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

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Poster #6

Background

Lorecivivint (SM04690) is an intra-articular (IA), small-molecule Wnt pathway inhibitor in development as a potential disease-modifying knee osteoarthritis (OA) drug (DMOAD)

- Preclinical studies demonstrated inhibition of inflammation and cartilage degradation compared to vehicle1
- A previous phase 2a study of lorecivivint demonstrated positive effects on knee OA pain, physical function, and medial joint space width (mJSW) at 52 weeks in key subgroups compared to placebo (PBO)1
- A 24-week phase 2b study was performed to refine patient-reported outcome (PRO) measures, target population, dose, and to evaluate safety; PRO results are presented

Conclusions

- In this phase 2b trial, lorecivivint showed statistically significant improvements from baseline in pain and function compared to PBO
  - All doses appeared safe and well tolerated
  - 0.07 mg and 0.23 mg are potentially efficacious doses
  - Further analyses of subject characteristics may refine target population
- The improvements seen in pain and function suggested that lorecivivint has a potential role in the treatment of signs and symptoms of knee OA
- Lorecivivint is undergoing further investigation as a potential DMOAD with long-term studies evaluating structure and morphology
- Pivotal studies are planned

Results and Discussion

Figure 1. PROs: Change from baseline compared to PBO over time

- 695 subjects (mean age 59.0 [±8.5] years, BMI 29.0 [±4.0] kg/m², female 58.4%, KL3 57.3%) were enrolled and dosed; 635 subjects (91.4%) completed the study
- Positive responses were seen in 0.03, 0.07, and 0.23 mg dose groups compared to PBO, with statistical significance achieved in 0.07 mg at most and 0.23 mg groups at all time points (Fig 1)
- The 0.15 mg group showed positive responses compared to baseline, similar in magnitude to PBO
- No differences in change from baseline in mJSW beyond measurement error or between PBO and treatment groups were seen
- Lorecivivint appeared safe and well tolerated. Arthralgia was the most common adverse event (AE). All AE rates were comparable between treatment and control groups. Six serious AEs were reported in 6 patients, all deemed unrelated by study physician

Methods

- Subjects had ACR-defined knee OA, Kellgren-Lawrence (KL) grades 2-3, and Pain Numeric Rating Scale (NRS) ≥4 and ≥6 in target knee and ≤4 in contralateral knee. A single IA injection of 2 mL lorecivivint (0.03, 0.07, 0.15, or 0.23 mg) or vehicle PBO was given in the target knee at baseline
- Subjects were stratified by presence of bilateral knee OA (50% bilateral, 50% unilateral) and Widespread Pain Index (WPI) & Symptom Severity (SS) Score (80% WPI ≤4 and SS ≤2, 20% WPI >4 and/or SS >2)
- PRO endpoints included change from baseline in weekly average of daily OA target knee pain by Numeric Rating Scale diary (NRS, [0-10]), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain [0-100], WOMAC Function [0-100], and Patient Global Assessment (PtGA) (VAS, [0-100])
- Radiographic endpoint of change from baseline in mJSW was measured at Week 24
- The sample size for this study was based upon accepted dose finding statistical practice2

References