NB-005: Best-in-Class DLL3-Targeted ADC

NAVIKA BIO

A breakthrough antibody-drug conjugate (ADC) targeting DLL3 for small cell lung cancer (SCLC) and other neuroendocrine tumors

NB-005: Best-in-Class DLL3-Targeted ADC

A next-generation antibody-drug conjugate (ADC) precisely engineered to target DLL3, a highly validated antigen in small cell lung cancer (SCLC) and other neuroendocrine tumors. This injectable therapeutic addresses a $5B market opportunity and is currently in IND-enabling studies with strong global patent protection.

DLL3 Targeting Advantage

DLL3 is highly expressed on SCLC tumor cells but minimally present on normal tissues, providing an exceptional therapeutic window. This Notch pathway protein represents one of the most validated targets in neuroendocrine malignancies.

DLL3 Antibody

Highly selective antibody component binds tumor-associated DLL3 with sub-picomolar affinity, ensuring precise tumor targeting.

Novel DLinker™ 1.0

Proprietary linker platform with exceptional plasma stability and optimized drug-release kinetics, a 1,000-fold improvement over conventional linkers.

TOP1 Inhibitor Payload

Potent topoisomerase I inhibitor payload delivers concentrated cytotoxic effect directly to tumor cells, sparing healthy tissue.

NB-005: Revolutionary Linker Technology Drives Differentiation

Best-in-Class Stability

Leverages the novel, patented **DLinker™ 1.0** platform. In plasma stability studies, only **0.0002%** of free payload is released after 30 days of incubation in both human and mouse plasma — versus 0.2% for conventional linkers.

0.0002%

Free Payload Released

After 30 days in plasma

1000X

Stability Improvement

Over standard ADC linkers in clinical use

Preclinical Efficacy & Safety

Preclinical studies using cell-derived xenograft (CDX) and patient-derived xenograft (PDX) mouse models demonstrate **robust inhibitory effects on SCLC**. NB-005 exhibits a favorable safety profile with no abnormal symptoms at doses from 50 to 100 mg/kg, supporting a wide therapeutic window and enabling aggressive clinical dosing strategies.

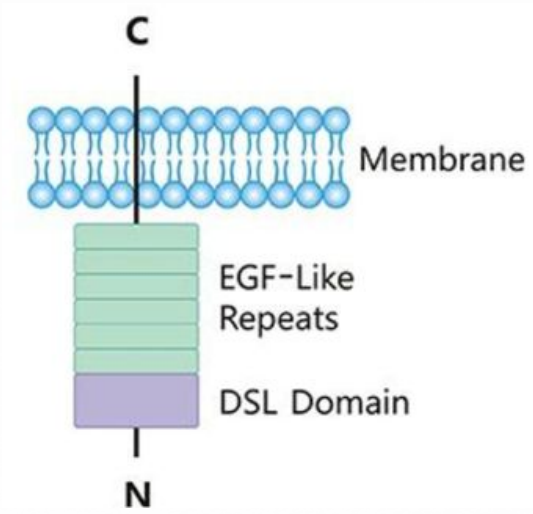
DLinker™ 1.0 directly addresses the key limitation of first-generation ADCs: premature payload release and associated off-target toxicity.

NB-005: DLL3 Target

Exceptionally Clean Expression Profile

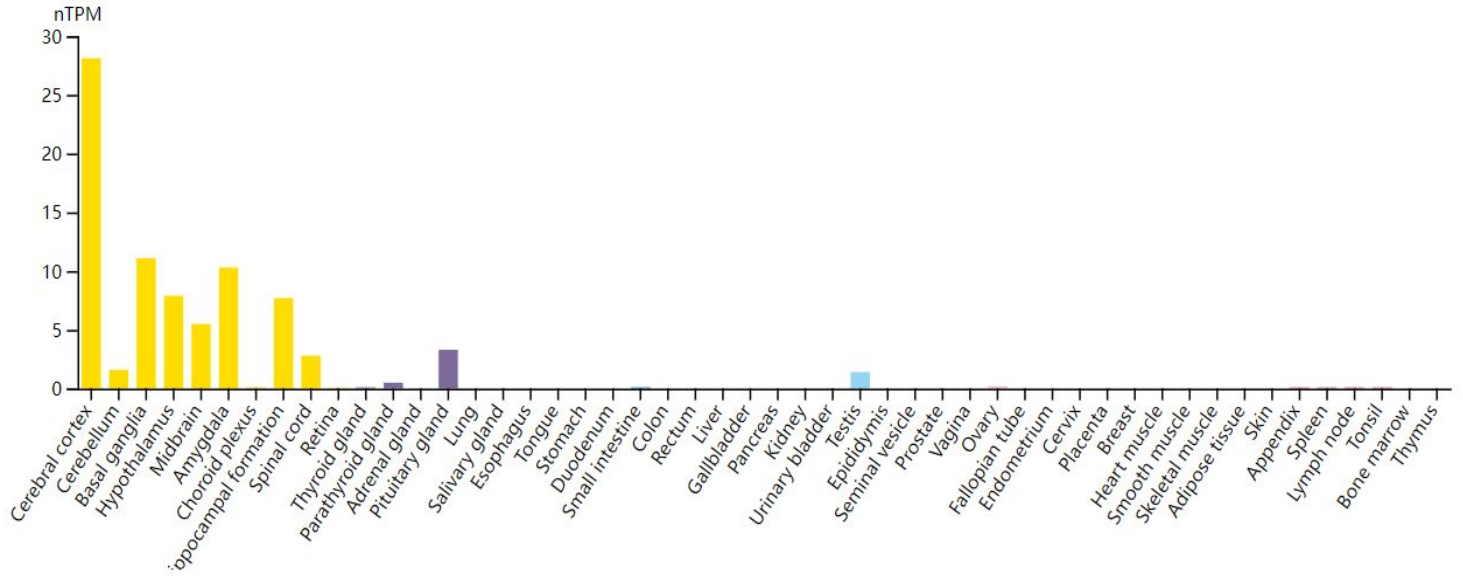
A single-pass transmembrane protein on the cell surface belonging to the Notch ligand family. Its complete structure comprises:

- One DSL domain for Notch receptor interaction
- One intracellular signaling domain
- Six epidermal growth factor-like (EGF-like) extracellular domain



DLL3 is highly expressed in SCLC and other neuroendocrine tumors, while showing minimal expression in normal tissues — making it an ideal ADC target with an exceptional therapeutic window.

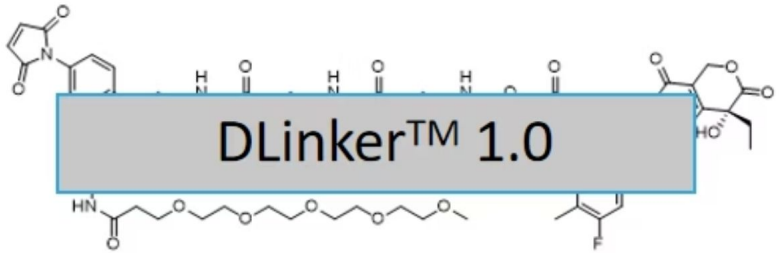
RNA expression (nTPM) data confirms DLL3 is detectable only in brain tissue among all normal tissues, virtually absent elsewhere in the body.



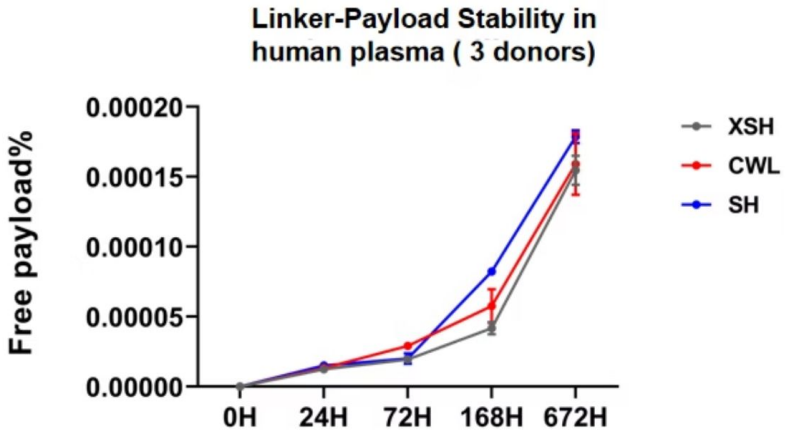
NB-005: DLinker™ 1.0

Efficiently Mitigating Payload Hydrophobicity

The DLinker™ 1.0 platform was engineered to solve two critical challenges in ADC design: **payload hydrophobicity**, which causes aggregation and accelerated clearance and **systemic circulation instability** that leads to premature drug release and off-target toxicity.



Linker-Payload Stability in Human Plasma



DLinker Reduces ADC Aggregation

By efficiently neutralizing payload hydrophobicity, DLinker™ 1.0 produces ADC constructs with remarkably low aggregation levels, a key indicator of manufacturability and clinical tolerability.

ADC Construct	DAR	Aggregation
ADC-18	DAR8	4.7%
ADC-12	DAR4	8.97%
ADC-16	—	1.67%
ADC-25	—	1.70%

ADC-16 and ADC-25 demonstrate the lowest aggregation levels, highlighting DLinker™'s capacity to maintain colloidal stability at high drug-to-antibody ratios.

Free payload remains at ≤0.0002% across 3 donors over 672 hours (28 days), confirming outstanding plasma stability.

NB-005: Antibody Characterization

Sub-Picomolar Binding Affinity

The antibody component (clone 13B) achieves exceptional affinity for human DLL3, with binding kinetics measured in both human and cynomolgus monkey cell systems to support cross-species translational studies and IND-enabling toxicology.

Human DLL3 Affinity

KD = **4.95×10^{-11} M**, sub-picomolar binding in human cells, enabling highly selective tumor engagement at low doses.

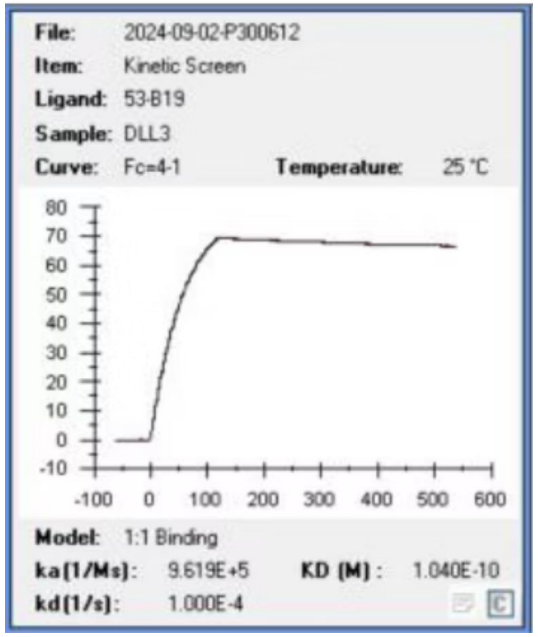
Monkey Cross-Reactivity

Strong binding confirmed in cynomolgus monkey DLL3, supporting non-human primate toxicology studies required for IND filing.

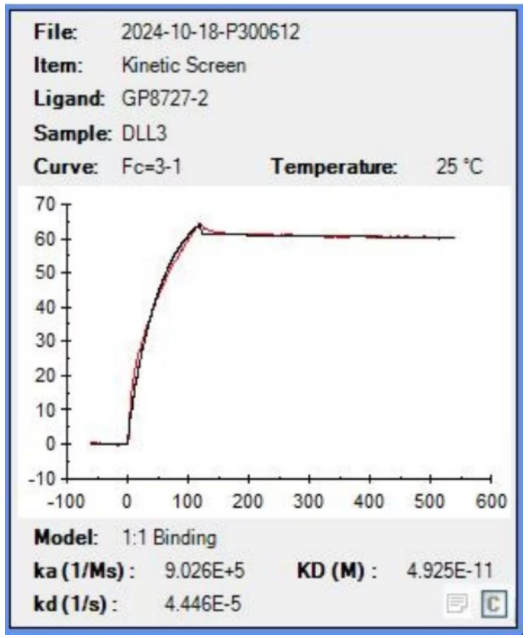
Clinical Relevance

High-affinity binding at picomolar concentrations enables effective tumor killing at clinically achievable ADC doses, widening the therapeutic window.

Human DLL3 binding kinetics



Cynomolgus monkey DLL3 binding kinetics



NB-005: Exquisite DLL3 Specificity — No Off-Target Binding

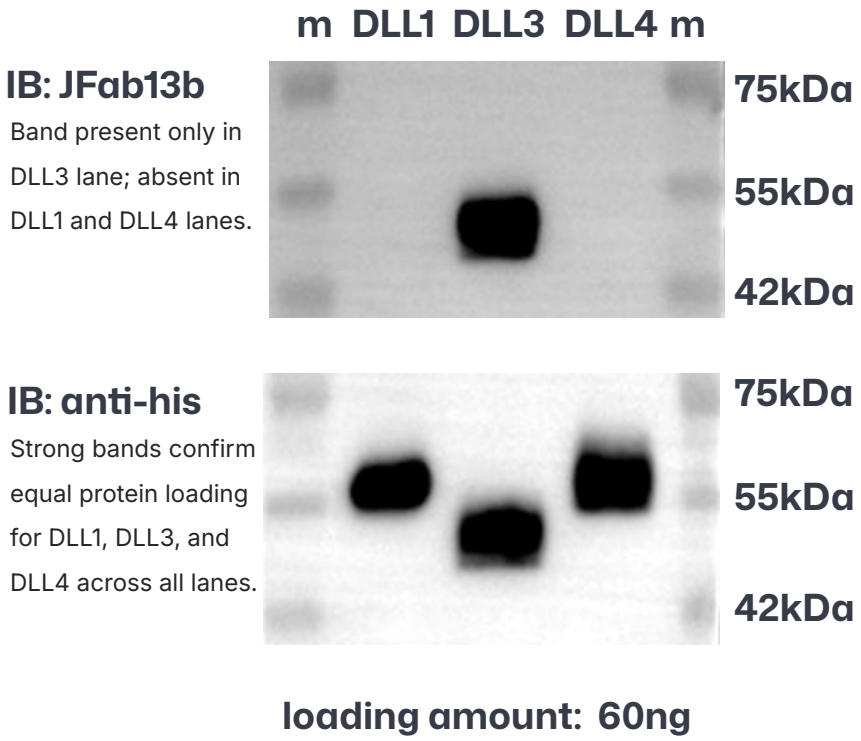
Antibody Specificity

A critical risk for any Notch-family targeting antibody is cross-reactivity with closely related ligands DLL1 and DLL4, which are expressed in normal vasculature and tissues. Western blot analysis confirms that **NB-005 binds exclusively to DLL3 protein** with no detectable cross-reactivity to DLL1 or DLL4.

- Anti-DLL3 (JFab13b) staining shows a single clean band only in the DLL3 lane at ~75 kDa
- Anti-His tag secondary antibody confirms equivalent protein loading across all three DLL family members
- Loading amount: 60 ng per lane — demonstrates high-sensitivity specificity

This specificity profile substantially de-risks on-target off-tumor toxicity and is a prerequisite for a favorable clinical safety profile.

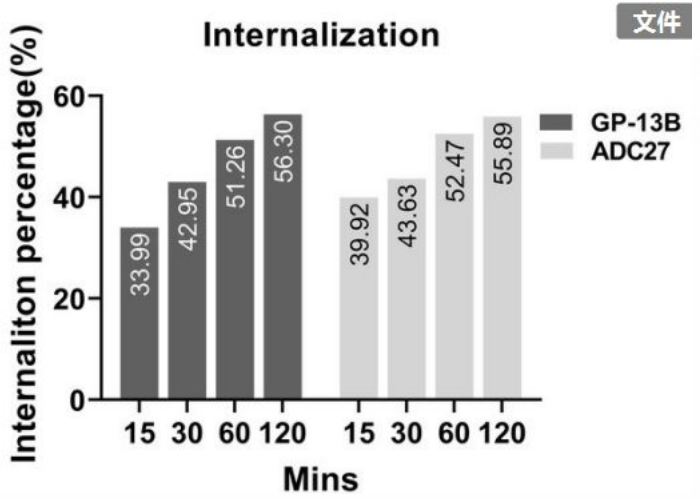
DLL Family Specificity (Western Blot)



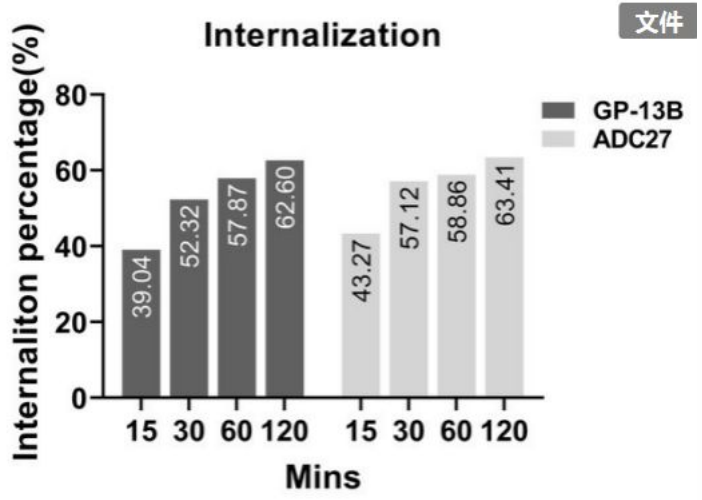
NB-005: Antibody: Efficient Internalization; Potent Bystander Effect

Mechanism of Action

Antibody Internalization

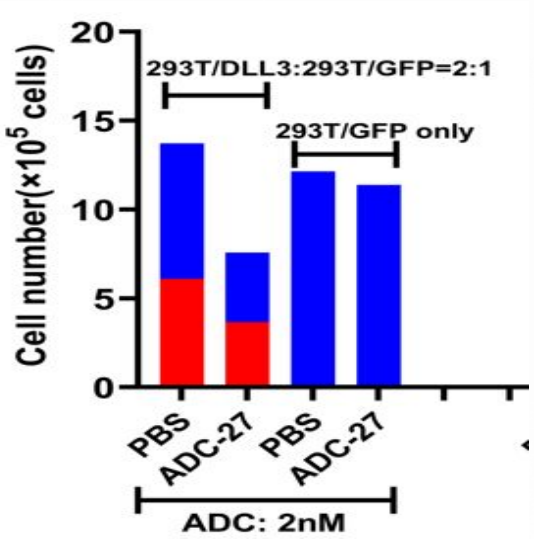


NB-005's antibody (GP-13B) demonstrates significant internalization in DLL3+ cells over time.



NB-005 (ADC27) internalization is parallel to its antibody. Effective ADC function requires robust antibody internalization upon target binding. The GP-13B antibody component of NB-005 demonstrates **significant and rapid internalization** in DLL3-expressing SCLC cells, a prerequisite for intracellular payload release and cytotoxicity.

ADC Internalization & Bystander Killing



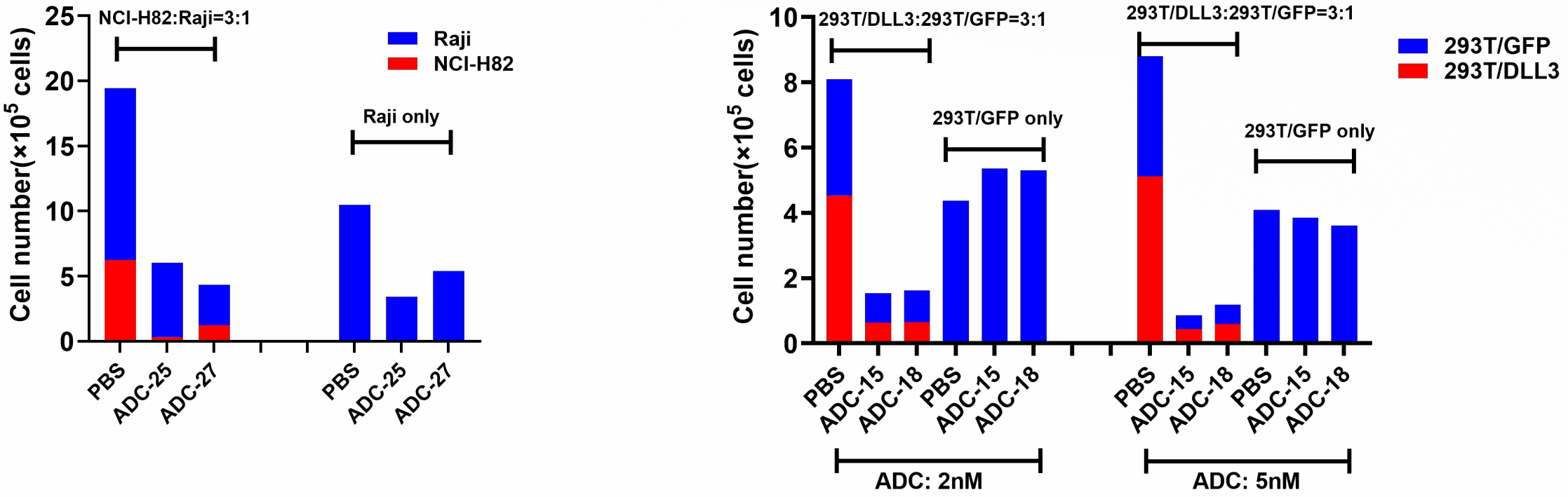
ADC-27 (NB-005) internalizes with kinetics parallel to its parental antibody, confirming that conjugation does not impair cellular uptake. Critically, NB-005 demonstrates a **strong bystander effect** in 293T-DLL3 co-culture assays, killing neighboring DLL3-negative cells, which is essential for tackling heterogeneous tumors.

NB-005: Strong Bystander Effect Confirmed by Flow Cytometry

Bystander Effect

Tumor heterogeneity is a major driver of ADC resistance. NB-005's potent bystander killing activity addresses this challenge directly. Flow cytometry co-culture assays demonstrate robust bystander killing when DLL3-positive cells (NCI-H82 or 293T-DLL3) are co-cultured with DLL3-negative cells (Raji or 293T).

- DLL3-positive NCI-H82 co-cultured with DLL3-negative Raji cells: strong bystander cytotoxicity observed in Raji population
- 293T-DLL3 co-cultured with parental 293T cells: equivalent bystander killing confirmed

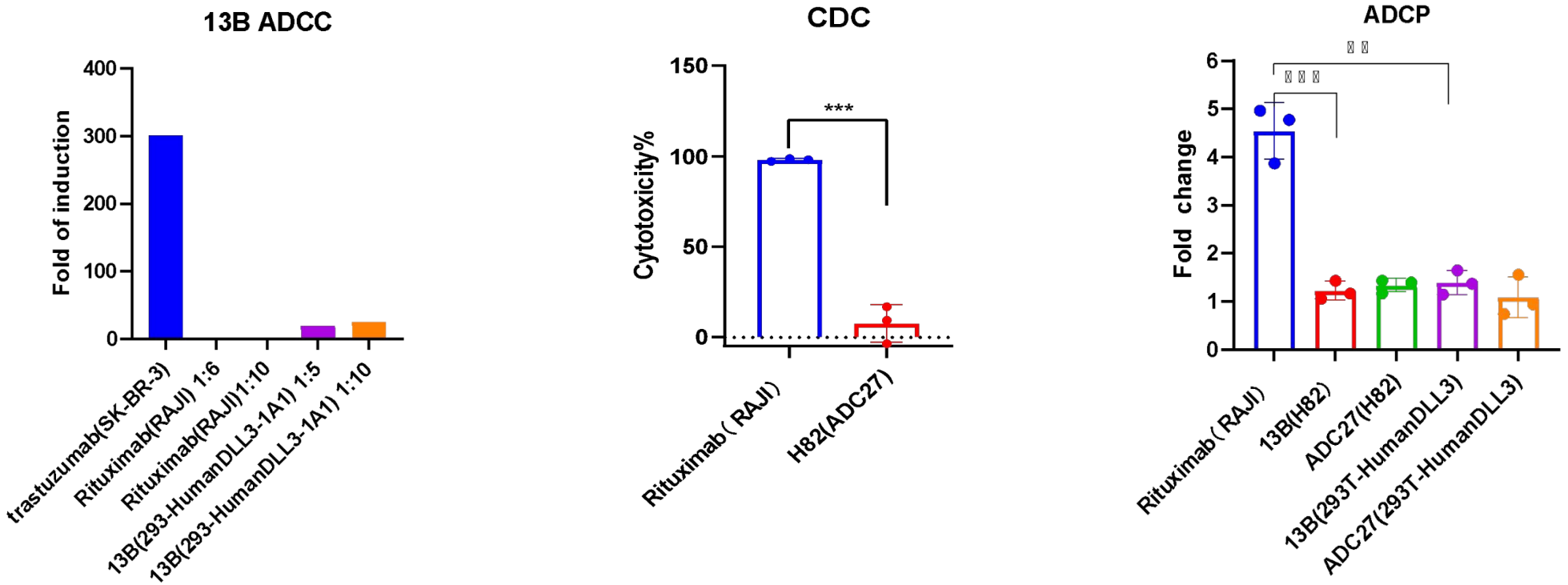


Bystander effect is critical for overcoming antigen heterogeneity in SCLC, a tumor type known for clonal diversity and rapid resistance emergence.

NB-005: Clean Effector Function Profile — No ADCC, ADCP, or CDC

Immune Function Profile

One important mechanistic consideration for ADC design is the absence of Fc-mediated immune effector functions, which can cause off-target immune activation and systemic toxicity. Functional assays confirm that the NB-005 **antibody (clone 13B) does not engage ADCC, ADCP, or CDC pathways** in human SCLC NCI-H82 or 293T-DLL3 cells.

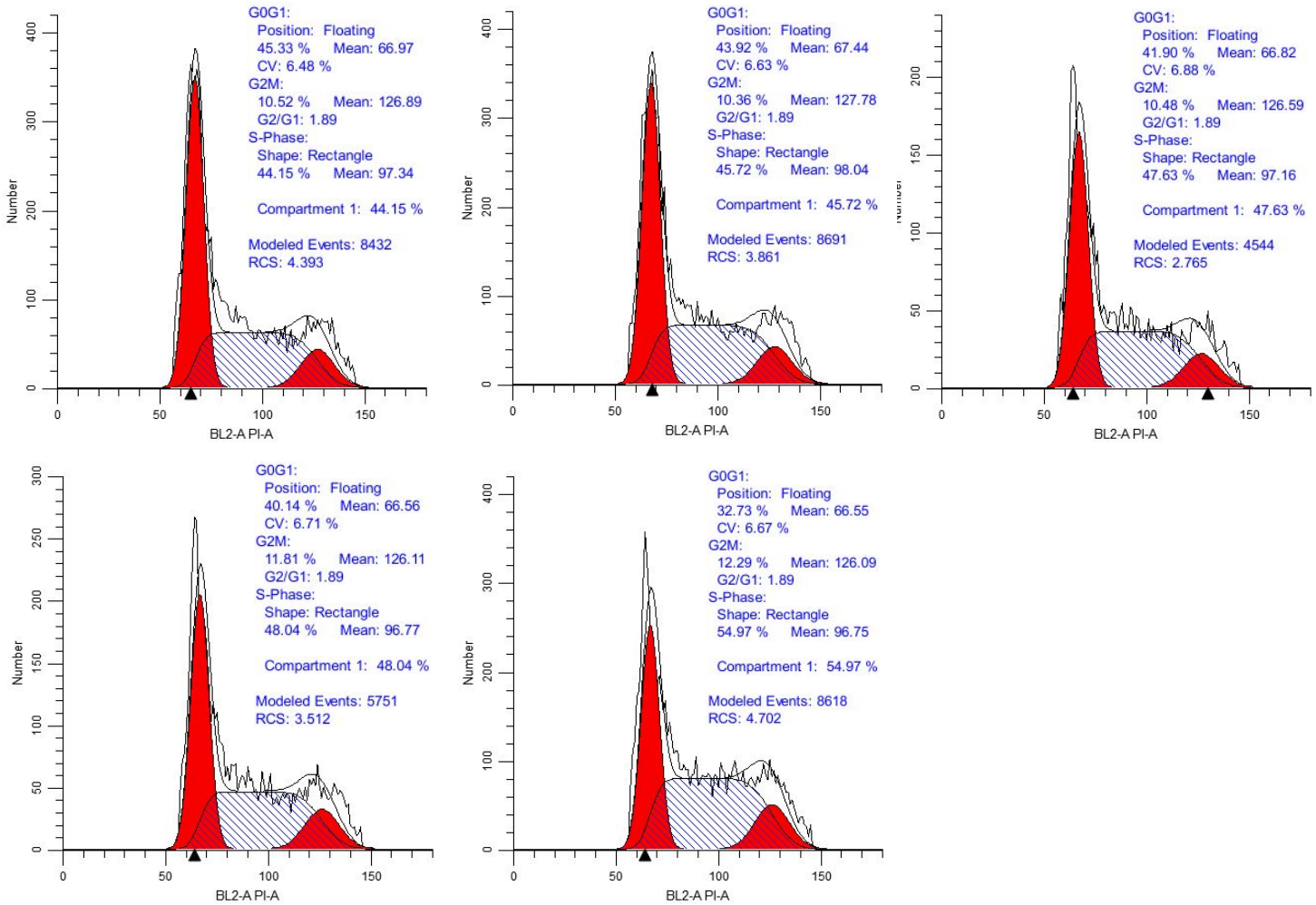


Trastuzumab (SK-BR-3 cells) and Rituximab (Raji cells) were used as positive controls, confirming assay validity. BP-A102 shows no effector function activity — consistent with a payload-dependent, ADC-mediated mechanism of action.

NB-005: Induces Dose-Dependent G2/M Cell Cycle Arrest

Mechanism of Action

Understanding the mechanism by which the TOP1 inhibitor payload kills cancer cells is critical for predicting clinical activity. Cell cycle analysis in NCI-H82 SCLC cells reveals a clear, **dose-dependent shift from G0/G1 into G2/M phase arrest**, the hallmark mechanism of topoisomerase I inhibitors.



Conc. (nM)	G0/G1	S Phase	G2/M
0 (control)	45.33%	44.15%	10.52%
0.046	43.92%	45.72%	10.36%
0.139	41.90%	47.63%	10.48%
0.417	40.14%	48.04%	11.81%
1.25	32.73%	54.97%	12.29%

G0/G1 fraction decreases significantly while G2/M fraction rises in a dose-dependent manner, confirming potent on-target mechanism at sub-nanomolar concentrations.

NB-005: Potent In Vitro Cytotoxicity Across SCLC Lines

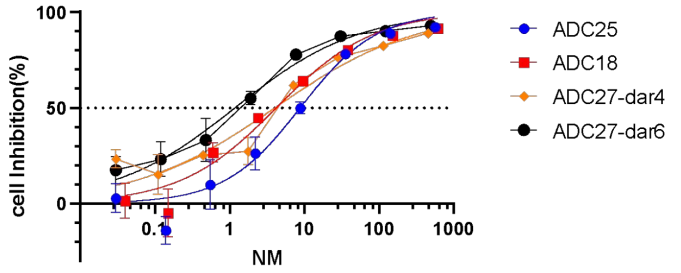
In Vitro Efficacy

NB-005 (ADC-27) was benchmarked against a deruxtecan-linker control ADC (ADC-18) and a GGFP linker comparator (ADC-25) across three SCLC cell lines with varying DLL3 expression levels. Results confirm superior potency of NB-005 across all lines tested.

Cell Line	NB-005 IC50	Deruxtecan ADC IC50	Fold Advantage
NCI-H82	1.0 nM	2.61 nM	~2.6×
SHP-77	202 nM	637 nM	~3.2×
DMS53	1.189 nM	4.2 nM	~3.5×

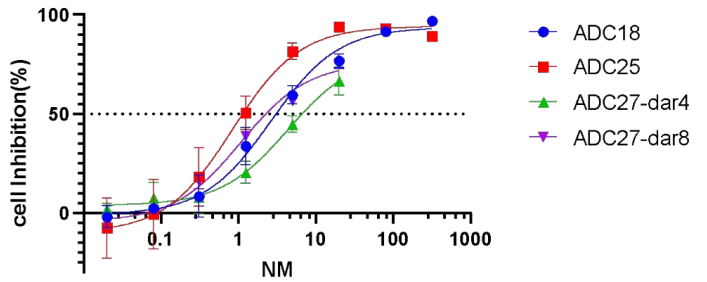
NB-005 outperforms the deruxtecan-linker ADC control across all three SCLC cell lines, demonstrating consistent potency advantage attributable to the DLinker™ 1.0 platform.

DMS53



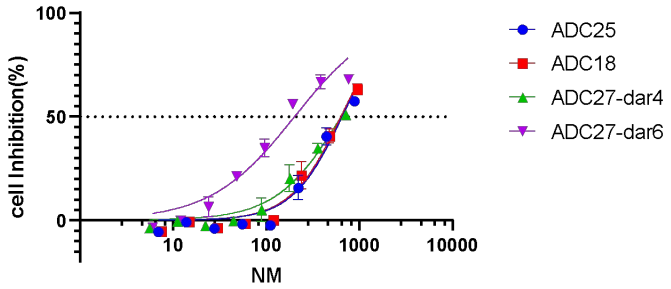
ADC25	ADC18	ADC27-dar4	ADC27-dar6
8.844	4.243	4.085	1.189

NCI-H82



ADC18	ADC25	ADC27-dar4	ADC27-dar8
2.639	0.8393	4.375	1.079

SHP77



ADC25	ADC18	ADC27-dar4	ADC27-dar6
657.9	637.3	640.7	202.2

NB-005: Favorable Half-Life Consistent with Benchmark ADCs

Pharmacokinetics

Following intravenous administration at 3 mg/kg, NB-005 exhibited similar metabolic kinetics to the unconjugated antibody, with a plasma half-life (t_{1/2}) of 3-4 days in mice. Complete degradation required approximately 15 days.

Key PK Parameters (Mouse, IV 3 mg/kg)

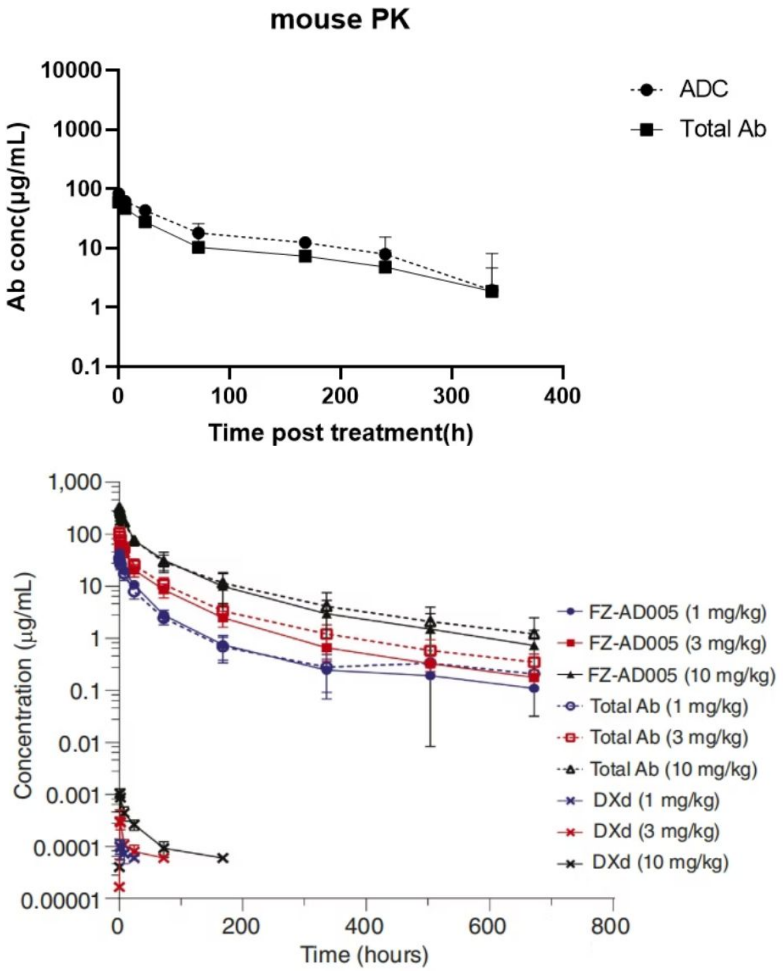
The ADC degrades slightly faster than the naked antibody — consistent with industry benchmark data for well-designed ADC constructs. This PK profile supports Q3W or Q4W dosing regimens typical in clinical ADC practice.

3–4 Days

Plasma half-life (t½) — comparable to unconjugated antibody

~15 Days

Complete degradation timeline following single IV dose



Plasma concentration-time curves for NB-005 vs. unconjugated antibody following IV administration at 3 mg/kg in mice.

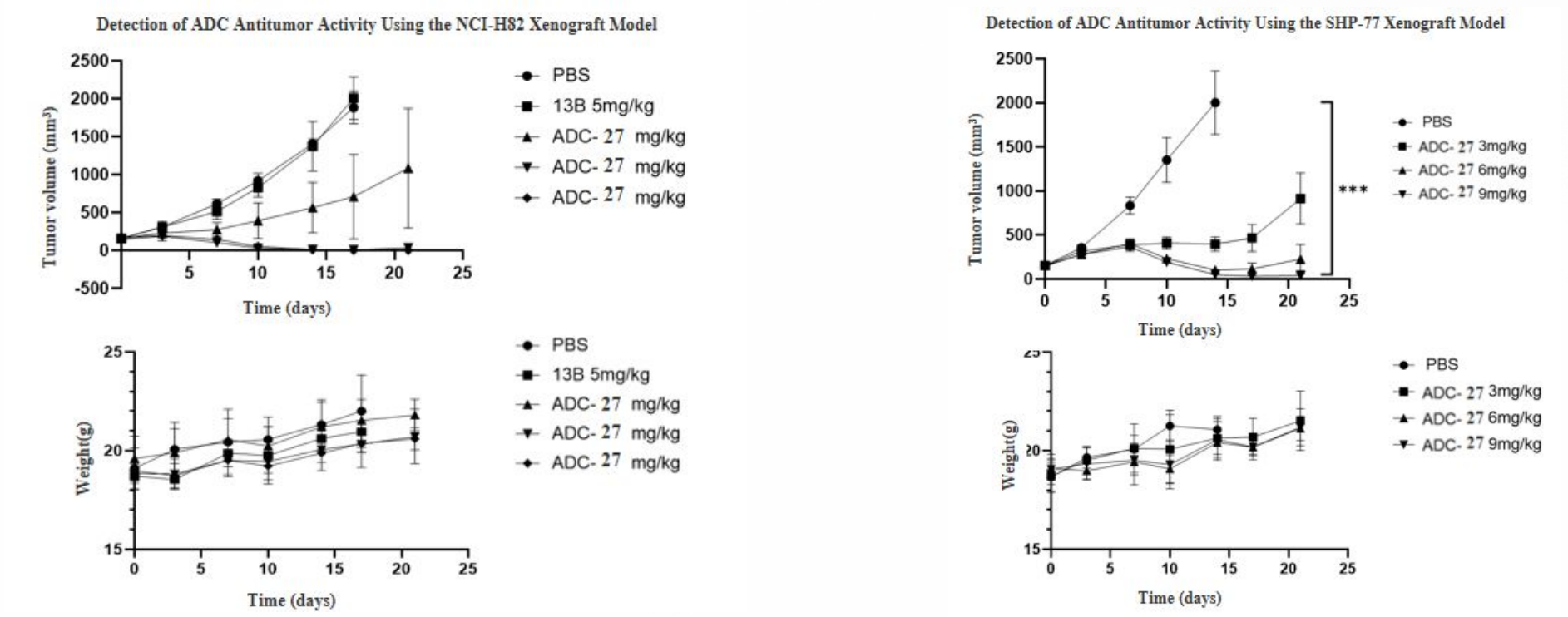
NB-005: Inhibits Tumor Growth in CDX Mouse Xenograft Model

In Vitro Efficacy - CDX Model

Cell-derived xenograft (CDX) studies demonstrate that NB-005 delivers potent and dose-dependent tumor growth inhibition in SCLC mouse models.
Key findings:

- Free payload alone shows limited anti-tumor activity, confirming that antibody-mediated tumor targeting is essential for efficacy
- NB-005 (DAR = 5.6) effectively inhibits tumor growth across dose levels of 1, 2, and 5 mg/kg
- No significant body weight loss observed at any dose, supporting a favorable tolerability profile

The clear separation between free payload and ADC efficacy validates the targeted delivery mechanism of BP-A102 and demonstrates that DLL3-directed tumor engagement is required for therapeutic activity.

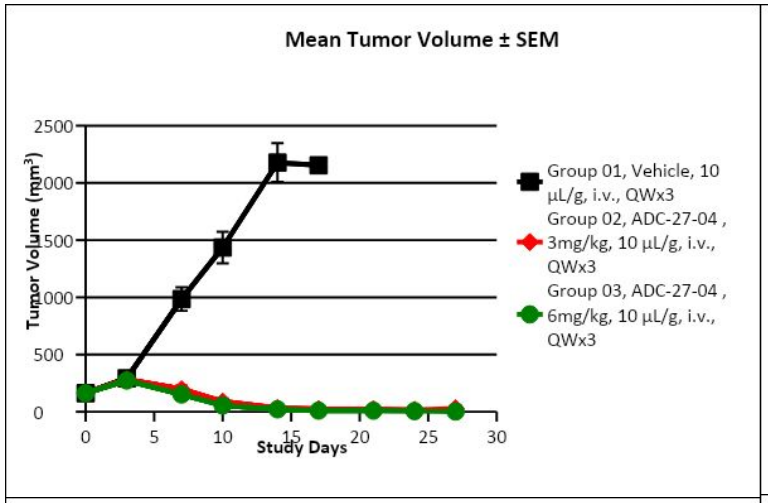


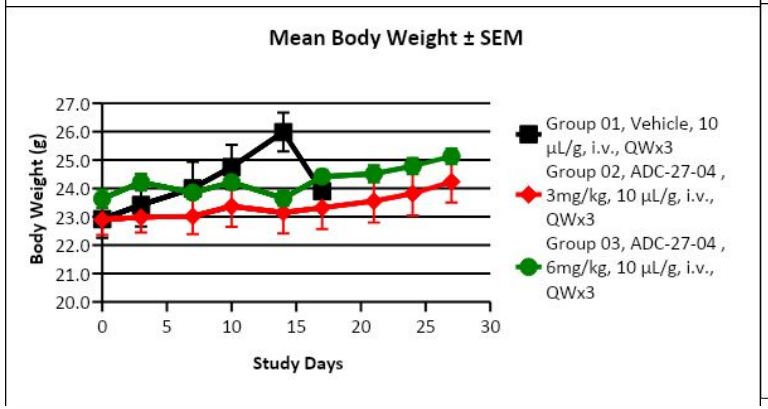
NB-005: Robust Efficacy Across Multiple PDX Lung Tumor Models

In Vitro Efficacy - PDX Models

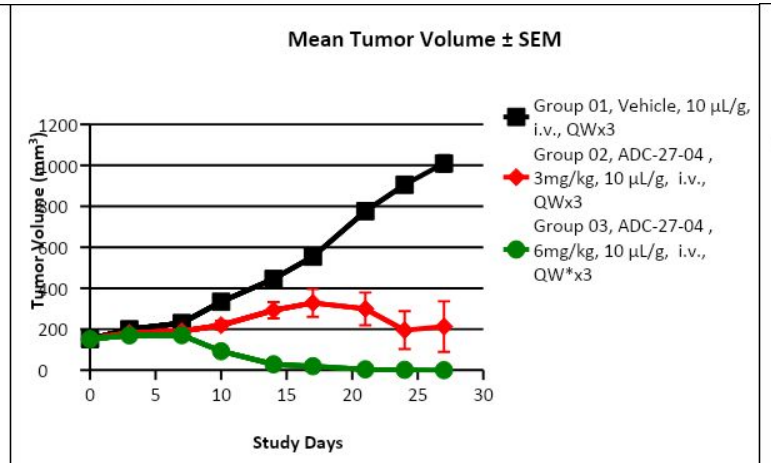
NB-005 demonstrated durable tumor growth inhibition across all three models, supporting broad clinical applicability in the SCLC patient population. Patient-derived xenograft (PDX) models provide the most clinically predictive preclinical data. NB-005 was evaluated in three independent SCLC PDX models, LU5188, LU5171 and LU5180, representing the heterogeneity of the patient population.

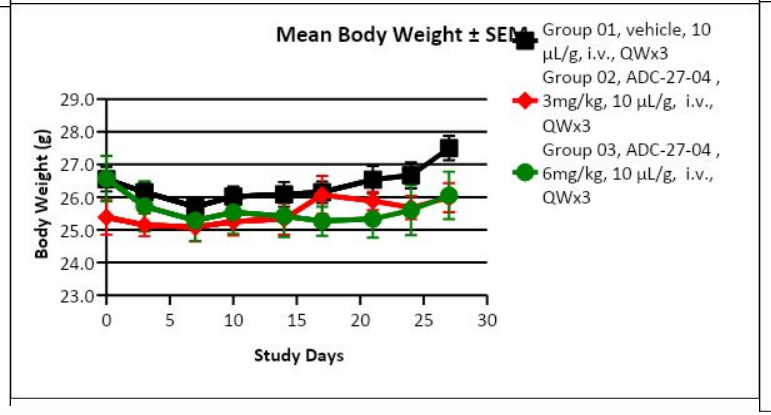
LU5188



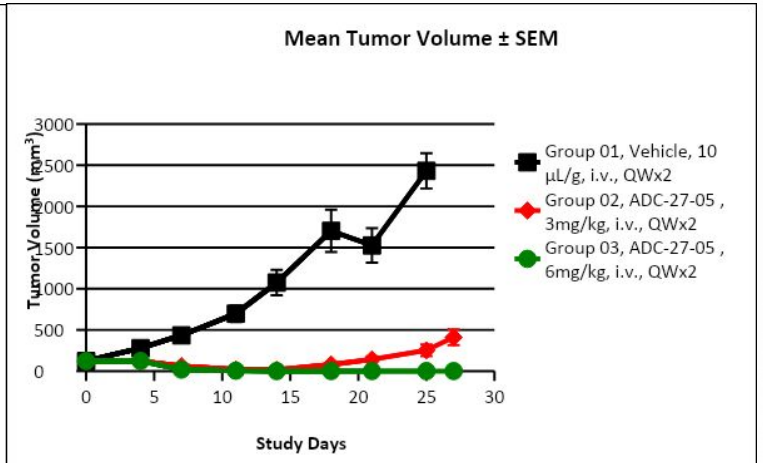


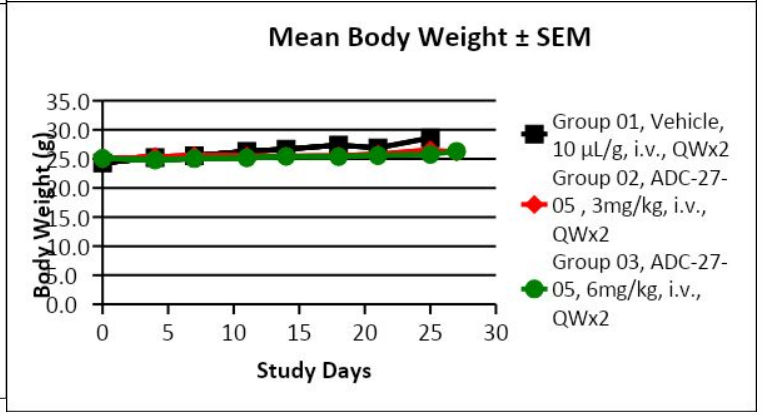
LU5171





LU5180





NB-005: Therapeutic Index of 50–100 — Wide Safety Margin

Therapeutic Index

Body weight curves following IV administration at 50 mg/kg and 100 mg/kg. Both groups maintain or gain weight, confirming well-tolerated profile at supratherapeutic doses.

Therapeutic Index (Ti): 50–100

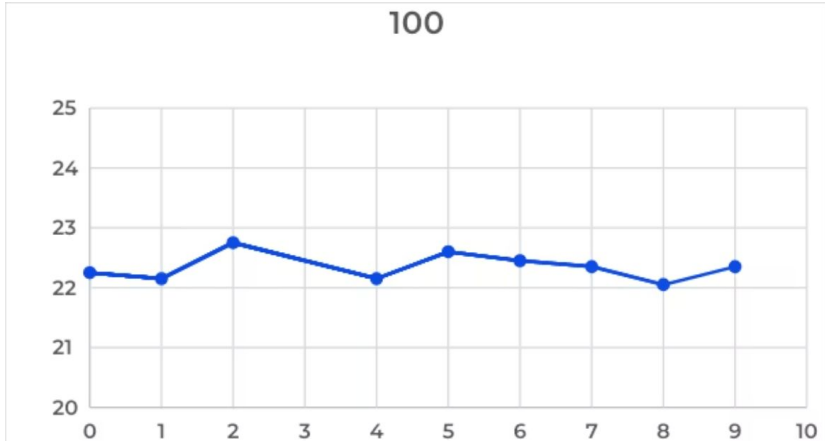
A therapeutic index of 50–100 represents a substantial safety margin, enabling aggressive clinical dosing and supporting broad patient eligibility in future trials.

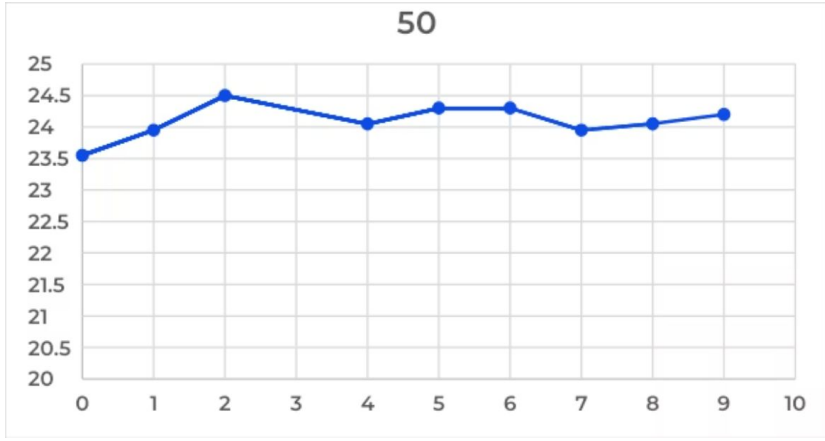
100 mg/kg

No obvious decrease in body weight observed. Normal vital signs throughout dosing period.

50 mg/kg

Body weight of mice **increased significantly** — indicating excellent systemic tolerability at the lower bound.

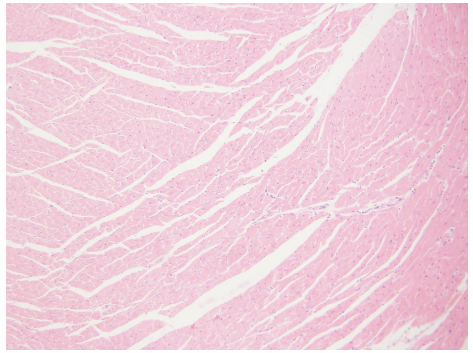




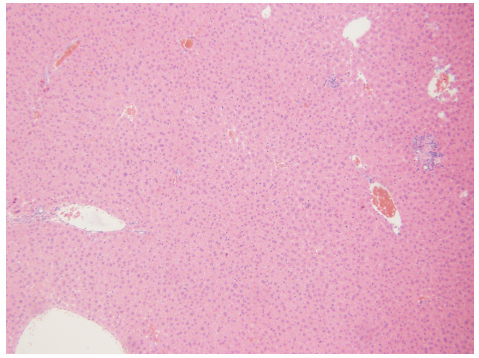
NB-005: No Significant Organ Toxicity

Clean Histopathological Profile

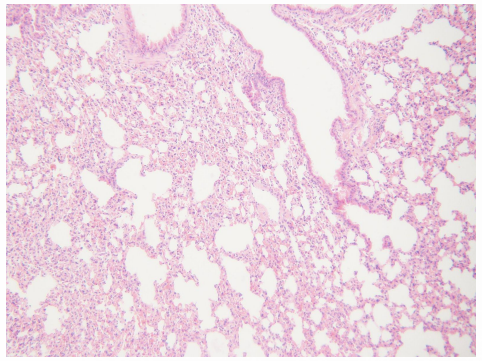
Comprehensive histopathological analysis of major organs following NB-005 treatment in xenograft mouse models reveals no significant toxicological findings — a critical milestone for advancing into formal IND-enabling GLP toxicology studies.



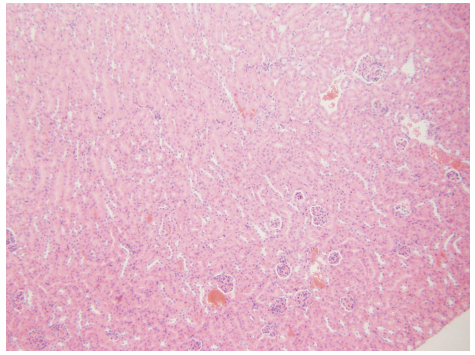
Heart



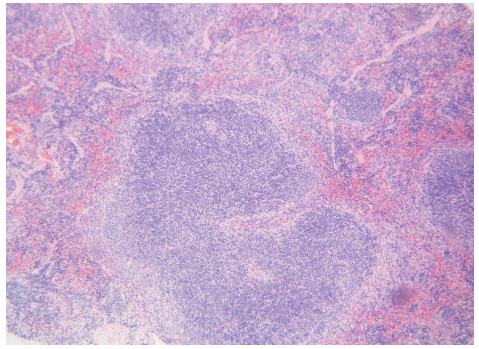
Liver



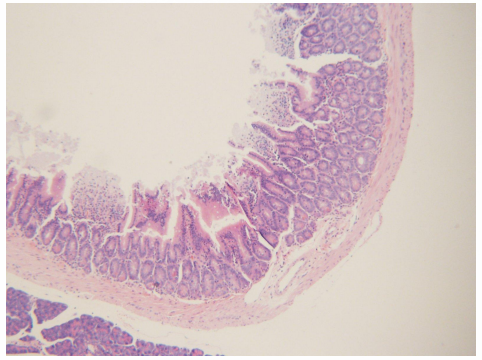
Lung



Kidney



Spleen



Duodenum

All organs examined histopathologically. No drug-related changes in any dose group. Consistent body weight gain across all groups further supports a manageable toxicity profile for NB-005.

NB-005: CMC Moving Forward - Stable Cell Line Established

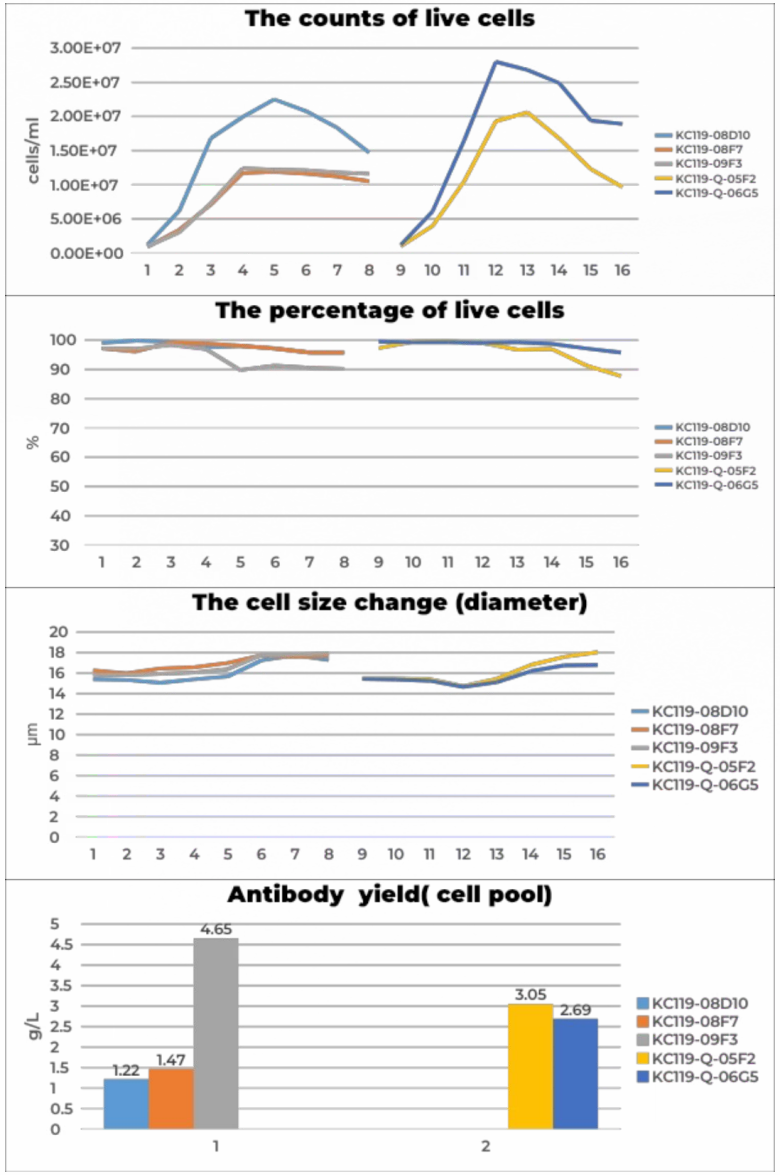
CMC Progress

Manufacturing readiness is a critical gating factor for IND filing. Navika Bio has established a stable CHO cell line producing the antibody, with productivity already exceeding the threshold required for clinical manufacturing scale-up.

4.65
mg/mL

The stable cell line underpins the path toward GMP manufacturing, IND submission, and Phase I dose escalation. Ongoing CMC activities include process development, analytical method qualification and formulation optimization.

Achievement of >4 mg/mL titers from a cell pool is an industry benchmark for advancing to clonal selection and GMP cell banking, confirming manufacturing viability.



NB-005: Summary - A Compelling Best-in-Class ADC Opportunity

Validated Target

DLL3 is highly expressed on SCLC and neuroendocrine tumors with minimal normal tissue expression — an exceptionally clean ADC target confirmed by RNA expression profiling across all human tissues.

Differentiated Linker

DLinker™ 1.0 achieves a **1,000-fold improvement** in plasma stability over conventional linkers (0.0002% vs. 0.2% free payload release at 30 days), directly addressing the core failure mode of first-generation ADCs.

Superior Preclinical Efficacy

outperforms a deruxtecan-linker ADC control across three SCLC cell lines in vitro and demonstrates robust tumor growth inhibition in CDX and PDX mouse models, including multiple patient-derived SCLC tumors.

Exceptional Safety Profile

A therapeutic index of 50–100, no organ toxicity on histopathology, and consistent body weight gain across dose groups support aggressive clinical dosing strategies and broad patient eligibility.

Manufacturing Ready

Stable cell line established with antibody yields of 4.65 mg/mL from cell pool. CMC program is on track to support IND submission and Phase I clinical entry for a **$5B addressable market**.

Accelerating Innovation to Improve Patients' Lives

Navika Bio connects groundbreaking biotech innovation with global pharmaceutical partners to deliver transformative therapies to patients worldwide.

NAVIKA BIO

Let's Connect

For more information about partnership opportunities and to join us on this exciting journey of bringing transformative therapies to patents worldwide, please reach out to:

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