AXS-07 (MoSEIC™ Meloxicam/Rizatriptan): Novel Oral Therapeutic in Clinical Development for the Acute Treatment of Migraine

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Introduction

Migraine is a disabling neurological disorder characterized by recurrent attacks of pulsating head pain accompanied by nausea and sensitivity to light and sound. These symptoms are often so severe and incapacitating, requiring bed rest.

Current treatments are suboptimal, with more than 70% of sufferers reporting dissatisfaction with existing acute treatments. The most commonly reported reasons for dissatisfaction are slow onset of pain relief, inconsistent pain relief, and recurrence of pain during the same day.1,2

Suboptimal acute treatment is associated with a significantly increased risk of new-onset chronic migraine, which may be prevented by improving acute treatment outcomes.3

AXS-07 is a novel, oral, investigational medicine, with distinct dual mechanisms of action, under development for the acute treatment of migraine. AXS-07 consists of MoSEIC™ meloxicam and rizatriptan. Meloxicam is a potent, COX-2 preferential NSAID which is limited by slow absorption, and rizatriptan is a potent 5-HT1c agonist with known efficacy in migraine.

AXS-07 utilizes proprietary MoSEIC™ (Molecular Solubility Enhanced Inclusion Complex) delivery technology (Figure 1) to substantially increase the solubility and speed of absorption of meloxicam after oral administration, while maintaining its extended plasma half-life.

Phase 1 Results

MoSEIC™ meloxicam was rapidly absorbed after oral administration of AXS-07 (20 mg MoSEIC™ meloxicam/10 mg rizatriptan), with a time to peak concentration (Tmax) of 1.98 hours compared to 71.81 minutes for the rizatriptan component of AXS-07, which compares to 21.5 hours for standard meloxicam.

Rizatriptan was rapidly absorbed after oral administration of AXS-07 (20 mg MoSEIC™ meloxicam/10 mg rizatriptan), with a time to peak concentration (Tmax) of 0.50 hours compared to 4.5 hours for 15 mg standard meloxicam (Mobic®).

Mean plasma elimination half-life (T1/2) for MoSEIC™ meloxicam was 18.2 hours after administration of AXS-07, which compares to 2.5 hours for standard meloxicam.

Figure 2: Mean Meloxicam Concentrations over Time for AXS-07 versus Standard Meloxicam®

Table 1: Meloxicam Pharmacokinetic Parameters for AXS-07

<table>
<thead>
<tr>
<th>AXS-07</th>
<th>Standard Meloxicam®</th>
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</thead>
<tbody>
<tr>
<td>Tmax (hr)</td>
<td>0.50</td>
</tr>
<tr>
<td>T1/2 (hr)</td>
<td>18.2</td>
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<tr>
<td>Maximal concentration (ng/mL)</td>
<td>46,865</td>
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</tbody>
</table>

Conclusions

AXS-07 was rapidly absorbed, resulting in therapeutic plasma concentrations of MoSEIC™ meloxicam in 17 minutes and maximum concentrations of rizatriptan in 38 minutes after oral administration, suggesting the potential for rapid onset of action with AXS-07.

The long elimination half-life of MoSEIC™ meloxicam (18.2 hours) after oral administration of AXS-07 suggests the potential for AXS-07 to reduce migraine pain recurrence.

The MOMENTUM Phase 3 trial of AXS-07 is enrolling only patients with a history of inadequate response to prior acute migraine treatments, assessed using the Migraine Treatment Optimization Questionnaire (mTOQ-4). The mTOQ-4 is a validated questionnaire that assesses efficacy response to prior acute treatments based on four aspects (two-hour pain freedom, efficacy for at least 24 hours with one dose, ability to plan activities, and disruption of daily activities).1

The majority of patients randomized to date in the MOMENTUM trial also report alldynia with their migraine attacks. Alldynia, which is pain from normally non-painful stimuli (such as brushing hair, wearing glasses, taking a shower, etc.), has been shown to be strongly associated with worse outcomes for pain freedom and pain relief after treatment with triptan medications.2,3

Disclosures: COGS, A, KJ, MJ & HT are employees of Axsome Therapeutics.