November 10, 2022

Sapience Therapeutics Presents Data on the Immune Activating Function of ST101 at Society for Immunotherapy of Cancer (SITC) 37th Annual Meeting

HARRISON, N.Y., Nov. 10, 2022 /PRNewswire/ -- Sapience Therapeutics, Inc., a clinical-stage biotechnology company focused on the discovery and development of peptide therapeutics to address oncogenic and immune dysregulation that drive cancer, announced today the presentation of non-clinical and clinical data supporting the immune activating activity of ST101 at the SITC 37th Annual Meeting in Boston, MA. ST101 is a first-in-class antagonist of C/EBPβ, currently being evaluated in the Phase 2 portion of an ongoing Phase 1-2 clinical study in patients with advanced unresectable and metastatic solid tumors (NCT04478279).

C/EBPβ is a leucine zipper family transcription factor that regulates macrophage differentiation, promoting the expression of M2 myeloid-derived suppressor cells (MDSCs) that contribute to suppression of antitumor immunity and correlate with poor prognosis. ST101 binds to C/EBPβ, preventing its dimerization and enhancing ubiquitin-proteasome dependent C/EBPβ degradation, resulting in repolarizing MDSCs from the immunosuppressive M2 to the pro-inflammatory M1 phenotype. In non-clinical studies, ST101 exposure to human peripheral blood mononuclear cells resulted in dose-dependent reduction in M2 macrophage and corresponding induction of pro-inflammatory M1 macrophage. At the highest ST101 concentration, a 40-fold increase in the M1/M2 ratio was observed. Validating these findings, subtherapeutic doses of ST101 significantly enhanced the anti-tumor activity of anti-PD1 antibodies in an orthotopic breast cancer tumor model. Sapience believes that reprogramming MDSCs from the M2 to the M1 phenotype represents a potential strategy to enhance antitumor immunity.

"These data validate the potential of ST101 to reprogram the tumor microenvironment to promote a more active immune system, which supports a novel, macrophage-driven mechanism of action for ST101," said Sapience CEO and President, Dr. Barry Kappel. "We are eager to broaden the development strategy of ST101 and explore combinations with immune-oncology molecules, such as checkpoint inhibitors, to treat solid tumor cancers with high unmet need."

"We are thrilled to present these data at SITC 2022, the premier scientific meeting that showcases novel immunotherapy approaches for cancer," added Jim Rotolo, Ph.D., Sapience's VP, Translational Pharmacology and Head of Research. "These data further elucidate the unique mechanism of action for ST101 and build upon our recent publication in *Molecular Cancer Therapeutics*, highlighting the therapeutic promise of disrupting C/EBPβ-

driven oncogenic activity. We look forward to exploring the activity of ST101 in immune-oncology therapeutic strategies."

Further details of the ST101 mechanism of action can be found on the company's website: ST101: Sapience Therapeutics, Inc.

SITC Poster Presentation Details:

Title: "*ST101, a peptide antagonist of novel I/O target CEBPβ, reprograms MDSC polarization and decreases tumor-associated Tregs, suggesting an immune component to observed clinical responses"*
Abstract Number: 1173
Location: Poster Hall C
Date/Time: Thursday, November 10, 2022 – Friday, November 11, 2022, 9am-9pm

The Sapience SITC poster has been published as a supplement in the *Journal for ImmunoTherapy of Cancer (JITC)*, the society's global, open access, peer-reviewed journal, and is available on the Presentations section of the company's website: Presentations :: Sapience Therapeutics, Inc.

About ST101

ST101, a first-in-class antagonist of C/EBPβ, is currently being evaluated in the Phase 2 portion of an ongoing Phase 1-2 clinical study in patients with advanced unresectable and metastatic solid tumors (NCT04478279). ST101-101 is an open-label, Phase 1-2 dose-finding study designed to determine the safety, tolerability, PK, PD, and proof-of-concept efficacy of ST101 in patients with advanced solid tumors. The study consists of two phases: Phase 1 dose escalation/regimen exploration and Phase 2 dose expansion. In the ongoing Phase 2 dose expansion, Sapience is actively enrolling patients with GBM, metastatic cutaneous melanoma, castration-resistant prostate cancer and locally advanced or metastatic hormone-receptor positive breast cancer. In the ongoing dose escalation part of the study, ST101 has demonstrated clinical proof-of-concept with a durable RECIST 1.1-confirmed partial response (PR) in a patient with cutaneous melanoma and evidence of long-lasting stable disease in several additional patients. In the ongoing Phase 2 dose expansion part of the study, ST101 has demonstrated clinical proof-of-concept with a mRANO-confirmed partial response in a patient with recurrent GBM and evidence of long-lasting stable disease in several additional patients.

ST101 has been granted Fast Track designation for recurrent GBM and advanced cutaneous melanoma in patients who have disease progression on or after anti-PD-1/anti-PD-L1 therapy, as well as orphan designations from the FDA for advanced melanoma, glioma and AML, and from the European Commission for the treatment of glioma.

About Sapience Therapeutics

Sapience Therapeutics, Inc. is a privately held, clinical-stage biotechnology company focused on discovering and developing peptide therapeutics to address oncogenic and immune dysregulation that drive cancer. Its pipeline of SPEARs™ (Stabilized Peptides Engineered Against Regulation) disrupt intracellular protein-protein interactions, enabling targeting of transcription factors which have traditionally been considered undruggable.

Sapience's lead program, ST101, is a first-in-class antagonist of C/EBPβ that has demonstrated clinical proof-of-concept in multiple indications. For more information on Sapience Therapeutics, please visit www.sapiencetherapeutics.com and engage with us on LinkedIn.

Cautionary Note on Forward-Looking Statements

This press release contains forward-looking statements. Any statements herein other than statements of historical fact could be deemed to be forward-looking statements. These forward-looking statements may include, among other things, statements regarding future events that involve significant risks and uncertainties (including with respect to Sapience's preclinical and clinical development programs). These forward-looking statements are based on management's current expectations, and actual results and future events may differ materially as a result of certain factors, including, without limitation, our ability to obtain additional funds, and meet applicable regulatory standards and receive required regulatory approvals. Forward-looking statements speak only as of the date of this press release. Sapience does not undertake any obligation to update any forward-looking statements as a result of new information, future events, changed assumptions or otherwise, except as required by law.

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