NB-010: Anti-PD-L1 ADC

NAVIKA BIO

First-in-class, IND-ready, anti-PD-L1 ADC with targeted cytotoxic delivery and immune checkpoint inhibition

NB-010: Anti-PD-L1 ADC

The Opportunity

IND-ready with a differentiated preclinical package: dual mechanism, superior pharmacology, stable linker, favorable PK and a wide safety margin — positioning for a compelling clinical development program.

Molecule Design

DAR8 with Hydrophilicity-Enhanced Linker
Maximizes drug loading while maintaining antibody-like biophysical properties; identical HIC retention time for ADC and parental antibody.

Dual-Function Payload
Top1 inhibition + DDX5 degradation delivers synergistic cytotoxicity with a novel mechanism distinct from MMAE and DXd.

Dual Mechanism of Action
Simultaneous PD-L1 checkpoint blockade and targeted intracellular cytotoxicity — immune activation + tumor killing in one molecule.

Species Cross-Reactivity
002mAb retains potent PD-L1 affinity in human and cynomolgus, enabling direct IND-enabling study translation.

Minimized FcγR Engagement
Preserves immune effector function while maintaining FcRn recycling for favorable PK.

Validated Target, Open Landscape

PD-L1 is expressed in 63% of solid tumors across 15,000+ patients. Only two αPD-L1 ADCs (Pfizer/Seagen Phase III; Henlius Phase II) have reached advanced development — far less crowded than HER2 or TROP2.

Significant Market Potential

Global PD-(L)1 market reached $58B in 2025; ADC sales exceeded $16B. Peak sales potential for a differentiated αPD-L1 ADC: $6–15B across NSCLC, TNBC, gastric, esophageal, urothelial, and other indications.

First-Mover Advantage

Blue-ocean competitive positioning with room to differentiate through superior molecule design, payload innovation, and clinical execution.

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Preclinical Data Package

NB-010 has demonstrated a best-in-class preclinical profile across pharmacology, PK, safety, and developability — supporting advancement into IND-enabling studies.

Superior Endocytosis & Cytotoxicity

Outperforms both clinical-stage αPD-L1 ADC competitors in receptor-mediated internalization. Potent, concentration-dependent tumor cell killing with minimal impact on immune effector cells, preserving the checkpoint inhibition mechanism.

Bystander Killing & MDR Resistance

Comparable bystander effect to Competitor 1 ADC across 4 heterogeneous tumor co-culture models. Full cytotoxic activity maintained in P-gp/BCRP efflux-competent MDR cell lines (HCT15, DMS53) — unlike MMAE and DXd-based ADCs.

Robust In Vivo Efficacy

Complete tumor regression in EBC-1 (lung SCC) CDX model at 10 mg/kg. Potent tumor growth inhibition in Karpas 299 (ALCL) model at doses as low as 3 mg/kg.

Plasma Stability & PK

Linker stable across human, cynomolgus, rat, and mouse plasma at 37℃ for ≥21 days. Rat IV PK: T½ = 162 h; TAb and ADC curves nearly identical (MRT 215 h) — confirming exceptional in vivo linker integrity.

Favorable Safety Profile

Tolerated at ≥120 mg/kg in rats and ≥20 mg/kg in cynomolgus monkeys. Only mild, reversible AEs (hair loss, loose stools) consistent with ADC class effects. Dose escalation ongoing with no dose-limiting toxicities identified.

Excellent Developability

High purity, high thermostability, low hydrophobicity (identical HIC RT for DAR8 ADC and parental antibody), and low non-specific binding — supporting CMC scale-up and standard cold-chain storage.

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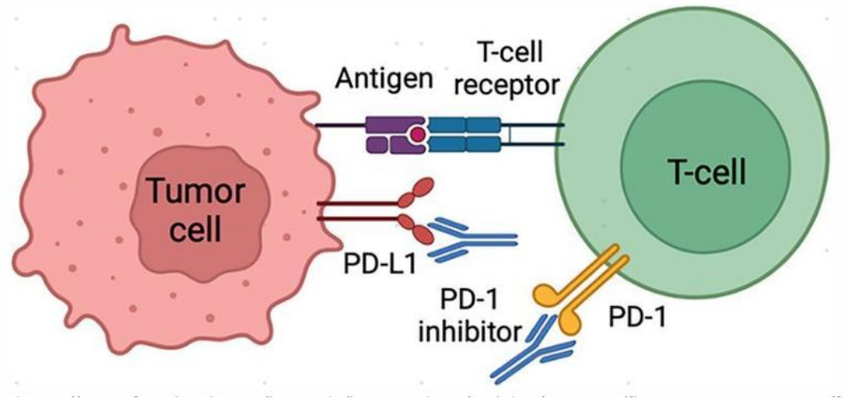
Rational Target of PD-L1

PD-L1 (Programmed Death-Ligand 1) is one of the most clinically validated targets in immuno-oncology, with a well-established mechanistic rationale across multiple tumor types. As a transmembrane protein with moderate endocytic capacity, PD-L1 is amenable to ADC-mediated delivery of cytotoxic payloads directly into the tumor microenvironment. Its broad and high expression across solid tumors makes it an ideal ADC target, enabling simultaneous immune checkpoint blockade and targeted cytotoxicity.



Tumor Type	N	PD-L1 Positive (TPS>1%)
Total (all types)	15,486	63.4% (high: 29.5%)
Metastatic cancer	1,208	61.5% (high: 30.7%)
Lung cancer	1,695	70.2% (high: 36.5%)
Stomach / gastric	545	50.3% (high: 20%)
Esophageal cancer	384	49.2% (high: 12%)
Colorectal cancer	1,142	31.5% (high: 5.3%)
Melanoma	555	56.0% (high: 14%)

*TPS: Tumor Proportion Score. Source: DOI: 10.1038/s41379-019-0210-3

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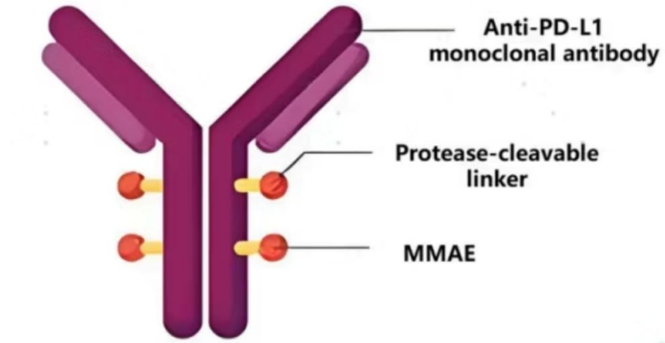
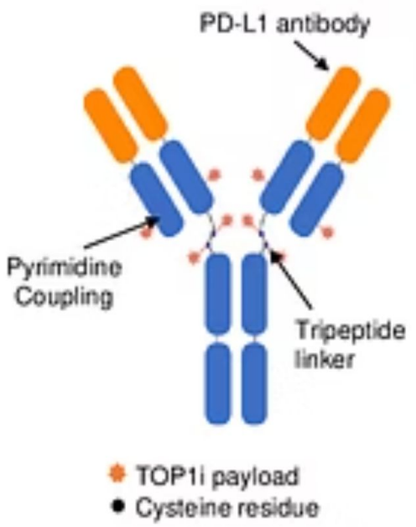
Competitive Landscape of αPD-L1 ADC

Only two αPD-L1 ADCs have reached advanced clinical development, leaving the competitive landscape notably open relative to more crowded ADC target classes such as HER2 and TROP2. Early clinical data for both candidates demonstrate promising safety and efficacy signals, validating the approach and creating a clear first-mover opportunity for differentiated entrants.

Target	ADC	Linker/Drug	Company / Status
PD-L1	PF-08046054 (SGN-PDL1V)	vcMMAE, DAR 4	Pfizer/Seagen — Phase III
PD-L1	HLX43	TMALIN-YL0014 (Medilink)	Henlius — Phase II

Both ADCs have advanced to later-stage clinical development based on favorable early safety and efficacy data. The PD-L1 ADC space remains a blue ocean — not crowded like HER2 or TROP2 — presenting a first-mover advantage and meaningful room to compete through differential design.





Key Features

- High PD-L1 binding affinity and internalizable humanized IgG1 with clinically proved safety.
- Cleavable, tumor microenvironment-activatable tripeptide linker with high stability in circulation.
- Topoisomerase 1 inhibitor payload with high potency, short half-life and strong bystander killing effects.
- Drug antibody ratio of eight.

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Commercial Value of αPD-L1 ADC

Indication	Global New Cases/yr	PD-L1 Positive Rate	Addressable Population
NSCLC	~2.2M	30–40%	0.7–0.9M
TNBC	~0.3M	15–20%	0.045–0.06M
Head & Neck SCC	~0.9M	20–30%	0.18–0.27M
Urothelial Carcinoma	~0.57M	20–25%	0.11–0.14M
Gastric Cancer	~1.0M	30–50%	0.3–0.5M
Esophageal Cancer	~0.6M	30–50%	0.18–0.3M
Cervical Cancer	~0.6M	30–40%	0.18–0.24M
Melanoma	~0.32M	30–40%	0.1–0.13M

Peak Sales Scenarios

Scenario	Market Penetration	Est. Peak Sales
Conservative	5–8% of PD-1/L1 & ADC market	$3–6B
Base	10–15%	$6–11B
Optimistic	Superior efficacy/safety; standard of care	$10–15B

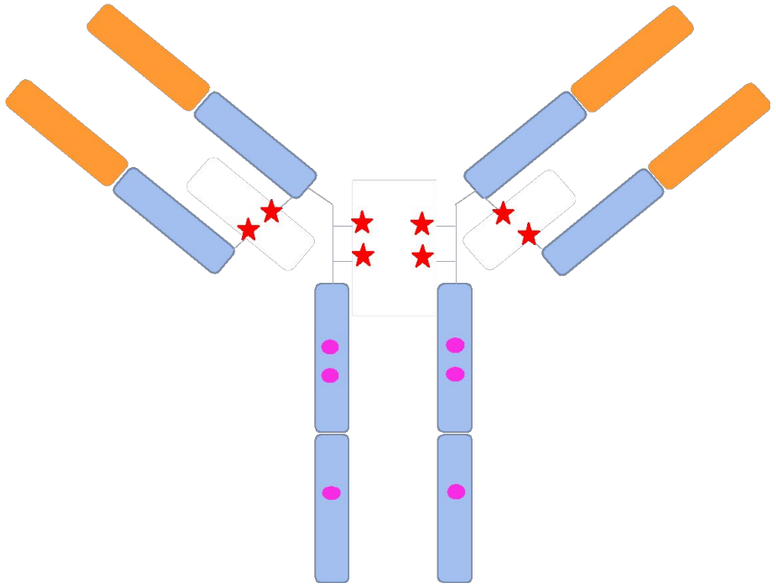
Global PD-(L)1 market (2025): **$58.1B**. Total global ADC sales already exceeded **$16.5B** in 2025. αPD-L1 ADC is positioned to capture a meaningful share through differentiation.

NB-010: Anti-PD-L1 ADC

Overview (αPD-L1 ADC, 002mAb-GSLP003)

A αPD-L1 ADC with DAR8, engineered around a **hydrophilicity-enhanced linker** paired with a **dual-function payload** (Top1i + DDX5 degrader — GSLP003). The antibody backbone (002mAb) retains potent PD-L1 affinity across human and cynomolgus species, with minimized FcγR engagement to preserve immune effector function while maintaining FcRn-mediated recycling for favorable PK.

αPD-L1 ADC (DAR8)



Hydrophilicity Enhanced Linker +
Top1i+DDX5 Degrader dual-functions payload

Key Preclinical Highlights

- → Excellent endocytosis & bystander effect
- → Efflux pump resistance (MDR)
- → Strong CDX in vivo efficacy
- → Stable in plasma ≥21 days at 37°C
- → Favorable PK: TAb/ADC curves tightly aligned
- → Tolerated ≥120 mg/kg (rodent) / ≥20 mg/kg (cyno)
- → Excellent developability (purity, thermostability, low hydrophobicity)

Dual Payload

Top1 inhibition + DDX5 degradation

DAR 8

High drug loading with hydrophilic linker

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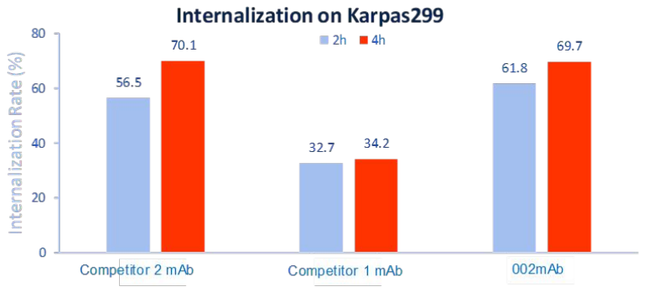
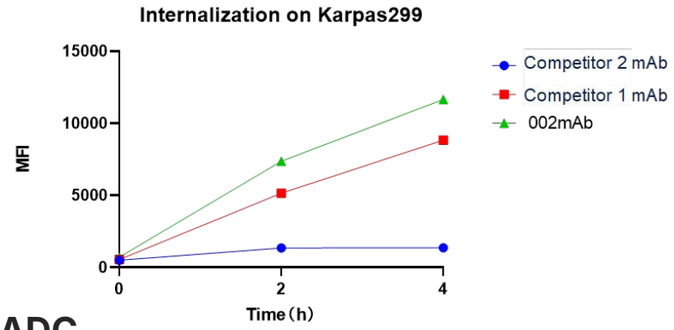
Endocytosis on Tumor Cell

Efficient receptor-mediated internalization is a prerequisite for effective intracellular payload delivery. Higher endocytic rates translate directly to greater intracellular drug accumulation and more potent tumor cell killing. The asset's antibody component was engineered to maximize PD-L1 internalization upon binding.

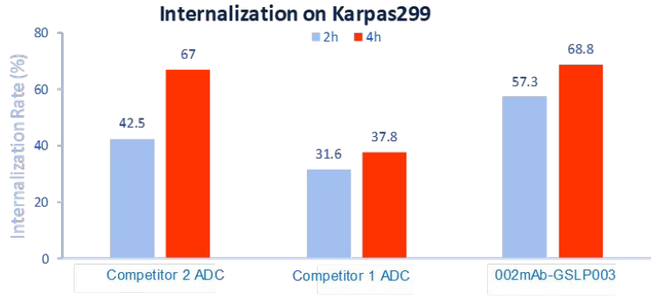
Naked Antibody

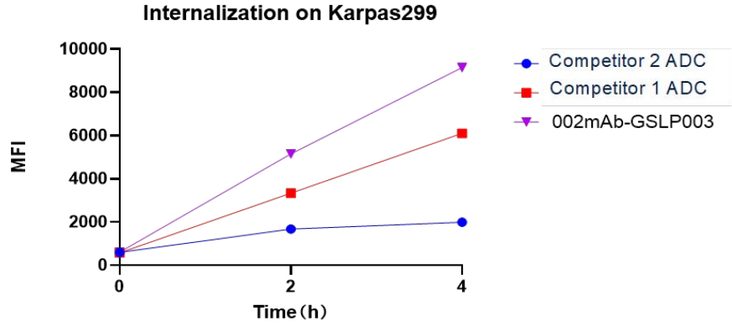




Baseline internalization of the parental 002mAb upon PD-L1 binding — establishes the inherent endocytic capacity of the targeting moiety.

ADC





ADC construct retains and enhances endocytic activity, outperforming both comparator ADCs in quantitative internalization assays across multiple PD-L1-expressing cell lines.

The asset demonstrated **superior endocytosis in tumor cells compared to both clinical-stage competitors**, supporting more efficient payload delivery and enhanced cytotoxic potential.

NB-010: Anti-PD-L1 ADC

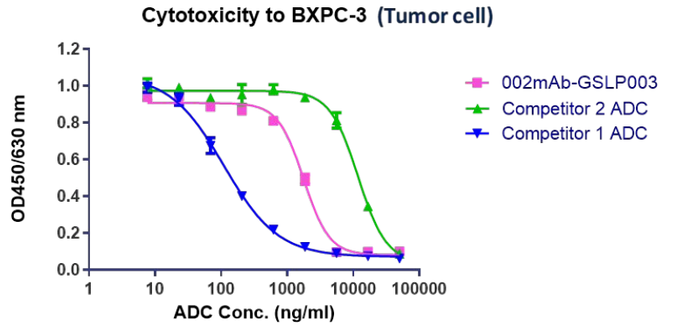
Cytotoxicity on Tumor Cells but Minimal Impact on Immune Cells

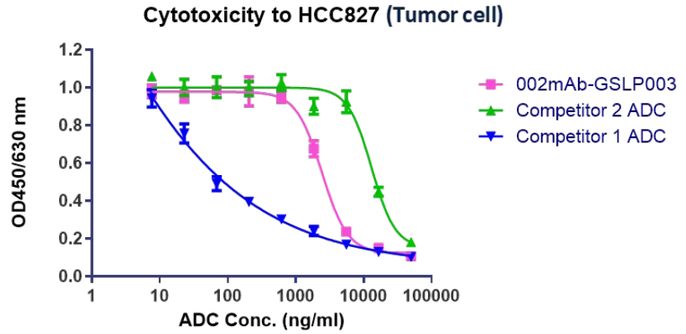
The asset showed potent cytotoxicity to tumor cells but minimal impact on immune cells, a key differentiator from immune-ablative payloads.

Selectivity Profile

Tumor Cells

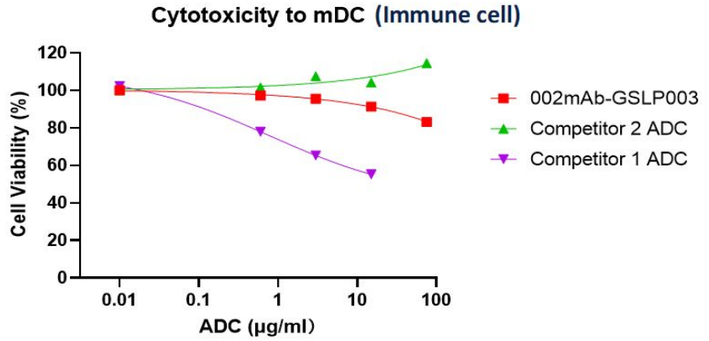
Potent, concentration-dependent cytotoxicity across PD-L1-positive cell lines

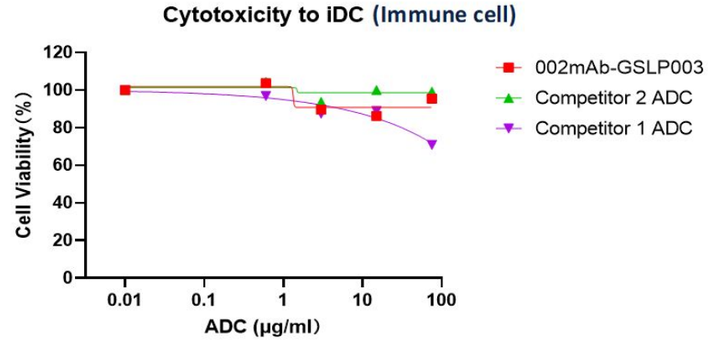




Immune Cells

Minimal impact on T cells and other immune effectors — preserving immunological function



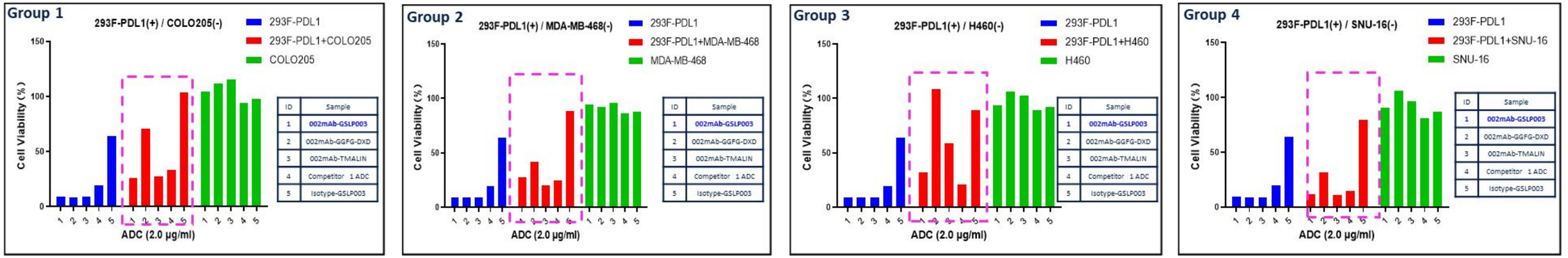


NB-010: Anti-PD-L1 ADC

Bystander Effect (Co-incubation Assay)

The bystander killing effect, the ability of released payload to eliminate adjacent PD-L1-negative tumor cells, is a critical attribute for ADC activity in heterogeneous tumors. The asset was evaluated in co-incubation assays across four cell line pairs, comparing performance against 002mAb-GGFG-DXd, 002mAb-TMALIN, and Competitor 1 ADC.

Group	PD-L1(−) Cell	Mixed Culture (+/−)	PD-L1(+) Cell
1	Colo205 (5,000)	Colo205 + 293F-PDL1	293F-PDL1 (4,000)
2	MDA-MB-468 (20,000)	MDA-MB-468 + 293F-PDL1	293F-PDL1 (4,000)
3	H460 (2,000)	H460 + 293F-PDL1	293F-PDL1 (4,000)
4	SNU-16 (2,000)	SNU-16 + 293F-PDL1	293F-PDL1 (4,000)

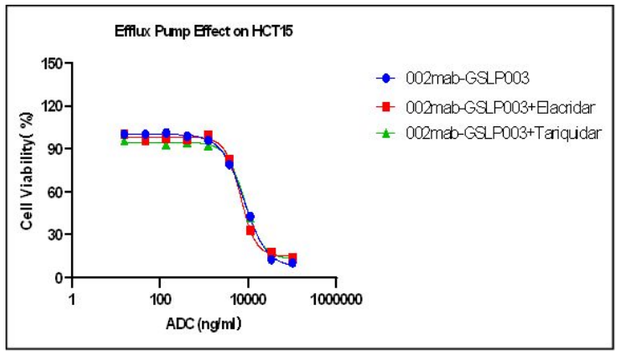


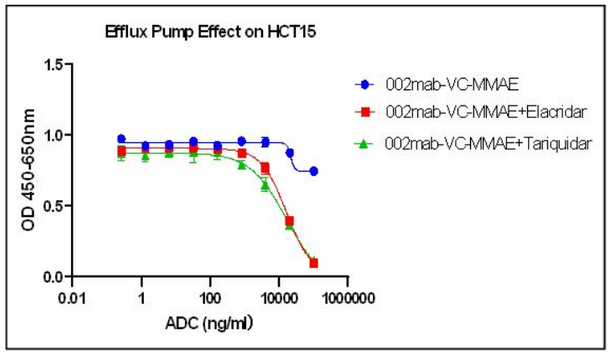
The asset demonstrated **comparable bystander effect to Competitor 1 ADC** and **superior bystander killing relative to 002mAb-GGFG-DXd**, confirming effective payload diffusion to antigen-negative neighboring cells across all four tumor cell models.

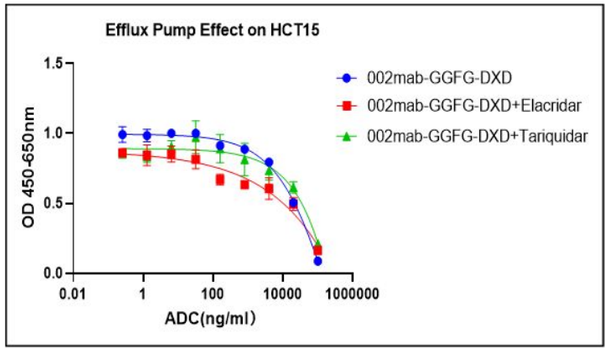
NB-010: Anti-PD-L1 ADC

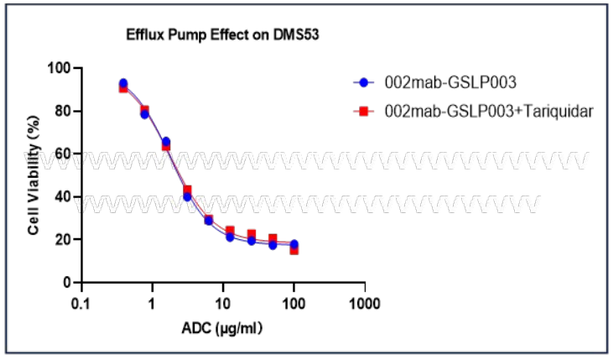
Efflux Pump Resistance / Multi-Drug Resistance

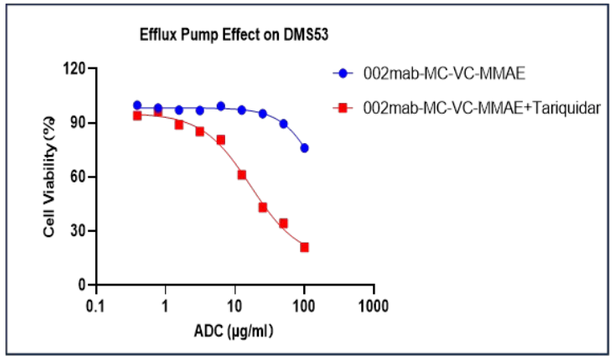
P-glycoprotein (P-gp) and BCRP efflux pumps are major drivers of multi-drug resistance (MDR) in solid tumors. Payloads susceptible to efflux, such as MMAE and DXd, can lose efficacy in resistant tumor cell populations. NB-010's GSLP003 payload was designed to be refractory to both P-gp and BCRP-mediated efflux. It was evaluated on the MDR cell lines HCT15 and DMS53. Unlike vcMMAE- and GGFG-DXd-conjugated ADCs, which show significantly reduced potency in efflux-competent cells, NB-010 maintained full cytotoxic activity in the absence of efflux inhibitors, demonstrating intrinsic resistance to pump-mediated drug export and a clear advantage in MDR tumor settings.

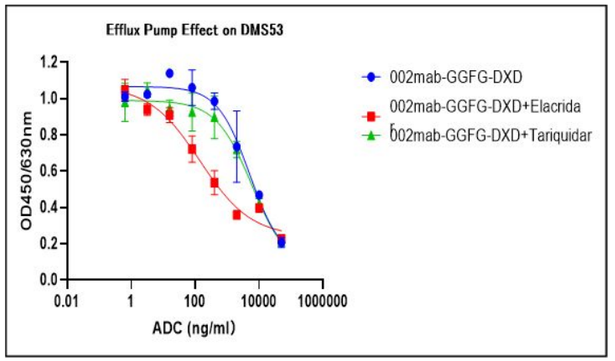












Tariquidar = P-gp inhibitor; Elacridar = P-gp/BCRP dual inhibitor. Sensitivity to efflux is confirmed when inhibitor addition rescues cytotoxicity.

NB-010: Anti-PD-L1 ADC

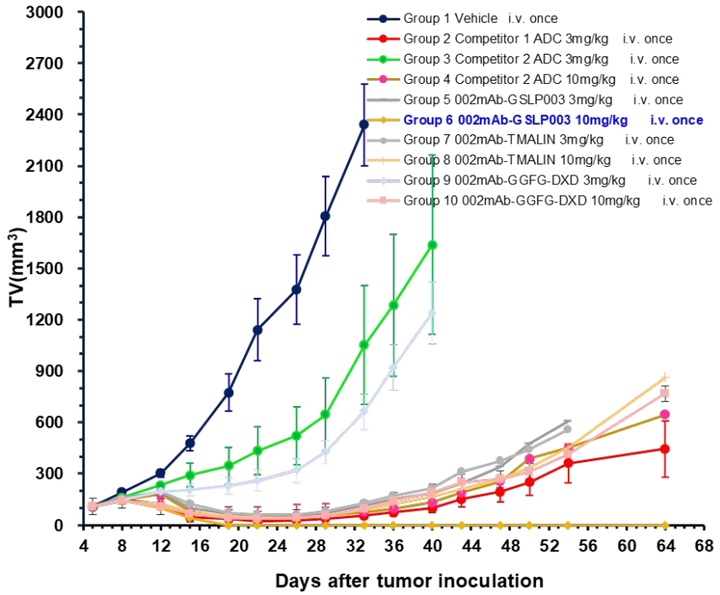
In Vivo Efficacy (EBC-1 & Karpas 299 CDX Models)

EBC-1 (lung squamous cell carcinoma, high PD-L1 expression) and Karpas 299 (anaplastic large cell lymphoma, PD-L1 positive) CDX models were selected to evaluate efficacy in two distinct PD-L1-expressing tumor contexts.

Tumor Growth Curves

EBC-1 — 10 mg/kg

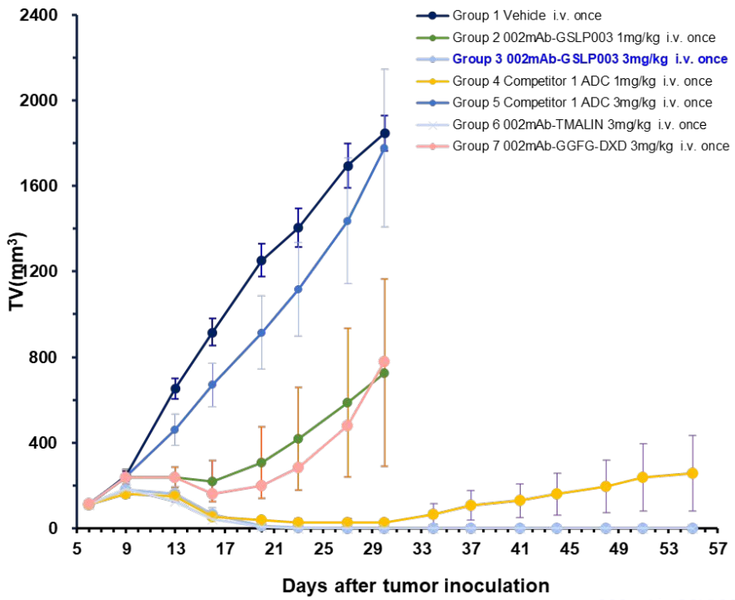
Complete tumor regression observed; durable response sustained post-dosing



002mAb-GSLP003, 10 mg/kg

Karpas 299 — 3 mg/kg

Potent tumor growth inhibition at low dose; dose-dependent activity confirmed



002mAb-GSLP003, 3 mg/kg

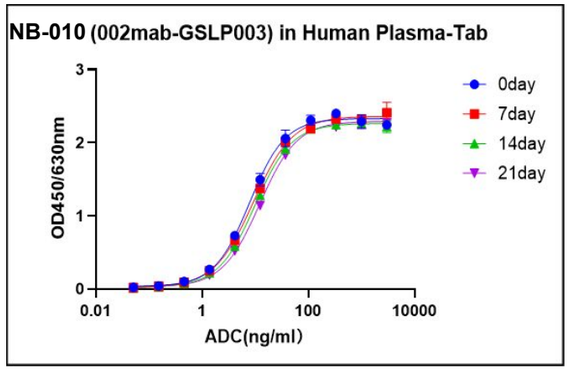
Excellent in vivo efficacy in both CDX models, with activity at doses as low as 3 mg/kg in the Karpas 299 model, underscoring the potency of the GSLP003 payload.

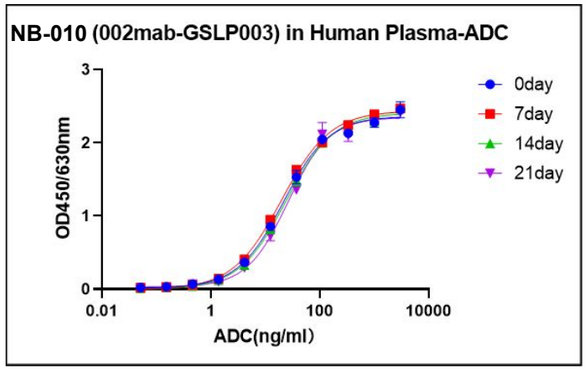
NB-010: Anti-PD-L1 ADC

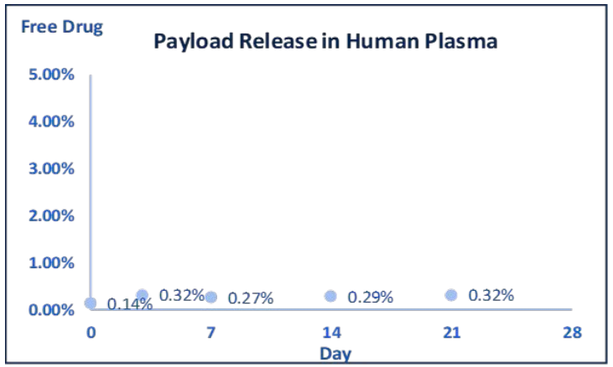
Human & Cynomolgus Plasma Stability

Remained highly stable in both human and cynomolgus plasma at 37°C for the full 21-day incubation period, demonstrating that the hydrophilicity-enhanced linker effectively prevents premature payload release, a prerequisite for a favorable therapeutic index in clinical development.

Human Plasma

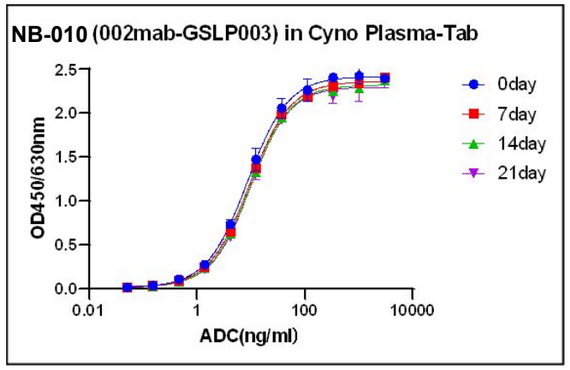


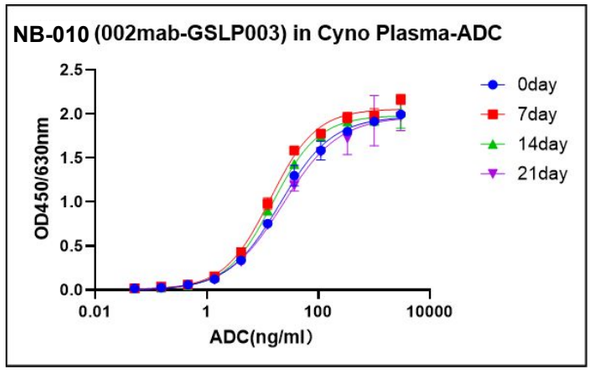


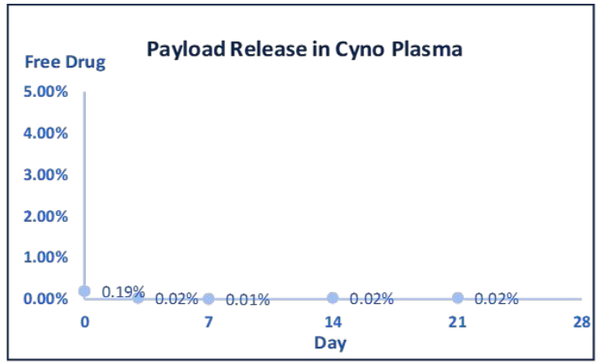


Stable over 21 days at 37°C, minimal drug-to-antibody ratio shift observed

Cyno Plasma







Equivalent stability profile, supports cross-species translatability and IND-enabling study design

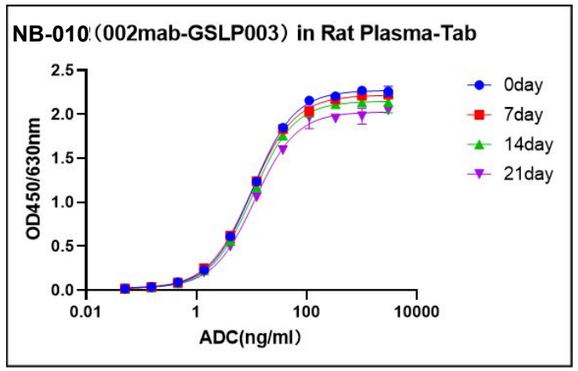
Premature payload release in systemic circulation is a leading cause of ADC-associated off-target toxicity. NB-010 was incubated in both human and cynomolgus monkey plasma at 37°C for up to 21 days to assess linker integrity under physiologically relevant conditions.

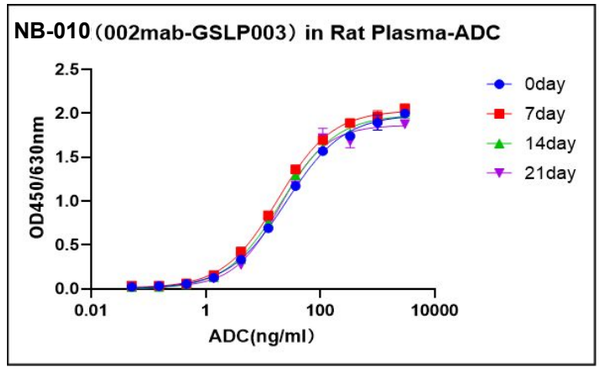
NB-010: Anti-PD-L1 ADC

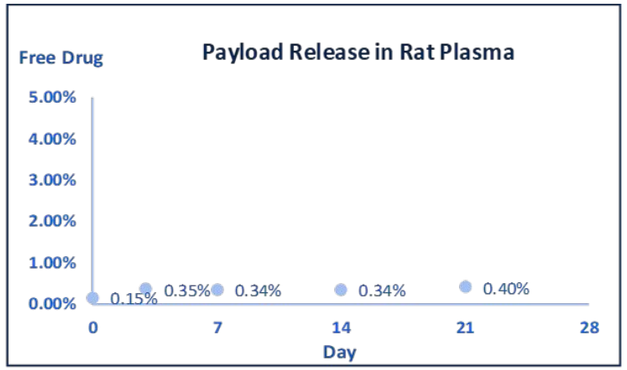
Rat & Mouse Plasma Stability

NB-010 (002mAb-GSLP003) remained stable in both rat and mouse plasma at 37℃ for up to 21 days, confirming the robustness of linker stability across all preclinical species used in safety and efficacy evaluation.

Rat Plasma

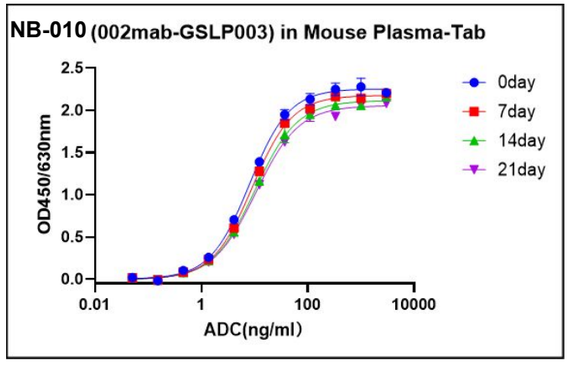


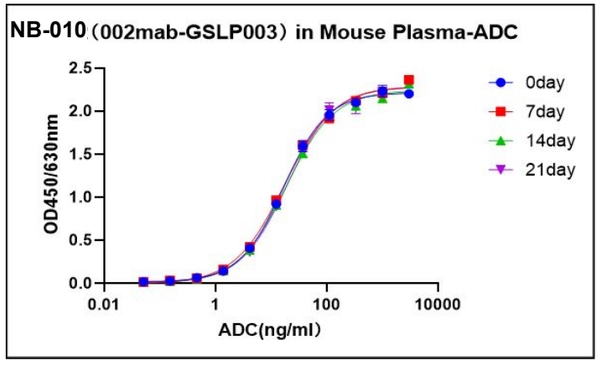


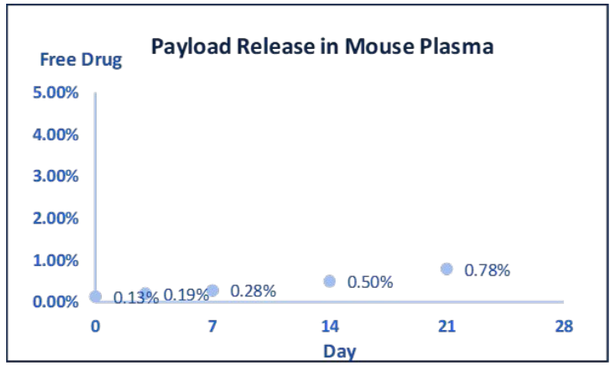


Full stability maintained over 21 days, consistent with data from higher species

Mouse Plasma







No significant payload release detected, supporting validity of mouse CDX efficacy models

Collectively, cross-species plasma stability data confirm that premature linker cleavage is not a confounding variable in any of the preclinical species used to characterize NB-010, providing high confidence in the integrity of in vivo pharmacology and safety findings.

NB-010: Anti-PD-L1 ADC

Rat Pharmacokinetic Study

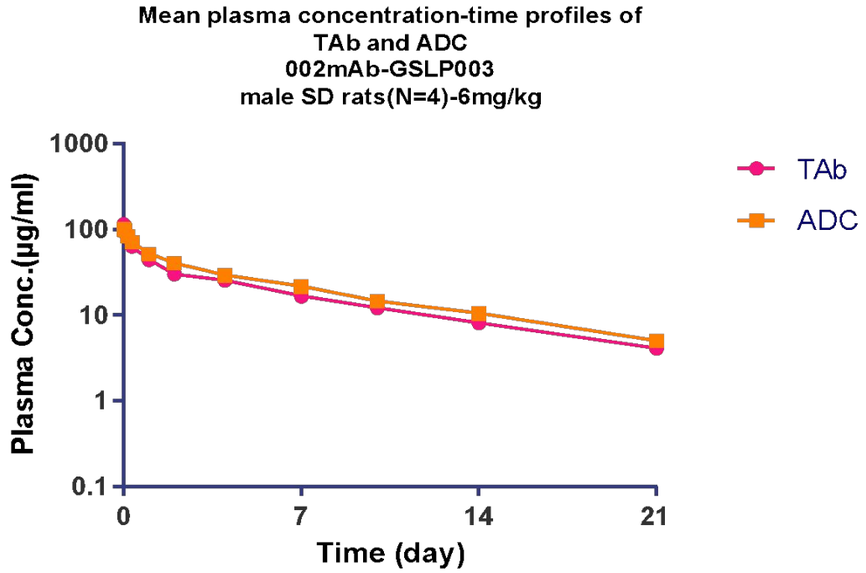
Exhibited favorable PK profiles with almost aligned curves of TAb and ADC. A key risk for ADCs is premature deconjugation leading to divergence between total antibody (TAb) and ADC exposure — a surrogate for linker instability in vivo. Administered IV to rats, with parallel PK sampling for both TAb and ADC components.

PK Parameter	Unit	TAb	ADC
Kel	1/h	0.00431	0.00430
T½	h	162	162
Tmax	h	0.250	0.667
Cmax	μg/mL	127	105
AUC_{0-t}	h·μg/mL	8,241	9,912
$AUC_{0-\infty}$	h·μg/mL	9,265	11,097
CL	mL/h/kg	0.656	0.541
Vss	mL/kg	140	116
$MRT_{0-\infty}$	h	215	215

Key PK Insight

The near-identical T½ (162 h), MRT (215 h), and Kel values for both TAb and ADC components demonstrate exceptional linker stability in vivo. The tightly aligned TAb and ADC concentration-time curves — a hallmark of a well-designed ADC — confirm that payload is retained on the antibody throughout the dosing interval, maximizing tumor exposure and minimizing systemic payload release.

Exhibited favorable PK with almost completely aligned TAb and ADC curves — a strong indicator of in vivo linker stability and predictable exposure.



NB-010: Anti-PD-L1 ADC

Pre-toxicity Study in Rat & Cynomolgus Monkey

Preliminary tolerability studies were conducted in both rodents and cynomolgus monkeys to assess the safety margins prior to formal GLP toxicology studies. These data establish a foundation for clinical dose range selection.

Rodent (Rat)

Demonstrated **favorable safety and tolerability at doses ≥120 mg/kg** — establishing a wide therapeutic window relative to anticipated clinical doses.

Cynomolgus Monkey

W**ell tolerated at doses ≥20 mg/kg**. Only mild, reversible adverse events observed (hair loss, loose stools). **Dose escalation is ongoing**, with no dose-limiting toxicities identified to date.

The adverse events observed in cynomolgus monkeys are consistent with on-target and class-effect findings typical for ADCs and are considered manageable in the clinical context.

NB-010: Anti-PD-L1 ADC

Developability Assessment

Why Developability Matters

Poor biophysical properties — aggregation, instability, high hydrophobicity, non-specific binding, are leading causes of late-stage ADC failures during CMC development and manufacturing scale-up. The asset was comprehensively characterized across all key developability parameters.

Exactly same retention time (RT) for ADC (DAR8) and its parental antibody — a hallmark of exceptional hydrophilicity and low aggregation propensity for a DAR8 construct.

High Purity

Excellent monomer content and minimal aggregation by SEC and HIC analytics

Thermostability

High Tm values supporting long-term stability and standard cold-chain storage

Low Hydrophobicity

Hydrophilicity-enhanced linker normalizes DAR8 HIC profile to match parental antibody RT

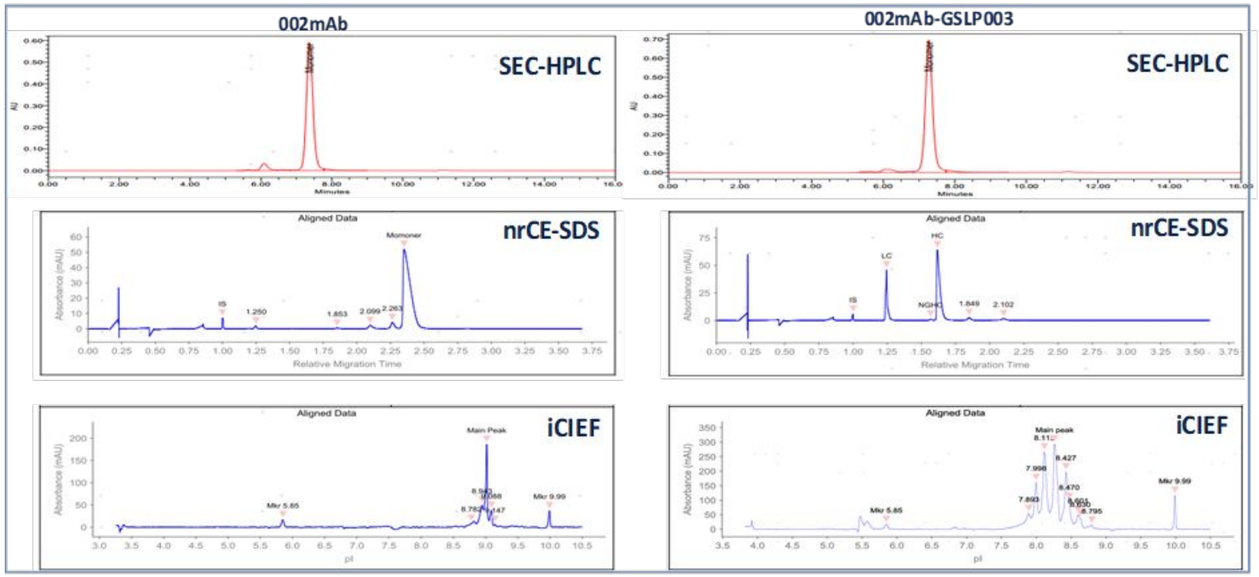
Low Non-Specific Binding & Charge Patches

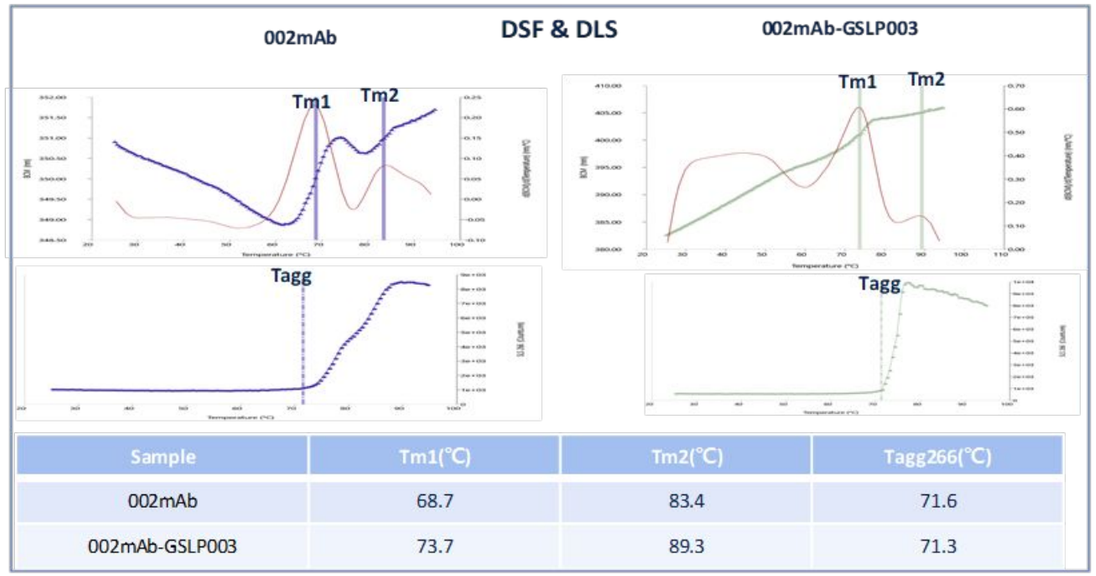
Minimal off-target binding and low positive charge patches — favorable for in vivo safety

NB-010: Anti-PD-L1 ADC

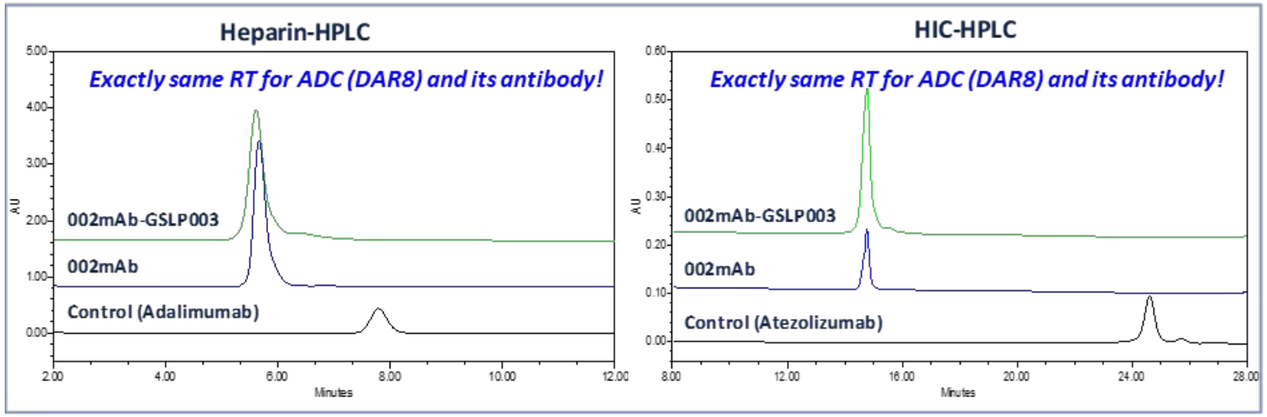
Developability Assessment

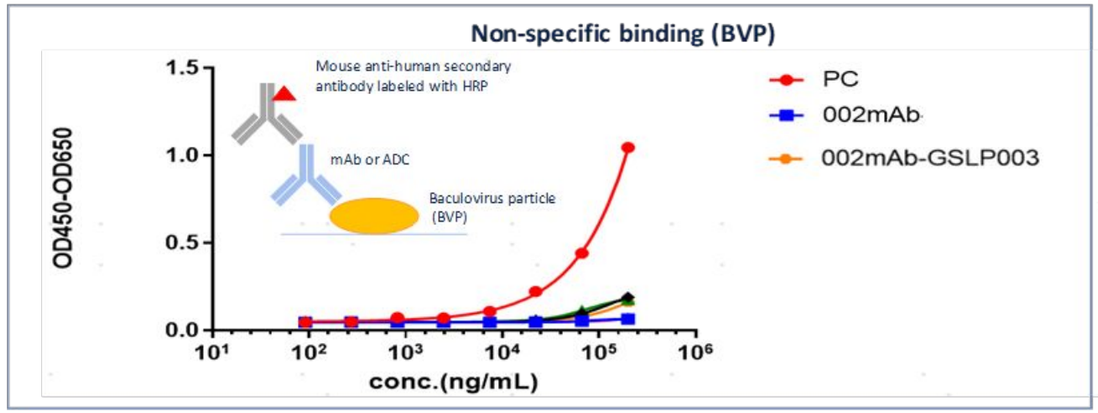
Excellent developability including high purities, good thermostability, low positive charge patches, hydrophobicity and non-specific binding





Sample	Tm1(℃)	Tm2(℃)	Tagg266(℃)
002mAb	68.7	83.4	71.6
002mAb-GSLP003	73.7	89.3	71.3





NB-010: Anti-PD-L1 ADC

Pharmacology Summary

Exhibits a compelling, differentiated preclinical profile that positions it as a best-in-class candidate in the emerging αPD-L1 ADC space.

Dual Mechanism of Action

Synergistic combination of targeted cytotoxicity (Top1i + DDX5 degradation) and immune checkpoint inhibition (PD-L1 blockade)

Potent Efficacy

Robust anti-tumor activity in vitro and in vivo; superior endocytosis, bystander killing and efflux resistance vs. comparators

Favorable PK & Plasma Stability

Aligned TAb/ADC curves, T½ ~162 h, and stable linker across all species for ≥21 days at 37°C

Favorable Safety

Tolerated at ≥120 mg/kg (rodent) and ≥20 mg/kg (cyno); only mild reversible AEs; dose escalation ongoing

Excellent Developability

High purity, thermostability, low hydrophobicity, low NSB — identical HIC RT for ADC and antibody at DAR8

Competitive Positioning

Highly differentiated profile vs. PF-08046054 and HLX43; blue-ocean market with $6–15B peak sales potential

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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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