SENTI BIO™

Engineering the Future of Cell and Gene Therapies

Corporate Presentation

May 2024

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Investment Highlights and Upcoming Clinical Catalysts

2024 Accomplishments

SENTI-202 for AML

- ✓ First patient dosed in 2Q 2024

Anticipated Clinical Catalysts

SENTI-202 for AML

- Initial clinical data expected by year-end 2024
- Durability data expected in 2025

SENTI-301A for HCC (Liver Cancer)

- First patient dosing in China expected in 2Q 2024

Central challenge in oncology:

Current therapies cannot precisely distinguish cancer vs healthy cells

Reduced therapeutic potential:

Lack of specificity leads to limited efficacy, relapse and safety issues

Senti's Approach:

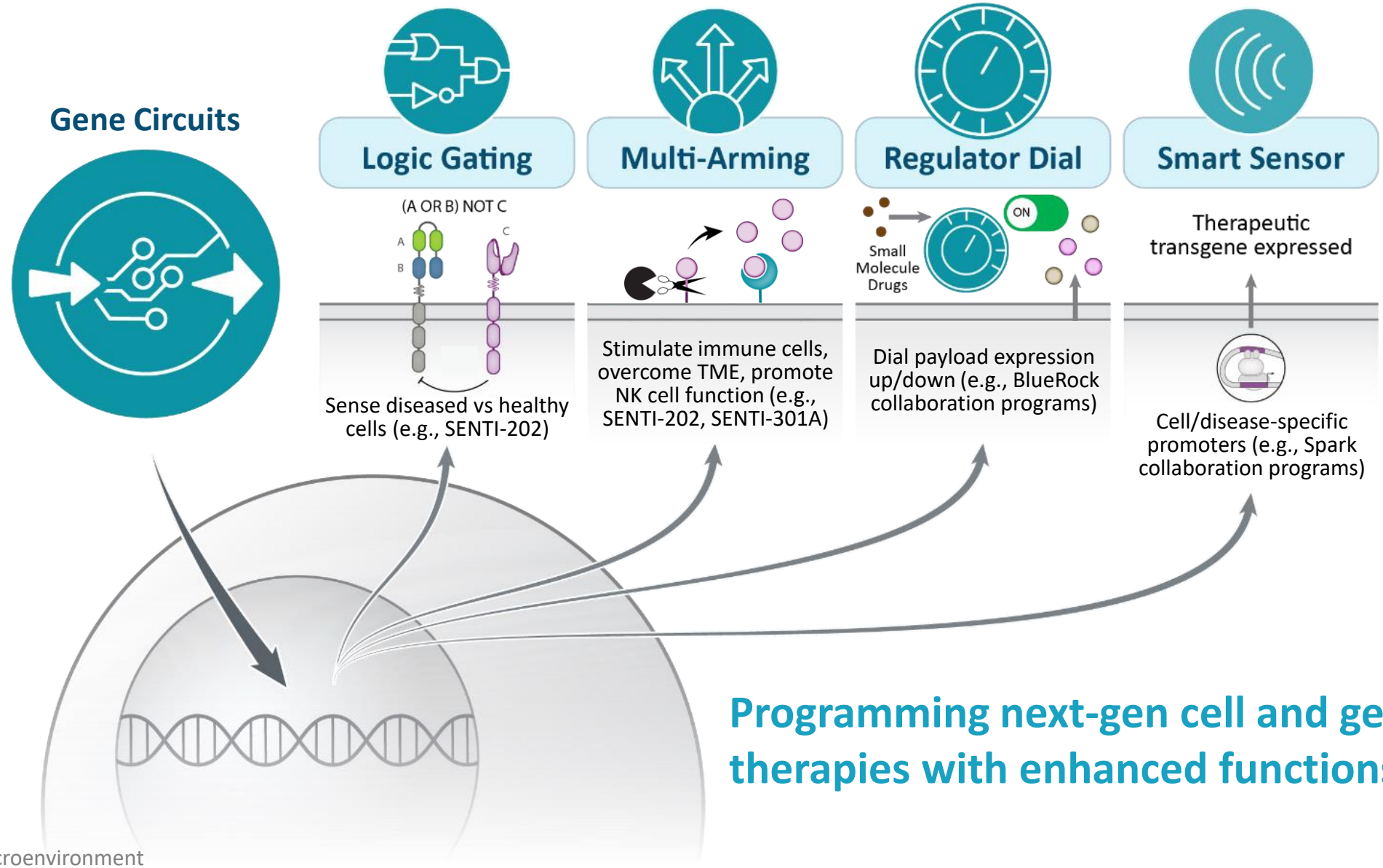
Senti's lead program, SENTI-202, utilizes proprietary Logic Gating technology designed to overcome AML disease heterogeneity by targeting LSCs while sparing healthy cells

Broad Applicability:

Potential to address a wide range of opportunities in oncology

AML: Acute Myeloid Leukemia; LSCs: Leukemic Stem Cells

Gene Circuits Could Enhance Precision, Control, and Activity of Cell & Gene Therapies



Programming next-gen cell and gene therapies with enhanced functions

TME: tumor microenvironment

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

Program	Target/Disease Candidate	Preclinical	Early Stage Clinical	Late Stage Clinical	Collaborator
SENTI-202	AML, MDS and other blood cancers		Initial clinical data expected by YE 2024		
SENTI-301A	HCC and other solid tumors		Enrollment of first patient expected in 2Q 2024		CELEST 晟临生物
Multiple Gene Therapy Programs	Eye, CNS and liver diseases				Spark Therapeutics; Roche
Multiple iPSC Cell Therapy Programs	Regenerative medicine				BlueRock Therapeutics; Bayer

HCC: Hepatocellular carcinoma; CNS: Central nervous system

Industry-Leading Management With Top-Tier Board and Scientific Advisors

Executive Team

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CEO & Co-Founder

Yvonne Li
Interim CFO and Treasurer

Kanya Rajangam, MD, PhD
Head of R&D and CMO

Scientific Advisors

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Scientific Co-Founder, MIT

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MD Anderson Cancer Center

Lawrence Fong, PhD
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Michael Kalos, PhD
Arsenal, Janssen, Lilly

Robin Taylor, PhD, MBA
SeaGen, Genentech

Wilson Wong, PhD
Scientific Co-Founder, Boston University

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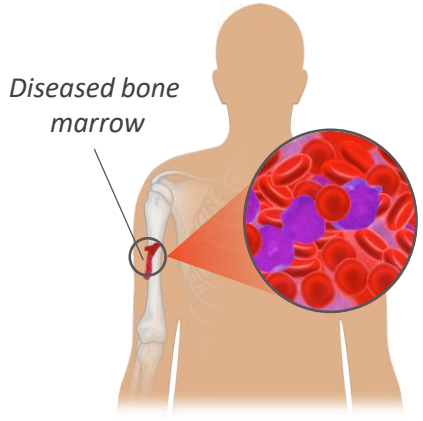
SENTI-202

Limited Standard of Care Options for R/R AML

R/R AML patient outcome



Median survival of 5.3 months[1]

5-year survival rate is 12.6%[1]

Major treatment challenges:

1. Disease heterogeneity
2. Durability of response
3. Healthy cell toxicity
4. Treatment tolerability

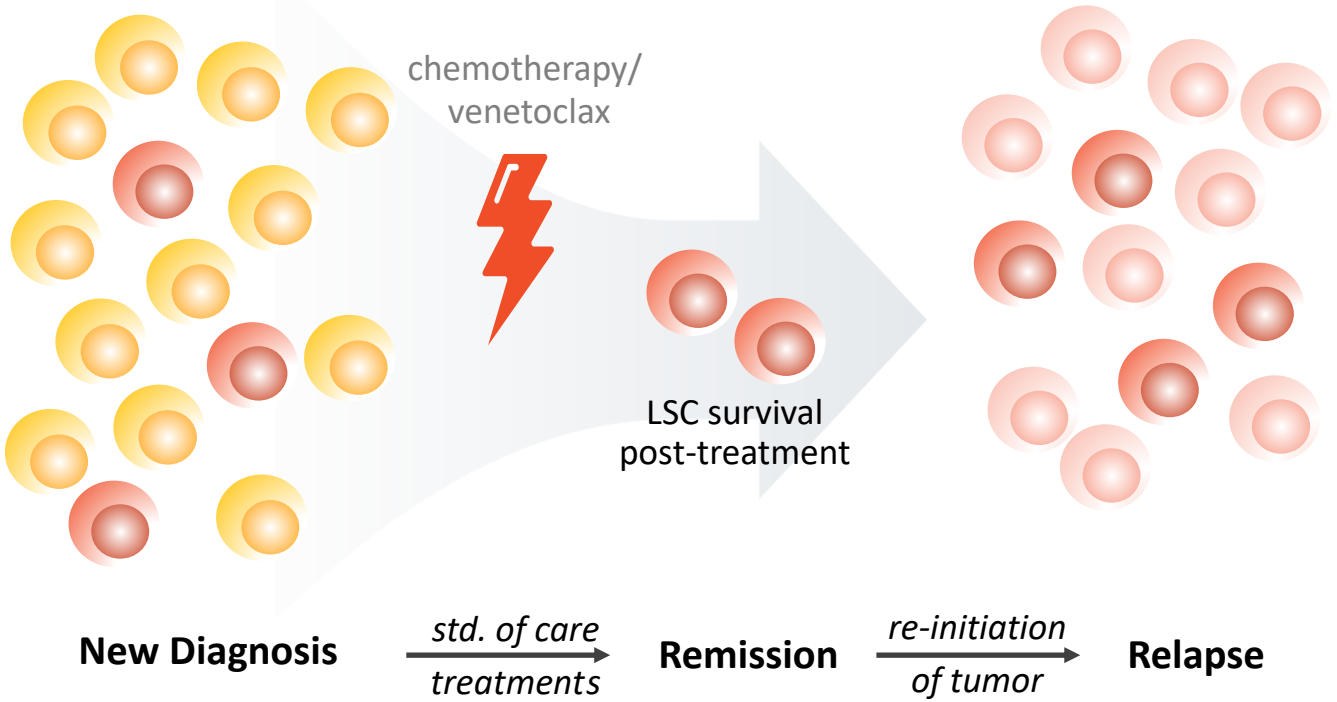
AML has the worst relapse rate of any blood cancer

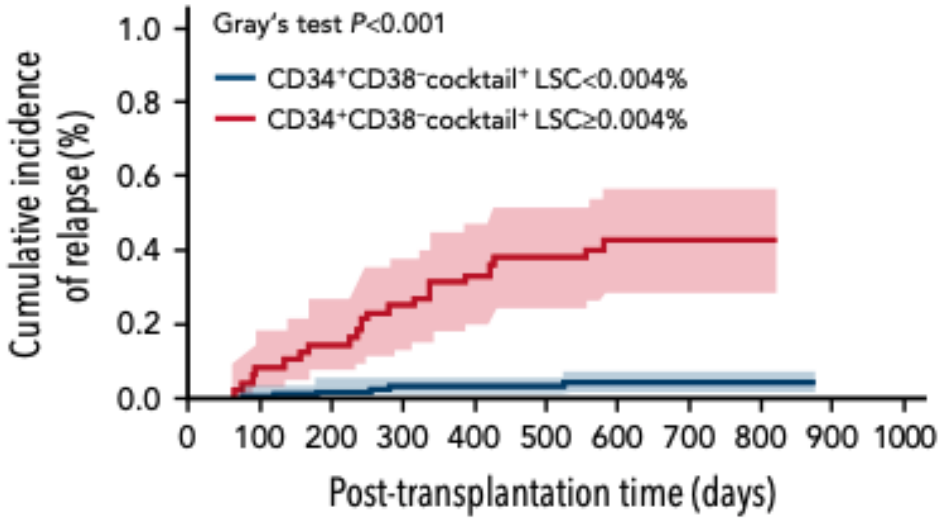
- 50%–70% of patients who obtain complete response (CR) eventually relapse[2]
- 21-32% CR/CRh rate with approved treatments for CD33+ AML, FLT3 and IDH1/2 mutated AML
  - No SOC after progression on mutationally targeted disease
- Allogeneic Hematopoietic Stem Cell Transplant (HSCT) is the only curative option but is limited to younger/ fit patients
- Presence of residual LSCs after treatment correlates with poorer prognosis and increased likelihood of relapse[3]
  - Residual LSCs contribute to worse prognosis and higher likelihood of relapse after treatment
  - Rare population that have markers similar to HSC; built in off-tumor on-target protection is key to effectively targeting LSCs

R/R: relapsed or refractory
CRh: complete remission with partial hematologic recovery; SOC: standard of care
[1] Brandwein AJBR 2020; [2] Heuser Annals of Oncology 2020; [3] Zeijlemaker Leukemia 2019

Targeting AML LSCs May Be Essential for Increased Durability and Longer Remissions

Etiopathology



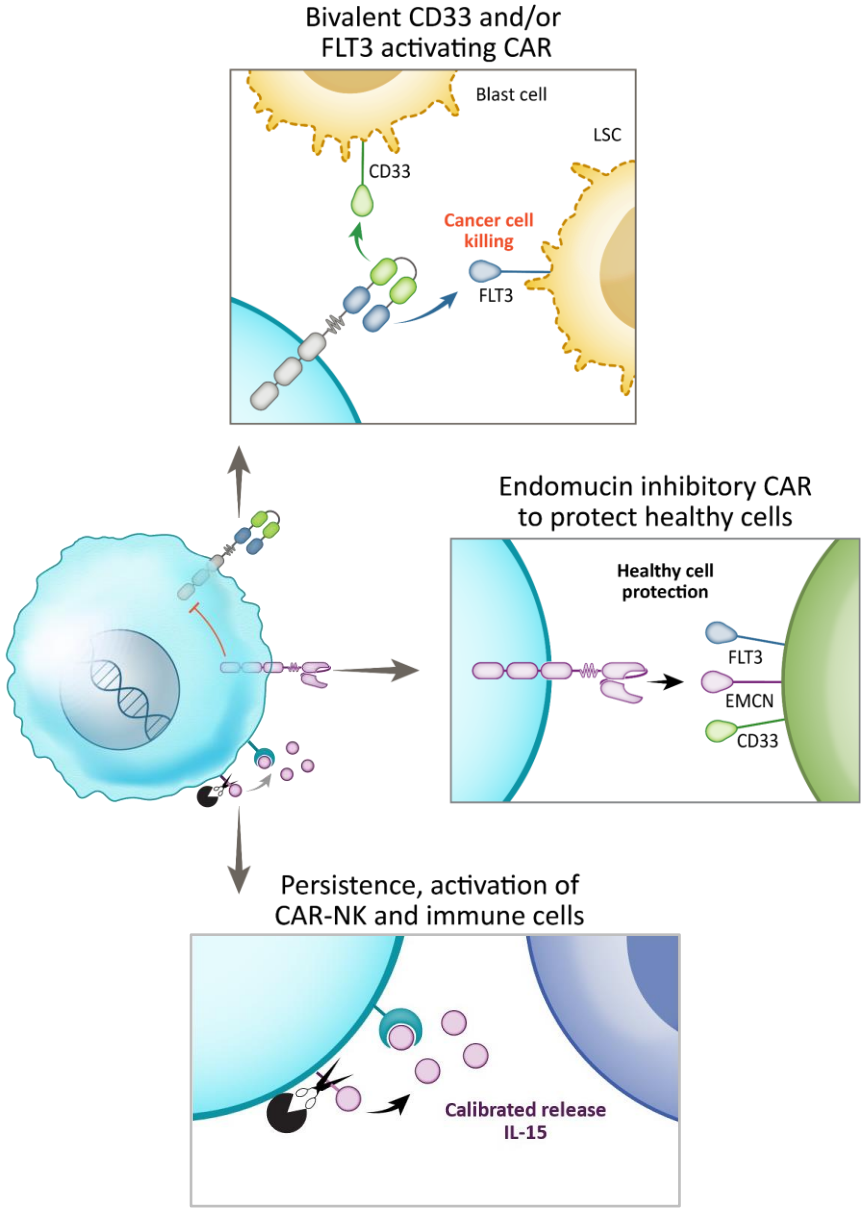


Relapses after initial successful treatment are thought to originate from the outgrowth of persistent LSCs[1]

- **Relapse correlates with LSC frequency[2]**
- **No available therapies specifically target LSCs**

[1] Zeijlemaker Leukemia 2019; Arnone Cancers 2020; van Gils Frontiers in Oncology 2021; Li Blood 2022; Hanekamp BJH 2020; Stelmach Haematologica 2023; [2] Li Blood 2022

SENTI-202 Is a First-In-Class Selective Off-the-Shelf Investigational Cell Therapy for Blood Cancers



Activating CAR – "kill" signal

- Bivalent CD33 and/or FLT3
- Potential for deep and durable responses in AML and other blood cancers

Inhibitory CAR – "protect" signal

- Inhibition by endomucin (EMCN) protective antigen
- EMCN selectively expressed on healthy hematopoietic stem cells (HSCs) for potentially improved safety and increased therapeutic window

Calibrated release IL-15

- Cell expansion, persistence, and tumor killing

Initial clinical data expected by year-end 2024
Durability data expected in 2025

SENTI-202 is Designed to Address AML Heterogeneity Which Contributes to Disease Relapse/Refractoriness

Treatment Challenges

1 Disease heterogeneity

AML cells have many antigen targets that are not uniformly expressed on all cancer cells

2 Durability of response

Limited durability from tumor escape, incomplete clearance of both leukemic blasts and LSCs

Other CAR-based therapies target a single AML antigen leading to tumor escape and eventual relapse[1]

CD33 allogeneic CAR-NK cell therapy: 60% CR rate as of 11/2022 (previously 80% on 6/2022)[2]

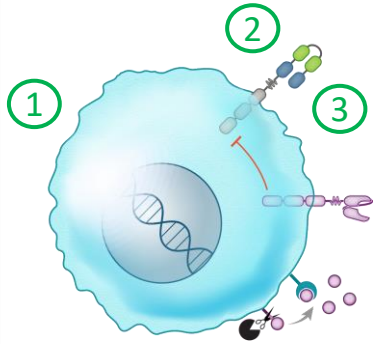
Targeting CD33 largely addresses blast cells and misses LSCs, leading to disease evasion and relapse

NKG2D allogeneic CAR-NK cell therapy: 22-67% CR/CRi rate and a short durability of <4 mo[3]

Leukemic stem cells downregulate NKG2D ligands leading to poor response durability[1]

Senti's Solution

SENTI-202 incorporates three key killing mechanisms to overcome AML heterogeneity with potential for deeper and longer remissions



Cancer killing mechanisms:

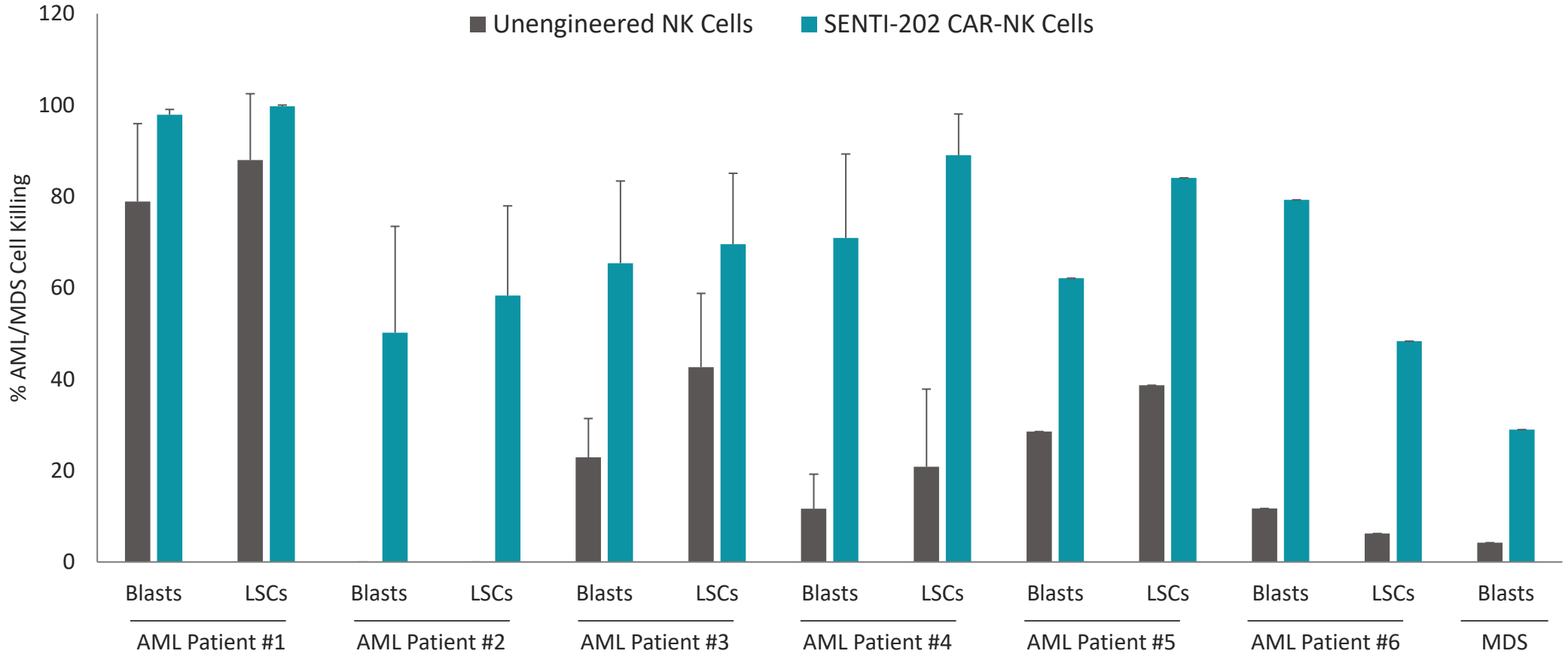
1. **NK cells innately kill cancer cells**
2. **CD33 CAR targets AML blasts**
3. **FLT3 CAR targets AML LSCs**

- Targeting FLT3 and CD33 addresses ~95% of AML patients
- **SENTI-202 is the only CAR-NK program utilizing the OR Logic Gate to target both CD33 and/or FLT3 for AML**

CRi: complete response with incomplete blood recovery

[1] Paczulla Nature 2019; [2] Huang Journal of Hematology & Oncology 2023; [3] Third-party data

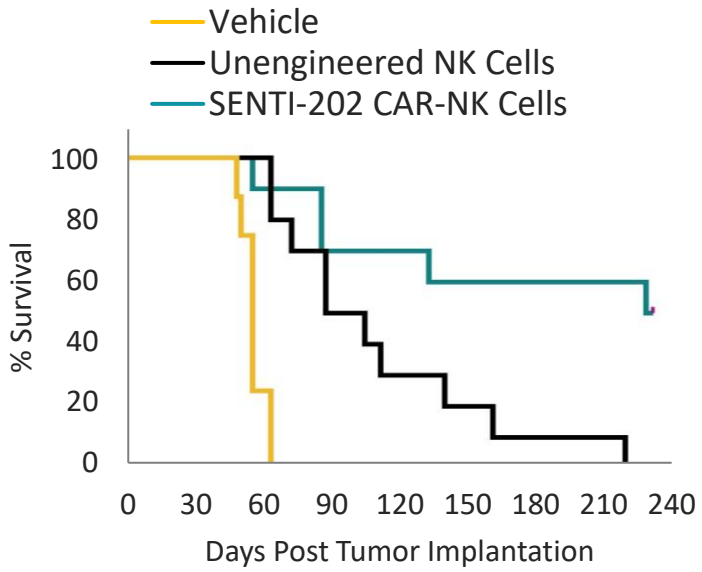
SENTI-202 Has Shown Robust Preclinical *In Vitro* Cancer Killing Against Patient Samples

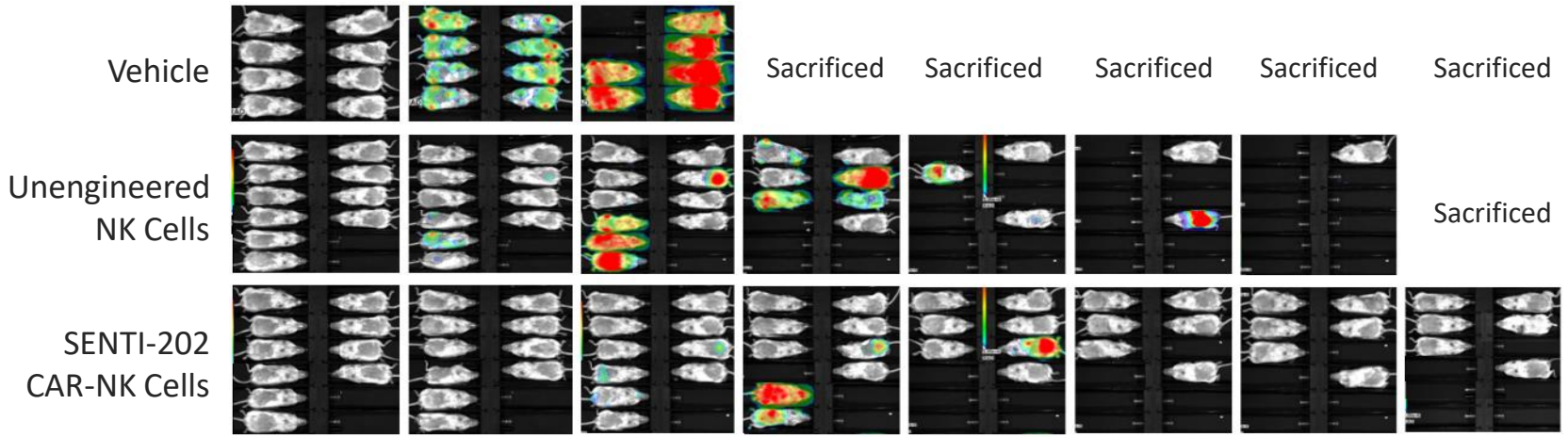


Broad *in vitro* killing of primary CD33+ and/or FLT3+[1] AML and MDS tumor cells compared to unengineered NK cells

[1] Both FLT3 wild-type and mutated AML patient samples

SENTI-202 Has Shown Robust Preclinical *In Vivo* Cancer Killing Activity





Group	Vehicle	Unengineered NK Cells	SENTI-202 CAR-NK Cells
Median Survival (Days)	*56*	*97*	*230*

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

SENTI-202 is Designed to Address the Lack of Clean AML Targets to Improve Selectivity

Treatment Challenges

3 Healthy cell toxicity

Many AML therapies kill cancer cells and HSCs because target antigens are expressed on both

4 Treatment tolerability

Killing of healthy HSCs leads to prolonged aplasia and myelosuppression

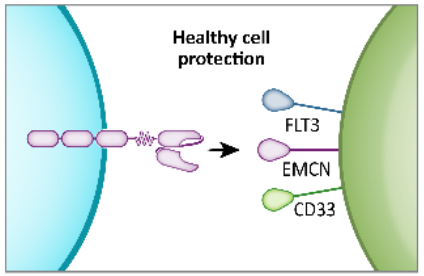
Other CAR-based therapies targeting AML antigens kill healthy cells, leading to adverse events and tolerability issues

Antigen expression on cells[1]			
Antigen	**LSCs**	**Blasts**	**HSCs**
CD33	+/-	+	+/-
FLT3	+	+/-	+
CLL-1	+/-	+	-
CD123	+	+	+/-
CD38	-	+	-
NKG2DL	-	+	-

Senti's Solution

SENTI-202 incorporates an inhibitory CAR designed to protect healthy HSCs, even when expressing FLT3 or CD33

Endomucin inhibitory CAR to protect healthy cells

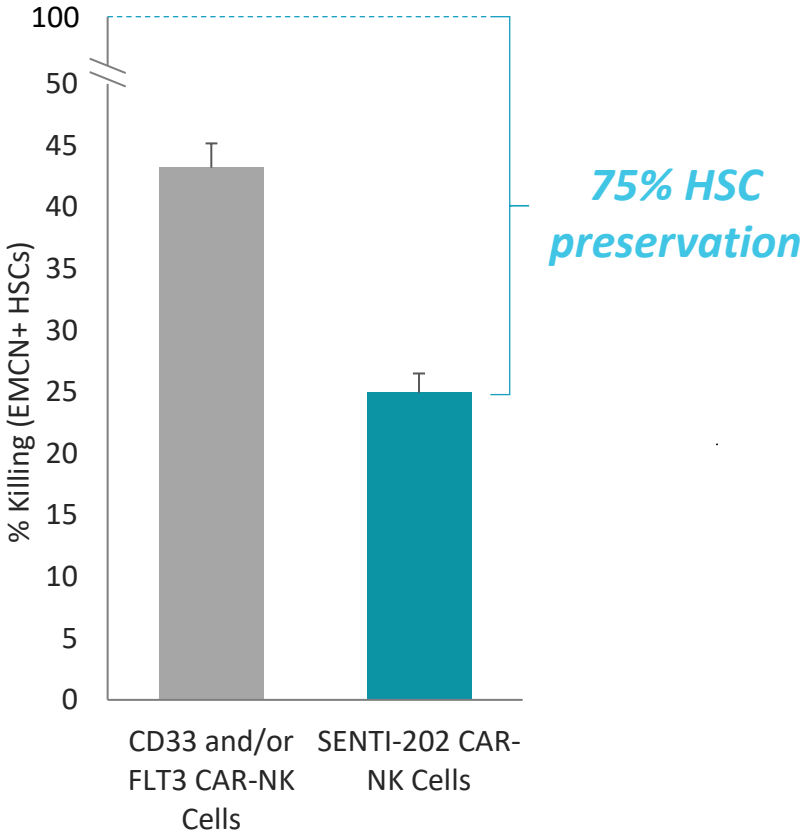


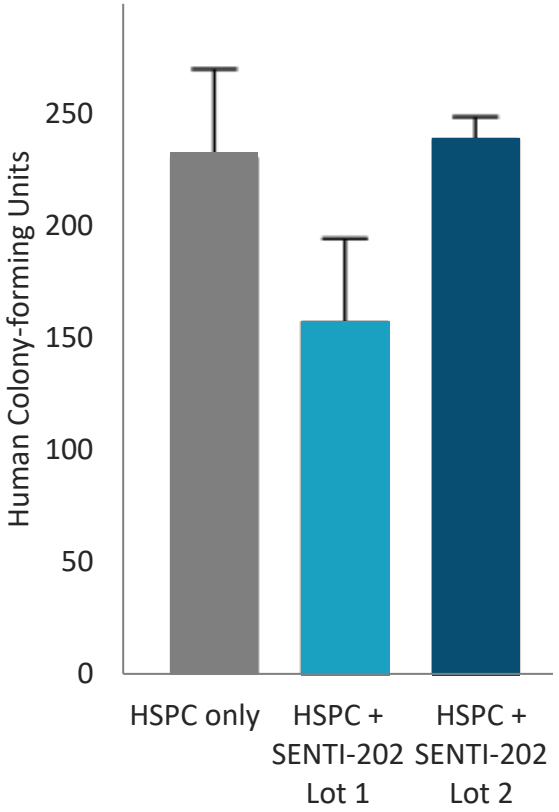
- EMCN was identified and validated as a protective antigen that is expressed on up to 76% of HSCs, but not on LSCs or blasts
- **SENTI-202 is the only known CAR-NK in development utilizing the NOT Logic Gate to protect healthy cells in AML**

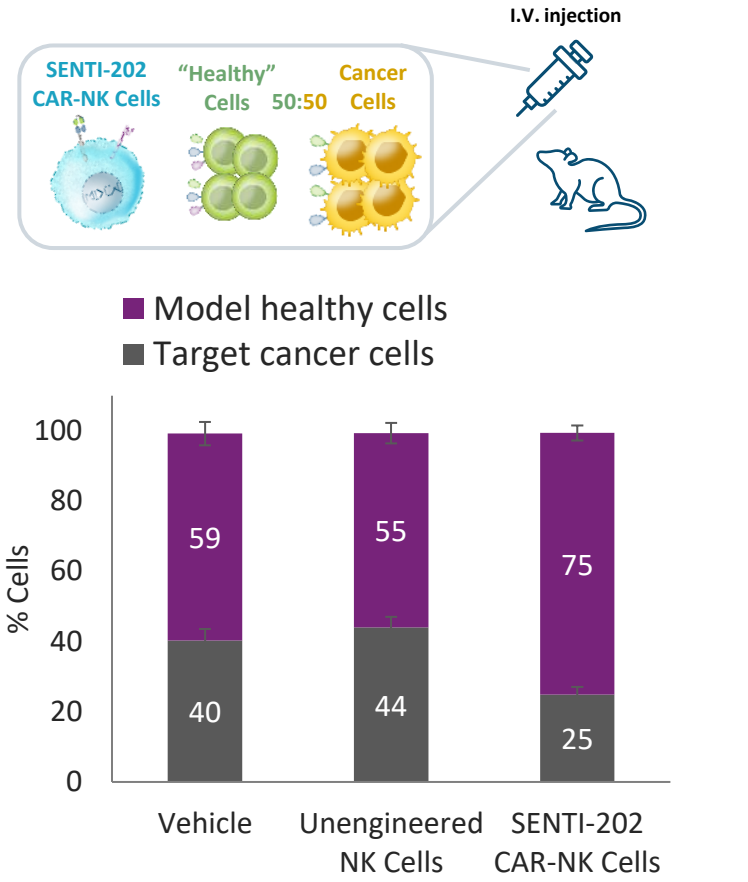
NKG2DL: NKG2D ligands

[1] Valent Stem Cell Translational Medicine 2020; Yoshimoto Blood 2009; Walter Blood 2012; Paczulla Nature 2019; Haubner Nature 2018; Pollyea Blood 2017

SENTI-202 Has Shown Strong Preclinical Selectivity and HSC Protection







In vitro protection of primary human HSCs expressing EMCN

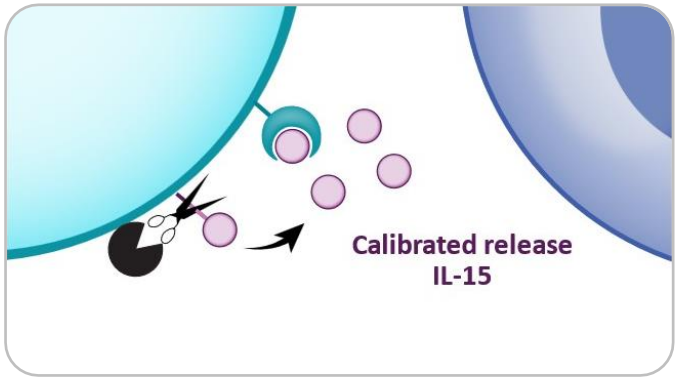
Preservation of colony forming activity of HSPCs

Killing target cancer cells and protecting model healthy cells

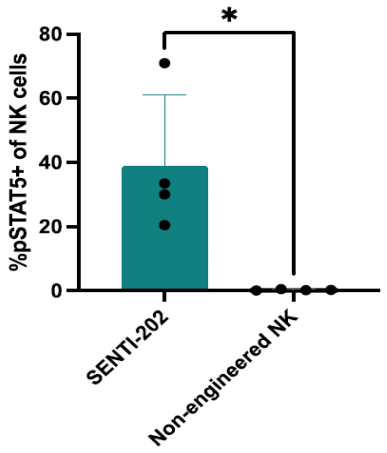
HSPCs: Hematopoietic Stem and Progenitor Cells

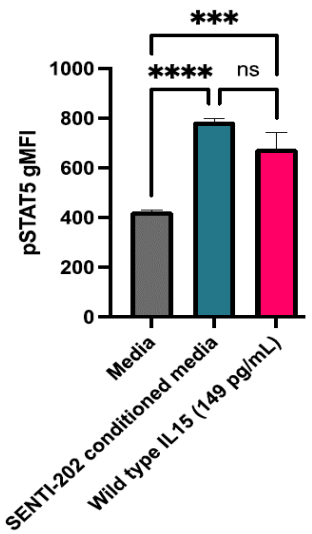
SENTI-202 Has Enhanced Proliferation and Persistence in Preclinical Studies and Can Activate Host Immune Cells

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

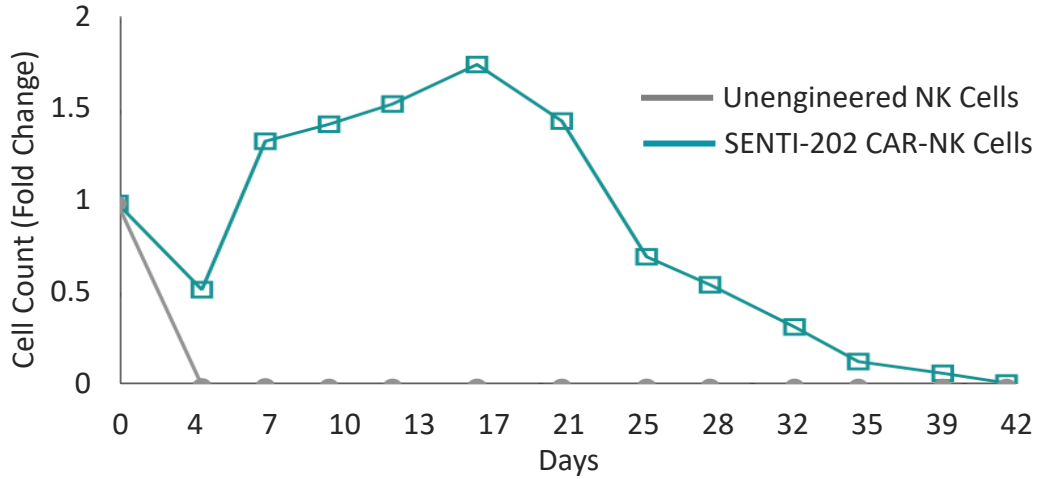


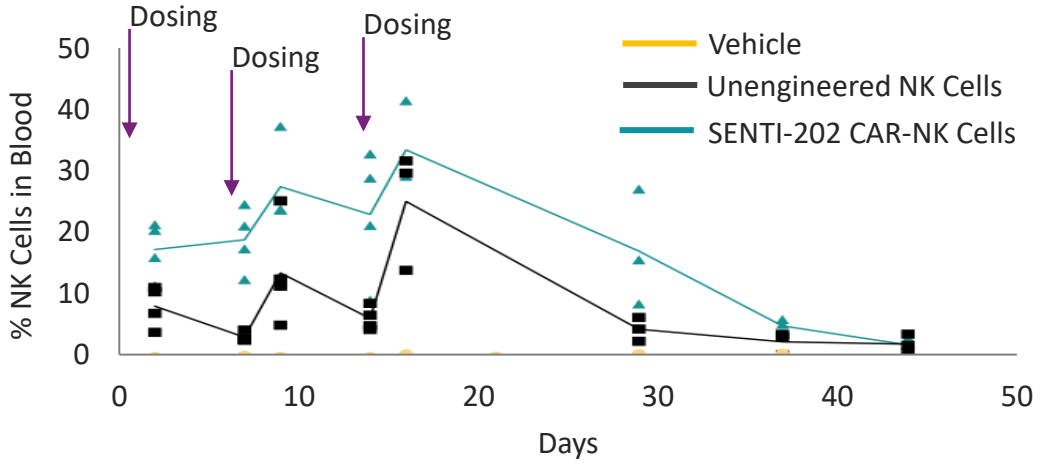
SENTI-202 demonstrated improved signaling in pSTAT5 assay





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





ns = not significant; *p < 0.05, *** p < 0.001, **** p < 0.0001

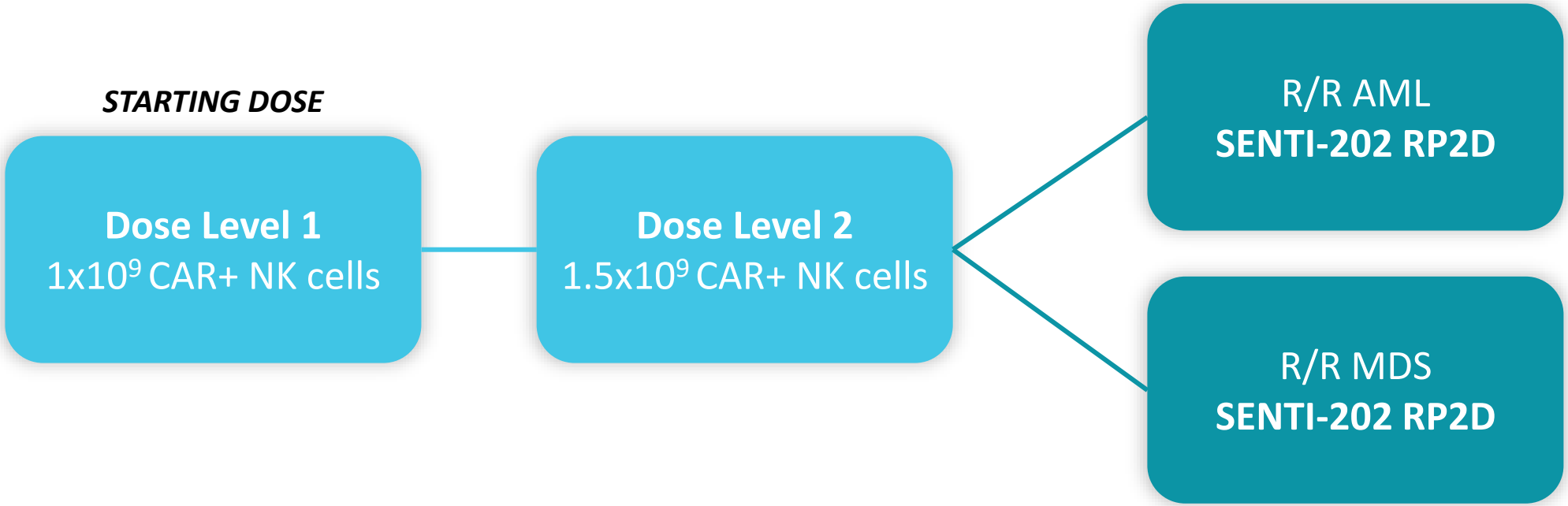
SENTI-202 Trial Design Incorporates Findings From Earlier CAR-NK Trials with Disease Specific Lymphodepletion, Multi-Dose and Multi-Cycles

Phase 1 Dose FINDING
"3+3" design

R/R CD33 or FLT3 expressing malignancies, focus on AML
Determine RP2D and assess frequency and types of safety events

Dose EXPANSION

Disease-specific expansion cohorts
AML and MDS



SENTI-202 Phase 1 Trial Design

Patient Population

- Adult patients
- R/R CD33 and/or FLT3 expressing heme malignancies
- 2 of 3 patients at each dose level with AML
- Received at least 1 prior treatment including targeted agents if FLT3, IDH1/2 mutation+

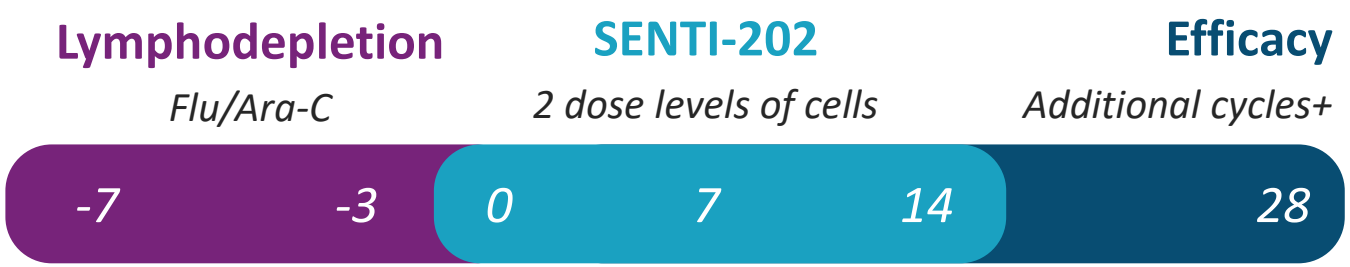
Study Design

- "3+3" study design
- Dose escalation followed by disease-specific expansion cohorts for AML and MDS
- Starting dose $1x10^9$ CAR+ NK cells and target dose $1.5x10^9$ CAR+ NK cells
- Plans to transition from Phase 1 to pivotal study

Planned Endpoints

- Safety, DLT, identify recommended Phase 2 dose
- Efficacy, including bone marrow recovery and MRD
- Pharmacokinetics (PK), pharmacodynamics (PD), biomarkers to supplement efficacy and immunogenicity

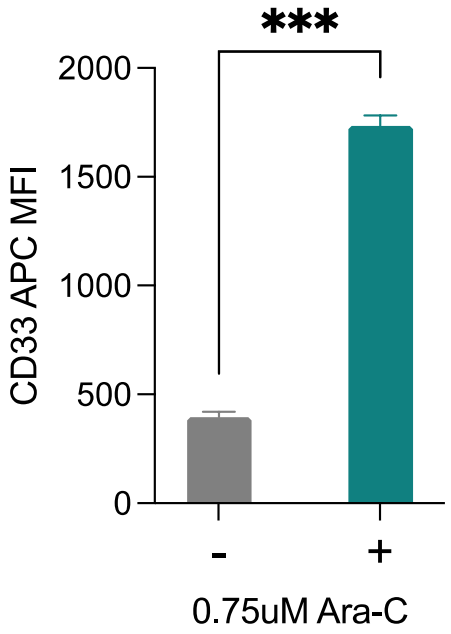
Multi-Dose & Multi-Cycle Dosing



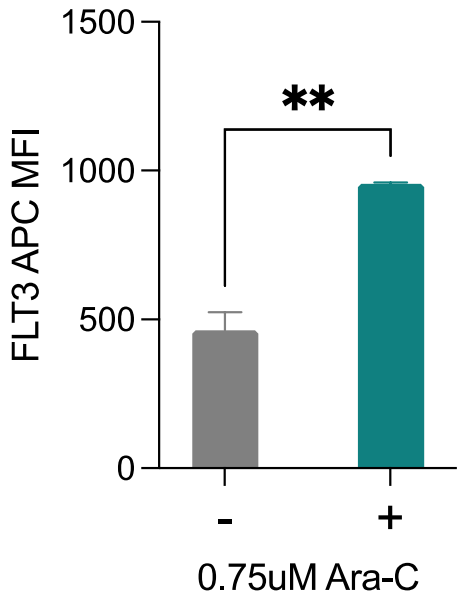
- ✓ Seamless Phase 1 to pivotal design
- ✓ Two initial dose levels
- ✓ Adaptive design with option to open IL2 cohort from emerging data

Ara-C Upregulated CD33 and FLT3 and Sensitized KG-1a Cells to SENTI-202

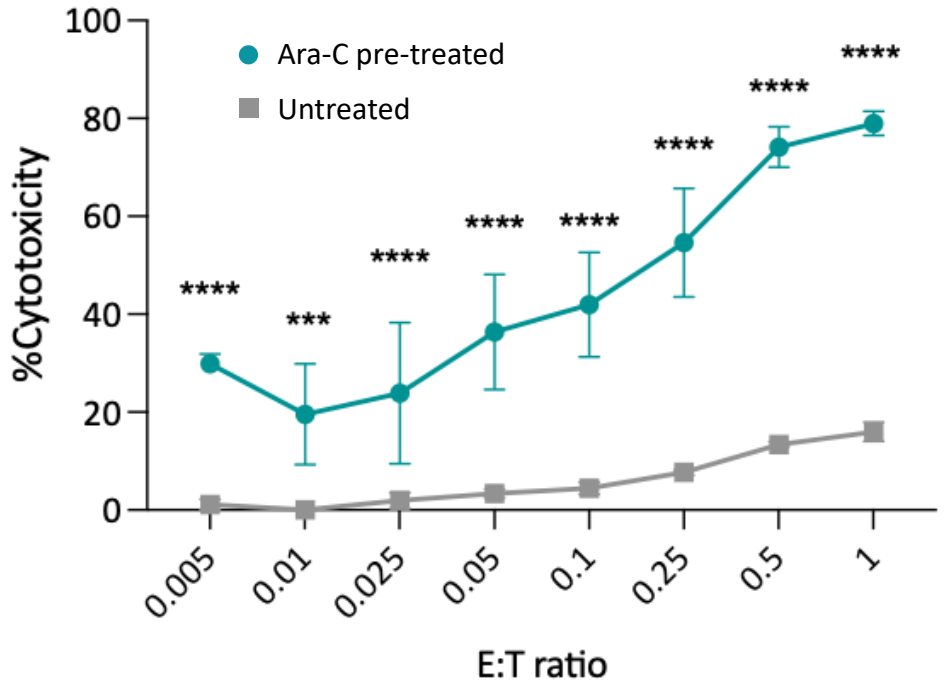
CD33 Expression



FLT3 Expression



Enhanced *In vitro* Cytotoxicity



- In the CD33 low/FLT3 low KG-1a cell line, 72h Ara-C treatment significantly upregulated CD33 and FLT3 MFI
- Ara-C pre-treated KG-1a cells are sensitized to SENTI-202-mediated cytotoxicity

APC: Allophycocyanin

SENTI-202 Mechanism of Action and Preclinical Data Could Result in Differentiated Clinical Profile

2024 Accomplishments

- ✓ First patient dosed in 2Q 2024

Clinical Catalysts

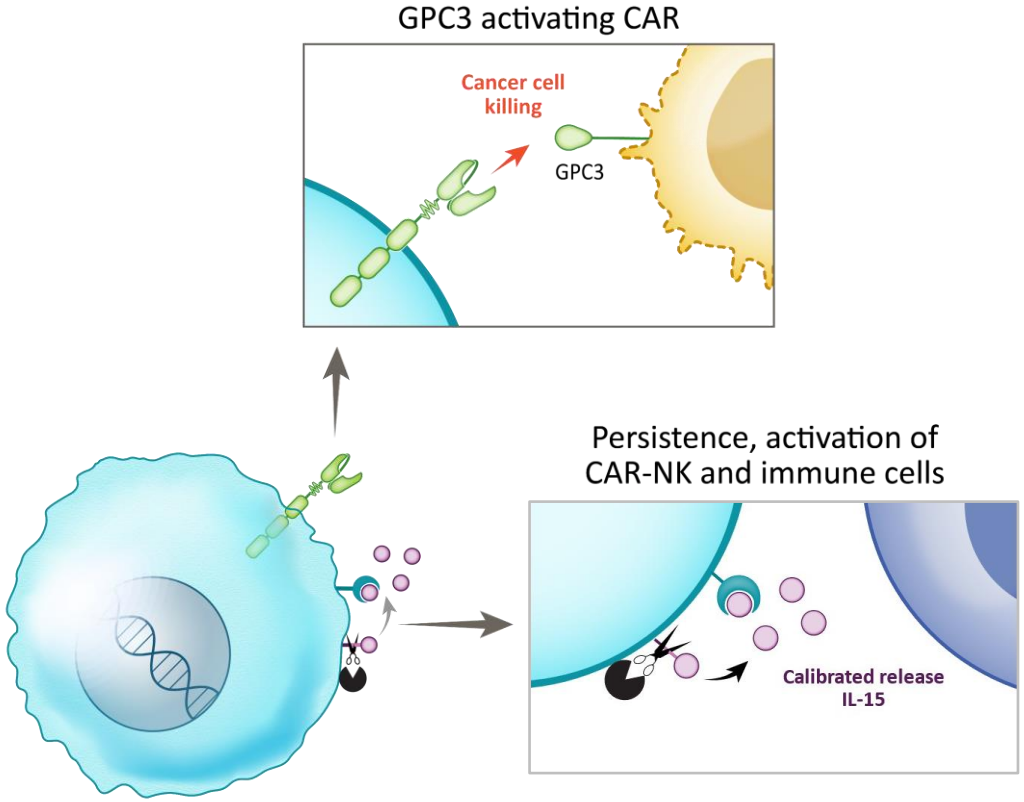
- ○ Initial clinical efficacy data expected by year-end 2024
- ○ Durability data expected in 2025

SENTI-202 was designed to integrate validated mechanisms together to solve key outstanding problems in AML

- Serial killing of LSCs and blasts *in vitro* and *in vivo*
- Pre-treatment with Ara-C sensitized CD33/FLT3 low AML
- Addition of EMCN shown to protect healthy hematopoietic stem cells
- crIL-15 engineered to increase persistence multiple times more compared to unengineered NK cells

SENTI-301A

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



Activating CAR – "kill" signal

- GPC3 for hepatocellular carcinoma (HCC) and other solid tumors

Calibrated release IL-15

- Potential for increased cell expansion, persistence, and tumor killing

Strategic collaboration with Celest Therapeutics for clinical development of SENTI-301A to treat solid tumors in China, starting with HCC

Collaboration with Celest Therapeutics to Develop SENTI-301A for HCC in China

Key Transaction Terms

- ✓ Up to $156 million in development milestones and potential tiered royalties post-commercialization
- ✓ Pilot trial to begin in mainland China with first patient dosing expected in 2Q 2024
- ✓ Potential to expand into Hong Kong, Macao, and Taiwan, with Senti retaining all commercialization rights outside of those regions and mainland China

Potential to expand into other regions with high prevalence of HCC

Dose-finding trial design, with two dose levels

9 initial patients with advanced GPC3 expressing liver cancer (HCC)

Pilot trial to include safety and efficacy endpoints

~400,000 new cases of liver cancer in China in 2020, which was ~65% of all liver cancer cases worldwide[1]

[1] Liu Cancers 2022

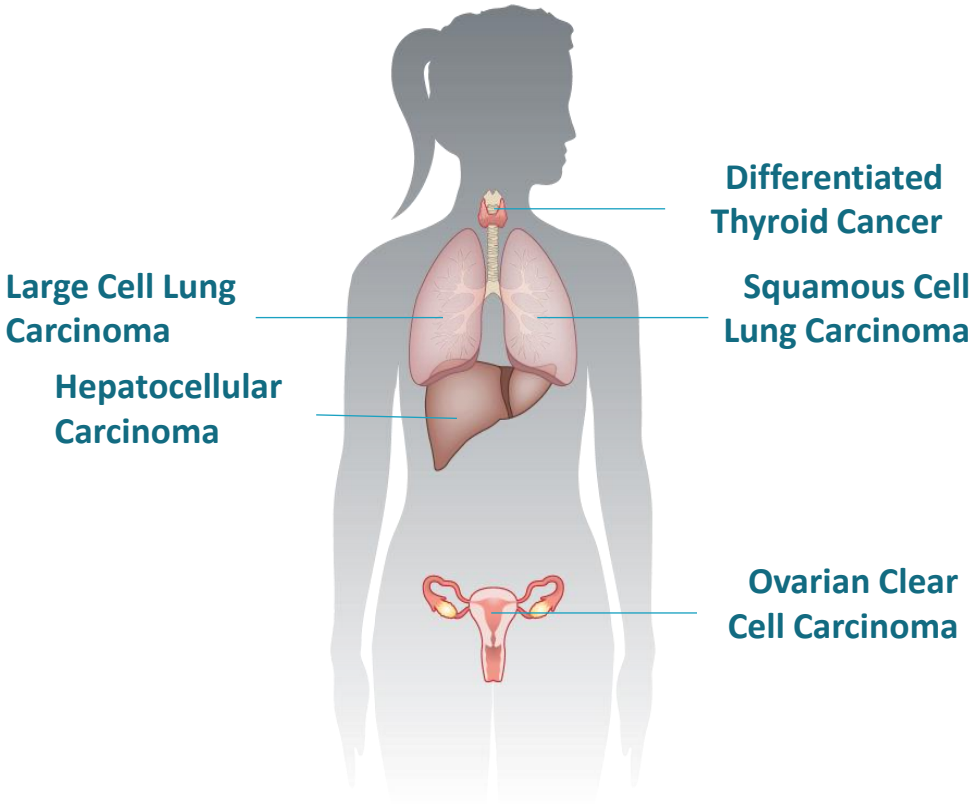
SENTI-301A Is Designed to Tackle GPC3+ Expressing Solid Tumors

GPC3 is expressed in multiple solid tumors

- HCC (70-90% GPC3+)[1] and other solid tumors – lung, ovarian, thyroid (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[2,3]**

SENTI-301A is designed to target GPC3+ tumors

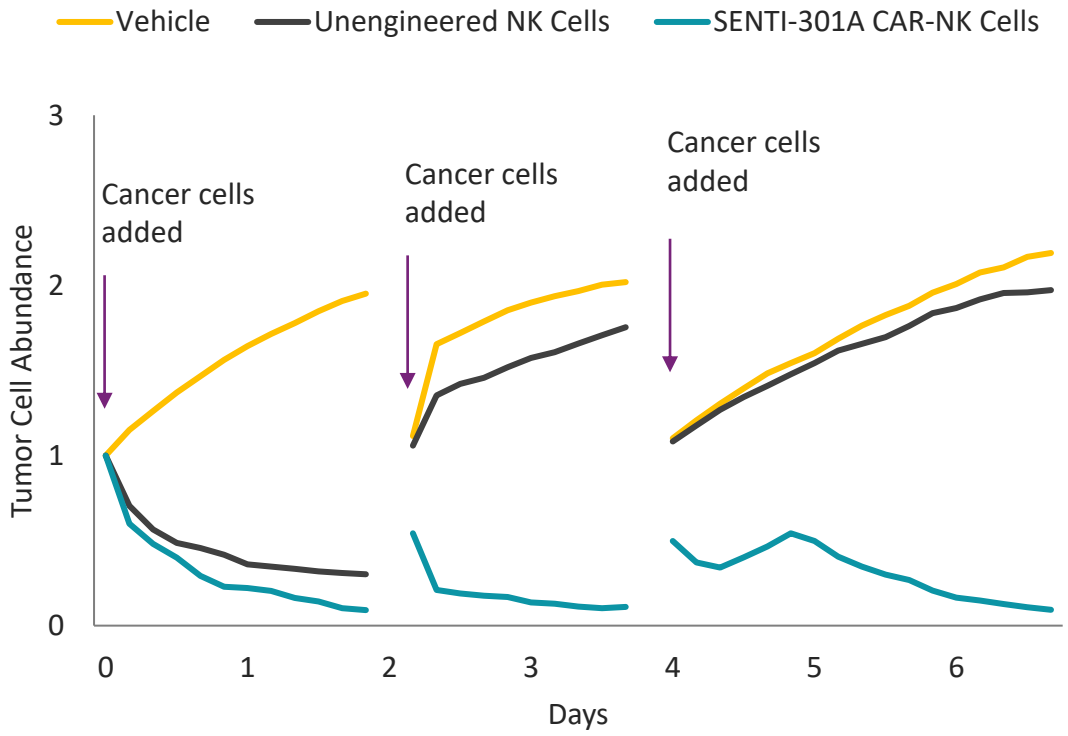
- Tackle multiple solid tumors with high GPC3 antigen expression via NKs multi-armed with GPC3 CAR and crIL-15

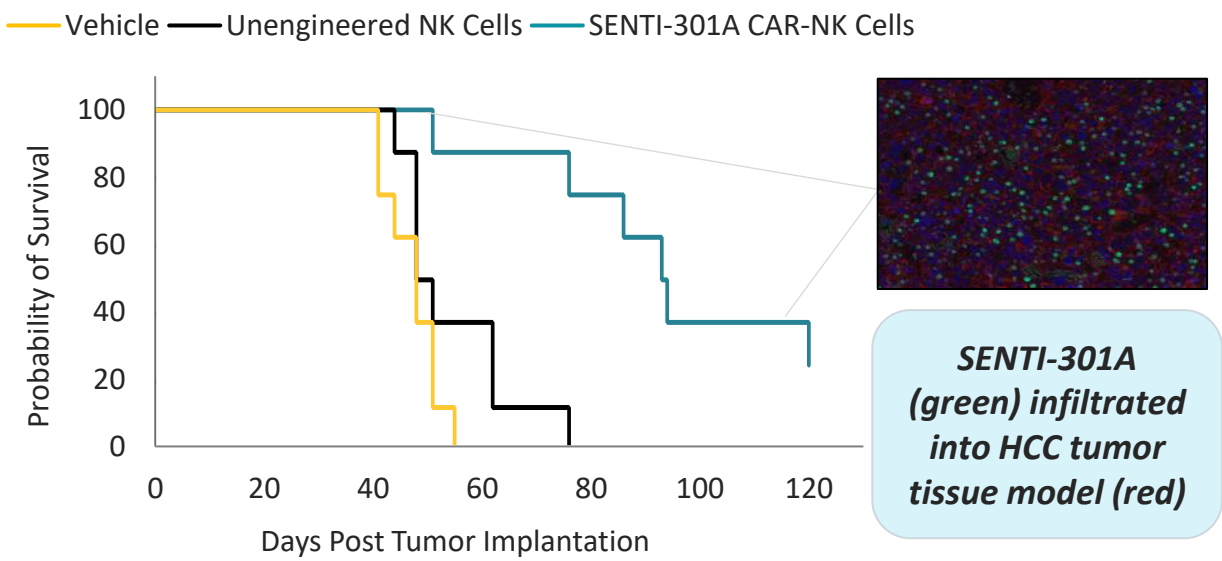


Common GPC3 expressing tumors

[1] Zheng Frontiers in Oncology 2022; [2] Moek American Journal of Pathology 2018; [3] Shi Clinical Cancer Research 2020

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





SENTI-301A (green) infiltrated into HCC tumor tissue model (red)

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

In vitro serial killing of HepG2 cell line observed

Increased survival, tumor infiltration and response in HepG2 mouse model

Planned Early Exploratory Clinical Study Design of SENTI-301A

Patient Population

- Adult patients
- Advanced GPC3-positive Hepatocellular Carcinoma
- Unresectable stage B or C (per BCLC)
- Failed at least 1 prior line, including PD1/L1 & TKIs

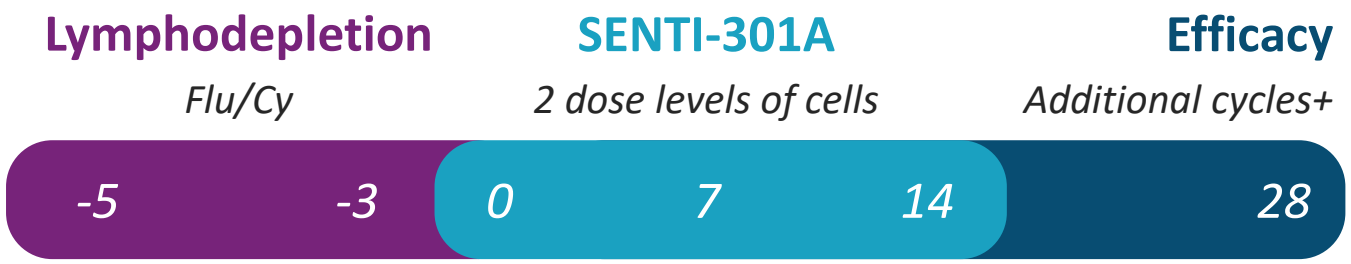
Study Design

- "3+3" study design
- Dose escalation followed by expansion cohort
- Starting dose $1x10^9$ CAR+ NK cells and target dose $1.5x10^9$ CAR+ NK cells
- Opportunity to transition to US clinical study

Planned Endpoints

- Safety, DLT, recommended Phase 2 dose
- Efficacy, using RECIST v1.1, mRECIST & iRECIST criteria
- Pharmacokinetics (PK), pharmacodynamics (PD), biomarkers to supplement efficacy and immunogenicity

Multi-Dose & Multi-Cycle Dosing



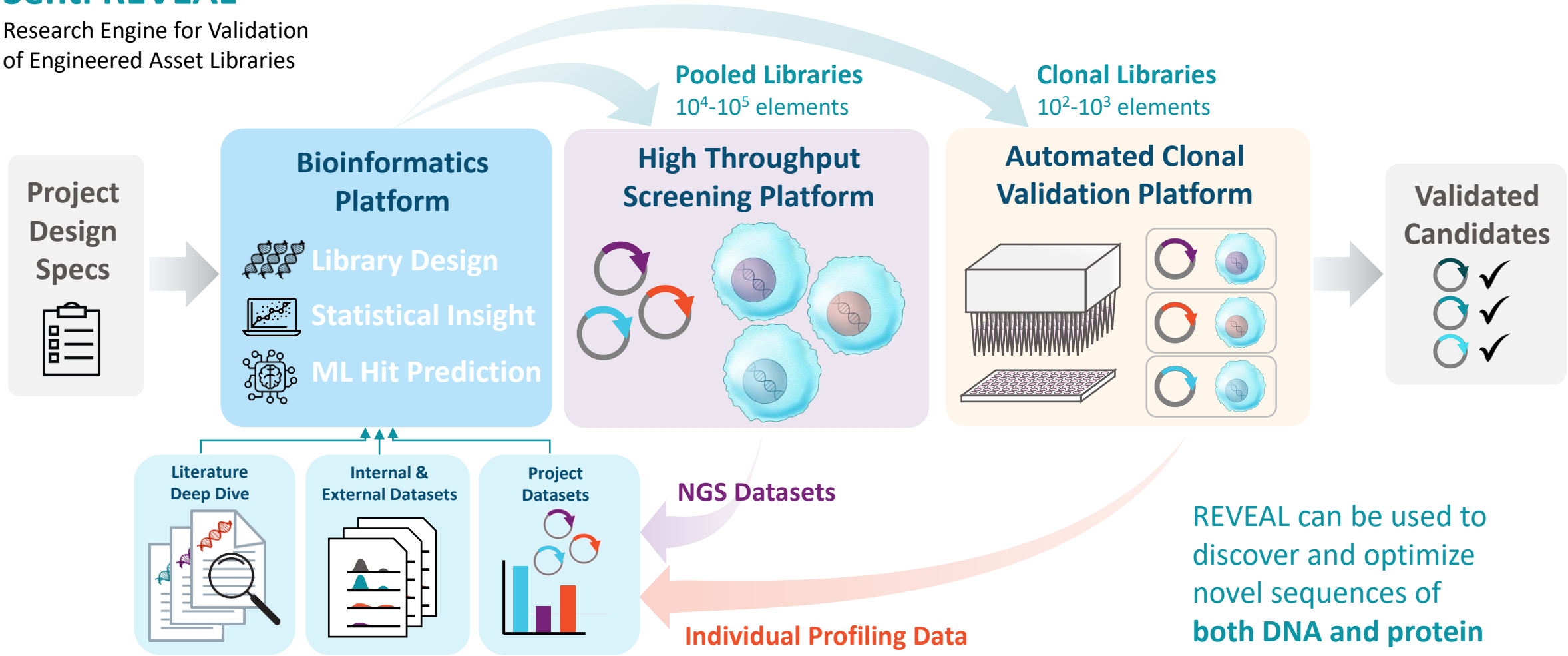
First patient dosing in China expected in 2Q 2024

Platform

Senti's Discovery and Optimization Engine For Novel DNA and Protein Assets

Senti REVEAL™

Research Engine for Validation of Engineered Asset Libraries



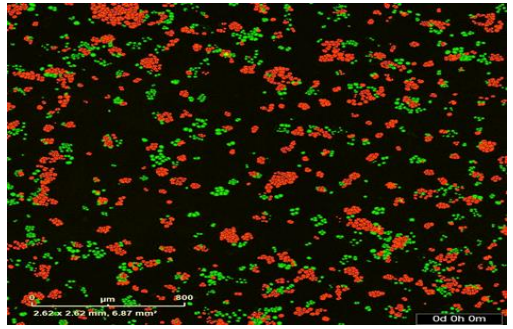
REVEAL can be used to discover and optimize novel sequences of **both DNA and protein**

Senti's REVEAL Platform Enables Rapid Optimization of Highly Potent and Protective Logic Gates for NK and T Cells

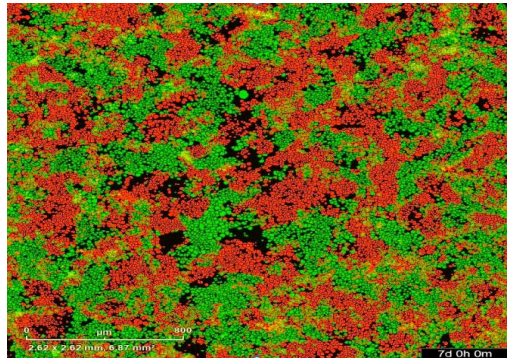
Cancer cells *(VSIG2⁻CEA⁺)*

Model healthy cells *(VSIG2⁺CEA⁺)*

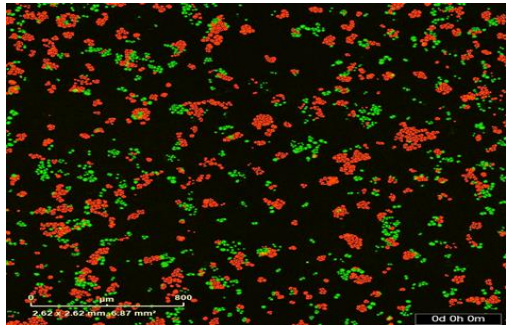
No NK Cells



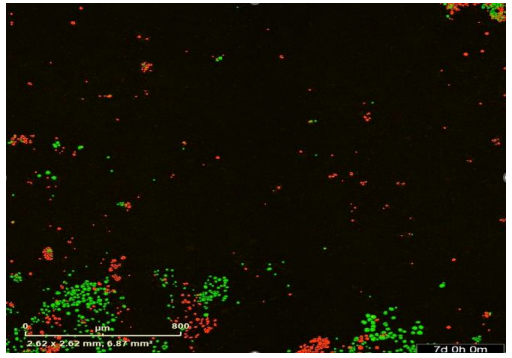
No killing of cancer or healthy cells



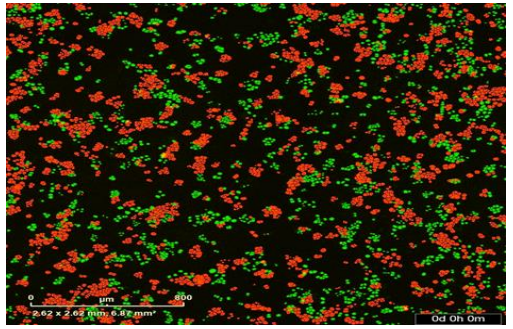
CEA CAR-NK Cells



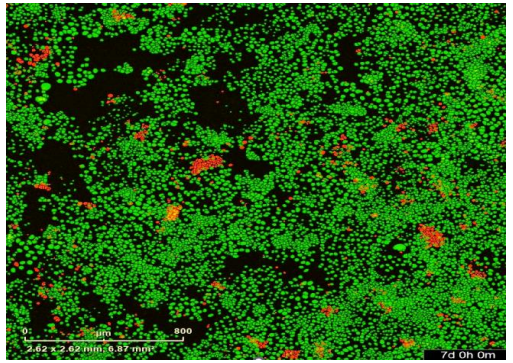
Significant killing of both cancer and healthy cells



CEA NOT VSIG2 CAR-NK Cells

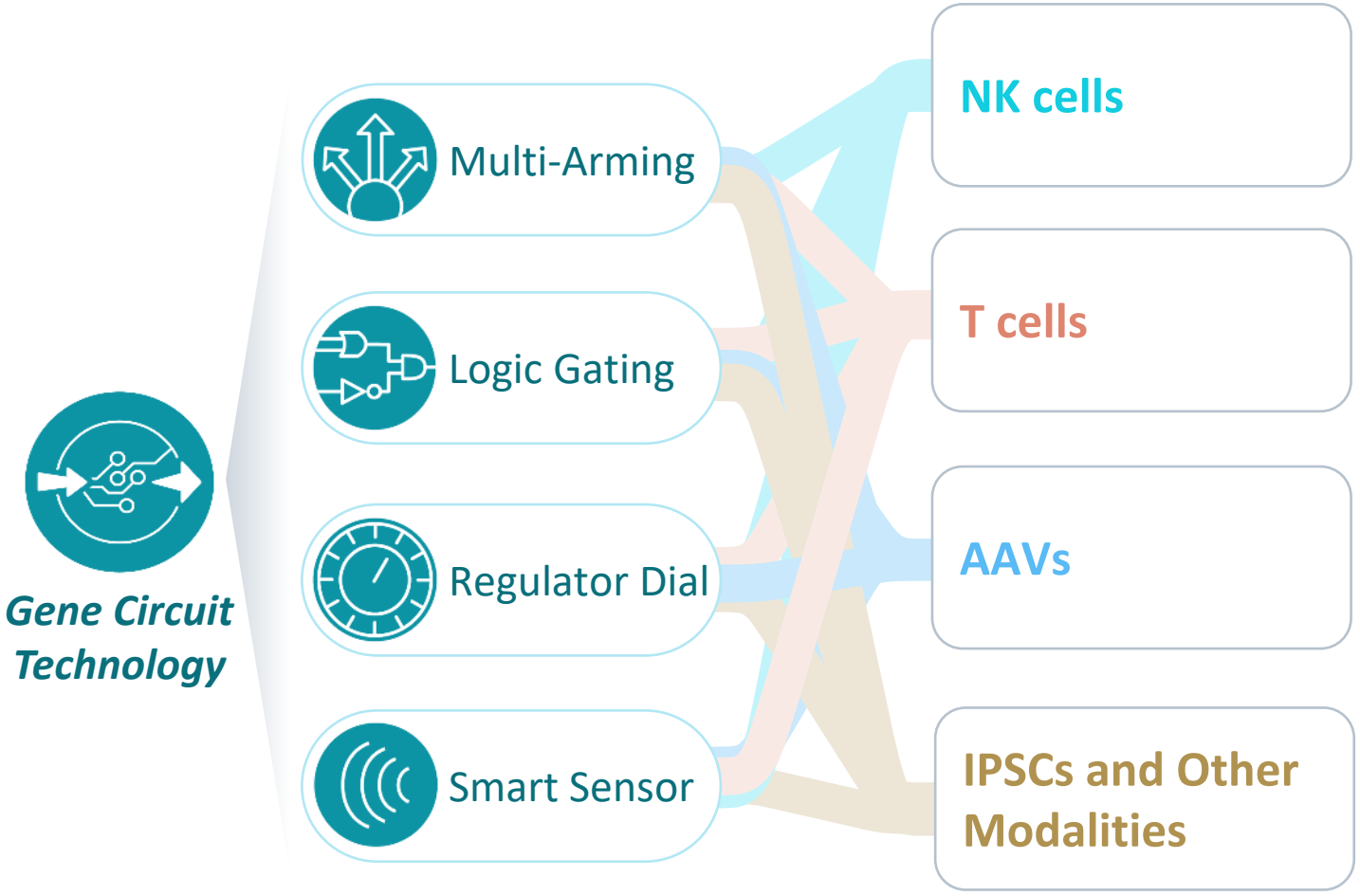


Precise killing of cancer cells while sparing healthy cells



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

Executing Towards Bringing Gene Circuit Medicines to Patients



- ✓ **SENTI-202 is a potential first-in-class Logic Gated CAR-NK program for AML**
  - ⇨ **Initial efficacy data anticipated YE 2024**
  - ⇨ **Durability data anticipated 2025**
- ✓ **SENTI-301A first patient dosing in China expected in 2Q 2024**
- ✓ **Experienced management team with track record of executing on timelines and accelerating innovative therapies**
- ✓ **Gene Circuit technology has been validated in NK cell, T cell, AAV, and iPSC applications**

SENTI BIO

Thank you