Efficacy and Safety of AXS-07 (MoSEIC™ Meloxicam/Rizatriptan) in the Acute Treatment of Migraine: Results from the INTERCEPT Phase 3 Trial

Amanda Jones[3], Cedric O'Gorman[3], Stewart J. Tepper[1], Richard B. Lipton[2], Herriot Tabuteau[3]

[1]Geisel School of Medicine at Dartmouth, Hanover, NH, USA; [2]Albert Einstein College of Medicine, New York, NY, USA; [3]Axsome Therapeutics Inc. New York, NY, USA

Presenter: Amanda Jones, PharmD

AXSOME THERAPEUTICS

Disclosures

Amanda Jones, Cedric O'Gorman, and Herriot Tabuteau are full-time employees of Axsome Therapeutics.

Stewart J. Tepper and Richard B. Lipton are consultants to Axsome Therapeutics.

Learning Objectives

1. Appreciate the seriousness of migraine and the continued unmet need in the acute treatment of migraine
2. Be able to describe the efficacy and safety results from INTERCEPT, a Phase 3 randomized, double-blind, placebo-controlled trial of AXS-07 in the acute treatment of migraine
3. Understand the multi-mechanistic approach of AXS-07 as an investigational agent for the acute treatment of migraine

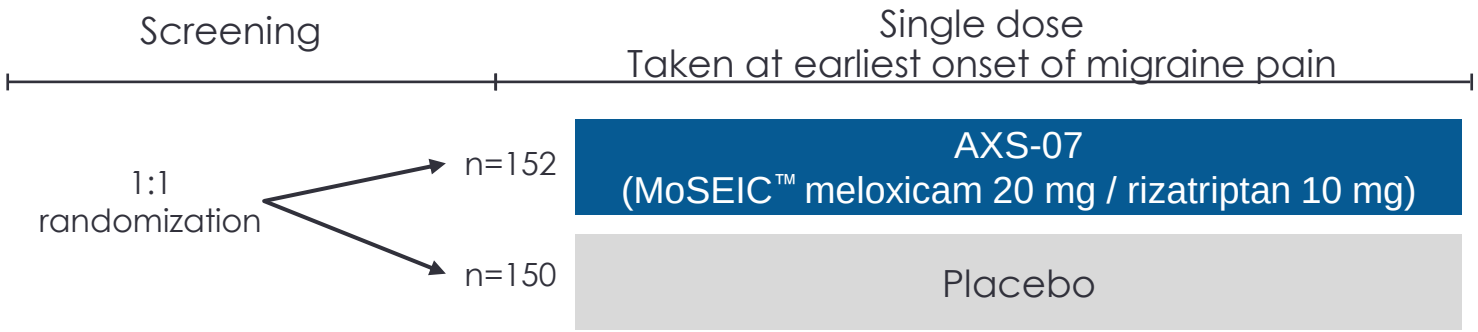
	AXS-07	
Migraine Process	Mechanism / Action	Component
CGRP Mediated	✓ Inhibition of CGRP release ✓ Reversal of CGRP-mediated vasodilation	Rizatriptan
Neuro-inflammation	✓ Cyclooxygenase inhibition ✓ PGE_2 synthesis inhibition	MoSEIC™ meloxicam
Pain Signal Transmission	✓ Decrease passage of pain signals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

Mechanism of AXS-07 addresses multiple disordered physiological processes observed during migraine attacks

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

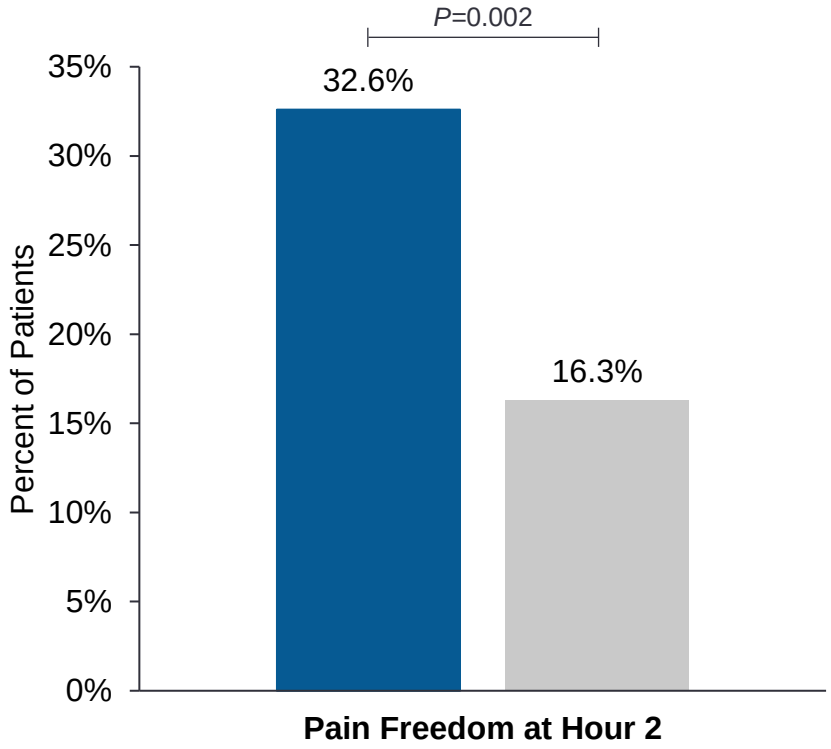
Secondary Endpoints include:
- Sustained pain freedom
- Freedom from migraine pain progression
- Change in functional disability
- Use of rescue medication

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

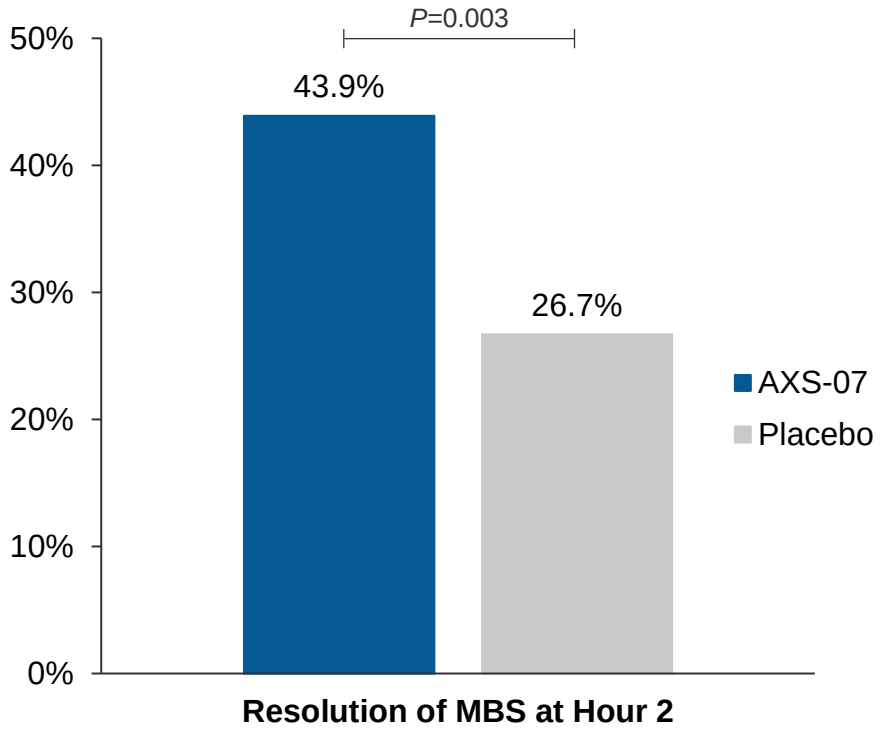
Exclusion Criteria
- Cluster headaches, tension headaches, or other types of migraines
- Chronic daily headache (≥15 non-migraine headache days per month)
- History of significant cardiovascular disease
- Uncontrolled hypertension

Abbreviations: ICHD-3 = International Classification of Headache Disorder, 3rd Edition; MBS = most bothersome migraine-associated symptom; MoSEIC = Molecular Solubility Enhanced Inclusion Complex

AXS-07 Achieved Co-Primary Endpoints:
Freedom from Pain and MBS at 2 Hours



Pain Freedom at Hour 2

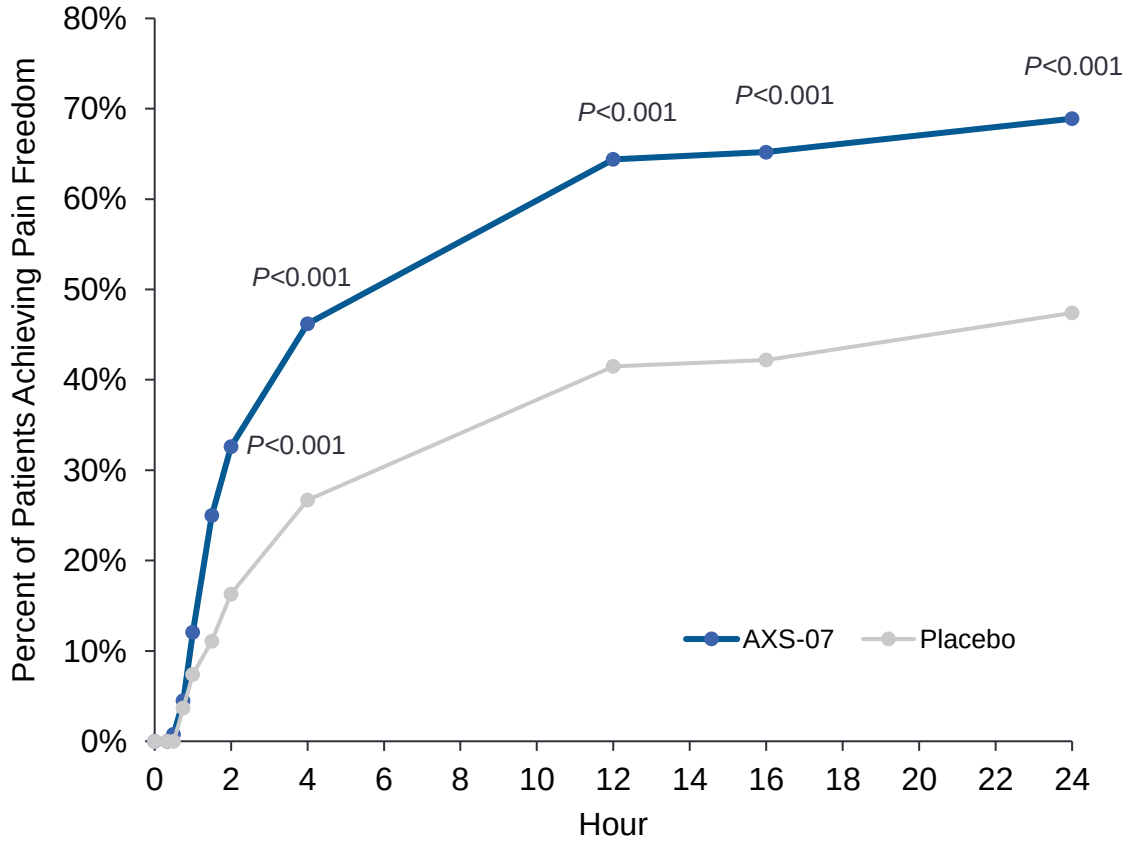


Resolution of MBS at Hour 2

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

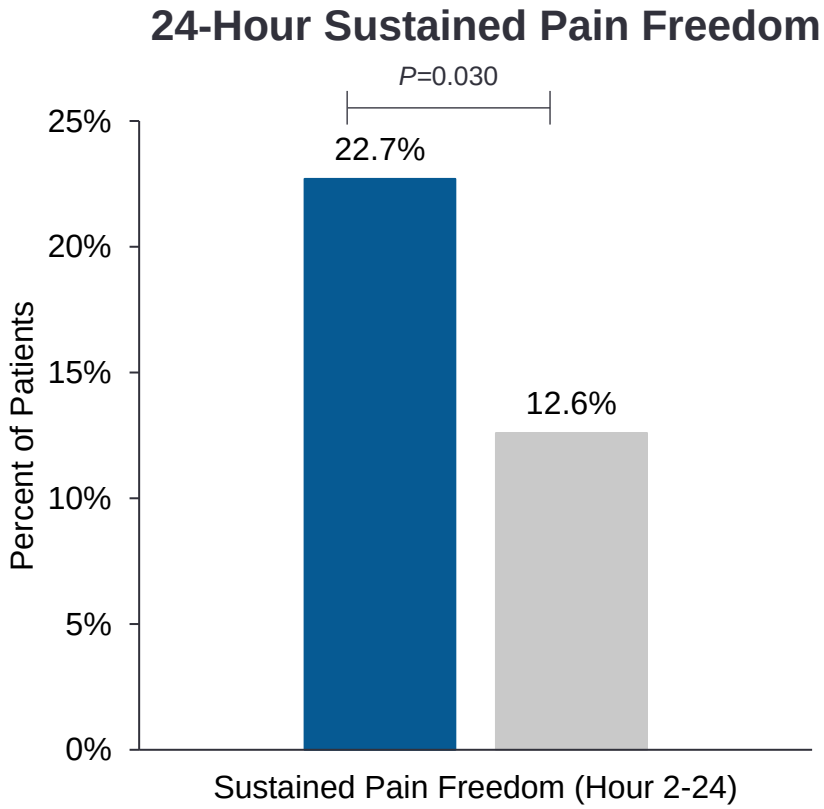
Most Bothersome Symptom = nausea, photophobia, or phonophobia

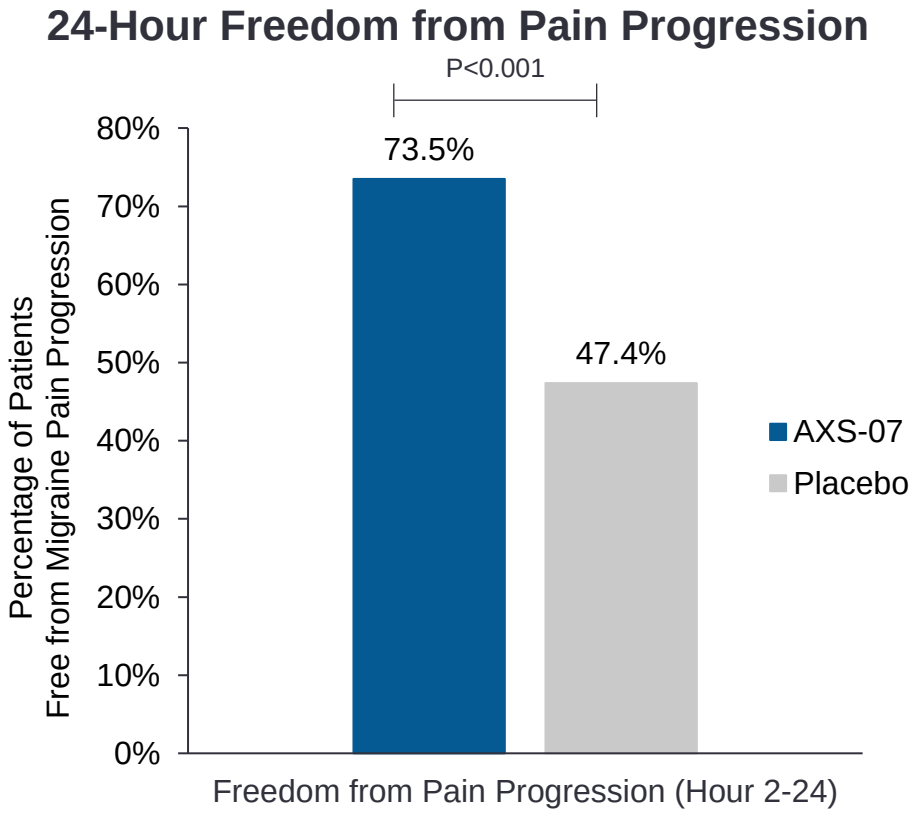
Rapid and Durable Freedom from Migraine Pain:
Migraine Pain Freedom over Time



- AXS-07 rapidly eliminated migraine symptoms, with a greater proportion of patients achieving pain freedom 30 minutes after a single dose, and statistically significant separation from placebo starting at 90 minutes (p=0.003) and at every timepoint thereafter
- 64% and 69% of AXS-07 patients were pain free at 12 and 24 hours, versus 42% and 47% of placebo, respectively

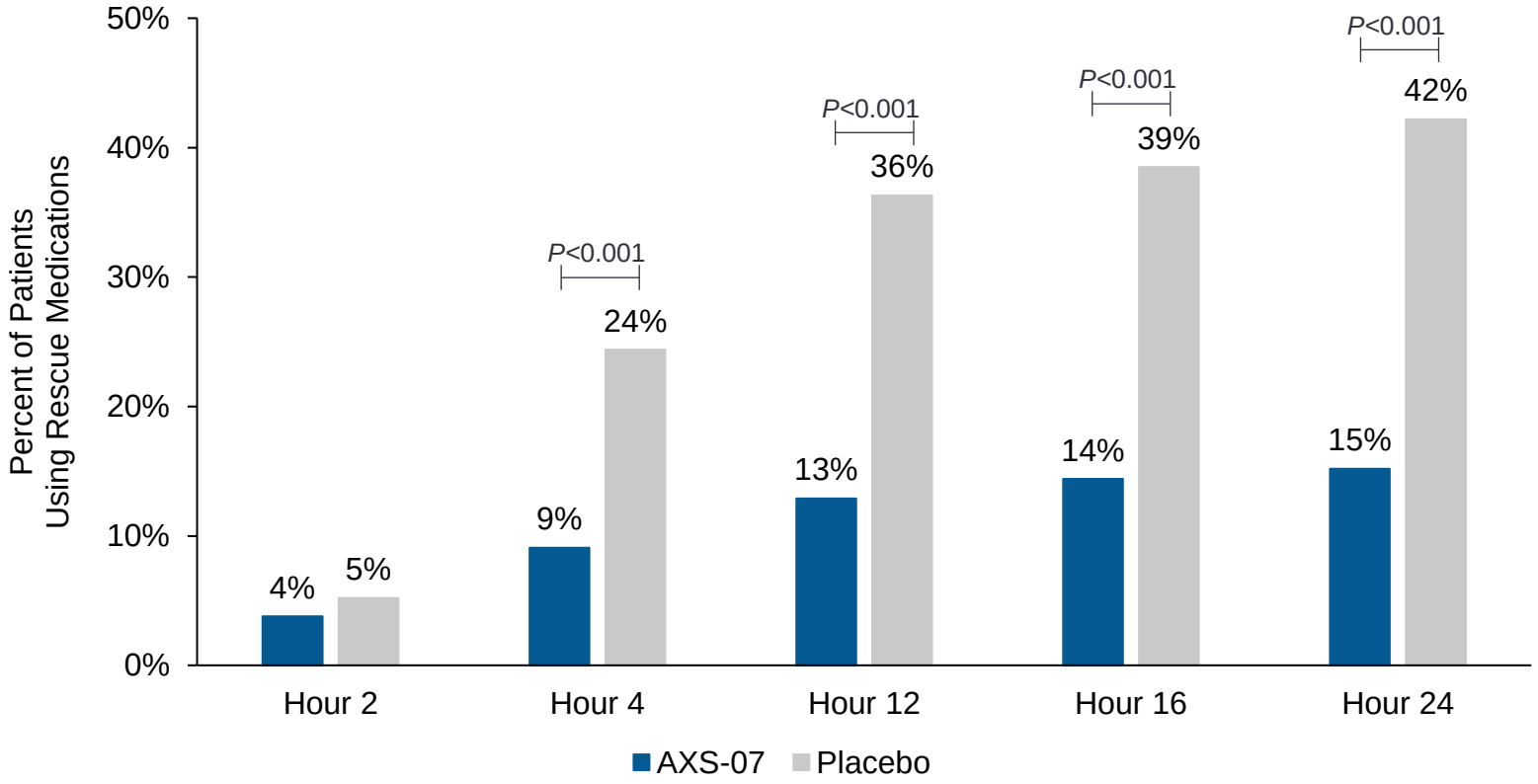
Sustained Pain Freedom and Prevention of Pain Progression





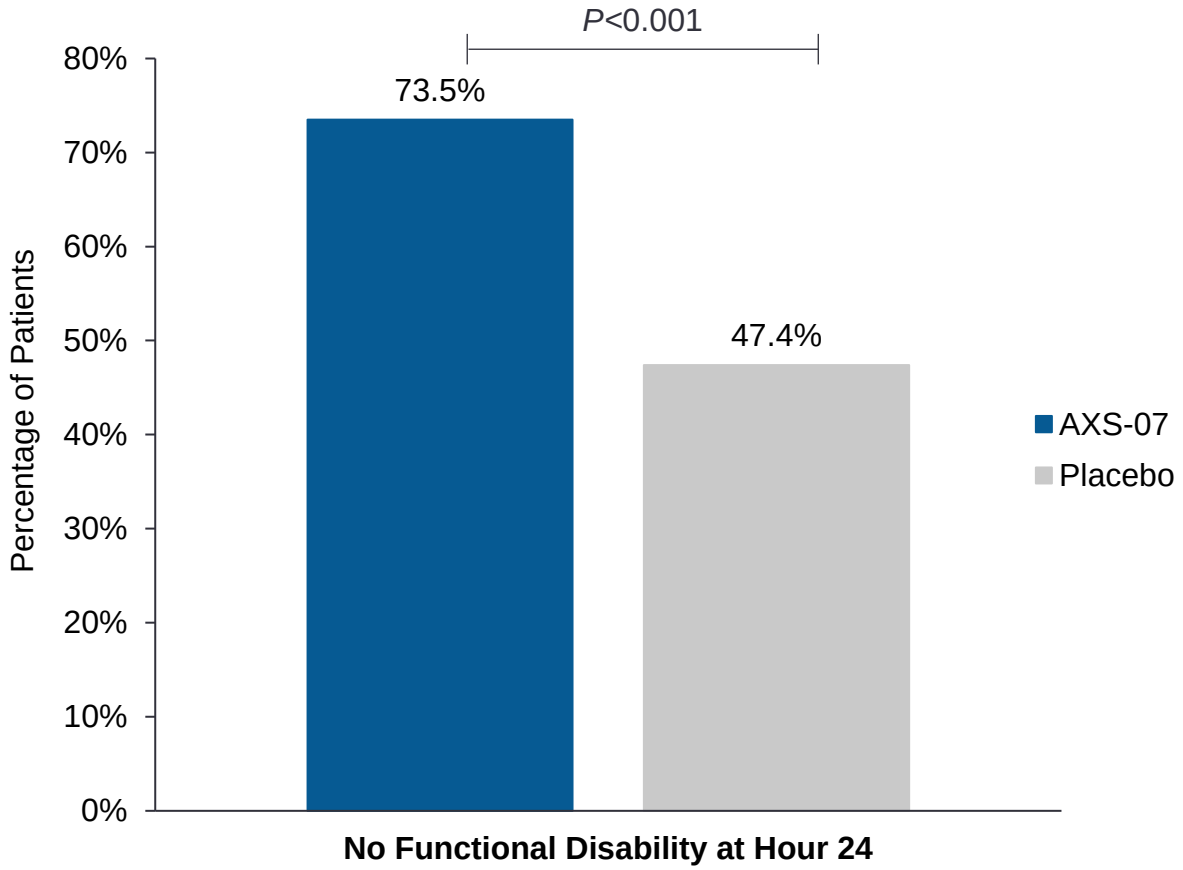
- Sustained pain freedom from 2 to 24 hours after dosing was experienced by 22.7% of patients treated with AXS-07, compared to 12.6% with placebo (p=0.030)
- AXS-07 prevented progression of migraine pain intensity beyond mild in 73.5% of patients versus 47.4% of placebo patients from 2 to 24 hours (p<0.001)

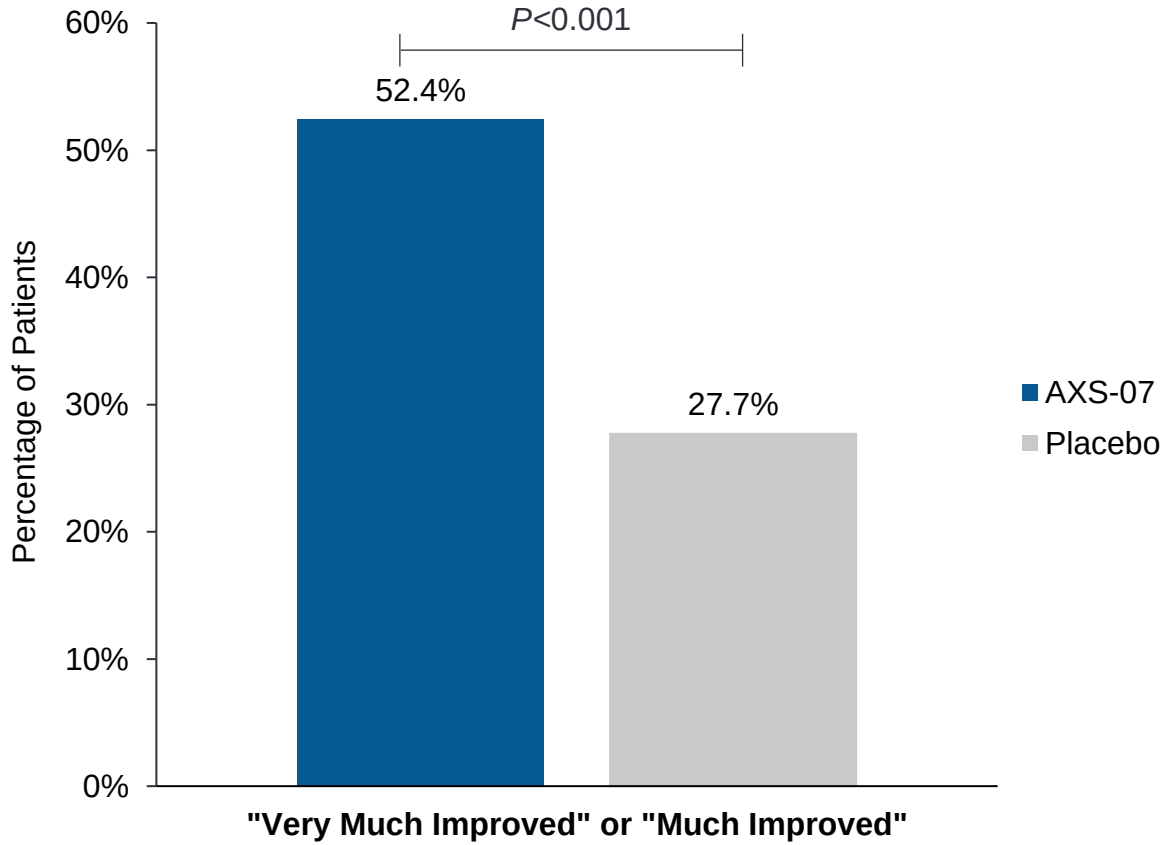
Significant Reduction in Rescue Medication Use with AXS-07



- Rescue medication was used by 15.3% of AXS-07 patients compared to 42.2% of placebo patients over 24 hours (p<0.001)

Significant Functional and Global Improvement with AXS-07





- A return to normal functioning was reported in 73.5% of AXS-07 patients, compared to 47.4% of patients receiving placebo, 24 hours after a single dose (p<0.001)
- On the Patient Global Impression of Change (PGI-C) scale, 52.4% of AXS-07 patients were very much or much improved compared to 27.7% of placebo patients at 2 hours (p<0.001)

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 serious adverse events in the trial

INTERCEPT Phase 3 Trial Results:
Summary

- AXS-07 achieved the two co-primary endpoints of pain freedom and freedom from most bothersome symptoms at 2 hours, compared to placebo
- AXS-07 resulted in rapid, substantial and sustained pain relief compared to placebo in patients who treated a single migraine attack at the earliest sign of migraine pain, while the pain was mild
- Early treatment with AXS-07 significantly prevented progression of migraine pain beyond mild in the majority of patients from 2 to 24 hours
- Efficacy benefits of AXS-07 translated into statistically significantly less rescue medication use, greater patient global response, and greater return to normal functioning after a single dose as compared to placebo
- AXS-07 was generally safe and well tolerated in this study