Senti Bio Highlights Preclinical Advances on Pipeline Candidate SENTI-202 at ASH 2021 Annual Meeting

- Preclinical data demonstrates complete functionality of SENTI-202 OR+NOT Logic Gated gene circuits for the elimination of AML cancer cells while sparing healthy stem cells -

- Presentation to be featured in virtual ASH Poster Walk intended to highlight recent NK cell advances for improved cancer therapies -

South San Francisco, Calif., December 13, 2021 —Senti Bio, a leading gene circuit company, announced new preclinical data from its gene circuit-engineered allogeneic CAR-NK cell therapy pipeline in a session yesterday at the American Society of Hematology (ASH) Annual Meeting and Exposition being held December 11–14. The presentation highlighted one of Senti Bio's pipeline candidates, SENTI-202, a next-generation cell therapy engineered with Logic Gated gene circuits.

In addition, the poster presentation was selected for inclusion in the virtual ASH Poster Walk on Natural Killer Cell-Based Immunotherapy taking place on Wednesday, December 15, 2021 from 5:00–6:00pm ET. The presenting author will discuss SENTI-202 and the role that a Logic Gated CAR-NK cell therapy product may have in potentially transforming the acute myeloid leukemia (AML) treatment landscape.

"Last night's presentation and the upcoming poster walk represent a significant milestone for Senti Bio—we have showcased our ability to engineer primary NK cells with sophisticated therapeutic gene circuits, demonstrating preclinical proof-of-concept of SENTI-202 on both killing of tumor cells and protection of healthy primary human hematopoietic stem cells," said Tim Lu, MD, PhD, co-founder and chief executive officer of Senti Bio. "I am incredibly proud of the team that made this possible, and could not be more excited about the potential that our allogeneic CAR-NK cell product candidate may hold for patients with AML."

In the abstract titled *FLT3 OR CD33 NOT EMCN Logic Gated CAR-NK Cell Therapy (SENTI-202) for Precise Targeting of AML*, the authors engineered allogeneic CAR-NK cells using Logic Gated gene circuits that broadly target AML cancer cells while sparing healthy cells. The OR GATE gene circuit is designed to address tumor heterogeneity and limit antigen escape by attacking multiple tumor-associated antigens, FLT3 OR CD33. The NOT GATE gene circuit is designed to widen the therapeutic window by preserving healthy primary cells while enabling effective killing of cancer cells. Senti Bio is developing an OR GATE + NOT GATE allogeneic CAR-NK cell therapy product candidate that targets and eliminates AML cells while sparing healthy hematopoietic stem and progenitor cells (HSCs/HSPCs). The preclinical results are summarized as follows:

- Efficient derivation of primary NK cells expressing all SENTI-202 components: 1. bivalent FLT3/CD33 *activating* CAR (OR GATE), 2. EMCN *inhibitory* CAR (NOT GATE), and 3. calibrated release IL-15 (crIL-15);
- OR Gated CAR-NK cells targeting FLT3 or CD33 demonstrated enhanced killing of AML cell lines in primary patient samples *in vitro*, and in multiple xenograft models *in vivo*, with the clinical aim of providing increased clearance of AML blasts and leukemic stem cells, respectively, and ultimately allowing for a deeper patient response and lower relapse rate;
- NOT Gated CAR-NK cells demonstrated significant *in vitro* and *in vivo* protection of model healthy cells from off-tumor killing via *inhibitory* CAR recognition of healthy cell safety antigen targets, as well as significant *in vitro* protection of primary healthy HSCs/HSPCs from off-tumor CAR-NK cell toxicity via the Endomucin (EMCN) healthy cell safety antigen, which is broadly expressed on healthy HSCs/HSPCs, but not on AML tumor cells;
- CAR-NK cells expressing Senti Bio's novel crIL-15 cytokine demonstrated significant tumor cell killing and persistence over CAR-NK cells expressing soluble IL-15 within an *in vitro* serial killing assay.

Rationale For Engineering CAR-NK Cells With Logic Gated Gene Circuits To Treat Cancer

An underlying challenge with oncology cell therapy is to effectively kill cancer cells while avoiding toxicity to healthy cells. This is particularly true in developing therapies to treat acute myeloid leukemia (AML), which lacks AML-specific tumor-associated antigens. SENTI-202 is a Logic Gated allogeneic CAR-NK cell therapy product candidate designed to target and eliminate multiple AML tumor cell types, including the critical leukemic stem cells that contribute to disease relapse, while sparing a patient's healthy hematopoietic stem and progenitor cells (HSCs/HSPCs).

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 activity 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.

Contact Senti Bio:

Deborah Knobelman, PhD, CFO

Email: corporate@sentibio.com

Denise Powell (Media)

Email: denise@redhousecomms.com

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