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): November 10, 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 2.02 Results of Operations and Financial Condition.

On November 10, 2022, Senti Biosciences, Inc. (the "Company") issued a press release announcing its financial results for the quarter ended September 30, 2022.

The information in this Item 2.02 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"), nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933 (the "Securities Act"), as amended.

Item 7.01 Regulation FD Disclosure.

Reference is made to the disclosure set forth above in Item 2.02 of this Current Report on Form 8-K which is incorporated herein by reference.

Beginning on November 10, 2022, the Company will participate in conferences with investors. A copy of the Company's presentation slide deck that will be presented is being furnished as Exhibit 99.2 to this report on Form 8-K and has been posted to the Company's website at https://investors.sentibio.com/events-presentations.

Limitation of Incorporation by Reference

In accordance with General Instruction B.2. of Form 8-K, the information in this Current Report on Form 8-K, including the exhibits, is intended to be furnished and shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934, or otherwise subject to the liabilities of that section and shall not be deemed to be incorporated by reference into any filing of the Company under the Securities Act 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.

Cautionary Statements

This filing and the presentation include "forward-looking statements" within the meaning of Section 27A of the Securities Act, and Section 21E of 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 "Risk Factors" contained in the Company's Form S-1 filed with the Securities and Exchange Commission (the "Commission") on September 12, 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 November 10, 2022
99.2	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: November 10, 2022

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

Senti Bio Reports Third Quarter Financial Results and Pipeline Updates

- SENTI-202 on track for IND filing in 2023; clinical plans for SENTI-202 expand beyond AML to CD33 and/or FLT3 expressing hematologic malignancies including MDS -

- Selected development candidate for program to treat GPC3-expressing solid tumors including HCC, SENTI-301A; expected IND filing in 2023 -

- Preclinical data from two solid tumor CAR-NK programs highlighted at SITC -

- Cash position of $114.9 million as of September 30, 2022; maintain expectation of cash runway into 2024 -

SOUTH SAN FRANCISCO, Calif., November 10, 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 reported financial results for the third quarter ended September 30, 2022, and highlighted recent pipeline advances, including an outline for its proposed Phase 1 clinical trial plans for SENTI-202, to include patients with CD33 and/or FLT3 expressing hematologic malignancies including acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). Senti Bio also selected SENTI-301A as the development candidate from its GPC3 targeting solid tumor program. SENTI-301A is a Multi-Armed off-the-shelf chimeric antigen receptor natural killer (CAR-NK) cell therapy candidate designed for the treatment of GPC3 expressing tumors including hepatocellular carcinoma (HCC), the most common form of liver cancer in adults.

In addition, Senti Bio's data presentation at the Society for Immunotherapy of Cancer (SITC) Annual Meeting outlined continued progress with the solid tumor CAR-NK product candidate SENTI-301A and the SENTI-401 program. Both programs use Senti Bio's proprietary gene circuit technology to potentially enhance activity against solid tumors by incorporating potent activating CARs and multifunctional cytokines to influence the tumor milieu as well as support enhanced CAR-NK activity. Specifically, SENTI-401 targets carcinoembryonic antigen (CEA) cell adhesion molecule 5 expressing solid tumors, including colorectal cancer (CRC), and also includes a NOT Logic Gate gene circuit to protect CEA expressing healthy cells from potential "on target, off tumor" killing. This Logic Gating strategy is designed to enable selective cytotoxicity of CAR-NK cells against tumor cells while protecting healthy cells.

"I am proud of our continued progress toward the clinic with our CAR-NK cell therapy oncology programs for both hematologic malignancies and solid tumors. With SENTI-202, we believe that we have generated compelling preclinical data demonstrating the killing of primary AML and MDS tumor cells, while maintaining protection of healthy hematopoietic stem cells, to support a clinical trial aimed at both cancer types, and we remain on track to file an IND in 2023," said Timothy Lu, MD, PhD, Chief Executive Officer and Co-Founder of Senti Bio. "In addition, we recently selected our development candidate, SENTI-301A, which is designed to treat GPC3 positive tumors including HCC, and are on track to file an IND in 2023."

Lu added, "Our scientists continue to generate exciting data across our pipeline; data from SENTI-301A and SENTI-401 are being highlighted today at the SITC Annual Meeting, and we are extremely excited to preview new data on SENTI-202 at the American Society of Hematology meeting next month. We remain steadfast in our vision of developing smarter medicines based on truly innovative advancements with our gene circuit technology platform."

RECENT PIPELINE HIGHLIGHTS

CAR-NK Cell Oncology Pipeline and Gene Circuit Platform Highlights:

SENTI-202: A Logic Gated off-the-shelf CAR-NK cell therapy development candidate designed to selectively target and eliminate CD33 and/or FLT3 expressing hematologic malignancies, such as AML and MDS, while sparing the healthy bone marrow.

- Announced the acceptance of an abstract for presentation at the American Society of Hematology (ASH) meeting in December 2022; preclinical data to highlight the use of Logic Gating gene circuits to target and eliminate AML cells while sparing healthy hematopoietic stem cells.
- Outlined plans for a proposed Phase 1 clinical trial, including a dose-finding phase in patients with relapsed and/or refractory CD33 and/or FLT3 expressing hematologic malignancies. Disease-specific expansion cohorts would include relapsed and/or refractory AML. Multiple doses of SENTI-202 administration following standard fludarabine/cyclophosphamide (Flu/Cy) lymphodepleting chemotherapy is planned along with a potential to receive multiple cycles. Clinical trial endpoints would evaluate safety and identification of a recommended Phase 2 dose of SENTI-202, as well as efficacy using standard disease-specific response criteria.
- Manufacturing efforts and GMP facility buildout remain on track towards enabling flexible clinical manufacturing of CAR-NK cells in 2023.
- An IND application for SENTI-202 is expected to be submitted to the U.S. Food and Drug Administration (FDA) in 2023.

SENTI-301A: A Multi-Armed off-the-shelf CAR-NK cell therapy development candidate designed for the treatment of GPC3 expressing tumors, including HCC.

- Selected a development candidate, SENTI-301A, based on extensive optimization using Senti Bio's proprietary screening platform for off-the-shelf CAR-NK cells with potent anti-tumor activity. SENTI-301A uses the following components:
  - Engineered NK cells that target glypican 3 (GPC3), which is highly expressed in 70% to 90% of HCCs and has low or no expression on normal adult tissues.
  - Calibrated release interleukin-15 (crIL-15), a multi-functional immuno-stimulatory payload designed to simultaneously stimulate surrounding immune cells and promote CAR-NK cell expansion, persistence and tumor killing.
- Preclinical data presented today at the SITC Annual Meeting demonstrates the use of gene circuits to improve the cytotoxicity and persistence of GPC3 targeting CAR-NK cells in treating HCC. Senti Bio's novel GPC3 targeting activating CAR combined with crIL-15 technology provide the CAR-NK cells multi-arming to enhance persistence and killing activity of the NK cells, and to leverage the endogenous immune system for increased anti-tumor activity. The data presents evidence of robust *in vitro* and *in vivo* killing of relevant tumor cells with SENTI-301A.
- An IND application for SENTI-301A is expected to be submitted to the FDA in 2023

The presentation at the SITC Annual Meeting also includes data from ongoing development of Regulator Dial gene circuits that control expression of crIL-12 in response to FDA-approved small molecules. These data indicate that the Company's Regulatory Dial gene circuits may be used with an expanded number

of FDA-approved drugs to modulate crIL-12 expression, including tamoxifen and grazoprevir, among others. These data give the Regulator Dial the potential for broader applicability beyond GPC3 expressing cancers and thus, the Company is actively exploring the continued development of this gene circuit for product opportunities across a wide range of additional solid tumors.

SENTI-401: A Logic Gated, Multi-Armed off-the-shelf selective CAR-NK cell therapy development program designed to precisely target CEA positive solid tumors (e.g., colorectal, pancreatic and lung cancers) while sparing healthy cells using the NOT Logic Gate.

- Presented preclinical proof-of-concept data at the SITC Annual Meeting that demonstrates the robust anti-cancer functionality of Logic Gated, Multi-Armed CAR-NK cells against a variety of colorectal cancer models:
  - Evaluated ways to enhance NK cell persistence and function using a combination of crIL-15 and IL-21, a previously undisclosed Multi-Arming combination, resulting in significantly enhanced and durable killing of CEA positive target cells *in vitro* and *in vivo.*
  - Long-term anti-tumor responses: a single dose of CEA targeting CAR-NK cells armed with crIL-15+IL-21 resulted in durable anti-tumor activity in human CRC xenograft models that express CEA, including complete tumor regressions.
  - CAR-NK cells equipped with an optimized inhibitory CAR (iCAR) suppressed activating CAR (aCAR)-mediated killing of healthy cells that co-expressed VSIG2-and CEA without diminishing aCAR-mediated anti-tumor activity of CEA expressing tumor cells.

THIRD QUARTER 2022 FINANCIAL RESULTS

- Cash and Cash Equivalents: As of September 30, 2022, Senti Bio held cash and cash equivalents of $114.9 million, which the Company believes is sufficient to fund operations into 2024.
- R&D Expenses: Research & development expenses were $8.1 million for the quarter ended September 30, 2022, compared to $5.4 million for the same period in 2021. The increase includes an additional $0.5 million in non-cash stock-based compensation expense.
- G&A Expenses: General and administrative expenses were $10.8 million for the quarter ended September 30, 2022, compared to $7.1 million for the same period in 2021. The increase includes an additional $1.2 million in non-cash stock-based compensation expense.
- Net Loss: Net loss was $16.6 million, or $0.38 per basic and diluted share, for the quarter ended September 30, 2022.
- CapEx: Capital expenditures were $14.2 million for the quarter ended September 30, 2022, primarily driven by the GMP manufacturing facility buildout and related equipment purchases.

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 estimates and forecasts of financial and cash runway and the sufficiency of such cash runway, Senti Bio’s ability to continue to advance its pipeline of preclinical programs and product candidates, Senti Bio’s research and development activities, the generation and release of additional preclinical data, commencement of IND-enabling studies and the timing of submission of IND filings, plans for a Phase 1 clinical trial, and GMP manufacturing start up activities, 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 events to differ materially from the forward-looking statements in this document, including but not limited to: (i) changes in domestic and foreign business, market, financial, political and legal conditions, (ii) changes in the competitive and highly regulated industries in which Senti Bio operates, variations in operating performance across competitors, changes in laws and regulations affecting Senti Bio’s business, (iii) the ability to implement business plans, forecasts and other expectations, (iv) the risk of downturns and a changing regulatory landscape in Senti Bio’s highly competitive industry, (v) risks relating to the uncertainty of any projected financial information with respect to Senti Bio, (vi) risks related to uncertainty in the timing or results of Senti Bio’s preclinical studies, IND filings, and GMP manufacturing startup activities, (vii) Senti Bio’s dependence on third parties in connection with preclinical and IND-enabling studies, IND filings, and GMP manufacturing buildout and startup activities, (viii) risks related to delays and other impacts from the COVID-19 pandemic, and (ix) the success of any future research and development efforts by Senti Bio. 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 registration statement on Form S-1 (File No. 333-267390), 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
Follow us on Linkedin: Senti Biosciences
Follow us on Twitter: @SentiBio

Senti Biosciences, Inc.
Unaudited Selected Consolidated Balance Sheet Data

(in thousands)

	September 30, 2022	December 31, 2021
Cash and cash equivalents	$ 114,940	$ 56,034
Restricted cash	3,295	3,257
Property and equipment, net	47,259	12,368
Operating lease right-of-use assets	18,883	20,708
Total assets	189,441	96,702
Total liabilities	49,098	36,326
Redeemable convertible preferred stock	—	171,833
Total stockholders' equity (deficit)	140,343	(111,457)

Senti Biosciences, Inc.
Unaudited Consolidated Statements of Operations

(in thousands, except share and per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Total revenue	$ 1,766	$ 1,103	$ 4,227	$ 1,968
Operating expenses:				
Research and development	8,056	5,410	24,904	15,548
General and administrative	10,795	7,116	29,936	15,981
Total operating expenses	18,851	12,526	54,840	31,529
Loss from operations	(17,085)	(11,423)	(50,613)	(29,561)
Total other income (expense), net	445	17	10,613	(14,854)
Net loss	$ (16,640)	$ (11,406)	$ (40,000)	$ (44,415)
Net loss per share, basic and diluted	$ (0.38)	$ (3.90)	$ (1.99)	$ (15.33)
Weighted-average shares outstanding, basic and diluted	43,424,172	2,925,957	20,150,459	2,897,850


SENTI BIO™
Corporate Presentation
November 2022
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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," "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 preclinical, clinical and therapeutic potential of our gene circuit platform and our product candidates, including our plans to submit INDs for our product candidates, the market opportunity for our product candidates, if approved, the progress and success of our existing collaborations and our ability to enter into new collaborations, our manufacturing capabilities and our plans to begin operating our cGMP facility, our cash position and runway, and the timing of these items, 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. 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. 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, uncertainty in the timing and results of our preclinical and clinical development activities, the risk that our product candidates may result in toxicities or adverse events that delay or preclude their further development, changes in the regulatory or competitive landscape for our product candidates and platform technology, our inability to maintain our existing collaborations or secure new partnerships, and changes in overall market conditions as well as those set forth in the section titled "Risk Factors" in our Registration Statement on Form S-1 (File No. 333-267390) filed with the Securities and Exchange Commission (the "SEC") on September 12, 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

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

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	Former CEO of Novartis Pharma
Tim Lu MD, PhD	CEO & Co-Founder


CAR-NK Cell Therapy
Pipeline
NOVEMBER 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 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	NA	✓
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

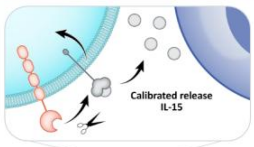
Limited activity beyond AML, persistence, durability, donor variability and select single clinical center usage

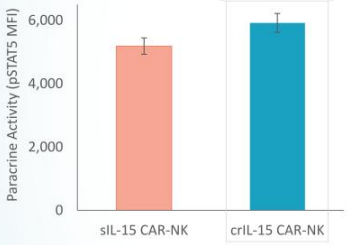
Senti's Gene Circuit technology, donor selection and scalable manufacturing address these limitations

[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

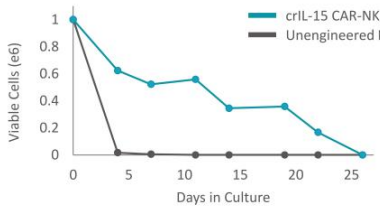
crIL-15: IL-15 released by local proteases → autocrine and paracrine effects



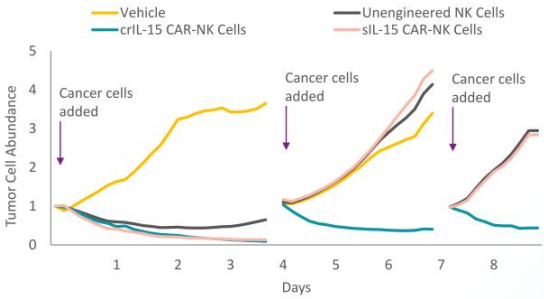


Phospho STAT5 levels increased in T cells exposed to supernatant from either crIL-15 or sIL-15 CAR-NK cell culture

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

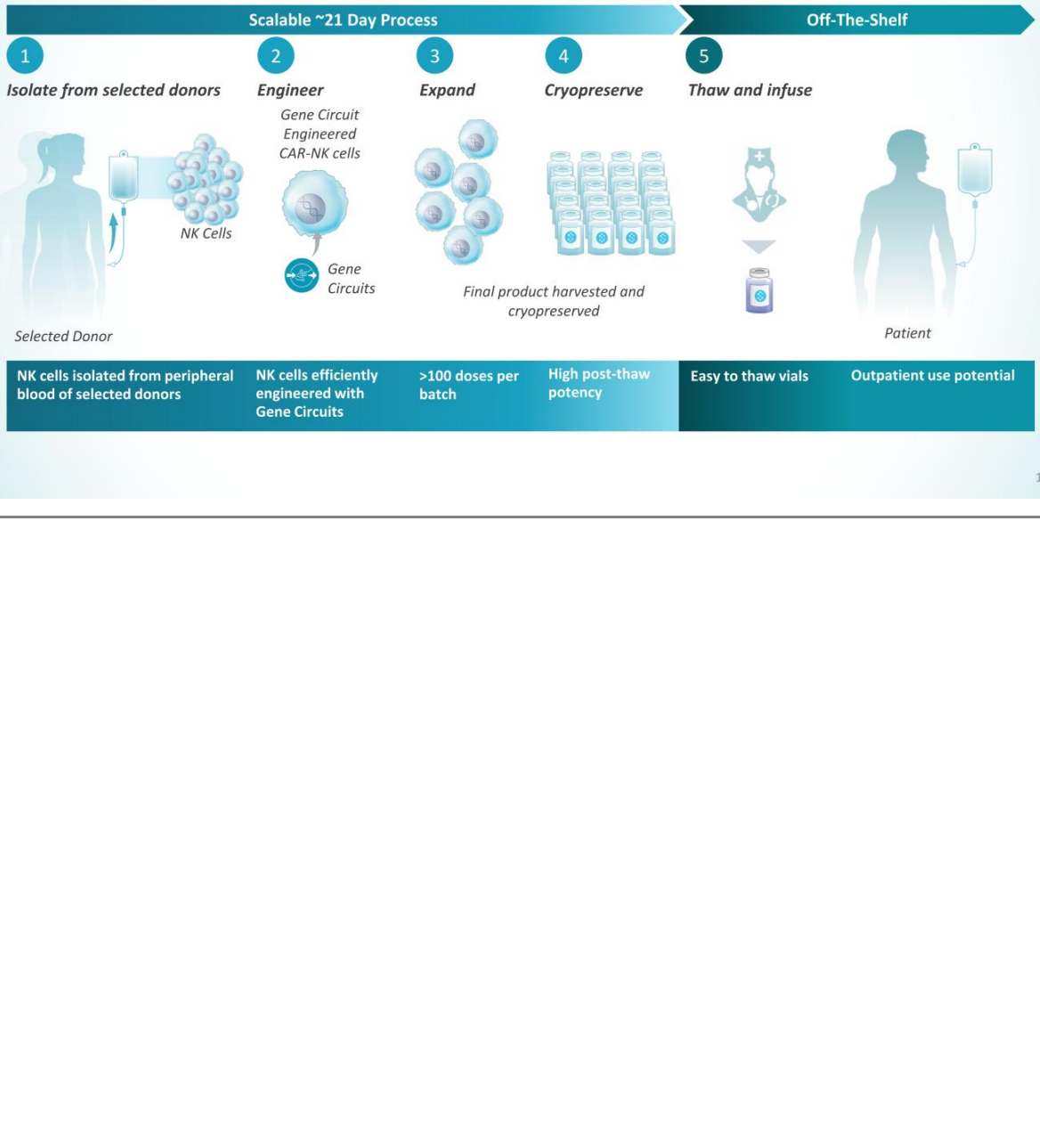
sIL-15: secreted wild-type IL-15

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

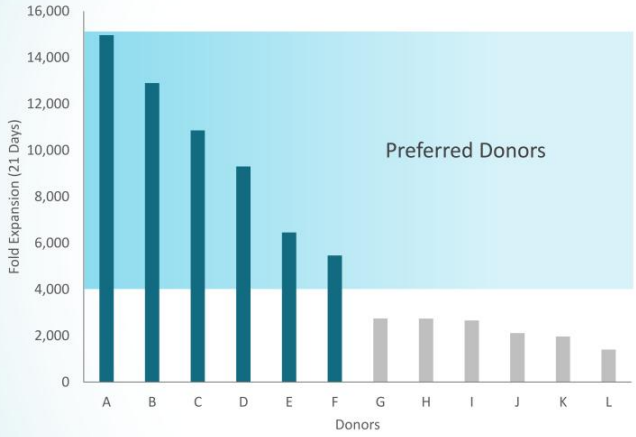
Program	Target	Indications	Discovery	IND enabling	Phase 1	Gene Circuits
SENTI-202	CD33, FLT3 bivalent	AML, MDS and other blood cancers		2023 IND		✓ Multi-Arming: designed for enhanced efficacy ✓ crIL-15: autocrine and paracrine activation ✓ OR GATE: bivalent activation ✓ NOT GATE selectivity: healthy 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
NOVEMBER 2022 | SENTI BIOSCIENCES

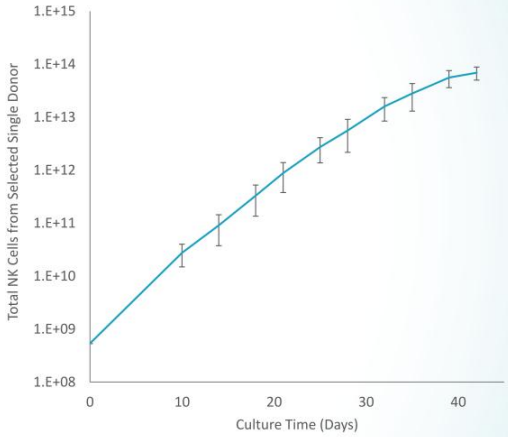
Scalable Manufacturing to Support Off-The-Shelf CAR-NK Products



Senti Selects NK Cell Donors to Support Robust Cell Expansion

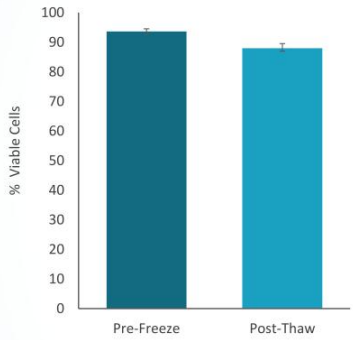


Senti screens and selects GMP donors using NK cell expansion and other functional attributes to minimize variability

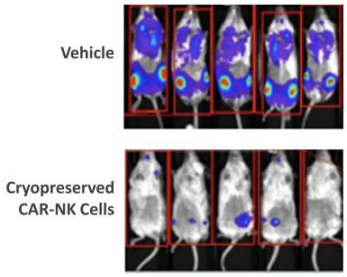


Senti process can potentially generate over 100 trillion NK cells from a single donor collection

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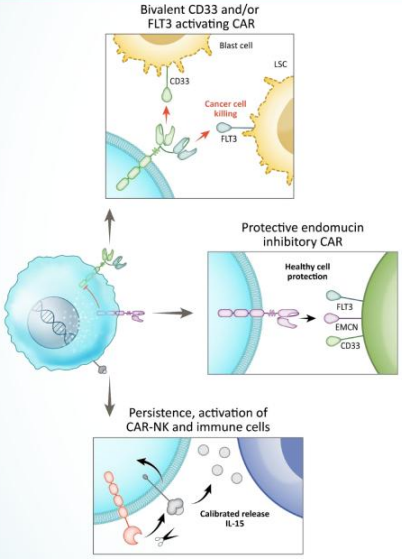
SENTI-202 for CD33 and/or FLT3 Expressing Blood Cancers



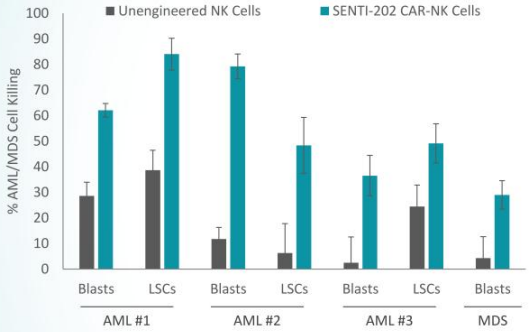
LSCs: Leukemic Stem Cells

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

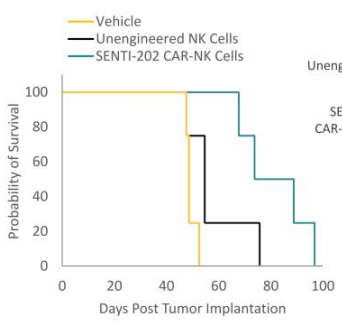
- ***OR GATE:*** *bivalent* CD33 and/or FLT3 activation → potential for deep and durable responses in acute myeloid leukemia (AML) and other blood cancers.
- ***NOT GATE:*** inhibition by endomucin (EMCN) protective antigen selectively expressed on healthy hematopoietic stem cells (HSCs) → potential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

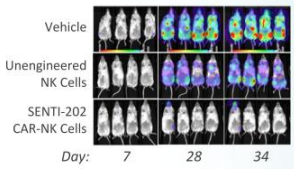
On track for IND in 2023

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



Broad in vitro killing of primary AML and MDS tumor cells



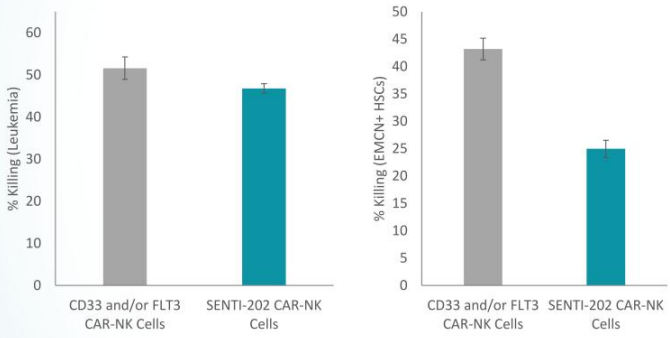


In vivo suppression of tumor and increased mouse survival in MV4-11 AML NSG mouse model

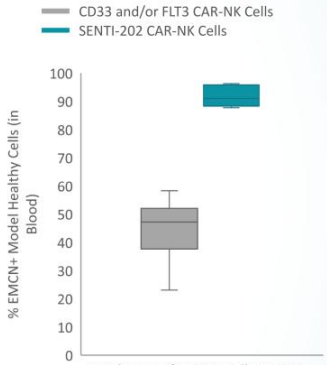
Group	Vehicle	Unengineered NK Cells	SENTI-202 CAR-NK Cells
Median Survival (Days)	*49*	*55*	*81.5*

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

- 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

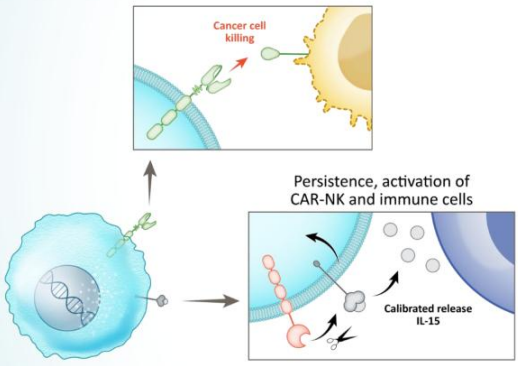
- Safety, DLT, identify recommended Phase 2 dose
- Efficacy using standard ELN 2022 criteria for AML and other disease specific consensus criteria
- PK, pharmacodynamics including endomucin protection, immunogenicity

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

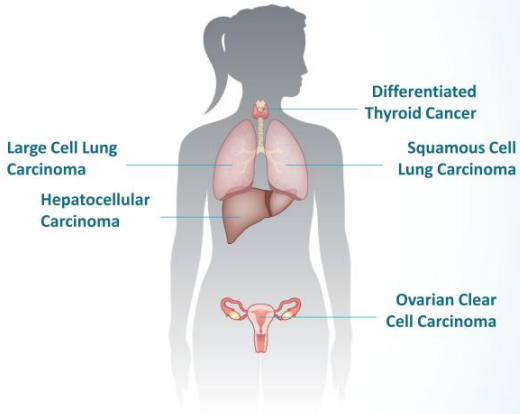
SENTI-301A Aims to Address Unmet Needs in GPC3 Expressing Solid Tumors With a Focus on HCC

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

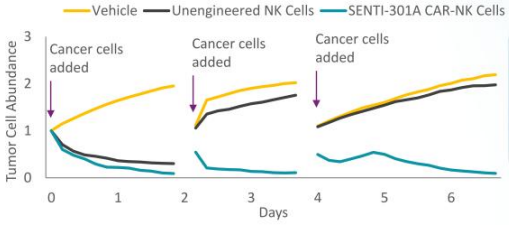
20.8% 5-year survival rate[1]

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

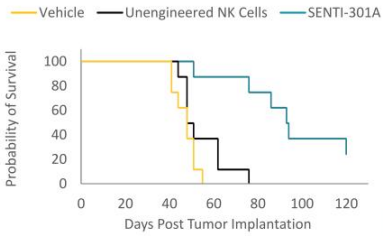
- Must have received standard of care
- Advanced solid tumors with focus on HCC during dose finding
- Disease specific expansion cohorts of advanced HCC and other solid tumors including lung cancer

Planned study treatment

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



Effective in vitro serial killing of HepG2 cell line

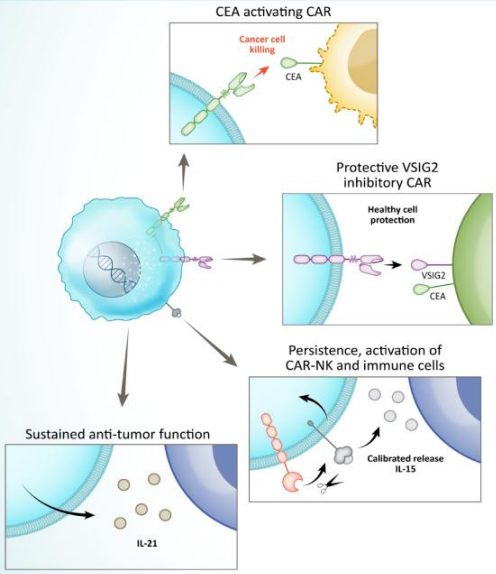


Increased survival and response in HepG2 mouse model

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

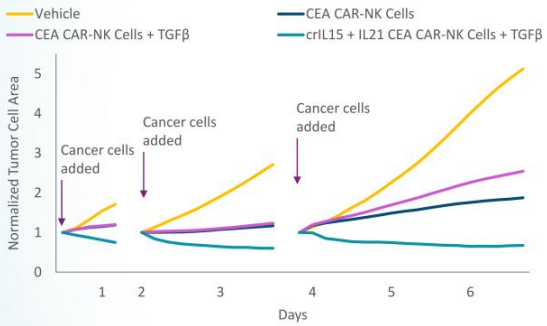


Multi-Armed, off-the-shelf, selective CAR-NK

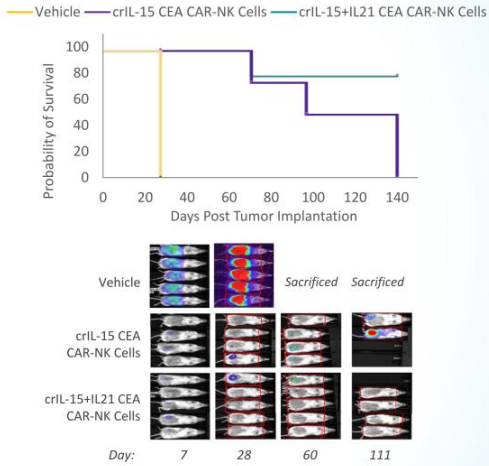
- ***CEACAM5 (CEA) activating CAR*** → colorectal cancer (CRC) and other solid tumors
- ***NOT GATE:*** inhibition by VSIG2 antigen on healthy epithelial cells → potential for improved safety, increased therapeutic window and reduced on-target, off-tumor toxicity
- ***crIL-15*** → potential for increased 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

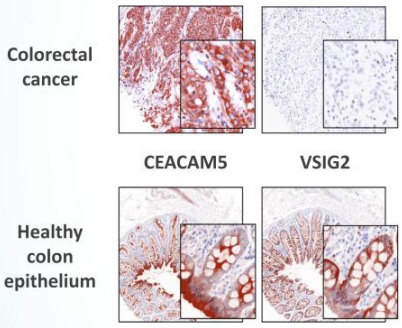


Arming CEA CARs with the combination of Senti's proprietary crIL-15 and IL-21 results in improved anti-tumor activity of NK cells

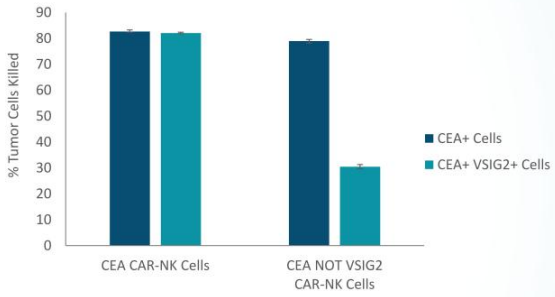
[1] Nature 2018

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



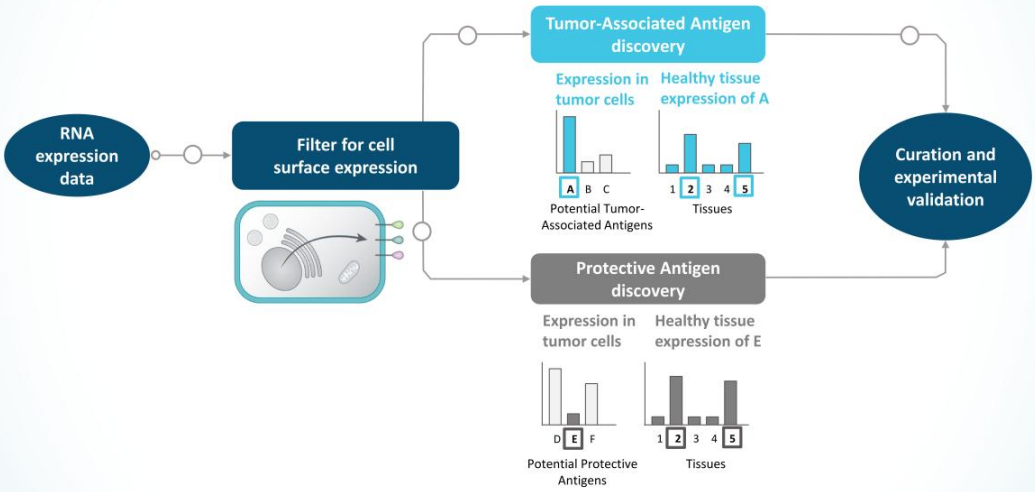
CEACAM5: 85-90% of CRC and 40-60% of other solid tumors including lung cancer[1]



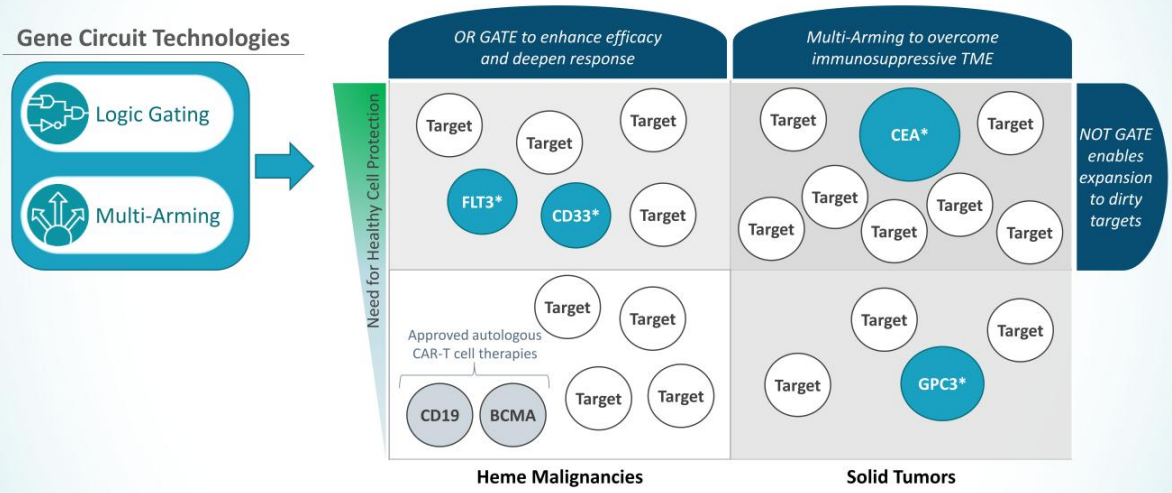
Decreased cell killing of VSIG2 expressing cells with addition of inhibitory CAR construct

[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

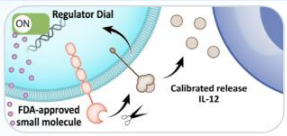


Gene Circuits Can Vastly Expand the Universe of Cancer Targets and Tumors That Can Be Addressed With Cell Therapies



* 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



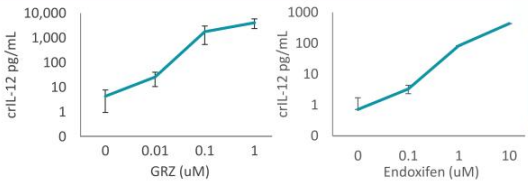
IL-12 is a well-known immuno-stimulatory cytokine

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

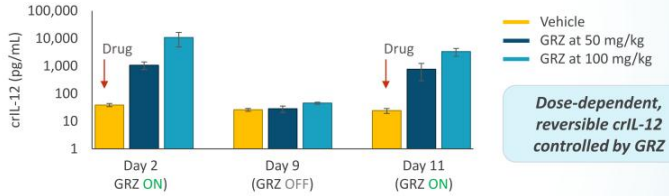
IL-12 clinical use has been limited by toxicities

- 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

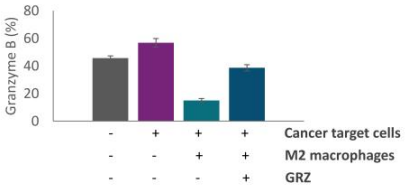
[1] Leonard 1997



Concentration dependent crIL-12 production



Dose-dependent, reversible crIL-12 controlled by GRZ



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

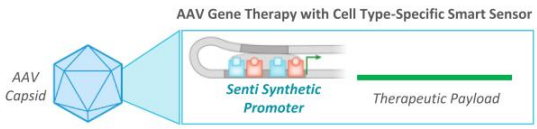
Program	Indications	Gene Circuit	Discovery	IND enabling	Phase 1	Rights
Gene Therapies for Tissue-Directed Targets						
GC-1001/GC-1002	Eye	Smart Sensor				Spark Therapeutics, Roche
GC-1003/GC-1004	CNS	Smart Sensor				
GC-1005	Liver	Smart Sensor				
Cell Therapies for Regenerative Medicine						
GC-1101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

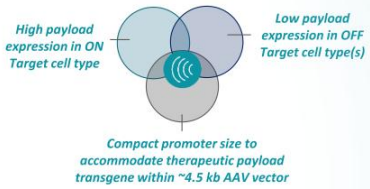
Spark

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

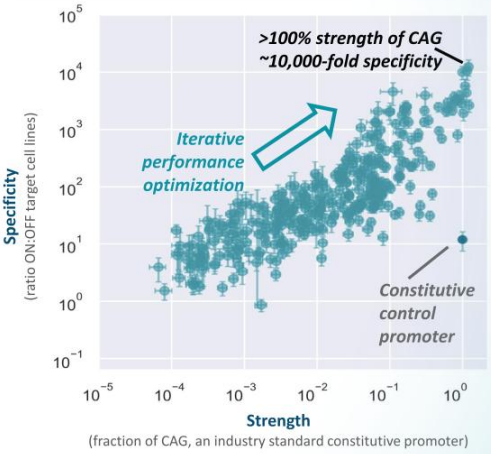
Smart Sensor Promoters Are Designed to Address Key Challenges in Gene Therapy

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

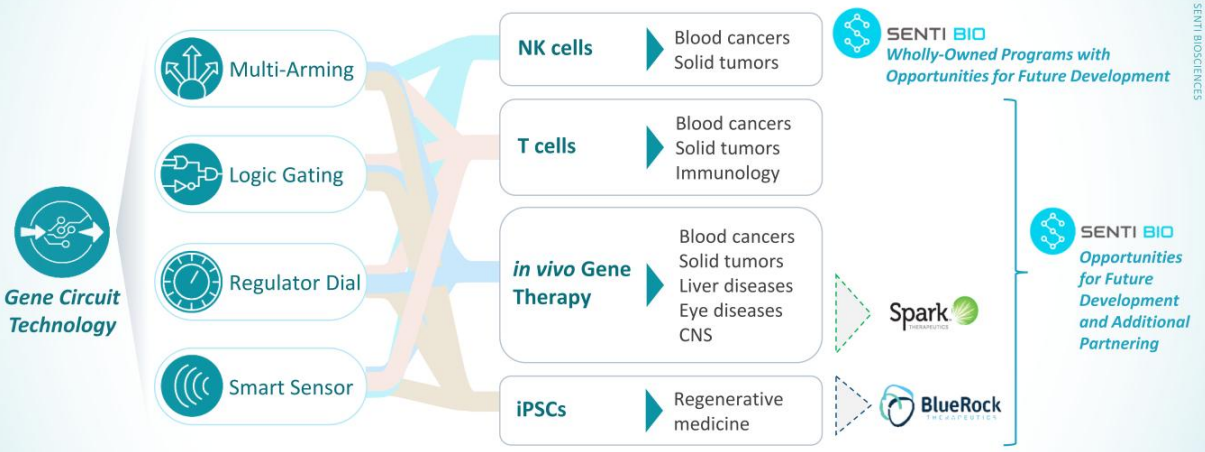
Smart Sensor Promoters enable next-generation gene therapy by:

- 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



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



Upcoming Value Driving Milestones

Program	2022 Anticipated Milestones	2023 Anticipated Milestones
SENTI-202 *CD33, FLT3 bivalent* *AML, MDS and other blood cancers*	Present data at key scientific conferences in 2H 2022 (accepted abstracts at ASH)	File IND application in 2023
SENTI-301A *GPC3* *HCC and other solid tumors*	Present data at key scientific conferences in 2H 2022 (abstracts published at SITC)	File IND application in 2023
SENTI-401 *CEA* *CRC and other solid tumors*	Present data at key scientific conferences in 2H 2022 (abstracts published at SITC)	Present data at key scientific conferences
Additional Programs *Other tumors*	Initiate preclinical work on additional CAR-NK pipeline programs	Pre-clinical PoCs for additional pipeline candidates
Manufacturing	Startup of manufacturing by YE 2022 Present data at key conferences	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Thank you!
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