



# NEXT-GENERATION IMMUNOMEDICINES

OCTOBER 2019

## 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 timing or likelihood of regulatory filings for our product candidates; (iii) our manufacturing capabilities and strategy; (iv) the potential benefits and activity of our product candidates; (v) our expectations regarding the nature of the biological pathways we are studying; (vi) our expectations regarding our FIND-IO platform; and (vii) the potential benefits of our relationships with Dr. Lieping Chen, Yale University and Eli Lilly and Company.

Various factors 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, 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 August 12, 2019. 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 of Immuno-medicines

- NC318: Phase 1 data to be presented November 9<sup>th</sup> at SITC\* 2019
- NC410 (LAIR-1): IND expected Q1 2020
- Additional research and development programs
- Manufacturing: dedicated, state-of-the-art facility

## Platform for Novel Target Discovery

- FIND-IO functional screening discovery engine
- Oncology partnership with Lilly: \$40M upfront and equity
- Expanding into autoimmune diseases

## Proven Abilities

- Experienced Management team
- Scientific founder Dr. Lieping Chen: discovered PD-L1 & other key targets
- Strong balance sheet to deliver on objectives

\*Title “Single agent anti-tumor activity in PD-1 refractory NSCLC: phase 1 data from the first-in-human trial of NC318, a Siglec-15-targeted antibody”

# THE UNMET NEEDS OF CANCER PATIENTS ARE SIGNIFICANT

NON-RESPONDERS

RAPID PROGRESSION

LIMITED TREATMENTS



We Need New Solutions

# COMMITTED TO DISCOVERING & DEVELOPING NOVEL, FIRST-IN-CLASS IMMUNOMEDICINES TO IMPROVE LIVES

**NEW**

therapeutic options

**POSITIVE**

clinical responses

**IMPROVED**

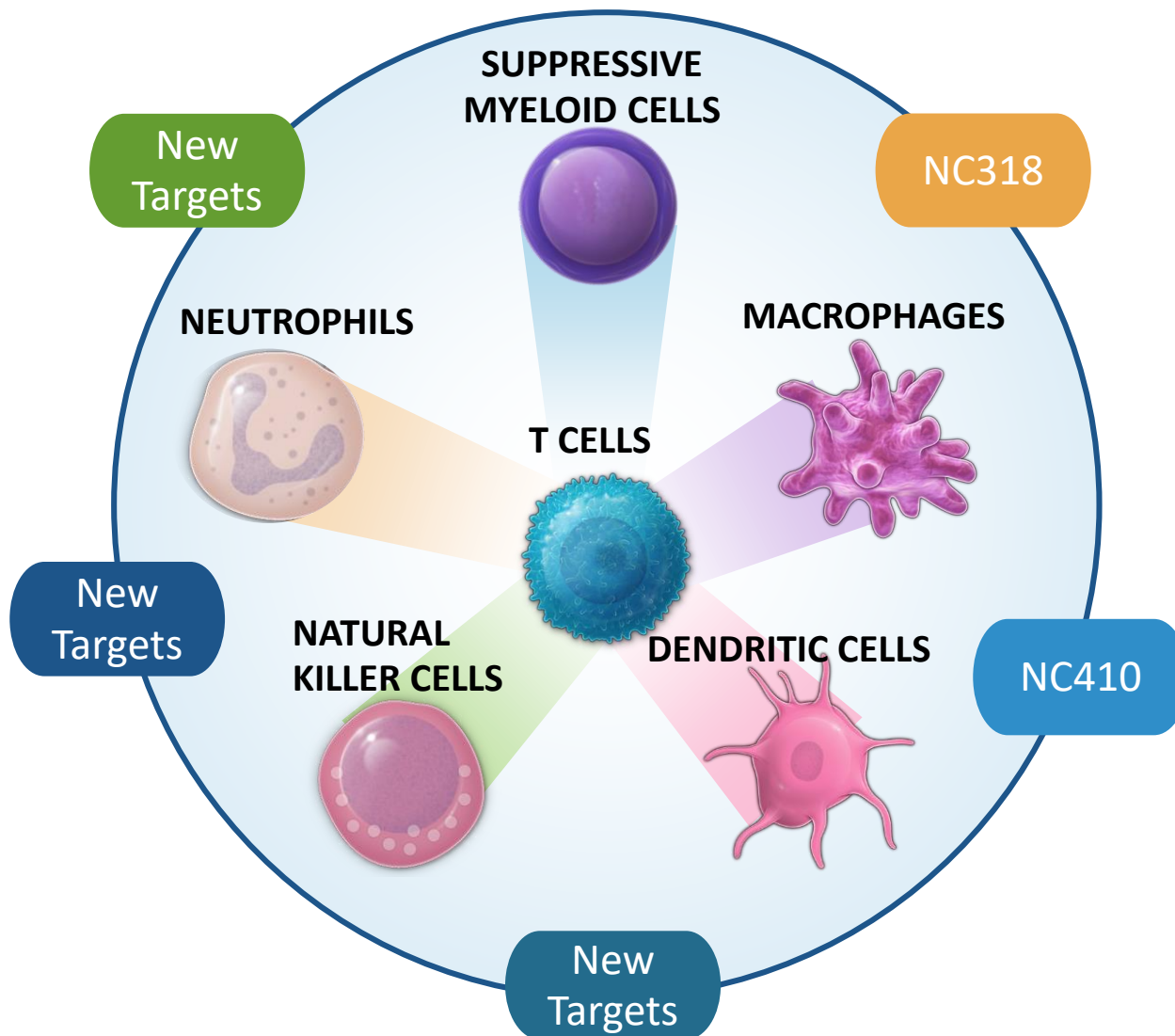
quality of life



Focused on Cancer Patients Not Adequately Addressed Today

**NextCure**

# EXPANDING TARGETS BEYOND T CELLS



# EXPERIENCED TEAM WITH STRONG TRACK RECORD

## HISTORY AND SUCCESS OF WORKING TOGETHER

Michael Richman CEO				
Timothy Mayer, PhD COO				
Steve Cobourn, CPA CFO				
Kevin N Heller, MD CMO				
Sol Langermann, PhD CSO				
Jim Bingham, PhD CDO				
Linda Liu, PhD SVP, Research				
Sebastien Maloveste, PhD VP, Business Development				
Dallas Flies, PhD VP, Discovery Research				

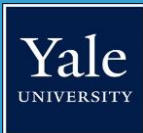
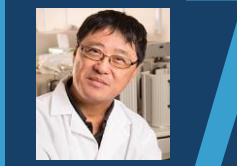


# WORLD-RENOWNED SCIENTIFIC FOUNDER AND KEY COLLABORATION

## YALE COLLABORATION

### LIEPING CHEN, MD, PhD

Discovered multiple  
key immune pathways,  
including PD-L1



### WORLD-RENOWNED INSTITUTION

Sponsored research, clinical  
samples, cell lines & models

### TEAM OF COLLABORATORS

Roy Herbst, MD, PhD  
David Rimm, MD, PhD  
Mario Sznol, MD

## NATURE MEDICINE PUBLICATION

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

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



# NEXTCURE HAS DELIVERED ROBUST PRODUCT PIPELINE IN *LESS THAN 3 YEARS*

PROGRAMS	CELLS	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT MILESTONE	WORLDWIDE RIGHTS
PRODUCT CANDIDATES								
NC318 (S15)	Tumors and macrophages	ONCOLOGY					Phase 1 complete in Q4 2019	NextCure
NC410 (LAIR-1)	Dendritic & T cells	ONCOLOGY					IND filing in Q1 2020	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	<div>Lilly</div> NextCure

# NC318

HUMANIZED  
MONOCLONAL  
ANTIBODY



## Phase 1/2 Clinical Trial

### TARGET

Siglec-15 (“S15”)

### CELL TYPES

Tumors &  
macrophages

### MOA

Designed to block  
S15-induced  
immunosuppression

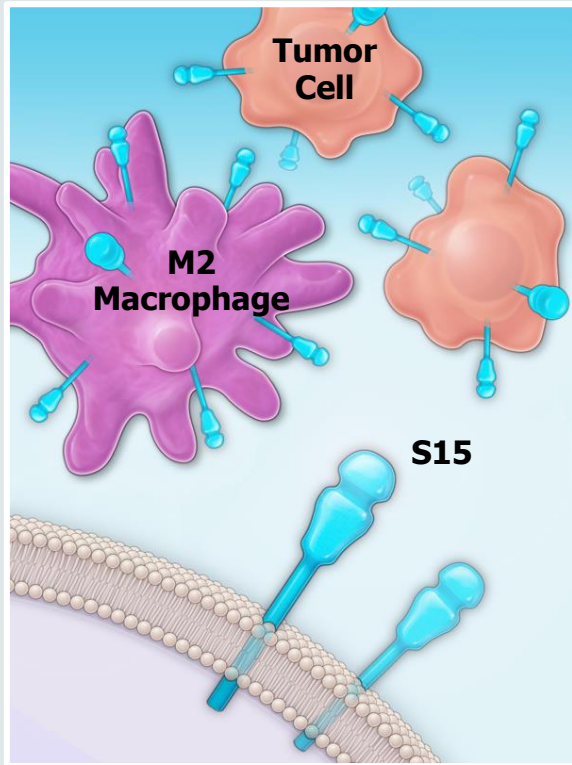
### INDICATIONS

Advanced or  
metastatic solid  
tumors, which could  
include ovarian,  
NSCLC, and head &  
neck cancers

# S15 AS A TARGET

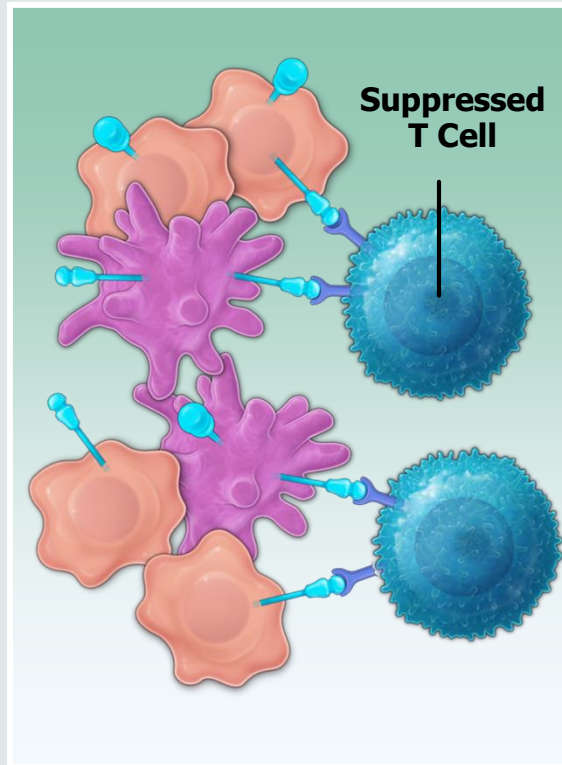
## EXPRESSION

Tumors &  
Macrophages



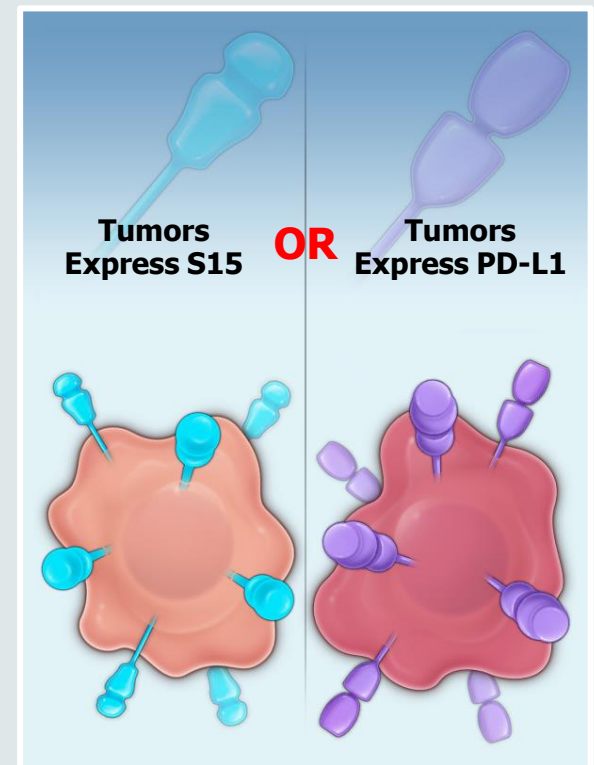
## FUNCTION

Potently Suppresses  
T Cell Function

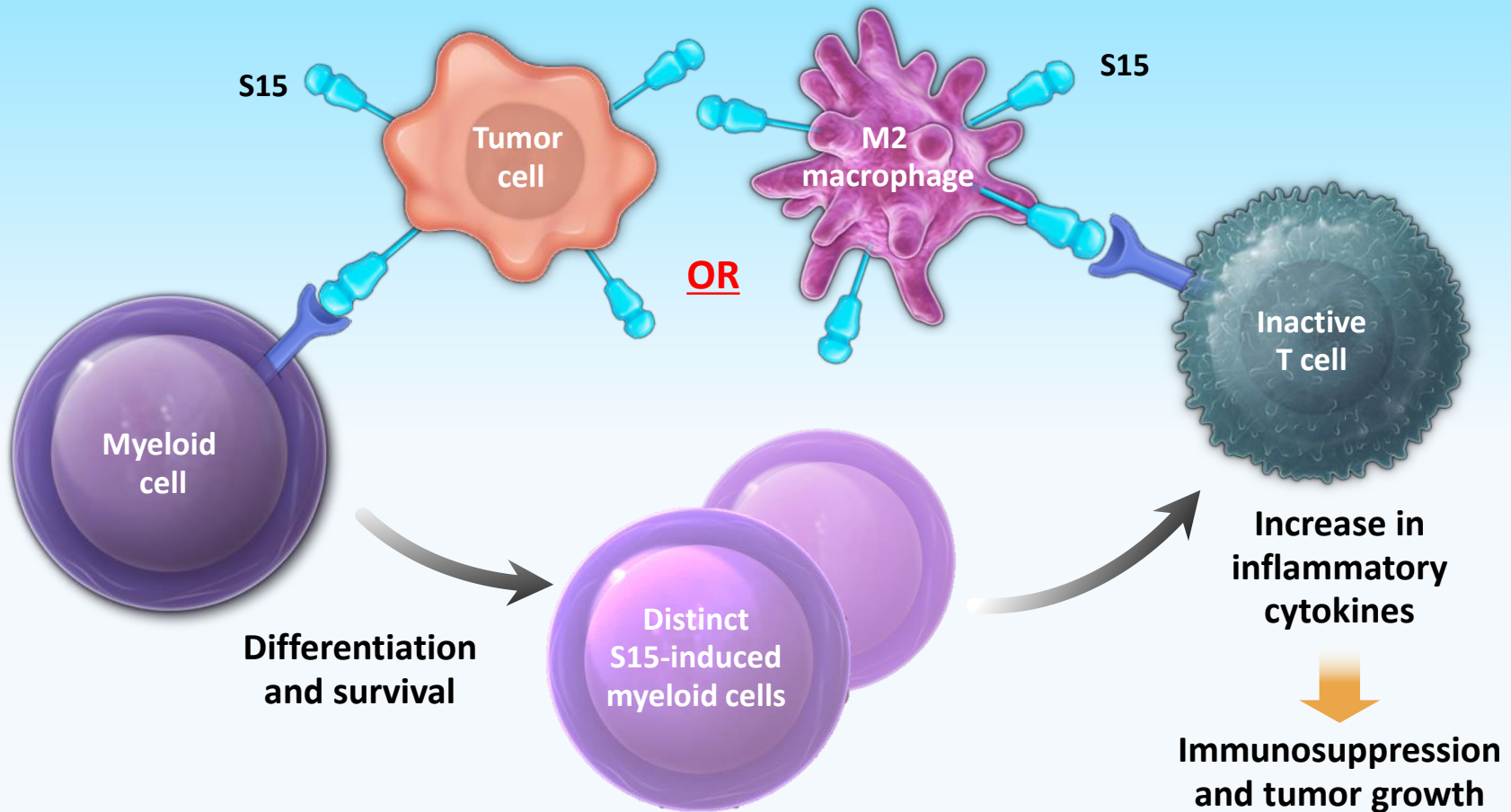


## NON-RESPONDERS

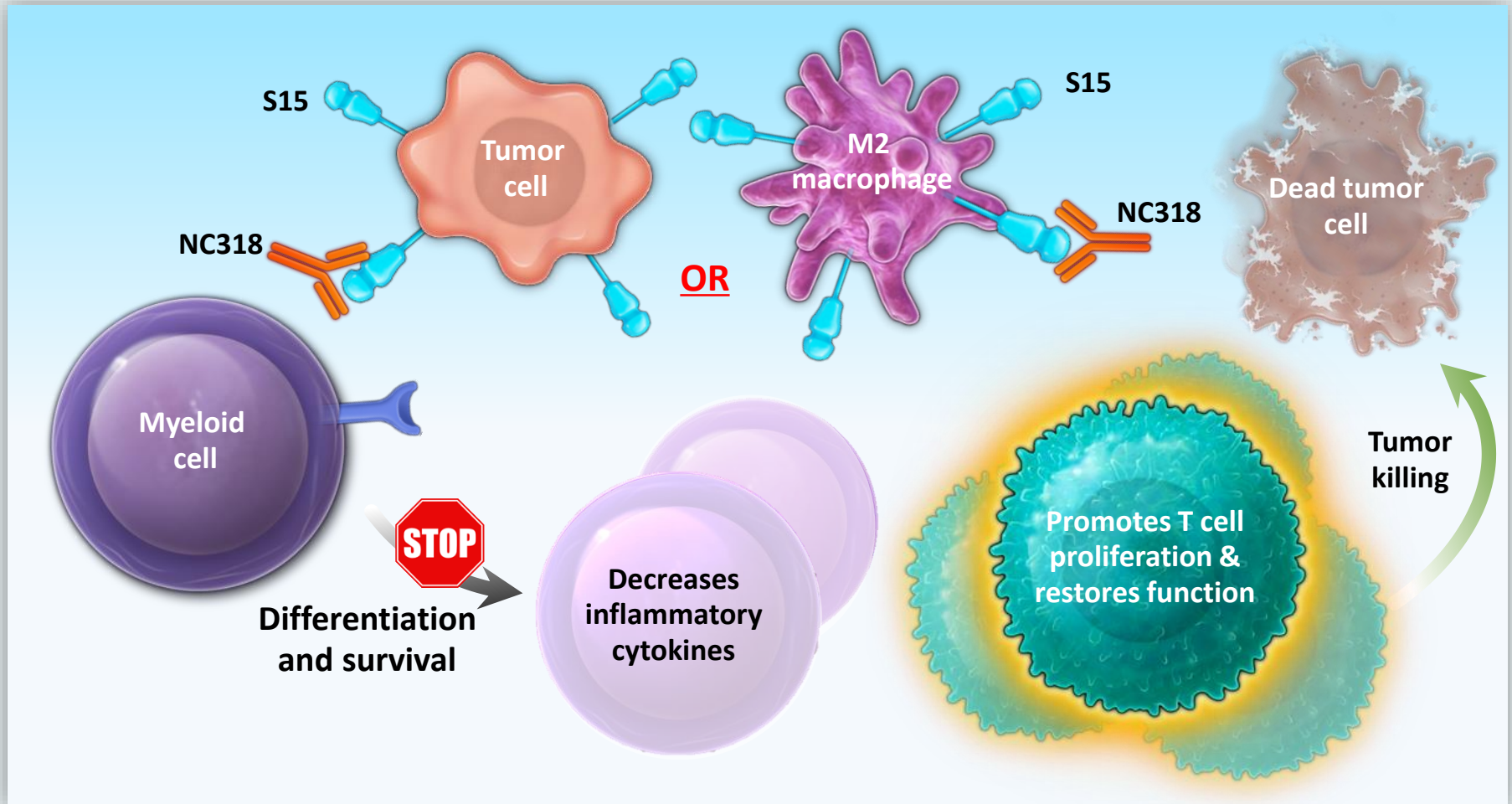
Generally Non-Overlapping  
with PD-L1 Expression



# S15 IS HIGHLY IMMUNOSUPPRESSIVE IN THE TME OF MULTIPLE TUMOR TYPES



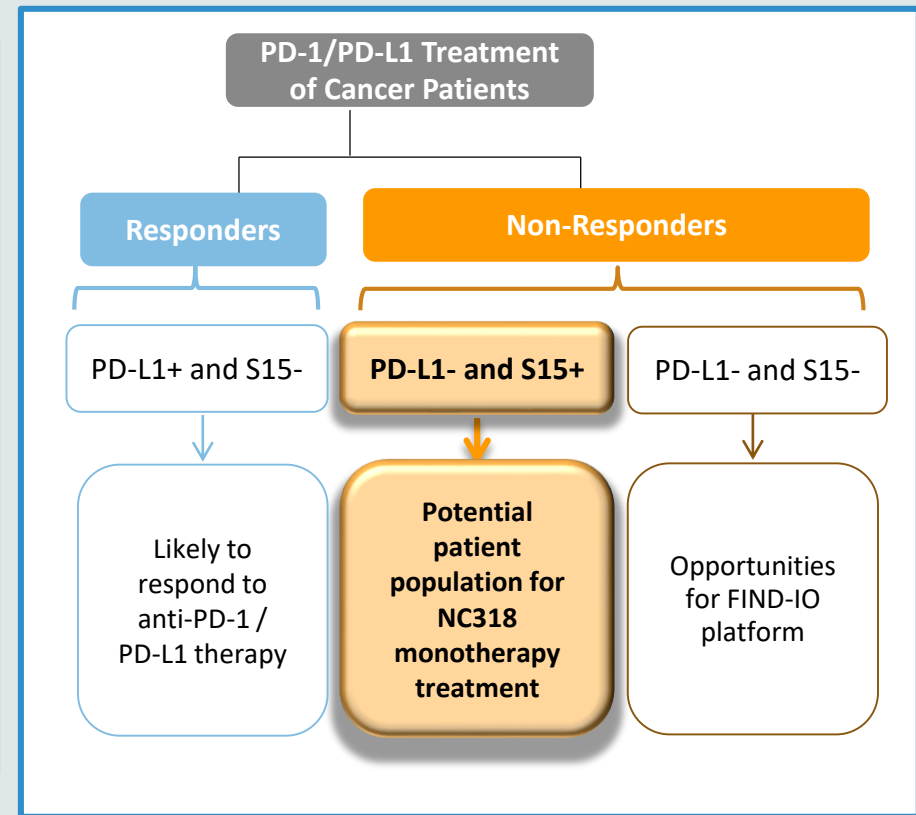
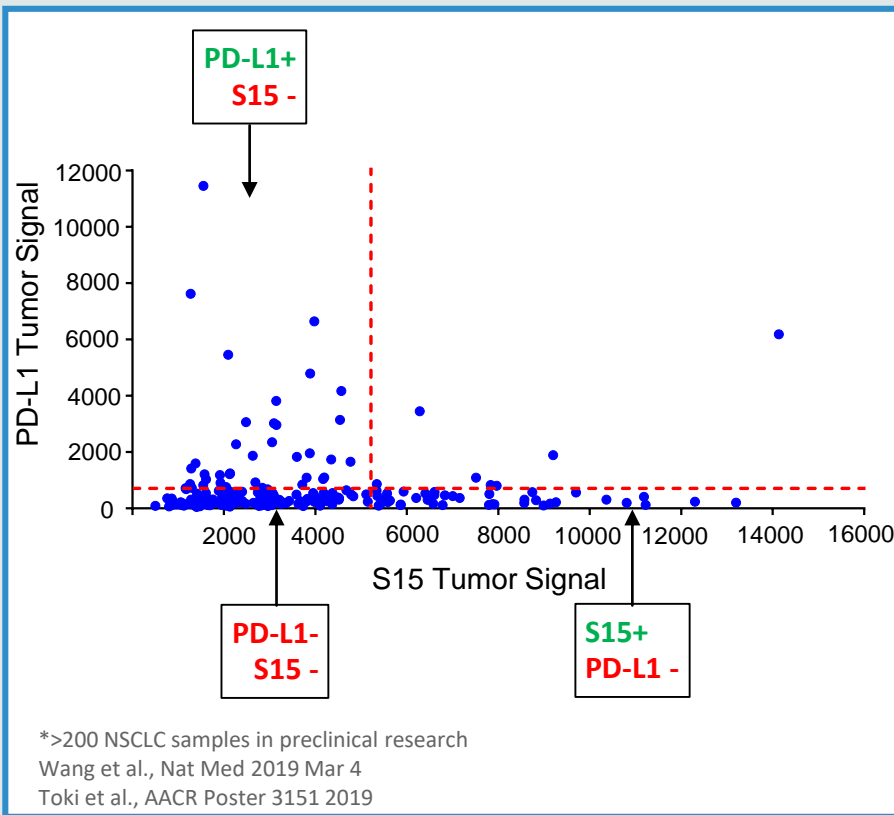
# NC318 IS DESIGNED TO BLOCK IMMUNOSUPPRESSIVE ACTIVITY INDUCED BY S15



# NC318: A POTENTIAL TREATMENT OPTION FOR PD-1/PD-L1 NON-RESPONDERS

S15 AND PD-L1 EXPRESSION GENERALLY DO NOT OVERLAP IN NSCLC TUMORS\*

POTENTIAL NEW TREATMENT OPTIONS FOR PD-1/PD-L1 NON-RESPONDERS

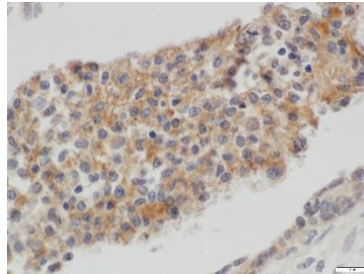




# S15 IS CLINICALLY AND FUNCTIONALLY RELEVANT

## Clinical Relevance

### S15 IN TUMORS



- Increased expression on tumor cells and immunosuppressive macrophages in multiple cancer types
- Minimal expression in normal tissues

## Functional Relevance

### S15 KNOCK-OUT MODEL



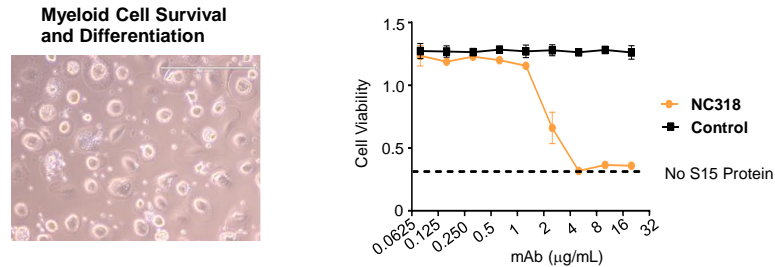
- S15-deficient mice showed
  - Enhanced antigen-specific T cell responses *in vivo*
  - Delayed tumor progression
  - Increase in survival



# NC318 RESTORED IMMUNE FUNCTION *IN VITRO*

## INHIBITED

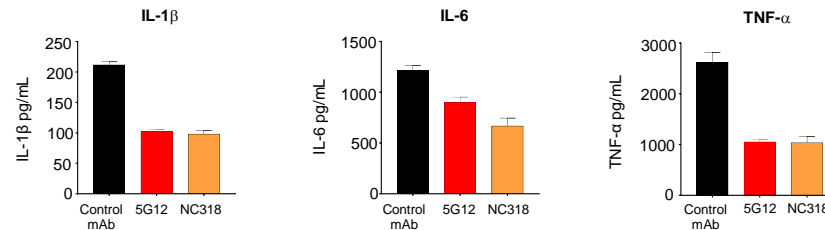
Myeloid Cell  
Differentiation  
and Survival



Blocked survival of  
myeloid cells

## DECREASED

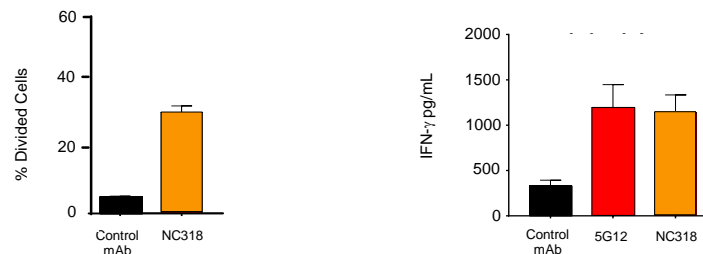
Pro-Inflammatory and  
Pro-Tumorigenic  
Cytokines



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

## PROMOTED

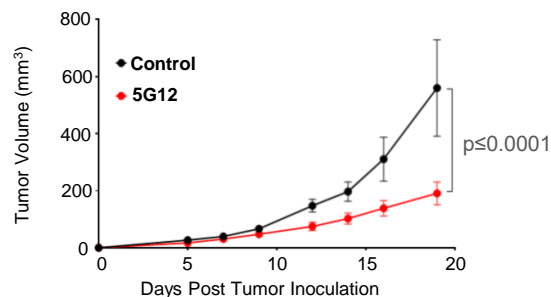
Tumor-Specific  
T Cell Function



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

# NC318\* HAS SHOWN MONOTHERAPY ACTIVITY IN A NUMBER OF ANIMAL MODELS

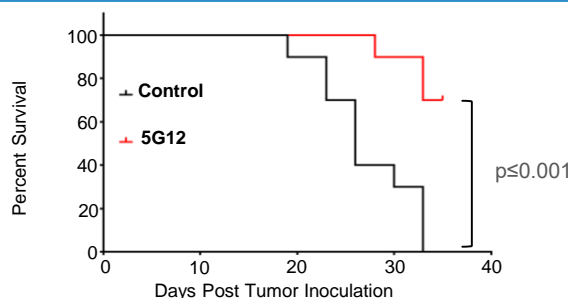
**REDUCED**  
Tumor Growth



CT26 tumor model

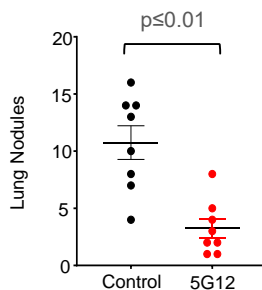
First 2 doses at 20 mg/kg followed by 10 mg/kg, Q4D, 7 doses

**INCREASED**  
Survival



CT26 tumor model

**DELAYED**  
Lung Metastasis



MC38 tumor model

30 mg/kg, Q7D, 4 doses

\*Murine surrogate is 5G12

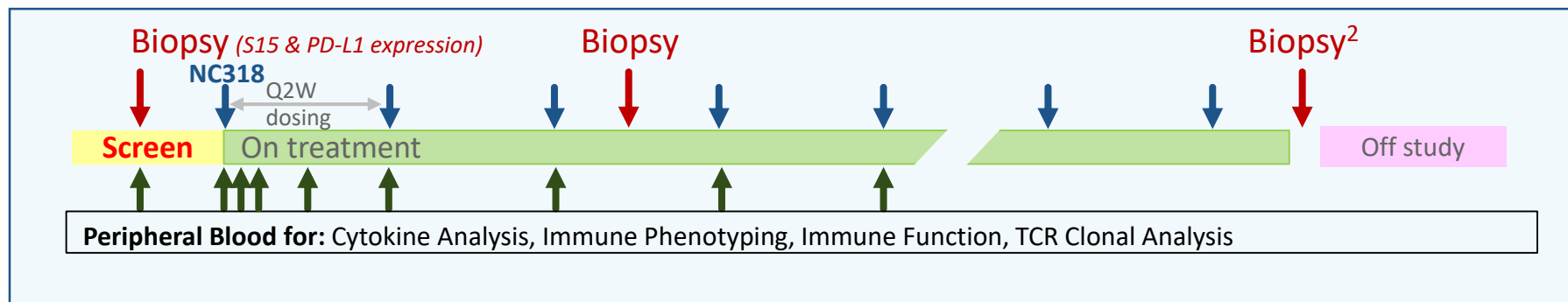
# NC318 MONOTHERAPY TRIAL UNDERWAY DESIGNED FOR RAPID PROOF-OF-CONCEPT

## PHASE 1

- Opened in 4Q 2018; Complete in 4Q 2019
- Dose-escalation<sup>1</sup>
- Safety, tolerability, and biomarker readouts
- Advanced or metastatic solid tumors

## PHASE 2

- Open in 1Q 2020; Complete in 4Q 2020
- Efficacy assessment
- Tumor types shown to have elevated S15 expression, including NSCLC, ovarian, and head & neck



(1) Dose escalation evaluates 6 dose cohorts (8 mg – 800 mg or approximately 0.1 - 10 mg/kg) administered every 2 weeks

(2) In Phase 2 portion of trial

# NC318 PHASE 1 TRIAL STATUS AS OF MARCH 31, 2019

## ENROLLMENT

- 21 subjects dosed
- 4<sup>th</sup> dose cohort open
- 10 different tumor types
- Recruitment on schedule

## SAFETY

- No dose limiting toxicities or drug-related SAEs
- 1 transient elevation of amylase (grade 3) and lipase (grade 4) that was deemed probably related to NC318<sup>(1)</sup>
- Possibly NC318-related AEs limited to transient asymptomatic lab findings or grade 1 events

## RESPONSES

- Evaluations every 8 weeks
- 1 confirmed partial response
- 6 stable disease
- 6 progressive disease
- 8 subjects not yet evaluated

• Angeles Clinic

• MSKCC

• Next Oncology

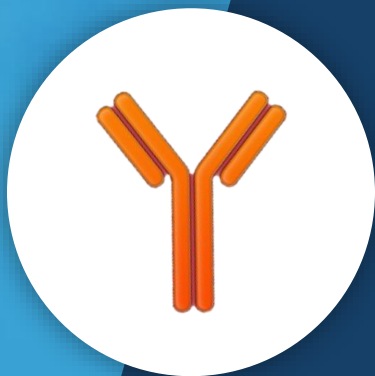
• NYU

• Yale University

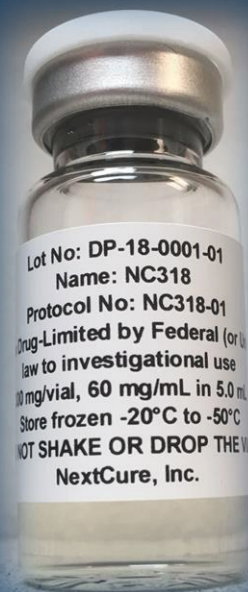
(1) The patient was asymptomatic and both elevations resolved without any interventions within 72 hours

# NC318

DESIGNED TO RESTORE  
IMMUNE FUNCTION IN A  
HIGHLY SUPPRESSIVE TUMOR  
MICROENVIRONMENT



- ☒ MOA / Preclinical studies complete
  - Relieved S15-mediated inhibition of T cells
  - Increased IFN- $\gamma$  production
  - Decreased inflammatory cytokines
- ☒ First-in-Human trial initiated in October 2018
- ☐ Complete Phase 1 and report data at SITC 2019
- ☐ Complete Phase 2 in Q4 2020



# NC410

## DECOY HUMAN FUSION PROTEIN TARGETING THE TME



### IND Filing Expected Q1 2020

#### TARGET

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

#### CELL TYPES

Dendritic cells  
and T cells

#### MOA

Promotes T cell  
function and  
dendritic cell activity

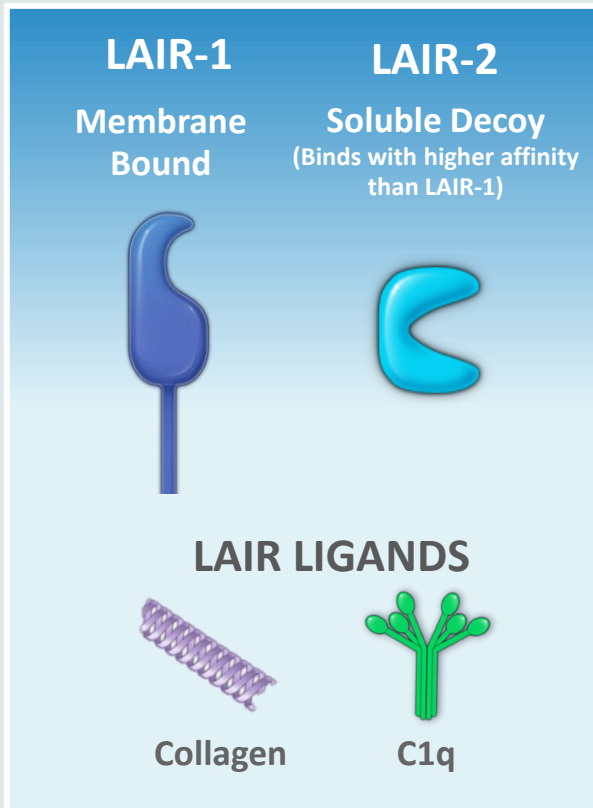
#### INDICATIONS

Advanced or  
metastatic solid  
tumors

# LAIR-1 & LAIR-2 FUNCTIONAL RELATIONSHIP

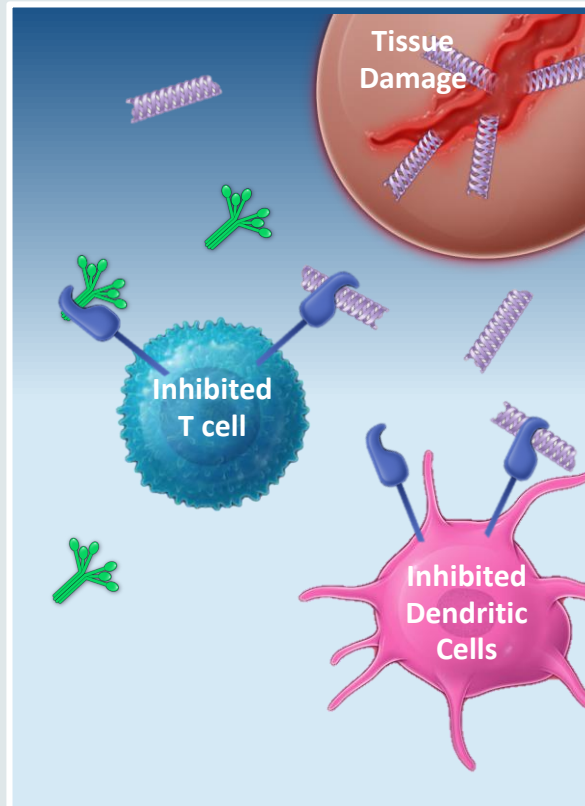
## LAIR & LIGANDS

LAIR-1 and LAIR-2 bind collagen and C1q



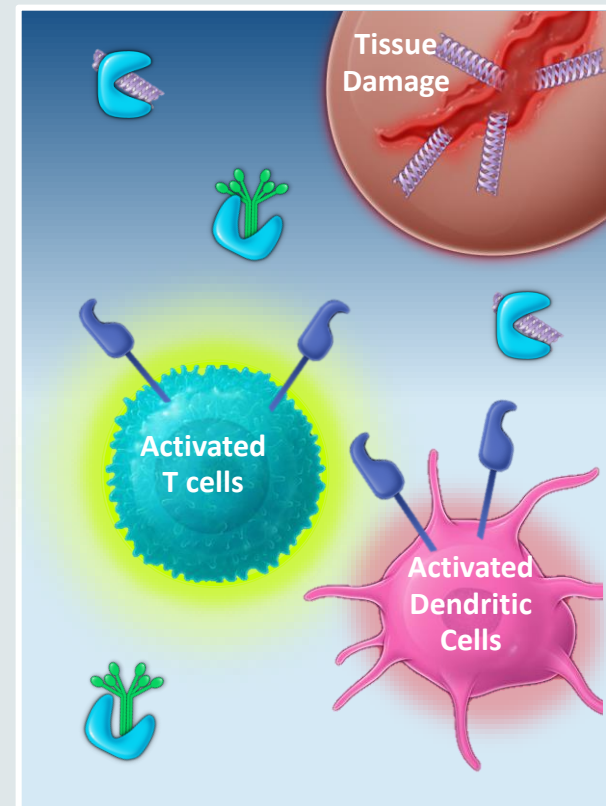
## LAIR-1

Ligands are expressed in response to inflammation & inhibit immune function



## LAIR-2

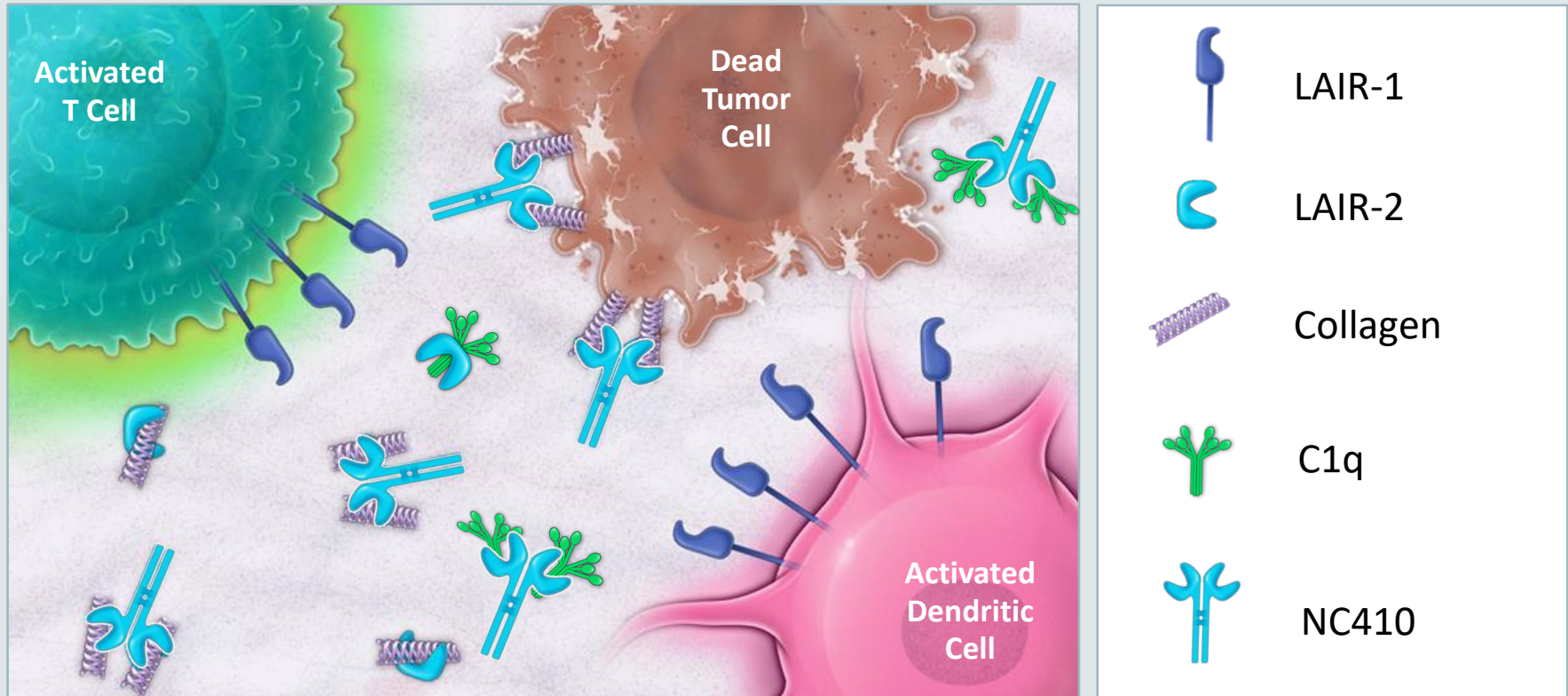
LAIR-2 modulates LAIR-1 mediated inhibition





# NC410 IS DESIGNED TO PREVENT IMMUNE SUPPRESSION CAUSED BY LAIR-1

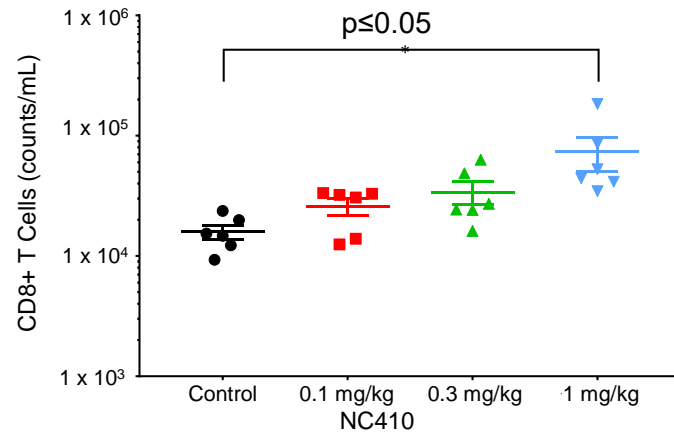
NC410 is a Fusion Protein of LAIR-2 and a Decoy for LAIR-1



NC410 Promotes T Cell Function and Dendritic Cell Activation

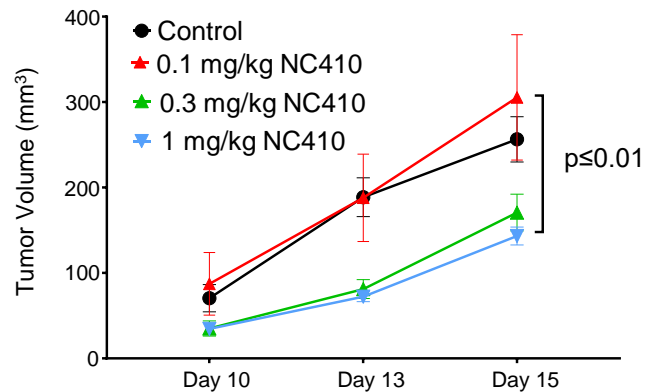
# NC410 ENHANCED T CELL EXPANSION AND RELIEVED IMMUNOSUPPRESSION

**BLOCKED**  
Suppression



Human CD8+ T cell  
expansion *in vivo*

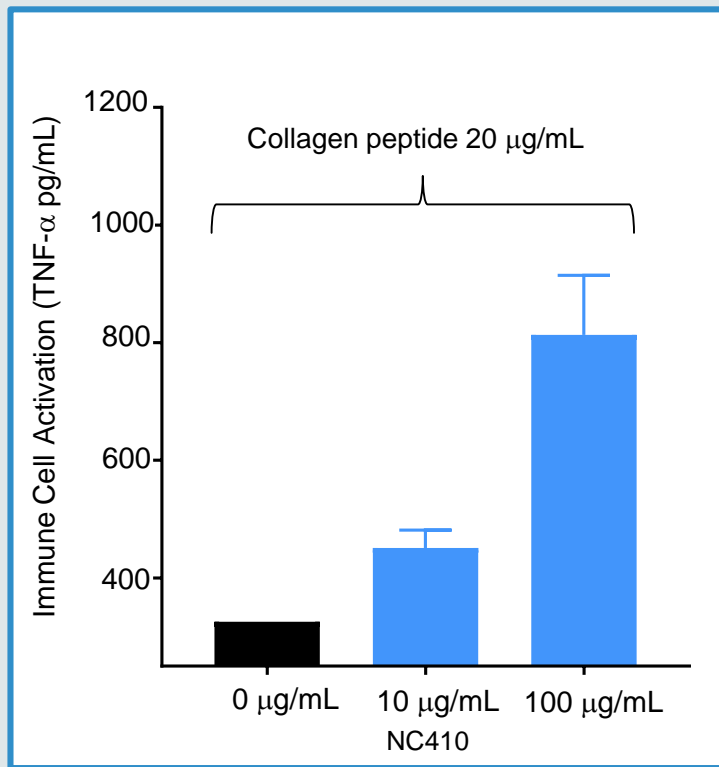
**DECREASED**  
Tumor Volume



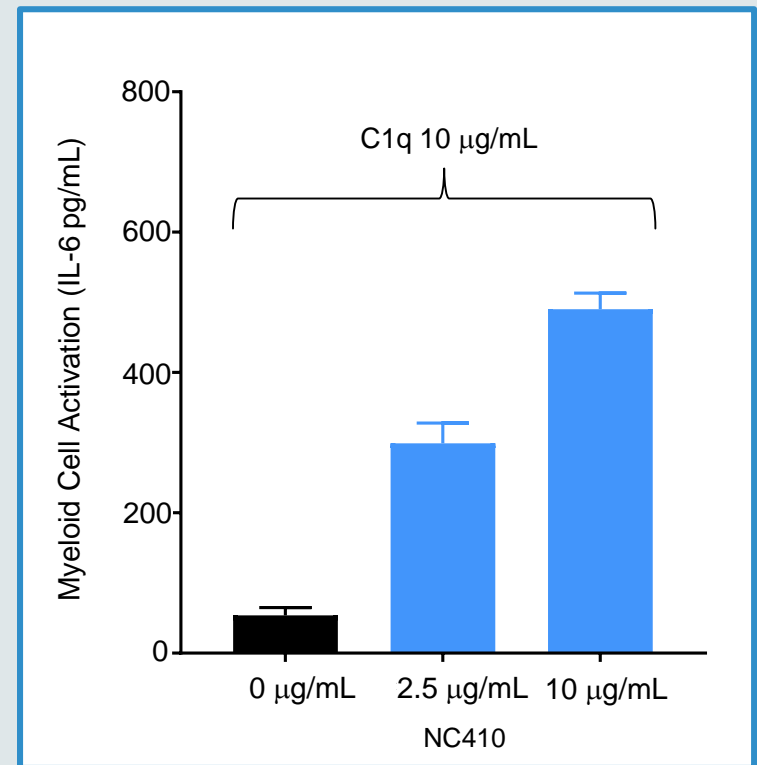
Human PBMCs in mice:  
CD8+ T cell activity  
decreased tumor volume

# NC410 PROMOTED IMMUNE CELL ACTIVATION IN THE PRESENCE OF COLLAGEN AND C1Q

## REVERSED COLLAGEN SUPPRESSION OF HUMAN PBMCS



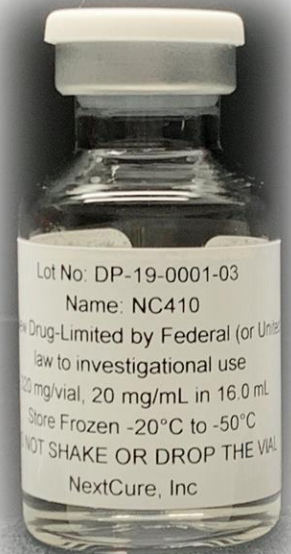
## REVERSED C1Q SUPPRESSION OF HUMAN MYELOID CELLS



# NC410 SUMMARY

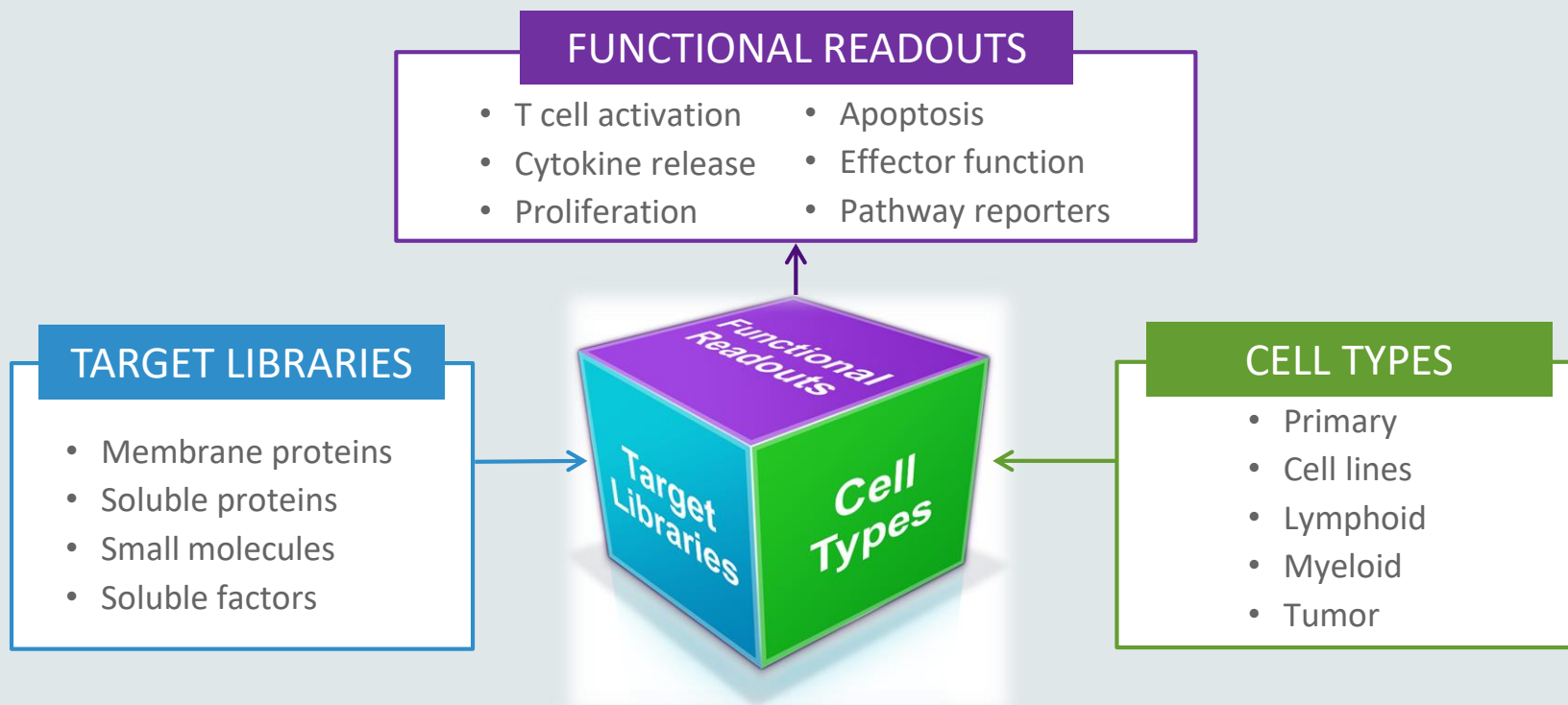


- ☒ Based on normal immune regulatory mechanism
- ☒ Promoted T cell function and dendritic cell activity in preclinical studies
- ☒ Designed to alleviate tumor-mediated immunosuppression
- ☒ IND-enabling tox studies complete
- ☒ cGMP manufacturing
- ☐ IND filing expected Q1 2020

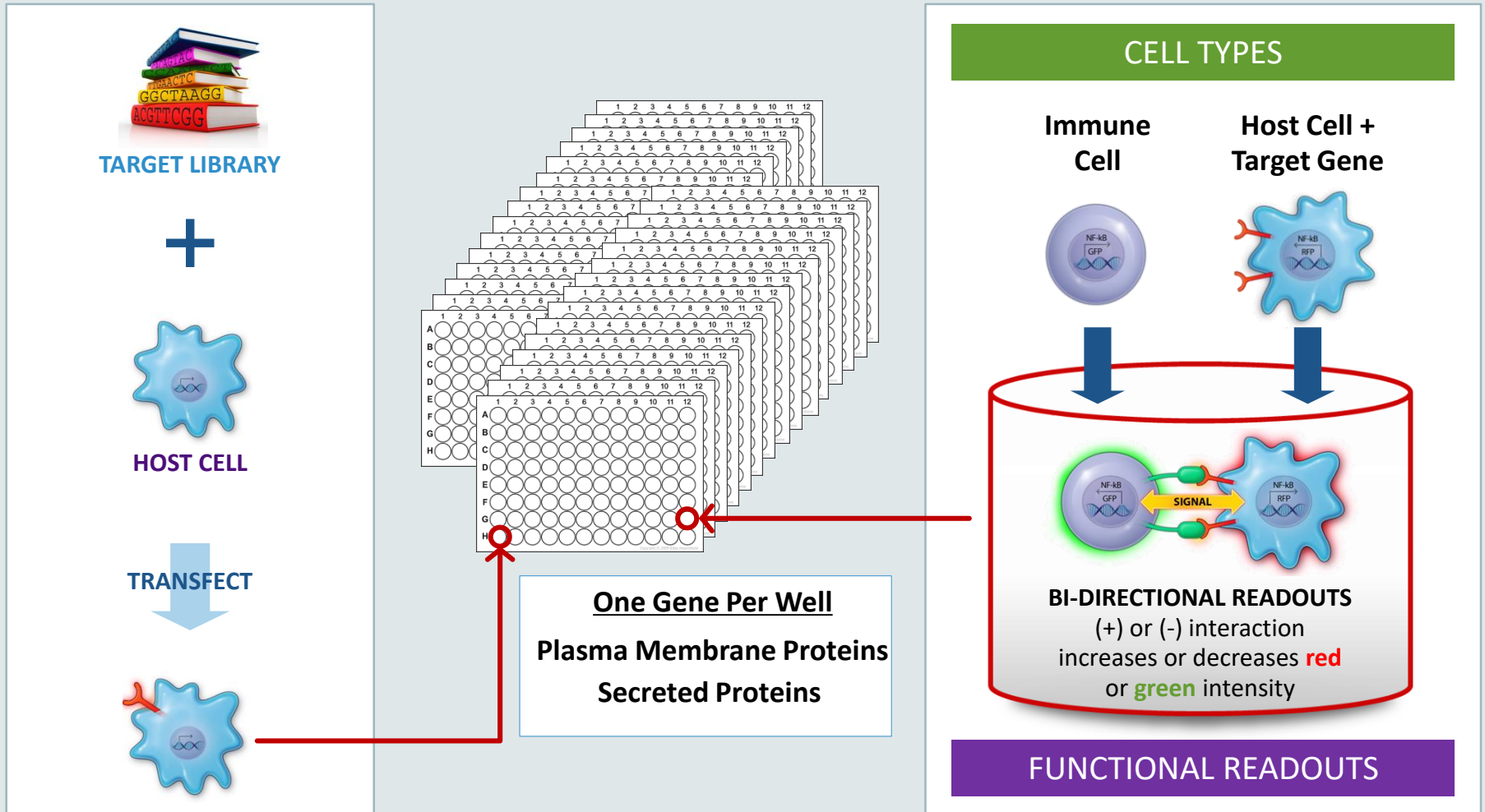


# FINDING SOLUTIONS WITH A POWERFUL DISCOVERY ENGINE

## Functional, Integrated, NextCure Discovery in Immuno-Oncology

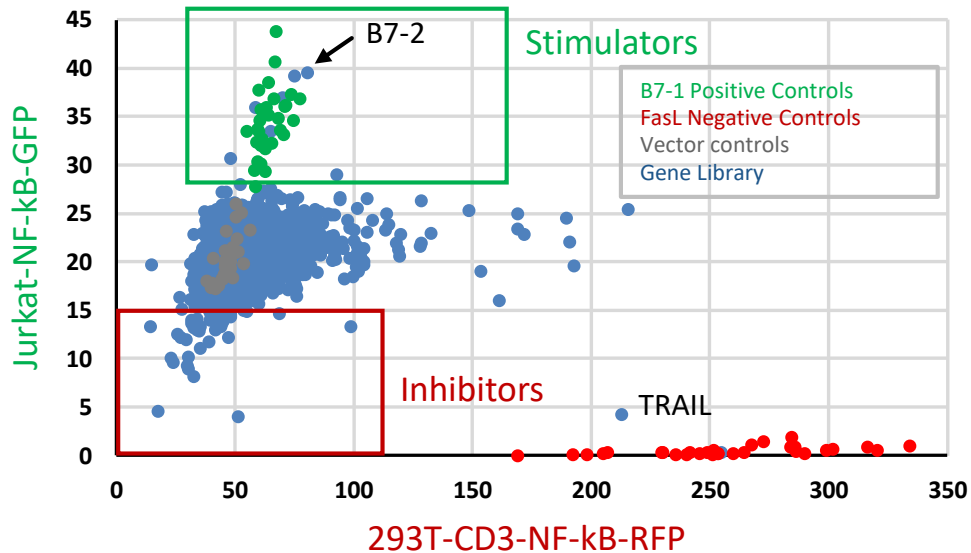


# FIND-IO SCREENING METHODOLOGY

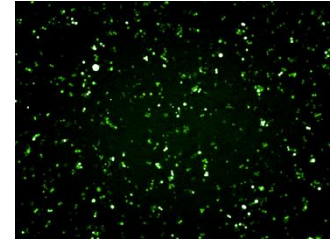


# JURKAT “T CELL LINE” SCREENING AND VALIDATING FIND-IO HITS

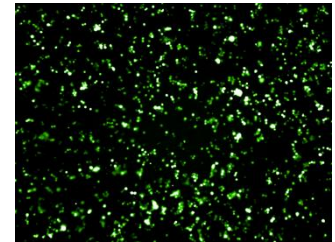
## Identified Novel T Cell Stimulators and Inhibitors



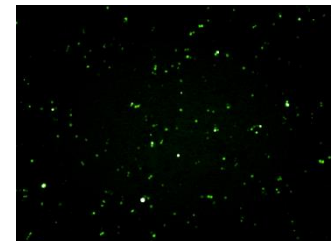
Vector Control



Stimulatory B7-2



Inhibitory TRAIL



REPRODUCIBILITY

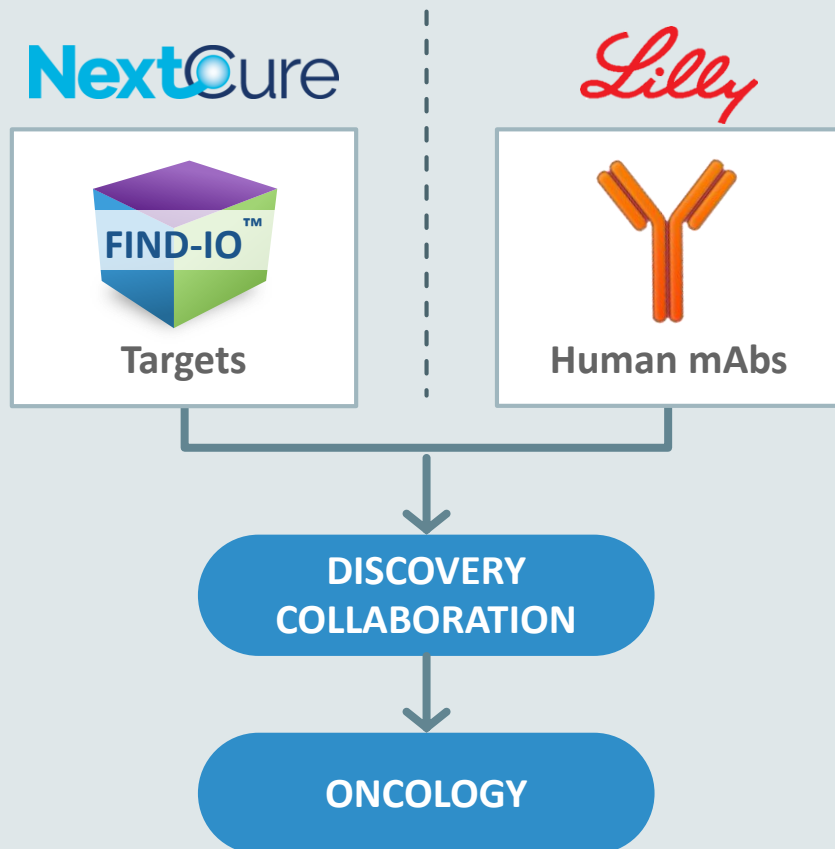
ROBUSTNESS

RELEVANCY



# LILLY – NEXTCURE PARTNERSHIP TO VALIDATE PLATFORM AND APPROACH

## Synergies



## Overview

### Structure

- Each party has options to exclusively license certain antibodies

### Terms

- Upfront: \$25M
- Equity investment: \$15M
- R&D support
- Option payments
- Development & sales milestones
- Royalties

# DIVERSIFICATION BEYOND ONCOLOGY

TODAY



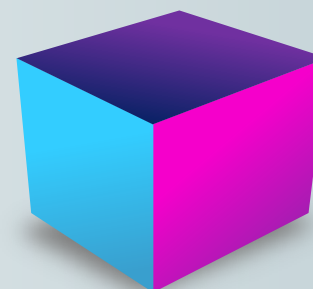
Oncology

TOMORROW



Autoimmunity

FUTURE



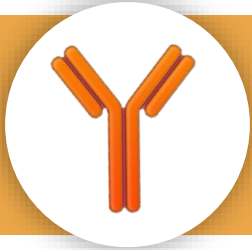
Neuro-Inflammation

Gene Libraries

Immune Cells

Functional Screening

# ANTICIPATED NEAR-TERM MILESTONES



**NC318**

- Complete Phase 1 and report data at SITC 2019
- Complete Phase 2 in Q4 2020



**NC410**

- Complete IND-enabling tox studies
- File IND in Q1 2020



**DISCOVERY**

- Identify novel targets and initiate validation



Committed to Addressing the Unmet Needs of Cancer Patients  
With New Solutions

**FOCUSED**  
Approach

**PROVEN**  
Momentum

**INNOVATIVE**  
Platform

**EXPERIENCED**  
Team

**FUTURE**  
Deliverables