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PRESS RELEASE

Samumed Presented Multiple Abstracts Supporting Potential Disease Modification at the Osteoarthritis Research Society International (OARSI) 2018 World Congress

SAN DIEGO – May 07, 2018 – Samumed, LLC, a leader in Wnt research and development, presented its most recent clinical and preclinical data for two of the company's investigational Wnt pathway inhibitors, SM04690 for the treatment of knee osteoarthritis (OA), and SM04755 for the treatment of tendinopathy, during the Osteoarthritis Research Society International World Congress held April 26-29, in Liverpool, U.K.

Additionally, Samumed held a scientific symposium titled "Advancing Disease Modification in Knee Osteoarthritis: Clinical Implications of Wnt Pathway Inhibition." Speakers Timothy McAlindon, MD, MPH, Rik Lories, MD, PhD, Nancy E. Lane, MD, and Yusuf Yazici, MD, provided an overview of the clinical implications of a potential injectable disease-modifying osteoarthritis drug (DMOAD), the Wnt pathway and OA, preclinical SM04690 data, and clinical SM04690 data, respectively.

"There is a lot of excitement surrounding the potential for disease-modifying products to treat OA. Our presentations and posters at OARSI demonstrate promising developments for the potential disease-modifying characteristics of our investigational Wnt inhibitor," said Yusuf Yazici, MD, Chief Medical Officer of Samumed.

Preclinical and clinical results from Samumed's SM04690 development program evaluating a single intra-articular (IA) injection of SM04690 in the knee as a potential DMOAD included:

- 52-week data from a phase 2 proof-of-concept study
- Post-hoc analyses of the phase 2 study
- Preclinical data from *in vivo* rat knee OA models

Samumed also presented preclinical data on its investigational drug candidate for tendinopathy, SM04755. Observations from acute- and repeat-injury delayed treatment tendinopathy models in rats demonstrated SM04755 promoted tendon healing compared with vehicle in both treatment models.

Highlights from Samumed's oral and poster presentations are below:

Oral Presentation #27

Experimental Tendinopathy Treatment with SM04755, a Topical Small Molecule Inhibitor of the Wnt Pathway

SM04755 demonstrated sustained tendon exposure with minimal systemic exposure over 24 hours following topical application (0.3 mg/cm^2). In an acute *in vivo* rat collagenase tendinopathy model, daily treatment with 0.3 mg/cm^2 topical SM04755 was shown to reduce inflammation, increase tendon regeneration markers, and improve tendon structure compared with vehicle at Day 21. A higher dose of SM04755 (0.9 mg/cm^2) led to faster tendon health score recovery at Day 14. Improvements in pain and

weight bearing function were observed in the same model at Day 18 and Day 7, respectively, and sustained through the end of the 21-day study. Additionally, treatment with 0.3 mg/cm^2 SM04755 promoted tendon healing in a repeat-injury delayed treatment model compared with vehicle at Day 21.

Poster #98

SM04690, a Wnt Pathway Inhibitor: Anti-Inflammatory and Cartilage Protective Effects in Preclinical Osteoarthritis Models

In vitro, SM04690 demonstrated significant ($p<0.05$) anti-inflammatory effects across a broad range of cytokines (small proteins important in cell signaling), including IL-1α, IL-1β, IL-2, IL-6, IL-8, TNF-α, and IL-17A, in cell co-cultures stimulated with super-antigen (sAG) or lipopolysaccharides (LPS), compared with vehicle. In multiple experiments using an *in vivo* rat knee OA model, a single IA injection of 0.3 µg SM04690 decreased inflammation at Day 11 and attenuated pain beginning at Day 6 and continuing through the last recorded measurement of the study (Day 22). Single injection of 0.3 µg SM04690 was also shown to protect cartilage as measured by improvements in Safranin-O staining and OARSI scores compared with vehicle at Day 28. Studies to further explore the anti-inflammatory effects of SM04690 are ongoing.

Poster #466

Radiographic Outcomes Were Concordant with Outcome Measures in Rheumatology Osteoarthritis Research Society International (OMERACT-OARSI) Strict Response: Post-Hoc Analysis from a Phase 2 Study of a Wnt Pathway Inhibitor, SM04690, for Knee Osteoarthritis Treatment

This post-hoc analysis of a 52-week phase 2 trial of SM04690 evaluated associations of mJSW with changes in pain and function. SM04690 treatment was shown to maintain or increase mJSW in 0.03 and 0.07 mg dose groups compared with placebo at 52 weeks in intent-to-treat and unilateral symptomatic subjects (with or without widespread pain). Changes in mJSW were concordant with OMERACT-OARSI strict response in the 0.07 mg and vehicle groups among unilateral symptomatic subjects, suggesting that an increase in mJSW may correspond to an overall improvement in pain and function of subjects with knee OA. These findings support further studies of SM04690 at a dose of 0.07 mg as a potential DMOAD for knee OA.

Poster #518

Joint Space Width Inclusion Criteria Can Reduce Knee Osteoarthritis Trial Heterogeneity: Post-Hoc Data from a Phase 2 Trial of Wnt Pathway Inhibitor, SM04690

This post-hoc analysis was conducted among a subject subgroup from the phase 2 OA study with mJSW [2-4] mm at baseline. In the 0.03 and 0.07 mg SM04690 groups, mJSW changes beyond the radiographic minimal detectable difference (>0.13 mm)^3 were observed, and were statistically significant compared with placebo at 52 weeks. These findings suggested that baseline cartilage thickness is an important determinant for detection of change. Additionally, a less heterogenous baseline mJSW reduced measurement variability, which may reduce the required population size in a clinical trial while maintaining statistical power. These data suggest that future trials using radiography to assess structure modification in knee OA should consider mJSW [2-4] mm as a specific inclusion criterion.

Poster #550

Results from a 52-Week Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study of a Novel, Intra-Articular Wnt Pathway Inhibitor (SM04690) for the Treatment of Knee Osteoarthritis

In this study, SM04690 appeared generally safe, with clinical and radiographic outcomes suggesting it may be a potential DMOAD for knee OA treatment. These findings also identified a target population of

knee OA subjects with unilateral symptoms and a potential optimal dose (0.07 mg) of SM04690. In this pre-specified subpopulation of subjects treated with 0.07 mg SM04690, mJSW as measured by x-ray was increased at 26 and 52 weeks compared with placebo. Improvement in WOMAC pain and function scores were also observed for the same subgroup at 52 weeks compared with placebo. Further studies assessing this molecule as a potential treatment for knee OA are ongoing.

The above presentations can be found on the Publications section of Samumed's website, accessible here: https://www.samumed.com/publications/default.aspx

About Osteoarthritis Research Society International
The Osteoarthritis Research Society International (OARSI) is the leading medical society for advancing the understanding, early detection, treatment and prevention of osteoarthritis (OA) through its exclusive dedication to research. OARSI's passion and area of focus is on OA, a debilitating disease affecting more than 600 million people around the world. With more than 30 years of experience serving the OA community, OARSI provides the necessary framework, expert resources and support for its international constituents to address the challenges of OA so that the knowledge gained can ultimately be used to help improve patient care and patient outcomes.

About SM04690
SM04690 is a small molecule inhibitor of the Wnt pathway administered as an intra-articular injection, and is being developed as a potential disease-modifying drug for osteoarthritis (DMOAD). Preclinical data suggested SM04690 has a dual mechanism of action with three specific effects on joint health – generation of articular cartilage, slowing down cartilage degradation, and reducing inflammation in the joint. Additional information on Samumed's SM04690 osteoarthritis program can be found here: https://www.samumed.com/pipeline/detail.aspx?id=20

About SM04755
SM04755 is a small-molecule Wnt pathway inhibitor and is being developed as a potential topical therapeutic for tendinopathy. Preclinical data has shown that SM04755 may inhibit inflammation, reduce fibrosis, and increase tenocyte differentiation (tendon repair). Additional information on Samumed's SM04755 tendinopathy program can be found here: https://www.samumed.com/pipeline/detail.aspx?id=13

About Samumed
Samumed's small-molecule drug platform is harnessing the innate restorative power of the Wnt pathway to reverse the course of severe and prevalent diseases. Samumed's clinical pipeline can be found here: https://www.samumed.com/pipeline/default.aspx

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