Senti Bio to Present Data from CAR-NK Cell Oncology Pipeline at ASGCT 24th Annual Meeting

- Using Logic Gating gene circuits, Senti Bio is engineering allogeneic CAR-NK cells to target and more precisely eliminate cancer cells while sparing healthy cells –

- Using a Regulator Dial gene circuit, Senti Bio regulated gene expression in preclinical in vivo models via FDA-approved, orally dosed NS3 inhibitors -

South San Francisco, Calif., May 11, 2021 —Senti Bio, a leading gene circuit company, announced presentations on its gene circuit-engineered allogeneic CAR-NK cell therapy pipeline at the American Society of Gene and Cell Therapy (ASGCT) 24th Annual Meeting. The presentations provide details of select gene circuit platform technologies being developed by the Company, specifically Logic Gating and Regulator Dial gene circuits. Logic Gating gene circuits are designed to enable cell and gene therapies to sense inputs, compute decisions and respond to their cellular environments. Regulator Dial gene circuits are designed to enable the precise tuning, via dosing of an oral small molecule drug, of therapeutic activity from cell and gene therapies once they have been delivered into patients.

Senti Bio is designing gene circuits to create a new generation of “smarter medicines" to potentially enhance the therapeutic effectiveness of cell and gene therapies against a broad range of diseases that cannot be readily addressed by current standards of care.

Precise Tumor Targeting with NOT Logic-Gated Chimeric Antigen Receptor Gene Circuits
Frankel et al. Digital Presentation: Tuesday May 11 from 8:00–10:00am ET (Abstract# 960)

Using a Logic Gated gene circuit (NOT GATE) in a preclinical study, the authors demonstrated the more precise killing of targeted cells by sparing healthy cells that express a Safety Antigen, to address the challenge of limiting on-target, off-tumor killing. NOT GATE gene circuits are designed to widen the therapeutic window by enabling effective killing of cancer cells while preserving healthy cells. The preclinical results are summarized as follows:

- The NOT GATE gene circuit enabled more precise killing of target cells, discriminating them from Safety Antigen (SA)-expressing healthy cells on a cell-by-cell basis; and
- The NOT GATE was shown to be broadly applicable across different sets of antigens and cell types, including NK cells and T cells.

Precise Targeting of AML with OR / NOT Logic-Gated Gene Circuits in CAR-NK Cells
Garrison et al. Oral Presentation: Wednesday May 12 from 6:00–6:15pm ET (Abstract# 77)

Using Logic Gated gene circuits, the authors engineered CAR-NK cells with the goal of overcoming some of the limitations of previous cell therapies for acute myeloid leukemia (AML), specifically the challenge of distinguishing between tumor cells and healthy cells. The OR GATE gene circuit is designed to address tumor heterogeneity and limit antigen escape. The NOT GATE gene circuit is designed to widen the therapeutic window by enabling effective killing of cancer cells while preserving healthy cells. Senti Bio is developing an OR GATE + NOT GATE allogeneic CAR-NK cell therapy that targets and eliminates AML cells while sparing healthy hematopoietic stem and progenitor cells (HSCs/HSPCs). Logic Gated allogeneic CAR-NK cell technology may have applicability to other tumor-associated antigens that are limited by potential off-tumor toxicity. The preclinical results are summarized as follows:

- The OR GATE was designed to target both tumor-associated antigens CD33 and FLT3, with the aim to provide increased clearance of AML blasts and leukemic stem cells respectively, to demonstrate the potential to allow for a deeper patient response and lower relapse rate; and
- The NOT GATE protected healthy HSCs/HSPCs from off-tumor killing via a Safety Antigen, Endomucin (EMCN).

Small Molecule-Regulated Gene Circuit for Controlling Cytokine Expression in Cell Therapies
Hung et al. Oral Presentation: Friday May 14 from 1:45–2:00pm ET (Abstract# 214)

Using a Regulator Dial gene circuit, the authors demonstrated control of gene expression in a preclinical model via FDA-approved, orally dosed nonstructural protein 3 (NS3) inhibitors as a way to potentially address the challenge of modulating the dose of cytokines (e.g. IL-12) produced by cell therapies even after they have been delivered *in vivo*. Controlling the induction of IL-12, if successfully transitioned to a clinical setting, would potentially enable the recruitment of endogenous immune cells to help further mount an antitumor immune response, while keeping IL-12 production at a safe and non-toxic level systemically. The preclinical results are summarized as follows:

- A Regulator Dial gene circuit capable of drug-inducible regulation of gene expression was optimized for safety (low basal gene expression) and inducibility (high fold change upon small molecule dosing) in primary immune cells;
- The Regulator Dial gene circuit was used to regulate IL-12 production in primary immune cells and demonstrated >100-fold dynamic range of control of IL-12 levels *in vivo*; and
- Regulator Dial gene circuits may also be applied to the regulation of additional cytokines and immune effectors to enhance efficacy of CAR immune cells.

Abstracts are available on the ASGCT website.

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 have built a synthetic biology platform that enables 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, reprogram cells with biological logic to sense inputs, compute decisions and respond to their cellular environments. We are designing 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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