



Investor Update

November 15, 2021

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

- NC318 (S15): Phase 2 mono – SITC presentation
- NC410 (LAIR-2): Phase 1 mono – SITC posters
- NC762 (B7-H4): Phase 1 mono
- New Product Candidate: NC525 - ASH poster

PRODUCT STRATEGY

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

PEOPLE

- Experienced team
- Fully integrated GMP manufacturing team

Advancing Product Development Pipeline

PROGRAMS	TARGET	CELLS	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
PRODUCT CANDIDATES							
NC318	S15	Tumors and macrophages	NSCLC, BREAST, H&N				
NC318 Anti-PD-1 Combo*	S15	Tumors and macrophages	NSCLC				
NC410	LAIR-2	Myeloid and T cells	NSCLC, H&N, GASTRIC, CRC, CERVICAL				
NC762	B7-H4	Tumors	NSCLC, BREAST, OVARIAN				
NC525	LAIR-1	Leukemic Stem Cells	AML				
DISCOVERY AND RESEARCH PROGRAMS							
Multiple Programs	Multiple Targets	Multiple cell types					

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

Worldwide Rights to All Programs

Agenda



NC318 – Ph1 & Ph2

Update, patient selection, dosing, sS15



Roy Herbst, MD, PhD

Unmet need in lung cancer



NC410 – Ph1

Safety, dose escalation, biomarkers



NC525 – PC

New program; IND 4Q 2022

Agenda – NC318 Phase 1 & Phase 2



NC318 – Ph1 & Ph2

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New program; IND 4Q 2022

NC318 Clinical Trial History and Update

SITC Data

Phase 1

- 3+3 design
- Dose escalation, 8 – 1600 mg
- 15 tumor types
- 49 patients

Phase 2

- Simon 2-stage design
- 400 mg Q2W
- NSCLC, ovarian, H&N and breast
- 47 patients



Amended Phase 2

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

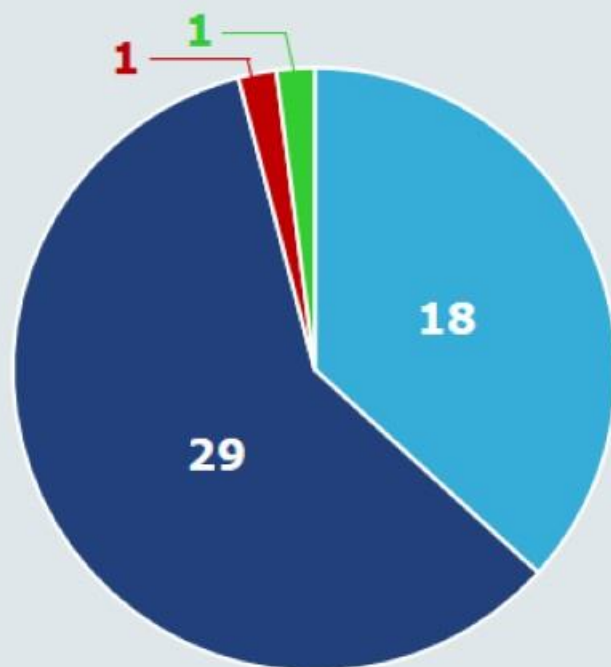
Yale Phase 2 (Combo)

- NSCLC
- Mono therapy: PD-1 refractory
- Pembro combo: PD-1 refractory
- Pembro combo: PD-1 naïve

NC318 Historical Clinical Outcomes

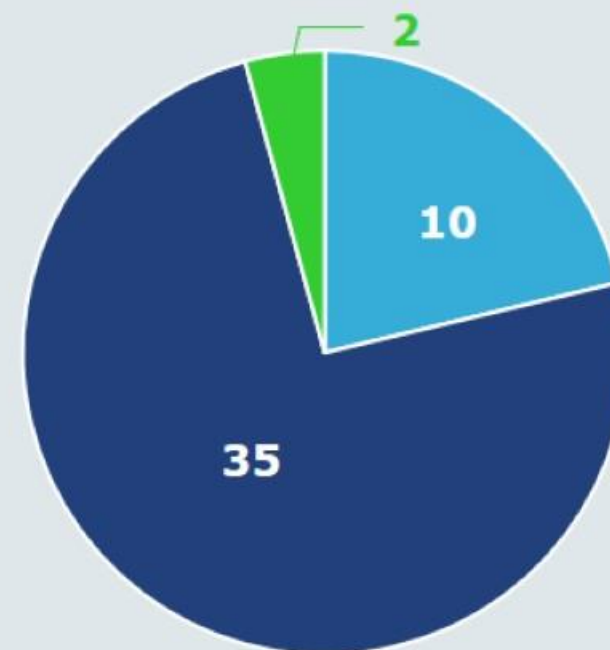
Phase 1

- 3+3 design
- Dose escalation, 8 – 1600 mg
- 15 tumor types
- 49 patients
- 1 CR (NSCLC); 1 PR (NSCLC); 18 SD



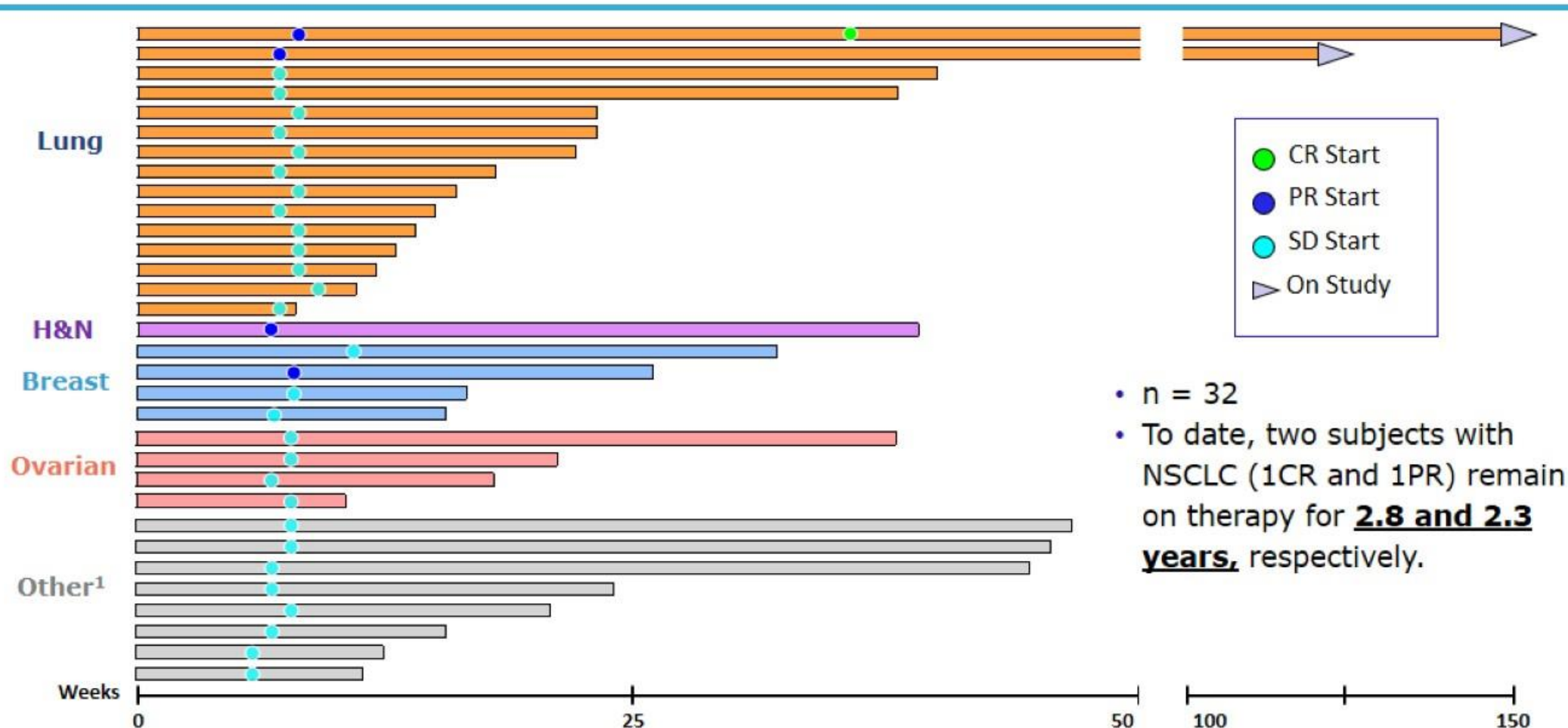
Phase 2

- Simon 2-stage design
- 400 mg Q2W
- NSCLC, ovarian, H&N and breast
- 47 patients
- 2 PRs (H&N and TNBC); 10 SD



■ Complete Response (CR)
■ Partial Response (PR)
■ Stable Disease (SD)
■ Progressive Disease (PD)

Time to & Duration of Disease Control



- n = 32
- To date, two subjects with NSCLC (1CR and 1PR) remain on therapy for **2.8 and 2.3 years**, 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)

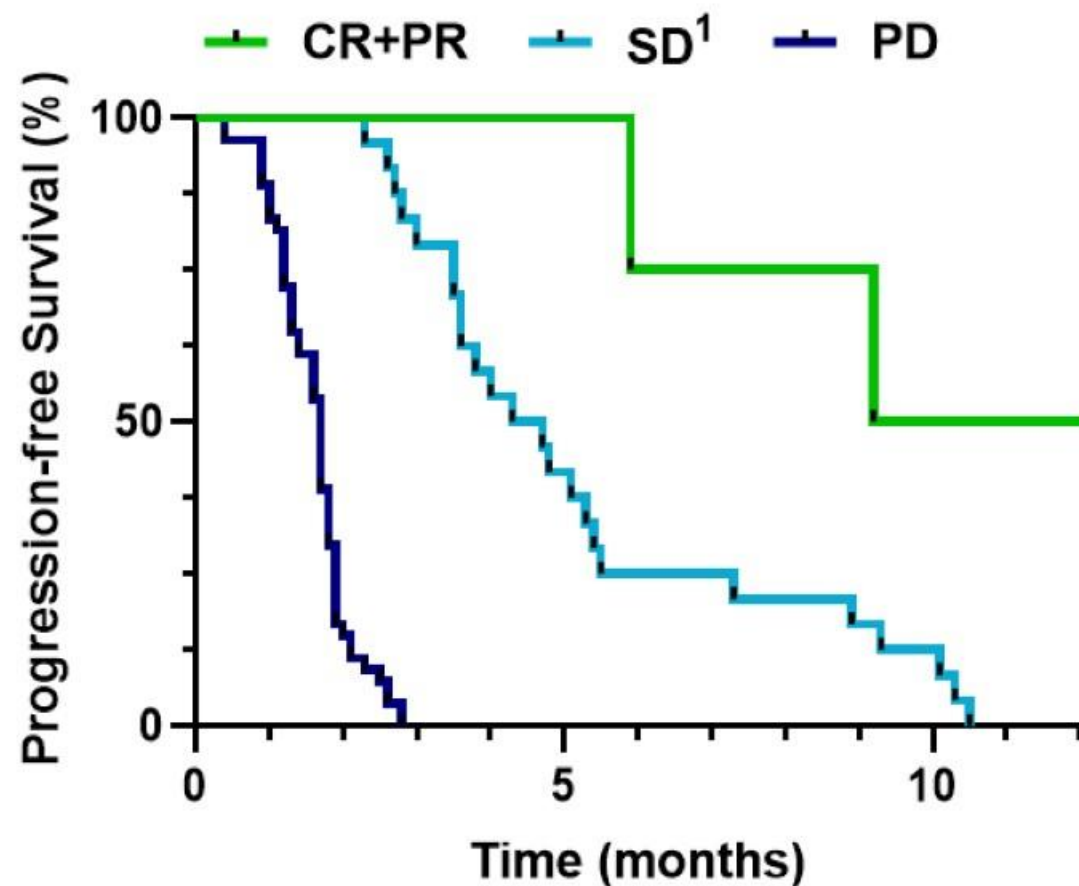
²Total of 96 subjects were treated with 10 subjects determined as non-evaluable (NE) for efficacy based on RECIST v1.1 and or clinical evaluations by principal investigators (PIs)

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

Progression-free Survival in the *Absence* of S15 Selection



Median PFS across all tumor types in Disease Control (DC; CR/PR/SD) is 5.0 months

- CR+PR: 18.3 months
- SD: 4.5 months
- PD: 1.7 months

¹4 SD subjects were lost to follow up for PFS

Retrospective Analysis in S15+ Patients

Disease Control Rate Increased in S15+ Patient Population

- Complete Response (CR)
- Partial Response (PR)
- Stable Disease (SD)
- Progressive Disease (PD)
- Not Evaluable (NE)

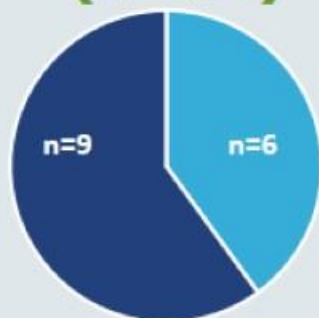
Subjects treated
with NC318
(n=96)

IHC available &
evaluable
(n=39)

All Subjects

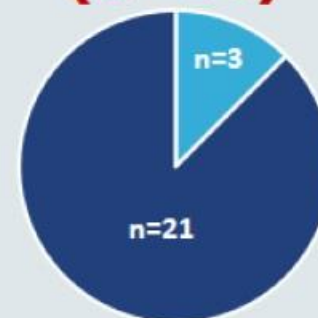


S15 Positive¹
(n=15)



40% Disease Control

S15 Negative
(n=24)



12% Disease Control

PD

- Lung = 5
- Other = 3
- Breast = 1

SD

- Lung = 3
- Other = 2
- Ovarian = 1

PD

- Lung = 8
- Ovarian = 6
- HNSCC = 3
- Breast = 2
- Other = 2

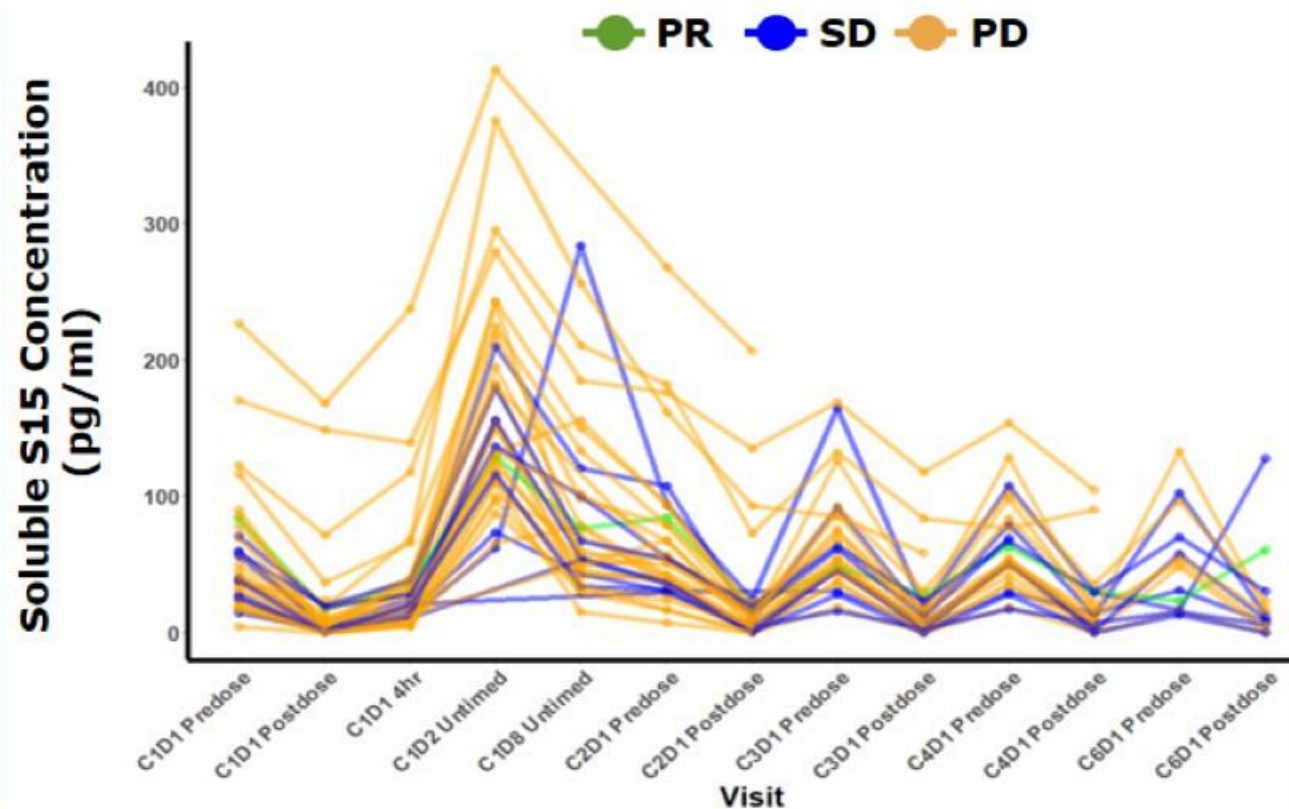
SD

- Lung = 2
- Breast = 1

¹H score ≥ 1

Soluble S15 Changes Associated with NC318 Dosing

- After infusion, soluble S15 (sS15) increased several fold compared to baseline
- PD was observed with a higher fold increase post-infusion (24 hours)
- PD may also correlate with a higher baseline sS15 level

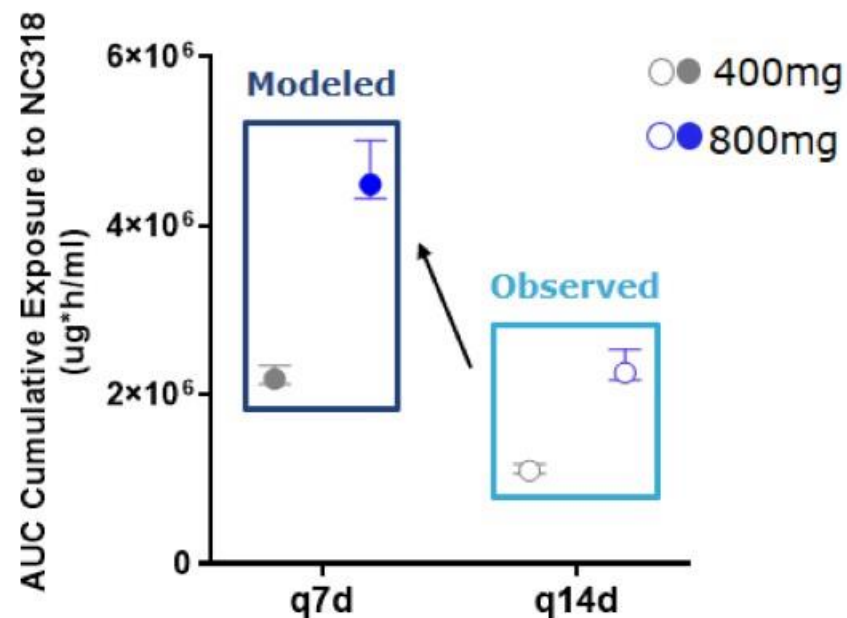


sS15 May Serve as NC318 Biomarker for Patient Selection & Monitoring

NC318 at 800mg Weekly Provides Increased Drug Exposure

PK/PD modeling showed 800mg Q1W would result in ~10-fold increase in drug exposure than achieved with 400mg Q2W

NC318 Area Under the Curve (AUC) by Dosing Schedule



Modeled AUC was estimated based on a 75kg subject

Increased Exposure May Impact Drug Activity and Clinical Outcomes

NC318 Phase 1 and Phase 2 Learnings & Current Trials

Phase 1 & Phase 2 Learnings

- ✓ Evidence of disease control at 400 mg Q2W
 - Lung: 45% Disease control; mPFS 5.2 months
 - All tumors: 37% Disease control; mPFS 5.0 months
- ✓ Enhanced outcomes in S15+ patients
- ✓ PK/PD modeling shows 800 mg Q1W results in ~10-fold increase



Current Trials

Amended Phase 2

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

Yale Phase 2 (Combo) NSCLC

- Mono therapy: PD-1 refractory
- Pembro combo: PD-1 refractory
- Pembro combo: PD-1 naïve

Agenda – Dr. Roy Herbst



NC318 – Ph1 & Ph2

Update, patient selection, dosing, sS15



Roy Herbst, MD, PhD

Unmet need in lung cancer



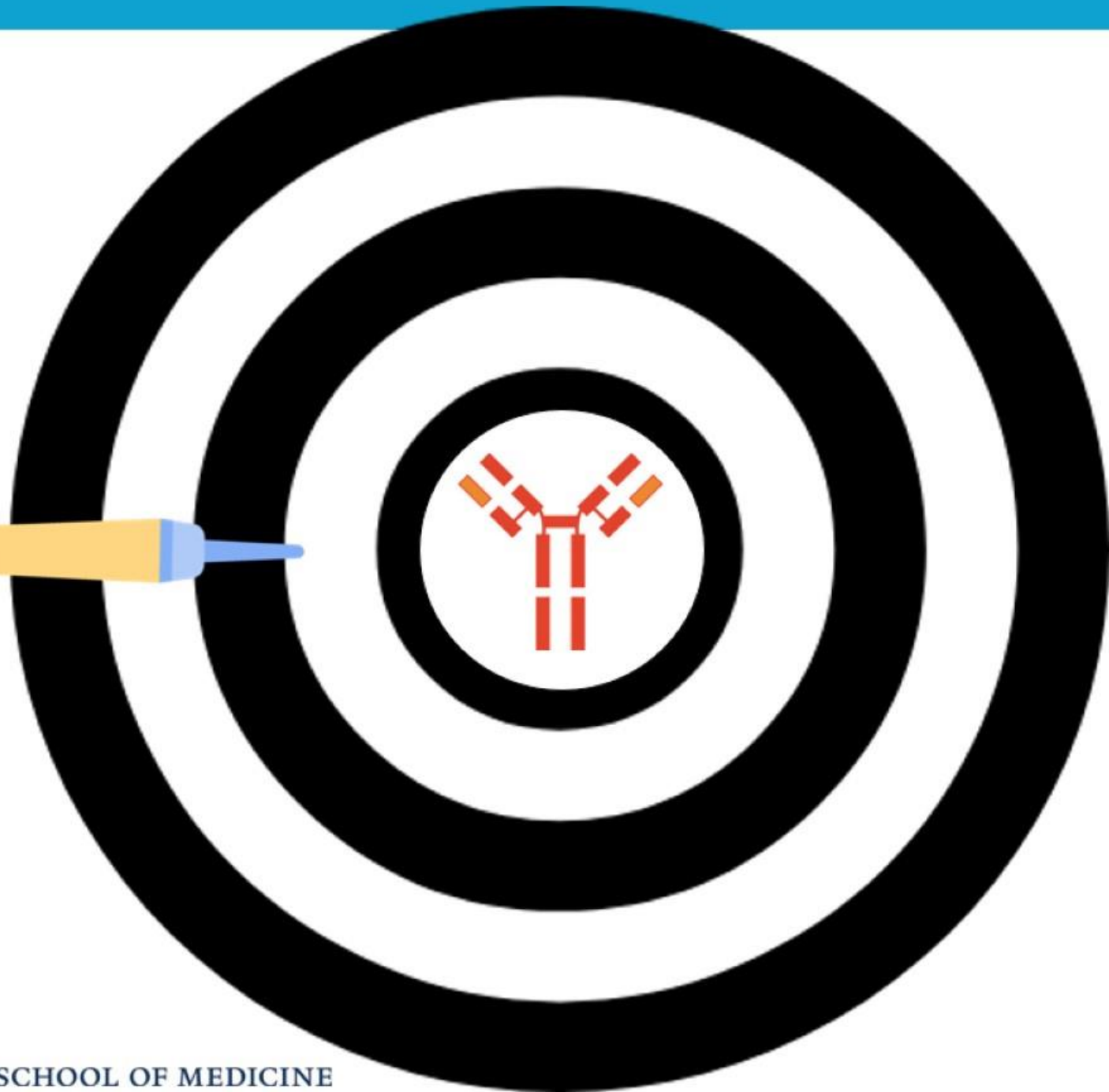
NC410 – Ph1

Safety, dose escalation, biomarkers



NC525 – PC

New program; IND 4Q 2022



**What are we waiting
for?**

**Time for more
targeted
immunotherapy!**

Siglec15 as a new target for lung cancer immunotherapy

nature
medicine

ARTICLES

<https://doi.org/10.1038/s41591-019-0334-x>

Siglec-15 as an immune suppressor and potential target for normalization cancer immunotherapy



Lieping Chen, MD PhD



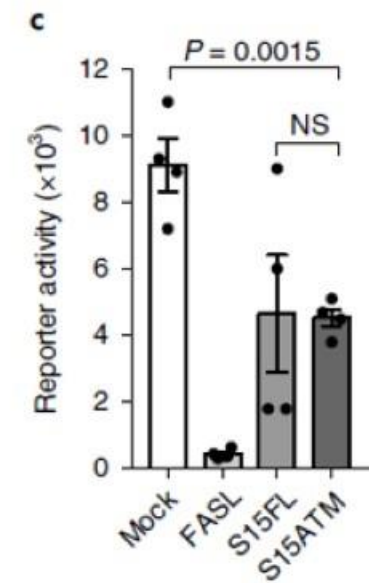
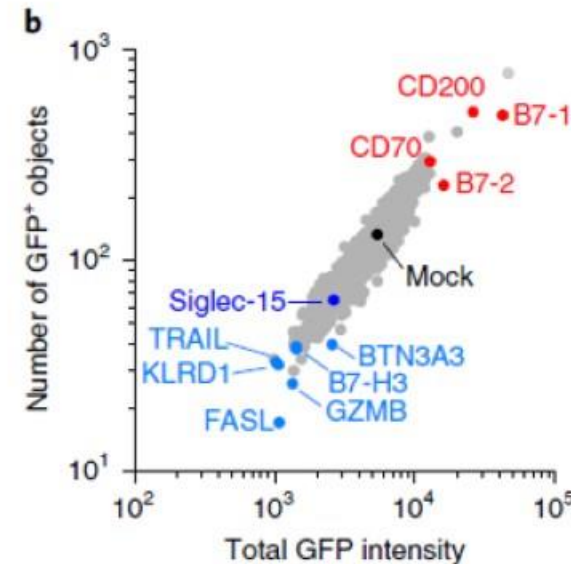
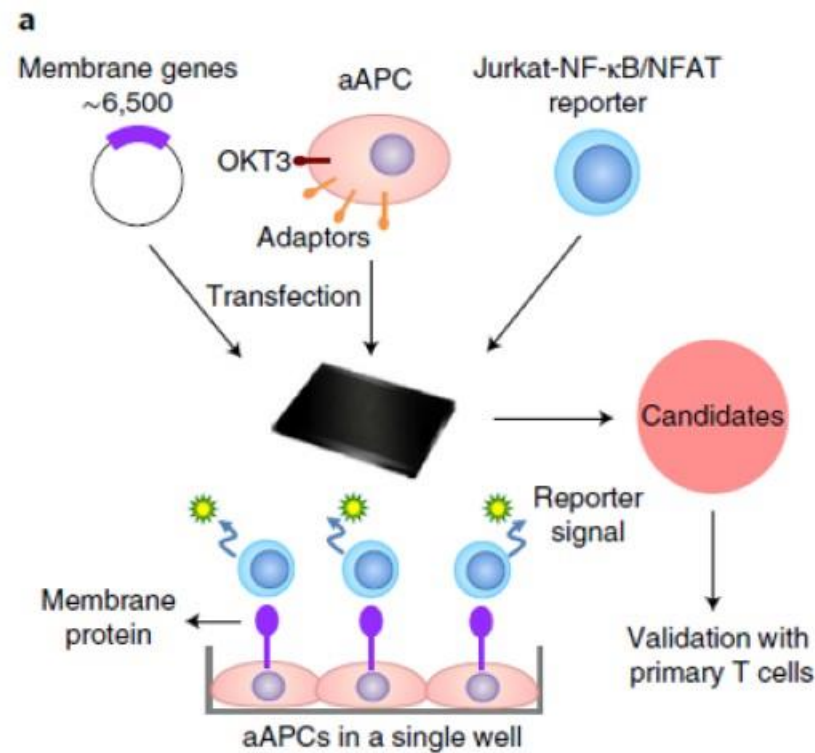
Roy Herbst, MD PhD



Scott Gettinger, MD



David Rimm, MD PhD



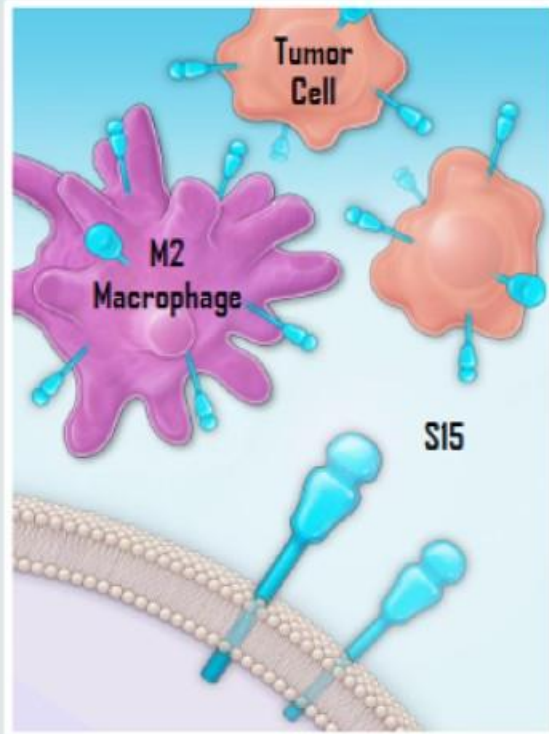
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	B7-1	B7-2	B7-H1	B7-DC	B7-H2	B7-H3	B7-H4	B7-H5	B7-H6
Identity (%)	28	22	24	21	28	23	19	20	24
Identity + similarity (%)	43	38	37	42	45	37	39	32	46

WHY DID WE SELECT S15?

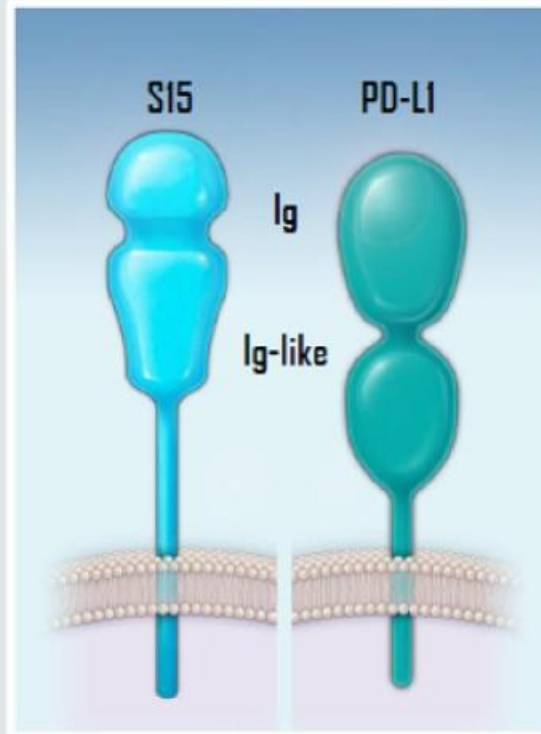
EXPRESSION

Expressed by Both Tumor Cells and Macrophages



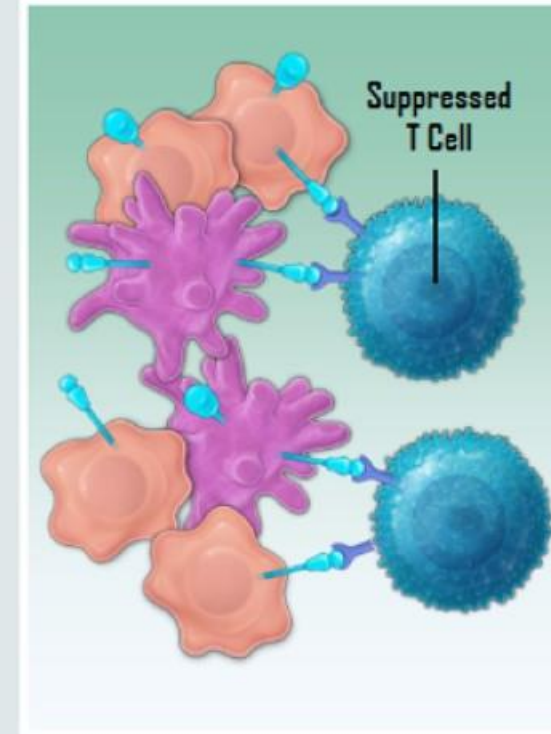
STRUCTURE

Similar to PD-L1

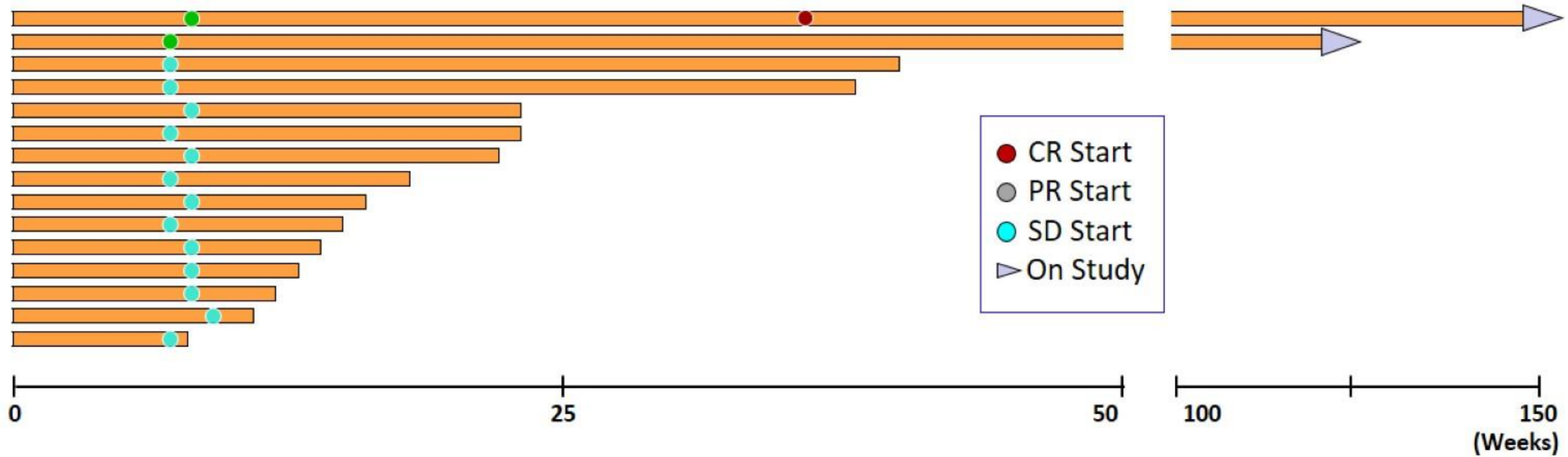


FUNCTION

Potently Suppresses T Cell Activities



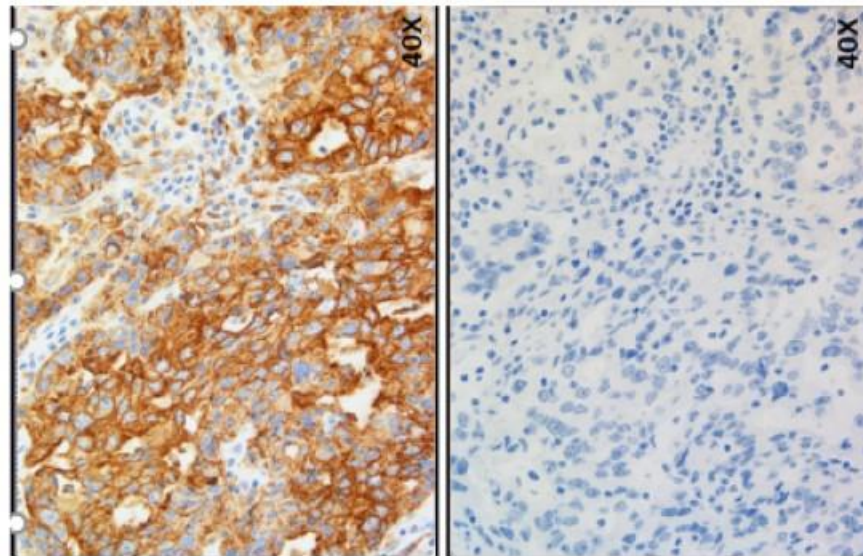
Time to & Duration of Disease Control In Lung Cancer



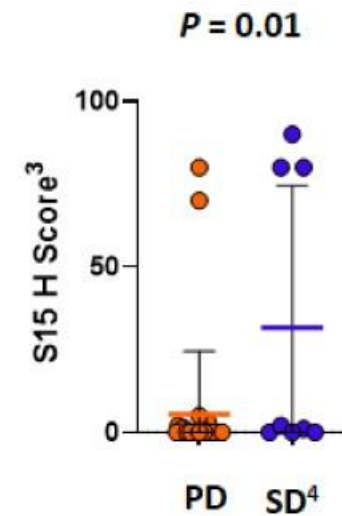
- $n = 15$
- To date, two subjects with NSCLC (1CR and 1PR) remain on therapy for **2.8 and 2.3 years**, respectively.

S15 mAb for use as a companion diagnostic test

- Tested extra-cellular domain antibodies
- Tested 2 batches (about 6 per batch) of NextCure produced intra-cellular domain mAbs
- Successfully identified IF-7 (below) for use in S15 CLIA validated diagnostic assays



David Rimm Lab



Confirmed Partial Response

74 y/o NSCLC dosed 400 mg every 2 weeks

Prior therapies:

- Immunotherapy: "LAG3/PD-1" (best response stable disease then progression)

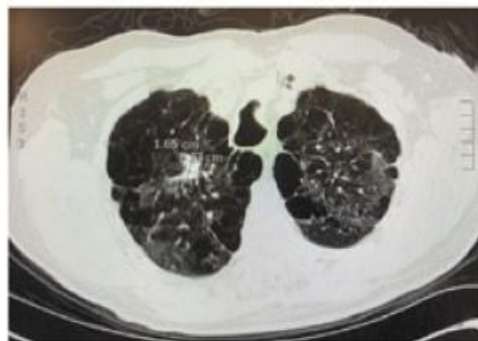
Diagnostic biopsy:	
S15	PD-L1 (TPS)
N/A	1-50%

BASELINE



Duration of PR: 15+ weeks.

Week 8



Target lesions -41%

Week 16



Target lesions -71%

DURATION ON STUDY 24+ Weeks

Conclusions

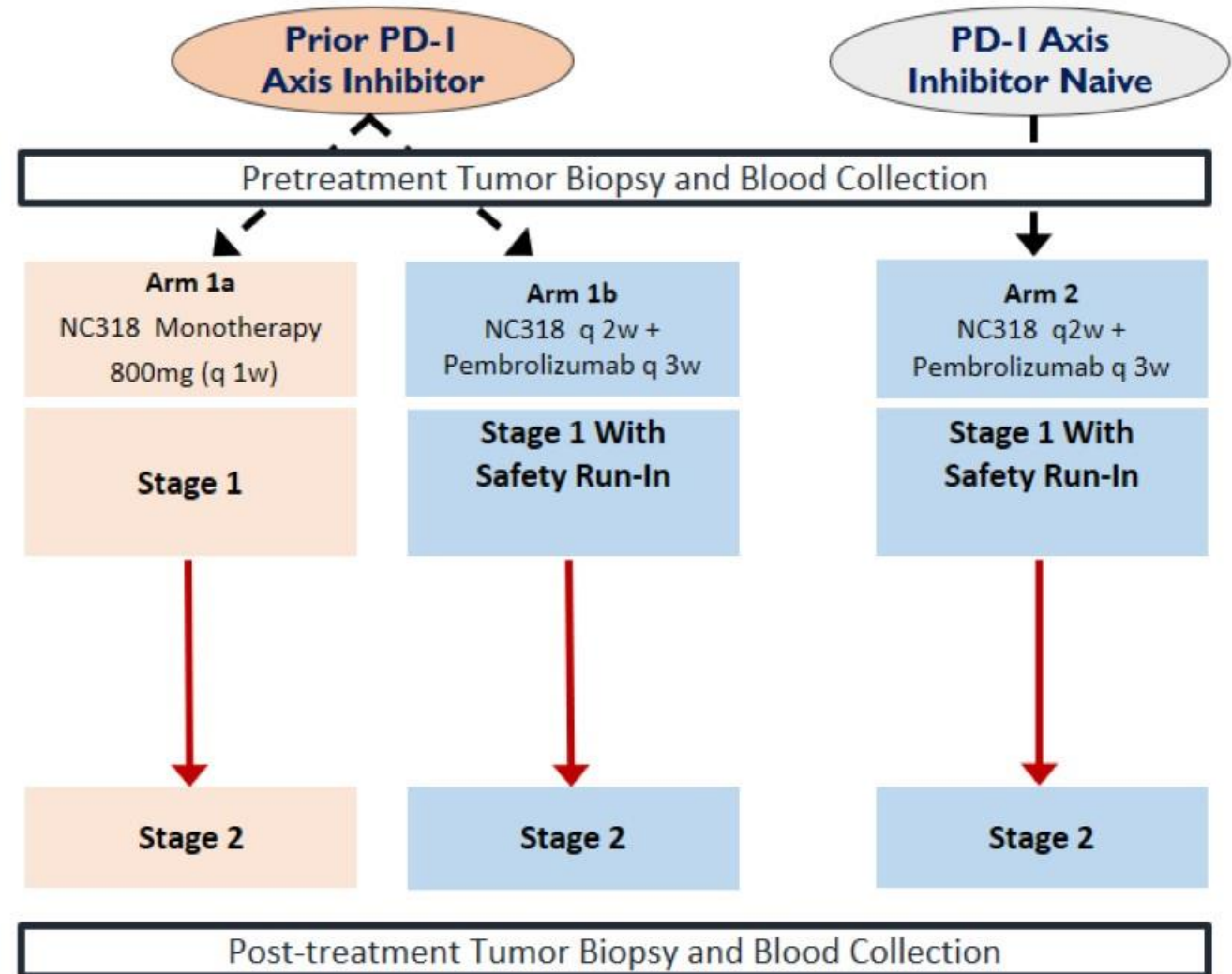
- NC318 has been well tolerated across multiple dose levels
- Adverse event profile consistent with other approved immunotherapies
- NC318 has shown encouraging single-agent anti-tumor activity
 - PD-1 refractory NSCLC: 1 CR, 1 PR, and stable disease in 13 patients (of 32 evaluable patients) with a median PFS of 5.2 months
 - Durable stable disease (>24 weeks observed in multiple tumor types)
- Phase 2 enrollment underway with revised protocol: 800mg Q1W in S15 positive patients

PROJECT 1 – Investigator Initiated SPORE Trial

TRIAL SCHEMA

NC318 dose will be determined by Ph I trial

- Advanced NSCLC
- ECOG 0-1
- Willing/able to undergo tumor biopsy
- ARM 1a and 1b: Progression on PD-1 axis Inhibitor (+/- chemo)
- ARM 2: No prior PD-1 axis Inhibitor or NC318; tumor PD-L1 < 50%
- No symptomatic or untreated CNS metastases



Agenda – NC410



NC318 – Ph1 & Ph2

Update, patient selection, dosing, sS15



Roy Herbst, MD, PhD

Unmet need in lung cancer



NC410 – Ph1

Safety, dose escalation, biomarkers

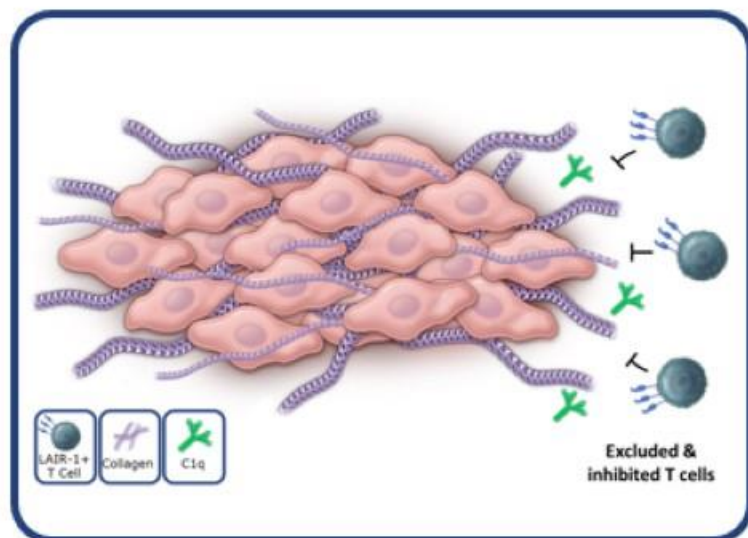


NC525 – PC

New program; IND 4Q 2022

LAIR Biology

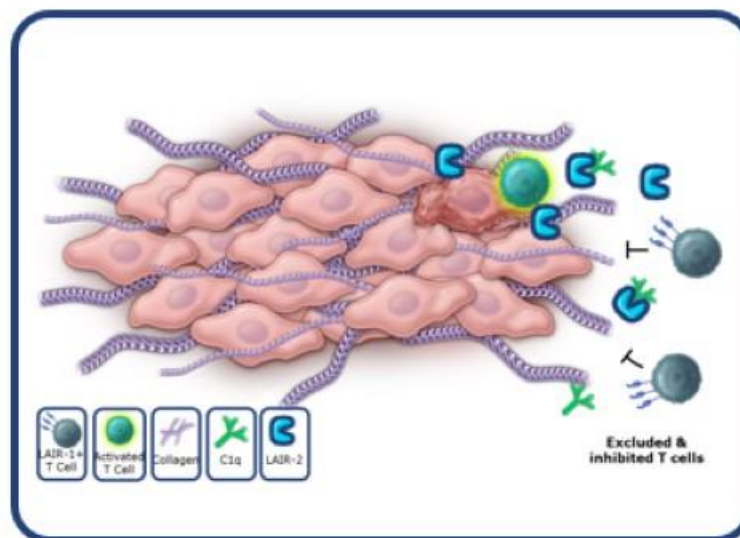
LAIR-1 IS IMMUNOSUPPRESSIVE



- **Binds collagen and C1q**

- Collagen density is a barrier to T cell migration and suppresses activation
- C1q enhances cancer cell proliferation

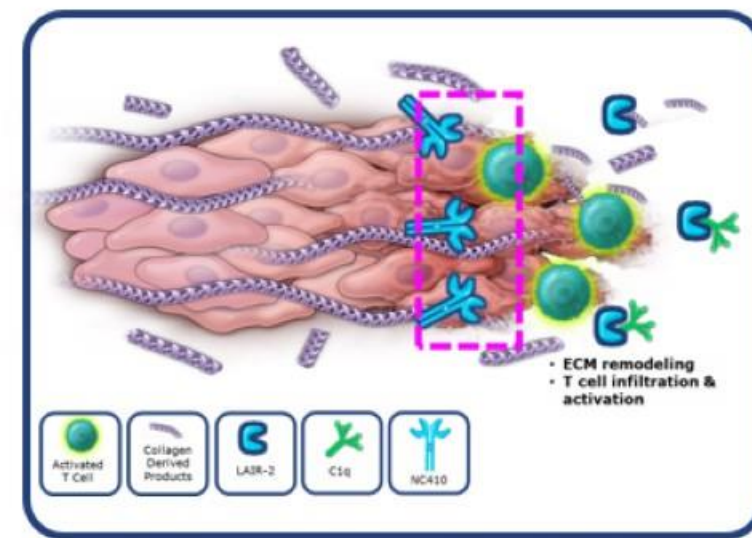
LAIR-2 ALLEVIATES IMMUNOSUPPRESSION



- **Differs from LAIR-1**

- Soluble
- Greater affinity for collagen & C1q
- **Modulates LAIR-1 inhibition**

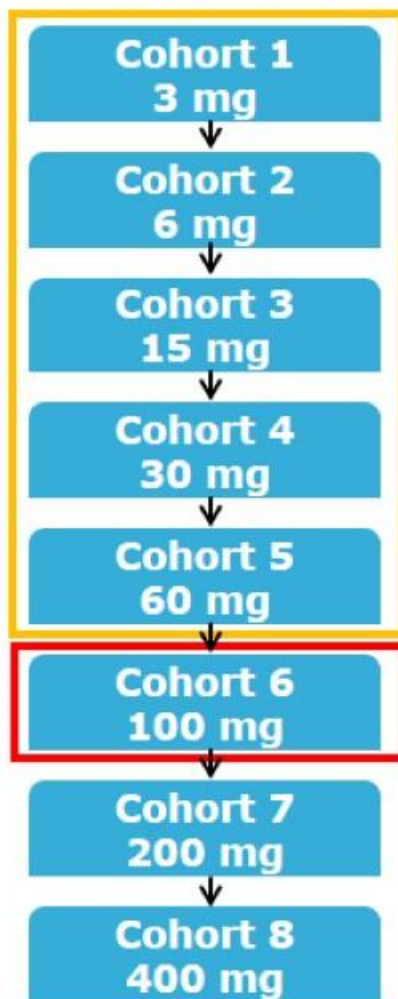
NC410 REMODELS COLLAGEN & NORMALIZES IMMUNE SYSTEM



- **NC410, fusion protein of LAIR-2**

NC410 Safety & Early Efficacy Data from Cohorts 1-5

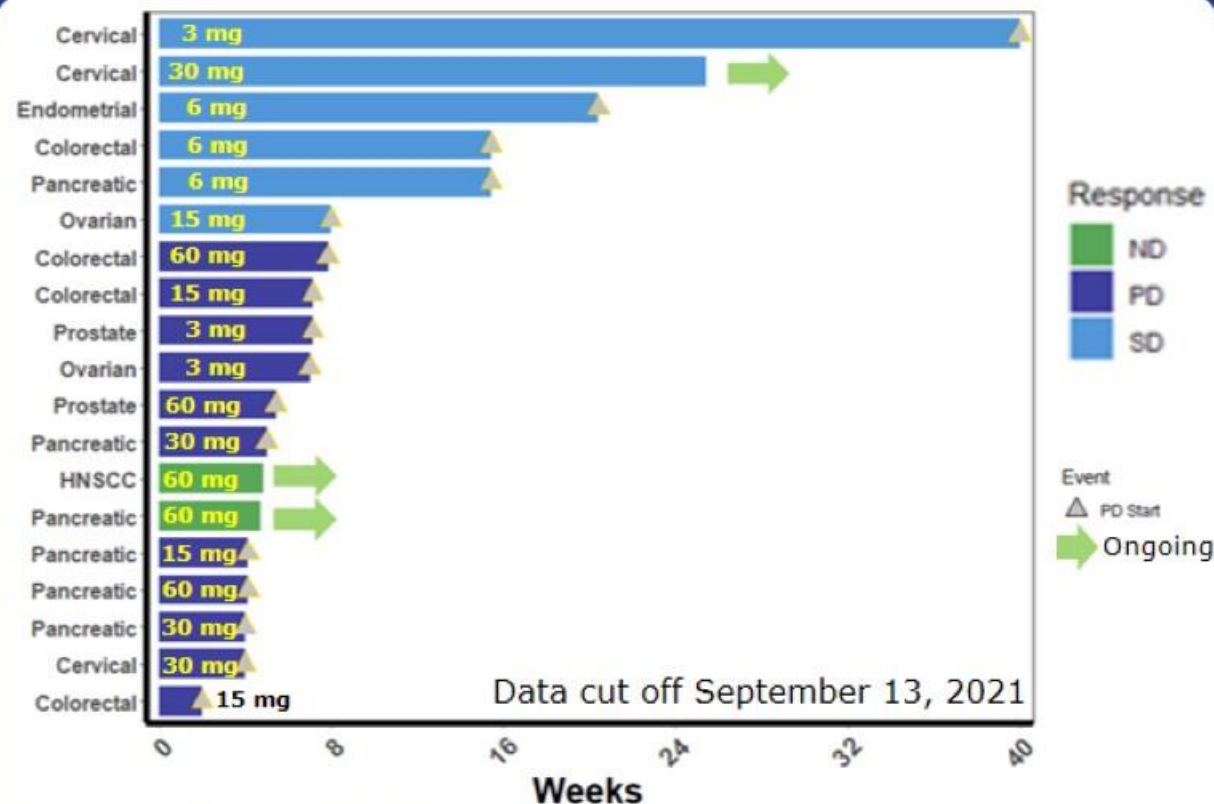
Phase 1a Dose Escalation



- 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

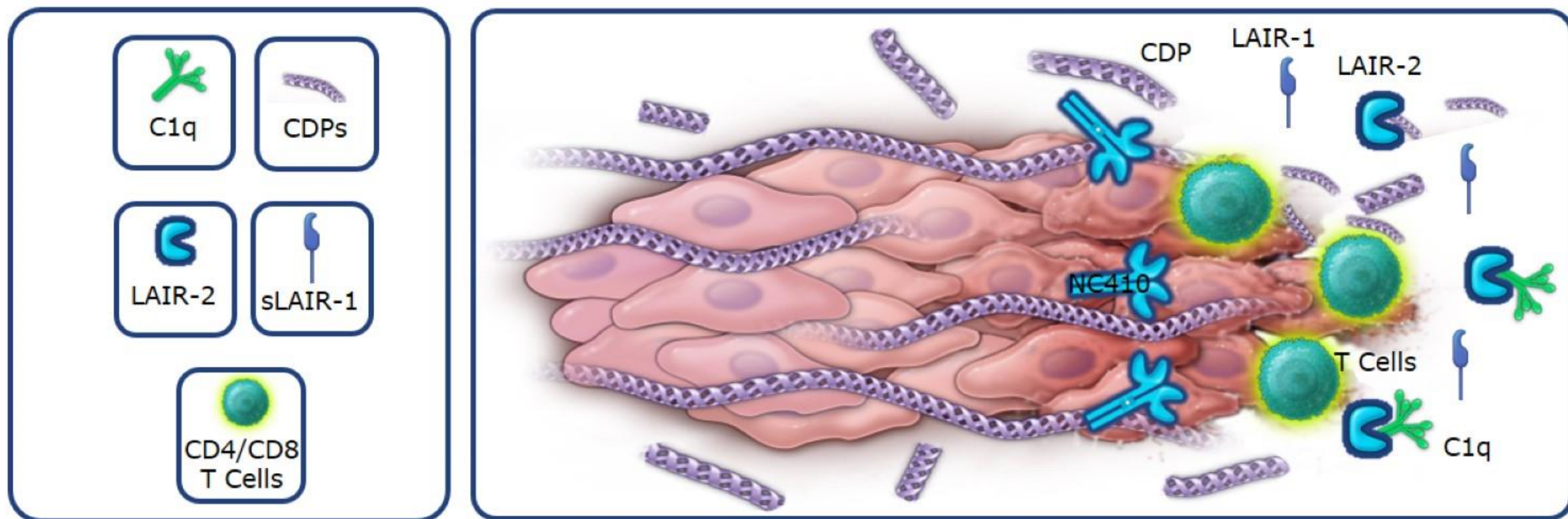
Phase 1b Dose Expansion

- 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 Biomarkers



LAIR

- Soluble LAIR-1
- LAIR-2

LIGANDS

- Collagen
- C1q

COLLAGEN REMODELING

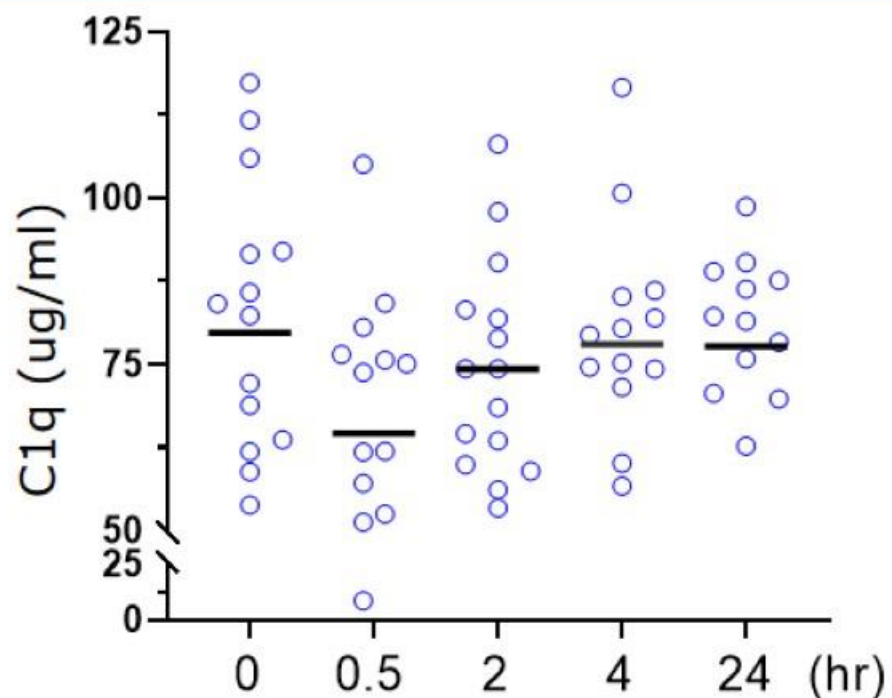
- Collagen derived products (CDPs)

NORMALIZATION OF IMMUNE RESPONSE

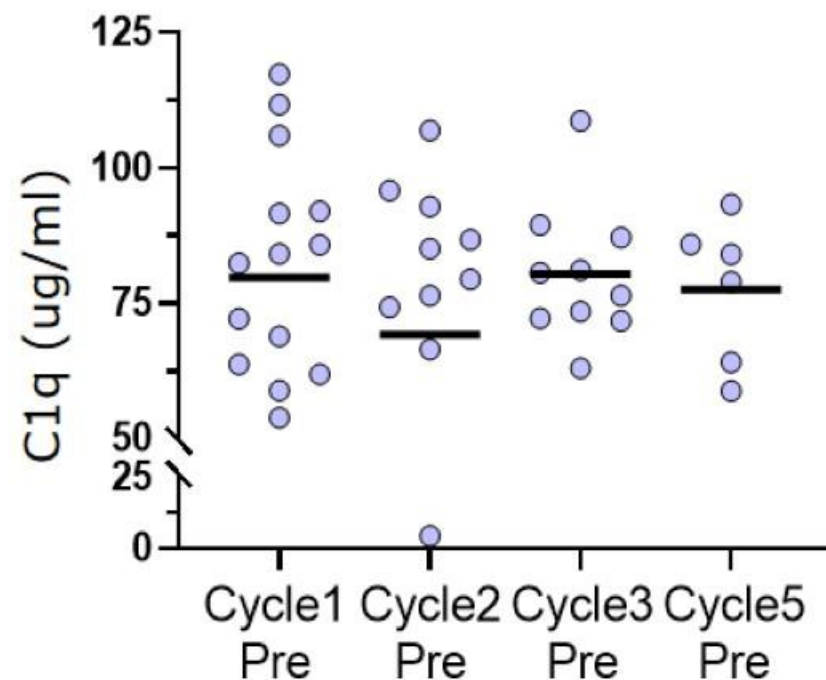
- CD4 / CD8 T cells

Transient Reduction of Soluble C1q: Evidence of NC410 Binding

C1Q Levels Pre- & Post-Dosing



Pre-Dose C1Q Levels



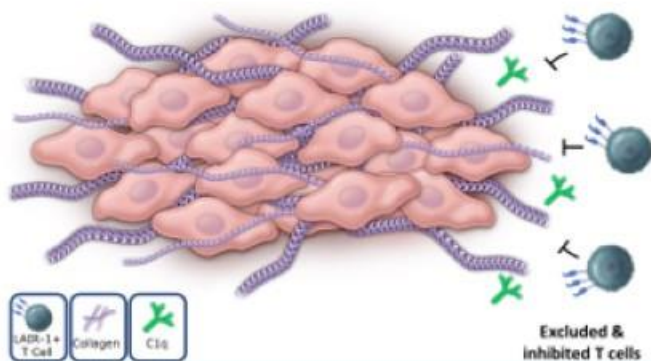
- Transient reduction in C1q is early peripheral pharmacodynamic marker
- Implies no safety concern regarding complement activity in circulation

ECM Remodeling

ECM Formation

Pro-C3 & Pro-C6

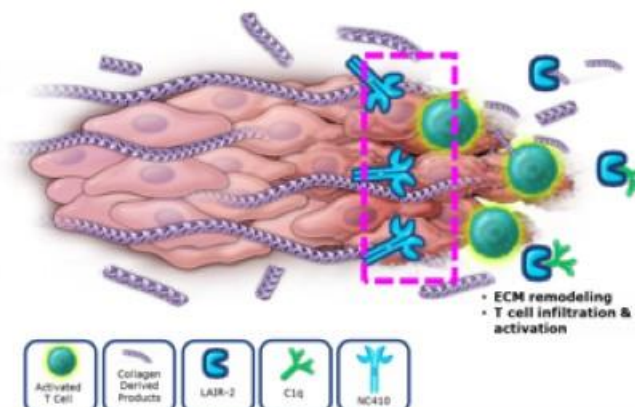
- Generated by collagen deposition
- ECM becomes dense and thick
- Excludes T cells



ECM Degradation

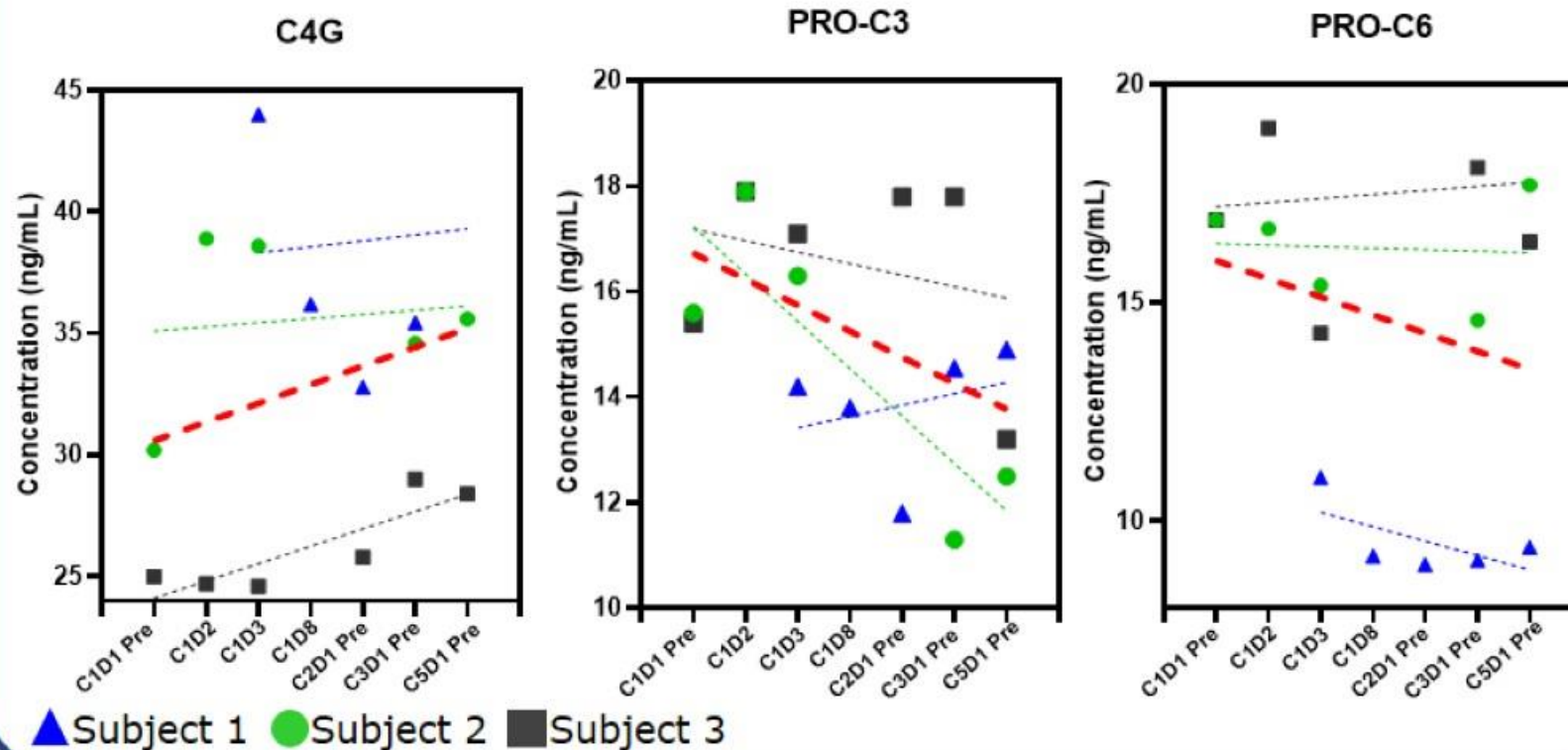
C4G

- Produced by cleavage from Granzyme B which is produced by activated T cells
- ECM becomes less dense
- Promotes T cell infiltration and activation

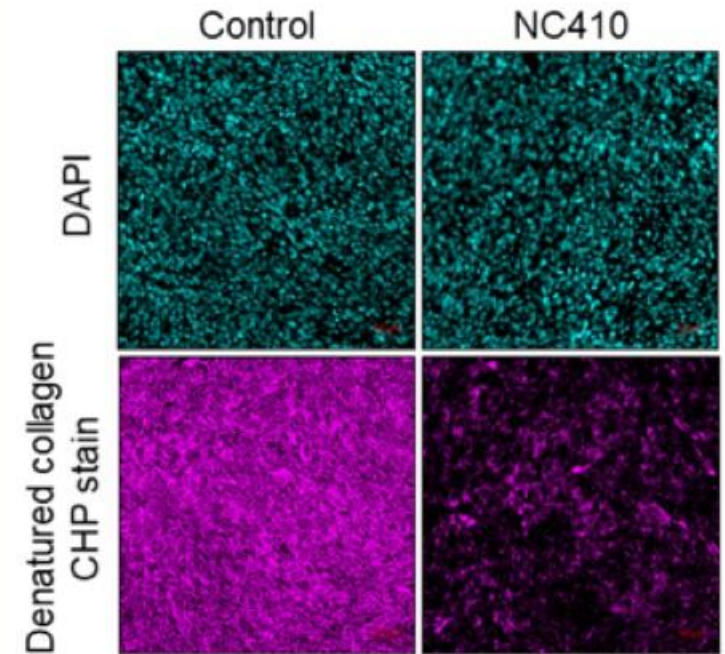


Collagen Derived Products - Early Evidence of Collagen Remodeling

Remodeling of Collagen in Clinical Samples



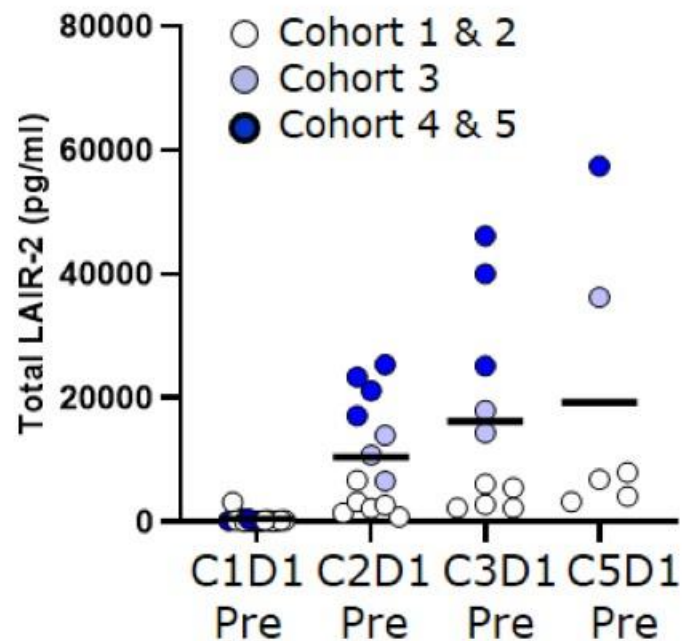
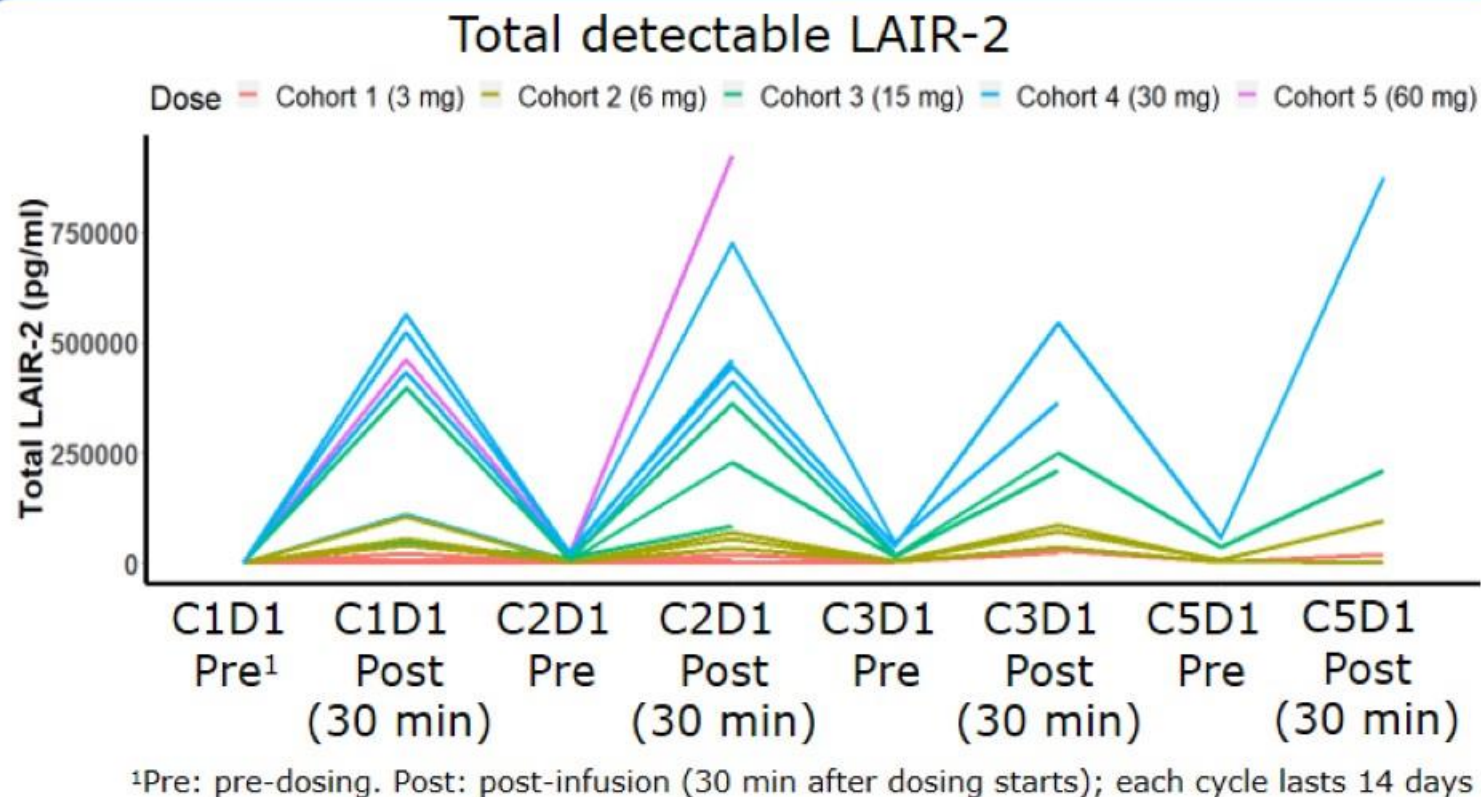
Remodeling of Collagen in Non-clinical Model



Horn et al., SITC 2021 (with permission)

- Increased C4G, Granzyme B-mediated collagen fragment, suggestive of immune activity
- Reduction in Pro-C3 and Pro-C6, prognosis markers of tumor progression

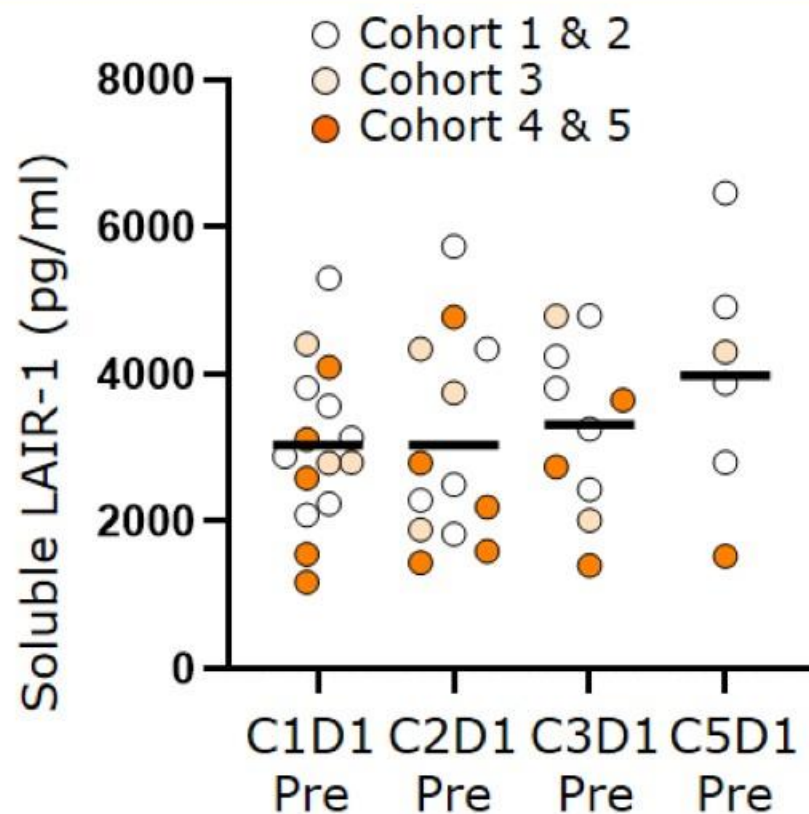
LAIR-2 Levels in Peripheral Blood Increase in a Dose-Dependent Fashion



- Suggest mechanistic evidence of immune modulation
- Current assay optimization to discern endogenous LAIR-2 and NC410

Soluble LAIR-1 in Peripheral Blood Over Time

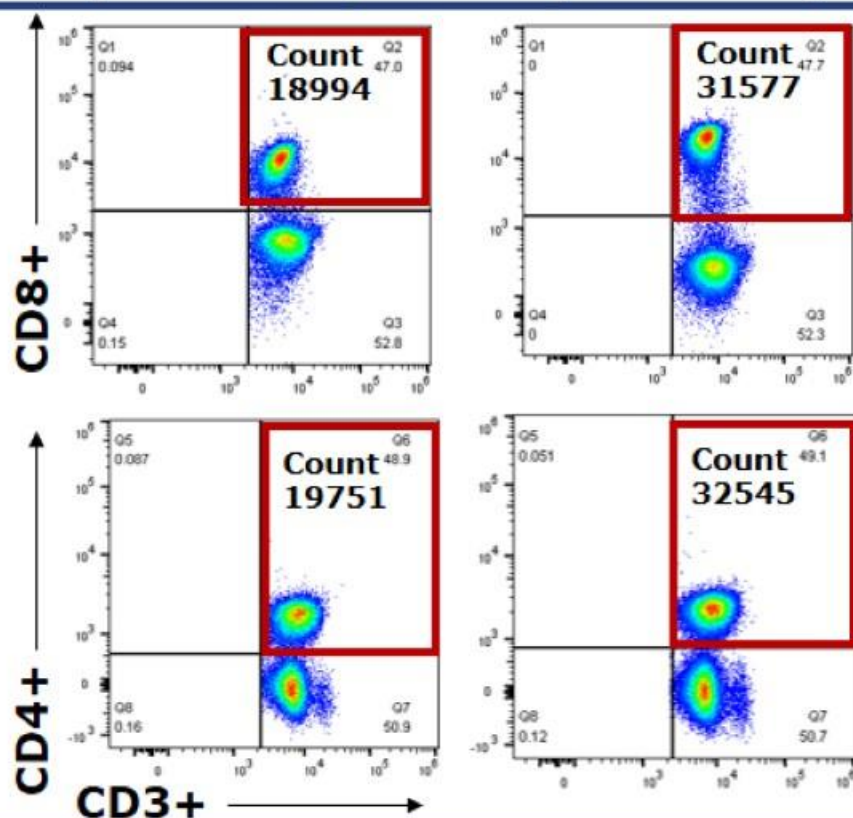
- Soluble LAIR-1 does not change overtime
- Continue to monitor at higher doses to assess mechanistic role in reducing immunosuppression



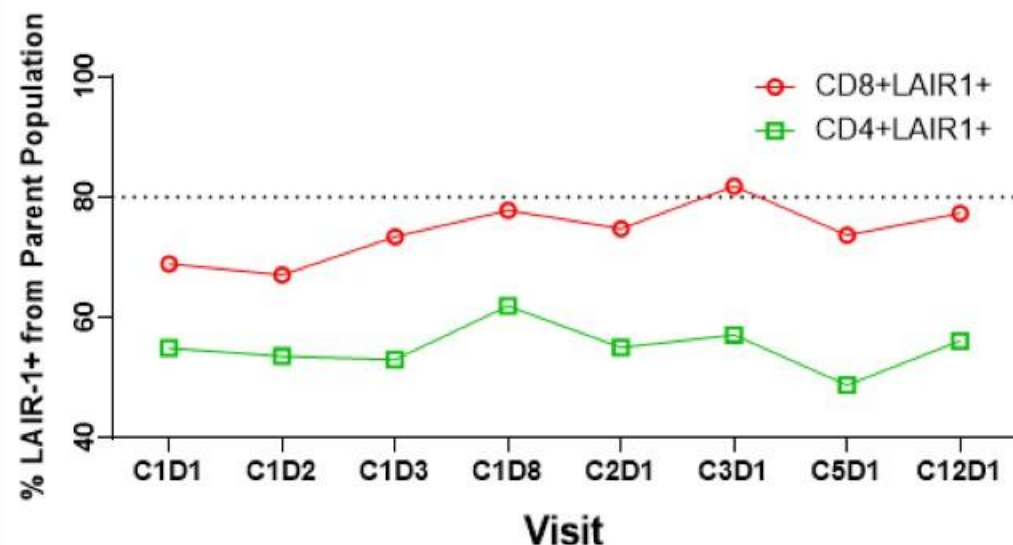
Early Evidence of Immune Activation in a Patient with Stable Disease

Cycle 1 Day 1

Cycle 3 Day 1



% LAIR-1+ CD8 & CD4 Cells



- Time-dependent increase in CD4+ and CD8+ T cells without increase in LAIR-1 expression
- Demonstrates NC410 enhanced T cell proliferation occurs without increase in LAIR-1 expression

NC410 Observations for Cohorts 1-5

C1Q

- Transient reduction is early peripheral pharmacodynamic marker
- Implies no safety concern regarding complement activity in circulation

CDPs

- Increased C4G, Granzyme B-mediated collagen fragment, suggests activity
- Reduction in Pro-C3 and Pro-C6, prognosis markers of tumor progression

LAIR-2

- Levels in peripheral blood increase in dose-dependent fashion
- Suggest mechanistic evidence of immune modulation

SOLUBLE LAIR-1

- Does not change overtime

CD4 / CD8

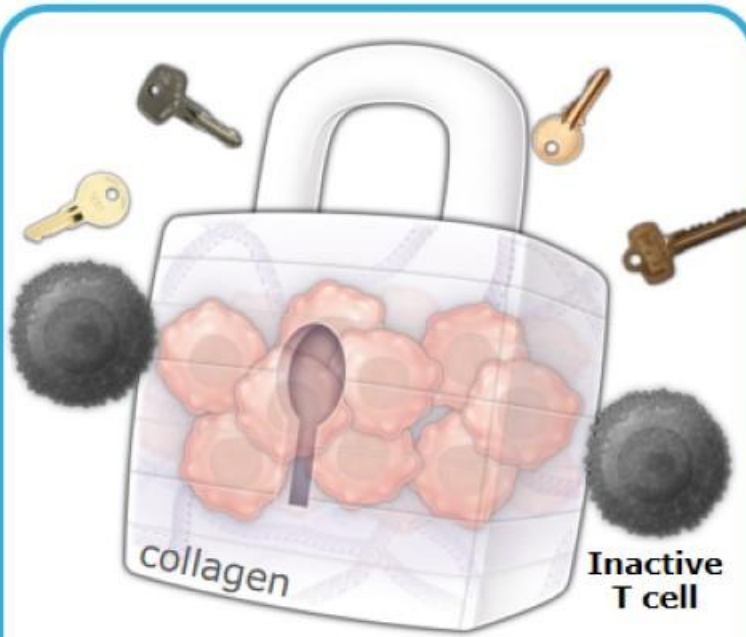
- Time-dependent increase without increase in LAIR-1 expression
- NC410 enhanced T cell proliferation occurs without increase in LAIR-1 expression

SAFETY & TOLERABILITY

- No DLTs through cohort 5
- Analyses ongoing for higher cohorts

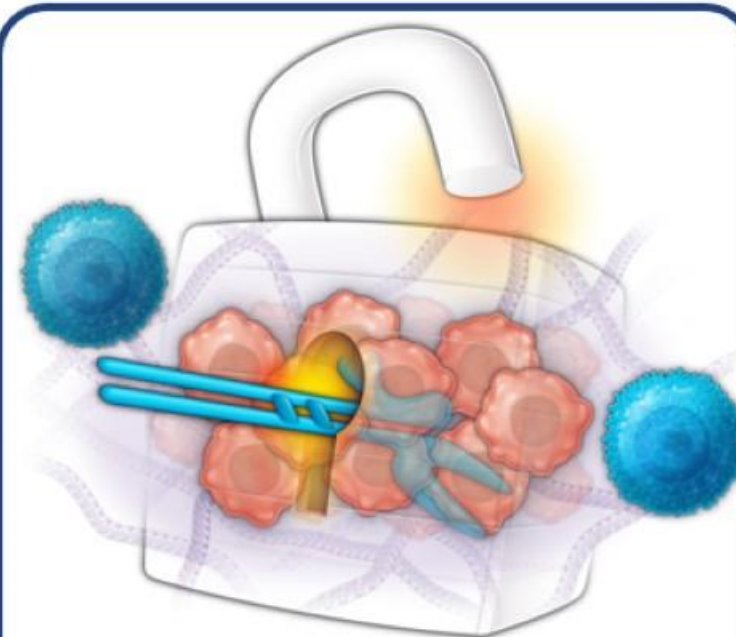
NC410: Key to Unlock TME and Normalize Immune Response

TME ACCESS LOCKED



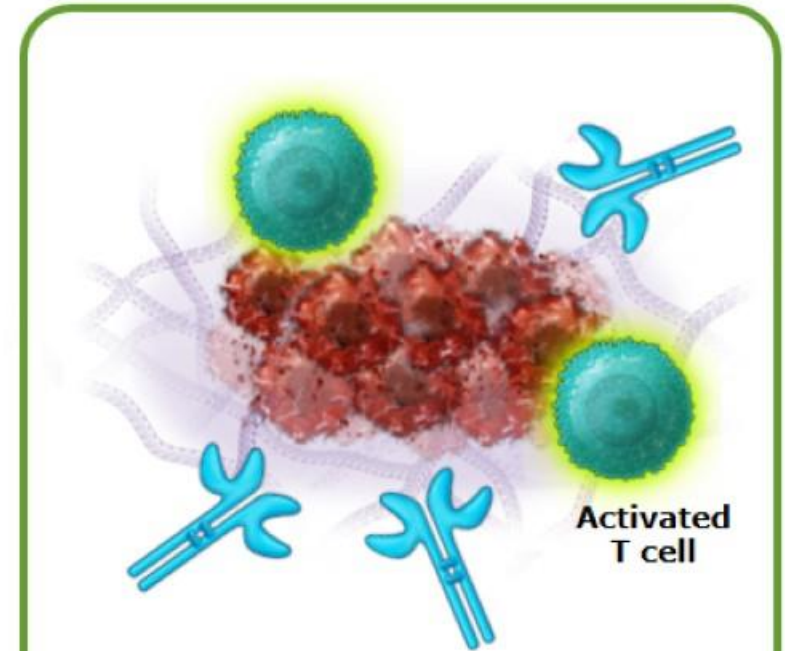
Many "keys" but none fit lock

NC410 UNLOCKS ECM



Enhances T cell infiltration

REMODELING & NORMALIZATION



Activated T cells kill tumor

Leveraging LAIR Biology and Distinct Candidate MOAs for Different Diseases

	CANDIDATE	TARGET	MOA	INDICATION
--	-----------	--------	-----	------------

NC410



LAIR-2 fusion

Collagen & C1q

ECM remodeling &
normalizing
immune response

Solid tumors

NC525



LAIR-1 mAb

LAIR-1

Blast & LSC killing

Heme-onc

Agenda – NC525



NC318 – Ph1 & Ph2

Update, patient selection, dosing, sS15



Roy Herbst, MD, PhD

Unmet need in lung cancer



NC410 – Ph1

Safety, dose escalation, biomarkers



NC525 – PC

New program; IND 4Q 2022

New Program - NC525 (LAIR-1 mAb)



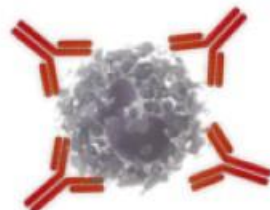
NC525

BIOLOGY

- LAIR-1 expression
 - High on AML blasts and leukemia stem cells (LSCs)
 - Minimal on hematopoietic stem and progenitor cells (HSPCs)
- Current AML treatments do not discriminate between leukemia blast cells and normal blood cells including 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 (CDX) *in vivo*
- Restricts AML progression in patient-derived xenografts (PDX) *in vivo*
- Preclinical data to be presented at ASH
- IND filing Q4 2022

Agenda – Closing Remarks



NC318 – Ph1 & Ph2

Update, patient selection, dosing, sS15



Roy Herbst, MD, PhD

Unmet need in lung cancer



NC410 – Ph1

Safety, dose escalation, biomarkers



NC525 – PC

New program; IND 4Q 2022

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

Product Development: Getting it Right



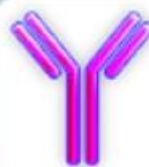
NC318

Phase 2



NC410

Phase 1



NC762

Phase 1



NC525

Pre-Clinical

**Patient
Selection**



**Triangulation
Strategy**



Combos

Biomarkers

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	Myeloid and T cells	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



Significant Momentum & Milestones in 2022

NC318
On Track

BUILDING PIPELINE
Momentum

EXPERIENCED
Team

RUNWAY
2H 2023