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NEXT-GENERATION IMMUNOMEDICINES

NOVEMBER 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 our prospectus dated November 14, 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 (S15): Phase 1 data presented at SITC 2019
- NC410 (LAIR-1): IND expected Q1 2020
- Manufacturing: dedicated, state-of-the-art facility

Platform for Novel Target Discovery

- FIND-IO functional screening discovery engine
- Oncology partnership with Lilly
- 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

THE UNMET NEEDS OF CANCER PATIENTS ARE SIGNIFICANT

NON-RESPONDERS **RAPID PROGRESSION** **LIMITED TREATMENTS**



We Need New Solutions

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

NEW
therapeutic options

POSITIVE
clinical responses

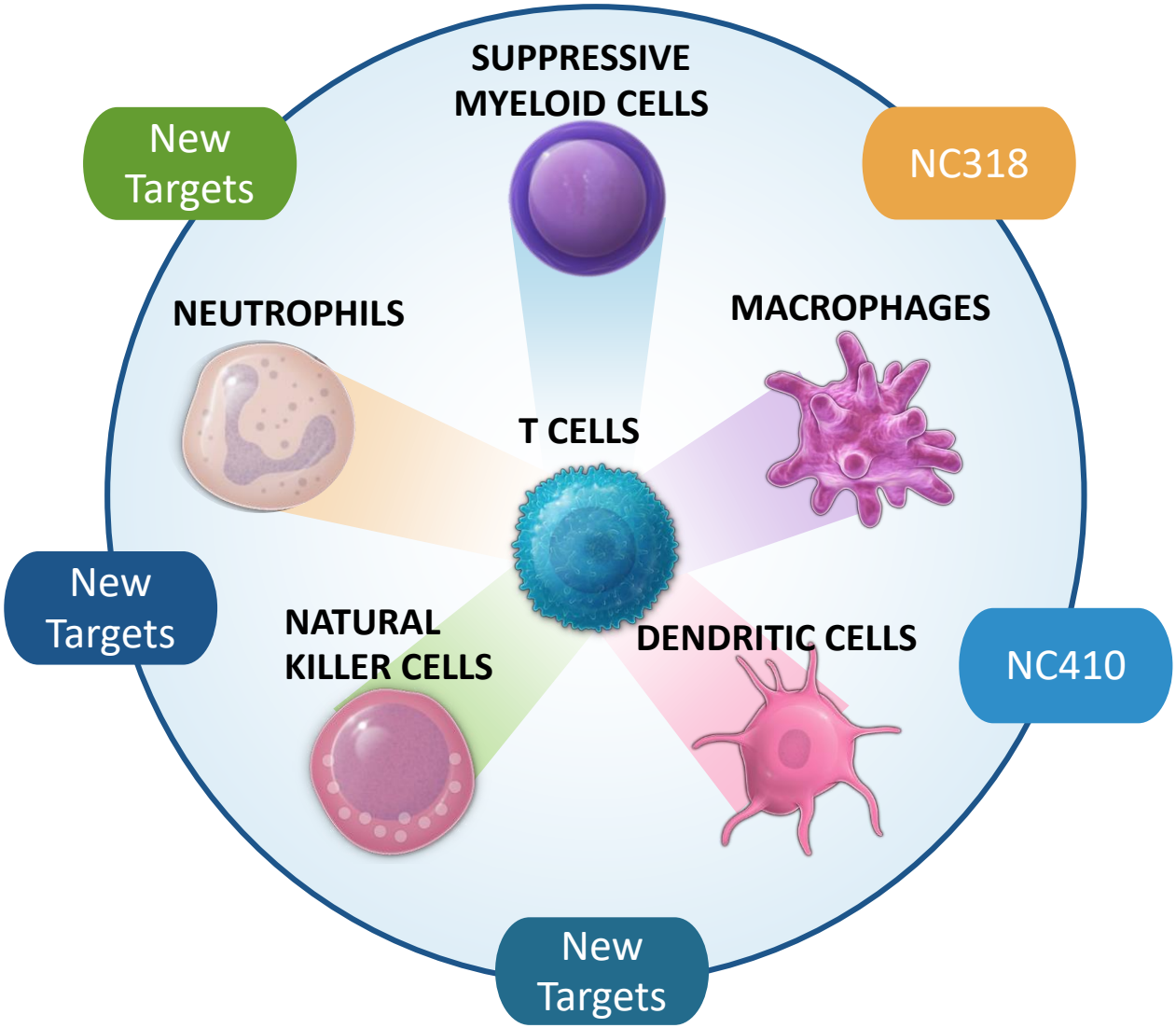
IMPROVED
quality of life



Focused on Cancer Patients Not Adequately Addressed Today

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EXPANDING TARGETS BEYOND T CELLS



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EXPERIENCED TEAM WITH STRONG TRACK RECORD

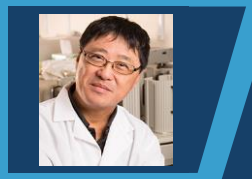
HISTORY AND SUCCESS OF WORKING TOGETHER

Michael Richman **CEO**	Amplimmune	MacroGenics	MedImmune	CHIRON
Timothy Mayer, PhD **COO**	MacroGenics	Banner & Witcoff, Ltd. Intellectual Property Law	invitrogen	life technologies
Steve Cobourn, CPA **CFO**	Vaccinex	Otsuka		
Kevin N Heller, MD **CMO**	Incyte	AstraZeneca	Bristol-Myers Squibb	The Rockefeller University
Sol Langermann, PhD **CSO**	Amplimmune	PharmAthene	MedImmune	
Jim Bingham, PhD **CDO**	Amplimmune	Lonza	Human Genome Sciences	MedImmune
Linda Liu, PhD **SVP, Research**	Amplimmune	MaxCyte	OSIRIS	St. Jude Children's Research Hospital
Sebastien Maloveste, PhD **VP, Business Development**	GenVec	Amplimmune		
Dallas Flies, PhD **VP, Discovery Research**	UNM	Yale University	Johns Hopkins Medicine	mayo

WORLD-RENOWNED SCIENTIFIC FOUNDER AND KEY COLLABORATION WITH YALE

YALE COLLABORATION

LIEPING CHEN, MD, PhD
Discovered multiple key immune pathways, including PD-L1

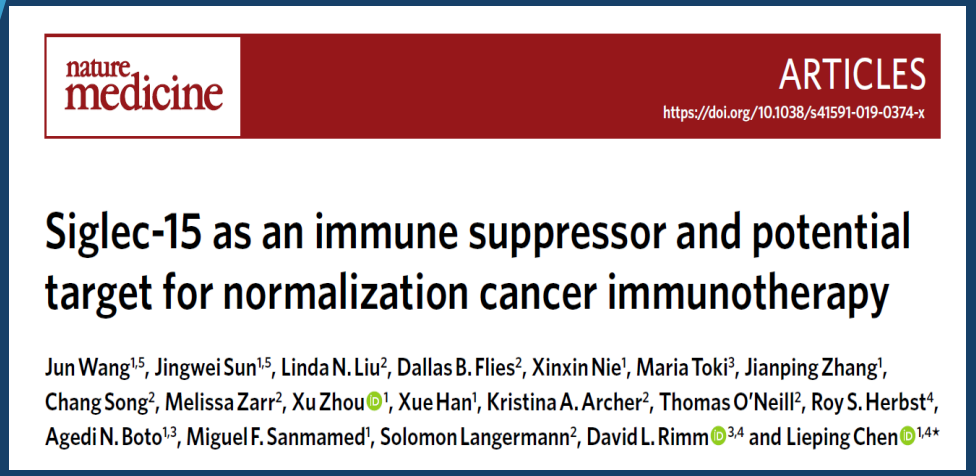


Yale UNIVERSITY

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[1,5], Jingwei Sun[1,5], Linda N. Liu[2], Dallas B. Flies[2], Xinxin Nie[1], Maria Toki[3], 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[3,4] and Lieping Chen[1,4*]

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NEXTCURE HAS DELIVERED A ROBUST PRODUCT PIPELINE

PROGRAMS	CELLS	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT MILESTONE	WORLDWIDE RIGHTS
PRODUCT CANDIDATES								
NC318 (S15)	Tumors and macrophages	ONCOLOGY					Phase 2 data by end of 2020	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	Lilly / 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

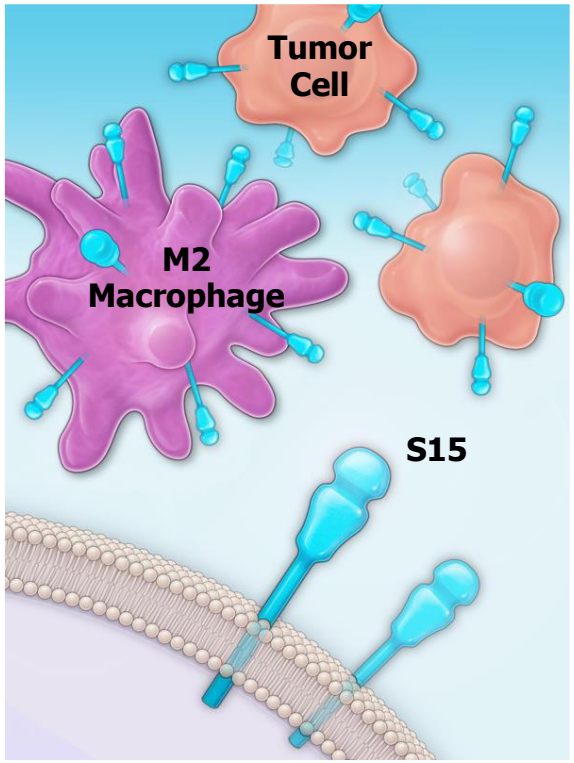
INDICATIONS

Advanced or metastatic solid tumors, including NSCLC, ovarian, head & neck and triple negative breast cancers

S15 AS A TARGET

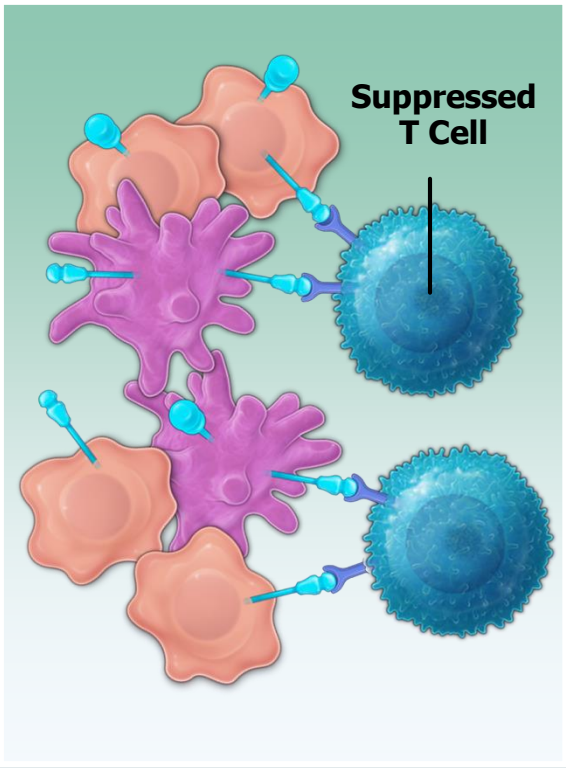
EXPRESSION

Tumors & Macrophages



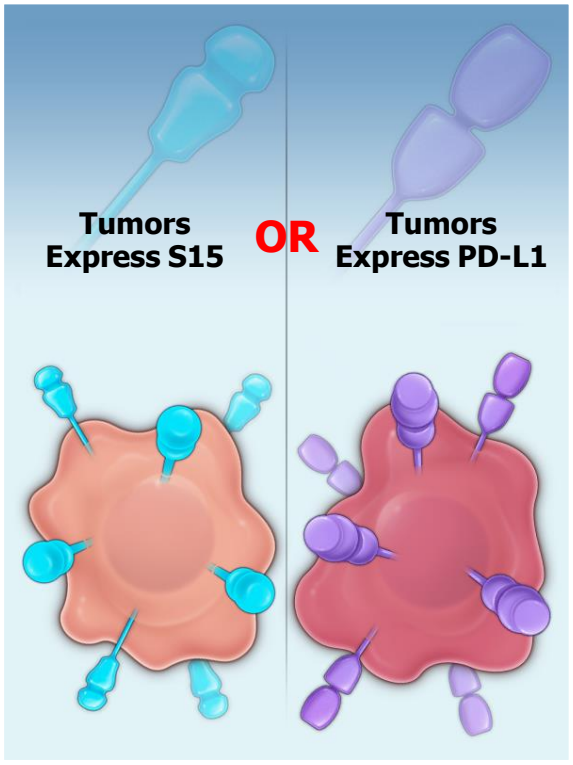
FUNCTION

Potently Suppresses T Cell Function



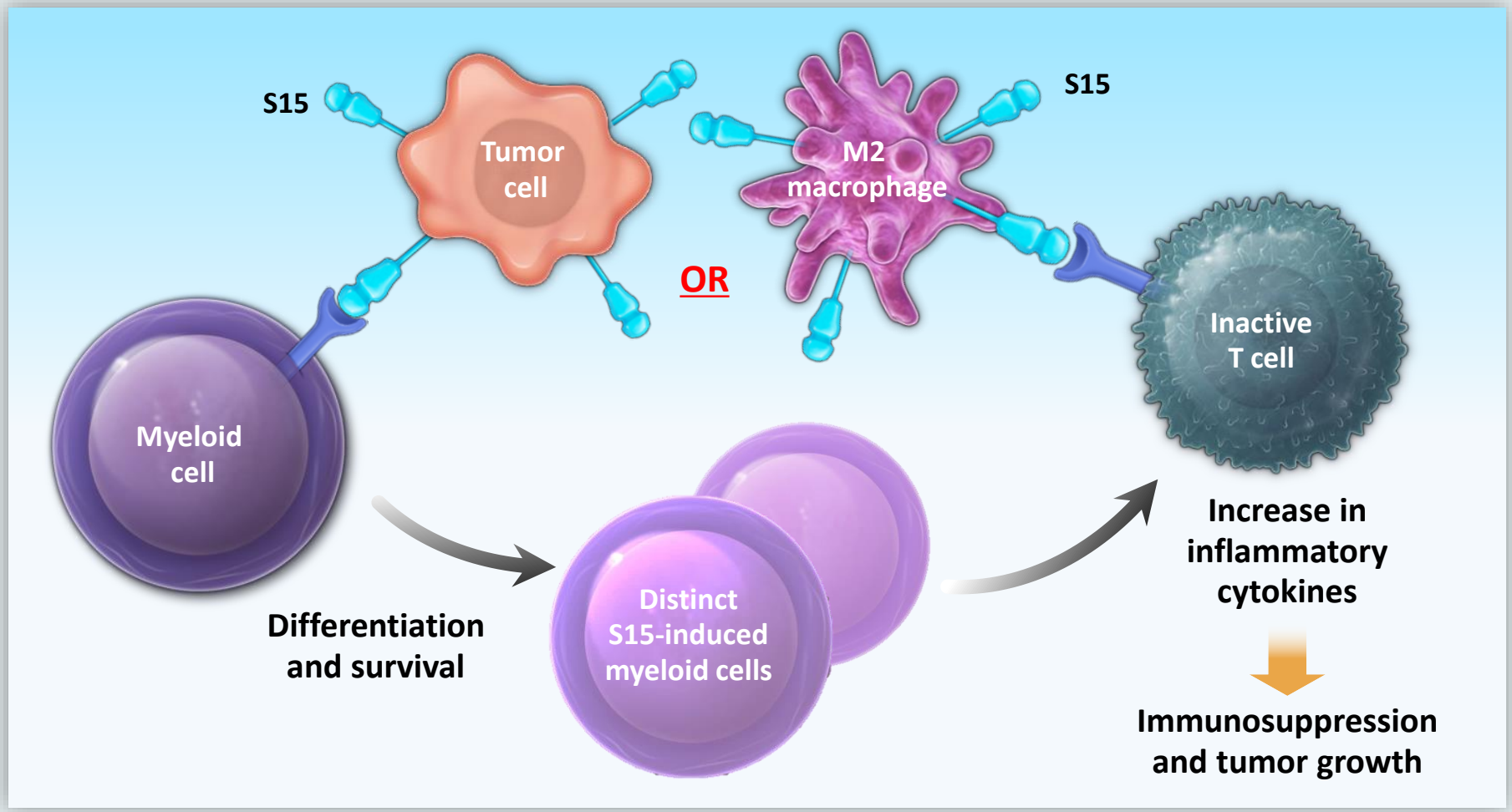
NON-RESPONDERS

Generally Non-Overlapping with PD-L1 Expression



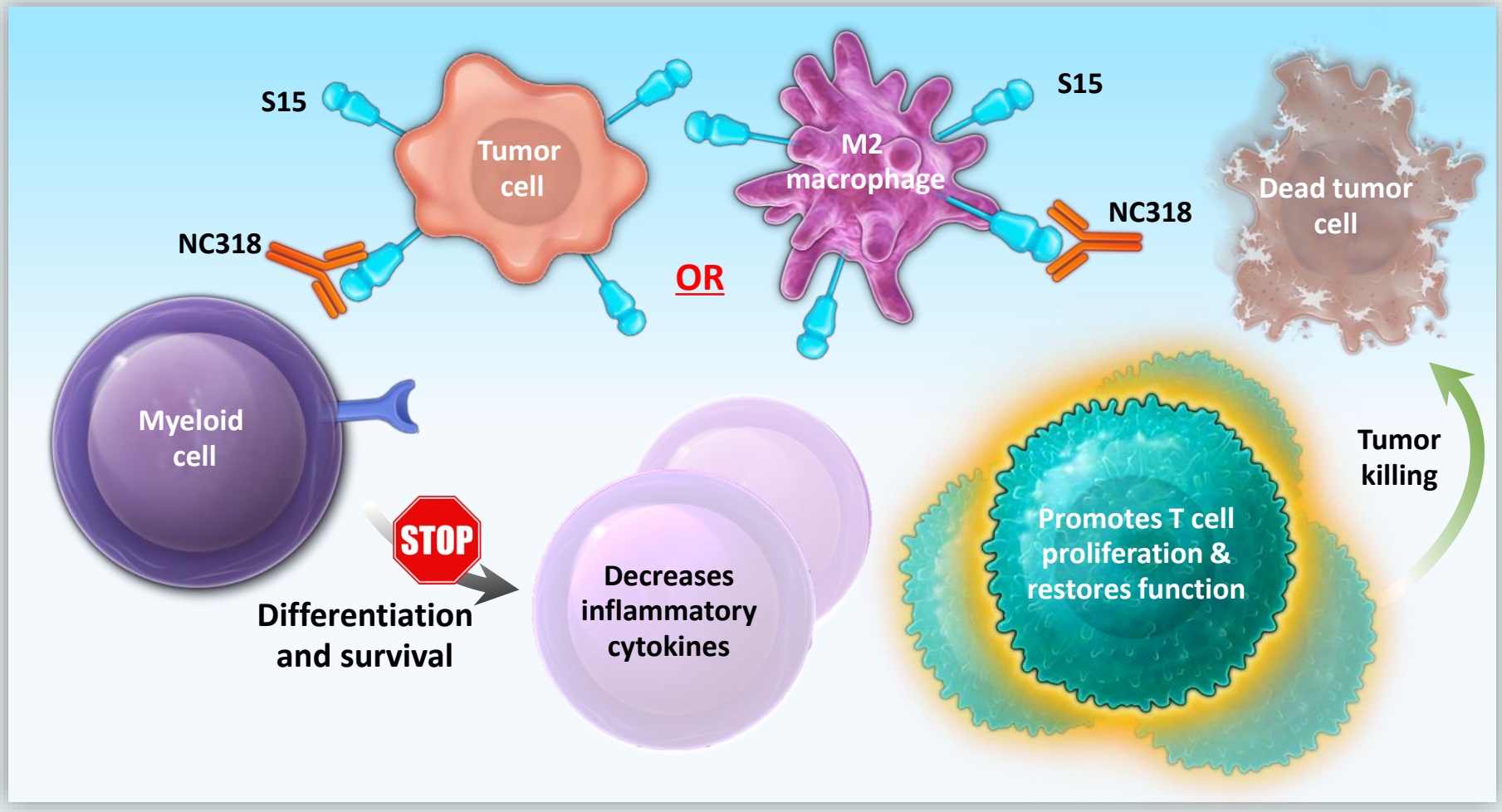
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S15 IS HIGHLY IMMUNOSUPPRESSIVE IN THE TME OF MULTIPLE TUMOR TYPES



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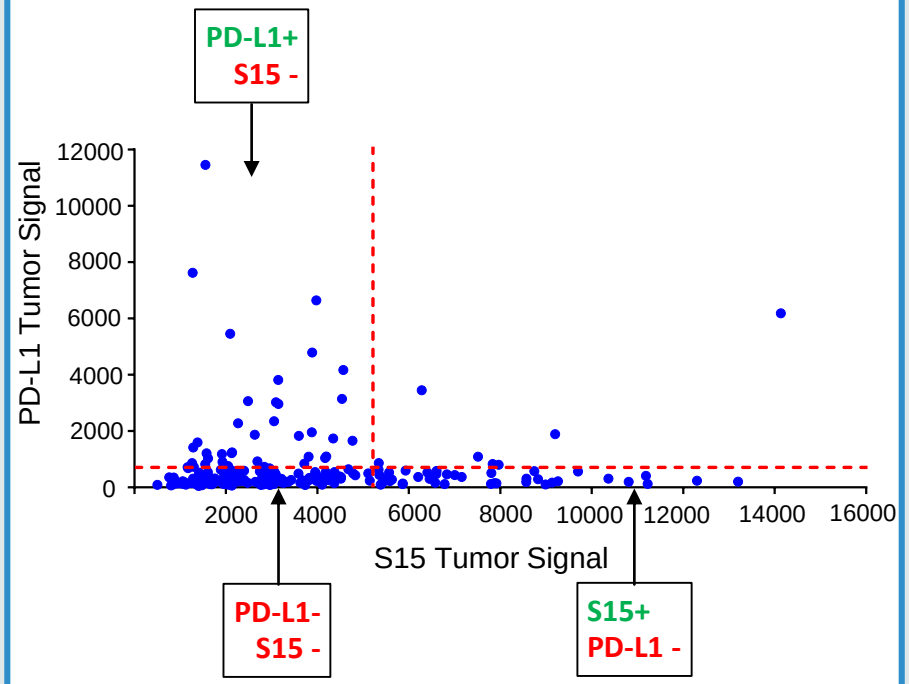
NC318 IS DESIGNED TO BLOCK IMMUNOSUPPRESSIVE ACTIVITY INDUCED BY S15



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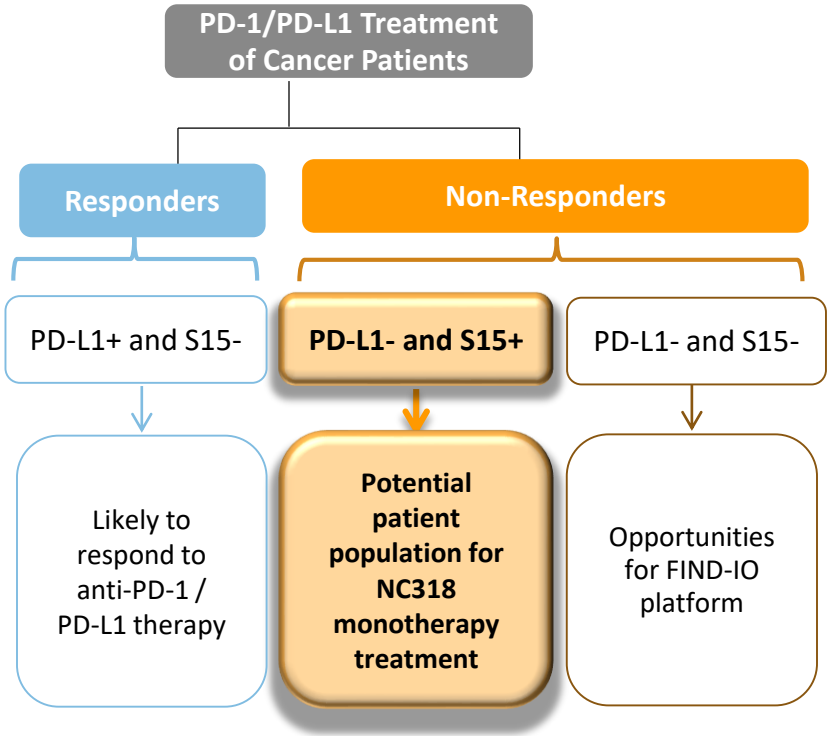
NC318: A POTENTIAL TREATMENT OPTION FOR PD-1/PD-L1 NON-RESPONDERS

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



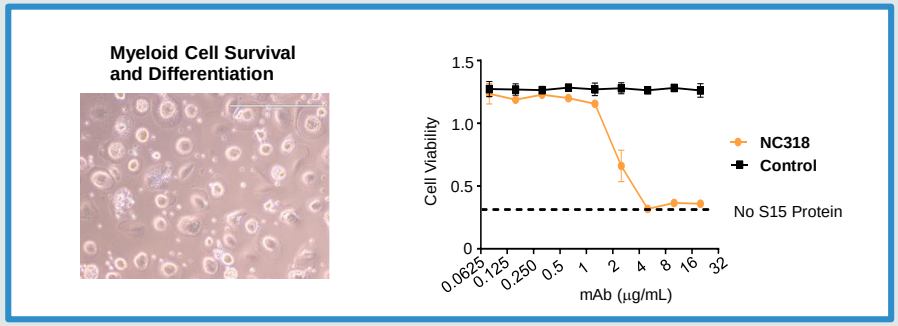
*>200 NSCLC samples in preclinical research
Wang et al., Nat Med 2019 Mar 4
Toki et al., AACR Poster 3151 2019

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



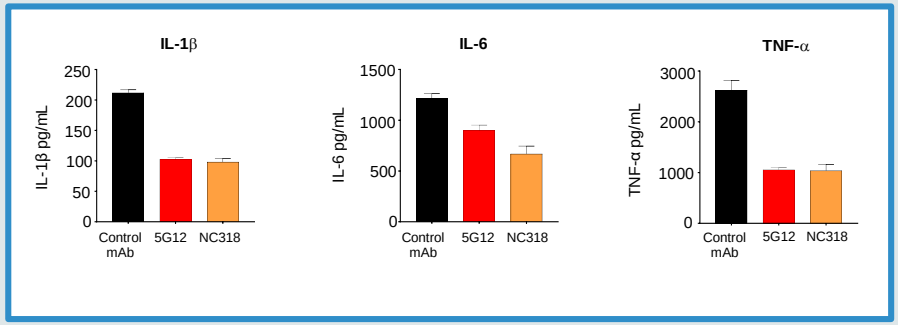
NC318 RESTORED IMMUNE FUNCTION *IN VITRO*

INHIBITED
Myeloid Cell Differentiation and Survival



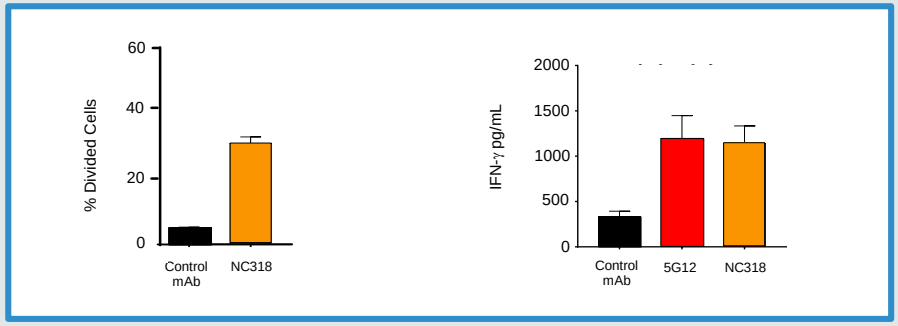
Blocked survival of myeloid cells

DECREASED
Pro-Inflammatory and Pro-Tumorigenic Cytokines



Decreased IL-1β, IL-6 & TNF-α

PROMOTED
Tumor-Specific T Cell Function



Increased T cell proliferation & IFN-γ production

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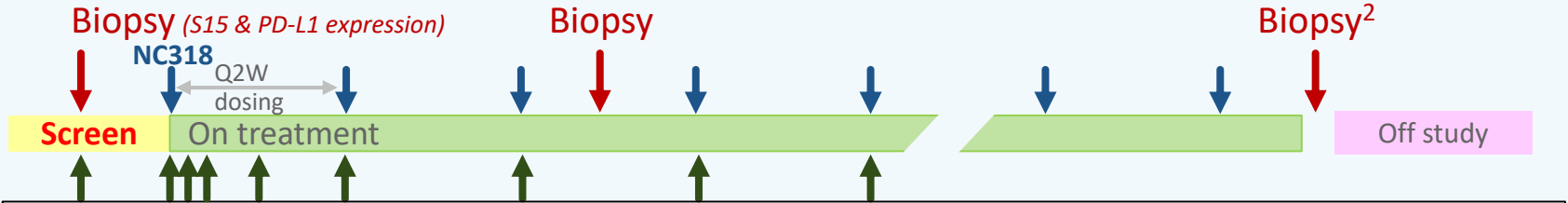
NC318 MONOTHERAPY TRIAL UNDERWAY DESIGNED FOR RAPID PROOF-OF-CONCEPT

PHASE 1

- Opened in 4Q 2018; preliminary data announced November 2019
- Dose-escalation[1]
- Safety, tolerability & biomarker readouts
- Advanced or metastatic solid tumors
- All comers regardless of PD-L1 or S15 expression status

PHASE 2

- Opened in 4Q 2019; initial data by end of 2020
- Efficacy assessment
- Tumor types shown to have elevated S15 expression, including NSCLC, ovarian, head & neck and TNBC
- PD-L1 TPS <50%



(1) Dose escalation evaluated 7 dose cohorts (8 mg – 1,600 mg or approximately 0.1 - 20 mg/kg) administered every 2 weeks

(2) In Phase 2 portion of trial

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NC318 PHASE 1 TRIAL STATUS AS OF NOVEMBER 9, 2019

Dose Escalation – Enrollment Complete

ENROLLMENT

- 49 patients dosed
- 15 different 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

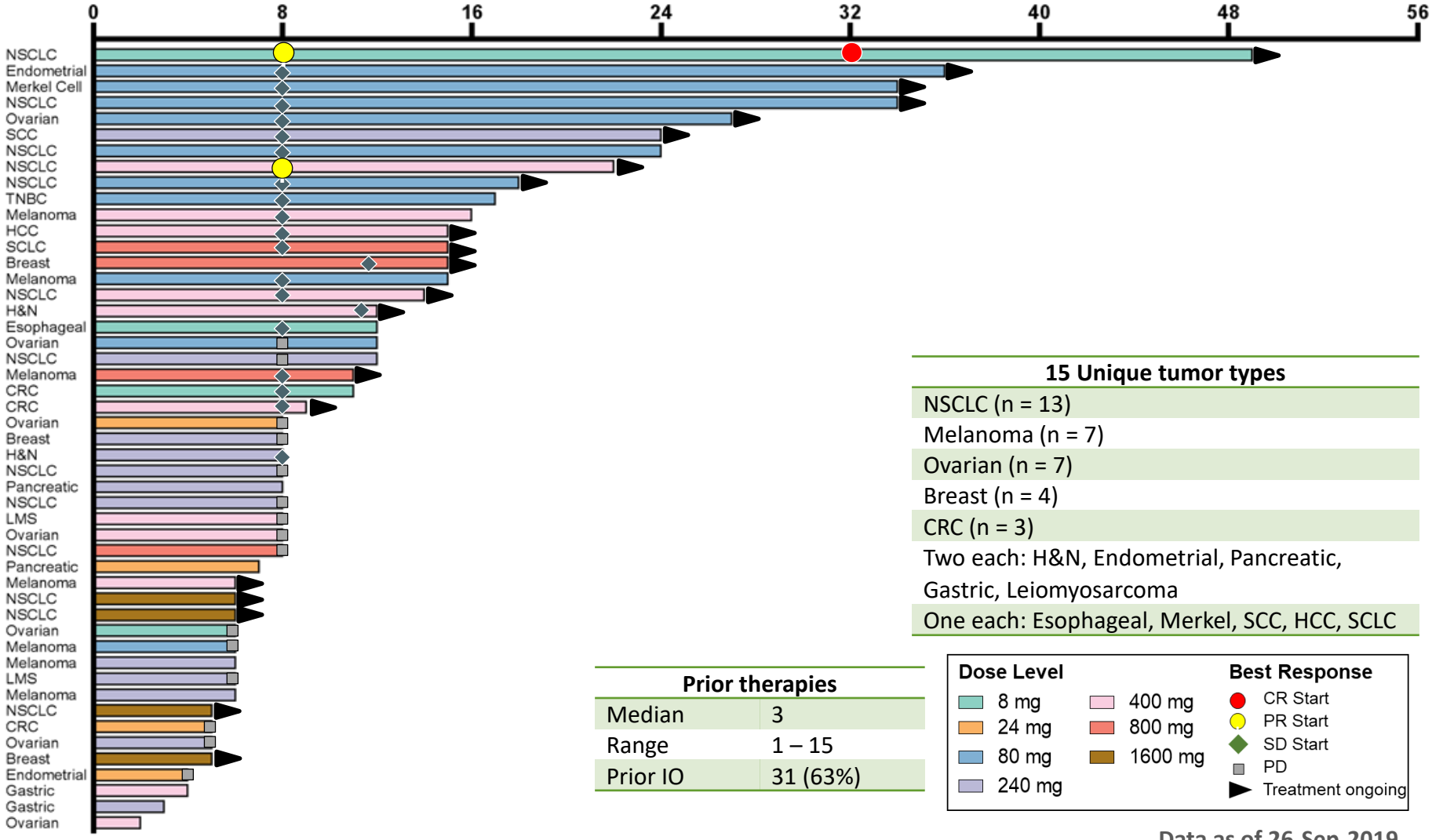
RESPONSES

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

- Angeles Clinic
- MSKCC
- Next Oncology
- NYU
- Yale University

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

TREATMENT DURATION IN WEEKS FOR ALL PHASE 1 PATIENTS



15 Unique tumor types
NSCLC (n = 13)
Melanoma (n = 7)
Ovarian (n = 7)
Breast (n = 4)
CRC (n = 3)
Two each: H&N, Endometrial, Pancreatic, Gastric, Leiomyosarcoma
One each: Esophageal, Merkel, SCC, HCC, SCLC

Prior therapies	
Median	3
Range	1 – 15
Prior IO	31 (63%)

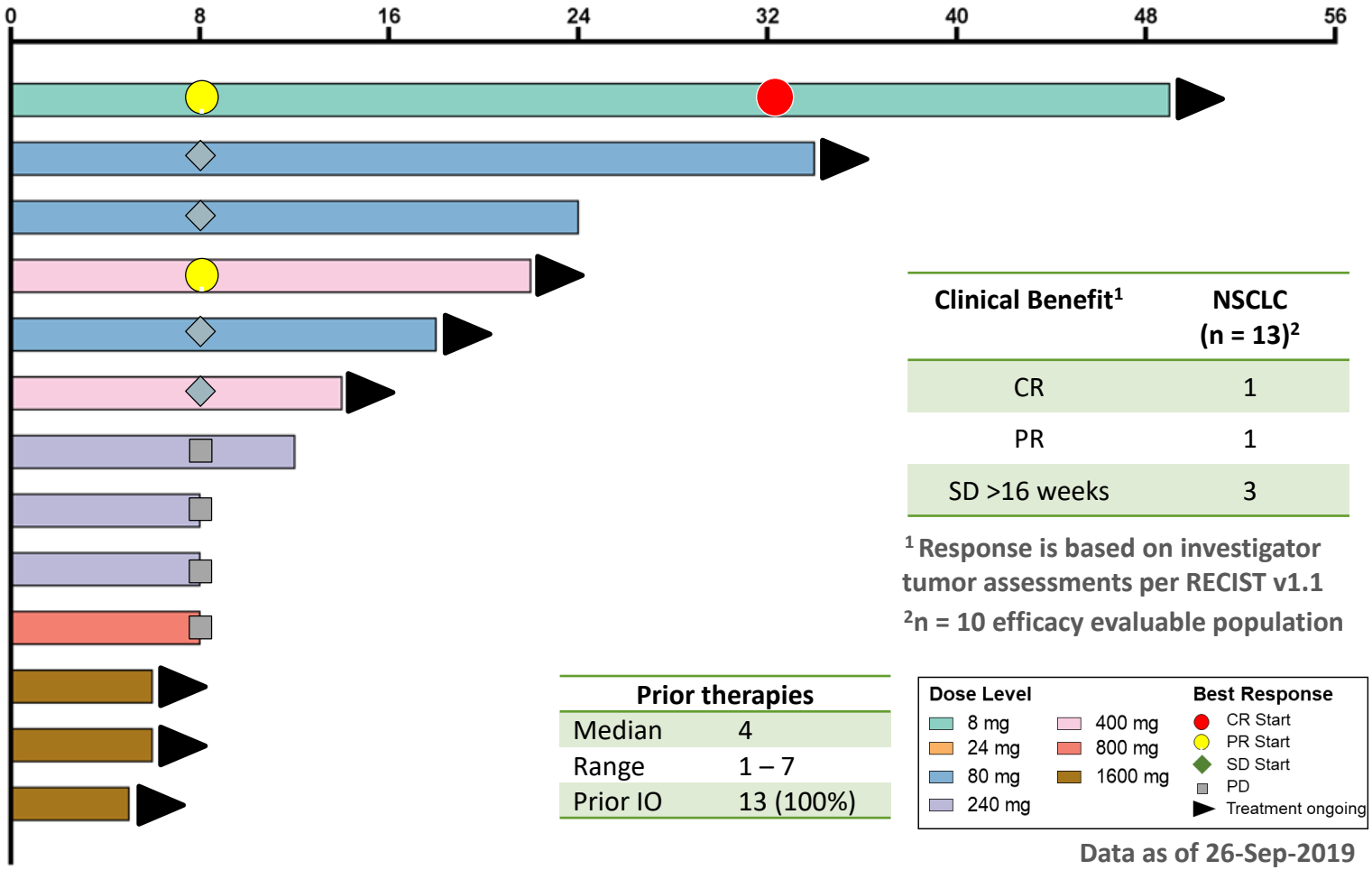
Dose Level
- 8 mg
- 24 mg
- 80 mg
- 240 mg
- 400 mg
- 800 mg
- 1600 mg

Best Response
- CR Start
- PR Start
- SD Start
- PD
- Treatment ongoing

Data as of 26-Sep-2019

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DURABLE CLINICAL BENEFIT FOR PD-1 REFRACTORY NSCLC PATIENTS



Clinical Benefit[1]	NSCLC (n = 13)[2]
CR	1
PR	1
SD >16 weeks	3

[1] Response is based on investigator tumor assessments per RECIST v1.1

[2] n = 10 efficacy evaluable population

Prior therapies	
Median	4
Range	1 – 7
Prior IO	13 (100%)

Dose Level
- 8 mg
- 24 mg
- 80 mg
- 240 mg
- 400 mg
- 800 mg
- 1600 mg

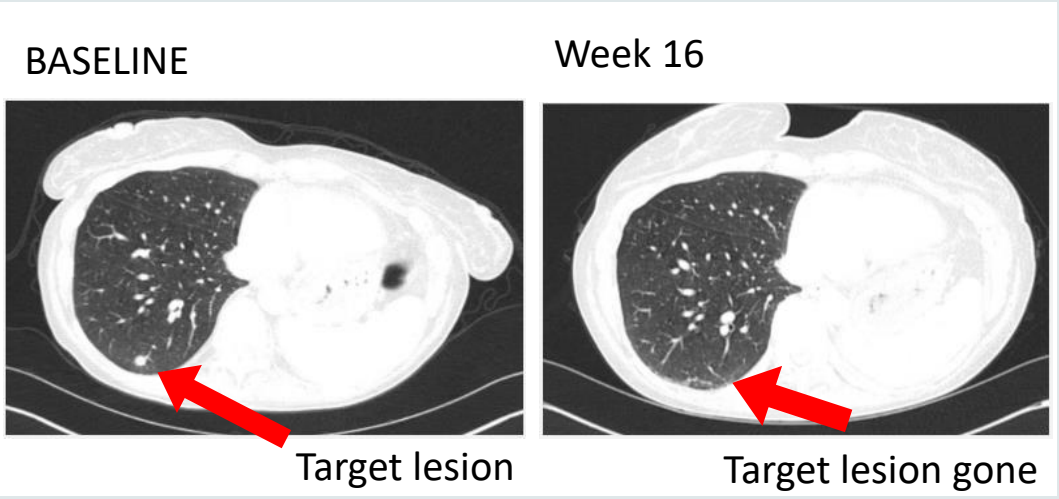
Best Response
- CR Start
- PR Start
- SD Start
- PD
- Treatment ongoing

Data as of 26-Sep-2019

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NC318: SINGLE AGENT ACTIVITY IN PD-1 REFRACTORY NSCLC

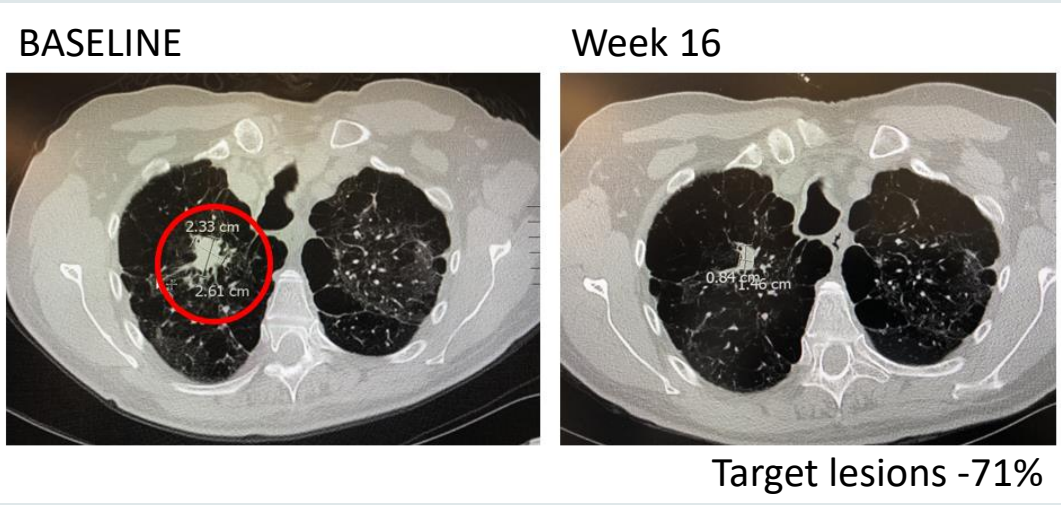
CONFIRMED COMPLETE RESPONSE



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

Prior therapies: Nivolumab (best response stable disease then progression)

CONFIRMED PARTIAL RESPONSE



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

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

CONCLUSIONS FROM PHASE 1 PORTION OF NC318 TRIAL

- NC318 has been well tolerated across multiple dose levels
- Adverse event profile consistent with other approved immunotherapies
- Predictable pharmacokinetic profile
- NC318 has shown encouraging single-agent anti-tumor activity
  - PD-1 refractory NSCLC: 1 CR, 1 PR, and stable disease in 3 patients
  - Durable stable disease (>24 weeks observed in multiple tumor types)
- Phase 2 enrollment underway

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
- Monotherapy
- 400 mg every 2 weeks

DELIVERABLES

Initial Phase 2 data by the end of 2020

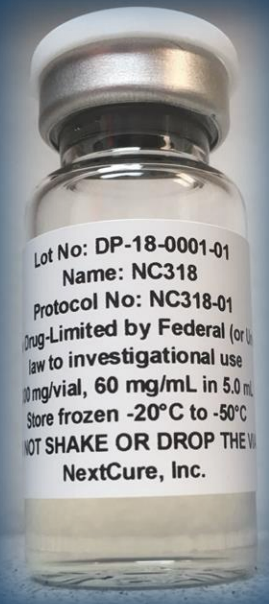
- Angeles Clinic
- MSKCC
- Next Oncology
- NYU
- Yale University

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-γ production
  - Decreased inflammatory cytokines
- ☑ Completed enrollment of Phase 1
- ☑ Reported preliminary data at SITC 2019
- ☐ Initiate Phase 2 combination trial with SOC chemotherapies
- ☐ Report initial Phase 2 data by end of 2020



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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

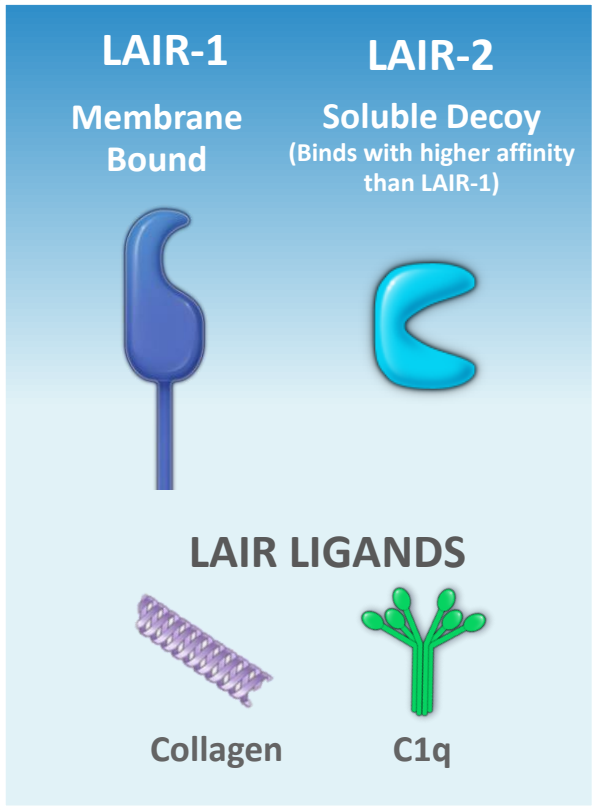
INDICATIONS

Advanced or metastatic solid tumors

LAIR-1 & LAIR-2 FUNCTIONAL RELATIONSHIP

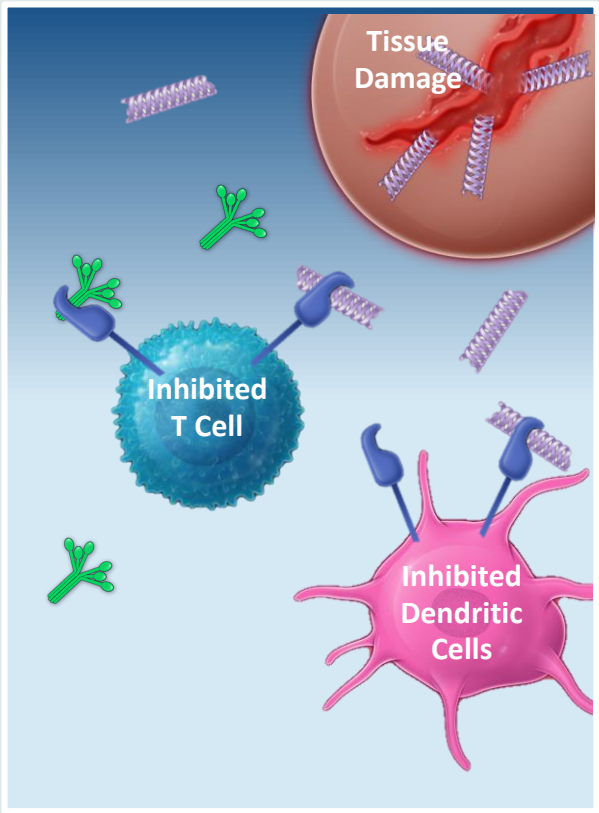
LAIR & LIGANDS

LAIR-1 and LAIR-2 bind collagen and C1q



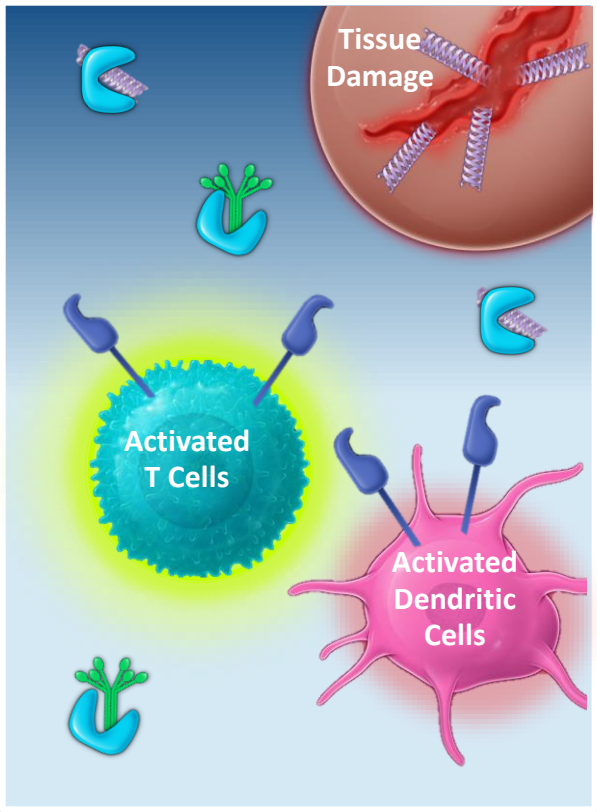
LAIR-1

Ligands are expressed in response to inflammation & inhibit immune function



LAIR-2

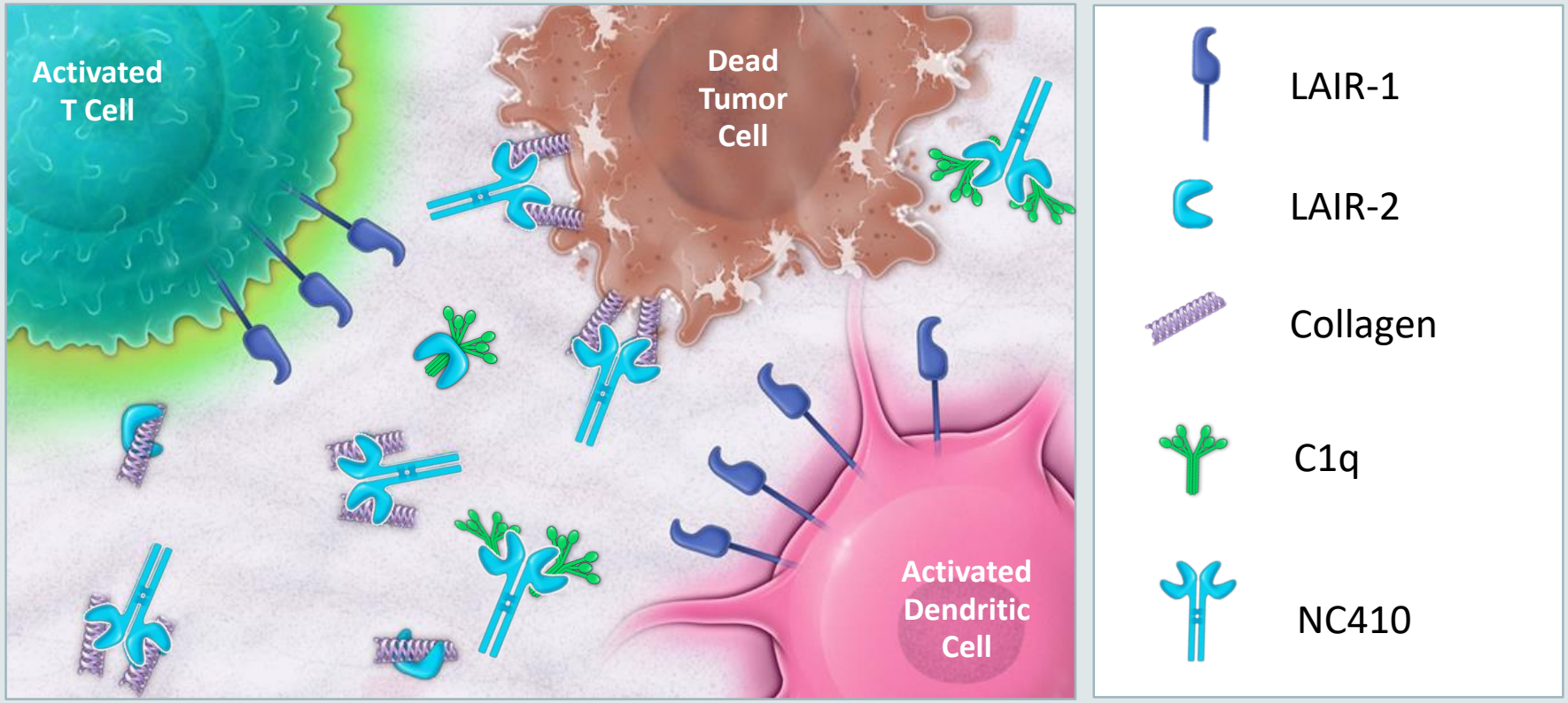
LAIR-2 modulates LAIR-1 mediated inhibition



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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

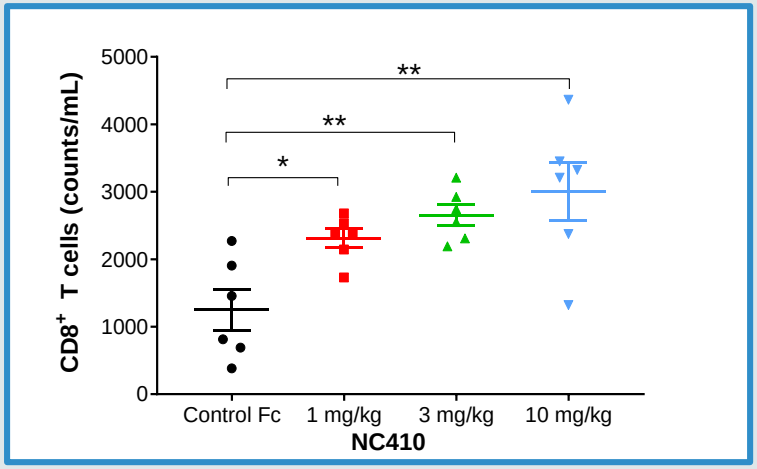


NC410 Promotes T Cell Function and Dendritic Cell Activation

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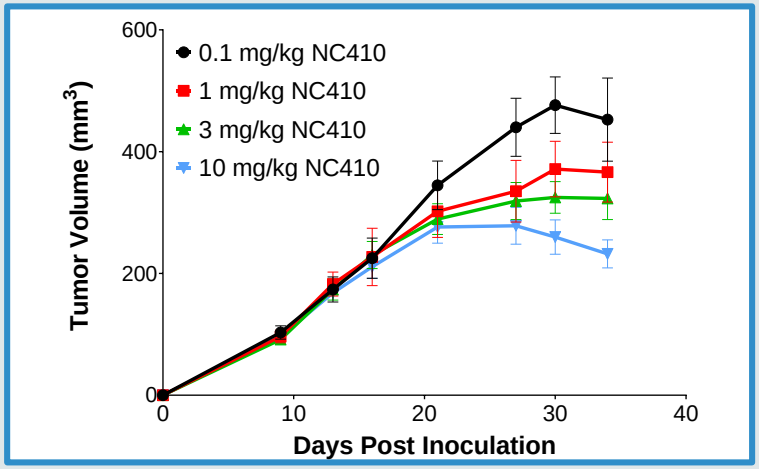
NC410 ENHANCED T CELL EXPANSION AND RELIEVED IMMUNOSUPPRESSION

BLOCKED
Suppression



Human CD8+ T cell expansion *in vivo*

DECREASED
Tumor Volume

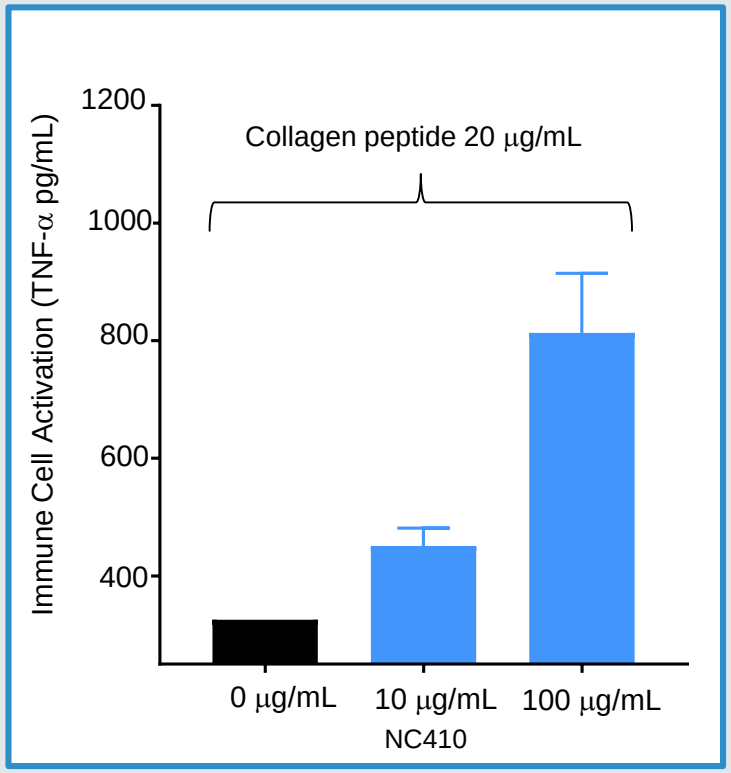


Human PBMCs in mice: CD8+ T cell activity decreased tumor volume in HT29 model

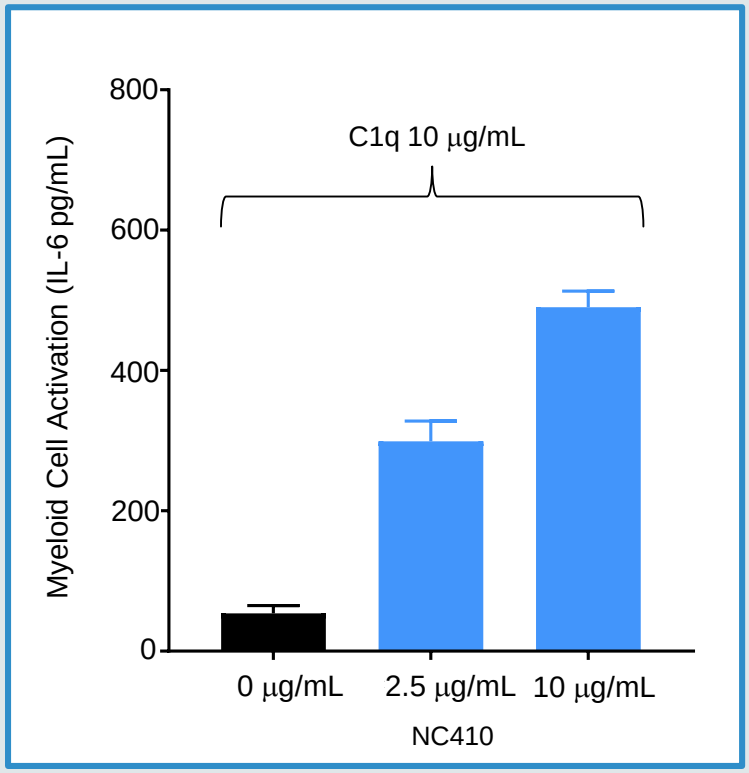
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NC410 PROMOTED IMMUNE CELL ACTIVATION IN THE PRESENCE OF COLLAGEN AND C1Q

REVERSED COLLAGEN SUPPRESSION OF HUMAN PBMCS



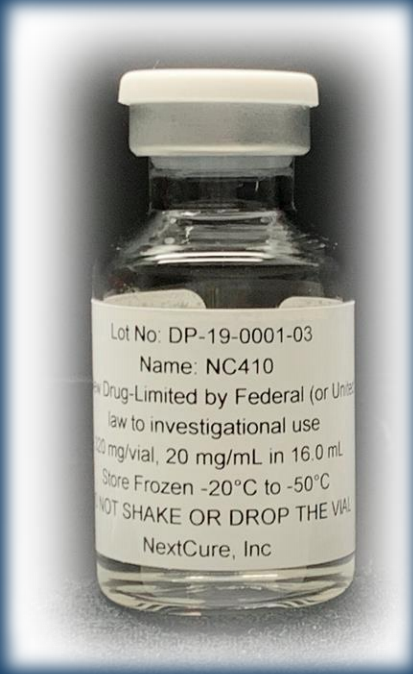
REVERSED C1Q SUPPRESSION OF HUMAN MYELOID CELLS



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



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FINDING SOLUTIONS
WITH A POWERFUL DISCOVERY ENGINE

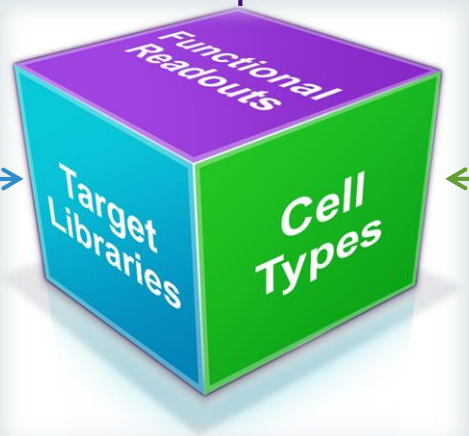
Functional, **I**ntegrated, **N**extCure **D**iscovery in **I**mmuno-**O**ncology

FUNCTIONAL READOUTS

- T cell activation
- Cytokine release
- Proliferation
- Apoptosis
- Effector function
- Pathway reporters

TARGET LIBRARIES

- Membrane proteins
- Soluble proteins
- Small molecules
- Soluble factors



CELL TYPES

- Primary
- Cell lines
- Lymphoid
- Myeloid
- Tumor

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FIND-IO SCREENING METHODOLOGY



TARGET LIBRARY

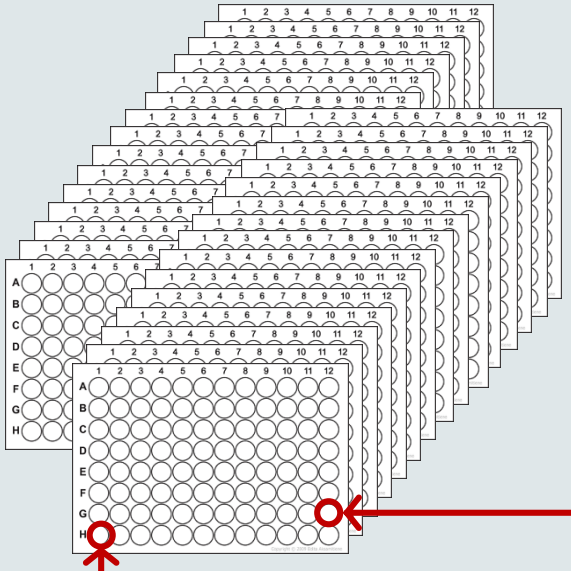
+



HOST CELL

TRANSFECT





One Gene Per Well

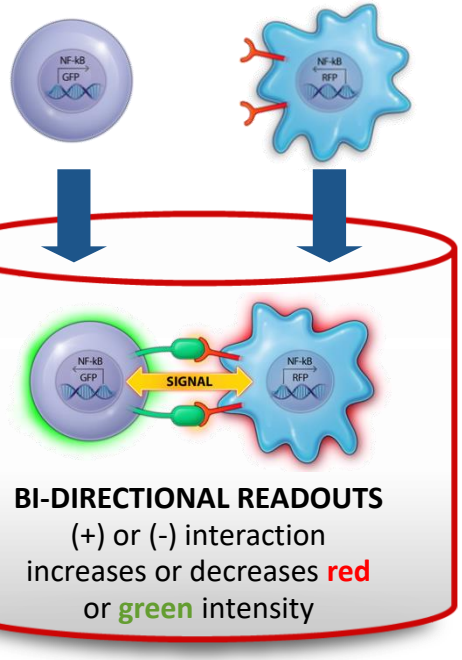
Plasma Membrane Proteins

Secreted Proteins

CELL TYPES

Immune Cell

Host Cell + Target Gene



BI-DIRECTIONAL READOUTS

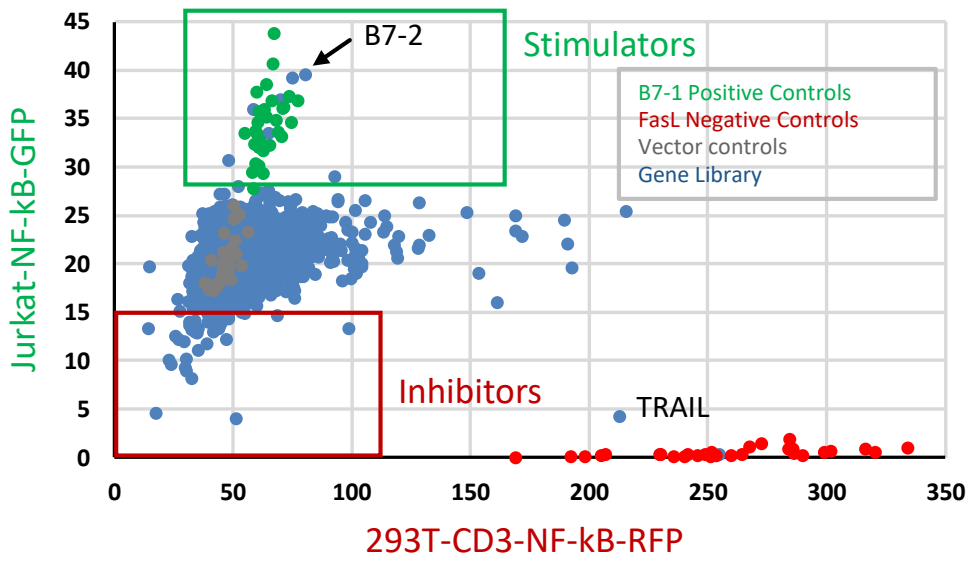
(+) or (-) interaction increases or decreases **red** or **green** intensity

FUNCTIONAL READOUTS

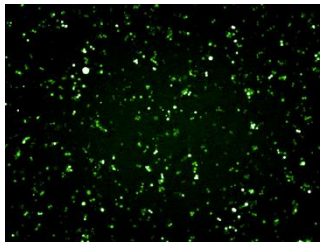
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JURKAT "T CELL LINE" SCREENING AND VALIDATING FIND-IO HITS

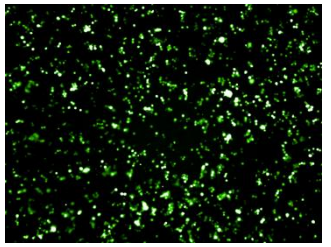
Identified Novel T Cell Stimulators and Inhibitors



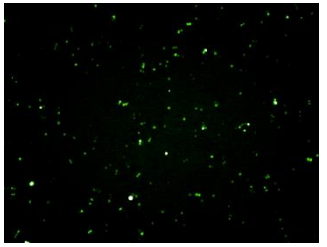
Vector Control



Stimulatory B7-2



Inhibitory TRAIL



REPRODUCIBILITY | **ROBUSTNESS** | **RELEVANCY**

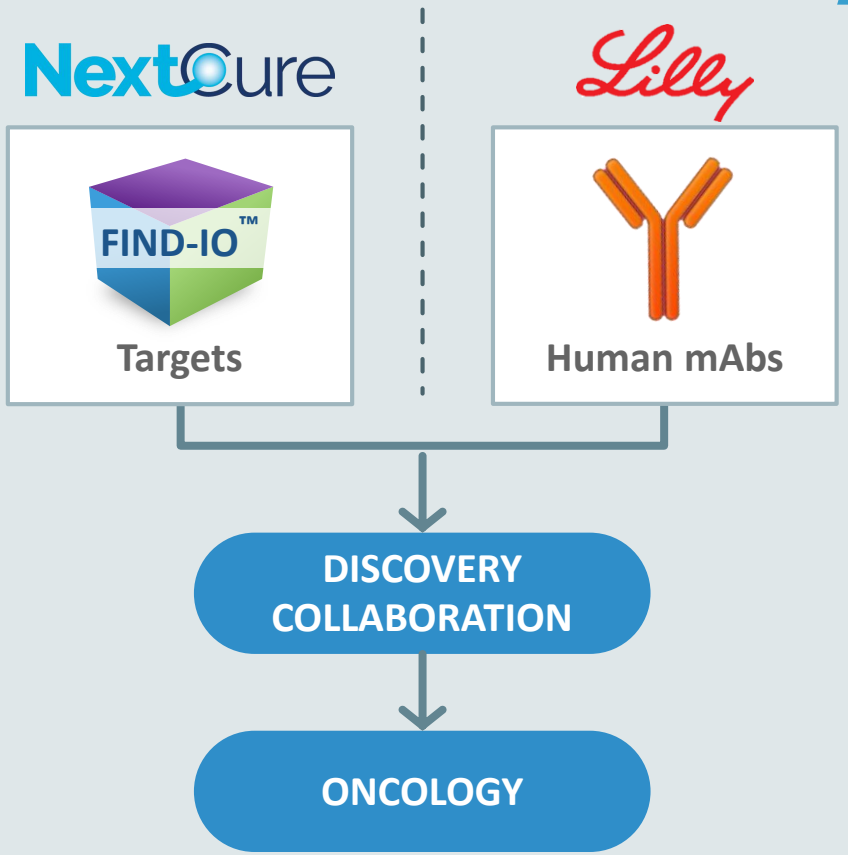
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LILLY – NEXTCURE PARTNERSHIP TO VALIDATE PLATFORM AND APPROACH

Synergies

NextCure — FIND-IO™ — Targets

Lilly — Human mAbs



Overview

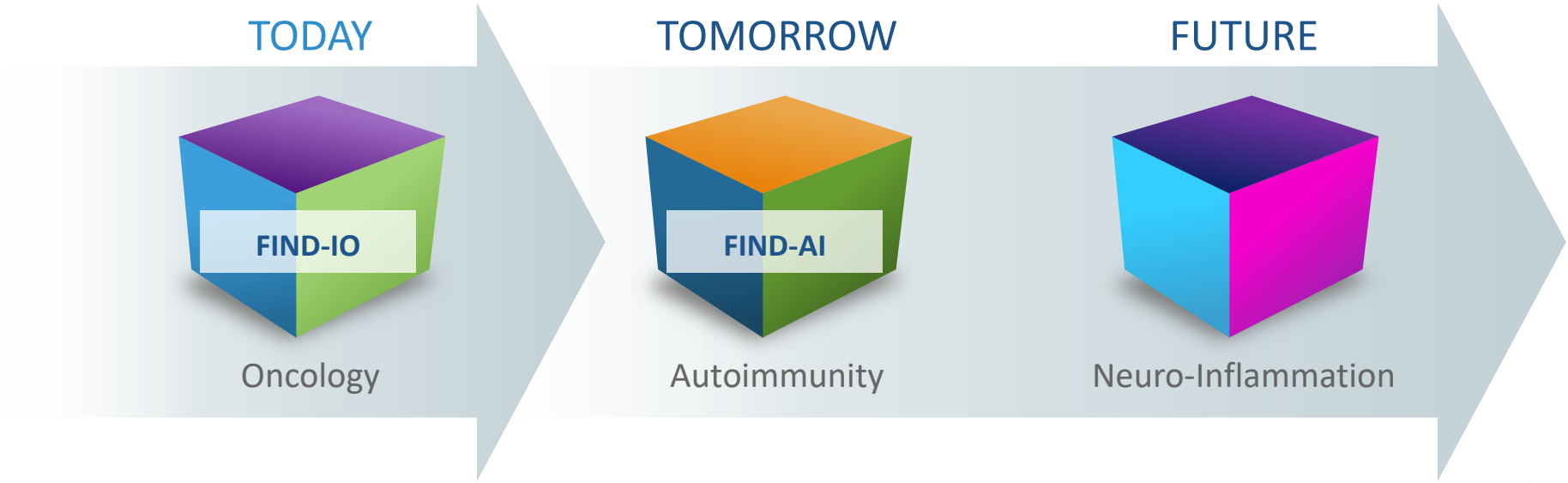
Structure

- 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



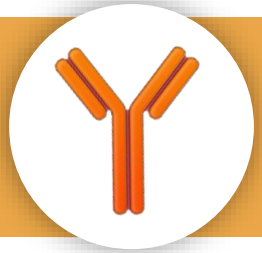
Gene Libraries

Immune Cells

Functional Screening

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ANTICIPATED NEAR-TERM MILESTONES



NC318

- Initiate Phase 2 combination trial with standard of care chemotherapies in 1H 2020
- Report initial Phase 2 data by end of 2020



NC410

File IND and initiate clinical development in Q1 2020



DISCOVERY

Identify novel targets and initiate validation

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

FOCUSED	PROVEN	INNOVATIVE	EXPERIENCED	FUTURE
Approach	Momentum	Platform	Team	Deliverables