NB-009 First-in-Class Candidate for RAS Tumors

Polysaccharide Drug Conjugate

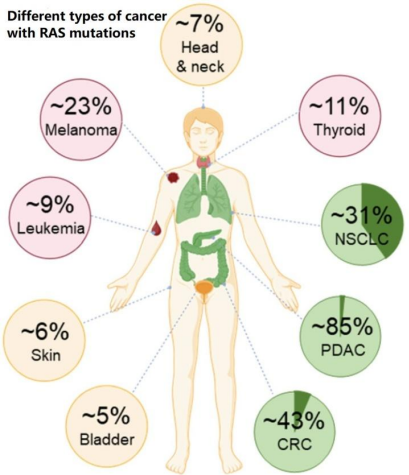
NAVIKA BIO

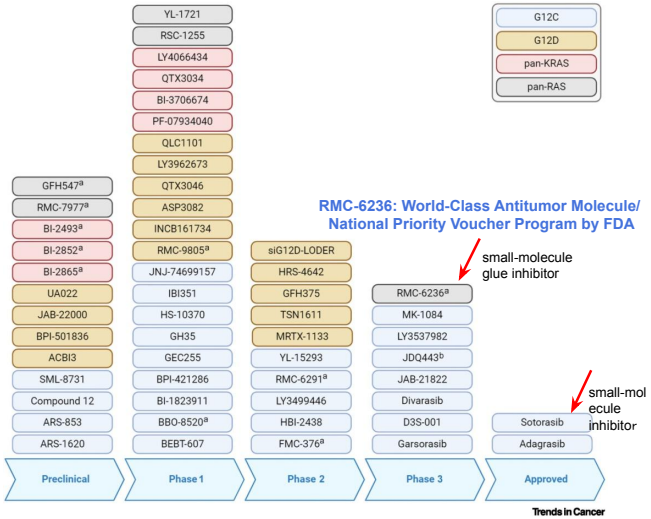
This asset has been selected for Oral Presentation in April, at the American Association Cancer Research Annual Meeting 2026, in San Diego

Global RAS-Targeted Therapy Landscape

Market Opportunity

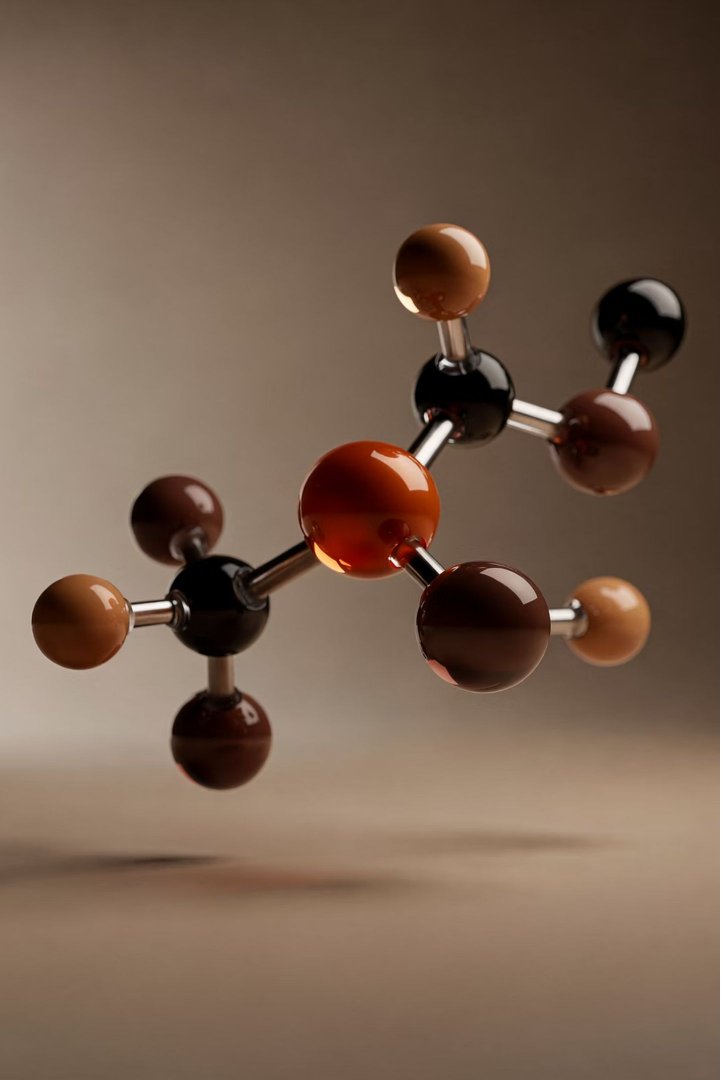
RAS mutations represent one of the largest and most challenging opportunities in oncology. Despite decades of research declaring RAS "undruggable," recent breakthroughs have validated this target, creating a market estimated at $20–30 billion USD with millions of patients in need of effective therapies. RAS mutations occur in approximately 19% of all cancer patients globally, representing about 3.4 million new cases annually. The distribution spans multiple high-incidence tumor types with significant unmet medical need.





RMC-6236: Best-in-Class Benchmark

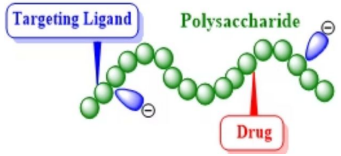
> RMC-6236 is a world-class small-molecule glue pan-RAS-ON inhibitor developed by Revolution Medicines. It was awarded The Commissioner's National Priority Voucher Program by the FDA, recognizing its high transformative impact and breakthrough potential for addressing large unmet medical needs. NB-009's superior performance vs. RMC-6236 in head-to-head xenograft studies establishes its best-in-class potential.



NB-009: First-in-Class for RAS Tumors

Our lead platform represents a revolutionary approach to targeted drug delivery, combining the specificity of targeted therapies with the potency of cytotoxic agents. This proprietary technology enables unprecedented tumor selectivity while minimizing systemic toxicity.

Our polysaccharide-drug conjugates exploit a fundamental biological difference between tumor cells and normal cells. Unlike conventional small molecules that rely on passive diffusion or receptor-mediated endocytosis, our platform harnesses macropinocytosis—a nutrient scavenging pathway that is dramatically upregulated in RAS-mutant tumors.



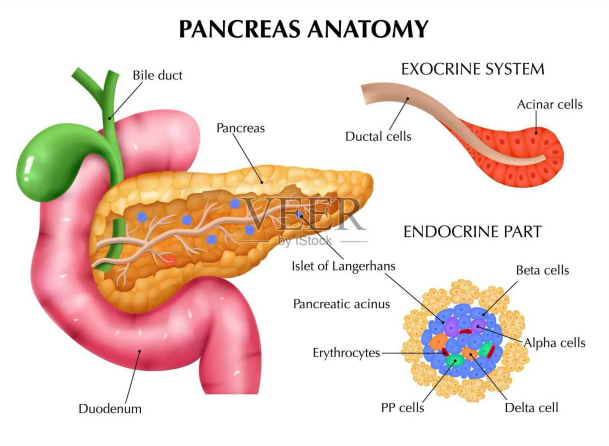
Versatile Targeting Ligands

- Unsaturated fatty acids (UFA)
- Aptamers for molecular recognition
- Oligosaccharides for cell surface binding
- Tumor-targeting peptides
- Antibody fragments for precision delivery

Drug

- Small molecule drugs
- Protein degraders (PROTACs)
- Small nucleic acids
- Proteins and peptides
- Radioactive elements
- Fluorescent dyes

NB-009: First-in-Class Pan RAS Inhibitor



Polysaccharide-Drug Conjugate (PSDC) Innovation

A first-in-class Polysaccharide-Drug Conjugate targeting Ras Mutant tumors via micropinocytosis. This novel Pan Ras inhibitor addresses a market 8 times the size of the current one for KRAS 12C inhibitors, i.e. potentially up to **$30B market opportunity**.

The program is in IND-enabling studies with strong global patent protection beyond 2040 (PCT filed). As the first Polysaccharide-Drug Conjugate using “Click Chemistry “ (Nobel-Prize-winning technology) , NB-009 as a Pan Ras inhibitor is a breakthrough treatment for High Mortality Cancers with high unmet need and poor prognoses, such as:

- Pancreatic Cancer (where KRAS mutations occur in ~88% of cases)
- Colorectal Cancer (~50%)
- Non-Small Cell Lung Cancer (~32%)

Broader Coverage Advantages

Significant inhibition of KRAS-driven tumor growth, including KRAS wild-type , G12C, G12D, G12V, G12R, etc.

Higher Antitumor Activity

Outperformed Revolution Medicine’s RMC-6236—the leading pan-RAS anti-tumor agent—in lung cancer models.

Higher Safety

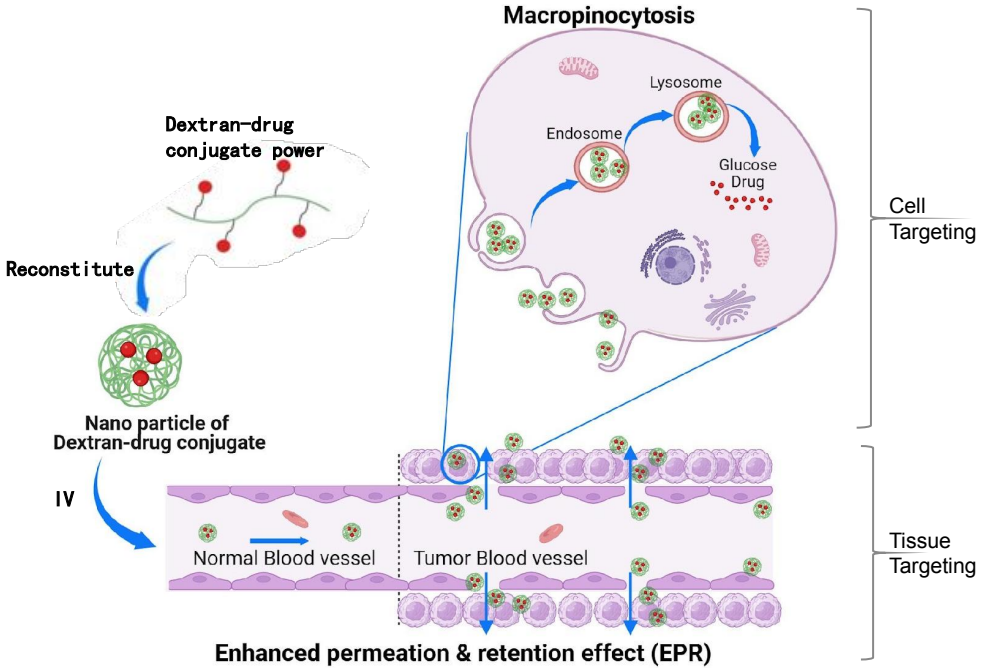
Excellent safety at a high dose of 15 mg/kg, representing a 2.5-fold improvement over free docetaxel with only minimal liver exposure.

NB-009: Novel Mechanism: Macropinocytosis

Our Unique Approach

We conjugate the payload drug to a dextran molecule. When tumor cells take up the dextran through macropinocytosis, the drug is simultaneously carried into the cell, achieving targeted intracellular delivery. (Dextran is a type of polysaccharide.)

Tumor-Targeting Mechanism Diagram



Macropinocytosis Activation

To support rapid proliferation, tumor cells actively take up nutrients such as polysaccharides and proteins from their surroundings through continuous membrane ruffling to "gulp" extracellular fluid.

RAS-Mutant Tumor Selectivity

RAS-mutant tumor cells actively scavenge polysaccharides and trigger intense macropinocytosis, creating a targetable vulnerability that normal cells lack.

Transmembrane Delivery

Polysaccharide-drug conjugates achieve efficient transmembrane delivery through macropinocytosis. Unlike other drugs where the cell membrane acts as a barrier, our approach bypasses this limitation entirely.

EPR Effect Enhancement

The Enhanced Permeability and Retention (EPR) effect allows nanoparticles and macromolecules to accumulate in tumor tissues due to leaky blood vessels and limited lymphatic clearance, providing passive tumor targeting. allows nanoparticles/macromolecules to accumulate in tumor tissues because of leaky blood vessels and limited lymphatic clearance

NB-009: First-in-Class Drug Candidate for RAS Tumors

Our Unique Approach

NB-009 represents a paradigm shift in treating RAS-mutant cancers. This novel modality combines a proven cytotoxic agent (docetaxel) with our proprietary polysaccharide delivery platform to create a first-in-class therapeutic specifically designed to target RAS-driven malignancies.

NB-009 Structure & Components

Dextran Carrier: Enables targeted delivery by exploiting RAS-driven dextran addiction in tumor cells

Docetaxel Payload: Induces apoptosis and kills tumor cells upon intracellular release

GLA Sensitizer: Provides synergistic antitumor activity, enhancing therapeutic efficacy

Glutamic Acid Modifier: Works with dextran to avoid clearance by the reticuloendothelial system (RES)

Average Molecular Weight: Approximately 130 kDa

Manufacturing Process

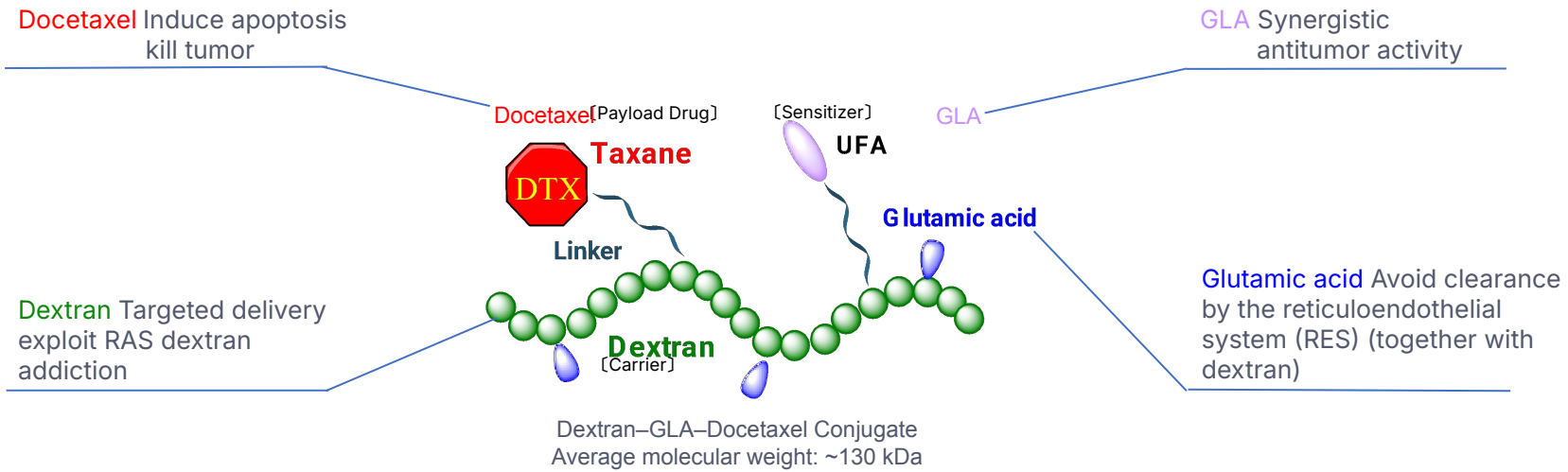
NB-009 is synthesized through a sophisticated multi-step process utilizing click chemistry (CuAAC) to conjugate functionalized dextran, GLA, and docetaxel components. This precise chemical coupling ensures consistent drug-to-carrier ratios and reproducible pharmacological properties.

Target Indications

- Non-small cell lung cancer (NSCLC)
- Pancreatic cancer (PDAC)
- Colorectal cancer (CRC)

NB-009: New modality for RAS tumors (First in class drug candidate)

Structure Diagram & Mechanism of Action



Dextran–GLA–Docetaxel Conjugate
Average molecular weight: ~130 kDa

Preparation of NB-009

Dextran
Di-Functionalization
Docetaxel Functionalization
GLA Functionalization

→ CuAAC Click Chemistry →

Dextran–GLA–Docetaxel Conjugate

Indications of NB-009

RAS-mutant tumors, such as:

- Non-small cell lung cancer (NSCLC)
- Pancreatic cancer PDAC)
- Colorectal cancer (CRC), etc.

NB-009: Robust Anti-Pan-KRAS Tumor Activity via Macropinocytosis

No Pan-RAS inhibitor approved for commercial sale yet; ~23% to 25% of malignant tumors have KRAS mutations. This translates to roughly 2.7M new patients globally each year.

NB-009 PSDC inhibits tumor growth by suppressing the PI3K-AKT , the p38 pathway and reduced proliferation (Ki-67). PSDC turn tumor cell membranes from natural “barriers” into “carriers” and enrich the drug inside tumor cells. Modified polysaccharides with negatively charged glutamic acid are non-immunogenic, fully biodegradable and avoid clearance by the reticuloendothelial system and markedly reduces uptake by normal cells.

First Click Chemistry Application

World- first to apply "click chemistry" to polysaccharide–drug conjugation. The reaction is simple, rapid, and highly specific.

- High yield (85-95%)
- High drug loading（30%）
- Allow coupling of a wide variety of drug molecules
- Capable of large-scale industrial production

Outstanding Efficacy

In RAS-driven lung cancer model, NB-009 at a dose of 15 mg/kg significantly inhibited H358 /KRAS G12C tumor growth, demonstrating in vivo antitumor efficacy 5.56-fold greater than RMC-6236 from Revolution Medicine and 9.4-fold greater than Adagrasib from BMS

Unique Biodistribution Profile

Selectively accumulating in tumor sites while sparing normal organs—unlike existing cancer therapies such as small molecules, macromolecules (including antibodies and ADCs) and nanoparticle formulations. Resulted in less drug resistance and minimal accumulation in liver and better safety profile

PSDC Platform Potential

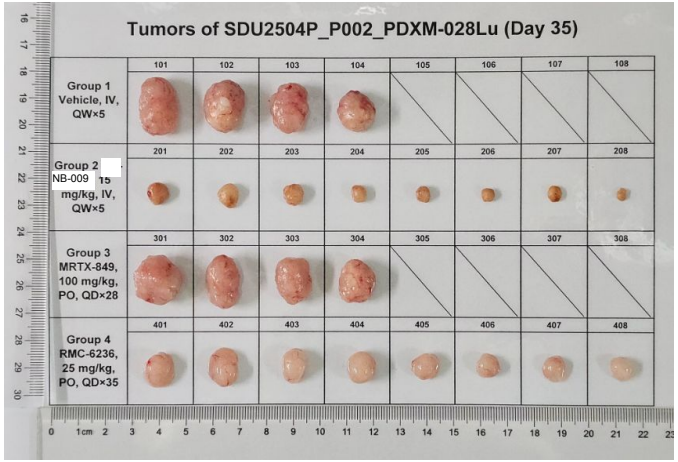
Difunctionalized polysaccharides with two different functional groups are the first one able to link both targeting ligand and drug in the world. Expansion to Additional Drug Classes: Small molecule, oligonucleic acids such as siRNA ASOs, protein, etc for various therapies.

NB-009: Differentiated Multidimensional Targeting Advantage

Patient Derived Xenograft Model

This independent third-party CRO study evaluated NB-009 performance in a patient-derived xenograft model of lung cancer harboring KRAS wild-type mutations, representing a clinically relevant therapeutic challenge in oncology.

NB-009 = CQ-0736



2.7× Superior TGI

At 15 mg/kg dosing, NB-009 achieved tumor growth inhibition 2.7-fold higher than RMC-6236 at Day 35, demonstrating exceptional anti-tumor activity in this preclinical lung cancer model.

Reduced Resistance Profile

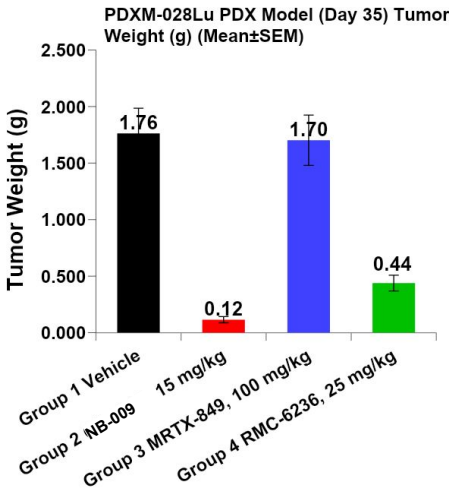
While RMC-6236 exhibited observable resistance emergence during treatment, NB-009 maintained durable efficacy with significantly lower tendency for resistance development throughout the study period.

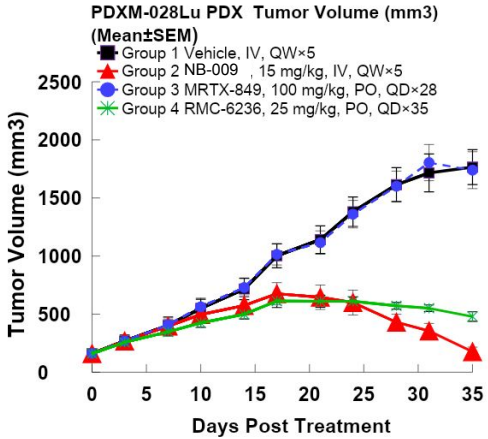
Clean Safety Profile

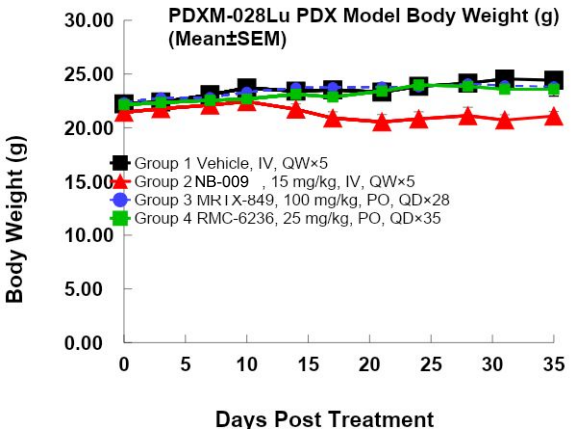
NB-009 treatment resulted in no body weight loss or observable toxicity, indicating a favorable therapeutic window critical for clinical translation and patient tolerability.

NB-009: Differentiated Multidimensional Targeting Advantage

Patient Derived Xenograft Model







Summary

NB-009 at a dose of 15 mg/kg significantly inhibited tumor growth in the PDX-028Lu KRAS/WT model. At Day 35, its tumor growth inhibition was 2.7-fold higher than that of RMC-6236, a leading RAS-targeted oncology drug candidate globally.

Resistance was observed in the RMC-6236 group. In contrast, NB-009 demonstrated a lower tendency for resistance and more durable efficacy.

NB-009 did not cause body weight loss or any observable toxicity.

NB-009: Demonstrates Durable Antitumor Activity

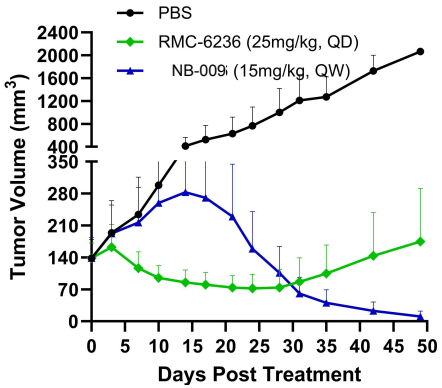
In both KRAS G12C and KRAS WT PDX models

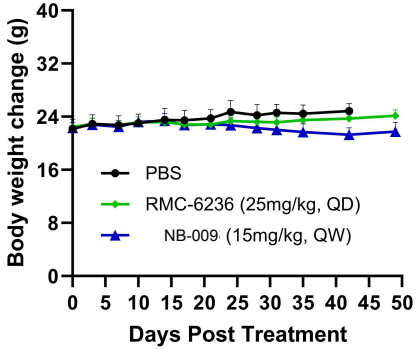
Kras G12C PDX M-170Lu Lung Cancer Models

At day 49, NB-009 group's tumor volume is **16.5** folders lower than RMC-6236

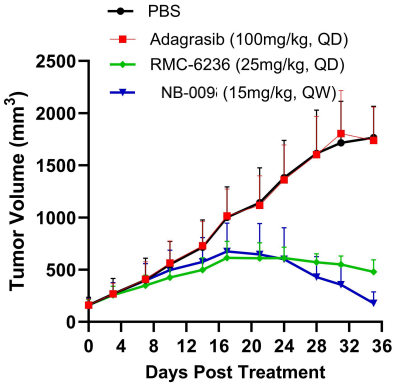
Resistance was observed in the RMC-6236 group, while NB-009 maintained durable tumor control without resistance over 49 days.

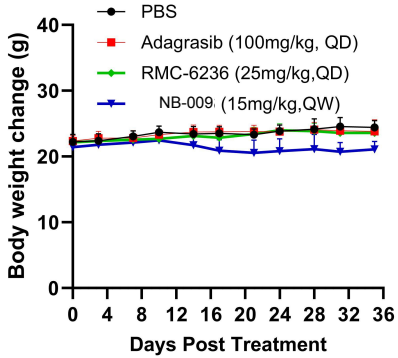
No significant body weight loss or observable toxicity.





Kras WT PDX-028Lu Lung Cancer Models





At day 35, NB-009's tumor volum is **2.7** folders lower than RMC-6236

Resistance was observed in the RMC-6236 group, while NB-009 maintained durable tumor control without resistance over 35 days.

No significant body weight loss or observable toxicity.

NB-009: Differentiated Multidimensional Targeting Advantage

Comparative analysis of therapeutic modalities targeting RAS-driven malignancies reveals distinct mechanistic and pharmacological profiles across drug classes. NB-009's dextran-docetaxel conjugate platform demonstrates unique advantages in targeting precision, resistance mitigation, and safety.

Drug Type	Tumor targeting				Efficacy	Durability / resistance	Safety	Liver accumulation
	Molecule targeting	Cell targeting	Tissues targeting	Overall targeting				
NB-009 Dextran- Docetaxel Conjugate	Related to RAS protein	⭐⭐⭐⭐ Macropinocytosis	⭐⭐⭐ EPR	⭐⭐⭐⭐	⭐⭐⭐⭐⭐	Less resistance	⭐⭐⭐⭐	NO
RMC series RAS macrocyclic molecular glues	RAS protein	⭐⭐⭐	NO	⭐⭐⭐	⭐⭐⭐⭐	Delayed resistance	⭐⭐⭐⭐	YES
Small-molecule direct RAS inhibitors	RAS protein	⭐⭐⭐	NO	⭐⭐⭐	⭐⭐⭐	Rapid resistance	⭐⭐⭐	YES
RAS protein degraders	RAS protein	⭐⭐⭐	NO	⭐⭐⭐	⭐⭐⭐	Delayed resistance	⭐⭐⭐	YES

Key Differentiators

NB-009 uniquely combines:

- **RAS protein-related targeting** with cell and tissue selectivity
- **Superior durability** with reduced resistance emergence
- **No hepatic accumulation**, addressing a critical safety limitation of competing modalities

NB-009: Demonstrates Potent Pan-KRAS Activity

In Vitro Efficacy

NB-009 exhibits remarkable inhibitory activity against pan-KRAS tumor cells in vitro, maintaining or exceeding the potency of parent docetaxel while providing the foundation for superior in vivo performance through its targeted delivery mechanism.

Figure 3: Growth Inhibition by NB-009

The inhibition of cancer cell growth by NB-009 was rigorously determined via CCK-8 assay across multiple KRAS-mutant cell lines.

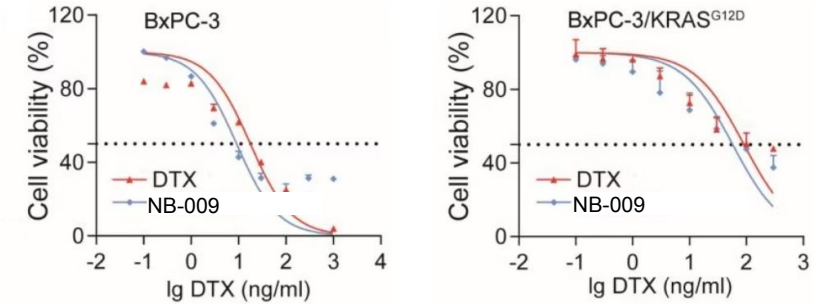


Table 1: IC50 Values (ng/mL) in Pancreatic Cancer Cells (72h Treatment)

Effects of NB-009 on tumor volume and body weight in nude mice bearing H358/KRAS G12C xenografts over 28 days.

Tumor Cells	DTX	CQ-0736
BxPc-3 WT	7.5 ± 1.2	5.7 ± 1.8
BxPc-3/KRAS G12D	7.9 ± 1.9	5.3 ± 1.3
MIA PaCa-2	6.7 ± 1.5	5.2 ± 1.2
MIA PaCa-2/KRAS G12C	9.1 ± 4.3	2.6 ± 1.4

Key Conclusion

> NB-009 significantly inhibits KRAS cancer cell growth in vitro compared to parent docetaxel (DTX), demonstrating maintained potent antitumor activity with complete release of the active drug upon cellular uptake. These results establish the foundation for the superior in vivo efficacy observed in xenograft models.

NB-009: Tumor Targeting

Dextran-Based Conjugates Target KRAS Pancreatic Cancer via Macropinocytosis

Using fluorescent imaging with Dex-GLA-Cy7.5, we definitively demonstrated that our polysaccharide conjugates achieve highly selective tumor accumulation through macropinocytosis. This selectivity is confirmed through inhibitor studies showing dramatic reduction in tumor uptake when macropinocytosis is blocked.

Figure 4a: *In Vivo* Fluorescence Imaging

Nude mice bearing MIA-paca-2 xenografts after intravenous administration of Dex-GLA-Cy7.5 demonstrate specific tumor accumulation over time.

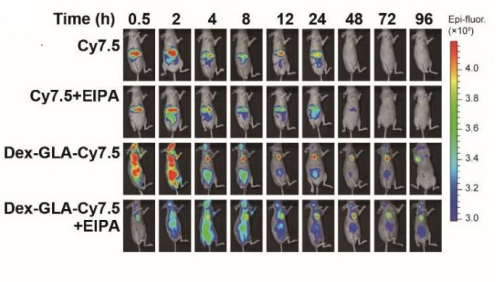


Figure 4b: Macropinocytosis Confirmation

Fluorescence intensity of tumors treated with Dex-GLA-Cy7.5 ± macropinocytosis inhibitor EIPA proves mechanism-dependent uptake.

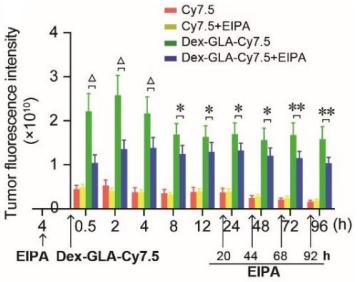


Figure 4c: Tissue Distribution Analysis

Optical and fluorescence imaging of tissues from mice treated with Dex-GLA-Cy7.5 and EIPA reveal striking tumor selectivity with minimal normal organ accumulation.

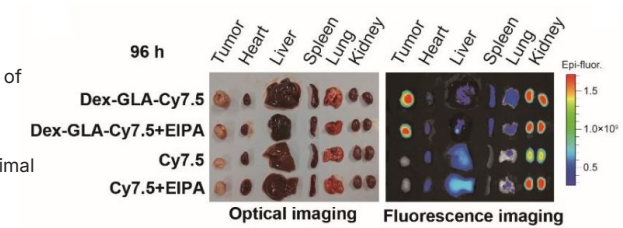
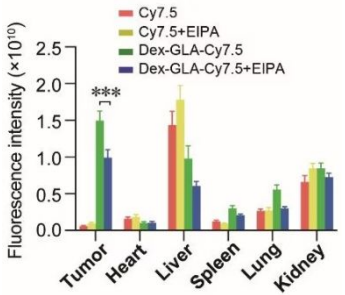


Figure 4d: Quantitative Biodistribution

Fluorescence intensity across tumor and major organs displayed as histogram.



Superior Tumor-to-Normal Tissue Ratio

> Dextran-GLA-Cy7.5 achieves tumor-selective accumulation via macropinocytosis with a superior tumor-to-normal tissue ratio compared to currently marketed cancer drugs. This exceptional selectivity translates into NB-009's remarkable therapeutic window observed in efficacy studies.

NB-009: Biodistribution: Exceptional Tumor Selectivity

Pharmacokinetics

Comprehensive biodistribution studies reveal NB-009's unprecedented tumor selectivity. Unlike conventional cancer therapeutics, NB-009 preferentially accumulates in tumor tissues while exhibiting minimal uptake in normal organs—a profile that directly translates into its superior safety and efficacy.

Figure 5a: Tumor Accumulation vs. Parent DTX

Free DTX concentration in tumors from BxPC-3 xenografts treated with NB-009 at 12 mg/kg compared to parent DTX at 24 hours demonstrates sustained delivery.

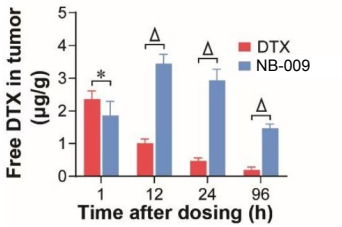


Figure 5b: Free vs. Total DTX in Tumors

Comparison of free DTX and total DTX (conjugated + free) of NB-009 in tumor tissues over time reveals controlled drug release kinetics.

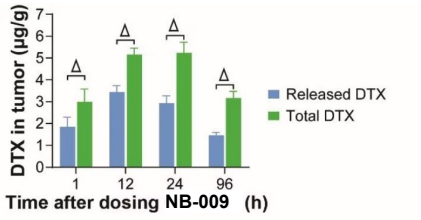


Figure 5c: Tissue Selectivity Profile

Free DTX levels of NB-009 in normal tissues versus tumor at 24 hours demonstrate preferential tumor accumulation.

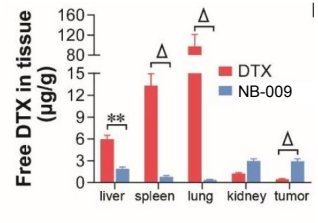
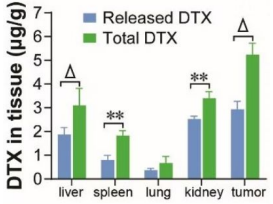


Figure 5d: Complete Biodistribution

Free DTX and total DTX distribution across normal tissues and tumor reveals the unique pharmacokinetic profile of NB-009.



Key Differentiators

Preferential Tumor Accumulation: NB-009 concentrates in tumor tissues rather than normal organs
Unique PK Profile: Unlike other macromolecular and small-molecule cancer drugs, NB-009's three key features—macromolecular polysaccharide structure, negative ionic charge, and lack of immunogenicity—dramatically reduce uptake into normal cells or tissues
Minimal Renal Clearance: Water-soluble polymers with molecular weight below 50,000 Da are typically filtered by kidneys; NB-009's 130 kDa structure avoids this rapid clearance

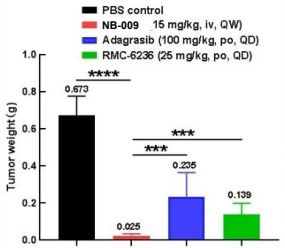
NB-009: In Vivo Efficacy Outperforms Leading KRAS G12C Inhibitors

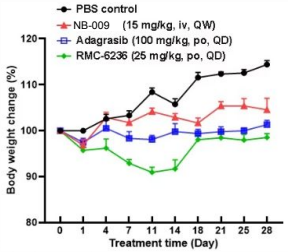
H358 Lung Cancer Xenograft Model (KRAS G12C)

In head-to-head comparisons against Revolution Medicines' RMC-6236 (pan-RAS-ON inhibitor awarded FDA's National Priority Voucher) and Mirati's adagrasib, NB-009 demonstrated dramatically superior efficacy with an improved safety profile and reduced resistance development.

Figure 6: Tumor Growth Inhibition

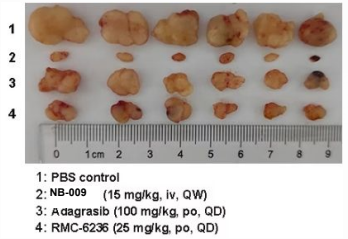
Effects of NB-009 on tumor volume and body weight in nude mice bearing H358/KRAS G12C xenografts over 28 days.





Treatment Regimens

NB-009: 15 mg/kg IV, once weekly × 4 weeks
Adagrasib: 100 mg/kg oral, daily × 4 weeks
RMC-6236: 25 mg/kg oral, daily × 4 weeks



5.56x
vs. RMC-6236
Tumor growth inhibition of NB-009 compared to Revolution Medicines' leading pan-RAS inhibitor

9.4x
vs. Adagrasib
Tumor growth inhibition of NB-009 compared to Mirati's approved KRAS G12C inhibitor

0%
Weight Loss
No body weight loss or observed toxicity at therapeutic doses with weekly administration

Critical Findings

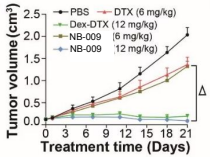
- NB-009 significantly inhibited H358 KRAS G12C tumor growth at 15 mg/kg without body weight loss or observed toxicity
- The adagrasib group showed rapid drug resistance, while RMC-6236 displayed delayed resistance. In contrast, NB-009 demonstrated less resistance and greater durability
- Both RMC-6236 and adagrasib groups exhibited slight body weight loss, while NB-009-treated mice maintained healthy weight
- Weekly dosing with NB-009 outperformed daily dosing of competitive agents, suggesting superior pharmacodynamics and patient convenience

NB-009: KRAS G12D Efficacy

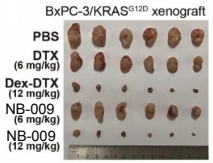
Exceptional Efficacy in BxPC-3/KRAS G12D Pancreatic Cancer

NB-009 demonstrated near-complete tumor growth inhibition in KRAS G12D pancreatic cancer xenografts—one of the most aggressive and treatment-resistant cancer subtypes. These results establish proof-of-concept for NB-009's pan-KRAS activity beyond G12C mutations.

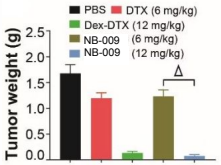
Study 1: Dose-Finding Efficacy (21-Day Study)



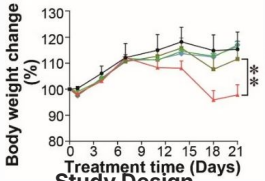
Tumor Volume



Tumor Weight



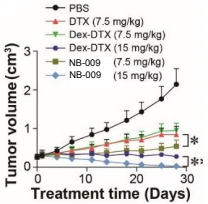
Body Weight



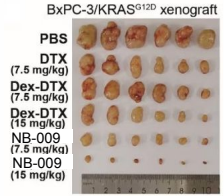
Study Design

Figure 7a: Effects on tumor parameters in BxPC-3/KRAS G12D xenografts. Mice received IV injections of DTX (6 mg/kg), Dex-DTX (12 mg/kg), or NB-009 (6 or 12 mg/kg DTX-equiv) on Days 0, 7, and 14.

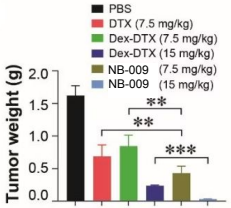
Study 2: Extended Efficacy Assessment (28-Day Study)



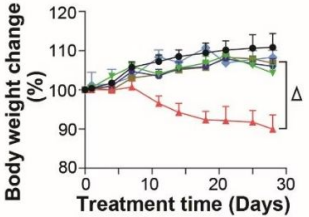
Tumor Volume



Tumor Weight



Body Weight



Study Design

Figure 7b: Effects in extended 28-day study. Mice received IV injections of DTX (7.5 mg/kg), Dex-DTX (7.5 or 15 mg/kg), or NB-009 (7.5 or 15 mg/kg DTX-equivalent) on Days 0, 7, 14, and 21.

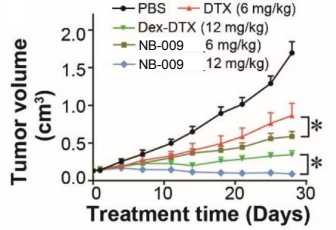
Breakthrough Results

> Significantly inhibited BxPC-3/KRAS G12D tumor growth, achieving a remarkable Tumor Growth Inhibition (TGI) of 98.5% without body weight loss or observed toxicity at the 15 mg/kg dose. Represents near-complete tumor suppression in a notoriously difficult-to-treat pancreatic cancer model.

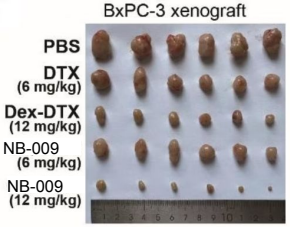
NB-009: Efficacy Extends Beyond KRAS Mutations

BxPC-3/KRAS Wild-Type Pancreatic Cancer Model

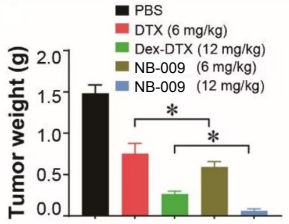
Remarkably, NB-009's efficacy is not limited to KRAS-mutant tumors. In wild-type KRAS pancreatic cancer models, NB-009 demonstrated exceptional tumor growth inhibition while parent docetaxel caused significant toxicity, highlighting the therapeutic advantage of targeted delivery even in non-mutant settings.



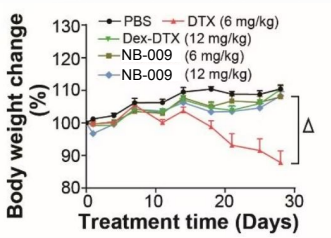
Tumor Volume Over Time



Final Tumor Weight



Body Weight Monitoring



Study Design

Figure 8: Effects on tumor volume, tumor weight, and body weight in nude mice bearing BxPC-3 wild-type KRAS xenografts. Mice received IV injections of DTX (6 mg/kg), Dex-DTX (12 mg/kg), or NB-009 (6 or 12 mg/kg DTX-equivalent) on Days 0, 7, 14, and 21 after tumor formation.

Superior Efficacy

NB-009 achieved **97% Tumor Growth Inhibition (TGI)** at 12 mg/kg dose without body weight loss or observed toxicity

Improved Safety

Parent DTX at 6 mg/kg caused **11% body weight loss**, indicating significant systemic toxicity

Broader Applicability

Efficacy in wild-type KRAS tumors expands the addressable patient population beyond KRAS-mutant cancers

Clinical Implications

> The exceptional efficacy of NB-009 in both KRAS-mutant and wild-type tumors demonstrates that macropinocytosis-mediated delivery provides therapeutic benefit across a broader spectrum of cancers than initially anticipated. This finding significantly expands the commercial opportunity and patient impact of the platform.

NB-009: Safety Profile: Hematological Parameters

28-Day Dose Range-Finding Toxicology Study

Comprehensive safety evaluation demonstrates that NB-009 maintains acceptable hematological parameters at therapeutic doses. While dose-dependent effects on white blood cells and lymphocytes were observed, critical parameters including red blood cells, platelets, and neutrophils remained within normal ranges.

Table 2: Blood Cell Counts and Clinical Signs After 28 Days of Treatment

Parameter	PBS	DTX 7.5	Dex-DTX 7.5	NB-009 7.5	NB-009 15
WBC (10^9/L)	6.90 ± 0.46	3.11 ± 0.55	3.23 ± 0.49	3.17 ± 0.39	2.00 ± 0.18
Neu (10^9/L)	1.53 ± 0.35	1.15 ± 0.12	0.98 ± 0.05	1.03 ± 0.07	0.85 ± 0.10
Lym (10^9/L)	5.42 ± 0.42	1.52 ± 0.36	2.06 ± 0.58	2.08 ± 0.44	1.19 ± 0.31
RBC (10^9/L)	9,746 ± 327	9,220 ± 180	9,087 ± 58	8,690 ± 81	8,070 ± 983
PLT (10^9/L)	1,406 ± 46	1,403 ± 6	1,451 ± 37	1,310 ± 40	1,449 ± 21
Activity	Active	Active	Active	Active	Active

Normal Mouse Ranges (×10^9/L): RBC: 7,500–11,500 | PLT: 800–2,200 | Neu: 0.50–3.00 | Lym: 3.00–11.00 | WBC: 4.00–14.00

RBC & Platelets: Within Normal Range

NB-009 at 15 mg/kg maintained red blood cell counts (8,070 × 10^9/L) and platelet counts (1,449 × 10^9/L) **within normal physiological ranges**, indicating no significant bone marrow suppression or bleeding risk.

Neutrophils: Maintained

Neutrophil counts remained adequate at both doses, preserving immune function and reducing infection risk compared to traditional chemotherapy.

Dose-Dependent Leukopenia

Total WBC and lymphocyte counts fell below normal range at 15 mg/kg, indicating leukopenia primarily driven by lymphopenia—an acceptable and manageable effect for oncology therapeutics.

No Severe Thrombocytopenia

Critically, NB-009 **did not cause severe thrombocytopenia**, a dose-limiting toxicity of many chemotherapeutics that leads to bleeding complications and treatment discontinuation.

Demonstrated a favorable hematological safety profile with preserved critical blood cell populations. The absence of severe thrombocytopenia and maintained RBC counts distinguish NB-009 from traditional chemotherapeutics and support its potential for chronic dosing.

NB-009: Safety Profile: Hepatic and Renal Function

28-Day Dose Range-Finding Toxicology Study

Comprehensive biochemical analysis reveals that NB-009 exhibits minimal hepatotoxicity and no apparent nephrotoxicity at therapeutic doses. These findings contrast sharply with parent docetaxel and support NB-009's superior safety margin for chronic administration.

Table 3: Serum Biochemical Parameters After 28-Day Treatment

Parameter	PBS	DTX 7.5	Dex-DTX 7.5	NB-009 7.5	NB-009 15
ALT (U/L)	28.9 ± 3.0	31.6 ± 1.6	52.0 ± 15.0	30.9 ± 2.4	34.3 ± 2.6
AST (U/L)	231.1 ± 14.3	222.1 ± 5.8	216.0 ± 11.6	197.2 ± 28.9	189.9 ± 34.6
UREA (mmol/L)	11.6 ± 3.4	19.9 ± 6.3	11.1 ± 0.1	9.2 ± 0.4	10.4 ± 1.0
CREA (μmol/L)	18.1 ± 2.4	23.2 ± 1.3	23.7 ± 3.7	18.6 ± 1.6	15.9 ± 2.3

Hepatic Function: Minimal Impact

ALT and AST: Remained within normal ranges across all treatment groups

Dex-DTX concern: Slight ALT elevation (52.0 ± 15.0 U/L) suggests potential hepatic stress

NB-009 advantage: Both 7.5 and 15 mg/kg doses showed near-control ALT levels (30–34 U/L)

AST trends: NB-009 groups showed slightly lower AST compared to PBS or DTX, indicating minimal hepatic stress

Conclusion: NB-009 appears **less hepatotoxic than both Dex-DTX and parent DTX**, supporting a favorable safety profile for chronic dosing.

Renal Function: No Apparent Toxicity

DTX toxicity: Parent docetaxel increased UREA (19.9 ± 6.3 mmol/L) and CREA (23.2 ± 1.3 μmol/L), consistent with renal burden

NB-009 preservation: Both doses maintained normal UREA (9–10 mmol/L) and CREA (16–19 μmol/L), comparable to PBS control

Dose independence: No dose-dependent increase in renal toxicity markers

Conclusion: These results indicate **no apparent nephrotoxicity** even at the higher 15 mg/kg NB-009 dose, a critical advantage over conventional chemotherapy.

Clinical Significance

> The absence of hepatic and renal toxicity is particularly significant for cancer therapeutics, as these organ systems are critical for drug metabolism and excretion. NB-009's safety profile in these parameters suggests potential for combination therapy approaches and treatment of patients with pre-existing organ dysfunction—expanding the treatable patient population.

NB-009: Histological Safety: Normal Tissue Preservation

H&E Staining After 28-Day Treatment

Microscopic examination of major organs provides definitive evidence of NB-009's exceptional safety profile. While parent docetaxel caused noticeable tissue injury in normal organs at 7.5 mg/kg, NB-009 preserved normal histology even at the higher 15 mg/kg dose, while simultaneously inducing extensive tumor necrosis.

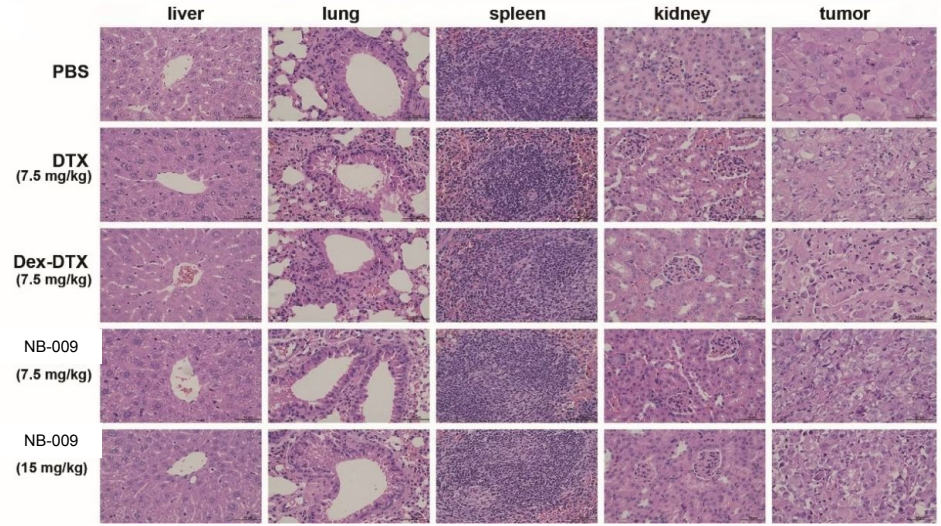


Figure 9: Representative H&E staining of major organs and tumor tissues from mice treated with PBS, DTX (7.5 mg/kg), Dex-DTX (7.5 mg/kg), or NB-009 (7.5 and 15 mg/kg). Images show liver, lung, spleen, kidney, and tumor sections.

Normal Organ Preservation

Free docetaxel caused noticeable tissue injury in normal organs (liver, lung, spleen, kidney) at 7.5 mg/kg, evidenced by cellular damage, inflammation, and architectural disruption.

Potent Antitumor Activity

Tumor sections from NB-009 -treated mice showed extensive necrosis, indicating potent antitumor activity that was achieved without obvious systemic toxicity to normal organs.

Safety at 2× Dose

In contrast, NB-009 preserved normal histology even at 15 mg/kg, double the dose that caused injury with parent DTX, demonstrating exceptional selectivity for tumor vs. normal tissues.

Therapeutic Window Advantage

> The histological data provides visual confirmation of NB-009's remarkable therapeutic window. The ability to induce extensive tumor necrosis while preserving normal tissue architecture at 2× the toxic dose of parent docetaxel represents a transformational improvement in the risk-benefit profile. This differential is the direct result of macropinocytosis-mediated tumor-selective delivery.

NB-009: Polysaccharide Drug Conjugate

Comparative Drug Properties Across Modalities

A comprehensive comparison of NB-009 against existing RAS-targeted modalities reveals clear differentiation. While each approach has merit, NB-009's polysaccharide-drug conjugate platform uniquely combines potent efficacy with exceptional safety and tumor selectivity—properties that no other modality can match.

Drug Property	Small Molecule Direct RAS Inhibitors	RAS Macrocyclic Molecular Glues (RMC)	RAS Protein Degraders (PROTACs)	Polysaccharide Drug Conjugate (NB-009)
Efficacy	⭐⭐⭐	⭐⭐⭐⭐	⭐⭐⭐	⭐⭐⭐⭐⭐
Safety	⭐⭐	⭐⭐⭐	⭐⭐	⭐⭐⭐⭐⭐
Tumor Targeting	⭐⭐⭐	⭐⭐⭐	⭐⭐⭐	⭐⭐⭐⭐
- Molecular Target	RAS protein	RAS protein	RAS protein	Not single RAS protein
- RAS Tumor Cell Targeting	⭐⭐⭐	⭐⭐⭐	⭐⭐⭐	⭐⭐⭐⭐ Macropinocytosis
- Tumor Tissue Targeting	No	No	No	EPR effect
Durability/Resistance	Rapid resistance	Delayed resistance	Delayed resistance	Less resistance
Accumulation in Liver	Yes	Yes	Yes	No
Overall Rating	⭐⭐	⭐⭐⭐⭐	⭐⭐	⭐⭐⭐⭐⭐

Unique Dual-Targeting Mechanism

Unlike all other modalities that target the RAS protein directly, NB-009 exploits **macropinocytosis at the cellular level** and the **EPR effect at the tissue level**, providing unprecedented tumor selectivity without requiring specific protein binding.

Minimal Hepatic Accumulation

A critical differentiator: NB-009 shows **no significant liver accumulation**, unlike all other RAS-targeted approaches. This property dramatically improves the safety profile and enables higher dosing for greater efficacy.

Superior Resistance Profile

By not relying on direct RAS protein binding, NB-009 demonstrates **less resistance development** compared to mutation-specific or pan-RAS inhibitors, which face inevitable resistance through secondary mutations or pathway bypass.

NB-009: Key Differentiators & Conclusions

The comprehensive preclinical dataset establishes NB-009 as a breakthrough therapeutic candidate with the potential to transform treatment for RAS-driven cancers. The combination of unprecedented efficacy, exceptional safety, and unique mechanism positions NB-009 as a best-in-class asset.

01

Superior Efficacy Across KRAS Variants

NB-009 demonstrated significant inhibition of KRAS-driven tumor growth across wild-type, KRAS G12D, and KRAS G12C variants. Notably, it **outperformed RMC-6236**,the leading pan-RAS anti-tumor agent—in lung cancer models, while also showing efficacy in pancreatic and colorectal cancer settings.

02

Exceptional Safety at Therapeutic Doses

NB-009 exhibited **excellent safety at 15 mg/kg**—a dose representing a **2.5-fold improvement** over free docetaxel. Hematological parameters, hepatic function, renal function, and tissue histology all confirm minimal systemic toxicity at efficacious doses.

03

Unique Biodistribution Profile

NB-009 displayed a **unique biodistribution profile** with selective accumulation in tumor sites while sparing normal organs. This tumor-to-normal tissue selectivity is **unprecedented among existing cancer therapies**, including small molecules, macromolecules (antibodies and ADCs), and nanoparticle formulations.

04

Deep Solid Tumor Penetration

The polysaccharide conjugate platform enables **powerful deep-penetration capabilities** in solid tumors, addressing a critical limitation of existing targeted therapies and enhancing therapeutic efficacy in poorly vascularized tumor regions.

05

Combination Therapy Potential

NB-009 can be strategically combined with RAS inhibitors to **overcome drug resistance**—a critical unmet need as resistance rapidly develops with current KRAS-targeted therapies.

06

Broad Pan-KRAS Activity

NB-009 is expected to demonstrate efficacy against **multiple KRAS mutations** (KRAS G12V, KRAS Q61H, KRAS G12A, etc.), offering more durable tumor suppression than mutation-specific (pan)-RAS inhibitors or RAS degraders.

Conclusions

Best-in-Class Potential

NB-009 **outperforms RMC-6236** and represents a highly promising drug candidate with strong potential to rival or exceed Revolution Medicines' RAS-targeted pipelines in both efficacy and safety.

Differentiated Drug Properties

NB-009 demonstrates **outstanding drug properties**—including excellent efficacy, favorable safety, high tumor targeting, deep solid-tumor penetration, and non-immunogenicity—distinguishing it from most cancer therapeutics in development or on the market.

Transformational Patient Impact

The successful development of NB-009 has the potential to **benefit millions of cancer patients worldwide**, particularly those with RAS-driven malignancies that currently lack effective, durable treatment options.

Accelerating Innovation to Improve Patients' Lives

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

How Navika Bio Adds Value

Navika Bio has identified and maintains relationships with over 25 licensable drug candidates across **Oncology**, **Autoimmune Diseases** and **Weight Loss**. Our curated pipeline continues to expand as we leverage our deep networks and scientific expertise.

01

Scout & Select

Asia's biotechnology sector is experiencing explosive growth, driven by government policy support, direct investment, and reverse brain drain. While these innovations were previously inaccessible to Western investors, funding gaps have created strategic entry points for partnerships.

02

Screen & In-License

Many pharmaceutical companies are actively scouting Asian biotech, but lack the scale, local presence, and trusted connections to identify the most compelling opportunities. Navika Bio understands their pipeline gaps and is uniquely positioned to identify, screen, and secure attractive assets from proven bioinnovation centers.

03

Curate & Accelerate

Navika Bio adds value beyond asset identification and rights negotiation. We leverage our scientific, regulatory, and commercial expertise to expedite development timelines, de-risk drug candidates, and facilitate successful business development transactions.

04

Out-License & Reinvest

We aim to out-license or divest assets to established biopharmaceutical companies seeking to strengthen their pipelines. Proceeds from successful transactions are strategically reinvested into new high-potential clinical opportunities, creating a sustainable cycle of innovation.

Founders

> In Sanskrit, **Nāvika** means "mariner." Our company was founded to navigate both sides of the Pacific, to act as a vessel to bring novel drug candidates from Asian innovation centers to Western markets.

Lawrence Hu

MEng MS PhD | Chief Technology Officer

- Product Development leader with deep expertise in Oncology and Cell Therapy CMC
- Successful exit as a biotech founder
- Over 20 years of experience in BioPharma and MedTech sectors
- Holder of 20+ US and international patents
- Extensively networked within the Asian biotech community

Richard Cunningham

MBA CMA | Advisor

- Finance and Commercial leader with 20 years of VP and Director-level experience at major pharmaceutical companies
- 20 successful drug launches across multiple therapeutic areas
- Executed 14+ M&A and licensing transactions
- Extensively networked within the US investor community

Expert Advisory Board

> Navika has assembled a distinguished team of advisors with deep expertise across licensing, product development, intellectual property, regulatory affairs, CMC, clinical trials, and commercialization. Our mission is to **accelerate innovation** and deliver transformative therapies that improve patients' lives worldwide.

Shuhua Xia, PhD
Scientific Leadership

- Molecular Biology expert and CEO of Nanjing Diligene Bio
- Former Scientist at Pfizer Drug Safety Research & Development
- Research Fellow, Cancer Research Center, Boston University School of Medicine
- Postdoctoral Fellow, Massachusetts General Hospital & Harvard Medical School

Howard Rutman, MD MBA FACC
Clinical Development

- Clinical Development expert with Chief Medical Officer experience at Xalud Tx
- Former VP and Head of Medical Affairs at Daiichi Sankyo
- Senior medical and development leadership roles at Pfizer and Taro Pharmaceuticals
- Board-certified cardiologist with extensive fundraising experience

Vic Clavelli, MBA
Commercial & Strategy

- CEO with 30-year distinguished career spanning pharma and biotech sectors
- Former Divisional President at Pfizer and Chief Commercial Officer at Optinose
- Built and scaled immunology, cardiovascular, and neuroscience business units
- Capital formation and strategic planning expertise in Board and C-Suite roles

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:

Lawrence Hu, PhD

Chief Technology Officer
Head of Business Development

Phone: 973-967-9949

Email: lawrence@navikabio.com