Sorrento Therapeutics Announces First Subject Dosed in a Phase I Clinical Study of STI-1558, an Oral Mpro Inhibitor as a Standalone Treatment and Prevention of COVID-19 Without Co-Administration of Ritonavir Booster

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- STI-1558, an oral SARS-CoV-2 main protease inhibitor, is specifically designed as a standalone treatment and prevention of COVID-19 without the co-administration of ritonavir as a booster for CYP3A4 inhibition.
- STI-1558 is also a Cathepsin L inhibitor, which may block effective viral entry into host cells without accelerating viral mutations and could work in conjunction with protease inhibition to further protect against COVID-19.
- STI-1558 showed good oral bioavailability of up to 85% in dogs and monkeys with a sufficient plasma exposure, suggesting that no CYP3A4 inhibitor co-administration is needed.
- No significant safety findings to date in GLP repeat-dose toxicology studies in rats and dogs at daily doses up to 2000 mg/kg and 300 mg/kg, respectively.

SAN DIEGO, June 03, 2022 (GLOBE NEWSWIRE) -- Sorrento Therapeutics, Inc. (Nasdaq: SRNE, "Sorrento") today announced the first subject was dosed in a Phase I clinical study (NCT05364840) of its oral main viral protease (M^{pro}) inhibitor, STI-1558.

The world has been experiencing repeated waves of infection of SARS-CoV-2 and its continually emerging variants. Current vaccines and EUA-approved antibodies offer diminished protection against transmission and infection by Omicron variants. Oral antiviral drugs with broad-spectrum antiviral activities and limited potential for drug-drug interaction risks are still urgently needed. EUA-cleared Nirmatrelvir (Paxlovid) has demonstrated encouraging data in preventing disease progression; however, in order to achieve therapeutic blood level, it requires the co-administration or “boosting” with Ritonavir, a strong inhibitor of cytochrome P450 (CYP) 3A4 (“CYP3A4"). This means it blocks the liver from metabolizing drugs that utilize this enzyme for metabolism and clearance, resulting in the potential for significant drug-drug interactions, which can limit its use, especially in at-risk patients on multiple medications.

STI-1558 is a potent M^{pro} inhibitor with an IC_{50} value of 2.7 nM and has demonstrated potent antiviral activity against all COVID-19 variants studied, including Omicron, with an IC_{90} value between 14 nM and 41 nM (an IC_{50}/IC_{90} is the concentration of drug need to produce a 50%/90% inhibition of activity) in vitro following infection of human bronchial epithelial cells. It is also a Cathepsin L inhibitor, which may block effective viral entry into host cells. In preclinical studies, STI-1558 showed an oral antiviral activity against SARS-CoV-2 in a humanized transgenic mice model. In these preclinical studies, STI-1558 protected virus infected mice from weight loss, viral replication in lungs, as well as associated lung pathology. STI-1558 possesses excellent off-target selectivity, is metabolically stable in human liver microsomes, and has demonstrated oral bioavailability of up to 85% in dogs and monkeys. In GLP repeat-dose toxicology studies in rats and dogs, there have been no significant safety findings to date, including blood chemistry, hematology and histopathology at daily doses of up to 2000 mg/kg and 300 mg/kg, respectively. Based on the safety and pharmacokinetic modeling, Sorrento expects the human efficacious dose to be between 300 mg and 600 mg BID without the need for a Ritonavir-boost.

The Phase I study will be conducted in Australia will evaluate the safety, tolerability, and pharmacokinetics of STI-1558 in single ascending doses (SAD) followed by multiple ascending doses (MAD) compared to placebo in healthy volunteers. A global pivotal Phase II/III trial will be initiated as soon as possible following the successful completion of the Phase I. “We are excited to reach the milestone of advancing STI-1558 to the clinical stage. With data achieved from the preclinical studies and potential standalone treatment without requiring a pharmacokinetic booster, STI-1558 has the potential to be a best-in-class oral antiviral therapeutic for COVID-19, appropriate for patients taking multiple medications, without requiring extra monitoring or dose adjustments. Sorrento has initiated a large-scale manufacture synthesis for API and drug product to prepare for global commercial supply if STI-1558 is successfully developed. Sorrento continues its commitment to develop and deliver effective anti-COVID-19 therapies to save patient lives and end the pandemic,” stated Dr. Henry Ji, Chairman and CEO of Sorrento.

About Sorrento Therapeutics, Inc.

Sorrento is a clinical and commercial stage biopharmaceutical company developing new therapies to treat cancer, pain (non-opioid treatments), autoimmune disease and COVID-19. Sorrento's multimodal, multipronged approach to fighting cancer is made possible by its extensive immuno-oncology platforms, including key assets such as fully human antibodies (“G-MAB™ library”), immuno-cellular therapies (“DAR-T™”), antibody-drug conjugates (“ADCs”), and oncolytic virus (“Seprehvec™”). Sorrento is also developing potential antiviral therapies and vaccines against coronaviruses, including Abivertinib, COVISHIELD™ and COVI-MSC™; and diagnostic test solutions, including COVIMARK™

Sorrento's commitment to life-enhancing therapies for patients is also demonstrated by our effort to advance a first-in-class (TRPV1 agonist) non-opioid pain management small molecule, resiniferatoxin (“RTX”), and SP-102 (10 mg, dexamethasone sodium phosphate viscous gel) (SEMDEXA™), a novel, viscous gel formulation of a widely used corticosteroid for epidural injections to treat lumbosacral radicular pain, or sciatica, and to commercialize ZTlido® (lidocaine topical system) 1.8% for the treatment of postherpetic neuralgia (PHN). RTX has been cleared for a Phase II trial for intractable pain associated with cancer and a Phase II trial in osteoarthritis patients. Positive final results from the Phase III Pivotal Trial C.L.E.A.R. Program for SEMDEXA™, its novel, non-opioid product for the treatment of lumbosacral radicular pain (sciatica), were announced in March 2022. ZTlido® was approved by the FDA on February 28, 2018.

For more information visit www.sorrentotherapeutics.com

Forward-Looking Statements

This press release and any statements made for and during any presentation or meeting contain forward-looking statements related to Sorrento Therapeutics, Inc., under the safe harbor provisions of Section 21E of the Private Securities Litigation Reform Act of 1995 and subject to risks and uncertainties that could cause actual results to differ materially from those projected. Forward-looking statements include statements regarding STI-1558, including the potential antiviral profile of STI-1558 with respect to SARS-CoV-2 and its variants; the preclinical testing of STI-1558; the potential safety and efficacy of STI-1558; the potential that no co-administration will be required with STI-1558; the potential for STI-1558 to effectively inhibit viral entry and replication, weight loss and lung pathology; the oral bioavailability of STI-1558; the potential success of the Phase I trial; the expected timing of a global Phase II/III trial; STI-1558's and Sorrento's position in the antiviral industry; the expected formulation, dosing and/or route of administration for STI-1558; and the preparation of a global commercial supply of STI-1558. Risks and uncertainties that could cause our actual results to differ materially and adversely from those expressed in our forward-looking statements, include, but are not limited to: risks related to Sorrento's technologies and prospects, including, but not limited to risks related to safety and efficacy of STI-1558 and seeking regulatory approval for STI-1558; clinical development risks, including risks in the progress, timing, cost, and results of clinical trials and product development programs; risk of difficulties or delays in obtaining regulatory approvals; risks that clinical study results may not meet any or all endpoints of a clinical study and that any data generated from such studies may not support a regulatory submission or approval; risks that prior test, study and trial results may not be replicated in continuing or future studies and trials; risks of manufacturing and supplying drug product; risks related to leveraging the expertise of its employees, subsidiaries, affiliates and partners to assist Sorrento in the execution of its product candidates' strategies; risks related to the global impact of COVID-19; and other risks that are described in Sorrento's most recent periodic reports filed with the Securities and Exchange Commission, including Sorrento's Annual Report on Form 10-K for the year ended December 31, 2021 and subsequent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission, including the risk factors set forth in those filings. Investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this release, and we undertake no obligation to update any forward-looking statement in this press release except as required by law.

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