Next Generation Immunomedicines

21st Annual Needham Healthcare Conference
April 12, 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 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

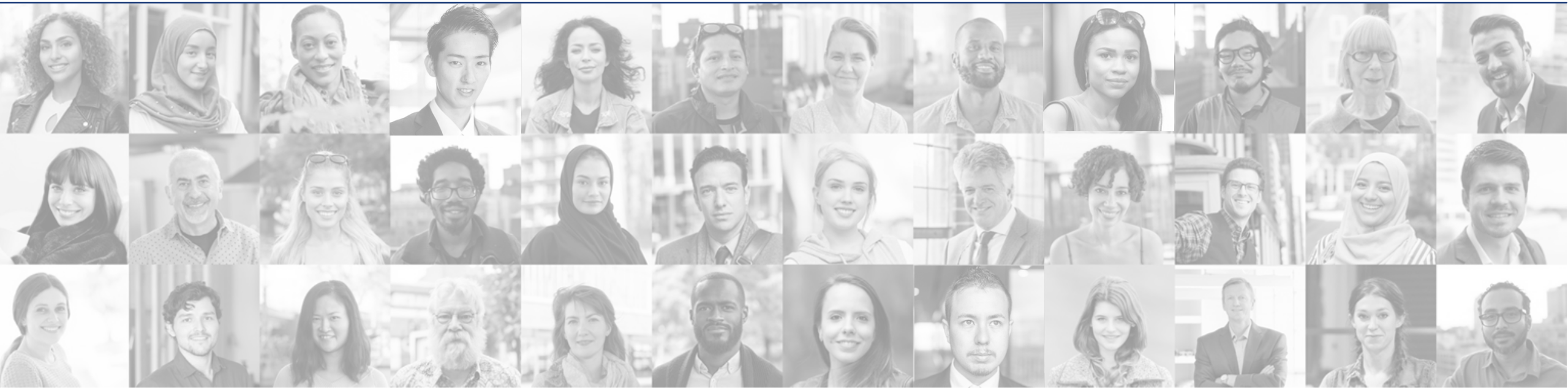
Significant Momentum & Milestones in 2022

NC318, NC410, NC762
On Track

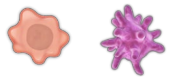
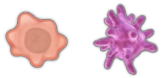
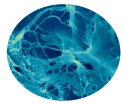
BUILDING PIPELINE
Momentum

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)

Worldwide Rights to All Programs

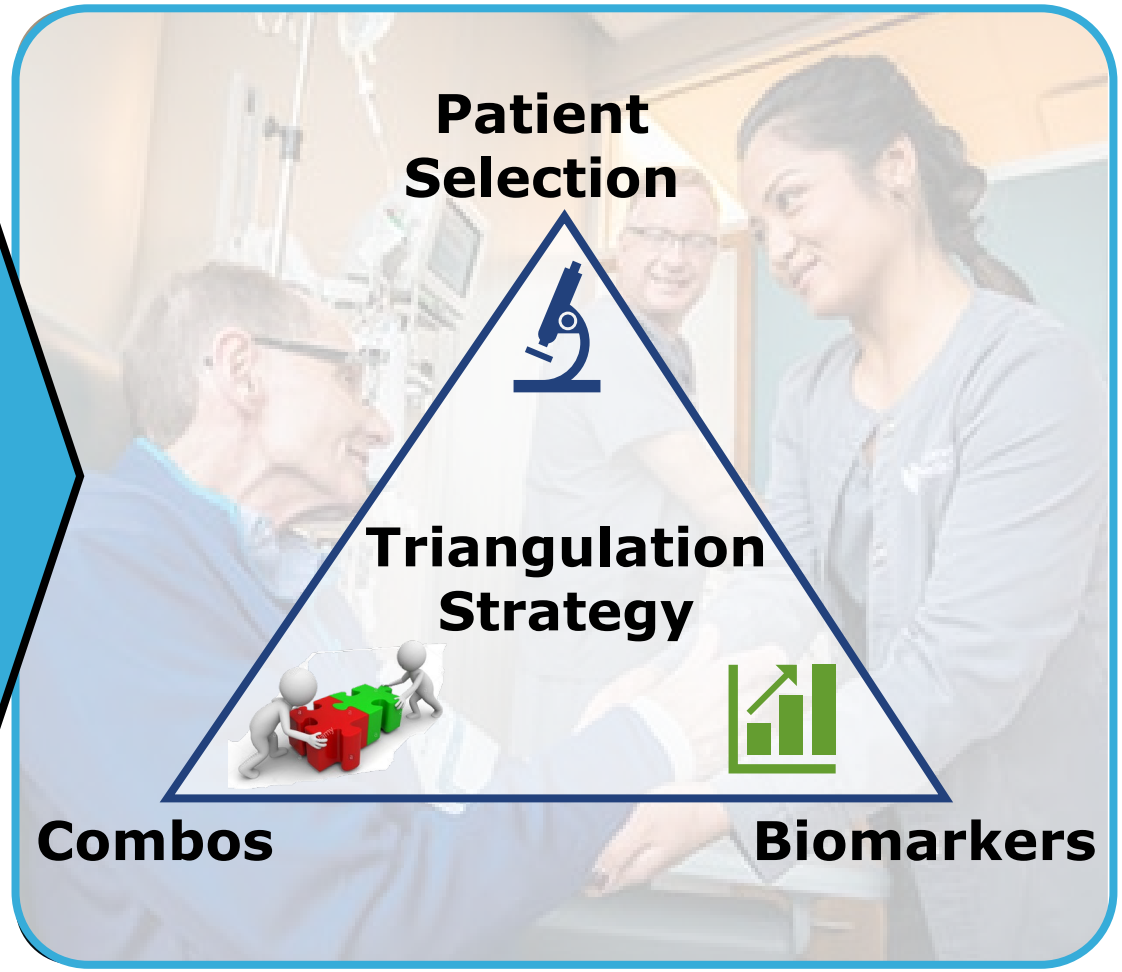
NextCure

Product Development: Getting it Right

Unmet Needs of Cancer Patients

- Non-Responders
- Rapid Progression
- Limited Treatments

We Need New Solutions



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NC318

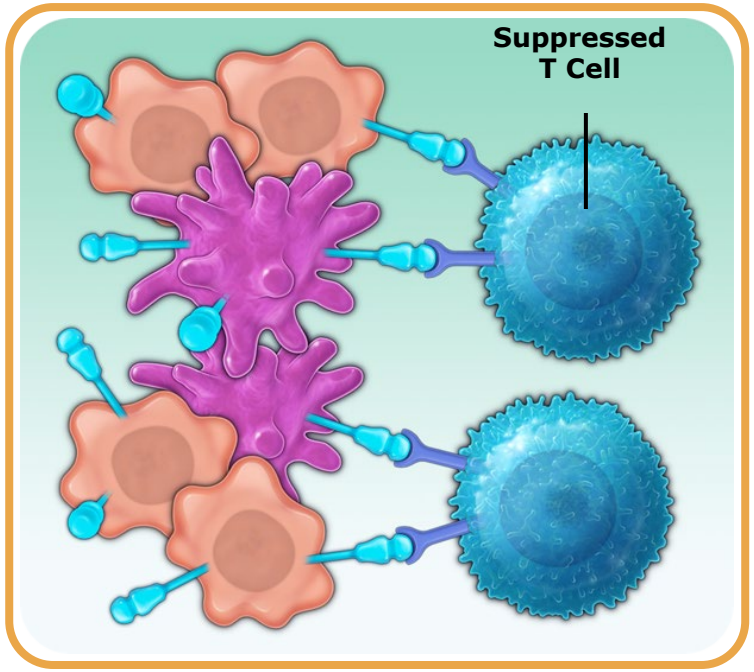
Humanized Siglec-15 (S15) Monoclonal Antibody

Phase 2 CLINICAL TRIALS

BIOLOGY

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

MOA



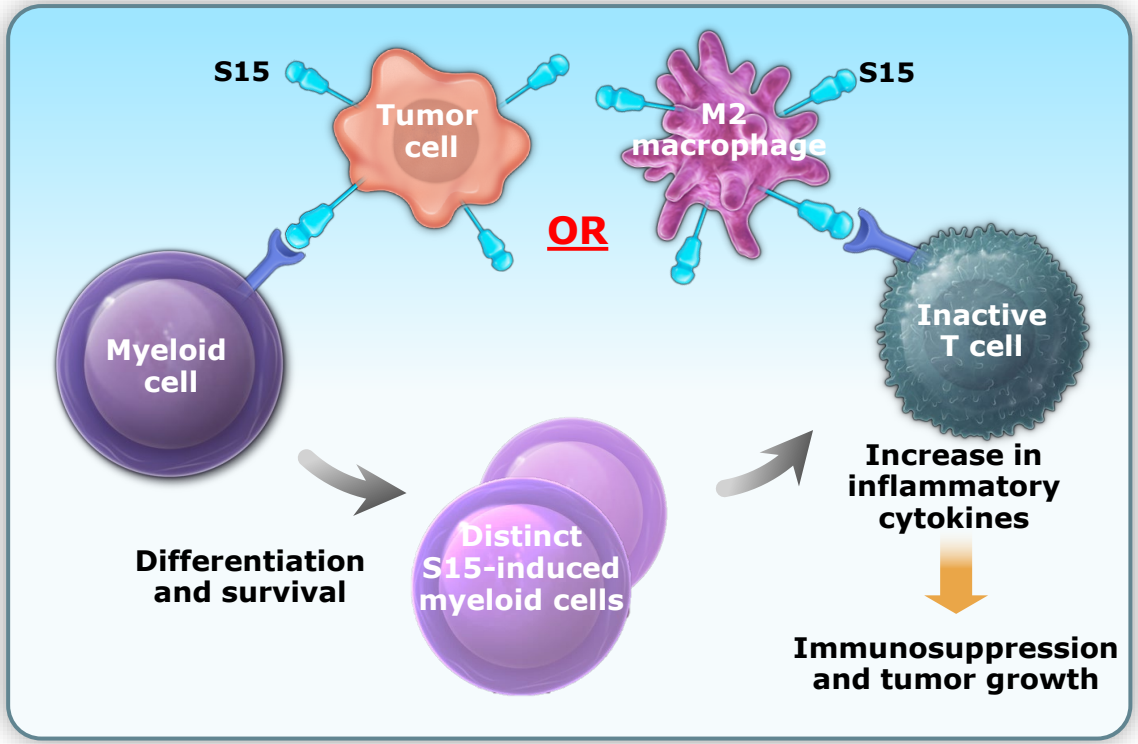
HIGHLIGHTS

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

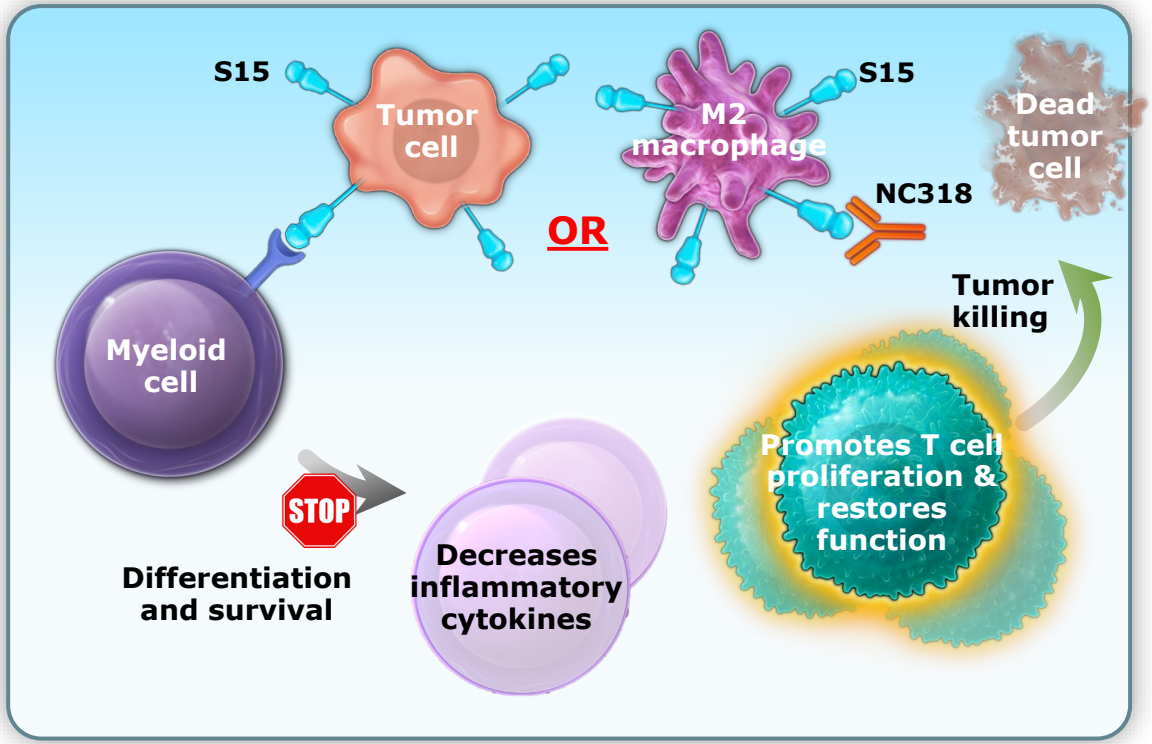
NextCure

NC318 Mechanism of Action

S15 is Immunosuppressive in the Tumor Microenvironment



NC318 Blocks Immunosuppressive Activity Induced by S15



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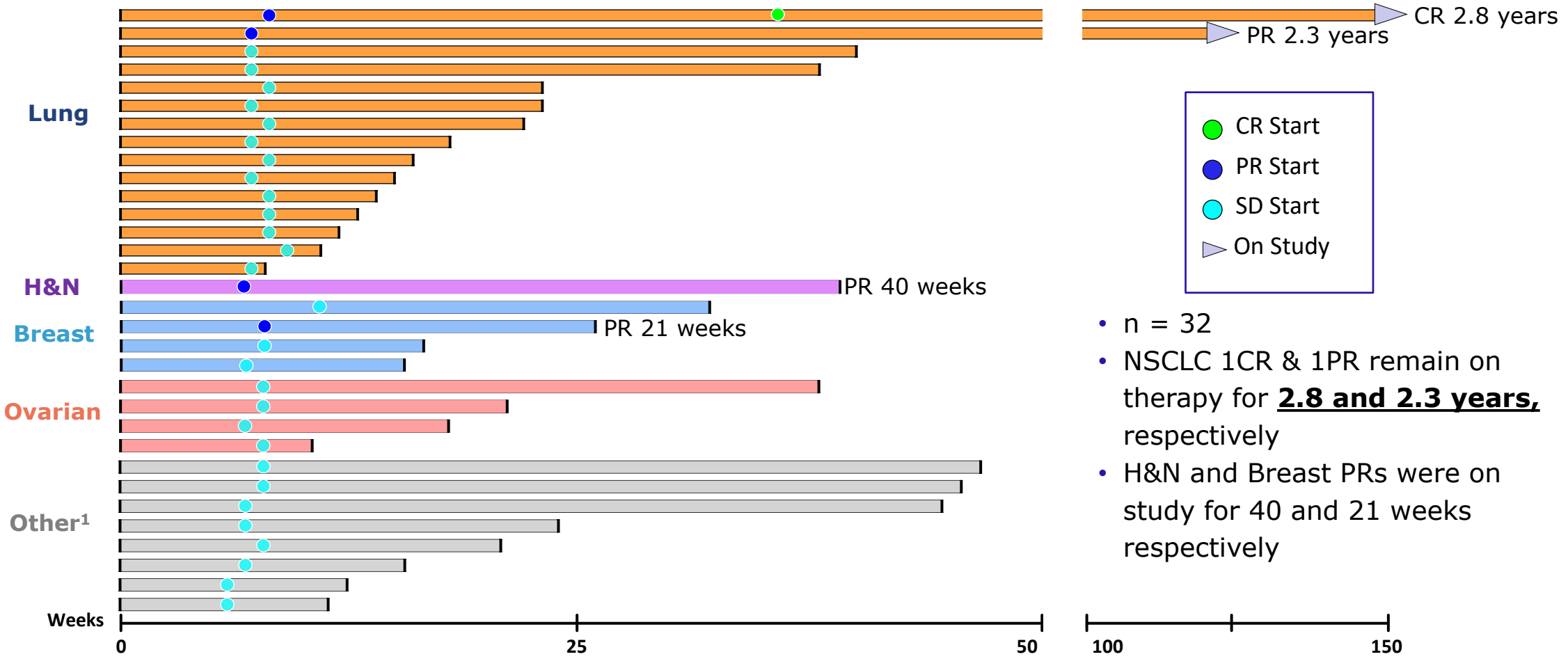
Time to & Duration of Disease Control



- 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

[1]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).

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

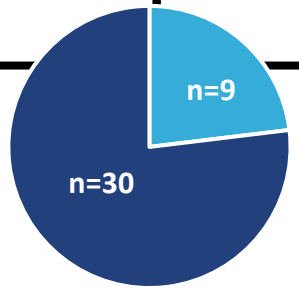
Cancer Types	Responses n=32	Disease Control (CR+PR+SD) n=32 (37%)	Progressive Disease (n=54)	Total Evaluable Subjects (n=86)[2]	mPFS in Disease Control (5.0 months)
Lung	1 CR, 1 PR, 13 SD	15 (45%)	18	33	5.2[3]
H&N	1 PR	1 (20%)	4	5	N/A
Breast	1 PR, 3 SD	4 (40%)	6	10	4.8
Ovarian	4 SD	4 (24%)	13	17	4.0[4]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

[1]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)
[2]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)
[3]3 SD subjects were censored for PFS analysis
[4]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

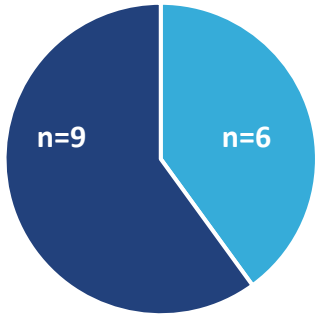
Subjects treated with NC318 (n=96)

IHC available & evaluable (n=39)



S15 Positive[1] (n=15)

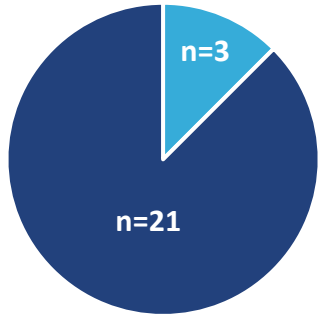
PD	SD
• Lung = 5	• Lung = 3
• Other = 3	• Other = 2
• Breast = 1	• Ovarian = 1



40% Disease Control

S15 Negative (n=24)

PD	SD
• Lung = 8	• Lung = 2
• Ovarian = 6	• Breast = 1
• HNSCC = 3	
• Breast = 2	
• Other = 2	



12% Disease Control

[1]H score ≥1

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NC318

Restores Immune Function in a Highly Suppressive TME

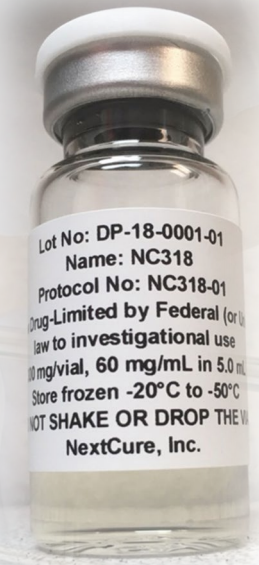
UPCOMING MILESTONES

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

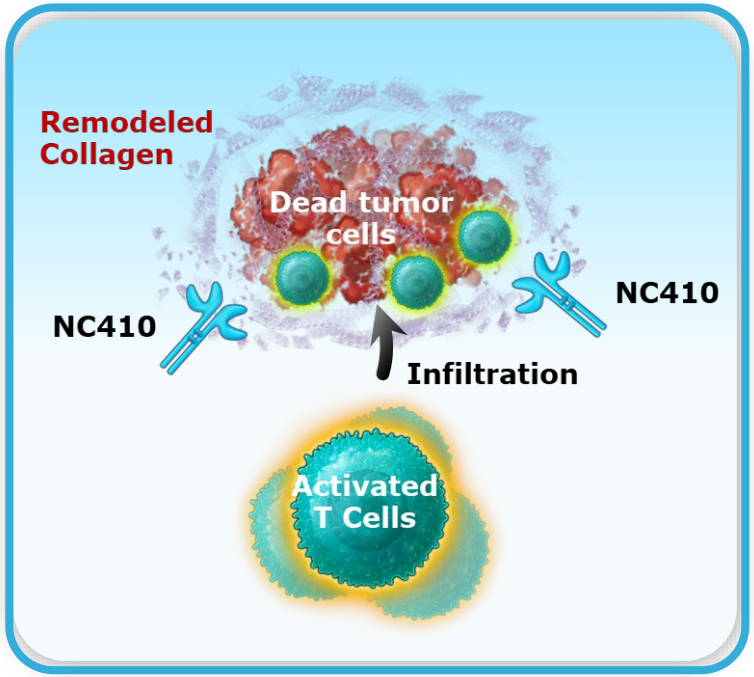
LAIR-2 (Collagen-Binding) Fusion Protein Decoy

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

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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

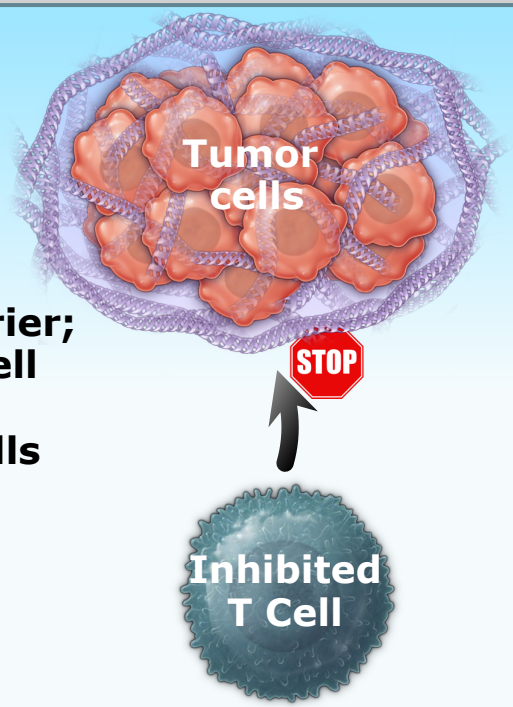
- Elevated collagen correlates with **PD-1/PD-L1 resistance**
- Changes in collagen expression correlate with **worse prognosis**
- LAIR-2 & NC410 **sensitizes** tumors

NC410 Mechanism of Action

Collagen is Immunosuppressive

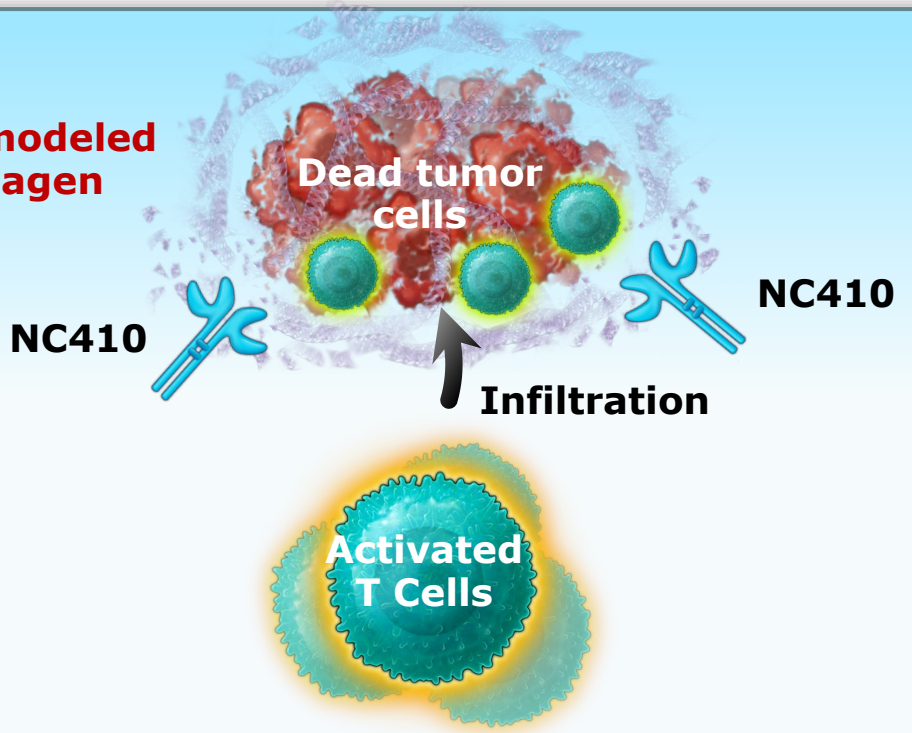
Tumor-specific Collagen

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



NC410 Normalizes Immune System

Remodeled Collagen



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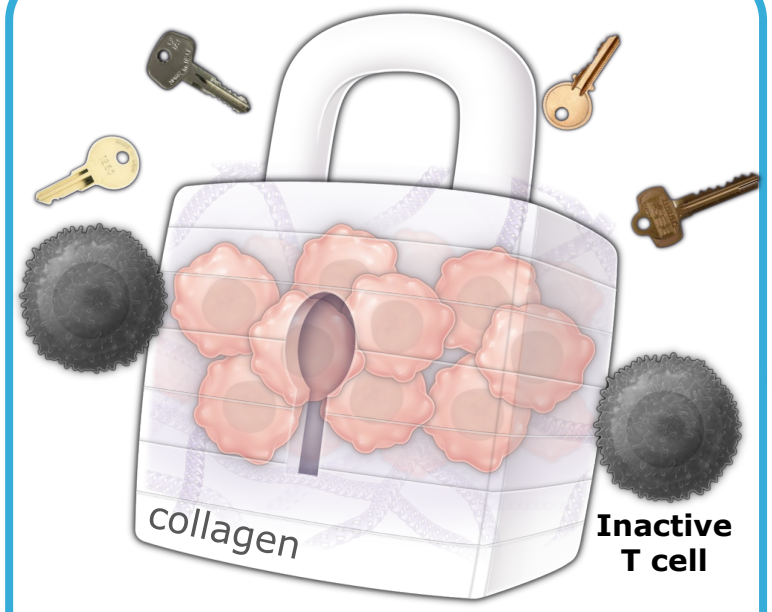
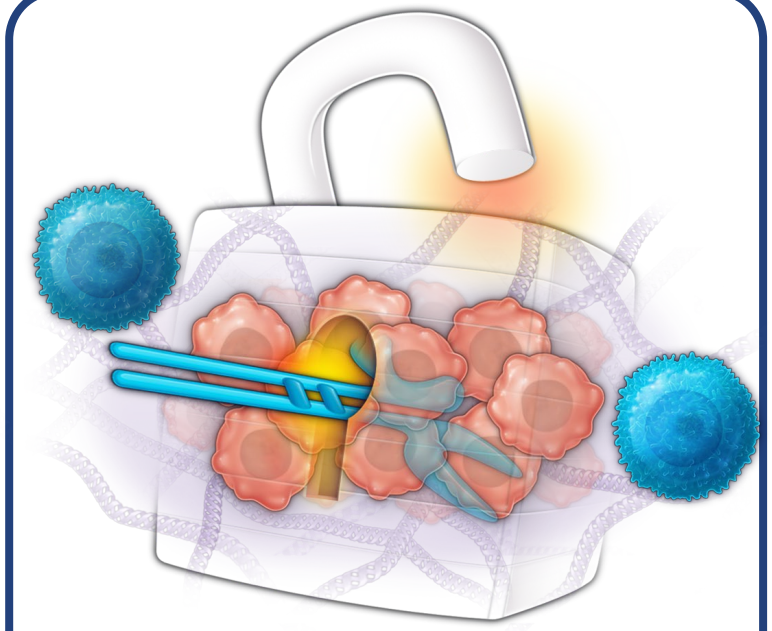
NC410: Key to Unlock TME and Normalize Immune Response

TME ACCESS LOCKED



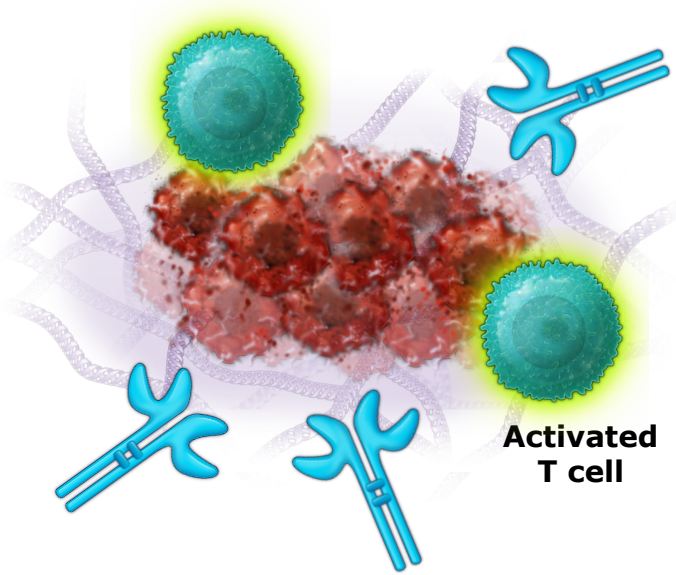
Many “keys” but none fit lock

NC410 UNLOCKS ECM



Enhances T cell infiltration

REMODELING & NORMALIZATION



Activated T cells kill tumor

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NC410 Safety & Early Efficacy Data from Cohorts 1-5

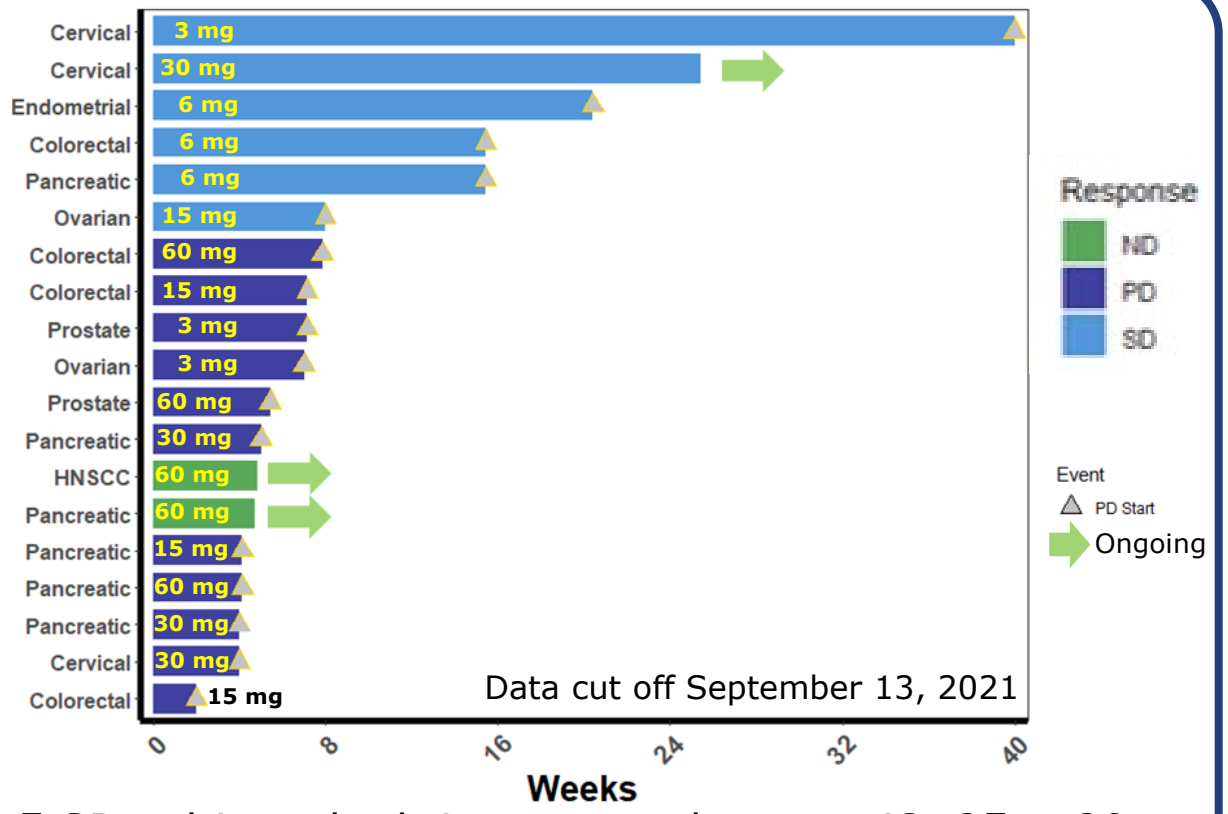
Phase 1a Dose Escalation

- Cohort 1 3 mg
- Cohort 2 6 mg
- Cohort 3 15 mg
- Cohort 4 30 mg
- Cohort 5 60 mg
- Cohort 6 100 mg
- Cohort 7 200 mg
- Cohort 8 400 mg

- 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

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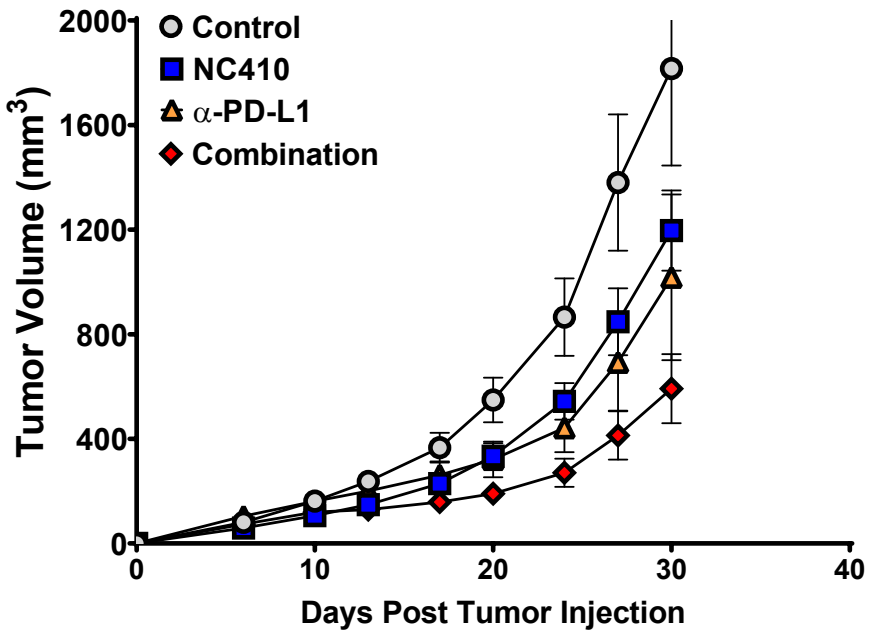
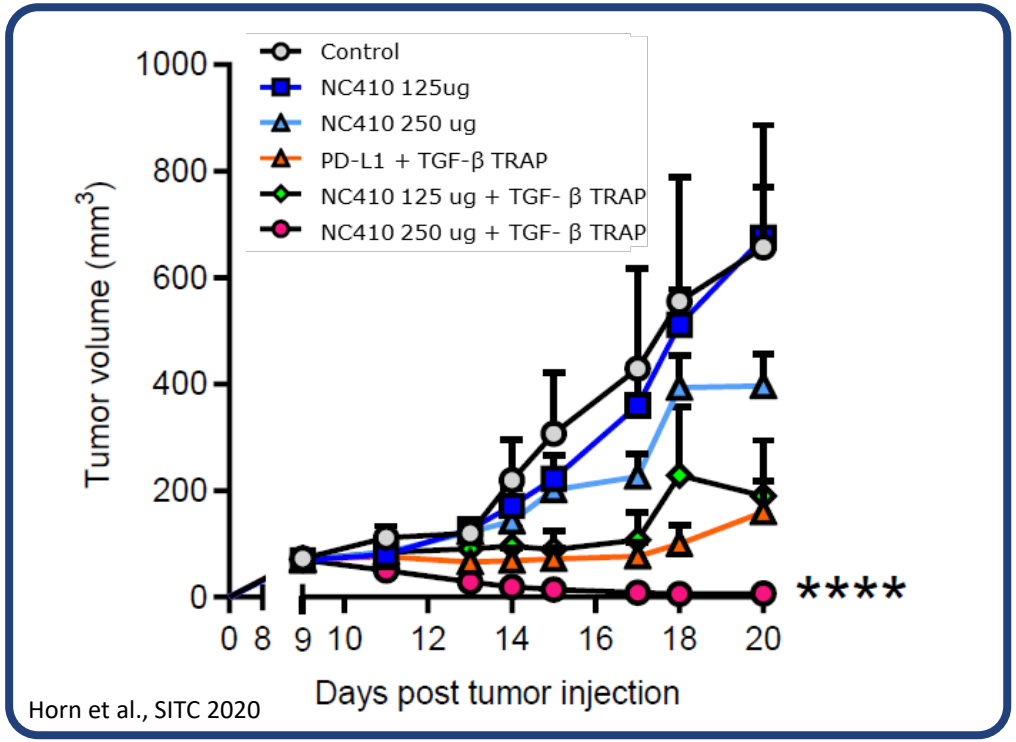
NC410 Demonstrates Synergistic Activity in Preclinical Models

PD-L1



PD-L1 TGF-β TRAP



Horn et al., SITC 2020

NC410

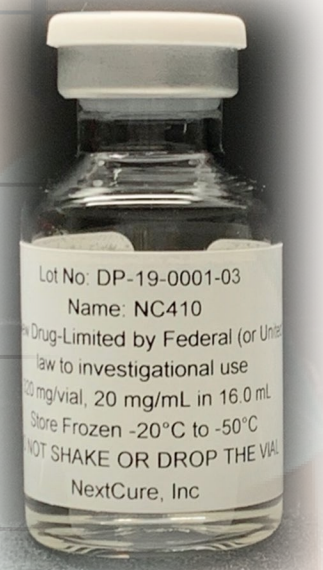
Remodels ECM Enhancing Immune Infiltration & Tumor Killing

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 2H 2022

NC762

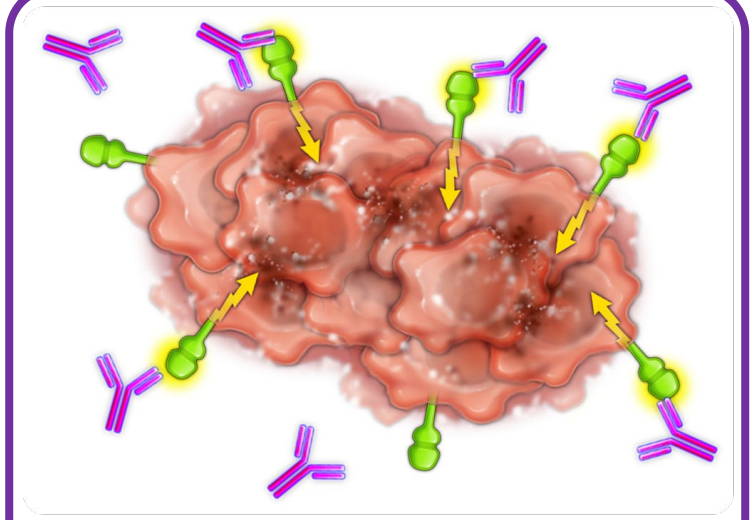
Humanized B7-H4 Monoclonal Antibody

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



B7-H4

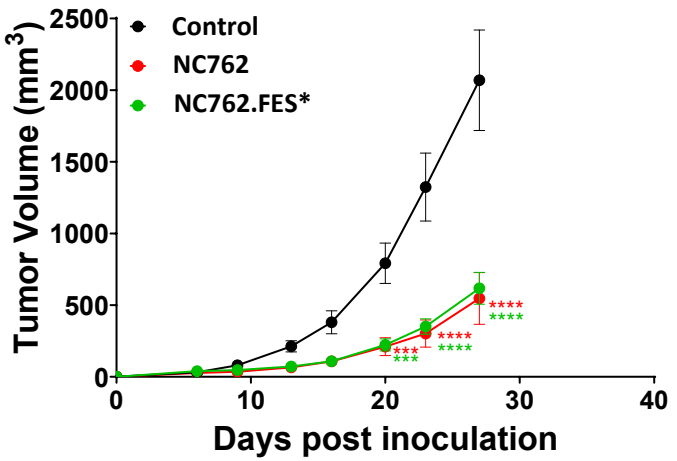
NC762 (B7-H4 mAb)

HIGHLIGHTS

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

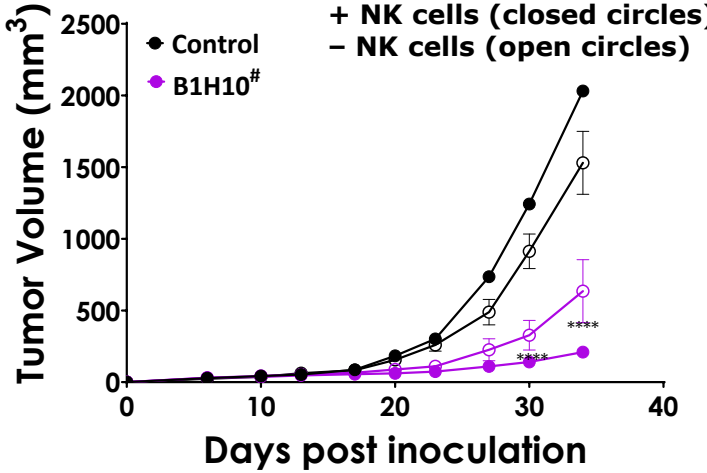
NC762 Inhibits Human Melanoma Tumor Growth *In Vivo*
Activity Enhanced by Human PBMCs

TUMOR INHIBITION



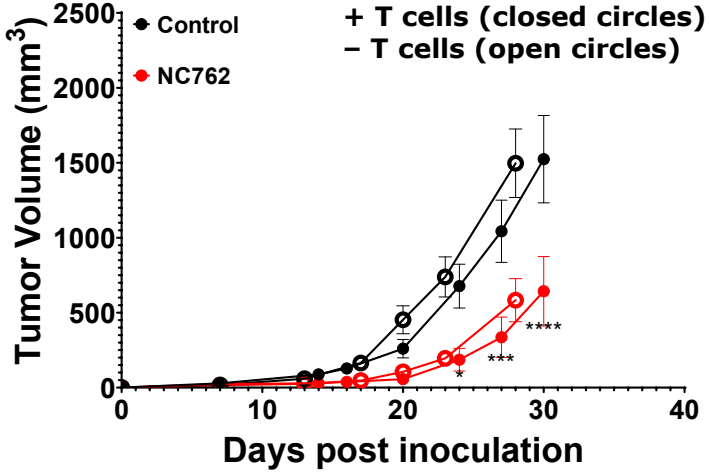
*Designed to reduce FcγR binding/restrict ADCC activity

NKs ENHANCE ACTIVITY



#Parent of NC762

T CELLS NOT REQUIRED



Archer et al., AACR 2021

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NC762

Summary & Upcoming Milestones

SUMMARY

Unique MOA

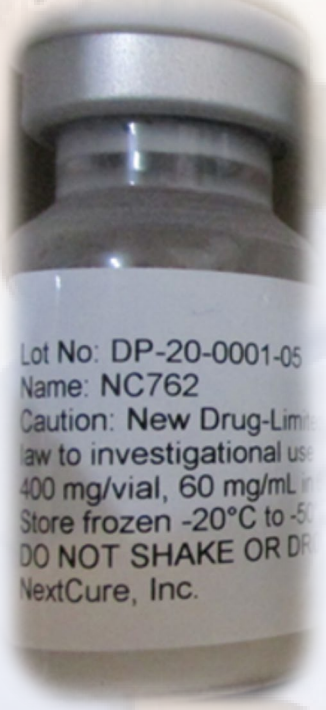
- mAb inhibits tumor cell growth
- Not dependent on immune cell infiltration into TME
- NK cells enhance activity

IND filed with FDA

Initiated Phase 1 trial

UPCOMING MILESTONE

Initial Phase 1 data 2H 2022



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New Program - NC525 (LAIR-1 mAb)

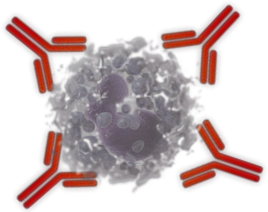
NC525
IND Q4 2022

BIOLOGY

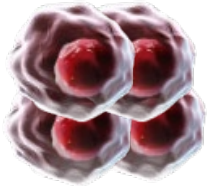
- LAIR-1 expression
  - High on AML blasts and leukemia stem cells (LSCs)
  - Minimal on hematopoietic stem and progenitor cells (HSPCs)

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

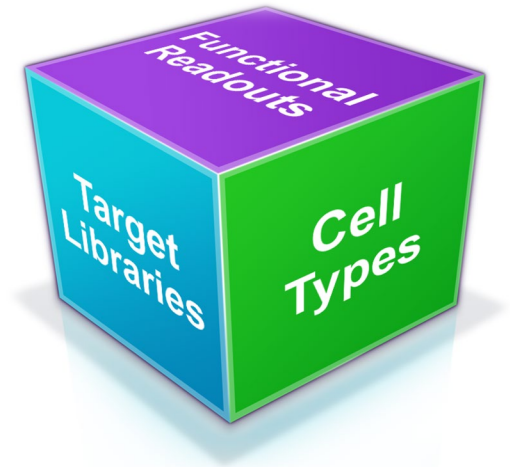
Functional, **I**ntegrated, **N**extCure **D**iscovery in **I**mmuno-**O**ncology

FUNCTIONAL READOUTS

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

TARGET LIBRARIES

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



CELL TYPES

- Primary
- Cell lines
- Lymphoid
- Myeloid
- Tumor

NextCure

GMP Manufacturing Facility: Added Additional Capacity

2,000L Capacity

Speed — **Use of a CMO adds ~8 months to timelines**

Flexibility — **Prioritization and scheduling**

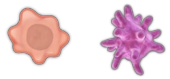
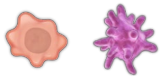
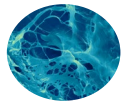
Efficiency — **Operational and capital efficiency**

Quality — **Controlling quality with experienced team**

Utilized to Produce Clinical Material for All Lead Programs

NextCure

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)

Worldwide Rights to All Programs

NextCure

Significant Momentum & Milestones in 2022

ON TRACK
NC318, NC410, NC762

MOMENTUM
Building Pipeline

TEAM
Experienced

Q1 2024
Runway