



Next Generation Immunomedicines

January 2023

Forward-Looking Statements

To the extent that statements contained in this presentation are not descriptions of historical facts, they may be deemed to be forward-looking statements under the Private Securities Litigation Reform Act of 1995. These statements are based on current expectations, forecasts, assumptions and other information available to NextCure as of the date hereof. Forward-looking statements include statements regarding NextCure's expectations, beliefs, intentions or strategies regarding the future and can be identified by forward-looking words such as "may," "will," "potential," "expects," "believes," "intends," "hope," "towards," "forward," "later" and similar expressions. Examples of forward-looking statements in this press release include, among others, statements about the development plans for our immunomedicines, statements about the progress and evaluation and expected timing of results of NextCure's ongoing clinical trial of NC410, NC762 or NC525, expectations regarding the potential benefits, activity, effectiveness and safety of NC410 or NC762, development plans for NC410, NC762 or NC525, NextCure's financial guidance, expected upcoming milestones, and NextCure's plans, objectives and intentions with respect to the discovery and development of immunomedicines. Forward-looking statements involve substantial risks and uncertainties that could cause actual results to differ materially from those projected in any forward-looking statement. Such risks and uncertainties include, among others: the impacts of the COVID-19 pandemic on NextCure's business, including NextCure's clinical trials, third parties on which NextCure relies and NextCure's operations; positive results in preclinical studies may not be predictive of the results of clinical trials; NextCure's limited operating history and no products approved for commercial sale; NextCure's history of significant losses; NextCure's need to obtain additional financing; risks related to clinical development, marketing approval and commercialization; the unproven approach to the discovery and development of product candidates based on NextCure's FIND-IO™ platform; and dependence on key personnel. More detailed information on these and additional factors that could affect NextCure's actual results are described in NextCure's filings with the Securities and Exchange Commission (the "SEC"), including in Item 1A of NextCure's most recent Form 10-K, subsequent Form 10-Q and elsewhere in the Company's filings with the SEC. You should not place undue reliance on any forward-looking statements. Forward-looking statements speak only as of the date of this press release, and NextCure assumes no obligation to update any forward-looking statements, except as required by law, even if expectations change.

NextCure Highlights

NC410 (LAIR-2)
Combo



Phase 1b/2

NC762 (B7-H4)



Phase 1b

NC525 (LAIR-1)



IND FILED
Q4 2022

PIPELINE *Progress*

- NC410 (LAIR-2): Phase 1b/2 combo
- NC762 (B7-H4): Phase 1b mono
- NC525 (LAIR-1): IND Q4 2022

PRODUCT *Strategy*

- Patient selection increasing probability of success
- Biomarkers for detecting early activity
- Combination therapy
- FIND-IO discovery platform

PEOPLE *Experience*

- Experienced team
- Fully integrated GMP manufacturing team



Momentum & Milestones

NC410, NC762, NC525
On Track

BUILDING PIPELINE
Momentum

EXPERIENCED
Team

RUNWAY
Mid-2025



Advancing Product Candidate Pipeline

PROGRAMS	TARGET	CELLS	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT MILESTONE
PRODUCT CANDIDATES								
NC410 COMBO	LAIR-2	Extracellular Matrix	CRC, ESOPHAGEAL, ENDOMETRIAL, H&N, OVARIAN					Phase 1b Data Mid-2023
NC762	B7-H4	Tumor Cells	OVARIAN, BREAST, NSCLC					Phase 1b Data Q4 2023
NC525	LAIR-1	Leukemia	LEUKEMIA (AML)					Trial Initiation Q1 2023
RESEARCH PROGRAMS								
Multiple Programs	Multiple Targets	Multiple Cells Types						

Worldwide Rights to All Programs

Product Development: Getting it Right

Unmet Needs of Cancer Patients

- Non-Responders
- Rapid Progression
- Limited Treatments

We Need New Solutions



**Patient
Selection**



**Triangulation
Strategy**



Combos

Biomarkers

NC410 Combo

LAIR-2 (Collagen-Binding) Fusion Protein Decoy

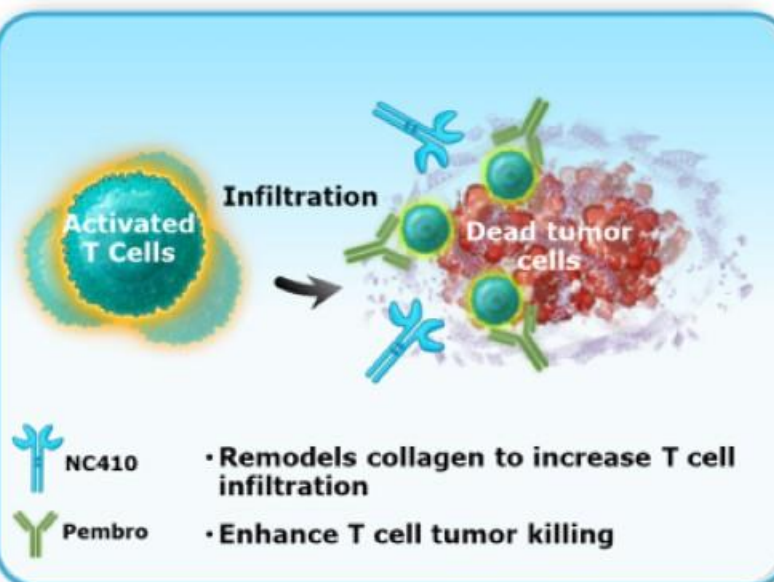


Phase 1b/2
CLINICAL
TRIAL

BIOLOGY

- Targets LAIR-1/LAIR-2 pathway
- Enhances T cell infiltration and tumor killing

MOA



HIGHLIGHTS

- Phase 1b/2
- Synergistic mechanisms of action
- Overcoming tumor resistance by collagen remodeling & enhancing T cell tumor killing

Scientific Advancement in Understanding Collagen Biology

2019 *Science Translational Medicine*
Targeted antibody and cytokine cancer immunotherapies through **collagen** affinity

2019 *Science Translational Medicine*
Anchoring of intratumorally administered cytokines to **collagen** safely potentiates systemic cancer immunotherapy

2020 *Nature Communication*
Collagen promotes anti-PD-1/PD-L1 resistance in cancer through LAIR1-dependent CD8⁺ T cell exhaustion

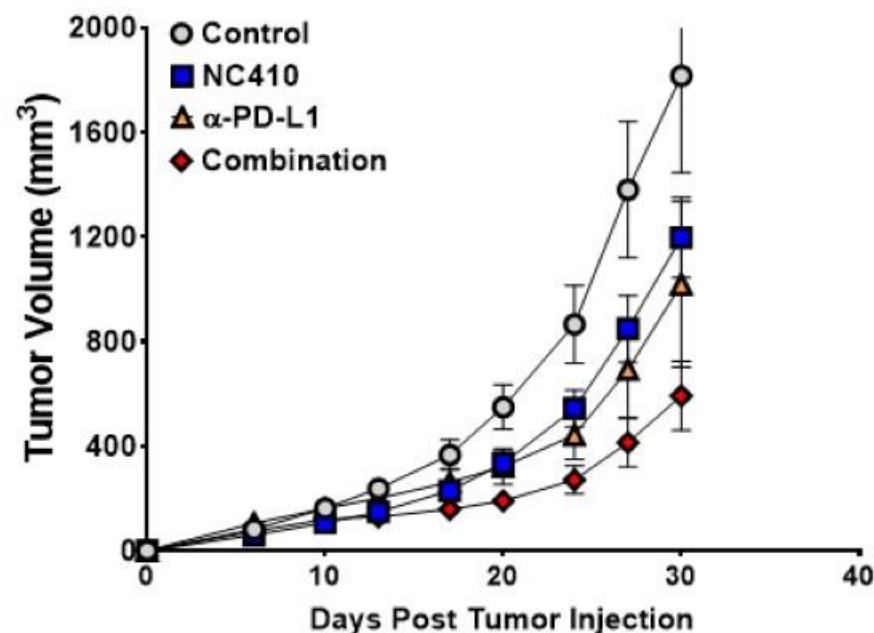
2021 *eLife*
Cancer immunotherapy by NC410, a LAIR-2 Fc protein blocking human LAIR-**collagen** interaction

2021 *Frontiers in Immunology*
Collagen Fragments Produced in Cancer Mediate T Cell Suppression Through Leukocyte-Associated Immunoglobulin-Like Receptor 1

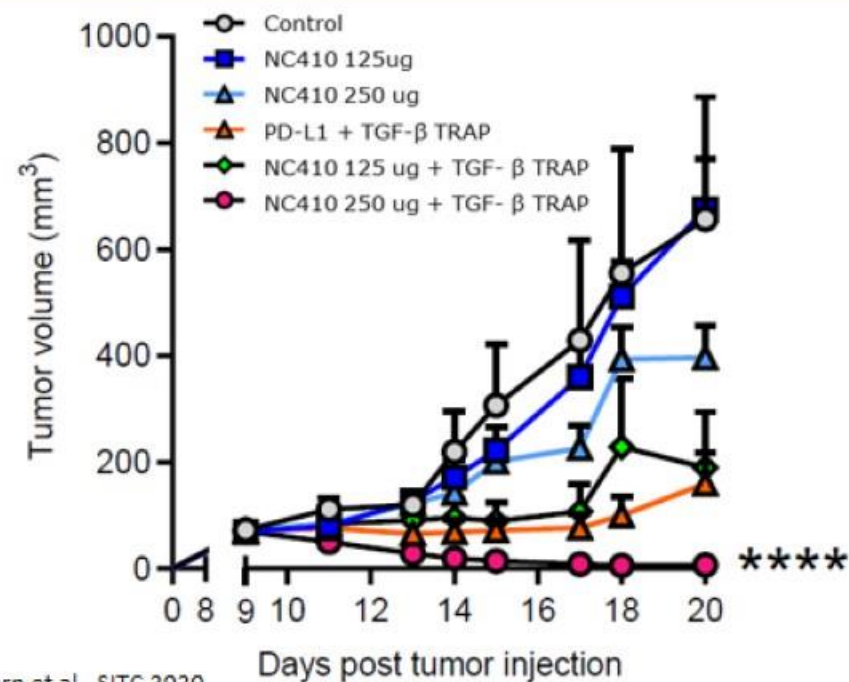
- Elevated collagen correlates with **PD-1/PD-L1 resistance**
- Changes in collagen expression correlate with **worse prognosis**
- LAIR-2 & NC410 **sensitizes** tumors

NC410 Demonstrates Synergistic Activity in Preclinical Models

PD-L1



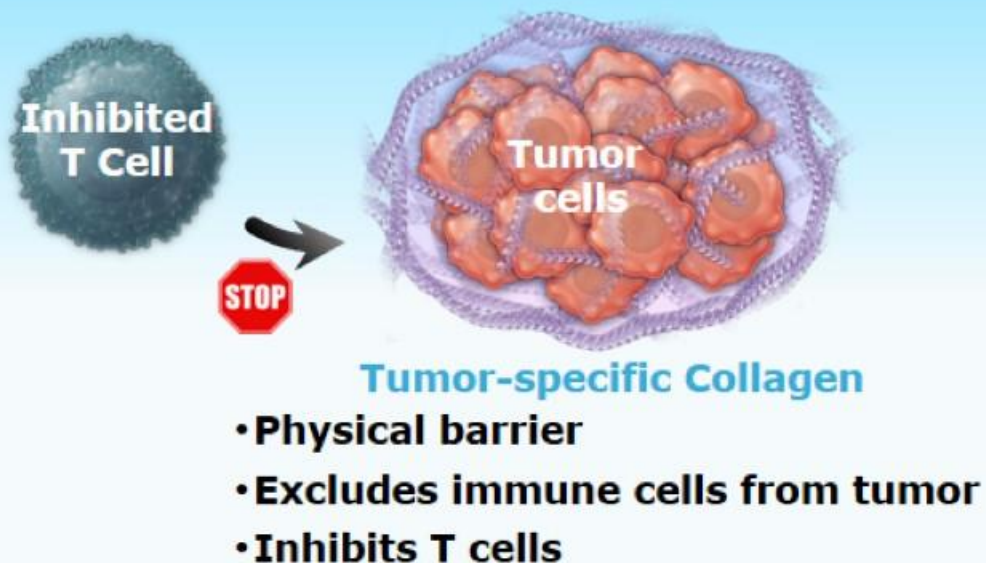
PD-L1 TGF-β TRAP



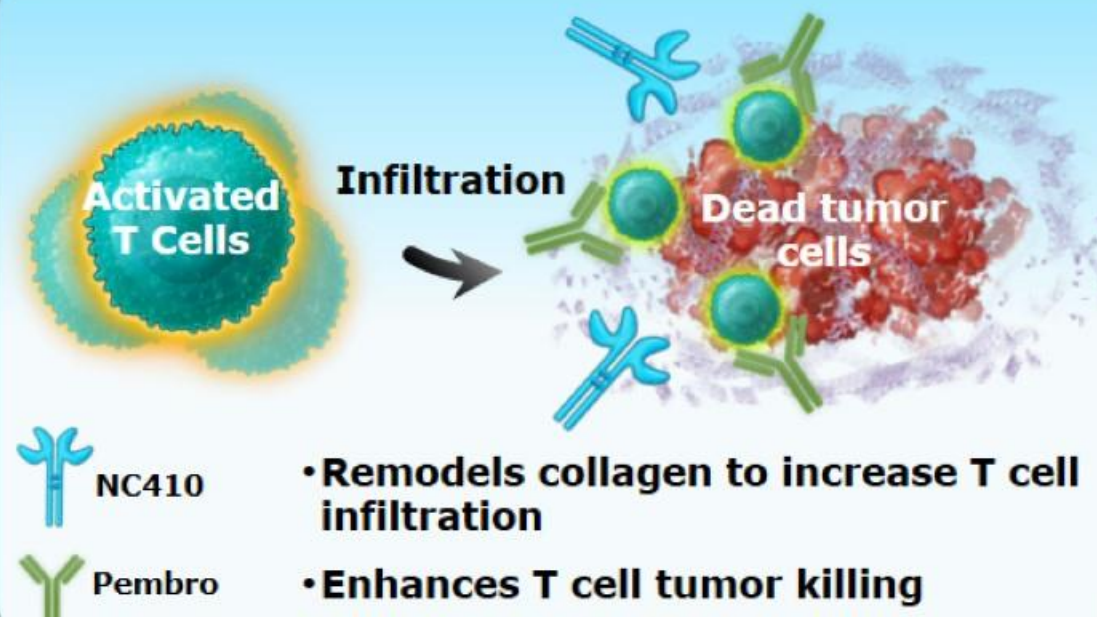
Horn et al., SITC 2020

NC410 Mechanism of Action

COLLAGEN IS IMMUNOSUPPRESSIVE

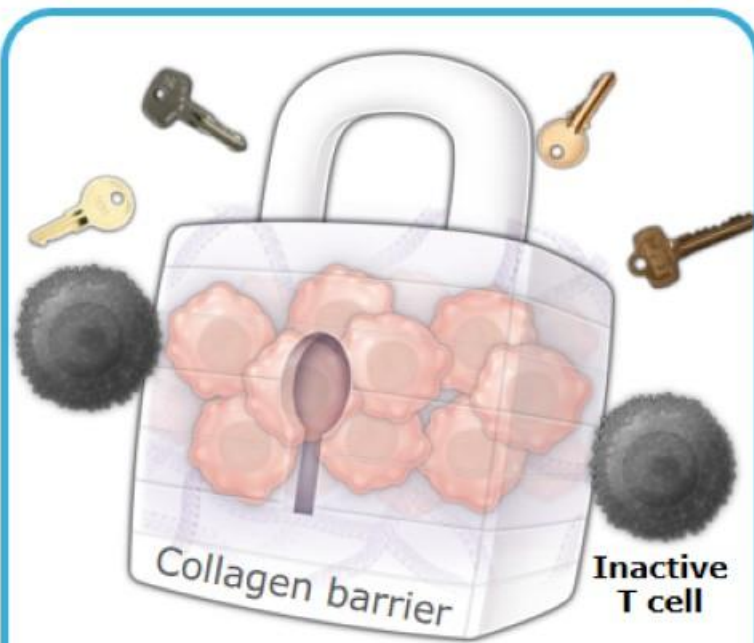


NORMALIZES IMMUNE SYSTEM



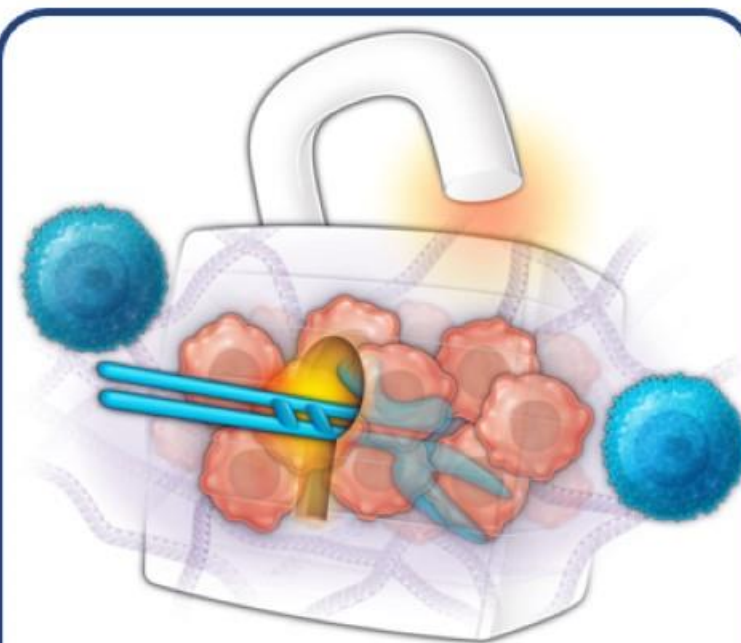
NC410: Penetrates TME and Normalizes Immune Responses

TME ACCESS LOCKED



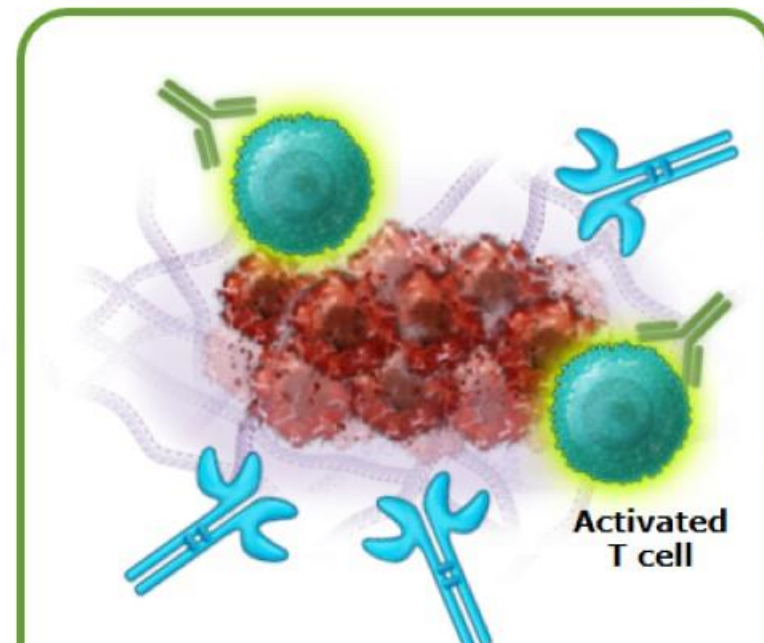
Many "keys" but none fit lock

NC410 UNLOCKS COLLAGEN BARRIER



Increased T cell infiltration

REMODELING & NORMALIZATION



Enhanced T cell tumor killing



NC410



Pembro

NC410 Phase 1 Results

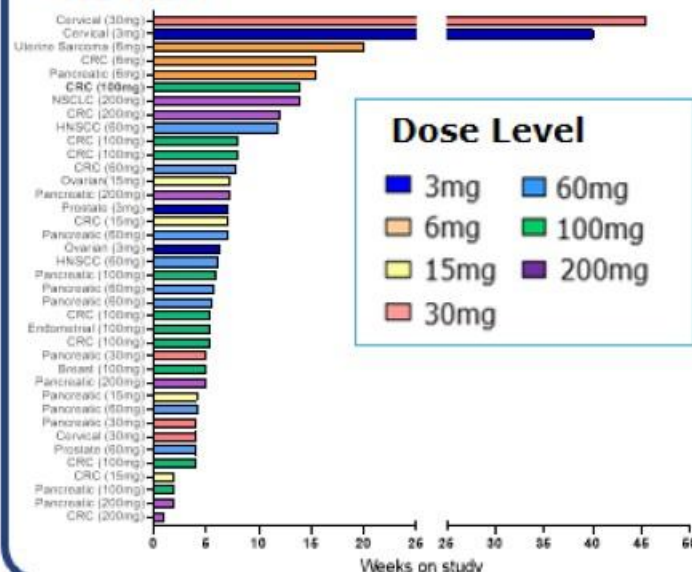
DESIGN

- 3+3 design
- 7 cohorts (3 – 200 mg)
- Dosing every 2 weeks
- Solid tumors

10 TUMOR TYPES ENROLLED TO DATE	NUMBER SUBJECTS (N=38)
Breast	n=1
Cervical	n=3
Colorectal	n=12
Endometrial	n=1
Head & Neck	n=2
NSCLC	n=1
Ovarian	n=2
Pancreatic	n=13
Prostate	n=2
Uterine sarcoma	n=1

SAFETY & EFFICACY

- No DLT
- Adverse events
 - Infusion Reactions (3): Grades 2 & 3
 - Anemia (3): Grades 2 & 3
 - Lymphopenia (1): Transient Grade 3
- Half-life: 54 hours
- No ADA



NEXT STEPS

- **Combo with Pembro**
- **Safety Run-In**
- **Phase 2:** PD-1 resistant/refractory & naive (MSS/MSI-L)* populations
- Merck supporting trial with drug supply
- Clinical POC in 2023

- *Microsatellites: short, repeated sequences of DNA
- Microsatellite instability (MSI): defect in ability to correct mistakes when DNA is copied
- Microsatellite stable (MSS) and MSI-Low tumors: do not respond to immune checkpoint inhibitors



NC410 Combo

Remodels Collagen
Enhancing Immune
Infiltration & Tumor
Killing

SUMMARY

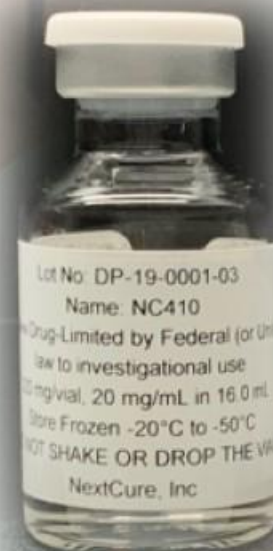
NC410 is safe and well tolerated

Binding collagen modulates and restores immune function

Combo therapy in PD-1 resistant / refractory & naive (MSS/MSI-L) populations

UPCOMING MILESTONE

Phase 1b data mid-2023



NC762

Humanized B7-H4 Monoclonal Antibody

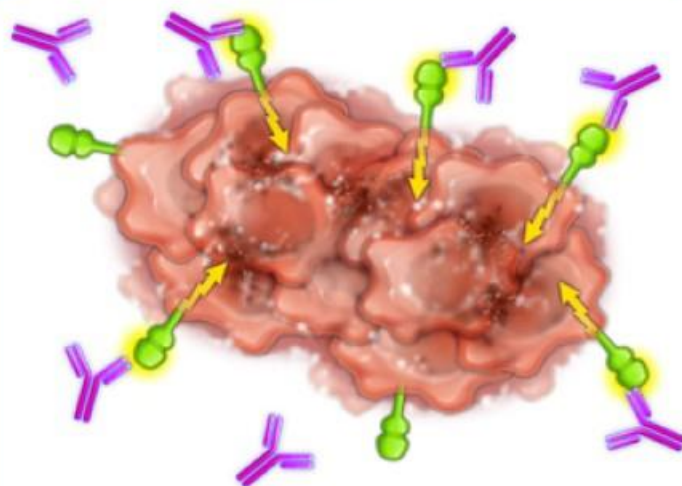


Phase 1b
CLINICAL
TRIAL

BIOLOGY

- Unique mechanism of action
- Inhibits tumor cell growth & is not dependent on T cells
- NK cells enhance anti-tumor activity

MOA



● B7-H4
Y NC762 (B7-H4 mAb)

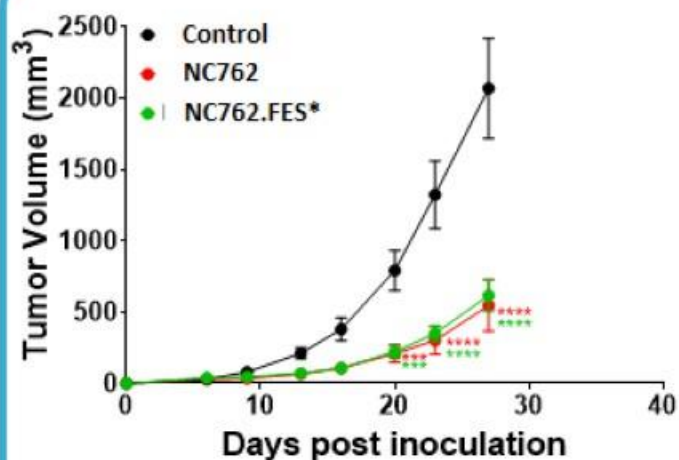
HIGHLIGHTS

- Expansion cohorts (ovarian, breast & NSCLC)
- Patient selection

NC762 Inhibits Human Melanoma Tumor Growth *In Vivo*

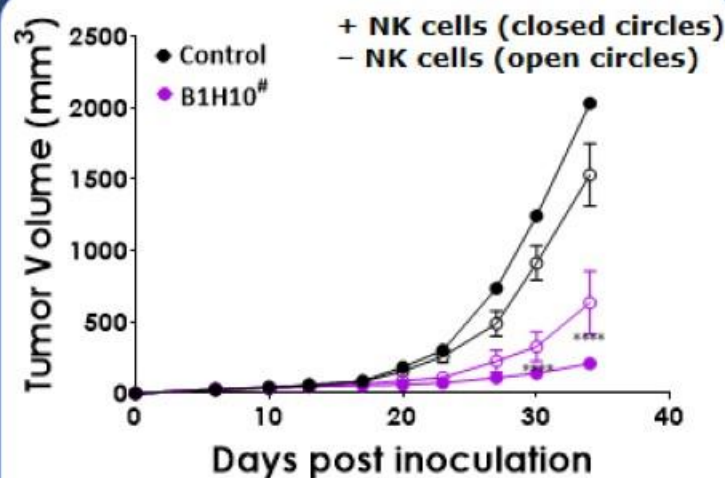
Activity Enhanced by Human PBMCs

TUMOR INHIBITION



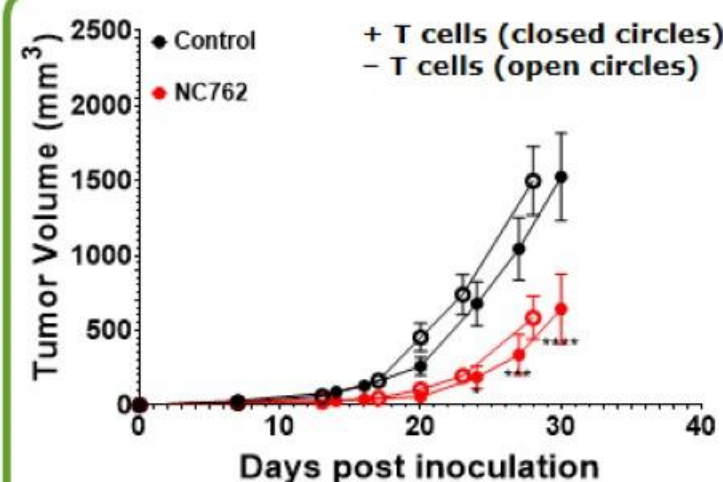
*Designed to reduce FcγR binding/restrict ADCC activity

NKs ENHANCE ACTIVITY



#Parent of NC762

T CELLS NOT REQUIRED



Archer et al., AACR 2021

NC762 Phase 1 Update

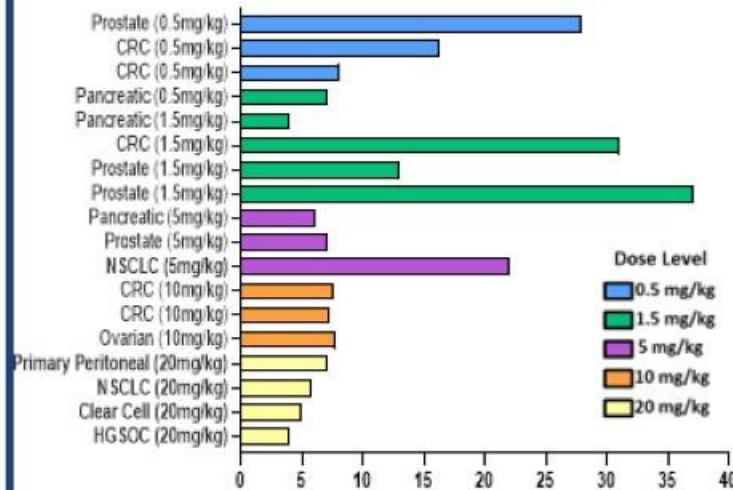
DESIGN

- 3+3 design
- 5 cohorts (0.5-20 mg/kg)
- Dosing every 2 weeks
- Solid tumors

5 TUMOR TYPES ENROLLED TO DATE	NUMBER SUBJECTS (N=18)
CRC	n=5
Lung	n=2
Ovarian	n=4
Pancreatic	n=3
Prostate	n=4

SAFETY & EFFICACY

- No DLTs through 20 mg/kg cohort



NEXT STEPS

- Dose expansion cohorts at 10 & 20 mg/kg
- Patient selection
- Indications: ovarian, breast & lung



NC762

Summary & Upcoming Milestones

SUMMARY

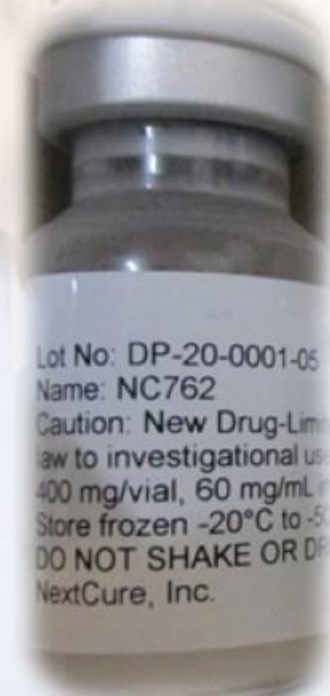
Unique MOA

- mAb inhibits tumor cell growth
- Not dependent on immune cell infiltration into TME
- NK cells enhance activity

Completed Phase 1a trial and initiated Phase 1b expansion study

UPCOMING MILESTONE

Phase 1b data Q4 2023



NC525

Humanized LAIR-1 Monoclonal Antibody



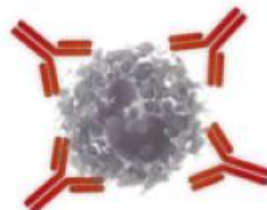
NC525
IND FILED

BIOLOGY

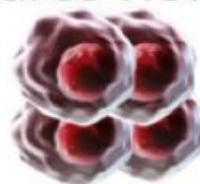
- LAIR-1 expression
 - High on AML blasts and leukemia stem cells (LSCs)
 - Minimal on hematopoietic stem and progenitor cells (HSPCs)

MOA

Kills AML Blast Cells & LSCs



Spares HSPCs



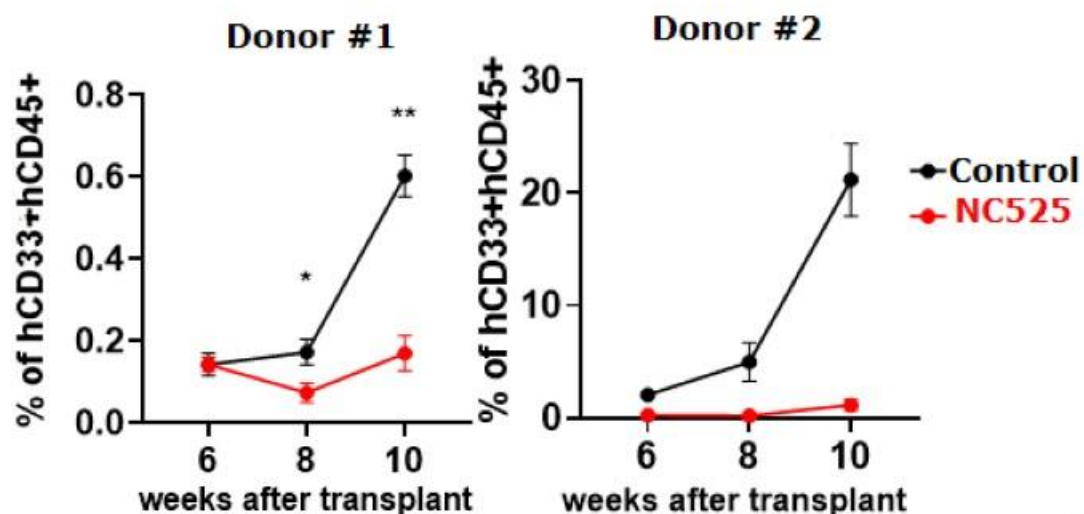
HIGHLIGHTS

- Eliminates leukemic stem cells preventing relapse
- Potential for lower incidence of neutropenia and thrombocytopenia by sparing normal blood cells

NC525 Clears Leukemia in Preclinical Model

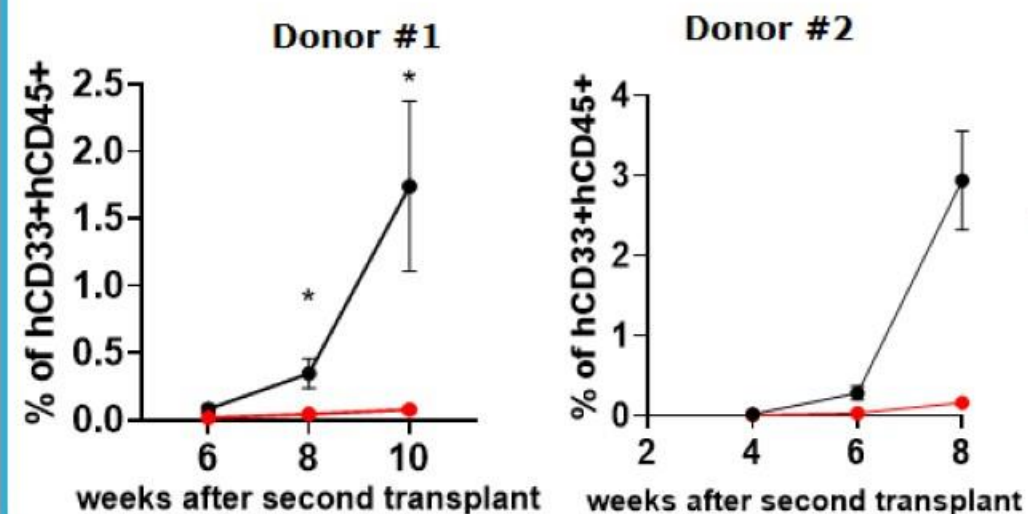
ELIMINATES LSC & CLEARS LEUKEMIA

Primary Transplant



PREVENTS PROPAGATION OF LEUKEMIA

Secondary Transplant

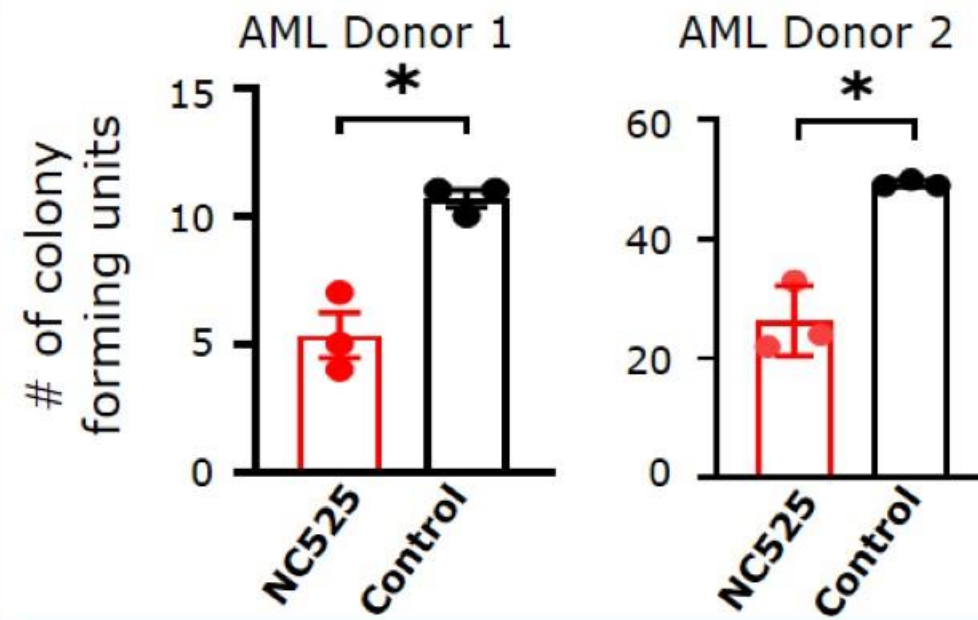


NC525 *Spare*s Healthy Blood Cells and Suppresses Leukemic Stem Cell Colony Formation

NO AFFECT ON NORMAL BLOOD CELLS



SUPPRESSES LSC COLONY FORMATION



Colony Forming Units Assay - measures the ability of hematopoietic progenitors to proliferate and differentiate into colonies in a semi-solid media in response to cytokine stimulation



NC525

First in Class Therapeutic Kills AML Cells

SUMMARY

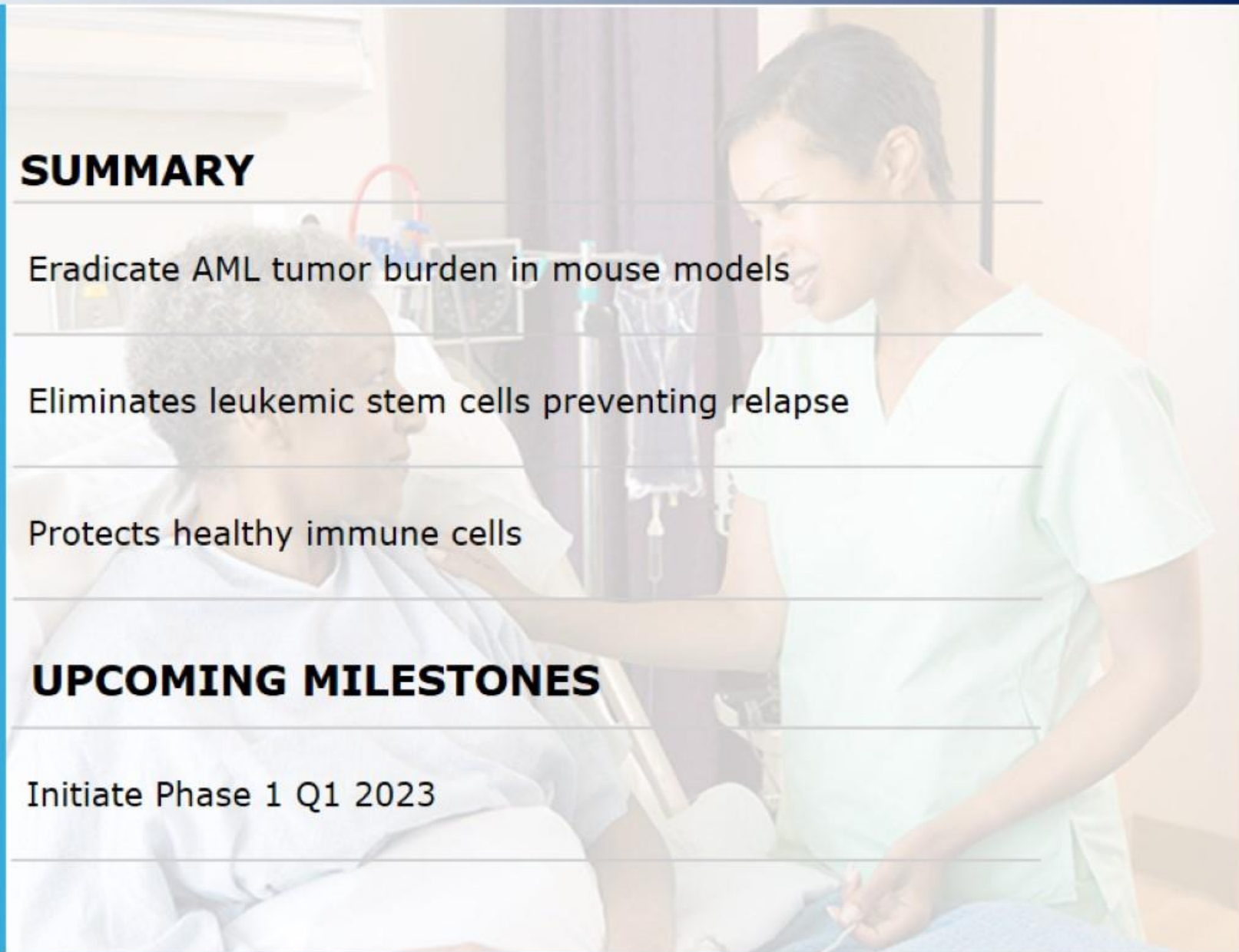
Eradicate AML tumor burden in mouse models

Eliminates leukemic stem cells preventing relapse

Protects healthy immune cells

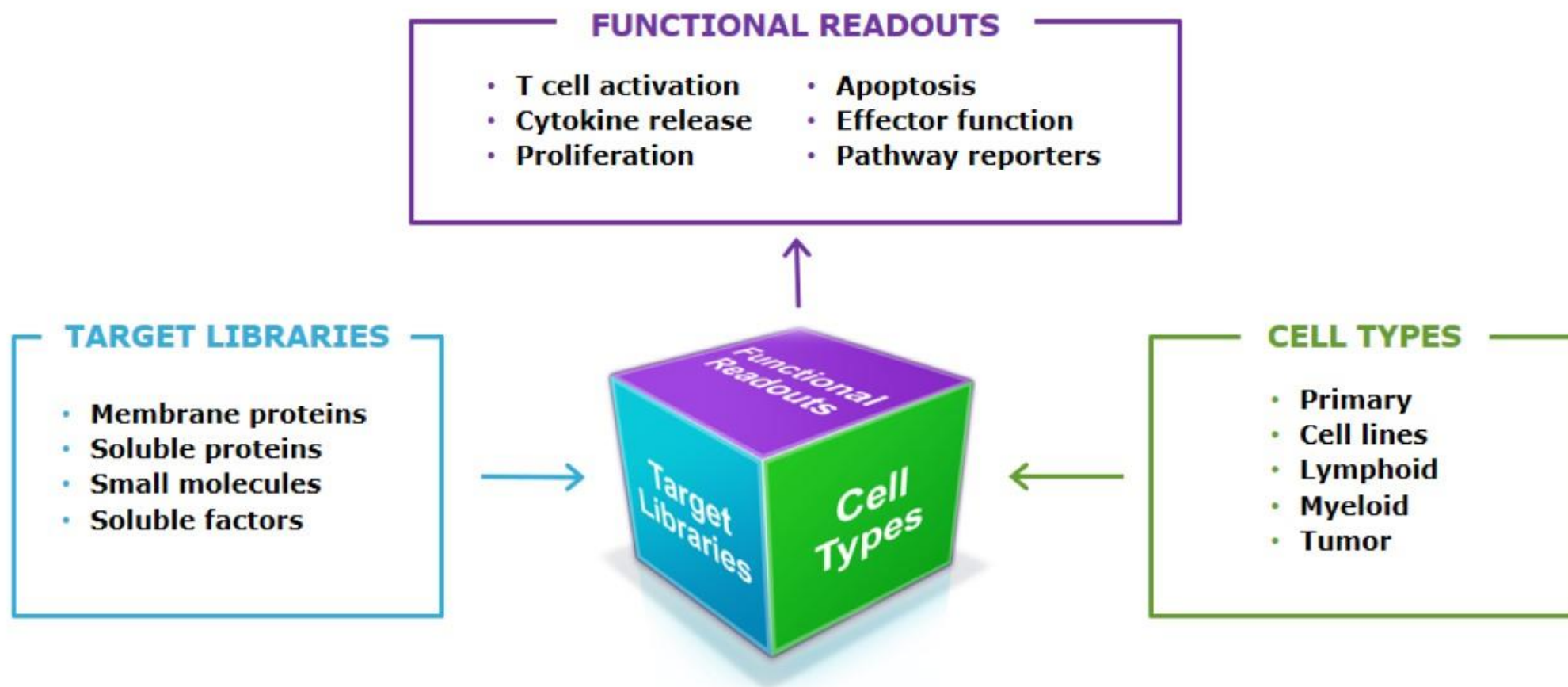
UPCOMING MILESTONES

Initiate Phase 1 Q1 2023



Finding Solutions with a Powerful Discovery Engine

Functional, Integrated, NextCure Discovery in Immuno-Oncology



GMP Manufacturing Facility: Added Additional Capacity

2,000L Capacity



Speed

Use of a CMO adds ~8 months to timelines

Flexibility

Prioritization and scheduling

Efficiency

Operational and capital efficiency

Quality

Controlling quality with experienced team

Utilized to Produce Clinical Material for All Lead Programs

Advancing Product Candidate Pipeline

PROGRAMS	TARGET	CELLS	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT MILESTONE
PRODUCT CANDIDATES								
NC410 COMBO	LAIR-2	Extracellular Matrix	CRC, ESOPHAGEAL, ENDOMETRIAL, H&N, OVARIAN					Phase 1b Data Mid-2023
NC762	B7-H4	Tumor Cells	OVARIAN, BREAST, NSCLC					Phase 1b Data Q4 2023
NC525	LAIR-1	Leukemia	LEUKEMIA (AML)					Trial Initiation Q1 2023
RESEARCH PROGRAMS								
Multiple Programs	Multiple Targets	Multiple Cells Types						

Worldwide Rights to All Programs



Momentum & Milestones

ON TRACK

NC410, NC762, NC525

MOMENTUM

Building Pipeline

TEAM

Experienced

Mid-2025

Runway

