

APRIL 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-K filed with the SEC on March 12, 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

# 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					Initiate Phase 1 Q2 2020 (Temporary delay)	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

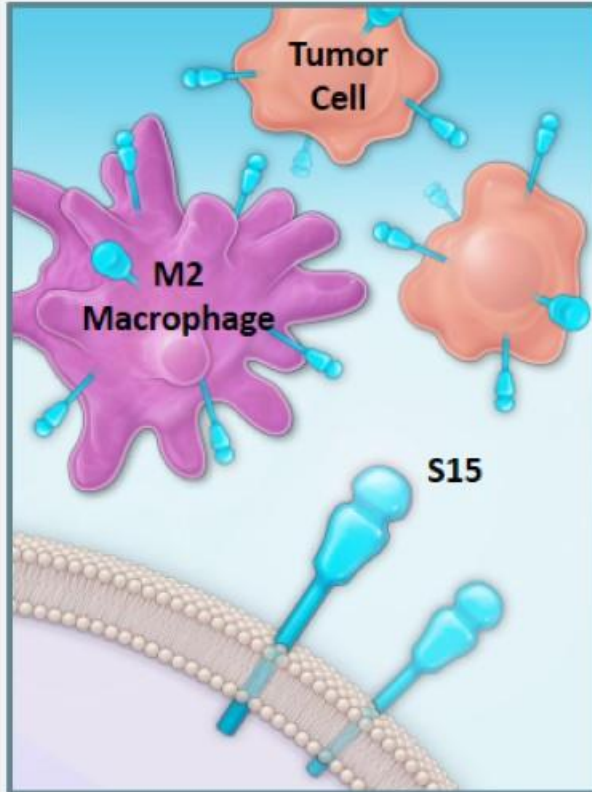
### INDICATIONS

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

# S15 as a Target

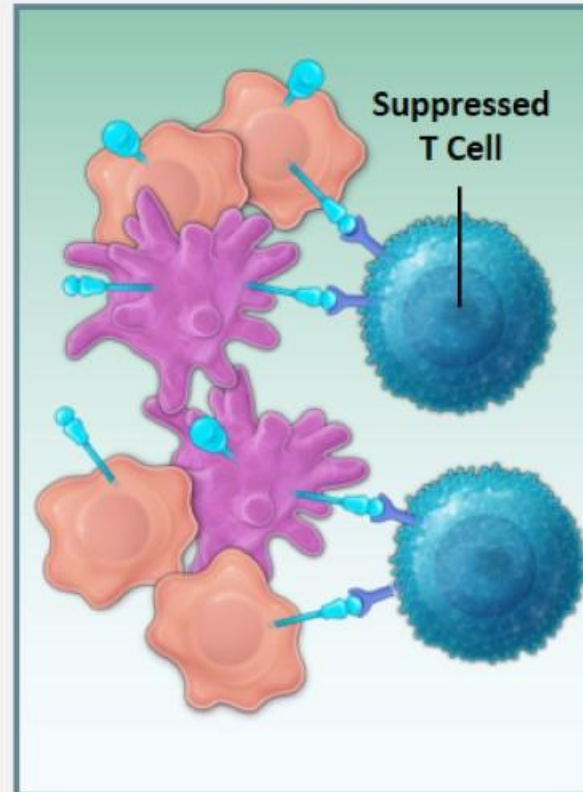
## EXPRESSION

Tumors and  
Macrophages



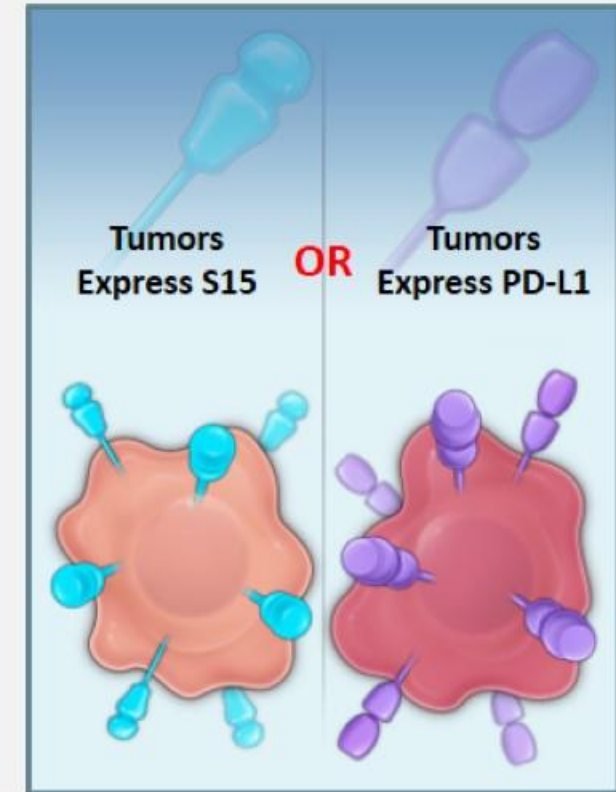
## FUNCTION

Potently Suppresses  
T Cell Function



## NON-RESPONDERS

Generally Non-Overlapping  
with PD-L1 Expression



Wang et al.,  
2019

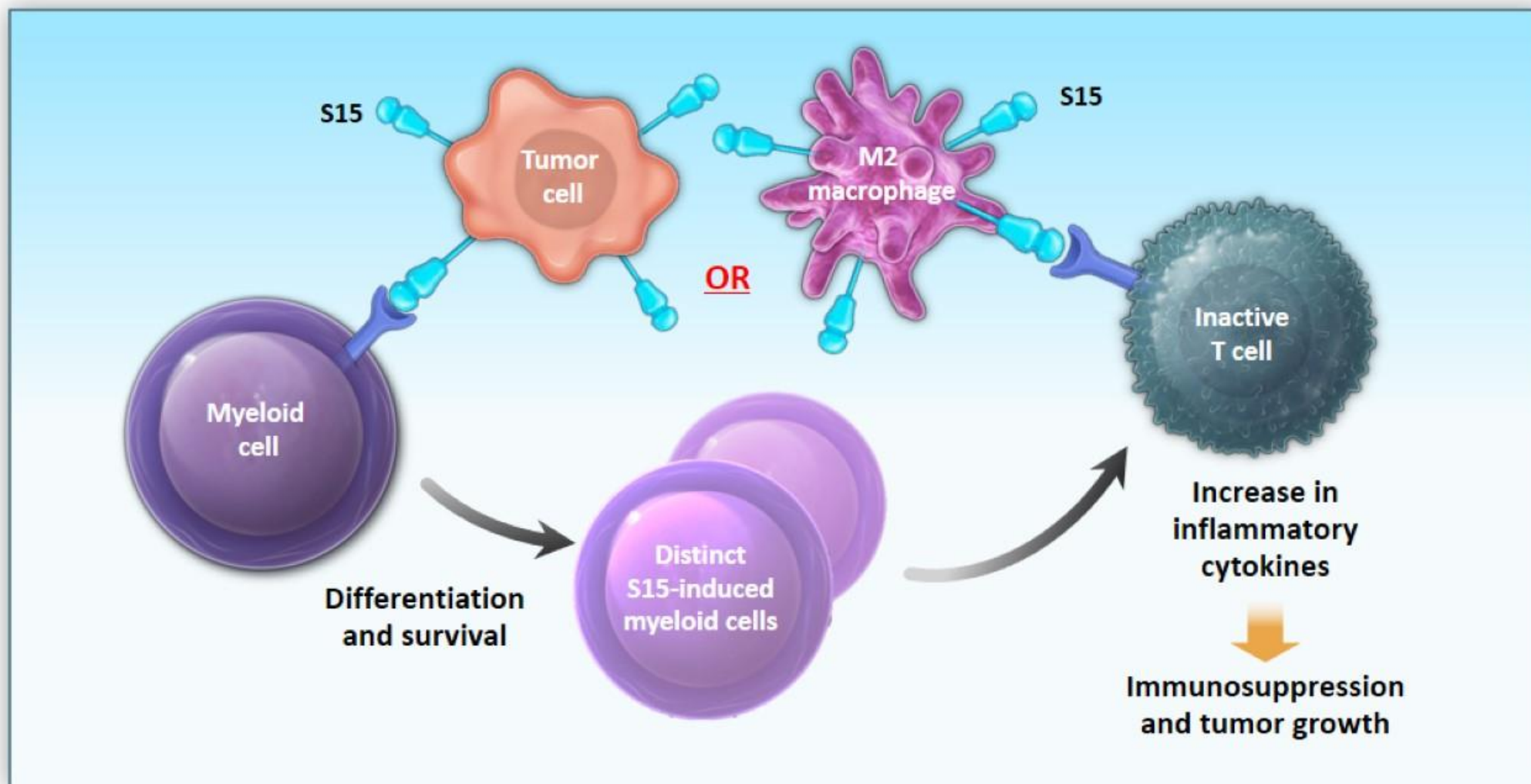
nature  
medicine

ARTICLES

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

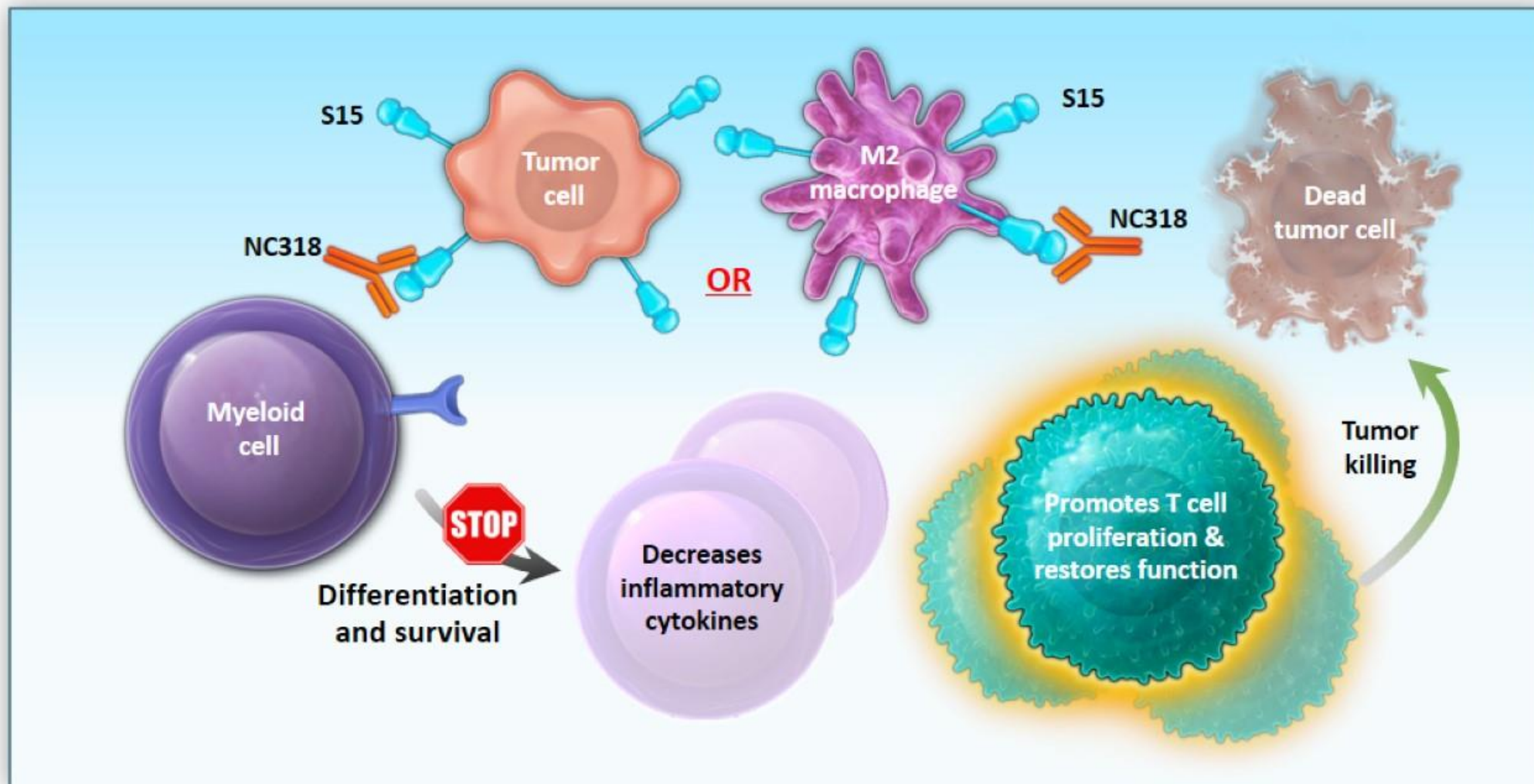
Siglec-15 as an immune suppressor and potential  
target for normalization cancer immunotherapy

## S15 is Immunosuppressive in the Tumor Microenvironment





## NC318 Blocks Immunosuppressive Activity Induced by S15

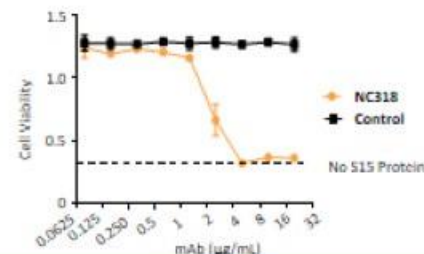
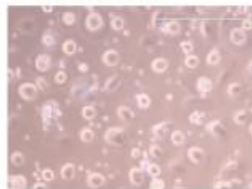


# NC318 Mechanism of Action Restores Immune Function *In Vitro*

## INHIBITS

Myeloid Cell  
Differentiation and Survival

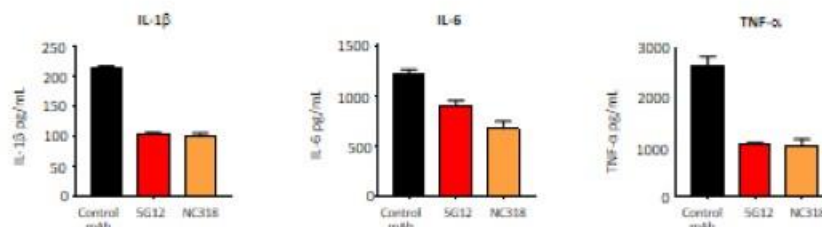
Myeloid Cell Survival and  
Differentiation



Blocks survival of  
myeloid cells

## DECREASES

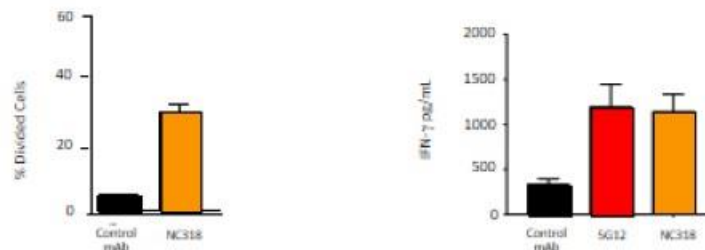
Pro-Inflammatory and  
Pro-Tumorigenic Cytokines



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

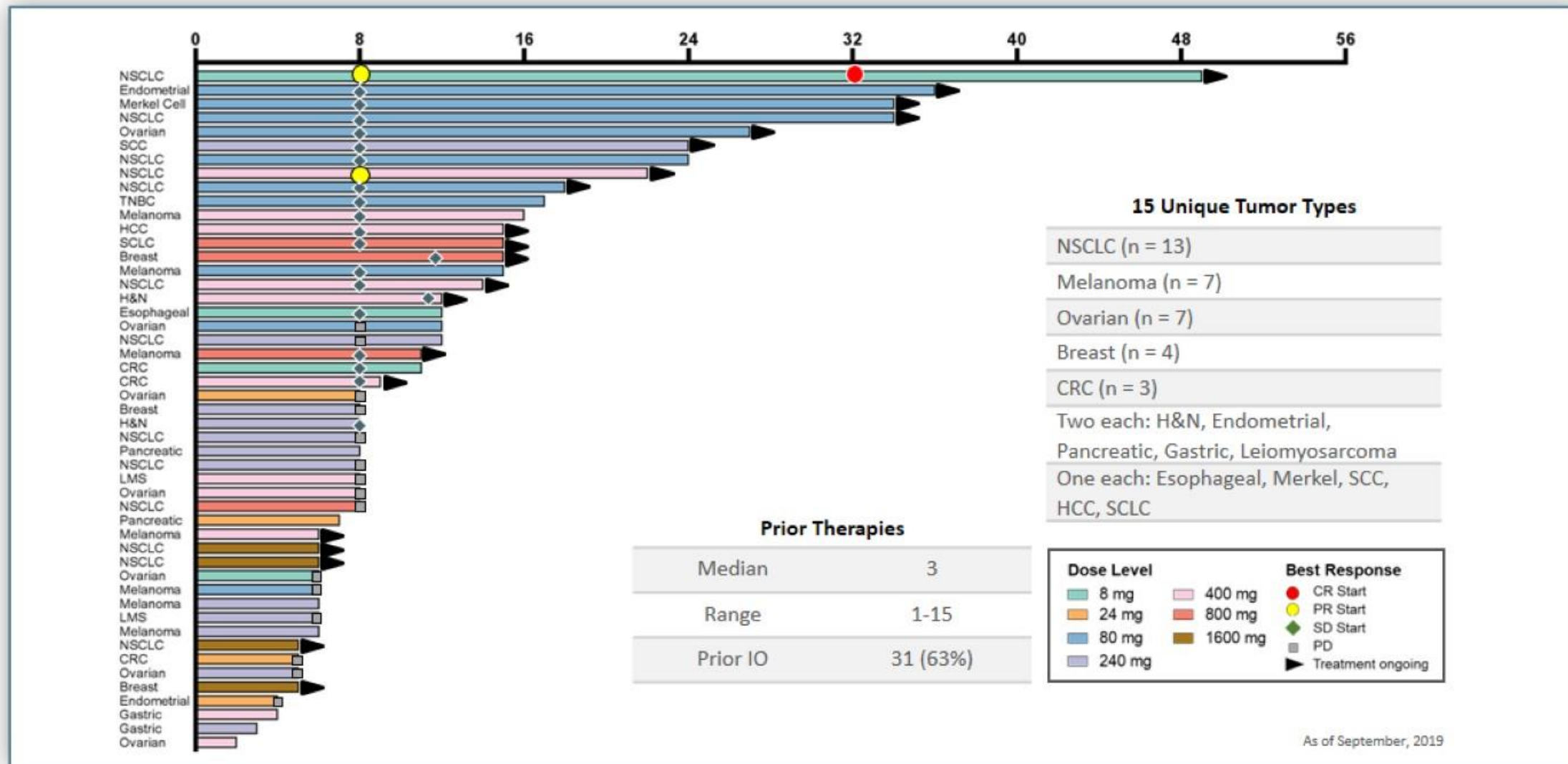
NYU Langone  
MEDICAL CENTER

John Theurer  
Cancer Center  
at Hackensack University Medical Center

Yale University

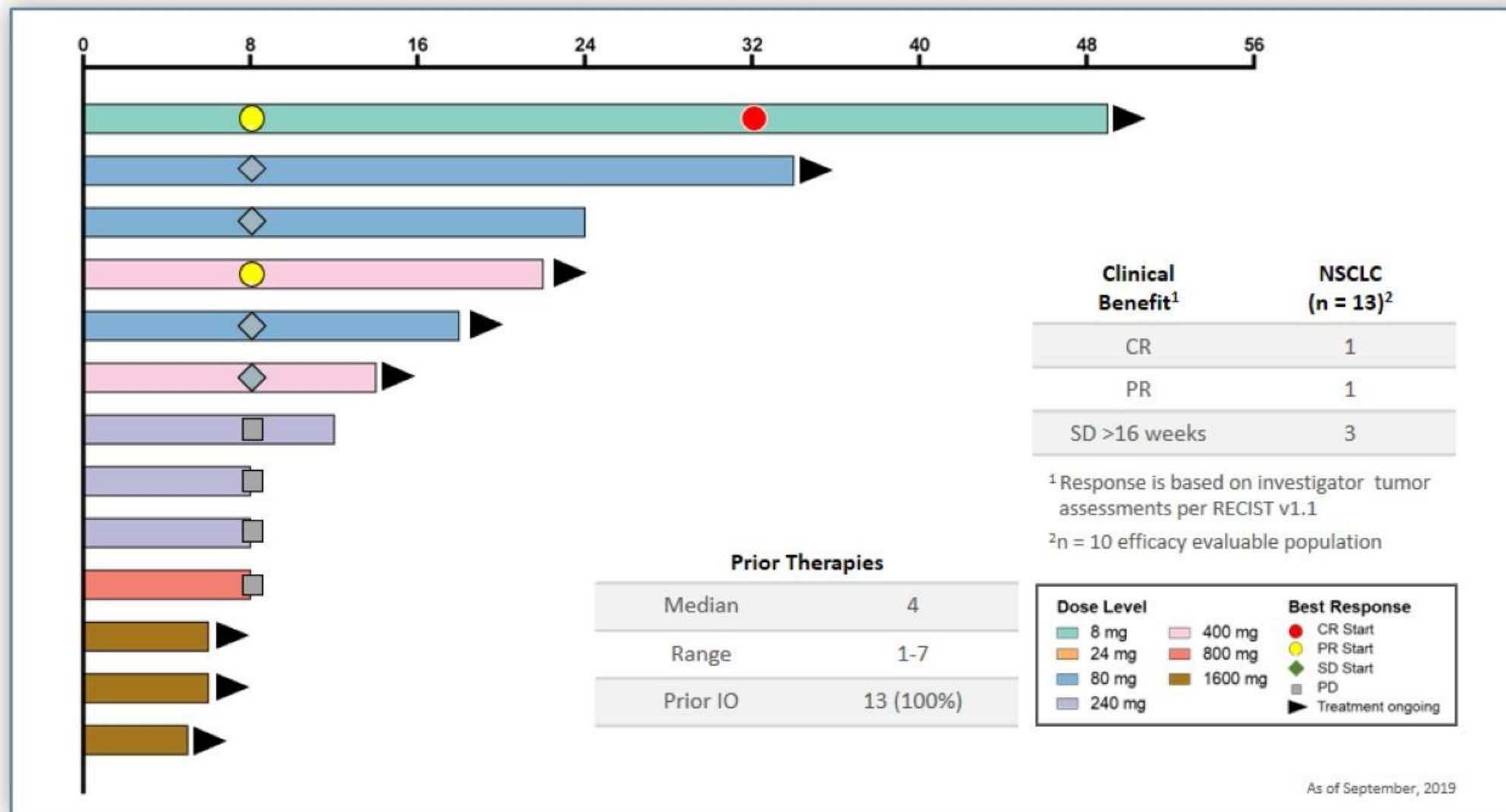
Most common AEs: infusion reactions, fatigue, headaches, pruritis, elevated amylase and elevated lipase

# Treatment Duration in Weeks for All Phase 1 Patients





# Durable Clinical Benefit for PD-1 Refractory NSCLC Patients

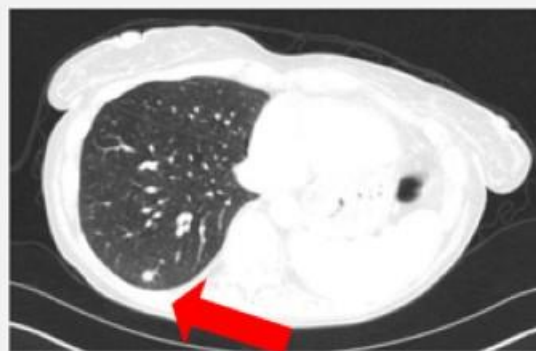


## NC318: Single-Agent Activity in PD-1 Refractory NSCLC

Confirmed

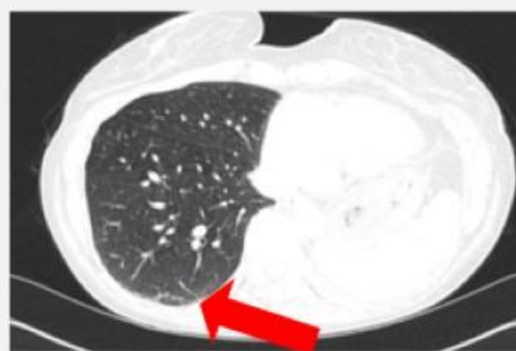
COMPLETE RESPONSE

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)



# 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)

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

# NC410

## Decoy Human Fusion Protein Targeting the TME



IND Filed  
Q1 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

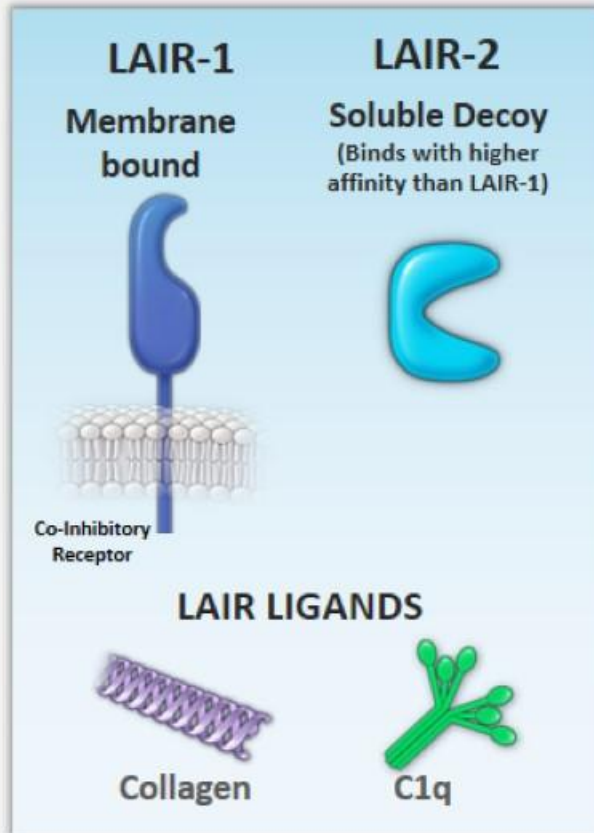
Advanced or  
metastatic solid  
tumors



# LAIR-1 & LAIR-2 Functional Relationship

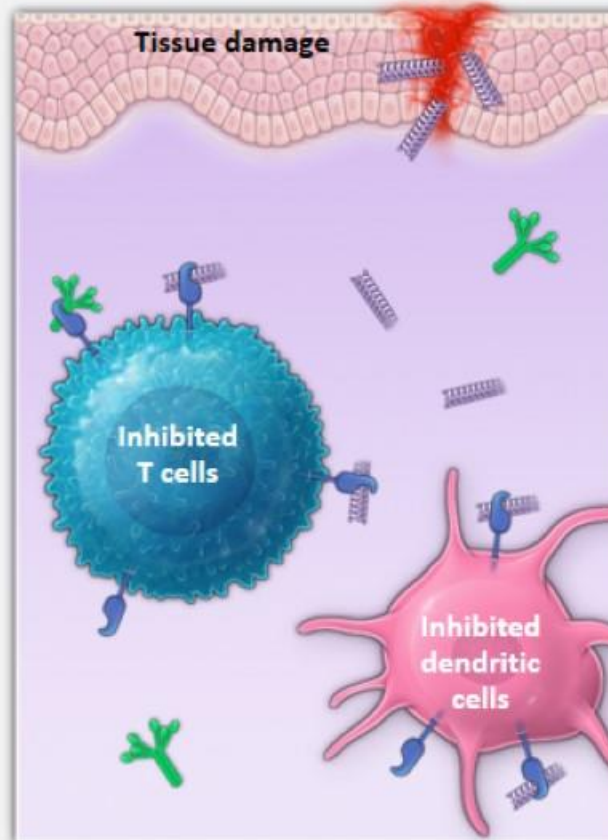
## LAIR & LIGANDS

LAIR-1 and LAIR-2 Bind  
Collagen and C1q



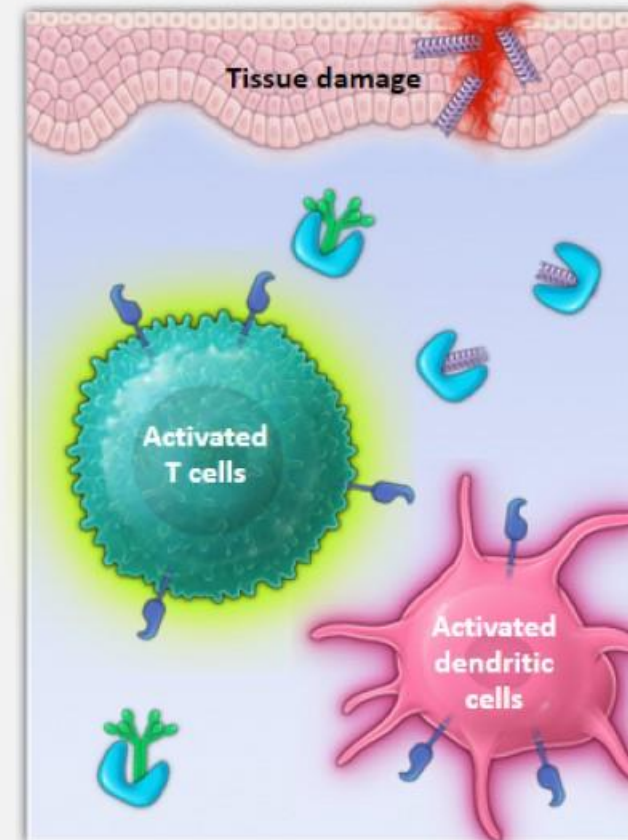
## LAIR-1

Ligands Expressed in Response to  
Inflammation & Inhibit Immune Function



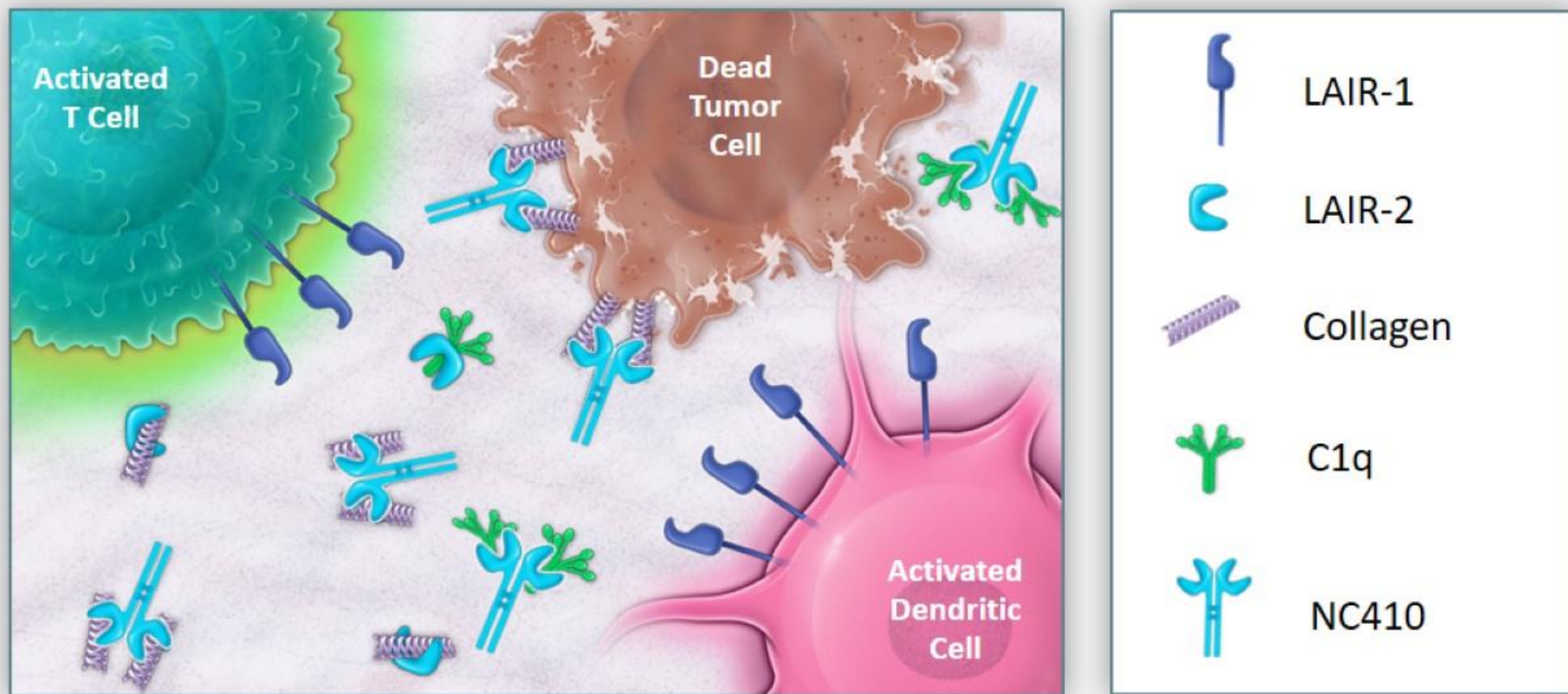
## LAIR-2

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

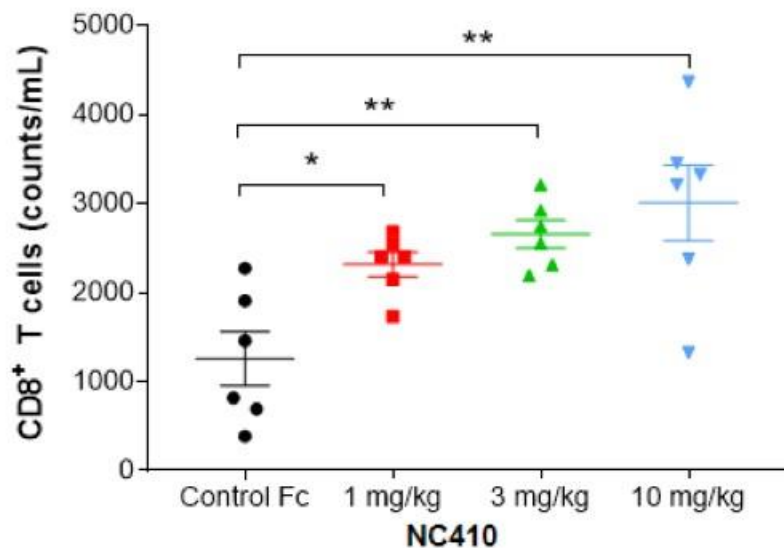




# NC410 Enhanced T Cell Expansion and Relieved Immunosuppression

Blocked

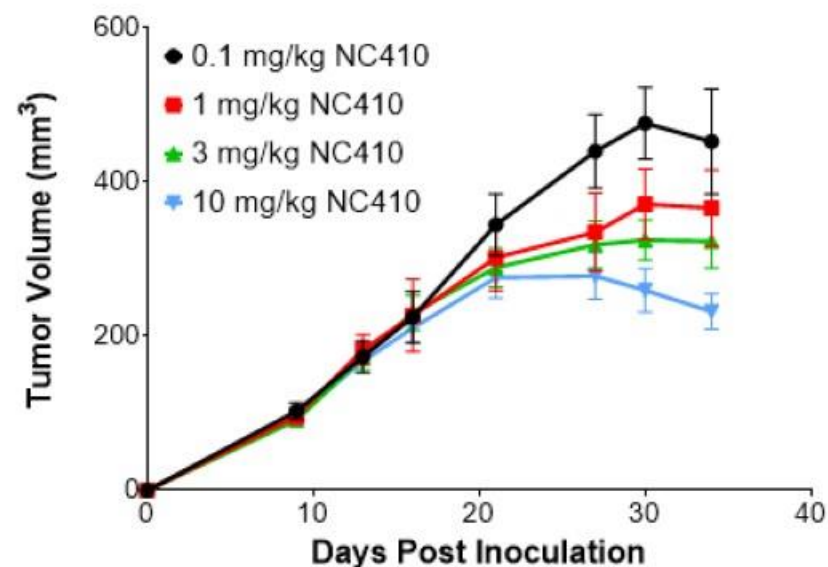
SUPPRESSION



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



IND-enabling tox studies complete



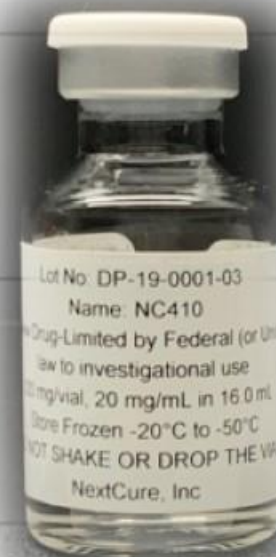
cGMP manufacturing complete



IND filed & received FDA clearance Q1 2020

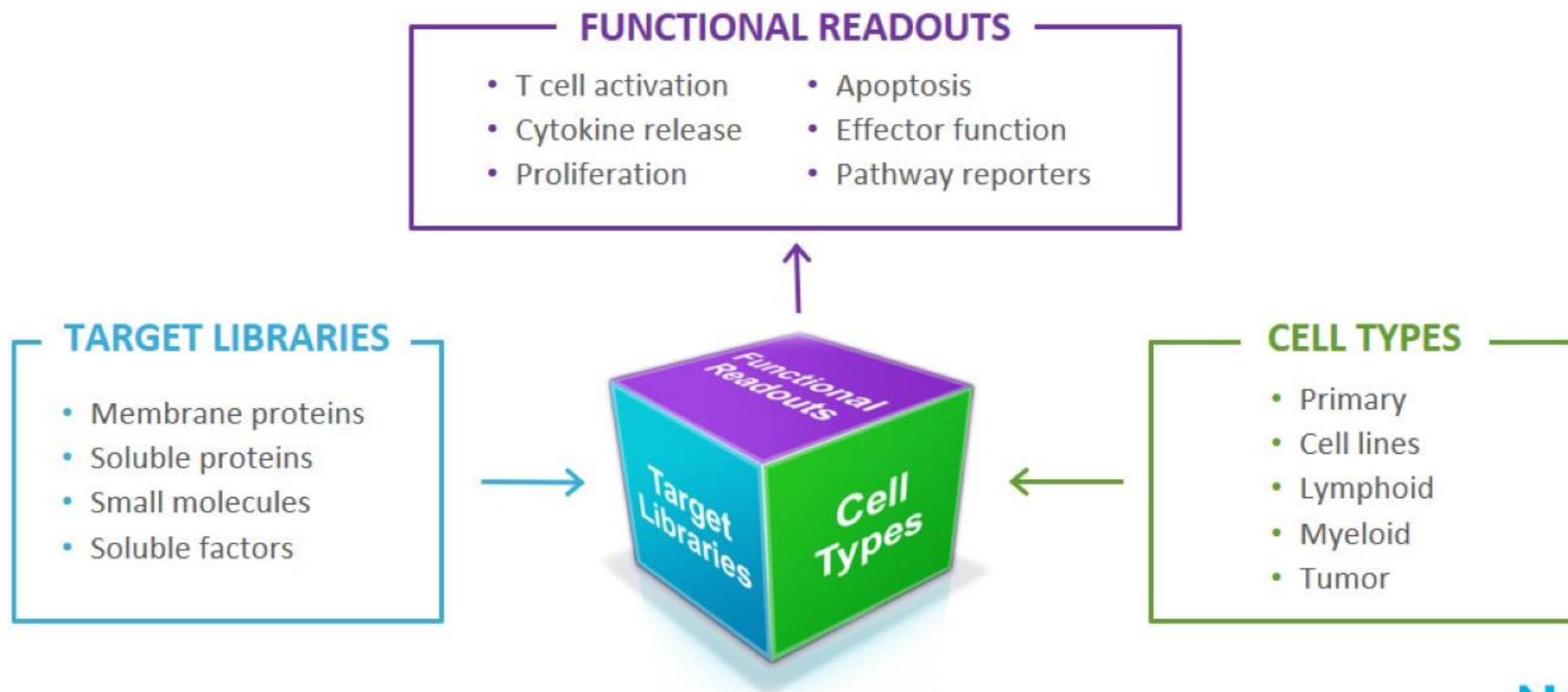


Initiate Phase 1 (temporarily delayed due to COVID-19)

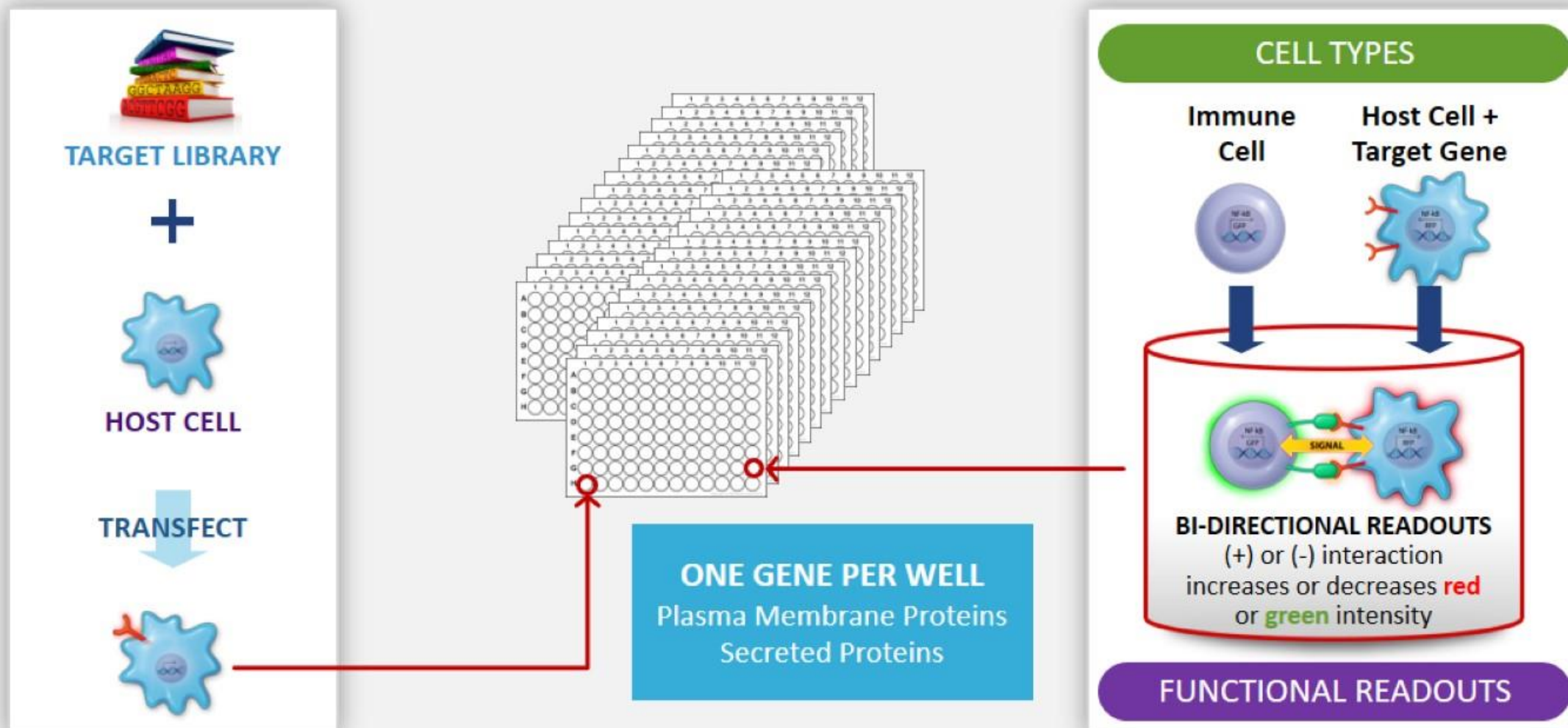


## Finding Solutions with a Powerful Discovery Engine

Functional, Integrated, NextCure Discovery in Immuno-Oncology

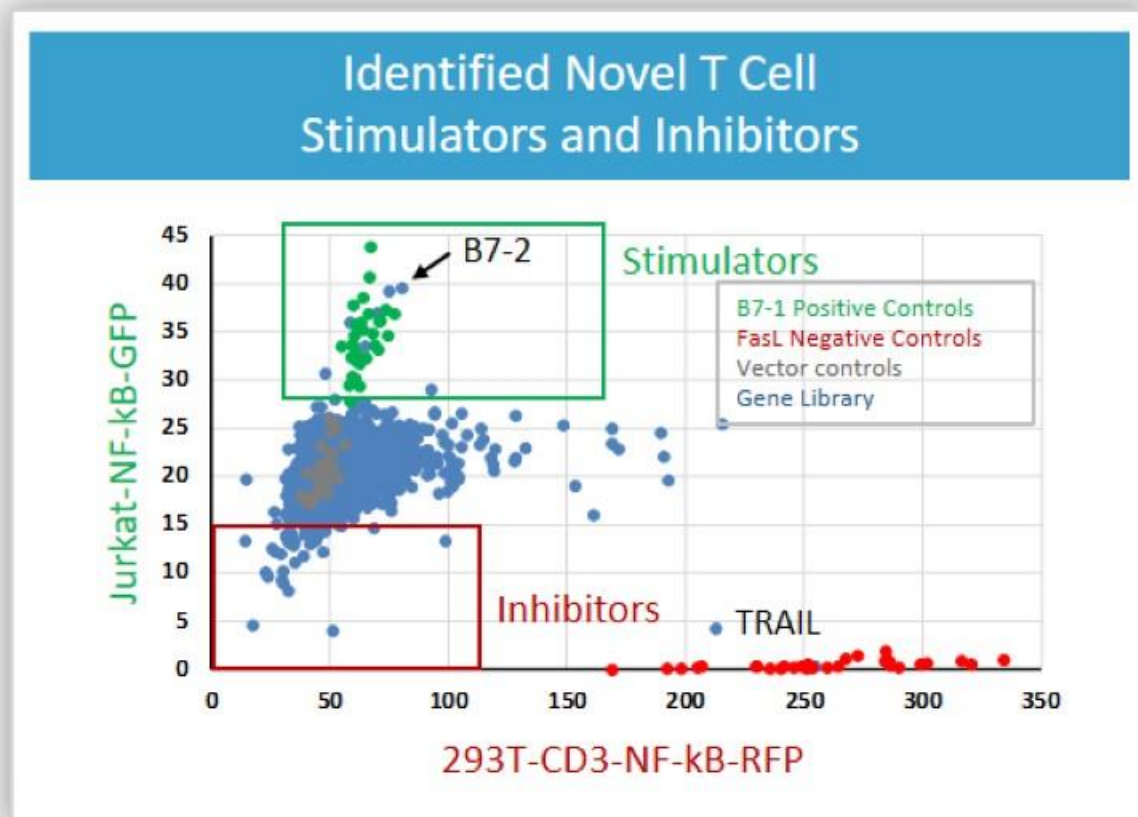


# FIND-IO Screening Methodology

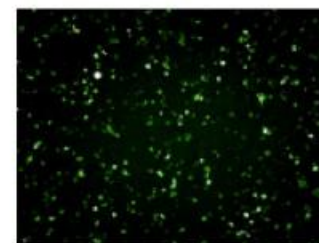




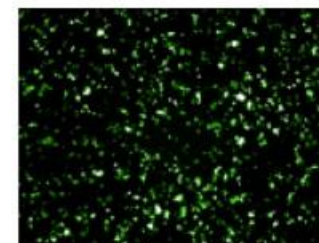
## Jurkat “T Cell Line” Screening and Validating FIND-IO Hits



Vector  
Control



Stimulatory  
B7-2



Inhibitory  
TRAIL



REPRODUCIBILITY

ROBUSTNESS

RELEVANCY

# 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