Silicon Therapeutics Announces Dosing of First Patient in Phase 1 Open-Label Clinical Trial of SNX281 for Advanced Solid Tumors or Lymphoma

SNX281 is a novel systemically available small molecule agonist of Stimulator of Interferon Genes (STING) and the company's first investigational candidate to enter the clinic

The study will be comprised of two treatment arms, one evaluating SNX281 as a monotherapy, and the other evaluating SNX281 in combination with the PD-1 inhibitor pembrolizumab

BOSTON, NOV. 23, 2020 — Silicon Therapeutics, a privately-held, integrated therapeutics company with a pioneering platform based on physics-driven molecular simulations, today announced treatment of the first patient with its therapeutic candidate SNX281 in a Phase 1 clinical trial in patients with advanced solid tumors or lymphoma. Wholly owned by Silicon Therapeutics, SNX281 is a small molecule Stimulator of Interferon Genes (STING) agonist with systemic exposure that was designed using unique insights and capabilities provided by the Silicon Therapeutics proprietary physics-driven drug discovery platform.

This Phase 1 open-label, multicenter, multidose, first-in-human clinical trial of SNX281 will evaluate the safety and tolerability of SNX281 alone and in combination with the PD-1 inhibitor pembrolizumab in subjects with relapsed or refractory solid tumors or lymphomas. The trial is designed to enroll up to 128 patients.

"The initiation of this study is a significant milestone for Silicon Therapeutics, as it marks the entry of our lead therapeutic into clinical development. The speed with which we have arrived at this milestone from our foundation in 2016 is a testament to Silicon Therapeutics' unique platform. Computational physics-driven drug discovery has truly come to fruition with our delivery of this new experimental medicine," said Lanny Sun, co-founder and chief executive officer. "As we navigate the unprecedented COVID-19 pandemic, we are leveraging virtual capabilities to initiate clinical trial sites, while ensuring patient and clinician safety is our top priority. We are incredibly grateful to the patients and their families, investigators and their clinical study sites, and our employees for advancing a program with the potential to treat patients suffering from challenging and life-threatening cancers."

The company's proprietary platform is being used to design additional first-in-class small molecules targeting key drivers of disease in cancer that have proven difficult to treat with prior approaches and thus previously considered undruggable. The discovery platform is fully integrated with Silicon Therapeutics' internal laboratories using cutting edge experimental capabilities in biophysics, biology and chemistry.

"There have been important advancements in immunotherapy treatments for cancer in recent years, but many patients do not benefit and therefore new approaches to stimulate effective anti-tumor responses are needed in the clinic," said Humphrey Gardner, M.D., F.C.A.P, chief medical officer. "We are excited about the potential of SNX281 to treat a broad array of cancers given its strong pre-clinical activity both as a single agent and in combination with a PD-1 inhibitor. We look forward to sharing the near- and long-term data as it becomes available."

About the SNX281 Clinical Trial

The purpose of this Phase 1 multi-center, open-label study is to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and clinical activity of SNX281 as a monotherapy and in combination with pembrolizumab, a monoclonal antibody immunotherapy for the treatment of cancers. Dose escalation in monotherapy and combination will be explored in patients with advanced solid tumors or lymphoma. After determination of the optimal dose of SNX281 as a single-agent and in combination with pembrolizumab, expansion cohorts to further evaluate safety and efficacy in specific populations will be examined, including colorectal and ovarian carcinoma in the monotherapy arm, and tumors refractory to or relapsed on checkpoint inhibitors in the combination arm.

For more information about the SNX281 clinical trial (NCT04609579), please visit: https://clinicaltrials.gov.

ABOUT SNX281

Activation of STING provides two critical anti-tumor responses: the "spark" for initiating a robust innate immune response as well as the priming and induction of a robust tumor directed T cell response, providing sustained antitumor immunity. First generation clinical compounds are structural mimetics of endogenous cyclic dinucleotides (CDNs) STING agonists and cannot be delivered systemically, thus limiting use to local delivery via intra-tumoral injection.

To address these limitations, the Silicon Therapeutics team has designed and developed the small molecule STING agonist SNX281 with unique drug properties permitting systemic delivery. SNX281 is potent, specific and active against all prevalent human isoforms of STING, rapidly activating downstream signaling and induction type I interferon (IFN). Treatment of primary immune cells from human donors results in the maturation and activation of antigen presenting cells. *In vivo*, SNX281 stimulates cross-presentation, antigen-specific T cell response and rapid multi-lineage anti-tumor immunity.

In preclinical disease models, treatment with SNX281 results in complete regression of tumors in mice harboring colorectal tumors (CT26) with a single intravenous dose. This anti-tumor activity was shown to be immune-mediated, as it did not occur in immunocompromised mice. Further, the combination of an anti-PD-1 antibody with SNX281 demonstrated both enhanced anti-tumor activity as well as increased survival in a variety of additional tumor models.

SNX281 drug characteristics and STING pharmacology allow for a unique dosing paradigm with robust tumor regression after a short duration of exposure, and durable anti-tumor immunity.

ABOUT SILICON THERAPEUTICS

Silicon Therapeutics is a privately-held, fully integrated drug design and development company focused on small molecule therapeutics. The Silicon Therapeutics proprietary physics-driven drug design platform combines quantum physics, statistical thermodynamics, molecular simulations, a dedicated HPC super-computing cluster, purpose-built software, in-house laboratories and clinical development capabilities. The platform was built from the ground up to address difficult targets using physics-based simulations and experiments to pioneer a new path for drug design with the prime goal of delivering novel medicines to improve the lives of patients.

Silicon Therapeutics is currently the only company that owns the entire spectrum of proprietary physics-driven drug discovery from chip-to-clinic. The company's lead program is a highly differentiated small molecule Stimulator of Interferon Genes (STING) agonist for the treatment of cancer. The company's

headquarters are located in Boston. To learn more about Silicon Therapeutics, please visit our website at www.silicontx.com or follow us on LinkedIn and Twitter.

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