Efficacy and Safety from a Phase 2b Trial of Lorecivivint (LOR; SM04690), a Novel Intra-articular Wnt Pathway Inhibitor for the Treatment of Osteoarthritis of the Knee

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Background

- Lorecivivint (LOR, SM04690) is an intra-articular (IA), small-molecule CLK/DYRK1A inhibitor that modulates the Wnt pathway. LOR is in development as a potential disease-modifying knee OA drug.

- Preclinical studies demonstrated LOR inhibited inflammation and cartilage degradation compared to vehicle1.

- A Phase 2a study demonstrated that LOR was well tolerated and had positive effects on Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain, WOMAC Function, and medial joint space width (mJSW) at 52 weeks in key subgroups of LOR compared to placebo (PBO)2.

- A 24-week Phase 2b study was performed to refine target population and dose as well as to evaluate patient-reported outcomes (PROs) and safety.

Results

- Subjects with ACR-defined knee OA, Kellgren-Lawrence (KL) grades 2-3, and Pain Numeric Rating Scale (NRS) ≥4 and ≤8 in the target knee and ≤4 in the contralateral knee were given single, 2 mL IA LOR injection (0.03, 0.07, 0.15, 0.23 mg) or vehicle (PBO) injection in the target knee.

- Subjects were stratified 50% unilateral symptomatic; 50% bilateral symptomatic: 80% Widespread Pain Index (WPI) ≤4, Symptom Severity Score (SSS) ≤2; 20% WPI >4 or SSS >2.

- PRO endpoints included change from baseline in weekly average daily target knee Pain and Function (WOMAC) Pain, WOMAC Function, and medial joint space width (mJSW).

- Sample size was based upon accepted dose.


- Safety assessments: AEs, vital signs, physical exam, laboratory panels

- LOR Phase 2b study design

Figure 1. Comparisons of LOR vs. PBO using a baseline-adjusted ANCOVA, presented at 4-week intervals (FAS). Data on X-axis offset for visual clarity.

- LOR showed statistically significant improvements in two dose groups for pain and function compared to PBO – 0.07 mg and 0.23 mg doses met Pain NRS primary endpoint.

- LOR appeared well tolerated.

- Improvements in pain and function suggested that LOR has a potential disease-modifying role in the treatment of knee OA.

- Phase 3 studies of LOR as a potential disease-modifying OA drug are ongoing.

Methods

- Subjects with ACR-defined knee OA, Kellgren-Lawrence (KL) grades 2-3, and Pain Numeric Rating Scale (NRS) ≥4 and ≤8 in the target knee and ≤4 in the contralateral knee were given single, 2 mL IA LOR injection (0.03, 0.07, 0.15, 0.23 mg) or vehicle (PBO) injection in the target knee.

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Conclusions

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References


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