NB-017: Best-in-Class Bispecific ADC Targeting PD-L1 & B7H3

A novel anti-PD-L1/B7H3 bispecific antibody-drug conjugate (BsADC, DAR8) engineered to overcome the key limitations of single-target ADCs and IO-refractory disease. By simultaneously engaging two broadly expressed tumor antigens (PD-L1 and B7H3), it delivers potent, selective cytotoxicity, while preserving immune cell integrity and activating immunogenic cell death.

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Novel mechanism targeting innate immune signaling at its molecular origin

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Dual-Target Rationale

PD-L1 + B7H3 co-expression in 70–90% of solid tumors; avidity-driven binding overcomes antigen heterogeneity and resistance

Best-in-Class Payload

Highly hydrophilic linker + Exatecan payload; efflux pump resistant; strong bystander effect; minimal immune cell toxicity

Clinical-Ready Profile

Favorable PK in rats; well-tolerated in cynomolgus monkeys at ≥30 mg/kg (Q3W×3); Fc-silenced to eliminate FcγR toxicity

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Preclinical Data Summary

Key Efficacy Highlights

- Complete responses at 3 mg/kg in EBC-1 CDX model; outperforming DB-1419 analogue and HLX43 analogue at the same dose
- Potent TGI in MDA-MB-231, A375, and H1975 CDX models; superior to all mono-target comparators
- Dose-dependent tumor growth inhibition at 1 and 5 mg/kg in triple-negative breast cancer model
- Synergistic dual-targeting effect confirmed across multiple tumor types

Differentiation vs. Competitors

- **vs. DB-1419 analogue:** Superior TGI across all CDX models tested; stronger bystander killing
- **vs. HLX43 analogue (PD-L1 ADC):** Enhanced internalization, broader tumor coverage via B7H3 co-targeting
- **vs. vc-MMAE class:** Efflux pump resistance confirmed via tariquidar inhibition assay
- **Immune safety:** Minimal cytotoxicity on myeloid dendritic cells; PD-1/PD-L1 blockade activity preserved

9.25nM

PD-L1 Affinity (KD)

Moderate, avidity-optimized binding

1.14nM

B7H3 Affinity (KD)

High-affinity second arm

30mg/kg

Cyno Tolerability

Well-tolerated Q3W×3, no DLTs

DAR8

Drug-Antibody Ratio

High payload load; hydrophilic linker

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Unmet Need for Novel Agents Beyond ADCs and IO

Despite remarkable advances in antibody-drug conjugates and immune checkpoint inhibitors, a significant proportion of solid tumor patients fail to achieve durable responses. Three converging challenges define the landscape of unmet need that this is designed to address.

1 Antigen Loss & Downregulation

Single-target ADCs are vulnerable to resistance via selective pressure: tumors downregulate or lose the targeted antigen, rendering the therapy ineffective over time. This is a well-documented mechanism for PD-L1 ADC and B7H3 ADC monotherapies.

2 IO-Refractory Disease

Patients who progress on checkpoint inhibitors have critically limited therapeutic options. Standard-of-care regimens offer modest benefit, and the immunosuppressive tumor microenvironment remains a profound barrier to durable IO responses.

3 Heterogeneous PD-L1 Expression

PD-L1 expression is spatially variable and dynamically regulated, making it an imperfect single biomarker. Tumors with heterogeneous or low PD-L1 expression are poorly served by PD-L1-directed monotherapy, limiting patient selection and response depth.

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Dual Targeting: PD-L1 × B7H3 — A Rational, Synergistic Strategy

Why PD-L1 + B7H3?

- **Broad overexpression**: B7H3 is broadly overexpressed across 70–90% of solid tumors with minimal expression in normal tissues, making it an ideal co-target.
- **Mechanistic link to immune evasion**: PD-L1 is mechanistically linked to immune evasion.
- **Frequent co-expression enabling**: Together, these two antigens are frequently co-expressed on the same tumor cells, enabling avidity-driven, highly selective binding that spares normal tissues.

Overcoming Heterogeneity

Dual targeting provides broader tumor coverage even in cases of heterogeneous antigen expression. If one antigen is downregulated, the second arm maintains ADC engagement, preventing the escape mechanisms that undermine mono-target approaches.

Avidity-Driven Selectivity

Bispecific binding to double-positive tumor cells enhances retention and penetration while reducing off-target engagement on single-positive normal cells

Synergistic Cytotoxicity

Direct tumor cell killing via Exatecan payload + immunogenic cell death (ICD) → activates innate and adaptive immune responses

IO Checkpoint Restoration

PD-1/PD-L1 blockade function preserved in NB-017 — comparable to parental BsAb and competitor ADC, adding an immune-activating dimension beyond cytotoxicity

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Molecular Architecture: Engineered for Precision & Safety

The asset integrates multiple engineering innovations to maximize therapeutic index, balancing potent anti-tumor activity with an acceptable safety profile across oncology indications.

Bispecific Antibody Backbone

15-002mAb: moderate affinity for PD-L1 (KD 9.25 nM) and high affinity for B7H3 (KD 1.14 nM); designed for avidity-driven tumor selectivity

Fc Silence Mutations

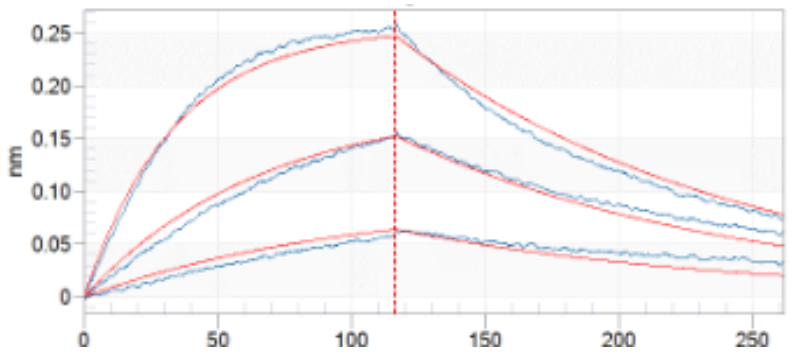
FcγR binding eliminated to remove immune activation-related toxicities; FcRn binding preserved to maintain favorable antibody half-life and PK

Hydrophilic Linker (GSLP001)

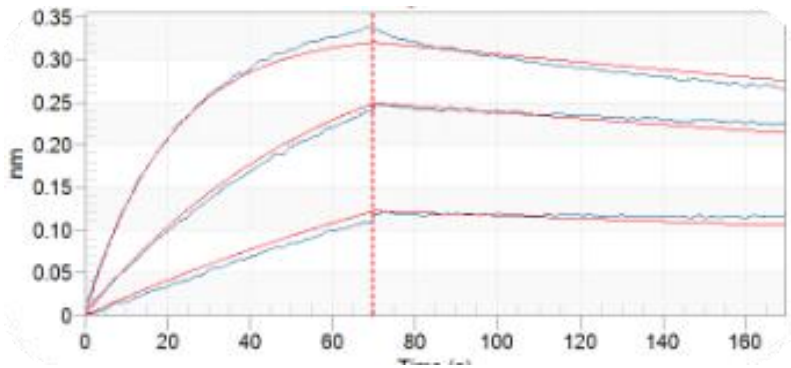
Highly hydrophilic linker reduces ADC aggregation, improves PK stability and enhances the bystander killing effect in antigen-heterogeneous tumor microenvironments

Exatecan Payload (DAR8)

Next-generation topoisomerase I inhibitor; potent, membrane-permeable for bystander effect; resistant to P-gp/MDR efflux pumps — a critical advantage over MMAE-based ADCs



BLI Fitting View: PD-L1 binding kinetics — KD 9.25 nM



BLI Fitting View: B7H3 binding kinetics — KD 1.14 nM

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Strong In Vitro Anti-Cancer Activity with Limited Impact on Immune Cells

The asset demonstrates superior internalization, potent cytotoxicity, robust bystander killing, efflux pump resistance and a favorable immune safety profile, a combination that distinguishes it from both competitor BsADCs and mono-target ADCs.

1

Superior Internalization

- NB-017 BsAb showed significantly higher internalization in Calu-6 and EBC-1 cells vs.:
  - PD-L1 mAb alone
  - Competitor BsAb
- Key Takeaway: Enhanced internalization is a prerequisite for intracellular payload delivery.

2

Potent Cytotoxicity

- Robust killing of HCC827 and Calu-6 cells
- Outperformed parental PD-L1 ADC and B7H3 ADC in head-to-head comparisons
- Key Takeaway: Confirms synergy of dual targeting.

3

Strong Bystander Effect

- Eradicated PD-L1-negative COLO205 and SNU-16 cells in co-culture with PD-L1-positive 293F-PDL1 cells
- Bystander effect exceeded DB-1419 analogue
- Key Takeaway: Effective against antigen-heterogeneous tumors.

4

Efflux Pump Resistance

- Retained full cytotoxic potency in DMS53 cells expressing P-gp efflux pumps
- Unlike vc-MMAE control (15-002mAb-vcMMAE)
- Confirmed by tariquidar inhibition assay
- Key Takeaway: Overcomes a major resistance mechanism of MMAE-based ADCs.

5

Immune Cell Safety

- Minimal cytotoxicity toward myeloid dendritic cells (mDCs)
- PD-1/PD-L1 blockade activity fully preserved at levels comparable to parental BsAb
- Key Takeaway: Clean immune safety profile; critical differentiator.

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Excellent In Vivo Anti-Tumor Efficacy Across Multiple CDX Models

- Consistent, superior anti-tumor efficacy demonstrated across four independent CDX models
- Indications: NSCLC, TNBC, Melanoma
- All models represent high unmet-need indications with documented PD-L1/B7H3 co-expression

Model 1: EBC-1 (NSCLC)

- Dose: 3 mg/kg
- Result: Induced complete responses
- Comparison: Outperformed DB-1419 analogue and HLX43 analogue at equivalent dose
- Key Finding: Dual-targeting synergy confirmed vs. mono-target PD-L1 ADC

Model 2: A375 (Melanoma)

- Dose: 8 mg/kg
- Result: Robust anti-tumor activity
- Comparison: Outperformed both DB-1419 analogue and HLX43 analogue
- Key Finding: Superior efficacy in melanoma model

Model 3: MDA-MB-231 (TNBC)

- Dose: 5 mg/kg (dose-dependent activity confirmed at 1 and 5 mg/kg)
- Result: Significantly greater TGI than DB-1419 analogue
- Comparison: Surpassed both PD-L1 ADC and B7H3 ADC arms
- Key Finding: Dual-targeting advantage in TNBC

Model 4: H1975 (NSCLC)

- Dose: 8 mg/kg
- Result: Outperformed DB-1419 analogue and HLX43 analogue
- Key Finding: Reinforces cross-model consistency of differentiated efficacy profile

- NB-017 consistently outperformed competitors across all four CDX models.
- Complete responses achieved at 3 mg/kg in EBC-1 (NSCLC).
- Dual-targeting synergy confirmed vs. mono-target ADCs.

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Favorable Pharmacokinetic & Safety Profile

Rat PK (6 mg/kg, Single Dose)

The asset exhibited well-aligned PK curves between the total antibody assay (measuring total Ab) and the ADC assay (measuring intact conjugate), indicating high linker stability in circulation and minimal premature payload release, a hallmark of a well-engineered ADC.

Closely matched curves are a strong predictor of predictable, dose-proportional exposure in future clinical studies.

Cynomolgus Monkey Exploratory Toxicity

In a multi-dose exploratory toxicology study, the asset was well-tolerated at 30 mg/kg administered Q3W × 3 doses, a clinically relevant dosing schedule. No dose-limiting toxicities were observed at this dose level.

Fc-silence mutations (ablating FcγR binding while preserving FcRn) are the key engineering feature enabling this favorable tolerability, by eliminating immune effector cell activation-related adverse effects.

Immune Cell Preservation

In vitro data confirm minimal impact on myeloid dendritic cells and full retention of PD-1/PD-L1 blockade, supporting a clean immune safety profile heading into IND-enabling studies.

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Vs. Competitive Benchmark: A Clear Differentiation Case

The asset has been benchmarked head-to-head against the leading PD-L1/B7H3 BsADC in the field (DB-1419 analogue) across in vitro and in vivo studies. The data consistently demonstrate superiority across multiple dimensions of preclinical performance.

DIMENSION	NB-017	DB-1419 ANALOGUE	HLX43 ANALOGUE (PD-L1 ADC MONO)
1. In Vivo Efficacy	Complete responses at 3 mg/kg	Partial responses	Inferior
2. Bystander Effect	Superior; exceeds DB-1419	Moderate	Limited
3. Efflux Pump Resistance	Resistant	Not tested	Not tested
4. Internalization	Significantly higher	Lower	Lowest
5. Immune Cell Safety	Minimal mDC toxicity	Comparable	Not reported
6. PK Stability	Excellent linker stability	Not disclosed	Standard

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Differentiated, Data-Driven and IND-Ready

NB-017 represents a compelling next-generation BsADC opportunity, combining best-in-class molecular engineering with a robust and reproducible preclinical efficacy and safety dataset. The program is positioned to advance into IND-enabling studies with a differentiated competitive profile.

01

Preclinical Package

Comprehensive in vitro & in vivo dataset across 4 CDX models; PK in rats; exploratory tox in cynomolgus monkeys — foundational data package complete

02

IND-Enabling Studies

GLP toxicology, ADME, and manufacturing scale-up under way; regulatory strategy for US IND and CTA submission being finalized

03

Phase I Trial

Dose-escalation study in PD-L1/B7H3-positive solid tumors; initial indications: NSCLC, TNBC, melanoma — informed by CDX model data

04

Partnership & Investment

Seeking strategic co-development partners and Series B capital to fund IND-enabling through Phase I; open to licensing discussions for ex-China rights

7 Preclinical Advantages Confirmed

Moderate affinity · Fc-silenced · Superior internalization · Potent cytotoxicity · Bystander effect · Efflux pump resistant · Favorable PK & Safety

Multiple High-Value Indications

NSCLC · TNBC · Melanoma · Broad solid tumor potential via 70–90% B7H3 co-expression across tumor types

Outperforms DB-1419 Analogue

Consistent superiority in all head-to-head CDX models — establishing NB-017 as the leading PD-L1/B7H3 BsADC in development

Accelerating Innovation to Improve Patients' Lives

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

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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 patients worldwide, please reach out to:

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