NASDAQ: AXSM

AXSOME THERAPEUTICS

MOMENTUM Phase 3 Trial of AXS-07 in Migraine Topline Results

Conference Call

December 30, 2019

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

Introduction	**Mark Jacobson**, Senior Vice President, Operations
Overview and Summary	**Herriot Tabuteau, MD**, Chief Executive Officer
MOMENTUM 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

CHIEF EXECUTIVE OFFICER
AXSOME THERAPEUTICS, INC.

AXSOME THERAPEUTICS

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

- AXS-07 is a novel, oral, multi-mechanistic investigational medicine for the acute treatment of migraine
- MOMENTUM enrolled only patients with a history of inadequate response to prior acute treatments and incorporated rizatriptan as an active comparator:
  - Rizatriptan is considered the fastest acting triptan, and one of the most effective migraine treatments
- AXS-07 met both co-primary endpoints, and key secondary endpoint (component contribution)
- AXS-07 provided substantially greater and more sustained migraine pain relief compared to rizatriptan and placebo
- Rapidly relieved migraine pain
- Significantly reduced use of rescue medication compared to rizatriptan
- AXS-07 was safe and well tolerated
- Positive MOMENTUM trial supports NDA filing of AXS-07 in the acute treatment of migraine, anticipated in 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]
- The majority of patients are not fully satisfied with their current treatment[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]Lipton and Stewart. *Headache*. 1999;39(suppl 2):S20-S26.

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

MOMENTUM Phase 3 Trial Design & Results

Cedric O'Gorman MD, MBA

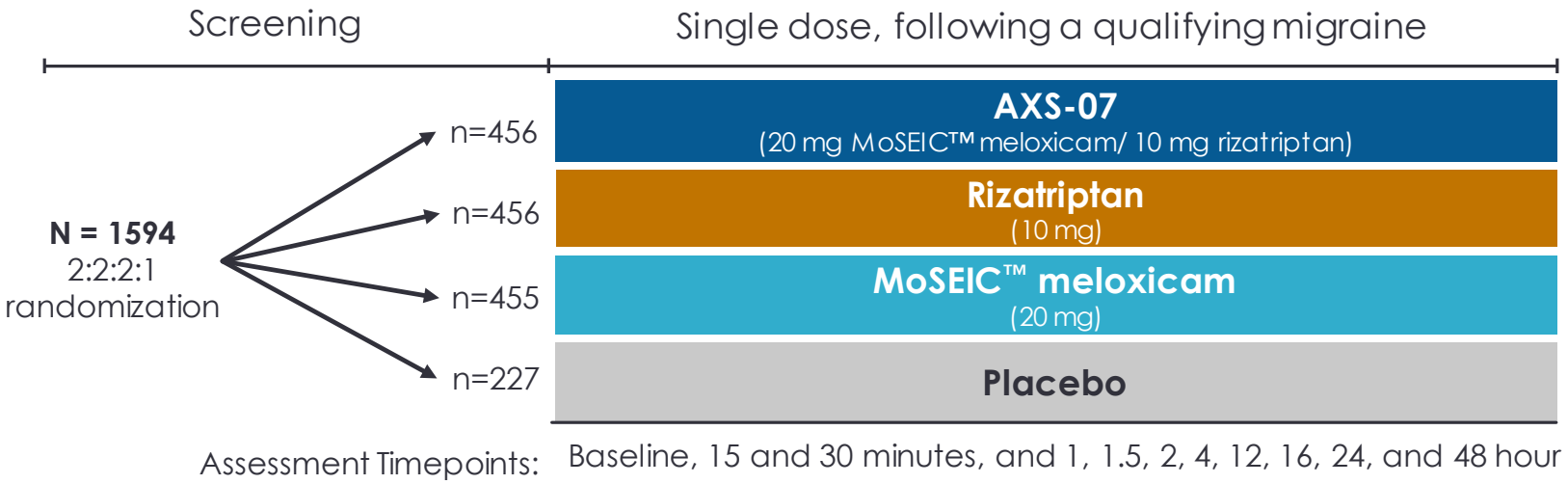
AXSOME THERAPEUTICS

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

MOMENTUM Phase 3 Trial: Design Summary

MOMENTUM STUDY

MOMENTUM: Maximizing **O**utco**ME**s i**N** **T**reating ac**U**te **M**igraine
Phase 3 study of AXS-07 for the acute treatment of migraine in adults with history of inadequate response to prior treatment



- **Co-Primary Endpoints (AXS-07 vs placebo)**
  - Pain Freedom at 2 hours
  - Freedom from MBS at 2 hours
- **Key Secondary Endpoint (AXS-07 vs rizatriptan and MoSEIC™ meloxicam)**
  - Superiority of AXS-07 to individual components (component contribution) based on sustained pain freedom 2-24 hours after dosing

MOMENTUM Phase 3 Trial: Key Entry Criteria

MOMENTUM 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 moderate to severe migraines per month, on average
- History of inadequate response as assessed by a score of ≤ 7 on the mTOQ-4

Exclusion Criteria

- Cluster 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.

MOMENTUM Baseline Characteristics:
Difficult-to-Treat Migraine Characteristics

	AXS-07 (20 mg MoSEIC MIx / 10 mg Riz)	Rizatriptan (10 mg)	MoSEIC Meloxicam (20 mg)	Placebo
	n=428	n=419	n=421	n=209
Total mTOQ-4 Score, mean (SD)	3.5 (2.17)	3.6 (2.25)	3.8 (2.14)	3.6 (2.19)
Presence of Allodynia, n (%)	336 (78.5%)	305 (72.8%)	322 (76.5%)	150 (71.8%)
Severe Pain Intensity, n (%)	184 (43.0%)	155 (37.0%)	181 (43.0%)	88 (42.1%)
Obese (>30mg/kg^2), n (%)	184 (43.0%)	197 (47.0%)	174 (41.3%)	90 (43.1%)
Morning Migraine, n (%)	162 (36.7%)	158 (36.4%)	159 (36.7%)	76 (34.9%)

Abbreviations: MIx = meloxicam; mTOQ-4 = Migraine Treatment Optimization Questionnaire; Riz = rizatriptan

MOMENTUM Baseline Characteristics: Demographics

	AXS-07 (20 mg MoSEIC MIx / 10 mg Riz)	Rizatriptan (10 mg)	MoSEIC Meloxicam (20 mg)	Placebo
	n=428	n=419	n=421	n=209
Age, years	41.2 (11.52)	41.4 (10.68)	41.0 (12.07)	40.8 (11.47)
Female gender, n (%)	346 (80.8%)	353 (84.2%)	355 (84.3%)	177 (84.7%)
Race, n (%)				
White	337 (78.7%)	320 (76.4%)	324 (77.0%)	154 (73.7%)
Black or African American	73 (17.1%)	83 (19.8%)	86 (20.4%)	47 (22.5%)
Asian	10 (2.3%)	6 (1.4%)	9 (2.1%)	5 (2.4%)
Other or Not Reported	4 (0.9%)	5 (1.2%)	0 (0%)	2 (1.0%)
BMI (mg/kg^2)	29.2 (5.67)	29.7 (5.67)	28.9 (5.69)	29.3 (5.63)
Prior triptan use, n (%)	171 (40.0%)	163 (38.9%)	147 (34.9%)	73 (34.9%)

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

Co-Primary Endpoints:
Pain and MBS Improvement

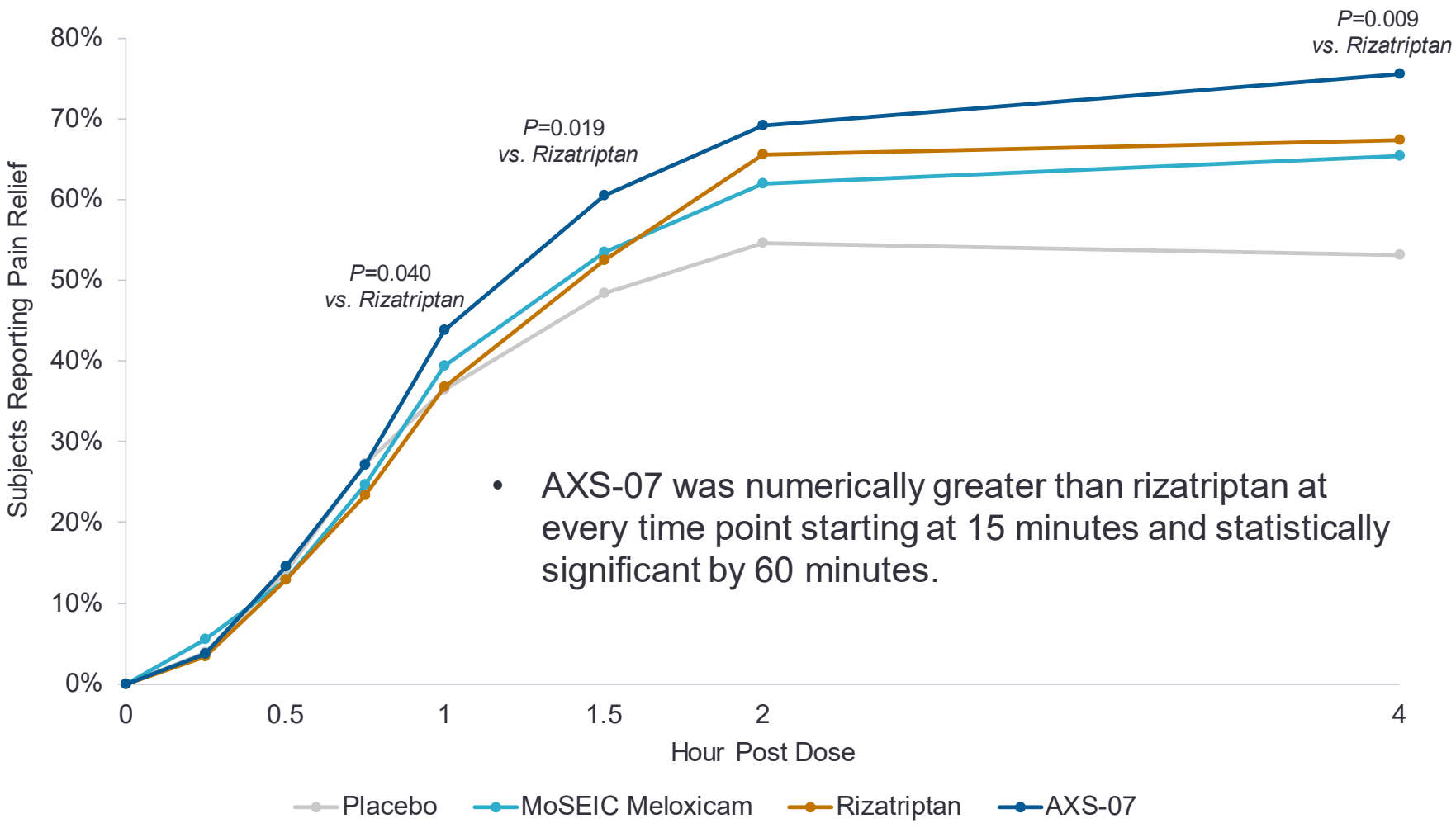
Endpoints	AXS-07 (n=428)	Placebo (n=209)	Difference	*P*-Value
Co-Primary Endpoint 1: *Pain Freedom 2 Hours after Dose, %*	19.9%	6.7%	-13.2%	<0.001
Co-Primary Endpoint 2: *Absence of Most Bothersome Symptom 2 Hours after Dose, %*	36.9%	24.4%	-12.5%	0.002

Most Bothersome Symptom = nausea, photophobia, or phonophobia

Key Secondary Endpoint:
2-24 Hour Sustained Pain Freedom

	AXS-07 (n=428)	**Rizatriptan** (n=419)	**MoSEIC Meloxicam** (n=421)	**Placebo** (n=209)
Sustained Pain Freedom, *Pain Freedom maintained from 2 to 24 Hours after Dose, %*	16.1%	11.2%	8.8%	5.3%
Difference from AXS-07		-4.9%	-7.3%	-10.9%
P-value vs. AXS-07		0.038	0.001	<0.001

Rapid Relief of Migraine Pain



- AXS-07 was numerically greater than rizatriptan at every time point starting at 15 minutes and statistically significant by 60 minutes.

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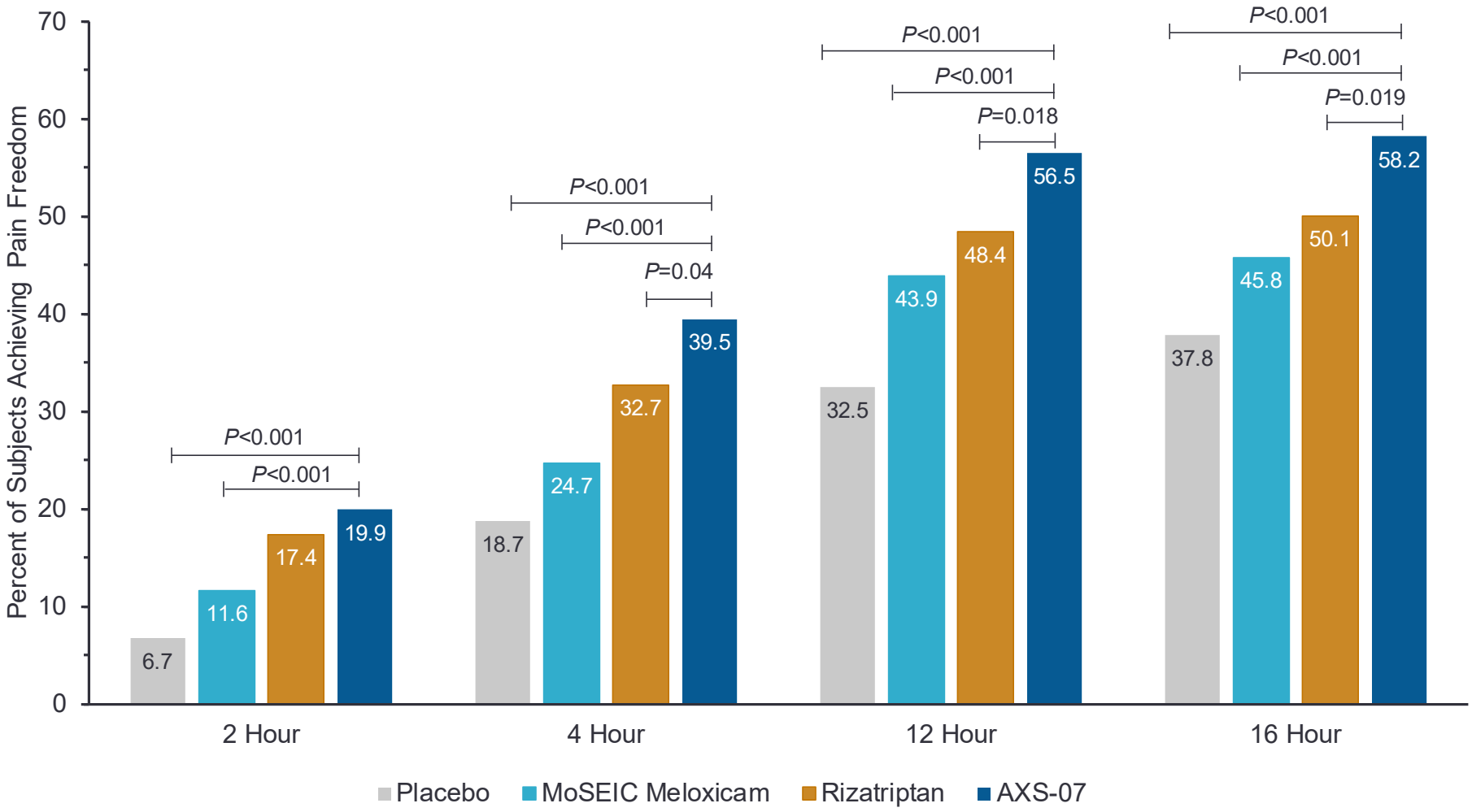
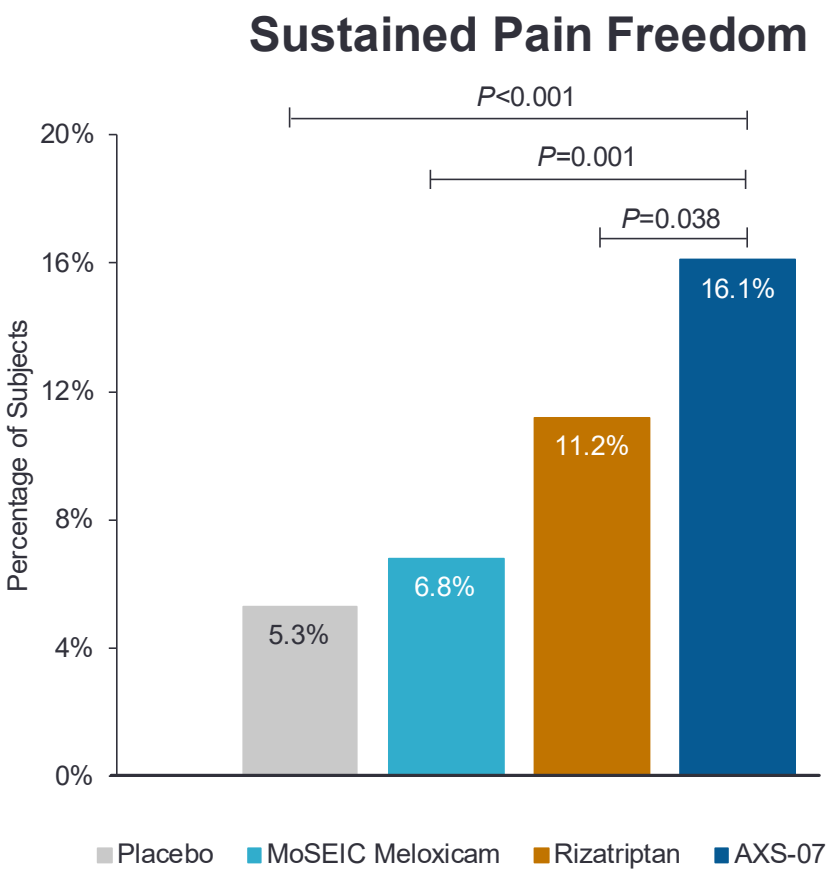
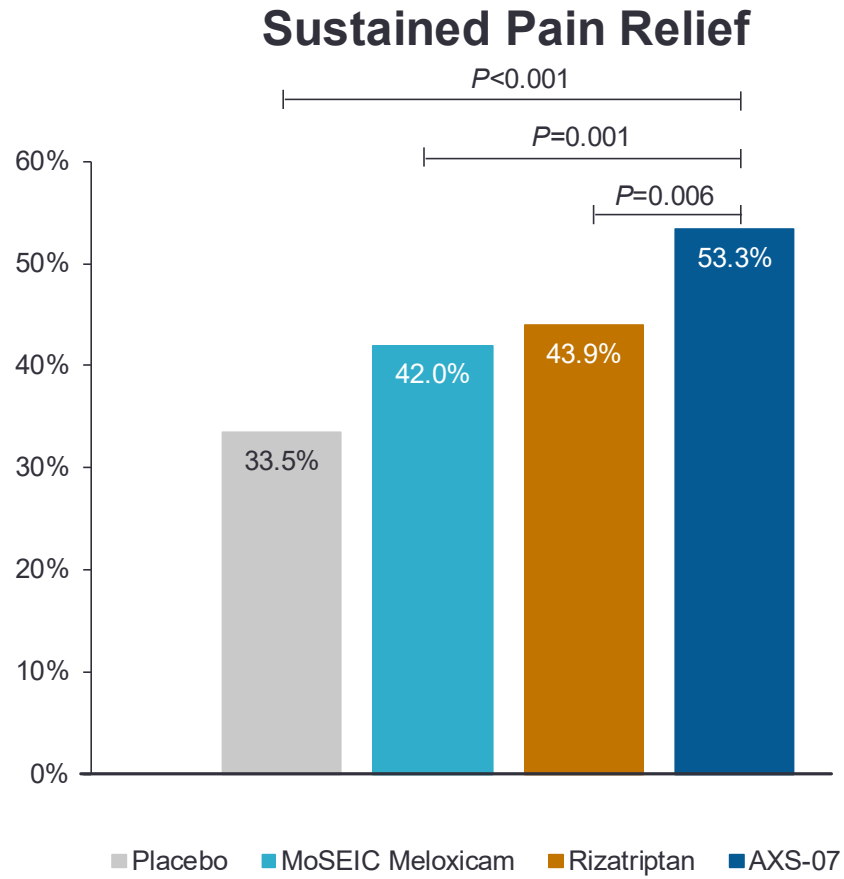
Pain Freedom Rates Over Time:
Significant Improvements in Pain Freedom



Sustained Effect from 2 to 24 hours: AXS-07 Superiority to Rizatriptan





- 80% of subjects treated with AXS-07 who achieved pain freedom at Hour 2 maintained it through Hour 24

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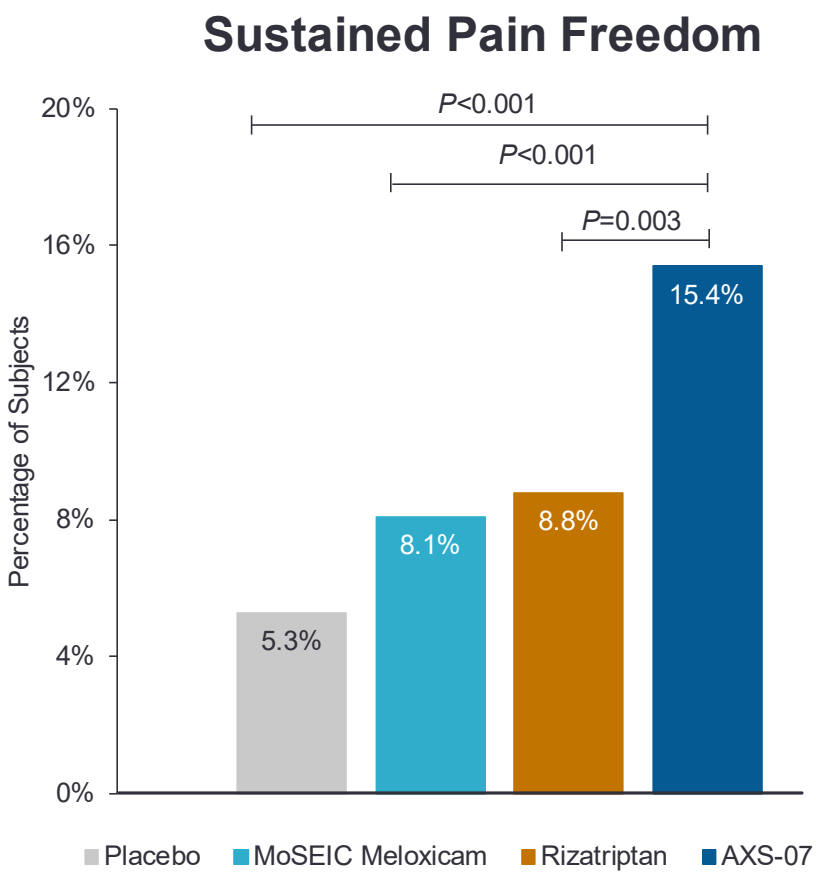
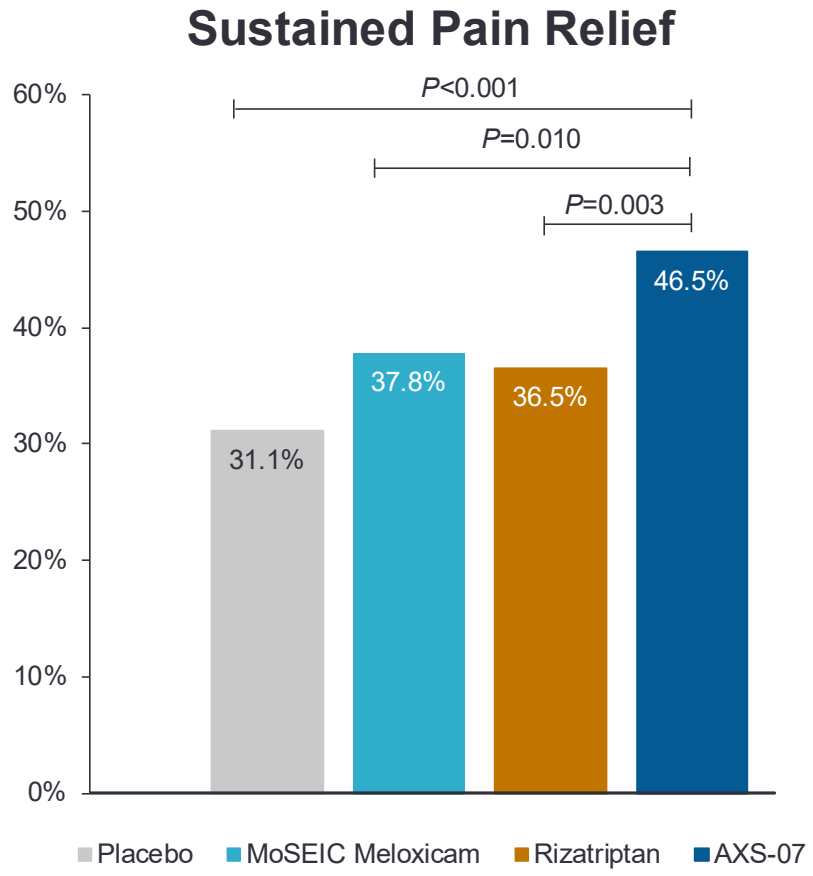
Sustained Effect from 2 to 48 hours: AXS-07 Superiority to Rizatriptan

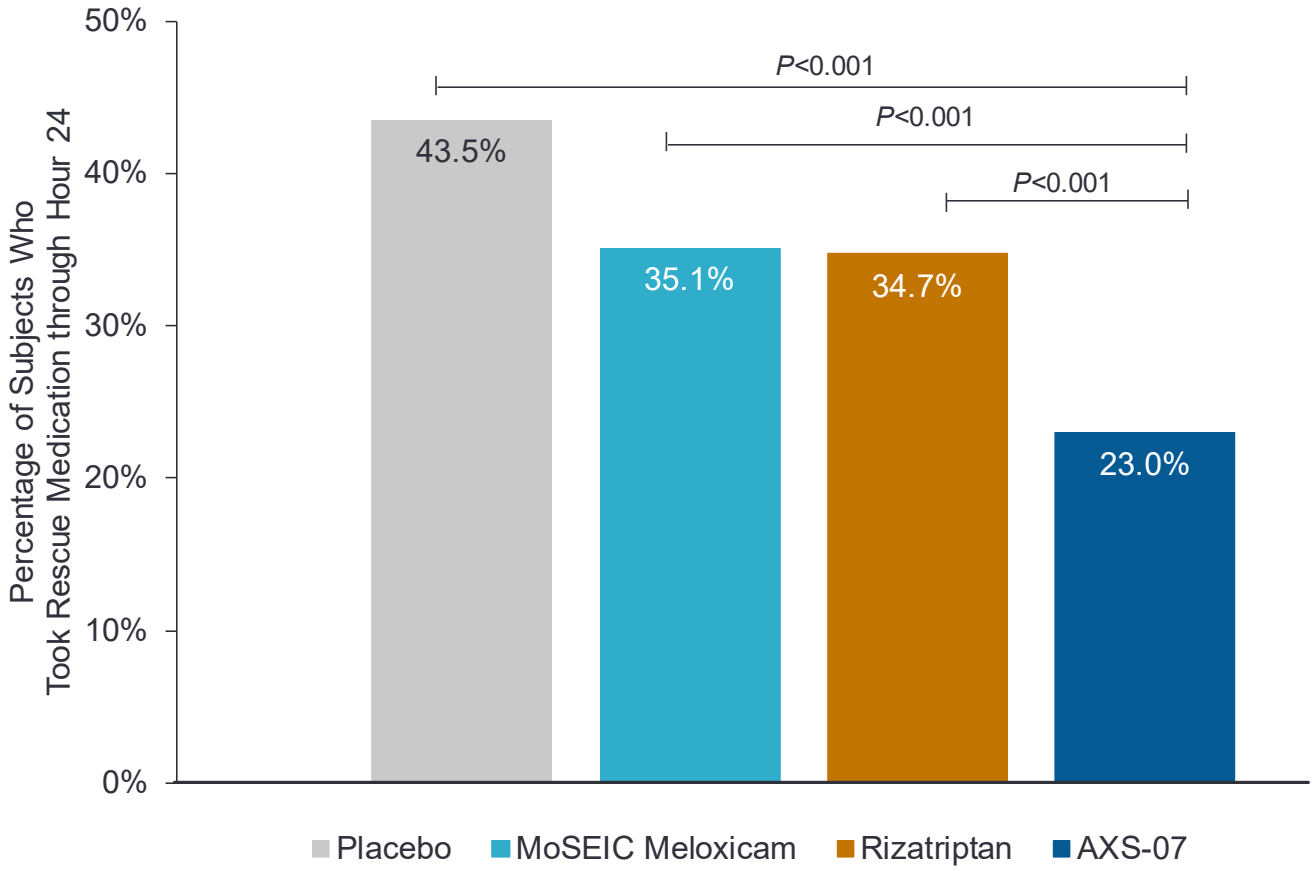




- 77% of subjects treated with AXS-07 who achieved pain freedom at Hour 2 maintained it through Hour 48

Reduced Use of Rescue Medication: AXS-07 Superiority to Rizatriptan

- 77% of subjects receiving AXS-07 did not require rescue medication



Multiple Efficacy-Related Endpoints: AXS-07 Superiority Over Rizatriptan

Endpoint	*P*-value AXS-07 vs. Rizatriptan
1 Hour Pain Relief	0.04
2-24 Hour Sustained Pain Relief	0.006
2-48 Hour Sustained Pain Relief	0.003
2-24 Hour Sustained Pain Freedom	0.038
2-48 Hour Sustained Pain Freedom	0.003
PGI-C	0.022
Functional Improvement at 24 hours	0.027
Use of Rescue Medication	<0.001

Abbreviations: PGI-C = Patient Global Impression – Change

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

	AXS-07 (N = 441)	Rizatriptan (N = 434)	Meloxicam (N = 433)	Placebo (N = 218)
Any Treatment-Emergent AE	**49 (11.1%)**	**67 (15.4%)**	**50 (11.5%)**	**13 (6.0%)**
Nausea	12 (2.7%)	21 (4.8%)	14 (3.2%)	8 (3.7%)
Dizziness	7 (1.6%)	9 (2.1%)	5 (1.2%)	5 (1.2%)
Somnolence	6 (1.4%)	9 (2.1%)	10 (2.3%)	6 (1.4%)

Data presented as number of subjects (% of subjects)

- One serious adverse event in the AXS-07 arm which was not treatment related

MOMENTUM Phase 3 Trial Results: Summary

- AXS-07 resulted in rapid, sustained, substantial and statistically significant efficacy as compared to placebo and rizatriptan in the acute treatment of migraine in patients with a history of inadequate response to prior acute treatments.
- The efficacy benefits of AXS-07 translated into significantly less use of rescue medication with AXS-07 as compared to rizatriptan and placebo.
- AXS-07 was safe and well tolerated in this study

Q&A

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Concluding Remarks

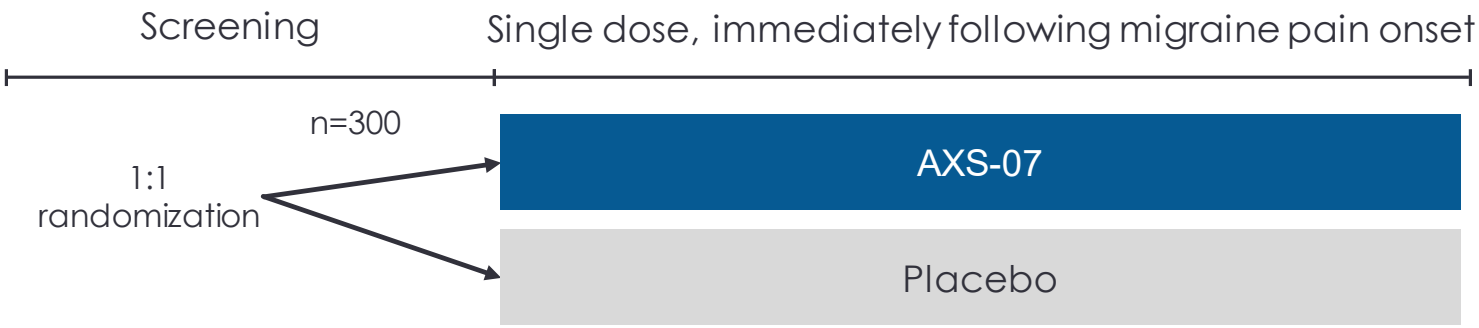
Herriot Tabuteau, MD

CHIEF EXECUTIVE OFFICER
AXSOME THERAPEUTICS, INC.

INTERCEPT Study of AXS-07
For the Acute Treatment of Migraine

INTERCEPT STUDY

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



Patient Population
- Adult subjects with an established diagnosis of migraine with or without aura
- Will initiate treatment at the first sign of migraine pain onset

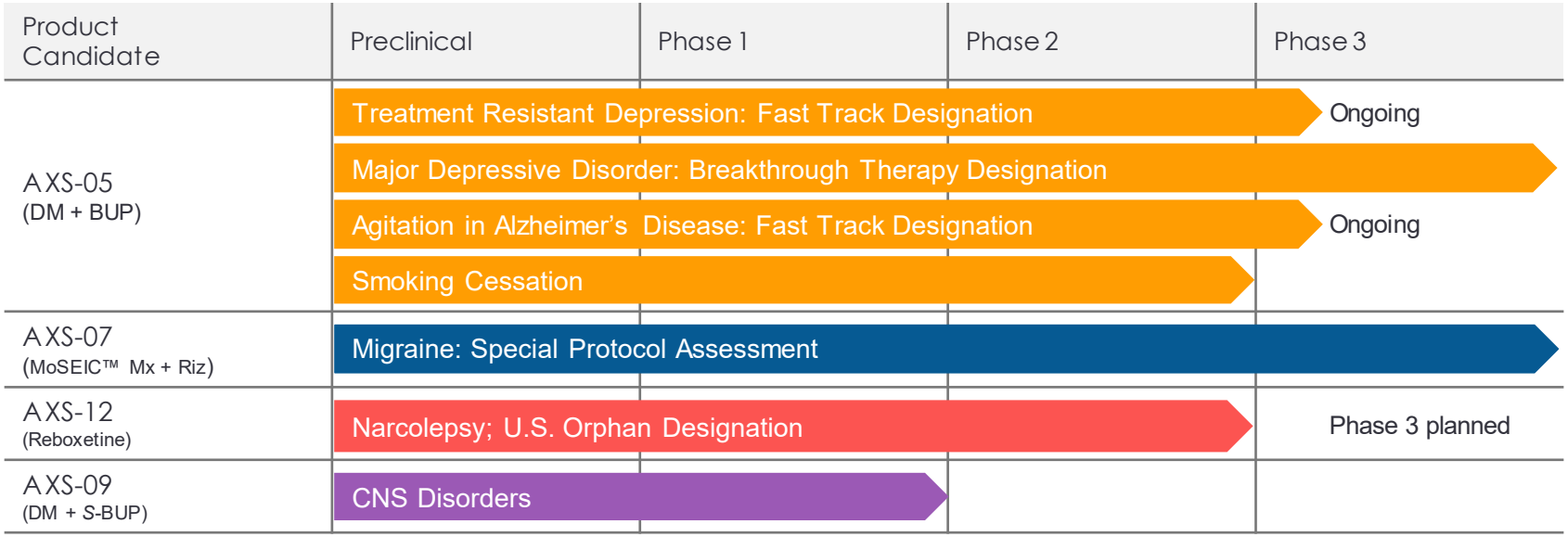
Co-Primary Endpoints (AXS-07 vs placebo)
- Pain Freedom at 2 hours
- Freedom from MBS at 2 hours

✓ On track to report topline results: Q1'20

Abbreviations: MBS, most bothersome migraine-associated symptom.

Our CNS Candidates and Pipeline

- Four differentiated clinical-stage CNS assets targeting significant and growing markets
- Patent protection to 2034-2036, worldwide rights



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

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Thank you.

For more information, please contact

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