UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 11, 2022

SENTI BIOSCIENCES, INC.
(Exact name of registrant as specified in its charter)

Delaware	001-40440	86-2437900
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

2 Corporate Drive, First Floor
South San Francisco, California 94080
(Address of principal executive offices including zip code)

Registrant's telephone number, including area code: (650) 382-3281

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	**SNTI**	**The Nasdaq Global Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Item 8.01 Other Events.

On December 11, 2022, Senti Biosciences, Inc., (the "Company") issued a press release announcing a presentation at the American Society of Hematology ("ASH") annual meeting in New Orleans. Copies of the press release and the presentation slide deck presented at the ASH annual meeting are filed herewith as Exhibits 99.1 and 99.2 to this Current Report on Form 8-K and incorporated by reference herein.

The Company has also updated certain corporate information in a presentation slide deck. A copy of this corporate presentation is filed herewith as Exhibit 99.3 to this Current Report on Form 8-K and incorporated by reference herein.

Cautionary Statement

This filing and the exhibits include "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). We intend these forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Exchange Act, and are making this statement for purposes of complying with those safe harbor provisions. These forward-looking statements reflect our current views about our plans, intentions, expectations, strategies, and prospects, which are based on the information currently available to us and on assumptions we have made. Important factors that may cause actual results to differ materially from those described in the forward-looking statements are disclosed in the respective exhibits and in the "Risk Factors" contained in the Company's Form 10-Q filed with the Securities and Exchange Commission (the "Commission") on November 10, 2022, and other filings we make with the Commission. All forward-looking statements are expressly qualified in their entirety by such factors. We do not undertake any duty to update any forward-looking statement except as required by law.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release, dated as of December 11, 2022
99.2	Presentation for American Society of Hematology annual meeting.
99.3	Corporate presentation.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

SENTI BIOSCIENCES, INC.

Date: December 12, 2022

By: /s/ Timothy Lu
Name: Timothy Lu, M.D., Ph.D.
Title: Chief Executive Officer & President

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

– 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, La., December 11, 2022 — 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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Find more information at sentibio.com
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Investor Event
December 2022
DECEMBER 2022 INVESTOR EVENT | SENTI BIOSCIENCES
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Disclaimer

Forward Looking Statements

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Trademarks

This document contains references to trademarks, trade names and service marks belonging to other entities. Solely for convenience, trademarks, trade names and service marks referred to in this presentation may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that the applicable owner will not assert, to the fullest extent under applicable law, its rights to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entities.

Agenda

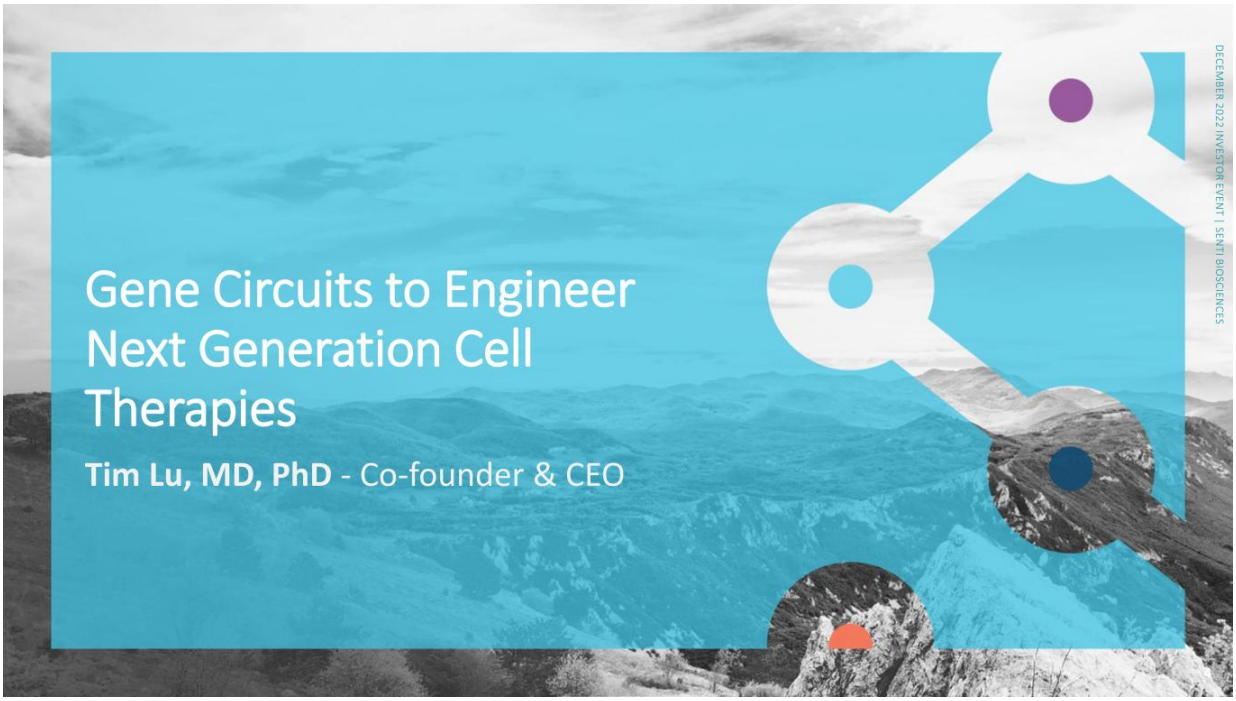
Gene Circuits to Engineer Next Generation Cell Therapies
Tim Lu, MD, PhD – Co-founder & CEO

Treatment Paradigm and Unmet Medical Need in AML
Stephen A. Strickland, Jr., MD, MSCI - Director of Leukemia Research at the Sarah Cannon Transplant & Cellular Therapy Network

Update on SENTI-202 For Heme Malignancies
Kanya Rajangam, MD, PhD – Chief Medical and Development Officer (CMDO)

Conclusions and Next Steps
Tim Lu, MD, PhD – Co-founder & CEO

Q&A


DECEMBER 2022 INVESTOR EVENT | SENTI BIOSCIENCES
Gene Circuits to Engineer Next Generation Cell Therapies
Tim Lu, MD, PhD - Co-founder & CEO

Senti's Next Generation Gene Circuit Technologies for Cancer Cell Therapy

Gene Circuits for Cell Therapy:


Multi-Arming


Logic Gating


Regulator Dial

Can be applied to:


NK Cells


T Cells


iPSCs


HSCs

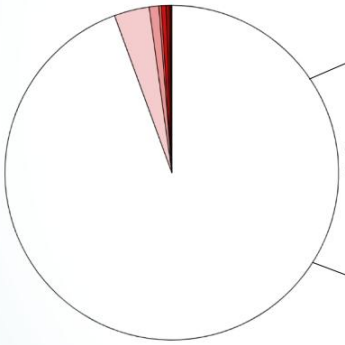
Aim to..

- Enhance durability and persistence
- Address efficacy AND safety
- Increase specificity and dosing window
- Broaden patient access
- Address large unmet needs across multiple solid and liquid tumors

NK Cells: Natural Killer Cells, iPSCs: induced pluripotent stem cells, HSCs: hematopoietic stem cells

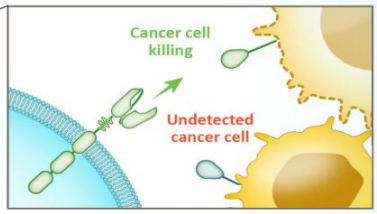
Today's Cell Therapies Are Largely Guided by Single CAR System and Limited to a Small Set of Potential Therapeutic Targets

Only ~5% of potential surface proteins have been utilized in CAR therapies

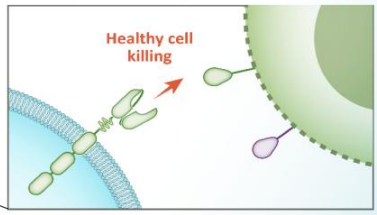


Two key limitations of today's cell therapies

Heterogeneous antigen expression leading to tumor escape

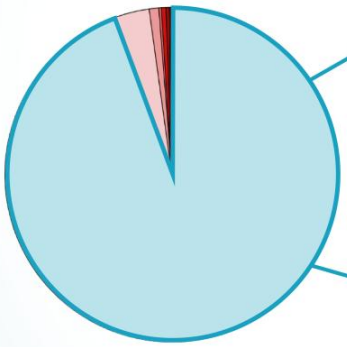


On-target / off-tumor killing leading to poor therapeutic window



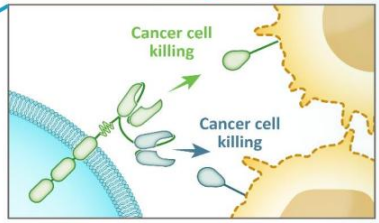
Senti's Gene Circuit Technology Has the Potential to Expand the Range of CAR Cell Therapies With Enhanced Efficacy and Precision

Expanding the range of potential therapeutics into the "empty" space

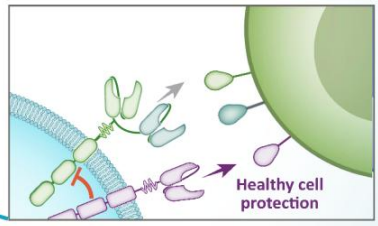


Senti's next-gen capabilities

Bivalent activating CAR: OR GATE



Inhibitory CAR: NOT GATE



Gene Circuits Designed to Solve for Key Cell Therapy Challenges

Cancer Cell Therapy Challenges	Senti's Gene Circuit Solutions	
Lack of NK cell expansion and persistence	Multi-Arming	Autocrine and paracrine activation with proprietary **Calibrated Release** IL-15 (crIL-15) and other complementary cytokines (e.g., IL-21)
Antigen escape and tumor heterogeneity	Logic Gating	Bivalent activating CAR with **OR Logic Gate**
Dirty targets (on-target / off-tumor toxicity)	Logic Gating	Inhibitory CAR protects healthy cells with **NOT Logic Gate**
Immunosuppressive tumor microenvironment	Regulator Dial	Pulsed Calibrated Release IL-12 with small molecule-controlled **Regulator Dial**

NK Cells Compare Favorably to T Cell Based Therapies, While Gene Circuits Have Potential to Further Improve Efficacy, Safety, and Durability Further

Capabilities	Current Auto T Cells	Senti's CAR-NK Cells
Off-the-shelf potential with broad patient accessibility	✗	✓
Designed with Logic Gates to achieve enhanced selectivity and safety	✗	✓
Engineered with enhanced persistence	N/A	✓
Engineered to stimulate the patient immune system	✗	✓

NK cells are an attractive modality vs T cells

- Extensive clinical experience with ~70 global peripheral blood derived unengineered NK cell therapy clinical trials[1]
- Well-tolerated with no/minimal CRS, neurotoxicity, GvHD
- Anti-tumor activity including CR observed in R/R AML

Key limitations noted with prior unengineered NK cell therapies

- Limited persistence
- Limited ability to cryopreserve
- Scale-up manufacture

Senti's Gene Circuit technology, donor selection and scalable manufacturing aim to address these limitations

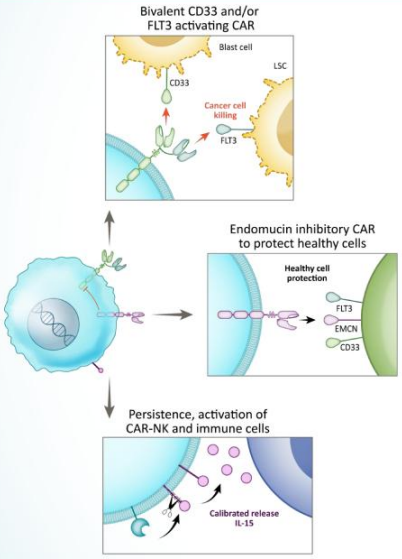
1 Lamers-Kok Journal of Hematology & Oncology 2022
CRS: cytokine release syndrome, GvHD: graft-versus-host disease, AML: acute myeloid leukemia

Senti's Next Generation CAR-NK Cell Therapy Pipeline Tackles Hard to Treat Cancers With Gene Circuits

Program	Target	Indications	Discovery	IND enabling	Phase 1	Gene Circuits
SENTI-202	CD33 and/or FLT3	AML, MDS and other blood cancers		2H 2023 IND		✓ Multi-Arming: designed for enhanced efficacy ✓ crIL-15: autocrine and paracrine activation ✓ OR GATE: bivalent activation ✓ NOT GATE selectivity: healthy cell protection
SENTI-301A	GPC3	HCC and other solid tumors		2023 IND		✓ Multi-Arming: designed for enhanced efficacy ✓ crIL-15: autocrine and paracrine activation
SENTI-401	CEA	CRC and other solid tumors		2024 IND		✓ Multi-Arming: designed for enhanced efficacy ✓ crIL-15: autocrine and paracrine activation ✓ NOT GATE selectivity: healthy cell protection ✓ IL-21: sustained anti-tumor function
Additional Programs	Undisclosed	Other tumors				Program candidates integrate Multi-Arming, Logic Gating and/or Regulator Dial Gene Circuits

MDS: myelodysplastic syndromes, HCC: hepatocellular carcinoma, CRC: colorectal cancerr

SENTI-202, a Novel, Multi-Armed, Off-The-Shelf, Selective CAR-NK Cell Therapy for Blood Cancers Including AML and MDS



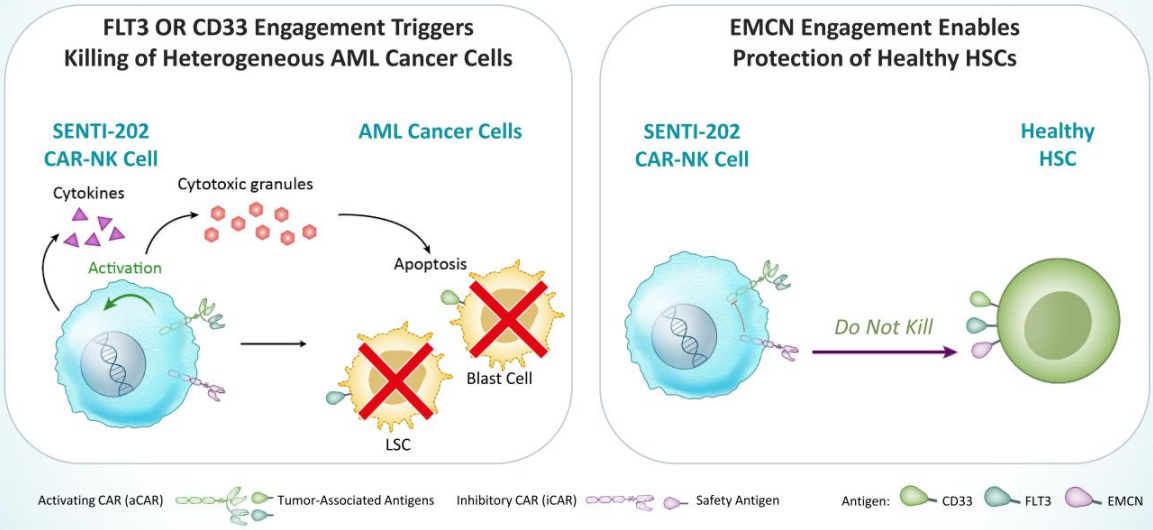
Multi-Armed, off-the-shelf, selective CAR-NK

- ***OR GATE:*** *bivalent* CD33 and/or FLT3 activation → potential for deep and durable responses in acute myeloid leukemia (AML) and other blood cancers.
- ***NOT GATE:*** inhibition by endomucin (EMCN) protective antigen selectively expressed on healthy hematopoietic stem cells (HSCs) → potential for improved safety and increased therapeutic window
- ***crIL-15*** → potential for increased persistence, autocrine and paracrine immune cell activation

On track for IND in 2H 2023

LSCs: Leukemic Stem Cells

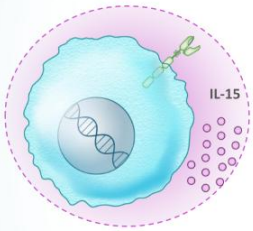
SENTI-202 Logic Gates Are Designed to Achieve Deep Clearance of AML Blasts and LSCs While Sparing Healthy HSCs



Senti's Proprietary crIL-15 Technology Aims to Enhances NK Cell Expansion, Persistence and Tumor Killing

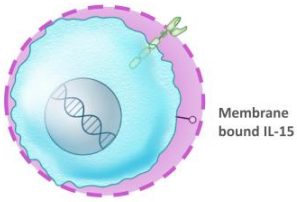
Enhanced NK Cell Expansion, Persistence and Tumor Killing

1. CYTOKINE SECRETION ONLY (PARACRINE)



Secreted IL-15 can activate neighboring immune cells present in the local tumor microenvironment (TME)

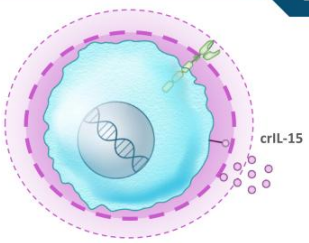
2. MEMBRANE-BOUND ONLY (AUTOCRINE)



Membrane-bound IL-15 on the cell surface leads to autocrine activity and increases CAR-NK cell activity/function

3. CALIBRATED RELEASE (cr) (PARACRINE AND AUTOCRINE)

Combines 1 & 2

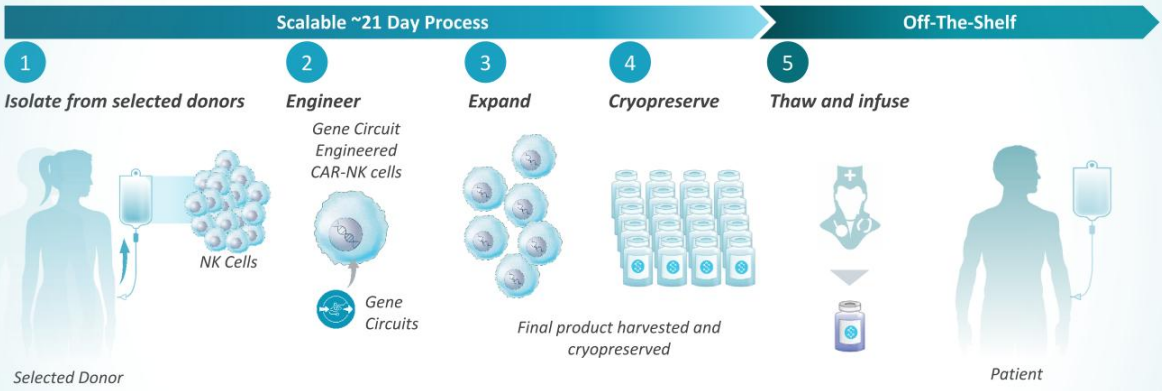


- Secreted IL-15 activates neighboring immune cells present in the local TME
- Membrane-bound IL-15 on the cell surface increases NK cell activity/function

Cell Therapies Using This Approach

SENTI BIO

Scalable Manufacturing to Support Off-The-Shelf CAR-NK Products

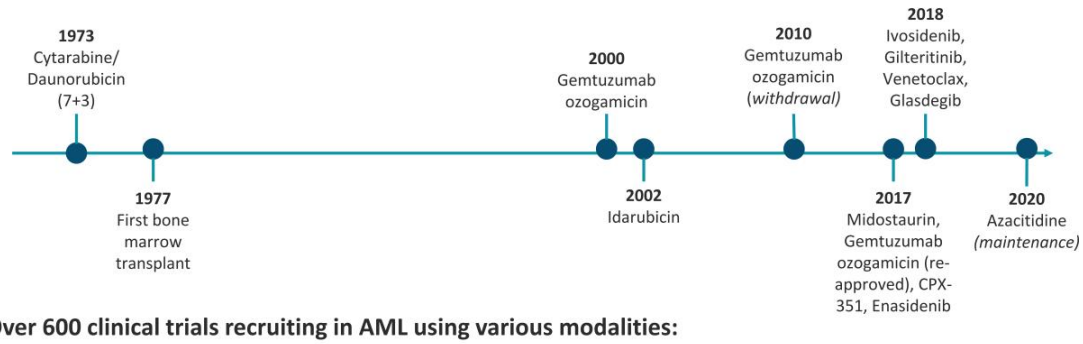


NK cells isolated from peripheral blood of selected donors	NK cells efficiently engineered with Gene Circuits	>100 doses per batch	High post-thaw potency	Easy to thaw vials	Outpatient use potential


DECEMBER 2022 INVESTOR EVENT | SENTI BIOSCIENCES
Treatment Paradigm and
Unmet Medical Need in AML
Stephen A. Strickland, Jr., MD, MSCI - Director of
Leukemia Research at the Sarah Cannon Transplant
& Cellular Therapy Network

History of FDA Approvals and Current Clinical Trials in AML

History of FDA Approvals in AML:



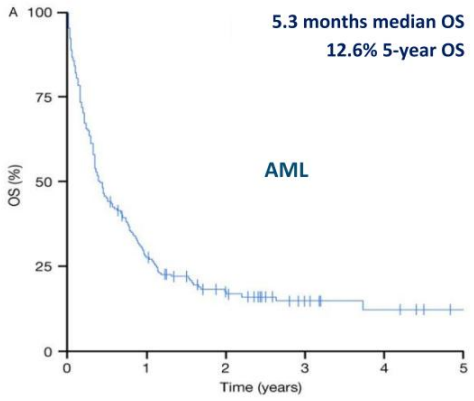
Over 600 clinical trials recruiting in AML using various modalities:

Cell therapies or immune cell engagers directed at AML cells	Cell therapies designed to improve transplant outcomes	Small molecules for genetically defined subsets	Small molecules against broad targets/pathways
ADCs	Monoclonal antibodies	Radiopharmaceuticals	Vaccines

SARAH CANNON

Significant Unmet Need in AML Even with Recent Approvals

- ~14,000 patients are newly diagnosed with AML in the US[1]
- Treatment at diagnosis generally includes intensive chemotherapy consolidated with HCT for younger fitter patients, and hypomethylating agents with venetoclax for older unfit patients
- Even with initial intensive treatment, 20-40% of patients fail to respond to up-front AML therapy while ~50% of those who attain an initial CR eventually relapse[2]
- Prognosis at relapse is grim with ~5-10 months overall survival in R/R AML patients and limited standard of care options that includes FLT3, IDH1/2 inhibitors if relevant mutations are present[3]



5.3 months median OS
12.6% 5-year OS

1 Clarivate source data 2022; 2 Mangan Ther Adv Hematology 2011; 3 Brandwein
Figure from Brandwein Am J Blood 2020

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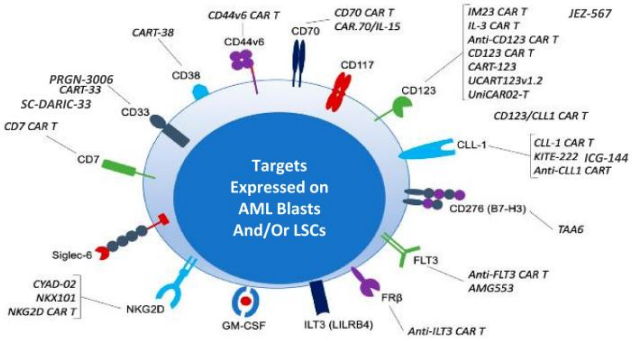
AML Is a Heterogenous Disease and Requires Multi-Antigen Targeting

AML targets are notoriously heterogenous:

Target Antigen Expression on Various Cells[1]			
Antigen	**LSCs**	**Blasts**	**HSCs**
CD33 (SIGLEC3)	+/-	+	+/-
FLT3 (CD135)	+	+/-	+
CLL-1 (CLEC12A)	+/-	+	-
CD123*	+/-	+	+/-
CD38	-	+	-
NKG2D ligands	-	+	-

CAR targets in AML and CAR cell therapies currently in clinical trials[2]:



Targeting LSCs Is Critical in the Treatment of AML but Most CAR-Based Therapies Target Only One Antigen Leading To Incomplete Clearance of Leukemic Blasts and Stem Cells (LSCs), Tumor Escape and Eventual Patient Relapse

1 Valent Stem Cell Trans. Med. 2020, 2 Marvin-Peek Cancers 2022
* Note: CD123 is highly expressed in endothelial cells

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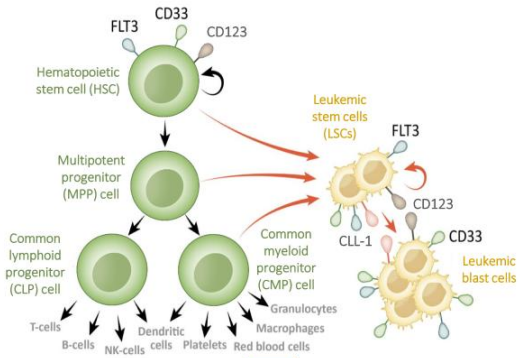
The Need to Limit On-Target / Off-Tumor Toxicity in AML

- **Common AML targets are largely expressed on cancer cells AND healthy hematopoietic stem and progenitor (HSPC) cells** leading to on-target, off-tumor toxicity
- Targeting HSPCs results in prolonged aplasia and myelosuppression leading to anemia, thrombocytopenia, neutropenia, and attendant complications like bleeding and infections
- **There is an urgent need for novel AML therapies with minimal bone marrow toxicities from off tumor effects**



Targeting HSPCs leads to…

Myelosuppression	Anemia	Thrombocytopenia	Neutropenia
Consequence	Fatigue	Risk of bleeding	Risk of infection

ESAs = Erythropoiesis-stimulating agents, G-CSF = Granulocyte colony stimulating factor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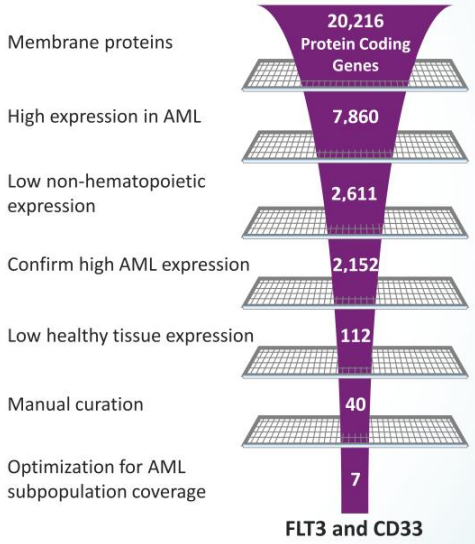
Update on SENTI-202 For Heme Malignancies
Kanya Rajangam, MD, PhD - CMDO

SENTI-202 for CD33 and/or FLT3 Expressing Blood Cancers Including AML

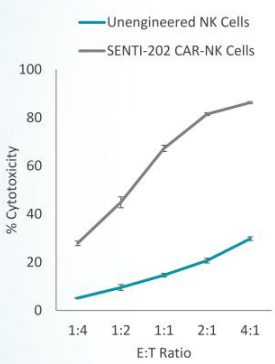
Proven Targets

- **FLT3 and/or CD33 expressed in ~95% of AML**
- Targeting FLT3 and CD33 with an OR GATE has potential of increased efficacy and deeper remission, due to decreased likelihood of tumor antigen escape
- Rigorous bioinformatics approach was used to identify CD33 and FLT3 as an optimal aCAR pair to provide broad coverage of blasts and LSCs

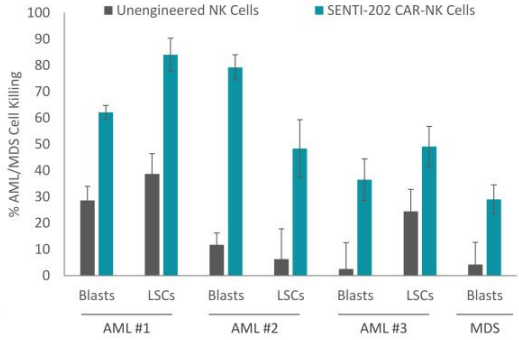
Bioinformatics approach to identify aCAR pair



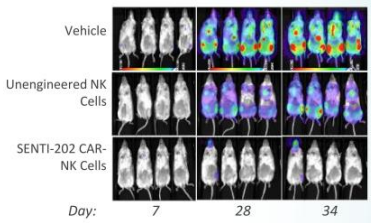
SENTI-202 Has Shown Robust Preclinical Anti-Tumor Activity



Significant in vitro killing of leukemia cell line



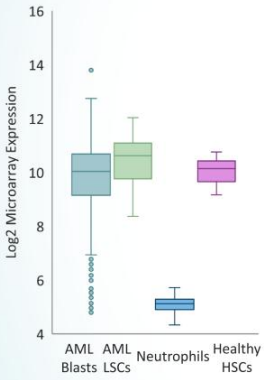
Broad in vitro killing of primary AML and MDS tumor cells

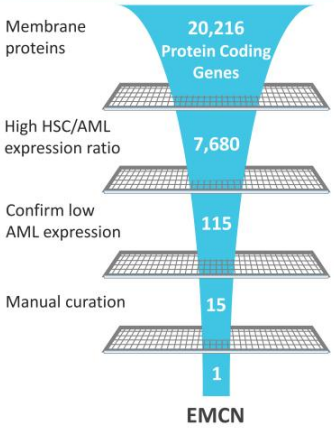


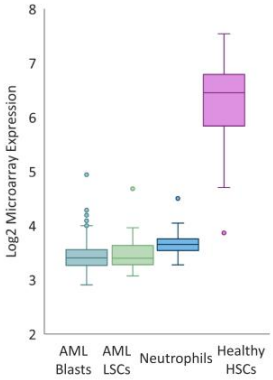
Robust suppression of tumor in AML MV4-11 xenotransplantation model

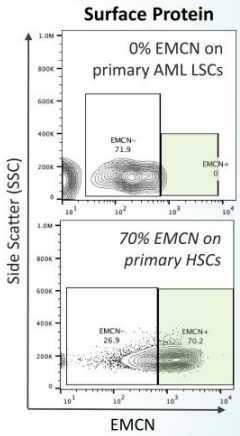
Senti's Discovery Platform Identified EMCN as a Key Protective Antigen for Healthy HSCs

Challenge | **Solution and Validation**







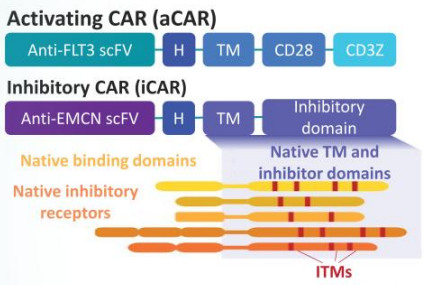


FLT3 is expressed on healthy HSCs

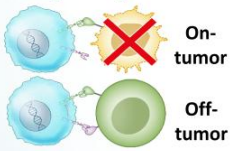
The NOT GATE uses EMCN as a Protective Antigen input to differentiate between healthy HSCs and AML cells

Senti's Discovery Platform Identified LIR1 as the Optimal iCAR ICD for SENTI-202

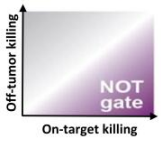
1- Screening and Identification of iCAR



2- Killing Assays

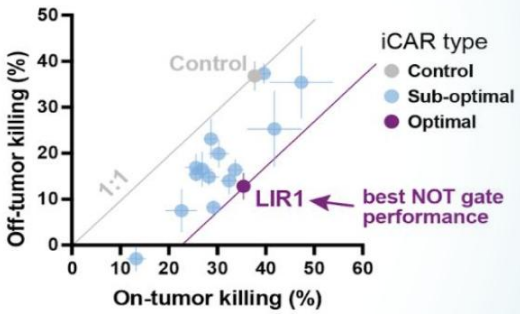


3- Logic Analysis



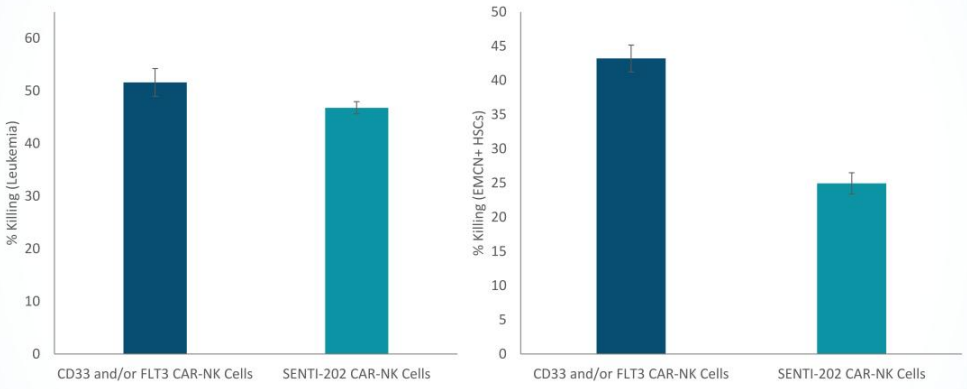
Systematic approach to identify optimal iCAR ICD for SENTI-202 using a screen of native inhibitory proteins

Screen of anti-EMCN iCARs with various transmembrane and intracellular domains



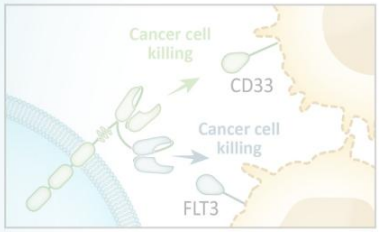
Comparative analysis between NOT gates with different iCAR ICDs identified LIR1 as optimal ICD for SENTI-202

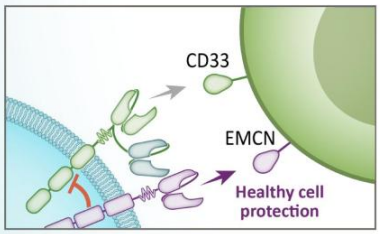
SENTI-202 Preclinical Selectivity via Inhibitory CAR Binding Endomucin to Protect Healthy Primary Human HSCs

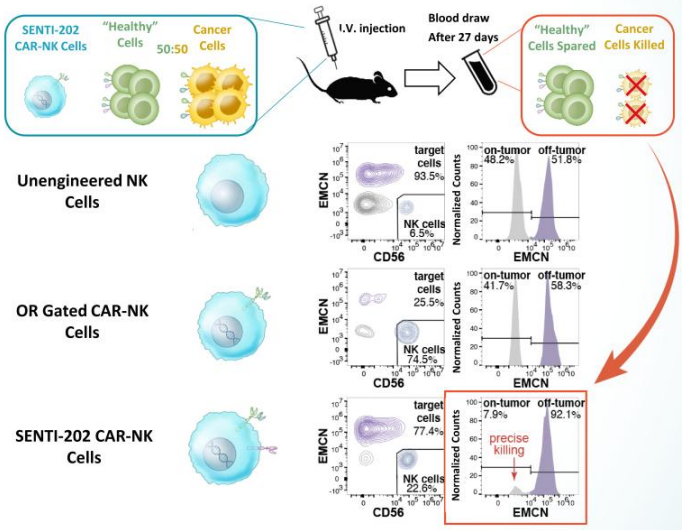


In vitro protection of healthy primary human HSC fraction expressing EMCN

SENTI-202 Preclinical Selectivity via EMCN iCAR Protects Model Healthy Cells *In Vivo* from aCAR-Mediated Killing

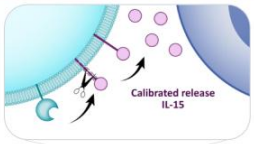


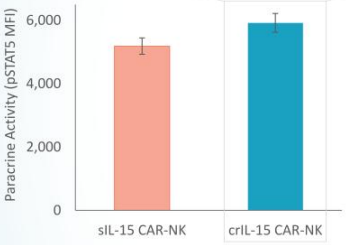




Calibrated Release IL-15 (crIL-15) Increases Persistence and Activation of Both CAR-NK and Immune Cells in Tumor Milieu

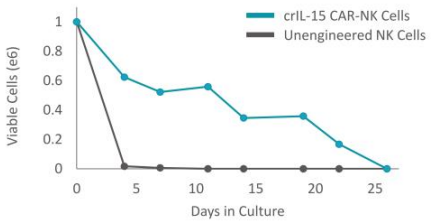
crIL-15: IL-15 released by local proteases → autocrine and paracrine effects



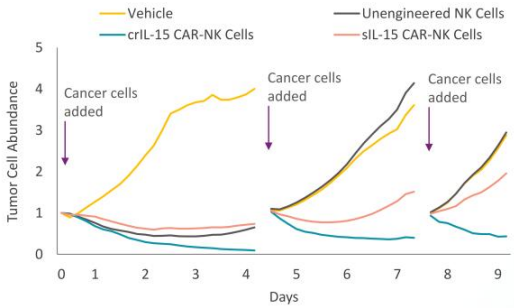


Phospho STAT5 levels increased in T cells exposed to supernatant from either crIL-15 or sIL-15 CAR-NK cell culture

crIL-15 has paracrine activity and activates resting immune cells



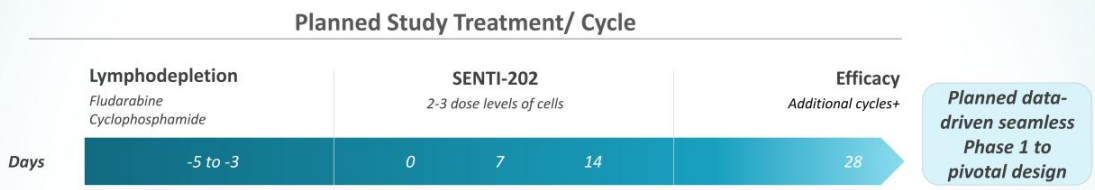
crIL-15 increases persistence of CAR- NK cells



crIL-15 increases CAR-NK serial killing compared to secreted IL-15

sIL-15: secreted wild-type IL-15

Proposed Phase 1 Study in R/R CD33+ And/or FLT3+ Malignancies With Focus on AML

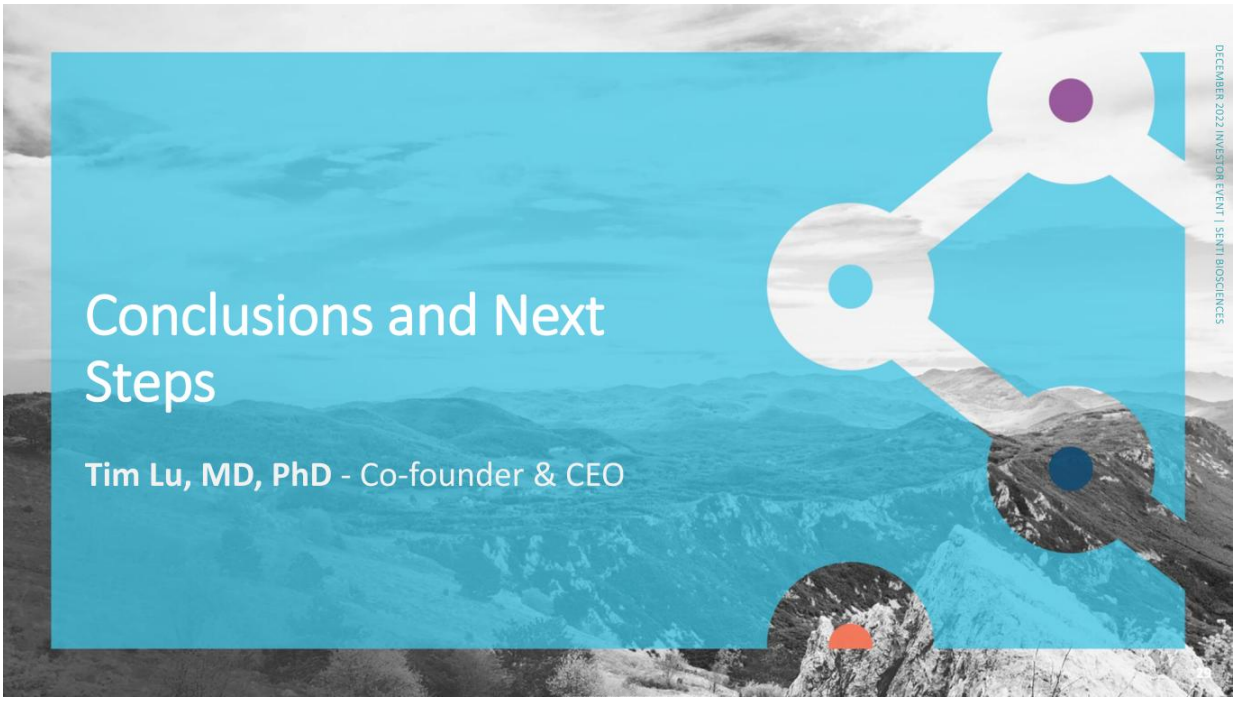


Proposed Phase 1 study anticipated to enroll R/R CD33+ and/or FLT3+ heme malignancies

- Modified "3+3" study design
- Enroll patients who have received at least 1 prior treatment including targeted agents if FLT3, IDH1/2 mutation+
- 2 of 3 patients at each dose level with AML
- Disease specific expansion cohorts for AML and MDS

Planned study endpoints

- Safety, DLT, identify recommended Phase 2 dose
- Efficacy using standard ELN 2022 criteria for AML and other disease specific consensus criteria
- PK, pharmacodynamics including endomucin protection, immunogenicity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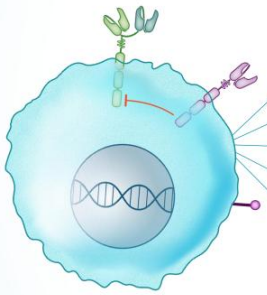
Conclusions and Next Steps
Tim Lu, MD, PhD - Co-founder & CEO

SENTI-202 Can Potentially Fulfill AML Treatment Gap



SENTI-202

Multi-Arming	Calibrated release IL-15 **enhances NK cell expansion, persistence, and tumor killing**
Multi-Antigen Targeting	Simultaneously targeting FLT3 and/or CD33 via Logic Gating to drive **deeper clearance of AML blasts and LSCs** and **prevent antigen escape and patient relapse**
Healthy Cell Protection	Protection of healthy HSCs via EMCN NOT Gate to **minimize on-target/off-tumor toxicity, prevent myelosuppression and allow for repeat dosing**
Redosing Potential	**Potential to increase durability and response** by re-dosing patients
Scalable Manufacturing	**Rigorous screening and selection of GMP donors** to minimize variability

SENTI-202 Aims to Fill Key Unmet Need of Targeting Both AML Blasts and AML LSCs

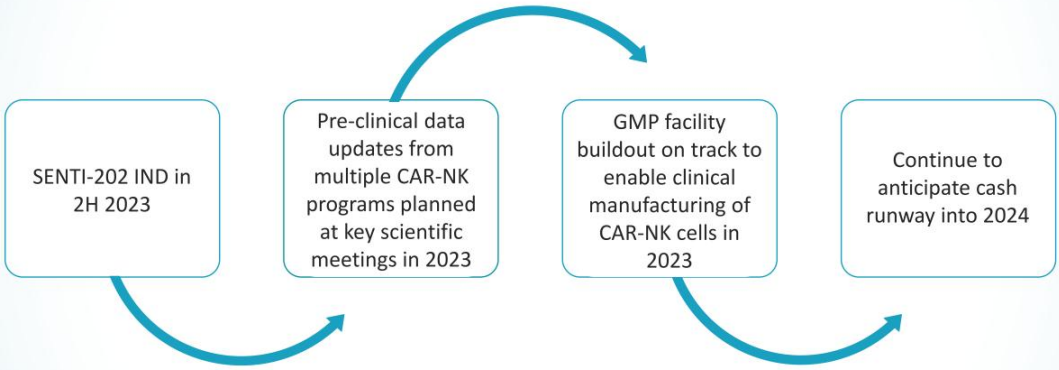
We believe that by *selectively targeting* FLT3 (LSCs) and/or CD33 (blasts), we have the potential to *provide AML patients with significantly deeper and longer remissions*. Our clinical program initially enrolls patients with R/R CD33 and/or FLT3 positive heme malignancies with focus on AML with the potential to expand into earlier lines of therapy

Select AML Cell Therapy Candidates in Development

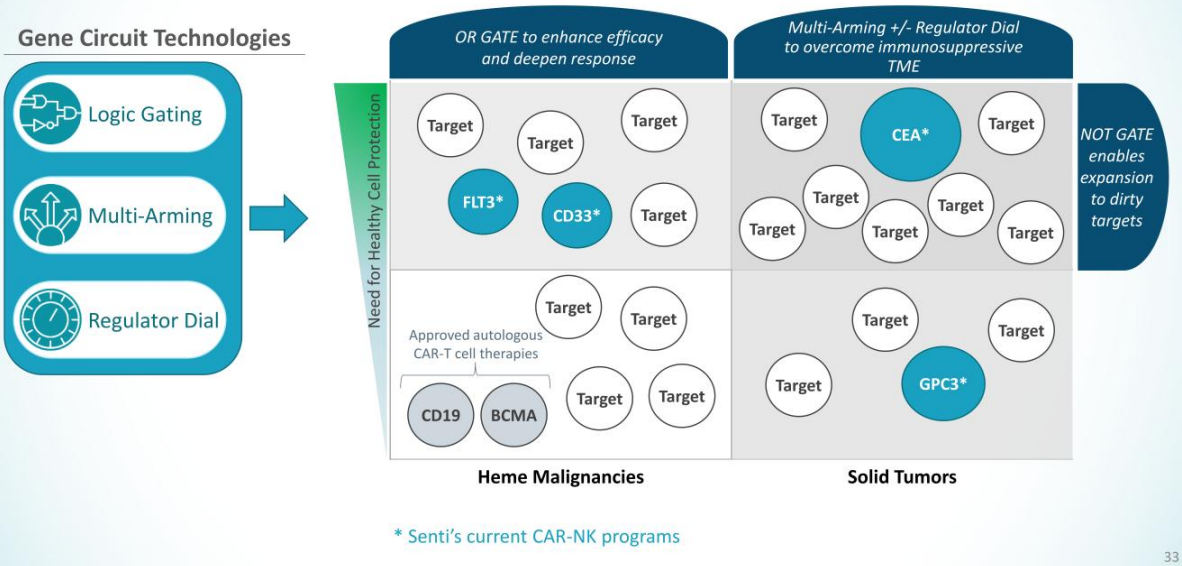
Manufacturer	Modality	MOA / Target[1]	Target Blasts	Target LSCs
KITE-222	Autologous CAR-T cells	CLL-1	+	+/-
UCART12	Allogeneic CAR-T cells	CD123	+	+/-
NKX101	CAR-NK Cells	NKG2D ligands	+	-
FT538	iPSC-derived NK Cells	--	+	-
SENTI-202	CAR-NK Cells	FLT3 OR CD33 NOT EMCN	✓	✓

[1] HSC toxicity was observed for several preclinical FLT3-targeted therapies, including CAR-T, ADCs and BiTes

YTD Progress and Planned Milestones in the Next 12 Months



Gene Circuits Can Vastly Expand the Universe of Cancer Targets and Tumors That Can Be Addressed With Cell Therapies



* Senti's current CAR-NK programs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Q&A
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SENTI BIO™
Corporate Presentation
December 2022
DECEMBER 2022 | SENTI BIOSCIENCES

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Forward Looking Statements

This presentation contains forward-looking statements. Statements we make in this presentation may include statements which are not historical facts and are considered forward-looking 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, which are usually identified by the use of words such as "anticipates," "believes," "estimates," "expects," "future," "opportunity," "proposed," "targets," "intends," "may," "plans," "projects," "seeks," "should," "will," and variations of such words or similar expressions. We intend these forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Securities Exchange Act and are making this statement for purposes of complying with those safe harbor provisions. These forward-looking statements, including statements relating to the attributes and benefits of our technology platform and our product candidates, including their therapeutic potential, our plans to submit INDs for our product candidates and the timing of such submissions, the generation and presentation of data regarding preclinical programs and the related timing, our proposed Phase 1 studies, including study design and endpoints, our ability to enter into new collaborations, our manufacturing process and its potential benefits, and our cash runway, reflect our current views about our plans, intentions, expectations, strategies and prospects, which are based on the information currently available to us and on assumptions we have made. 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. Although we believe that our plans, intentions, expectations, strategies and prospects as reflected in or suggested by those forward-looking statements are reasonable, we can give no assurance that the plans, intentions, expectations or strategies will be attained or achieved. Many actual events and circumstances are difficult or impossible to predict, are beyond our control and will differ from assumptions. Furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a variety of risks and factors that are beyond our control including, without limitation, the risk that results observed in studies of our product candidates, including preclinical studies and future clinical trials of any of our product candidates, will not be observed in ongoing or future studies involving these product candidates, the risk that we may cease or delay clinical development of any of our 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 our product candidates for preclinical and clinical testing, and any adverse events or other negative results that may be observed during preclinical or clinical development), our ability to obtain, maintain and protect our intellectual property, our dependence on third parties for development and manufacture of product candidates, our ability to manage expenses and to obtain additional funding when needed to support our 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 our product candidates may not produce therapeutic benefits or may cause other unanticipated adverse effects, as well as those set forth in the section titled "Risk Factors" in our Form 10-Q filed with the Securities and Exchange Commission (the "SEC") on November 10, 2022, and our subsequent SEC filings. Except as required by law, we assume no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

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Pioneering Smarter Next Generation Cell and Gene Therapies

SENTI BIO

Gene Circuits

Multi-Arming
Logic Gating (OR and NOT GATEs)
Regulator Dial
Smart Sensor

to

reprogram cells to sense, compute, and respond to disease

Two INDs Anticipated in 2023

Pipeline of CAR-NK Cell Therapies

Diseases: blood cancers and solid tumors
Gene Circuit advantages: multi-arming, selectivity and control
Manufacturing: off-the-shelf, scalable with outpatient potential

Spark, BlueRock

Platform Collaborations

Precise gene therapy for eye, CNS and liver applications
Targeted and controllable iPSC cell therapies for regenerative medicine

Founded 2016 | Public June 2022 | Anticipated Cash Runway into 2024 | Headquartered South San Francisco, CA

CNS: Central Nervous System

Industry-Leading Management With Top-Tier Board and Scientific Advisors

Executive Team

Tim Lu, MD, PhD
CEO & Co-Founder

Philip Lee, PhD
CTO & Co-Founder

Deb Knobelman, PhD
CFO

Kanya Rajangam, MD, PhD
Chief Medical and Development Officer (CMDO)

Scientific Advisors

James Collins, PhD	Scientific Co-Founder, MIT
Michael Andreeff, MD, PhD	MD Anderson Cancer Center
Lawrence Fong, PhD	UCSF
Martin Fussenegger, PhD	ETH Zurich
Michael Kalos, PhD	Arsenal, Janssen, Lilly
Ahmad (Mo) Khalil, PhD	Boston University
Robin Taylor, PhD, MBA	SeaGen, Genentech
Michael Varney, PhD	Erasca, Genentech
Wilson Wong, PhD	Scientific Co-Founder, Boston University

Board of Directors

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Ed Mathers	NEA
James Collins, PhD	Scientific Co-Founder, MIT
Omid Farokhzad, MD	Seer Inc.
David R. Epstein	Former CEO of Novartis Pharma
Tim Lu MD, PhD	CEO & Co-Founder


CAR-NK Cell Therapy
Pipeline
DECEMBER 2022 | SENTI BIOSCIENCES

Gene Circuits Designed to Solve for Key Cell Therapy Challenges

Cancer Cell Therapy Challenges	Senti's Gene Circuit Solutions	
Lack of NK cell expansion and persistence	Multi-Arming	Autocrine and paracrine activation with proprietary **Calibrated Release** IL-15 (crIL-15) and other complementary cytokines (e.g., IL-21)
Antigen escape and tumor heterogeneity	Logic Gating	Bivalent activating CAR with **OR Logic Gate**
Dirty targets (on-target, off-tumor toxicity)	Logic Gating	Inhibitory CAR protects healthy cells with **NOT Logic Gate**
Immunosuppressive tumor microenvironment	Regulator Dial	Pulsed Calibrated Release IL-12 with small molecule-controlled **Regulator Dial**

NK Cells Compare Favorably to T Cell Based Therapies

Capabilities	Current Auto T Cells	Senti's CAR-NK Cells
Off-the-shelf potential with broad patient accessibility	✗	✓
Designed with Logic Gates to achieve enhanced selectivity and safety	✗	✓
Engineered with enhanced persistence	N/A	✓
Engineered to stimulate the patient immune system	✗	✓

Extensive clinical experience with allogeneic donor-derived unengineered NK cells[1]

- Nearly 600 patients treated across 30+ single center academic trials
- Well-tolerated
  - No (or minimal) CRS, neurotoxicity, GvHD
- Anti-tumor activity observed in AML
  - 19% CR in 105 R/R AML patients aggregated from multiple trials

Key limitations of unengineered NK cells

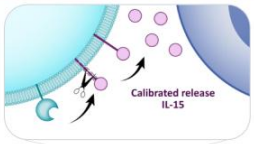
Limited activity beyond AML, persistence, durability, donor variability and select single clinical center usage

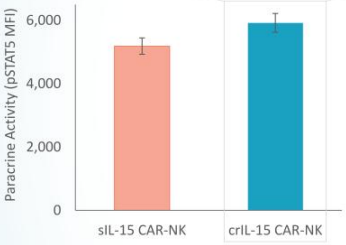
Senti's Gene Circuit technology, donor selection and scalable manufacturing address these limitations

[1] Velluchamy 2017, Bachier 2021

Calibrated Release IL-15 (crIL-15) Increases Persistence and Activation of Both CAR-NK and Immune Cells in Tumor Milieu

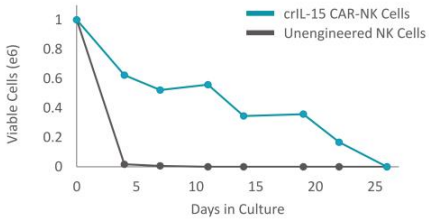
crIL-15: IL-15 released by local proteases → autocrine and paracrine effects



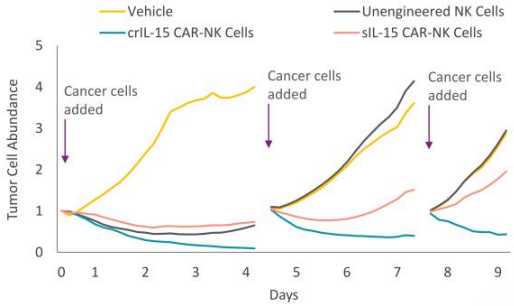


Phospho STAT5 levels increased in T cells exposed to supernatant from either crIL-15 or sIL-15 CAR-NK cell culture

crIL-15 has paracrine activity and activates resting immune cells



crIL-15 increases persistence of CAR- NK cells



crIL-15 increases CAR-NK serial killing compared to secreted IL-15

sIL-15: secreted wild-type IL-15

Senti's Next Generation CAR-NK Cell Therapy Pipeline Tackles Hard to Treat Cancers

Program	Target	Indications	Discovery	IND enabling	Phase 1	Gene Circuits
SENTI-202	CD33 and/or FLT3	AML, MDS and other blood cancers		2H 2023 IND		✓ Multi-Arming: designed for enhanced efficacy ✓ crIL-15: autocrine and paracrine activation ✓ OR GATE: bivalent activation ✓ NOT GATE selectivity: healthy cell protection
SENTI-301A	GPC3	HCC and other solid tumors		2023 IND		✓ Multi-Arming: designed for enhanced efficacy ✓ crIL-15: autocrine and paracrine activation
SENTI-401	CEA	CRC and other solid tumors		2024 IND		✓ Multi-Arming: designed for enhanced efficacy ✓ crIL-15: autocrine and paracrine activation ✓ NOT GATE selectivity: healthy cell protection ✓ IL-21: sustained anti-tumor function
Additional Programs	Undisclosed	Other tumors				Program candidates integrate Multi-Arming, Logic Gating and/or Regulator Dial Gene Circuits


Manufacturing
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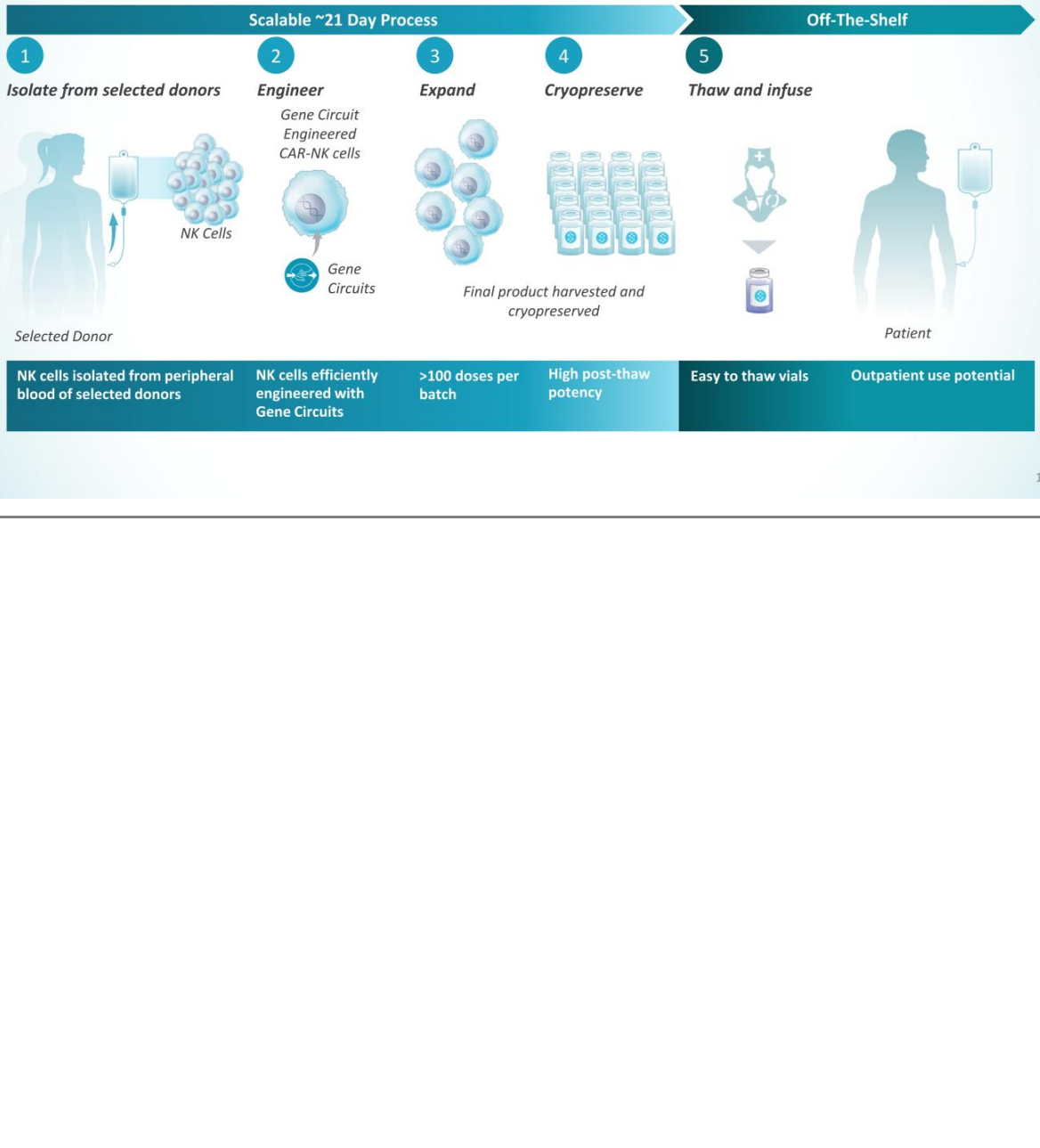
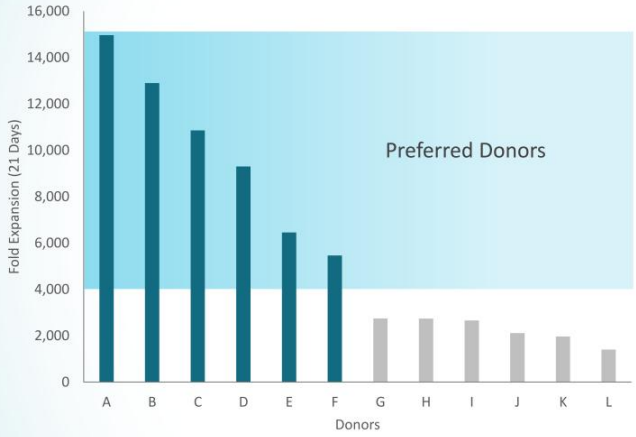
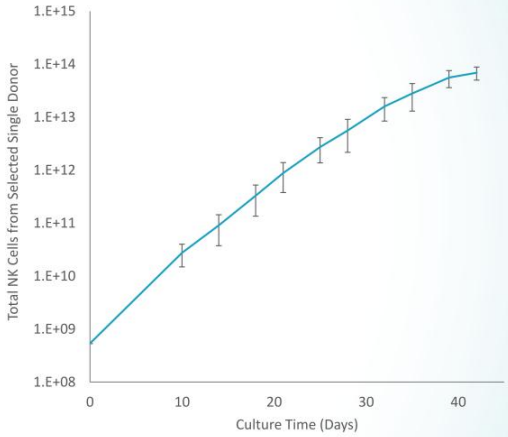
Scalable Manufacturing to Support Off-The-Shelf CAR-NK Products



Senti Selects NK Cell Donors to Support Robust Cell Expansion

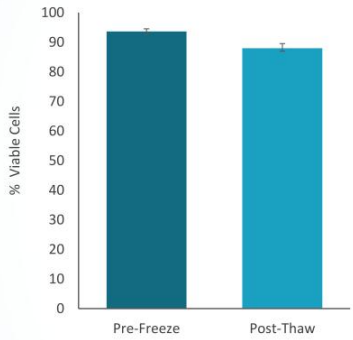


Senti screens and selects GMP donors using NK cell expansion and other functional attributes to minimize variability

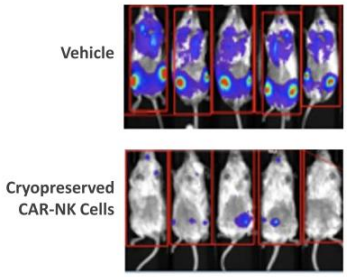


Senti process can potentially generate over 100 trillion NK cells from a single donor collection

Senti's Cryopreservation Process Retains High Potency of CAR-NK Products Supporting Multi-Country and Multi-Site Clinical Evaluation



CAR-NK cell viability retained post-thaw in vitro



In vivo activity with cryopreserved CAR NK cells in MOLM13 AML NSG mouse model
(10 days after single dose)


Pipeline Products
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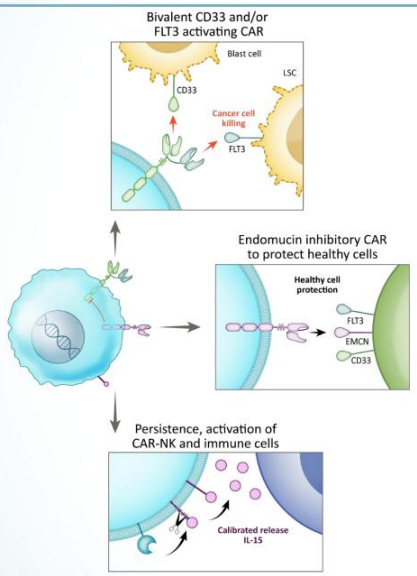
SENTI-202 for CD33 and/or FLT3 Expressing Blood Cancers



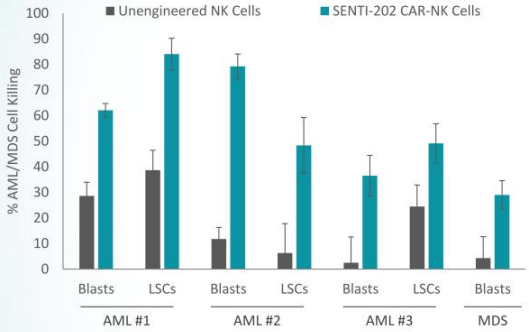
LSCs: Leukemic Stem Cells

Multi-Armed, off-the-shelf, selective CAR-NK

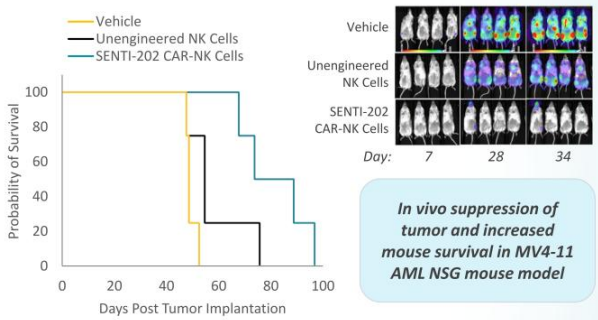
- ***OR GATE:*** *bivalent* CD33 and/or FLT3 activation → potential for deep and durable responses in acute myeloid leukemia (AML) and other blood cancers.
- ***NOT GATE:*** inhibition by endomucin (EMCN) protective antigen selectively expressed on healthy hematopoietic stem cells (HSCs) → potential for improved safety and increased therapeutic window
- ***crIL-15*** → potential for increased persistence, autocrine and paracrine immune cell activation

On track for IND in 2H 2023

SENTI-202 Has Shown Robust Preclinical Activity Across Multiple AML / MDS Models



Broad in vitro killing of primary AML and MDS tumor cells

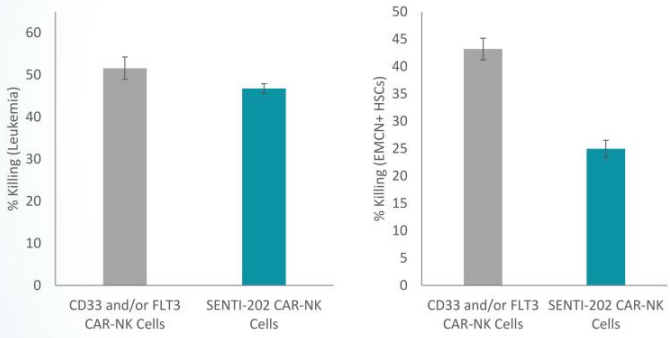


In vivo suppression of tumor and increased mouse survival in MV4-11 AML NSG mouse model

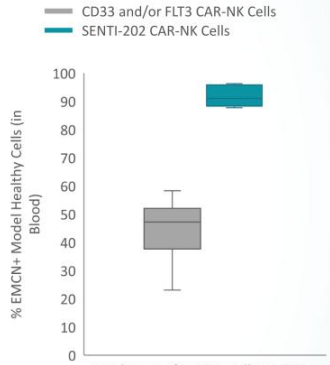
Group	Vehicle	Unengineered NK Cells	SENTI-202 CAR-NK Cells
Median Survival (Days)	*49*	*55*	*81.5*

SENTI-202 Preclinical Selectivity via Inhibitory CAR Binding Endomucin to Protect Healthy Primary Human HSCs

Endomucin was identified and validated by bioinformatics, flow cytometry, and functional assays, and is expressed on up to 76% of HSCs, but not on leukemic stem cells or blasts. FLT3 and/or CD33 expressed on tumor cells in ~95% of AML patients



In vitro protection of healthy primary human HSC fraction expressing EMCN



Enrichment of EMCN+ cells in NSG mouse model 3 weeks after injecting 1:1 EMCN-/+ cells with CAR-NK cells

In vivo protection of EMCN+ model healthy cells

Proposed Phase 1 Study in R/R CD33+ and/or FLT3+ Malignancies With Focus on AML

High unmet need in patients with AML

- 30.5% 5-year survival[1]
- 5 months median overall survival at relapse[2]

Proposed Phase 1 study anticipated to enroll R/R CD33+ and/or FLT3+ heme malignancies

- Modified "3+3" study design
- Received at least 1 prior treatment including targeted agents if FLT3, IDH1/2 mutation+
- 2 of 3 patients at each dose level with AML
- Disease specific expansion cohorts for AML and MDS

Planned study endpoints

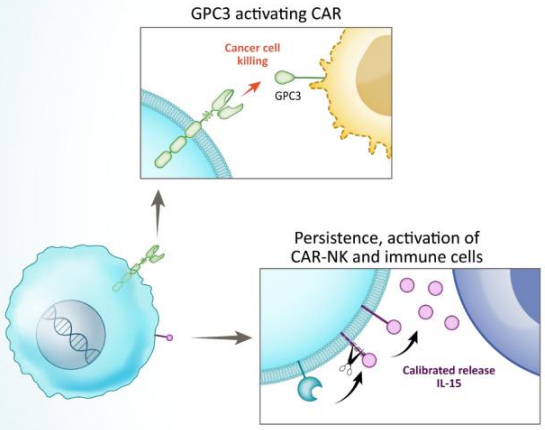
- Safety, DLT, identify recommended Phase 2 dose
- Efficacy using standard ELN 2022 criteria for AML and other disease specific consensus criteria
- PK, pharmacodynamics including endomucin protection, immunogenicity

Planned Study Treatment/ Cycle

Planned data-driven seamless Phase 1 to pivotal design

[1] Seer 2020; [2] Brandwein 2020

SENTI-301A for GPC3 Expressing Solid Tumors



Multi-Armed, off-the-shelf, selective CAR-NK

- ***GPC3 activating CAR*** → hepatocellular carcinoma (HCC) and other solid tumors
- ***crIL-15*** → potential for increased persistence, autocrine and paracrine immune cell activation

On track for IND in 2023

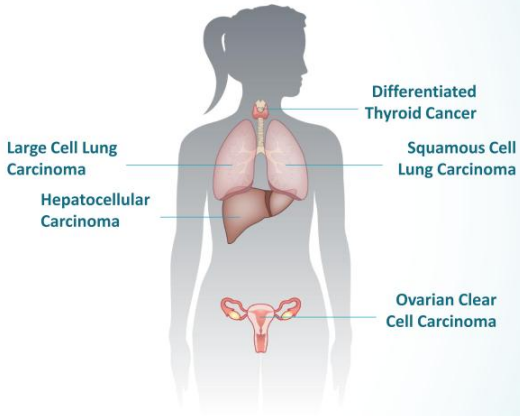
SENTI-301A Aims to Address Unmet Needs in GPC3 Expressing Solid Tumors With a Focus on HCC

GPC3 is a validated cancer target

- Glypican-3 (GPC3) is a membrane-bound protein normally expressed in fetal tissues such as liver and placenta.
- After birth, GPC3 is not expressed in healthy liver tissue or other human organs but is overexpressed in different tumor types, notably in HCC (70-90% GPC3+)[1] and other solid tumors (29-54%[2] GPC3+)
- Academic GPC3 CAR-T cell trials have shown promising activity but limited by CAR-T toxicities precluding multiple dosing and limited durability[3]

SENTI-301A is designed to target GPC3 expressing tumors

- Aim to address unmet need in HCC as the initial focus given the lack of targeted therapies and lack of effective immunotherapies
- Tackle multiple solid tumors with high GPC3 antigen expression via NKs multi-armed with GPC3 CAR and crIL-15



Common GPC3 expressing tumors

[1] Zheng 2022, [2] Moek 2018, [3] Shi 2020

SENTI-301A Preclinical Anti-Cancer Activity and Proposed Phase 1 Study in Advanced Solid Tumors With Focus on HCC

High unmet need in patients with liver cancer

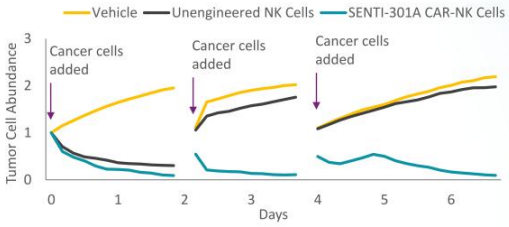
20.8% 5-year survival rate[1]

Proposed Phase 1 study anticipated to enroll an advanced metastatic GPC3 solid tumor population

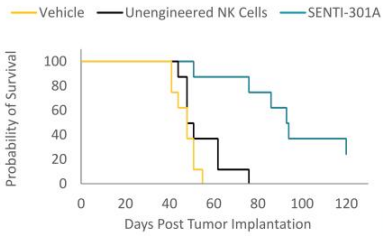
- Must have received standard of care
- Advanced solid tumors with focus on HCC during dose finding
- Disease specific expansion cohorts of advanced HCC and other solid tumors including lung cancer

Planned study treatment

- Multi-dose and multi-cycle following conditioning
- 2-3 cell dose levels



Effective in vitro serial killing of HepG2 cell line

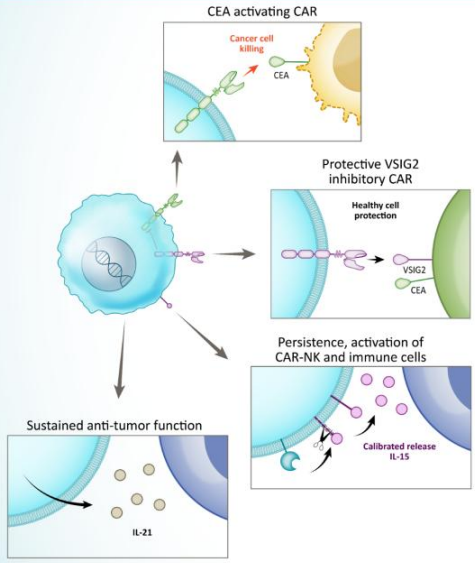


Increased survival and response in HepG2 mouse model

Group	Vehicle	Unengineered NK Cells	SENTI-301A CAR-NK Cells
Median Survival (Days)	*48*	*49.5*	*93.5*

[1] Seer 2020 (liver and intrahepatic bile duct cancer combined)

SENTI-401 for CEA Expressing Solid Tumors

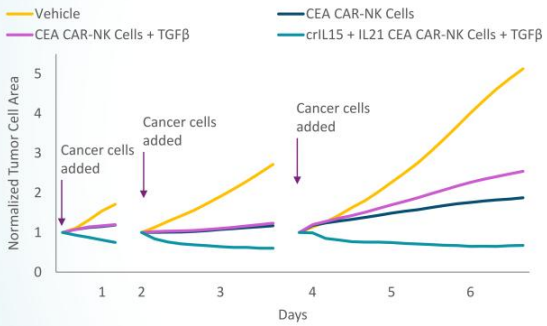


Multi-Armed, off-the-shelf, selective CAR-NK

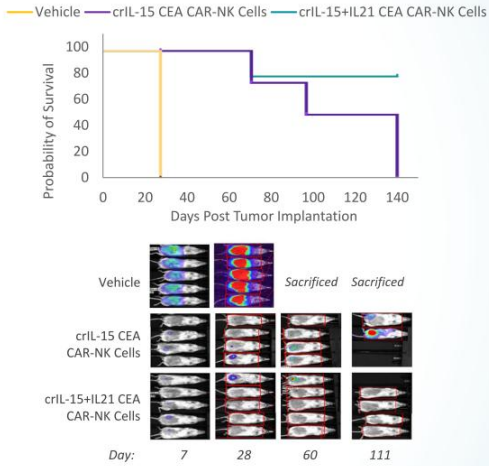
- ***CEACAM5 (CEA) activating CAR*** → colorectal cancer (CRC) and other solid tumors
- ***NOT GATE:*** inhibition by VSIG2 antigen on healthy epithelial cells → potential for improved safety, increased therapeutic window and reduced on-target, off-tumor toxicity
- ***crIL-15*** → potential for increased persistence and autocrine and paracrine immune cell activation
- ***IL-21*** → construct to further potentiate persistence and efficacy of CAR-NK cells and to stimulate endogenous immune cells

Robust Preclinical Activity With CEA CAR-NK Cells That Is Augmented by Multi-Arming With Both crIL-15 and IL-21

TGFβ is an immunosuppressive tumor factor highly expressed in CRC, known to suppress immune activation and help tumor escape[1]



Sustained serial killing with CEA CAR-NK cells expressing crIL-15 and IL-21 in the presence of the immunosuppressive cytokine TGFβ

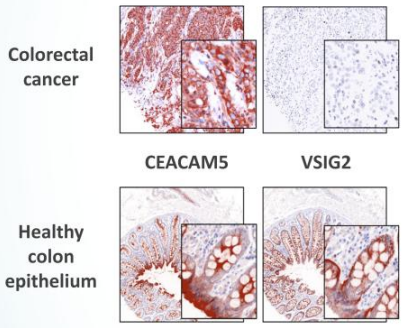


Arming CEA CARs with the combination of Senti's proprietary crIL-15 and IL-21 results in improved anti-tumor activity of NK cells

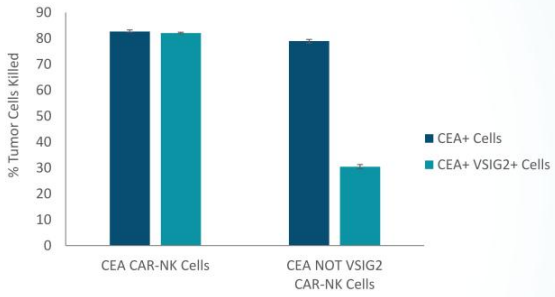
[1] Nature 2018

Senti's Approach to Select Paired Target and Protective Antigens Translates to Rapid Preclinical Proof of Principle for SENTI-401

VSIG2 was identified by bioinformatics using single cell RNA sequencing and validated as protective antigen with immunohistochemistry



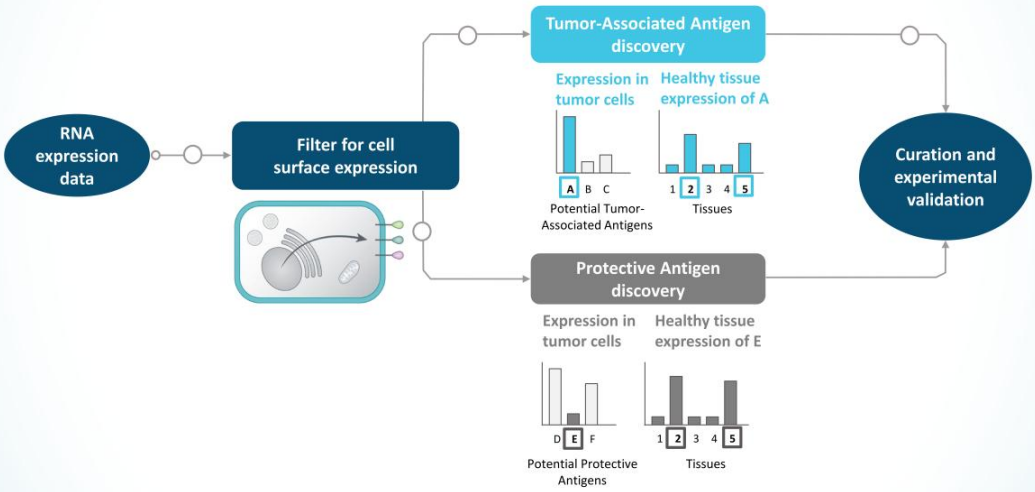
CEACAM5: 85-90% of CRC and 40-60% of other solid tumors including lung cancer[1]



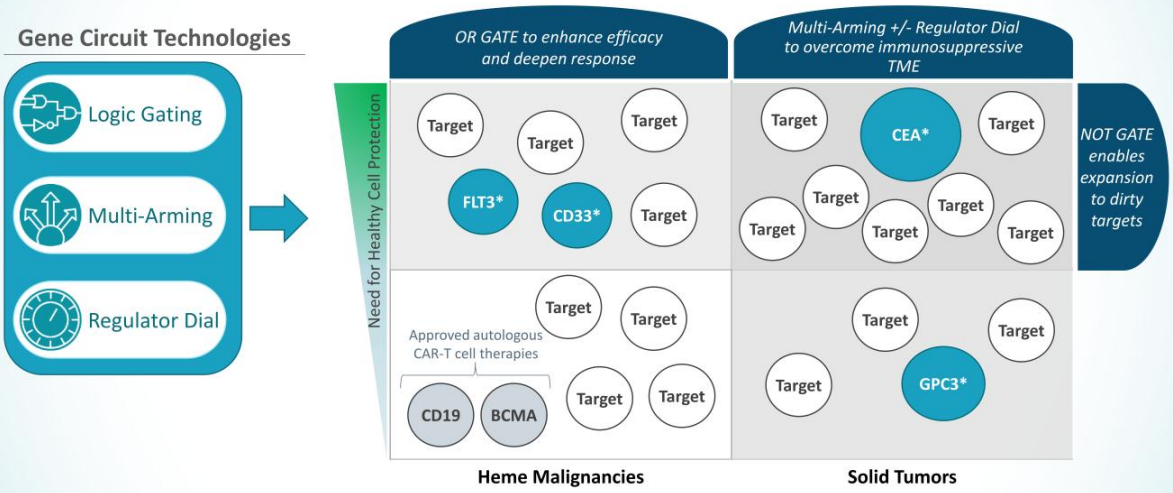
Decreased cell killing of VSIG2 expressing cells with addition of inhibitory CAR construct

[1] Goldstein 2005

Senti's Discovery Platform for Tumor-Associated Antigen and Protective Antigen to Generate Many Targets for New Logic Gated CAR-NK Candidates

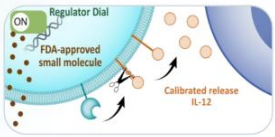


Gene Circuits Can Vastly Expand the Universe of Cancer Targets and Tumors That Can Be Addressed With Cell Therapies



* Senti's current CAR-NK programs

Senti's Regulator Dial Enables On-Demand Production of crIL-12 Controlled via Multiple Distinct FDA-Approved Small Molecule Oral Drugs

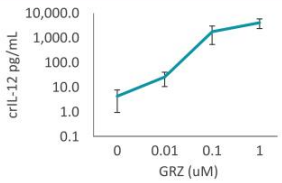


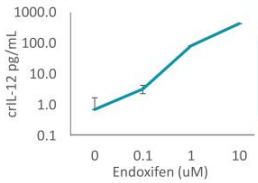
IL-12 is a well-known immuno-stimulatory cytokine

- Increases NK and T cell activation and inhibits immunosuppressive cells such as tumor-associated macrophages
- Responses noted with systemic administration of IL-12[1]

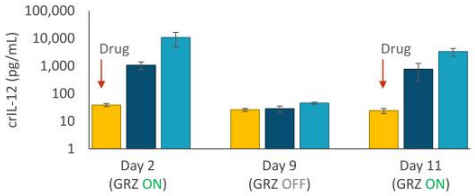
IL-12 clinical use has been limited by toxicities

- Regulator Dials control IL-12 production with FDA approved oral drugs such as grazoprevir (GRZ) and endoxifen (active metabolite of tamoxifen)
- Opportunities for application across multiple solid tumor indications

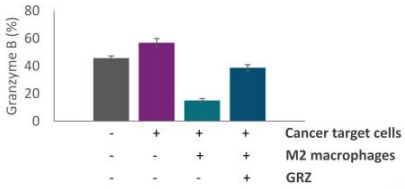




Concentration dependent crIL-12 production



Dose-dependent, reversible crIL-12 controlled by GRZ in vivo



CAR-NK activity suppressed by M2 macrophages → Activity restored by GRZ induced crIL-12 via Regulator Dial

[1] Leonard 1997


Platform and Collaboration Opportunities
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Multiple Platform Collaborations Extend Utility of Gene Circuits

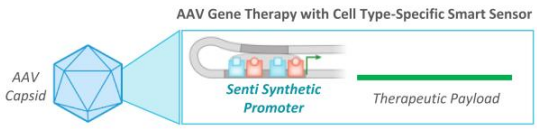
Program	Indications	Gene Circuit	Discovery	IND enabling	Phase 1	Rights
Gene Therapies for Tissue-Directed Targets						
GC-1001/GC-1002	Eye	Smart Sensor				Spark Therapeutics, Roche
GC-1003/GC-1004	CNS	Smart Sensor				
GC-1005	Liver	Smart Sensor				
Cell Therapies for Regenerative Medicine						
GC-1101	Regenerative Medicine	Regulator Dial				BlueRock Therapeutics, Bayer
GC-1102	Regenerative Medicine	Regulator Dial				
GC-1103	Regenerative Medicine	Smart Sensor				

Two Collaborations to Develop Next Generation Cell and Gene Therapies

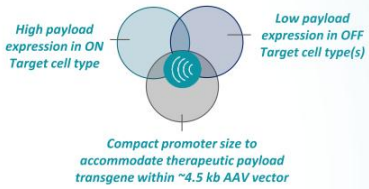
Spark

Collaboration for gene therapies

AAV Gene Therapy with Cell Type-Specific Smart Sensor



Synthetic Promoter Performance Profile:



BlueRock THERAPEUTICS

Collaboration for cell therapies

Gene Circuit-Engineered "Smart" Regenerative Medicines

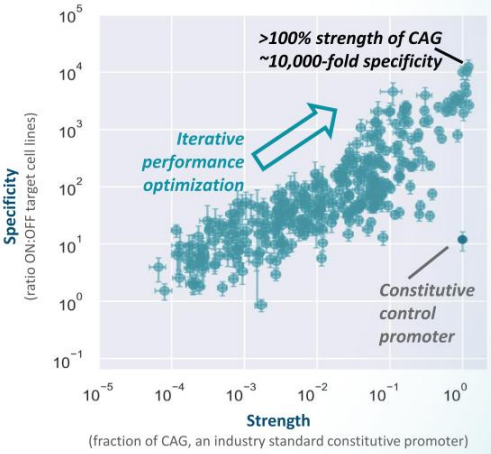
Smart Sensor Promoters Are Designed to Address Key Challenges in Gene Therapy

Gene Therapy Challenges	Senti's Gene Circuit Solutions
Off-target tissue toxicity	Smart Sensor ▶ Enhance target tissue specificity and limit off-target tissue toxicity
Sub-optimal therapeutic performance	Smart Sensor ▶ Improve expression and increase potency

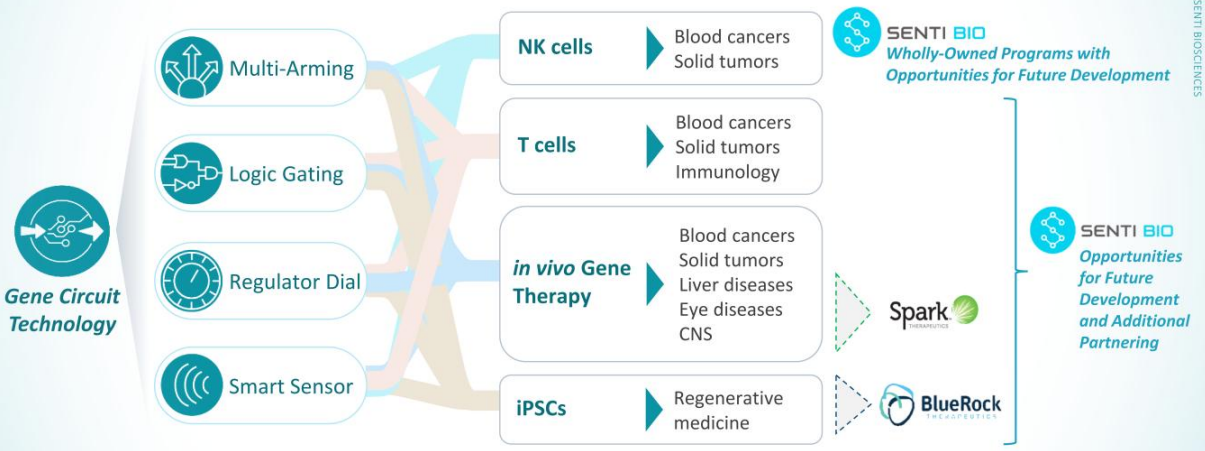
Smart Sensor Promoters enable next-generation gene therapy by:

- Enhancing specificity to target tissue(s) (and thus limiting off-target tissue toxicities) and
- Increasing strength, potentially enabling more efficacious therapies

Smart Sensor Promoter Data

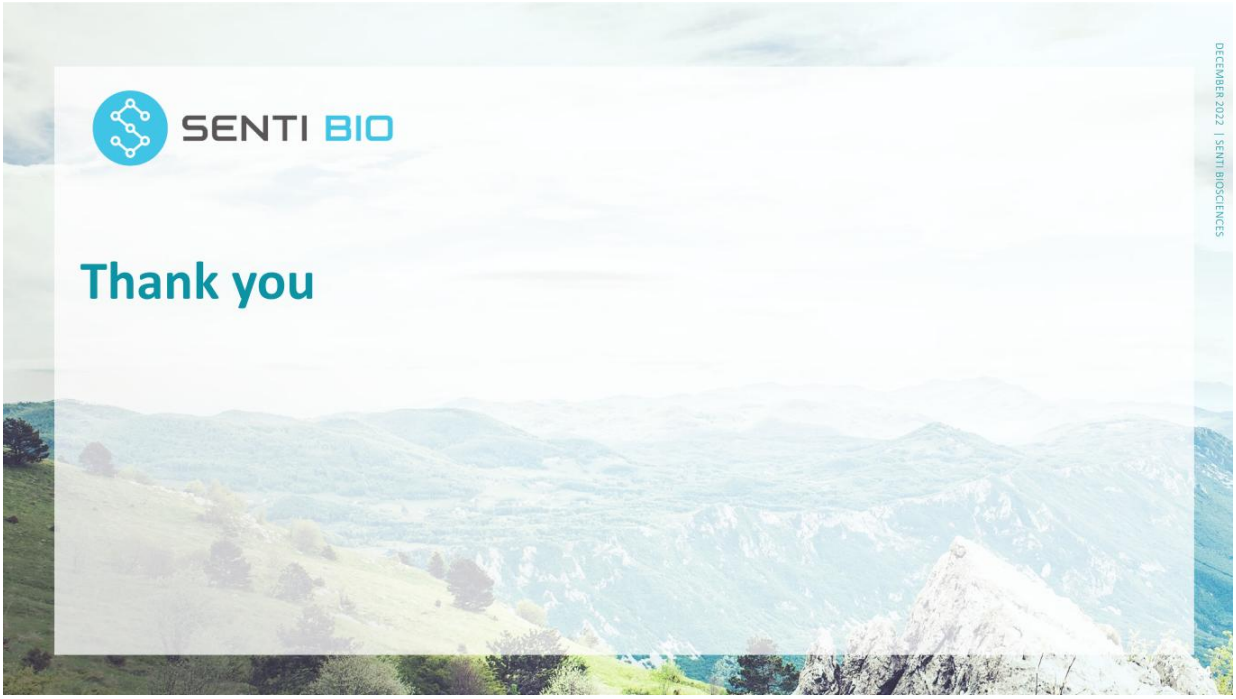


Senti's Gene Circuit Technology Has Broad Potential Across Modalities and Therapeutic Areas



2022 Milestones and Upcoming Value Driving Milestones

Program	2022 Completed Milestones	2023 Anticipated Milestones
SENTI-202 *CD33 and/or FLT3* *AML, MDS and other blood cancers*	Presented key preclinical data at ASH in December 2022	File IND application in 2H 2023
SENTI-301A *GPC3* *HCC and other solid tumors*	Presented preclinical data at SITC in November 2022	File IND application in 2023
SENTI-401 *CEA* *CRC and other solid tumors*	Presented preclinical data at SITC in November 2022	Present data at key scientific conferences
Additional Programs *Other tumors*	Initiated research work on additional CAR-NK pipeline programs	Pre-clinical PoCs for additional pipeline candidates
Manufacturing	Initiated manufacturing activities and presented data at key conferences	


SENTI BIO
Thank you
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