NASDAQ: NXTC

NextCure

Treating Cancer by Restoring Immune Function

22nd Annual Needham Virtual Healthcare Conference
April 19, 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 trials of NC410, NC762 and NC525, expectations regarding the potential benefits, activity, effectiveness and safety of NC410, NC762 and 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.

The NextCure Opportunity

DIFFERENTIATED PIPELINE

Multiple clinical programs, novel targets and diverse indications

NEAR TERM VALUE CREATION

Multiple milestones in 2023

CAPITAL EFFICIENCY

$159.9M balance sheet, runway into mid-2025

QUALITY PRODUCT DEVELOPMENT

Fully integrated operations drive innovation, internal manufacturing and capital efficiency

Developing First-in-Class Immunomedicines to Treat Cancer

CLINICAL STAGE COMPANY
Strong Pipeline With Differentiated Mechanism of Actions

	**NC410 Combo** Phase 1b/2	LAIR-2	**Overcoming tumor resistance** by remodeling ECM
	**NC762** Phase 1b	B7-H4	**Inhibiting tumor growth** independent of immune cells
	**NC525** Phase 1	LAIR-1	**Specifically kills leukemia** stem cells

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How Are We Improving Cancer Treatment?

CANCER

UNDERSTANDING Tumor Biology

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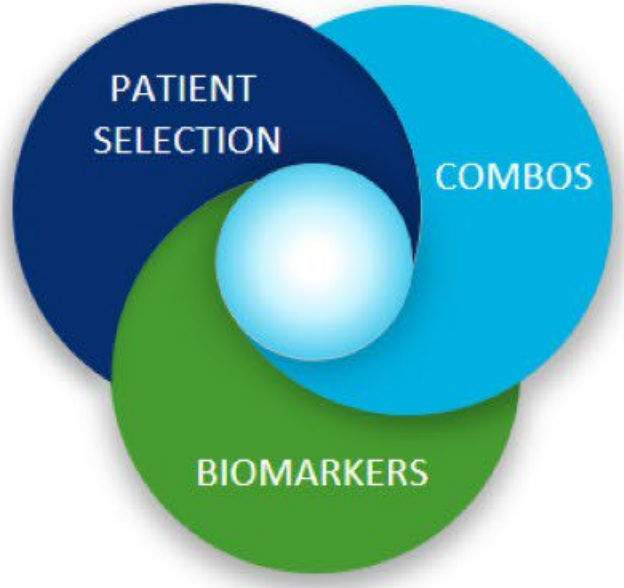
FOCUSED Product Development



MOA – mechanism of action; ECM – extracellular matrix; TME – tumor microenvironment

Advancing Product Development 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 Update Mid-2023
NC762	B7-H4	Tumor Cells	OVARIAN, BREAST, NSCLC					Phase 1b Update Q4 2023
NC525	LAIR-1	Leukemia	ACUTE MYELOID LEUKEMIA					Phase 1a Update Q4 2023
RESEARCH PROGRAMS								
Multiple Programs	Multiple Targets	Multiple Cell Types						

Partnering Optionality and Value Creation

MID-2023

PHASE 1b UPDATE

NC410

Overcoming tumor resistance by remodeling the extracellular matrix (ECM) to enhance T cell infiltration and tumor killing

COMPLETED

Phase 1a Dose Escalation & Safety

- ✓ Monotherapy
- ✓ Safe and well tolerated
- ✓ No anti-drug antibodies
- ✓ No dose-limiting toxicity

INITIATED

Phase 1b/2 NC410 + Pembro

- Combo therapy
- Immune checkpoint refractory or naïve solid tumors

TARGETING THE ECM

CRC	Esophageal	Endometrial	Head and Neck	Ovarian

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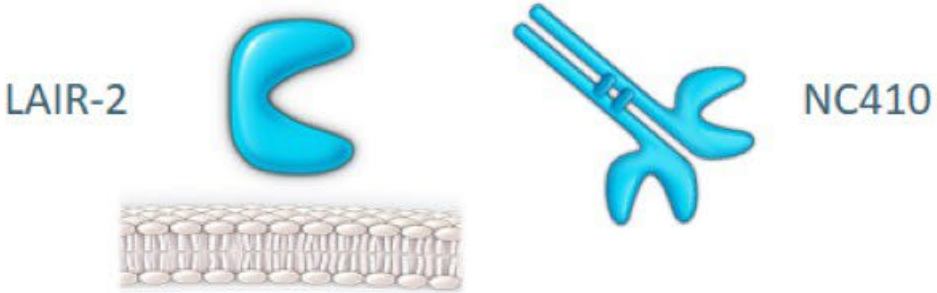
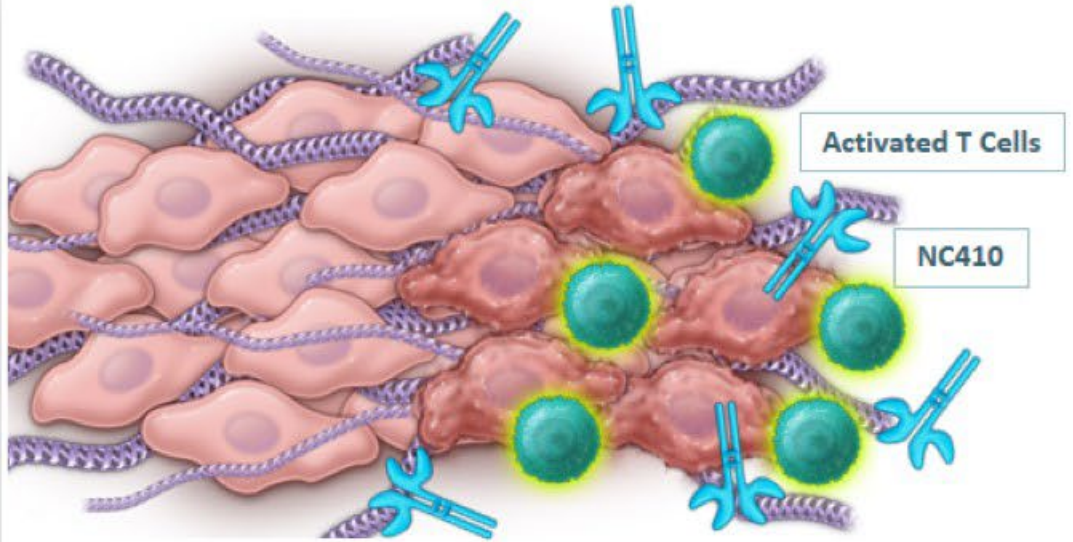
NC410: Fusion Protein and Biomimic for LAIR-2

NC410 RECOGNIZES COLLAGEN



Natural decoy
and immune modulator

NC410 ALLEVIATES IMMUNOSUPPRESSION



Remodels collagen to
increase T cell infiltration

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NC410 Phase 1a Monotherapy Dose Escalation and Safety Study

PHASE 1A – COMPLETE

DESIGN

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

SAFETY

- Safe and well tolerated
- No dose-limiting toxicity
- No anti-drug antibodies

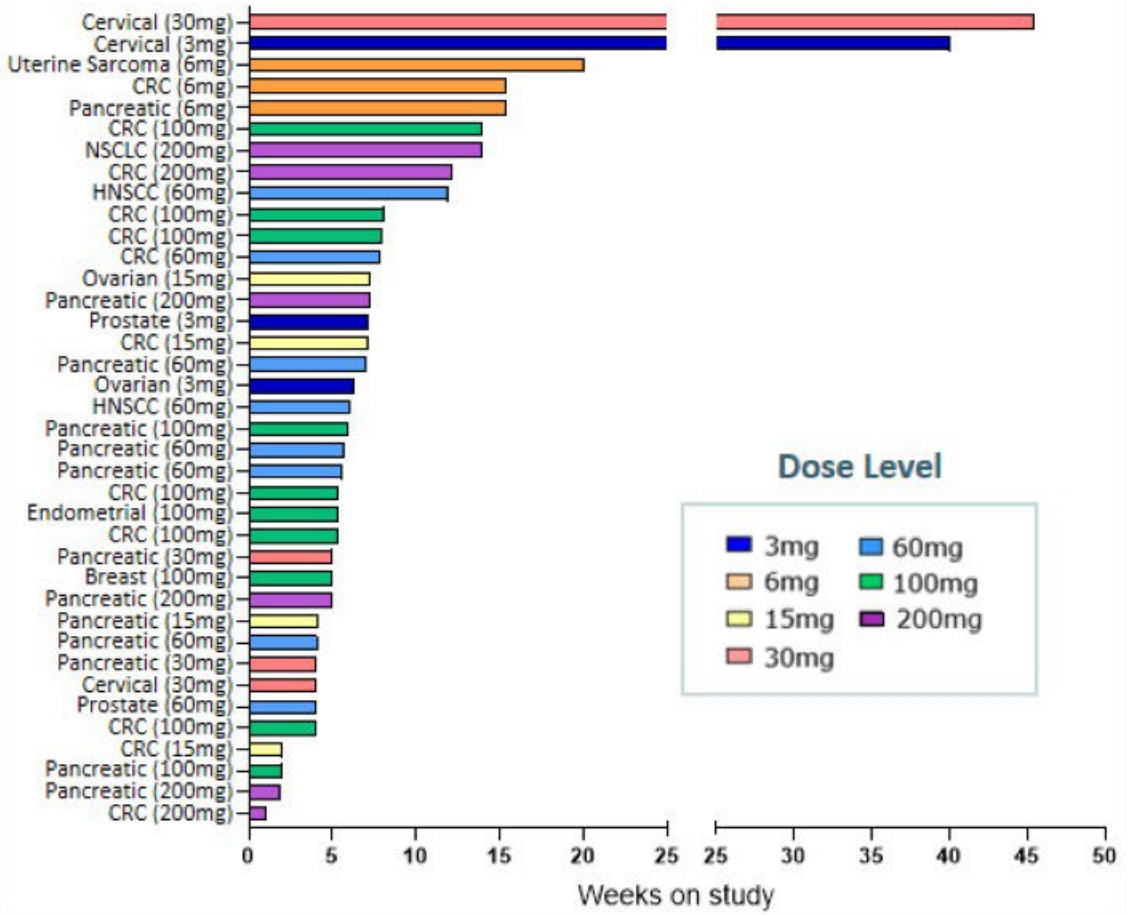
METRICS

- Treated 41 patients
- 10 tumor types

RESULTS

- Best responses stable disease (22%) >12 weeks
- Collagen derived products supporting mechanism of ECM remodeling
- Expansion of T cells demonstrating immune activation
- Selected Phase 2 doses (30 & 60 mg)

SWIMLANE PLOT



Christenson et al., SITC 2022

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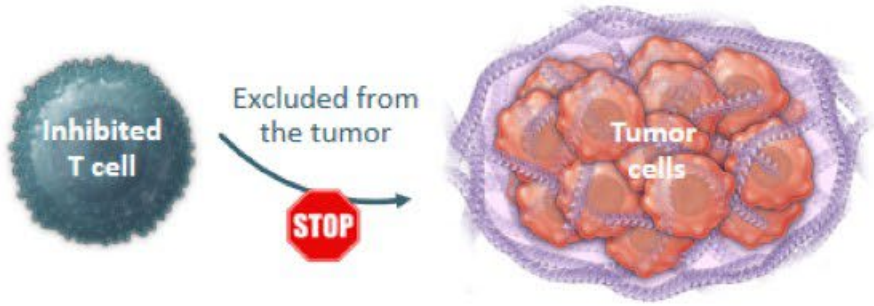
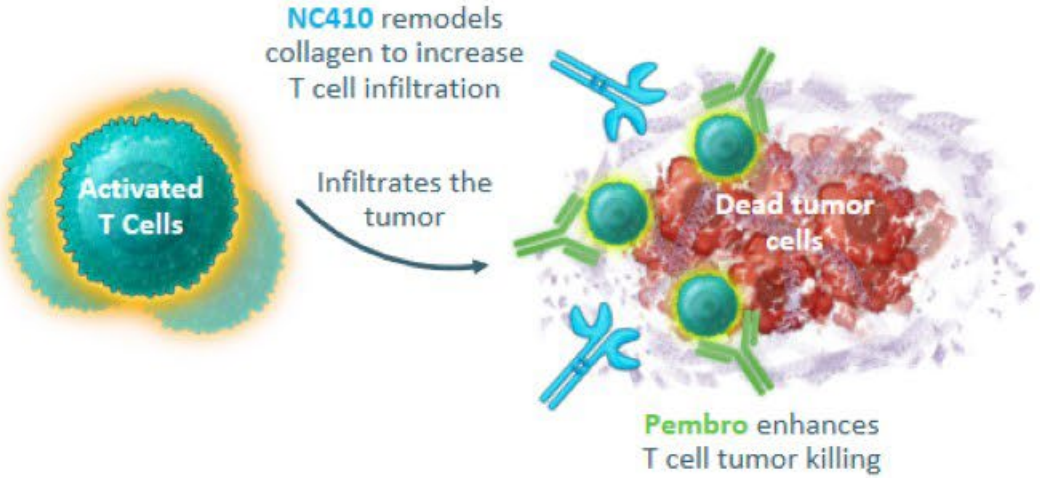
NC410 + Pembro Combo: A Synergistic Approach to Breaking the Collagen Barrier and Restoring Anti-Tumor Activity

COLLAGEN BUILDUP AND DENSITY LEAD TO RESISTANCE



Tumor cells proliferate and become resistant

NC410 COMBO REMODELING RESTORES NORMAL IMMUNE FUNCTION



T cells infiltrate and kill the tumor

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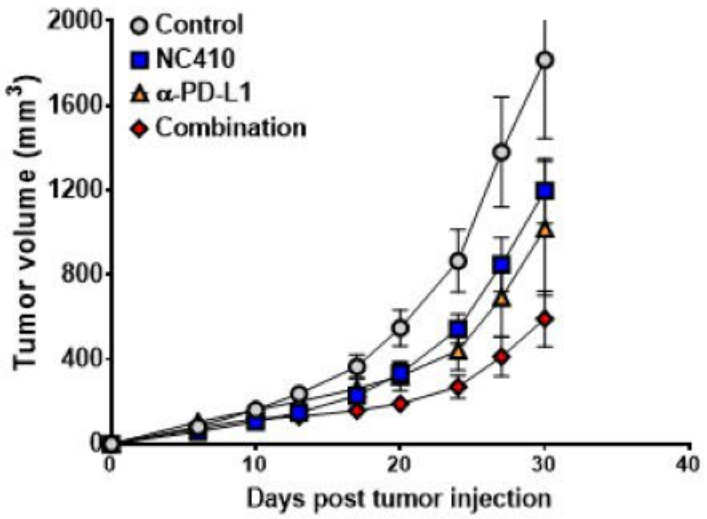
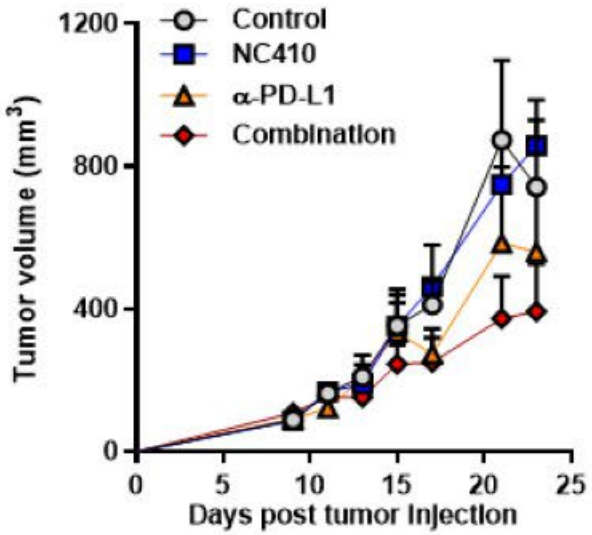
NC410 + Anti-PD-L1 Results in Reproducible Tumor Killing in Murine Models

NEXTCURE



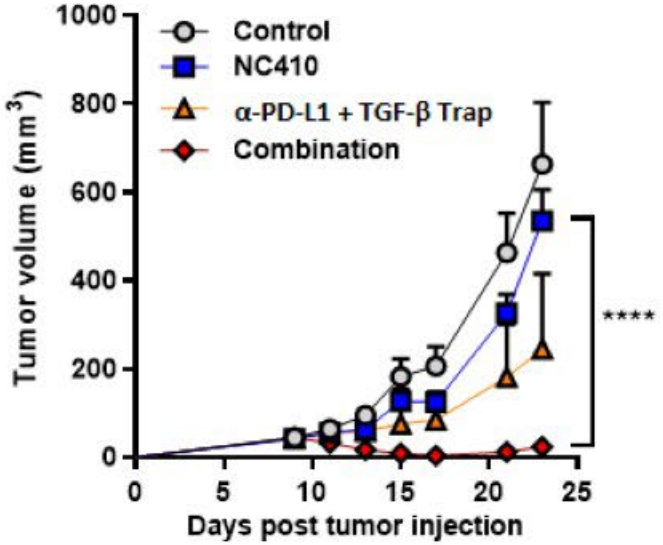
NC410 at 200ug Q4D for 5 doses and/or PD-L1 at 100ug Q7D for 2 doses

UTRECHT COLLABORATION



NC410 at 200ug and/or PD-L1 at 200ug twice a week for three weeks

NCI COLLABORATION



Horn et al., SITC 2020
Horn et al., JCI 2022

NC410 at 250ug and/or PD-L1 + TGF-B trap at 492ug on days 9, 11 and 13

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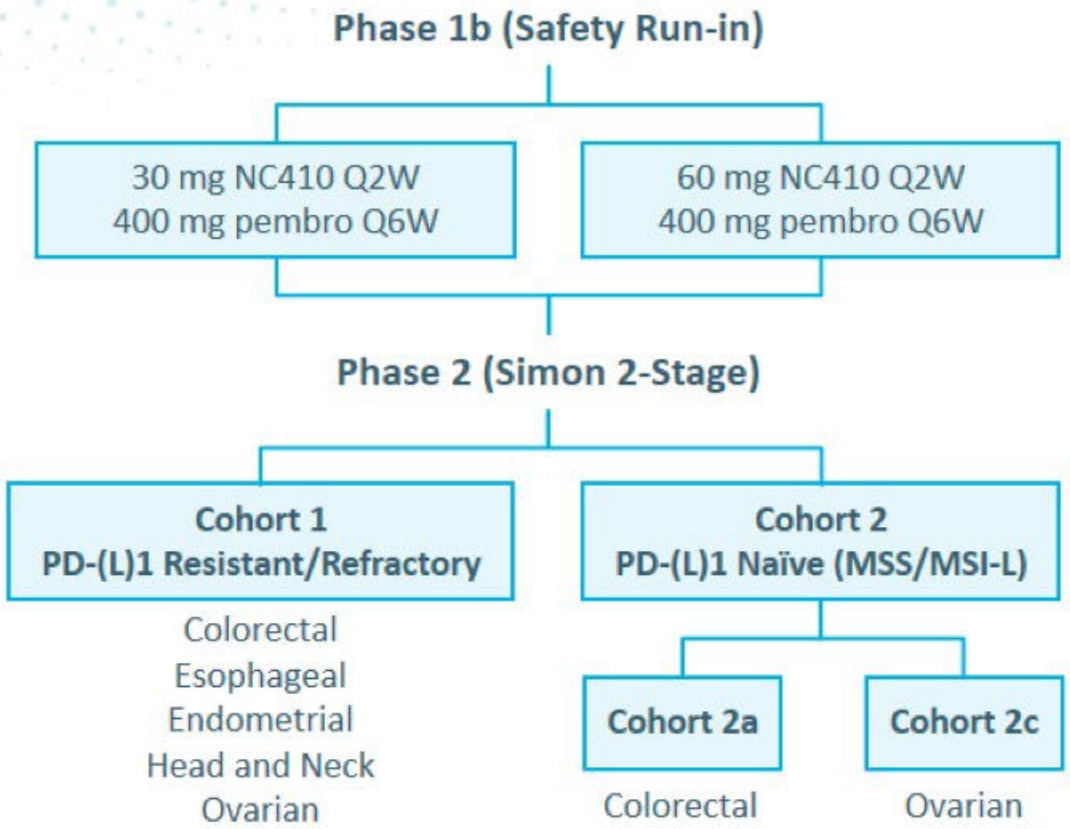
Phase 1b/2 NC410 + Pembro Combo Study – Ongoing

TRIAL DESIGN



BIOMARKERS

TUMOR BIOPSIES

PRE-DOSE

- LAIR
- Collagen
- PD-L1
- MSS/MSI status

WEEK 8

- Collagen degradation
- Immune cell infiltration

PERIPHERAL BLOOD

- Collagen derived products
- Cytokines & chemokines
- Immunophenotyping
- Soluble factors

MSS – microsatellite stable; MSI-L – microsatellite instable, low

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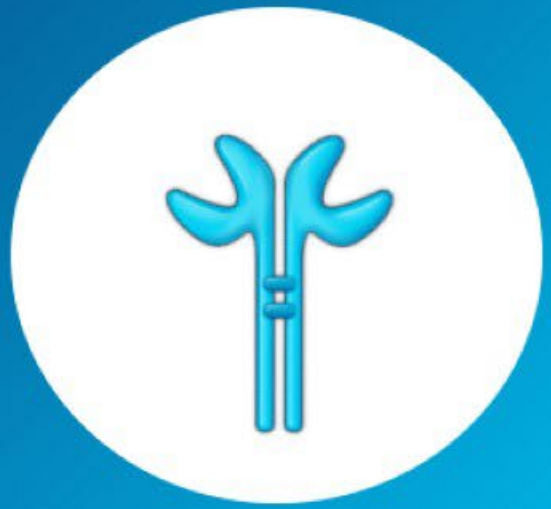
NC410 Summary



Significant Momentum, Continued Progress

COMPLETED

- ✓ Phase 1a monotherapy dose escalation & safety
- ✓ N = 41 patients; 10 tumor types;
  7 dose cohorts: 3 – 200 mg
- ✓ Safe & tolerated; Responses: 22% SD
- ✓ RP2D (30 & 60 mg)

ONGOING & NEXT STEPS

- Phase 1b/2 NC410 + pembro combo initiated
- ICI refractory and naïve
- Biomarkers
- **Phase 1b update mid-2023**

Q4 2023

PHASE 1b UPDATE

NC762

Monoclonal antibody that inhibits tumor cell growth independent of immune cell infiltration into tumor microenvironment (TME)

COMPLETED

Phase 1a Dose Escalation & Safety

- ✓ Monotherapy
- ✓ Safe and well tolerated
- ✓ No anti-drug antibodies
- ✓ No dose-limiting toxicity

INITIATED

Phase 1b Dose Expansion

- Monotherapy
- Dose expansion cohorts at 10 and 20 mg/kg

TARGETING TUMOR CELLS

Ovarian	Breast	NSCLC

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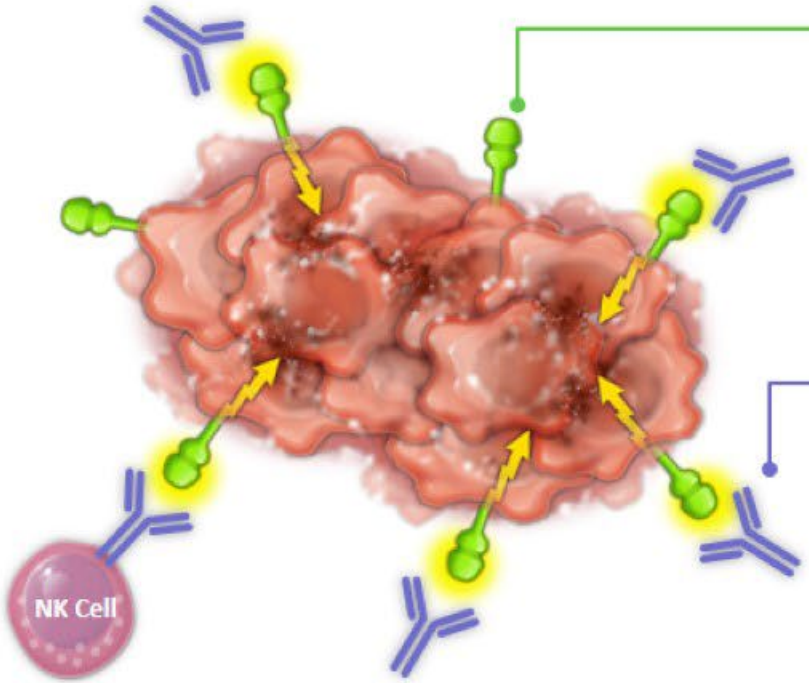
NC762 Targets B7-H4 Positive Tumors



B7-H4

- Transmembrane protein commonly expressed by several tumor types
- Correlated with poor clinical outcomes

NC762

- Unique mechanism of action
- Inhibits tumor cell growth and is not dependent on T cells
- Natural Killer (NK) cells enhance anti-tumor activity

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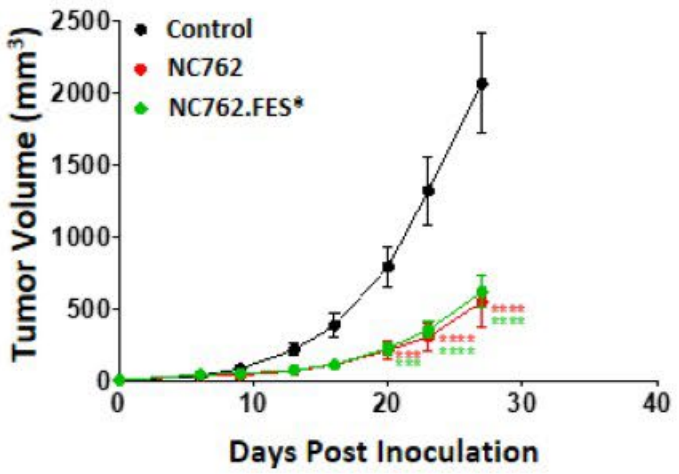
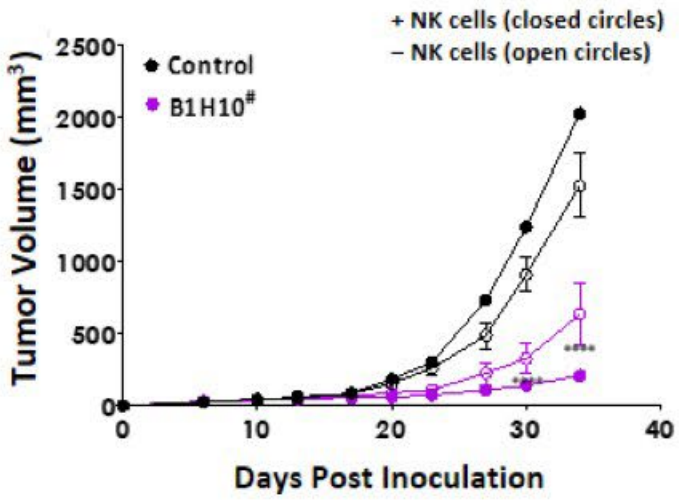
NC762 Inhibits Human Tumor Growth *In Vivo*

TUMOR INHIBITION



NC762 at 200ug starting on day 3
Q7D for 4 doses

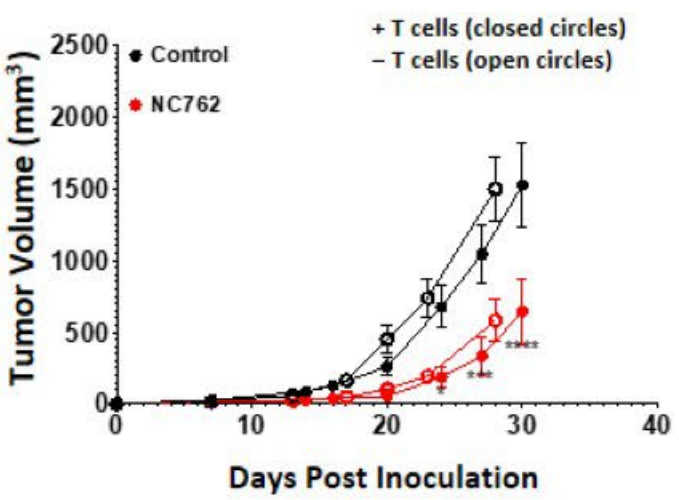
NKs ENHANCE ACTIVITY



#Parent of NC762

B1H10 at 200ug starting on day 3
Q7D for 4 doses

T CELLS NOT REQUIRED



NC762 at 200ug starting on day 3
Q7D for 4 doses

Archer et al., AACR 2021

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NC762 Phase 1a Monotherapy Dose Escalation & Safety Study

PHASE 1A – COMPLETE

DESIGN

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

METRICS

- Treated 18 patients
- 5 tumor types

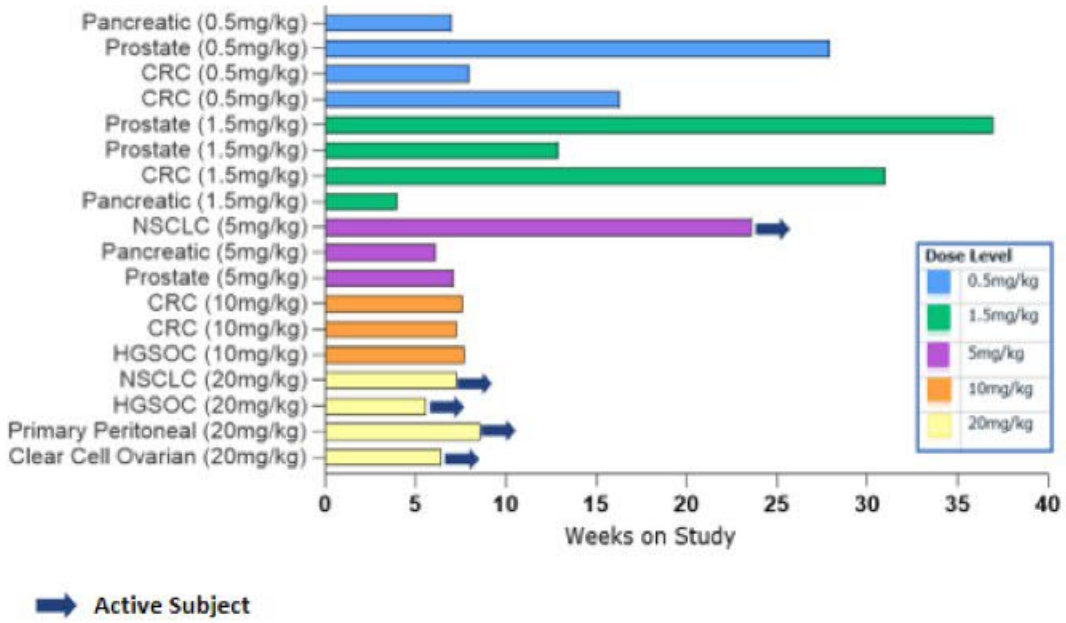
SAFETY

- Safe and well tolerated
- No dose-limiting toxicity
- No anti-drug antibodies

RESULTS

- Best responses stable disease (33%) >12 weeks
- Increases in cytokines and chemokines were observed 24 hours post treatment
- Early signs of immune activation and modulating NK cell activity
- Selected Phase 2 doses (10 & 20 mg)

SWIMLANE PLOT



Zsiros et al., SITC 2022

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NC762 Phase 1b Monotherapy Dose Expansion

TRIAL DESIGN

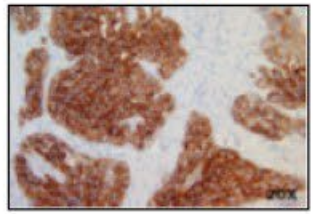
Phase 1b
NC762 (10 & 20 mg/kg, Q2W)

- Ovarian
- Breast
- NSCLC

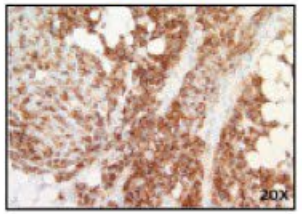
PATIENT SELECTION

- CLIA validated immunohistochemical (IHC) assay
- High expression of B7-H4

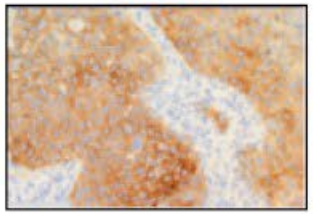
Ovarian



Breast



NSCLC



BIOMARKERS

TUMOR BIOPSIES

PRE-DOSE

- B7-H4
- PD-L1

WEEK 8

- Immune cell infiltration
- B7-H4
- PD-L1

PERIPHERAL BLOOD

- Cytokines & chemokines
- Immunophenotyping
- Soluble factors (B7-H4, PD-L1, others)

NC762 Summary

Significant Momentum, Continued Progress

COMPLETED

- ✓ Phase 1a monotherapy dose escalation & safety
- ✓ N = 18 patients; 5 tumor types
- ✓ 5 dose cohorts: 0.5 – 20 mg/kg
- ✓ Safe & tolerated; Responses: 33% SD
- ✓ RP2D (10 & 20 mg/kg)

ONGOING & NEXT STEPS

- Phase 1b monotherapy dose expansion initiated
- B7-H4+ patient selection
- Biomarkers
- **Phase 1b update Q4 2023**

Q4 2023

PHASE 1a UPDATE

NC525

Killing leukemic stem cells while preserving healthy immune cells

COMPLETED

Investigational New Drug (IND) Application

- ✓ Clearance to proceed with Phase 1 trial
- ✓ Initiated clinical trial Q1 2023

ONGOING

Phase 1a Dose Escalation & Safety

- Monotherapy
- AML; 5 cohorts: 2 – 30 mg/kg

TARGETING LAIR-1

Leukemia (AML)

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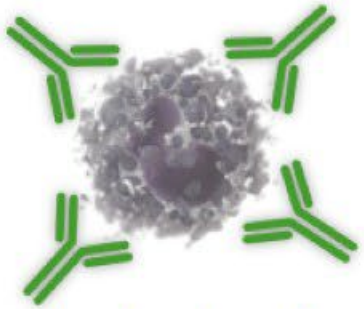
NC525 Delivers the Best of Both Worlds

AML

NC525

Targets LAIR-1, which is essential for AML development and cell survival

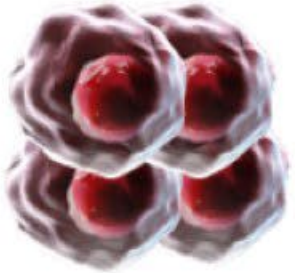
ELIMINATES



Leukemia cells and leukemia stem cells (LSC)

Prevents relapse due to chemotherapy resistant LSCs

SPARES

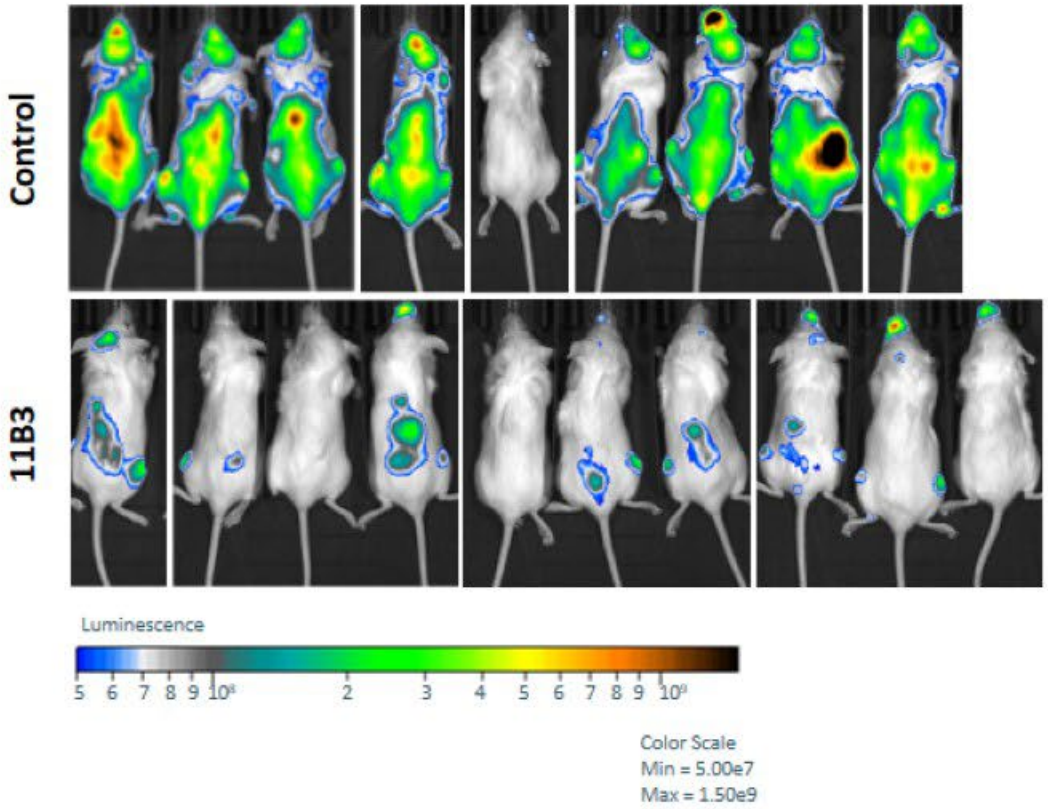


Normal hematopoietic stem and progenitor cells (HSPCs)

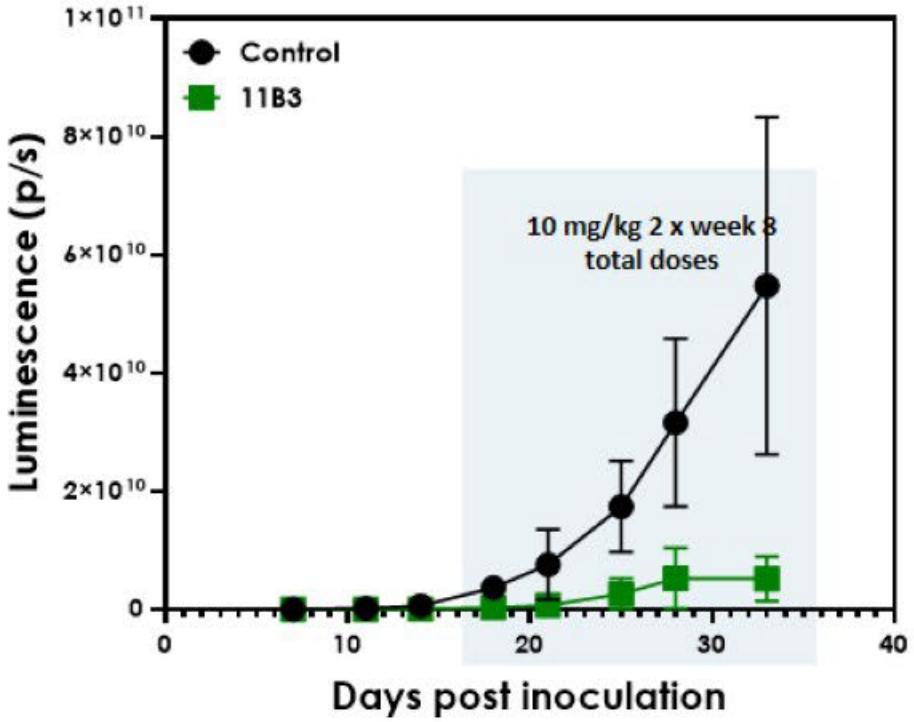
Potential for improved safety with lower incidence of neutropenia and thrombocytopenia

LAIR-1 Antibody 11B3* Reduces Tumor Burden in Murine Leukemia Model

FULL BODY LUMINESCENCE (DAY 33)



LUMINESCENCE MEASUREMENTS



*11B3: NC525 Murine Parent

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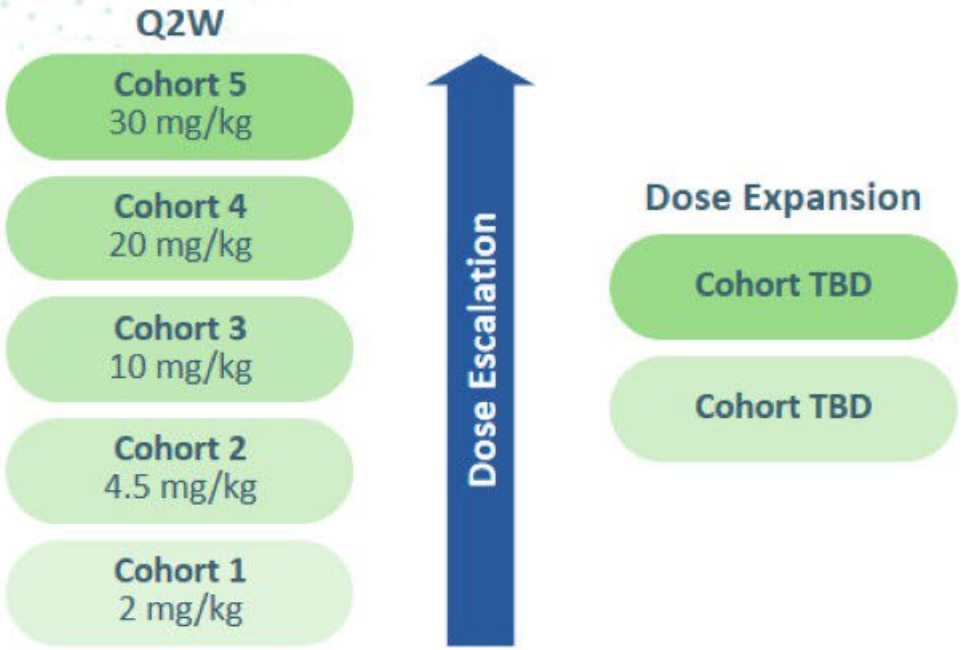
NC525 Phase 1 Monotherapy Dose Escalation and Safety Study Plans

TRIAL DESIGN



PATIENT SELECTION

Acute myeloid leukemia (AML)
(<25,000 white blood cells)

BIOMARKERS

BIOPSIES

- Bone marrow blast clearance
- LAIR-1 expression on blasts correlated with responses
- Effects on LSCs and HSPCs

PERIPHERAL BLOOD

- Blast clearance & normal blood cell recovery
- Cytokines & chemokines
- Immunophenotyping
- Soluble factors (LAIR-1)

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NC525 Summary

Significant Momentum, Continued Progress

COMPLETED

- ✓ Pre-clinical research
- ✓ Submitted & cleared IND
- ✓ Initiated clinical trial

ONGOING & NEXT STEPS

- Phase 1 monotherapy dose escalation & safety
- AML; 5 cohorts: 2 – 30 mg/kg
- Biomarkers
- **Phase 1a update Q4 2023**

Powerful, Proven, and Productive Discovery Engine Fuels Our Pipeline Growth

Functional, Integrated, NextCure Discovery in Immuno-Oncology

FIND-IO

TARGET LIBRARIES

- Membrane proteins
- Soluble proteins
- Small molecules
- Soluble factors

CELL TYPES

- Primary
- Cell lines
- Lymphoid
- Myeloid
- Tumor

FUNCTIONAL READOUTS

- T cell activation
- Cytokine release
- Proliferation
- Apoptosis
- Effector function
- Pathway reporters

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Integrated Development Capabilities Are Major Advantages

- R&D labs
- Vivarium
- Antibody generation
- GLP clinical testing lab
- Biomarker lab
- GMP manufacturing
- Environmental testing lab
- Supply chain warehouse

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CREATIVE APPROACHES

+

CLINICAL DEVELOPMENT

+

CAPITAL EFFICIENCY

+

CAPABILITIES

2,000L Capacity

Produces clinical material for all programs

High Quality GMP Clinical Supply Manufacturing Provides Many Advantages

SPEED

Saves ~8 months on timelines vs. CDMO

FLEXIBILITY

Prioritization and scheduling

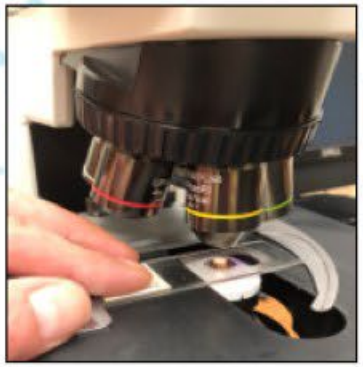
EFFICIENCY

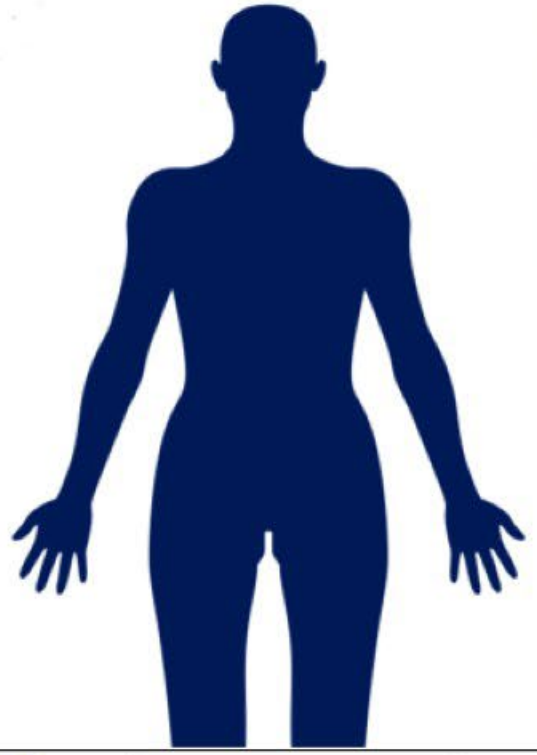
Operational and capital efficiency

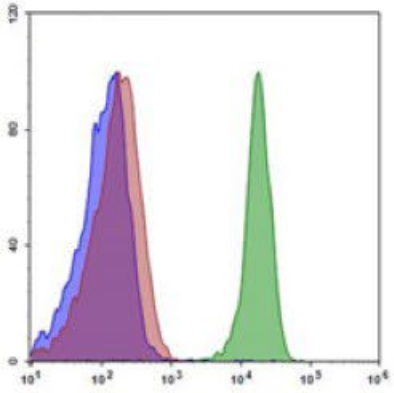
QUALITY

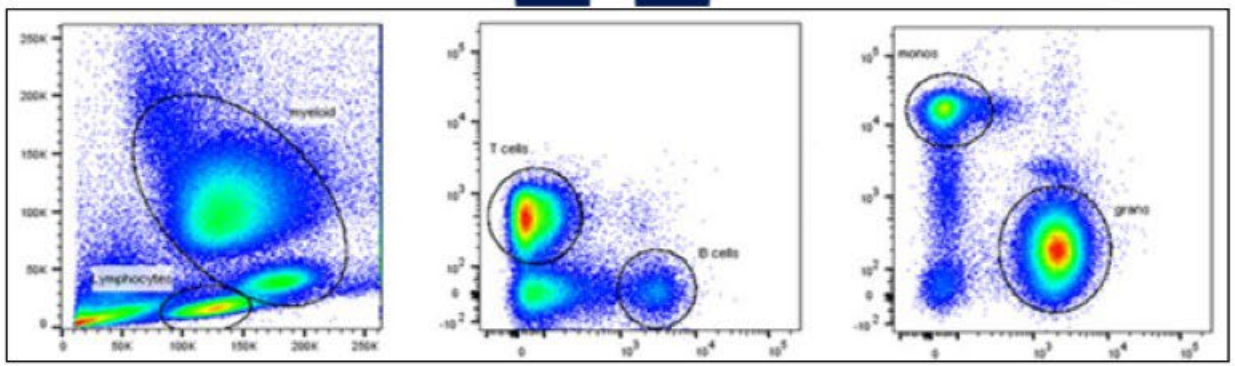
Controlling quality with experienced team

Biomarkers









VALUE

- Real-time feedback to clinicians
- MOA/POC
- Clinical response correlations
- Patient selection

CAPABILITIES

- Critical reagents
- Assay development & validation
- Analytics
- GLP lab

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Multiple Collaborations Will Drive Continued Growth

COLLABORATIONS

MERCK

- NC410 + pembro combo
- Supply arrangement

LCB LegoChemBio

- B7-H4 ADC + additional target options
- Co-development and co-commercialization

FUTURE PARTNERSHIPS

3 clinical candidates

Multiple pre-clinical programs

Flexibility and optionality

3 Clinical Candidates and Strong Balance Sheet

MULTIPLE NEAR-TERM MILESTONES IN 2023

	Q1	Q2	Q3	Q4
NC410 Combo		Phase 1b update		
NC762				Phase 1b update
NC525	Phase 1 initiated			Phase 1a update

FINANCIAL POSITION

BALANCE SHEET	RUNWAY	CAP STRUCTURE
Strong Cash Position	Significant Momentum	No Debt or Warrants
$159.9M as of Q4 2022	Mid-2025	27.75M Outstanding

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Treating Cancer by Restoring Immune Activity

3 First-in-Class Clinical Candidates

DIFFERENTIATED	CONTINUED	NEAR TERM	CAPITAL	HIGH QUALITY
pipeline	momentum	value creation	efficiency	infrastructure