



Next Generation Immunomedicines

11th Annual SVB Leerink Global Healthcare Conference
February 16, 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. Words such as “may,” “will,” “expect,” “anticipate,” “estimate,” “intend,” “next,” “near-term,” “future” and similar expressions, as well as other words and expressions referencing future events, conditions, or circumstances, are intended to identify forward-looking statements. Examples of forward-looking statements in this presentation may include, among others, statements regarding: (i) the timing, progress and results of our preclinical and clinical trials; (ii) the evaluation of biomarkers; (iii) the impact of the COVID-19 pandemic on the initiation, progress or expected timing of those trials and the timing of related data, as well as our efforts to adjust trial-related activities to address the impact of the COVID-19 pandemic; (iv) the timing or likelihood of regulatory filings for our product candidates; (v) our manufacturing capabilities and strategy; (vi) the potential benefits and activity of our product candidates; (vii) our expectations regarding the nature of the biological pathways we are studying; (viii) our expectations regarding our FIND-IO platform; and (ix) the potential benefits of our relationships with Dr. Lieping Chen and Yale University.

Various factors could cause actual results to differ materially from those projected in any forward-looking statement. Such risks and uncertainties include, among others: the impact of the ongoing COVID-19 pandemic on our business, including our clinical trials, third parties on which we rely and our operations; our limited operating history and no products approved for commercial sale; our history of significant losses; our need to obtain additional financing; risks related to clinical development, marketing approval and commercialization; and the unproven approach to the discovery and development of product candidates based on our FIND-IO platform. No forward-looking statement is a guarantee of future results or events, and one should avoid placing undue reliance on such statements. For further discussion of these and other factors that could affect the outcome of our forward-looking statements, see our filings with the Securities and Exchange Commission, including in “Risk Factors” and “Special Note Regarding Forward-Looking Statements” in the Risk Factors section and throughout NextCure’s Form 10-Q filed with the SEC on November 4, 2021. Except as otherwise indicated, this presentation speaks as of the date indicated herein. Except as required by law, we assume no obligation to update any forward-looking statements, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future. The information in this presentation is not complete and may be changed.

NextCure Highlights

NC318 (S15)



Phase 2

NC410 (LAIR-2)



Phase 1

NC762 (B7-H4)



Phase 1

NC525 (LAIR-1)



IND 4Q 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 4Q 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
2H 2023



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 1H 2022
NC410	LAIR-2	ECM	NSCLC, H&N, GASTRIC, CRC, CERVICAL					Phase 1 update Q2 2022
NC762	B7-H4	Tumors	NSCLC, BREAST, OVARIAN					Initial Phase 1 data Q2 2022
NC525	LAIR-1	Leukemic Stem Cells	AML					IND filing 2H 2022
DISCOVERY AND RESEARCH PROGRAMS								
Multiple Programs	Multiple Targets	Multiple cell types						IND filing in 2023

*Investigator-initiated (IIT) trial (Yale University)

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

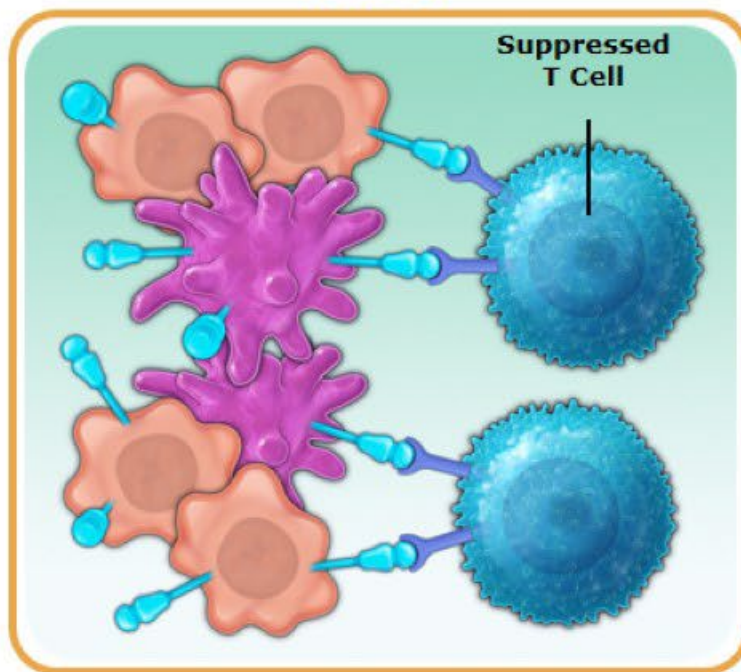


Phase 2
CLINICAL
TRIALS

BIOLOGY

- Decreases suppressive myeloid cells & pro-tumorigenic cytokines
- Promotes T cell function & IFN- γ production

MOA

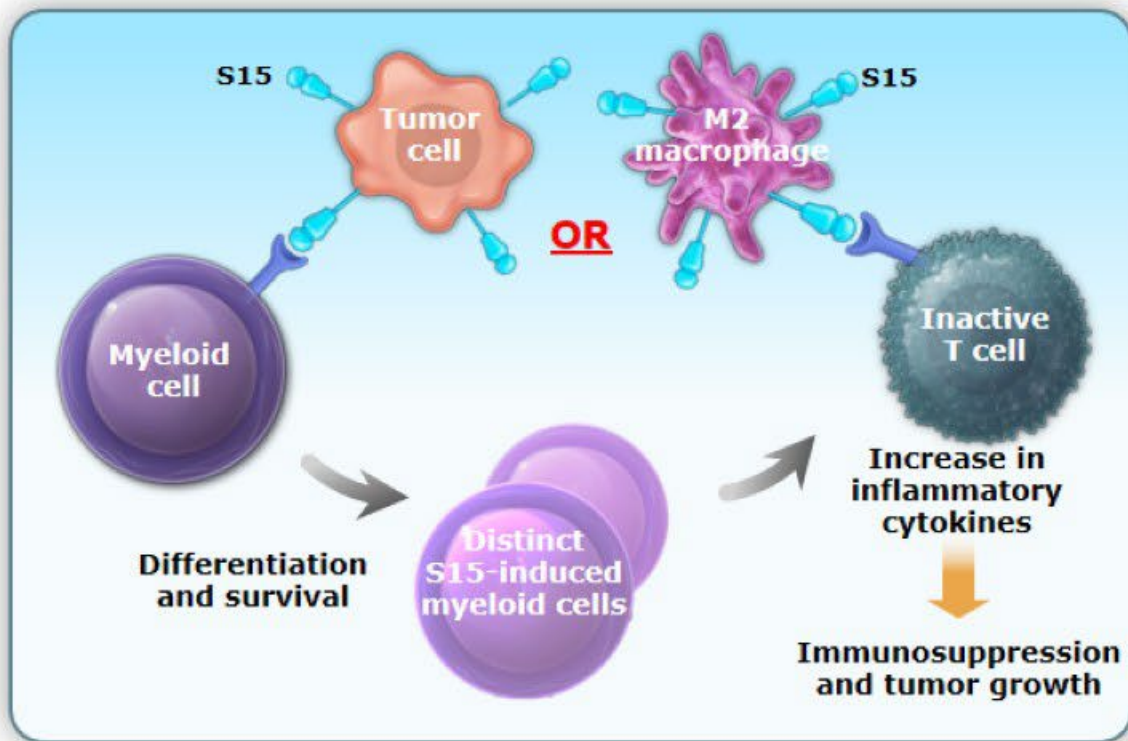


HIGHLIGHTS

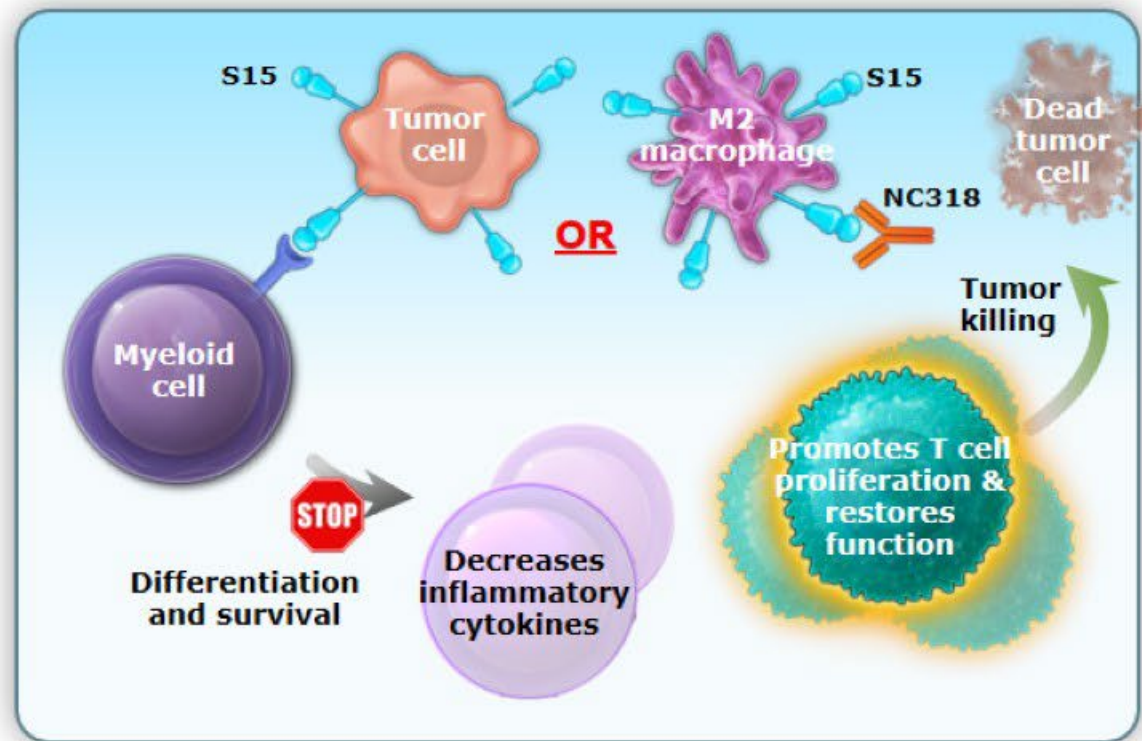
- NSCLC, Breast, H&N
- Evidence of disease control
- Enhanced outcomes in S15+ patients

NC318 Mechanism of Action

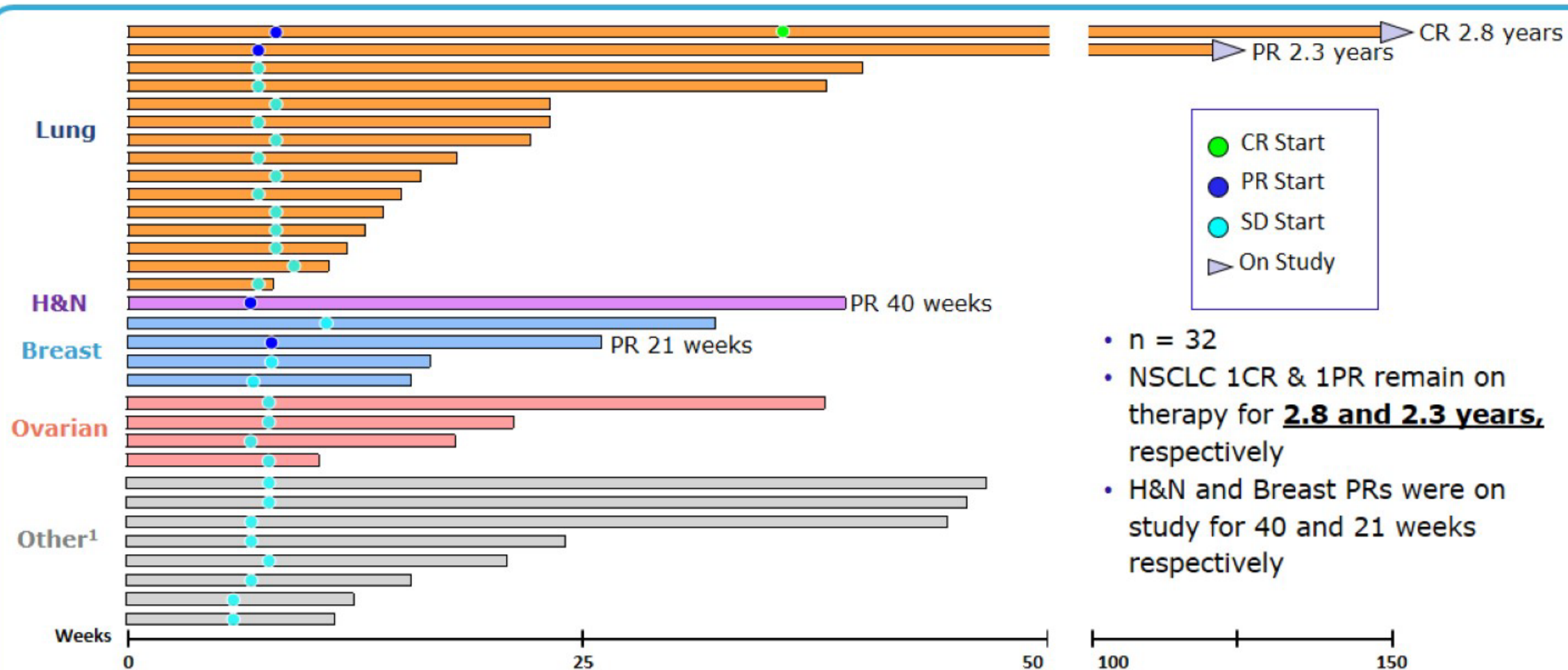
S15 is Immunosuppressive in the Tumor Microenvironment



NC318 Blocks Immunosuppressive Activity Induced by S15



Time to & Duration of Disease Control



- n = 32
- NSCLC 1CR & 1PR remain on therapy for **2.8 and 2.3 years**, respectively
- H&N and Breast PRs were on study for 40 and 21 weeks respectively

¹SD 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).

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

Cancer Types	Responses n=32	Disease Control (CR+PR+SD) n=32 (37%)	Progressive Disease (n=54)	Total Evaluatable Subjects (n=86) ²	mPFS in Disease Control (5.0 months)
Lung	1 CR, 1 PR, 13 SD	15 (45%)	18	33	5.2 ³
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 ⁴
Other ¹	8 SD	8 (38%)	13	21	5.1

¹SD 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)

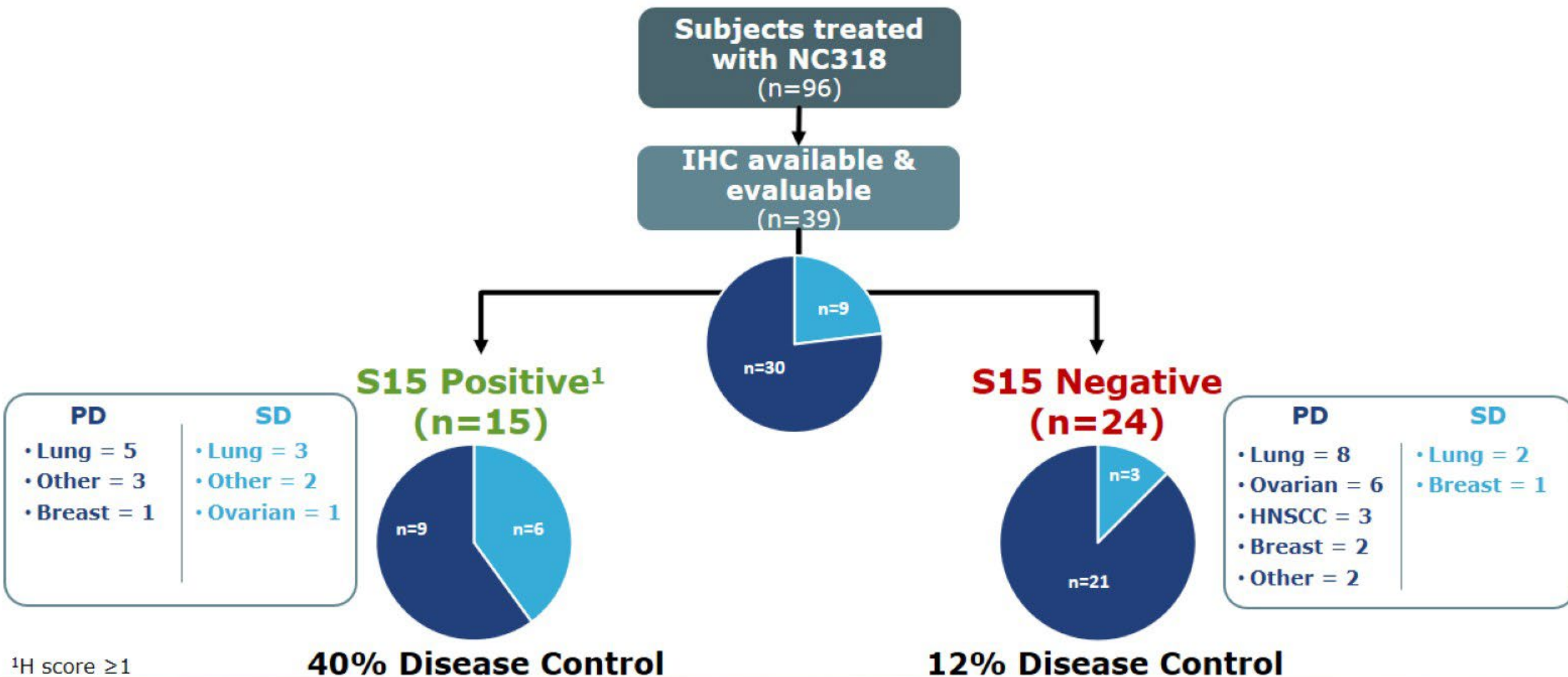
²Total of 96 subjects were treated with 10 subjects determined as non-evaluable (NE) for efficacy based on RECIST v1.1 and or clinical evaluations by principal investigators (PIs)

³3 SD subjects were censored for PFS analysis

⁴1 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

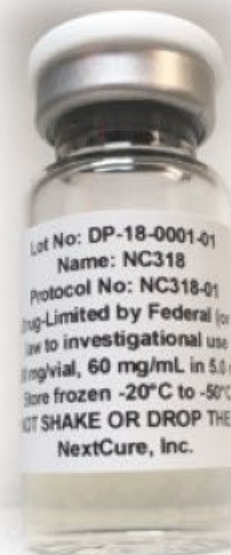
UPCOMING MILESTONES

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 1H 2022**



NC410

LAIR-2 (Collagen-Binding) Fusion Protein Decoy

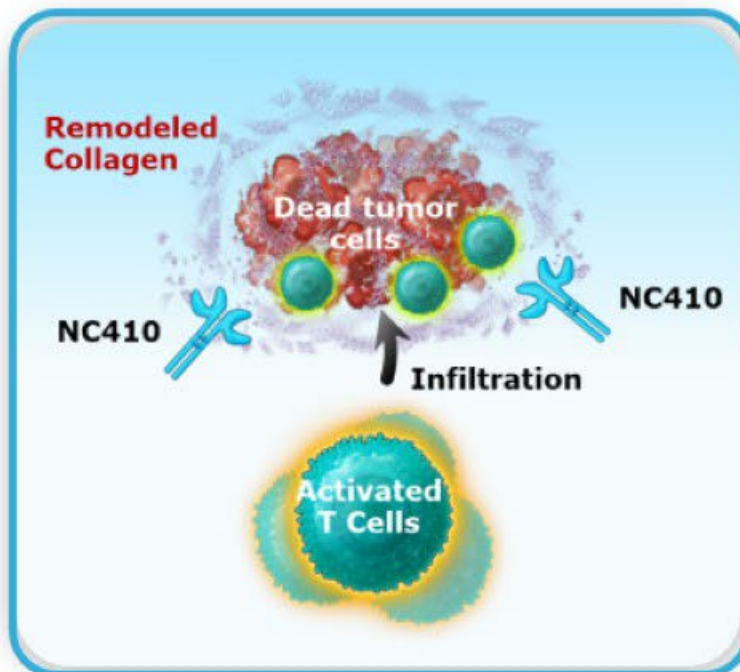


Phase 1/2
CLINICAL
TRIAL

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⁺ 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

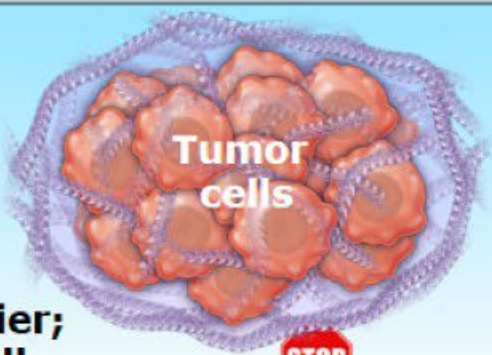
- Elevated collagen correlates with PD-1/PD-L1 resistance
- Changes in collagen expression correlate with worse prognosis
- LAIR-2 & NC410 sensitizes tumors

NC410 Mechanism of Action

Collagen is Immunosuppressive

Tumor-specific Collagen

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



STOP



NC410 Normalizes Immune System

Remodeled Collagen

Dead tumor cells

NC410



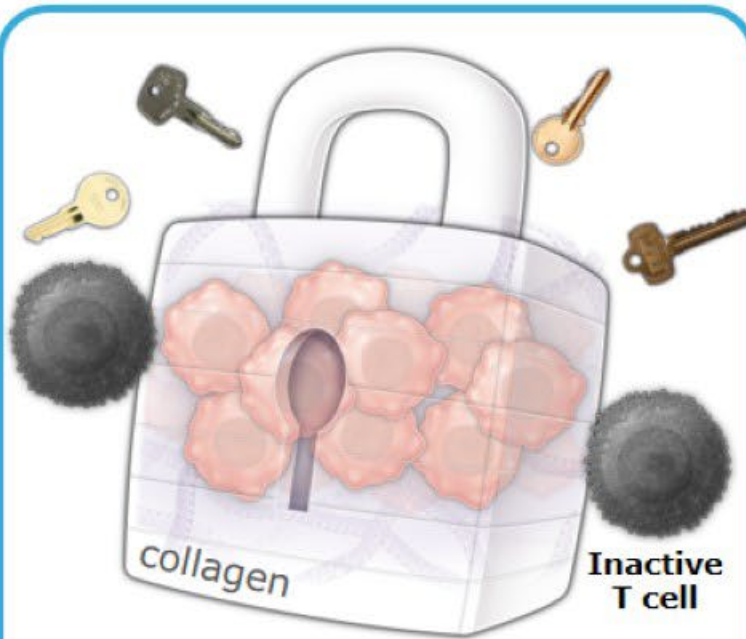
Infiltration

NC410



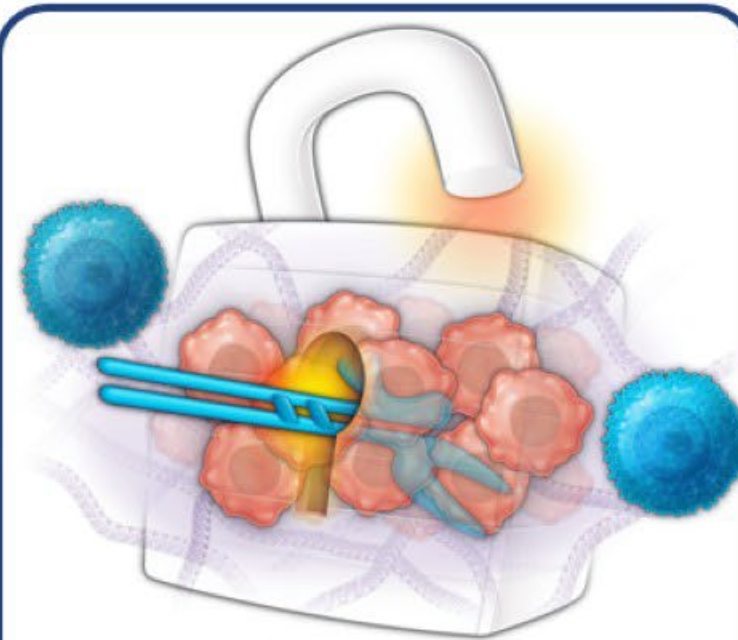
NC410: Key to Unlock TME and Normalize Immune Response

TME ACCESS LOCKED



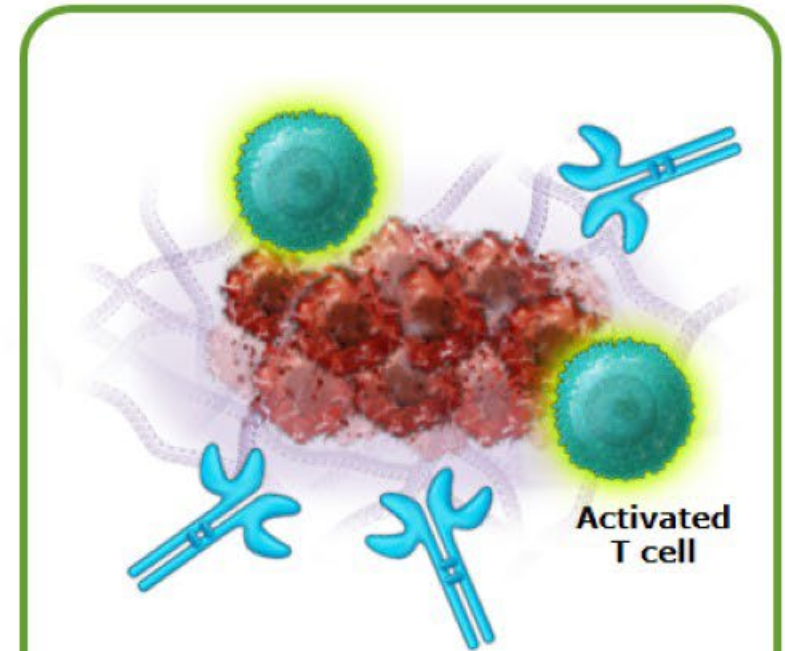
Many "keys" but none fit lock

NC410 UNLOCKS ECM



Enhances T cell infiltration

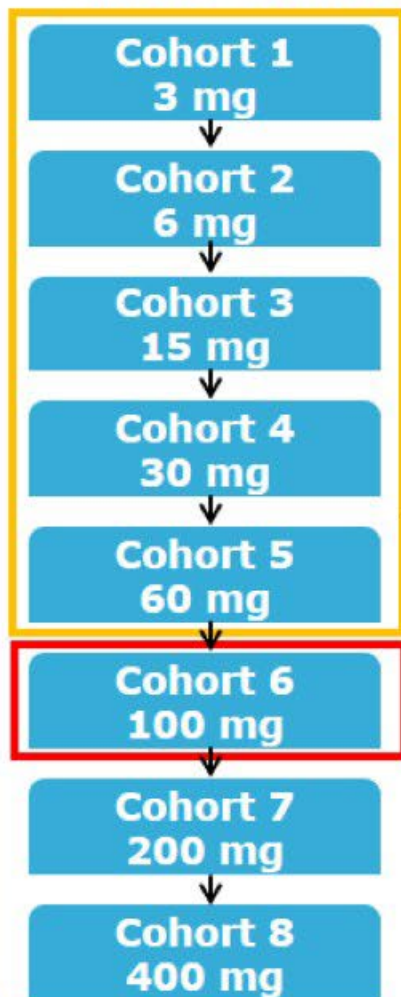
REMODELING & NORMALIZATION



Activated T cells kill tumor

NC410 Safety & Early Efficacy Data from Cohorts 1-5

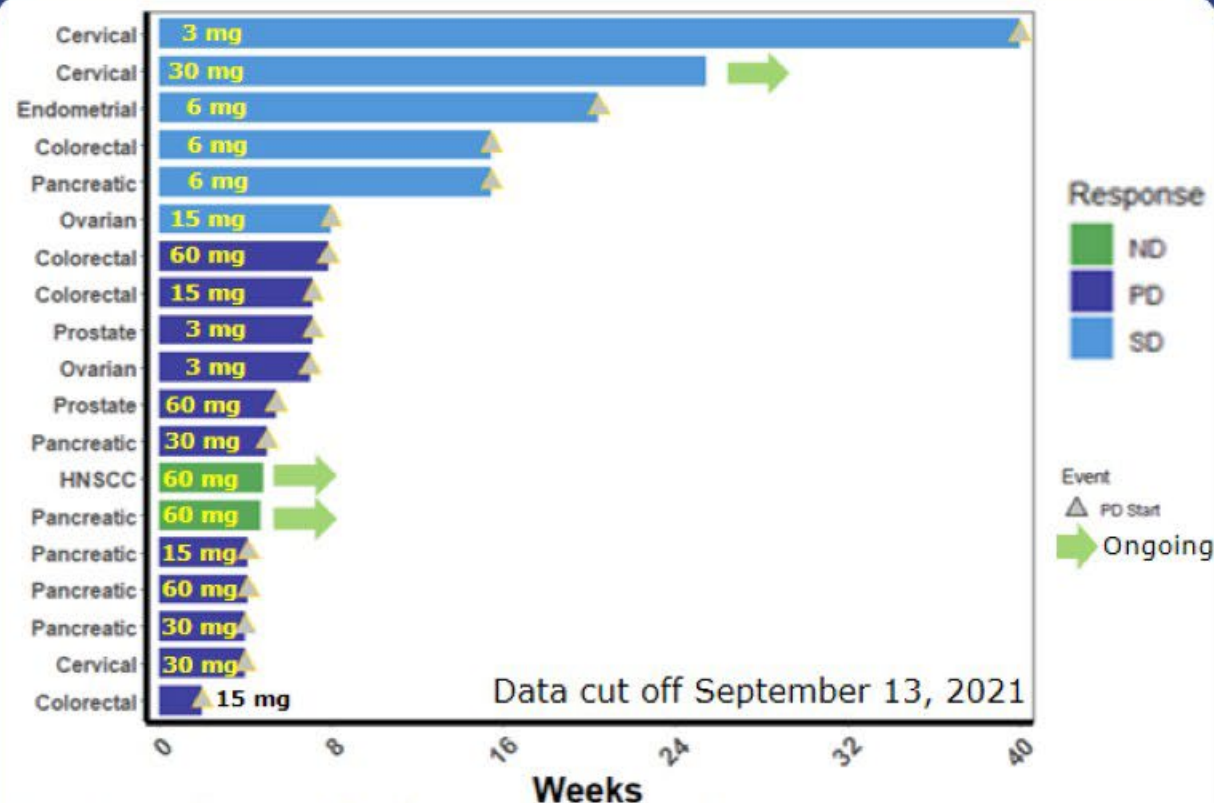
Phase 1a Dose Escalation



- 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

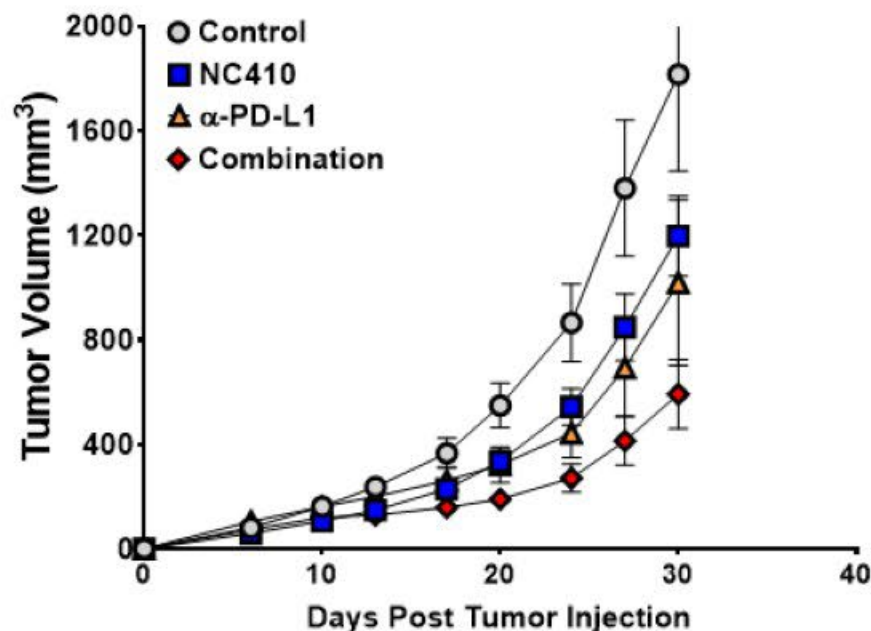
- Confirm PK and PD
- Biopsy analysis
- Determine RP2D



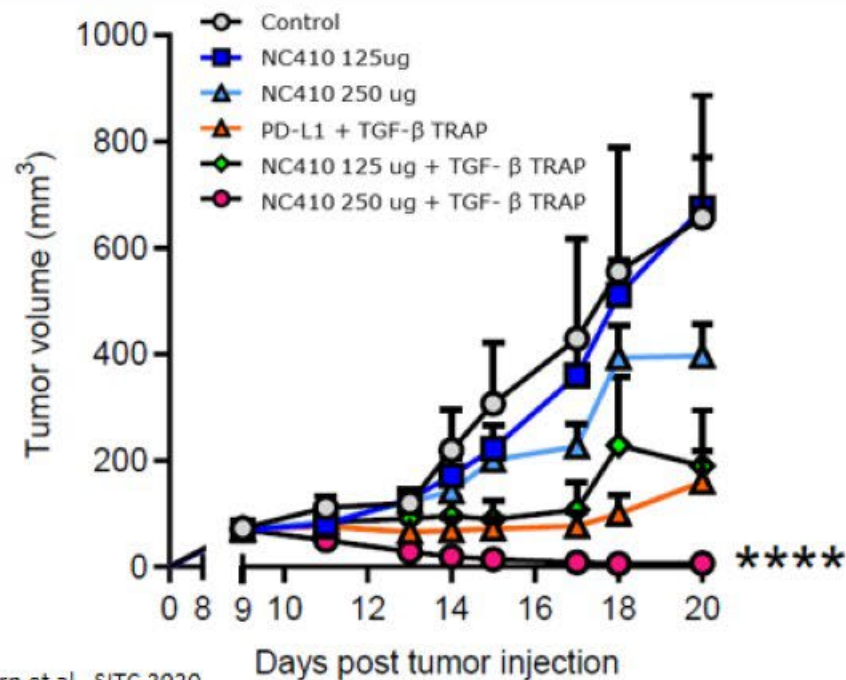
- 5 SD subjects had time-on-study up to 42, 25+, 20, 16 and 16, respectively
- 3 active subjects ongoing: one at 25+ and two at 5+ weeks

NC410 Demonstrates Synergistic Activity in Preclinical Models

PD-L1



PD-L1 TGF-β TRAP



Horn et al., SITC 2020



NC410

Remodels ECM Enhancing
Immune Infiltration &
Tumor Killing

SUMMARY

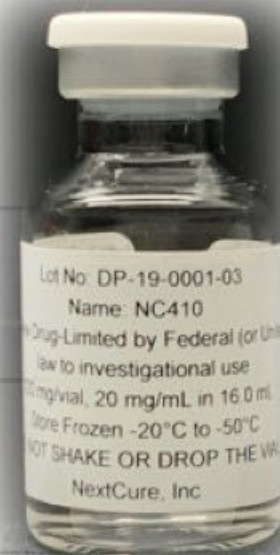
NC410 is safe and well tolerated with no DLTs
up to cohort 5; dose escalation continues

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 2Q 2022



NC762

Humanized B7-H4 Monoclonal Antibody

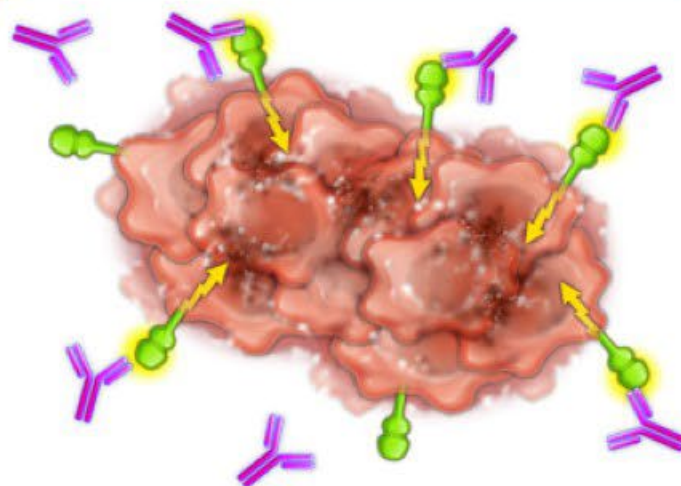


Phase 1/2
CLINICAL
TRIAL

BIOLOGY

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

MOA



B7-H4

NC762 (B7-H4 mAb)

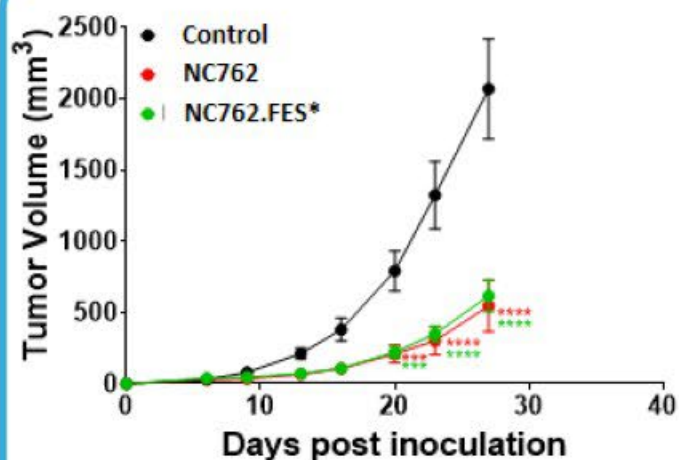
HIGHLIGHTS

- Initiated Phase 1 trial
- IHC assay for patient selection
- Biomarkers
- AACR 2021 poster
- Initial Phase 1 data Q2 2022

NC762 Inhibits Human Melanoma Tumor Growth *In Vivo*

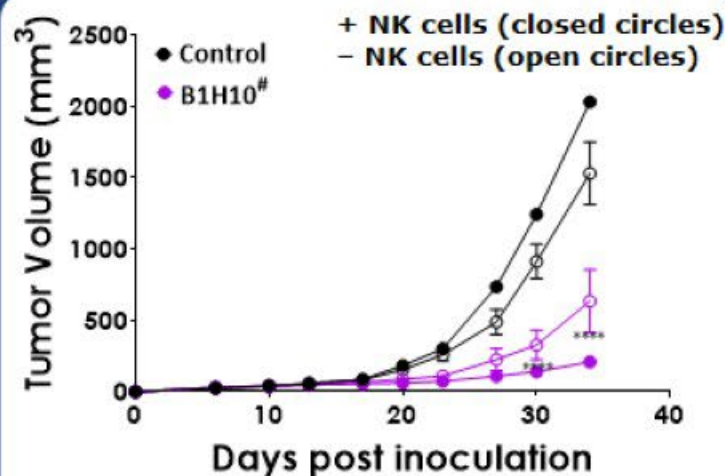
Activity Enhanced by Human PBMCs

TUMOR INHIBITION



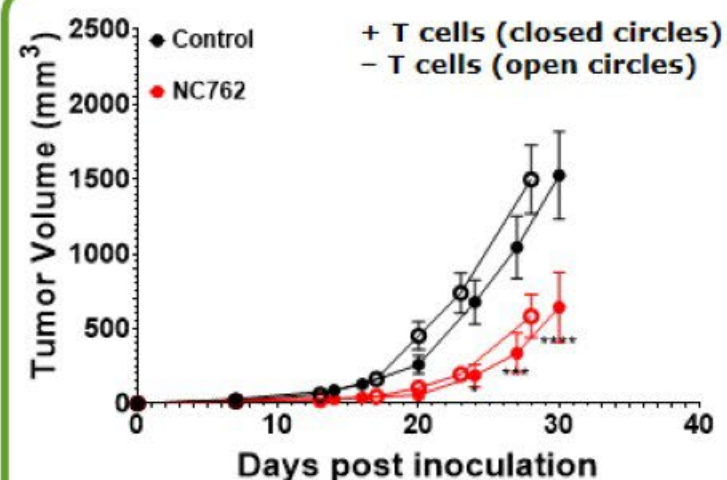
*Designed to reduce FcγR binding/restrict ADCC activity

NKs ENHANCE ACTIVITY



#Parent of NC762

T CELLS NOT REQUIRED



Archer et al., AACR 2021



NC762

Summary & Upcoming Milestones

SUMMARY

Unique MOA

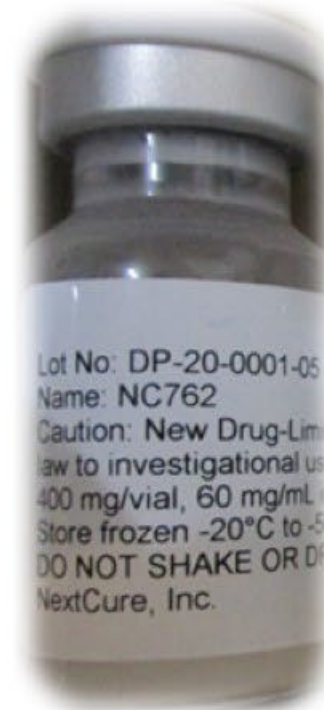
- mAb inhibits tumor cell growth
- Not dependent on immune cell infiltration into TME
- NK cells enhance activity

IND filed with FDA

Initiated Phase 1 trial

UPCOMING MILESTONE

Initial Phase 1 data Q2 2022



New Program - NC525 (LAIR-1 mAb)



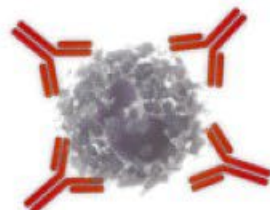
NC525
IND Q4 2022

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

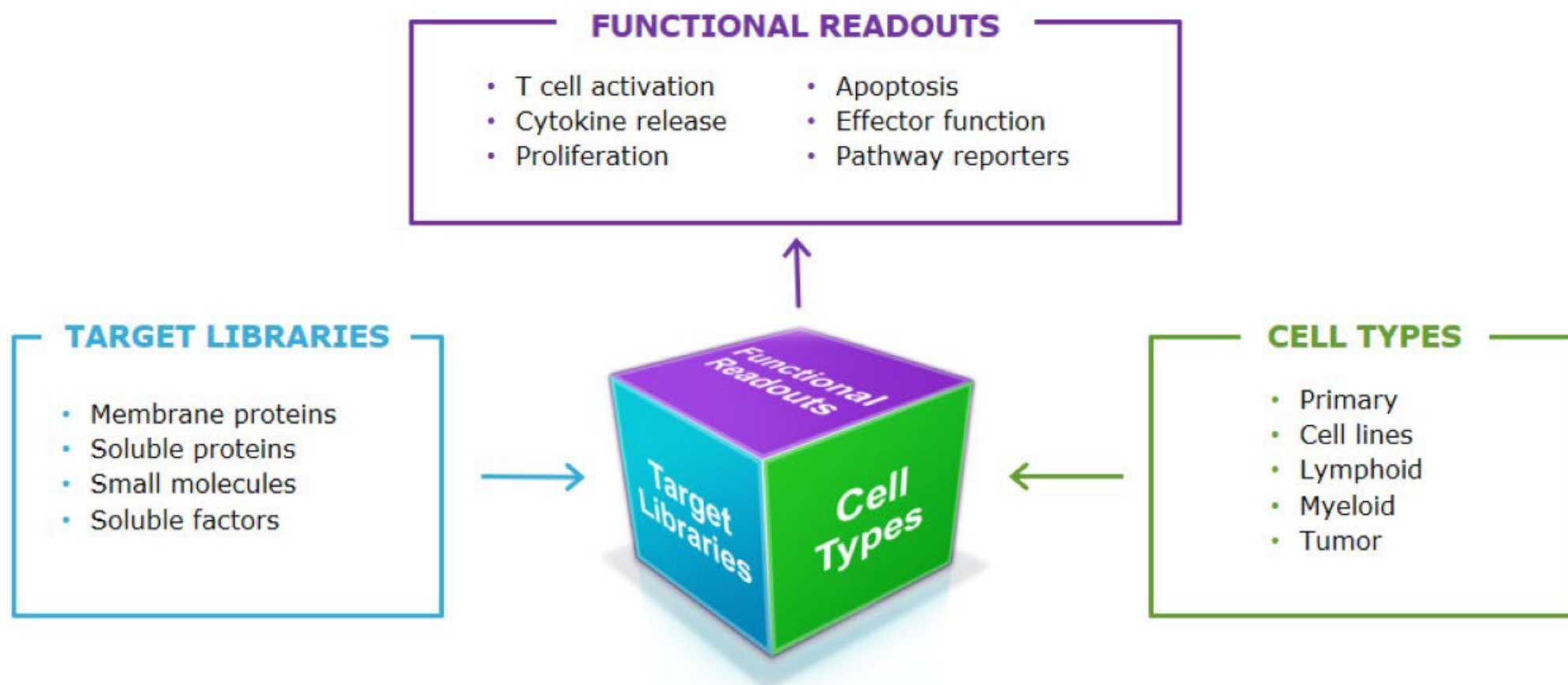


UPDATE

- 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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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 – Partnership Opportunities



Significant Momentum & Milestones in 2022

ON TRACK

NC318, NC410, NC762

MOMENTUM

Building Pipeline

TEAM

Experienced

2H 2023

Runway

