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Results from a Phase 2b Trial of SM04690, a Novel Intra-articular Wnt Pathway Inhibitor for the Treatment of Knee Osteoarthritis

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Objective: A phase 2a study of SM04690 demonstrated improvements in knee pain, physical function, and medial joint space width (mJSW) at 52 weeks in key subgroups of subjects with knee osteoarthritis (OA) compared to placebo (PBO).¹ A 24-week phase 2b study was conducted to refine patient-reported outcomes (PROs), target population, dose, and to assess safety. PRO results (Weeks 12 and 24) are presented.

Materials and Methods: Subjects with knee OA, Kellgren-Lawrence (KL) grades 2-3, and Pain Numeric Rating Scale (NRS) ≥ 4 and ≤ 8 in the target knee (< 4 in non-target knee) were given a single, 2 mL, IA injection of SM04690 (0.03, 0.07, 0.15, or 0.23 mg), vehicle PBO, or sham (dry needle only) on Day 0. PROs included change from baseline in weekly average of daily pain in target knee (NRS) [0-10], Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain [0-100], WOMAC Function [0-100], and Patient Global Assessment (PtGA) [0-100].

Results: 635 subjects (91.4%) completed the study. No safety signals were observed.

Significant improvements from baseline compared to PBO were observed in Pain NRS for 0.07 mg and 0.23 mg groups at Weeks 12 and 24 (**Figure**). Similar improvements were observed in WOMAC Pain, WOMAC Function, and PtGA for 0.07 mg (Week 12) and 0.23 mg (Weeks 12 and 24) dose groups.

Conclusion: SM04690, in development as a potential disease-modifying OA drug, showed in this phase 2b study statistically significant improvements from baseline compared to PBO for PROs in pain, function, and PtGA. Phase 3 studies are planned.

Reference: 1. Yazici Y, et al. *Arthritis Rheum.* 2017.

Disclosures: All authors are employees or consultants of Samumed, LLC

Figure. Actual observations over time and ladder plots depicting mean improvement (\pm 95% CI) of SM04690 compared to baseline-adjusted PBO for Pain NRS

