

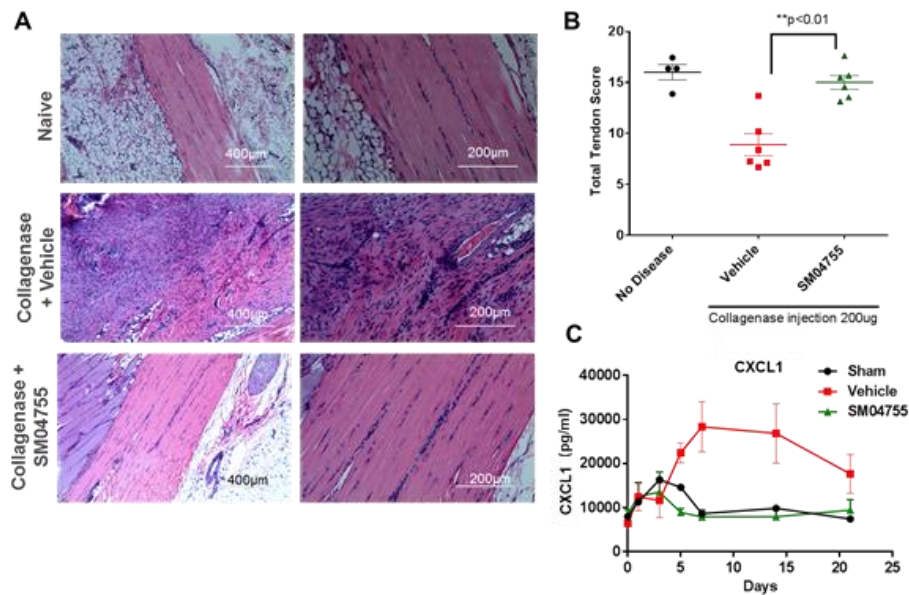
SAMUMED PRESENTS DATA FOR A SMALL MOLECULE MODULATOR OF WNT PATHWAY AS A POTENTIAL TOPICAL TREATMENT FOR CHRONIC TENDINOPATHY

San Diego, CA—November 14, 2016 – Samumed presented at the 2016 American College of Rheumatology (ACR) Annual Meeting results from *in vitro* and *in vivo* studies regarding the use of its small molecule compound SM04755 as a potential topical treatment of chronic tendinopathy. SM04755 is one of two small molecule Wnt pathway modulators (together with SM04690, which is in clinical trials for osteoarthritis and degenerative disc disease) about which Samumed has presented clinical and preclinical data across five different rheumatic diseases. Chronic tendinopathy is a degenerative and fibrotic condition caused by injuries or overuse; it is characterized by pain and impaired function. (Khan KM, et al. *BMJ*. 2002;324.2; Kountouris A and Cook J. *Pract Res Clin Rheumatol*. 2007; 21(2):295-316; Maffulli N, et al. *Arthroscopy: The J of Arthro and Rel Surg*. 1998;14(8):4.)

In preclinical studies, SM04755 demonstrated potential to promote healing in chronic tendinopathy. Specifically, *in vitro* testing demonstrated that SM04755 prevented and reversed fibrosis and promoted the formation of tendon cells. From *in vivo* studies, SM04755 topically applied to rat tendinopathy models reduced markers of tendon inflammation in plasma, showed evidence of tendon regeneration, and increased tendon health scores compared to rats treated with inactive vehicle.

Samumed presented, inter alia, the following data and images related to its *in vivo* studies as part of its abstract for ACR on this potential treatment for chronic tendinopathy:

Figure. SM04755 inhibited inflammation and promoted tendon healing in a rat collagenase-induced tendinopathy model



(A) Images of rat tendons stained with H&E from sham or collagenase-injected and vehicle- or SM04755 (0.3 mg/cm²) treated rats on day 21; (B) histological score of inflammation, linearity and density of tendon fibers, shape of tenocytes and hemorrhage for the rat tendons. Mean \pm SEM, day 21: N=4 sham, n+6 vehicle & SM0755; (C) levels of circulating CXCL1 in peripheral blood following treatment as measured by ELISA.

In vivo efficacy of topical SM04755 was evaluated in an intra-tendon collagenase-induced rodent tendinopathy model by scoring (range 5-20) several histological indicators of tendon health. Inflammation in the rodent model was measured by chemokine ligand 1 (CXCL1) levels in plasma by ELISA and other inflammatory markers in the tendon by qPCR. Tendon regeneration was evaluated by qPCR based gene expression of tenocyte differentiation markers scleraxis A and tenascin C.

In the collagenase-induced model, compared to vehicle, SM04755 treatment significantly increased the mean tendon health score ($p < 0.01$, $n=6$), decreased the plasma levels of CXCL1 ($p < 0.05$, $n=6$), reduced gene expression of pro-inflammatory markers (IL-6, TNF- α , IL-1 β , INF- γ , IL-8) ($p < 0.05$, $n=3$), and increased expression of scleraxis A and tenascin C in tendon ($p < 0.05$, $n=6$).

The abstract for the presentation is available at ACR's website here: [Discovery of a Small Molecule Inhibitor of the Wnt Pathway \(SM04755\) As a Potential Topical Treatment for Chronic Tendinopathy](#). Details of methodology and results are covered in the poster presented at ACR available [here](#).

"Based on our preclinical study results, we are extremely excited about SM04755's potential as a treatment for chronic tendinopathy, for which current therapeutic options focus on alleviating the symptoms and pain rather than treating the underlying disease," said Yusuf Yazici, M.D., Chief Medical Officer of Samumed. "For this potential treatment, we just opened an IND, and we are planning to initiate a Phase 1 clinical trial before the end of 2016."

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ABOUT SAMUMED, LLC

Based in San Diego, CA, Samumed (www.samumed.com) is a pharmaceutical platform company focused on advancing regenerative medicine and oncology applications through research and innovation. Samumed has discovered new targets and biological processes in the Wnt pathway, allowing the team to develop small molecule drugs that potentially address numerous degenerative conditions as well as many forms of cancer.