TRISALUS LIFE SCIENCES' PRESSURE-ENABLED DRUG DELIVERY (PEDD) INCREASES PENETRATION AND ANTITUMOR ACTIVITY OF ANTI-CEA CAR-T IN MOUSE MODEL OF LIVER METASTASES

- **High-pressure PEDD delivery of chimeric antigen receptor T cell (CAR-T) significantly increased antitumor activity compared with low-pressure delivery**
- **No increase in liver inflammation or toxicity**
- **PEDD -18% tumor burden compared to +148 in low-pressure delivery (*P*=0.05), and +178% in saline controls (*P*=0.04)**
- **Checkpoint inhibitors delivered regionally with high-pressure PEDD also significantly increased the therapeutic index for colorectal liver metastases, while limiting systemic exposure**

SAN DIEGO, CA—May 11, 2019—A preclinical trial to be presented at the annual meeting of the American Association of Immunologists (AAI) demonstrates that administering anti–carcinoembryonic antigen (anti-CEA) CAR-T to liver metastases using high delivery pressure in an animal model simulating TriSalus™ Life Sciences' innovative Pressure-Enabled Drug Delivery™ (PEDD™) significantly increased penetration and antitumor activity when compared with standard low-pressure (LP) delivery.

PEDD delivery of CAR-T: Increased penetration, greater therapeutic effect

In the anti-CEA CAR-T study performed by Dr. Steven Katz, MD, director of the Office of Therapeutic Development at the Roger Williams Medical Center, mice with CEA+ liver metastases were infused employing simulated PEDD technology (HP cohort) or by standard means (LP cohort). Hepatic interstitial fluid pressures were simultaneously recorded. One day after infusion, flow cytometry assessment demonstrated a significantly greater cell therapy product delivery in the PEDD/HP cohort, 15.9% CD3+CAR, compared with 5.1% in the LP cohort (*P*=0.0004).

"Higher delivery pressure, such as that achieved with TriSalus devices in patients, correlated with higher CAR-T penetration that better controlled tumor growth," said Dr. Katz, who is also the principal investigator of the ongoing clinical Phase 1b trial using

Sorrento's (Sorrento Therapeutics, Inc. [NASDAQ: SRNE]) CEA–CAR-T cells for the treatment of liver metastases. "We have seen excellent CEA–CAR-T delivery in our clinical studies using PEDD. Follow-up to this proof-of-concept study will investigate combination approaches, with the goal of durable tumor eradication."

PEDD delivery of checkpoint inhibitors shown to reduce colorectal liver metastases — even with 10-fold lower dose

In a separate poster presentation at the AAI annual meeting, significant increases in therapeutic index also occurred when PEDD was used to deliver anti–PD-1 checkpoint inhibitors (CPI) regionally to colorectal liver metastases.

In this study, mice with colorectal liver metastases treated with regional PEDD high-pressure delivery (HP cohort) were administered a 3- or 10-fold *lower* dose of CPI than is typically given systemically to patients. Mice treated with regional HP CPI infusions showed significantly lower tumor burden than animals given a low-pressure (LP) infusion (P=0.04 and P=0.0001, respectively) at early time points. Importantly, HP regional delivery at the lower doses resulted in similar tumor control to mice receiving conventional systemic doses, with significantly less systemic CPI exposure.

"These results add to the growing body of clinical evidence that TriSalus Life Sciences' PEDD technology overpowers high pressure to penetrate solid tumors and enhance the reach and efficacy of therapeutic agents while reducing systemic toxicity," said Mary T. Szela, CEO and president of TriSalus Life Sciences.

About TriSalus™ Life Sciences

TriSalus Life Sciences is committed to transforming outcomes for patients with pancreatic cancer and other solid tumors. Our solution is bold: to integrate novel and proprietary therapeutics with the TriSalus Pressure-Enabled Drug Delivery™ (PEDD™) technology. It's a comprehensive approach intended to improve treatment response and, ultimately, outcomes.

The PEDD platform increases drug concentration in the tumor by generating favorable pressure to overcome the infusion barriers of the tumor microenvironment. The integration of PEDD with chemotherapy, immunotherapy, and other emerging therapies may improve treatment efficacy while reducing the toxicity challenges of traditional delivery methods.

Acknowledging that meaningful progress in this difficult-to-treat disease is not easy, we're committed to transforming the battle with pancreatic cancer through deep science, novel technology innovation, and an absolute focus on the patient.

For more information, please visit www.trisaluslifesci.com.

About Sorrento Therapeutics, Inc.

Sorrento is a clinical stage, antibody-centric biopharmaceutical company developing new therapies to turn malignant cancers into manageable and possibly curable diseases. Sorrento's multimodal, multipronged approach to fighting cancer is made possible by its extensive immuno-oncology (I-O) platforms, including key assets such as fully human antibodies (G-MAB™ library), clinical-stage immunocellular therapies (CAR-T), intracellular targeting antibodies (iTAbs), antibody-drug conjugates (ADCs), and clinical-stage oncolytic virus (Seprehvir®).

Sorrento's commitment to life-enhancing therapies for cancer patients and osteoarthritis (OA) patients is also demonstrated by its effort to advance Resiniferatoxin (RTX), a first-in-class (TRPV1 agonist) nonopioid pain management small molecule, ZTlido® and SP-102, a nonopioid corticosteroid gel. Resiniferatoxin is completing a Phase 1b trial in terminal cancer patients and a Phase 1b trial for OA. ZTlido was approved by US FDA on 02/28/18. SP-102 (Semdexa™) is in Phase 3 pivotal study for the treatment of lumbar radicular pain/sciatica.

For more information, visit www.sorrentotherapeutics.com. More information on Sorrento clinical trials can be found at www.clinicaltrials.gov.

Media contact:

Edna Kaplan
KOGS Communication
kaplan@kogspr.com
781-639-1910 – office
617-974-8659 – mobile