NASDAQ: AXSM

AXSOME THERAPEUTICS

INTERCEPT Phase 3 Trial of AXS-07 in Migraine

Topline Results

Conference Call

April 6, 2020

AXS-07 in Migraine Acute Treatment
INTERCEPT Phase 3 Trial Topline Results

Introduction	**Mark Jacobson**, Chief Operating Officer
Overview and Summary	**Herriot Tabuteau, MD**, Chief Executive Officer
INTERCEPT Trial Design & Results	**Cedric O'Gorman, MD**, Senior Vice President, Clinical Development & Medical Affairs
Q&A	**Presenters, Nick Pizzie**, Chief Financial Officer and **Dave Marek,** Chief Commercial Officer
Concluding Remarks	**Herriot Tabuteau, MD**, Chief Executive Officer

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Overview and Summary

Herriot Tabuteau, MD

AXSOME THERAPEUTICS

CHIEF EXECUTIVE OFFICER
AXSOME THERAPEUTICS, INC.

AXS-07 INTERCEPT Phase 3 Trial:
Summary of Topline Results

- AXS-07 is a novel, oral, multi-mechanistic investigational medicine for the acute treatment of migraine
- The INTERCEPT trial randomized patients to treat a single migraine attack with a single dose of AXS-07 or placebo, at the earliest sign of migraine pain, while the pain was mild
- AXS-07 met the two co-primary endpoints, demonstrating robust rates of migraine pain freedom and and most bothersome symptom freedom at 2 hours compared to placebo
- AXS-07 significantly prevented progression of migraine pain beyond mild in the majority of patients from 2 to 24 hours
- Treatment with AXS-07 enabled return to normal functioning for the majority of patients at 24 hours
- AXS-07 significantly reduced rescue medication use
- With the INTERCEPT and MOMENTUM Phase 3 trials, the efficacy of AXS-07 has been demonstrated in two positive trials, across a spectrum of migraine attack settings
- The positive INTERCEPT trial results strengthen the planned NDA filing for AXS-07 in the acute treatment of migraine, which remains on track for 4Q 2020

Migraine: Disabling Disease in Need of New Treatments

- The World Health Organization classifies severe migraine attacks as among the most disabling illnesses, comparable to dementia, quadriplegia and active psychosis[1,2]
- Debilitating pain, and the often-constant fear of the next migraine attack, damage family life, social life and employment[3]
- Depression and anxiety are twice as common in people with migraine than in healthy individuals[4]
- Widespread misperception of the seriousness of migraine contributes to its under-recognition and under-treatment[3]
- Migraine treatment guidelines encourage rapid early treatment of migraines to limit reoccurance[5]

There is an urgent need for new treatments that provide improved efficacy for this serious neurological disease

[1]Menken et al. *Arch Neurol*. 2000;57:418-420.
[2]Shapiro and Goadsby. *Cephalalgia*. 2007;27:991-4.
[3]Global Burden of Disease Study. *Lancet.* 2017;390:1211-1259
[4]Antonaci et al. *J Headache Pain*. 2011;12:115–125.
[5] Silberstein. *Neurology*. 2000 Sep 26;55(6):754-62.

AXS-07 (MoSEIC™ Meloxicam/Rizatriptan)
Multi-Mechanistic Treatment for Migraine

	AXS-07	
Migraine Process	Mechanism / Action	Component
CGRP Mediated	✓ Inhibition of CGRP release ✓ Reversal of CGRP-mediated vasodilation	Rizatriptan
Neuroinflammation	✓ Cyclooxygenase inhibition ✓ PGE_2 synthesis inhibition	MoSEIC™ meloxicam
Pain Signal Transmission	✓ Decrease passage of pain signals to trigeminal nucleus caudalis	Rizatriptan
Central Sensitization	✓ Reversal of central sensitization	MoSEIC™ meloxicam

Mechanisms of AXS-07 address multiple disordered physiological processes observed during migraine attacks

INTERCEPT Phase 3 Trial Design & Results

Cedric O'Gorman MD, MBA

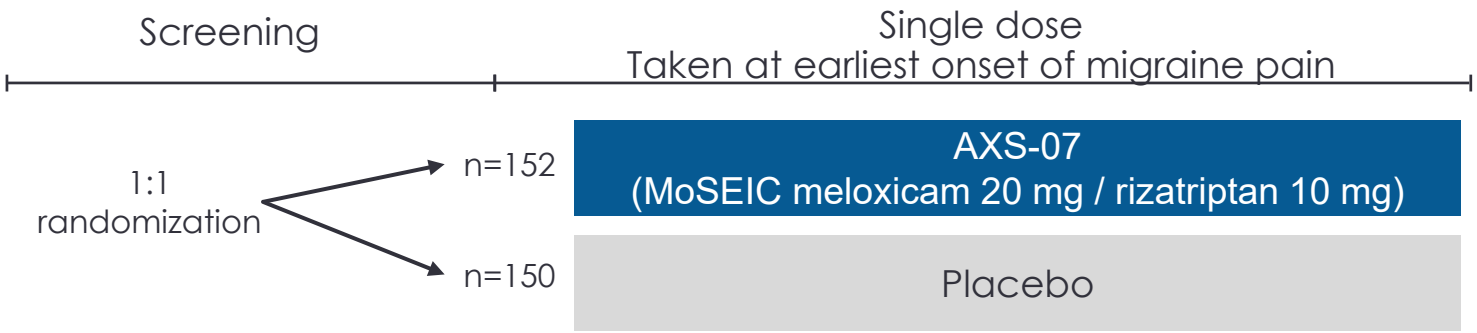
AXSOME THERAPEUTICS

SENIOR VICE PRESIDENT, CLINICAL DEVELOPMENT
AND MEDICAL AFFAIRS
AXSOME THERAPEUTICS, INC.

INTERCEPT Phase 3 Trial: Design Summary

INTERCEPT STUDY

INTERCEPT: INiTiating EaRly Control of MigrainE Pain & Associated SympToms
Phase 3 trial of AXS-07 for the acute treatment of migraine



Co-Primary Endpoints:

- Pain Freedom at 2 hours
- Freedom from MBS at 2 hours

Secondary Endpoints include:

- Sustained pain freedom
- Freedom from migraine pain progression
- Change in functional disability
- Use of rescue medication

Abbreviations: MBS, most bothersome migraine-associated symptom.

INTERCEPT Phase 3 Trial: Key Entry Criteria

INTERCEPT STUDY

Inclusion Criteria

- Male or female, 18 to 65 years of age, inclusive
- Established diagnosis (at least 1 year) of migraine with or without aura as defined by the ICHD-3 criteria
- An average 2 to 8 migraines per month

Exclusion Criteria

- Cluster headaches, tension headaches, or other types of migraines
- Chronic daily headache (≥15 non-migraine headache days per month)
- History of significant cardiovascular disease
- Uncontrolled hypertension

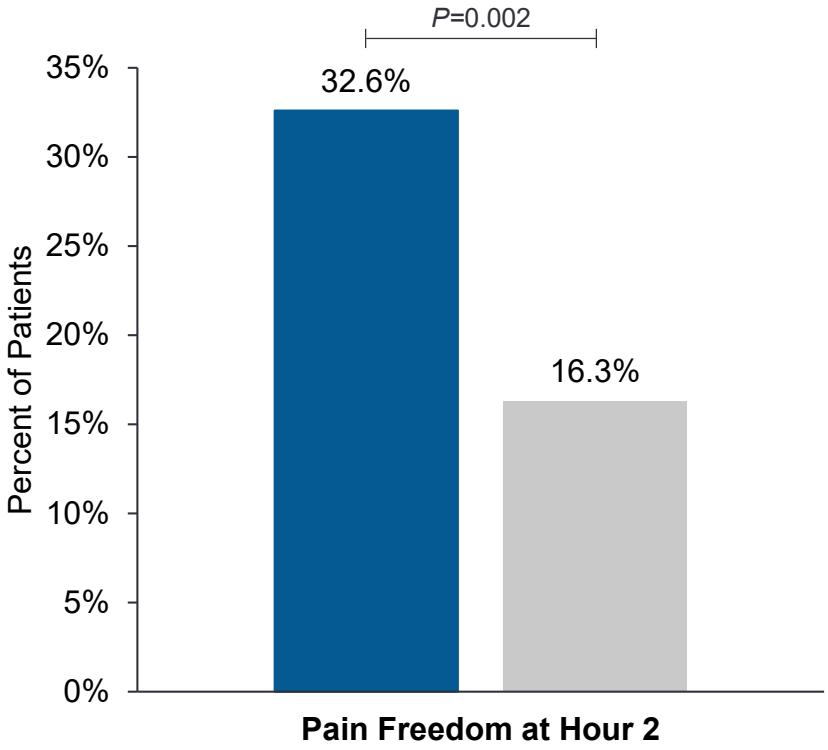
Abbreviations: ICHD-3 = International Classification of Headache Disorder, 3rd Edition; mTOQ-4 = Migraine Treatment Optimization Questionnaire.

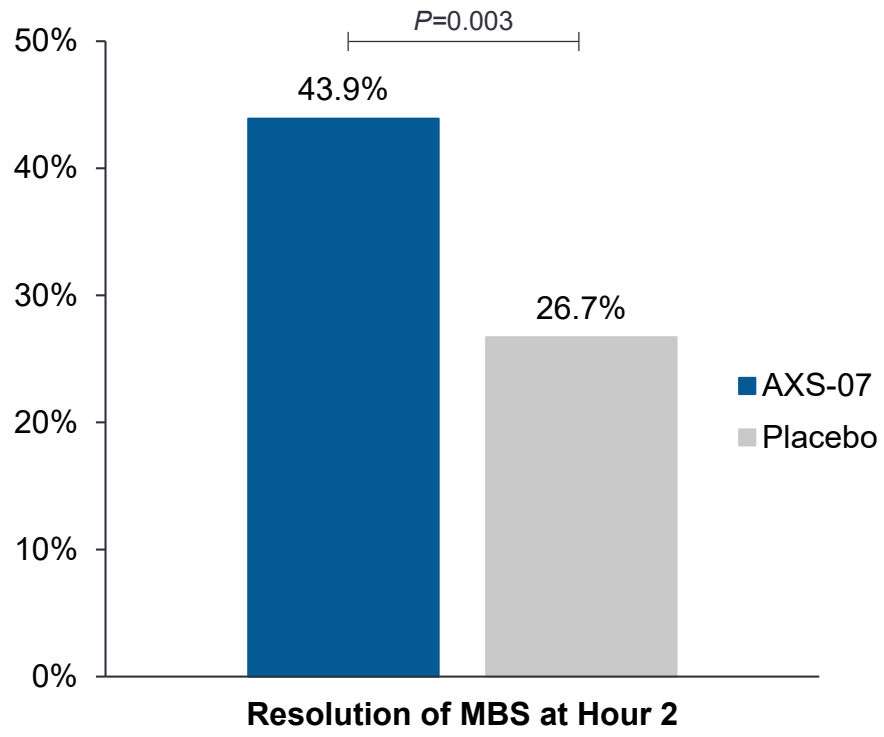
INTERCEPT Baseline Characteristics: Demographics

	AXS-07 (20 mg MoSEIC MIx / 10 mg Riz)	Placebo
	n=140	n=143
Age, years	41.7 (11.58)	41.4 (11.11)
Female gender, n (%)	119 (85.0%)	122 (85.3%)
Race, n (%)		
White	118 (84.3%)	116 (81.1%)
Black or African American	18 (12.9%)	17 (11.9%)
Asian	1 (0.7%)	7 (4.9%)
Other or Multiple	3 (2.1%)	3 (2.1%)
BMI (mg/kg^2)	28.7 (5.68)	28.4 (5.76)
Baseline pain intensity, mild	100%	100%

Data are mean (SD) unless otherwise stated.
Abbreviations: BMI = Body Mass Index; MIx = meloxicam; Riz = rizatriptan

Co-Primary Endpoints:
Pain Freedom and MBS Freedom at 2 Hours

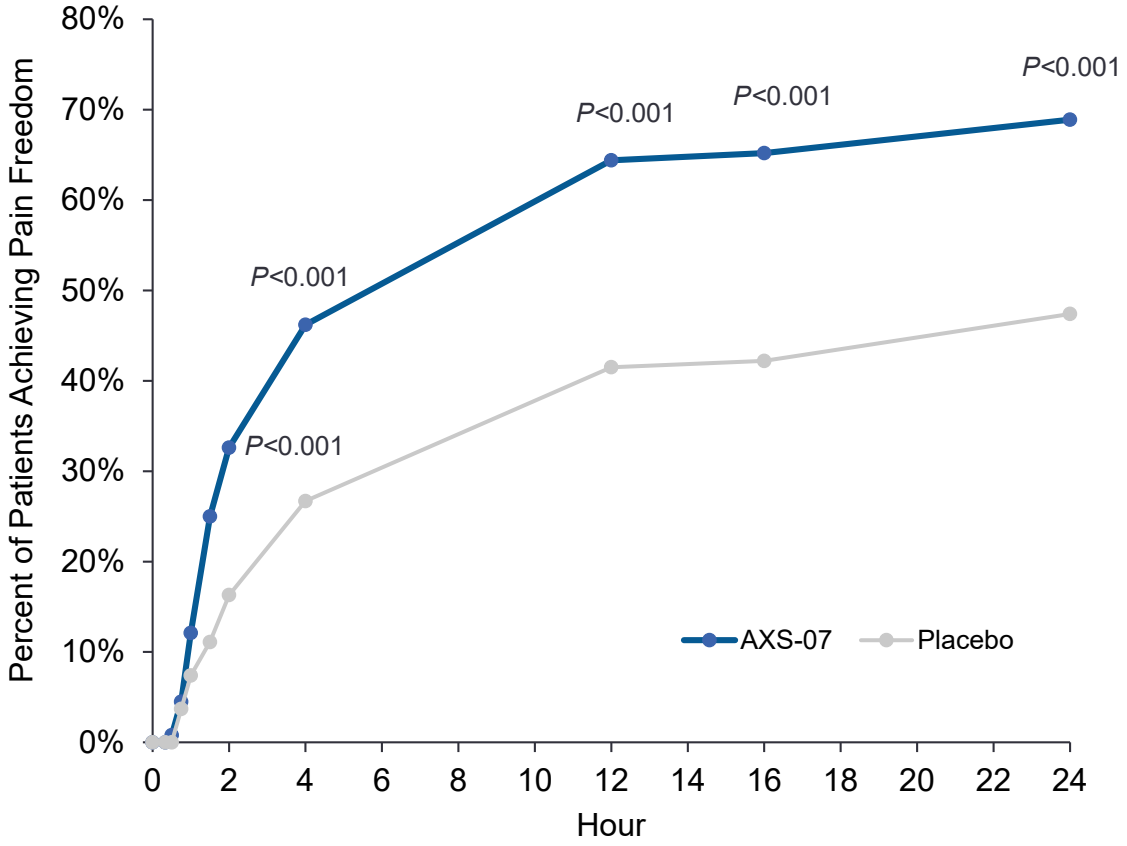




Co- Primary Endpoints	Difference AXS-07 - Placebo	*P*-Value
Pain Freedom 2 Hours after Dose	16.3%	0.002
Resolution of Most Bothersome Symptom 2 Hours after Dose	17.3%	0.003

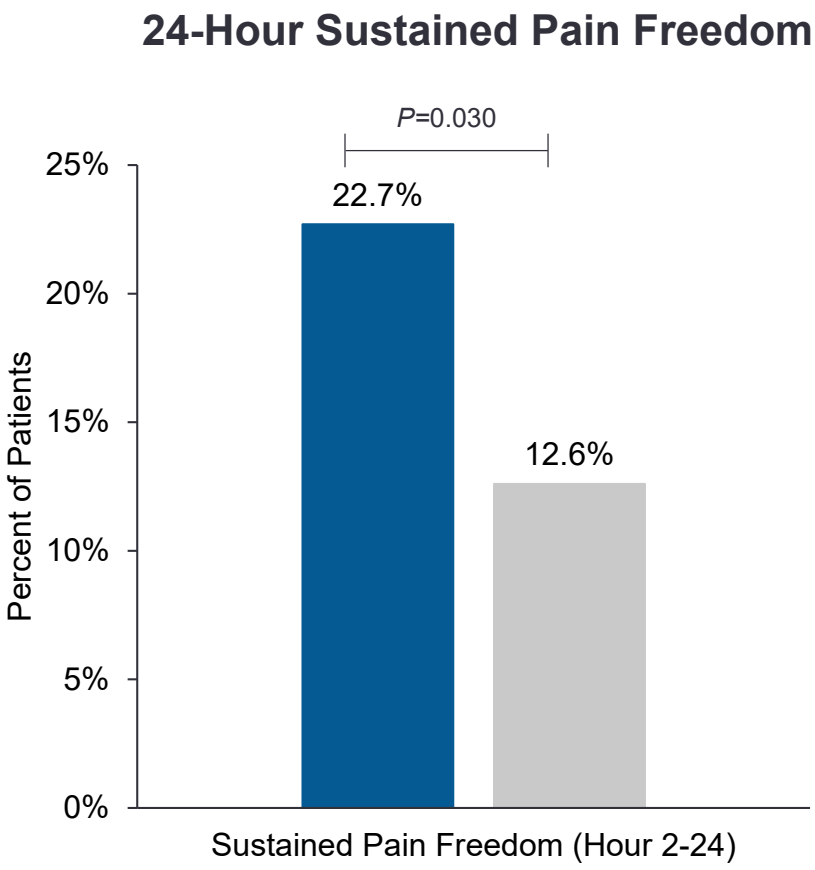
Most Bothersome Symptom = nausea, photophobia, or phonophobia

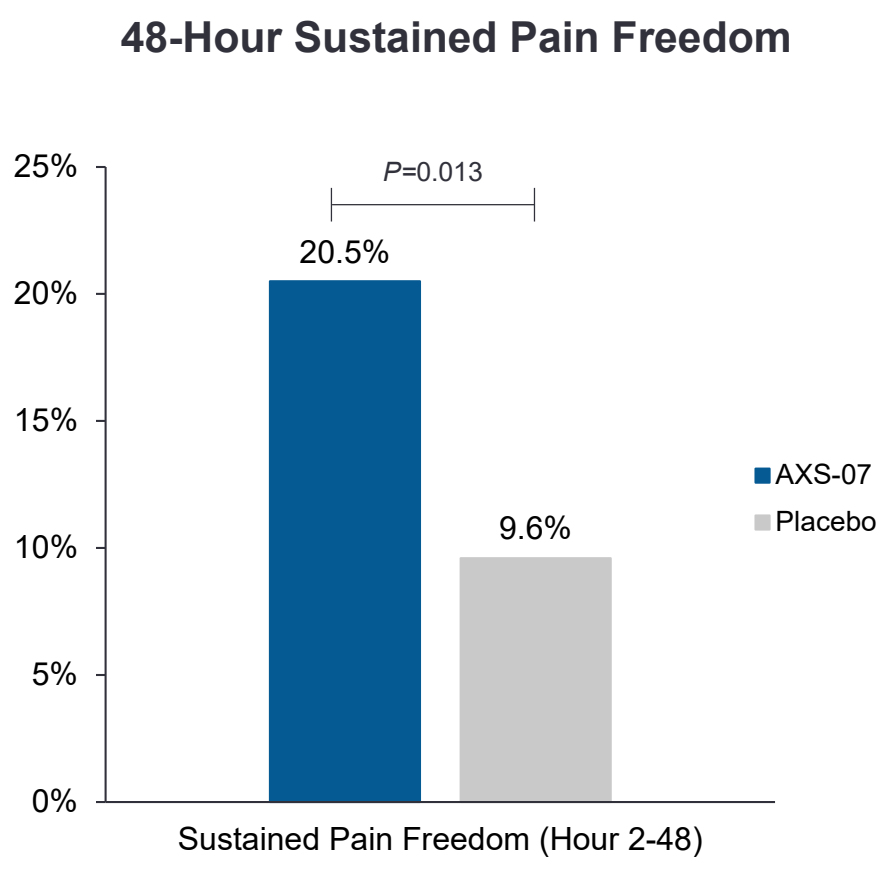
Rapid and Durable Freedom from Migraine Pain: Migraine Pain Freedom over Time



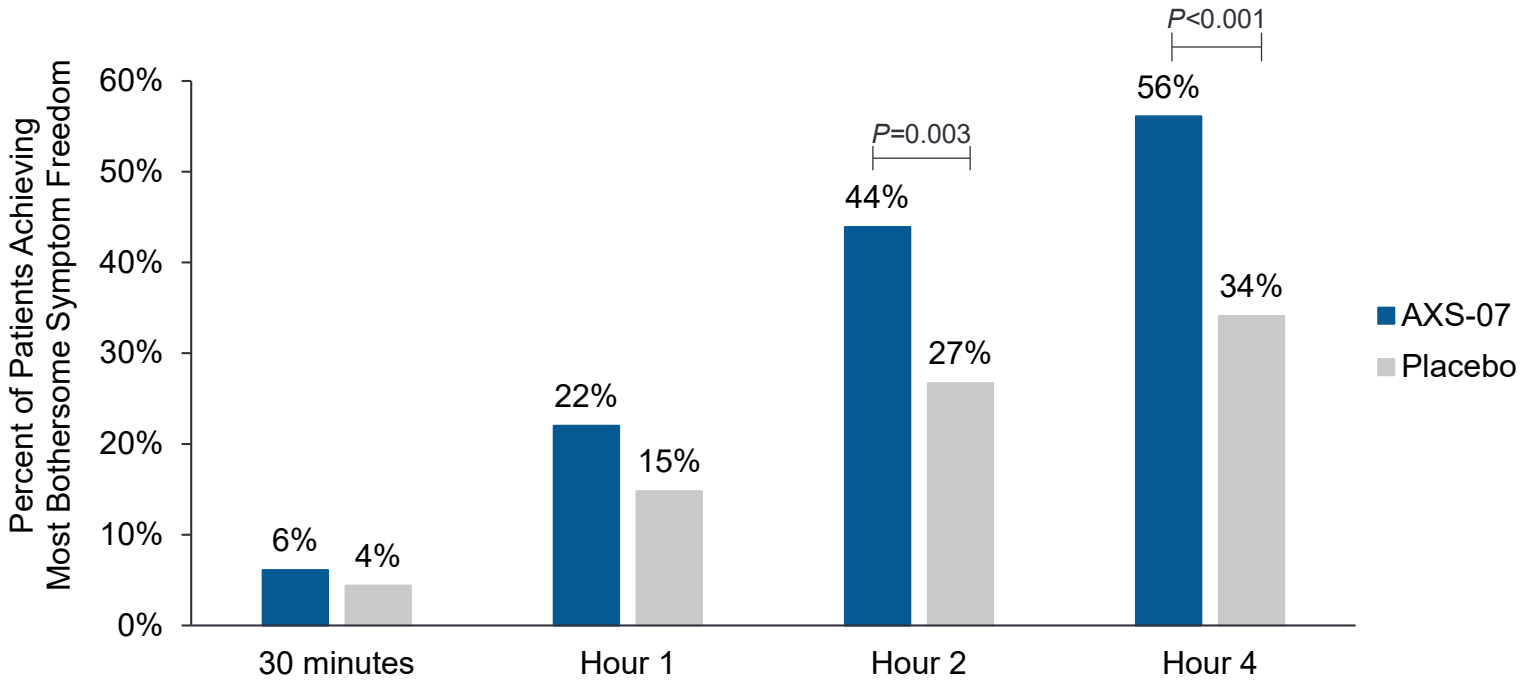
- Numerical separation from placebo as early as 30 minutes after dosing
- 64% and 69% of AXS-07 patients pain free at 12 and 24 hours, versus 42% and 47% of placebo, respectively.

Rapid and Durable Freedom from Migraine Pain: Sustained Pain Freedom



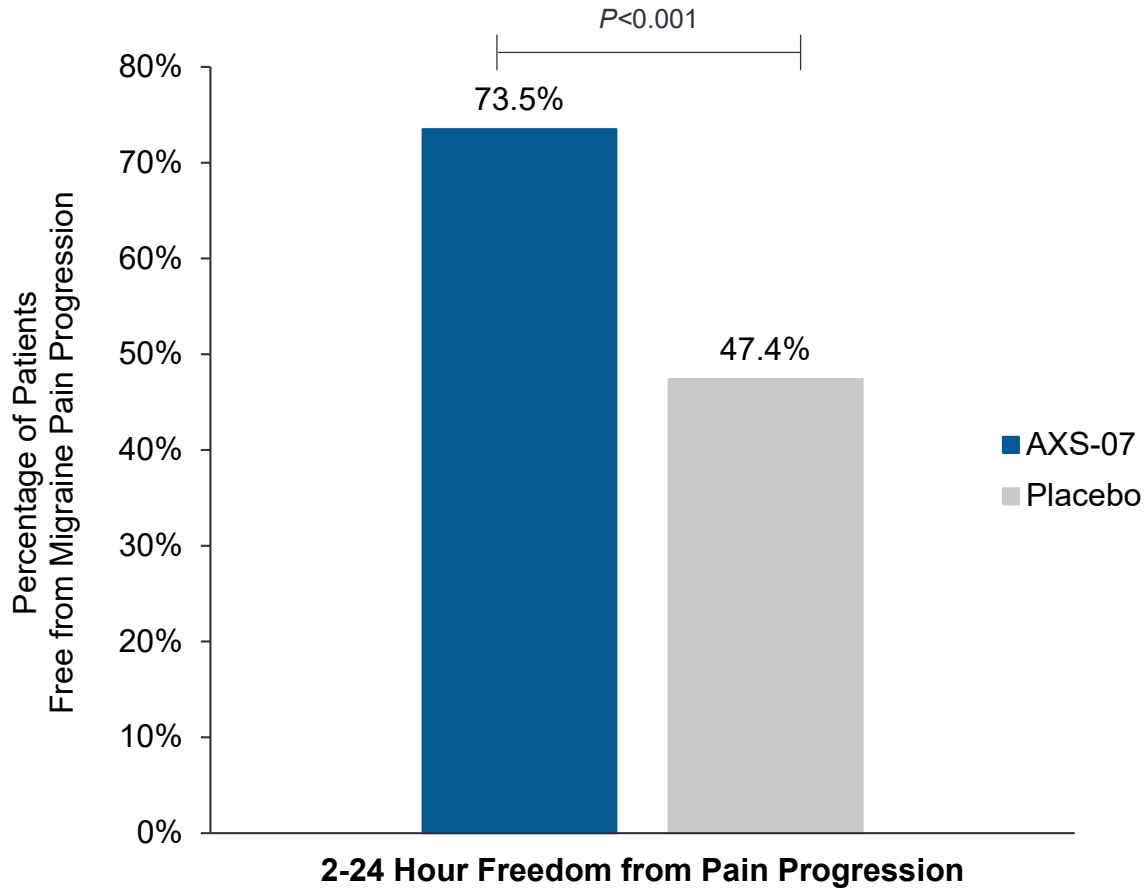


Rapid Freedom from Most Bothersome Symptom:
Most Bothersome Symptom Freedom over Time



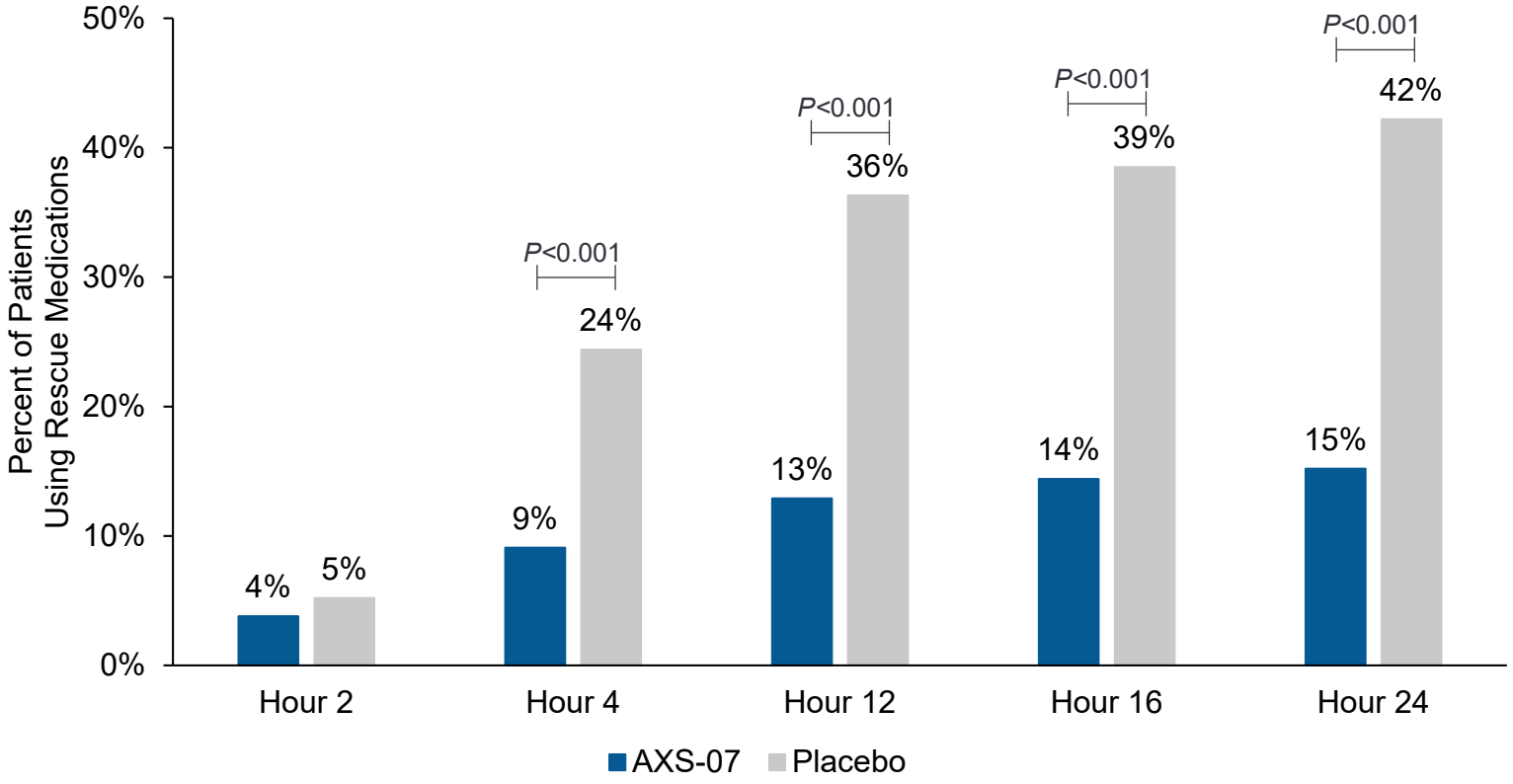
- Numerical separation from placebo as early as 30 minutes after dosing
- Most bothersome symptoms: nausea, photophobia, or phonophobia

Prevention of Worsening Migraine Pain: Freedom from Pain Progression 2-24 Hours

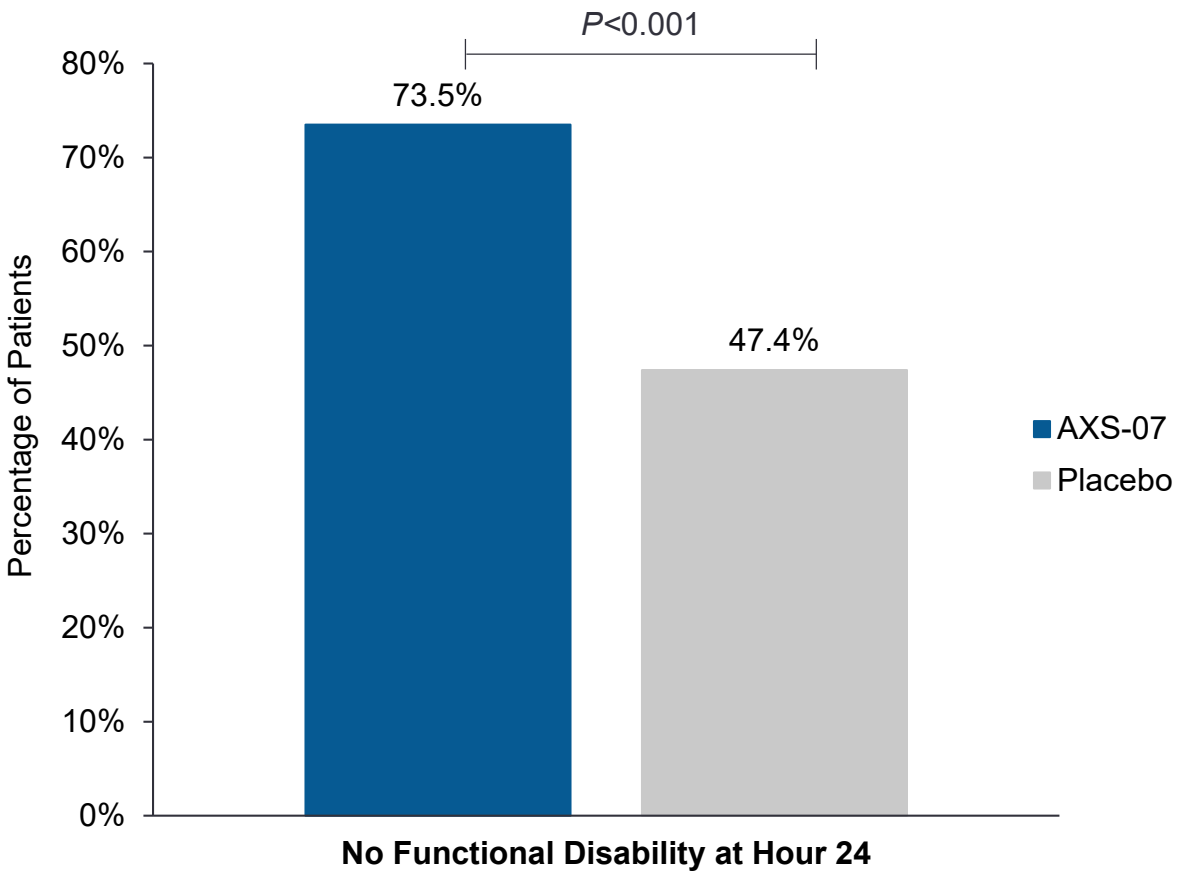


- A single dose of AXS-07 significantly prevented migraine pain progression beyond mild

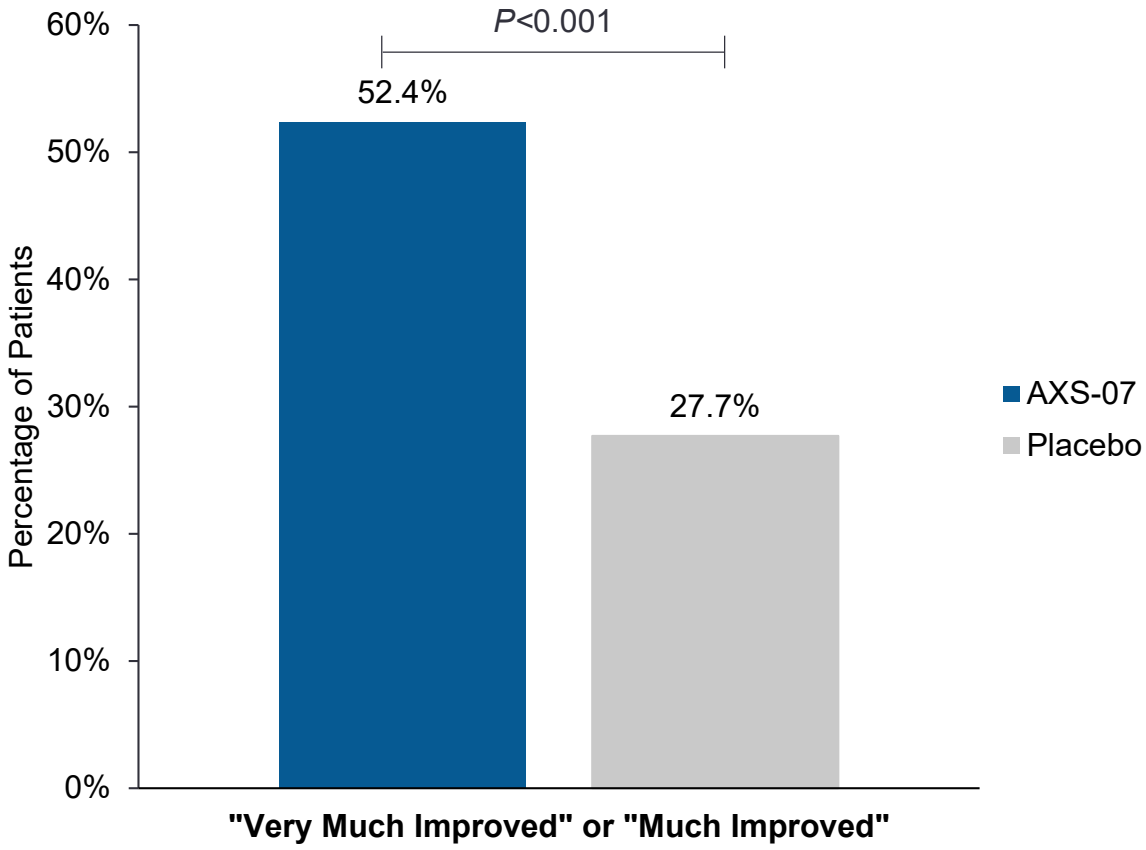
Prevention of Worsening Migraine Pain: Rescue Medication Use Over Time



Return to Normal Functioning:
Functional Disability at Hour 24



Global Improvement in Migraine Symptoms:
Patient Global Impression of Change at Hour 2



Safety of AXS-07:
Adverse Events Occurring in ≥2% of Subjects

	AXS-07 (N = 140)	Placebo (N = 143)
Any Treatment-Emergent AE	**25 (17.9%)**	**11 (7.7%)**
Somnolence	6 (4.3%)	3 (2.1%)
Dizziness	4 (2.9%)	2 (1.4%)
Paraesthesia	3 (2.1%)	0

Data presented as number of subjects (% of subjects)

- There were no SAEs in the trial

INTERCEPT Phase 3 Trial Results: Summary

- Treatment with AXS-07 resulted in rapid, sustained, and statistically significant efficacy as compared to placebo
- Early treatment with AXS-07 resulted in significant prevention of migraine pain progression
- Efficacy benefits of AXS-07 translated into significantly less use of rescue medication and return to normal functioning in the vast majority of AXS-07 treated patients
- AXS-07 was generally safe and well tolerated in this study

Q&A

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Concluding Remarks

Herriot Tabuteau, MD

CHIEF EXECUTIVE OFFICER
AXSOME THERAPEUTICS, INC.

AXS-07: Clinical Development in Migraine

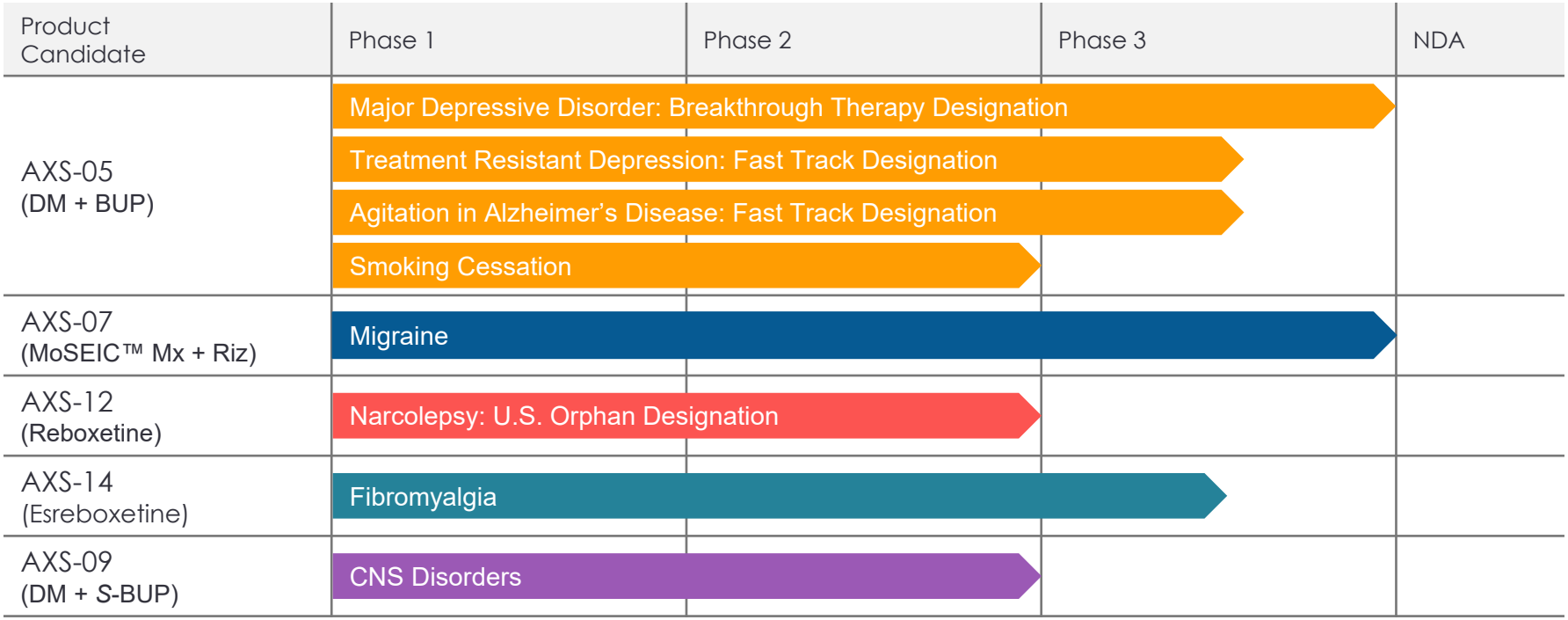
	Clinical Program		
	MOMENTUM	**INTERCEPT**	**AXS-07 / OL**
Indication	Acute treatment of migraine	Acute treatment of migraine	Acute treatment of migraine
Patient population	History of inadequate response to prior treatments	All comers	Participation in MOMENTUM or INTERCEPT
Migraine pain severity and treatment timing	Moderate or severe migraine pain	Earliest onset of migraine pain, while pain is mild	Treat all attacks, as needed
Phase	Pivotal Phase 3	Supportive Phase 3	Open-label Phase 3
Objectives	Efficacy of AXS-07 vs. Riz vs. MoSEIC™ Mlx vs. PBO	Efficacy of AXS-07 vs. PBO	Long-term safety of AXS-07
Status	Completed	Completed	Ongoing
Patients Dosed	1526	283	751

Abbreviations: OL = Open-label; PBO = placebo; Riz = rizatriptan; Mlx = meloxicam

- NDA filing of AXS-07 for the acute treatment of migraine, based on positive results from MOMENTUM study, on track for 4Q 2020

Our CNS Candidates and Pipeline

- Five differentiated clinical-stage CNS assets targeting significant and growing markets
- Patent protection to 2034-2036, worldwide rights for most product candidates



Abbreviations: BUP = Bupropion; CNS = Central Nervous System; DM = Dextromethorphan; Mx = Meloxicam; Riz = Rizatriptan; *S*-BUP = Esbupropion.

Our Clinical and Regulatory Milestones

Product Candidate	Indication	2020
AXS-05 (DM + BUP)	**MDD**	● **NDA** submission (4Q)
	TRD	✓ **STRIDE-1** topline results ● **Phase 3** trial start (Q3 2020)
	AD Agitation	● **ADVANCE-1** Phase 2/3 topline results (early 2Q)
	Smoking Cessation	● **FDA** meeting (2020)
AXS-07 (MoSEIC™ Mx + Riz)	**Migraine**	✓ **INTERCEPT** Phase 3 topline results ● **NDA** submission (4Q)
AXS-12 (Reboxetine)	**Narcolepsy**	● **Phase 3** trial start (2020)
AXS-14 (Esreboxetine)	**Fibromyalgia**	● **FDA** feedback (2020)

Abbreviations: AD = Alzheimer's Disease; BUP = Bupropion; DM = Dextromethorphan; MDD = Major Depressive Disorder; Mx = Meloxicam; Riz = Rizatriptan; TRD = Treatment Resistant Depression.

✓ Accomplished milestone.

● Upcoming milestone.

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Thank you.

For more information, please contact

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