Senti Bio Highlights Preclinical Data from Logic-Gated Gene Circuit CAR-NK Cell Therapy SENTI-202 at ASH Annual Meeting and Investor Event

December 11, 2022

– ASH poster presentation summarizes preclinical data from SENTI-202, an off-the-shelf CAR-NK cell therapy candidate engineered with a logic-gated gene circuit and multi-armed with crIL-15, that is advancing toward clinical development for hematologic malignancies –

– SENTI-202 is on track for IND filing in 2H 2023 –

– SENTI-202 aims to more precisely target tumor cells in CD33 and/or FLT3 expressing tumors such as acute myeloid leukemia and myelodysplastic syndrome, while sparing healthy cells –

– Senti Bio Investor Event to include an AML expert; in-person and webcast at 12:30 p.m. ET/11:30 a.m. CT today –

NEW ORLEANS, Dec. 11, 2022 (GLOBE NEWSWIRE) -- Senti Biosciences, Inc. (Nasdaq: SNTI) (“Senti Bio”), a biotechnology company innovating next-generation cell and gene therapies using its proprietary gene circuit platform, today announced a presentation at the American Society of Hematology (ASH) Annual Meeting in New Orleans. The presentation highlights preclinical data that led to the selection of SENTI-202 as the Company's lead oncology candidate. Senti Bio plans to evaluate SENTI-202 in patients with CD33 and/or FLT3 expressing hematologic malignancies including acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS), with an anticipated filing of an Investigational New Drug (IND) application in the second half of 2023.

“The preclinical data presented at ASH demonstrates the progress made with our lead logic-gated gene circuit CAR-NK cell therapy, SENTI-202, which incorporates our OR gate, NOT gate, and calibrated release IL-15 technologies," said Tim Lu, MD, PhD, Chief Executive Officer and Co-Founder of Senti Bio. "In both *in vitro* and *in vivo* models, we observed that SENTI-202 had significant and precise cancer-killing activity against AML, and significant protection of healthy cells from off-tumor cytotoxicity. We are hopeful that these preclinical results will translate into the clinic for patients with AML and MDS. The success of these gene circuits in the clinic would broadly enable off-the-shelf CAR-NK cells that precisely kill cancer cells while sparing healthy cells across multiple tumor indications."

In addition to Senti Bio presenting these data and the initial SENTI-202 clinical development plan, today’s Investor Event will also feature a presentation by Stephen A. Strickland, Jr., MD, MSCI, Director of Leukemia Research for the Sarah Cannon Transplant & Cellular Therapy Network, who will review the current treatment landscape as well as the potential role for next-generation cell therapies in AML and MDS.

"I am excited about the potential for next-generation cell therapies, like SENTI-202, to target multiple disease pathways to overcome the often harsh tumor microenvironment and provide enhanced cancer-killing activity," said Dr. Strickland. "The outcome for patients with AML is poor, with a 5 year relative survival rate of approximately 30% at diagnosis and 5 month overall survival when relapsed/refractory[1]. New therapies with novel mechanisms of action are needed to combat this aggressive disease. I look forward to seeing possible improved treatment for patients and am hopeful that these novel technologies can enable greater tumor clearance with less off-tumor toxicity, and ultimately deeper and longer remissions."

SENTI-202, a Selective, Off-the-Shelf, Preclinical CAR-NK Cell Therapy with CD33 and/or FLT3 Activating CAR, Healthy Cell Protection from Endomucin (EMCN) Inhibitory CAR and Calibrated Release IL-15 for Hematologic Malignancies Including AML, Garrison et al. (Poster presentation: December 10, 2022)
New preclinical data for SENTI-202 were presented supporting Senti Bio’s approach of using an OR Gate to provide robust targeting of AML disease (blasts and leukemic stem cells (LSCs)), and a NOT Gate to protect healthy hematopoietic stem cells (HSCs) from off-tumor toxicity.

- **SENTI-202 demonstrated significant aCAR-mediated anti-tumor activity, including *in vivo* tumor suppression in an AML xenotransplantation model, and significant *in vitro* killing of primary AML blasts and LSCs from patient samples.** Targeting AML LSCs is believed to be essential for achieving longer-lasting remissions and/or curative outcomes and is, the Company believes, a potentially significant differentiating aspect of SENTI-202 compared to available therapies.

- **SENTI-202 demonstrated significant iCAR-mediated *in vitro* protection of primary healthy donor EMCN+ HSCs from off-tumor toxicity, and significant *in vivo* protection of EMCN+ model healthy cells from off-tumor toxicity.** HSCs are responsible for lifelong hematopoiesis, and protecting them from off-tumor toxicity may broaden the therapeutic window for SENTI-202, enabling more precise and potentially more effective treatment.

- **SENTI-202 demonstrated sufficient crIL-15 expression to activate the IL-15 receptor pathway, shown to result in increased CAR-NK cell persistence and killing activity.**

The SENTI-202 poster is available on the Senti Bio website.

To access the Investor Event via webcast, please visit the Events & Presentations page on the Senti Bio website.

1. Am J Blood Res. 2020 Aug 25;10(4):124-133. eCollection 2020.
https://pubmed.ncbi.nlm.nih.gov/32923092/

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 novel and proprietary Gene Circuits 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 off-the-shelf chimeric antigen receptor natural killer (CAR-NK) cells, outfitted with Gene Circuit technologies, to target particularly challenging liquid and solid tumor oncology indications. Our lead product candidate is SENTI-202 for the treatment of CD33 and/or FLT3 expressing hematologic malignancies, such as AML and MDS. We are developing an additional CAR-NK product candidate, SENTI-301A, for the treatment of hepatocellular carcinoma (HCC) and other GPC3 positive cancers. We also have a CAR-NK program for the treatment of colorectal cancer (CRC) and other CEA positive cancers, SENTI-401. We have also demonstrated the breadth of our Gene Circuits in other modalities and diseases outside of oncology and have executed partnerships with Spark Therapeutics and BlueRock Therapeutics to advance these capabilities.

Forward-Looking Statements

This document contains certain statements that are not historical facts and are considered forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These forward-looking statements generally are identified by the words “believe,” “could,” “predict,” “continue,” “ongoing,” “project,” “expect,” “anticipate,” “explore,” “estimate,” “intend,” “strategy,” “future,” “opportunity,” “plan,” “may,” “should,” “will,” “would,” “will be,” “will continue,” “will likely result,” “forecast,” “seek,” “target” and similar expressions that predict or indicate future events or trends or that are not statements of historical matters. Forward-looking statements are predictions, projections and other statements about future events that are based on current expectations of Senti Bio’s management and assumptions, whether or not identified in this document, and, as a result, are subject to risks and uncertainties. Forward-looking statements include, but are not limited to, statements regarding Senti Bio’s research and development activities, including the development of product candidates, progress of IND-enabling studies and the timing of submission of IND filings, plans for advancing SENTI-202 into the clinic, presentation plans at the Investor Event, as well as statements about the potential attributes and benefits of Senti Bio’s product candidates, including their clinical and therapeutic potential, and Senti Bio’s platform technology. These forward-looking statements are provided for illustrative purposes only and are not intended to serve as, and must not be relied on as a guarantee, an assurance, a prediction or a definitive statement of fact or probability. Many actual events and circumstances are difficult or impossible to predict, are beyond the control of Senti Bio and will differ from assumptions. Many factors could cause actual future events to differ materially from the forward-looking statements in this document, including but not limited to the risk that results observed in studies of its product candidates, including preclinical studies and future clinical trials of any of its product candidates, will not be observed in ongoing or future studies involving these product candidates, the risk that Senti Bio may cease or delay clinical development of any of its product candidates for a variety of reasons (including requirements that may be imposed by regulatory authorities on the initiation or conduct of clinical trials, the amount and type of data to be generated, or otherwise to support regulatory approval, difficulties or delays in subject enrollment and continuation in current and planned clinical trials, difficulties in manufacturing or supplying Senti Bio’s product candidates for preclinical and clinical testing, and any adverse events or other negative results that may be observed during preclinical or clinical development), Senti Bio’s ability to obtain, maintain and protect its intellectual property, Senti Bio’s dependence on third parties for development and manufacture of product candidates, Senti Bio’s ability to manage expenses and to obtain additional funding when needed to support its business activities and establish and maintain strategic business alliances and new business initiatives, the impacts of macroeconomic and geopolitical events, including changing conditions from the COVID-19 pandemic, the hostilities in Ukraine, increasing rates of inflation and rising interest rates on business operations and expectation, and the risk that its product candidates may not produce therapeutic benefits or may cause other unanticipated adverse effects. The foregoing list of factors is not exhaustive. You should carefully consider the foregoing factors and the other risks and uncertainties described in the “Risk Factors” section of Senti Bio’s Form 10-Q filed with the SEC on November 10, 2022, and other documents filed by Senti Bio from time to time with the SEC. These filings identify and address other important risks and uncertainties that could cause actual events and results to differ materially from those contained in the forward-looking statements in this document. There may be additional risks that Senti Bio does not presently know, or that Senti Bio currently believes are immaterial that could also cause actual results to differ from those contained in the forward-looking statements in this document. Forward-looking statements speak only as of the date they are made. Senti Bio anticipates that subsequent events and developments may cause Senti Bio’s assessments to change. Except as required by law, Senti Bio assumes no obligation to update publicly any forward-looking statements, whether as a result of new information, future events, or otherwise.

Availability of Other Information About Senti Bio

For more information, please visit the Senti Bio website at https://www.sentibio.com or follow Senti Bio on Twitter (@SentiBio) and LinkedIn (Senti Biosciences). Investors and others should note that we communicate with our investors and the public using our company website (www.sentibio.com), including, but not limited to, company disclosures, investor presentations and FAQs, Securities and Exchange Commission filings, press releases, public conference call transcripts and webcast transcripts, as well as on Twitter and LinkedIn. The information that we post on our website or on Twitter or LinkedIn could be deemed to be material information. As a result, we encourage investors, the media and others interested to review the information that we post there on a regular basis. The contents of our website or social media shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended.

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