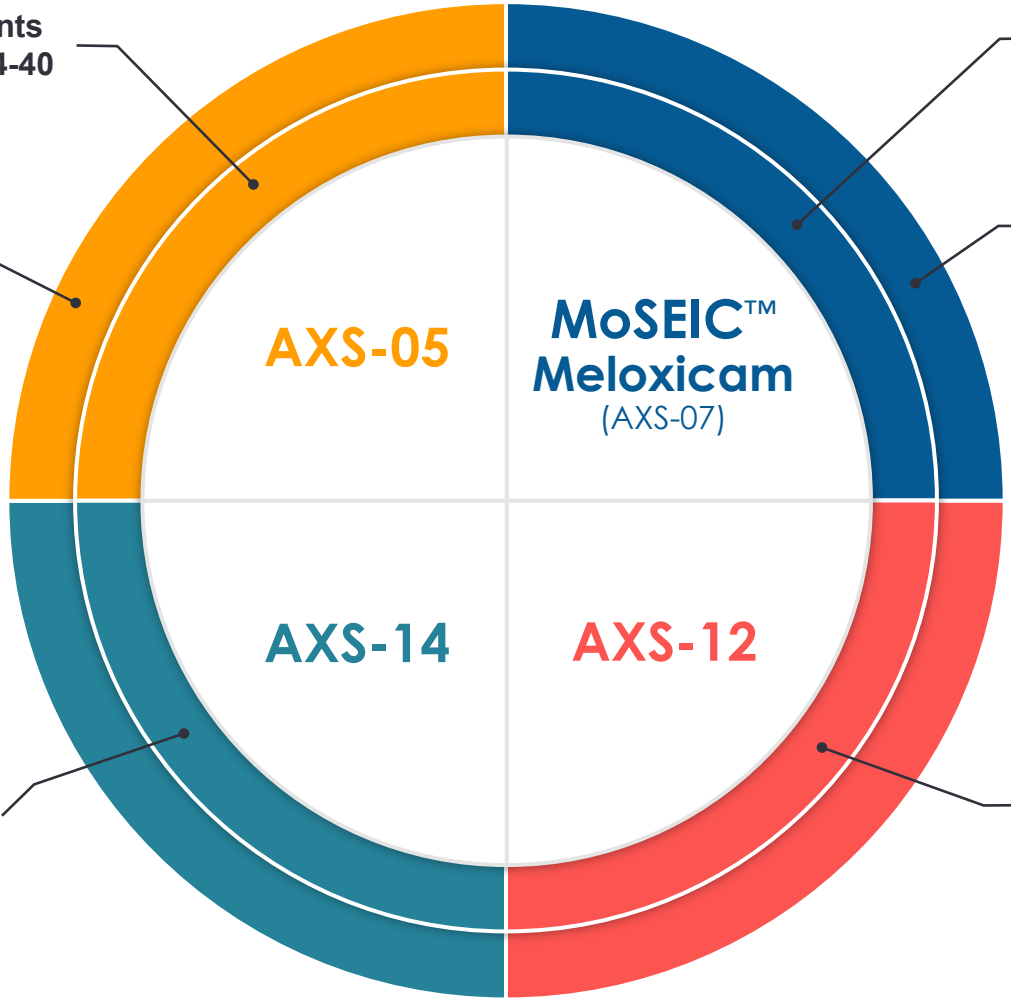
Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-14 (Esreboxetine)	Fibromyalgia			

1. Decision Resources Group 2019

Barriers to Entry

>50 Issued U.S. Patents
>40 Issued O-U.S. Patents
Claims extending to **2034-40**
>40 pending

Proprietary Manufacturing
Drug Product Formulation



>50 issued U.S. Patents
>40 issued O-U.S. Patent
Claims extending to **2036**
>40 pending

Proprietary Manufacturing
Drug Product Formulation

Pending U.S. Patents

Pending U.S. Patents
Orphan Drug Designation

Our Team

Management

Herriot Tabuteau, MD
Founder & CEO

Nick Pizzie, CPA, MBA
Chief Financial Officer

Mark Jacobson, MA
Chief Operating Officer

Kevin Laliberte, PharmD
EVP, Product Strategy

Lori Englebert
SVP, Commercial & Business Dev.

Amanda Jones, PharmD
SVP, Clinical Development

Cedric O'Gorman, MD, MBA
SVP, Medical Affairs

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United Therapeutics Corp.
Prior positions at Amgen and Burroughs Wellcome

Mark Saad
Former CFO
Bird Rock Bio, Inc.
Former COO of the Global Healthcare Group at UBS

Mark Coleman, MD
President
National Spine and Pain Centers
Diplomat of the American Board of Anesthesiology

Herriot Tabuteau, MD
Chairman

Our Clinical and Regulatory Milestones

Product Candidate	Indication	Milestone
AXS-05 NMDA receptor antagonist with multimodal activity	**MDD**	✓ **NDA** submission ✓ **NDA** Priority Review • **MERIT** results (2H 2021)
	AD Agitation	✓ **Accord** trial start
	Smoking Cessation	• **FDA** meeting (3Q 2021)
AXS-07 MoSEIC™ COX-2 pref. inhibitor + 5-$HT_{1B/1D}$ agonist	**Migraine**	• **NDA** submission (2Q 2021)
AXS-12 Highly selective NE reuptake inhibitor	**Narcolepsy**	• **Phase 3** trial start (3Q 2021)
AXS-14 Highly selective NE reuptake inhibitor	**Fibromyalgia**	✓ **FDA** meeting

Abbreviations: AD = Alzheimer's Disease; MDD = Major Depressive Disorder; TRD = Treatment Resistant Depression

✓ Accomplished milestone

• Upcoming milestone

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THERAPEUTICS

Thank you.

For more information, please contact

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