Treatment of Migraine Pain and Associated Symptoms with AXS-07: Results from MOVEMENT, a Long-term Efficacy and Safety Study

Amanda Jones[1], Cedric O'Gorman[1], Herriot Tabuteau[1]

[1]Axsome Therapeutics, New York, NY

22 Cortlandt Street, 16th Floor, New York, NY 10007

For more information, please contact Cedric O'Gorman at **cogorman@axsome.com**

Introduction

- **Migraine is a highly disabling neurological disorder:**
  - Characterized by recurrent attacks of pulsating head pain accompanied by nausea and sensitivity to light and sound. These symptoms are often severe and incapacitating, requiring bed rest[1]
  - The World Health Organization classifies severe migraine attacks as among the most disabling illnesses, comparable to dementia, quadriplegia, and active psychosis[2,3,4]
  - Widespread misperception of the seriousness of migraine contributes to its under-recognition and under-treatment[1]
- **Suboptimal acute treatment is associated with an increased risk of chronic migraine:** which may be prevented by improving acute treatment outcomes[5]
- **Migraine treatment guidelines encourage rapid early treatment:** failure to use an effective treatment promptly may increase pain, disability, and the impact of the headache[6]
- **Current treatments are suboptimal:**
  - More than 70% of sufferers report dissatisfaction with existing acute treatments
  - The most commonly reported reasons for patient dissatisfaction are slow onset of pain relief, inconsistent pain relief, and recurrence of pain during the same day[7,8]
- **There is an urgent need for new acute treatments:** that provide rapid, sustained, and improved efficacy for this serious neurological disease

AXS-07: A Multi-Mechanistic Approach

- **AXS-07 consists of MoSEIC™ meloxicam and rizatriptan:**
  - MoSEIC™ meloxicam is a potent, oral, rapidly absorbed, COX-2 preferential NSAID
  - Rizatriptan is a potent 5-$HT_{1B/1D}$ agonist and is considered one of the most effective and fastest-acting acute migraine therapies
- **MoSEIC™ delivery technology:** A proprietary technology which substantially increases the solubility and speed of absorption of meloxicam, after oral administration, while maintaining an extended plasma half-life
- **Multiple mechanisms of actions:** AXS-07 provides multiple mechanisms of action which combined with a favorable PK profile, may result in improved efficacy in acute migraine treatment

	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

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

References

1. Dodick DW. Migraine. Lancet. 2018;391(10127):1315–1330. **2.** Menken et al. Arch Neurol. 2000;57:418-420. **3.** Shapiro and Goodsby. Cephalalgia. 2007;27:991-4. **4.** Global Burden of Disease Study. Lancet. 2017;390:1211-1259 **5.** Lipton RB et al. Neurology. 2015;84(7):688-695. **6.** Silberstein. Neurology. 2000 Sep 26;55(6):754-62. **7.** Smelt AF et al. PLoS One. 2014;9(6):e98933. **8.** Lipton RB, Stewart WF. Headache. 1999;39(suppl 2):S20-S26.

Trial Objective

- The MOVEMENT (Multi-mechanistic Treatment over Time of Migraine Symptoms) was a Phase 3, trial to evaluate the long-term safety and efficacy of AXS-07 (20mg MoSEIC™ meloxicam-10mg rizatriptan), dosed for up to 12 months, in patients with migraine

Trial Design

- The MOVEMENT trial was a Phase 3, multi-center, open-label U.S. trial
- The study enrolled patients who had completed the previous pivotal studies of AXS-07: the MOMENTUM and INTERCEPT trials
- Enrolled patients (N=706) experienced at least 2 migraines per month, on average, and were allowed to treat up to 10 migraine attacks per month during the up to 12-month period, with one dose of AXS-07 for each migraine
- Efficacy evaluations were collected for the first 4 migraines

Efficacy Outcome Measures:

- Migraine Pain Relief
- Migraine Pain Freedom
- Freedom from MBS (most bothersome migraine-associated symptoms)
- Freedom from Rescue Medication Use over 24 and 48 hours
- Sustained Pain Relief from 2-24 and 2-48 hours
- Sustained Pain Freedom from 2-24 and 2-48 hours

Baseline Demographics and Clinical Characteristics

Characteristic	AXS-07 (N=706)
Age, mean (range)	42.0 (19-65)
Female sex, n (%)	578 (81.9%)
Race, n (%)	
White	544 (77.1%)
Black	132 (18.7%)
Asian	12 (1.7%)
Obese (BMI ≥ 30 kg/m²)	324 (45.9%)
Years since migraine diagnosis, mean (range)	18.2 (1.0-54.0)
mTOQ-4 score, n (%)	
Maximum treatment efficacy	53 (7.5%)
Moderate treatment efficacy	389 (55.1%)
Poor or very poor efficacy	264 (37.4%)

Abbreviations: BMI = body mass index; mTOQ-4=Migraine Treatment Optimization Questionnaire, 4-item

- Patients represented a difficult-to-treat population, with 37% reporting poor or very poor treatment efficacy on the mTOQ-4 and 46% being obese

Safety and Tolerability

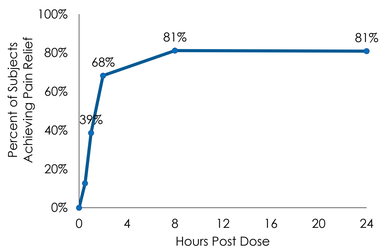
- AXS-07 was well-tolerated with long-term dosing in this study
- The safety profile of AXS-07 over the 12-month treatment period was consistent with that previously reported in short-term controlled trials
- The most commonly reported adverse events were nausea, dizziness, somnolence, and vomiting
- During the 12-month trial, 1.8% of patients discontinued due to adverse events, no event term occurring in more than one subject
- A total of 8 subjects experienced an SAE, with no event term occurring in more than one subject

Adverse Events Occurring in ≥2% of Subjects

Adverse Event	AXS-07 N (%)
Nausea	40 (5.7%)
Vomiting	33 (4.7%)
Somnolence	20 (2.8%)
Diarrhea	16 (2.3%)
Upper respiratory tract infection	14 (2.0%)

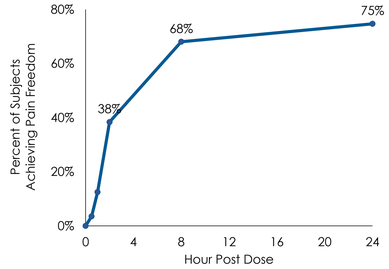
Efficacy Results

Rapid and Substantial Relief of Migraine Pain



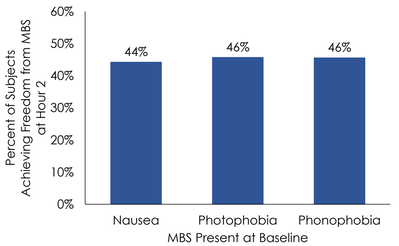
- Pain relief with AXS-07 was achieved in 39% of treated migraines at 1 hour, 68% at 2 hours and over 80% through 24 and 48 hours

Rapid and Substantial Freedom from Migraine Pain



- Pain freedom with AXS-07 was achieved in 38% of treated migraines at 2 hours and over 75% through 24 and 48 hours

Freedom from Most Bothersome Migraine-associated Symptoms

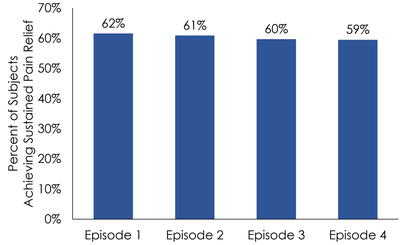


- Overall 47% of treated migraines resulted in freedom from most bothersome symptom (photophobia, phonophobia, or nausea) within 2 hours after dosing

Prevention of Pain Relapse and Freedom from Rescue Medication Use

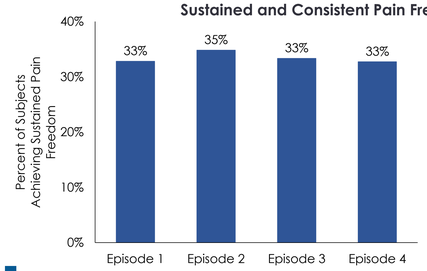
	AXS-07
Prevention of Pain Relapse, % of treated episodes	83.9%
Freedom from use of rescue medication through Hour 24, % of treated episodes	84.8%

Sustained and Consistent Pain Relief



- Rates of sustained pain relief from 2 to 24 hours and 2 to 48 hours were high (approx. 60%) and consistent across migraine attacks

Sustained and Consistent Pain Freedom



- Rates of sustained pain freedom from 2 to 24 hours and 2 to 48 hours were high (32-35%) and consistent across migraine attacks

Conclusions

- **Treatment with AXS-07, rapidly, substantially, and durably relieved migraine pain and associated symptoms**
- **The efficacy of AXS-07 was high and consistent across sequential migraine attacks**
- **AXS-07 was well tolerated with long-term episodic treatment over 1 year, with a safety profile consistent with that observed in previously reported controlled trials**
- **These long-term data are consistent with the rapid and substantial efficacy of AXS-07 observed in controlled trials**
- **AXS-07, as a multi-mechanistic treatment for the acute treatment of migraine, may help address the current unmet need for more efficacious treatments**

Disclosures: AJ, COG and HT are employees of Axsome Therapeutics.