



# NextCure

## Corporate Presentation

NASDAQ: NXTC



## Forward-Looking Statement

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. These statements are based on current expectations, forecasts, assumptions and other information available to NextCure as of the date hereof. Forward-looking statements include statements regarding NextCure's expectations, beliefs, intentions or strategies regarding the future and can be identified by forward-looking words such as "may," "will," "potential," "expects," "believes," "intends," "hope," "towards," "forward," "later" and similar expressions. Examples of forward-looking statements in this presentation include, among others, statements about the development plans for our products, statements about the progress and evaluation and expected timing of results of NextCure's ongoing or planned clinical trials, expectations regarding the potential benefits, activity, effectiveness and safety of our research stage, preclinical stage, and clinical stage therapeutic candidates, NextCure's financial guidance, expected upcoming milestones, and NextCure's plans, objectives and intentions with respect to the discovery and development of therapeutic products. Forward-looking statements involve substantial risks and uncertainties that could cause actual results to differ materially from those projected in any forward-looking statement. Such risks and uncertainties include, among others: the impacts of the COVID-19 pandemic on NextCure's business, including NextCure's clinical trials, third parties on which NextCure relies and NextCure's operations; positive results in preclinical studies may not be predictive of the results of clinical trials; NextCure's limited operating history and no products approved for commercial sale; NextCure's history of significant losses; NextCure's need to obtain additional financing; risks related to clinical development, marketing approval and commercialization; the unproven approach to the discovery and development of product candidates based on NextCure's discovery platform; and dependence on key personnel. More detailed information on these and additional factors that could affect NextCure's actual results are described in NextCure's filings with the Securities and Exchange Commission (the "SEC"), including in Item 1A of NextCure's most recent Form 10-K, subsequent Form 10-Q and elsewhere in the Company's filings with the SEC. You should not place undue reliance on any forward-looking statements. Forward-looking statements speak only as of the date of this press release, and NextCure assumes no obligation to update any forward-looking statements, except as required by law, even if expectations change.

## Focus on Two Promising Programs

### NC410 COMBO

- Early Clinical Responses in Ovarian & CRC
- Additional Clinical Data Expected 2024


### LNCB74

- Differentiated B7-H4 ADC
- Collaboration with LigaChem Biosciences
- IND 2024

**~\$86 M - RUNWAY THROUGH 2H 2026**



# Advancing Our Prioritized Programs

PROGRAMS	TARGET	CELLS	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT MILESTONE
NC410 COMBO (Pembro)	LAIR-2	Extracellular Matrix	Ovarian					Ph1b Data 4Q 2024
			Colorectal (CRC)					Ph1b Update 4Q 2024
LNCB74 (ADC) <small>Co-development with</small> 	B7-H4	Tumor Cells	Breast, Ovarian, Endometrial					IND 4Q 2024



**Ovarian**  
CANCER

**PH1B DATA 4Q 2024**



**Colorectal**  
CANCER

**PH1B UPDATE 4Q 2024**

**NC410 COMBO**

**BUILDING ON CLINICAL RESPONSES & BIOMARKER OBSERVATIONS**

## DIFFERENTIATED APPROACH

Remodeling tumor architecture  
removing physical barrier and allowing  
T cells to kill tumors

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## LARGE UNMET NEEDS

Ovarian cancer  
Colorectal cancer

LAIR-2 FUSION

NextCure

NC410 COMBO

Addressing Unmet Needs  
for Non-Responders



## DEEP EXPERTISE

Extracellular matrix collagen drives  
tumor resistance

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## POTENTIALLY FIRST-IN-CLASS

Improved safety profile  
Addresses tumor resistance



## Leader in Understanding *LAIR & Extracellular Matrix (ECM) Biology*



**Regulation of tumor immunity and immunotherapy by the tumor collagen extracellular matrix**



**Cancer immunotherapy by NC410, a LAIR-2 Fc protein blocking human LAIR-collagen interaction**



**Collagen Fragments Produced in Cancer Mediate T Cell Suppression Through Leukocyte-Associated Immunoglobulin-Like Receptor 1**



**A Phase 1b/2, open-label, safety, tolerability and efficacy study of NC410 plus pembrolizumab for participants with immune checkpoint inhibitor (ICI) refractory or MSS/MSI-low ICI naïve advanced or metastatic solid tumors**



**NC410 (LAIR-2-Fc Fusion Protein): Overcoming Clinical Limitations to Immunotherapy Through Targeting and Remodeling Tumor ECM**



**Targeting LAIR-1 abrogates neutrophil-mediated suppression of T cell responses in ovarian cancer microenvironment**



**Remodeling the tumor microenvironment via blockade of LAIR-1 and TGF- $\beta$  signaling enables PD-L1-mediated tumor eradication**

**An Emerging Area of Interest for New Therapies**

# NC410 Combo

Overcoming tumor resistance by remodeling ECM to remove physical barrier and enhance T cell tumor killing



## COMPLETED

- ✓ Safe & well tolerated
- ✓ No dose limiting toxicities
- ✓ Evidence of clinical activity in ovarian & colorectal

## ONGOING

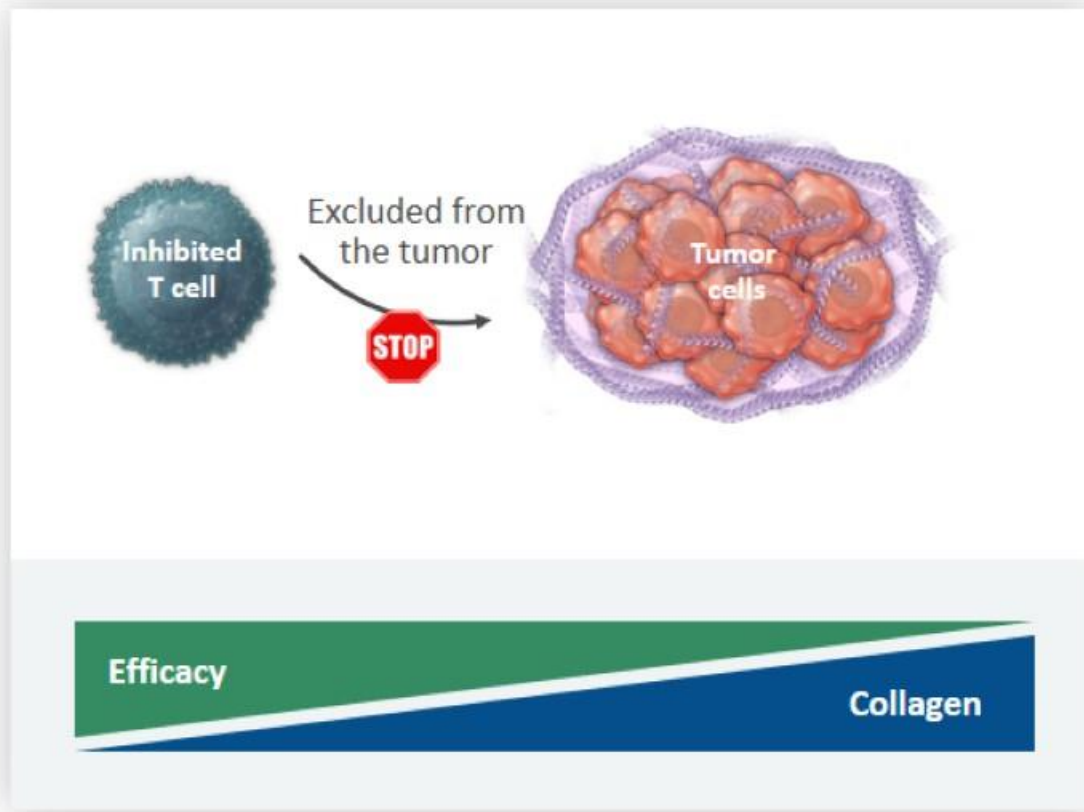
- Expansion of ovarian cohort
- 2024 anticipated data (ovarian n=~25)





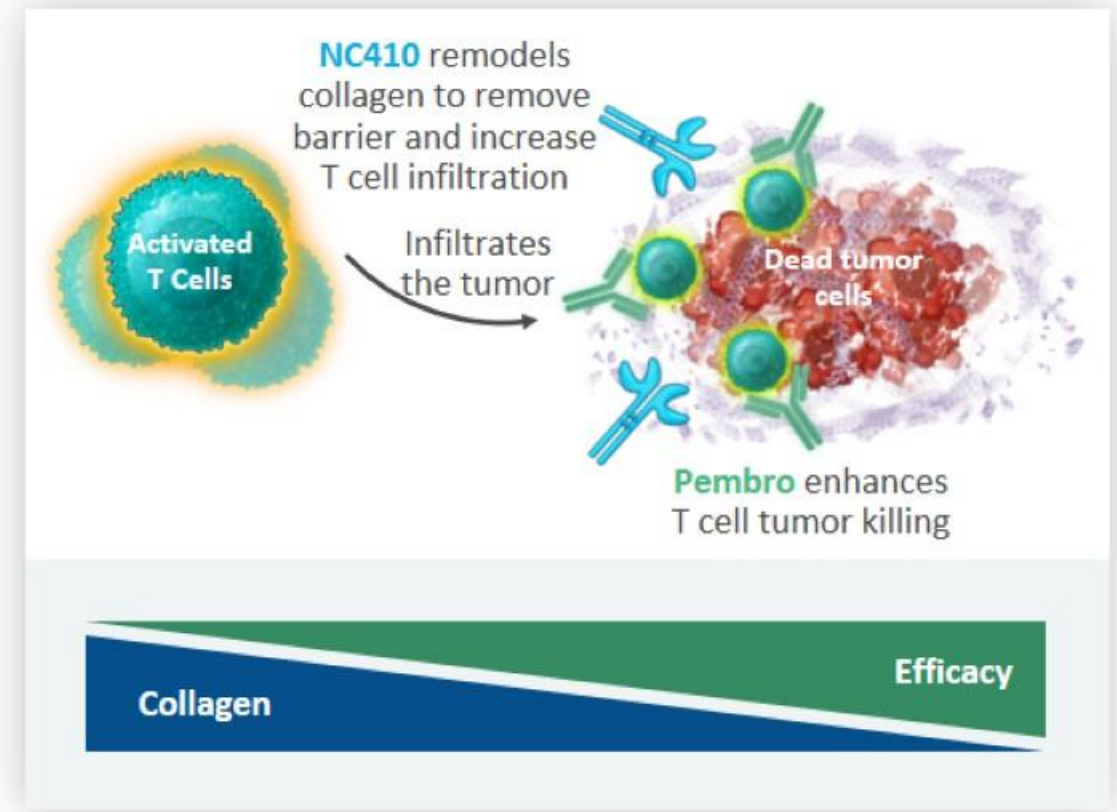
# NC410 Combo: A Synergistic Approach to Breaking the Collagen Barrier and Enhancing Anti-Tumor Activity

COLLAGEN BUILDUP AND DENSITY LEAD TO RESISTANCE



Tumor cells proliferate and become resistant

ECM REMODELING LEADS TO GREATER ANTI-TUMOR FUNCTION



T cells kill the tumor

# NC410 Combo Phase 1 Study



## POPULATION

PD-(L)1 Naïve

## DOSE & REGIMEN

100 mg NC410 Q2W | 200 mg NC410 Q2W  
400 mg pembro Q6W | 400 mg pembro Q6W

## FINDINGS TO DATE

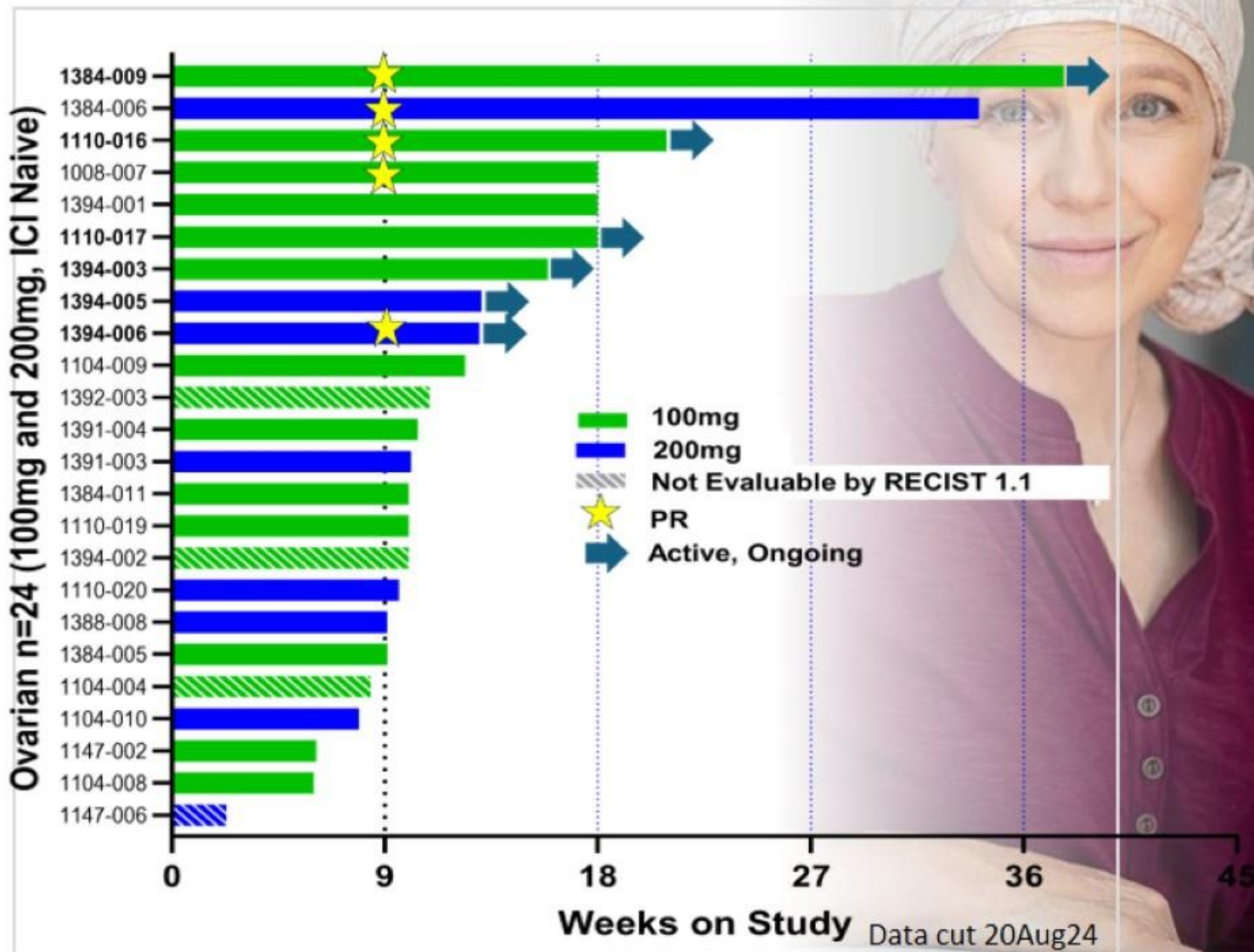
ORR 25% (5/20)  
DCR 50% (10/20)  
Biomarker evidence supporting mechanism of action

## NEXT STEPS

Continue following ongoing patients

## DATA EXPECTED

4Q 2024

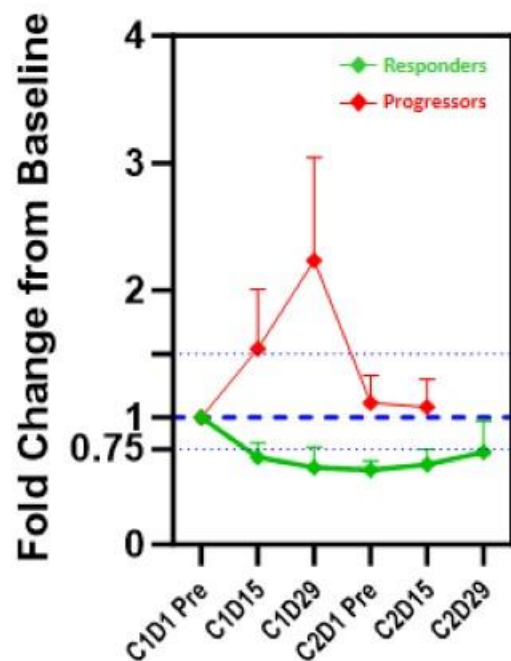




# Evidence of Peripheral Immune Modulation and TME Infiltration in Responders from Ovarian Cohort

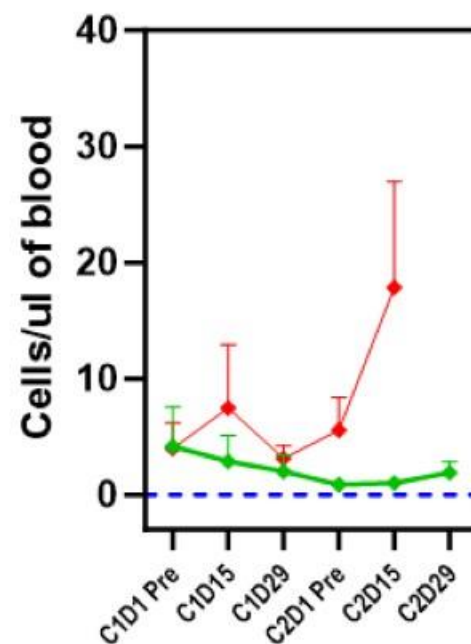
## Decrease *Granzyme B*-expressing *CD8+* T cells

- Remodels ECM allowing effector immune cell infiltration into TME from periphery



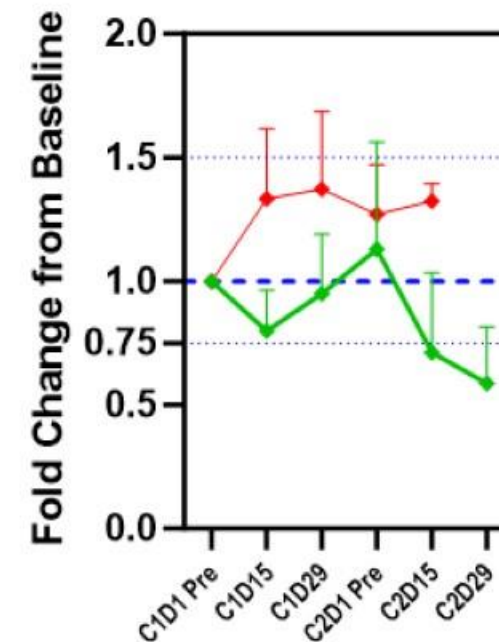
## Decrease suppressive MDSCs

- Reduces suppressive effects
- Enhances activation of immune cells and anti-tumor activity



## Decrease *CCR7+* *CD4+* T cells

- Induces chemokine guided migration of immune cells to TME



# Colorectal CANCER

## NC410 Combo Phase 1 Study

### POPULATION

PD-(L)1 Naïve, MSS/MSI-L\*, without Liver Metastasis

### DOSE & REGIMEN

100 mg NC410 Q2W  
400 mg pembro Q6W

### FINDINGS TO DATE

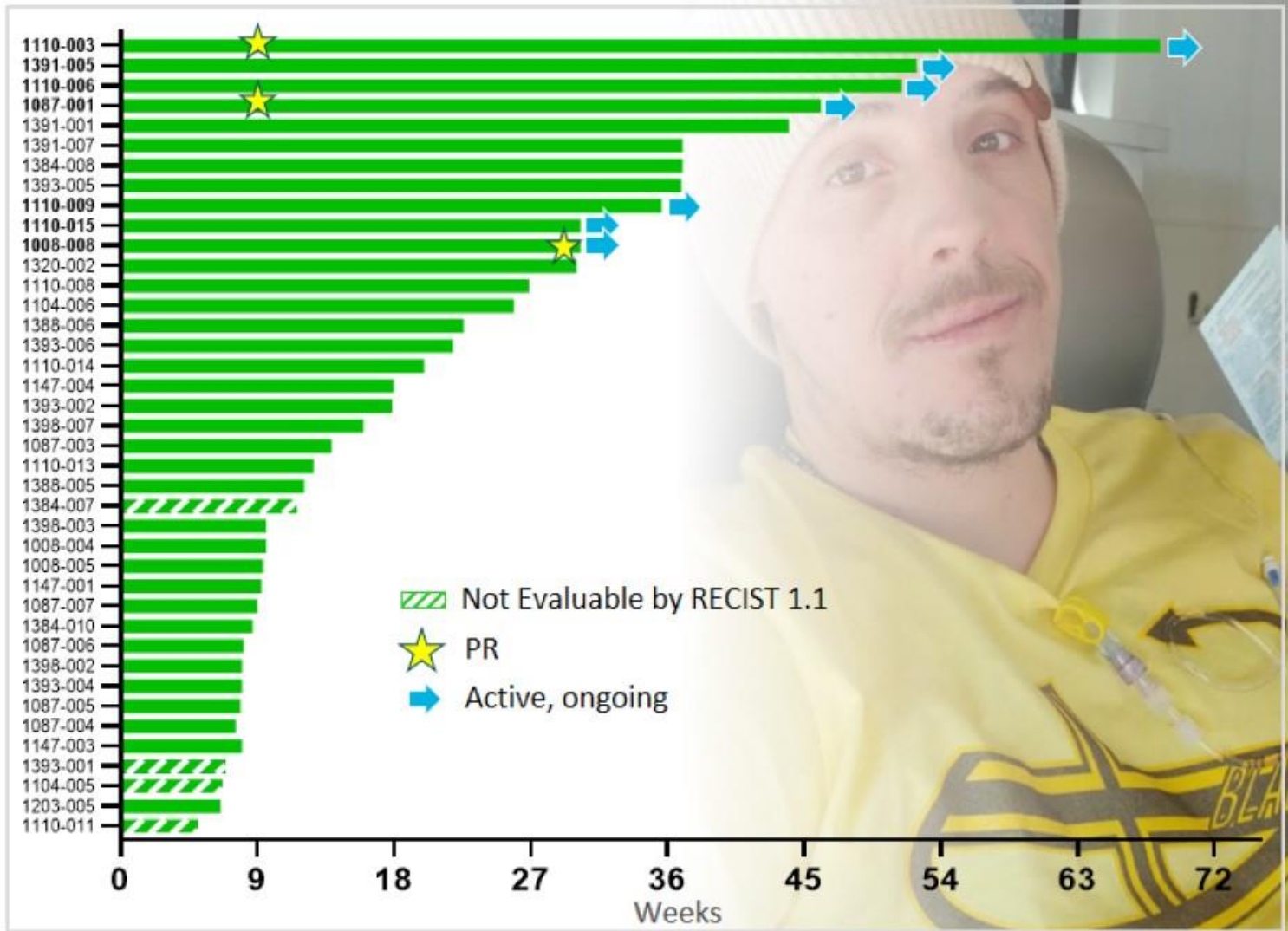
ORR 8.3% (3/36)  
DCR 47% (17/36)  
mPFS 4.1 months

### NEXT STEPS

Continue to follow patients on study

### UPDATE EXPECTED

4Q 2024



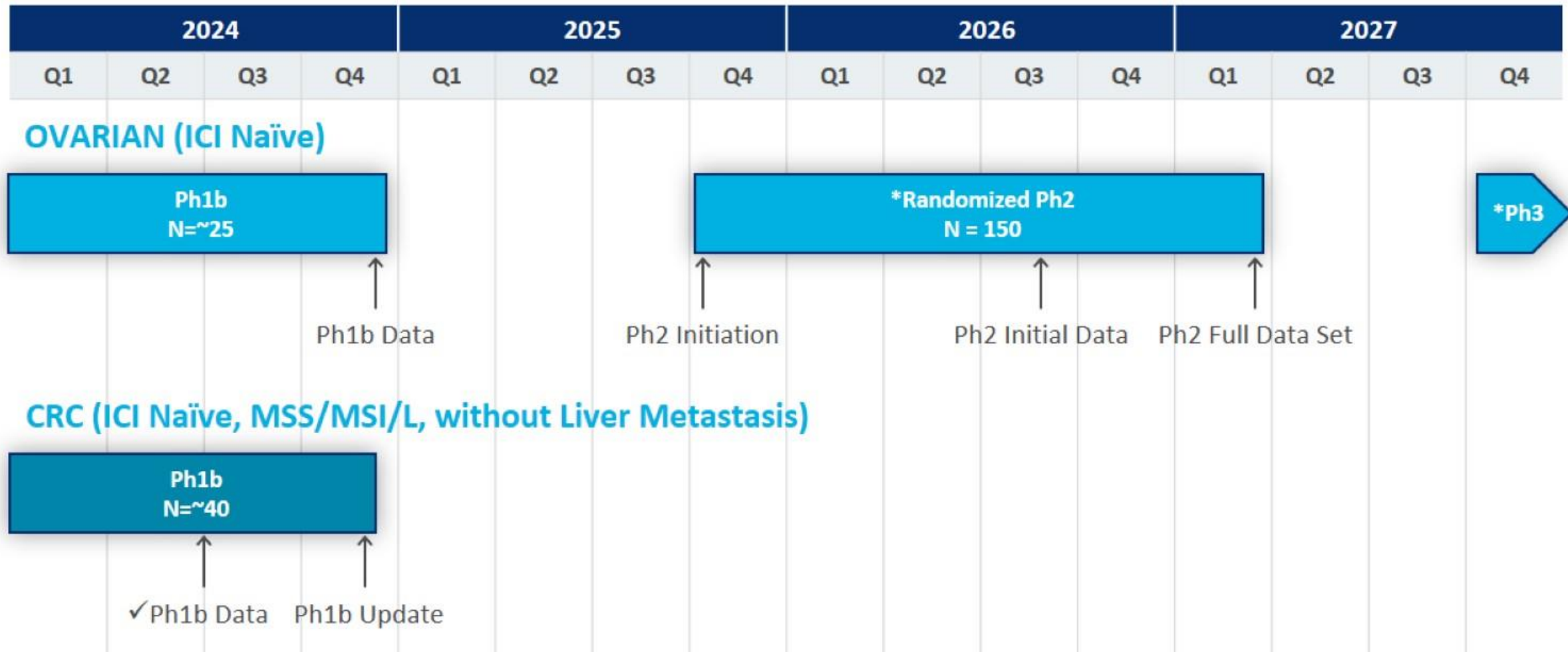
\*Microsatellite stable/microsatellite instability-low

PR – Partial Response  
SD – Stable Disease ≥16 weeks

Data cut 21Aug24



# NC410 Combo Timeline and Potential Catalysts



\*Pending partnership or financing

# Opportunity to Treat Large Unmet Needs



**EARLY CLINICAL  
ACTIVITY**

**ADDITIONAL CLINICAL DATA 2024**





## LNCB74

**LEVERAGING OUR DEEP EXPERTISE IN B7-H4 AND COLLABORATION WITH LCB TO DEVELOP A DIFFERENTIATED THERAPEUTIC**

**IND 4Q 2024**

## NOVEL APPROACH

Unique antibody linker strategy

Co-development partnership  
with LCB

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## PATIENT SELECTION STRATEGY

CLIA validated IHC  
biomarker assays

B7-H4 ADC

NextCure

LNCB74

Differentiated ADC



## DEEP EXPERTISE

Significant B7-H4 experience  
LCB's substantial ADC know-how

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## THERAPEUTIC POSITIONING

Improved safety and efficacy



# B7-H4 is the Next Target of Interest in Women's Cancer



**NextCure, LegoChem\* join big-league rivals in antibody-drug conjugate race**

\*Currently known as LigaChemBio

Journal of  
Clinical  
Oncology\*

Phase 1 study of SGN-B7H4V, a novel, investigational vedotin antibody–drug conjugate directed to B7-H4, in patients with advanced solid tumors (SGNB7H4V-001, trial in progress).

ANNALS of  
ONCOLOGY  
Official journal of the American Society of  
Clinical Oncology

381O First-in-human/phase I trial of HS-20089, a B7-H4 ADC, in patients with advanced solid tumors

Journal of  
Clinical  
Oncology\*

XMT-1660: A phase 1b trial of a B7-H4 targeted antibody drug conjugate (ADC) in breast, endometrial, and ovarian cancers.

ApexOnco  
OncologyPipeline

**Pfizer shuffles its deck post-Seagen**

The group's B7-H4-targeting bispecific is out, in favour of Seagen's ADC.

AAGR  
American Association  
for Cancer Research

Abstract 2947: Preclinical evaluation of a novel B7-H4 targeted antibody-drug conjugate AZD8205 as a single agent and in combination with novel PARP inhibitor and checkpoint blockade



**In 2nd big deal of the day, GSK inks \$1.4B pacy for Hansoh gynecology cancer asset**

## Deep Expertise in B7-H4



NextCure

- Extensive publications
- Expertise in expression
- Repertoire of models
- Top-tier KOL collaborative network
- Validated patient selection assay



LCB  
LigachemBio

- Co-development partner since 2022
- Significant success advancing ADCs
- Differentiated linker technology

Option to Develop Additional Targets



# LNCB74

## On Track for an IND Year-End 2024



### COMPLETED

- ✓ Potent pre-clinical activity *in vitro* and *in vivo*
- ✓ DRF & GLP tox studies – safe and tolerable
- ✓ Favorable pre-IND feedback from FDA

### ONGOING

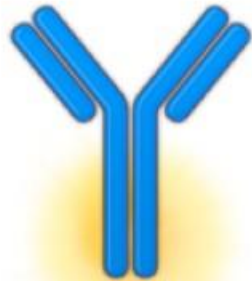
- GMP manufacturing
- Planning for Ph1



# LNCB74 Is an Anti-B7-H4 MMAE ADC

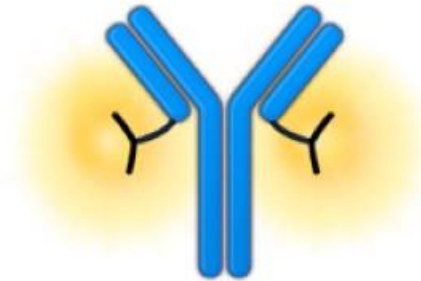
## STRUCTURAL DIFFERENTIATION

Antibody



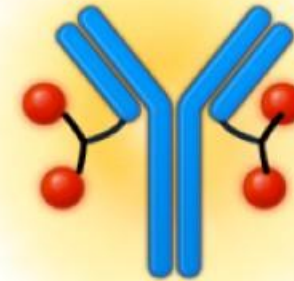
**Fc Modification**  
Protects immune cells

Linker



**Tumor Selectivity**  
Glucuronidase cleavable linker  
provides greater selectivity  
and specificity

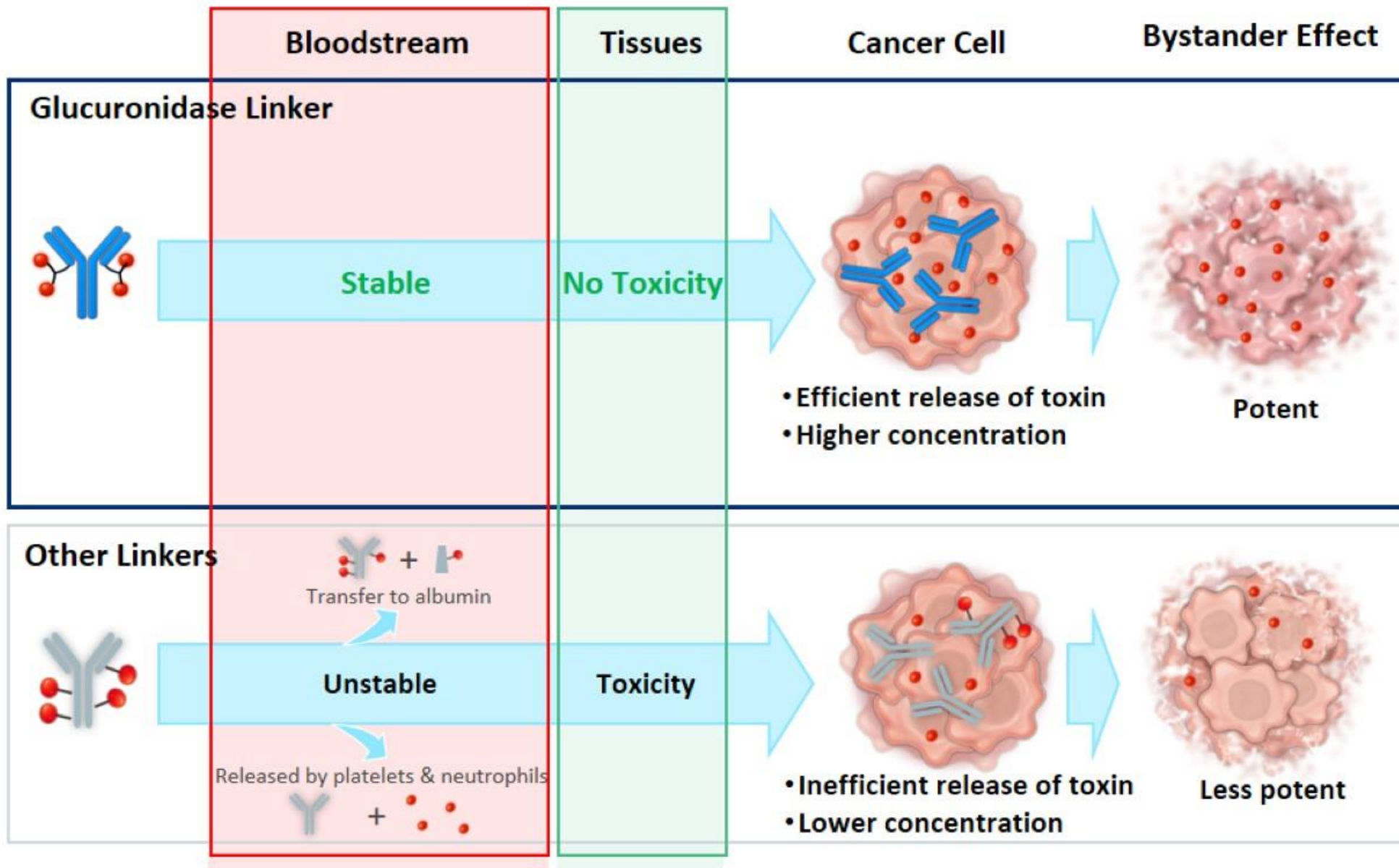
Payload



**MMAE DAR 4**  
Improves safety and control  
over how the payload  
is dispersed



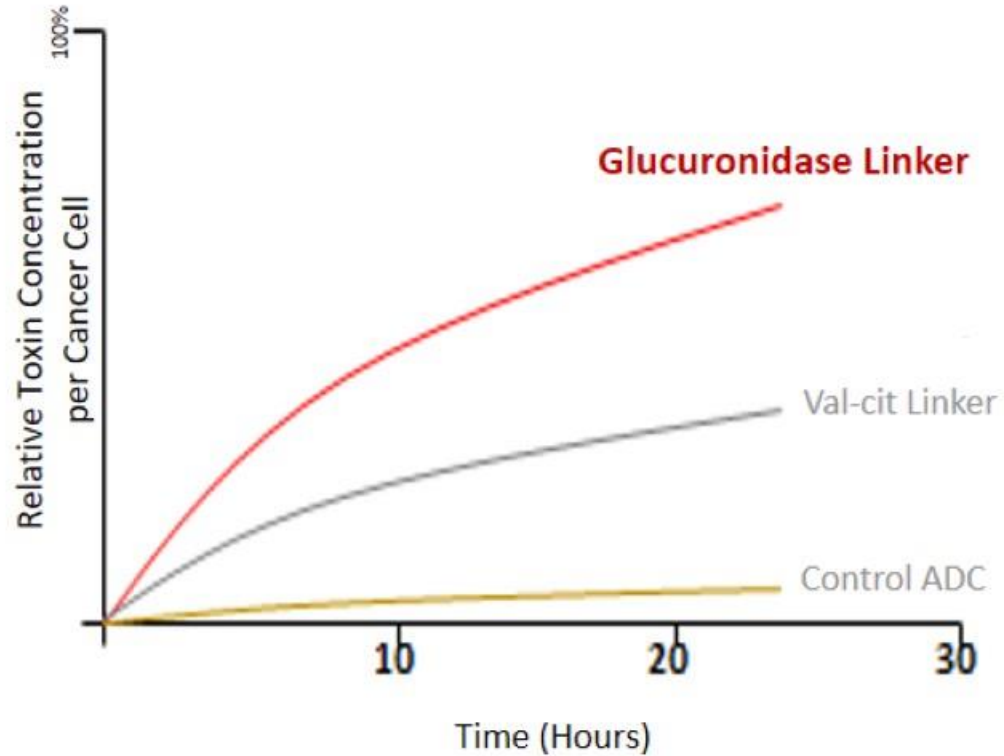
# Differentiating Glucuronidase & Other Linkers



Linker	Glucuronidase cleavable
Payload	Tubulin inhibitor
Conjugation	Site Specific
DAR	4

Linker	Protease or esterase cleavable
Payload	Tubulin or Topo-1 inhibitors
Conjugation	Site Specific or cysteine
DAR	~4, 6, 8

# Key Differentiating Features of Glucuronidase Linkers



## Glucuronidase Linker

- Site specific attachment to mAb
- Highly stable linkage
- Specifically cleaved in cancer cells
- Efficient release of payload
- Higher concentration of toxin per cancer cell

## Val-Cit Linker

- Non-specific attachment to mAb
- Unstable linkage
  - Prone to transferring to albumin
  - Increases toxicity
- Susceptible to cleavage by platelets and neutrophils, increasing toxicity
- Less efficient release of payload
- Lower concentration of toxin per cancer cell

- Improved therapeutic index
- Higher efficacy
- Lower toxicity
- Less frequent dosing

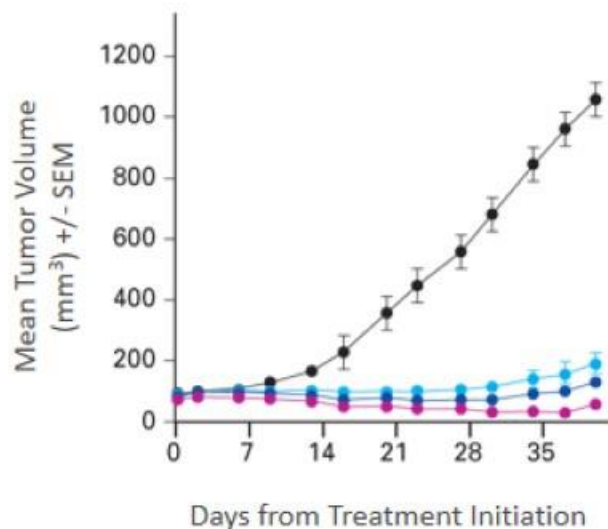


# LNCB74 Shows Potent Anti-Tumor Activity in CDX and PDX Models

## CDX

### BREAST (ZR-75-1)

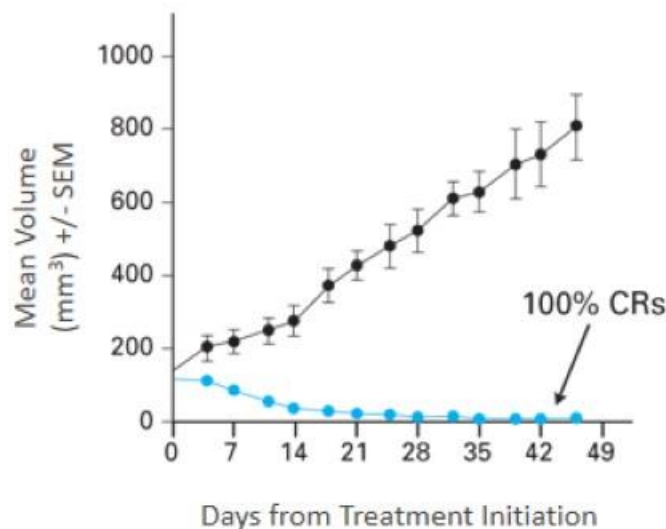
- Vehicle
- LNCB74 (3 mg/kg)
- LNCB74 (1 mg/kg)
- LNCB74 (6 mg/kg)



Q7D x 3

### OVARIAN (OVCAR-3-B7-H4-OE)

- No Treatment
- LNCB74 (6 mg/kg = 0.114 MMAE)

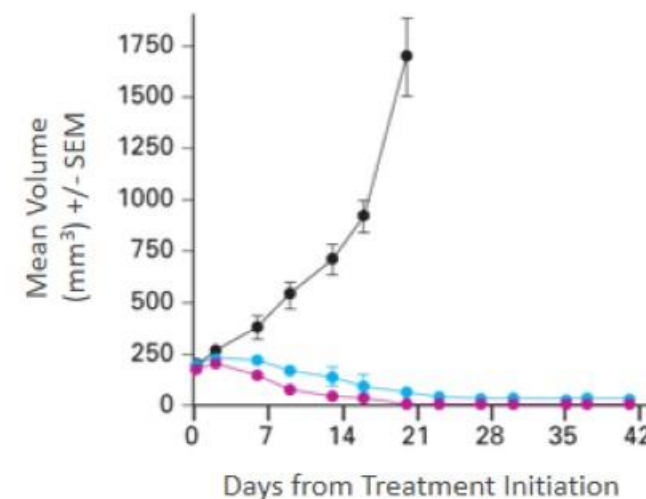


Single dose

## PDX

### TNBC (CTG-0012)

- No Treatment
- LNCB74 (1.5 mg/kg = 0.0275 MMAE)
- LNCB74 (4.5 mg/kg = 0.08 MMAE)



1.5 mg/kg: Q7D x 3  
4.5 mg/kg: single dose

Dosing

## LNCB74 on Track for 4Q 2024 IND

### TOX STUDY

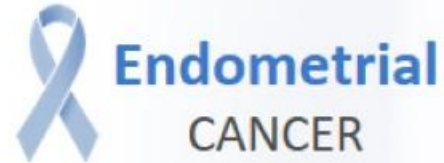
<b>Species</b>	Cynomolgus
<b>Dose Range</b>	4, 7 & 10 mg/kg Q3W, i.v.
<b>Evaluation</b>	Toxicology profiling, pathology, hematology, immunotoxicology
<b>Status</b>	Complete

### GMP MANUFACTURING

- Master cell bank generated
- Process development complete
- Antibody being manufactured
- Drug conjugation



# LNCB74 Ph1 Monotherapy Study Plans



## DOSE ESCALATION

- 5 dose cohorts
- Regimen Q3W
- N=65 subjects



**Readout:** Scans every 6 weeks  
**Endpoint:** Safety

## DOSE EXPANSION

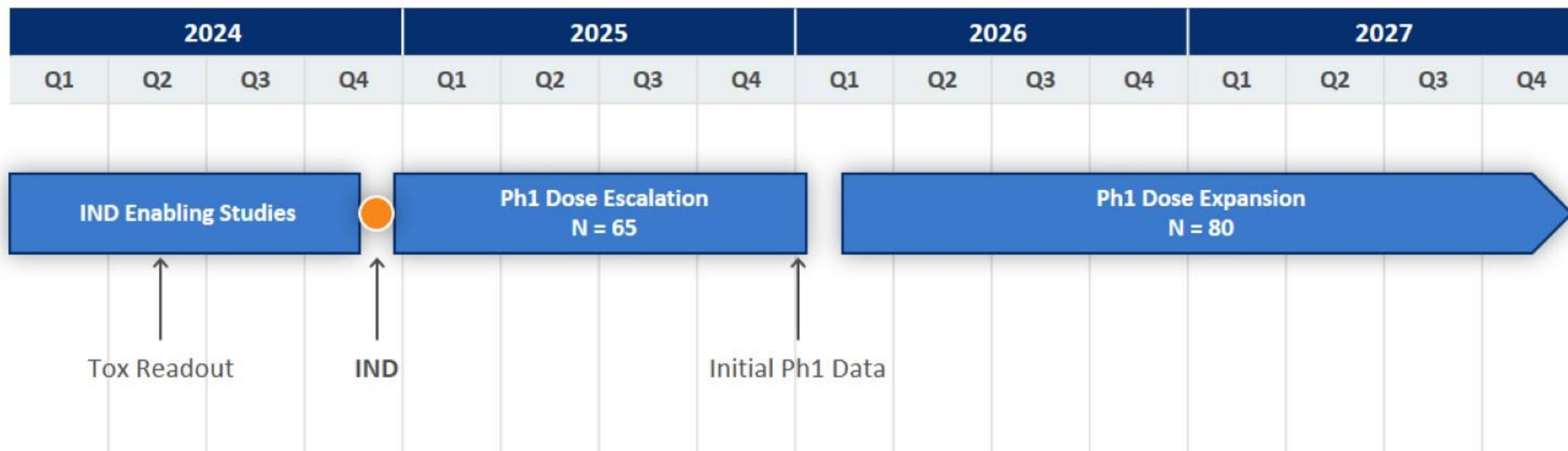
- 2 dose cohorts
- 2 tumor types
- N=80 subjects
- Pre-treatment & on study biopsies



**Readouts:** Scans every 6 weeks  
**Endpoints:** Safety and ORR



# LNCB74 Timeline and Potential Catalysts





# Opportunity to Develop Differentiated B7-H4 ADC Therapeutic



B7-H4 ADC



VALUE CREATION

IND

PH1 INITIATION

## Programs Available for Partnering

PROGRAMS	TARGET	CELLS	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT MILESTONE
NC525	LAIR-1	Leukemia	Acute Myeloid Leukemia					Ph1a Data 4Q 2024
NC605	S15	Osteoclasts	Osteogenesis Imperfecta					Tox Studies
NC181	APOE4	Microglia & Neurons	Alzheimer's Disease					Master Cell Bank
FIND-ADC	New Targets	Tumor Cells	Oncology					Lead Selection



## Anticipated 2024 Milestones

	Q1	Q2	Q3	Q4
NC410 Combo Ovarian				Ph1b Data
CRC		✓ Ph1b Data		Ph1b Update
LNCB74				IND Filing

# NextCure

## Advancing Innovative Medicines for Cancer



Differentiated  
Programs

ADCs

Treatments for  
Non-Responders



The logo for NextCure, featuring the word "Next" in blue and "Cure" in white, with a blue circle around the letter "C".

**NextCure**

**APPENDIX**

# 1087-001 CRC: Partial Response

## 71% Reduction in Sum of Target Lesions

BASELINE – 9.15.2023

WEEK 9 – 11.20.2023

WEEK 18 – 1.19.2024

**TARGET  
LESION 1**Right Axillary  
lymph node**TARGET  
LESION 2**Right Pelvic  
lymph node



# 1110-003 CRC: Partial Response

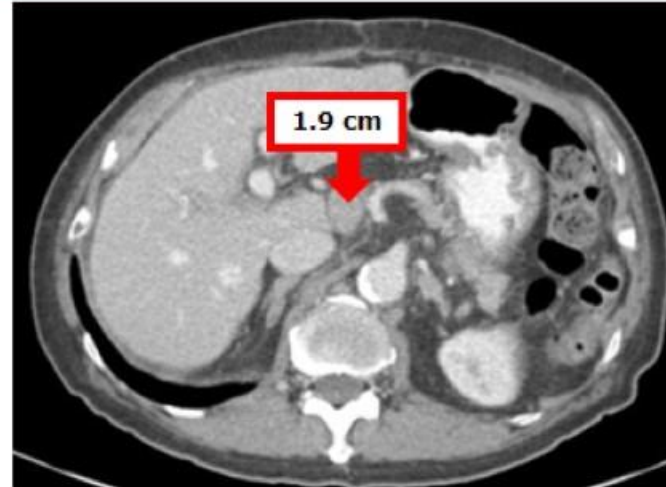
## 59% Reduction in Sum of Target Lesions

BASELINE – 4.8.2023

WEEK 9 – 6.20.2023

### TARGET LESION 1

Gastrohepatic lymph node



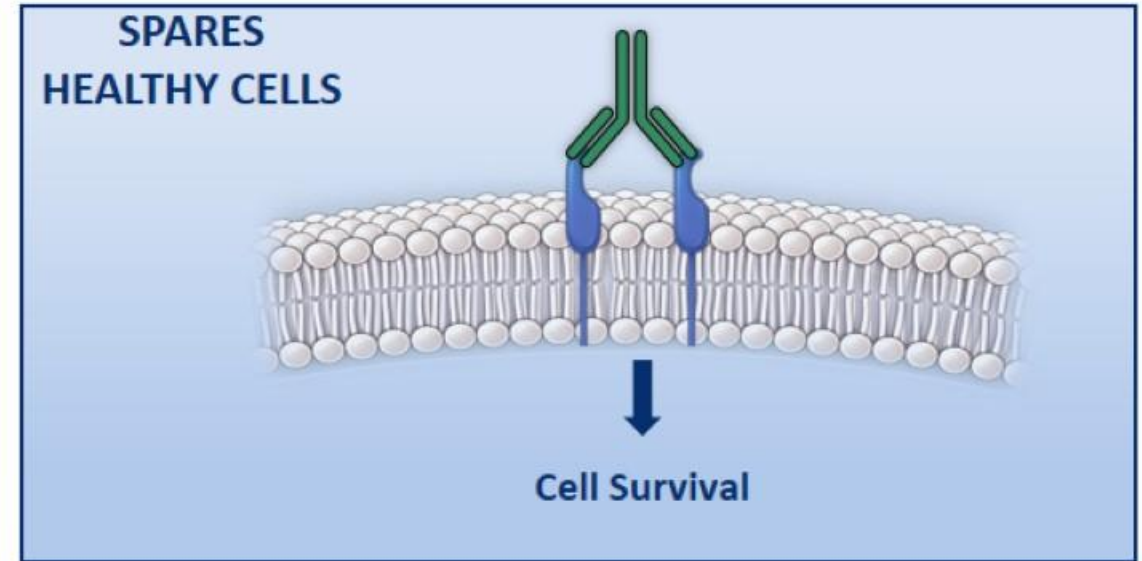
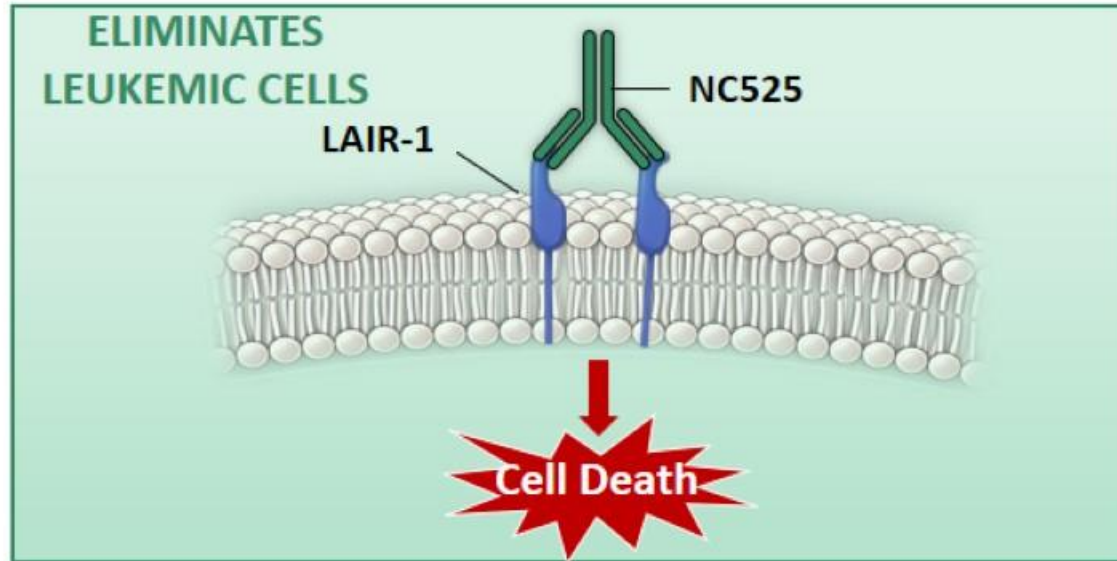
### TARGET LESION 2

Paraaortic lymph node



# NC525

## LAIR-1 MAB



- LAIR-1 is essential for AML development and cell survival
- Data defining MOA recently published (Lovewell RR et al., J Clin Invest 2023)

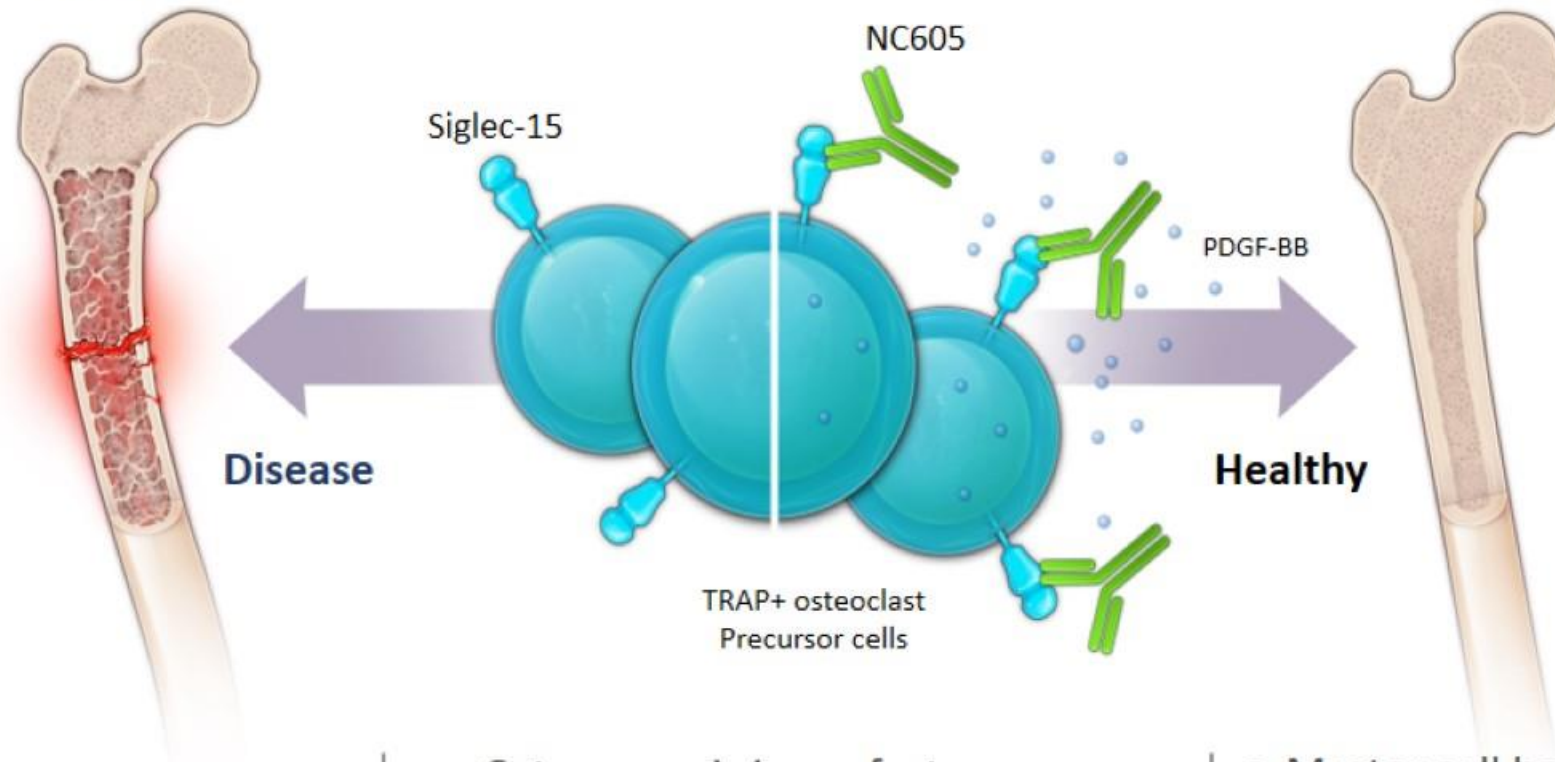
- Leukemia (AML)
- High-risk myelodysplastic syndrome
- Chronic myelomonocytic leukemia

- Ph1 dose escalation study ongoing
- Phase 1a data 4Q 2024
- Currently seeking partner



# NC605

## SIGLEC-15 MAB



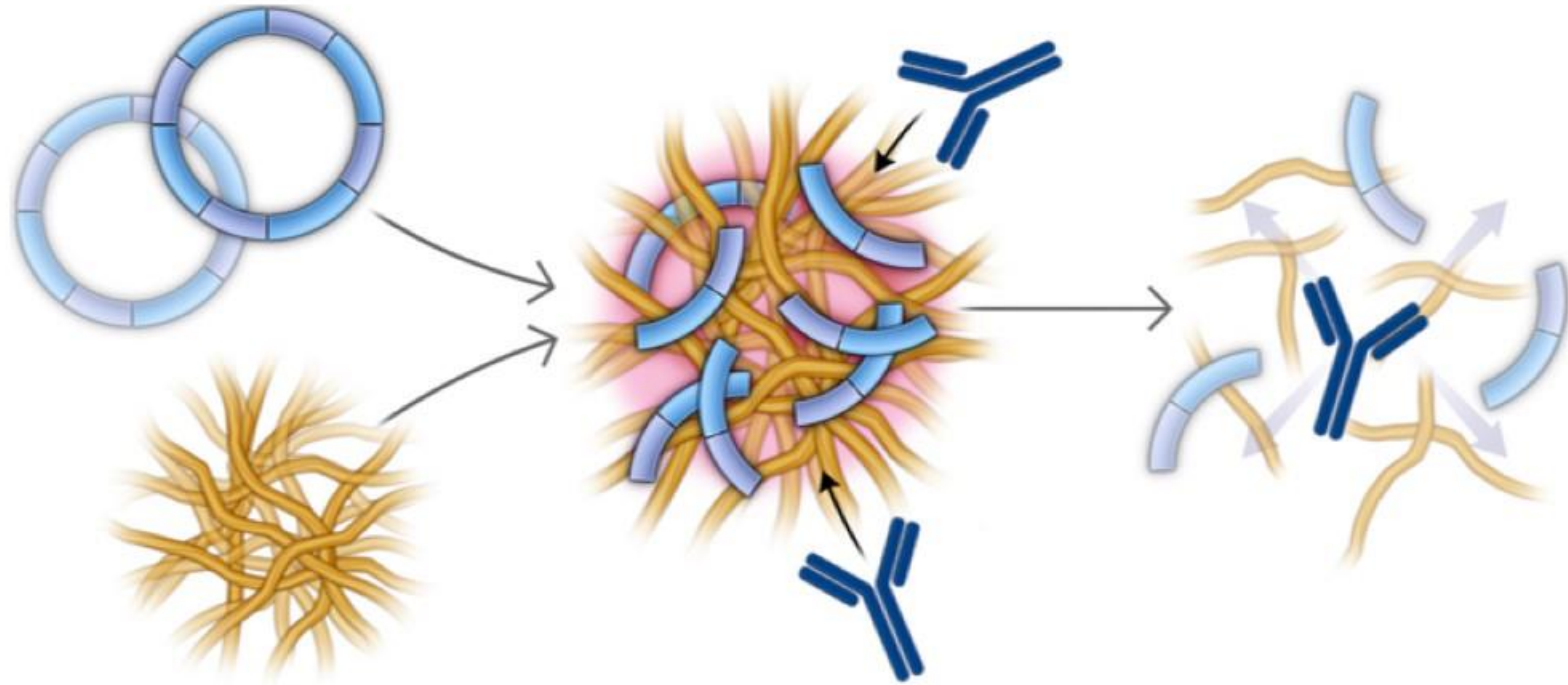
- Prevents bone loss
- Promotes bone formation
- Decreases fractures

- Osteogenesis imperfecta
- Osteoporosis
- Non-union fracture

- Master cell bank available
- Initiating tox studies
- Currently seeking partner

# NC181

## APOE4 MAB



- Reduces amyloid plaques
- Suppresses neuroinflammation
- Improves cerebrovascular function

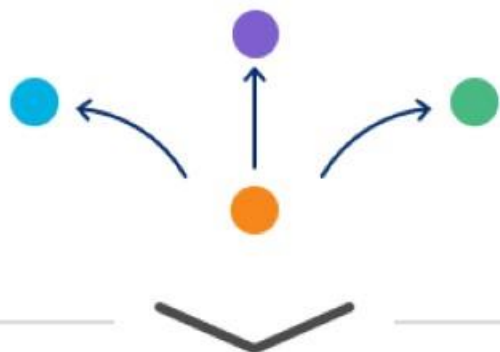
- Alzheimer's disease
- Cerebral amyloid angiopathy (CAA)
- Parkinson's disease

- Master cell bank being generated
- Currently seeking partner



# FIND-ADC™ Technology Uniquely Unlocks New Targets for ADCs

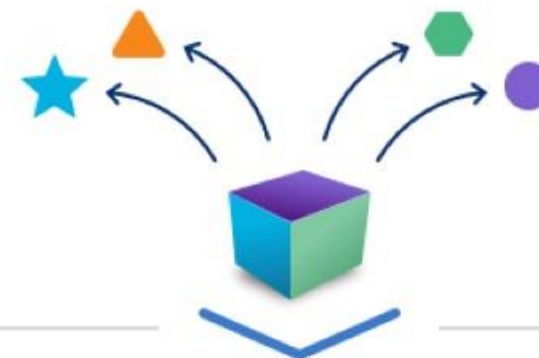
## TRADITIONAL DISCOVERY



Incremental payload and linker improvements to the **same pool of existing targets** (HER2, EGFR, FR $\alpha$ , TROP-2, CLDN18.2, BCMA, CD19)

## NextCure

## FIND-ADC



**Identifying new targets** for ADCs that unlock novel products and value