Senti Bio Highlights Colorectal Cancer Preclinical Data from Logic Gated CAR-NK Cell Program at 36th SITC Annual Meeting

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- SENTI-401 engineered to target colorectal cancer cells while sparing healthy cells -

- Preclinical proof-of-concept data suggest that Logic Gated gene circuits can be used in CAR-NK cells to prevent target-mediated toxicity on healthy epithelial tissues -

SOUTH SAN FRANCISCO, Calif., November 12, 2021 —Senti Bio, a leading gene circuit company, today announced results from SENTI-401, one of its preclinical stage oncology programs, that aims to more precisely target tumors while sparing healthy cells. The poster presentation, which is on display starting today at the Annual Meeting of the Society for Immunotherapy of Cancer (SITC), describes preclinical data from SENTI-401, a Logic Gated allogeneic, chimeric antigen receptor natural killer (CAR-NK) cell therapy development program for the treatment of colorectal cancer (CRC). The results support the Company's vision of using gene circuits to create next-generation, "smart" cell and gene therapies with computer-like logic in human cells.

Targeting of tumor-associated antigens, such as carcinoembryonic antigen (CEA), can result in severe clinical toxicities due to the killing of healthy epithelial cells whose cell surfaces also express CEA. This includes toxicity risk to cells in the colon and gastrointestinal tract as well as the lungs. SENTI-401 is designed to incorporate logic gating to target and kill CEA-expressing tumor cells, while preventing the killing of CEA-expressing healthy epithelial cells. The SENTI-401 NOT GATE pairs a CEA-targeting activating-CAR (aCAR) with an inhibitory-CAR (iCAR) that recognizes a safety antigen (SA) uniquely expressed in certain healthy gastrointestinal and lung epithelial cells. The SA was identified and validated through Senti Bio's proprietary Bioinformatics-Driven Antigen Pairing (B-DAP) discovery platform. The poster highlights the SENTI-401 development program's NOT GATE gene circuit technology as follows:

Killing of colorectal cancer cells:

- Generated, tested and optimized anti-CEA CAR constructs for optimal performance in NK cells using Senti Bio's Design-Build-Test-and-Learn (DBTL) platform.
- Evaluated CAR-NK cells for anti-tumor activity, and demonstrated potent killing of CEA-expressing CRC target cells in vitro. A single dose of these CAR-NK cells also demonstrated anti-tumor activity in a human CRC xenograft model, reducing tumor burden in >33% of the treated mice.

Preservation of healthy cells:

- iCAR suppressed aCAR mediated killing ($p<0.05$) in a SA-dependent manner without diminishing aCAR-mediated anti-tumor activity.
- V-set and Immunoglobulin Domain Containing 2 (VSIG2), a membrane protein, was identified as the SA via Senti Bio's B-DAP discovery platform and validated in healthy tissue samples. VSIG2 is uniquely expressed in CEA-positive healthy cells but not in tumor cells.
- Used Senti Bio's DBTL platform to evaluate multiple iCAR designs that utilize inhibitory domains that can selectively prevent CAR-mediated killing in an SA-dependent manner.

"Existing cancer therapies generally target only a single tumor-associated antigen, which means that they can only be used safely and effectively where that antigen is expressed primarily on tumor cells," said Alba Gonzalez, PhD, presenter of the abstract and Associate Director, Research at Senti Bio. "What is so exciting about our Logic Gating platform is the potential to advance a highly novel approach to CAR-NK based therapy that may more precisely treat colon cancer, and other solid tumors, with a reduced risk for on-target, off-tumor toxicities, thereby offering the potential to increase the therapeutic window and provide meaningful benefit to patients."

The abstract (Poster #116) is available on the SITC website. The poster is available on the Senti Bio website.

About Logic Gating and NOT GATE Gene Circuits

Logic Gating gene circuits are designed to enable cell and gene therapies to control their therapeutic activity in response to the presence or absence of multiple disease biomarkers. NOT GATE gene circuits are one type of Logic Gates that are designed to widen the therapeutic window by enabling killing of cancer cells while preserving healthy cells. The NOT GATE functions by recognizing Safety Antigens on the cell surface, or antigens that are selectively expressed on healthy cells and not on cancer cells, thus limiting on-target, off-tumor killing. By protecting healthy cells, the NOT GATE has the potential to enable more effective on-target, on-tumor killing of tumor cells that express tumor-associated antigens.

About Senti Bio

Our mission is to create a new generation of smarter medicines that outmaneuver complex diseases in ways previously inconceivable. To accomplish this mission, we are building a synthetic biology platform that we believe may enable us to program next-generation cell and gene therapies with what we refer to as “gene circuits.” These gene circuits, which are created from novel and proprietary combinations of DNA sequences, are designed to reprogram cells with biological logic to sense inputs, compute decisions and respond to their cellular environments. We aim to design gene circuits to improve the “intelligence” of cell and gene therapies in order to enhance their therapeutic effectiveness against a broad range of diseases that conventional medicines do not readily address. For more information, please visit the Senti Bio website at https://www.sentibio.com.

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