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SENTI-202:

Positive Preliminary Results in the Treatment of Relapsed/Refractory Hematologic Malignancies Including AML in Ongoing Phase 1 Trial (SENTI-202-101)

April 28, 2025

Conference Call and Webcast

NASDAQ: SNTI | sentibio.com

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Company Highlights

Potential best-in-class Logic-Gated cell therapy pipeline, initially targeting AML

Scalable **off-the-shelf** manufacturing process streamlines treatment

Gene Circuits platform provides blockbuster opportunity to **selectively and effectively target liquid and solid tumors while sparing healthy cells**

Platform technology can be utilized with both NK and T cell therapies

Lead program SENTI-202

First-in-Class Off-the-Shelf Logic-Gated Selective CD33 OR FLT3 NOT EMCN CAR NK Cell Therapy

- Demonstrated positive preliminary efficacy data in ongoing Phase 1 trial for treatment in R/R AML
- Dose finding completed, CR* and durability data presented at AACR 2025 along with correlative data supporting Logic Gating mechanism of action

Pipeline of NK and T cells for hard-to-treat cancers

Investment from Leading Healthcare Institutional Investors

NEA Celadon Partners leaps BAYER

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*CR: Complete Remission

Logic Gates in Cell Therapy

Enable CAR-NK / CAR-T Cells to Address Broad Liquid and Solid Tumor Applications

Senti Bio's Logic Gate Approach

SENTI-202 and Other Undisclosed Programs

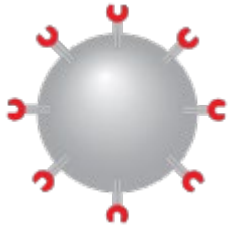
Recognizes Multiple Antigen Targets

OR Gate (aCAR)
Kill if you see Antigens CD33 or FLT3

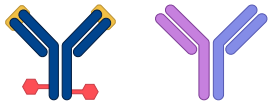
NOT Gate (iCAR)
Do Not Kill if you see Antigen EMCN even if you see CD33 or FLT3

Cancer Cells	Healthy Cells
KILL	PROTECT (DO NOT KILL)

Non-Logic Gate Approaches



Commercially approved CAR T cell therapies



Biologics (ADC/TCE)*

Recognize Single Antigen Target
Single Antigen Target may be found on both cancer and healthy cells

Cancer Cells	Healthy Cells
KILL	KILL

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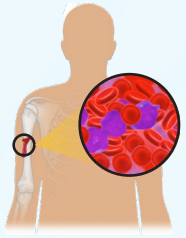
*ADC: antibody drug conjugate; TCE: T cell engagers

Acute Myeloid Leukemia (AML) Is an Aggressive Leukemia with Poor Prognosis

AML Estimated Disease Burden

- 20,800 newly diagnosed AML patients in US every year[1]
  - ~60% patients experience relapse or death within 12 months[2]

Relapsed/Refractory AML Patient Outcome



Median survival of 5.3 months[3]

5-year survival rate is 12.6%[3]

- Current standard of care responses[4,5]
  - CR rate ~15-25%
  - CR/CRh rate ~20-33%

Effective Anti-AML Therapies Need To:

1. Target heterogenous clones / leukemia stem cells (LSCs)[6]
   - To achieve deep / MRD negative CR
   - Leading to durable remissions / longer survival[4,6]
2. Selectively kill AML blasts and LSCs, and spare HSCs
   - To support normal blood cell count recovery
   - Leading to improved prognosis / longer survival[7]

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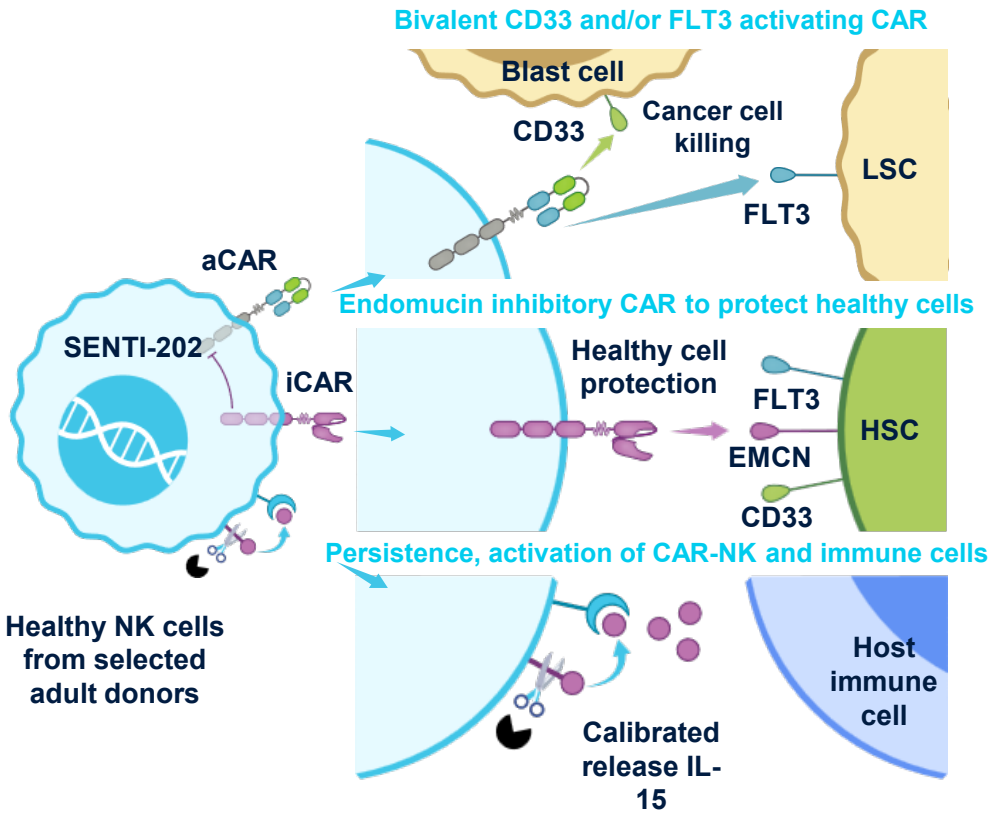
CR: complete remission; CRh: complete remission with partial hematologic recovery; MRD: measurable residual disease; HSC: hematopoietic stem cell

[1]SEER 2024; [2]Tenold Frontiers in Oncology 2021; [3]Brandwein AJBR 2020; [4]Dohner Blood 2022; [5]USPI Idhifa, Xospata, Tibsovo; [6]Zeijlemaker Leukemia 2019; [7]Innes Blood 2018

SENTI-202:
Intelligently Designed CAR-NK May Overcome Limitations of Current Therapies Against AML



SENTI-202 Gene Circuit Design

- **OR Logic Gate "Kills"** leukemia blasts and LSCs via CD33 OR FLT3 activating CAR (aCAR)
  - CD33 and/or FLT3 expressed in ~95% of AML patients with CD33 being predominantly expressed on bulk blasts and FLT3 on LSCs
- **NOT Logic Gate "Protects"** healthy HSC/HSPCs from 'off-tumor, on-target' effects
  - Protection of HSC/HSPCs via Endomucin (EMCN) inhibitory CAR (iCAR), even when they express CD33 and/or FLT3
  - EMCN found predominantly on healthy HSC/HSPC surface, rarely on AML blasts
- **Calibrated release IL-15 "Enhances"** SENTI-202 and host immune cell activity and persistence

SENTI-202 is designed to selectively kill both AML blasts and LSCs while protecting healthy HSC/HSPCs using its novel CD33 OR FLT3 NOT EMCN Logic-Gated gene circuit

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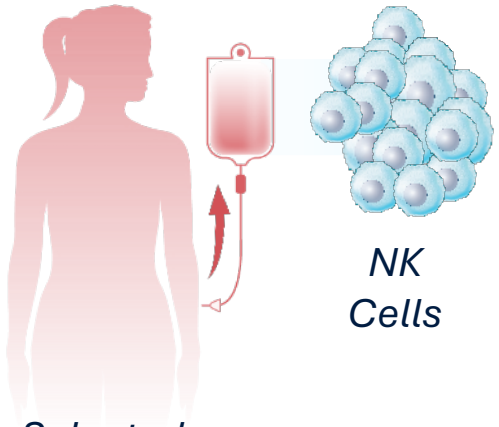
LSC: Leukemia stem cell; HSC: hematopoietic stem cell; HSPC: hematopoietic stem and progenitor cell

SENTI-202 Scalable Manufacturing Process

Off-the-Shelf Allogeneic CAR-NK

Scalable Process

1 ***Isolate from selected donors***

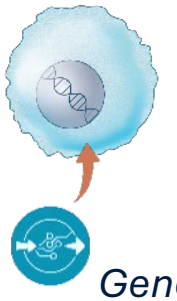


Selected Donor

NK Cells

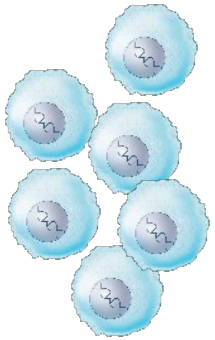
2 ***Engineer***

Gene Circuit Engineered CAR-NK cells



Gene Circuit delivered through single transduction step

3 ***Expand***



4 ***Cryopreserve and Store***

Final product harvested and cryopreserved

NK cells isolated from peripheral blood of selected donors

NK cells efficiently engineered with Gene Circuits

High post-thaw potency

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1 ***Thaw and Infuse Off-the-Shelf***

Patient

Easy to thaw vials

Outpatient use potential

SENTI-202 Phase 1 Trial (SENTI-202-101) Design

A multicenter, multinational, open-label study (NCT06325748)

Key Eligibility Criteria

- ≥18 and <75 years
- ECOG 0-1
- R/R CD33 and/or FLT3 expressing heme malignancies
  - CD33+ by local assessment
- R/R AML (1-3 prior Rx)
- R/R MDS with increased blasts[1] (1-2 prior Rx)
- Must have received targeted agents if applicable mutations

Study Design

"3+3"

Dose finding followed by AML, MDS and other expansion cohorts at RP2D

Study Dosing

2 Dose Levels and 2 schedules planned

Opening dose cohort anticipated to be biologically active

Study Objectives

- Primary objective- safety and determination of MTD/RP2D
- DLT definition includes:
  - ≥ G3 non-hematologic toxicities
  - Prolonged G4 neutropenia /thrombocytopenia not due to underlying disease
- Other key objectives
  - Efficacy based on ELN 2022 criteria (AML)
  - MRD assessed per local standard of care
  - Pharmacokinetics (PK)
  - Pharmacodynamics (PDn) using CyTOF on serial BM samples

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ECOG: European Cooperative Oncology Group; RP2D: recommended phase 2 dose; MTD: Maximum tolerated dose; DLT: dose limiting toxicity; G: Grade by CTCAE v5.0 and other applicable Grading systems; ELN: European LeukemiaNet; CyTOF: Cytometry by Time-of-Flight; BM: bone marrow

[1]Per WHO 2022 Classification;

SENTI-202 Phase 1 Trial (SENTI-202-101) Dosing Schema- Preliminary RP2D Identified

SENTI-202 Dose Levels

Dose Level	CAR+ NK Cells/Dose
1	1×10^9
2	1.5×10^9

Multi-Dose Cycle

Lymphodepletion
Fludarabine/Cytarabine (Ara-C)

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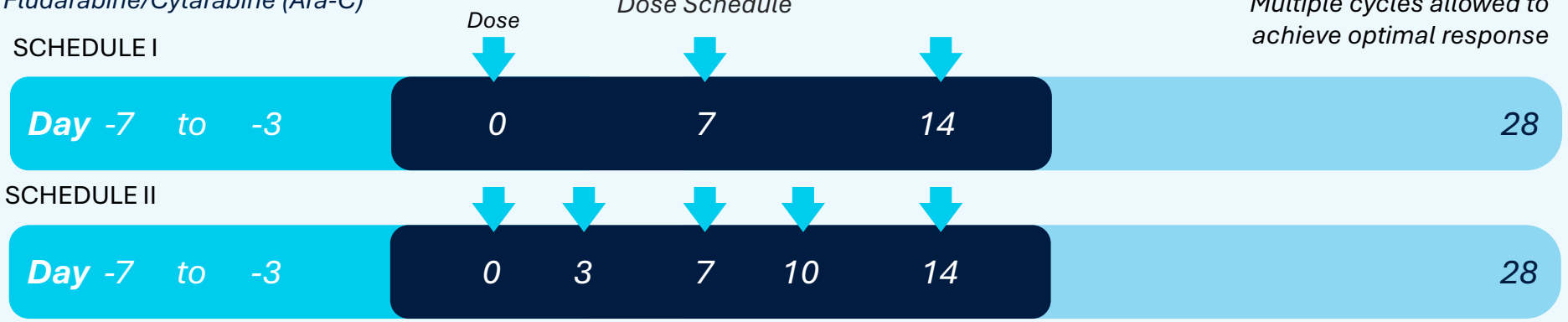
Dose Schedule

Efficacy Assessment
Multiple cycles allowed to achieve optimal response



Opening Dose Cohort was Anticipated to be Biologically Active
Schedule I Dose Level 1, N = 3
No DLTs

Schedule I Dose Level 2, N = 3
No DLTs
Identified as preliminary RP2D based on totality of clinical data

Schedule II Dose Level 1, N = 3
No DLTs

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Study Enrolled a High-Risk R/R AML Population with Multiple Baseline Adverse Characteristics

Baseline Characteristics	Dose Level 1		Dose Level 2	All Patients N = 9
	Schedule I N = 3	Schedule II N = 3	Schedule I N = 3	
Age, yr, median (range)	64 (26,72)	41 (36, 67)	**63 (51, 69)**	63 (26, 72)
Male, n (%)	1 (33)	2 (67)	**3 (100)**	6 (67)
AML, n (%)	3 (100)	3 (100)	**3 (100)**	9 (100)
Years from AML diagnosis, median (range)	2.84 (0.5, 6.2)	0.49 (0.3, 0.8)	**0.94 (0.5, 1.0)**	0.75 (0.3, 6.2)
Adverse risk by ELN 2022, n (%)	2 (67)	2 (67)	**3 (100)**	7 (78)
Baseline bone marrow blasts, %, median (range)	20 (15, 69)	30 (18, 31)	**45 (10, 93)**	30 (10, 93)
Baseline platelet count < 50 x 10^9/L , n (%)	0 (0)	2 (67)	**2 (67)**	4 (44)
			preliminary RP2D	

- Median of <1 yr from diagnosis to trial entry across all patients and in preliminary RP2D cohort
- Majority of patients (all in preliminary RP2D cohort) with adverse risk genetics by ELN 2022 criteria

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Data from an open clinical database of an ongoing study as of 7 Apr 2025

Study Subjects had Received Multiple Prior Therapies

Prior Therapy	Dose Level 1		Dose Level 2	All Patients N = 9
	Schedule I N = 3	Schedule II N = 3	Schedule I N = 3	
Number of prior lines, median (range)	1 (1,1)	2 (1, 2)	**2 (2, 3)**	2 (1,3)
Chemotherapy, n(%)	3 (100)	3 (100)	**3 (100)**	9 (100)
Fludarabine and/or Ara-C, n (%)	3 (100)	3 (100)	**3 (100)**	9 (100)
Anthracycline, n (%)	3 (100)	2 (67)	**3 (100)**	8 (89)
Venetoclax, n (%)	1 (33)	3 (100)	**3 (100)**	7 (78)
Hypo-methylating Agents, n (%)	2 (67)	3 (100)	**3 (100)**	8 (89)
FLT3/IDH2 targeted therapy, n (%)	1 (33)	1 (33)	**1 (33)**	3 (33)
Bone marrow transplant, n (%)	1 (33)	0 (0)	**1 (33)**	2 (22)
Primary refractory*, n (%)	1 (33)	2 (67)	**2 (67)**	5 (56)

preliminary RP2D

- Median of 2 lines before study entry overall and in preliminary RP2D cohort
- All patients with previous chemotherapy exposure including fludarabine and/or cytarabine (4 received both) and majority with previous venetoclax exposure

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Data from an open clinical database of an ongoing study as of 7 Apr 2025; * Primary refractory defined as failure to achieve cCR or cCR lasting <3 mo with front-line therapy

Patients Received a Median of 2 Cycles of SENTI-202 Therapy

Exposure	Dose Level 1		Dose Level 2	All Patients N = 9
	Schedule I N = 3	Schedule II N = 3	Schedule I N = 3	
Number of SENTI-202 treatment cycles, median (range)	2 (1, 2)	2 (1, 2)	**2 (1, 2)**	2 (1, 2)
Subjects continuing treatment as of data-cut, n (%)	0	2 (67)	**0**	2 (22)
Subjects discontinuing treatment, n (%)	3 (100)	1 (33)	**3 (100)**	7 (78)
Adverse Event	0	0	**0**	0
Achieved Optimal Response (cCR)	2 (67)	0	**2 (67)**	4 (44)
Disease Progression/ Stable Disease	1 (33)	1 (33)	**1 (33)**	3 (33)

preliminary
RP2D

- Median of 2 cycles across dose cohorts
- Majority of patients discontinued SENTI-202 after achieving cCR with none discontinuing due to adverse event

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Data from an open clinical database of an ongoing study as of 7 Apr 2025; cCR: composite CR includes CR, CRh, CRi

Preliminary Safety Data Indicate that SENTI-202 is Well Tolerated

Any Grade 3-4* AEs Regardless of Relationship	Dose Level 1		Dose Level 2	All Patients N = 9
	Schedule I N = 3	Schedule II N = 3	Schedule I N = 3	
Any Grade ≥ 3 AEs, n (%)	3 (100)	3 (100)	**3 (100) ^**	9 (100)
Febrile Neutropenia	1 (33)	1 (33)	**2 (67) ^**	4 (44)
Platelet Count Decreased	2 (67)	0	**2 (67) ^**	4 (44)
Anemia	1 (33)	1 (33)	**0**	2 (22)
Abdominal Pain	1 (33)	1 (33)	**0**	2 (22)
**No Grade 5 AEs, ^ 1 patient with G3 febrile neutropenia and G4 platelet count decreased assessed as possibly related to SENTI-202*				

preliminary
RP2D

SENTI-202 was well tolerated

- In general, G3-4 AEs on study were hematologic, unrelated to SENTI-202 and consistent with R/R AML patients receiving LD
- No single type of SAE reported in > 1 patient
- No significant difference in AE profile across dose cohorts

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AEs: treatment emergent adverse events includes adverse events with onset after SENTI-202 dosing and within 30 days of last dose of study treatment; Grading per CTCAE v5.0
Data from an open clinical database of an ongoing study as of 7 Apr 2025

SENTI-202 Related AEIs Were Low Grade and Manageable with Standard of Care

Patient # (Dose Cohort)	Event Term (Grade)	Onset from SENTI-202 Dose (days)	Duration (days)
001-0004, (1)	Chills, G1	0	1
	Pyrexia, G1	0	1
008-005, (1)	Pyrexia, G1	0	5
	Hypotension, G1	3	1
102-007, (prelim. RP2D)	Pyrexia, G1	1	1
	Hypoxia, G2	1	1

- 3 pts experienced G1 pyrexia with either hypotension or hypoxia in 1 each, typically within 1 day of SENTI-202 dosing that were reported as Cytokine Release Syndrome (CRS)
  - Events resolved rapidly with standard of care; None were serious
- Likely represent delayed infusion reactions described with NK cell therapies
- No other AEIs or DLTs reported on study

AEIs: AEs of Interest; Grading per ASTCT criteria
Data from an open clinical database of an ongoing study as of 7 Apr 2025

Responses Observed Across All Dose Cohorts

Best Overall Response on Study, n (%)	Dose Level 1		Dose Level 2	All Patients N = 7*
	Schedule I N = 3	Schedule II N = 1*	Schedule I N = 3	
Overall Response Rate (ORR)	2 (67)	1 (100)	**2 (67)**	5 (71)
composite CR Rate (cCR)^	2 (67)	0	**2 (67)**	4 (57)
Negative MRD Status in cCR Patients	2/2 (100)	N/A	**2/2 (100)**	4/4 (100)
Response Category, n(%)				
CR	2 (100)	0	**1 (33)**	3 (43)
CRh	0	0	**1 (33)**	1 (14)
MLFS	0	1 (100)	**0**	1 (14)
SD	0	0	**1 (33)**	1 (14)
PD	1 (33)	0	**0**	1 (14)
**Two patients continuing into second Cycle after achieving SD with blast reduction from 31% to 13% and 5% to 3% respectively are excluded from best overall response assessment; ^CR + CRh + CRi*				
			preliminary RP2D	

AML Response

- 5 of 7 patients overall achieved ORR
- 2/3 and 4/7 patients achieved cCR respectively in preliminary RP2D cohort and all patients
- 4/4 cCR patients were MRD-
- All cCR responses are ongoing as of data-cut with median duration of response not reached

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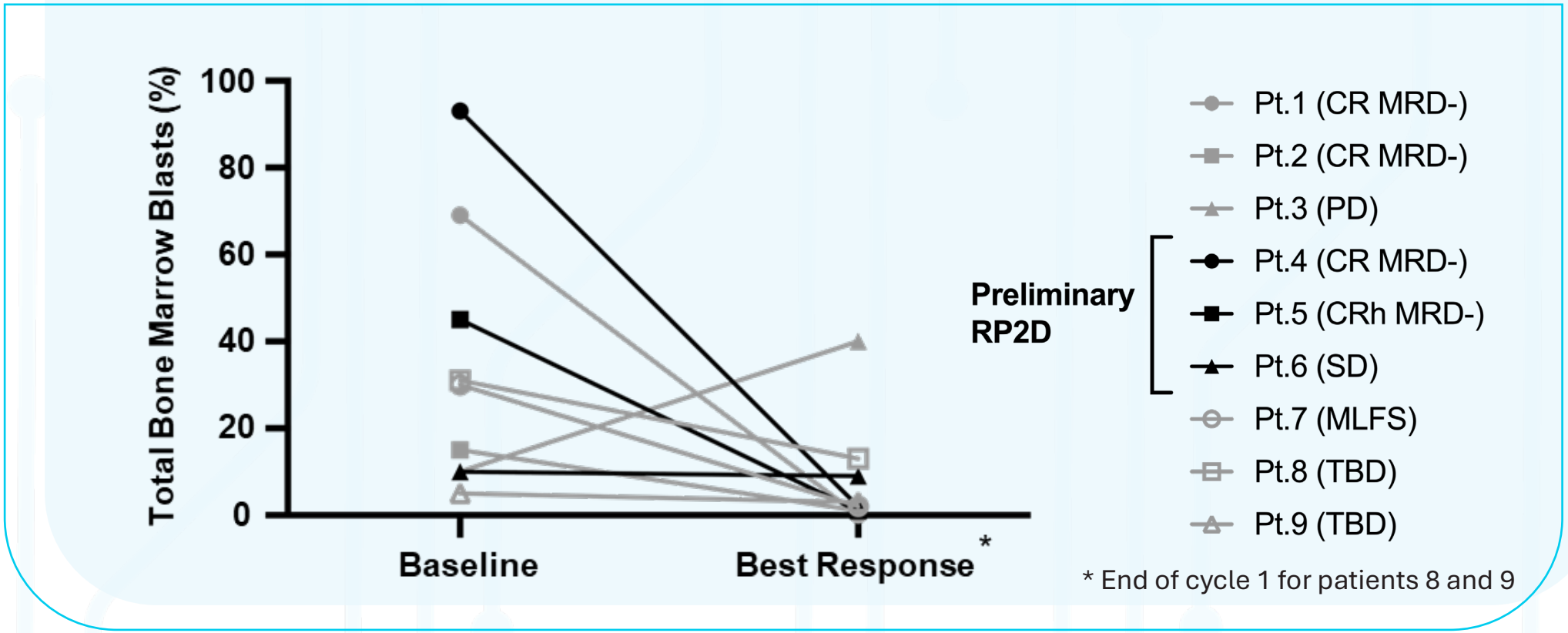
Data from an open clinical database of an ongoing study as of 7 Apr 2025

Rapid Bone-Marrow Blast Reduction Observed Across All Dose Cohorts



Blast Reduction Noted in Majority of Patients Across All Dose Cohorts

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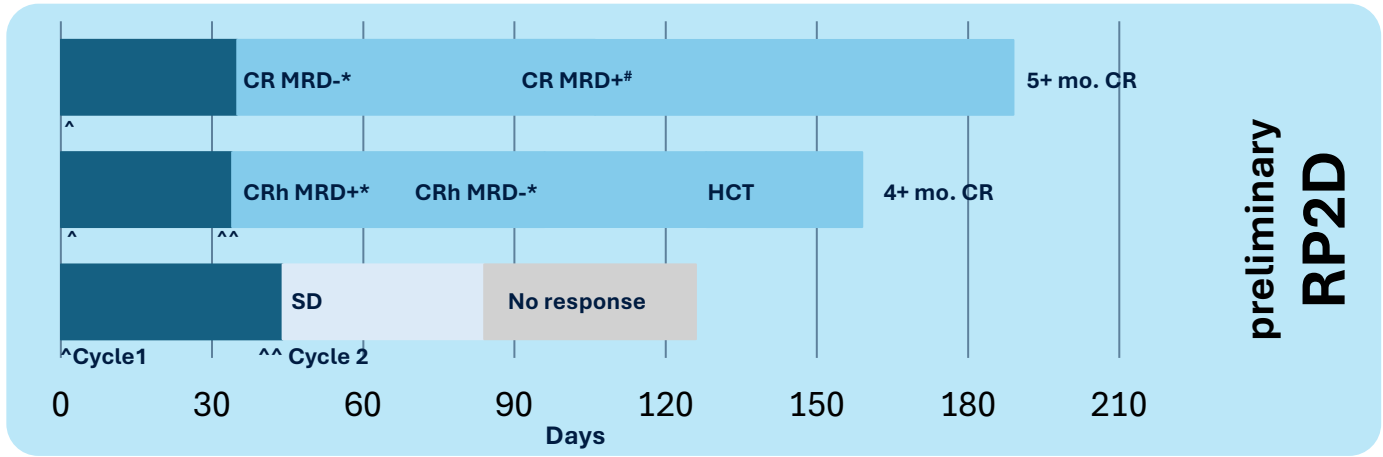
Data from an open clinical database of an ongoing study as of 7 Apr 2025

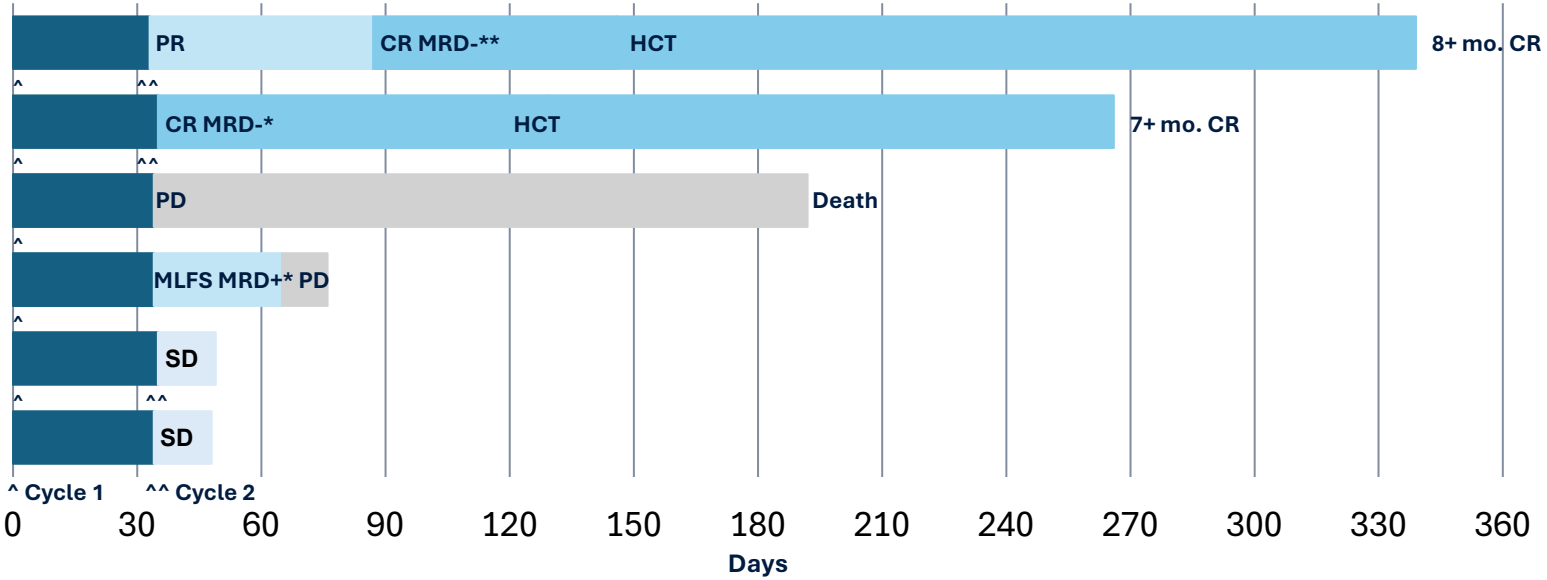
Early Deep Responses Noted Across Dose Levels with Durability 8+ Months

Pt	I⁰ Ref	Adv. Risk	FA Exp	FA Ref
Pt4	Yes	Yes	Yes-both	Yes-both
Pt5	No	Yes	Yes-both	No
Pt6	Yes	Yes	Yes	Yes



*MRD by multi-parametric flow (sensitivity ≤ $1/10^{-4}$), **MRD by NGS (sensitivity ≤ $1/10^{-2}$)

Pt	I⁰ Ref	Adv. Risk	FA Exp	FA Ref
Pt1	No	Yes	Yes	No
Pt2	No	No	Yes	No
Pt3	Yes	Yes	Yes	Yes
Pt7	Yes	No	Yes-both	Yes-both
Pt8	Yes	Yes	Yes	Yes
Pt9	Unk	Yes	Yes-both	Unk



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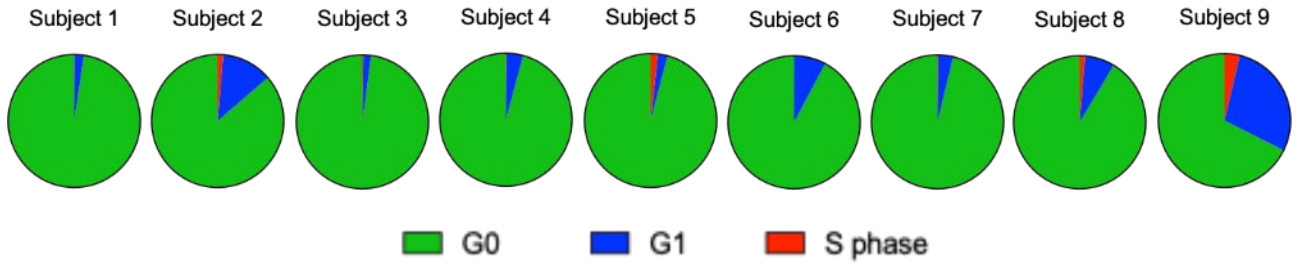
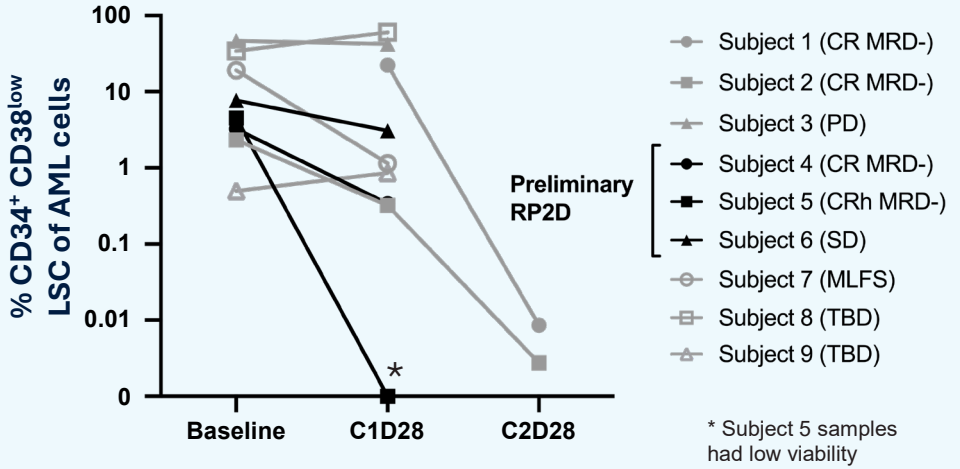
I⁰ Ref: Primary refractory defined as failure to achieve cCR or cCR lasting <3 mo with front-line therapy; Adv. Risk: Adverse Risk genetics by ELN 2022; FA Exp: fludarabine and/or Ara-C Exposed, both indicates exposed to both agents; FA Ref: Fludarabine and/or Ara-C refractory (failure to achieve cCR or cCR lasting < 3 mo), both indicates refractory to both agents; #Patient had detectable IDH2 mutation by NGS while in morphologic remission and started on venetoclax/enasidenib; Data from an open clinical database of an ongoing study as of 7 Apr 2025

CyTOF Bone Marrow Data Reveals SENTI-202 Treatment Resulted in Decreased LSCs in Responders

LSCs in bone marrow at baseline are largely non-cycling when analyzed by Ki67 and IdU



LSC ($CD34^{+}$ $CD38^{low}$) in Bone Marrow



- CyTOF measured 49 different proteins in serial bone marrow derived mononuclear cells samples from baseline and end of each Cycle
- At baseline, majority of leukemic stem cells (LSCs) were in G0 phase and not expected to be susceptible to chemotherapy
- With SENTI-202 treatment, LSCs decreased > 10-fold in all patients who achieved cCR

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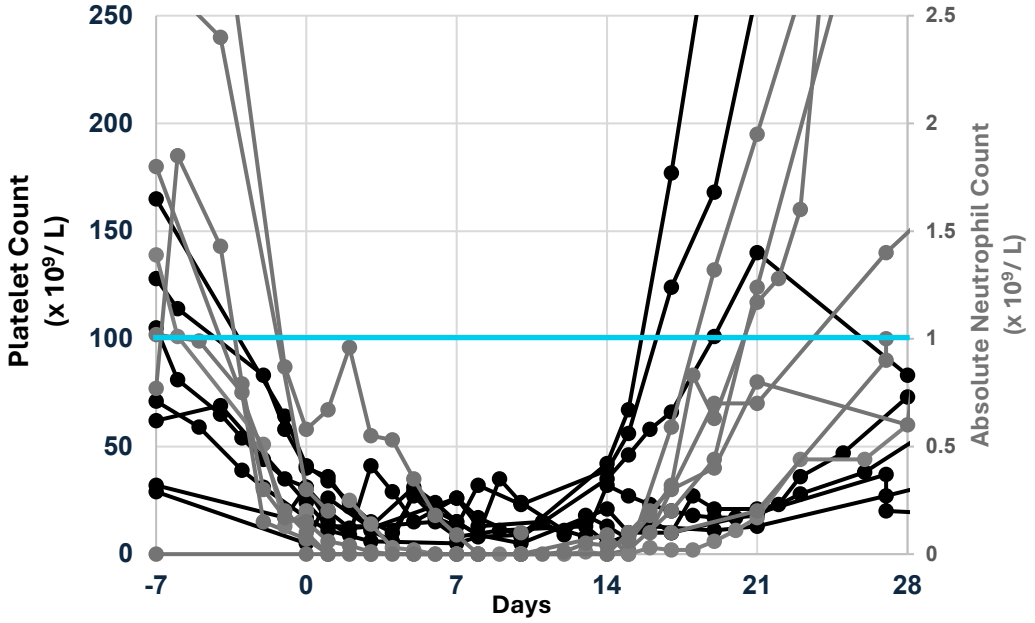
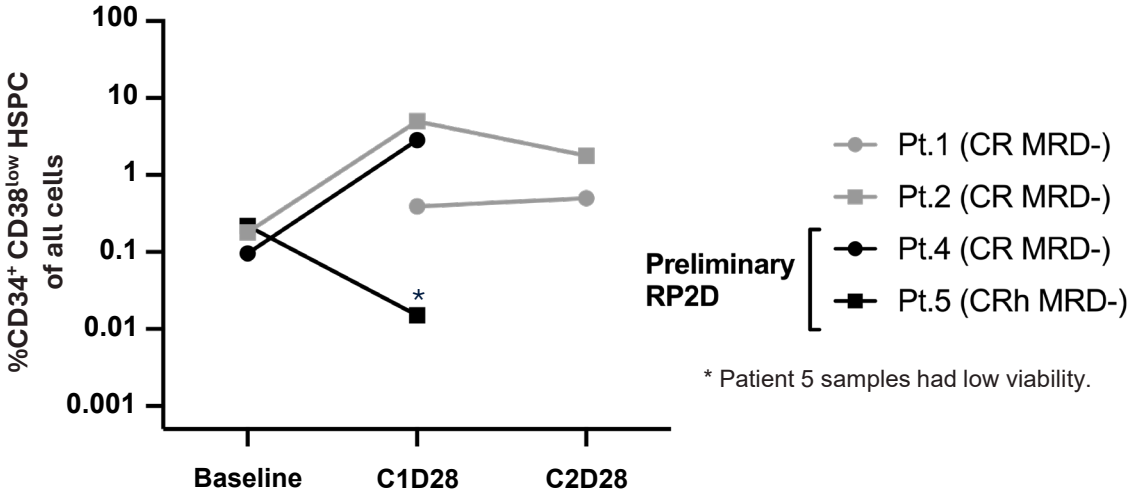
IdU: 5-Iodo-2'-Deoxyuridine; Data from an open clinical database of an ongoing study as of 7 Apr 2025

Rapid Normalization of Peripheral Blood Cell Count along with Protection of BM HSPCs in Patients who Achieved cCR

Peripheral Blood Cell Counts



HSPC (CD34+ CD38^{low}) in Bone Marrow (BM)



* Patient 5 samples had low viability.

Rapid blood cell count recovery in periphery in patients who achieved cCR

- Median of 21 days for neutrophil count ≥ 0.5 and 1 x10^9/ L, and 28/35 days to platelet count ≥ 50 and 100 x10^9/ L
- CyTOF analyses revealed HSPCs were maintained or increased in bone marrow of patients who achieved cCR consistent with SENTI-202 Logic Gate mechanism of action

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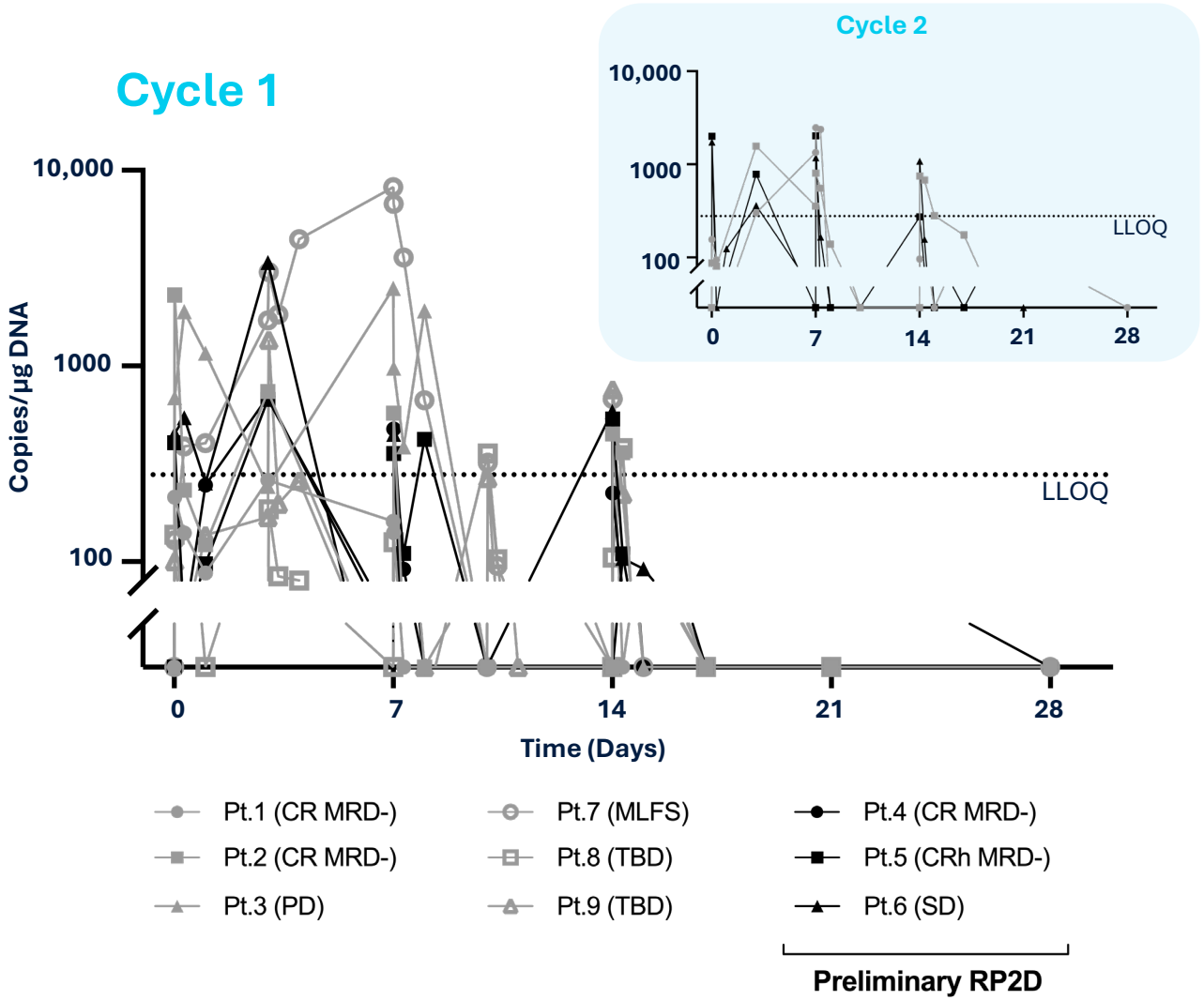
Data from an open clinical database of an ongoing study as of 7 Apr 2025

SENTI-202 Is Detected in Periphery of All Treated Patients Consistent with Allo-NK Profile



- PK profile consistent with allogeneic NK cell therapy
  - Modest peripheral expansion in first 14 days consistent with NK biology and safety of SENTI-202
  - Clearance >14 days from periphery
- No significant difference in exposure across patients who achieved cCR or not
- No significant difference in exposure across Dose Cohorts
- No significant difference in exposure between Cycle 1 and 2

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Interim PK data as of 7 Apr 2025; value of 1 assigned for timepoints with non-measurable transgene, LLOQ estimated using equivalent DNA loading and is the lower limit of quantitation

Dosing and Safety Conclusions- SENTI-202 Generally Well Tolerated in R/R AML Patients

- SENTI-202 is a First-In-Class Off-the-Shelf Logic Gated selective CD33 OR FLT3 NOT EMCN CAR NK cell therapy
  - Designed to selectively kill both AML blasts and LSCs while protecting healthy HSPCs with a novel OR/NOT logic gate gene circuit
- SENTI-202-101 trial enrolled heavily treated R/R AML patients with poor prognosis
- SENTI-202 is well tolerated
  - Most frequent Grade 3+ AEs were hematologic and consistent with R/R AML patients receiving LD
  - MTD not reached and preliminary RP2D identified as 1.5B cells/ dose x 3 weekly doses/ 28 days

Efficacy Conclusions- Promising Preliminary Efficacy Noted with SENTI-202 in R/R AML Patients

- **Efficacy**
  - 5/7 ORR and 4/7 cCR across all patients including 2/3 cCR in preliminary RP2D cohort
  - 4/4 cCR MRD- as assessed per local standard of care
  - All cCR patients maintaining morphologic remission with longest follow up of 8+ mo
- **PK**
  - SENTI-202 detected in all treated patients, consistent with other allogeneic CAR NK cell therapy PK profiles and its well tolerated safety profile
- **CyTOF analyses of BM**
  - SENTI-202 treatment decreased LSC frequencies and maintained (or increased) healthy HSPC frequencies in patients achieving cCR consistent with SENTI-202 Logic Gated gene circuit design

Also at AACR...

- First-In-Human, Multicenter Study of SENTI-202, a CD33/FLT3 Selective Off-the-Shelf Logic Gated CAR NK Cell Therapy in Hematologic Malignancies including AML: Correlative Data (#10977)

  Session: PO.CT01.02 - First-in-Human Phase I Clinical Trials 2

  Location: Section 48, #9

  Time: 4/29/2025 9:00:00 - 12:00:00 PM

- SENTI-202 CD33 OR FLT3 NOT EMCN Logic-Gated Gene Circuit Components Selectively Target AML while Protecting Human HSC/HPCs from Off-Tumor Toxicity in a Humanized Mouse Model (#6833)

  Session: PO.IM01.17 - Novel In Vivo, In Vitro, and In Silico Models

  Location: Section 38, #18;

  Time: 4/30/2025 9:00:00 - 12:00:00 PM

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    - UCLA Department of Medicine, Los Angeles, CA
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Q&A

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