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PRESS RELEASE

Samumed Announces Publication of Phase 2 Data on Lorecivivint, Now in Pivotal Trials for Knee Osteoarthritis

X-ray results and pain and function responses highlight
the potential of lorecivivint as a first-in-class drug for the treatment of knee osteoarthritis

SAN DIEGO – May 22, 2020 – Samumed, LLC, announced today the publication of results from the Phase 2a trial of lorecivivint, an investigational CLK/DYRK1A inhibitor that modulates the Wnt pathway, for the potential treatment of knee osteoarthritis (OA). The article was published in *Arthritis & Rheumatology* and demonstrates the disease-modifying promise of lorecivivint.

"We are pleased to publish exciting data on lorecivivint for the treatment of knee OA. Limiting structural progression remains an acute unmet medical need for OA patients. Joint space narrowing, suggestive of cartilage loss, is a biomarker of disease progression in knee OA. These Phase 2a data highlight the disease modifying promise of lorecivivint based on its ability to slow joint space narrowing, while durably improving pain and function over one year," said Yusuf Yazici, M.D., Chief Medical Officer of Samumed.

The paper titled "Lorecivivint, a Novel Intra-articular CLK/DYRK1A Inhibitor and Wnt Pathway Modulator for Treatment of Knee Osteoarthritis: A Phase 2 Randomized Trial" included the clinical results from Samumed's proof-of-concept, multicenter, randomized, double-blind, placebo-controlled Phase 2a study (NCT02536833). The trial evaluated the safety, tolerability, and efficacy of lorecivivint after a single injection into the target knee joint of moderately to severely symptomatic OA patients over 52 weeks.

Published data include:

- 455 subjects were randomized to receive a single intra-articular knee injection of 0.03, 0.07, or 0.23 mg lorecivivint, or placebo
- Subjects in the prespecified subgroup with unilateral symptoms (164 subjects) showed statistically significant improvements in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain, WOMAC Function, and medial joint space width (mJSW), as measured by X-ray, at 52 weeks when treated with 0.07 mg lorecivivint compared with placebo
- In a post hoc analysis, unilateral symptomatic subjects without widespread pain (128 subjects) receiving 0.07 mg lorecivivint compared with placebo showed statistically significant improvements in WOMAC Pain, WOMAC Function, and mJSW at Weeks 26 and 39
- A post hoc analysis of both subgroups demonstrated that the radiographic (mJSW) improvements in the 0.07 mg dose group were concordant with clinical improvements

(WOMAC Pain and Function), indicating the potential connection between changes in structural measures and clinical responses that may be due to treatment
- Intra-articular injection with lorecivivint appeared generally safe and well tolerated

Lorecivivint is currently being studied in the STRIDES-X-ray Phase 3 trial (NCT03928184), a 56-week, multicenter, randomized, double-blind, placebo-controlled study utilizing patient-reported pain and function endpoints and radiographic outcomes to evaluate the efficacy and safety of a single intra-articular injection of 0.07 mg lorecivivint in patients with moderately to severely symptomatic knee OA.

About Osteoarthritis
Arthritis is the leading cause of adult disability. As the most common type of arthritis, osteoarthritis (OA) is characterized by the destruction of articular cartilage and structural changes in bone, which contribute to pain and loss of joint function. An estimated 30 million U.S. adults suffer from OA, primarily due to an aging population and an increasing prevalence of obesity. The combination of direct medical costs, pain and suffering, and loss of workplace productivity elevates OA to a major socioeconomic problem for health systems, the economy, and suffering patients. Currently, there are no approved disease-modifying treatments for osteoarthritis.

About Lorecivivint
Lorecivivint (SM04690) is a small-molecule CLK/DYRK1A inhibitor that modulates the Wnt pathway and is in development as a potential disease-modifying osteoarthritis drug (DMOAD). Vehicle-controlled preclinical data suggest that lorecivivint has a dual mechanism of action with three potential effects on joint health: generation of cartilage, slowing of cartilage breakdown, and reduction of inflammation. Additional information on Samumed's investigational lorecivivint osteoarthritis program can be found here: https://www.samumed.com/pipeline/detail.aspx?id=20.

About Samumed
Samumed's investigational small-molecule drug platform is harnessing the potential restorative power of the Wnt pathway to reverse the course of severe and prevalent diseases. Learn more about Samumed's potential regenerative drug candidates and broad clinical pipeline at https://www.samumed.com/pipeline/default.aspx.

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