Senti Bio Presents New Preclinical Data on Cancer-Killing Allogeneic CAR-NK Cells at AACR Annual Meeting

April 8, 2022

- Preclinical data demonstrate the use of gene circuits to improve the therapeutic potential of allogeneic CAR-NK cells for the treatment of solid tumors -

- CAR-NK cells armed with calibrated release IL-15 achieve optimal cytokine distribution and result in superior killing and persistence -

South San Francisco, Calif., April 8, 2022—Senti Bio, a leading gene circuit company, today announced new data from preclinical studies that further demonstrates the Company's ability to arm allogeneic chimeric antigen receptor natural killer (CAR-NK) cells with proprietary gene circuits. The results indicate superior tumor killing and persistence of CAR-NK cells as well as optimal activation of other anti-tumor immune cells.

The authors' preclinical research illustrates the benefits of Senti Bio's calibrated release gene circuit technology to improve CAR-NK cell functions aimed at enhancing solid tumor killing. The poster, titled "Driving anti-tumor activity in solid tumors with controlled arming of allogeneic CAR-NK cells," outlines findings that are potentially relevant to multiple programs that Senti Bio plans to advance into Investigational New Drug (IND)-enabling studies and towards clinical development.

"We observed tumor shrinkage in 62% of the mice treated with CAR-NK cells armed with our crIL-15, whereas in mice treated with CAR-NK cells alone, there was no tumor shrinkage at all, just continued tumor growth, which I believe to be quite dramatic," said Alba Gonzalez, PhD, presenter of the poster and Associate Director, R&D at Senti Bio. "What is so exciting about our Multi-Arming platform is the potential to enhance the function of allogeneic CAR-NK cells—maximizing paracrine and autocrine benefits of cytokines with the aim of increasing the therapeutic window of these cells for the treatment of solid tumors."

- Researchers highlight their ability to arm CAR-NK cells with Senti Bio's proprietary calibrated release interleukin-15 (crIL-15), which results in both cell-surface and secreted IL-15
- CAR-NK cells armed with crIL-15 have superior anti-tumor activity and persistence *in vivo* and demonstrate enhanced activation as measured by increased levels of interferon gamma (IFN-γ) production when co-cultured with tumor cells *ex vivo*
- These studies illustrate the combined advantage of both secreted and cell-surface cytokines that result in optimal engagement of the local immune tumor microenvironment and stimulation of the CAR-NK cells as well
- Further studies with CAR-NK cells containing Multi-Armed gene circuits that express both
- IL-15 and IL-21 show improved CAR-NK anti-tumor activity and persistence

While secreted cytokines are well known to stimulate the immune system to fight solid tumors by activating neighboring cells (paracrine signaling), they are often associated with systemic toxicity. Cell-surface cytokines, by contrast, can cause a more localized (autocrine signaling) and potent stimulation of CAR-NK cells but have limited impact on the broader tumor microenvironment. Senti Bio's novel calibrated release technology provides both paracrine and autocrine effects, resulting in improved CAR-NK cell function in solid tumor models.

Senti Bio's gene circuit technology is being applied in the design of multiple product candidates including SENTI-202 for the potential treatment of acute myeloid leukemia (AML), SENTI-301 for the potential treatment of hepatocellular carcinoma (HCC) and SENTI-401 for the potential treatment of colorectal cancer (CRC). The Company plans to submit IND applications in 2023 to support the clinical evaluation of SENTI-202 and SENTI-301, and in 2024 to support the clinical evaluation of SENTI-401.

The full poster presentation is available on the Senti Bio and AACR websites.

About Senti Bio

Our mission is to create a new generation of smarter medicines that outmaneuver complex diseases using novel and unprecedented approaches. To accomplish this, we are building a synthetic biology platform that 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, precision, and durability against a broad range of diseases that conventional medicines do not readily address. Our synthetic biology platform utilizes allogeneic chimeric antigen receptor natural killer (CAR-NK) cells, outfitted with these Gene Circuit technologies, to target particularly challenging liquid and solid oncology indications, including acute myeloid leukemia, hepatocellular carcinoma, and colorectal cancer. We have also demonstrated the breadth of our Gene Circuits in other modalities and diseases outside of oncology, and have executed partnerships with Spark and BlueRock to advance these capabilities. 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

Find more information at sentibio.com

Follow us on Linkedin: Senti Biosciences

Follow us on Twitter: @SentiBio