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): September 30, 2022

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

Delaware	**333-262707**	**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

N/A
(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.

Beginning on October 3, 2022, Senti Biosciences, Inc. (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 99.1 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 report, including the Exhibit, is furnished pursuant to Item 7.01 and shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section. 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 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 Securities 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 on September 12, 2022. 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	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: September 30, 2022

By: /s/ Tim Lu
Name: Tim Lu
Title: President and Chief Executive Officer


SENTI BIO™
Corporate Presentation
October 2022
OCTOBER 2022 | SENTI BIOSCIENCES
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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

MIT · HARVARD MEDICAL SCHOOL

Philip Lee, PhD
CTO & Co-Founder

UCSF · Merck

Deb Knobelman, PhD
CFO

Penn · Pfizer

Kanya Rajangam, MD, PhD
CMDO

Northwestern University · Atara Bio · nkarta Therapeutics

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
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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 cytokines
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 Have Compared Favorably to Current Approved T Cell Therapies In Clinical Trials

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	✗	✓
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

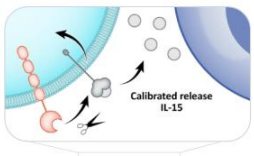
Limited activity beyond AML, persistence, durability, donor variability and select single clinical center usage

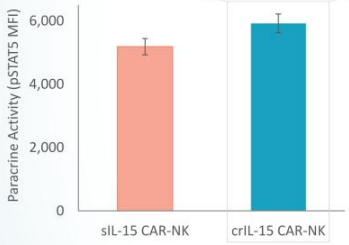
Senti's Gene Circuit technology, donor selection and scalable manufacturing address these limitations

[1] Velluchamy 2017, Bachier 2021

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

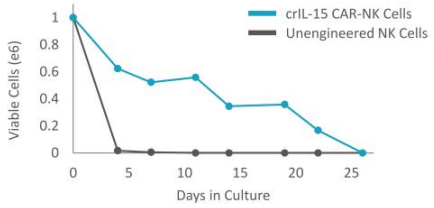
crIL-15: IL-15 released by local proteases → autocrine and paracrine effects



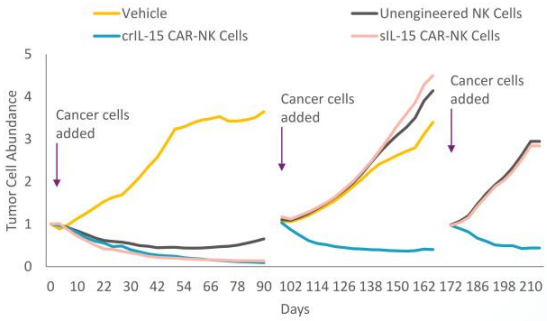


Phospho STAT5 levels increased in T cells exposed to supernatant from either crIL-15 or sIL-15 CAR-NK cell culture

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-301	GPC3	HCC and other solid tumors		2023 IND		✓ Multi-Arming: designed for enhanced efficacy ✓ crIL-15: autocrine and paracrine activation ✓ Control: Regulator Dial crIL-12
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 ✓ Undisclosed: combo immune effectors
Additional Programs	Undisclosed	Other tumors				Undisclosed


Manufacturing
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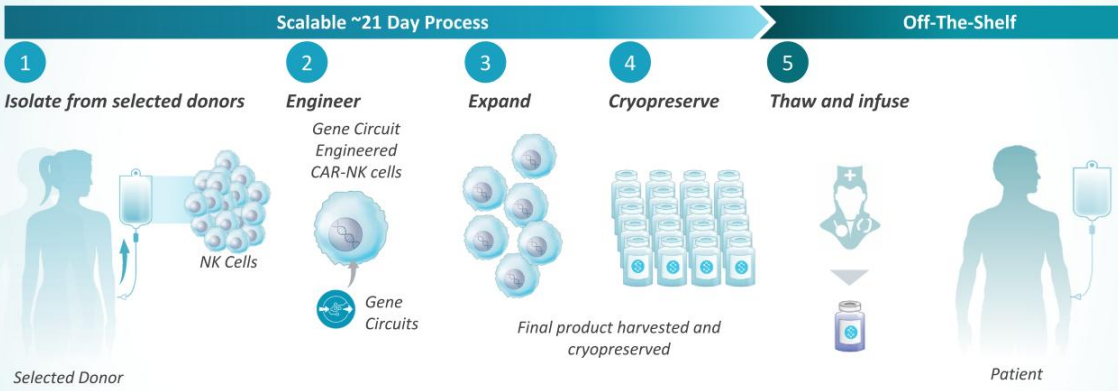
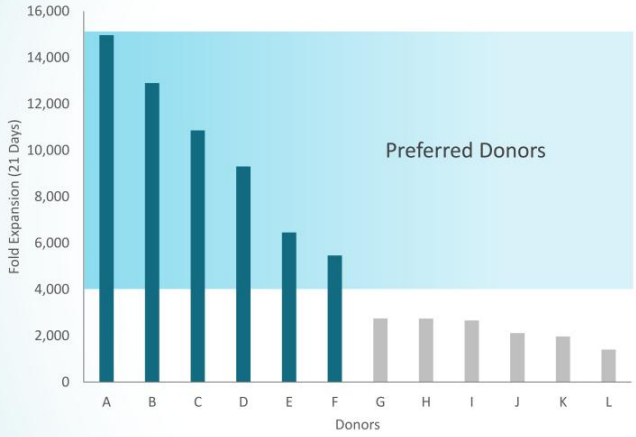
Scalable Manufacturing to Support Off-The-Shelf Products

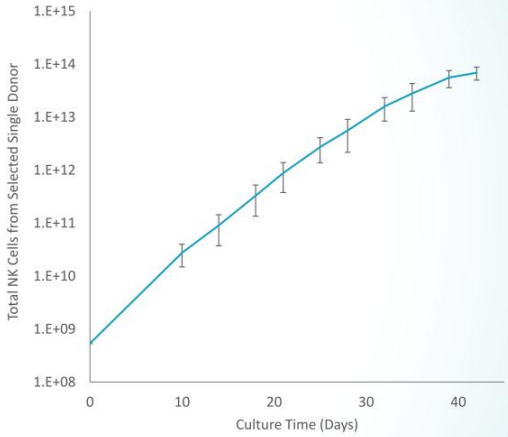


NK cells isolated from peripheral blood of selected donors	NK cells efficiently engineered with Gene Circuits	>100 doses per batch	High post-thaw potency	Easy to thaw vials	Outpatient use potential

Senti Selects NK Cell Donors to Support Robust Cell Expansion

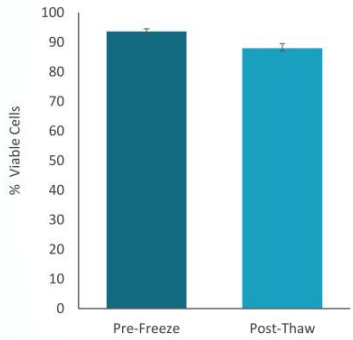


Senti screens and selects GMP donors using NK cell expansion and other functional attributes to minimize variability

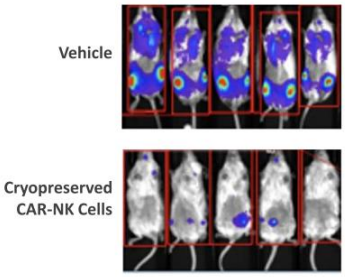


Senti process can potentially generate over 100 trillion NK cells from a single donor collection

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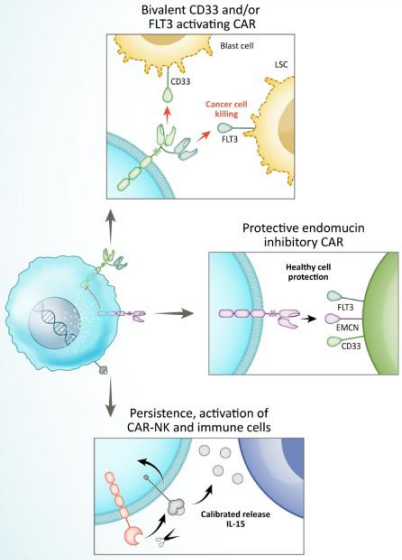
SENTI-202 for CD33 and/or FLT3 Expressing Blood Cancers



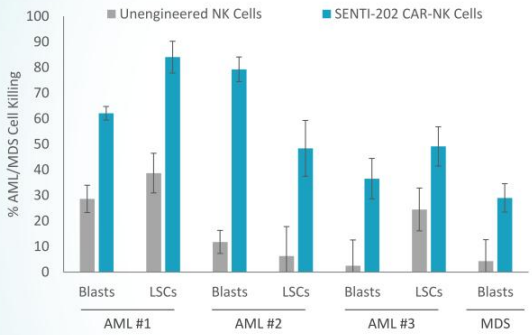
LSCs: Leukemic Stem Cells

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

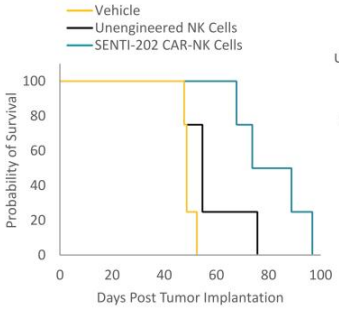
- ***OR GATE:*** *bivalent* CD33 and/or FLT3 activation → potential for deep and durable responses in acute myeloid leukemia (AML) and other blood cancers
- ***NOT GATE:*** inhibition by endomucin (EMCN) protective antigen selectively expressed on healthy cells → potential for improved safety and increased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

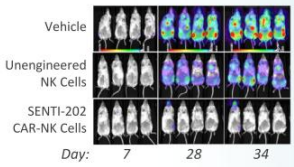
On track for IND in 2023

SENTI-202 Shows Robust Preclinical Activity



Broad in vitro killing of primary AML and MDS tumor cells



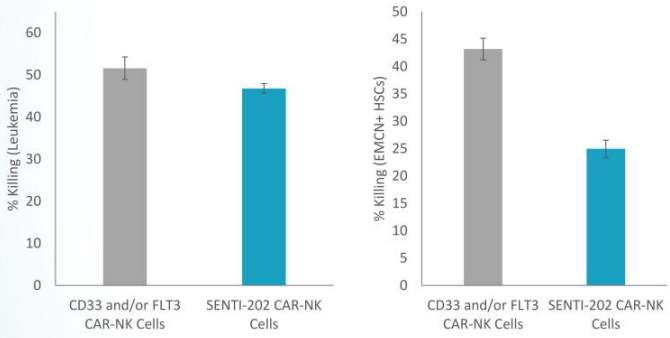


In vivo suppression of tumor and increased mouse survival in MV4-11 AML NSG mouse model

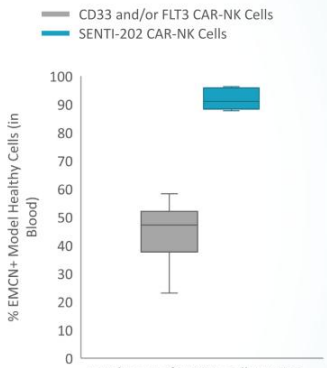
Group	Vehicle	Unengineered NK Cells	SENTI-202 CAR-NK Cells
Median Survival	*49*	*55*	*81.5*

SENTI-202 Preclinical Selectivity via Inhibitory CAR Binding Endomucin on Healthy Primary Human Hematopoietic Stem Cells (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



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]

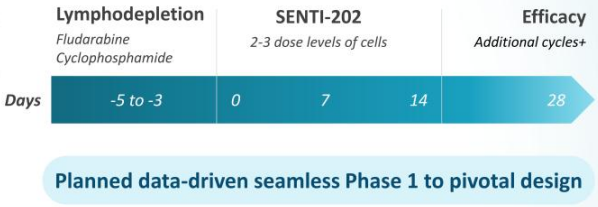
Proposed Phase 1 study anticipated to enroll R/R CD33+ and/or FLT3+ heme malignancies

- 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

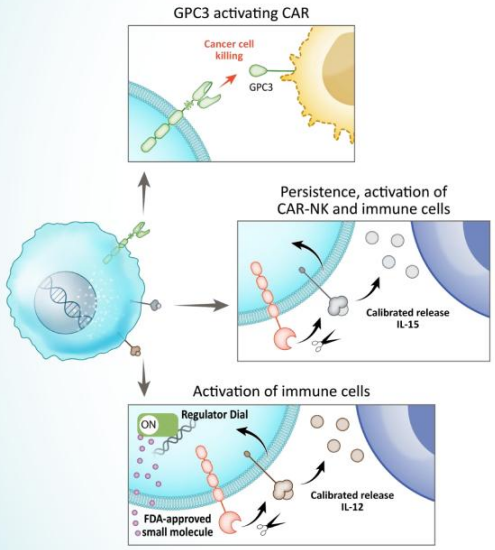
Planned Study Treatment/ Cycle



Planned data-driven seamless Phase 1 to pivotal design

[1] Seer 2020; [2] Brandwein 2020

SENTI-301 for GPC3 Expressing Solid Tumors



Multi-Armed, off-the-shelf, Regulator Dial controlled CAR-NK

- ***GPC3 activating CAR*** → hepatocellular carcinoma (HCC) and other solid tumors
- ***crIL-15*** → potential for increased persistence, autocrine and paracrine immune cell activation
- ***Pulsed crIL-12*** controlled by FDA-approved drug via Regulator Dial → potential to remodel tumor micro-environment and increase anti-tumor immune responses with improved safety

On track for IND in 2023

crIL-15 GPC3 CAR-NK Cells Preclinical Anti-Cancer Activity

High unmet need in patients with liver cancer

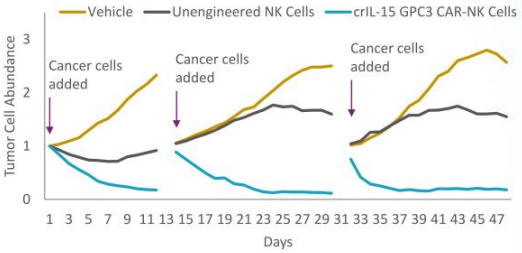
- 20.8% 5-year survival rate[1]

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

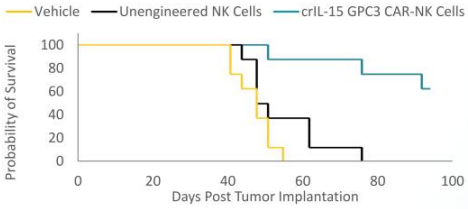
- Must have received standard of care
- Advanced solid tumors with focus on HCC (70-90% GPC3+) during dose finding
- Disease specific expansion cohorts of advanced HCC and other solid tumors (29-54%[2] GPC3+) including lung cancer

Planned study treatment

- Multi-dose and multi-cycle following conditioning
- Small molecule administered as needed
- 2-3 cell dose levels



Effective in vitro serial killing of HepG2 HCC cell line



Increased survival in HepG2 HCC NSG mouse model

Group	Tumor Cells	Unengineered NK Cells	crIL-15 GPC3 CAR-NK Cells
Median Survival	*48*	*49.5*	*Not reached*

[1] Seer 2020 (liver and intrahepatic bile duct cancer combined); [2] Moek 2018

Senti's Regulator Dial Enables On-Demand Production of crIL-12 Controlled via FDA-Approved Small Molecule Drug

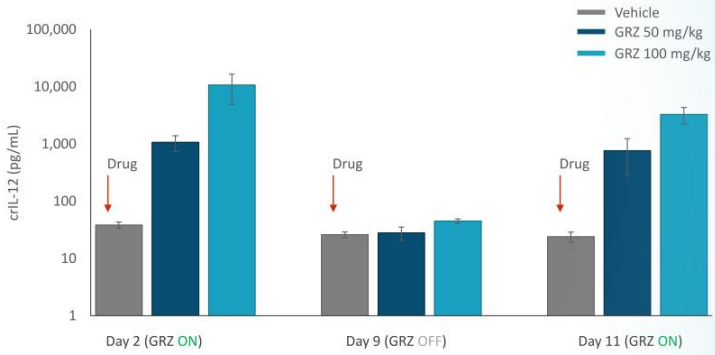
IL-12 is a potent pro-inflammatory type 1 cytokine

- Increases NK and T cell activation
- 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

- Narrow therapeutic window with systemic IL-12

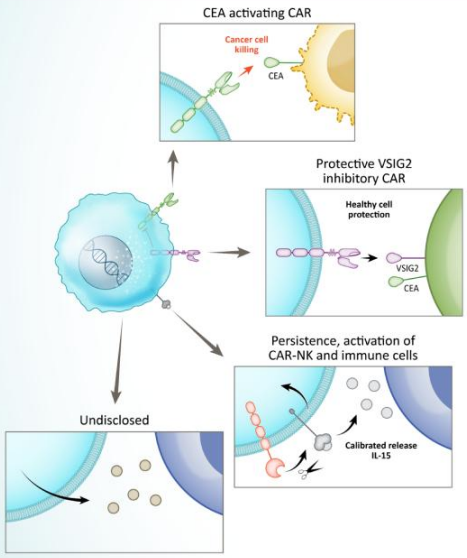
Senti's proprietary Regulator Dial is controlled by FDA-approved small molecule releasing crIL-12



crIL-12 release controlled by small molecule drug administered 2 days prior to sampling in a dose-dependent manner in vivo

[1] Leonard 1997

SENTI-401 for CEA Expressing Solid Tumors

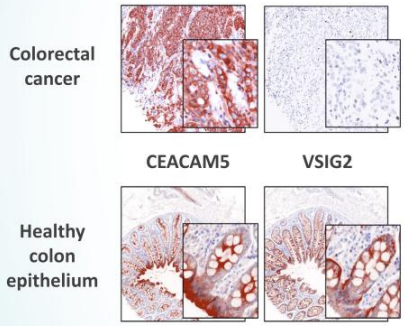


Multi-Armed, off-the-shelf, selective CAR-NK

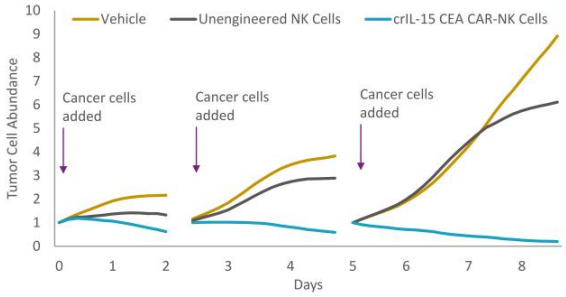
- ***CEACAM5 (CEA) activating CAR*** → colorectal cancer (CRC) and other solid tumors
- ***NOT GATE:*** inhibition by VSIG2 antigen on healthy epithelial cells → potential for improved safety, increased therapeutic window and reduced on-target, off-tumor toxicity
- ***crIL-15*** → potential for increased persistence and autocrine and paracrine immune cell activation
- ***Undisclosed 4th arming*** → construct to further potentiate persistence, efficacy of CAR-NK cells and stimulate endogenous immune cells

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

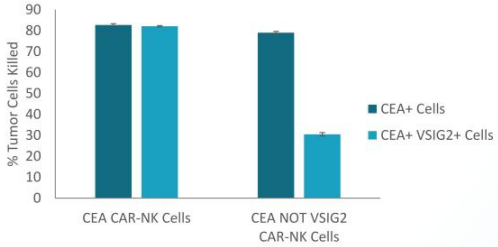
VSIG2 was identified by bioinformatics using single cell RNA sequencing and validated as protective antigen with immunohistochemistry



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



Effective in vitro serial killing of LOVO cell line by Multi-Armed CEA CAR



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

[1] Goldstein 2005


Platform Collaborations
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Multiple Platform Collaborations Extend Utility of Gene Circuits

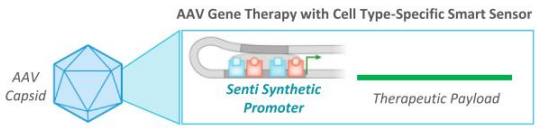
Program	Indications	Gene Circuit	Discovery	IND enabling	Phase 1	Rights
Gene Therapies for Tissue-Directed Targets						
GC-1001/GC-1002	Eye	Smart Sensor				Spark Therapeutics, Roche
GC-1003/GC-1004	CNS	Smart Sensor				
GC-1005	Liver	Smart Sensor				
Cell Therapies for Regenerative Medicine						
GC-1101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

Two Collaborations to Develop Next Generation Cell and Gene Therapies

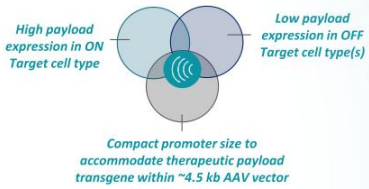
Spark

Collaboration for gene therapies

AAV Gene Therapy with Cell Type-Specific Smart Sensor



Synthetic Promoter Performance Profile:



BlueRock THERAPEUTICS

Collaboration for cell therapies

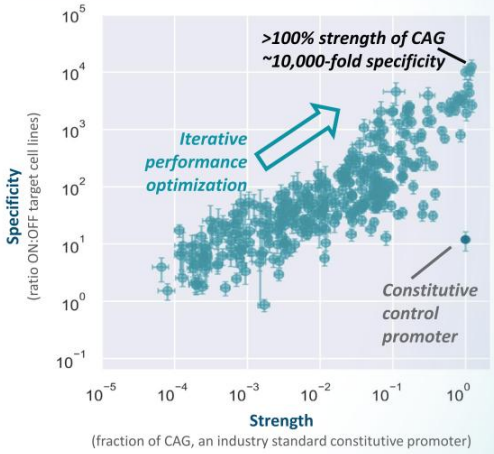
Gene Circuit-Engineered "Smart" Regenerative Medicines

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

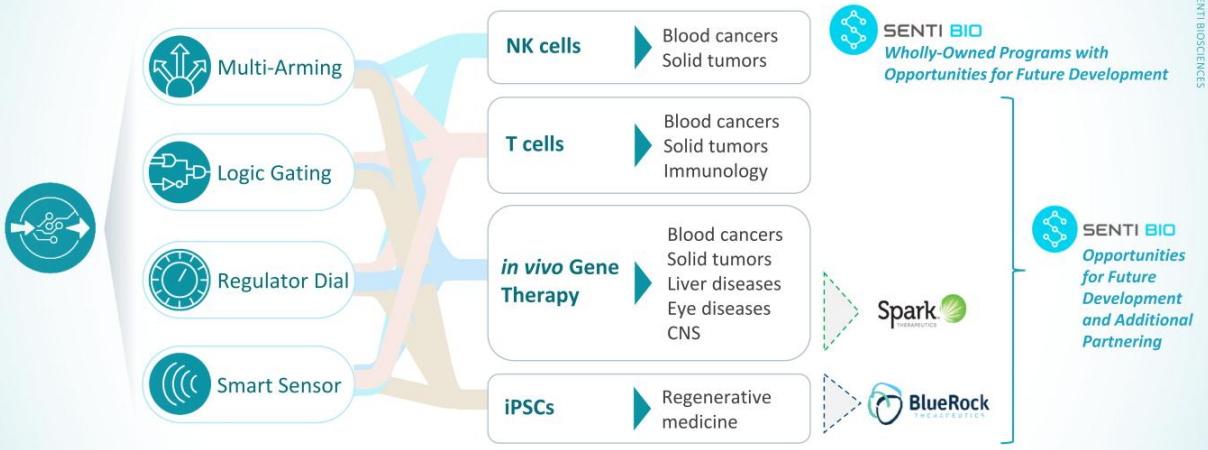
Gene Therapy Challenges	Senti's Gene Circuit Solutions
Off-target tissue toxicity	Smart Sensor ▶ Enhance target tissue specificity and limit off-target tissue toxicity
Sub-optimal therapeutic performance	Smart Sensor ▶ Improve expression and increase potency

Smart Sensor Promoters designed to 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 (e.g., ASH)	File IND application in 2023
SENTI-301 *GPC3* *HCC and other solid tumors*	Present data at key scientific conferences in 2H 2022 (e.g., SITC)	File IND application in 2023
SENTI-401 *CEA* *CRC and other solid tumors*		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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