samumed

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SAMUMED, LLC ANNOUNCES SUCCESSFUL MODULATION OF THE WNT PATHWAY FOR POTENTIAL CARTILAGE REGENERATION

SAN FRANCISCO—November 9, 2015—At the American College of Rheumatology (ACR) Annual Meeting, Samumed unveiled groundbreaking pre-clinical and clinical research that demonstrated successful modulation of the Wnt pathway for potential applications in regenerative medicine. Samumed researchers have developed an injectable investigational drug that inhibits the Wnt pathway, causing endogenous stem cells to regenerate knee cartilage in animals. Clinical data indicate that the same investigational drug may slow joint space narrowing and possibly increase joint space in the knee. Clinicians generally perceive an increase in joint space as evidence of preservation or regrowth of cartilage.

"The results of our Phase I study of SM04690 for the treatment of osteoarthritis of the knee are very encouraging," said Yusuf Yazici, M.D., Chief Medical Officer of Samumed. "We believe that the clinical trial results we have seen to date, combined with the success of our animal results, demonstrate that our technology could potentially be the basis of a safe and effective treatment for the millions of patients suffering from osteoarthritis of the knee."

OSTEOARTHRITIS CLINICAL TRIAL

Samumed recently concluded a 24 week placebo-controlled, double-blind, randomized Phase I clinical trial, studying the safety and preliminary efficacy of SM04690 in patients with moderate to severe osteoarthritis of the knee. Subsequently, Samumed began enrollment in an approximately 400-patient Phase II clinical trial. SM04690 is a small molecule inhibitor of the Wnt pathway administered via intra-articular (IA) injection.

In the Phase I trial, a total of 61 subjects were enrolled across 3 dose cohorts, in ratios of 4:1 treatment to placebo, with each subject receiving a single IA injection (i.e., 16 patients injected with SM04690 versus 4 administered placebo at each of the 3 dose levels). The study's primary objectives were to evaluate the safety and tolerability of SM04690, determine the dose-limiting toxicities, and assess its pharmacokinetic behavior. The study's secondary exploratory objective was to estimate clinical response to treatment, using, among other measures, change from baseline for function, pain and stiffness scores using the Western Ontario and McMaster Universities Arthritis Index (WOMAC), and physician global assessment of disease activity. Magnetic resonance imaging (i.e., MRI) at 12 weeks and 24 weeks and radiographic (i.e., x-ray) imaging data at 24 weeks were also collected to study safety and potential disease modification effect.

At the ACR Annual Meeting, the company presented two posters relating to the 12 week safety and efficacy interim results from this Phase I trial, as well as the preliminary 24 week safety and radiographic imaging results (see Poster # 312: *Safety, Efficacy and Biomarker Outcomes of a Novel, Intra-Articular, Injectable, Wnt Inhibitor (SM04690) in the Treatment of Osteoarthritis of the Knee: Interim, Exploratory Analysis of Results from a Randomized, Double-Blind, Placebo-Controlled Phase 1 Study* & Poster # 313: *Magnetic Resonance Imaging Outcomes Using an Intra-Articular Injection (SM04690) in the Treatment of Osteoarthritis of the Knee: Interim, Exploratory Analysis of Results from a Randomized, Double-Blind, Placebo-Controlled, Phase 1 Study*). Radiographic imaging suggests a slowing/stopping of joint space narrowing compared to placebo, with one dose level demonstrating statistically significant improved joint space width. The results also suggested that a single IA injection with SM04690 appeared to be safe and potentially effective in improving function and reducing pain for patients with osteoarthritis of the knee. More than 9 million Americans have symptomatic osteoarthritis of the knee. According to the Arthritis Foundation, osteoarthritis (in any joint) affects 27 million Americans—more than 10 percent of the U.S. adult population—and is the most common cause of disability in the United States.

PRECLINICAL RESEARCH RESULTS

Osteoarthritic joints are characterized by degradation of the articular cartilage, which provides the cushioning between bones, and by bony protrusions called osteophytes, which interfere with function and exacerbate the pain associated with osteoarthritis. An overactive Wnt pathway in the affected joint causes the formation of more (spurious) bone instead of (healthy) cartilage, leading to pain, loss of function, stiffness, and deformity.

“The Wnt pathway has been extensively studied because it is a master regulator of tissue regeneration. Our research has uncovered previously-unknown targets in the Wnt pathway and we are developing small molecule drugs that stimulate tissue repair and regeneration,” said John Hood, Ph.D., Chief Scientific Officer and Co-Founder of Samumed.

Samumed has demonstrated that its investigational compound SM04690 modulated the Wnt pathway in cellular and animal models, leading endogenous adult stem cells to differentiate into cartilage-forming chondrocyte cells (see Dr. Hood’s presentation at the ACR Annual Meeting: *Discovery of an Intra-Articular Injection Small Molecule Inhibitor of the Wnt Pathway (SM04690) As a Potential Disease Modifying Treatment for Knee Osteoarthritis*). Samumed has shown that in vitro inhibition of the Wnt pathway caused adult human mesenchymal stem cells to differentiate into chondrocyte cells at a rate 50 fold higher than control, while simultaneously reducing the levels of cartilage degrading protease enzymes by a similar factor. In animal studies modeling osteoarthritis of the knee, the net effect of the inhibition of the Wnt pathway has been the regeneration of articular cartilage and suppression of inflammation in the knee joints of the study animals.

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.

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