

JANUARY 2021



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 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 5, 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): Phase 1
- 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

NextCure

Unmet Medical Needs of Cancer Patients

NEW Therapeutic Options

POSITIVE Clinical Responses

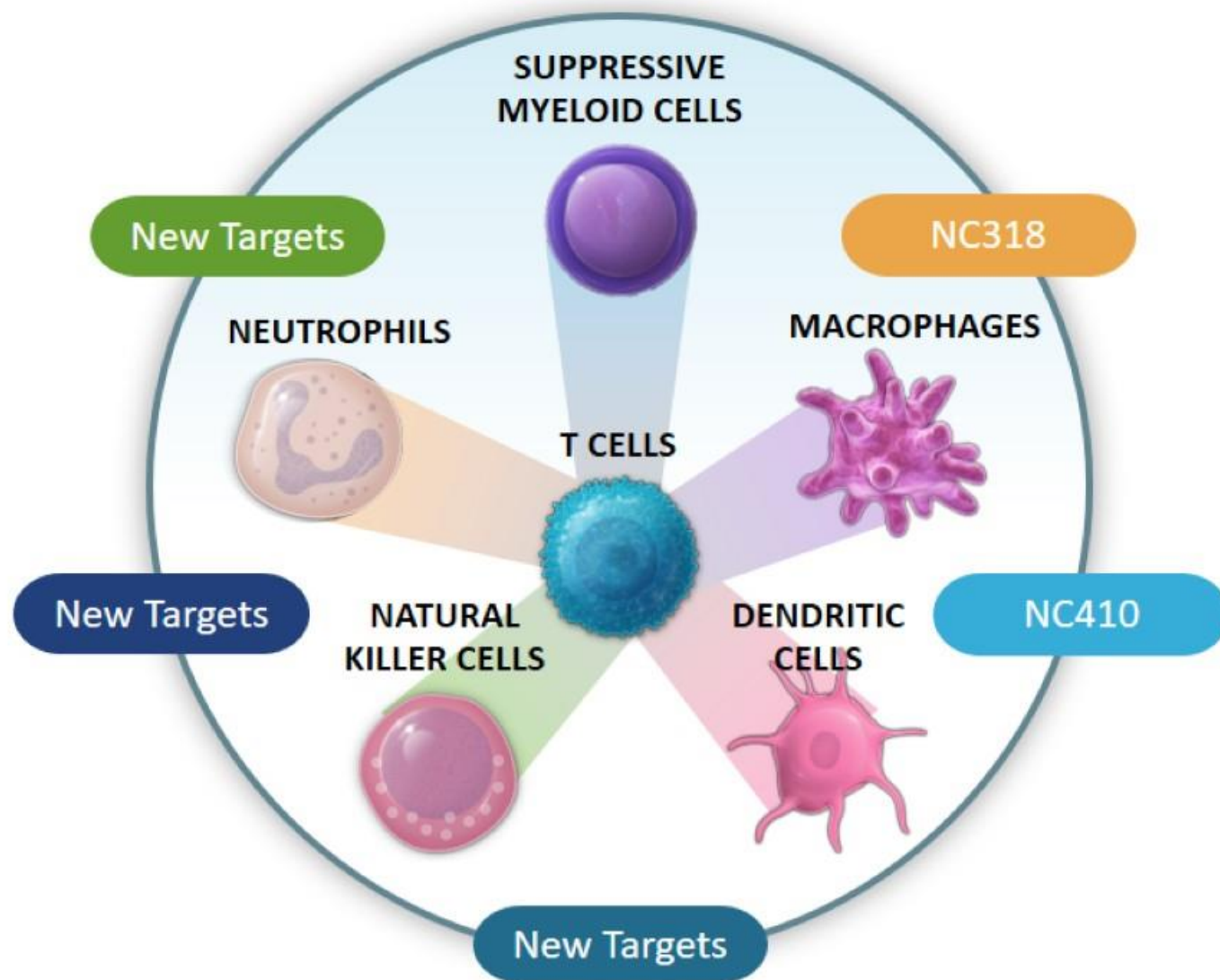
IMPROVED Quality of Life



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	NEXT MILESTONE	WORLDWIDE RIGHTS
PRODUCT CANDIDATES								
NC318 (S15) Monotherapy	Tumors and macrophages	ONCOLOGY					Report next steps in early 2021	NextCure
NC318 (S15) Anti-PD-1 Combo	Tumors and macrophages	ONCOLOGY					Initiate Phase 1 TBD	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

NC318

Humanized Monoclonal Antibody



Phase 1/2
CLINICAL
TRIAL

TARGET

Siglec-15
("S15")

CELL TYPES

Tumors &
macrophages

MOA

Blocks S15-induced
immunosuppression

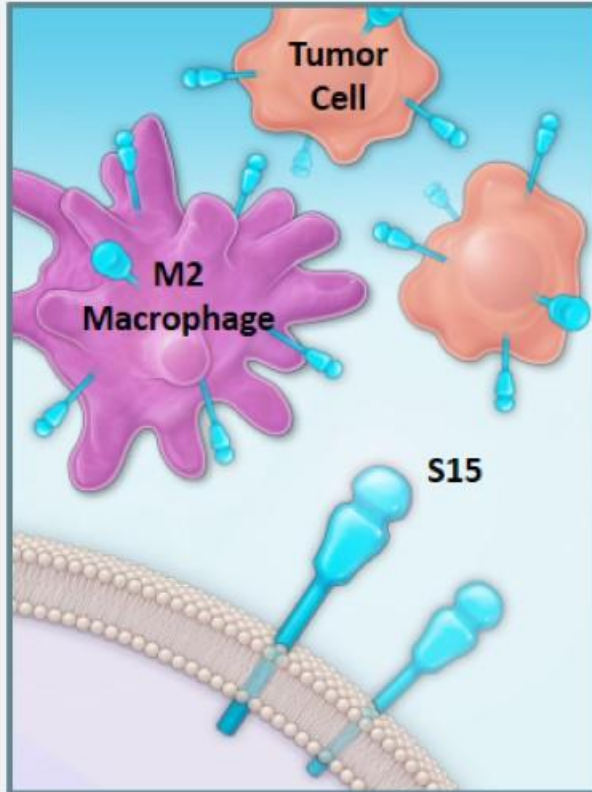
INDICATIONS

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

S15 as a Target

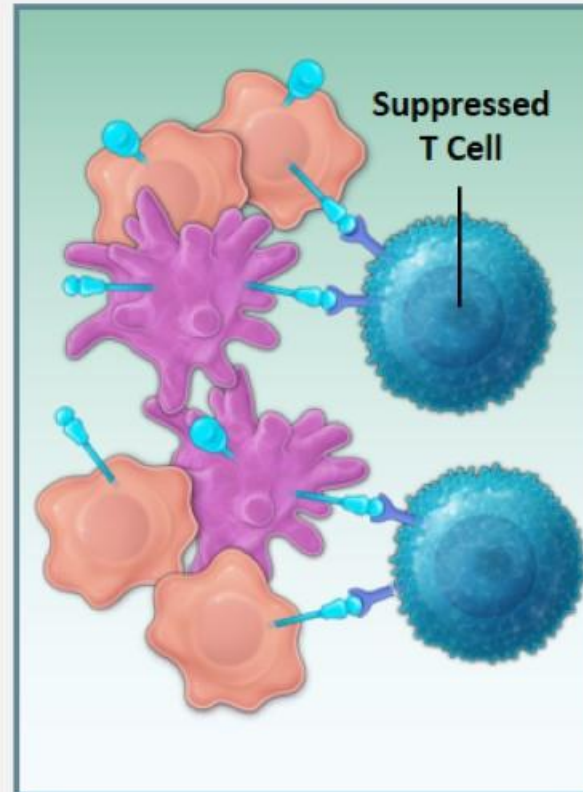
EXPRESSION

Tumors and
Macrophages



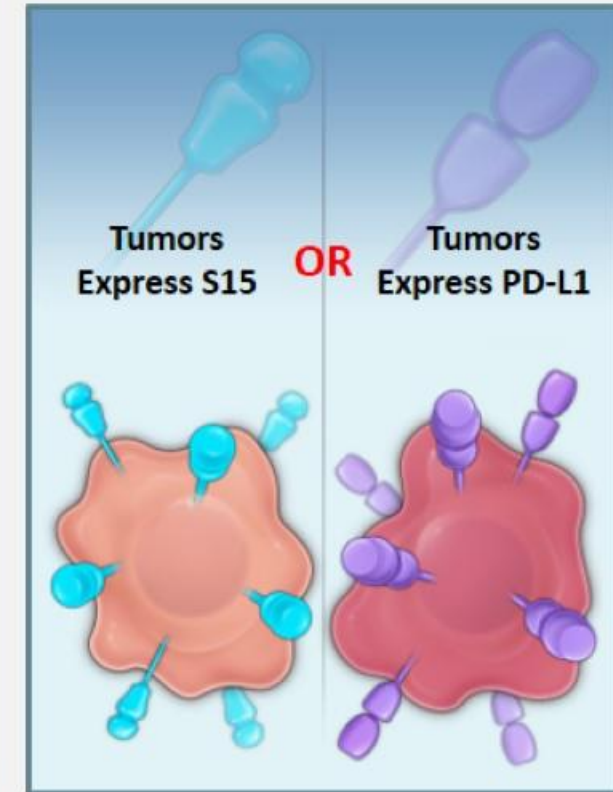
FUNCTION

Potently Suppresses
T Cell Function



NON-RESPONDERS

Generally Non-Overlapping
with PD-L1 Expression



Wang et al.,
2019

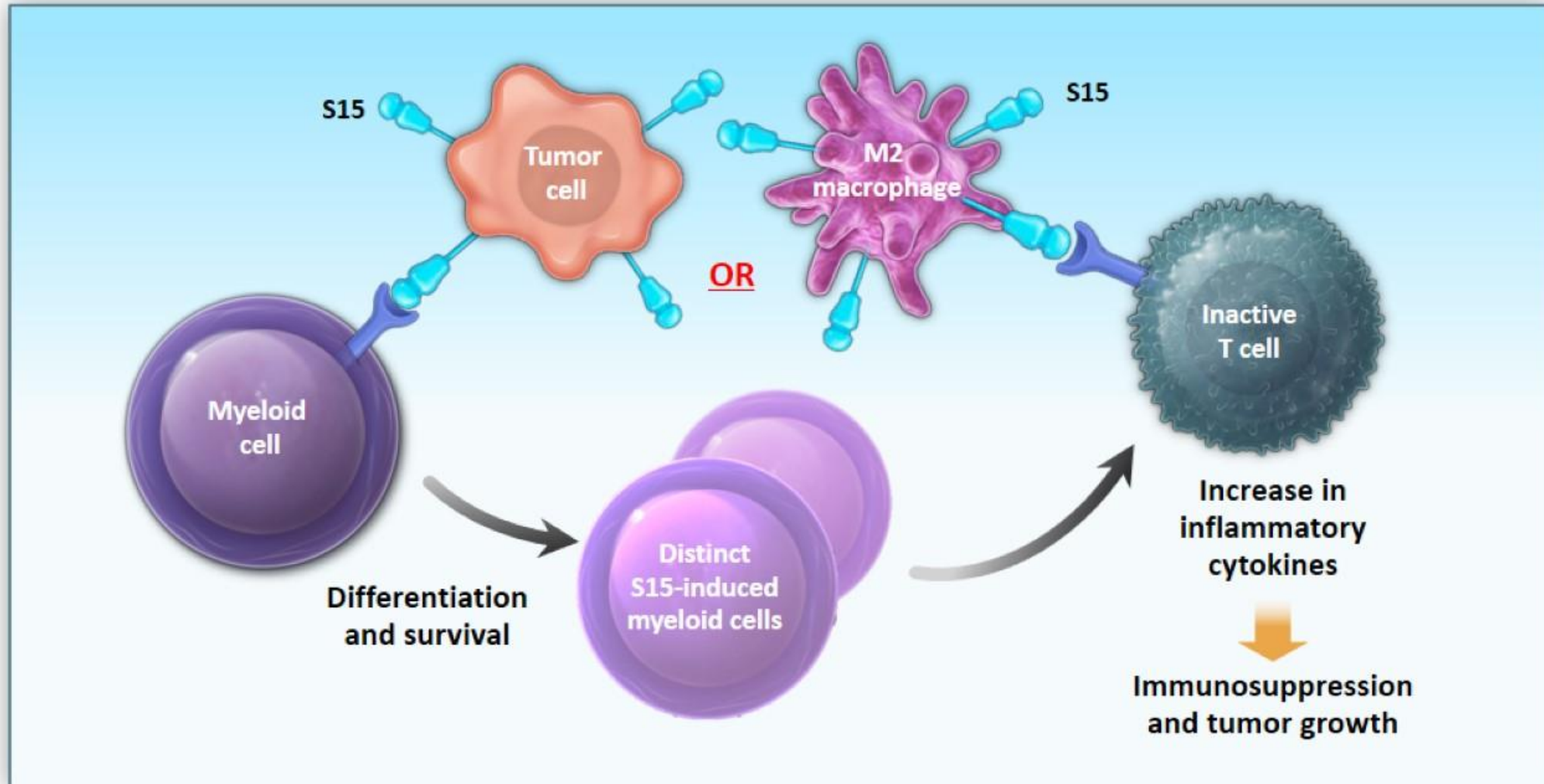
nature
medicine

ARTICLES

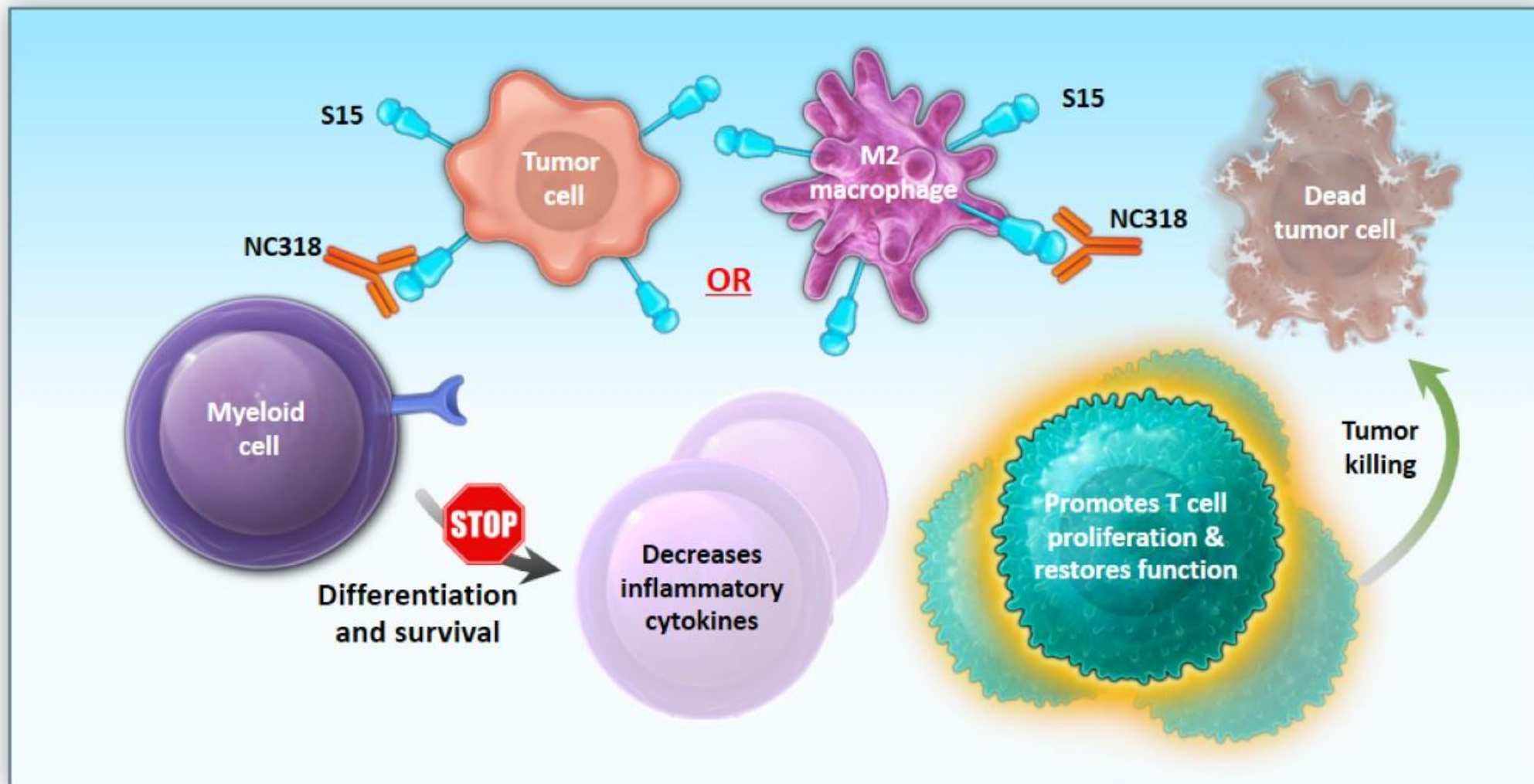
<https://doi.org/10.1038/s41591-019-0374-x>

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

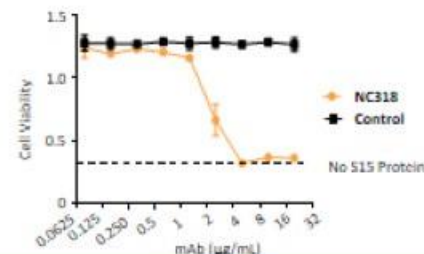
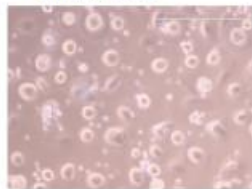


NC318 Mechanism of Action Restores Immune Function *In Vitro*

INHIBITS

Myeloid Cell
Differentiation and Survival

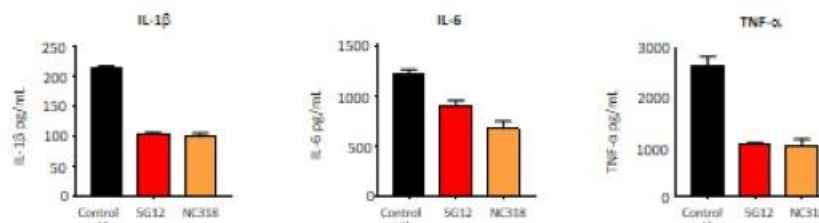
Myeloid Cell Survival and
Differentiation



Blocks survival of
myeloid cells

DECREASES

Pro-Inflammatory and
Pro-Tumorigenic Cytokines



Decreases IL-1 β ,
IL-6 & TNF- α

PROMOTES

T Cell Function



Increases T cell
proliferation &
IFN- γ production

NC318 Phase 1 Trial Status

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 (104+ weeks)
- 1 confirmed PR (78+ weeks)
- 10 durable SD (≥24 weeks)

The Angeles Clinic
AND RESEARCH INSTITUTE
A CEDARS-SINAI AFFILIATE

next
ONCOLOGY

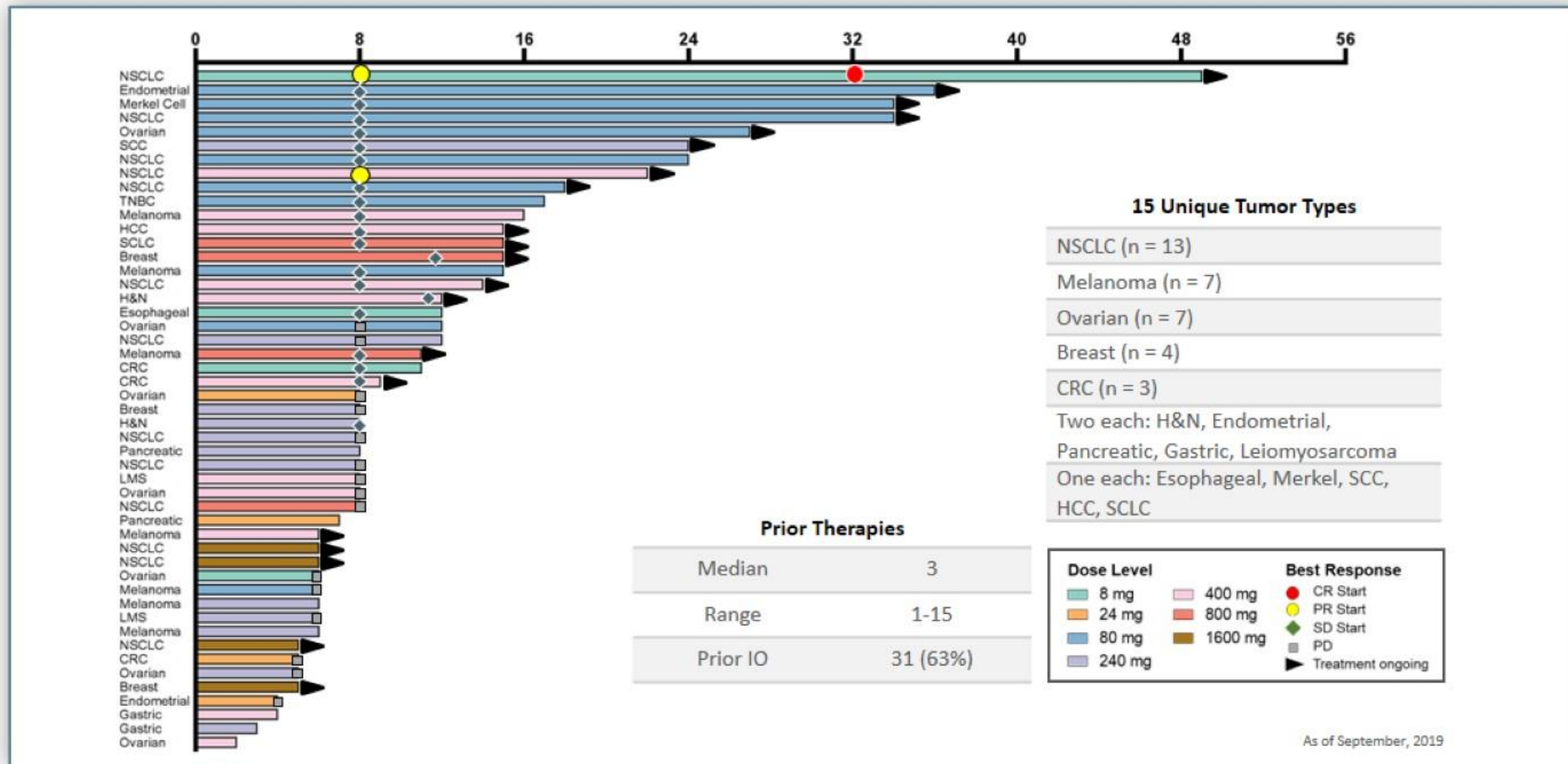
NYU Langone
MEDICAL CENTER

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

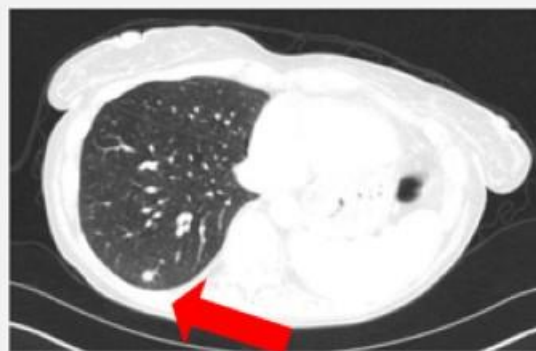


NC318: Single-Agent Activity in PD-1 Refractory NSCLC

Confirmed

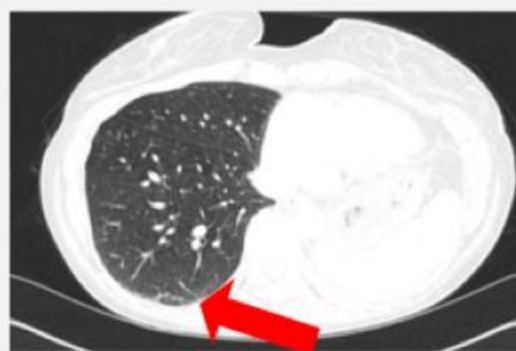
COMPLETE RESPONSE

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 December 17, 2020

TUMOR TYPES

NSCLC

Ovarian

H&N

TNBC

DESIGN

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

INTERIM RESULTS

- H&N and TNBC continue to enroll
- 1 confirmed PR in H&N (32+ weeks)
- S15 expression determined; 13% of evaluable biopsies had S15-positive tumors
- Selection criterion did not result in enough S15-positive patients
- Biomarker analysis demonstrated increase in peripheral immune modulation markers
- Next steps and plans early 2021



NC318

Restores Immune
Function in a Highly
Suppressive TME



MOA / Preclinical studies complete

- Relieves S15-mediated inhibition of T cells
- Increases IFN- γ production
- Decreases inflammatory cytokines



Completed enrollment of Phase 1



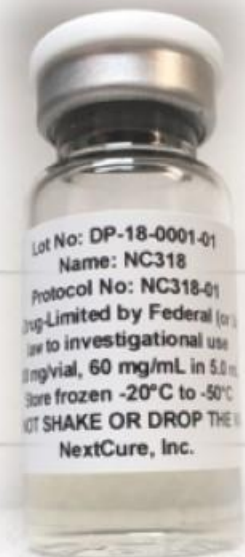
Reported preliminary data at SITC 2019



Report next steps early 2021



Initiate Phase 2 combination trial with anti-PD-1 (TBD)



NC410

Decoy Human Fusion Protein Targeting the TME



Phase 1/2
CLINICAL
TRIAL

TARGET

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

CELL TYPES

Dendritic cells and
T cells

MOA

Promotes T cell
function & dendritic
cell activity

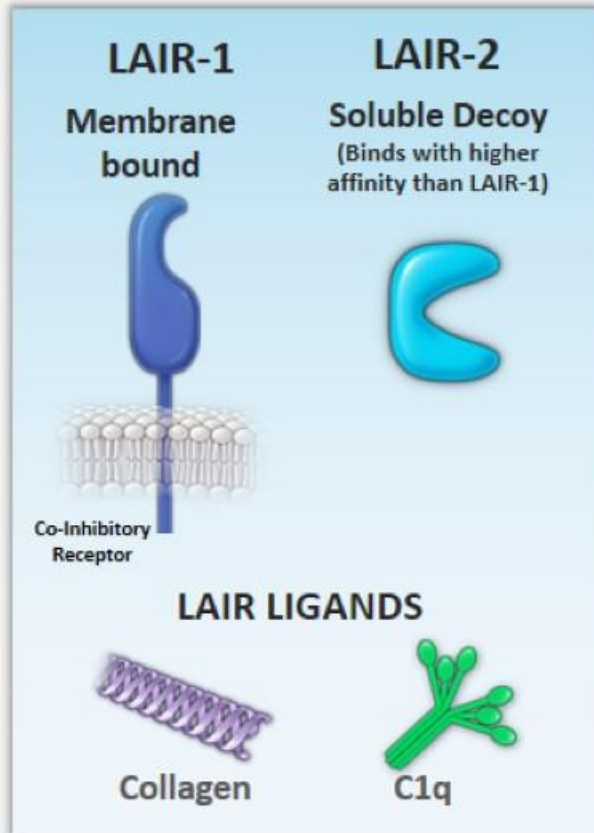
INDICATIONS

Advanced or
metastatic solid
tumors

LAIR-1 & LAIR-2 Functional Relationship

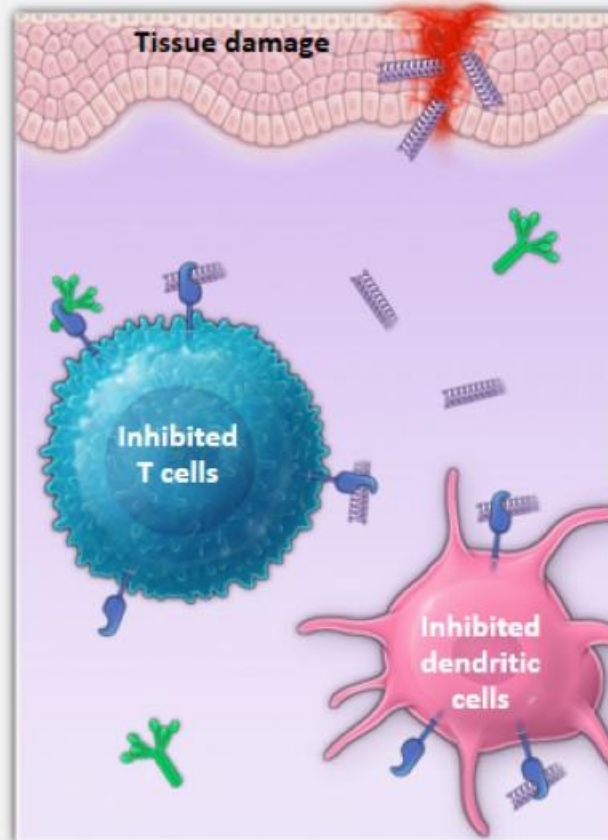
LAIR & LIGANDS

LAIR-1 and LAIR-2 Bind
Collagen and C1q



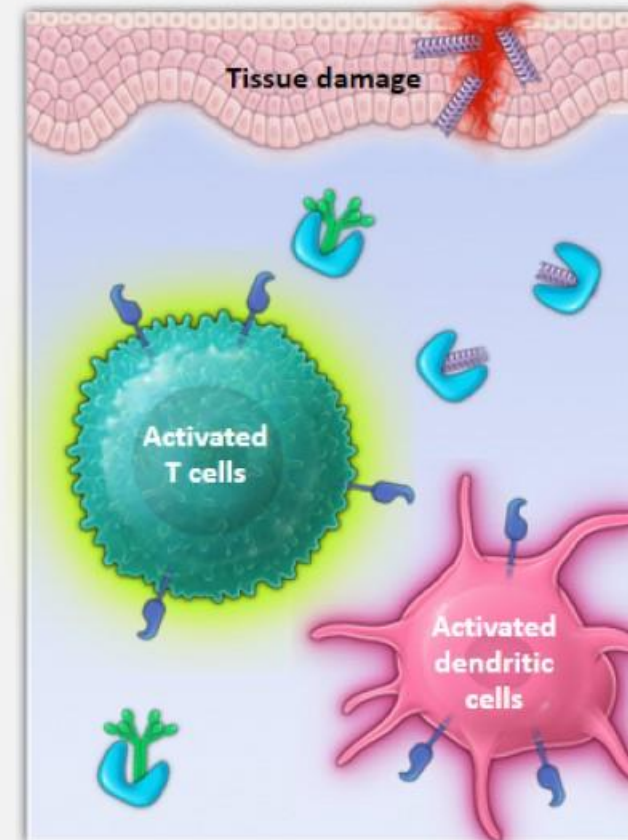
LAIR-1

Ligands Expressed in Response to
Inflammation & Inhibit Immune Function



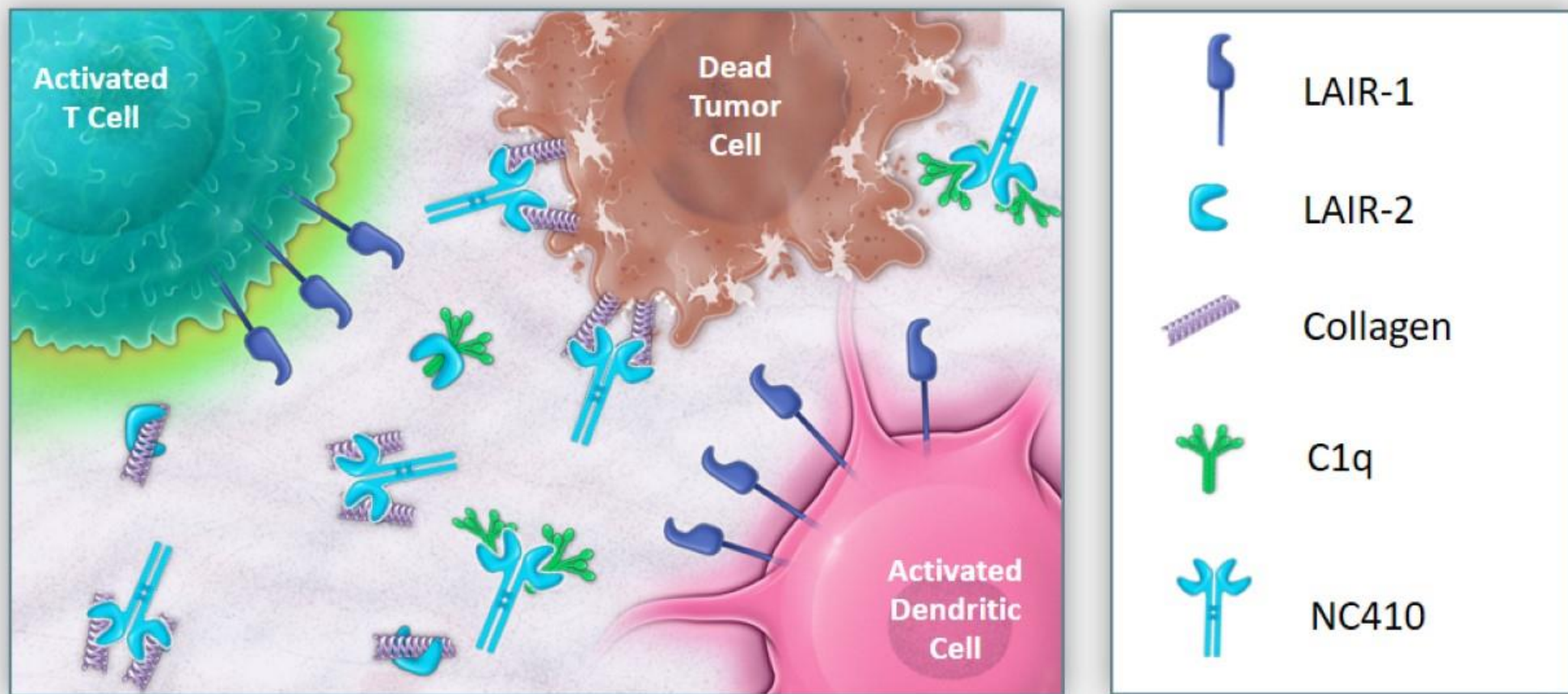
LAIR-2

LAIR-2 Modulates LAIR-1
Mediated Inhibition



NC410 Prevents Immune Suppression

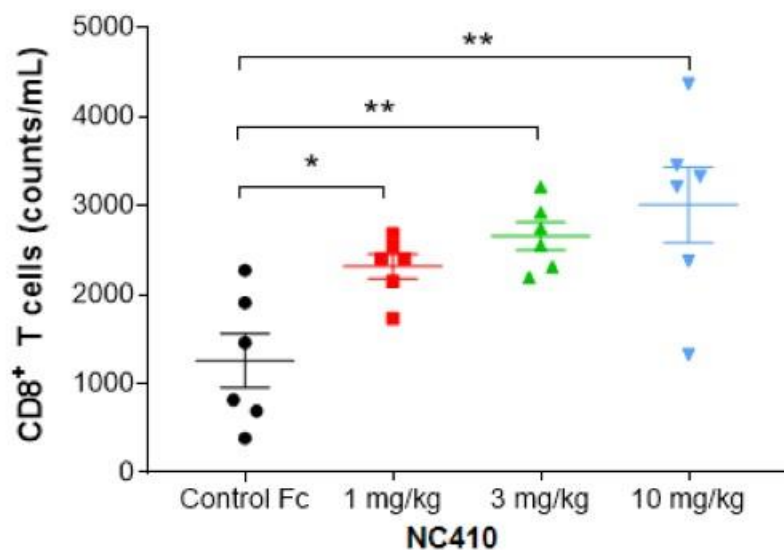
NC410 IS A FUSION PROTEIN OF LAIR-2 AND A DECOY FOR LAIR-1 AND PROMOTES T CELL FUNCTION AND DC ACTIVATION



NC410 Enhanced T Cell Expansion and Relieved Immunosuppression

Blocked

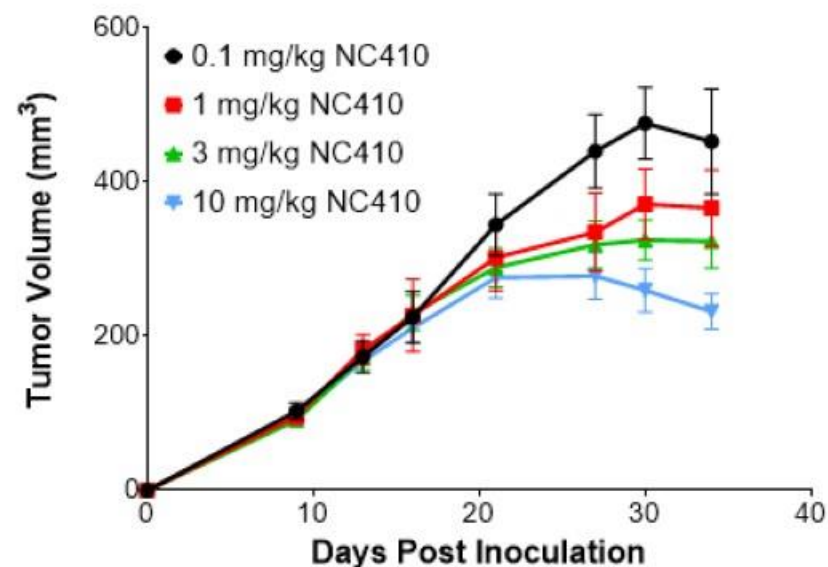
SUPPRESSION



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 Phase 1 Portion of Phase 1/2 First-in-Human Trial

DESIGN

- Dose-escalation
- Safety, tolerability, and biomarker readouts

TUMOR TYPES

Advanced or metastatic solid tumors

DELIVERABLES

Initial Phase 1 data 2H2021



NATIONAL CANCER INSTITUTE
Center for Cancer Research



John Theurer
Cancer Center
at Hackensack University Medical Center



NC410 Summary



Promotes T cell function and dendritic cell activity
in preclinical studies



cGMP manufacturing complete



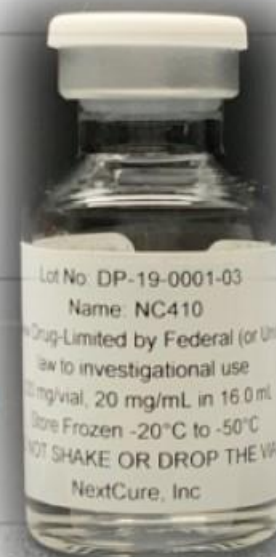
IND filed & received FDA clearance Q1 2020



Initiated Phase 1 trial

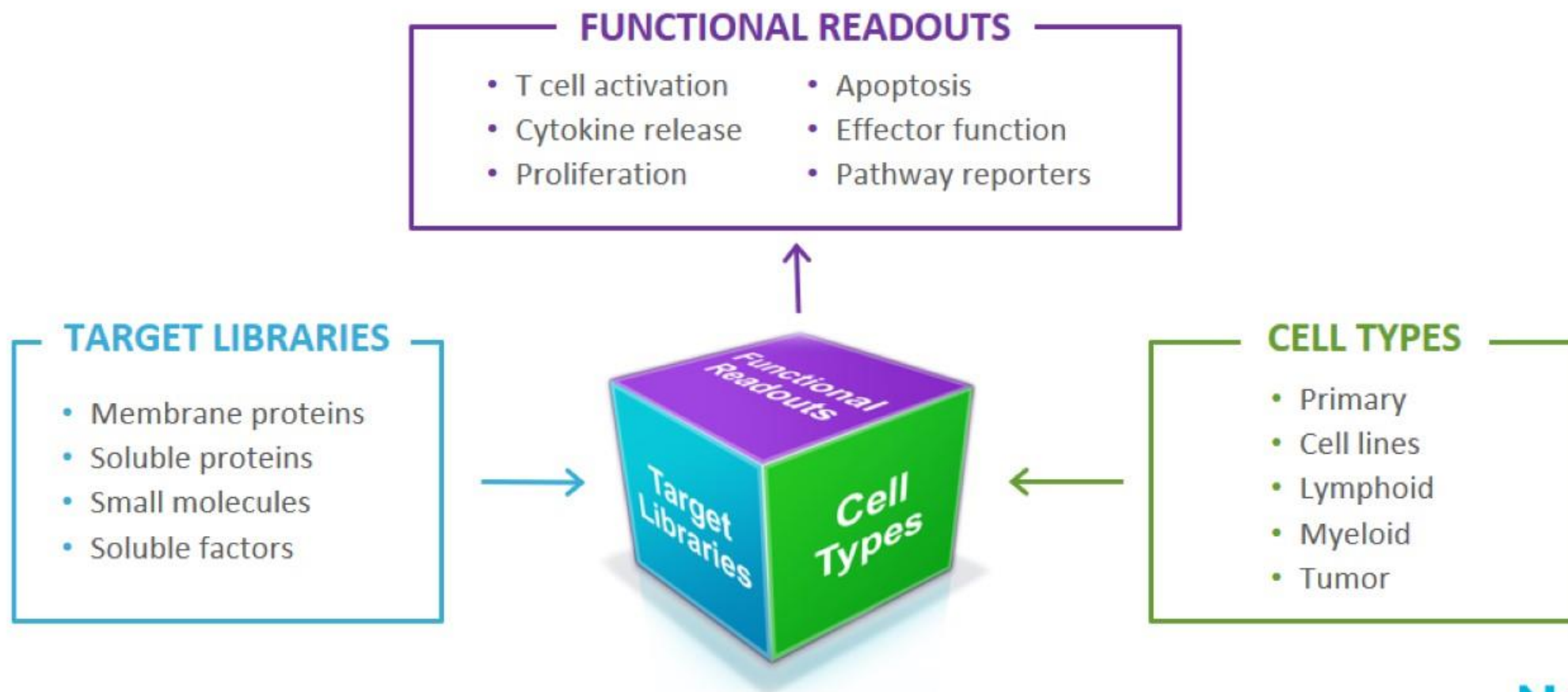


Initial Phase 1 data 2H 2021



Finding Solutions with a Powerful Discovery Engine

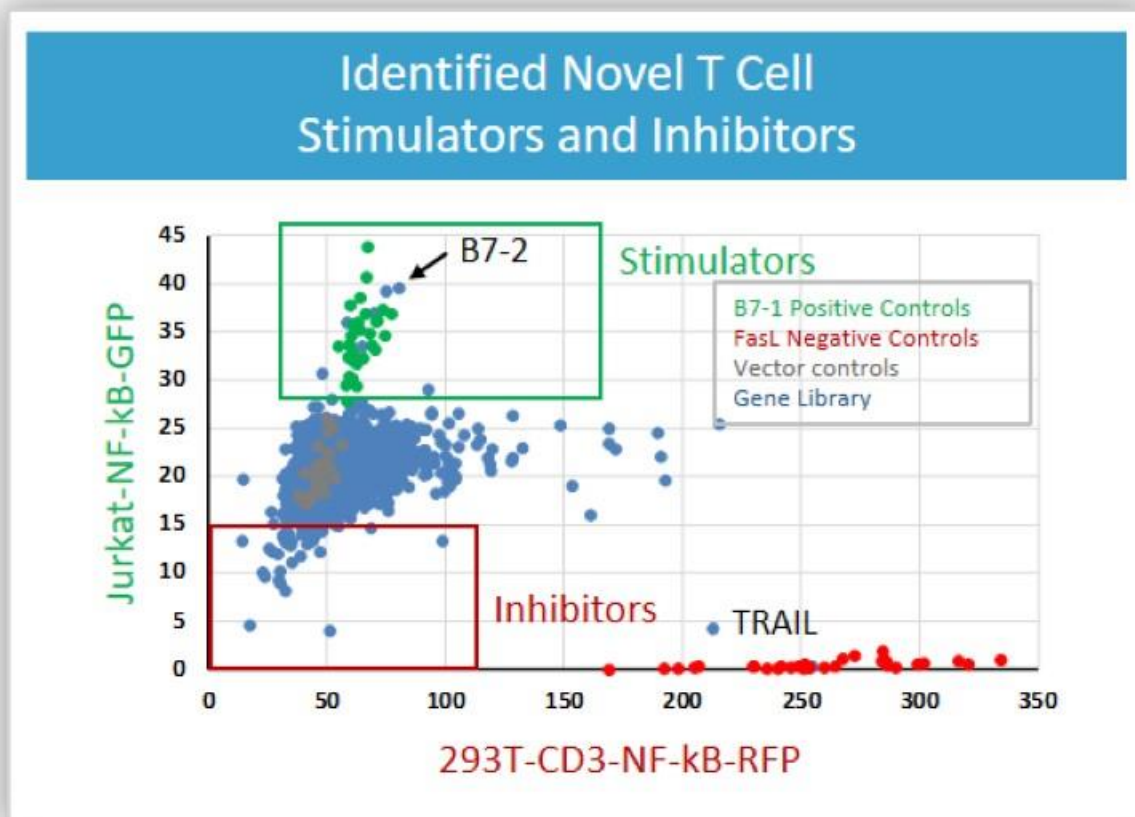
Functional, Integrated, NextCure Discovery in Immuno-Oncology



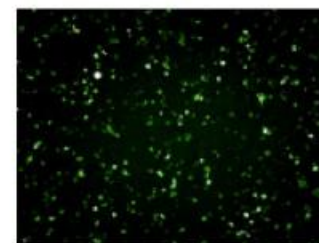
FIND-IO Screening Methodology



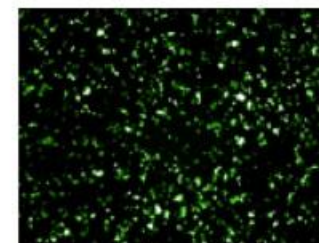
Jurkat “T Cell Line” Screening and Validating FIND-IO Hits



Vector
Control



Stimulatory
B7-2



Inhibitory
TRAIL

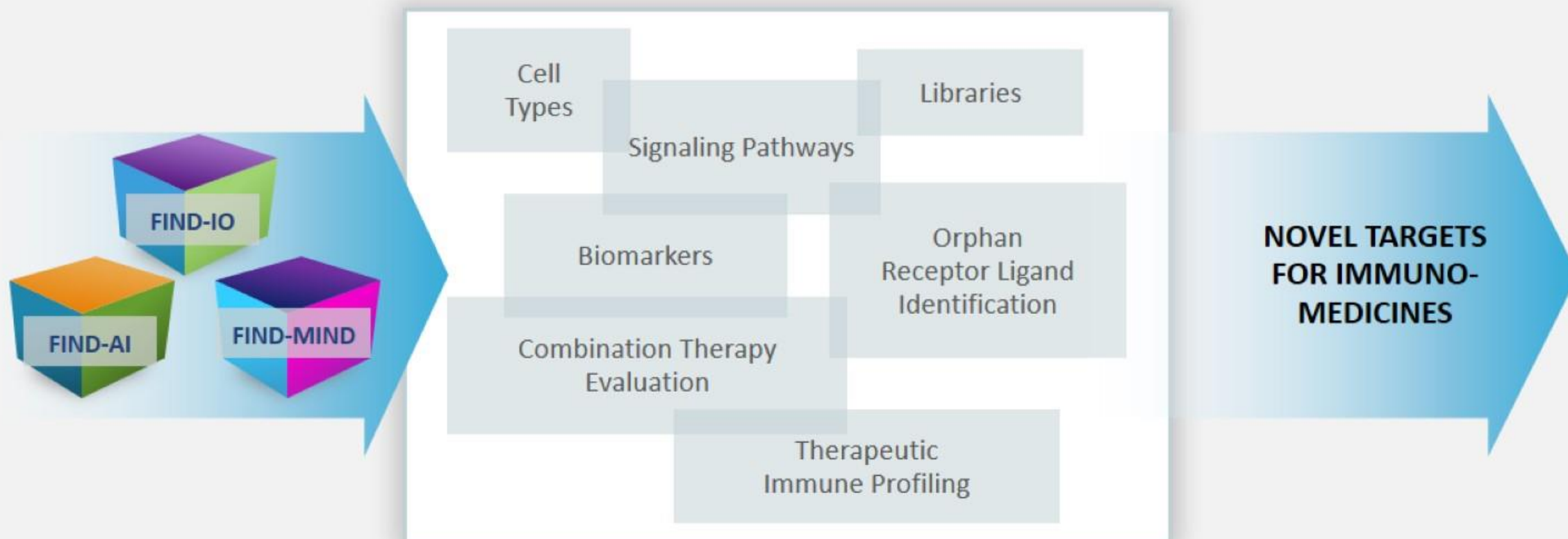


REPRODUCIBILITY

ROBUSTNESS

RELEVANCY

Versatile, Flexible, and Comprehensive Approach for Target Identification



Anticipated Near-Term Milestones



NC318

- Report next steps early 2021
- Initiate Phase 2 combination trial with anti-PD-1 (TBD)



NC410

- Report initial Phase 1 data 2H 2021



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