



SENTI BIO<sup>TM</sup>

# Outsmarting Complex Diseases with Intelligent Medicines

Corporate Overview

January 2022





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SENTI BIO

Senti Bio designs gene circuits for next-gen cell and gene therapies

**Proprietary gene circuit technology platform** enables the development of “smart” next-gen cell and gene therapies with enhanced efficacy, safety and control

**Multiple therapeutic modalities** (e.g. NK cells, T cells, iPSCs, gene therapy, mRNA, etc.) offering vast opportunities

**Potential to address patients with high unmet needs** in oncology, immunology, genetic diseases, neurology, cardiology, ophthalmology, and more

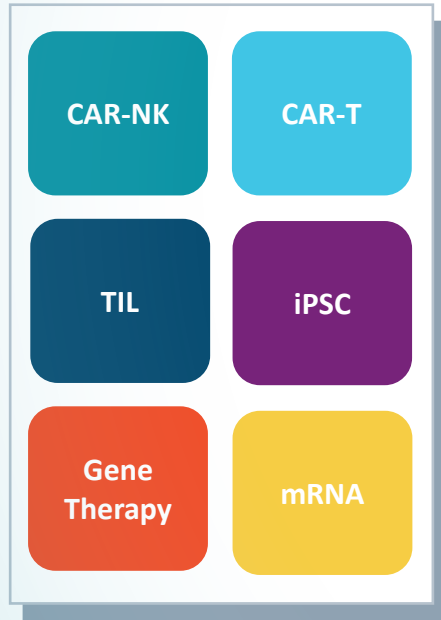
**Differentiated Allogeneic CAR-NK Oncology Pipeline and Collaborations** with Spark (Roche) and BlueRock (Bayer)

**Allogeneic CAR-NK Anticipated IND filings in 2023 for product candidates SENTI-202 (AML) and SENTI-301 (HCC)**



# Today's Cell and Gene Therapies Cannot Resolve Fundamental Disease Challenges

## CURRENT CELL AND GENE THERAPIES ARE SIMPLISTIC...



Unable to precisely distinguish diseased versus healthy cells



TARGET HETEROGENEITY

Unable to overcome multiple disease mechanisms



DISEASE EVASION

Unable to be regulated after delivery into patients



NARROW THERAPEUTIC WINDOW

Unable to adapt to disease conditions



DYNAMIC DISEASE CONDITIONS



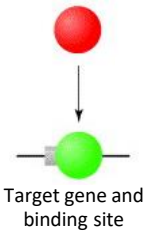


# Senti's Gene Circuits Use Biological Computation to Solve Biological Problems

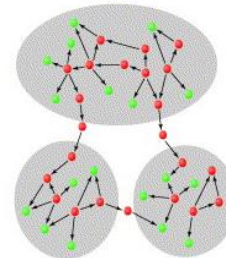
Evolution has selected for natural genetic circuits

## Genetic Parts

Transcription factor



## Gene Circuits



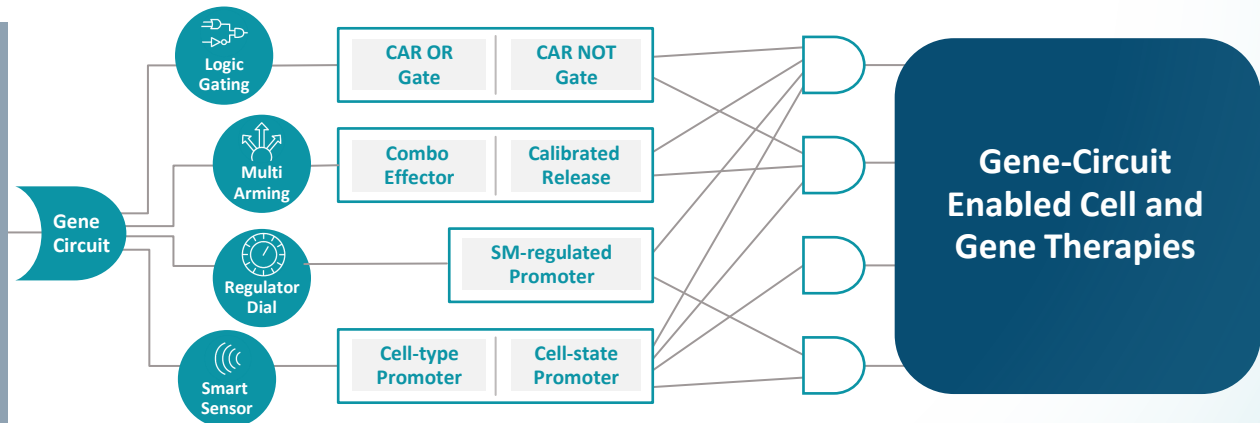
## Gene Networks



Adapted from Babu et al. Curr Opin in Structural Bio, 14(3), 2004



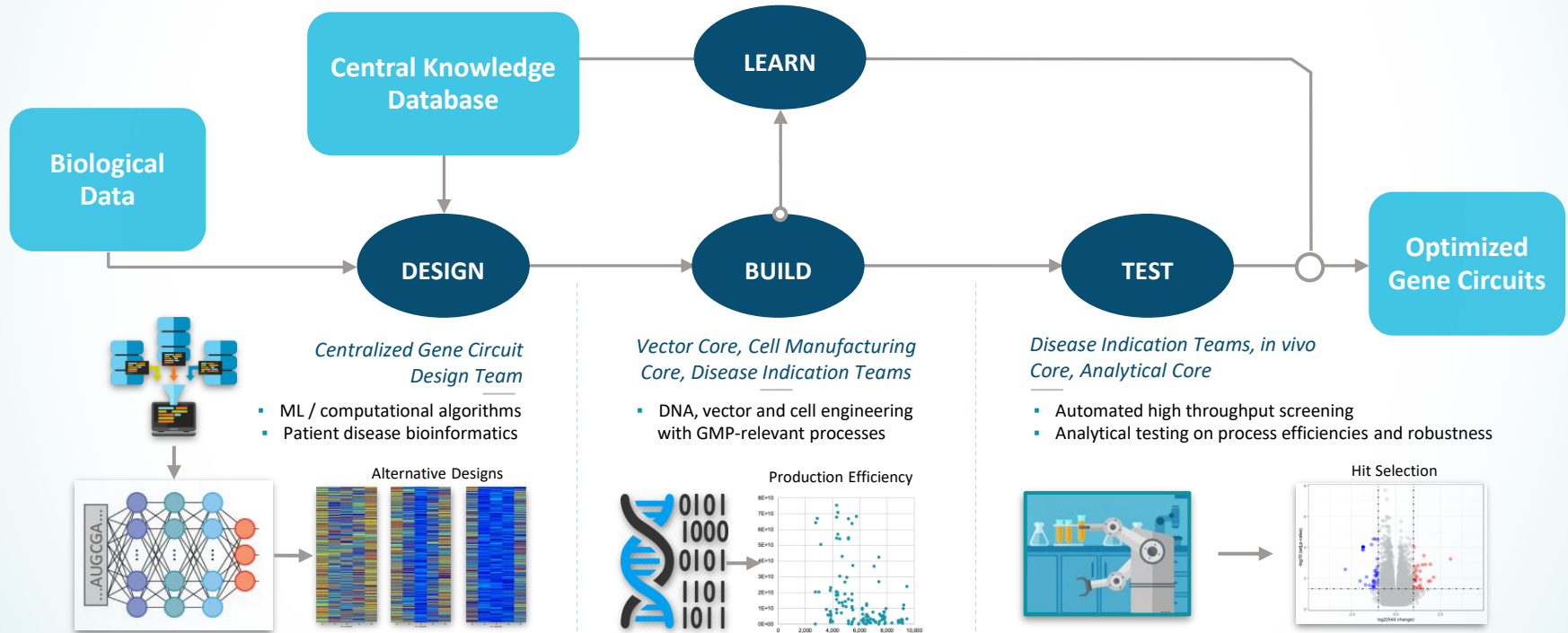
Learning from evolution, Senti creates intelligent gene circuits





# Powerful and Scalable Engine Optimizes Gene Circuits to Enable Creation of Intelligent Medicines

## SENTI'S DESIGN-BUILD-TEST-LEARN ENGINE





# Senti's Gene Circuit Platform is Designed to Overcome Fundamental Disease Challenges

## FUNDAMENTAL DISEASE CHALLENGES...



TARGET HETEROGENEITY



DISEASE EVASION

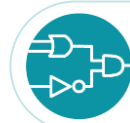


NARROW THERAPEUTIC WINDOW



DYNAMIC DISEASE CONDITIONS

## ...ARE TACKLED THROUGH INTELLIGENT GENETIC PROGRAMMING



LOGIC GATING

Integrates multiple targets to pinpoint diseased cells and spare healthy ones



MULTI-ARMING

Targets multiple disease pathways within a single all-in-one drug



REGULATOR DIAL

Dynamically regulates therapies *in vivo* using FDA-approved oral drugs

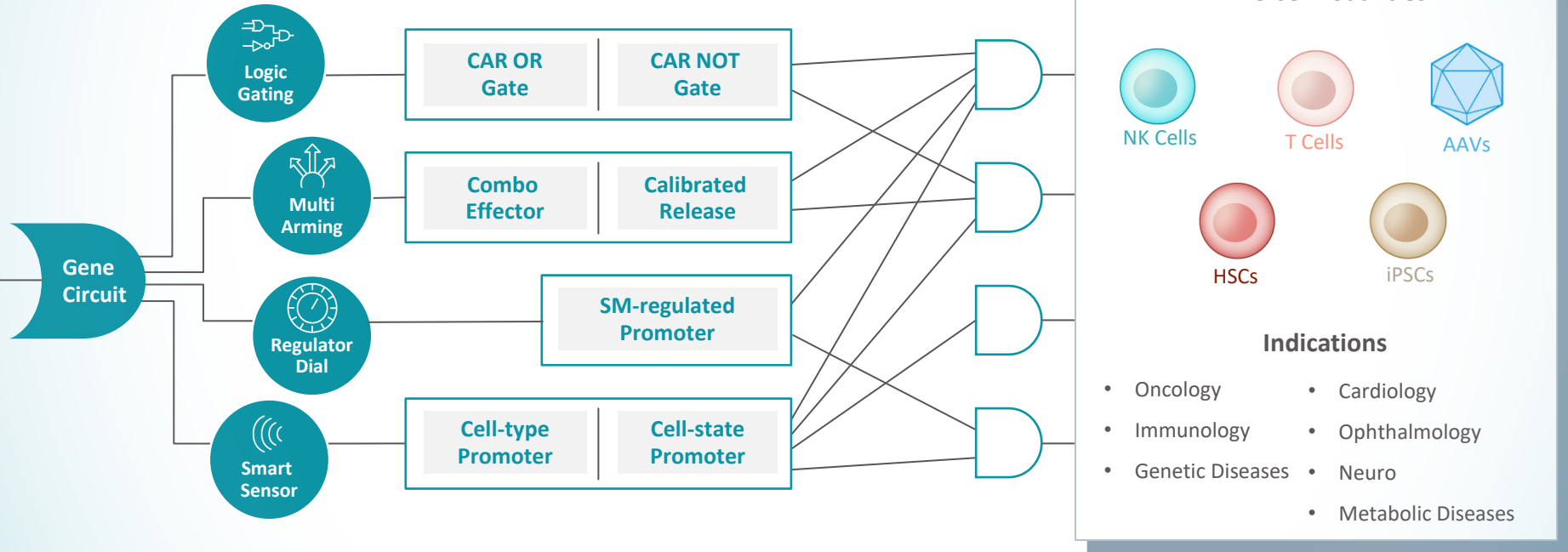


SMART SENSOR

Precisely detects and responds to disease environments



# Gene Circuits Could Potentially Power Multiple Cell and Gene Therapy Modalities for Broad Therapeutic Potential

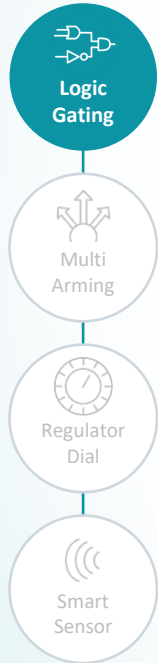




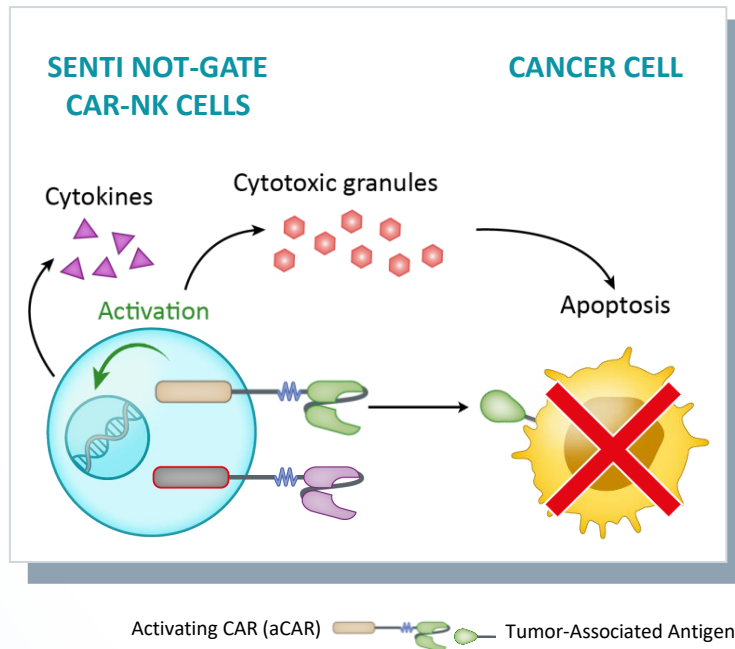


# Logic Gating Enables Highly Specific Therapies by Recognizing Multiple Antigens

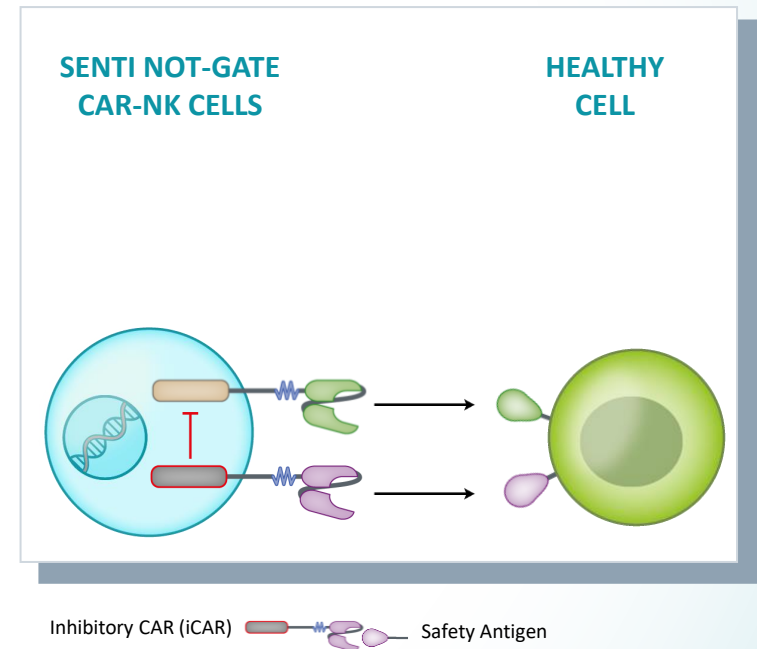
Toolbox of  
Gene Circuits



## TUMOR-ASSOCIATED ANTIGENS (TAA) ENGAGEMENT TRIGGERS CANCER CELL KILLING



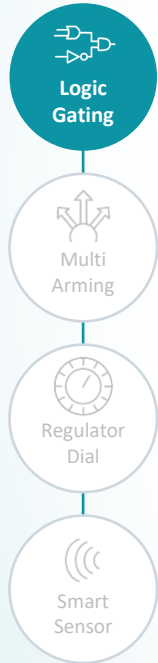
## SAFETY ANTIGEN ENGAGEMENT ENABLES PROTECTION OF HEALTHY CELLS





# NOT Logic Gate Functions In Vivo to Specifically Kill Cancer Cells and Spare Healthy Cells

Toolbox of  
Gene Circuits

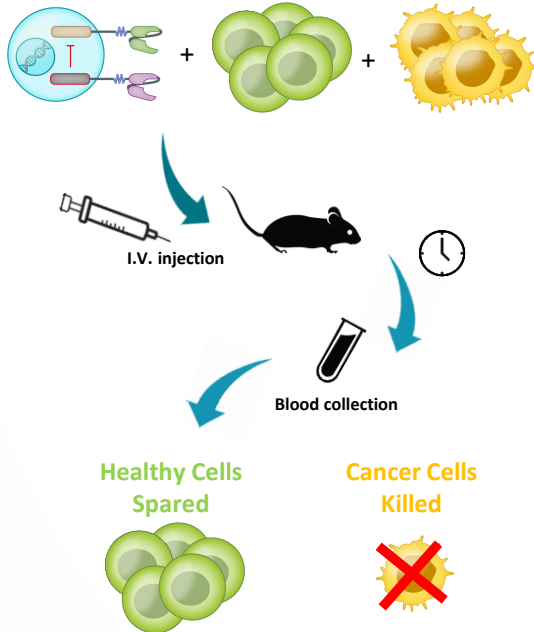


NOT-Logic-Gated  
CAR-NK Cells

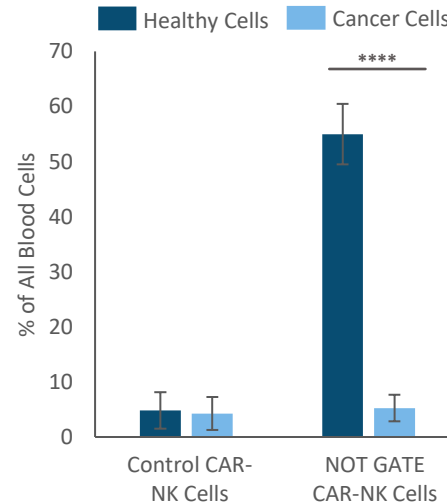
Healthy  
Cells

50:50

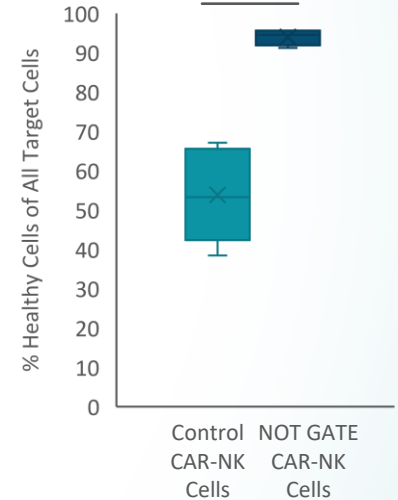
Cancer  
Cells



NOT-GATED CAR-NK CELLS REDUCE  
KILLING OF HEALTHY CELLS



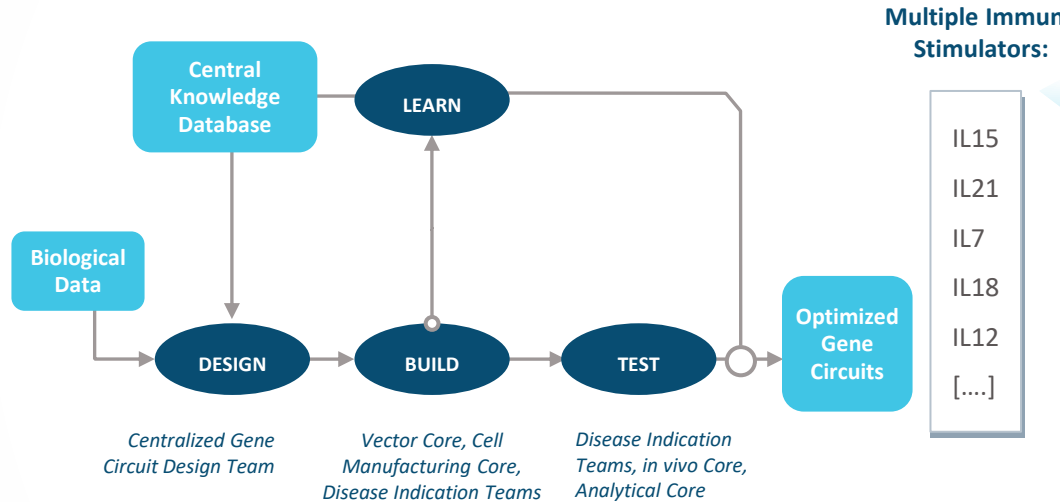
RESULTING IN ENRICHMENT  
OF HEALTHY CELLS





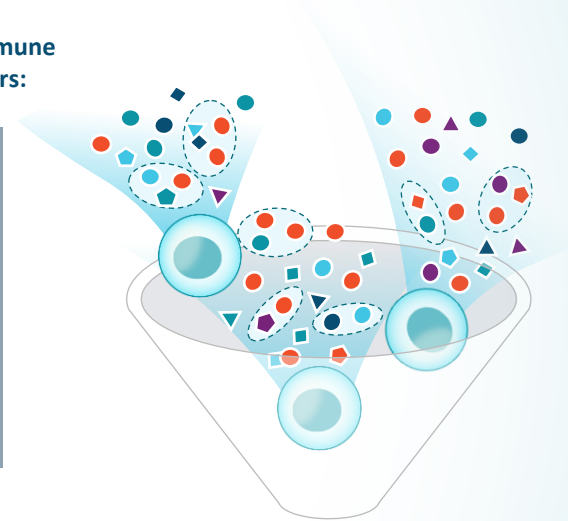
# Multi-Arming Circuits Enable All-in-One Combination Cell and Gene Therapies

## Toolbox of Gene Circuits



## Multiple Immune Stimulators:

IL15  
IL21  
IL7  
IL18  
IL12  
[...]



**Use of Senti's Design-Build-Test-Learn Engine optimizes each payload's expression level and which combinations are expressed from Multi-Arming gene circuits to enhance therapeutic activity**

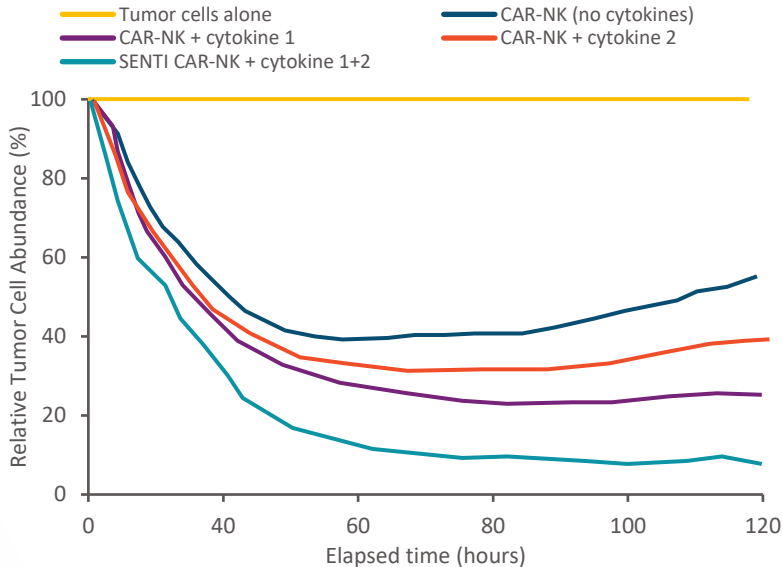


# Multi-Armed CAR-NK Cells Exhibit Significantly Improved Killing of Cancer Cells

## Toolbox of Gene Circuits

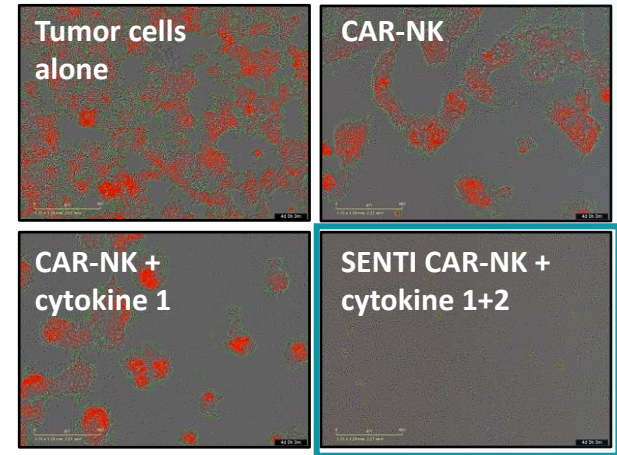


## IN VITRO TUMOR CELL KILLING (INCUCYTE)



## TUMOR CELL KILLING

(day 5 post co-culture, 2:1 ratio)



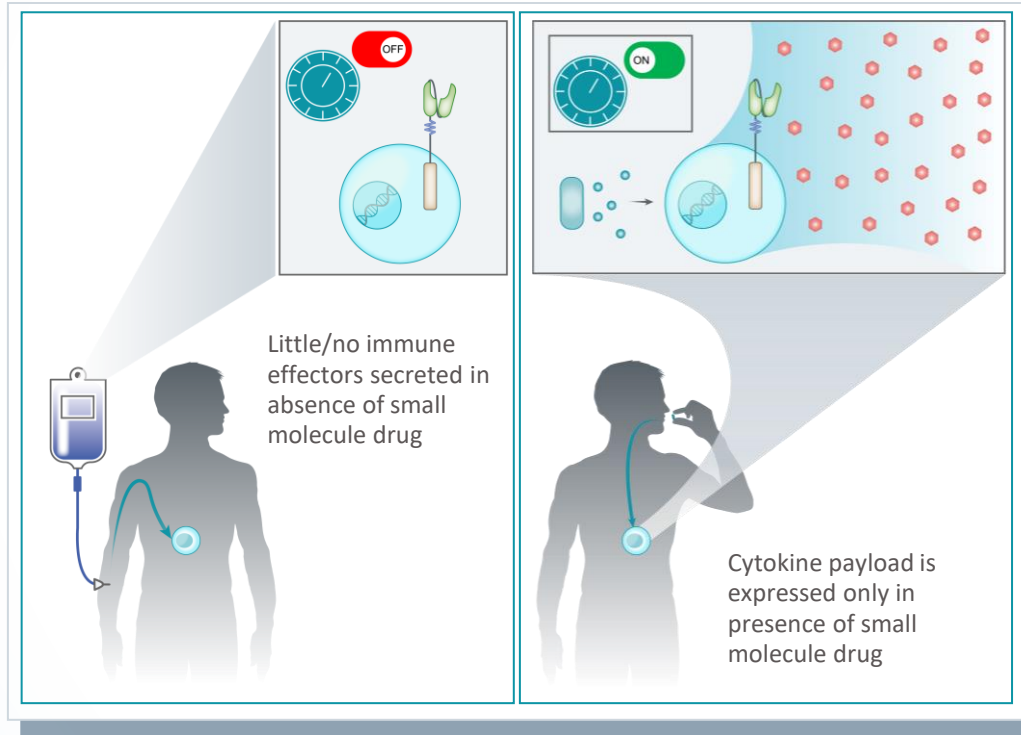
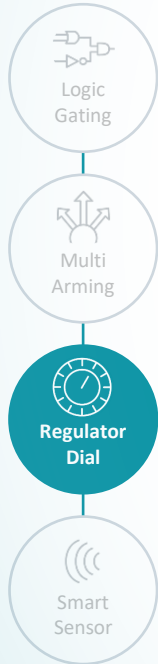
Red fluorescence = tumor cells

Arming of CAR-NK cells using **a combination of cytokines** results in potent and durable killing



# Regulator Dial Circuit Potentially Enables Control of Cell Therapies Using FDA-Approved Drugs

## Toolbox of Gene Circuits



## MULTIPLE DRUG SWITCHES:

- HCV protease inhibitors
- IMiDs
- Tamoxifen

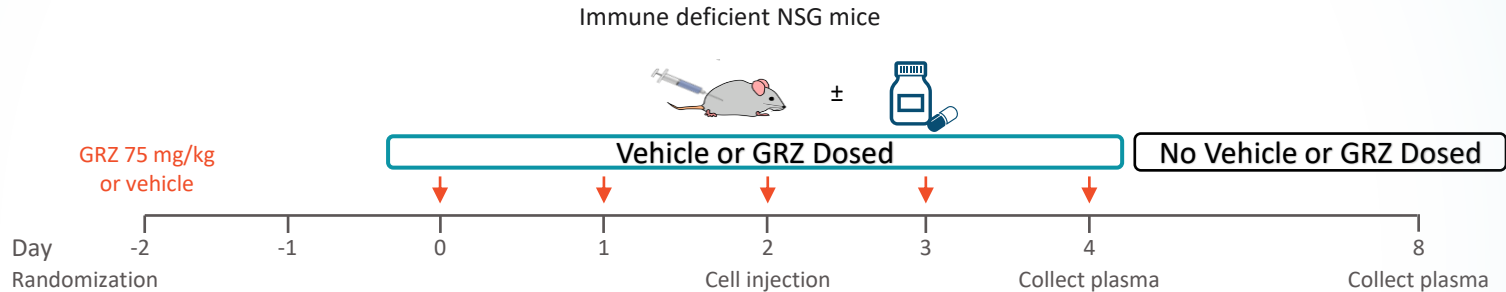


# Regulator Dial Enables ~90-fold ON/OFF Control of IL-12 Secretion *In Vivo*

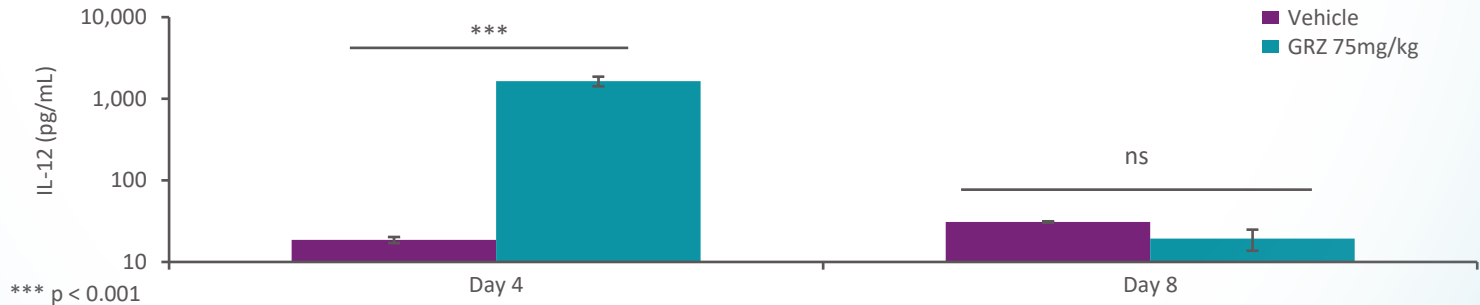
## Toolbox of Gene Circuits



## STUDY DESIGN



## IL-12 DETECTED IN MOUSE PLASMA

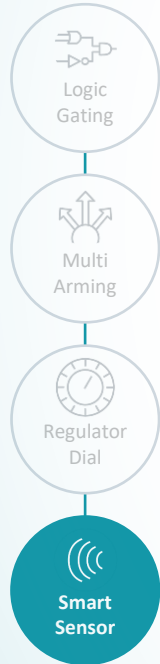




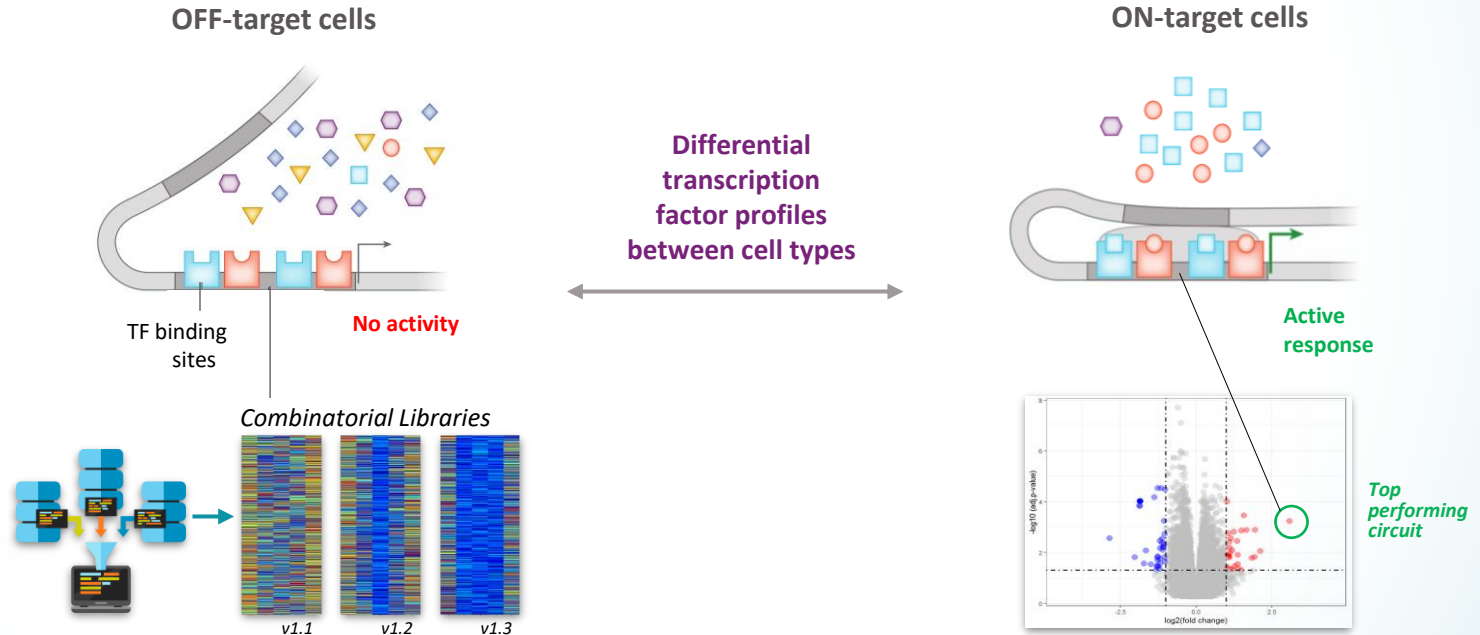


# Smart Sensors Enable Precise and Dynamic Recognition of Diseased Cells

## Toolbox of Gene Circuits



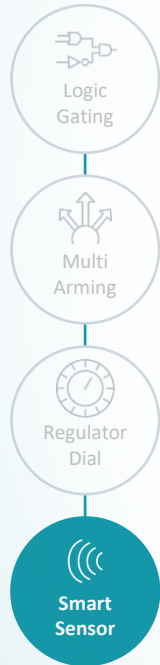
## CURRENT GENE THERAPIES LACK SPECIFICITY FOR SPECIFIC DISEASED CELL TYPES



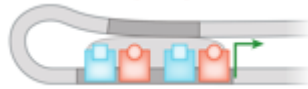


# Smart Sensor Promoters Enable up to 1,000-fold Selectivity for Diseased Cells

## Toolbox of Gene Circuits

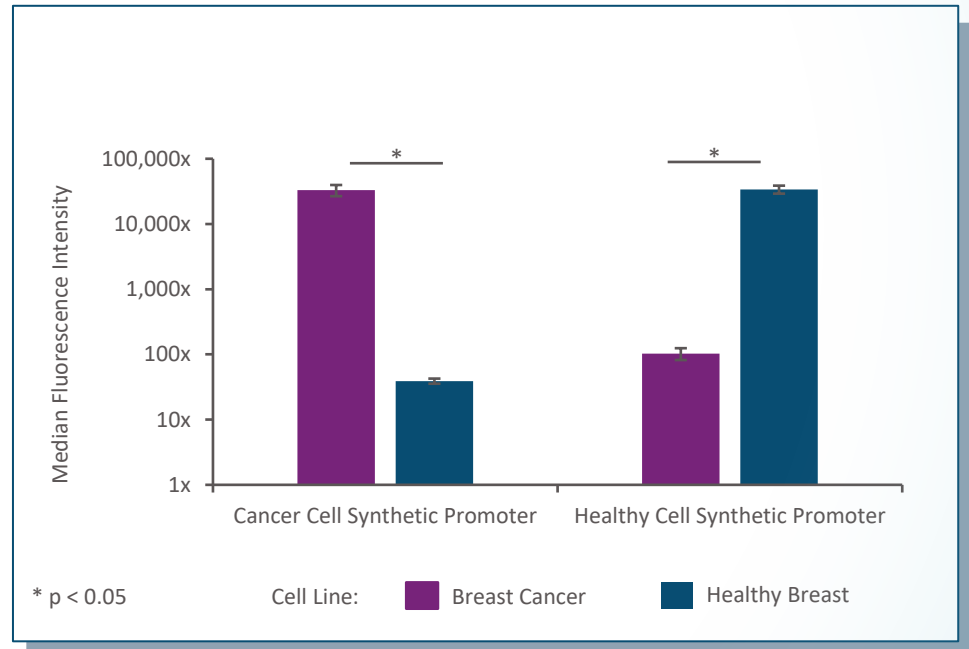


## SIGNALS SUCH AS TRANSCRIPTION FACTOR(S)



**Cancer-specific  
transcription factor(s)**














## GENE THERAPY WITH TRANSGENE EXPRESSION UP TO ~1,000X CELL TYPE SELECTIVITY



Source: Wu et al. Nature Communications 10, Article number 2880 (2019)



# Gene Circuit Enabled Pipeline With Additional Collaboration Opportunities

Modality	Gene Circuit	Name	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Rights
 Allogeneic NK Cells for Oncology	 Logic Gating	SENTI-202	Acute Myeloid Leukemia	<div><div></div></div>					 SENTI BIO
		SENTI-401	Colorectal Cancer	<div><div></div></div>					
		SENTI-411	Solid Tumors	<div><div></div></div>					
		SENTI-421	Solid/Liquid Tumors	<div><div></div></div>					
	 Multi-Arming	SENTI-301	Hepatocellular Carcinoma	<div><div></div></div>					
		SENTI-311	Solid Tumors	<div><div></div></div>					
 Gene Therapies for Tissue-Directed Targets	 Smart Sensor	GC-1001 /-1002	Ocular	<div><div></div></div>					 Spark THERAPEUTICS 
		GC-1003 /-1004	Central Nervous System	<div><div></div></div>					
		GC-1005	Liver	<div><div></div></div>					
 Cell Therapies for Regenerative Medicine	 Regulator Dial	GC-1101	Regenerative Medicine	<div><div></div></div>					 BlueRock THERAPEUTICS 
		GC-1102	Regenerative Medicine	<div><div></div></div>					
	 Smart Sensor	GC-1103	Regenerative Medicine	<div><div></div></div>					

Note: Spark is a wholly owned subsidiary of Roche; BlueRock is a wholly owned subsidiary of Bayer



# Natural Killer (NK) Cells are an Ideal Modality for Gene-Circuit Enhanced Cancer Cell Therapy



## Innate Killing

- ✓ Natural ability to kill tumor cells and spare healthy ones based on multi-receptor engagement
- ✓ Anti-tumor activity and persistence validated



## Immune Activation

- ✓ Proinflammatory cytokine and chemokine secretion
- ✓ Elicit endogenous response for durable anti-tumor immunity



## Favorable Safety

- ✓ Low/no incidence of GvHD vs. CAR-T
- ✓ Low risk of CRS and neurotoxicity



## Broad Access

- ✓ Does not require patient derived cells
- ✓ Potential for outpatient administration
- ✓ Amenable to large scale allogeneic manufacturing



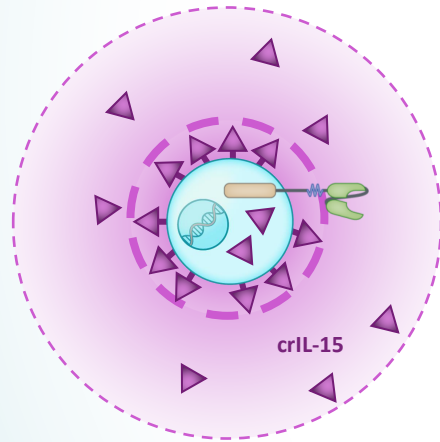
## Clinical Validation

- ✓ **MD Anderson CD19 CAR-NK study in advanced B cell malignancies: 7/11 (64%) CRs and no reported CRS, GvHD or neurotoxicity**
- ✓ **Fate Therapeutics study with FT516 in B-cell lymphoma: 6/11 (55%) CRs and no CRS, GvHD or neurotoxicity**

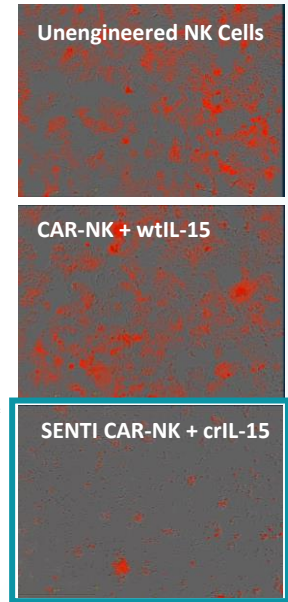
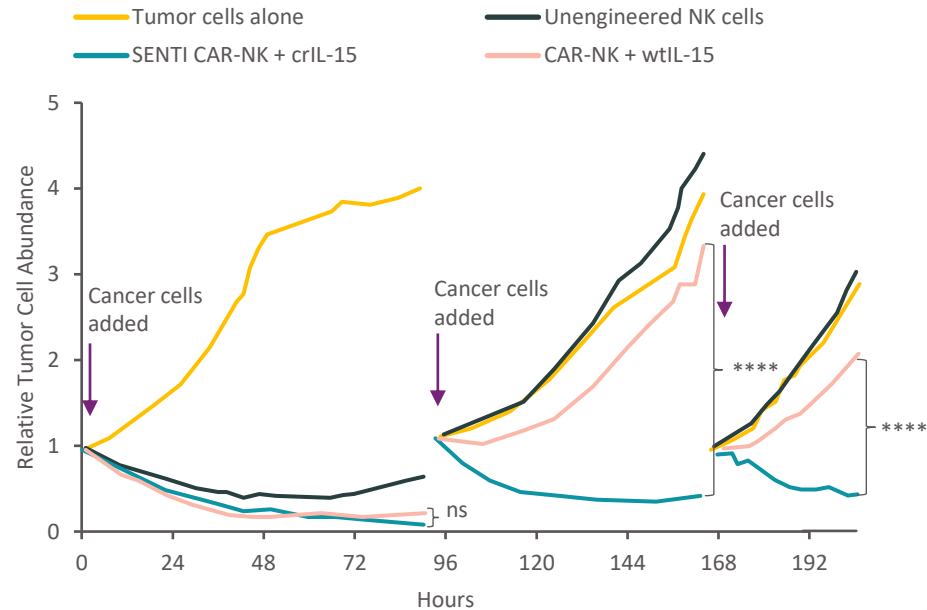


# Senti's Proprietary Calibrated Release IL-15 (crIL-15) Enhances NK Cell Persistence and Tumor Killing

crIL-15 ENABLES BOTH AUTOCRINE  
AND PARACRINE SIGNALING



## crIL-15 IMPROVES NK PERSISTENCE AND SERIAL KILLING



Red fluorescence = tumor cells

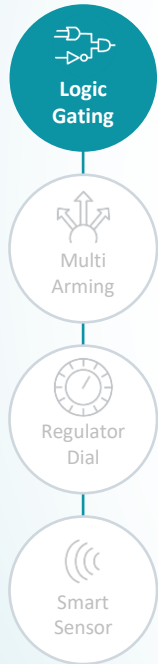
Images taken from 3<sup>rd</sup> round

ns = not significant; \*\*\*\* p = <0.0001



# SENTI-202: Designed to Address Unmet Needs in the Treatment of Acute Myeloid Leukemia (AML)

## Toolbox of Gene Circuits



## SENTI'S LOGIC GATES SOLVE KEY DISEASE CHALLENGES IN AML

### CHALLENGES

#### Target heterogeneity

Relapse due to incomplete targeting of leukemic stem cells (LSCs)

#### Target heterogeneity

Off-tumor toxicity and limited efficacy due to lack of AML-specific targets

### SENTI GENE CIRCUIT SOLUTIONS

#### OR Logic Gate

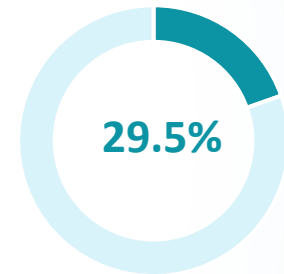
Targets multiple AML tumor associated antigens

#### NOT Logic Gate

Enables broad targeting of AML while preserving healthy blood stem cells

## UNMET NEED IN AML

### 5-Year Survival<sup>1</sup>



**DUE TO DISEASE RELAPSE  
DRIVEN BY  
LEUKEMIC STEM CELLS (LSCs)**

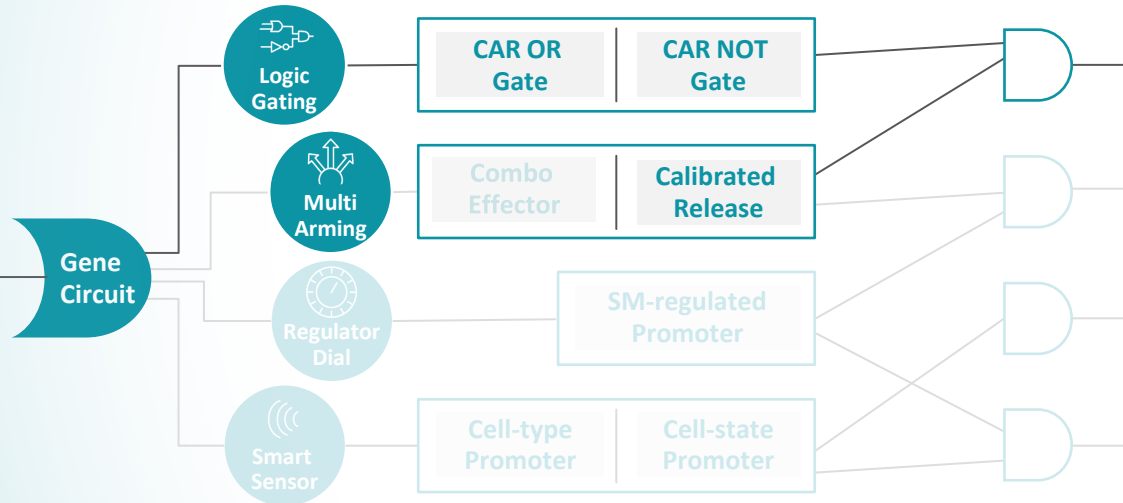
**SENTI'S LOGIC-GATED CAR-NK PROGRAM OFFERS POTENTIAL TO DEVELOP A CURE FOR AML PATIENTS  
IN THE ABSENCE OF A BONE MARROW TRANSPLANT**

<sup>1</sup>SEER Cancer Stat Facts: Acute Myeloid Leukemia

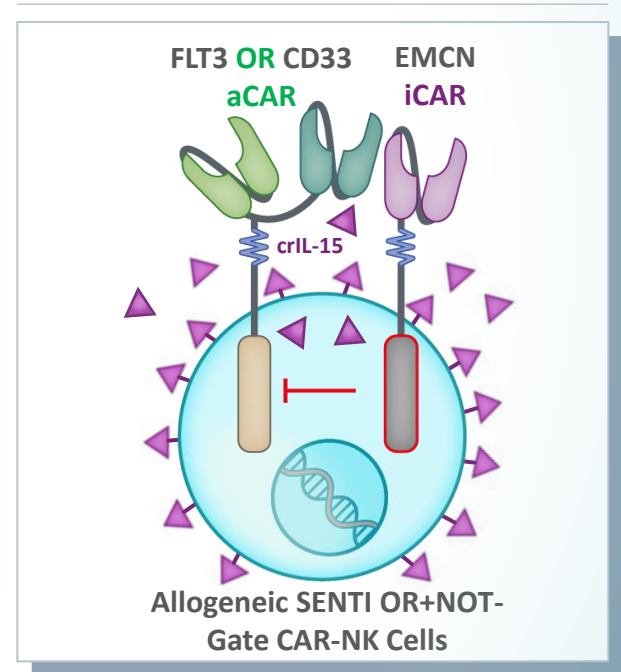




# SENTI-202: Potential to Develop a Cure With No Bone Marrow Transplant Needed



## PRODUCT SCHEMATIC



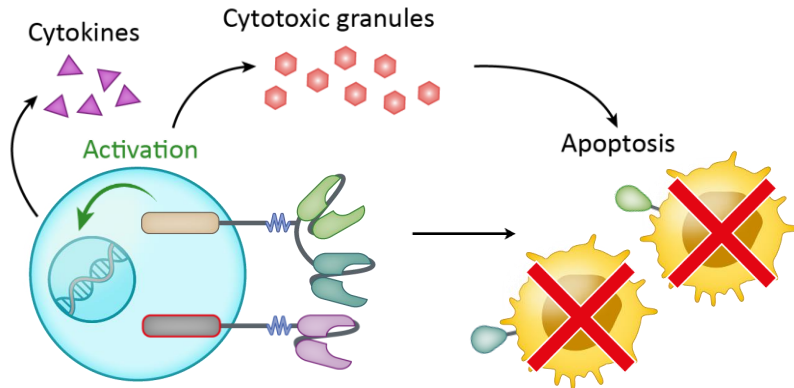


# SENTI-202 OR/NOT Logic Gating: Deep Clearance of AML Blasts and AML LSCs While Sparing Healthy Hematopoietic Stem Cells (HSCs)

FLT3 OR CD33 ENGAGEMENT TRIGGERS  
KILLING OF HETEROGENEOUS AML CANCER CELLS

SENTI-202 CAR-  
NK CELL

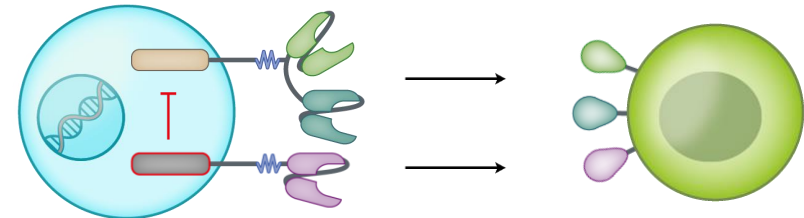
AML CANCER  
CELLS



EMCN ENGAGEMENT ENABLES  
PROTECTION OF HEALTHY HSCs

SENTI-202 CAR-  
NK CELL

HEALTHY  
HSC



*Protecting 10-20% of HSCs May Be Clinically Meaningful*

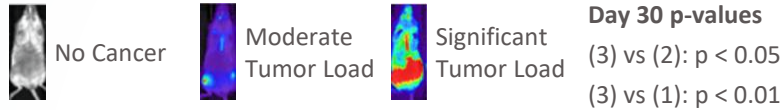
Activating CAR (aCAR) Tumor-Associated Antigens

Inhibitory CAR (iCAR) Safety Antigen

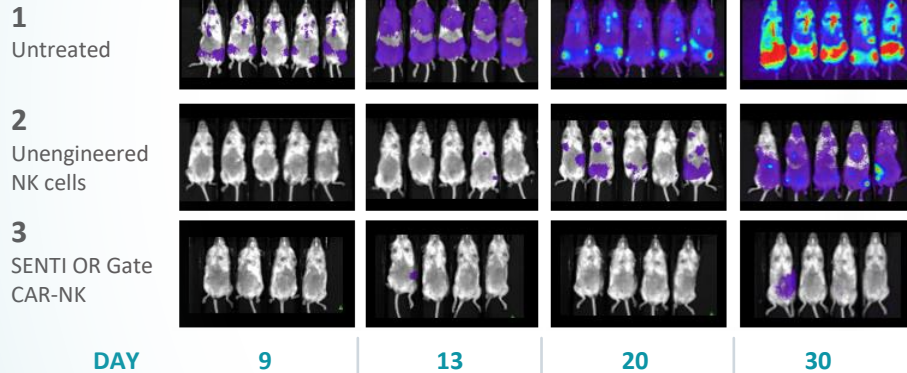
Antigen: CD33 FLT3 EMCN



# FLT3 OR CD33 CAR-NK Cells Significantly Suppressed Tumor Growth, Reduced Tumor Burden and Improved Survival

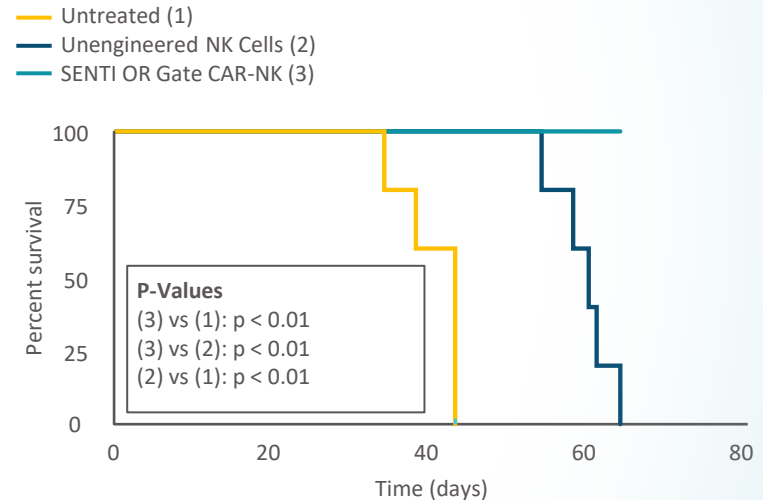


## Groups



**SENTI FLT3 OR CD33 CAR-NK cells achieved statistically significantly greater anti-tumor activity compared to untreated control mice ( $p < 0.01$ ) and mice treated with unengineered NK cells ( $p < 0.05$ )**

## MV4-11-BASED AML XENOTRANSPLANTATION MODEL

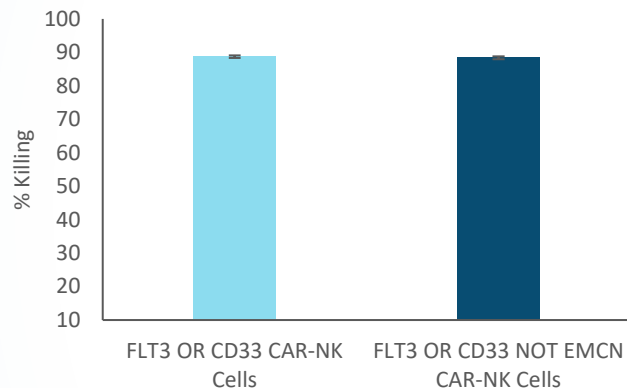


**FLT3 OR CD33 CAR-NK cells significantly suppressed tumor growth and increased survival**

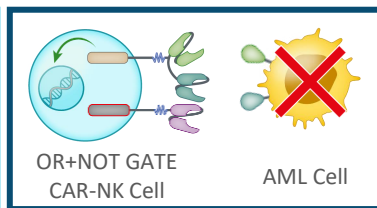
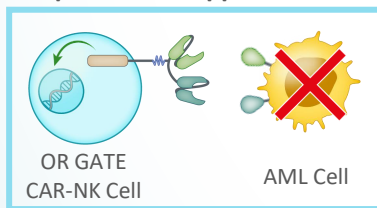


# SENTI-202 Product Candidate Protects Primary Donor HSCs While Maintaining On-Target Killing of Cancer Cells

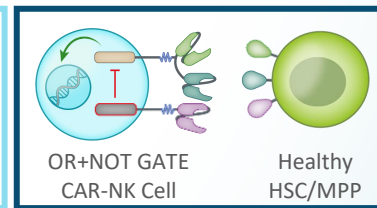
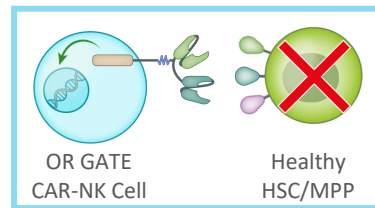
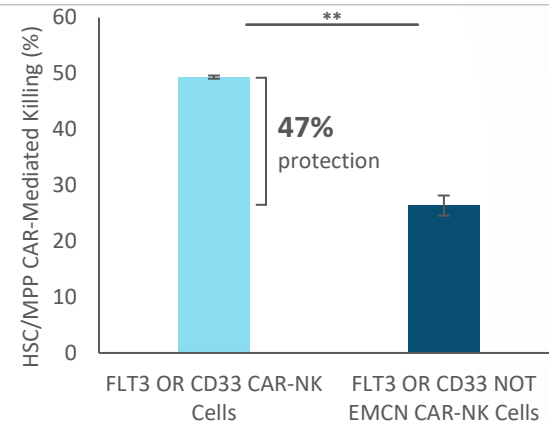
## EMCN NOT-GATE CAR-NK CELLS EFFECTIVELY KILL AML CANCER CELLS



### Experimental Approach:



## EMCN NOT-GATE CAR-NK CELLS PROTECT HEALTHY HSCs/MPPs



We believe that **protecting 10-20%** of Healthy HSCs is clinically meaningful.



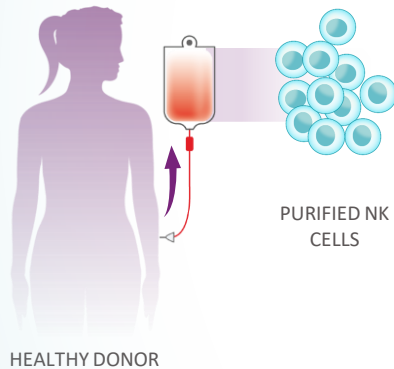
# Senti's Allogeneic Manufacturing Designed to Enable Widespread Distribution

Senti Anticipates Scalable ~21 Day Process to Manufacture NK Cell Product

With Off-the-Shelf Availability for Patients

1

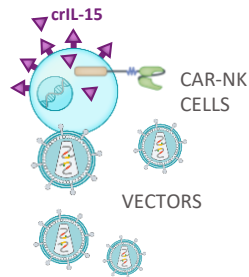
Starting Cells



High purity and functional NK cells isolated from peripheral blood

2

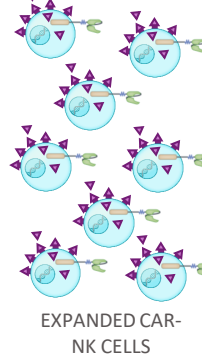
Gene Modification



Vectors optimized for NK cell transduction

3

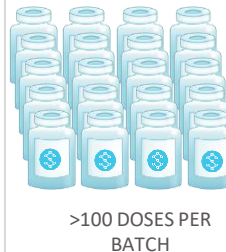
Expansion



Proprietary expansion and cryopreservation process for >100 doses per batch and high post-thaw potency

4

Freezing & Distribution



5

Prescription

Patient receives prescription

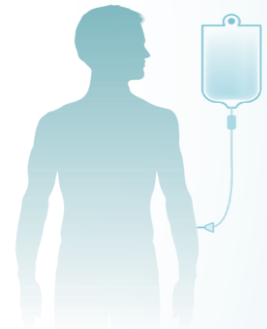


Product arrives and is thawed at clinic

Patient requests a prescription from physician

6

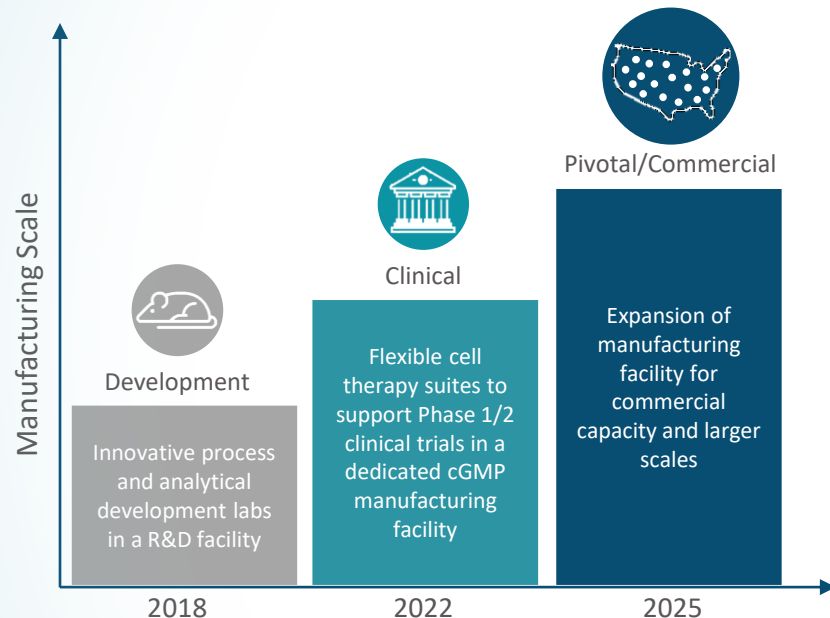
Infusion



Patient receives "Off-the-shelf" infusion at a clinical site



# Strategy to Build, Control, and Scale In-House GMP Allogeneic Cell Manufacturing



## Key Takeaways

- Senti plans to operate in-house facilities and develop proprietary processes for manufacturing and testing of CAR-NK cell therapies
- Industry-leading contract manufacturing and testing partners leveraged for standardized components

Clinical / Pivotal / Commercial



GMP manufacturing, product testing, and storage (~92,000 sf) - Alameda, CA

Development



Multi-modal preclinical research labs (~40,000 sf) - South San Francisco, CA





# 2021 Progress Sets The Stage For Upcoming Value Driving Milestones

## 2021 Achievements

### Data readouts:

- ☒ Presented pre-clinical POC data at AACR, demonstrating proprietary antigen discovery platform and NOT Logic Gate functionality
- ☒ Presented preclinical data at ASGCT for SENTI-202 and SENTI-301
  - SENTI-202: Demonstrated AML antigen-specific OR Gate and NOT Gate efficacies
  - SENTI-301: Demonstrated use of Regulator Dial gene circuit for *in vivo* control of IL-12 expression

### Manufacturing:

- ☒ ISCT and CAR-TCR Summit presentations demonstrating a GMP relevant allogeneic CAR-NK process

### Business development and financial:

- ☒ Signed collaborations with Spark and BlueRock
- ☒ Raised \$105mm Series B round

## Anticipated 2022 Milestones

- ☐ Present SENTI-301 and SENTI-202 IND-enabling pharmacological data at key scientific conferences (AACR, ASGCT, SITC or equivalent)
- ☐ Pre-IND meetings for SENTI-301 and SENTI-202
- ☐ Apply for Orphan Drug Designation for SENTI-301 and SENTI-202
- ☐ Initiate preclinical work on additional CAR-NK pipeline programs
- ☐ Complete first stage of construction for clinical-scale GMP facility
- ☐ Present clinical-scale GMP manufacturing process for gene-circuit-engineered NK cells at key technical conferences

## Anticipated 2023 Milestones

- ☐ File INDs for SENTI-301 and SENTI-202
- ☐ Present SENTI-401 IND-enabling pharmacological data at key scientific conferences (AACR, ASGCT, SITC or equivalent)
- ☐ Pre-IND meeting for SENTI-401
- ☐ Pre-clinical POCs for additional pipeline candidates
- ☐ Present further platform validating data in gene therapy

## Anticipated 2024+

- ☐ Approximately one IND per year



**SENTI BIO**

**Thank you**