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Results from a 52-week, phase 2a study of an intra-articular, small molecule Wnt pathway inhibitor, SM04690, for knee osteoarthritis

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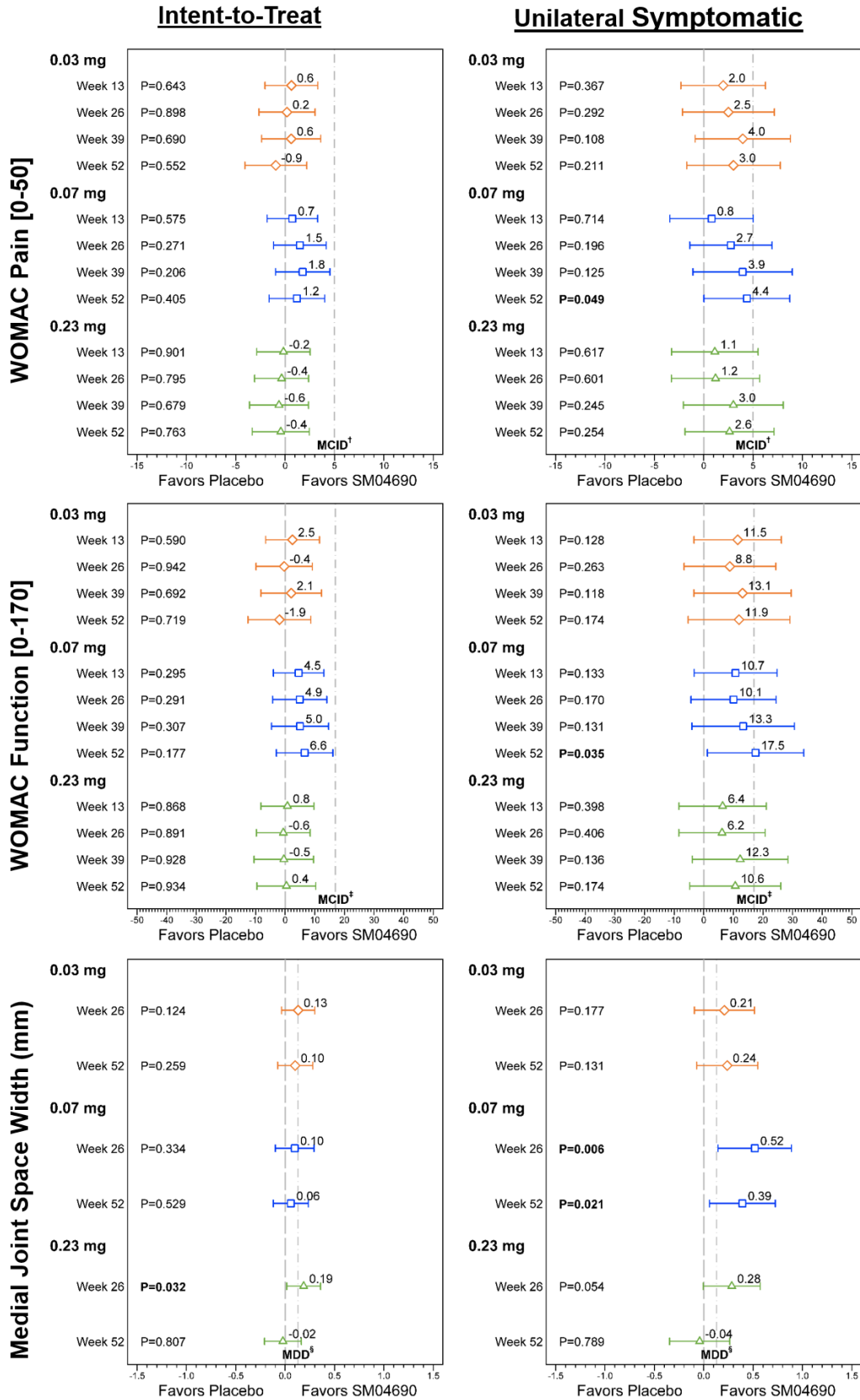
Background: Wnt signaling is upregulated in osteoarthritis (OA) and involved in cartilage degradation. SM04690 is a Wnt pathway inhibitor in development as a potential disease-modifying knee OA drug. A phase 2a study was conducted to identify target population and dose. Primary endpoint was change from baseline in WOMAC Pain at Week 13. Key secondary endpoints included change from baseline in WOMAC Pain, Function and radiographic knee medial joint space width (mJSW) at Week 52.

Methods: Kellgren-Lawrence (KL) grades 2-3 knee OA subjects received a single 2 mL injection of SM04690 (0.03 mg, 0.07 mg, 0.23 mg) or saline (placebo; PBO) in target (most painful) knee. WOMAC Pain and Function subscores were measured (Weeks 0, 4, 13, 26, 39, 52) and knee radiographs (PA, weight-bearing, positioned) taken (Weeks 0, 26, 52). Analysis of covariance adjusted for baseline with multiple imputation in the ITT population and a pre-specified subgroup analysis of subjects with unilateral symptoms (UNI) were performed.

Results: 455 subjects (KL 3 [64.4%], UNI [36.0%]) were enrolled. SM04690 appeared safe and well-tolerated. In ITT, clinically important differences from baseline were seen in all WOMAC subscores at all timepoints, but differences were not significant compared with PBO. In UNI (n=164), 0.07 mg SM04690 showed significant improvements in WOMAC Pain ($P=0.049$), WOMAC Function ($P=0.035$) and mJSW ($P=0.021$) at Week 52 compared with PBO (Figure).

Conclusion: Further investigation of 0.07 mg SM04690 in the unilateral symptomatic population is warranted based upon Week 52 improvements in WOMAC Pain and Function and mJSW compared with PBO.

Improvement of SM04690 over Placebo



†Minimal clinically important difference (MCID) defined as 10% of WOMAC Pain scale, or 5 points. ‡MCID defined as 10% of WOMAC Function scale, or 17 points. §Minimum detectable difference (MDD) defined as 0.13 mm of mJSW.