

Efficacy and Safety of Symbravo[®] (MoSEIC[™] Meloxicam/Rizatriptan), a Novel Acute Migraine Treatment: Data from 3 Clinical Trials

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Key Objective

- Evaluate the efficacy and safety of SYMBRAVO for the acute treatment of episodic migraine compared to placebo and active controls in two single-attack Phase 3 trials (MOMENTUM, INTERCEPT)
- Evaluate the long-term safety and efficacy of SYMBRAVO in an open-label, long-term up to 12-months trial (MOVEMENT)

Introduction

- Migraine is a highly disabling, typically episodic neurological disorder with characteristic symptoms of pulsating head pain, nausea, and sensitivity to light and sound that can be severe and incapacitating¹
- Existing acute migraine treatments are often limited by inconsistent pain relief, slow onset, and high symptom recurrence within 24 hours, resulting in patient dissatisfaction²⁻⁴
- Suboptimal treatment is associated with increased risk of progression from episodic to chronic migraine⁵
- SYMBRAVO is a novel fixed-dose combination of MoSEIC[™] meloxicam (a COX-1/COX-2 inhibitor NSAID) and rizatriptan, a serotonin 5-HT_{1B/1D} receptor agonist (triptan), approved by the US Food and Drug Administration for the acute treatment of migraine with or without aura in adults⁶
- Three clinical trials, INTERCEPT, MOMENTUM, and MOVEMENT, evaluated the short-term (INTERCEPT and MOMENTUM) and long-term (MOVEMENT) efficacy and safety of SYMBRAVO, an FDA-approved, multi-mechanistic medication indicated for the acute treatment of migraine with or without aura in adults⁷⁻⁸

References

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Acknowledgments

Axsome Therapeutics funded and conducted the reported trials. The authors would like to express their appreciation to the trial participants and their families as well as the investigators and site personnel.

QR Code

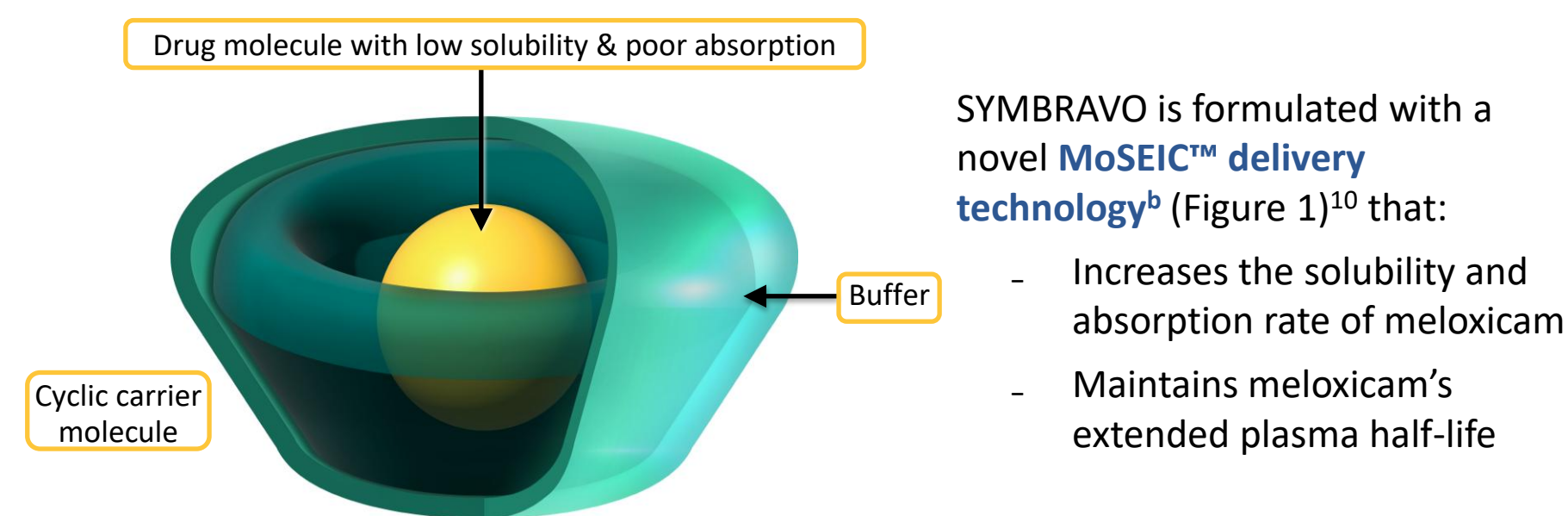
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SYMBRAVO Mechanism of Action

- The combination of MoSEIC[™] meloxicam and rizatriptan is thought to provide a multi-mechanistic approach to acute migraine treatment by targeting multiple pathophysiological pathways^a:
 - Meloxicam: **reduces inflammation** both peripherally and centrally by inhibiting cyclooxygenase and PGE₂ synthesis; reverses **central sensitization**⁹
 - Rizatriptan: reduces transmission of **pain signals** by inhibiting release of CGRP through activation 5-HT_{1B/1D} receptors in the dura⁹
 - SYMBRAVO was purposefully designed to address the inherent limitations of the individual components

Figure 1. Novel MoSEIC[™] Technology



^aThe exact mechanism of action of SYMBRAVO is not completely understood. ^bThe clinical significance of the MoSEIC[™] formulation is not known. MoSEIC, Molecular Solubility Enhanced Inclusion Complex; PGE₂, prostaglandin E₂.

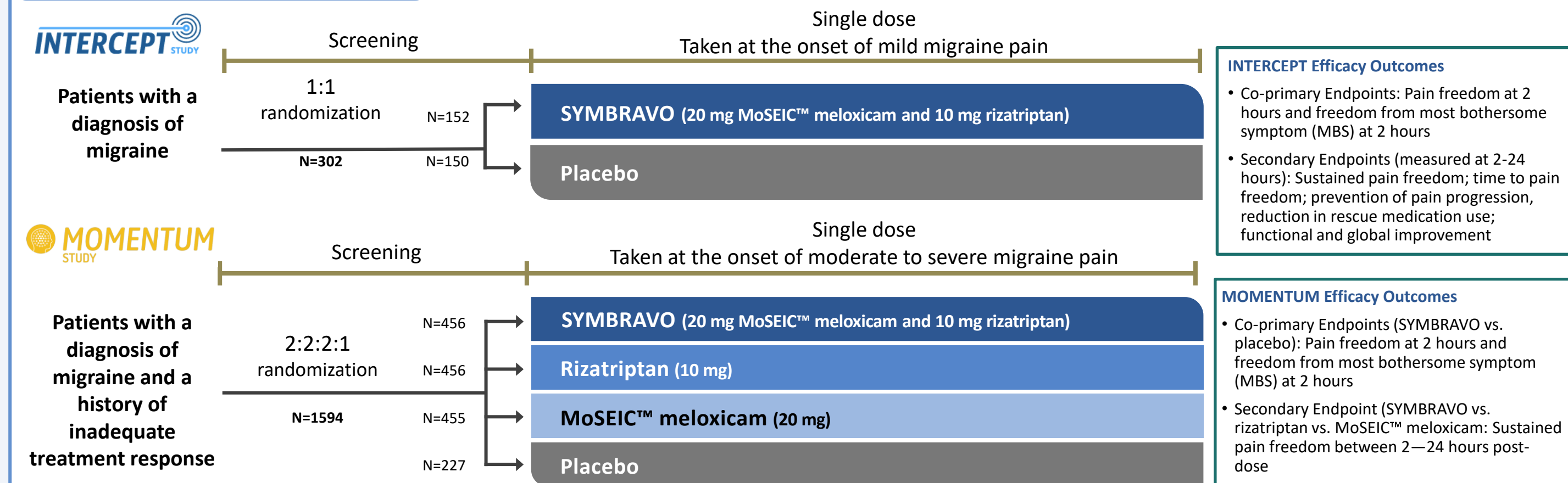
SYMBRAVO is formulated with a novel **MoSEIC[™] delivery technology^b** (Figure 1)¹⁰ that:

- Increases the solubility and absorption rate of meloxicam
- Maintains meloxicam’s extended plasma half-life

Methods

- The **INTERCEPT** and **MOMENTUM** trials were Phase 3, randomized, double-blind trials that assessed the efficacy and safety of SYMBRAVO vs placebo for the treatment of moderate to severe migraine attacks. MOMENTUM also compared the efficacy and safety to SYMBRAVO to the active controls of meloxicam and rizatriptan

Figure 1. Trial Designs



- The **MOVEMENT** trial was a Phase 3, multicenter, single arm, open-label trial that assessed the long-term safety and efficacy of SYMBRAVO dosed up to 12 months in patients who had completed the MOMENTUM or INTERCEPT trials (N = 706)⁷
 - Safety was evaluated for up to 10 migraine attacks/month, with each patient taking one dose of SYMBRAVO at the onset of a migraine regardless of severity. Efficacy outcomes, including pain relief and pain freedom at 2-24 hours, were evaluated for the first 4 migraine attacks
 - Primary endpoint: long-term safety of chronic intermittent use of SYMBRAVO, as measured by the incidence of treatment-emergent adverse events

Results

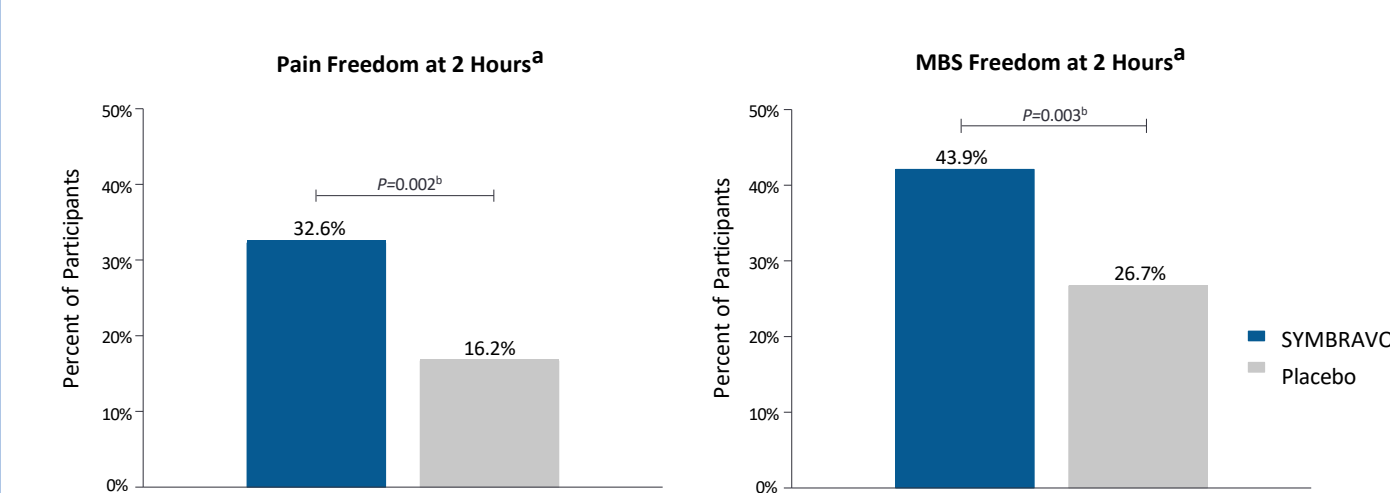
Table 2. Baseline Characteristics^a

Characteristics	INTERCEPT		MOMENTUM			MOVEMENT	
	SYMBRAVO (n = 140)	Placebo (n = 143)	SYMBRAVO (n = 428)	Rizatriptan (n = 419)	MoSEIC [™] Mix (n = 421)	Placebo (n = 209)	SYMBRAVO (n = 706)
Age, mean (SD)	41.7 (11.58)	41.4 (10.67)	41.1 (11.64)	41.5 (10.72)	41.0 (12.13)	41.0 (11.71)	42.0 (10.94)
Female gender, n (%)	119 (85.0)	122 (85.3)	357 (81.0)	366 (84.3)	363 (83.8)	185 (84.9)	580 (82.2)
Race, n (%)							
White	118 (84.3)	116 (81.1)	345 (78.2)	332 (76.5)	330 (76.2)	160 (73.4)	544 (77.1)
Black or African American	18 (12.9)	17 (11.9)	76 (17.2)	84 (19.4)	88 (20.3)	48 (22.0)	132 (18.7)
Other ^b	4 (2.8)	10 (7.0)	20 (4.5)	18 (4.3)	15 (3.4)	10 (4.5)	30 (4.3)

- Patients in the MOMENTUM trial had a history of inadequate response to prior acute treatments, with an average mTOQ-4 total score ranging from 3.5-3.8 (“poor treatment efficacy”) across all 4 treatment arms; In the MOMENTUM trial, 37% of patients reported poor or very poor treatment efficacy

^aBaseline characteristic analyses were based on the safety population, defined as all subjects who received study drug. ^bIn the INTERCEPT trial, the “Other” race category includes American Indian or Alaska Native, Asian, or Multiple races. In the MOVEMENT and MOMENTUM trials, the “Other” race category includes American Indian or Alaska Native, Asian, Multiple, and Other races as well as Not Reported in the former. Mix, Meloxicam; mTOQ-4, Migraine Treatment Optimization Questionnaire, 4-item.

Figure 2. INTERCEPT Efficacy Co-Primary Endpoints



- The percentage of participants achieving headache pain freedom and freedom from MBS at 2 hours post-dose was statistically significantly greater for SYMBRAVO compared to placebo
 - Secondary endpoints, including sustained pain freedom, freedom from pain progression, avoidance of rescue medication use, and return to normal functioning were also met.

^aEfficacy analyses were based on the ITT population which included all subjects randomized who had a qualifying migraine episode with a mild pain intensity (1 on a 4-point scale). ^bP-values were based on Chi-square test. ITT, intent-to-treat; MBS, most bothersome symptom (nausea, photophobia, or phonophobia).

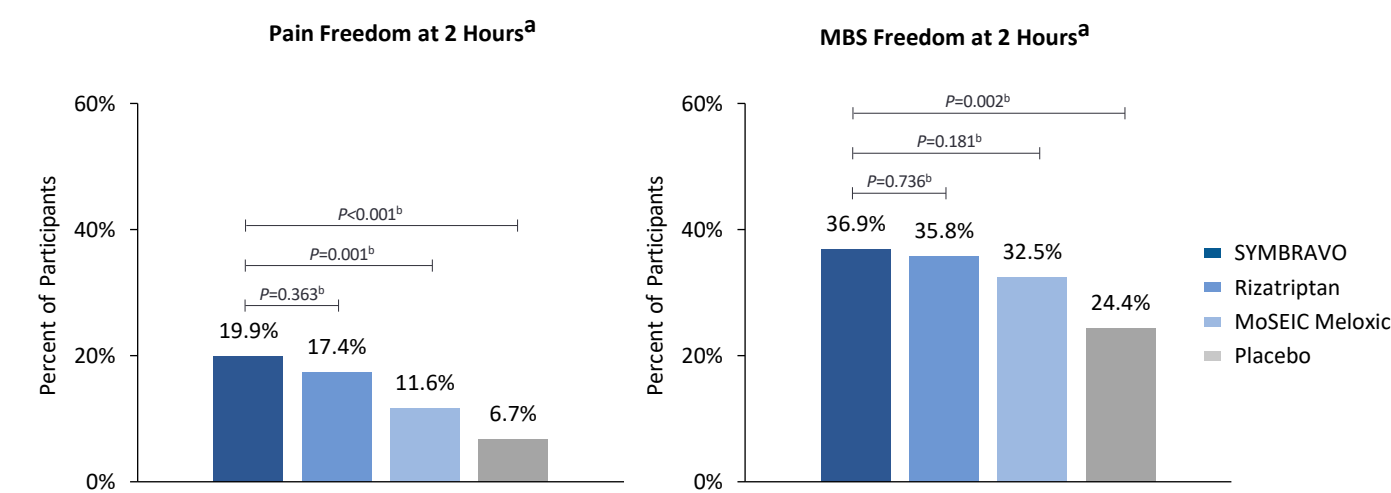
Table 3. Safety

	INTERCEPT ^a			MOMENTUM			MOVEMENT ^b
	SYMBRAVO (n = 140)	Placebo (n = 143)	SYMBRAVO (n = 441)	Rizatriptan (n = 434)	MoSEIC™ Mix (n = 433)	Placebo (n = 218)	SYMBRAVO (n = 706)
Any TEAE, n (%)	25 (17.9)	11 (7.7)	49 (11.1)	67 (15.4)	50 (11.5)	13 (6.0)	293 (41.5)
Somnolence	6 (4.3)	3 (2.1)	6 (1.4)	9 (2.1)	10 (2.3)	1 (0.5)	20 (2.8)
Dizziness	4 (2.9)	2 (1.4)	7 (1.6)	9 (2.1)	5 (1.2)	2 (0.9)	22 (3.1)
Nausea	2 (1.4)	1 (0.7)	12 (2.7)	21 (4.8)	14 (3.2)	8 (3.7)	40 (5.7)

- SYMBRAVO was generally safe and well-tolerated over the short- and long-term dosing periods. The most common reported adverse events across trials included somnolence, dizziness, and nausea.

^aAdverse events occurring in ≥1% of subjects are presented. For the MOMENTUM and MOVEMENT trials, Adverse events occurring in ≥2% of subjects are presented. ^bSafety data are presented for multiple exposures; For the INTERCEPT and MOMENTUM trials, safety data is presented for a single attack. Mix, Meloxicam; TEAE, treatment-emergent adverse event.

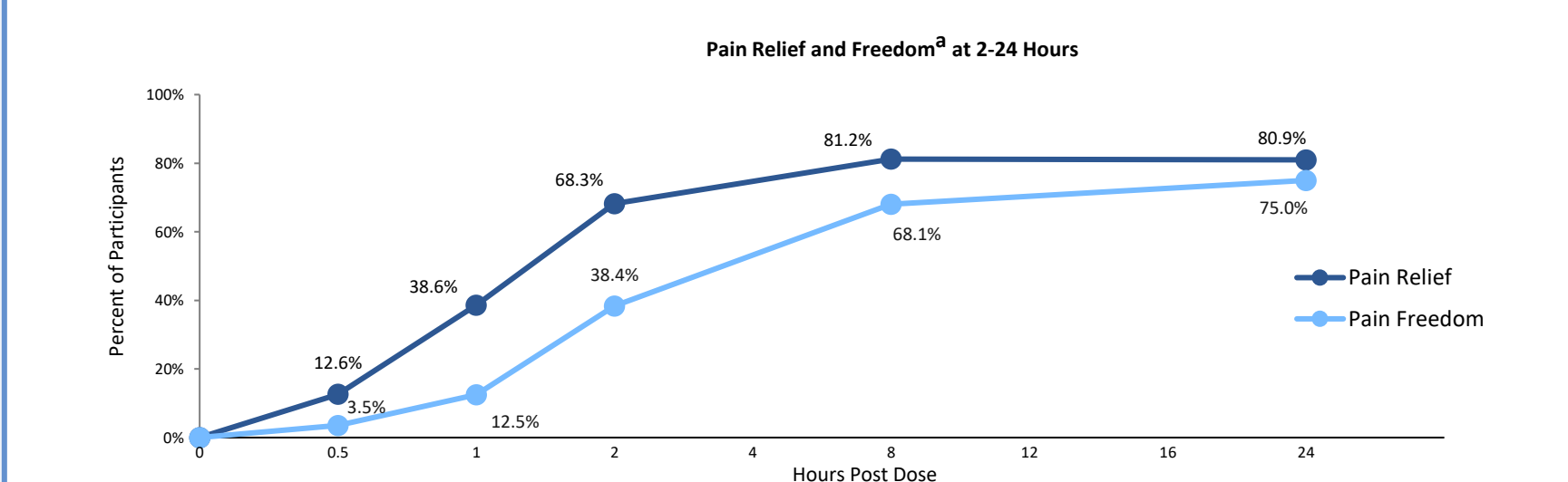
Figure 3. MOMENTUM Efficacy Co-Primary Endpoints



- The percentage of participants achieving headache pain freedom and freedom from MBS at 2 hours post-dose was statistically significantly greater for SYMBRAVO compared to placebo
 - The secondary endpoint was also met as a statistically significant greater percentage of participants achieved 24-hour sustained pain freedom with SYMBRAVO compared to rizatriptan and MoSEIC[™] meloxicam

^aEfficacy analyses were based on the ITT population which included all subjects randomized who had a qualifying migraine episode with a mild pain intensity (1 on a 4-point scale). ^bP-values were based on Chi-square test. ITT, intent-to-treat; MBS, most bothersome symptom (nausea, photophobia, or phonophobia).

Figure 4. MOVEMENT Open-Label Effectiveness



- Treatment with SYMBRAVO resulted in migraine pain relief and freedom in a high proportion of treated episodes. These effects were sustained through 48 hours post-dose.

^aPain relief is defined as experiencing a moderate (2) or severe (3) headache at baseline which became mild (1) or none (0), or a mild (1) headache at baseline which became none (0), and without taking rescue medication. Pain freedom was defined as reported pain intensity of none (0) and without taking rescue medication. N = 2734 migraine episodes.

Table 1. Key Eligibility Criteria^a

Inclusion	Exclusion
• Male or female, 18 to 65 years of age inclusive	• Cluster headaches or other types of migraine
• Established diagnosis of migraine (at least 1 year) with or without aura as defined by ICHD-3 criteria	• Chronic daily headache (≥15 non-migraine headache days per month)
• Average of 2-8 migraines per month	• >8 migraine attacks per month per month during 2 months prior to screening
• MOMENTUM trial additional criteria: mTOQ-4 score ≤7 out of 8 (8=maximum treatment efficacy) with prior acute treatment for migraine ⁹	• Cardiovascular disease/uncontrolled hypertension
	• History of neurological condition associated with headache

^aFor all three trials. ICHD-3, International Classification of Headache Disorders-3; mTOQ-4, Migraine Treatment Optimization Questionnaire, 4-item

Conclusions

- SYMBRAVO, a novel, oral, fixed-dose combination of MoSEIC[™] meloxicam and rizatriptan approved for the acute treatment of migraine in adults, was evaluated in three clinical trials
 - In the INTERCEPT and MOMENTUM trials, SYMBRAVO was associated with a statistically significantly greater percentage of participants experiencing freedom from pain and MBS at 2 hours post-dose compared to placebo and its individual components
 - Across the first 4 attacks, rapid and substantial pain freedom was also observed 2 to 48 hours post-dose (MOVEMENT)
- SYMBRAVO was safe and well-tolerated across all trials, and its safety profile over a 12-month treatment period was consistent with that reported in short-term trials
- These results provide evidence for the efficacy and safety of SYMBRAVO in the treatment of acute migraine in adults