samumed

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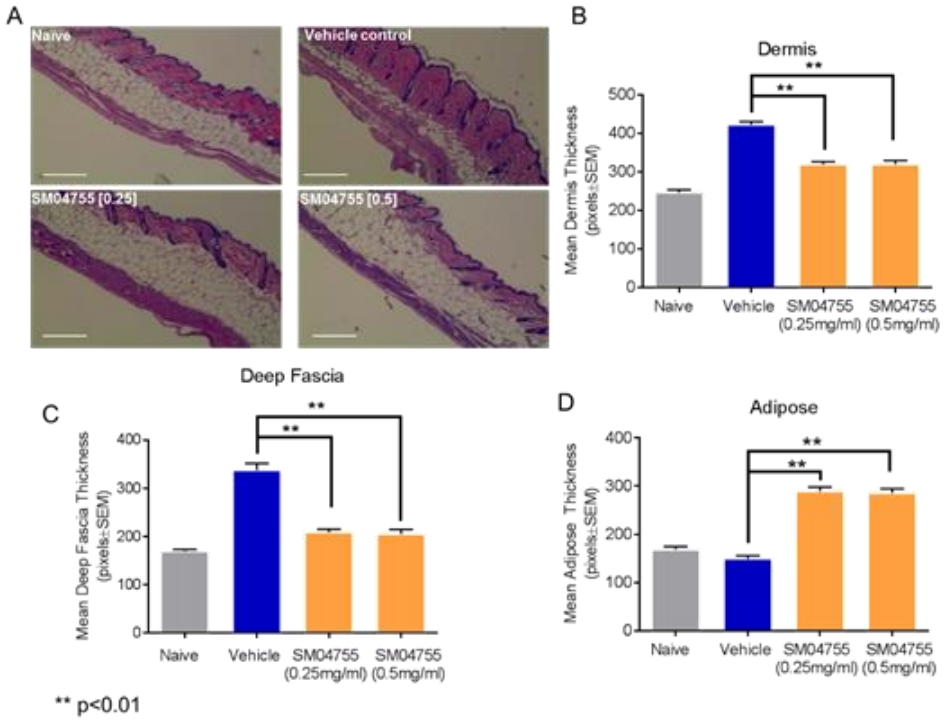
SAMUMED, LLC PRESENTS DATA FOR SMALL MOLECULE MODULATOR OF WNT PATHWAY AS A POTENTIAL TOPICAL TREATMENT FOR SCLERODERMA

San Diego, CA—November 14, 2016 – Samumed presented at the 2016 American College of Rheumatology (ACR) Annual Meeting preclinical results from *in vitro* and *in vivo* studies regarding the use of its small molecule compound SM04755 as a potential topical treatment for scleroderma. 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/or preclinical data across five different rheumatic diseases.

Scleroderma is an autoimmune fibrotic disease, which presents skin manifestations, among other signs and symptoms. From *in vitro* studies, SM04755 inhibited inflammation and reversed dermal fibrosis. From an *in vivo* mouse model, topically applied SM04755 reversed dermal fibrosis, increased adipose tissue, and reduced vasculopathy compared to vehicle, with minimal exposure to plasma or systemic toxicity. These studies demonstrated that SM04755 has potential as a topical therapy for scleroderma.

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

Figure. SM04755 reduced the thickness of the dermis and deep fascia relative to control in a bleomycin-induced scleroderma model in mice



(A) Histological evaluation of H&E stained skin sections from normal or bleomycin-injected and vehicle- or SM04755-treated mice on day 28. (B)–(D) Quantification of the thickness measured in pixels of the layers of skin in (A). Mean ± SEM, n=7 mice/group for treatment, 6 mice/group for vehicle, and 3 mice/group for normal.

From the *in vitro* studies, anti-inflammatory activity was evaluated by measuring IL-6 and TNF-α secretion using ELISA in lipopolysaccharides-stimulated THP-1 monocytes and anti-CD3/anti-CD28-stimulated peripheral blood mononuclear cells. Effects on fibrosis were assessed in TGF-β-stimulated human dermal fibroblasts by measuring smooth muscle actin (αSMA), plasminogen activator inhibitor, connective tissue growth factor, and collagen expression by qRT-PCR. The effect on myofibroblast differentiation and reversion was measured by immunocytochemistry for αSMA.

In vivo efficacy was evaluated in a subcutaneous bleomycin (50μg)-induced mouse model of scleroderma by histological measurements of the thickness of the layers of the skin, CD31 immunohistochemistry for vasculopathy, and qRT-PCR based expression of Wnt signaling and fibrotic markers. Pharmacokinetics were evaluated following topical application in rats by analysis of compound concentrations in skin and plasma.

The details of methodologies and results were presented at a poster at ACR which can be found here. 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 Scleroderma.

"Based on our study results, we are excited about SM04755's potential as a treatment for scleroderma," said Yusuf Yazici, M.D., Chief Medical Officer of Samumed. "We expect to expand our ongoing clinical trials for SM04755 from chronic tendinopathy to psoriasis and scleroderma in 2017."

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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.