NextCure

DECEMBER 2024

Corporate Presentation

NASDAQ: NXTC

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Value-Driven ADC Opportunity

SIGNIFICANT OPPORTUNITY

- Antibody-drug conjugate targeting B7-H4
- Differentiated linker for improved safety and increased efficacy
- Completed GLP tox study and GMP manufacturing for Ph 1 trial

2024-2025 DELIVERABLES

- IND submitted Q4 2024
- Breast, endometrial and ovarian cancers
- FIH expected in Q1 2025

RUNWAY

- Balance sheet, ~$75 M, end of Q3
- Runway 2H 2026

Breast CANCER

Ovarian CANCER

Endometrial CANCER

LNCB74

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

Focused on a Clinically Validated Target with High Unmet Need

PROGRAMS	TARGET	CELLS	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	ANTICIPATED MILESTONES
LNCB74 (ADC) Co-development with LCB LigaChemBio	B7-H4	Tumor Cells	**Breast, Ovarian, Endometrial**					**FIH Q1 2025**

NOVEL APPROACH

Unique antibody linker strategy

Co-development partnership with LCB

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

THERAPEUTIC POSITIONING

Improved safety and efficacy

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

FIERCE Biotech

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

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.

AACR 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

FIERCE Biotech

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 & cost-sharing
- Significant success advancing ADCs
- Differentiated linker technology

LNCB74
Initiation of Phase 1

COMPLETED

- ✓ Potent pre-clinical activity *in vitro* and *in vivo*
- ✓ DRF & GLP tox studies – favorable safety and tolerability profile
- ✓ Favorable pre-IND feedback from FDA
- ✓ GMP manufacturing
- ✓ IND filing

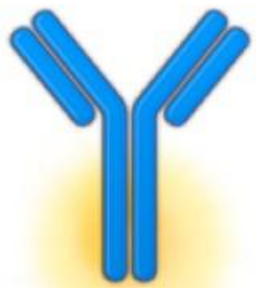
ONGOING

- Planning for Ph1 initiation

LNCB74 Is an Anti-B7-H4 MMAE ADC

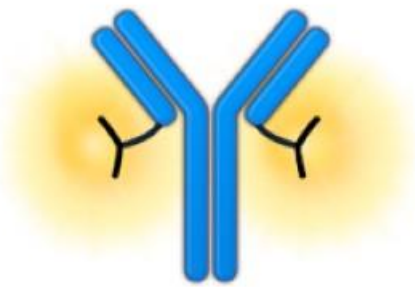
STRUCTURAL DIFFERENTIATION

Antibody



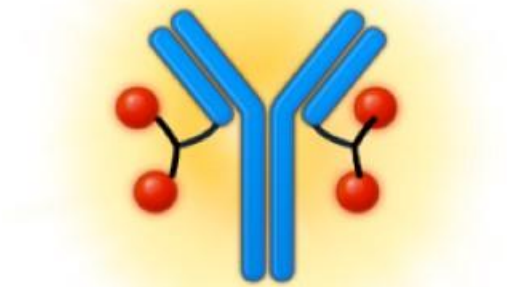
Fc Modification
Protects immune cells

Linker



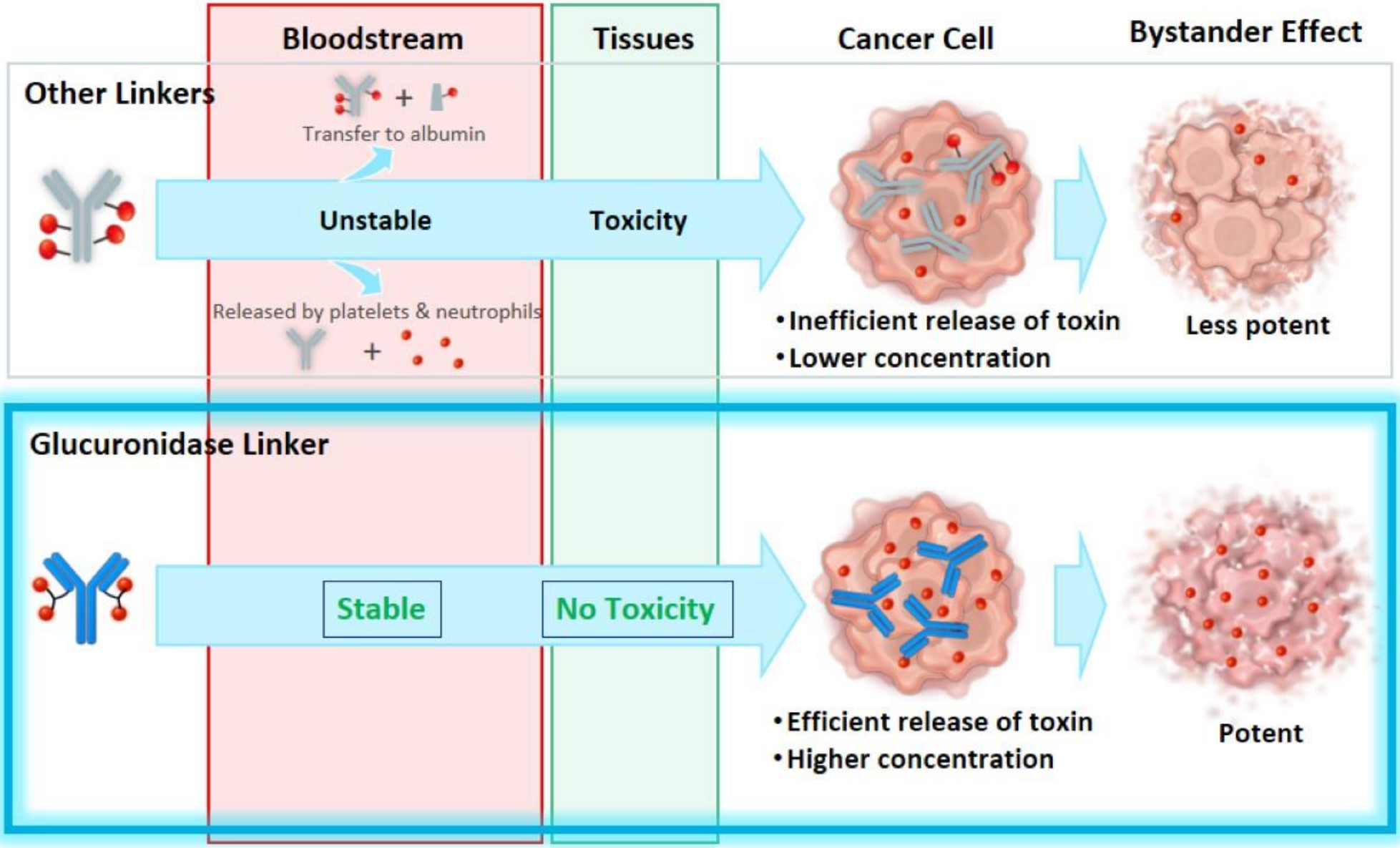
Tumor Selectivity
Glucuronidase cleavable linker provides greater selectivity and specificity

Payload



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

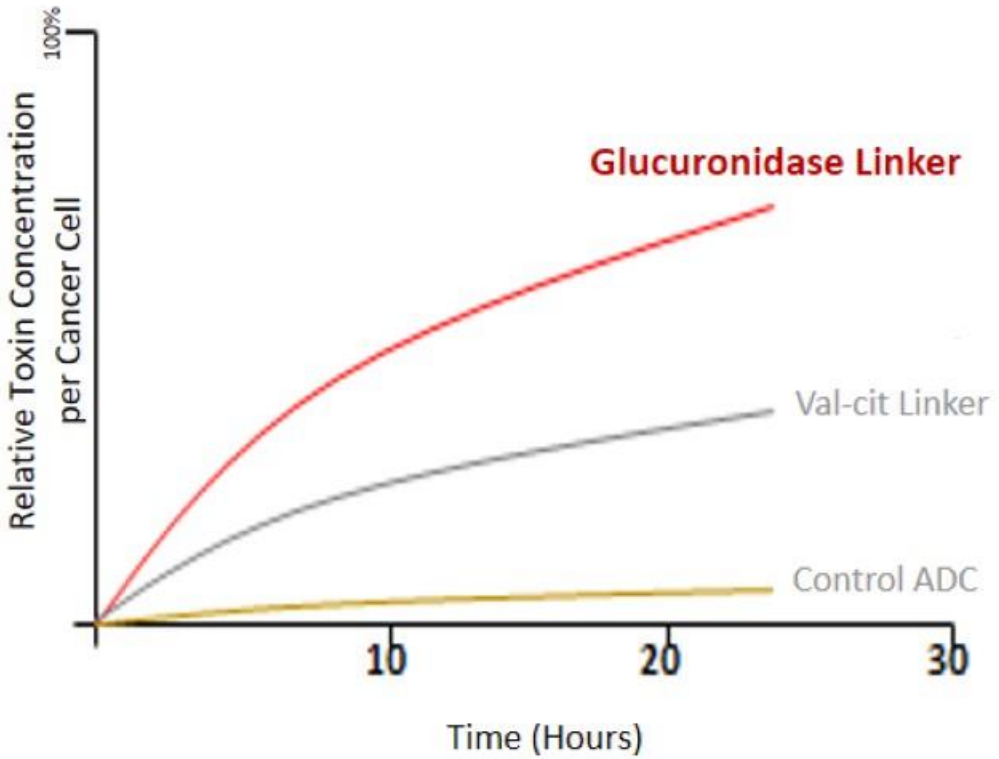
LNCB74 Uses Differentiating Glucuronidase Linker for Potentially Improved Safety & Efficacy



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

Linker	Glucuronidase cleavable
Payload	Tubulin inhibitor
Conjugation	Site Specific
DAR	4

Key Differentiating Features of Glucuronidase Linkers



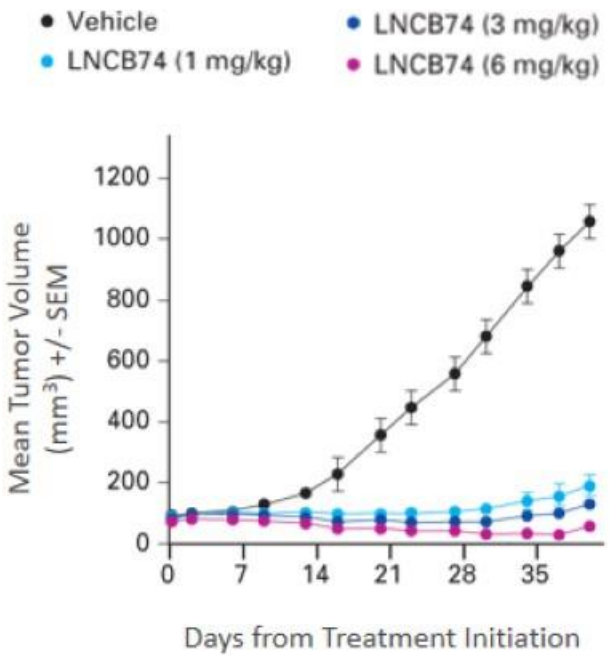
Glucuronidase Linker	Val-Cit Linker
☑ Site specific attachment to mAb	☐ Non-specific attachment to mAb
☑ Highly stable linkage	☐ Unstable linkage – Prone to transferring to albumin – Increases toxicity
☑ Specifically cleaved in cancer cells	☐ Susceptible to cleavage by platelets and neutrophils, increasing toxicity
☑ Efficient release of payload	☐ Less efficient release of payload
☑ Higher concentration of toxin per cancer cell	☐ Lower concentration of toxin per cancer cell

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

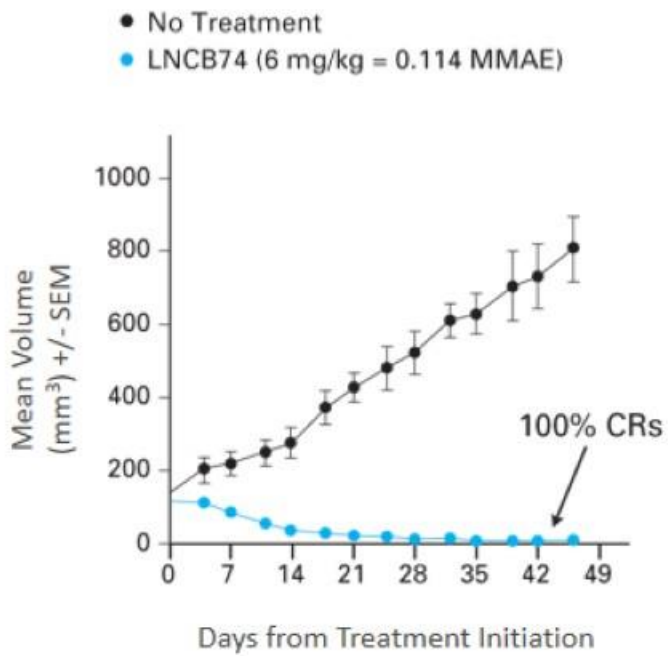
LNCB74 Shows Potent Anti-Tumor Activity in CDX and PDX Models

CDX

BREAST (ZR-75-1)

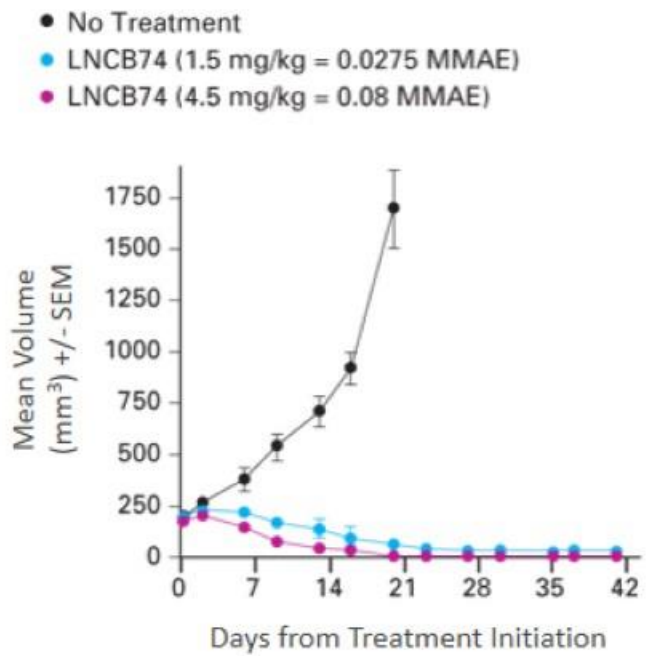


OVARIAN (OVCAR-3-B7-H4-OE)



PDX

TNBC (CTG-0012)

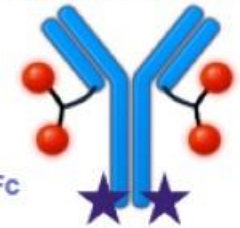


Dosing	Q7D x 3	Single dose	1.5 mg/kg: Q7D x 3 4.5 mg/kg: single dose

LNCB74 is More Effective than Comparator B7-H4-MMAE

LNCB74 (B7-H4 ADC)

LCB site-specific conjugation
[GUSB-cleavable, light-chain linker]



MMAE payload (DAR4)

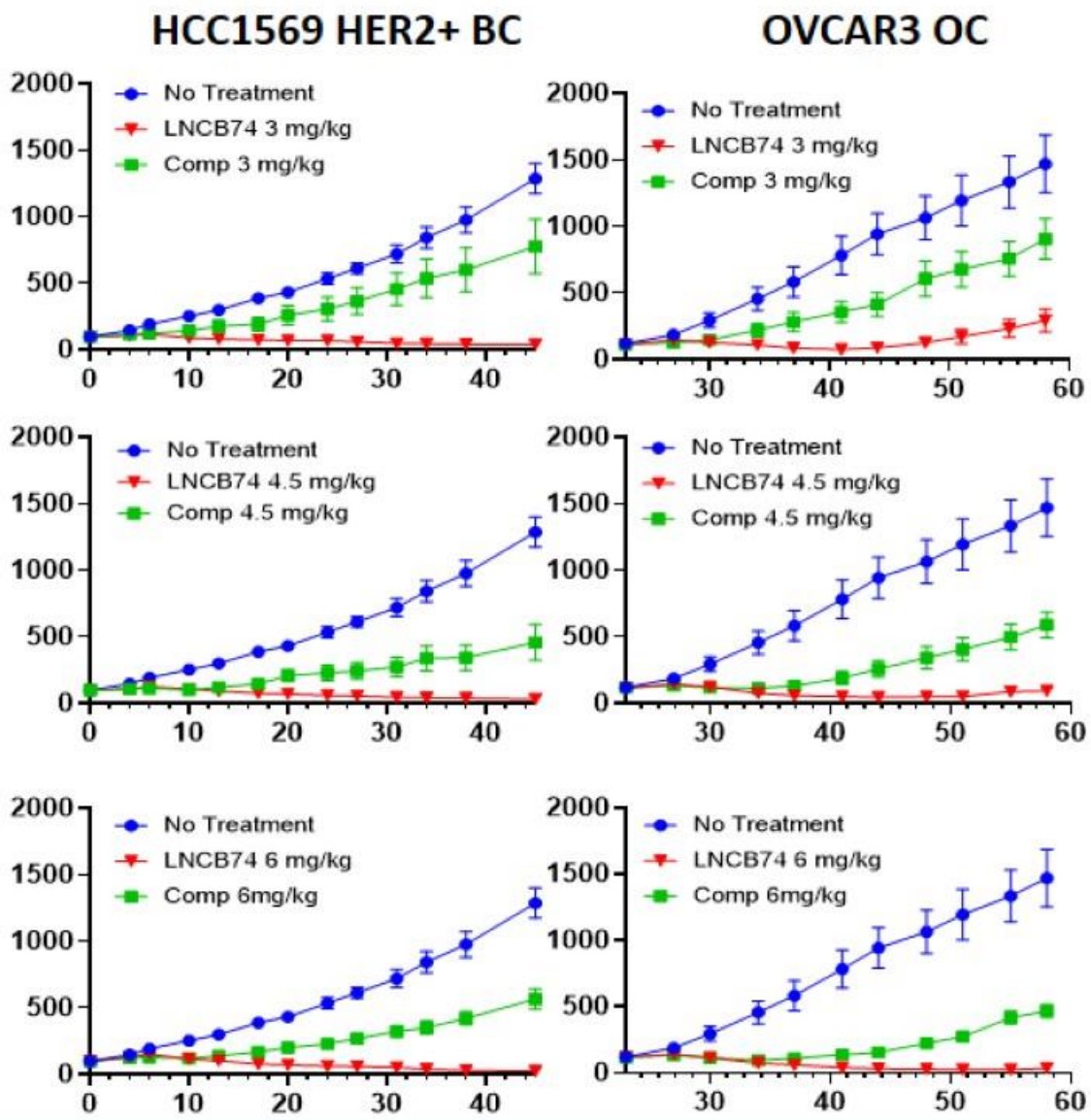
hG1-LALA Fc
↓↓↓
Limited immune cell engagement

Comparator val-cit MMAE (B7-H4 ADC)

Stochastic, reduced cystine conjugation
[CTSB-cleavable, inter-chain linker]

MMAE payload (DAR4)

WT hG1 Fc
↑
immune cell engagement



B7-H4 is a Validated ADC Target

Key Features	LNCB74	SGN-B7H4V	XMT-1660	HS-20089	AZD8205	DB-1312 / BG-C9074
	NextCure LCB LigaChemBio	Seagen Pfizer	Mersana	Partnership with HANSOH PHARMA GSK	AstraZeneca	DualityBio BeiGene
ADC Design	• B7-H4 mAb • Glucuronidase cleavable linker • Monomethyl Auristatin E (MMAE) • DAR 4	• B7-H4 mAb • Val-Cit cleavable linker • Monomethyl Auristatin E (MMAE) • DAR ~4	• B7-H4 mAb • Protease cleavable linker • Auristatin F-HPA (Dolasynthen) • DAR 6	• B7-H4 mAb • Protease cleavable linker • TOPO1 inhibitor (Exatecan) • DAR 6	• B7-H4 mAb • Pegylated Val-Ala cleavable linker • TOPO1 inhibitor (Proprietary) • DAR 8	• B7-H4 mAb • GGFG cleavable linker • Non-Pgp substrate payload • DAR 6
DLT	Safe and tolerable up to 10 mg/kg*	1.25 (N=1) or 1.5 mg/kg (N=2)	TBD	7.2 mg/kg (N=2)	3.2 mg/kg (N=2)	TBD
Common Aes	No major toxicity observed in NHPs	Neutropenia, Peripheral sensory neuropathy, Nausea, Fatigue, Anemia, Dyspnea, Hypotension, and Pneumonia	TBD	Leukopenia, Neutropenia, Nausea, Anemia, Vomiting, Fatigue, Thrombocytopenia, Increased ALT and AST, Anorexia, and Hyponatremia	Nausea, Neutropenia, Thrombocytopenia, Anemia and WBC decrease	TBD
RESPONSES	• IND Submitted Q4 2024	• TNBC: 1 CR / 8 PR (N=42)* • HR+/HER2- Breast: 5 PR (N=24)* • Ovarian: 2 PR (N=15) • Endometrial: 1 CR (N=16)	• Dose escalation progressed to 115 mg/m^2 w/o MTD • Anticipated Ph1 read out (safety, efficacy and biomarker analysis) – YE • Expected initiation of TNBC expansion cohort in post topo-1 ADC patients – YE	• TNBC: 6 PR (N=16) • Ovarian: 2 PR (N=3)	• Ovarian 3 PR (N=7) • Breast 3 PR (N=17) • Endometrial 3 PR (N=12)	TBD
Data Source	AACR 2024	ESMO 2023		ESMO 2023	ESMO 2024	

*Cyno tox study

*Pfizer Oncology Innovation Day February 29, 2024

GLP Tox and GMP Manufacturing Complete

TOX STUDY	
Species	Cynomolgus
Dose Range	4, 7 & 10 mg/kg Q3W, i.v.
Evaluation	Toxicology profiling, pathology, hematology, immunotoxicology
Findings	Favorable safety and tolerability profile

GMP MANUFACTURING
☑ Master cell bank generated
☑ Process development complete
☑ Antibody manufactured
☑ Clinical supply ready

LNCB74 Ph1 Monotherapy Study Plans

Breast CANCER

Ovarian CANCER

Endometrial CANCER

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

Opportunity
to Develop Differentiated B7-H4 ADC Therapeutic

B7-H4 ADC

- POTENTIAL FOR IMPROVED SAFETY & EFFICACY
- UNMET NEED IN BREAST & GYNECOLOGICAL CANCERS
- PATIENT SELECTION STRATEGY

Programs Available for Partnering

PROGRAMS	TARGET	CELLS	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
NC410 Combo	LAIR-2	Extracellular Matrix	**Ovarian**				
			Colorectal (CRC)				
NC525	LAIR-1	Leukemia	**Acute Myeloid Leukemia**				
NC605	S15	Osteoclasts	**Osteogenesis Imperfecta**				
NC181	APOE4	Microglia & Neurons	**Alzheimer's Disease**				

Anticipated Milestones

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