SENTI BIO™

Engineering the Future of Cell and Gene Therapies

June 2023

Disclaimer

Forward Looking Statements

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Mission to Create Life-Saving Therapies For Patients With Cancer and Other Diseases With High Unmet Needs

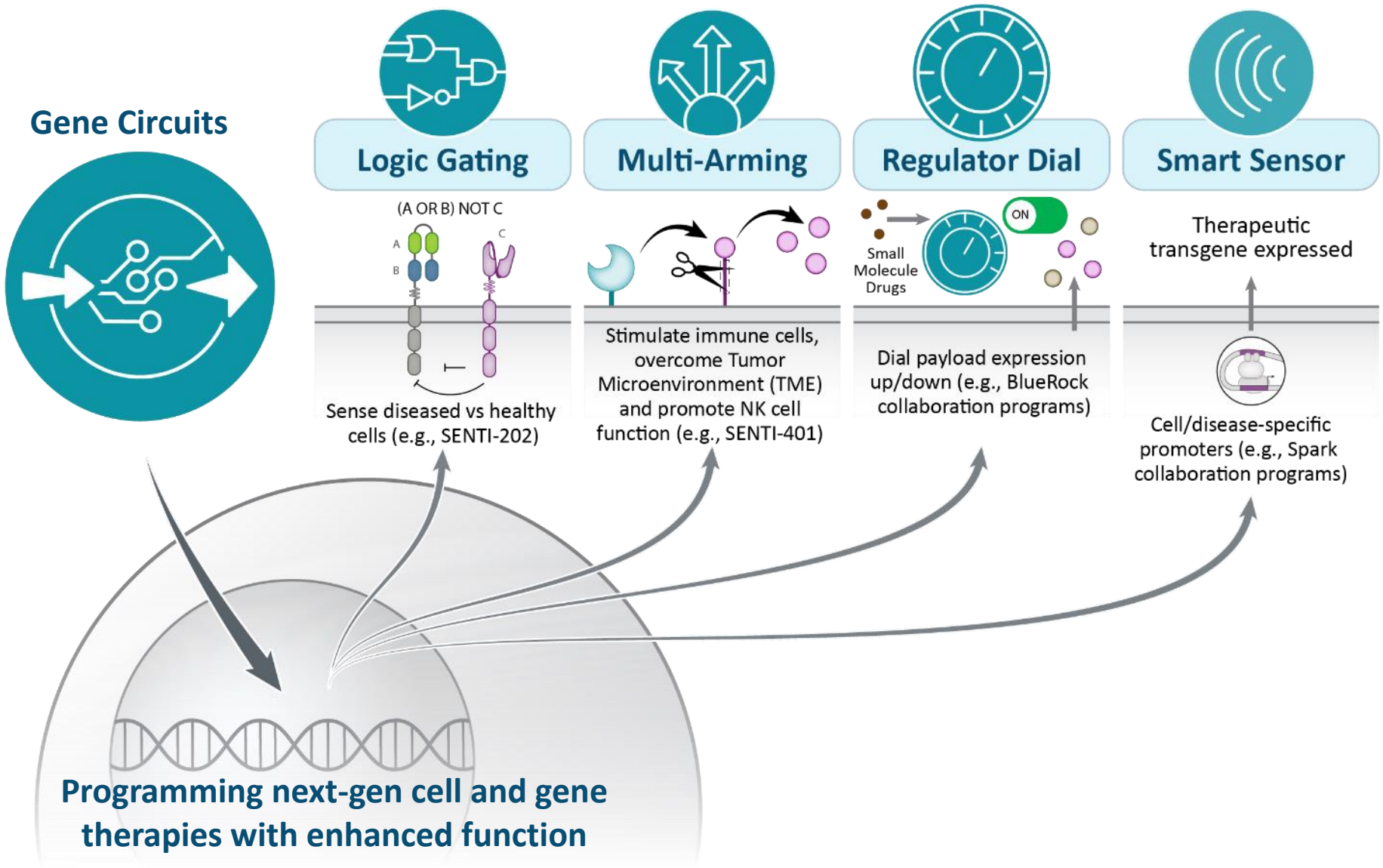
SENTI BIO

Proprietary Gene Circuit Technologies
Synthetic biology platform enables enhanced precision, control, and activity to be programmed into cell and gene therapies

IND for First-in-Class CAR-NK Cell Therapy in 2H 2023
Pipeline aims to solve challenges of liquid and solid tumors with Logic Gating and Multi-Arming, starting with SENTI-202 in AML

Strategic Partnerships in Non-Oncology Indications
Collaborations with Spark (Roche) and BlueRock (Bayer) to program gene circuits into next-gen AAV and iPSC-derived cell therapies

Gene Circuit Technologies for Enhanced Precision, Control, and Activity



Internal Focus on Oncology, Partnering to Support Non-Oncology Indications

Program	Target	Application	Discovery	IND enabling	Clinical	Collaborator
Wholly Owned CAR-NK Programs for Oncology						
SENTI-202	CD33 and/or FLT3	AML, MDS and other blood cancers		2H 2023 IND		
SENTI-401	CEA	CRC and other solid tumors				
SENTI-301A	GPC3	HCC and other solid tumors	*Potential for partnering or future clinical development*			
Additional Programs	Undisclosed	Other tumors				
Collaboration Programs						
Multiple Gene Therapy Programs	Undisclosed	Eye, CNS and liver diseases				Spark Therapeutics, Roche
Multiple iPSC Cell Therapy Programs	Undisclosed	Regenerative medicine				BlueRock Therapeutics, Bayer

CAR-NK Pipeline and Manufacturing

Re-imagining Cancer Treatment with Gene Circuit-Powered CAR-NK Cells

Gene circuits for smarter cancer therapies

- ✓ Protect healthy cells with NOT Logic Gate
- ✓ Avoid antigen escape with OR Logic Gate
- ✓ Increase cancer killing with cytokine Multi-Arming
- ✓ Empower a variety of modalities including NK and T cells

Peripheral blood NKs unlock many advantages

- ✓ True NK function over other cell sources such as iPSCs
- ✓ Extensive clinical experience[1]
- ✓ Well-tolerated with no/minimal CRS, neuro tox, GvHD[2]
- ✓ 19% CR rate (aggregated) in 105 R/R AML patients[2]

Proprietary crIL-15 to increase NK cell function

Persistence and durability are key limitations of unengineered NK cells

- ✓ crIL-15 increases CAR-NK cancer killing and persistence
- ✓ crIL-15 activates neighboring immune cells in the endogenous immune system – a key feature for treating solid tumors

Off-the-shelf manufacturing for broader access

- ✓ Scalable and cost-effective manufacturing process
- ✓ Proprietary expansion and cryopreservation processes
- ✓ Extensive donor selection process to minimize variability

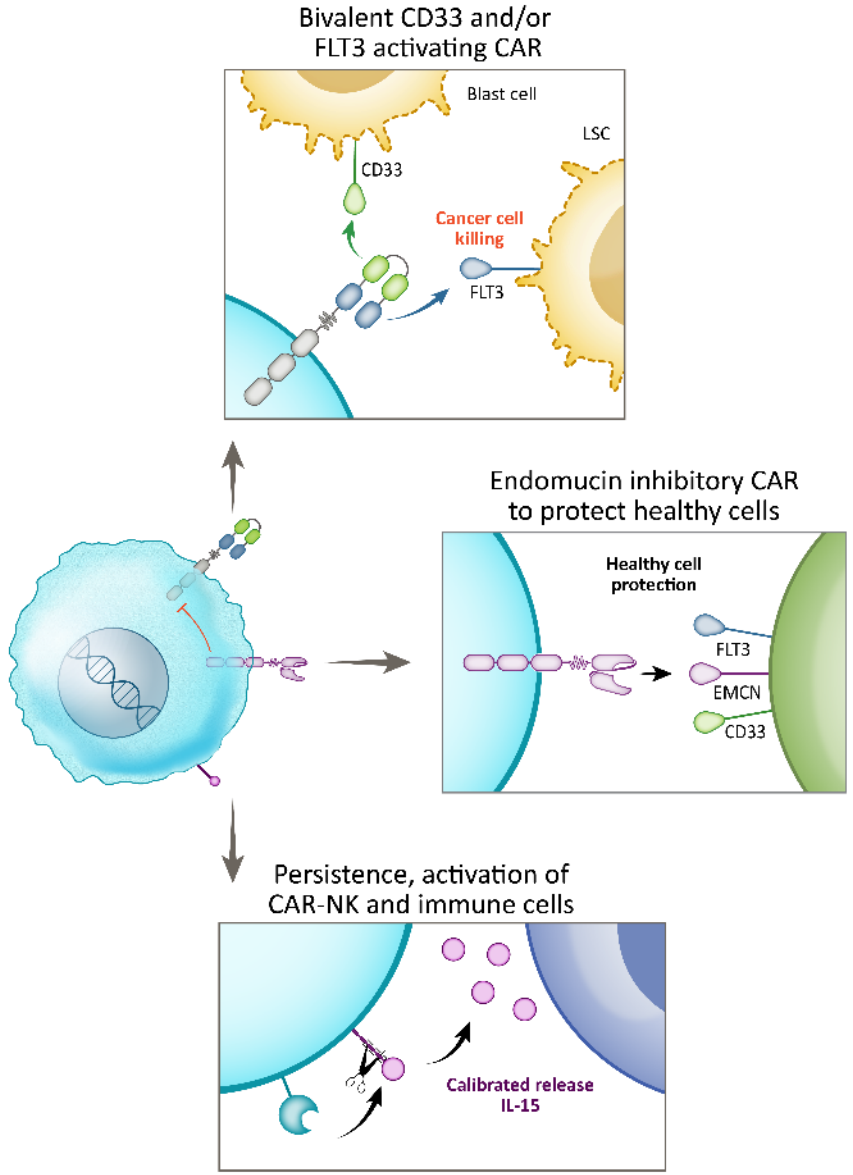
[1] Lamers-Kok Journal of Hematology & Oncology 2022; [2] Bachier 2021
crIL-15: Calibrated Release IL-15

Expanding the Range of CAR Cell Therapies Beyond CD19/BCMA With Potentially Enhanced Efficacy and Precision

	SENTI-202 (Focus on AML)	SENTI-401 (Focus on CRC)	SENTI-301A (Focus on HCC)
+ Activating CAR *Elimination of cancer cells*	✓	✓	✓
+ Inhibitory CAR *Protection of healthy cells*	✓	✓	NA*
+ Calibrated release IL-15 (crIL-15) *Enhanced NK cell expansion, persistence and tumor killing*	✓	✓	✓
+ IL-21 Multi-Arming *Overcoming immunosuppressive TME*		✓	

* GPC3 is selectively expressed on cancer cells

SENTI-202 Is a First-In-Class Cell Therapy Program With Focus on AML



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 cell expansion, persistence, and tumor killing

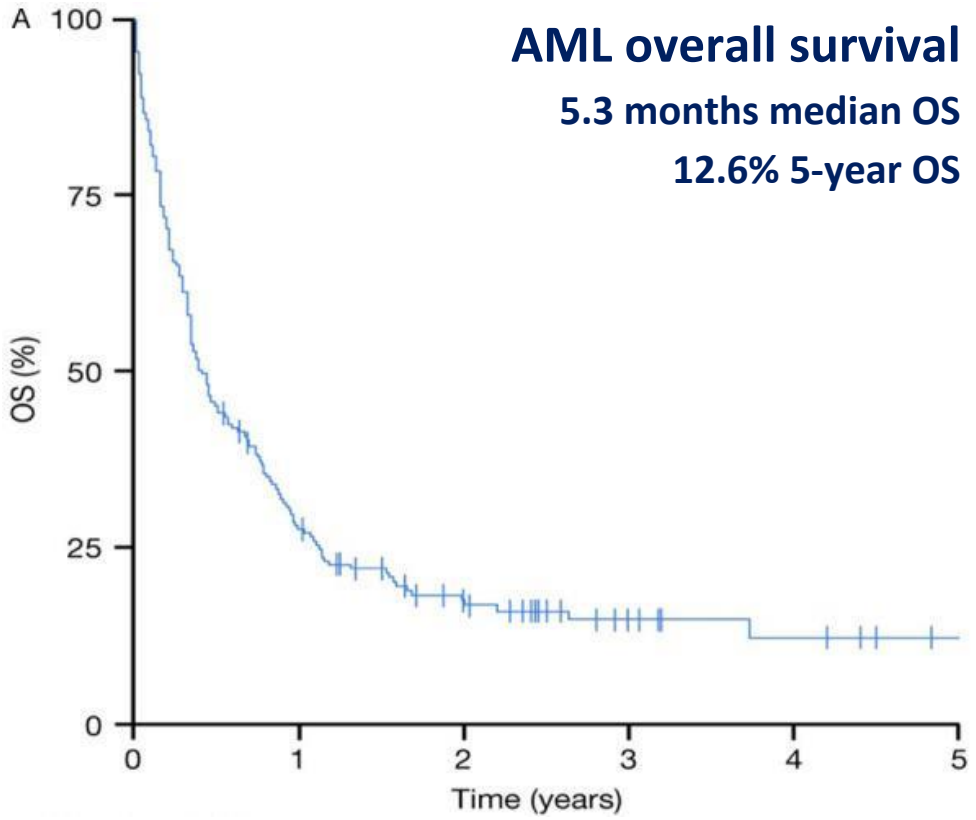
On track for IND in 2H 2023

LSCs: Leukemic Stem Cells

Significant Unmet Need in AML Even with Recent Approvals

AML is a cancer with very high unmet need

- 20,050 newly diagnosed AML patients in the US with 30.5% 5-year survival[1]
- Majority of patients fail to respond or relapse after up-front therapy
- Prognosis at relapse is grim with ~5-10 months overall survival in R/R AML patients and limited standard of care options that includes FLT3, IDH1/2 inhibitors if relevant mutations are present[2]



AML overall survival

5.3 months median OS

12.6% 5-year OS

[1] Seer estimates; [2] Brandwein
Figure from Brandwein Am J Blood 2020

AML is a Heterogenous Disease and Requires Multi-Antigen Targeting

Other CAR-based therapies currently in clinical development target only one AML antigen leading to tumor escape and eventual patient relapse

Manufacturer	Modality	MOA / Target	Antigen Expression on LSCs[1]	Blasts[1]	HSCs
SENTI-202	Allogeneic CAR-NK Cells	**FLT3 OR CD33**	+	+	+
KITE-222	Autologous CAR-T cells	**CLL-1**	+/-	+	-
UCART123	Allogeneic CAR-T cells	**CD123**	+/-	+	+/-
NKX101	Allogeneic CAR-NK Cells	**NKG2D ligands**	-	+	-
VCAR33	Autologous CAR-T Cells	**CD33**	+/-	+	+/-
CYTO NK-201	Allogeneic CAR-T Cells	**FLT3**	+	+/-	+

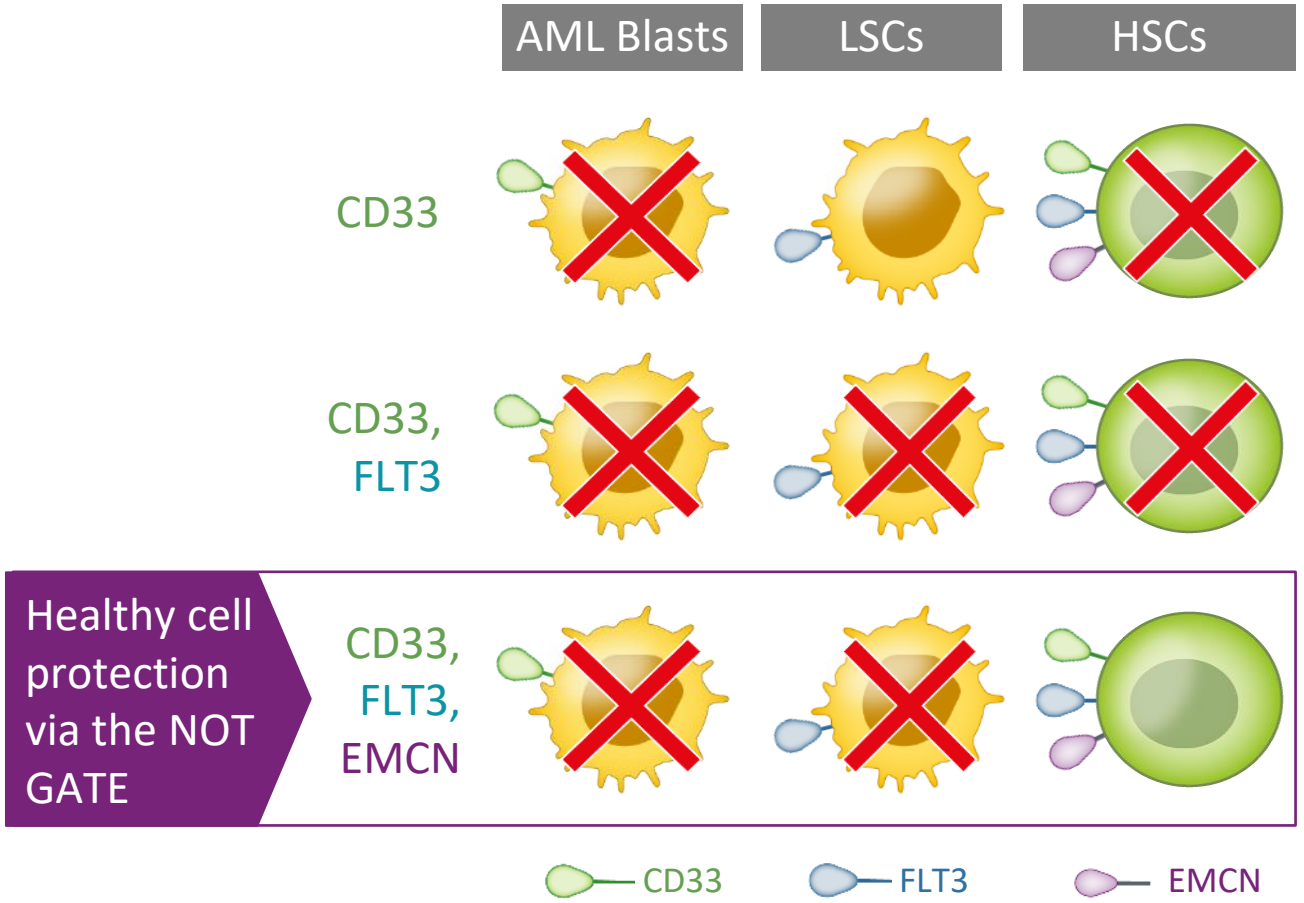
Selectively targeting both FLT3 (LSCs) and/or CD33 (blasts) with SENTI-202 has the potential to *provide AML patients with deeper and longer remissions.*

[1] Valent Stem Cell Trans. Med. 2020

Protecting Healthy Bone Marrow Stem Cells Is Integral to Driving Better Patient Outcomes

AML therapies are typically constrained by on-target, off-tumor toxicity

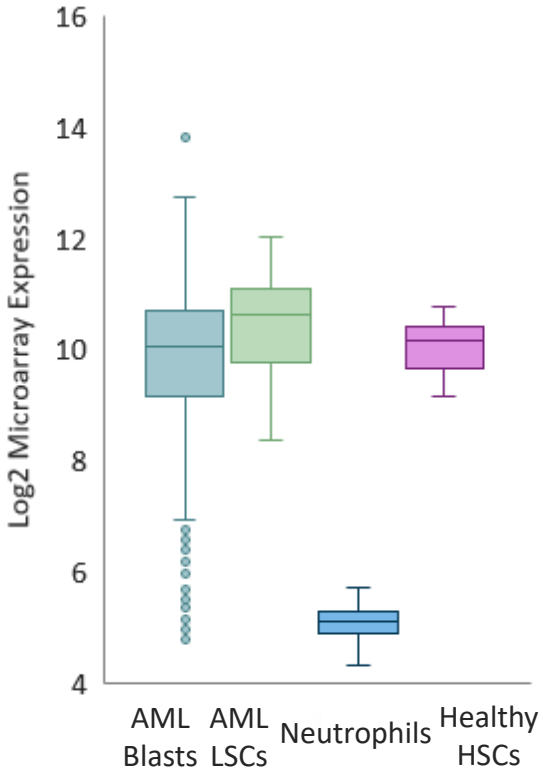
- Common AML targets are expressed on cancer cells AND healthy HSCs, leading to prolonged aplasia and myelosuppression
- Endomucin was identified and validated as a NOT GATE protective antigen that is expressed on up to 76% of HSCs, but not on LSCs or blasts
- **Utilizing the NOT GATE technology enables protection of healthy HSCs, with the potential to widen the therapeutic window**

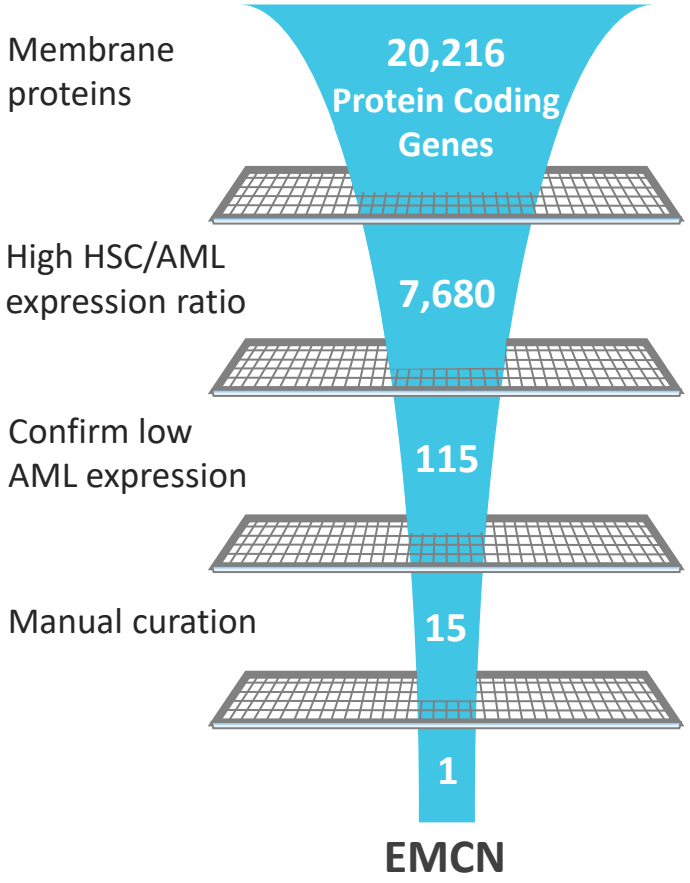


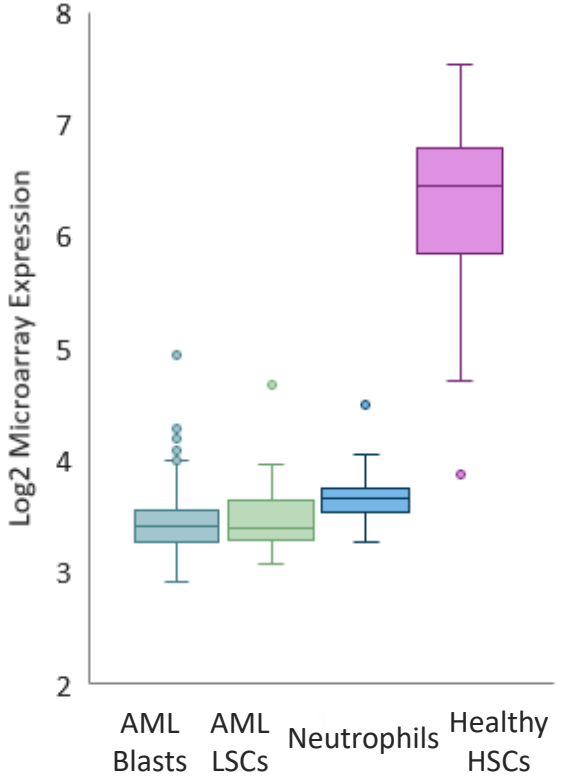
Senti's Discovery Platform Identified EMCN as a Key Protective Antigen for Healthy HSCs

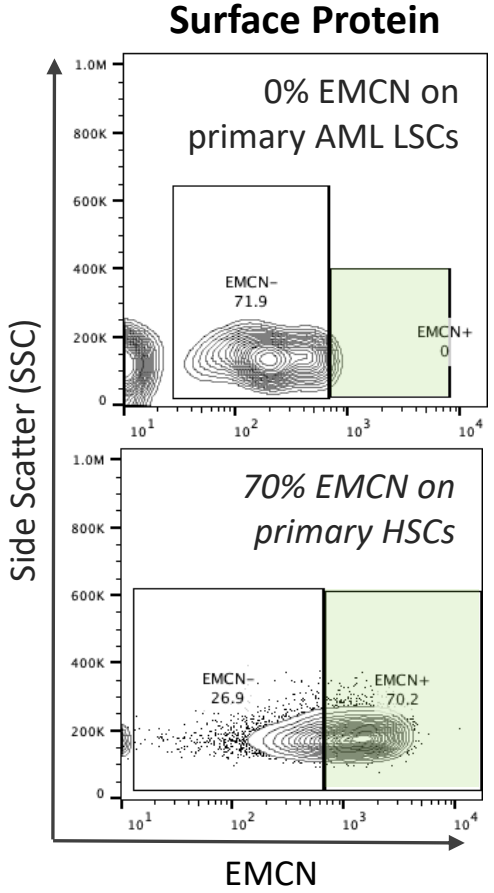
Challenge with FLT3

Solution and Validation with EMCN Protective Antigen







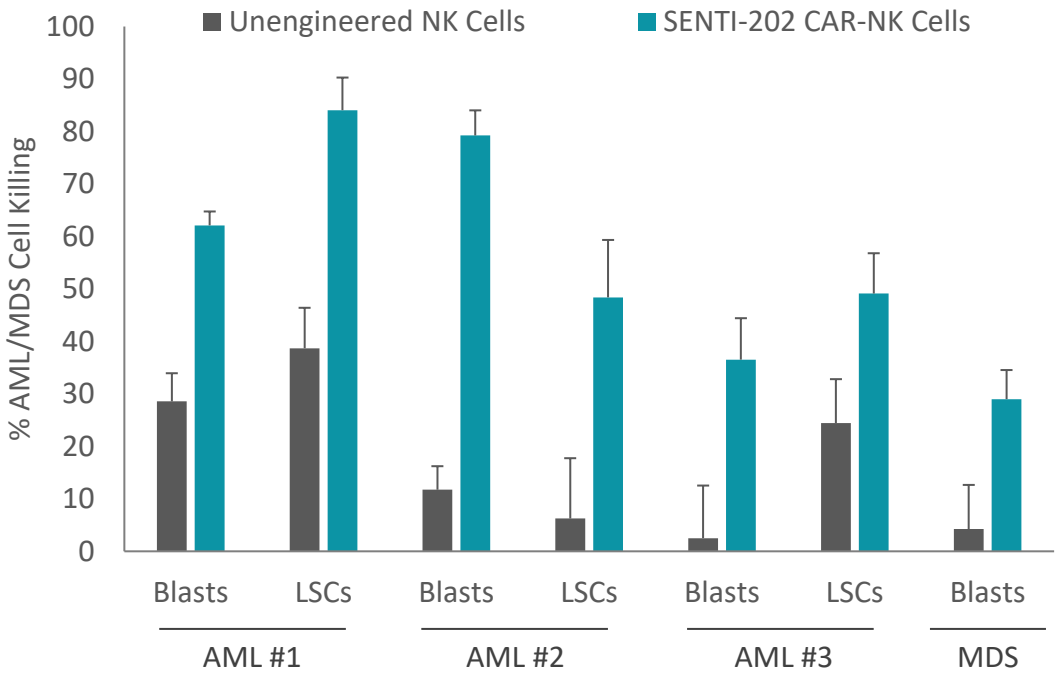


FLT3 is expressed on healthy HSCs

The NOT GATE is designed to use EMCN as a Protective Antigen input to recognize and protect healthy HSCs from off-tumor killing

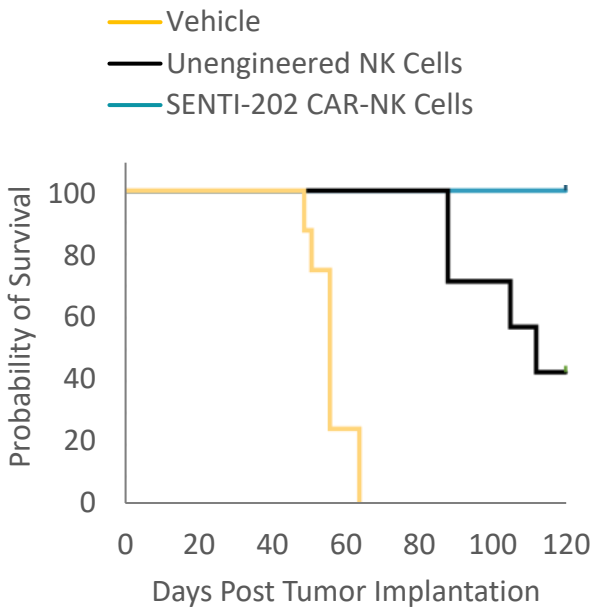
SENTI-202 Has Shown Robust Preclinical Cancer Killing Activity

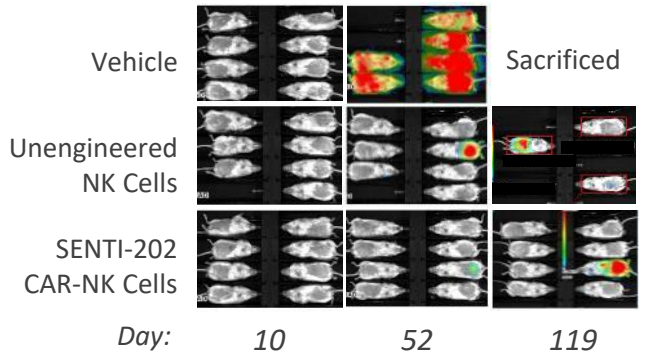
In Vitro Data



Broad in vitro killing of primary AML and MDS tumor cells and enhanced serial killing activity compared to unengineered NK cells

In Vivo Data

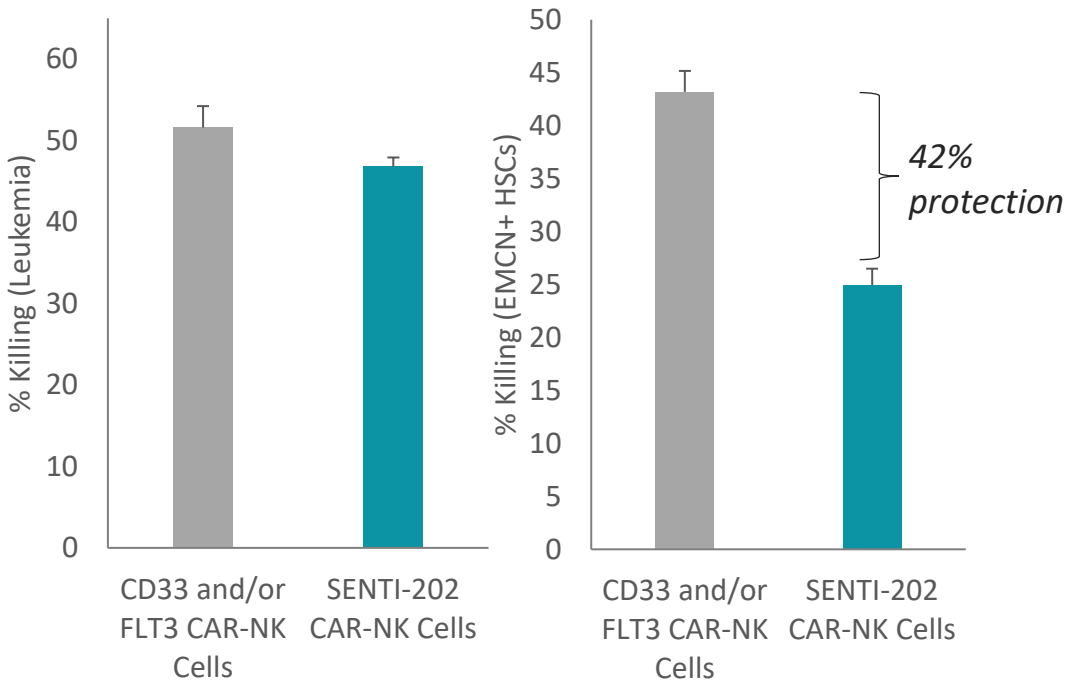




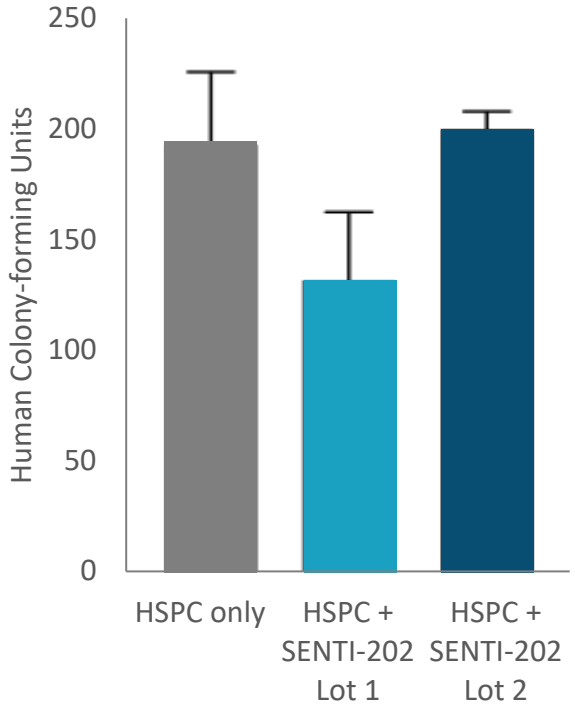
In vivo suppression of tumor and increased mouse survival in MV4-11 AML NSG mouse model

Group	Vehicle	Unengineered NK Cells	SENTI-202 CAR-NK Cells
Median Survival (Days)	*56*	*112*	*Undefined*

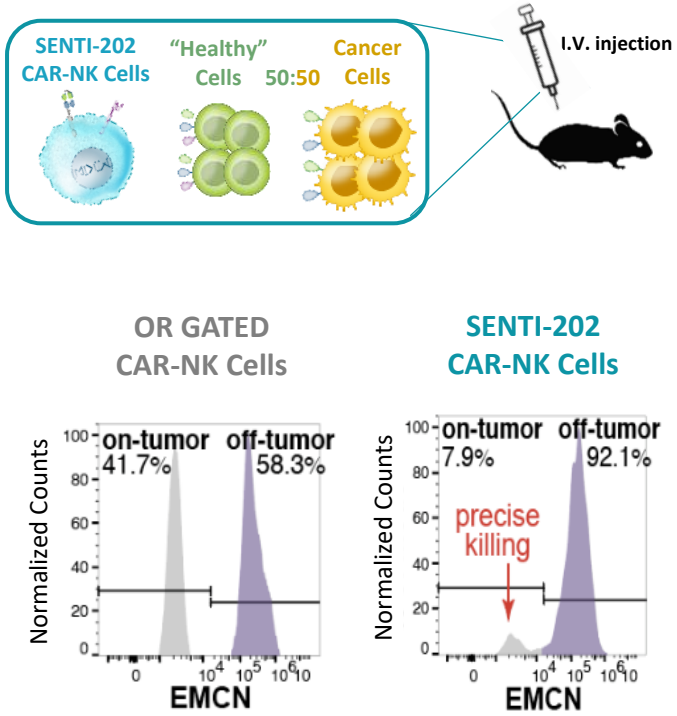
SENTI-202 Has Shown Strong Preclinical Selectivity and HSC Protection



In vitro protection of primary human HSCs expressing EMCN



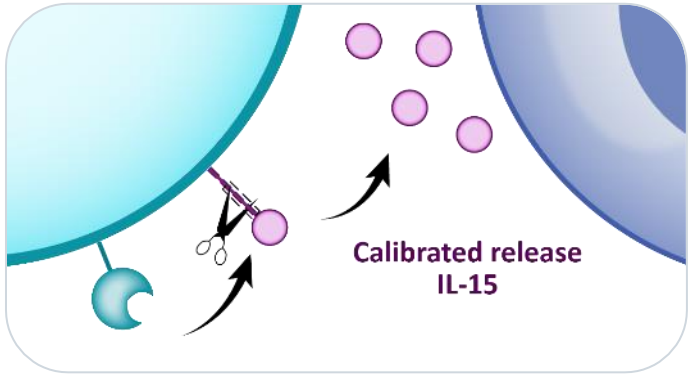
SENTI-202 preserves colony forming activity of HSPCs



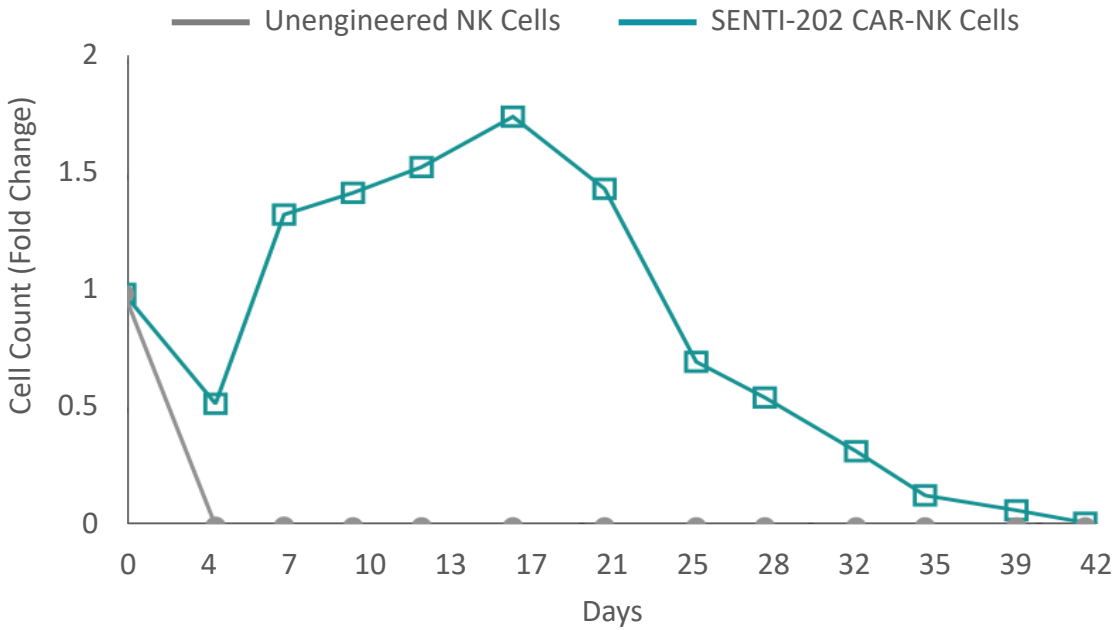
In vivo protection of EMCN+ model healthy cells

SENTI-202 Has Enhanced Proliferation and Persistence in Preclinical Studies

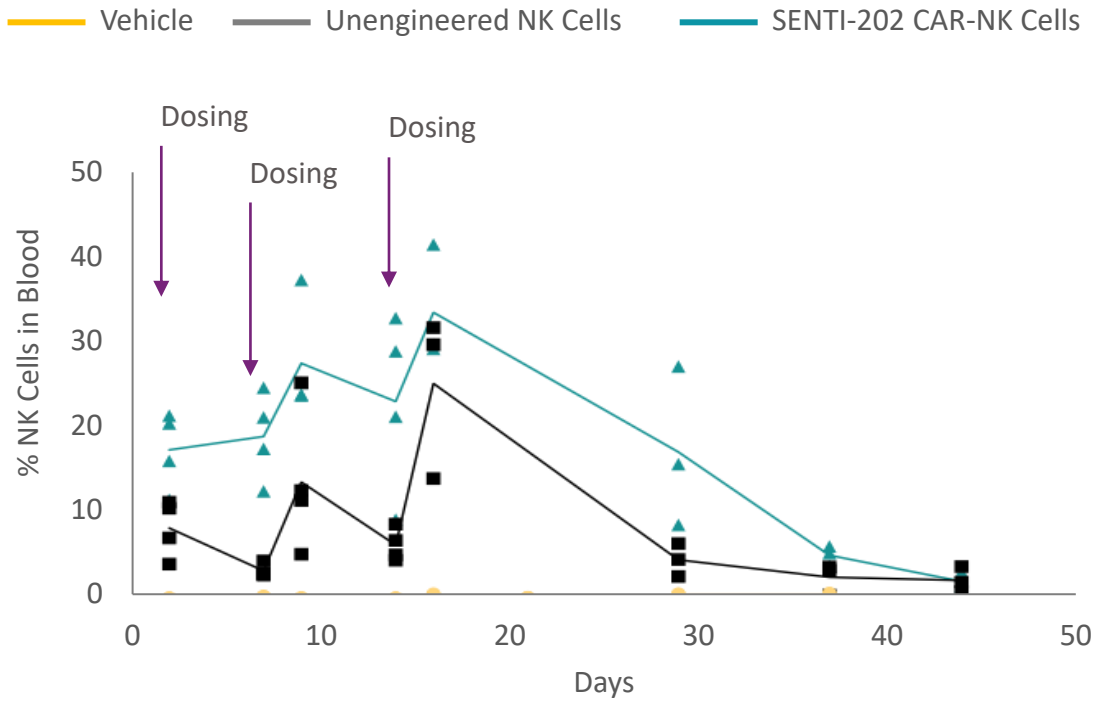
crIL-15: calibrated release by local proteases -> enhanced NK cell persistence



In Vitro Data



In Vivo Data



crIL-15 increases persistence of SENTI-202 CAR-NK cells vs unengineered NK cells in vitro and in vivo

Proposed Phase 1 Study in R/R Heme Malignancies With Focus on AML

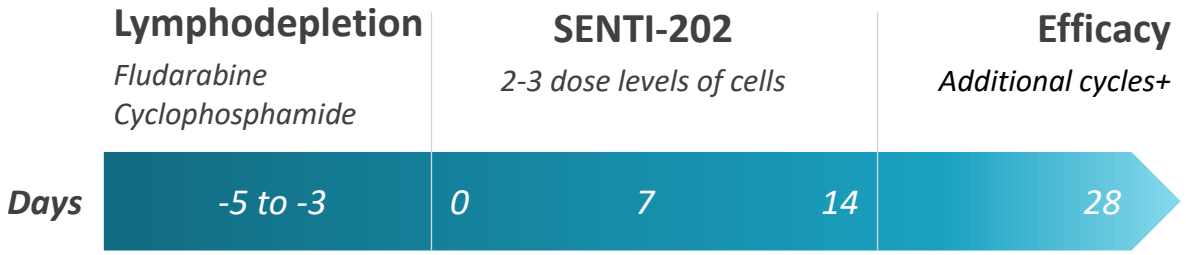
Proposed Phase 1 study anticipated to enroll R/R CD33+ and/or FLT3+ heme malignancies

- Modified “3+3” study design
- 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

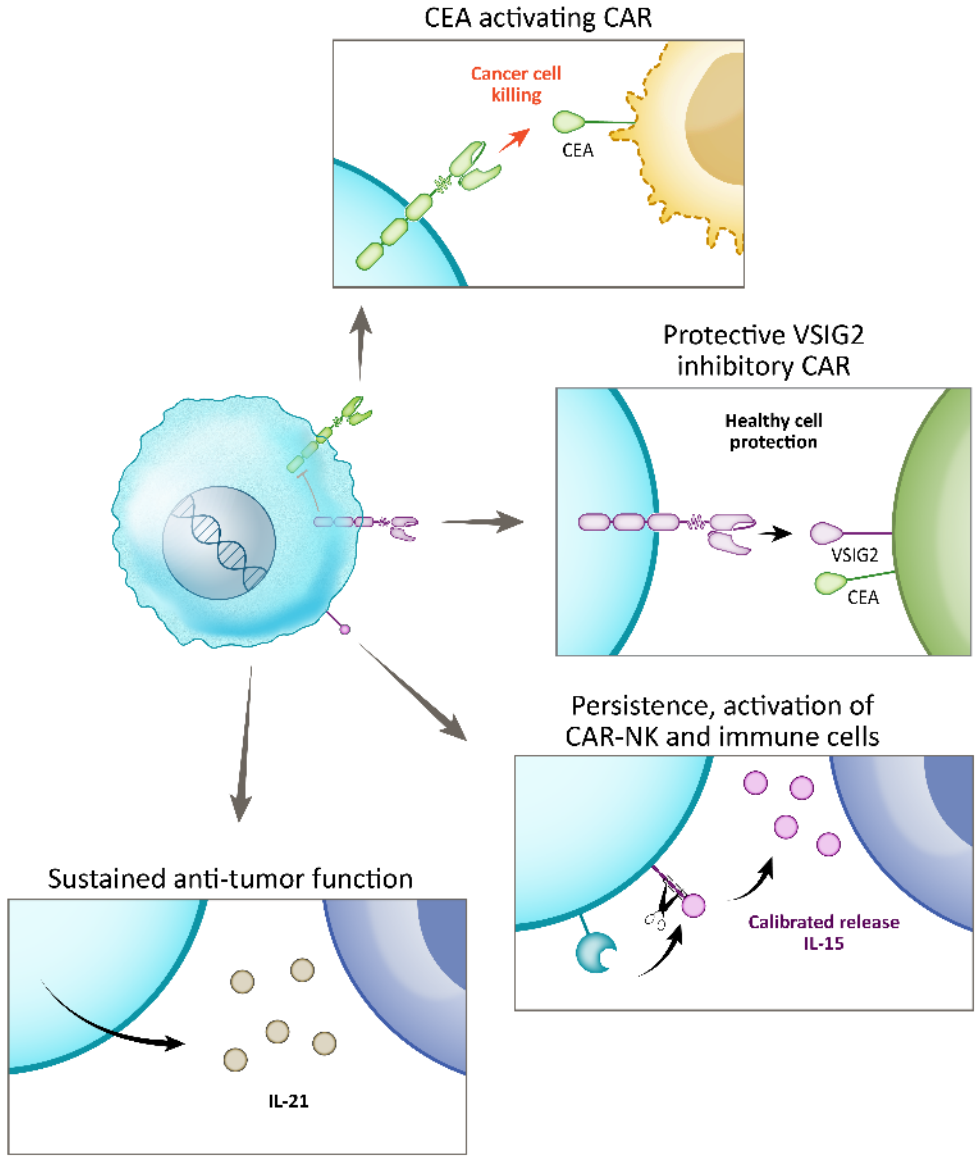
- Safety, DLT, identify recommended Phase 2 dose
- Efficacy using standard ELN 2022 criteria for AML and other disease specific consensus criteria
- PK, pharmacodynamics including endomucin protection, immunogenicity

Planned Study Treatment/ Cycle



Planned data-driven seamless Phase 1 to pivotal design

SENTI-401 Aims to Enhance the Treatment of Solid Tumors Starting With mCRC



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 cell expansion, persistence, and tumor killing
- ***IL-21*** → construct to further potentiate persistence and efficacy of CAR-NK cells and to stimulate endogenous immune cells

SENTI-401 Addresses Key Limitations of Cell Therapies for Solid Tumors Like CRC

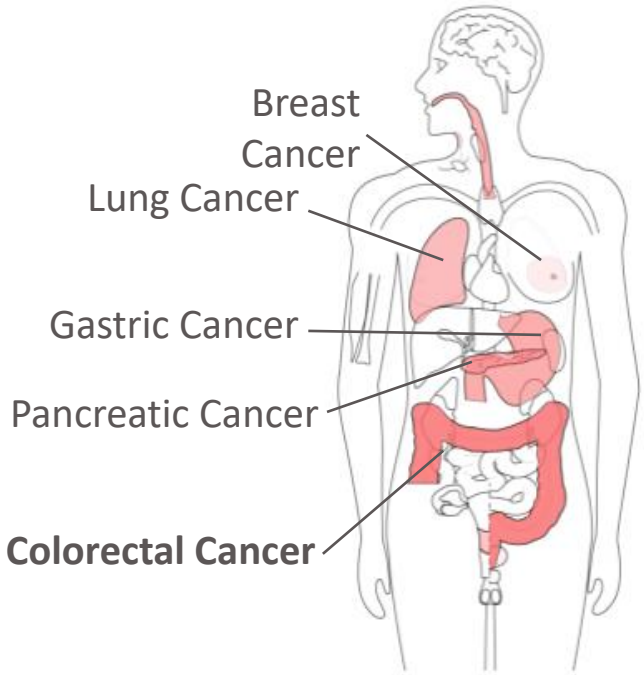
CEA is an attractive cancer target

- 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 and lung toxicity potentially from on-target, off-tumor toxicity[1]

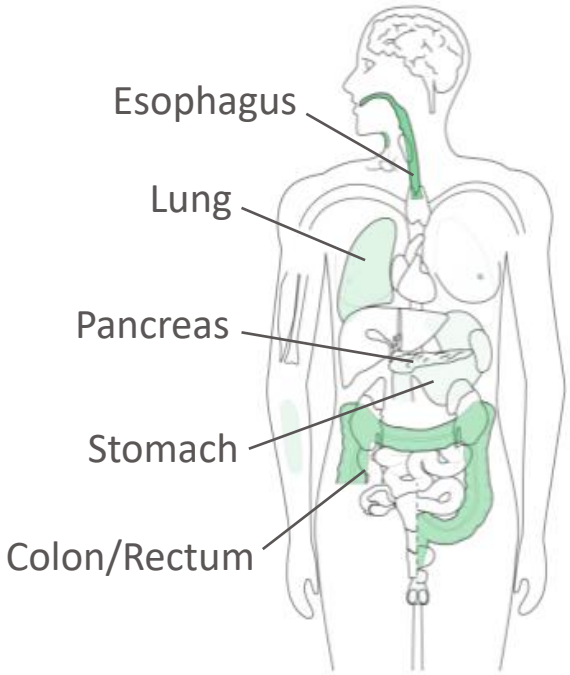
Cell therapies need to overcome the TME

- SENTI-401 is designed to target CEA expressing tumors while minimizing on-target, off-tumor toxicity using a NOT GATE
- SENTI-401 is Multi-Armed with crIL-15 and IL-21 to overcome the immunosuppressive milieu of solid tumors

Tumor Types With CEA Overexpression[2]

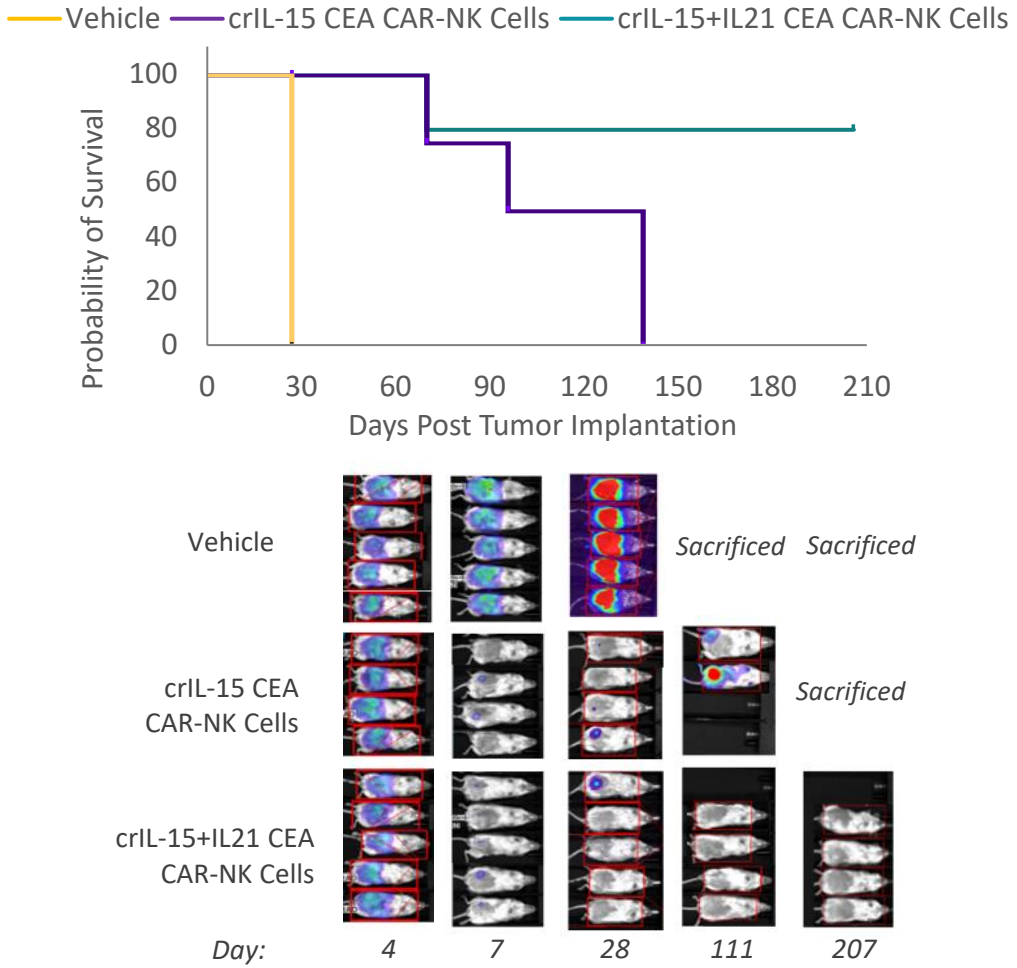


Healthy Tissues With CEA Overexpression[2]



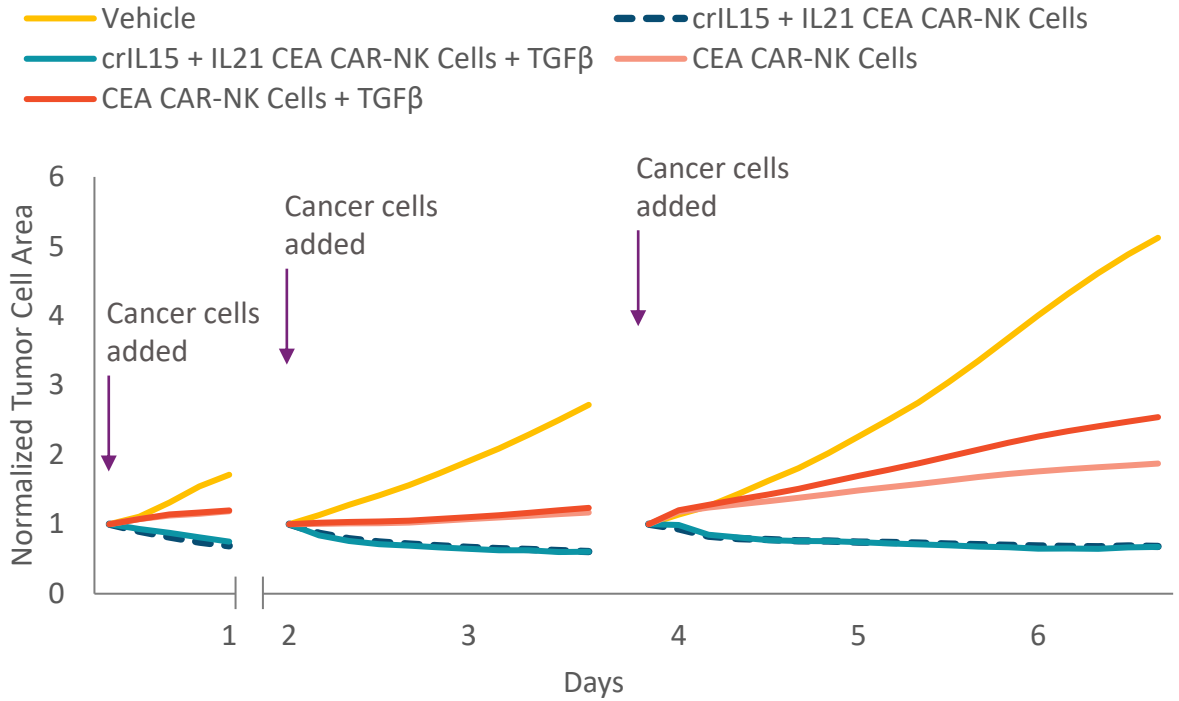
[1] Parkhurst, et al., [2] Median expression of tumor and normal samples in body map (Log2 (TPM+1) scale) source: TCGA, Gtex and Nat Genetics 2020 [GSE132465],

SENTI-401 Preclinical Killing Activity Is Enhanced by crIL-15 and IL-21 Multi-Arming



Arming CEA CAR-NKs with the combination of Senti's proprietary crIL-15 and IL-21 results in improved anti-tumor activity of NK cells against LoVo CRC model

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

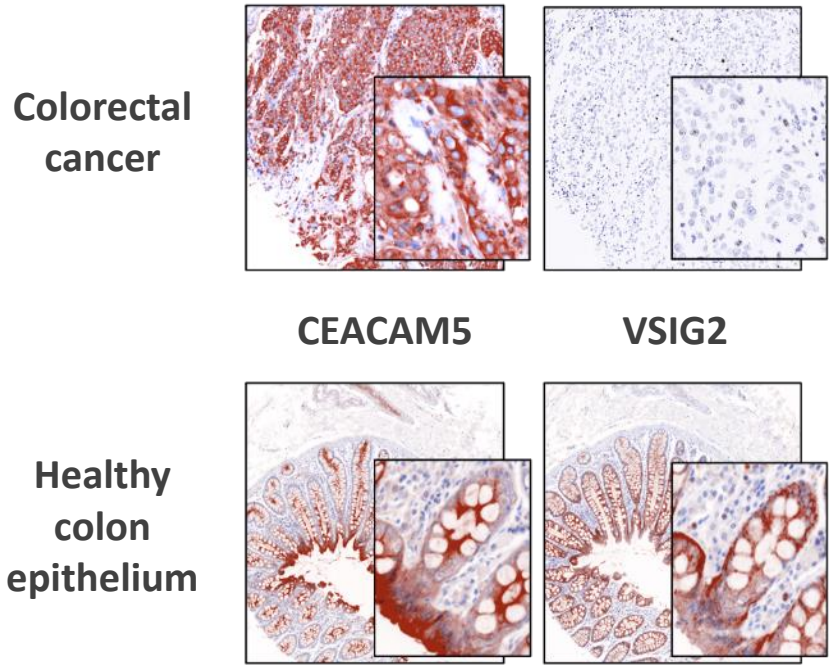


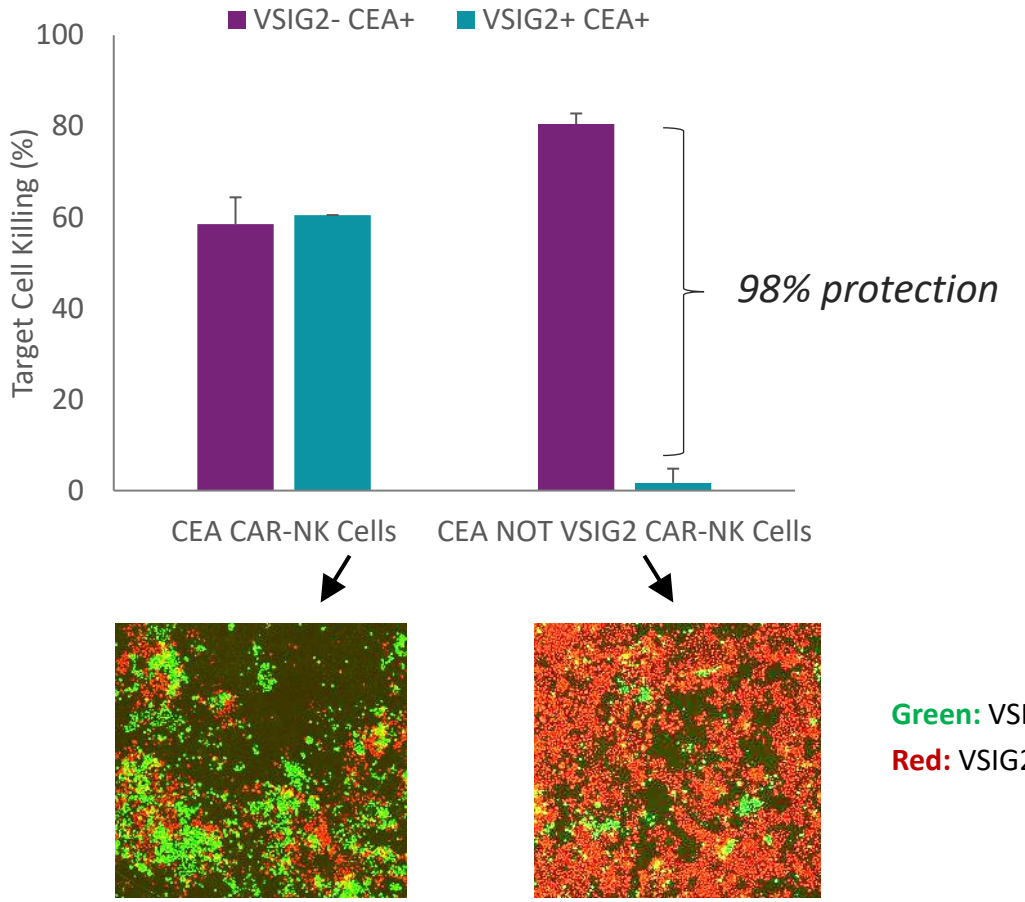
crIL-15 increases CAR-NK cell persistence and IL-21 sustained serial killing against Ls174t CRC cell line even in the presence of the immunosuppressive cytokine TGFβ

[1] Nature 2018

SENTI-401 Includes an iCAR Recognizing VSIG2 to Potentially Reduce On-Target, Tumor Toxicity

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 model healthy cells in DLD1 CRC cell line with addition of inhibitory CAR construct

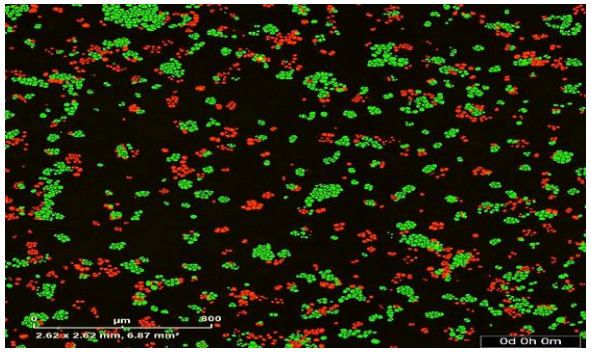
[1] Goldstein 2005

NOT GATE Spares VSIG2+ Expressing Cells While Maintaining CEA+ Cancer Killing

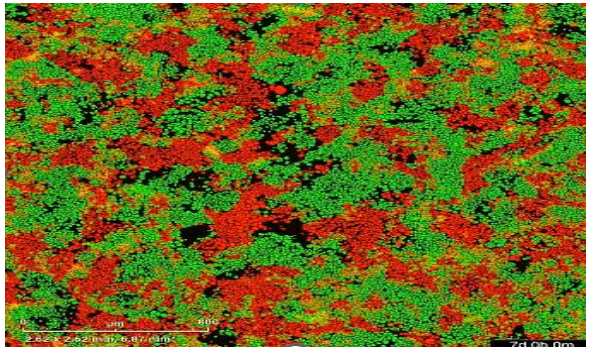
Cancer cells (VSIG2-CEA+)

Model healthy cells (VSIG2+CEA+)

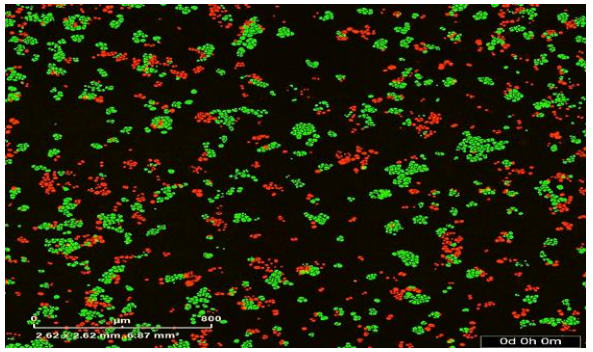
No NK Cells



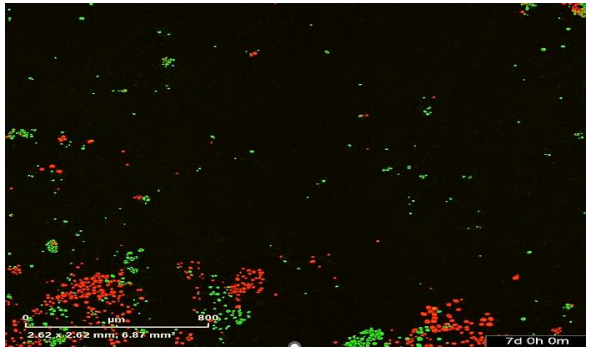
No killing of cancer or healthy cells



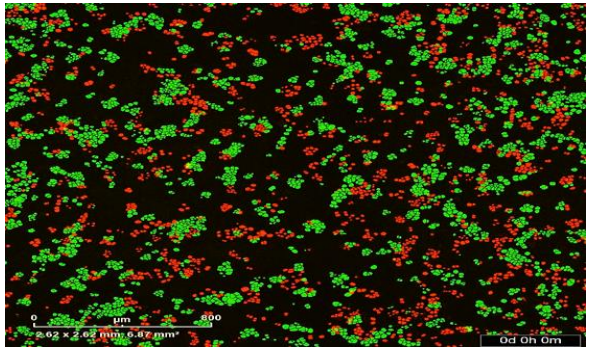
CEA CAR-NK Cells



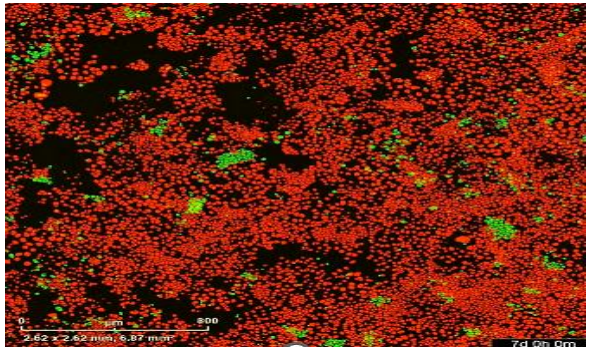
Significant killing of both cancer and healthy cells



CEA NOT VSIG2 CAR-NK Cells

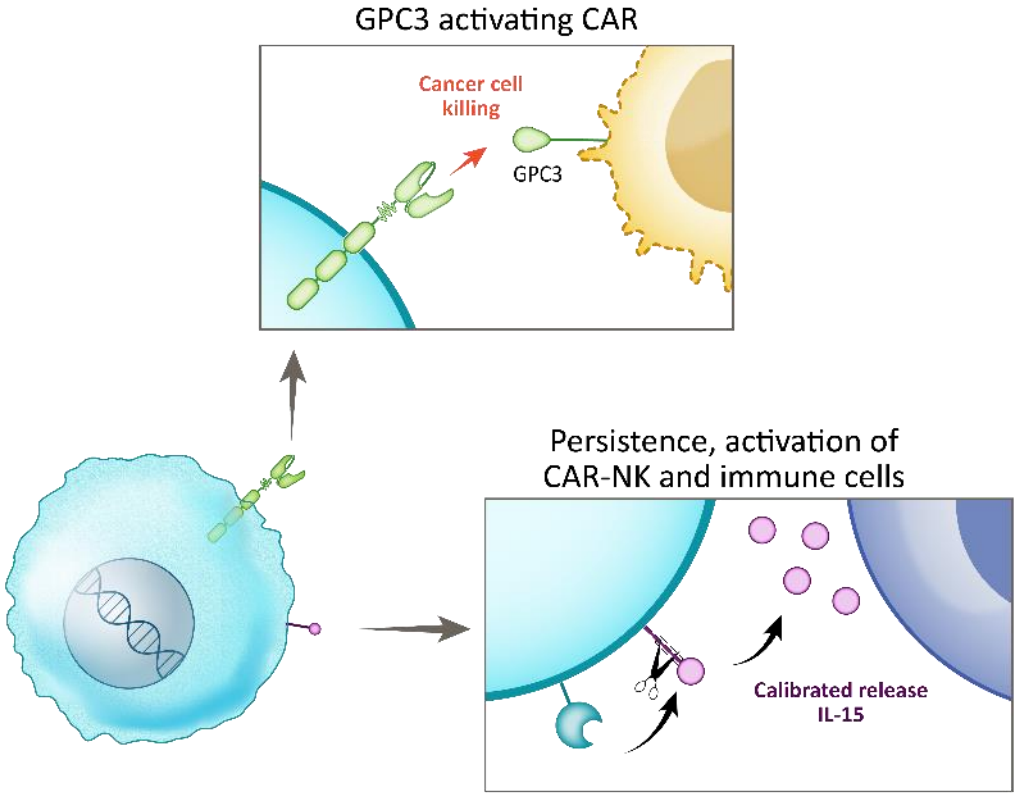


Precisely kills cancer cells and spares healthy cells



CEA NOT VSIG2 CAR-NK cells spare VSIG2-expressing model healthy cells while maintaining robust on-target, on-tumor killing of CEA+ cancer cells

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



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

- ***GPC3 activating CAR*** → hepatocellular carcinoma (HCC) and other solid tumors
- ***crIL-15*** → potential for increased cell expansion, persistence, and tumor killing

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

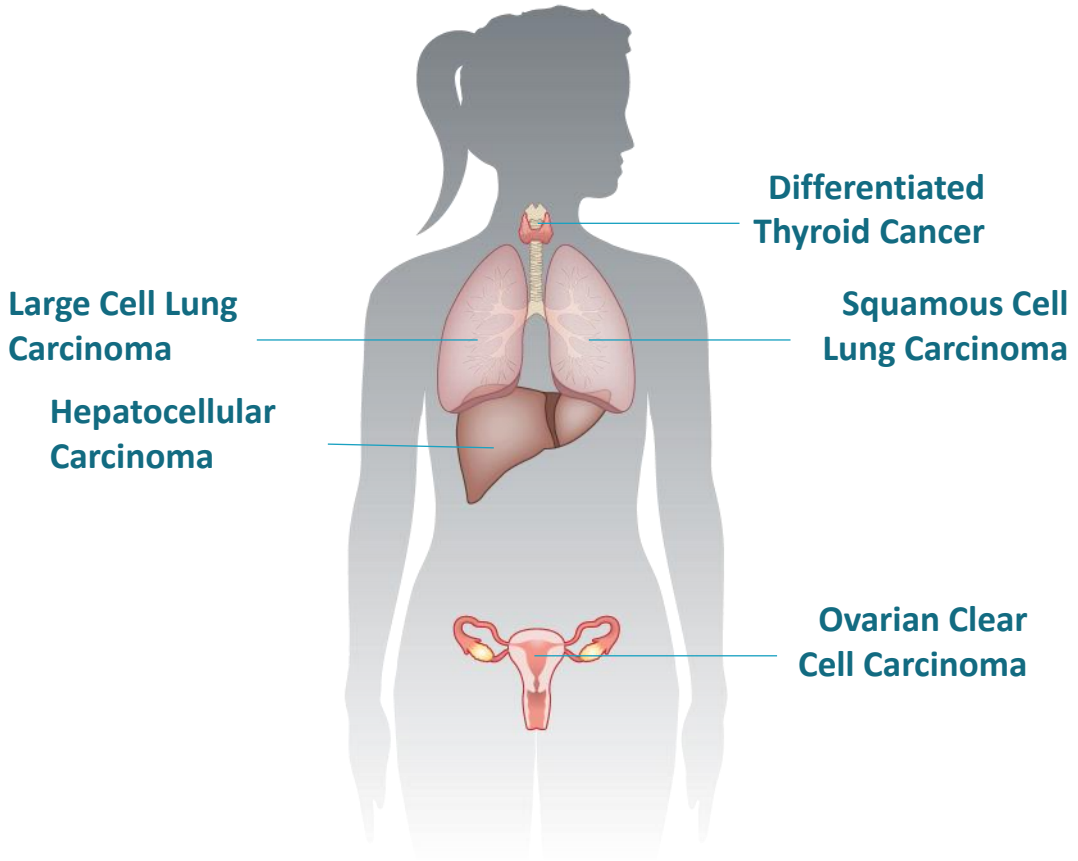
SENTI-301A Is Designed to Tackle GPC3+ Expressing Solid Tumors

GPC3 is an attractive cancer target

- Glypican-3 (GPC3) is a membrane-bound protein normally expressed in fetal tissues such as liver and placenta.
- GPC3 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

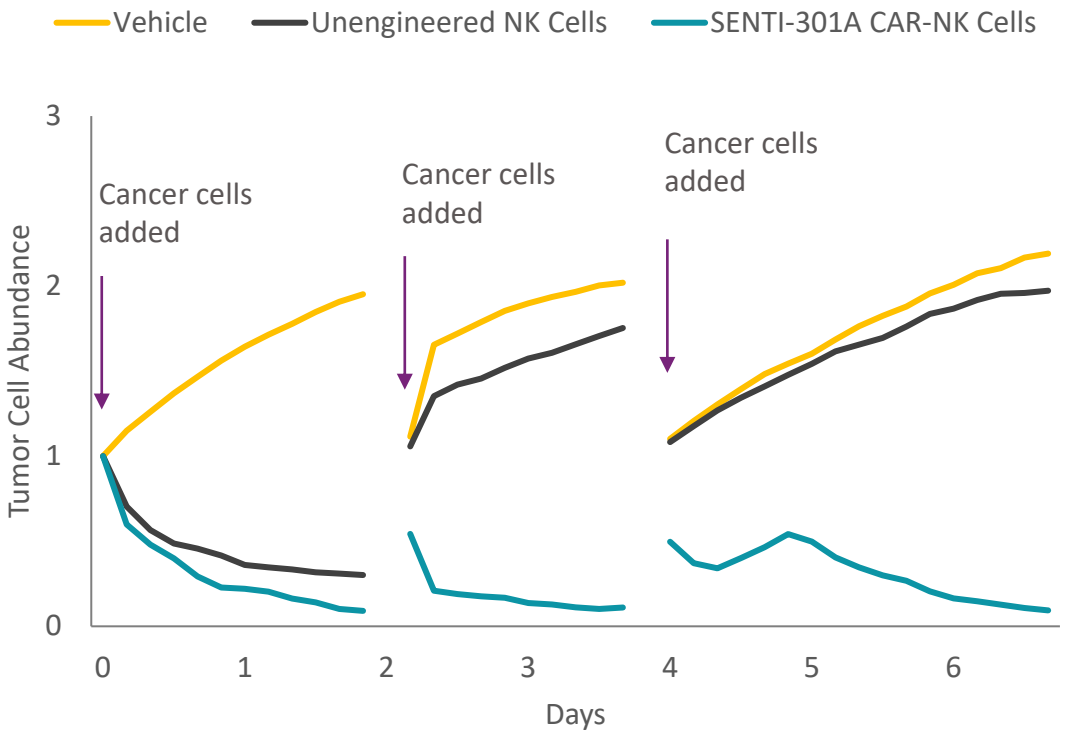
- Aim to address unmet need in HCC as the initial focus given the lack of targeted therapies and lack of effective immunotherapies
- Tackle multiple solid tumors with high GPC3 antigen expression via NKs multi-armed with GPC3 CAR and crIL-15

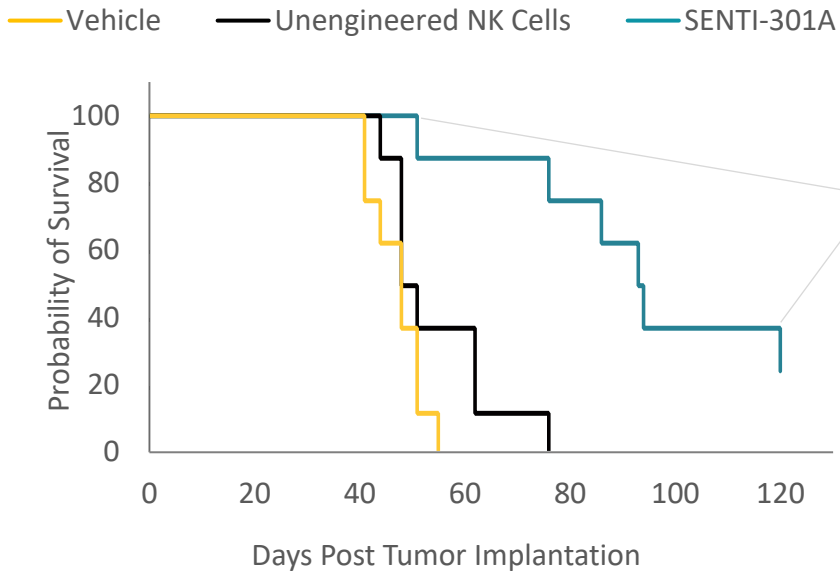


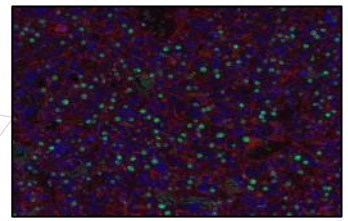
Common GPC3 expressing tumors

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

SENTI-301A Has Robust Preclinical Activity in Preclinical Models of Liver Cancer







SENTI-301A infiltrates into tumors (green)

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

Effective in vitro serial killing of HepG2 cell line

Increased survival, tumor infiltration and response in HepG2 mouse model

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

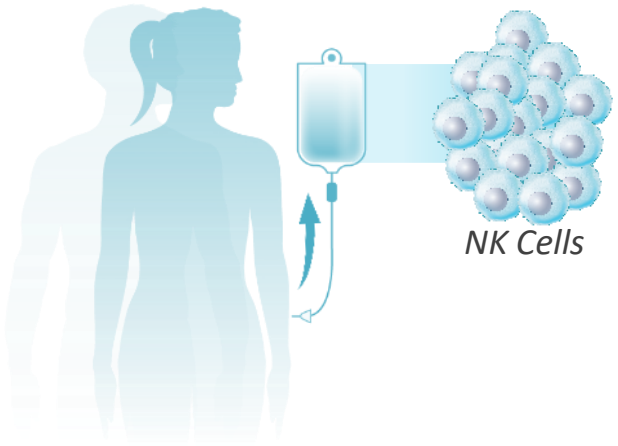
Features	Cord Blood NK Cells	iPSC-Derived NK-Like Cells	Peripheral Blood NK Cells
NK Cell Expandability	Increased expansion potential but smaller number of starting cells	Similar expandability to peripheral blood	Established methods for 1,000-10,000-fold expansion in 14-21 days
Potency and Function	More 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 ~70 clinical trials using peripheral NK cells

Peripheral blood-sourced NK cells provide a full repertoire of functional NK cells, a mature GMP process, and extensive clinical experience to enable our next generation CAR-NK cell therapies

Senti's Scalable Manufacturing Process to Support Off-The-Shelf CAR-NK Products

Scalable ~21 Day Process | **Off-The-Shelf**

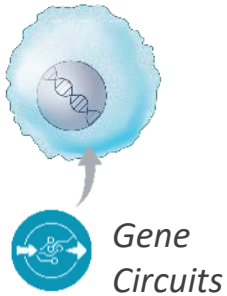
1 ***Isolate from selected donors***



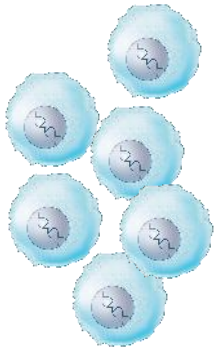
Selected Donor

2 ***Engineer***

Gene Circuit Engineered CAR-NK cells



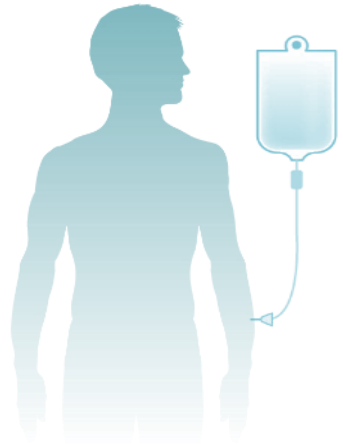
3 ***Expand***



4 ***Cryopreserve***

Final product harvested and cryopreserved

5 ***Thaw and infuse***

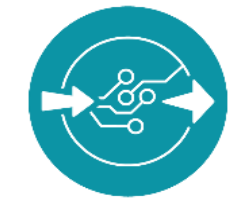


Patient

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**

Gene Circuit Platform

Gene Circuit Technology Has Broad Applicability Across Multiple Modalities and Therapeutic Areas



Gene Circuit Technology

- Multi-Arming
- Logic Gating
- Regulator Dial
- Smart Sensor

NK cells	Blood cancers Solid tumors
T cells	Blood cancers Solid tumors Immunology
***in vivo* Gene Therapy**	Blood cancers Solid tumors Liver diseases Eye diseases CNS
iPSCs	Regenerative medicine

SENTI BIO

Wholly-Owned Programs with Opportunities for Future Development

Spark THERAPEUTICS

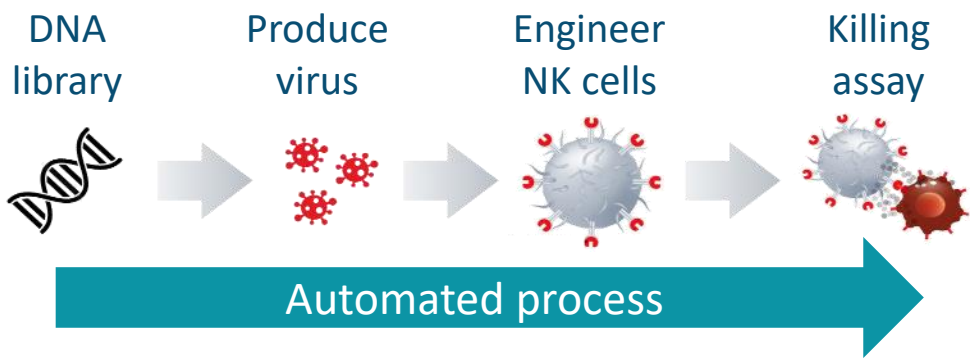
BlueRock THERAPEUTICS

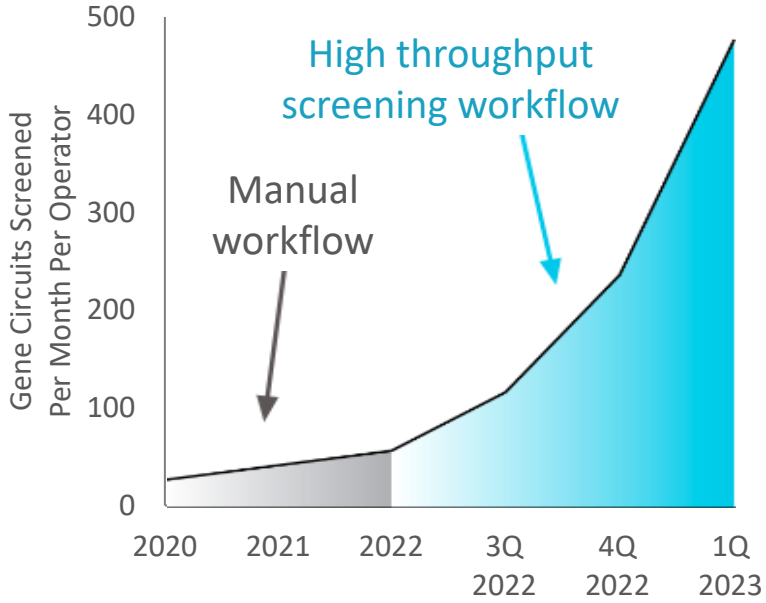
SENTI BIO

Opportunities for Future Development and Additional Partnering

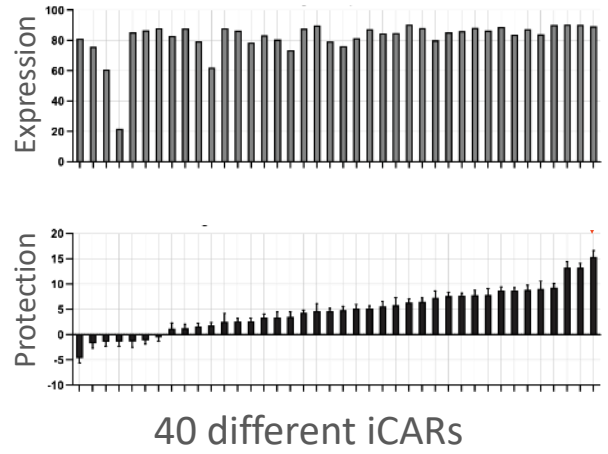
High Throughput Screening (HTS) Of Gene Circuits in NK and T Cells

State-of-the-art, integrated system for screening gene circuit libraries in one continuous process within primary human NK cells

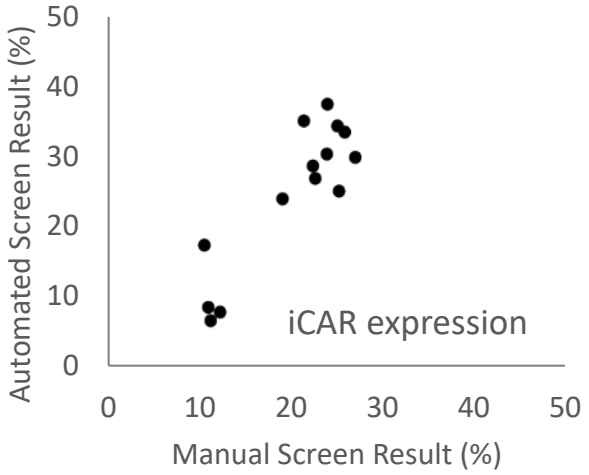


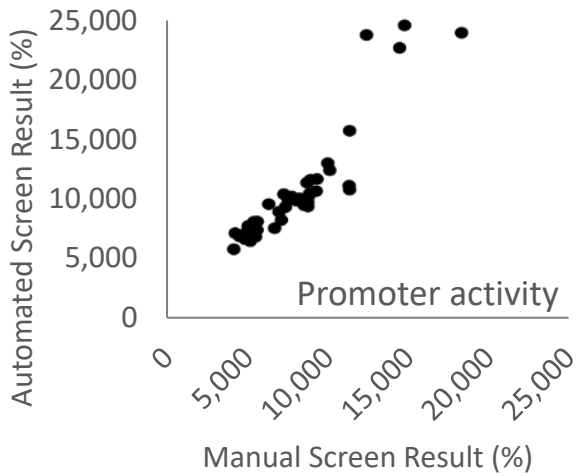


iCAR profiling

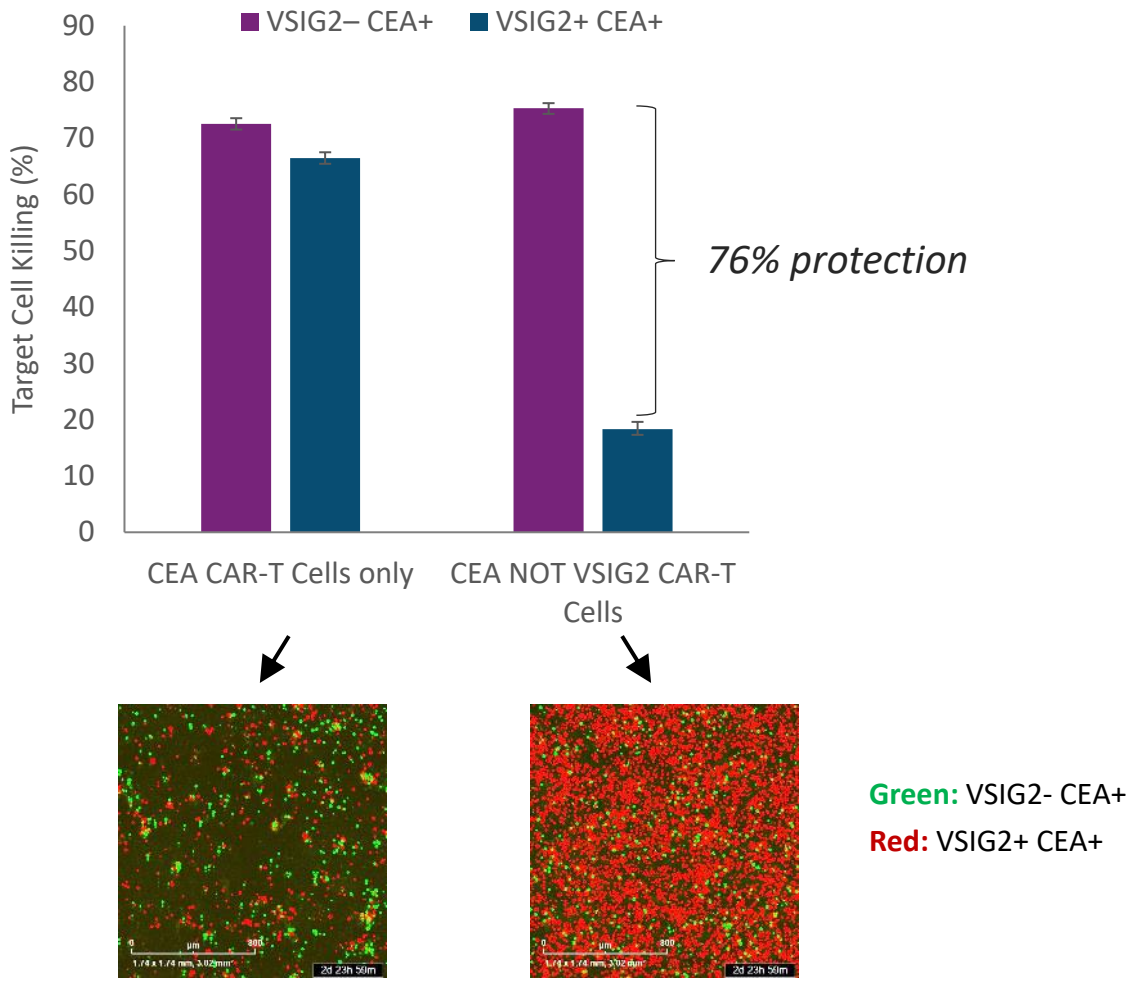


Automated vs Manual Screening





NOT GATE Gene Circuit Validation in CAR-T Cells



Green: VSIG2- CEA+

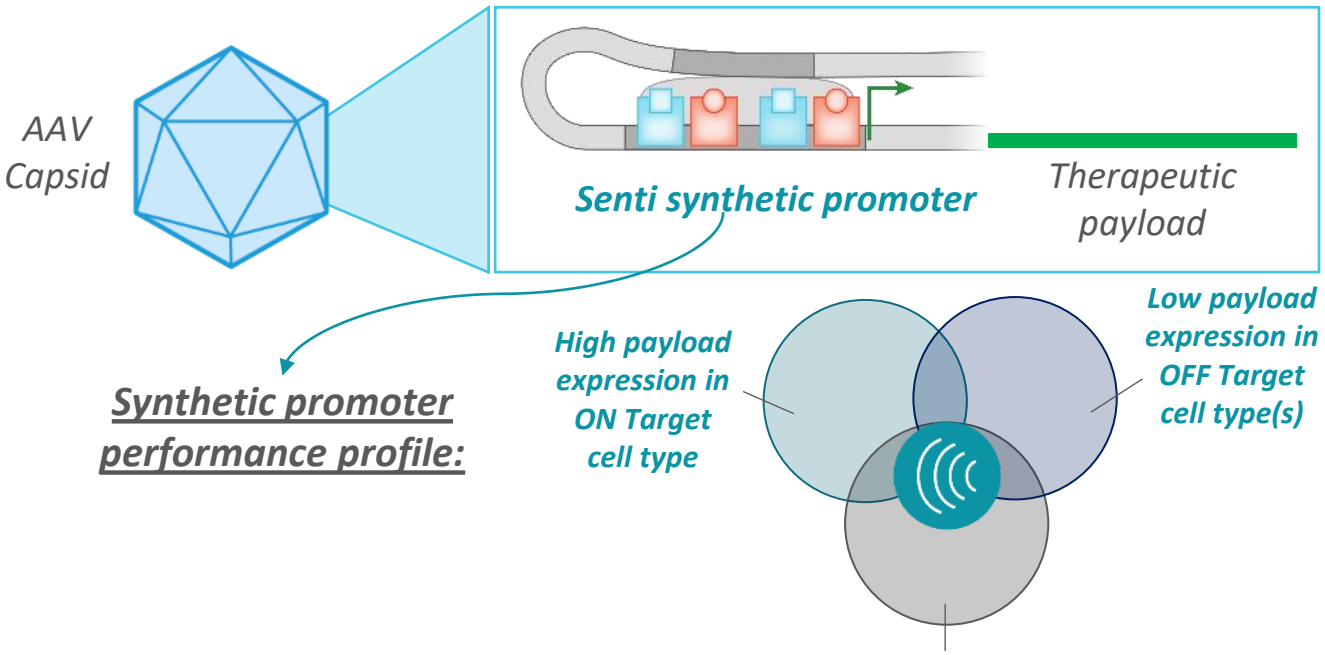
Red: VSIG2+ CEA+

VSIG2 inhibitory CAR-T construct achieves robust protection of model healthy cells while effectively killing cancer cells

Gene Circuit Technology For AAV Gene Therapy

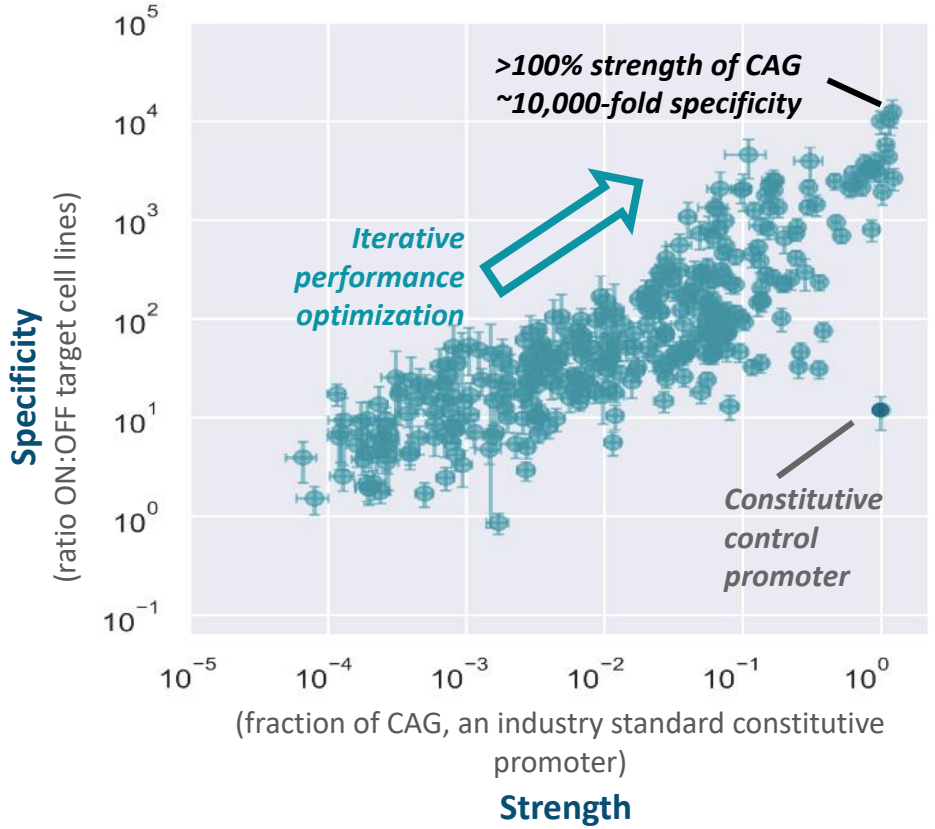
Spark

AAV gene therapy with cell type-specific Smart Sensor for CNS, eye and liver applications



Compact promoter size to accommodate therapeutic payload transgene within ~4.5 kb AAV vector

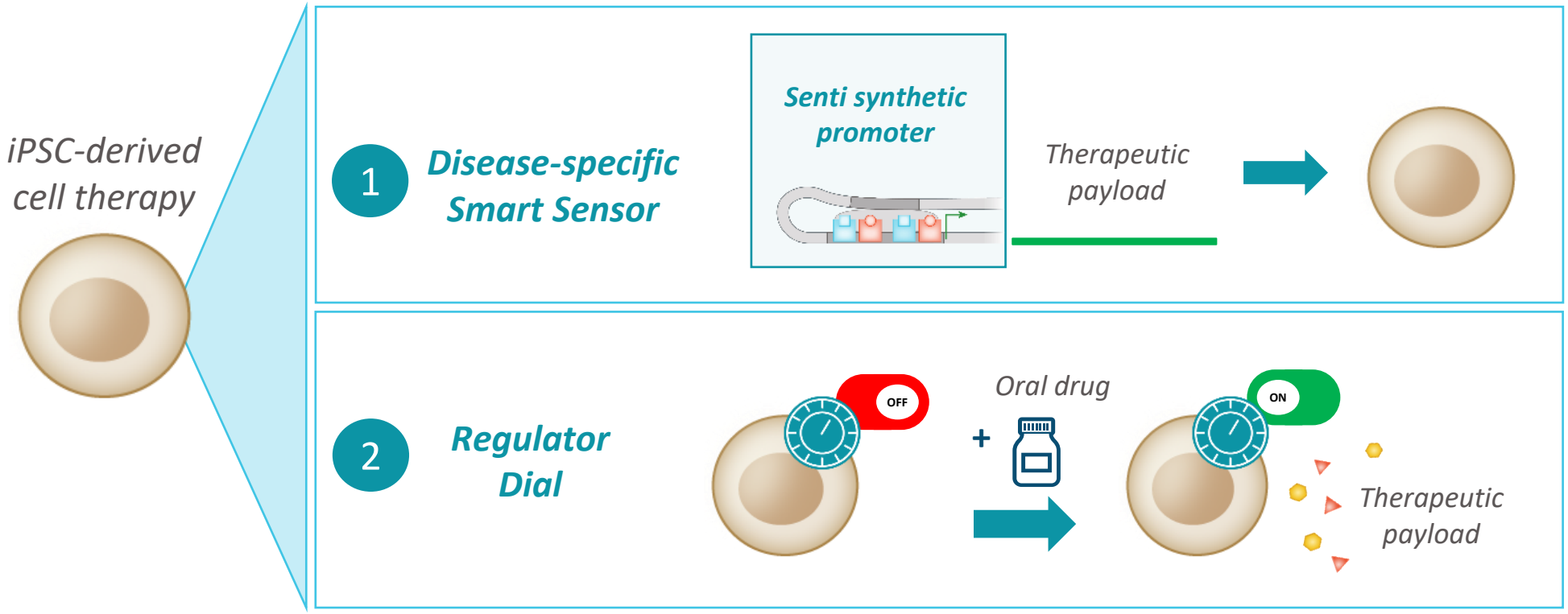
Smart Sensor promoter data



Smart Sensor promoters increase specificity to target cells thus limiting off-target cell toxicities and increase strength, potentially enabling more efficacious therapies

Gene Circuit Technology For iPSC-Derived Cell Therapy

BlueRock THERAPEUTICS *iPSC-derived cell therapy with disease-specific Smart Sensor and Regulator Dial for regenerative medicine*



Collaboration aims to use Regulator Dial to control IL-12 expression using FDA approved small molecule drugs as well as Smart Sensors promoters to control macrophage polarization logic

Continued Execution Across Wholly Owned and Partnered Programs

Preclinical validation across multiple applications

- Gene circuit technology being applied across NK cells, T cells, AAVs and IPSCs
- Platform enables smarter cell and gene therapies for oncology, ocular disease, neurodegenerative disease and more

Clear focus on bringing gene circuits into the clinic

- SENTI-202 is a first-in-class CAR-NK program for AML on track for IND submission and clearance in 2H 2023
- SENTI-401 is a pipeline in a product for multiple solid tumors
- Gene circuit-enabled collaborations for applications outside of oncology are advancing with continued validation

Strong execution on pipeline and manufacturing timelines

- Experienced management team with track record of executing on timelines and accelerating innovating therapies
- Strategic plan for 2023:
  - Validate gene circuit-powered CAR-NK and partnered programs at key conferences
  - Manufacture GMP batches to support SENTI-202 IND filing
  - Pursue strategic geographic partnerships for SENTI-301A
- Cash runway expected to fund operations through at least 1Q 2024

SENTI BIO

Thank you