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): January 27, 2023

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 7.01. Regulation FD Disclosure.

Reference is made to the disclosure set forth below in Item 8.01 of this Current Report on Form 8-K which is incorporated herein by reference.

On January 27, 2023, Senti Biosciences, Inc., (the "Company") issued a press release (the "Press Release") titled, "Senti Bio Announces Pipeline Prioritization to Focus on Logic Gated Cell Therapies; Updates Cash Runway Guidance," a copy of which is furnished herewith as Exhibit 99.1. The information in this Item 7.01 of Form 8-K and Exhibit 99.1 attached hereto is furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933 (the "Securities Act"), as amended or the Exchange Act. The information in this Item 7.01 of this Current Report on Form 8-K will not be deemed an admission as to the materiality of any information that is required to be disclosed solely by Regulation FD.

Item 8.01. Other Events.

On January 27, 2023, the Company announced a strategic plan to focus internal resources on SENTI-202, SENTI-401 and, with potential partners, to develop Gene Circuits for other programs. The Company also announced that it does not intend to devote its own resources to the development of SENTI-301A for the treatment of hepatocellular carcinoma at this time, and is actively pursuing strategic geographic partnerships for further clinical development of SENTI-301A. This business realignment will streamline internal efforts and is expected to extend the Company's cash runway through at least the first quarter of 2024. In connection with this announcement, the Company has also updated certain corporate information in a presentation slide deck. A copy of this corporate presentation is filed herewith as Exhibit 99.2 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 January 27, 2023
99.2	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: January 27, 2023

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

Senti Bio Announces Pipeline Prioritization to Focus on Logic Gated Cell Therapies; Updates Cash Runway Guidance

– R&D focus is on lead oncology candidate SENTI-202 for the treatment of AML and other CD33 and/or FLT3 expressing hematologic malignancies, and SENTI-401 to target colorectal cancer and other CEA-positive solid tumors –

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

– Cash runway guidance extended through at least Q1 2024 –

SOUTH SAN FRANCISCO, Calif., January 27, 2023 — Senti Biosciences, Inc. (Nasdaq: SNTI) ("Senti Bio"), a biotechnology company innovating next-generation cell and gene therapies using its proprietary Gene Circuit technology platform, today announced a strategic plan to focus internal resources on SENTI-202, SENTI-401 and, with potential partners, to continue to pursue the development of Gene Circuits for other programs, including solid tumors. The Company does not intend to invest in the clinical development of SENTI-301A, for the treatment of hepatocellular carcinoma (HCC), on its own at this time; however, the Company believes there is significant market opportunity for SENTI-301A, especially in territories within Asia where HCC is more prevalent than in the United States. Accordingly, the Company is actively pursuing strategic geographic partnerships for clinical development of SENTI 301A. This business realignment will streamline internal efforts and is expected to extend the Company's cash runway through at least the first quarter of 2024.

With SENTI-202, a Logic Gated (OR+NOT) off-the-shelf CAR-NK cell product candidate that is designed to target and eliminate acute myeloid leukemia (AML) cells while sparing the healthy bone marrow, the Company has commenced IND-enabling studies and remains on track to file an IND application in the second half of 2023. In addition, the Company has initiated the technology transfer to its cGMP manufacturing facility as part of its goal to provide clinical-scale manufacturing for its off-the-shelf CAR NK cell product candidates, including SENTI-202.

"We are laser focused on developing cell therapies engineered with Gene Circuits to enable selective killing of tumor cells while protecting healthy cells. Our Gene Circuits, especially our NOT gate, are designed to enable advanced cell and gene therapies to potentially have enhanced precision, activity and control, across therapeutic areas and delivery modalities, including NK cells and T cells," said Timothy Lu, MD, PhD, Chief Executive Officer and Co-Founder of Senti Bio. "By focusing on SENTI-202 and SENTI-401, both of which incorporate NOT gates, we believe that we are well positioned to maximize opportunities across these two oncology programs while advancing Gene Circuits in a variety of other disease areas with potential partners."

Dr. Lu added, "The team's accomplishments with SENTI-202 have generated very promising data over the past year that was presented at the American Society of Hematology (ASH) Annual Meeting last month. The data included human cell models and *in vivo* models that showcase the ability of our OR gate to broadly kill CD33 and/or FLT3 expressing leukemic blasts and leukemic stem cells, and our NOT gate to protect healthy cells expressing the EMCN protective antigen, including human hematopoietic stem cells. The team has completed pre-IND interactions with the FDA and believes that our planned IND-enabling studies and manufacturing and analytical processes will support a Phase 1 trial for SENTI-202, with the ultimate goal of targeting patients with CD33 and/or FLT3 expressing hematologic malignancies including AML and myelodysplastic syndrome (MDS). Initiating process and analytical technology transfer to our Alameda cGMP facility is another milestone that puts us one step closer to providing clinical-scale manufacturing for our CAR-NK cell development candidates."

The SENTI-401 program incorporates multiple Gene Circuit technologies to target solid tumors expressing the CEA tumor antigen, including colorectal cancer. Senti Bio has recently demonstrated, including data presented at the Society for Immunotherapy of Cancer (SITC) conference in November 2022, that CAR-NK cells expressing a potent CEA-targeting activating CAR along with two multifunctional cytokines (calibrated-release IL-15 and IL-21) exhibited significant activity in killing CEA-expressing tumors *in vitro*, even in the presence of inhibitory TGF-beta, and in mice. Furthermore, Senti Bio's optimized NOT gate technology was shown to achieve up to 98% protection of model healthy cells that express CEA along with a protective antigen, VSIG2. The Company believes the

combination of Logic Gating and Multi Arming Gene Circuits within a single CAR-NK development candidate demonstrates the potential for Senti Bio's Gene Circuit technologies to be expanded to a wide range of solid tumor indications beyond SENTI-202 and SENTI-401.

Beyond oncology, the Company is continuing its strategic research collaborations with Spark Therapeutics on next-generation AAV gene therapy, and BlueRock Therapeutics on iPSC-derived cell therapies.

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. Additionally, our SENTI-401 program is being designed for the treatment of colorectal cancer (CRC) and other CEA-positive cancers. We have also demonstrated in preclinical studies the potential breadth of our Gene Circuits in other modalities, including T cells, AAVs and iPSCs, and diseases outside of oncology; and we have executed partnerships with Spark Therapeutics and BlueRock Therapeutics to advance these capabilities.

Forward-Looking Statements
This press release and document contain 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," "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 the Company's SENTI-202 product candidate and the advancement of its SENTI-401 program, its interactions with regulatory authorities and plans to submit an IND application for SENTI-202, its plans to pursue potential strategic partnerships for SENTI 301A and other programs, its projected cash runway; and its continuation of its collaborations with Spark Therapeutics and BlueRock Therapeutics, as well as the timing of these events, as well as statements about the potential attributes and benefits of Senti Bio's product candidates and 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 by any investor as, a guarantee, an assurance, a prediction, or a definitive statement of fact or probability. Actual events and circumstances are difficult or impossible to predict and will differ from assumptions. Many actual events and circumstances are beyond the control of Senti Bio. Many factors could cause actual future results to differ materially from the forward-looking statements in this document, including but not limited to: the risk that results observed in studies of the Company's 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 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 of 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 Senti Bio's product candidates may not have beneficial attributes 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 Quarterly Report on 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 Biosciences, Inc.
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 social media. The information that we post on our website or on social media 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.

Find more information at sentibio.com
Follow us on Linkedin: Senti Biosciences

Contact Senti Bio:
Email: investors@sentibio.com

Kelli Perkins (Media)
Email: kelli@redhousecomms.com


SENTI BIO™
Engineering the Future of Cell and Gene Therapies
January 2023
JANUARY 2023 | SENTI BIOSCIENCES

Disclaimer

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 an IND and the timing of such submission, 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 and pursuit of new collaborations, our manufacturing process and its potential benefits, the benefits of our cell source, 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.

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.

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

IND Anticipated in 2H 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

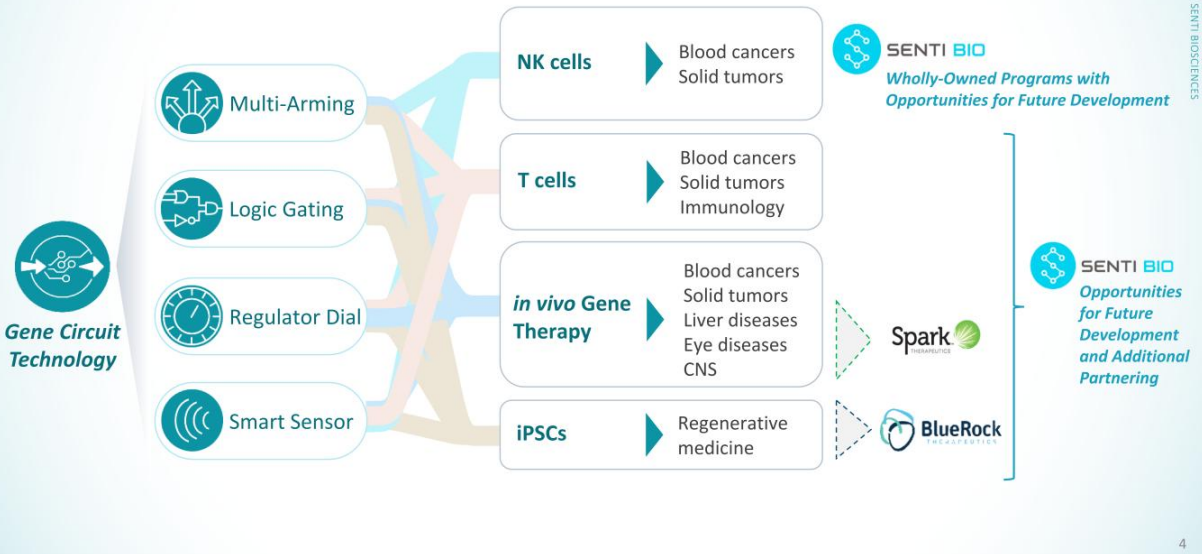
Platform Collaborations

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

Public June 2022 | Anticipated Cash Runway Through At Least Q1 2024 | Headquartered South San Francisco, CA

CNS: Central Nervous System

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



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

Susan Berland	Senior Financial Executive
Brenda Cooperstone, MD	Pfizer Rare Disease
Ed Mathers	NEA
James Collins, PhD	Scientific Co-Founder, MIT
Omid Farokhzad, MD	Seer Inc.
David R. Epstein	Seagen Inc.
Tim Lu MD, PhD	CEO & Co-Founder


CAR-NK Cell Therapy
Pipeline
JANUARY 2023 | SENTI BIOSCIENCES

Gene Circuits Designed to Solve for Key Cell Therapy Challenges

Cancer Cell Therapy Challenges	Senti's Gene Circuit Solutions	
Lack of 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	✗	✓
Scalable and cost-effective manufacturing process	✗	✓

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

- ~70 global peripheral blood derived unengineered NK cell therapy clinical trials[1]
- Well-tolerated (~500 patients clinical experience)[2]
  - No (or minimal) CRS, neurotoxicity, GvHD
- Anti-tumor activity observed in AML[2]
  - 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, proprietary expansion and cryopreservation processes and extensive donor selection address these limitations

[1] Lamers-Kok Journal of Hematology & Oncology 2022; [2] Bachier 2021

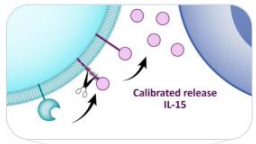
Peripheral Blood-Sourced NK Cells Provide Multiple Advantages for Next Generation CAR-NK Cell Therapies

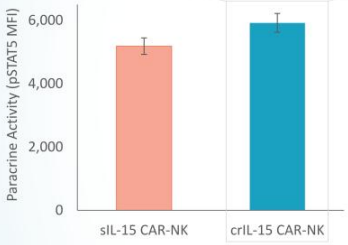
Features	Cord Blood NK Cells	iPSC-Derived NK-Like Cells	Peripheral Blood NK Cells
NK Cell Expandability	Increased expansion potential but smaller number of starting cells	Similar expandability to peripheral blood	Established methods for 1,000-10,000-fold expansion in 14-21 days
Potency and Function	More immature repertoire of NK cells	Unclear if identical to primary NK cells	Full repertoire of functional and mature NK cells
Genetic Engineering	Well established protocols for genetic engineering	iPSC engineering and clone selection with extensive pre-clinical characterization	Well established protocols for genetic engineering
GMP Process Maturity	Established unit operations for clinical process	More complex, multistage process	Well established unit operations for clinical process with defined path for commercial scaling process
Clinical Experience	Modest clinical experience with 30+ clinical trials using cord-derived NK cells	Limited clinical experience - 4 clinical trials using iPSC derived NK cells	Widely used NK cell source in clinical trials with 200+ clinical trials using peripheral NK cells

Peripheral blood-sourced NK cells allow us to immediately leverage an established supply chain, a mature GMP process, and extensive clinical experience to develop our next generation CAR-NK cell therapies

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

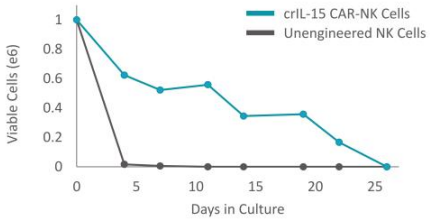
crIL-15: IL-15 released by local proteases → autocrine and paracrine effects



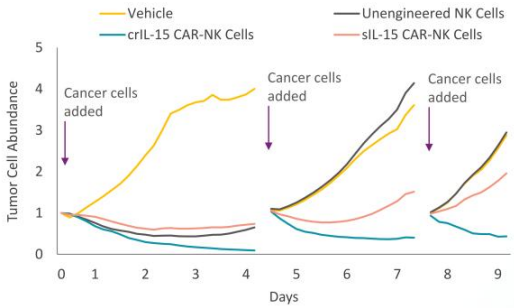


Phospho STAT5 levels increased in T cells exposed to supernatant from either crIL-15 or sIL-15 CAR-NK cell culture

crIL-15 has paracrine activity and activates resting immune cells



crIL-15 increases persistence of CAR- NK cells

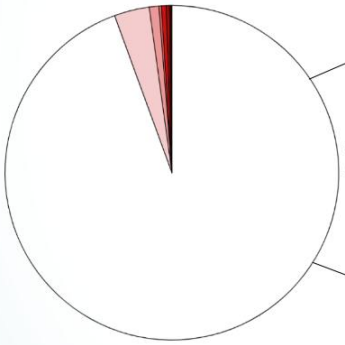


crIL-15 increases CAR-NK serial killing compared to secreted IL-15

sIL-15: secreted wild-type IL-15

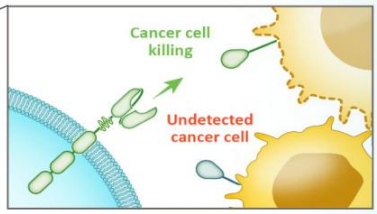
Today's Cell Therapies Are Largely Guided by Single CAR System and Limited to a Small Set of Potential Therapeutic Targets

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

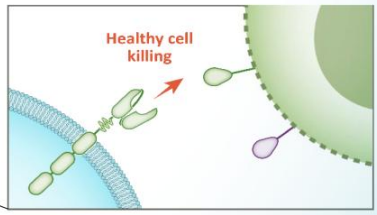


Two key limitations of today's cell therapies

Heterogeneous antigen expression leading to tumor escape

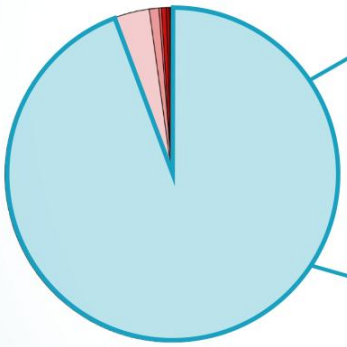


On-target / off-tumor killing leading to poor therapeutic window



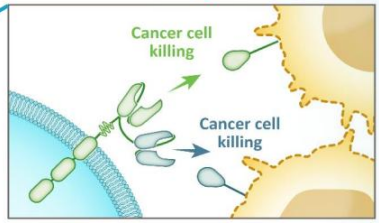
Senti's Gene Circuit Technology Has the Potential to Expand the Range of CAR Cell Therapies With Enhanced Efficacy and Precision

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

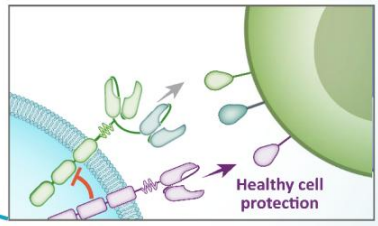


Senti's next-gen capabilities

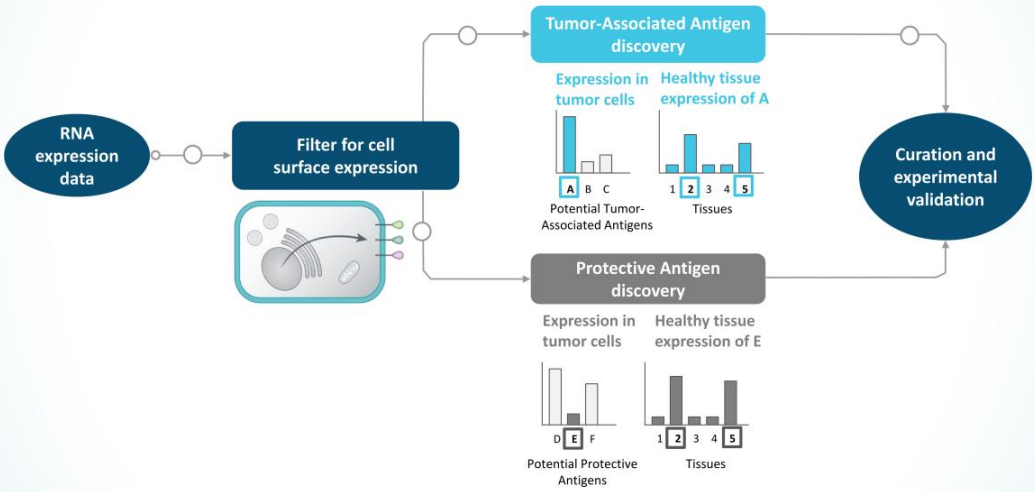
Bivalent activating CAR: OR GATE



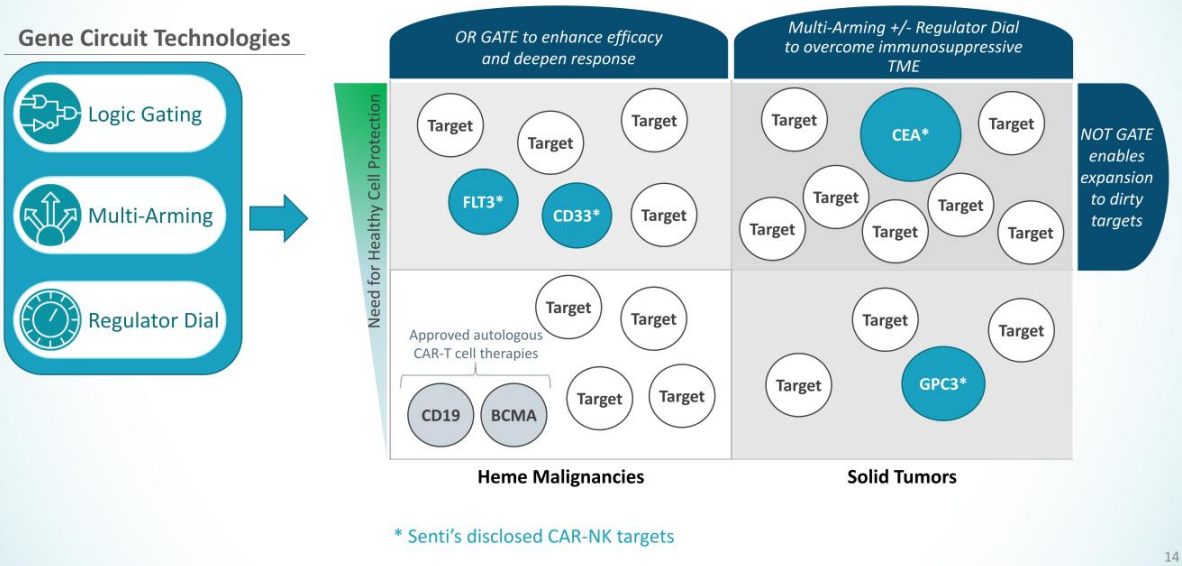
Inhibitory CAR: NOT GATE



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 disclosed CAR-NK targets

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-401	CEA	CRC and other solid tumors				✓ Multi-Arming: designed for enhanced efficacy ✓ crIL-15: autocrine and paracrine activation ✓ NOT GATE selectivity: healthy cell protection ✓ IL-21: sustained anti-tumor function
SENTI-301A	GPC3	HCC and other solid tumors		*Potential for partnering or future clinical development*		✓ Multi-Arming: designed for enhanced efficacy ✓ crIL-15: autocrine and paracrine activation
Additional Programs	Undisclosed	Other tumors				Program candidates integrate Multi-Arming, Logic Gating and/or Regulator Dial Gene Circuits


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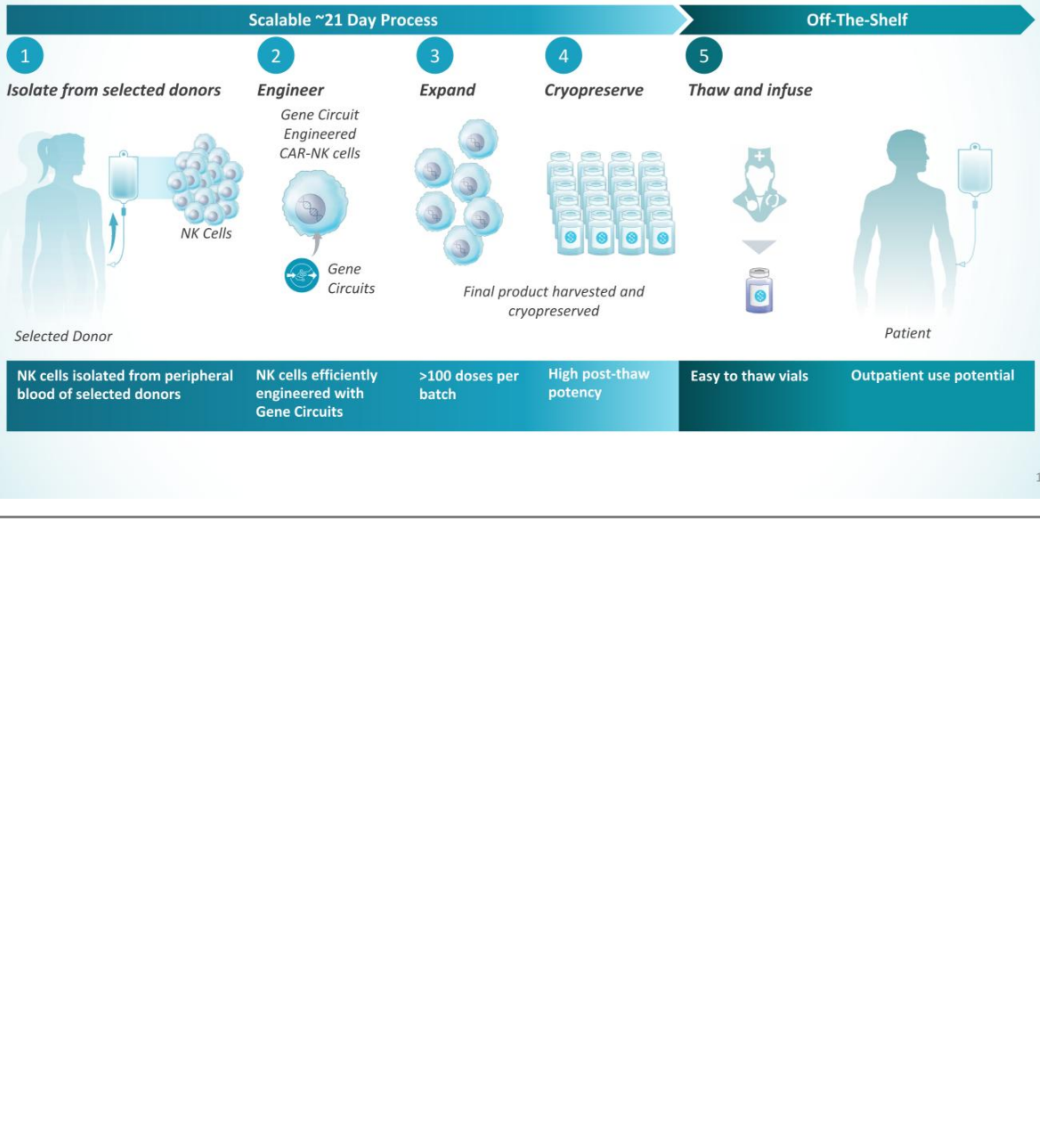
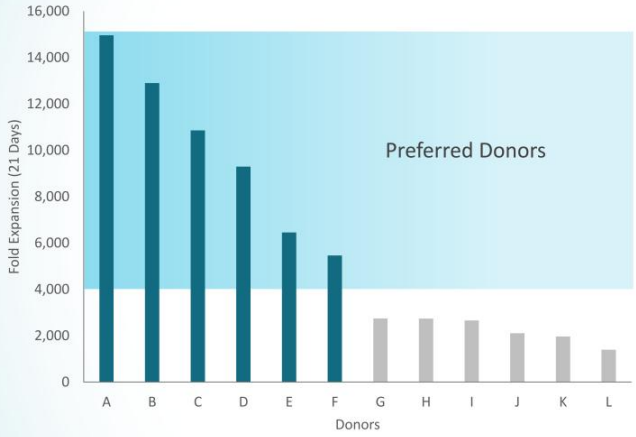
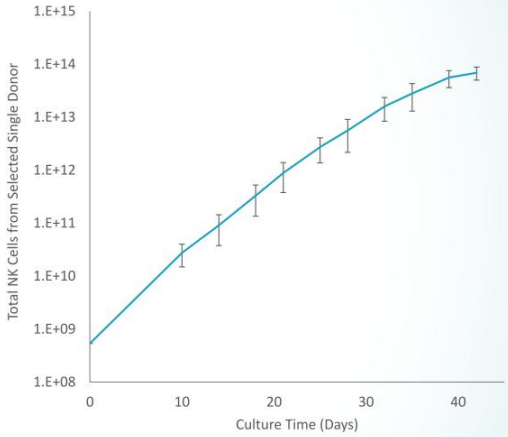
Scalable Manufacturing to Support Off-The-Shelf CAR-NK Products



Senti Selects NK Cell Donors to Support Robust Cell Expansion

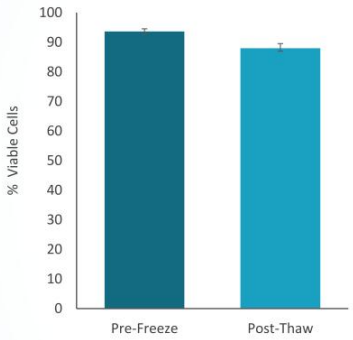


Senti screens and selects GMP donors using NK cell expansion and other functional attributes to minimize variability

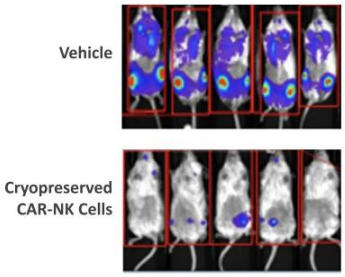


Senti process can potentially generate over 100 trillion NK cells from a single donor collection

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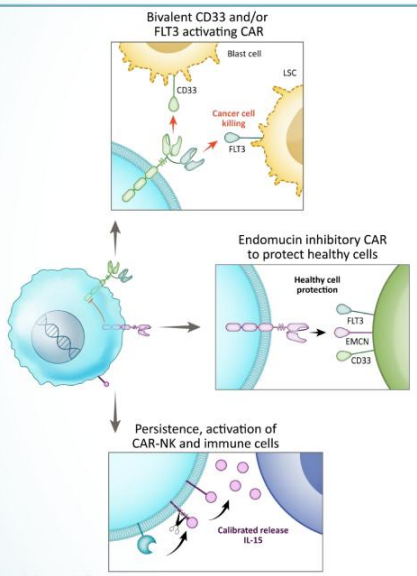
SENTI-202 for CD33 and/or FLT3 Expressing Blood Cancers



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

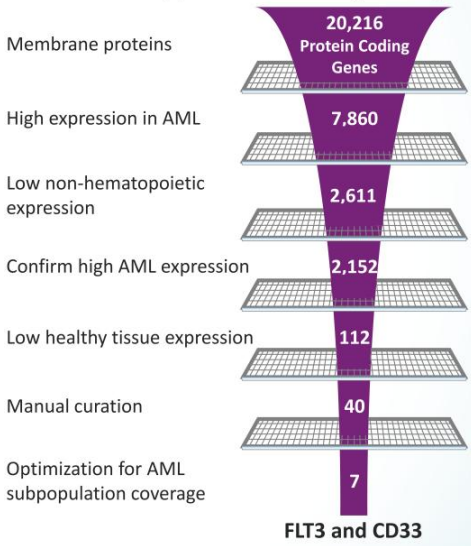
On track for IND in 2H 2023

SENTI-202 Aims to Address Unmet Needs in FLT3 and/or CD33 Expressing Blood Cancers With a Focus on AML

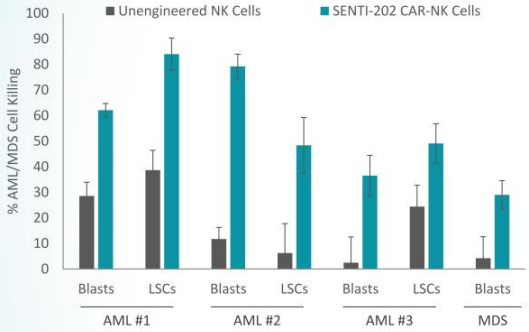
Proven Targets

- **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

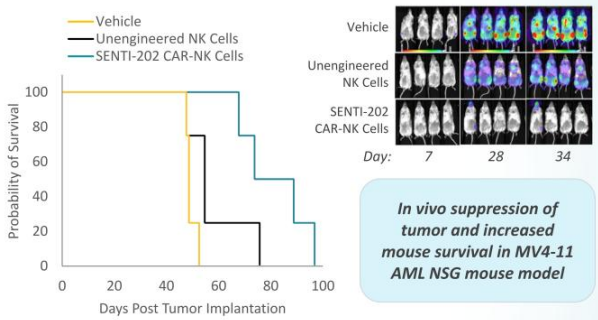
Bioinformatics approach to identify aCAR pair



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



Broad in vitro killing of primary AML and MDS tumor cells

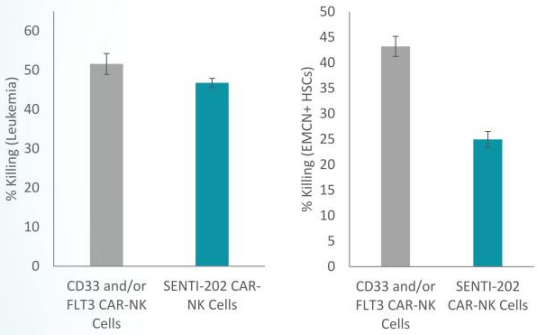


In vivo suppression of tumor and increased mouse survival in MV4-11 AML NSG mouse model

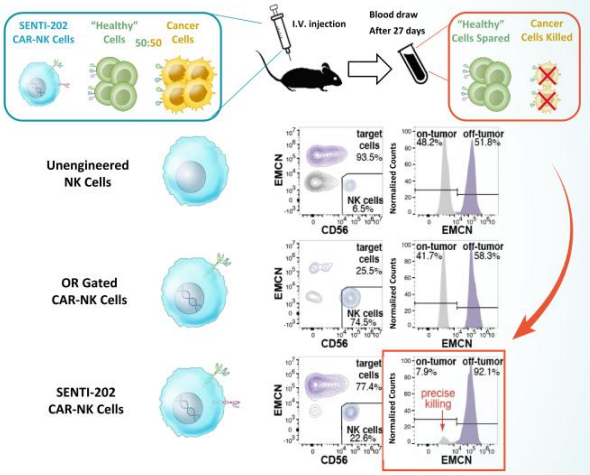
Group	Vehicle	Unengineered NK Cells	SENTI-202 CAR-NK Cells
Median Survival (Days)	*49*	*55*	*81.5*

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.



In vitro protection of healthy primary human HSC fraction expressing EMCN



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

- 20,050 newly diagnosed AML patients in the US[1]
- 30.5% 5-year survival[1]

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

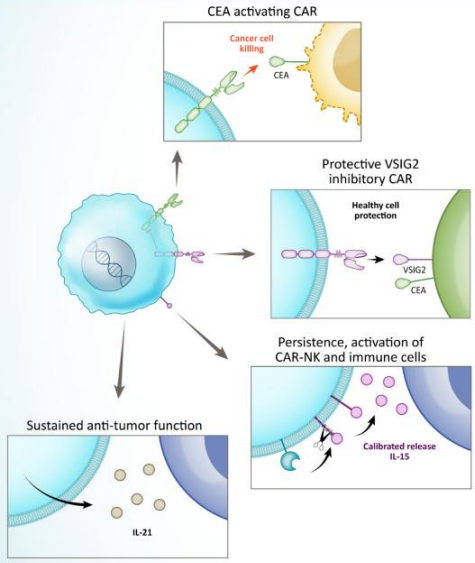
- Safety, DLT, identify recommended Phase 2 dose
- Efficacy using standard ELN 2022 criteria for AML and other disease specific consensus criteria
- PK, pharmacodynamics including endomucin protection, immunogenicity

Planned Study Treatment/ Cycle

Planned data-driven seamless Phase 1 to pivotal design

[1] Seer estimates

SENTI-401 for CEA Expressing Solid Tumors



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

- ***CEACAM5 (CEA) activating CAR*** → metastatic colorectal cancer (mCRC) 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

SENTI-401 Aims to Address Unmet Needs in CEA Expressing Solid Tumors With a Focus on mCRC

High unmet need in patients with colorectal cancer

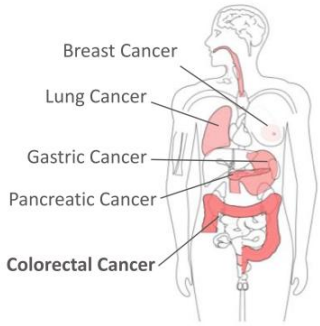
- 151,030 newly diagnosed CRC patients in the US[1]
- 65.1% 5-year survival rate[1]

CEA is an attractive cancer target

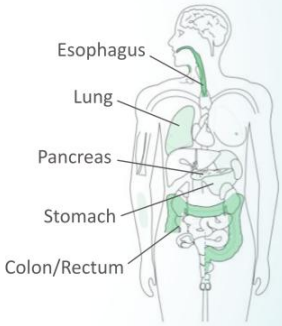
- CEA is overexpressed in several solid tumors, including CRC (~85-90% CEA+) as well as NSCLC, gastric and esophageal cancers
- CEA-targeted adoptive T cell trials reported objective regression but also observed colitis potentially from on-target, off-tumor toxicity[2]

SENTI-401 is designed to target CEA expressing tumors while minimizing on-target, off-tumor toxicity using a NOT GATE

Tumor Types With CEA Overexpression[3]

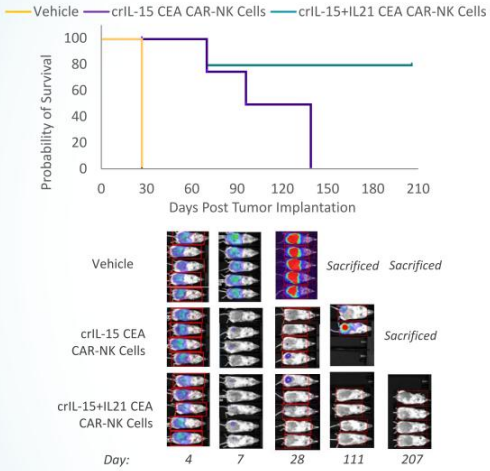


Healthy Tissues With CEA Overexpression[3]



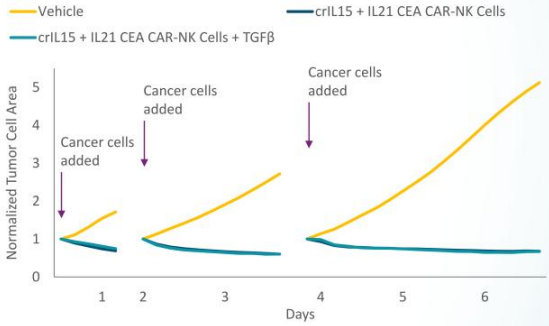
[1] Seer estimates, [2] Parkhurst, et al. [3] Median expression of tumor and normal samples in body map (Log2 (TPM+1) scale). Source: TCGA, Gtex and Nat Genetics 2020 [GSE132465]

Robust Preclinical Activity With CEA CAR-NK Cells Multi-Armed With Both crIL-15 and IL-21



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

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

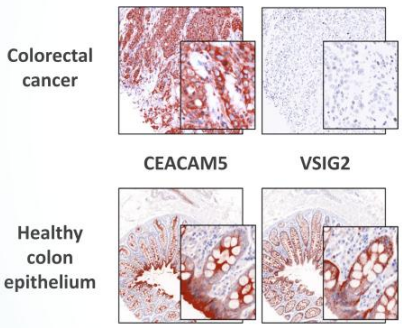


Sustained serial killing with CEA CAR-NK cells expressing crIL-15 and IL-21 even in the presence of the immunosuppressive cytokine TGFβ

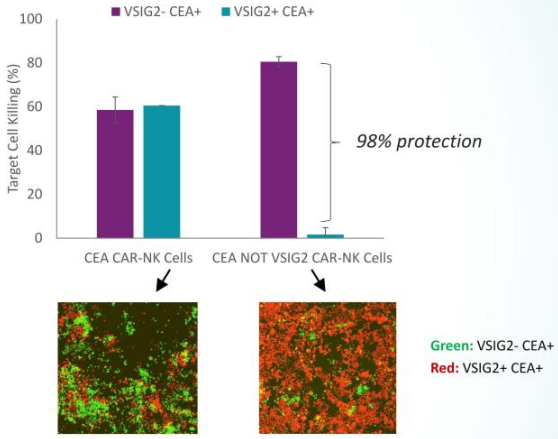
[1] Nature 2018

Senti's Approach to Select Paired Target and Protective Antigens Translates to Rapid Preclinical Proof of Principle for Protecting Healthy VSIG2+ cells

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



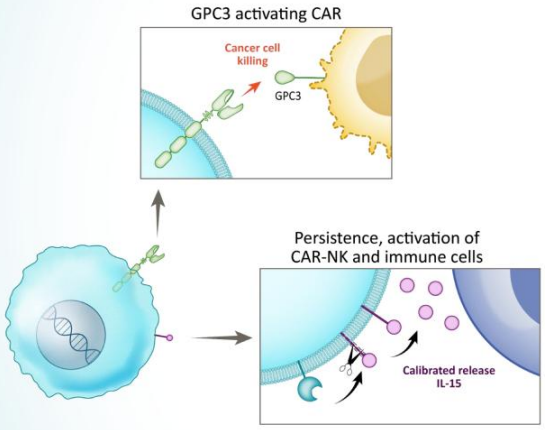
CEACAM5: 85-90% of CRC and 40-60% of other solid tumors including lung cancer[1]



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

[1] Goldstein 2005

SENTI-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

Pursuing strategic geographic partnerships to enable clinical development in areas with high HCC incidence such as in China

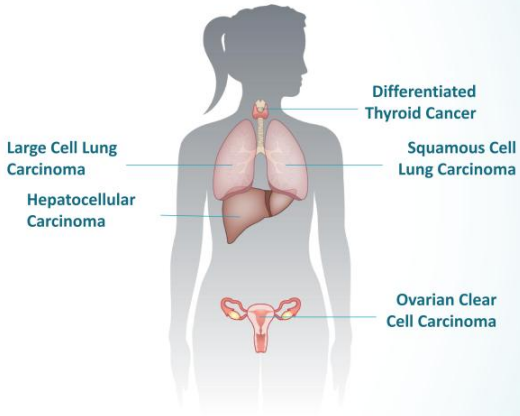
SENTI-301A Aims to Address Unmet Needs in GPC3 Expressing Solid Tumors With a Focus on HCC

GPC3 is an attractive 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

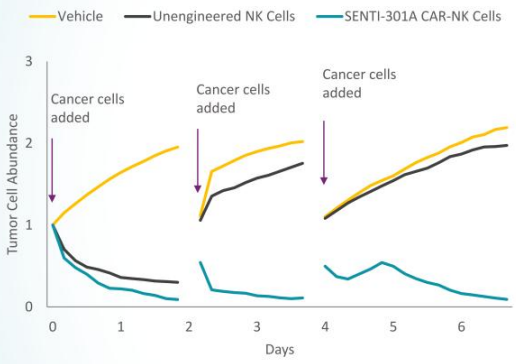
- Aim to address unmet need in HCC as the initial focus given the lack of targeted therapies and lack of effective immunotherapies
- Tackle multiple solid tumors with high GPC3 antigen expression via NKs multi-armed with GPC3 CAR and crIL-15



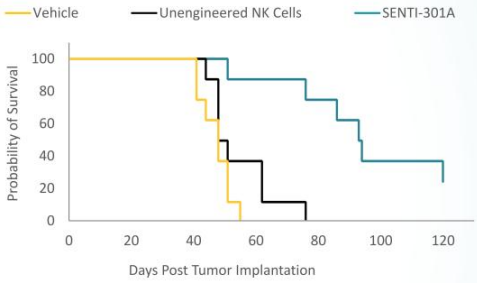
Common GPC3 expressing tumors

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

SENTI-301A Preclinical Anti-Cancer Activity



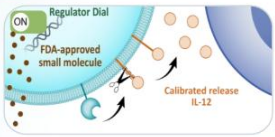
Effective in vitro serial killing of HepG2 cell line



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

Increased survival and response in HepG2 mouse model

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



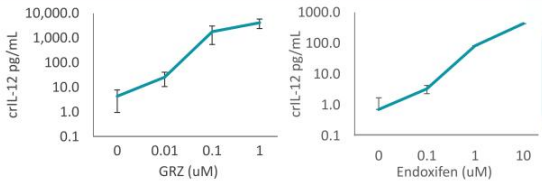
IL-12 is a well-known immuno-stimulatory cytokine

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

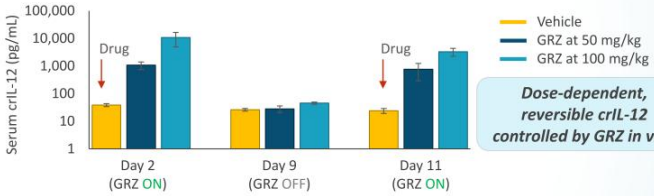
IL-12 clinical use has been limited by toxicities

- 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

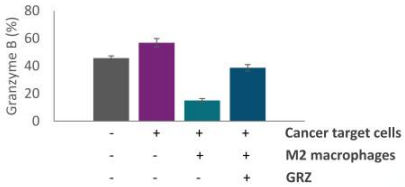
[1] Leonard 1997



Drug dose-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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Platform and Collaboration Opportunities

Multiple Platform Collaborations Extend Utility of Gene Circuits

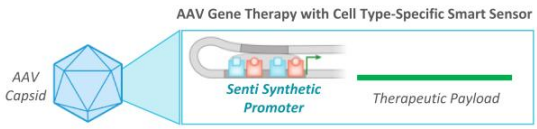
Program	Indications	Gene Circuit	Discovery	IND enabling	Phase 1	Rights
Gene Therapies for Tissue-Directed Targets						
GC-1001/GC-1002	Eye	Smart Sensor				Spark Therapeutics, Roche
GC-1003/GC-1004	CNS	Smart Sensor				
GC-1005	Liver	Smart Sensor				
Cell Therapies for Regenerative Medicine						
GC-1101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

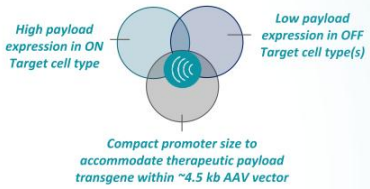
Spark

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

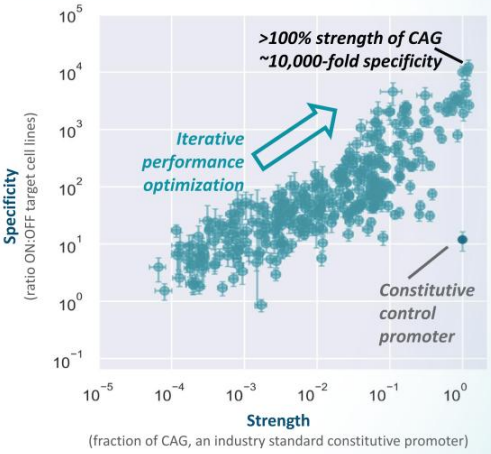
Smart Sensor Promoters Are Designed to Address Key Challenges in Gene Therapy

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:

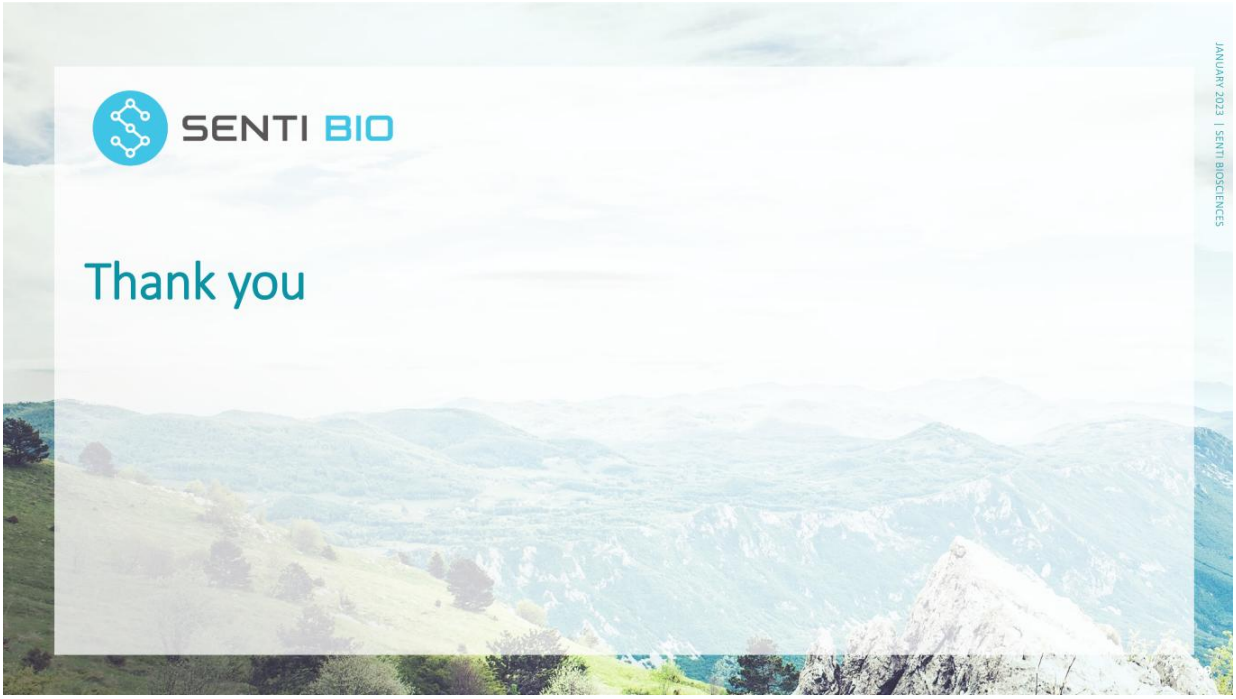
- Enhancing specificity to target tissue(s) (and thus limiting off-target tissue toxicities) and
- Increasing strength, potentially enabling more efficacious therapies

Smart Sensor Promoter Data



Completed 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-401 *CEA* *CRC and other solid tumors*	Presented preclinical data at SITC in November 2022	Present data at key scientific conferences
SENTI-301A *GPC3* *HCC and other solid tumors*	Presented preclinical data at SITC in November 2022	
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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