

JULY 2020



# Next-Generation Immunomedicines

# 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 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; (iii) the timing or likelihood of regulatory filings for our product candidates; (iv) our manufacturing capabilities and strategy; (v) the potential benefits and activity of our product candidates; (vi) our expectations regarding the nature of the biological pathways we are studying; (vii) our expectations regarding our FIND-IO platform; and (viii) 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 May 7, 2020. 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
- NC410 (LAIR-1): IND filed and received FDA clearance Q1 2020
- Manufacturing: dedicated, state-of-the-art facility

## PLATFORM

- FIND-IO functional screening discovery engine
- Validation of novel cancer targets
- Expanding into autoimmune diseases

## PEOPLE

- Experienced management team
- Founder Dr. Lieping Chen: discovered PD-L1
- Strong immunology capabilities

# Unmet Medical Needs of Cancer Patients



We Need New Solutions

**Next**Cure

# Unmet Medical Needs of Cancer Patients

**NEW** Therapeutic Options

**POSITIVE** Clinical Responses

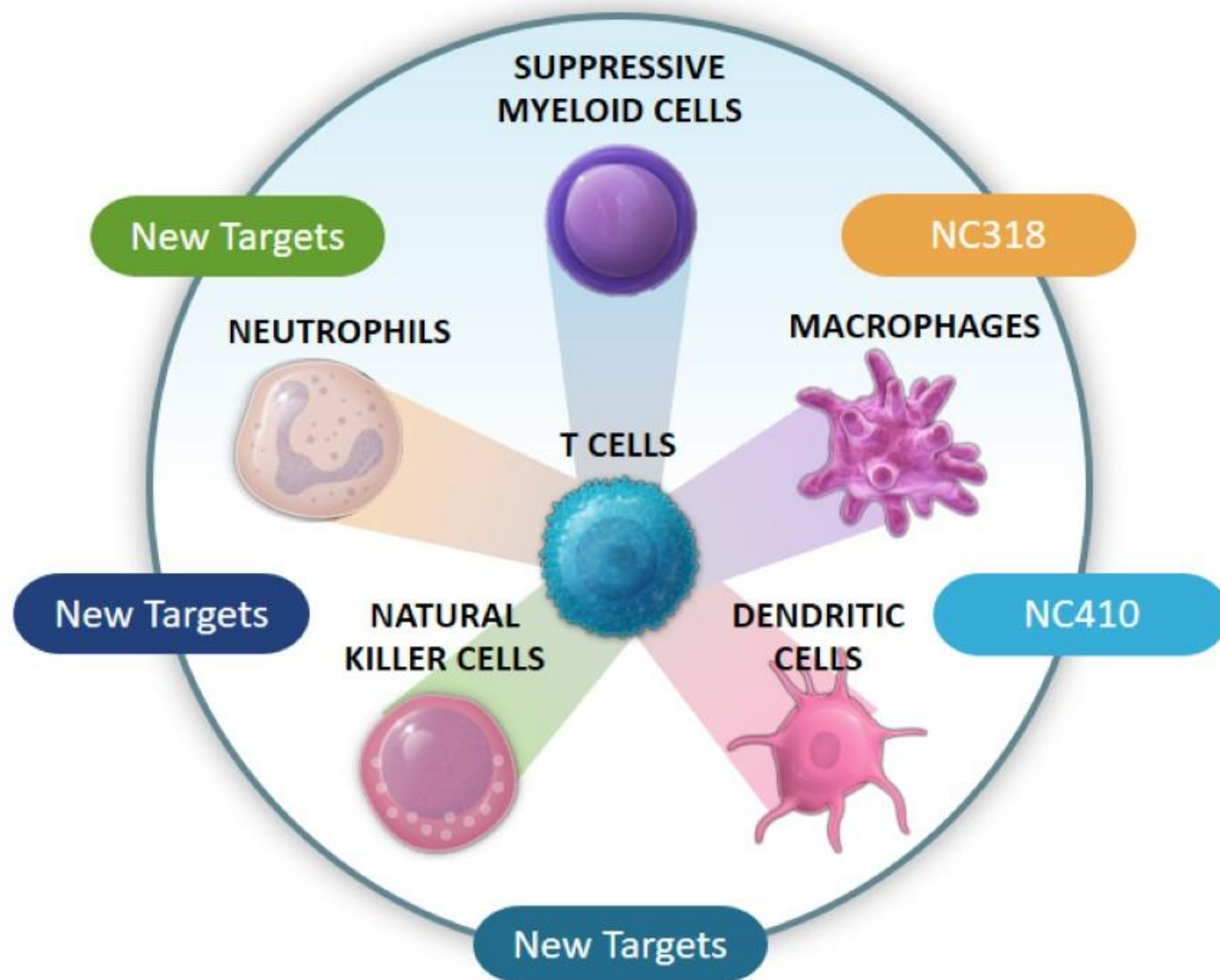
**IMPROVED** Quality of Life



Focused on Patients Not Adequately Addressed Today

**NextCure**

# Expanding Targets Beyond T Cells



# Product Development Pipeline

| PROGRAMS                        | CELLS                  | DISCOVERY | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 | ORIGINAL MILESTONE                            | WORLDWIDE RIGHTS |
|---------------------------------|------------------------|-----------|-------------|---------|---------|---------|-----------------------------------------------|------------------|
| PRODUCT CANDIDATES              |                        |           |             |         |         |         | (UPDATED GUIDANCE*)                           |                  |
| NC318 (S15) Monotherapy         | Tumors and macrophages | ONCOLOGY  |             |         |         |         | Phase 2 data by end of Q4 2020 (Expect delay) | NextCure         |
| NC318 (S15) Chemo Combo         | Tumors and macrophages | ONCOLOGY  |             |         |         |         | Initiate Phase 1 mid-2020 (Temporary delay)   | NextCure         |
| NC410 (LAIR-1)                  | Dendritic and T cells  | ONCOLOGY  |             |         |         |         | Initial Phase 1 data 2H 2021                  | NextCure         |
| DISCOVERY AND RESEARCH PROGRAMS |                        |           |             |         |         |         |                                               |                  |
| Multiple Programs               | Immune cells           |           |             |         |         |         | First IND filing in early 2021                | NextCure         |
| FIND-IO Platform                | Multiple cell types    |           |             |         |         |         | First IND filing in late 2022                 | NextCure         |

\*Updated guidance noted in parentheses indicates delays or expected delays due to the ongoing COVID-19 pandemic. Where delays are indicated or expected, the original milestone should be disregarded.

# NC318

## Humanized Monoclonal Antibody



Phase 1/2  
CLINICAL  
TRIAL

### TARGET

Siglec-15  
("S15")

### CELL TYPES

Tumors &  
macrophages

### MOA

Blocks S15-induced  
immunosuppression

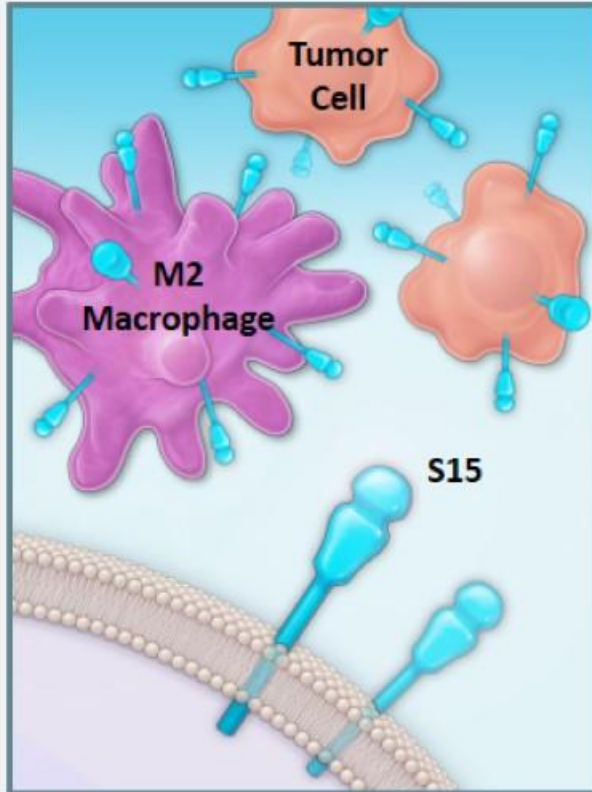
### INDICATIONS

NSCLC, ovarian,  
head & neck and  
triple negative  
breast cancers

# S15 as a Target

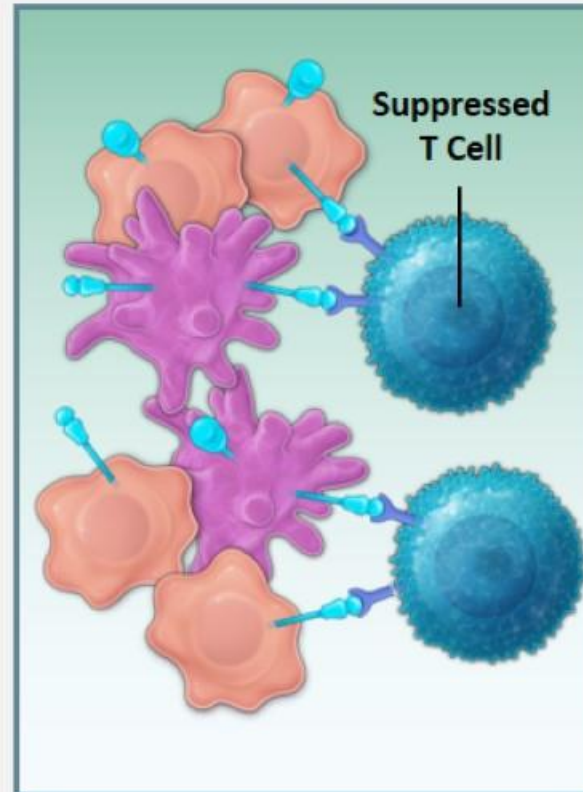
## EXPRESSION

Tumors and  
Macrophages



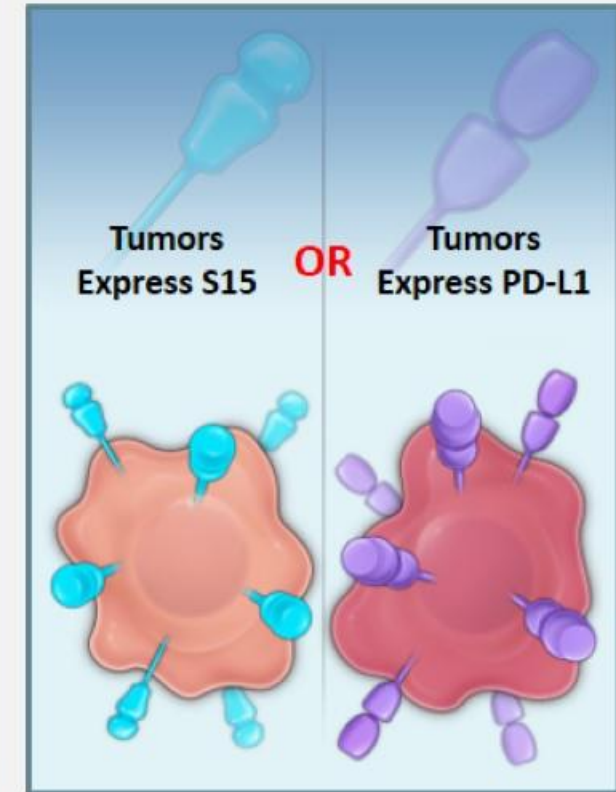
## FUNCTION

Potently Suppresses  
T Cell Function



## NON-RESPONDERS

Generally Non-Overlapping  
with PD-L1 Expression



Wang et al.,  
2019

nature  
medicine

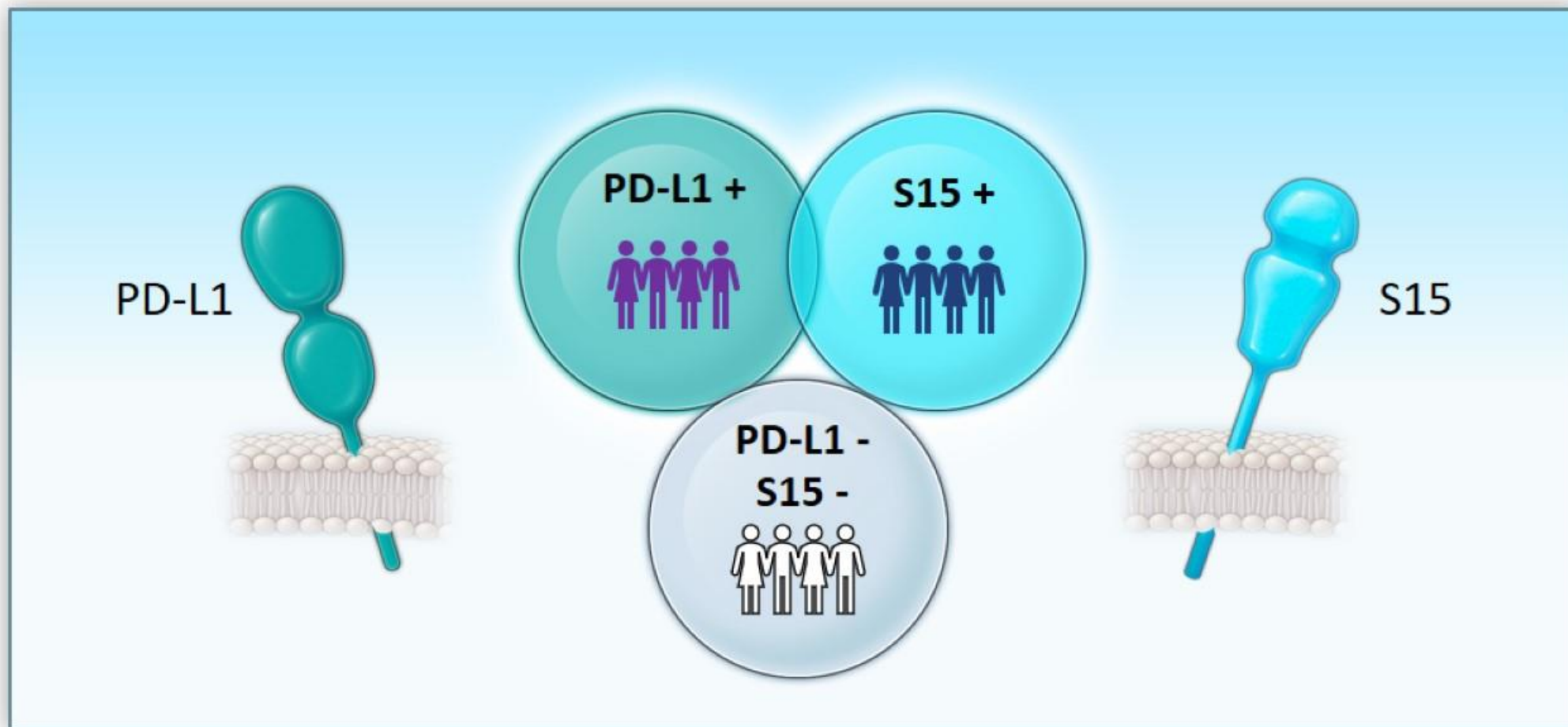
ARTICLES

<https://doi.org/10.1038/s41591-019-0374-x>

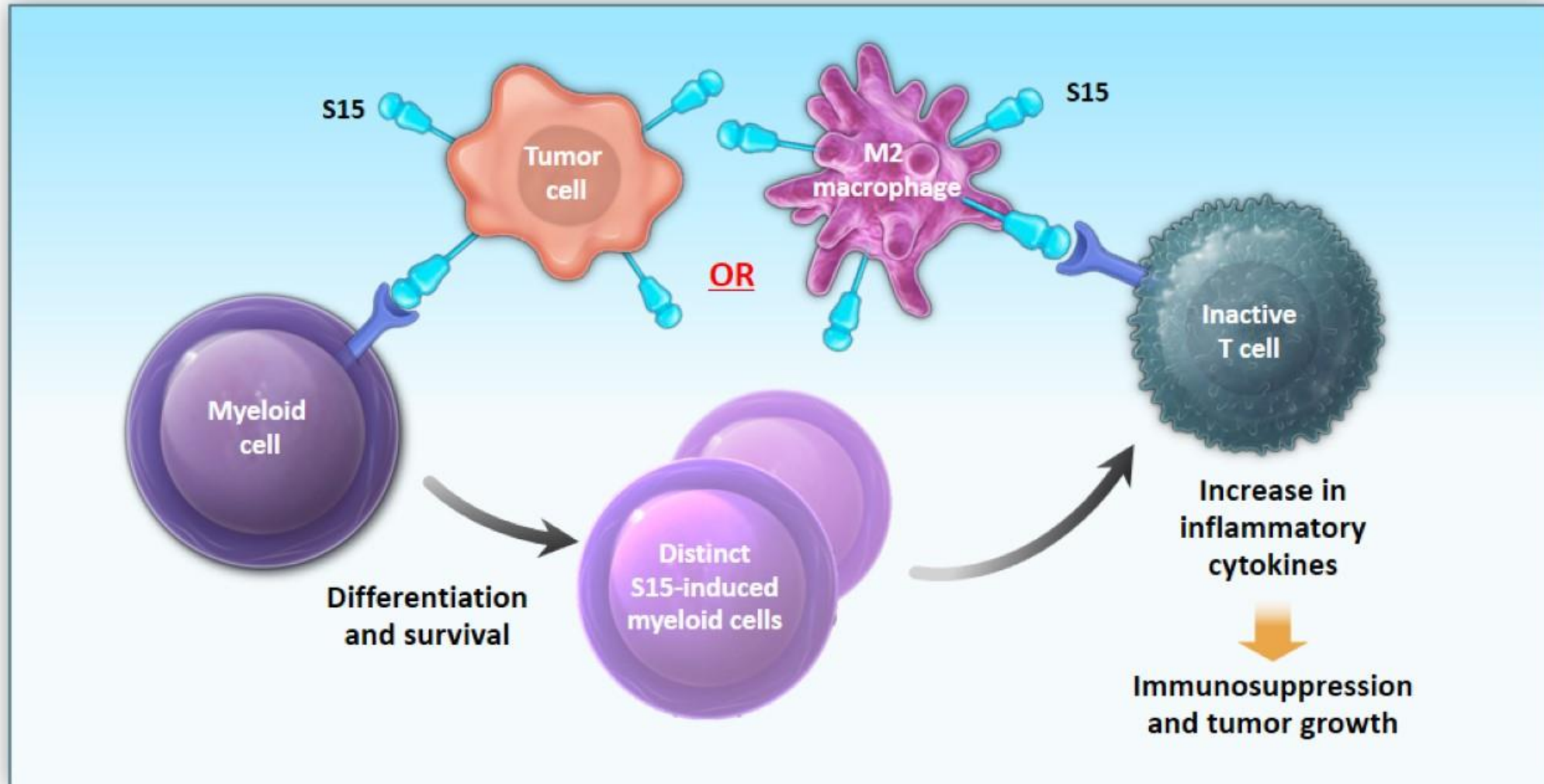
Siglec-15 as an immune suppressor and potential  
target for normalization cancer immunotherapy

# NC318: A Potential Treatment Option for PD-1/PD-L1 Non-Responders

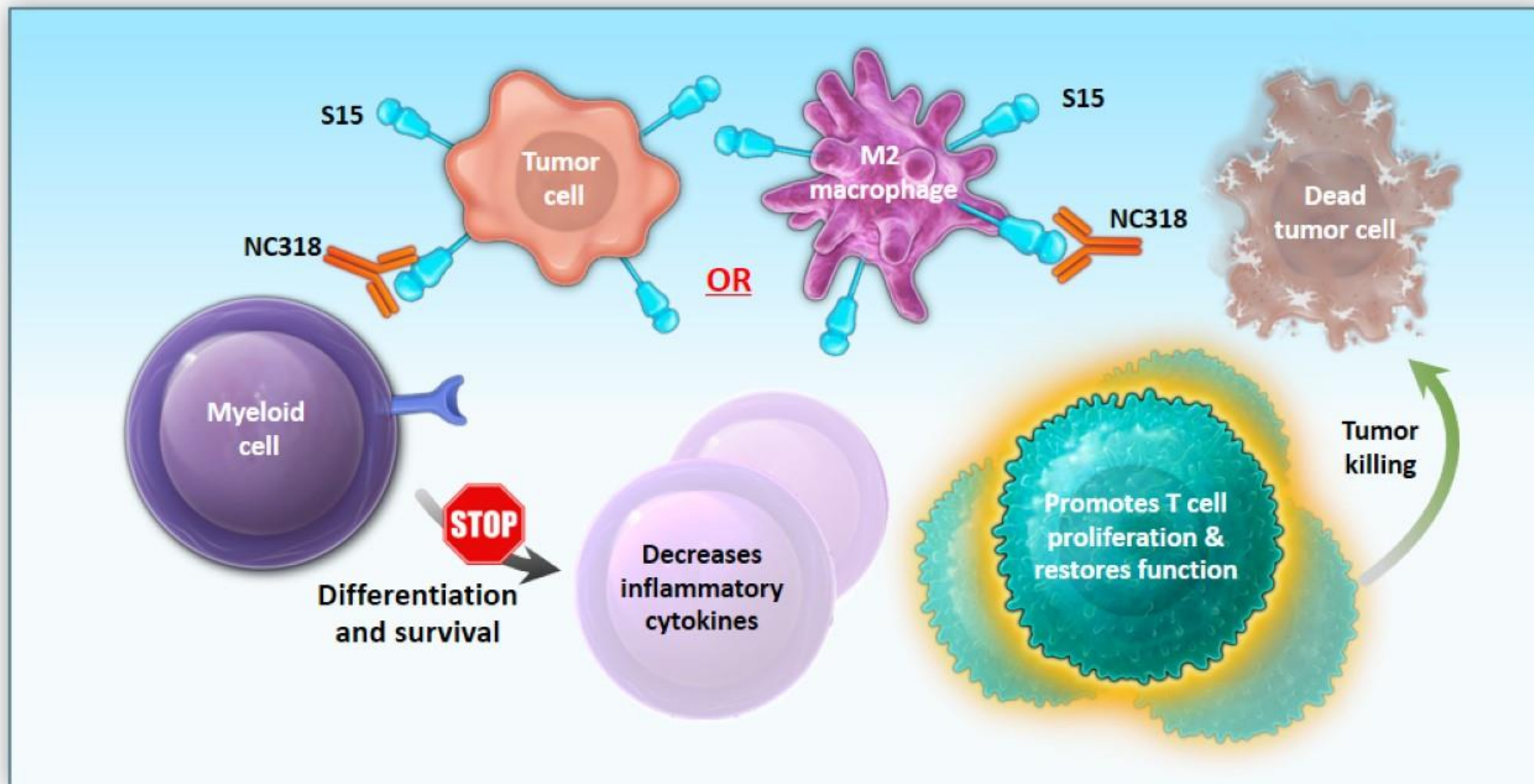
**S15 AND PD-L1 EXPRESSION GENERALLY DO NOT OVERLAP**



## S15 is Immunosuppressive in the Tumor Microenvironment



## NC318 Blocks Immunosuppressive Activity Induced by S15

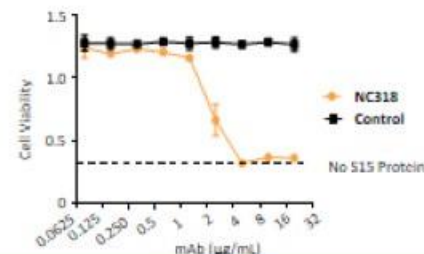
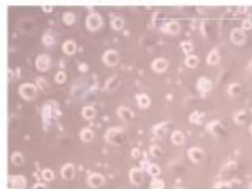


# NC318 Mechanism of Action Restores Immune Function *In Vitro*

## INHIBITS

Myeloid Cell  
Differentiation and Survival

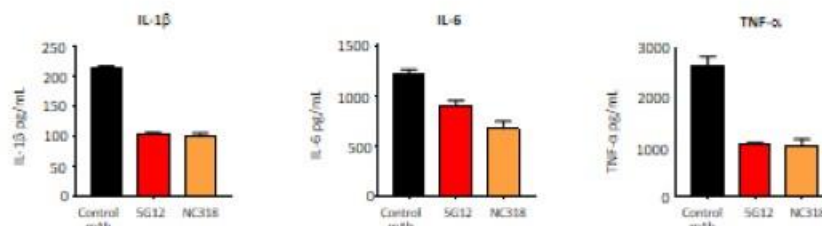
Myeloid Cell Survival and  
Differentiation



Blocks survival of  
myeloid cells

## DECREASES

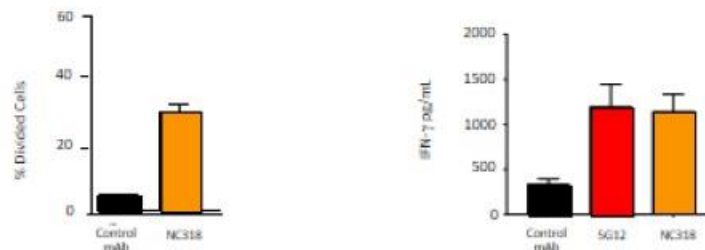
Pro-Inflammatory and  
Pro-Tumorigenic Cytokines



Decreases IL-1 $\beta$ ,  
IL-6 & TNF- $\alpha$

## PROMOTES

T Cell Function



Increases T cell  
proliferation &  
IFN- $\gamma$  production

# NC318 Phase 1 Trial Status as of November 9, 2019 (SITC Presentation)

## DOSE ESCALATION AND SAFETY AND TOLERABILITY

### Completed

#### ENROLLMENT

- 49 patients
- 15 tumor types
- Median of 3 prior therapies
- All comers regardless of PD-L1 or S15 expression status

#### SAFETY

- No DLTs through 800 mg
- 1 DLT at 1600 mg: Grade 3 pneumonitis
- Common irAEs observed, including diarrhea, rashes, vitiligo, arthralgias

#### RESPONSES

- Evaluations every 8 weeks
- 1 confirmed CR (55+ weeks)
- 1 confirmed PR (28+ weeks)
- 14 durable SD ( $\geq 16$  weeks)

The Angeles Clinic  
AND RESEARCH INSTITUTE  
A CEDARS-SINAI AFFILIATE

next  
ONCOLOGY

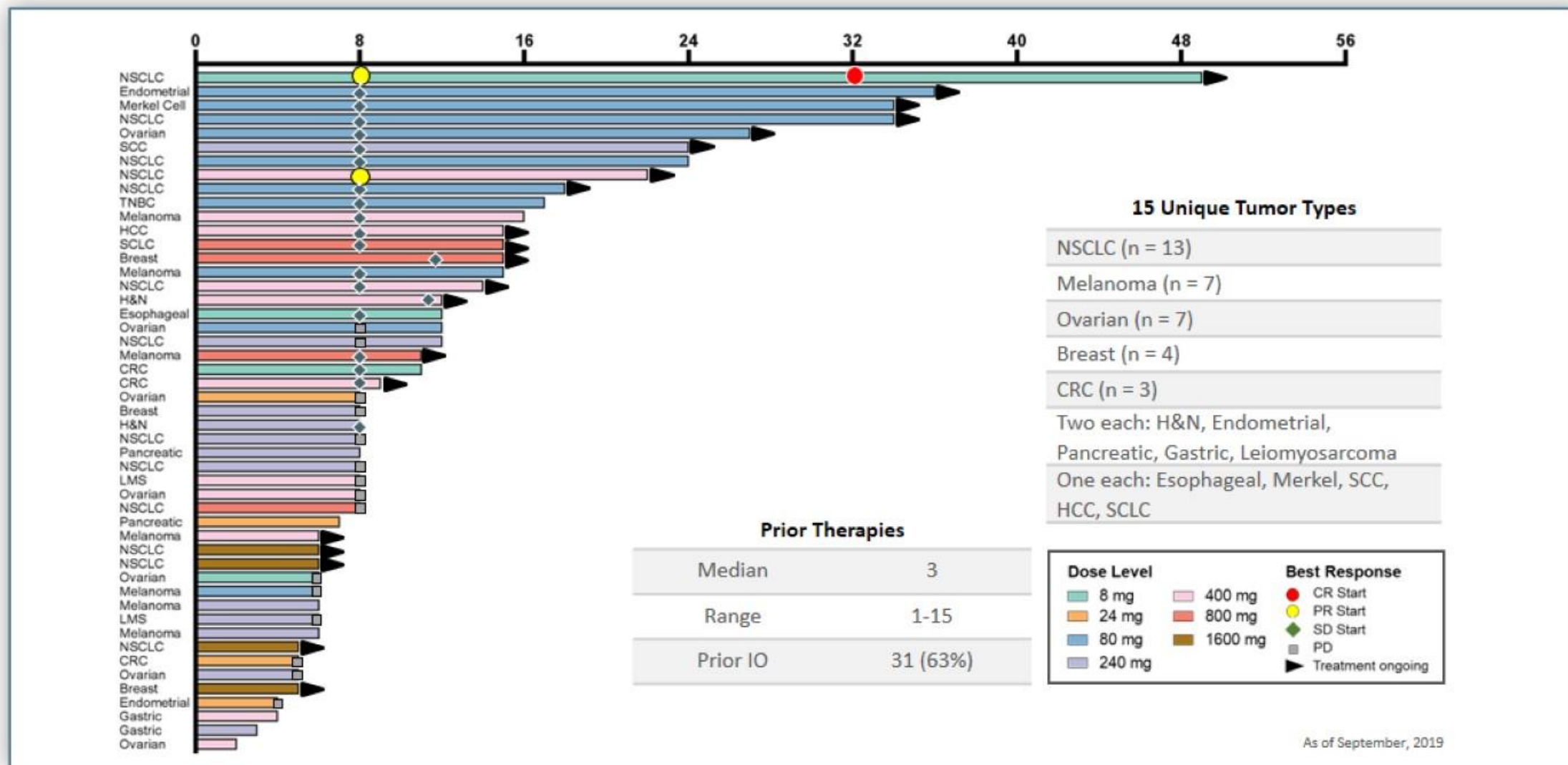
NYU Langone  
MEDICAL CENTER

John Theurer  
Cancer Center  
at Hackensack University Medical Center

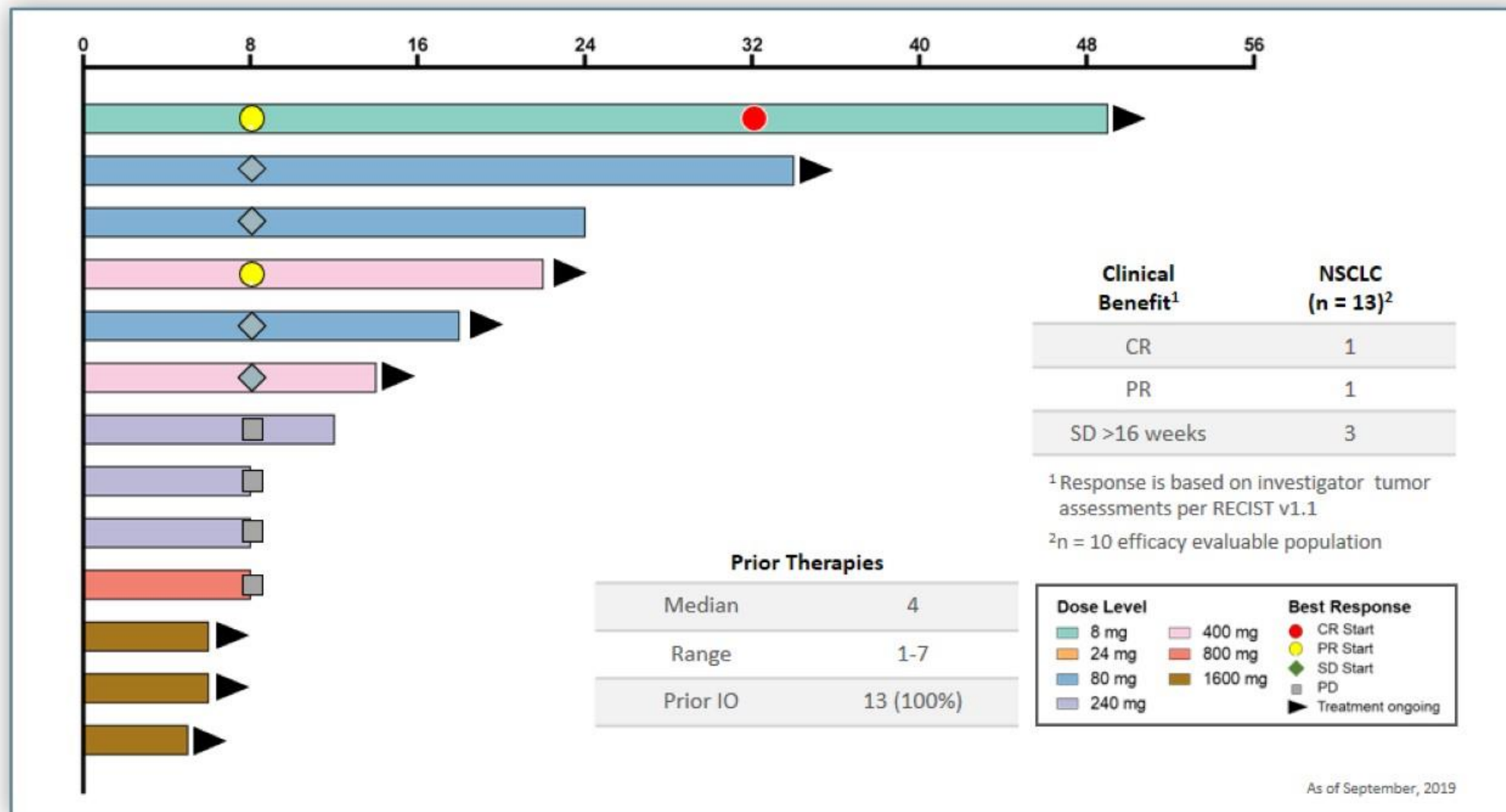
Yale University

Most common AEs: infusion reactions, fatigue, headaches, pruritis, elevated amylase and elevated lipase

# Treatment Duration in Weeks for All Phase 1 Patients



# Durable Clinical Benefit for PD-1 Refractory NSCLC Patients

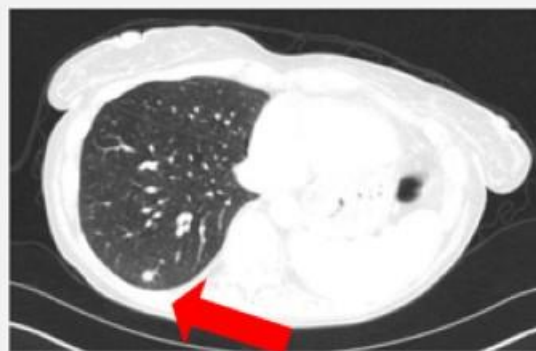


## NC318: Single-Agent Activity in PD-1 Refractory NSCLC

Confirmed

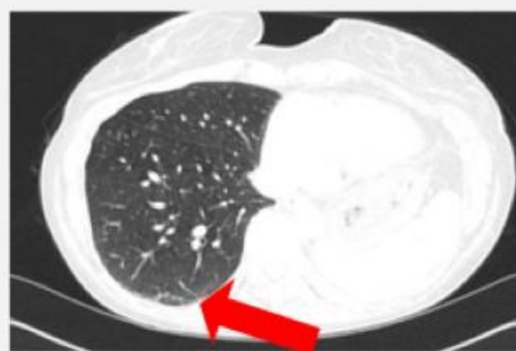
COMPLETE RESPONSE

BASELINE



Target lesion

WEEK 16



Target lesion gone

56 y/o NSCLC with  
multiple lesions  
(PD-L1 TPS <50%)  
8 mg every 2 weeks

**PRIOR THERAPIES:**  
Chemotherapy (x3)  
Nivolumab (best response  
stable disease then  
progression)

Confirmed

PARTIAL RESPONSE



Target lesions -71%



74 y/o NSCLC  
(PD-L1 TPS <50%)  
400 mg every 2 weeks

**LAST PRIOR THERAPY:**  
Immunotherapy:  
LAG3/PD-1 (best response  
stable disease then  
progression)

## Conclusions from Phase 1 Portion of NC318 Trial

- Well tolerated across multiple dose levels
- AE profile consistent with approved immunotherapies
- Predictable PK profile
- Encouraging single-agent anti-tumor activity
  - PD-1 refractory NSCLC: 1 CR, 1 PR, and 3 SD
  - Other tumor types: SD >24 weeks in endometrial, Merkel cell, and ovarian cancers
- Phase 2 initiated October 2019



# NC318 Phase 2 Trial Status as of November 9, 2019

## DOSE EXPANSION - ENROLLING

### TUMOR TYPES

NSCLC

H&N

Ovarian

TNBC

### DESIGN

- Biopsies required
- PD-L1 TPS <50%
- S15 evaluated retrospectively
- Biomarker evaluation
- Monotherapy
- 400 mg every 2 weeks

### DELIVERABLES

- Initial Phase 2 data (expect delay due to COVID-19)



# NC318

Restores Immune  
Function in a Highly  
Suppressive TME



MOA / Preclinical studies complete

- Relieves S15-mediated inhibition of T cells
- Increases IFN- $\gamma$  production
- Decreases inflammatory cytokines



Completed enrollment of Phase 1



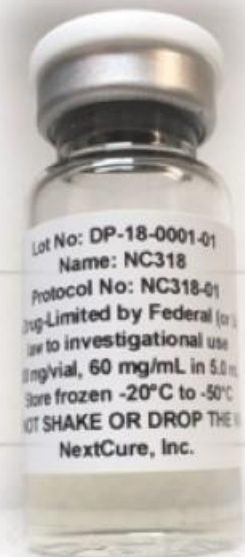
Reported preliminary data at SITC 2019



Initiate Phase 2 combination trial with SOC  
chemotherapies (temporarily delayed due to COVID-19)



Report initial Phase 2 data (expect delay due to COVID-19)



# NC410

## Decoy Human Fusion Protein Targeting the TME



Phase 1  
Started  
July 2020

### TARGET

Leukocyte-Associated  
Immunoglobulin-like  
Receptor-1 (LAIR-1)

### CELL TYPES

Dendritic cells and  
T cells

### MOA

Promotes T cell  
function & dendritic  
cell activity

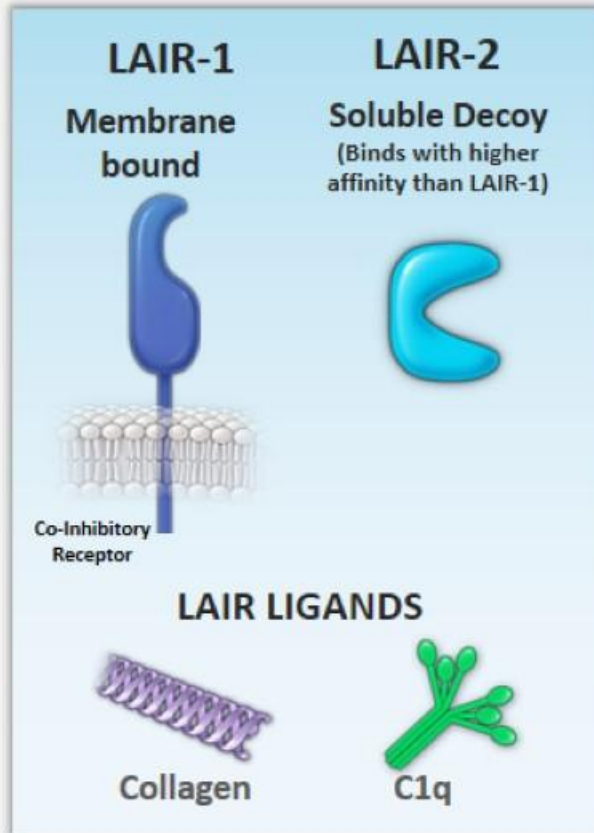
### INDICATIONS

Advanced or  
metastatic solid  
tumors

# LAIR-1 & LAIR-2 Functional Relationship

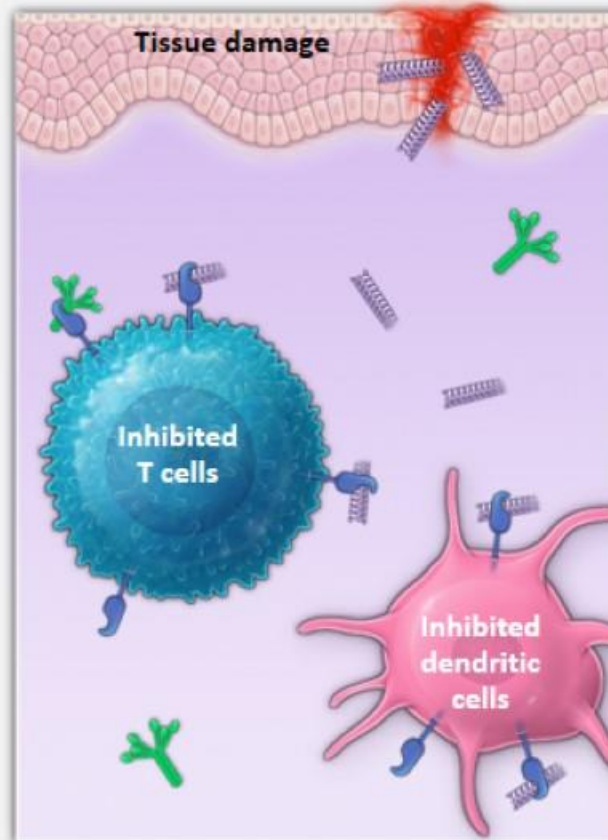
## LAIR & LIGANDS

LAIR-1 and LAIR-2 Bind  
Collagen and C1q



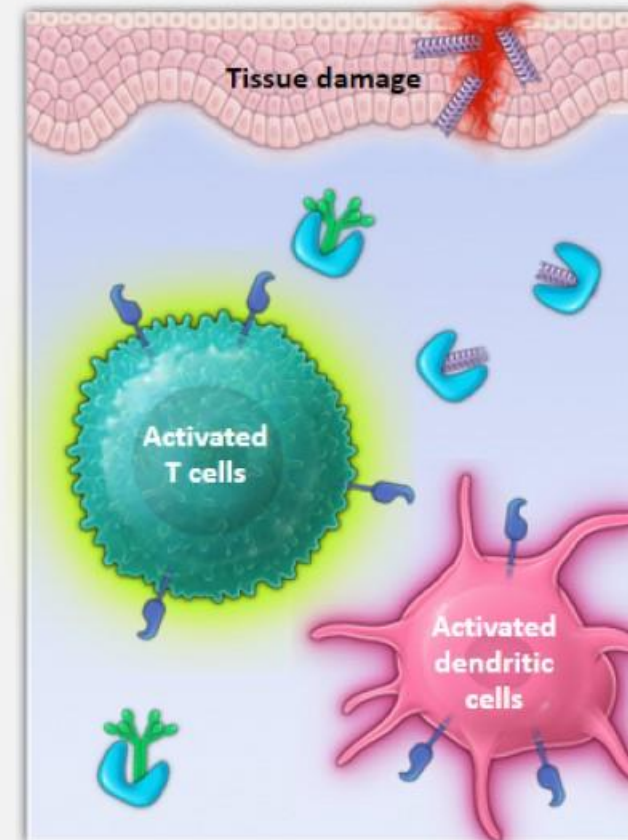
## LAIR-1

Ligands Expressed in Response to  
Inflammation & Inhibit Immune Function



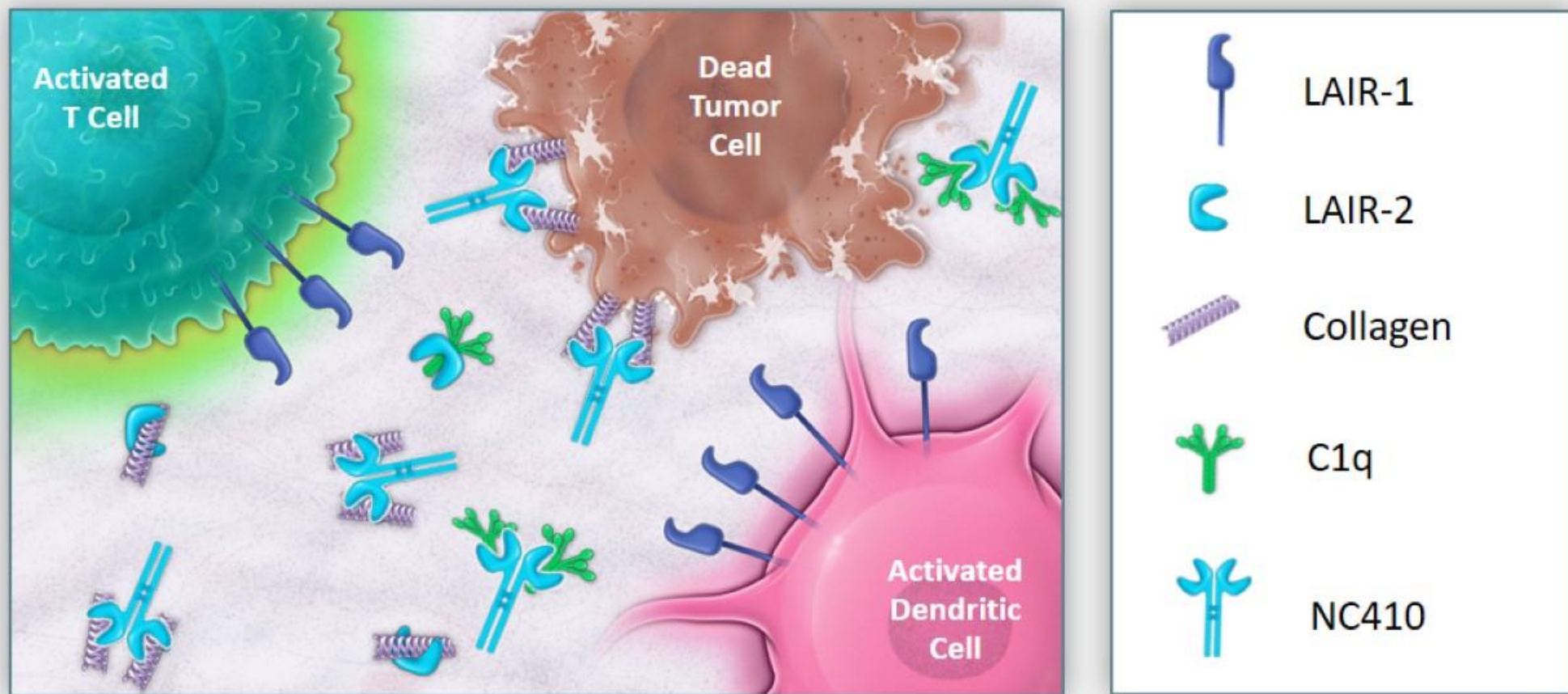
## LAIR-2

LAIR-2 Modulates LAIR-1  
Mediated Inhibition



# NC410 Prevents Immune Suppression

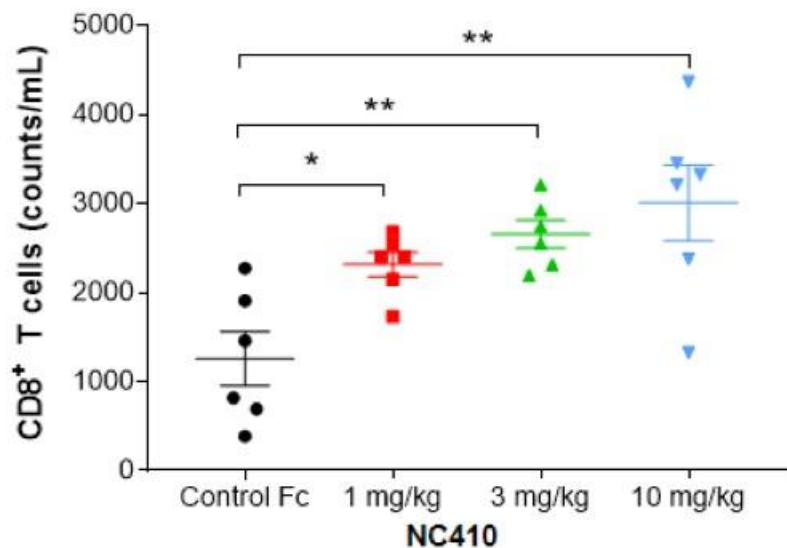
NC410 IS A FUSION PROTEIN OF LAIR-2 AND A DECOY FOR LAIR-1 AND PROMOTES T CELL FUNCTION AND DC ACTIVATION



# NC410 Enhanced T Cell Expansion and Relieved Immunosuppression

Blocked

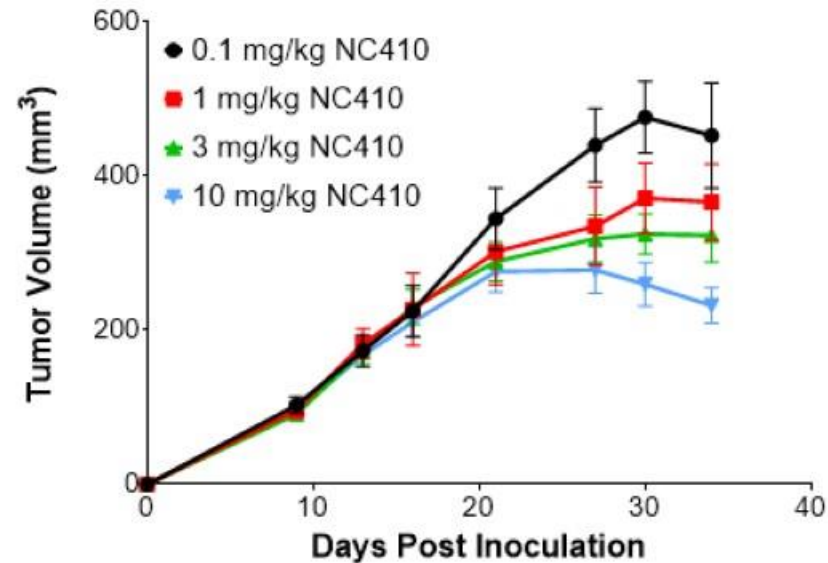
SUPPRESSION



Human CD8+ T cell expansion  
*in vivo*

Decreased

TUMOR VOLUME



Human PBMCs in mice: CD8+ T cell activity  
decreased tumor volume in HT29 model



## NC410 Summary



Promotes T cell function and dendritic cell activity  
in preclinical studies



cGMP manufacturing complete



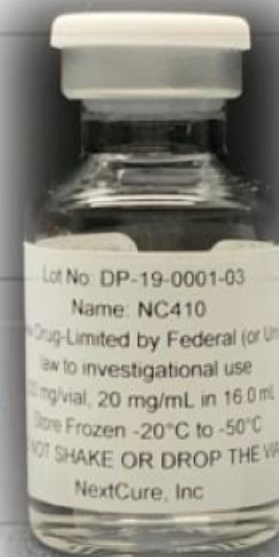
IND filed & received FDA clearance Q1 2020



Initiated Phase 1 trial

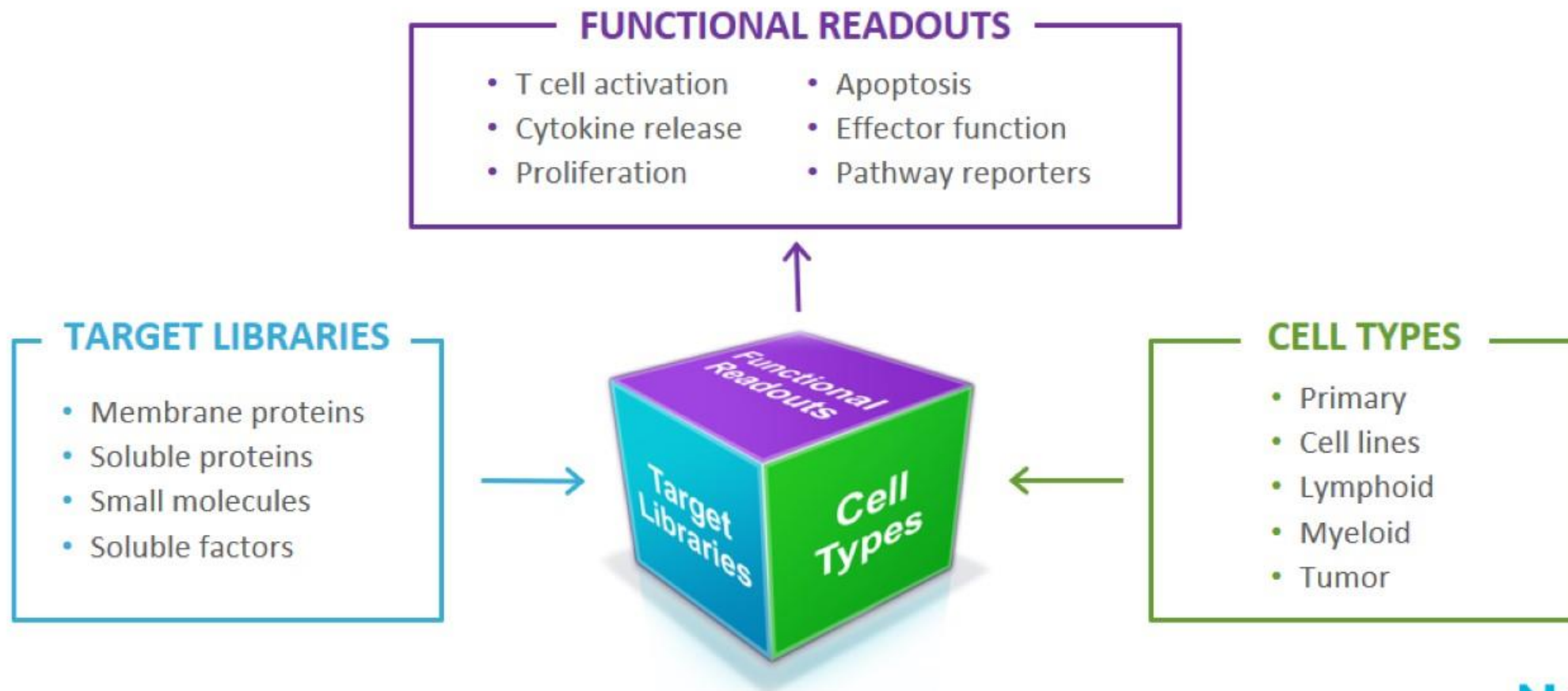


Initial Phase 1 data 2H 2021



## Finding Solutions with a Powerful Discovery Engine

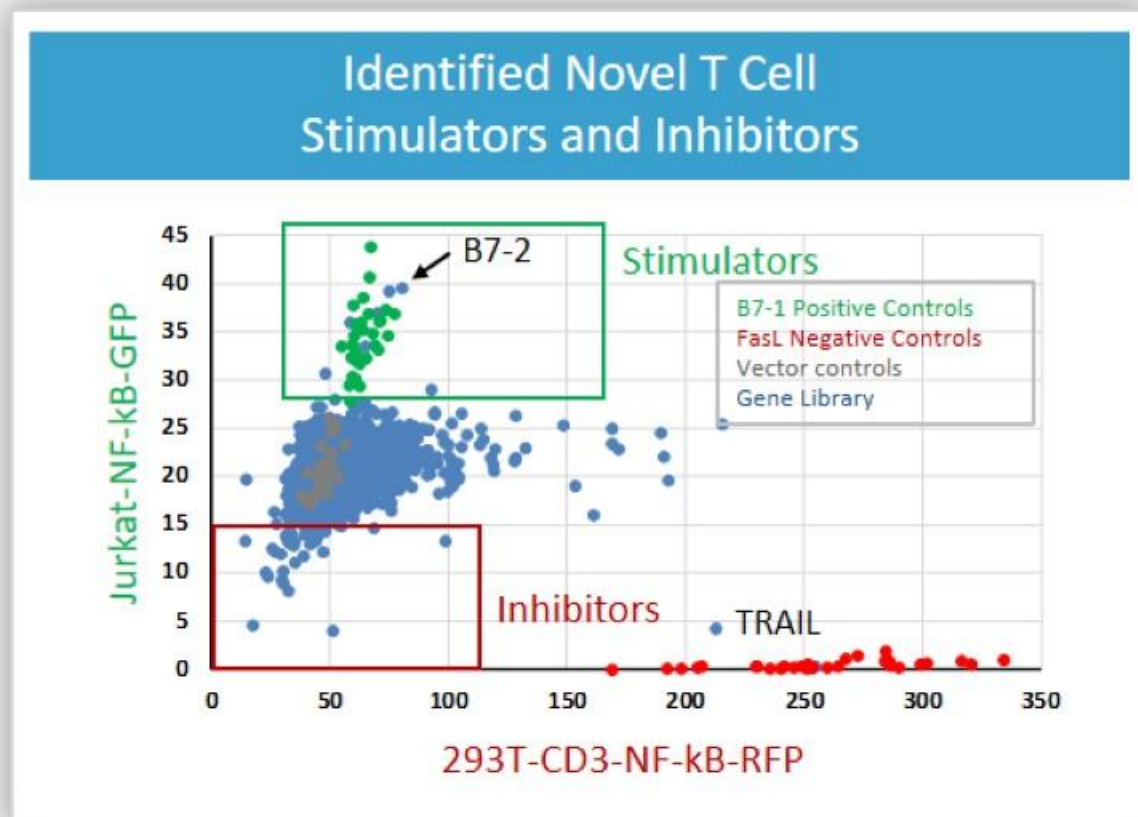
Functional, Integrated, NextCure Discovery in Immuno-Oncology



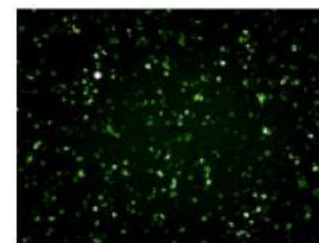
# FIND-IO Screening Methodology



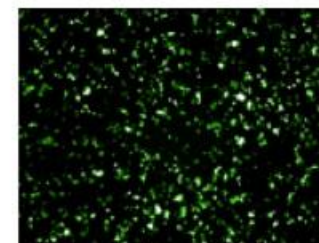
## Jurkat “T Cell Line” Screening and Validating FIND-IO Hits



Vector  
Control



Stimulatory  
B7-2



Inhibitory  
TRAIL

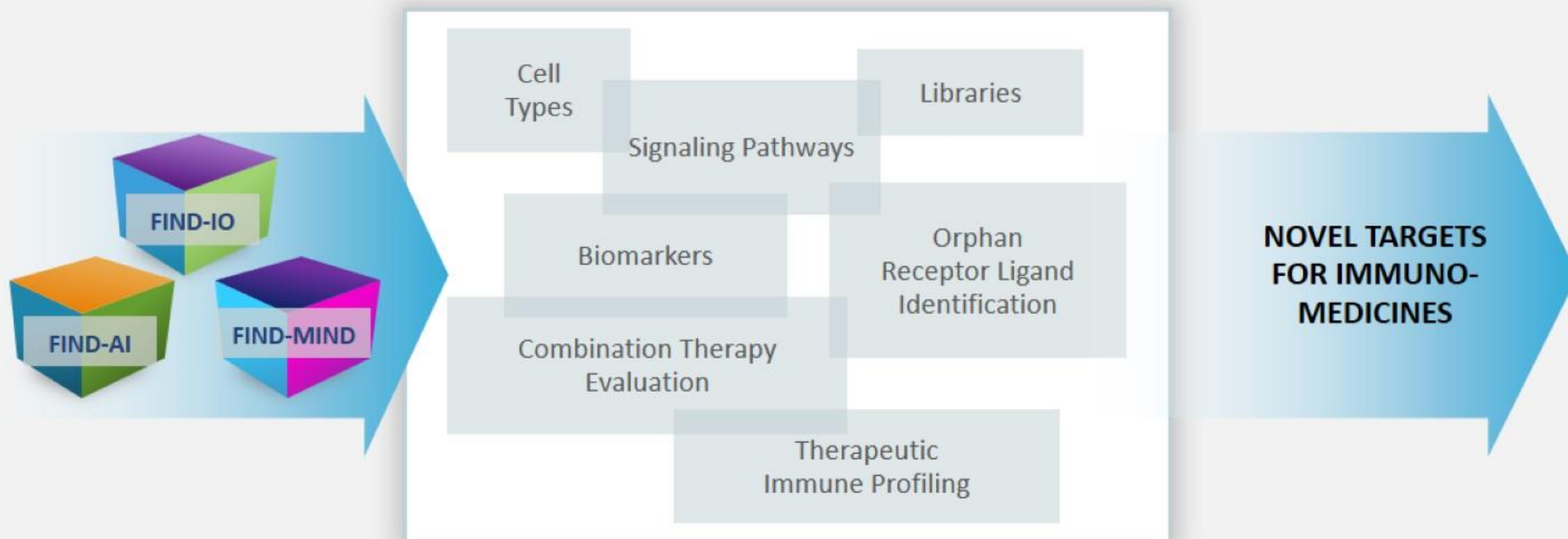


REPRODUCIBILITY

ROBUSTNESS

RELEVANCY

# Versatile, Flexible, and Comprehensive Approach for Target Identification



# Anticipated Near-Term Milestones



## NC318

- Initiate Phase 2 combination trial with standard of care chemotherapies (temporarily delayed due to COVID-19)
- Report initial Phase 2 data (expected delay due to COVID-19)



## NC410

- Initiate Phase 1 (temporarily delayed due to COVID-19)



## DISCOVERY

- Identify novel targets and initiate validation



Committed to Addressing the Unmet Needs of Patients with New Solutions

**FOCUSED**  
Approach

**PROVEN**  
Momentum

**INNOVATIVE**  
Platform

**EXPERIENCED**  
Team

**FUTURE**  
Deliverables