UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15(d) of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **November 13, 2021**

NextCure, Inc.
(Exact name of registrant as specified in charter)

Delaware	**001-38905**	**47-5231247**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

9000 Virginia Manor Road, Suite 200 Beltsville, Maryland	**20705**
(Address of principal executive offices)	(Zip Code)

(240) 399-4900
Registrant's telephone number, including area code

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	NXTC	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure

On November 13, 2021, NextCure, Inc. (the "Company") issued a press release announcing new data from two clinical studies and one research study presented at the Society for Immunotherapy of Cancer (SITC) annual meeting in Washington, D.C., and on a virtual platform. The data come from clinical studies evaluating NC318, a Siglec-15 (S15) antibody, and NC410, a fusion protein of LAIR-2, in patients with advanced/metastatic solid tumors, as well as from a research study evaluating NC410's impact on T cell activation and myeloid cell polarization conducted in collaboration with the National Cancer Institute at the National Institutes of Health. The Company is furnishing a copy of the press release, which is attached hereto as Exhibit 99.1.

On November 15, 2021, the Company is hosting a Virtual Oncology Pipeline Update Event. The presentation for such virtual event is being furnished as Exhibit 99.2 hereto. A live webcast of the event will be available through the Investors section of the Company's website at www.nextcure.com. A replay of the webcast will be available approximately two hours after the event and archived on the website for 30 days. The Company's website and any information contained on the website are not incorporated into this Current Report on Form 8-K.

The information furnished in this Item 7.01 (including Exhibit 99.1 and Exhibit 99.2) shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, and is not incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits.

Exhibit Number	Description
99.1	Press release issued by NextCure, Inc. dated November 13, 2021
99.2	Investor presentation issued by NextCure, Inc. dated November 15, 2021
104	Cover Page Interactive Data File (the cover page XBRL tags are embedded within the inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: November 15, 2021

NEXTCURE, INC.

/s/ Steven P. Cobourn
Steven P. Cobourn
Chief Financial Officer

NextCure and Collaborators Provide Clinical and Research Updates on NC318 and NC410 Candidates at Society for Immunotherapy of Cancer Annual Meeting

BELTSVILLE, Md. – November 13, 2021 -- NextCure, Inc. (Nasdaq: NXTC), a clinical-stage biopharmaceutical company committed to discovering and developing novel, first-in-class immunomedicines to treat cancer and other immune-related diseases, today announced new data from two clinical studies and one research study presented at the Society for Immunotherapy of Cancer (SITC) annual meeting in Washington, D.C., and on a virtual platform. The data come from clinical studies evaluating NC318, a Siglec-15 (S15) antibody, and NC410, a fusion protein of LAIR-2, in patients with advanced/metastatic solid tumors, as well as from a research study evaluating NC410's impact on T cell activation and myeloid cell polarization conducted in collaboration with the National Cancer Institute at the National Institutes of Health.

"We are pleased to share promising data from our NC318 and NC410 programs at this year's SITC annual meeting," said Han Myint, MD, NextCure's chief medical officer. "Results from our ongoing Phase 1 and Phase 2 trials suggest that NC318 may have a clinical benefit in patients. Retrospective analysis of patient biopsies from the Phase 1 and Phase 2 trials showed better outcomes in S15+ patients compared to S15- patients receiving NC318. Selecting for patients with S15+ expression coupled with a higher and more frequent dosing regimen that increases overall drug exposure is anticipated to impact clinical outcomes. Additionally, data from our NC410 program show that NC410 is safe and well-tolerated

in patients and demonstrates early indications of immune modulation. We look forward to continuing the advancement of both programs to improve the treatment landscape for cancer patients."

Details of the oral and poster presentations are below:

Clinical benefit through S15 targeting with NC318 antibody in subjects with S15 positive advanced solid tumors

Combined Phase 1 and Phase 2 data from the NC318 study show early evidence of possible clinical benefit in patients with lung cancer, squamous cell carcinoma of the head and neck and breast cancer and other advanced/metastatic solid tumors with dosing once every two weeks during dose escalation and with the 400mg dose selected for the Phase 2 studies. Highlights include:

- Data are derived from patient cohorts in both Phase 1 (n=49) and Phase 2 (n=47) of these studies.
- One NSCLC CR and one NSCLC PR patient from the Phase 1 study remain on therapy for 2.8 and 2.2 years, respectively.
- NC318 appears to show evidence of disease control with better outcomes in S15+ patients compared to S15- patients.
- The disease control rate across all tumors in both studies was 37% with a median progression-free survival (PFS) of 5.0 months.
- Patients in the lung cohort from both studies showed 45% disease control rate with a median PFS of 5.2 months.

- Data indicate that soluble S15 (sS15) level may serve as a biomarker for patient selection.
- Pharmacokinetic and pharmacodynamic modeling predict that a dose of 800 mg once a week results in nearly 10 times greater drug exposure which may impact drug activity and clinical outcomes.

NC410, a fusion protein of LAIR-2 (Leukocyte Associated Immunoglobulin-like Receptor) fused to human IgG1 Fc domain appears safe and well-tolerated with evidence of immune modulation in subjects with advanced solid tumors

Interim data presented from the Phase 1 dose-escalation study show that NC410 appears to be safe and well-tolerated in patients with advanced tumors and show evidence of immune modulation. Highlights include:

- The data come from the first five patient cohorts (n=19), who received doses of NC410 up to 60 mg once every two weeks.
- There were no dose-limiting toxicities.
- Data show a transient reduction in peripheral C1q, suggesting target binding of NC410.
- LAIR-2 levels in peripheral blood increase in a dose-dependent fashion and may suggest mechanistic evidence of immune normalization.
- Early evidence of extracellular matrix (ECM) remodeling and immune activation was shown by an increase in serum C4G, a Granzyme B-mediated collagen fragment, and a reduction in serum Pro-C3 and Pro-C6 fragments.
- Time-dependent increase in CD4+ and CD8+ T cells without an increase in LAIR-1 expression provides further early evidence of immune activation.
- Safety, tolerability, efficacy, and biomarker analyses are ongoing in higher dose cohort patients.

Blockade of the inhibitory collagen receptor LAIR-1, PD-L1, and TGF-β promotes anti-tumor activity through T cell activation and myeloid cell polarization

Non-clinical data from a research study conducted in collaboration with the National Cancer Institute at the National Institutes of Health show NC410's impact on T cell activation, myeloid cell polarization and anti-tumor activity. Highlights include:

- NC410 and bintrafusp alpha, a TGF-beta trap molecule, synergize for effective tumor control in a mouse model of colon cancer.
- Tumor control is mediated by an increase in activated CD8+ T cells and a reduction in M2 tumor-associated macrophages in tumor infiltrates.
- Collagen remodeling is demonstrated in tumors treated with NC410.

About NC318

NC318 is a first-in-class immunomedicine against Siglec-15 (S15), a novel immunomodulatory target found on highly immunosuppressive cells called M2 macrophages in the tumor microenvironment and on certain tumor types including lung, ovarian and head and neck cancers. In preclinical research, it was observed that S15 promoted the survival and differentiation of suppressive myeloid cells and negatively regulated T cell function, allowing cancer to avoid immune destruction. In preclinical studies, NC318 blocked the negative effects of S15. NextCure believes NC318 has the potential to treat multiple cancer types.

About NC410

NC410 is a first-in-class immunomedicine designed to block immune suppression mediated by LAIR-1, an immunomodulatory receptor expressed on T cells and myeloid cells, including dendritic cells, a type of antigen presenting cell. In preclinical research, it has been shown that LAIR-1 inhibits T cell function and myeloid activity. In preclinical studies, NC410 blocks the negative effects of LAIR-1 and promotes T cell function and myeloid cell activity. NextCure believes NC410 has the potential to treat multiple cancer types.

About NextCure, Inc.

NextCure is a clinical-stage biopharmaceutical company committed to discovering and developing novel, first-in-class immunomedicines to treat cancer and other immune-related diseases. Through our proprietary FIND-IO™ platform, we study various immune cells to discover and understand targets and structural components of immune cells and their functional impact in order to develop immunomedicines. Our initial focus is to bring hope and new treatments to patients who do not respond to current cancer therapies, patients whose cancer progresses despite treatment and patients with cancer types not adequately addressed by available therapies. http://www.nextcure.com

Cautionary Statement Regarding Forward-Looking Statements

Statements made in this press release that are not historical facts are forward-looking statements. Words such as “expects,” “believes,” “intends,” “hope,” “forward” and similar expressions are intended to identify forward-looking statements. Examples of forward-looking statements in this press release include, among others, statements about NextCure’s plans, objectives, and intentions with respect to the discovery of immunomedicine targets and 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: 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, including that early clinical data may not be confirmed by later clinical results; risks that pre-clinical research may not be confirmed in clinical trials; risks related to marketing approval and commercialization; and the unproven approach to the discovery and development of product candidates based on our FIND-IO platform. 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 NextCure’s most recent Form 10-K and subsequent Form 10-Q. You should not place undue reliance on any forward-looking statements. NextCure assumes no obligation to update any forward-looking statements, even if expectations change.

Investor Inquiries

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NextCure, Inc.
Chief Operating Officer
(240) 762-6486
IR@nextcure.com

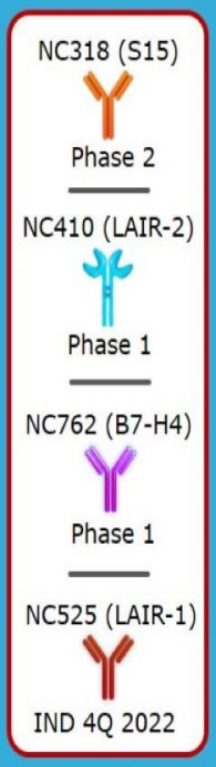

NextCure
Investor Update
November 15, 2021

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



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
Update, patient selection, dosing, sS15

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Safety, dose escalation, biomarkers

NC525 - PC
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

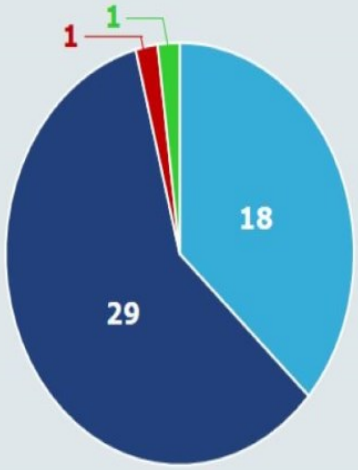
Amended Phase 2
- S15+ selection (CLIA assay)
- 800 mg Q1W: drug exposure
- NSCLC, H&N and breast

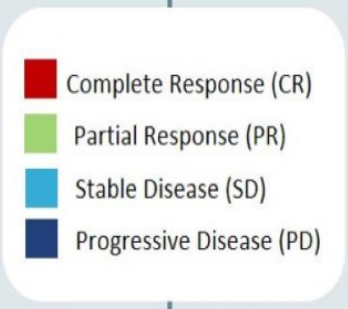
Yale Phase 2 (Combo)
- NSCLC
- Mono therapy: PD-1 refractory
- Pembro combo: PD-1 refractory
- Pembro combo: PD-1 naïve

NC318 Historical Clinical Outcomes

Phase 1

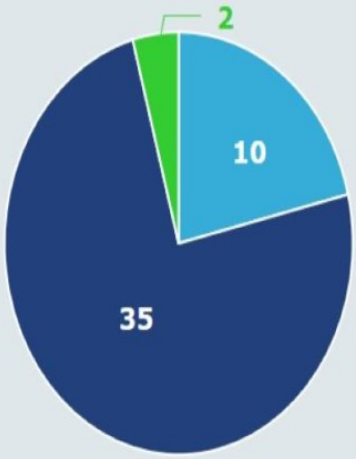
- 3+3 design
- Dose escalation, 8 – 1600 mg
- 15 tumor types
- 49 patients
- 1 CR (NSCLC); 1 PR (NSCLC); 18 SD





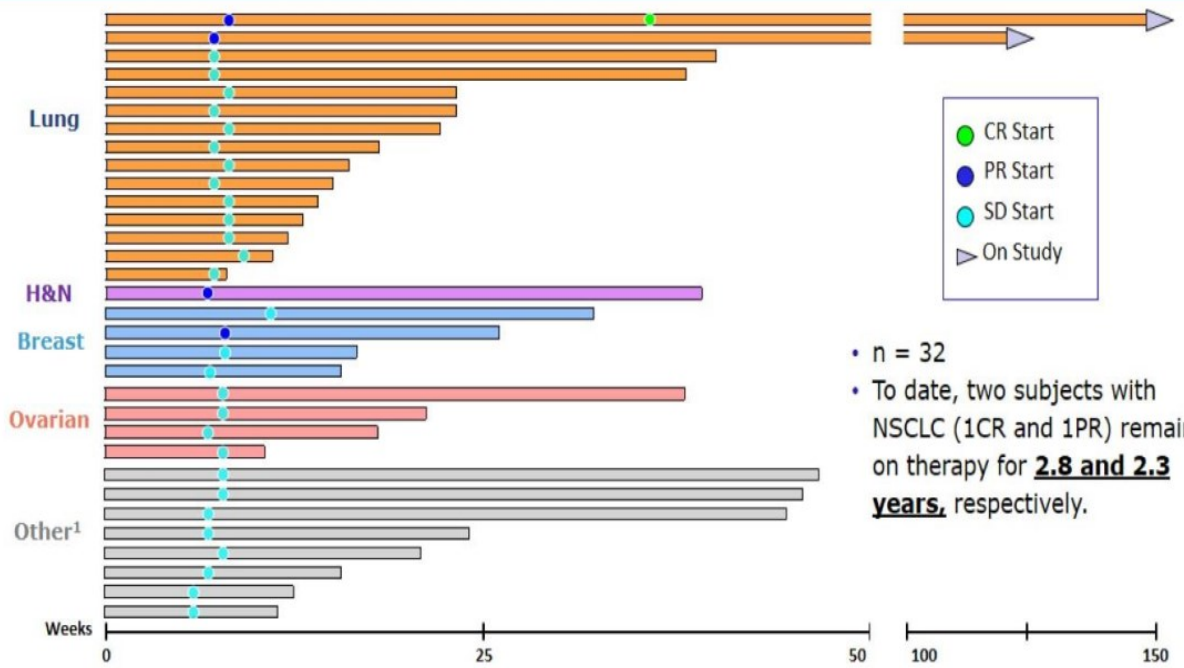
Phase 2

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



NextCure

Time to & Duration of Disease Control



[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).

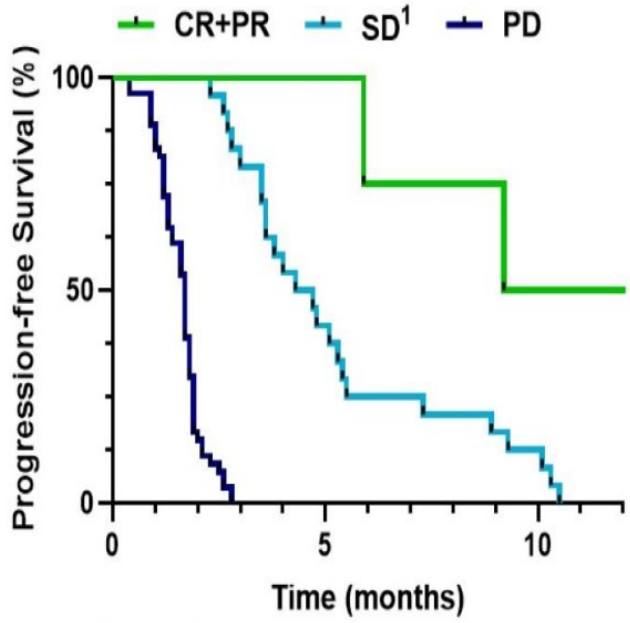
Analysis in All Patients

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

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



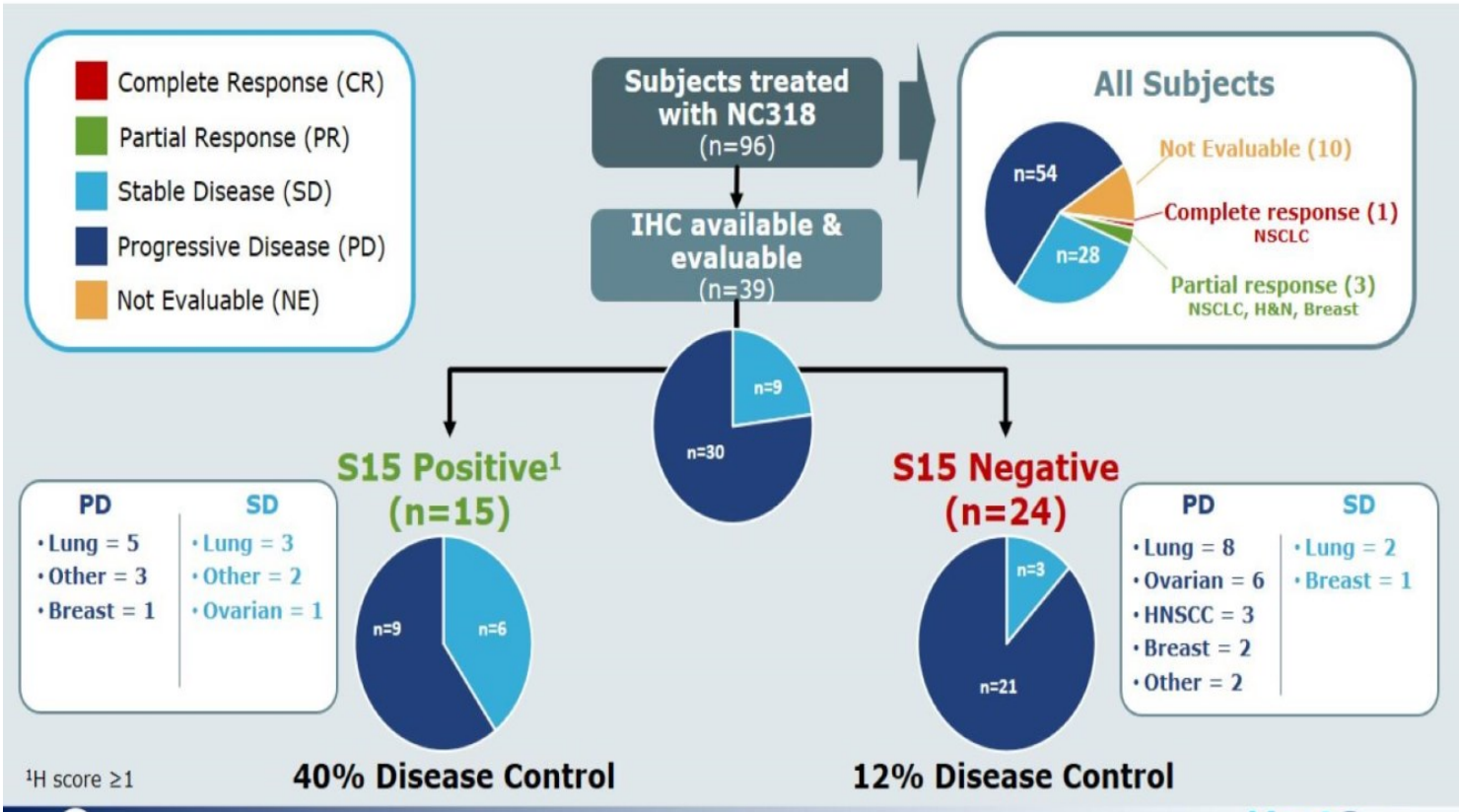
[1]4 SD subjects were lost to follow up for PFS

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

Retrospective Analysis in S15+ Patients

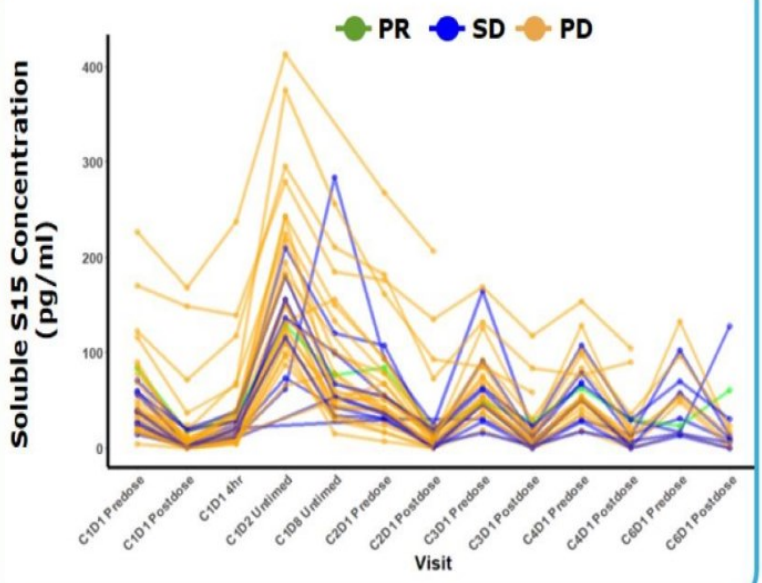
Disease Control Rate Increased in S15+ Patient Population



NextCure

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



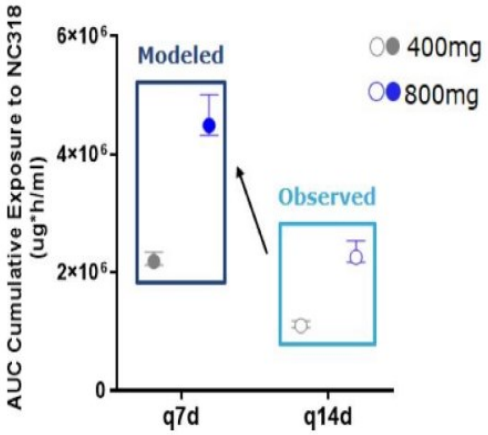
sS15 May Serve as NC318 Biomarker for Patient Selection & Monitoring

NextCure

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!

YaleNewHavenHealth
Smilow Cancer Hospital

Yale CANCER CENTER
A Comprehensive Cancer Center Designated by the National Cancer Institute

Yale SCHOOL OF MEDICINE

Siglec15 as a new target for lung cancer immunotherapy

Lieping Chen, MD PhD

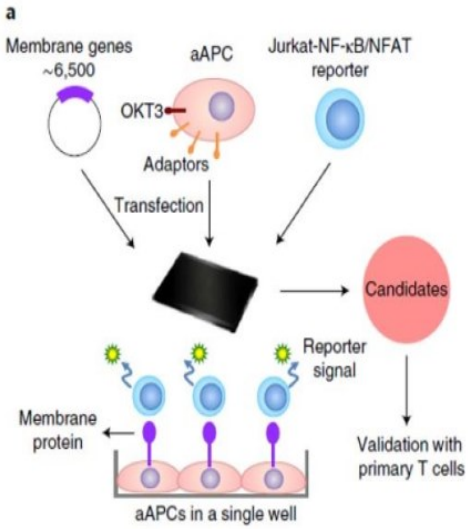
Roy Herbst, MD PhD

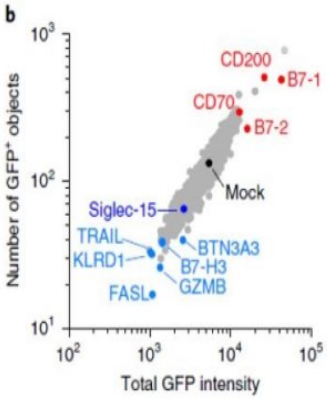
Scott Gettinger, MD

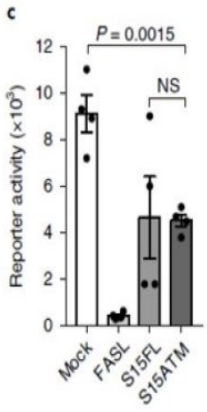
David Rimm, MD PhD

nature medicine ARTICLES

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







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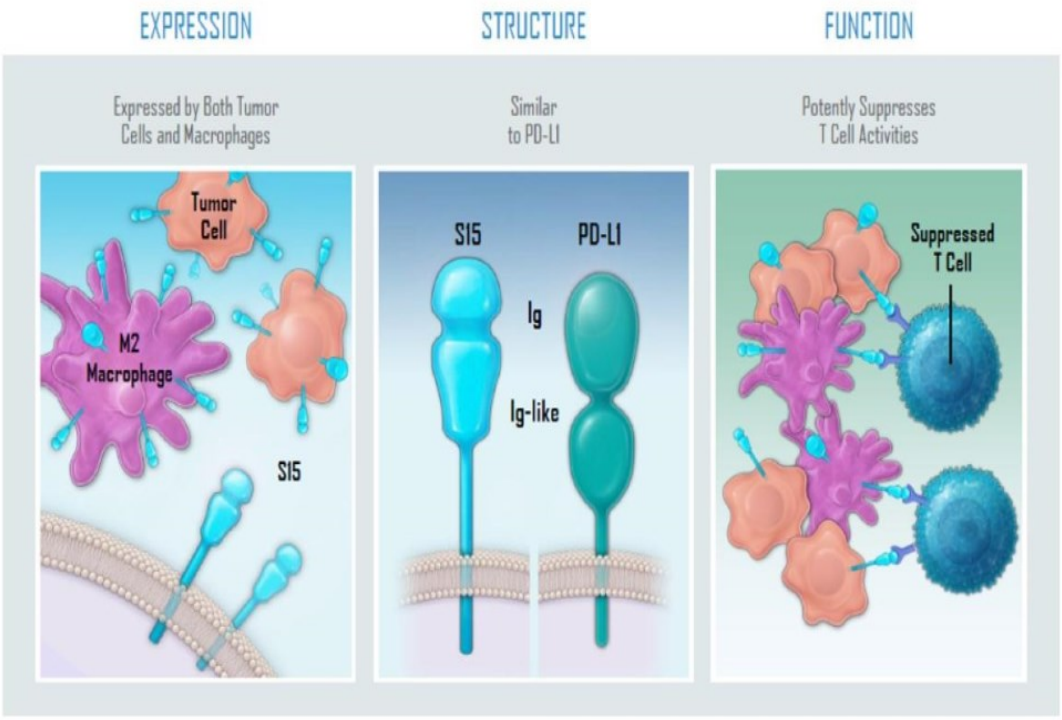
	B7-1	B7-2	B7-H1	B7-DC	B7-H2	B7-H3	B7-H4	B7-H5	B7-H6
Identity (%)	28	22	24	21	28	23	19	20	24
Identity + similarity (%)	43	38	37	42	45	37	39	32	46

YaleNewHavenHealth Smilow Cancer Hospital | Yale CANCER CENTER | Yale SCHOOL OF MED

Jun Wang[1,5], Jingwei Sun[1,5], Linda N. Liu[2], Dallas B. Flies[2], Xinxin Nie[1], Maria Toki[1], Jianping Zhang[1], Chang Song[2], Melissa Zarr[2], Xu Zhou[1], Xue Han[1], Kristina A. Archer[2], Thomas O'Neill[2], Roy S. Herbst[4], Agedi N. Boto[1,3], Miguel F. Sanmamed[1], Solomon Langermann[2], David L. Rimm[1,4] and Lieping Chen[1,4*]

WHY DID WE SELECT S15?

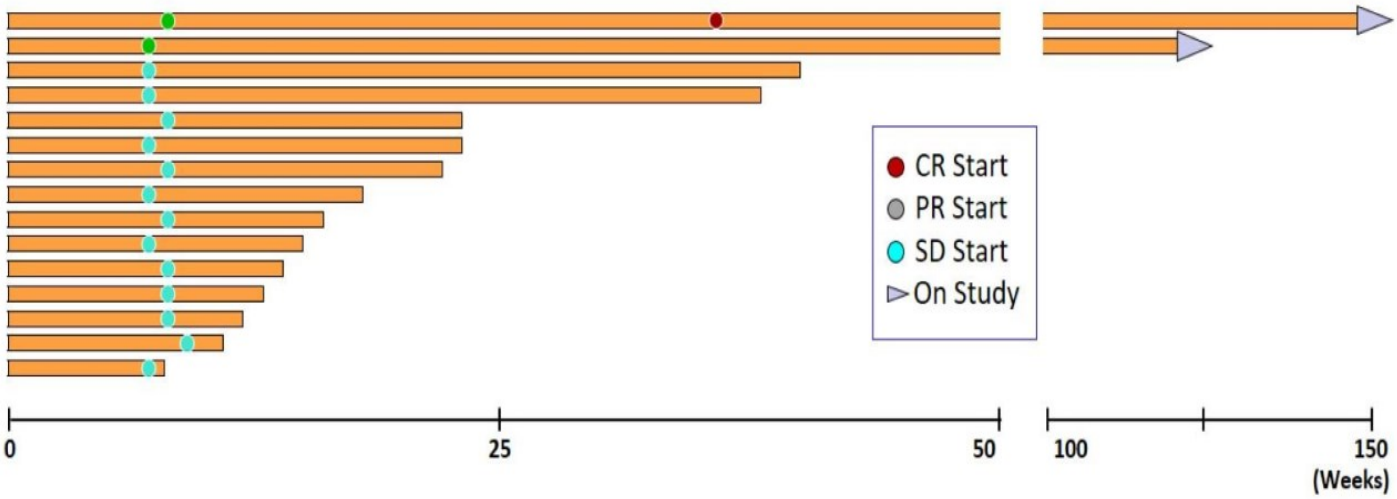


YaleNewHavenHealth
Smilow Cancer Hospital

Yale CANCER CENTER
A Comprehensive Cancer Center Designated by the National Cancer Institute

Yale SCHOOL OF MEDICINE

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.

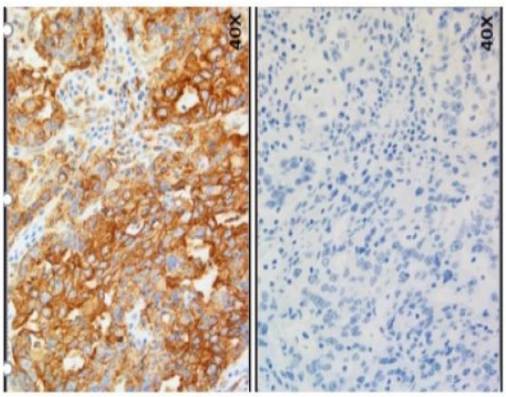
YaleNewHavenHealth
Smilow Cancer Hospital

Yale CANCER CENTER
A Comprehensive Cancer Center Designated by the National Cancer Institute

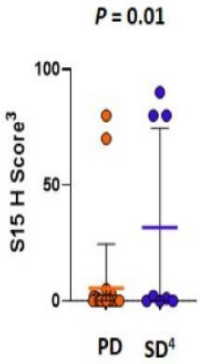
Yale SCHOOL OF MEDICINE

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



YaleNewHavenHealth Smilow Cancer Hospital | Yale CANCER CENTER | Yale SCHOOL OF MEDICINE

Shum et al SITC 2021

Confirmed Partial Response

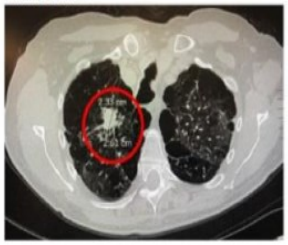
74 y/o NSCLC dosed 400 mg every 2 weeks

Prior therapies:

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

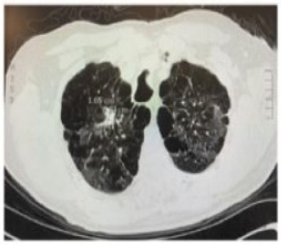
Diagnostic biopsy:	
S15	PD-L1 (TPS)
N/A	1-50%

BASELINE



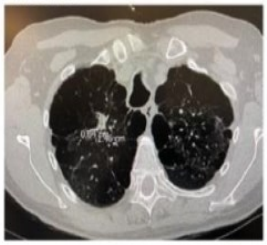
Duration of PR: 15+ weeks.

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

YaleNewHavenHealth
Smilow Cancer Hospital

Yale CANCER CENTER
A Comprehensive Cancer Center Designated by the National Cancer Institute

Yale SCHOOL OF MEDICINE

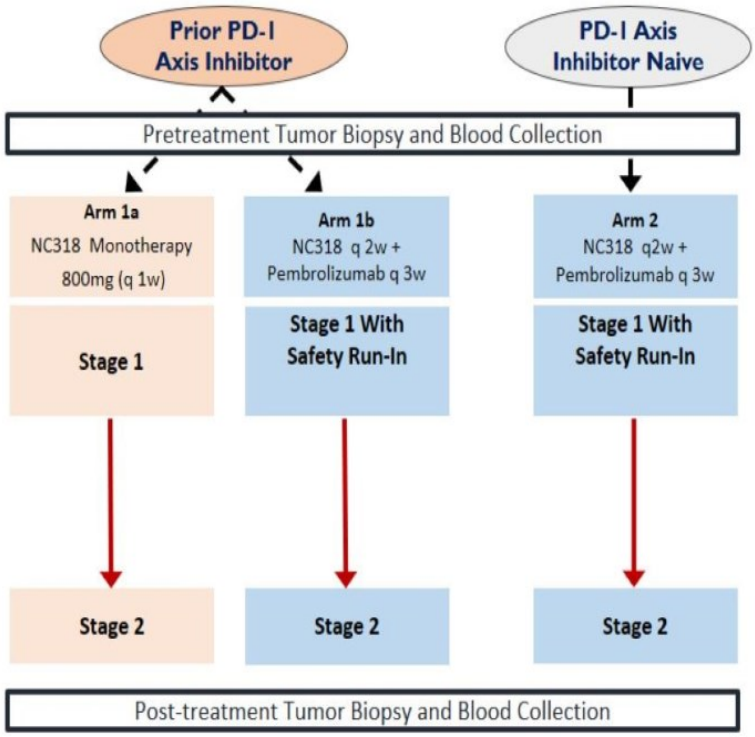
Tolcher et al. SITC 2019 (Yale PI LoRusso)
Shum et al SITC 2021

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



YaleNewHavenHealth Smilow Cancer Hospital | Yale CANCER CENTER | Yale SCHOOL OF MEDICINE

Scott Gettinger PI

Agenda – NC410

NC318 – Ph1 & Ph2

Update, patient selection, dosing, sS15

Roy Herbst, MD, PhD

Unmet need in lung cancer

NC410 – Ph1

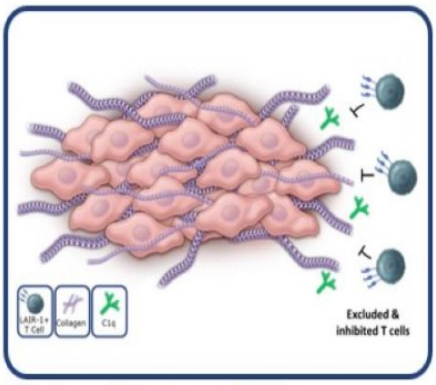
Safety, dose escalation, biomarkers

NC525 - PC

New program; IND 4Q 2022

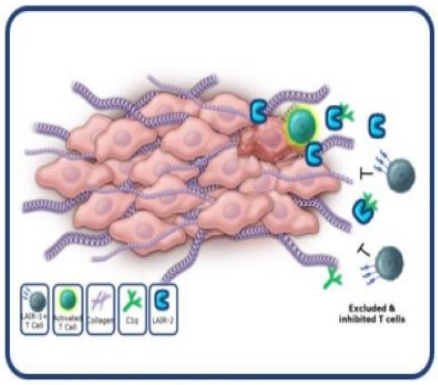
LAIR Biology

LAIR-1 IS IMMUNOSUPPRESSIVE



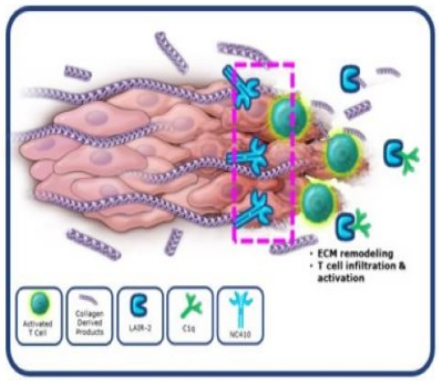
- **Binds collagen and C1q**
  - Collagen density is a barrier to T cell migration and suppresses activation
  - C1q enhances cancer cell proliferation

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**

NextCure

NC410 Safety & Early Efficacy Data from Cohorts 1-5

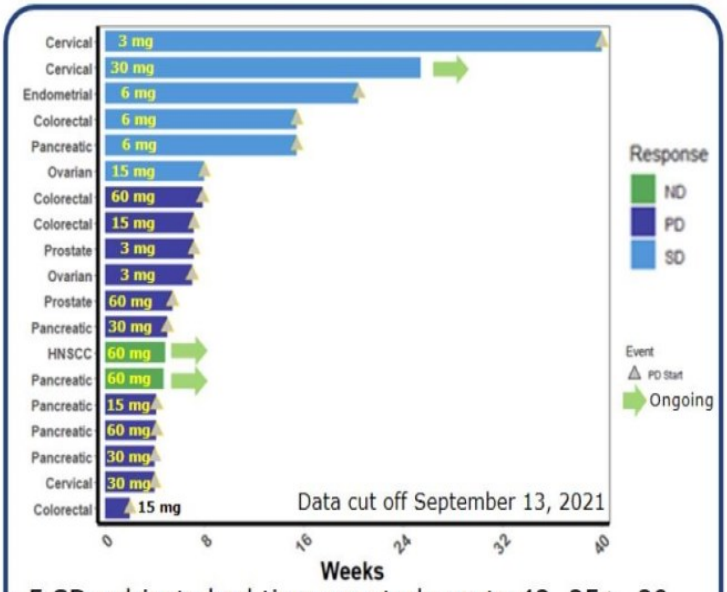
Phase 1a Dose Escalation

- 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

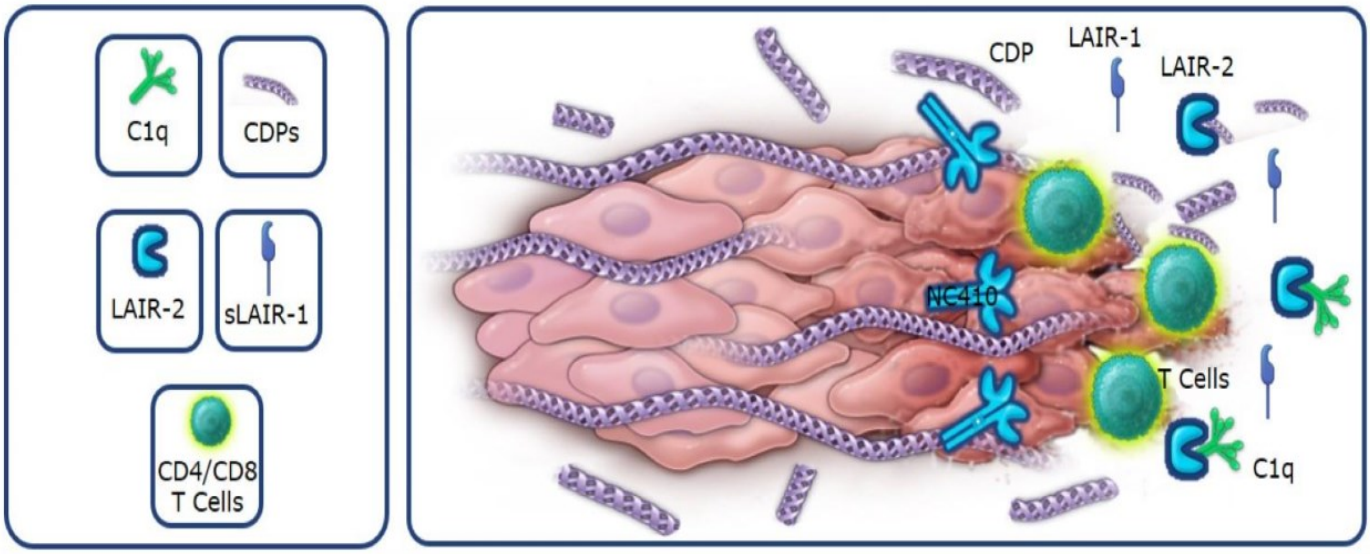
- Confirm PK and PD
- Biopsy analysis
- Determine RP2D



- 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

NextCure

NC410 Biomarkers

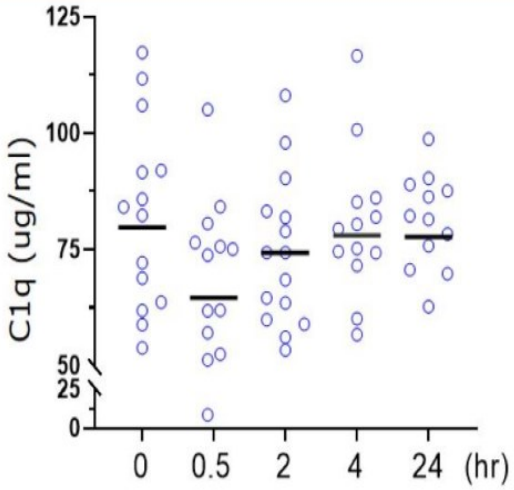


LAIR	LIGANDS	COLLAGEN REMODELING	NORMALIZATION OF IMMUNE RESPONSE
•Soluble LAIR-1 •LAIR-2	•Collagen •C1q	•Collagen derived products (CDPs)	•CD4 / CD8 T cells

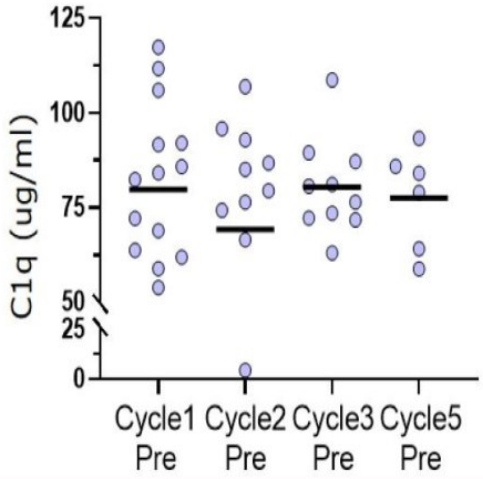
NextCure

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

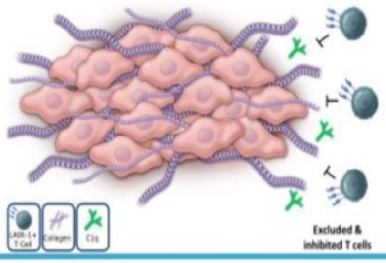
NextCure

ECM Remodeling

ECM Formation → **ECM Degradation**

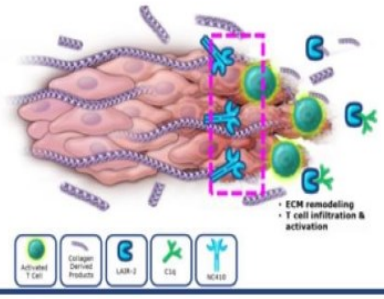
Pro-C3 & Pro-C6

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



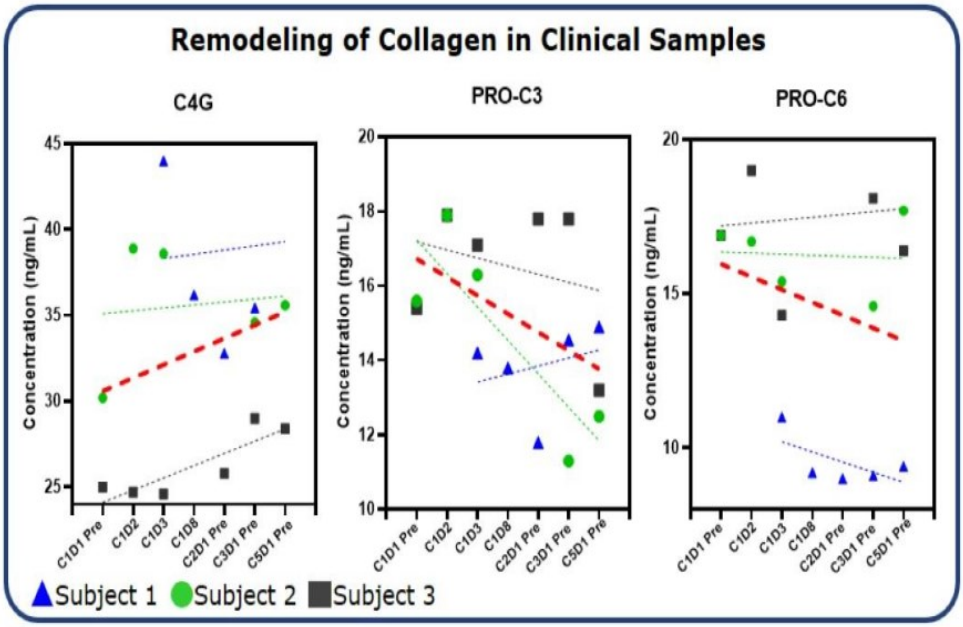
C4G

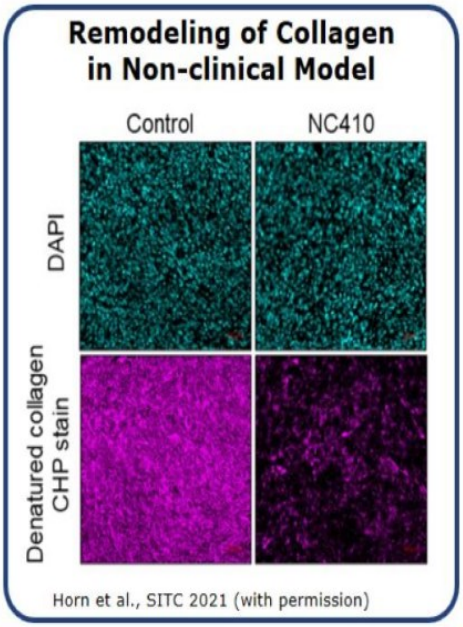
- Produced by cleavage from Granzyme B which is produced by activated T cells
- ECM becomes less dense
- Promotes T cell infiltration and activation



NextCure

Collagen Derived Products - Early Evidence of Collagen Remodeling

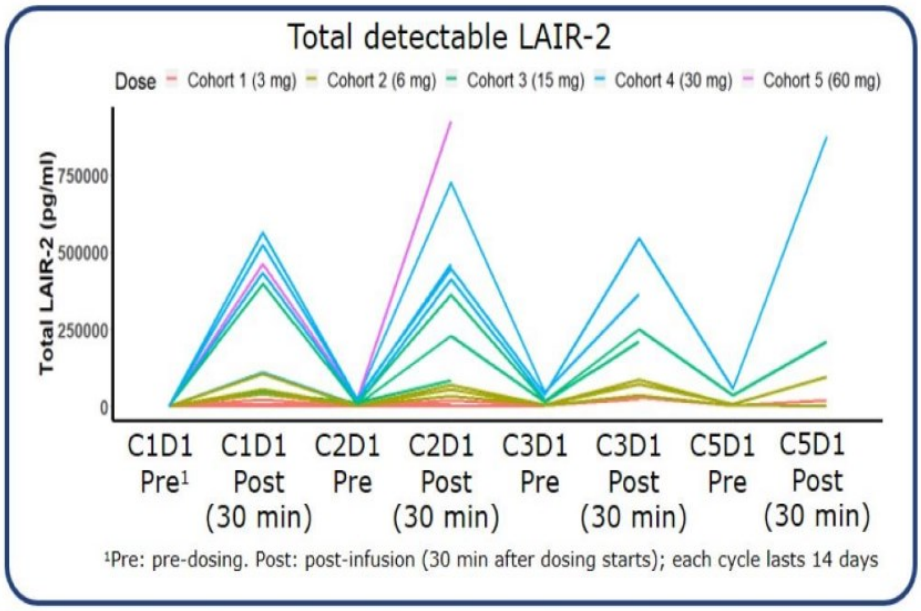


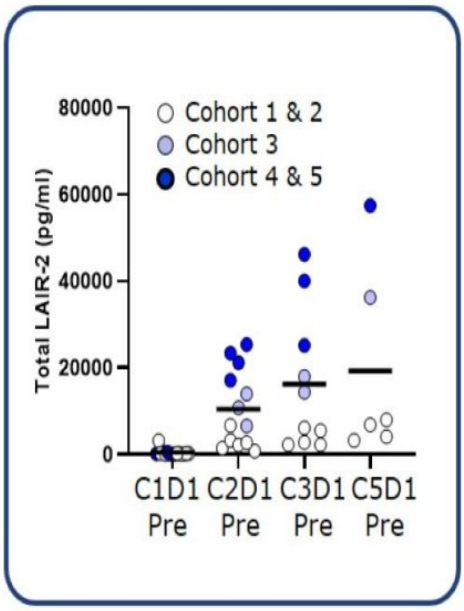


- Increased C4G, Granzyme B-mediated collagen fragment, suggestive of immune activity
- Reduction in Pro-C3 and Pro-C6, prognosis markers of tumor progression

NextCure

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



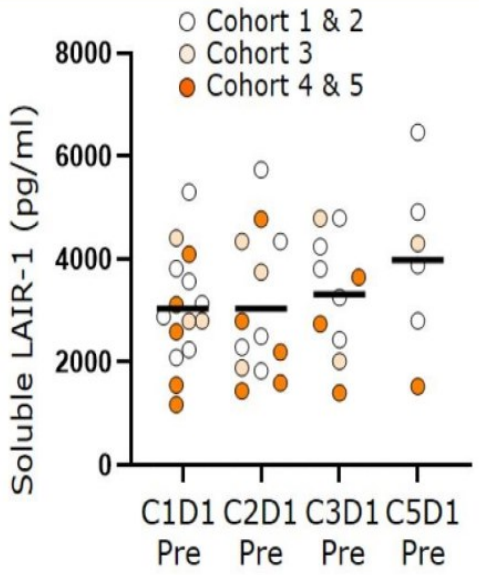


- Suggest mechanistic evidence of immune modulation
- Current assay optimization to discern endogenous LAIR-2 and NC410

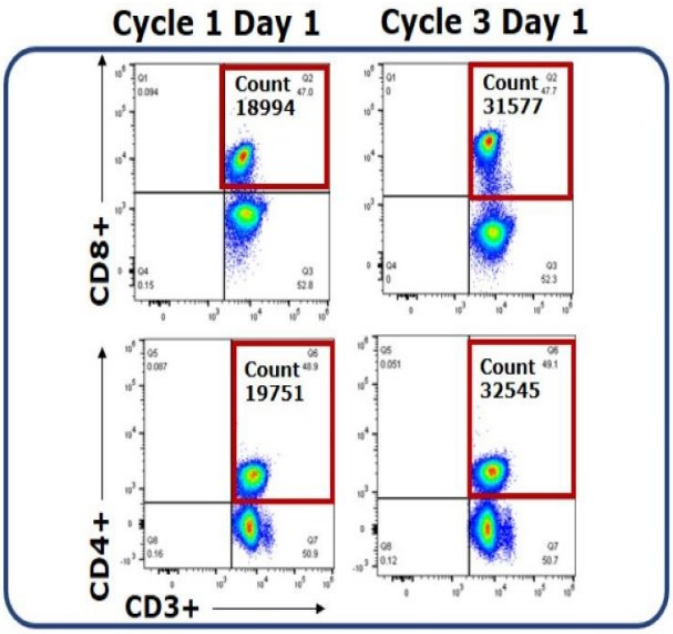
NextCure

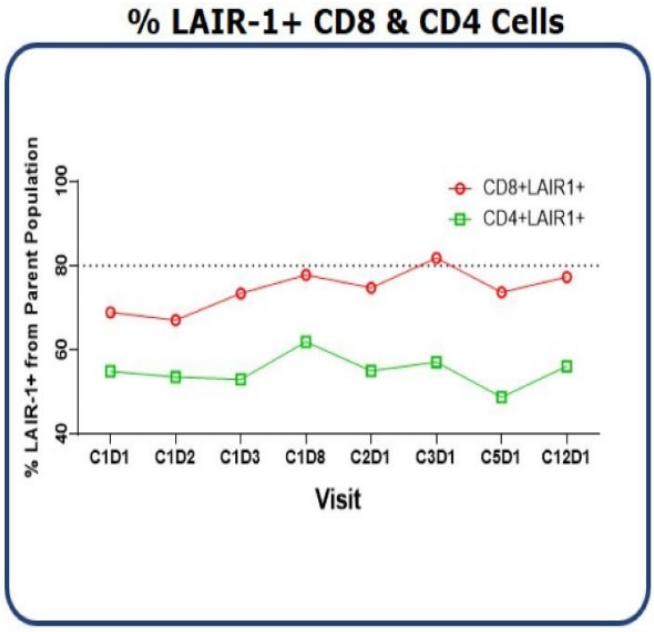
Soluble LAIR-1 in Peripheral Blood Over Time

- 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





- 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

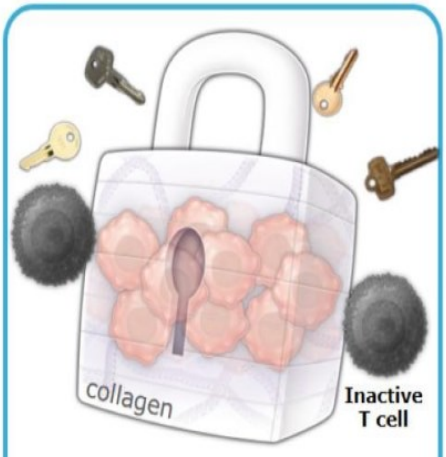
NextCure

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

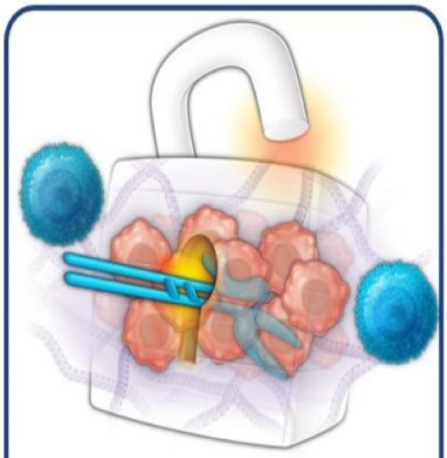
NC410: Key to Unlock TME and Normalize Immune Response

TME ACCESS LOCKED



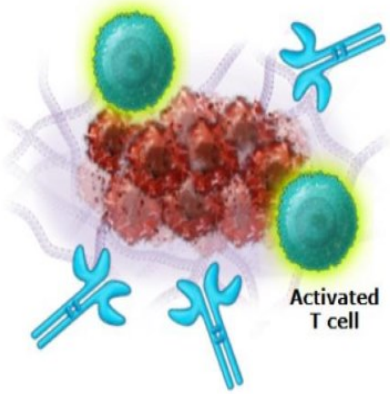
Many "keys" but none fit lock

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)

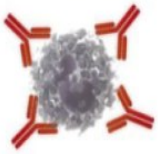
NC525

BIOLOGY

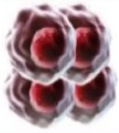
- LAIR-1 expression
  - High on AML blasts and leukemia stem cells (LSCs)
  - Minimal on hematopoietic stem and progenitor cells (HSPCs)
- Current AML treatments do not discriminate between leukemia blast cells and normal blood cells including HSPCs

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

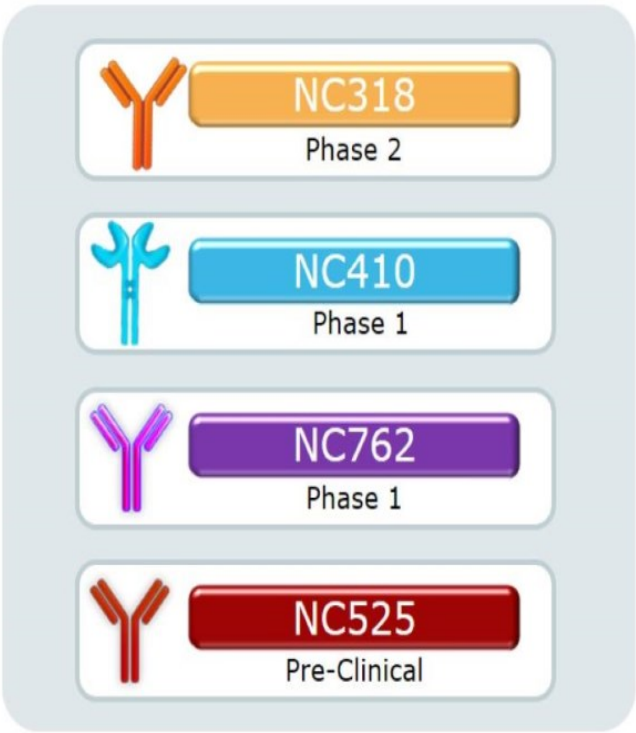
GMP Manufacturing Facility: Added Additional Capacity

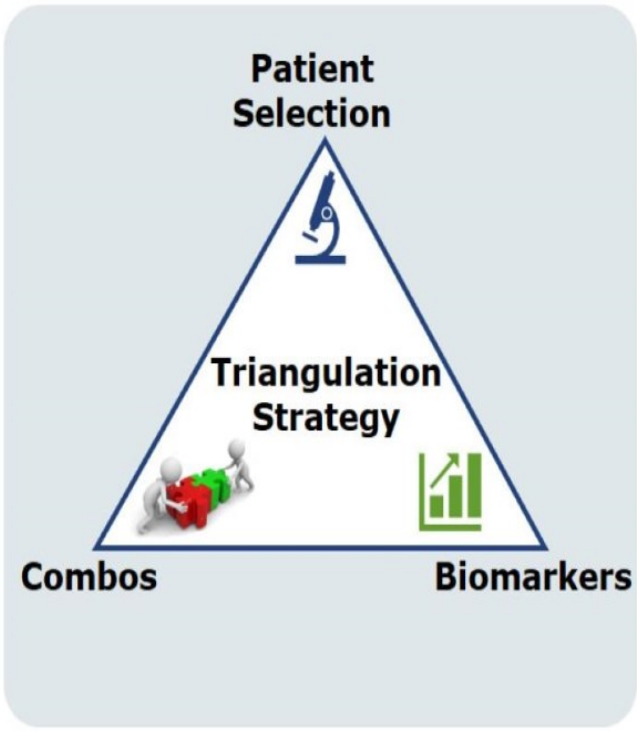
2,000L Capacity

- **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





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

NextCure

Significant Momentum & Milestones in 2022

NC318	BUILDING PIPELINE	EXPERIENCED	RUNWAY
On Track	Momentum	Team	2H 2023