

SEPTEMBER 13, 2021



Next-Generation Immunomedicines

H.C. Wainwright 23rd Annual Global Investment Conference

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-K filed with the SEC on August 5, 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-1)



Phase 1

NC762
(B7-H4)



Phase 1

PIPELINE *Progress*

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

PRODUCT *Strategy*

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

PEOPLE *Experience*

- Fully integrated GMP manufacturing
- Experienced team
- Founder/SAB Head: Dr. Lieping Chen (discovered PD-L1)

Product Development Pipeline

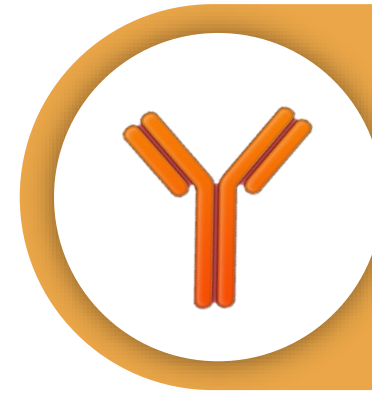
PROGRAMS	CELLS	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT MILESTONE
PRODUCT CANDIDATES							
NC318 (S15) Monotherapy	Tumors and macrophages	ONCOLOGY					Data update 4Q 2021
NC318 (S15) Anti-PD-1 Combo*	Tumors and macrophages	ONCOLOGY					Initial data 1H 2022
NC410 (LAIR-1)	Dendritic and T cells	ONCOLOGY					Initial data 2H 2021
NC762 (B7-H4)	Tumors	ONCOLOGY					Initial data Mid-2022
DISCOVERY AND RESEARCH PROGRAMS							
Multiple Programs	Multiple cell types						IND filing in 2022

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

Retains Worldwide Rights to All Programs

NC318

Humanized Siglec-15 (S15) Monoclonal Antibody

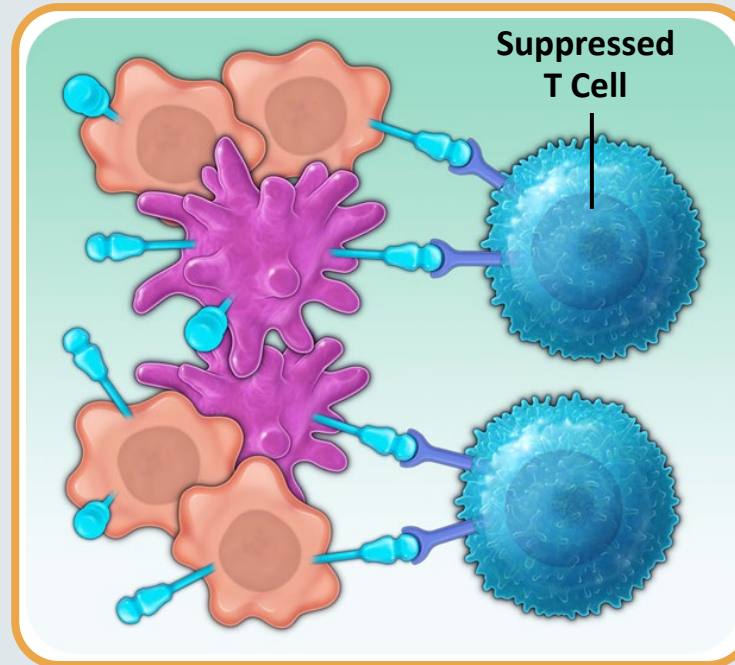


Phase 1/2
CLINICAL
TRIAL

BIOLOGY

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

MOA



HIGHLIGHTS

- CLIA test for patient selection
- Increase drug exposure
- Biomarker evaluation
- Yale NSCLC trial

NC318 Phase 1/2 Monotherapy Trial Status

PHASE 1

- Dose escalation
- 49 patients
- 15 tumor types
- All comers regardless of PD-L1 or S15 expression status
- 1 confirmed CR NSCLC (118+ weeks)¹
- 1 confirmed PR NSCLC (92+ weeks)¹

PHASE 2

- S15+ patient selection
- Resumed enrollment of NSCLC adenocarcinoma cohort
- 800 mg weekly
- 1 confirmed PR H&N (40 weeks)^{1,2}
- 1 confirmed PR TNBC (21 weeks)^{1,2}

The Angeles Clinic
AND RESEARCH INSTITUTE
A CEDARS-SINAI AFFILIATE

next
ONCOLOGY

NYU Langone
MEDICAL CENTER

John Theurer
Cancer Center
at Hackensack University Medical Center

Adding sites

1-As of March 4, 2021; 2-Prior dose regimen (400 mg, q2w)

Yale Investigator-Initiated Phase 2 Trial in Non-Small Cell Lung Cancer

PRINCIPAL INVESTIGATORS

- Roy Herbst, MD, PhD
- Scott Gettinger, MD



MONO

- S15+ patients
- PD-1 refractory

COMBO

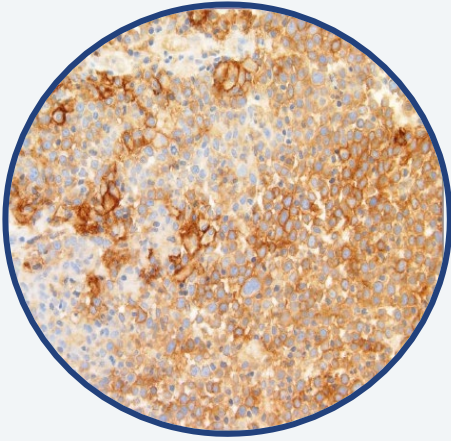
- Pembrolizumab
- 2 arms
 - PD-1 refractory
 - PD-1 naïve

NCT04699123

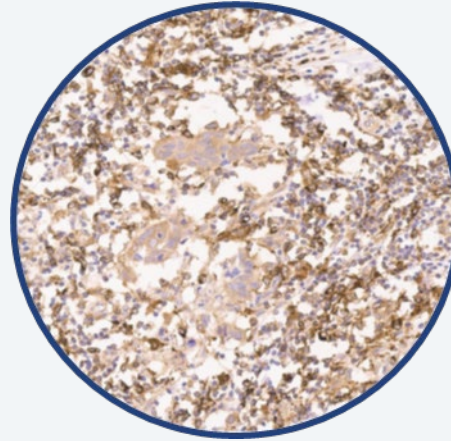
Trial Initiated April 2021

Selecting S15 Positive Patients for NC318 Study

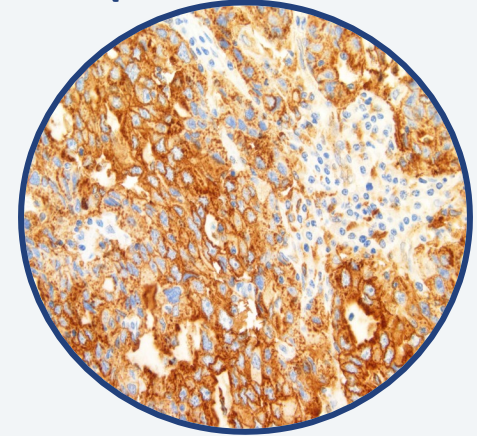
Head & Neck



Breast



NSCLC (adenocarcinoma)



Tissue Biopsies



CLIA Validated Assay



Enrich S15+ Patients

NC410

Decoy Human Fusion Protein
Targeting the TME

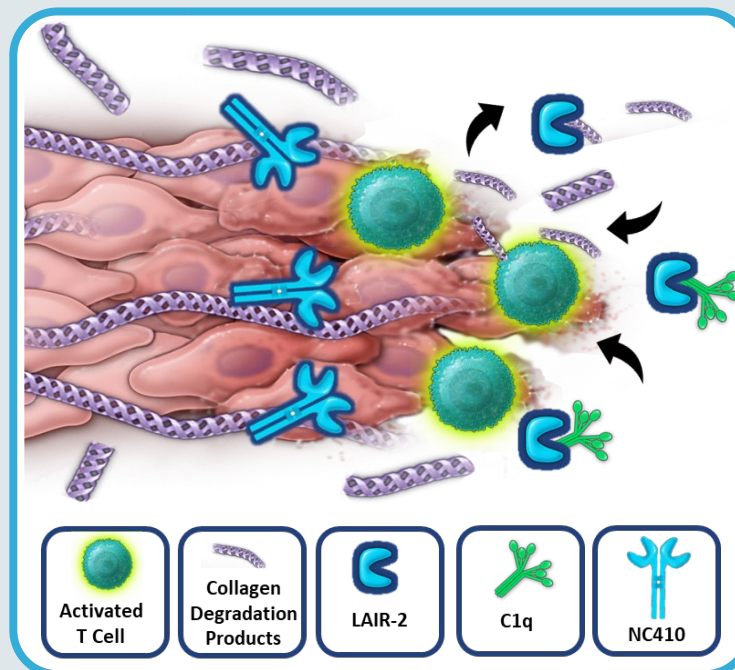


Phase 1/2
CLINICAL
TRIAL

BIOLOGY

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

MOA



HIGHLIGHTS

- IHC assay for patient selection
- Biomarkers
- Synergistic combinations
- ASCO 2021 poster
- eLife 2021 publication

Scientific Advancement in Understanding Collagen and LAIR Biology

2019

Science Translational Medicine

Targeted antibody and cytokine cancer immunotherapies through **collagen** affinity

Jun Ishihara^{1*}, Ako Ishihara^{1*}, Koichi Sasaki^{1†}, Steve Seung-Young Lee², John-Michael Williford¹, Mariko Yasui³, Hiroyuki Abe³, Lambert Potin^{1,4}, Peyman Hosseini¹, Kazuto Fukunaga^{1‡}, Michal M. Racz¹, Laura T. Gray¹, Aslan Mansurov¹, Kiyomitsu Katsumata^{1§}, Masashi Fukayama³, Stephen J. Kron², Melody A. Swartz^{1,5}, Jeffrey A. Hubbell^{1||}

2019

Science Translational Medicine

Anchoring of intratumorally administered cytokines to **collagen** safely potentiates systemic cancer immunotherapy

Noor Momin^{1,2}, Naveen K. Mehta^{1,2*}, Nitasha R. Bennett^{1*}, Leyuan Ma^{1,3*}, Joseph R. Palmeri^{1,4}, Magnolia M. Chinn^{1,2}, Emi A. Lutz^{1,2}, Byong Kang^{1,2}, Darrell J. Irvine^{1,2,3,5,6}, Stefani Spranger^{1,7}, K. Dane Wittrup^{1,2,4†}

2020

Nature Communication

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

David H. Peng¹, Bertha Leticia Rodriguez¹, Lixia Diao², Limo Chen¹, Jing Wang², Lauren A. Byers¹, Ying Wei³, Harold A. Chapman³, Mitsuo Yamauchi⁴, Carmen Behrens⁵, Gabriela Raso⁵, Luisa Maren Solis Soto⁵, Edwin Roger Parra Cuentas⁵, Ignacio I. Wistuba⁵, Jonathan M. Kurie¹ & Don L. Gibbons^{1,6,§§}

2021

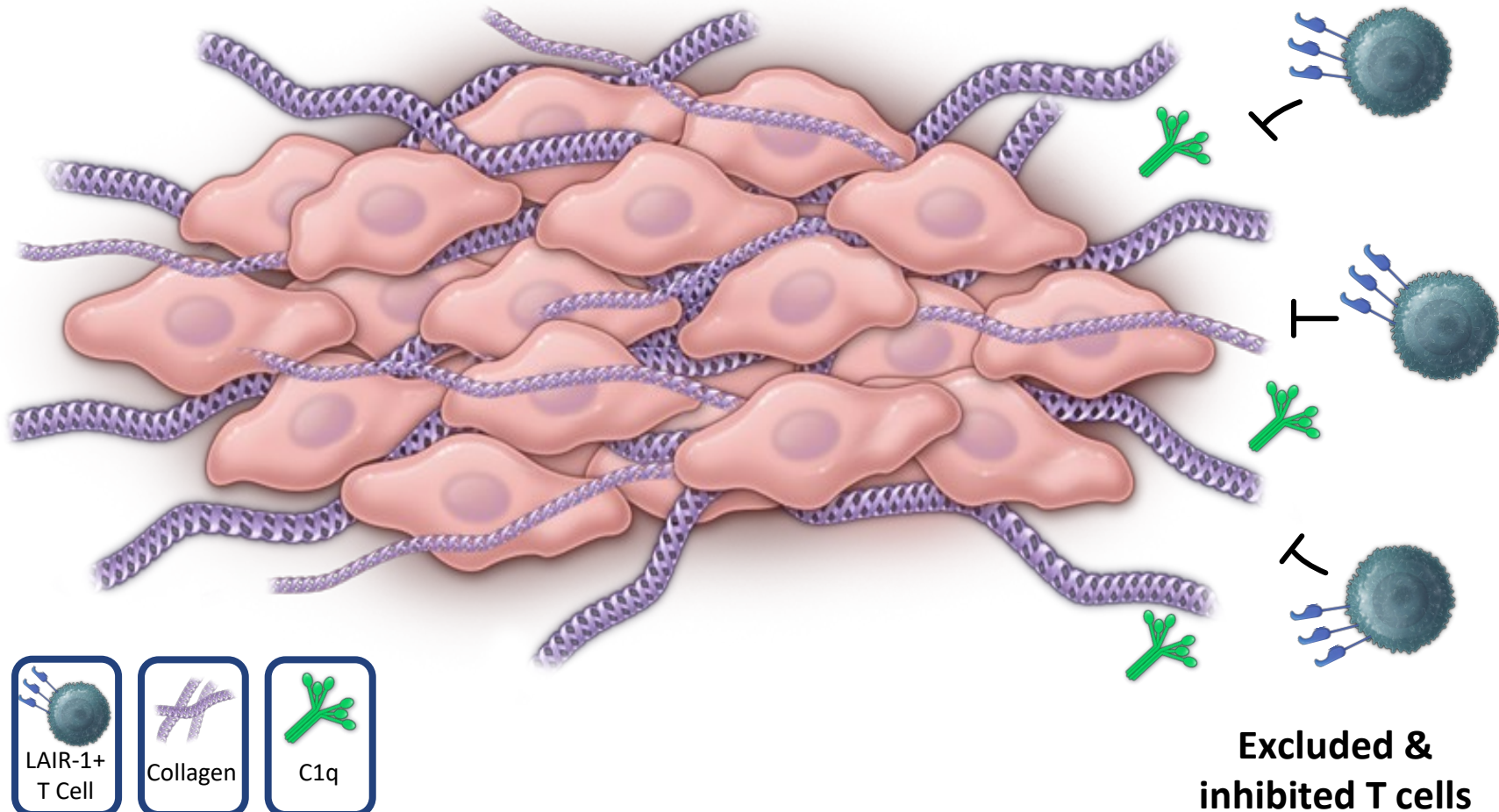
eLife

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

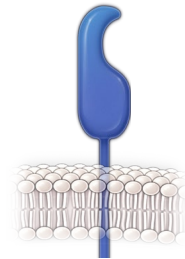
M Ines Pascoal Ramos^{1,2†}, Linjie Tian^{3†}, Emma J de Ruiter⁴, Chang Song³, Ana Paucarmayta³, Akashdip Singh^{1,2}, Eline Elshof^{1,2}, Saskia V Vijver^{1,2}, Jahangheer Shaik³, Jason Bosiacki³, Zachary Cusumano³, Christina Jensen⁴, Nicholas Willumsen⁴, Morten A Karsdal⁴, Linda Liu³, Sol Langermann³, Stefan Willems^{5§}, Dallas Flies^{3†*}, Linde Meyaard^{1,2‡*}

- ECM associated with suppression
- Elevated collagen correlates with
 - PD-1/PD-L1 resistance
 - Decreased T cells
 - Increased exhausted T cells
- LAIR-2 overexpression sensitizes tumors

Collagen Inhibits T Cells through LAIR-1 Pathway

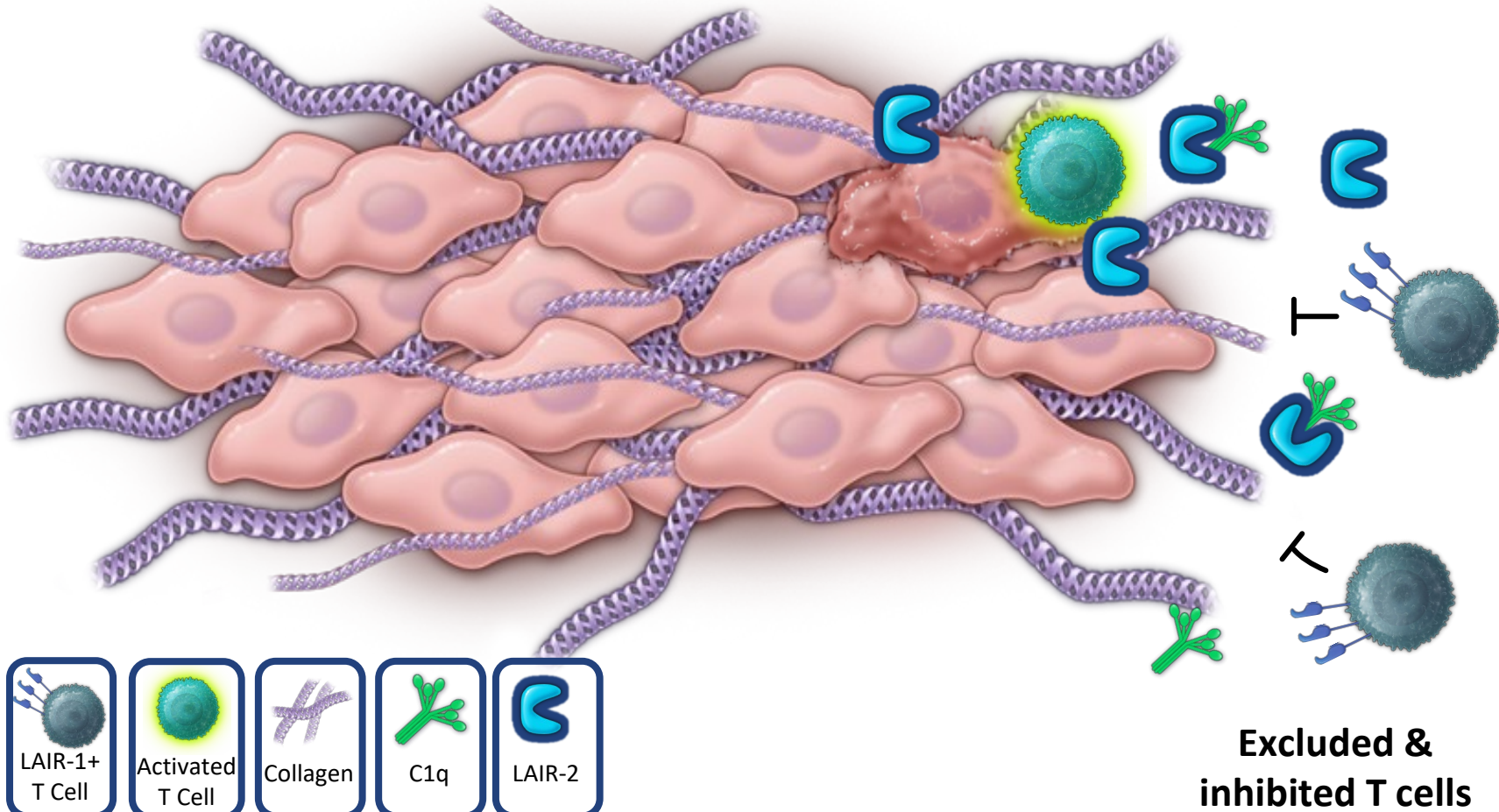


LAIR-1



- LAIR-1:
 - Co-inhibitory receptor
 - Binds collagen and C1q
- Collagen density is a barrier to T cell migration and suppresses activation
- C1q enhances cancer cell proliferation

LAIR-2 is a Natural Decoy of LAIR-1

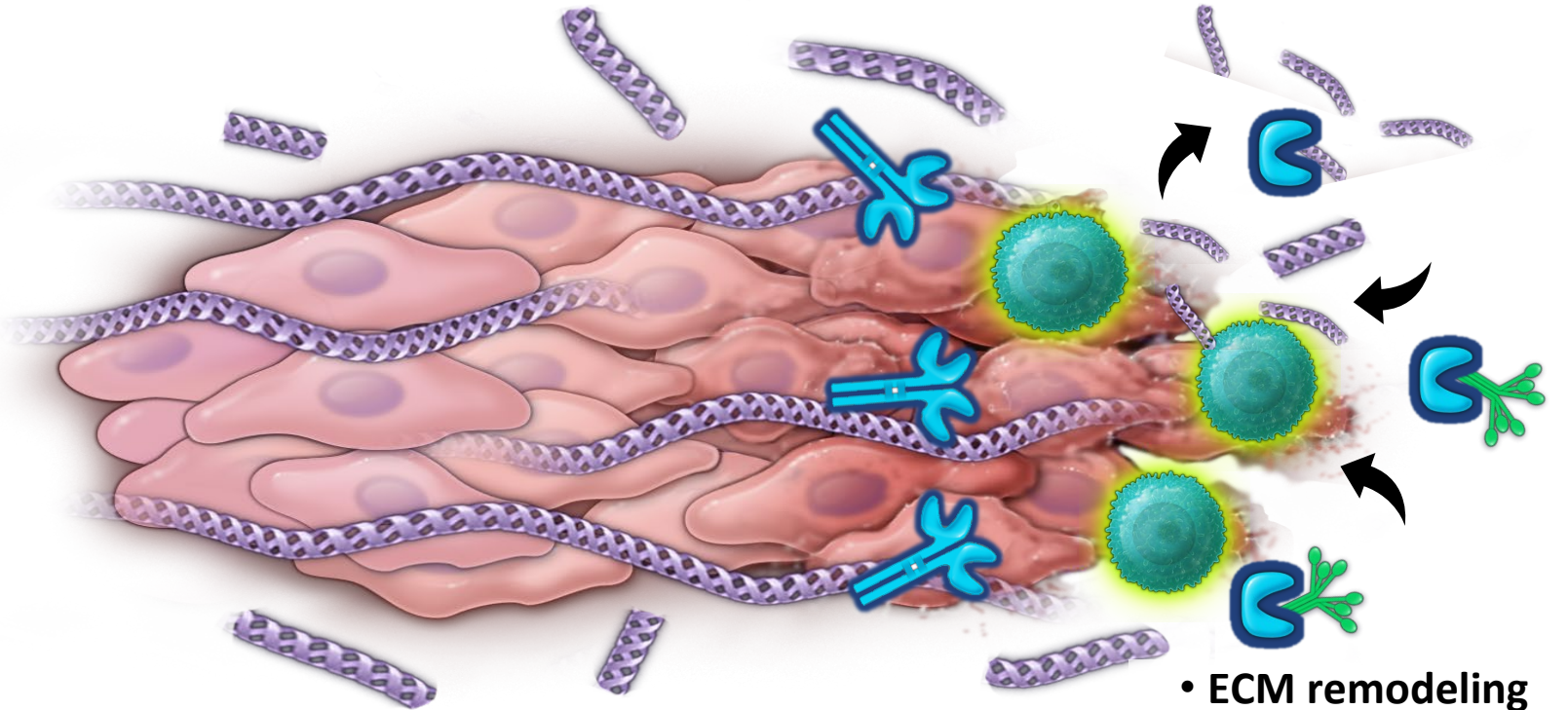


LAIR-2



- LAIR-2 is a decoy molecule
- Differs from LAIR-1
 - Naturally soluble
 - Binds ligands with greater affinity
- Modulates LAIR-1 inhibition

NC410 Remodels Extracellular Matrix (ECM) & Restores Immune Activity



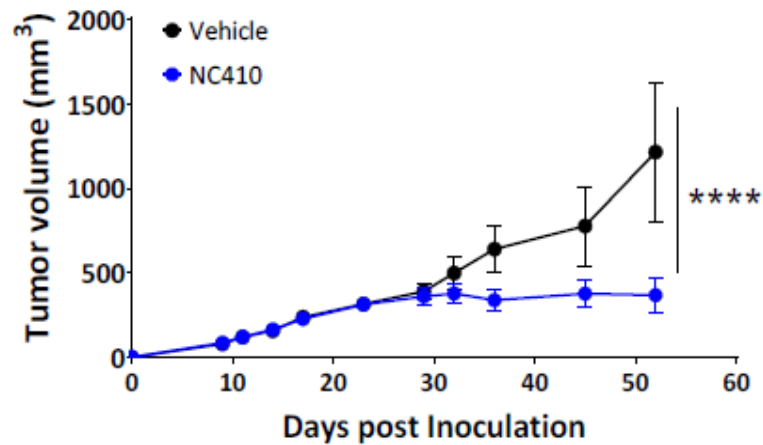
NC410



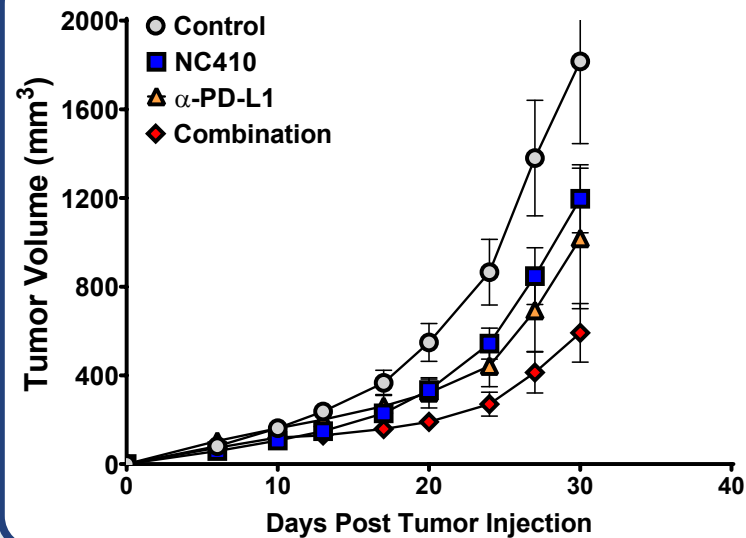
- NC410 is a fusion protein of LAIR-2
- Decreases tumor progression
- Blocks collagen mediated suppression
- Mediates T cell infiltration and restores activation
- Collagen degradation fragments (biomarkers of ECM remodeling)

NC410 Demonstrates Activity in Preclinical Models

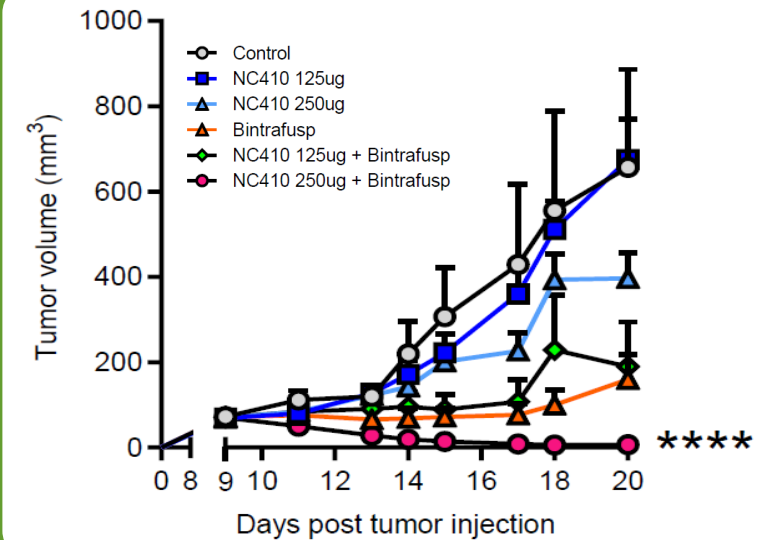
MONO



PD-L1 COMBO



BINTRAFUSP ALPHA COMBO



Horn et al., SITC 2020

NC410 Phase 1 Portion of Phase 1/2 First-in-Human Trial

DESIGN

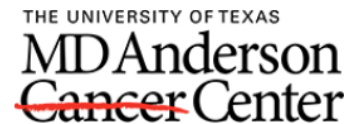
- Dose-escalation
 - 8 dose cohorts
 - 3 mg to 400 mg
- Safety & tolerability

TUMOR TYPES

- Advanced or metastatic solid tumors
- NSCLC
 - Ovarian cancer
 - Pancreatic cancer

DELIVERABLES

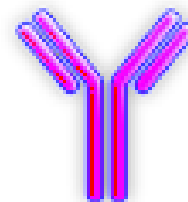
Initial Phase 1 data
4Q 2021



Adding sites

NC762

Humanized B7-H4 Monoclonal Antibody

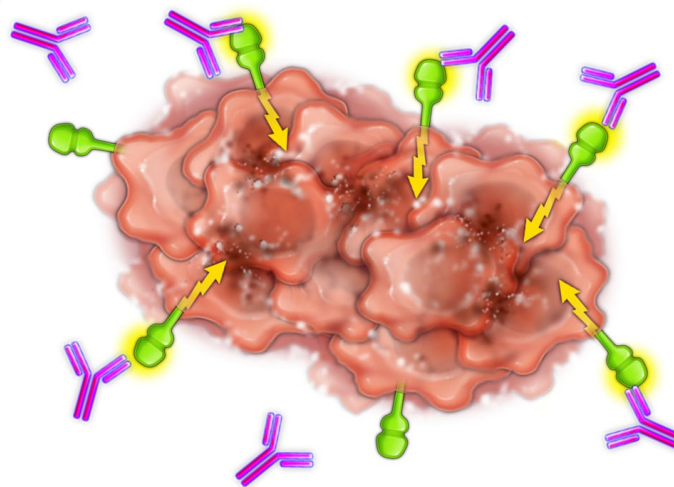



Phase 1/2
CLINICAL
TRIAL


BIOLOGY

- Unique mechanism of action
- Inhibits tumor cell growth and 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

NC762 Phase 1 Portion of Phase 1/2 First-in-Human Trial

DESIGN

- Dose-escalation
- Safety & tolerability

TUMOR TYPES

- Advanced or metastatic solid tumors
- NSCLC
 - Breast cancer
 - Ovarian cancer

DELIVERABLES

Initial Phase 1 data
mid-2022



Adding sites

GMP Manufacturing Facility: Capacity to Produce Clinical Material for All Programs

2,000L Capacity



Speed

Use of a CMO adds ~8 months to timelines

Flexibility

Prioritization and scheduling

Efficiency

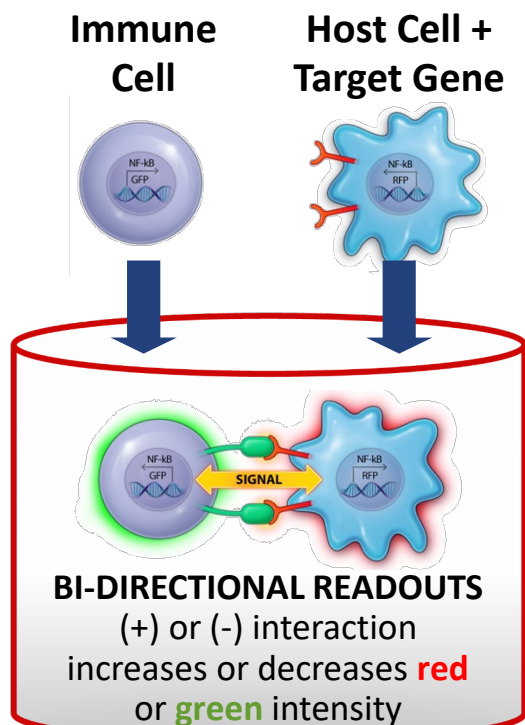
Operational and capital efficiency

Quality

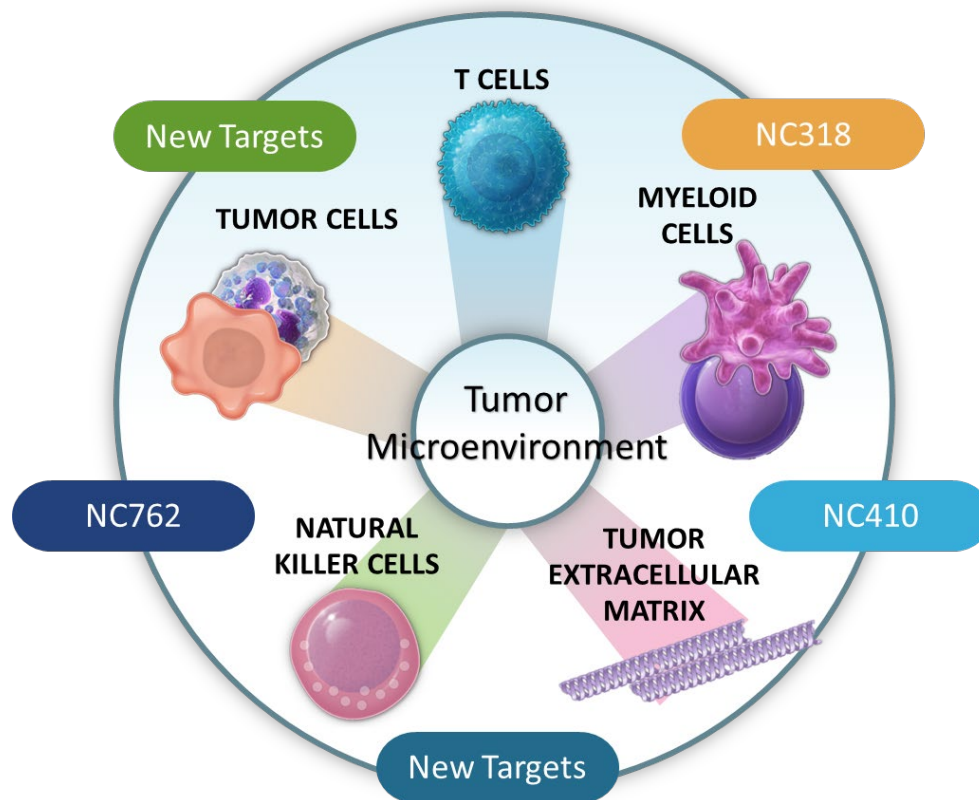
Controlling quality with experienced team

FIND-IO: Finding Solutions with a Powerful Discovery Engine

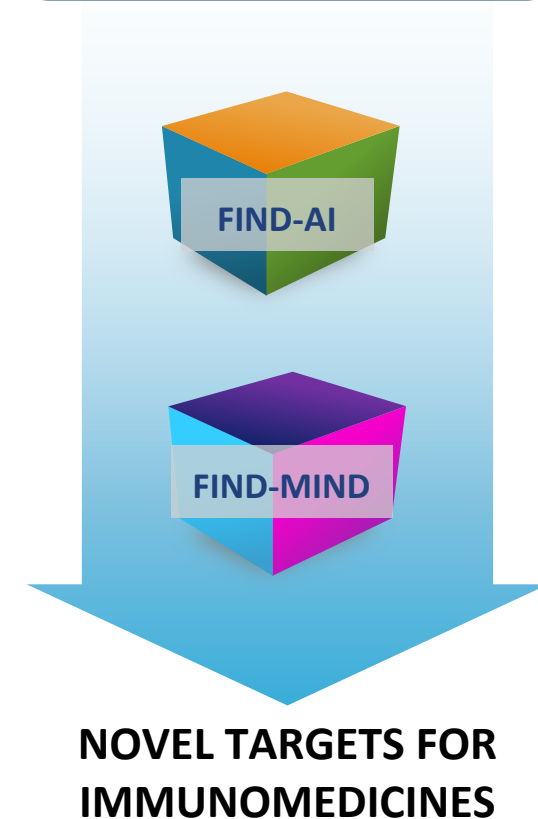
FUNCTIONAL READOUTS



FUTURE PIPELINE



DIVERSIFICATION



Anticipated Near-Term Milestones

Cash Position: \$249.5M Runway: 2H 2023

PROGRAMS	2021					2022			
	Q1	Q2	Q3	Q4		Q1	Q2	Q3	Q4
PRODUCT CANDIDATES									
NC318 (S15) Monotherapy					Phase 2 update				
NC318 (S15) Anti-PD-1 Combo*		Started Phase 2 ✓				Anticipate initial data			
NC410 (LAIR-1)					Initial data				
NC762 (B7-H4)		Started Phase 1 ✓					Initial data		

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

 **September**



Committed to Addressing the Unmet Needs of Patients with New Solutions

FOCUSED
Approach

PROVEN
Momentum

INNOVATIVE
Platform

EXPERIENCED
Team

FUTURE
Deliverables