



# Next Generation Immunomedicines

August 2022

# 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 NC318, expectations regarding the potential benefits, activity, effectiveness and safety of NC318, expectations regarding the investigator initiated trial conducted by Yale, the expected timing of results of NextCure's ongoing clinical trial of NC410, the development plans for NC762, 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

NC318 (S15)



Phase 2

NC410 (LAIR-2)



Phase 1

NC762 (B7-H4)



Phase 1

NC525 (LAIR-1)



IND Q4 2022

## PIPELINE

*Progress*

- NC318 (S15): Phase 2 monotherapy & combo therapy
- NC410 (LAIR-2): Phase 1 monotherapy
- NC762 (B7-H4): Phase 1 monotherapy
- NC525 (LAIR-1): IND Q4 2022

## PRODUCT

*Strategy*

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

## PEOPLE

*Experience*

- Experienced team
- Fully integrated GMP manufacturing team



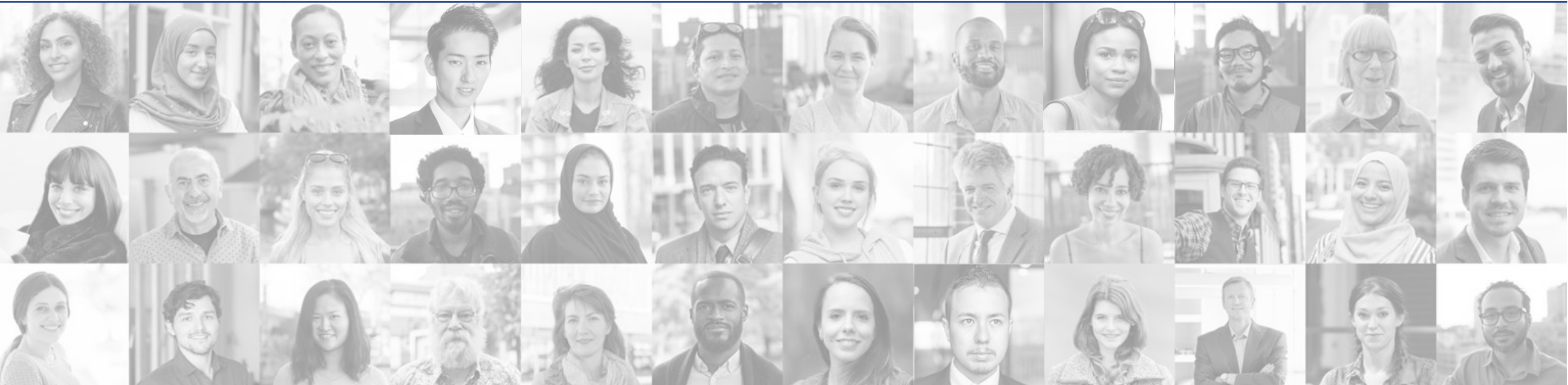
## Significant Momentum & Milestones in 2022

**NC318, NC410, NC762**  
On Track





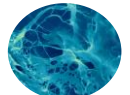




**BUILDING PIPELINE**  
Momentum

**EXPERIENCED**  
Team

**RUNWAY**  
Q1 2024



# Advancing Product Development Pipeline

PROGRAMS	TARGET	CELLS	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT MILESTONE
PRODUCT CANDIDATES								
NC318	S15	 	Tumors and macrophages	NSCLC, BREAST, H&N				Phase 2 update Q4 2022
NC318 Anti-PD-1 Combo*	S15	 	Tumors and macrophages	NSCLC				Initial Data 2H 2022
NC410	LAIR-2		ECM	NSCLC, H&N, GASTRIC, CRC, CERVICAL				Phase 1 update 2H 2022
NC762	B7-H4		Tumors	NSCLC, BREAST, OVARIAN				Initial Phase 1 data 2H 2022
NC525	LAIR-1		Leukemic Stem Cells	AML				IND filing Q4 2022
DISCOVERY AND RESEARCH PROGRAMS								
Multiple Programs	Multiple Targets	 	Multiple cell types					IND filing in 2023
*Investigator-initiated (IIT) trial (Yale University)								

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**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**

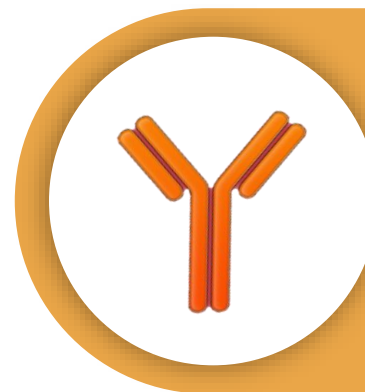


**Combos**

**Biomarkers**

# NC318

Humanized Siglec-15 (S15) Monoclonal Antibody

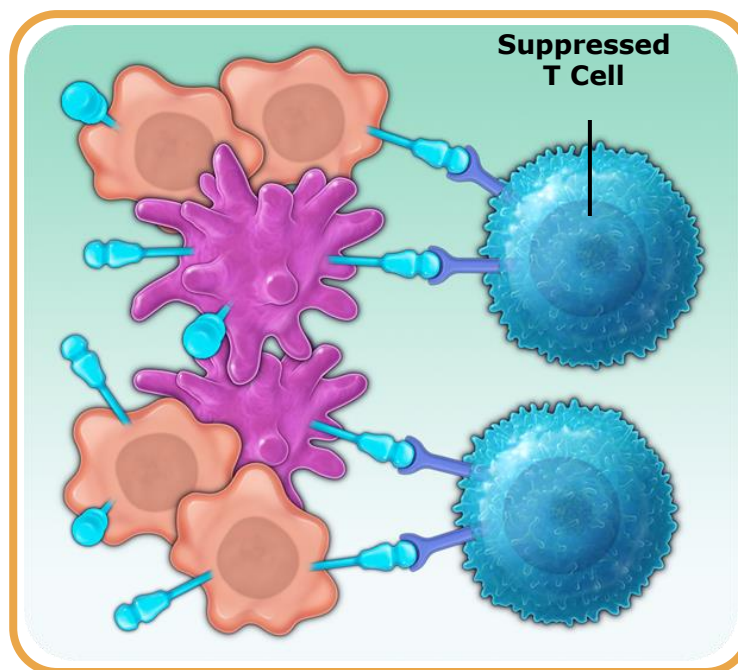


Phase 2  
CLINICAL  
TRIALS

## BIOLOGY

- Decreases suppressive myeloid cells & pro-tumorigenic cytokines
- Promotes T cell function & IFN- $\gamma$  production

## MOA

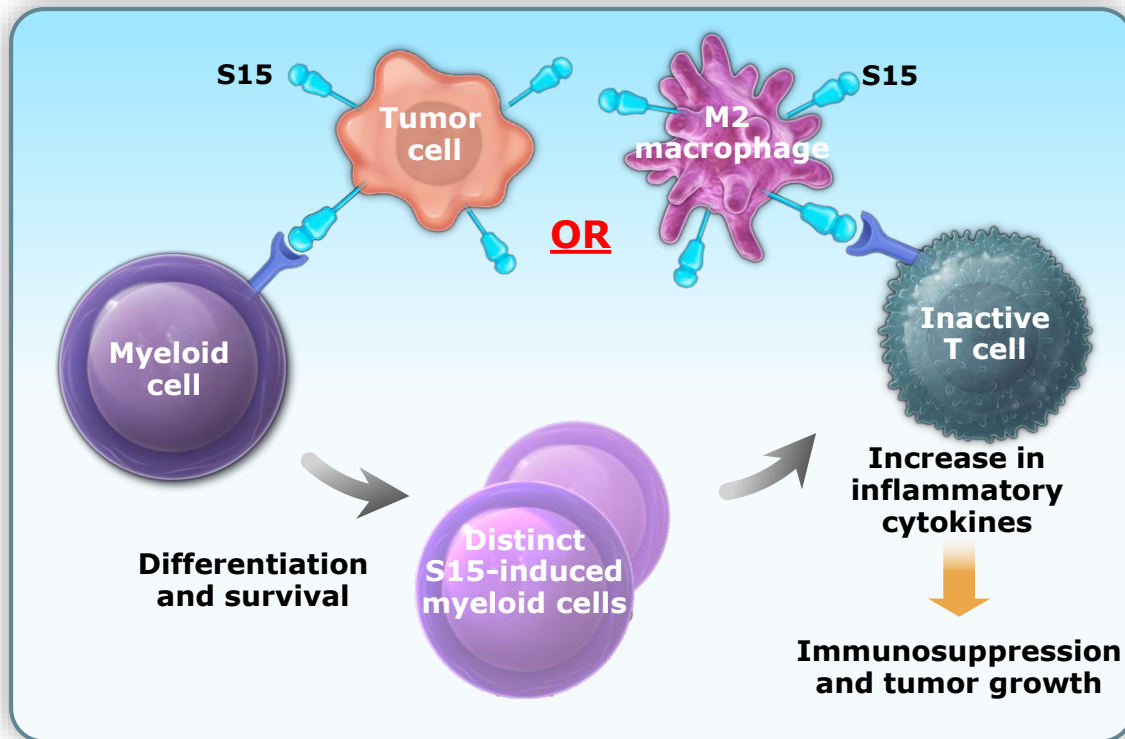


## HIGHLIGHTS

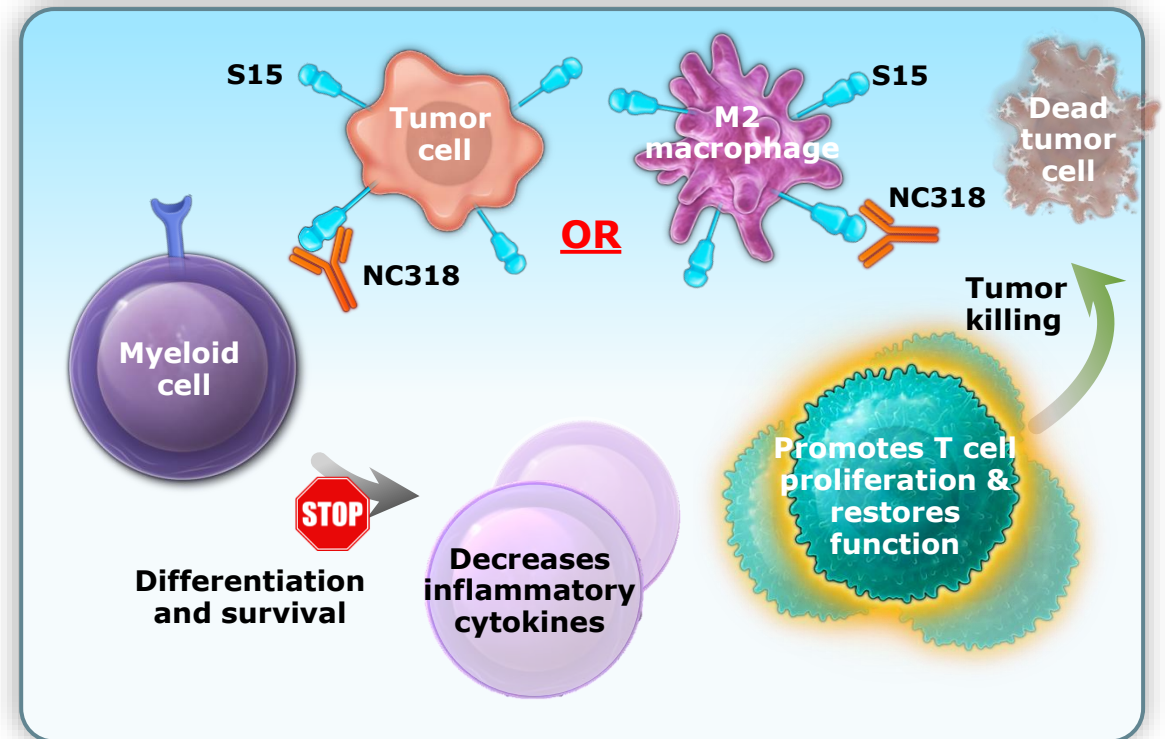
- NSCLC, Breast, H&N
- Evidence of disease control
- Enhanced outcomes in S15+ patients

# NC318 Mechanism of Action

## S15 is Immunosuppressive in the Tumor Microenvironment

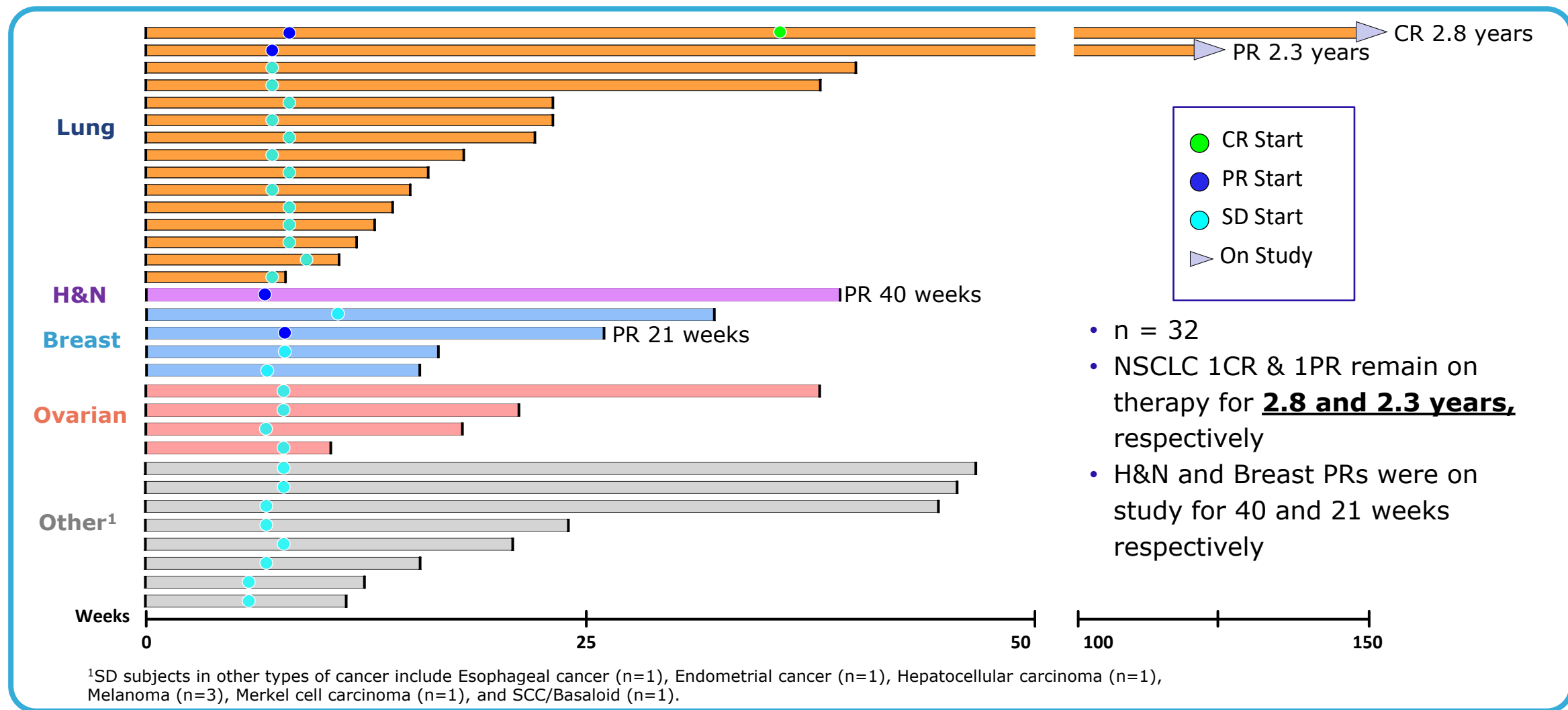


## NC318 Blocks Immunosuppressive Activity Induced by S15





# Time to & Duration of Disease Control



## Analysis in All Patients: Early Evidence of Disease Control Without S15 Selection in Ph1 & Ph2

Cancer Types	Responses n=32	Disease Control ( <b>CR+PR+SD</b> ) n=32 (37%)	Progressive Disease (n=54)	Total Evaluable Subjects (n=86) <sup>2</sup>	mPFS in Disease Control (5.0 months)
Lung	1 CR, 1 PR, 13 SD	15 (45%)	18	33	5.2 <sup>3</sup>
H&N	1 PR	1 (20%)	4	5	N/A
Breast	1 PR, 3 SD	4 (40%)	6	10	4.8
Ovarian	4 SD	4 (24%)	13	17	4.0 <sup>4</sup>
Other <sup>1</sup>	8 SD	8 (38%)	13	21	5.1

<sup>1</sup>SD subjects in other types of cancer include Esophageal Cancer (n=1), Endometrial Cancer (n=1), Hepatocellular Carcinoma (n=1), Melanoma (n=3), Merkel cell carcinoma (n=1), and SCC/Basaloid (n=1)

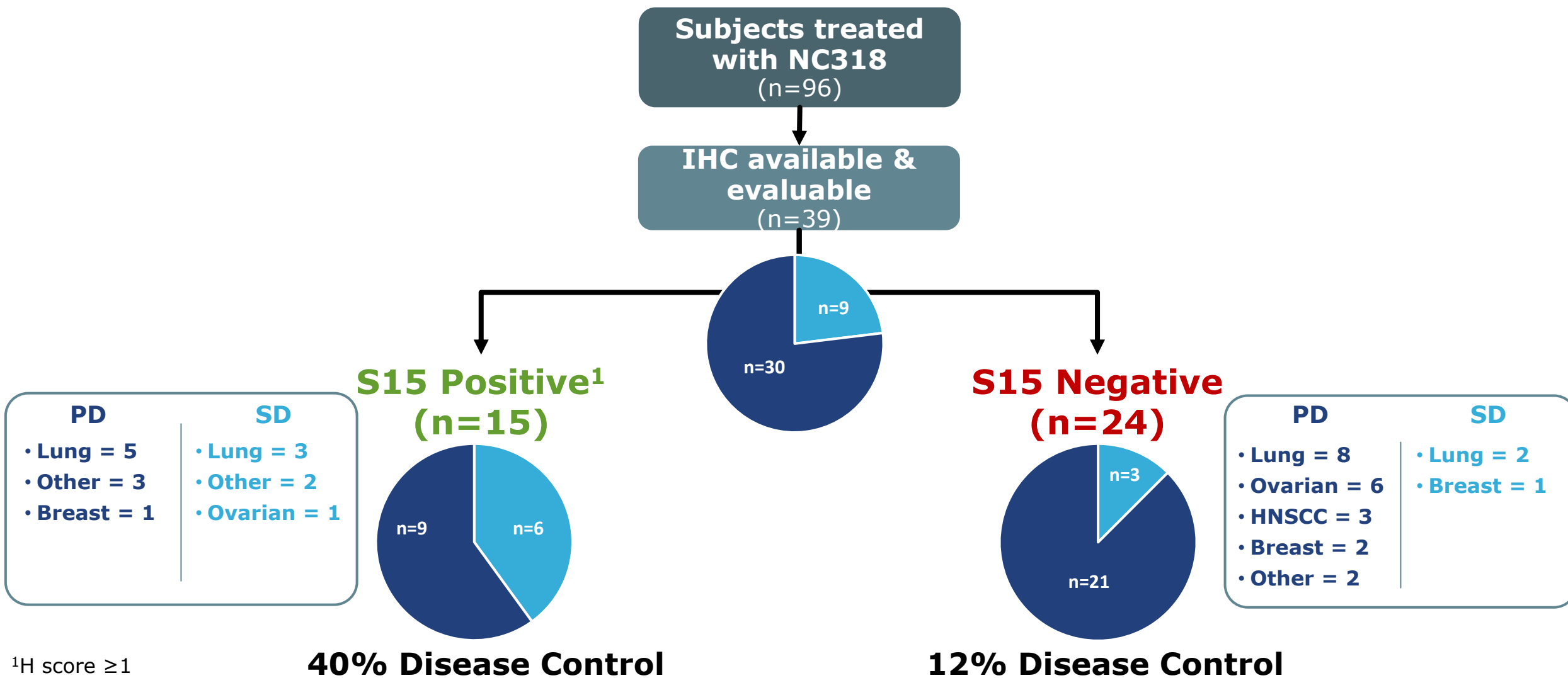
<sup>2</sup>Total of 96 subjects were treated with 10 subjects determined as non-evaluable (NE) for efficacy based on RECIST v1.1 and or clinical evaluations by principal investigators (PIs)

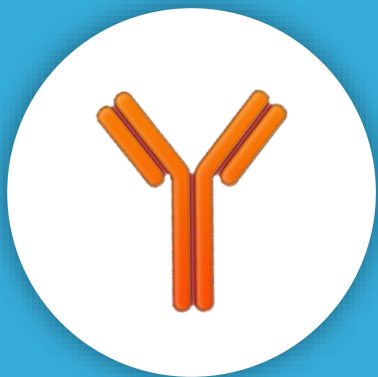
<sup>3</sup>3 SD subjects were censored for PFS analysis

<sup>4</sup>1 SD subject lost to follow up for PFS analysis

N/A: Not Applicable is used where sample size is less than 3 for median analysis. The data extract date is as of 18AUG2021

# Retrospective Analysis: Disease Control Rate Increased in S15+ Patients





# NC318

Restores Immune  
Function in a Highly  
Suppressive TME

## UPCOMING MILESTONES

### Amended Phase 2

- S15+ selection (CLIA assay)
- 800 mg Q1W: drug exposure
- NSCLC, H&N and breast
- **Update 4Q 2022**

### Yale Phase 2 (Combo) NSCLC

- Mono therapy: PD-1 refractory
- Pembro combo: PD-1 refractory
- Pembro combo: PD-1 naïve
- **Initial data 2H 2022**





# NC410

LAIR-2 (Collagen-Binding) Fusion Protein Decoy

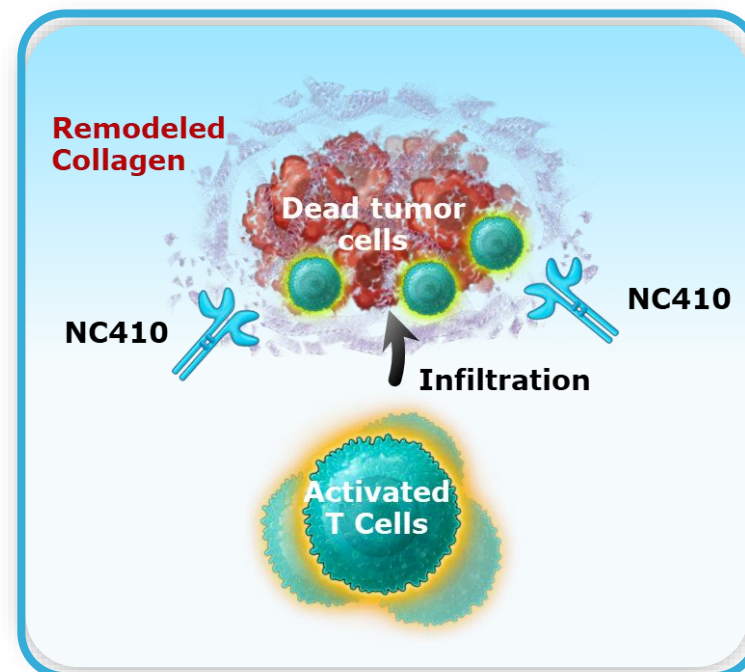


Phase 1/2  
CLINICAL  
TRIAL

## BIOLOGY

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

## MOA



## HIGHLIGHTS

- Patient selection assay
- Evidence of immune activation
- Synergistic combinations
- 2021 posters & publications
  - ASCO
  - SITC
  - eLife
  - Frontiers in Immunology

# 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<sup>+</sup> 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

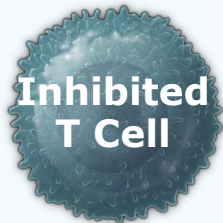
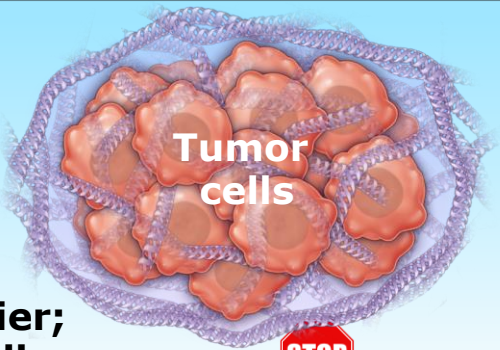
- Elevated collagen correlates with **PD-1/PD-L1 resistance**
- Changes in collagen expression correlate with **worse prognosis**
- LAIR-2 & NC410 **sensitizes** tumors

# NC410 Mechanism of Action

## Collagen is Immunosuppressive

### Tumor-specific Collagen

- Physical barrier; excludes T cell from TME
- Inhibits T cells



## NC410 Normalizes Immune System

### Remodeled Collagen

### Dead tumor cells

NC410

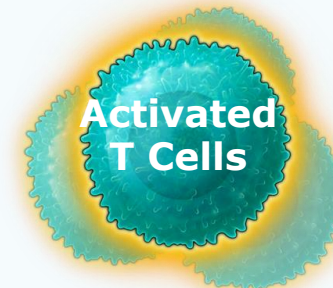


Infiltration

NC410

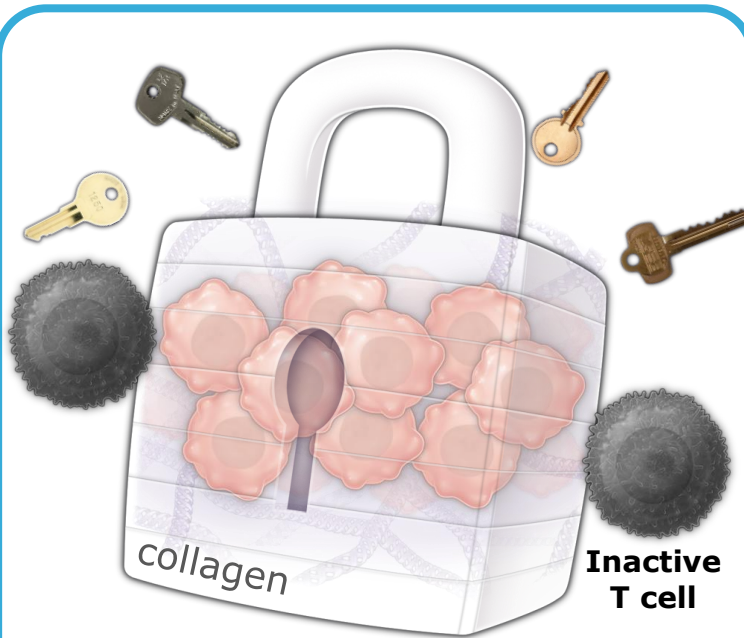


Activated T Cells



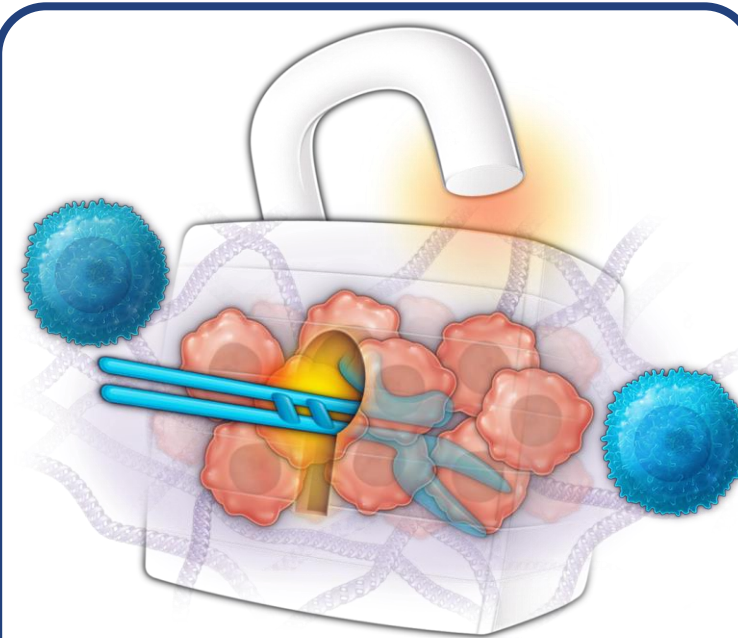
# NC410: Key to Unlock TME and Normalize Immune Response

## TME ACCESS LOCKED



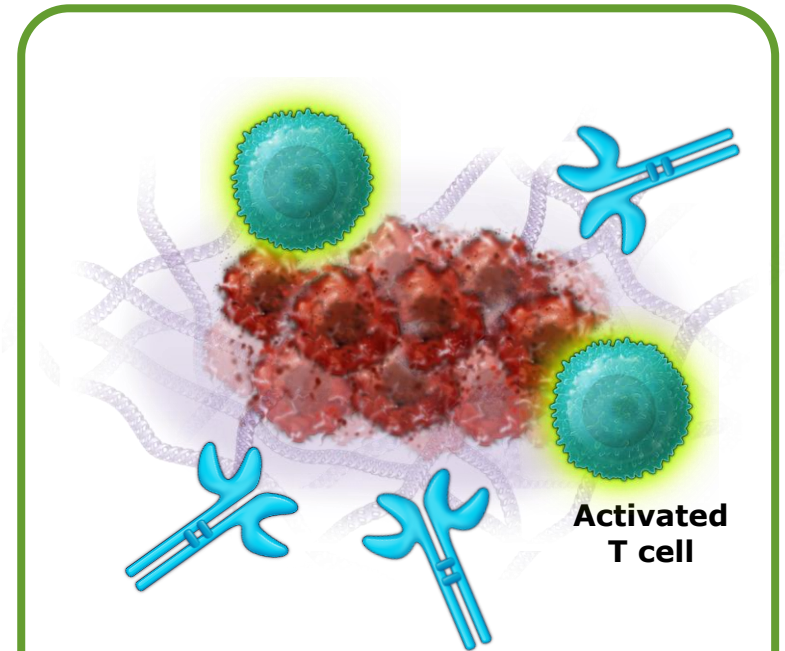
Many "keys" but none fit lock

## NC410 UNLOCKS ECM



Enhances T cell infiltration

## REMODELING & NORMALIZATION

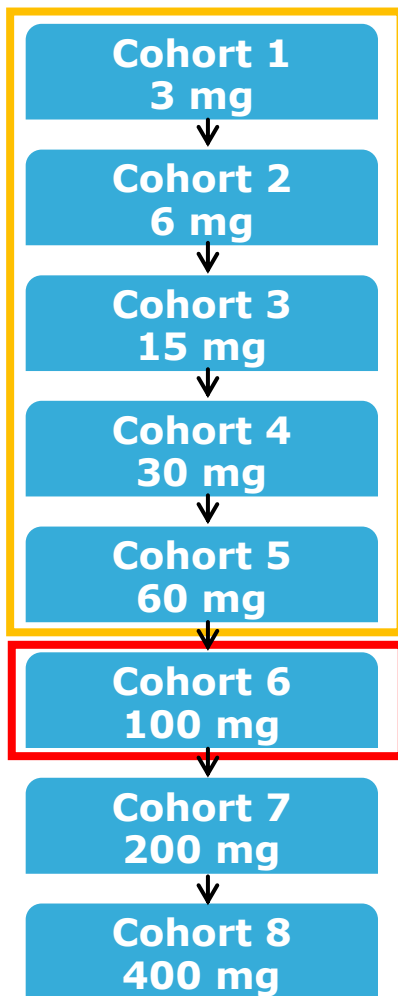


Activated T cells kill tumor



# NC410 Safety & Early Efficacy Data from Cohorts 1-5

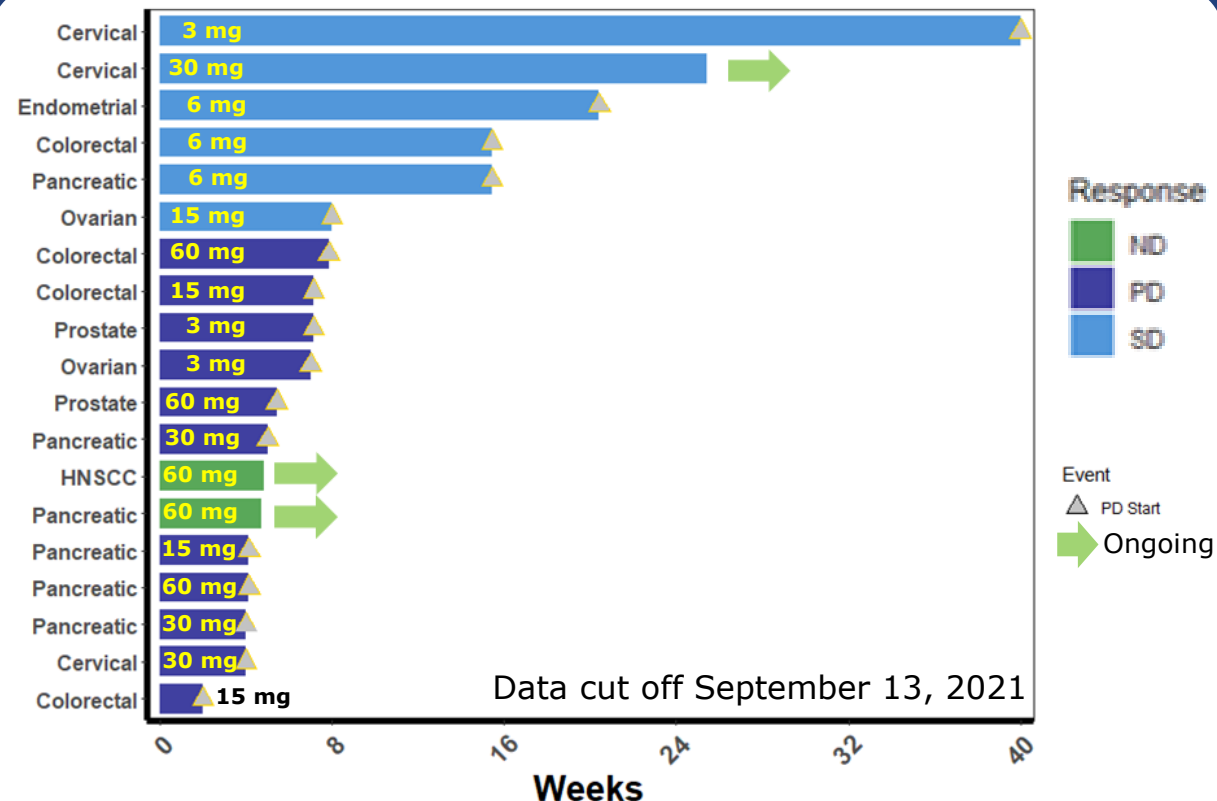
## Phase 1a Dose Escalation



- 3+3 design
- Dosing every 2 weeks
- Solid tumors
- No DLTs through cohort 5
- Two subjects reported with worsening Grade 3: lymphopenia (1); anemia (1); no treatment related grade 4 adverse events were reported

## Phase 1b Dose Expansion

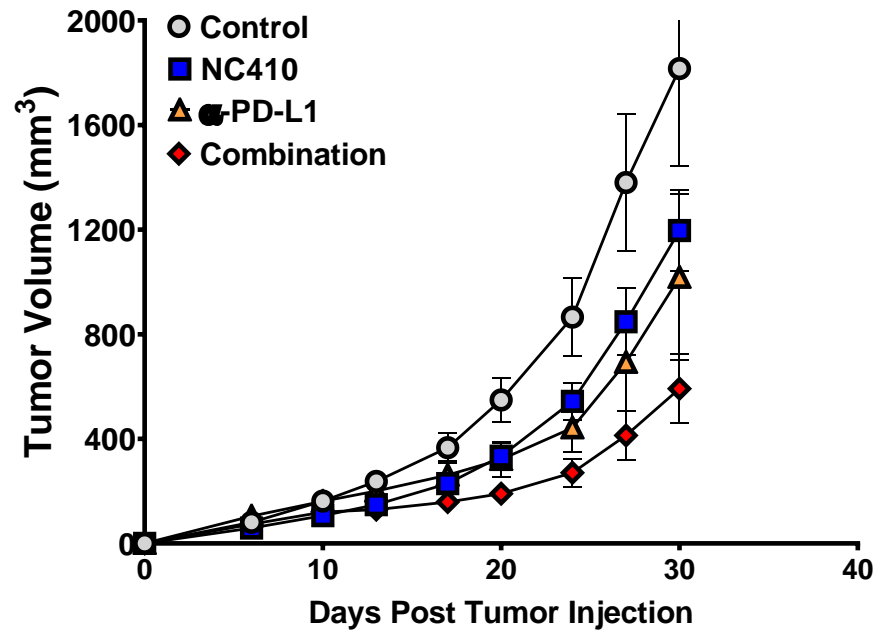
- Confirm PK and PD
- Biopsy analysis
- Determine RP2D



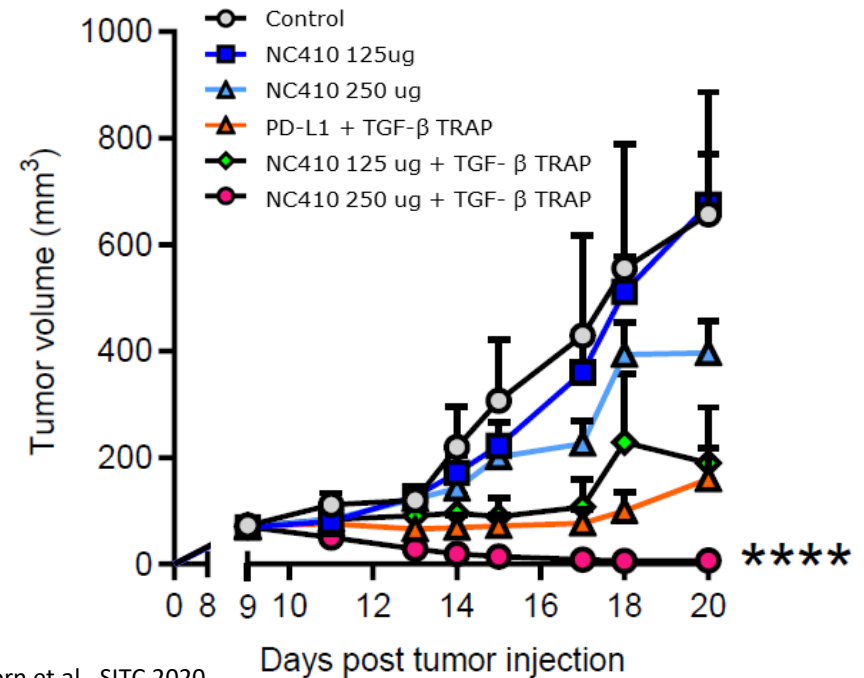
- 5 SD subjects had time-on-study up to 42, 25+, 20, 16 and 16, respectively
- 3 active subjects ongoing: one at 25+ and two at 5+ weeks

# NC410 Demonstrates Synergistic Activity in Preclinical Models

## PD-L1



## PD-L1 TGF- $\beta$ TRAP



Horn et al., SITC 2020



# NC410

Remodels ECM Enhancing  
Immune Infiltration &  
Tumor Killing

## SUMMARY

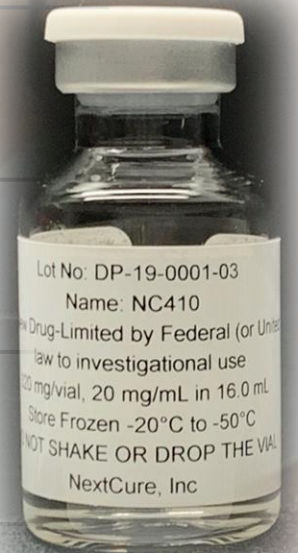
NC410 is safe and well tolerated with no DLTs up to cohort 5; dose escalation continues

Binding to C1q and collagen, modulates and restores immune function

Increase in T cells, remodeling of ECM, and enhanced infiltration of T cells supports MOA

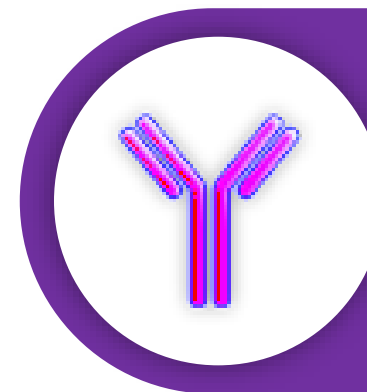
## UPCOMING MILESTONE

Phase 1 monotherapy update 2H 2022



# NC762

Humanized B7-H4 Monoclonal Antibody

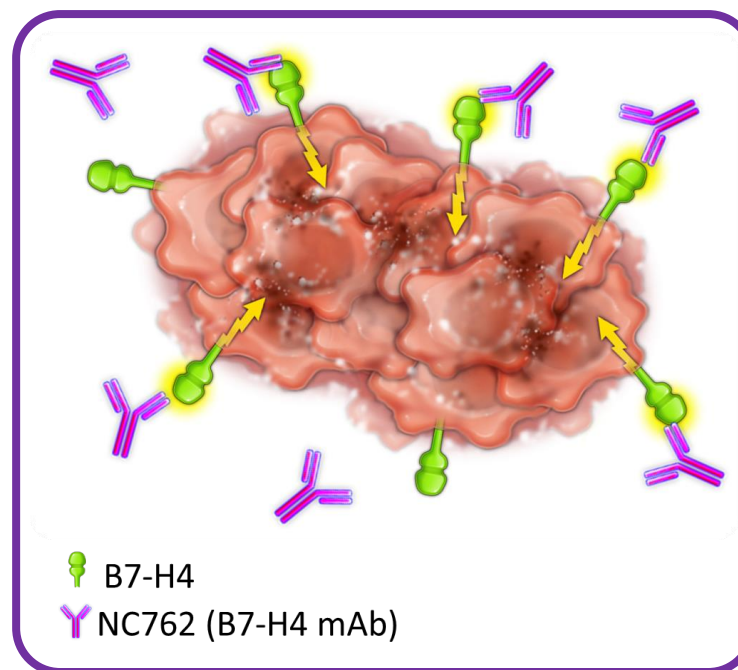


Phase 1/2  
CLINICAL  
TRIAL

## BIOLOGY

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

## MOA



## HIGHLIGHTS

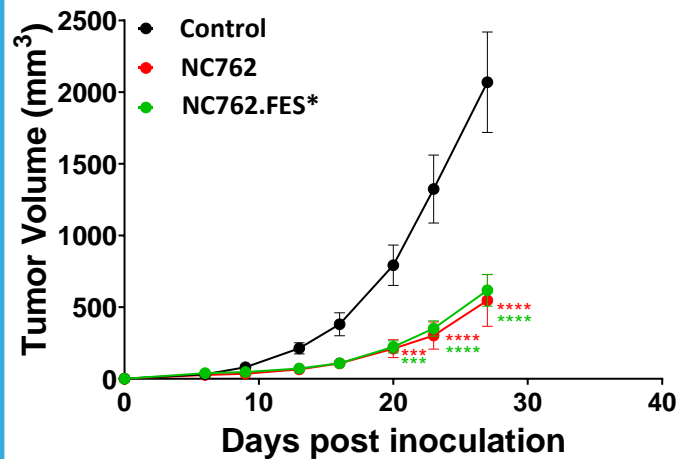
- Initiated Phase 1 trial
- IHC assay for patient selection
- Biomarkers
- AACR 2021 poster
- Initial Phase 1 data 2H 2022



# NC762 Inhibits Human Melanoma Tumor Growth *In Vivo*

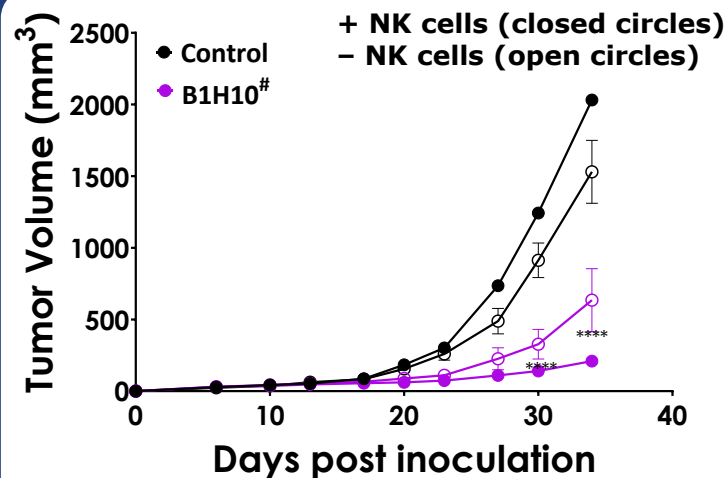
## Activity Enhanced by Human PBMCs

### TUMOR INHIBITION



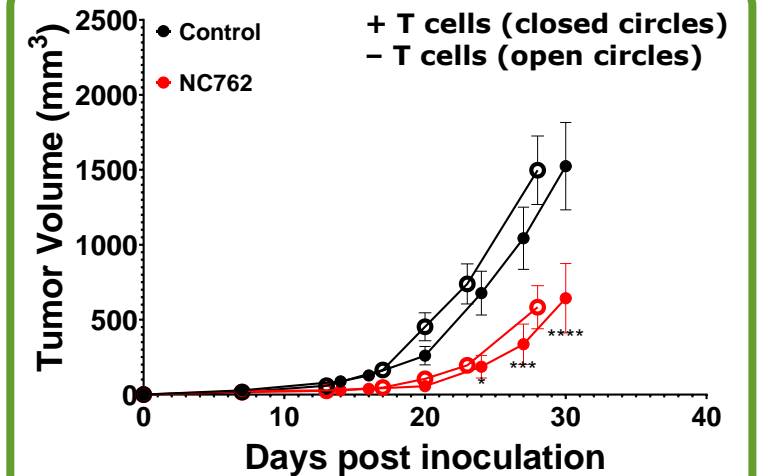
\*Designed to reduce FcγR binding/restrict ADCC activity

### NKs ENHANCE ACTIVITY

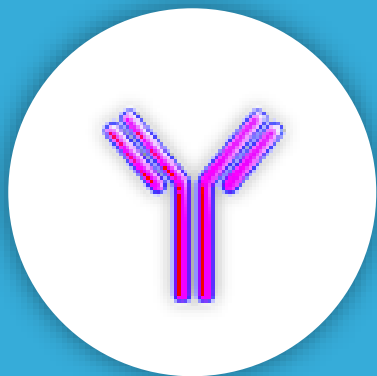


#Parent of NC762

### T CELLS NOT REQUIRED



Archer et al., AACR 2021



# NC762

## Summary & Upcoming Milestones

### SUMMARY

#### Unique MOA

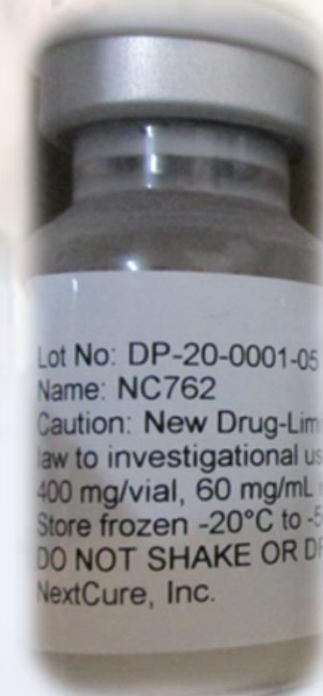
- mAb inhibits tumor cell growth
- Not dependent on immune cell infiltration into TME
- NK cells enhance activity

IND filed with FDA

Initiated Phase 1 trial

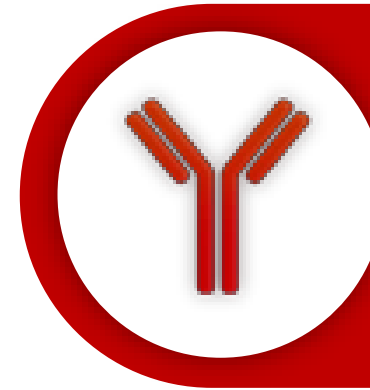
### UPCOMING MILESTONE

Initial Phase 1 data 2H 2022



# NC525

Humanized LAIR-1 Monoclonal Antibody



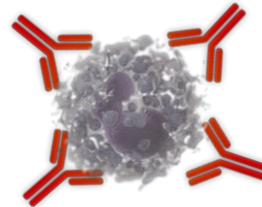
NC525  
IND Q4 2022

## 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

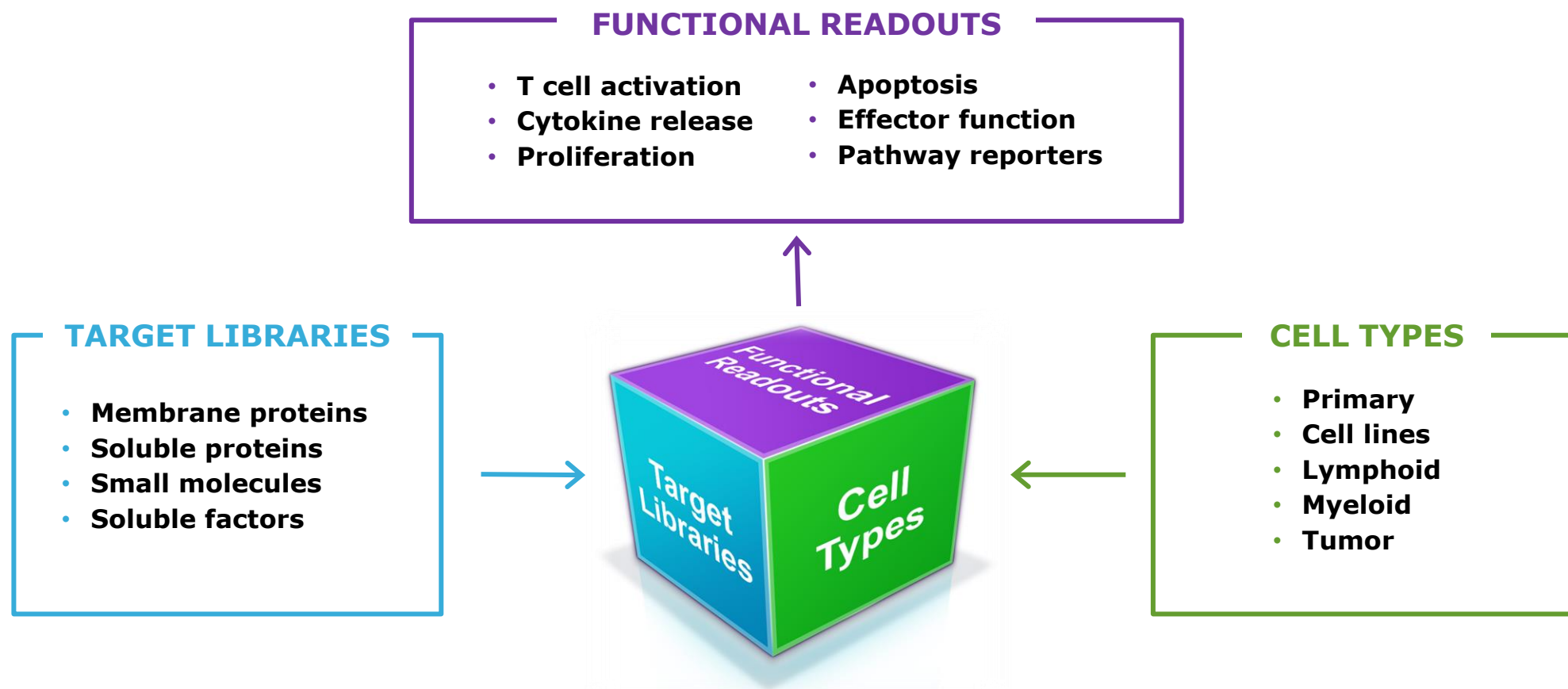


## HIGHLIGHTS

- Inhibits colony formation of AML LSCs *in vitro*
- Inhibits AML growth in MV4-11 derived xenografts
- Restricts AML progression in patient-derived xenografts

# 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**





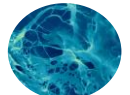




**Operational and capital efficiency**

**Quality**

**Controlling quality with experienced team**

**Utilized to Produce Clinical Material for All Lead Programs**

# Advancing Product Development Pipeline

PROGRAMS	TARGET	CELLS	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT MILESTONE
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NC525	LAIR-1		Leukemic Stem Cells	AML				IND filing Q4 2022
DISCOVERY AND RESEARCH PROGRAMS								
Multiple Programs	Multiple Targets	 	Multiple cell types					IND filing in 2023
*Investigator-initiated (IIT) trial (Yale University)								

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**Worldwide Rights to All Programs**



## Significant Momentum & Milestones in 2022

### ON TRACK

NC318, NC410, NC762

### MOMENTUM

Building Pipeline

### TEAM

Experienced

### Q1 2024

Runway

