Triple Payload Targeted RNA Nanostructures with Staggered Intracellular Drug Activation

RNA nanobiotics

Validated multiple payload (chemo, RNAi, radiotherapy) RNA Nanostructures that enable clinically relevant sequential drug activation within the same cell-supporting combination therapy not achievable with existing delivery systems.

Exclusive rights to foundational RNA Nanostructure IP (4WJ and related architectures/platforms) enabling defined multidrug stoichiometry and controlled intracellular activation, supported by additional linker, payload and individual drug patents.

James Carroll, President & CEO

May 1, 2026

Multi-Payload RNA Platform with Staggered Intracellular Drug Release

- **In vivo validated multi-payload efficacy with defined stoichiometry and linker-dependent staggered intracellular drug release:** RNA nanostructures demonstrate superior tumor response vs monotherapy across multiple in vivo models, with architecture enabling multi-payload including validated three-payload architectures.

- **Lead Clinical Program:** EpCAM-targeted SN-38 RNA nanostructure advancing via 505(b)(2) pathway, leveraging known drug safety to enable rapid clinical entry.

- **Large, scalable clinical opportunity:** Lead program targets EpCAM+ metastatic colorectal cancer (~$10B market), with expansion across multiple EpCAM-expressing solid tumors (~$30B–$50B opportunity)

- **Market validation and comparable transactions:** Eli Lilly acquired CrossBridge (~$300M preclinical) to advance dual-payload ADCs; RNA Nanobiotics has already validated triple-payload systems with defined stoichiometry and staggered intracellular release and activation of individual drug payloads.

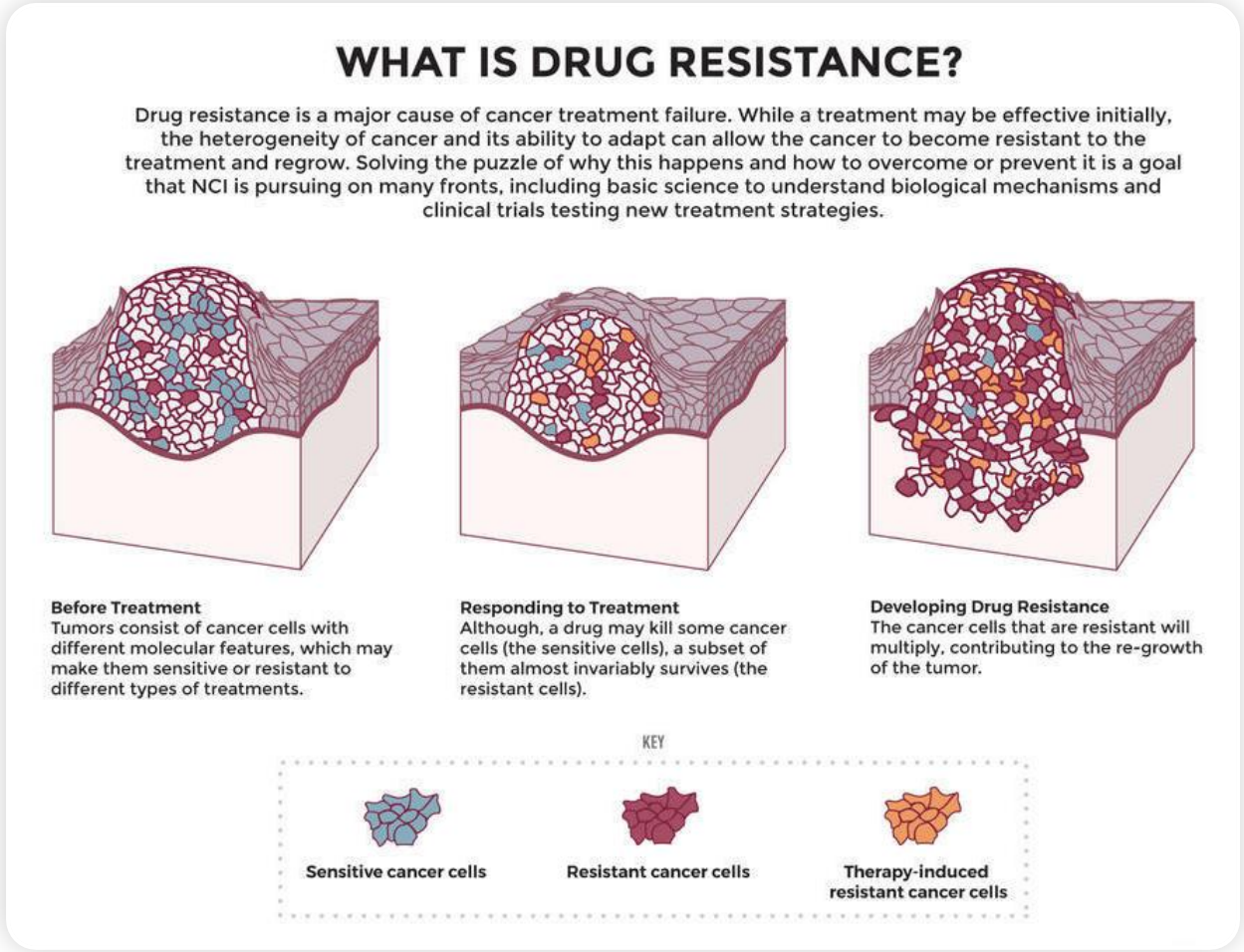
- **Structural advantage vs ADCs:** Small (deformable to < 5 nm) RNA nanostructures enable deep tumor penetration and effective cytosolic delivery; intrinsic anionic charge supports preferential tumor interaction and rapid system clearance reduces off-target exposure; fixed architecture enables defined multi-drug stoichiometry and enables payload-dependent activation timing not achievable with ADCs

- **Manufacturing de-risked:** External validation by Eli Lilly and others confirms scalable, reproducible drug manufacturing.

- **Near-term value inflection:** Defined 505(b)(2) regulatory strategy for SN-38 reduces cost, faster clinical entry, and near-term value inflection

The Current Challenges In Cancer Treatment

- Cancer is adaptive, heterogeneous, and spatially complex, particularly in advanced disease.
- Therapies must be targeted to cancer cells with multiple synergistic drugs (frequently 3 or more) to overcome resistance.
- Clinical practice relies on precisely sequenced drug administration to optimize efficacy- but current targeted delivery systems cannot reproduce this within the same cancer cell.
- Delivering drugs with sufficient precision across heterogeneous tumors and to the correct intracellular location (cytosol) remains a fundamental challenge.
- Many promising therapies fall short because of systemic off-target toxicity.



The Future of Oncology: Targeted Multi-Payload Combination Therapies & RNA-Based Medicines

"Most cancers will not be controlled with single agents. Rationally designed combination therapies are required to address resistance and tumor heterogeneity."

— Fabrice André — Nat Rev Clin Oncol (2020)

"Cancer drug development is increasingly focused on combination strategies rather than monotherapies."

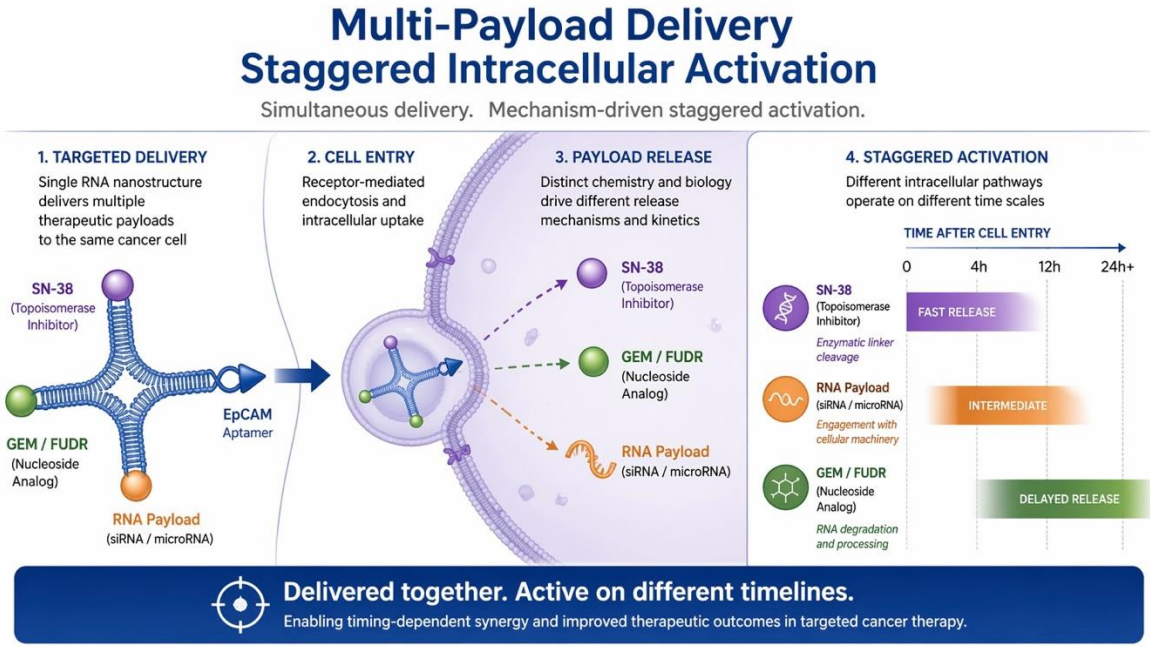
— Richard Pazdur — FDA OCE (2019–2021)

"RNA-based therapeutics provide access to disease drivers that are not reachable with conventional small molecules or biologics."

— National Cancer Institute — RNA Therapeutics Workshop (2021)

"RNA interference has clear potential in oncology, particularly when paired with effective delivery systems and used in combination regimens."

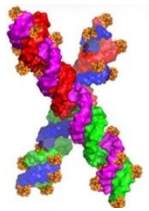
— Craig Mello — CSHL Symposium (2019)

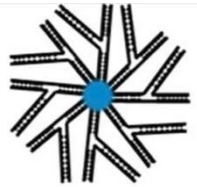


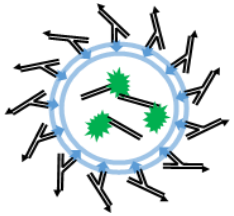
Next-generation delivery systems must enable both combination therapy and staggered intracellular drug release.

RNA NanoBiotics Platforms with Validated Multi-Payload Therapeutic Combinations

Exclusive Licensed Patent Portfolio Covers All Applications







Delivery Constraint	4WJ Nanoparticles	RNA Micelles	RNA Exosome Systems
Deep Tissue Penetration	Yes-Primary Strength	Moderate	Variable
Drug Load Capacity	Moderate	High-Primary Strength	Moderate
Circulation Stability	High	Moderate	Good
CNS/Biological Access	Limited	Limited	Yes-Primary Strength
Multi-Payload Capacity	Yes	Limited	Yes
Staged Timed Deliver	Yes	No	No
Representative Therapeutic Fit	Solid Tumors, RNA + Chemotherapy Combo	High-Burden Disease, hydrophobic Payloads	CNS Delivery, Gene/RNA Editing, mRNA

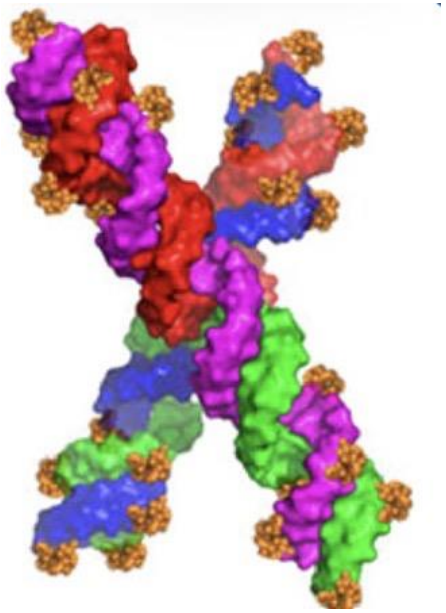
4WJ serves as the primary oncology backbone, with complimentary architectures expanding therapeutic landscape

Exclusive, Broad and Defensible RNA Platform IP

- Worldwide exclusive licenses to > 10 foundational RNA nanotechnology patents (Ohio State University, University of Kentucky and University of Cincinnati)
- Broad compensation-of-matter coverage: RNA nanostructures, targeting aptamers, RNAi and miRNA therapeutics, chemotherapeutics, imaging and radiopharmaceutical payloads
- Multiple delivery modalities covered: RNA Nanoparticles, targeted RNA exosomes, and RNA micelle systems
- Platform-level claims covering design, targeting, payload flexibility, and therapeutic use across solid and liquid tumors
- Manufacturing and scalability IP: synthesis, assembly and production of RNA Nanostructures
- Continuously expanding portfolio driven by ongoing academic and translational research adds new drugs, technologies, and patent filings

>$50M invested in platform R&D across licensed institutions

4WJ RNA Nanostructures: Core Oncology Platform



Optimized 4-Way-Junction (4WJ) Nanostructure

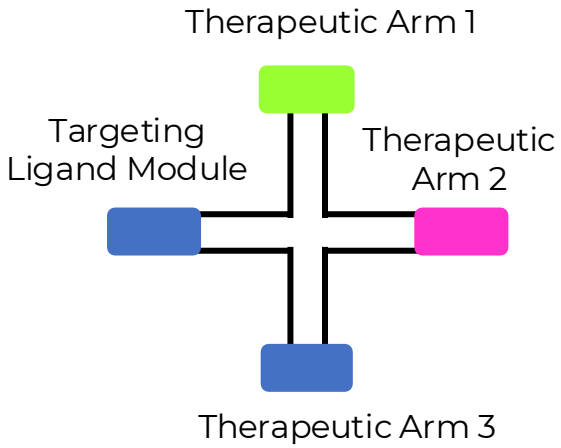
Engineered RNA architecture designed on **modularity.**

- **Defined Stoichiometry: Precise control of payload number and spatial positioning on each arm**
- **Multi-Payload Design: Simultaneous delivery of three chemotherapeutics, RNAi, and targeting ligands within a single construct. (Expandable to more than three)**
- **Mechanism-Driven Release: Distinct payload classes activate via different intracellular pathways enabling, staggered intracellular drug release (e.g., linker cleavage vs RNA processing)**
- **Structural Stability: Rigid 4WJ architecture maintains integrity in circulation while enabling efficient cellular uptake**
- **Programmable Functionality: Each arm independently engineered for targeting, payload delivery, or release control**

The platform's behavior is driven by molecular architecture, not formulation or encapsulation

Engineering 4WJ Release RNA Nanostructures for Precision Oncology

Four Engineered Modules Combine



Targeting Ligand Arm– Aptamer sequences engineered into module

Therapeutic Arms– miRNA, siRNA, nucleoside and chemo Drugs , and radioisotope linkers engineered into arms

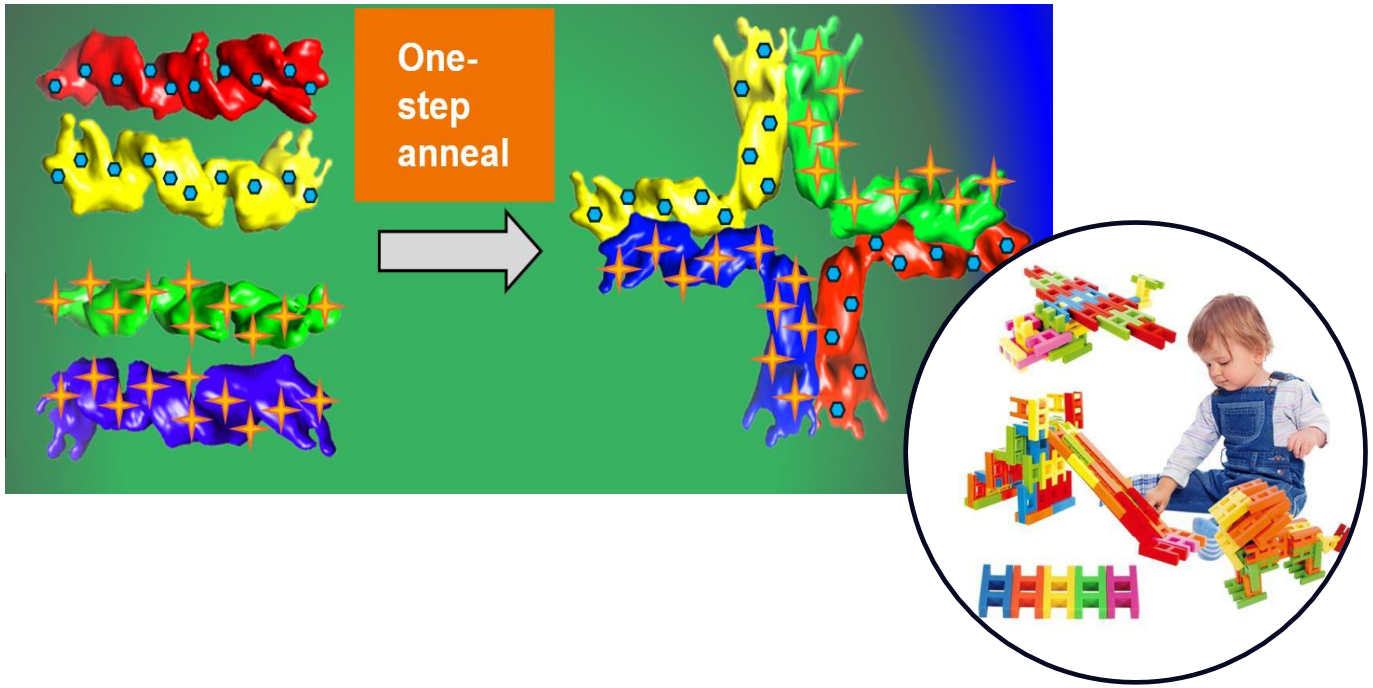
- Target cancer and identified, Literature Search, Manual Layout of Drugs
- High-affinity aptamer(s) chosen or identified via Literature and testing
- Best-fit therapeutic payload(s) selected by public availability:
  - RNAi, microRNA, Chemo, Radiation
- Click chemistry sites and best linkers selected for each drug payload
- Stabilizing modified nucleosides placed for serum durability
- Drug cleavage points ranked and mapped to linker chemistry
- Aptamer surface orientation and density optimized

AI End-to-End System Architecture

- Target module: Literature + trial mining → aptamer targets.
- Design module: Generative LLM for aptamers + 4WJ scaffolds.
- Payload module: siRNA + miRNA optimizer.
- Drugs Synthesized. Screened in Cell Culture and on to Animal Testing

Modular 4WJ architecture enables progression from validated single, double and triple-payload combination therapies within the same structural framework…other arms can be added to expand payloads if necessary

Like “LEGO Assembly”: Modular Arm Design Allows Combination Drugs or Retargeting



ARM DESIGN CHOICES:

- Non-Active Stability Arm - Standardized
- Targeting Ligand – Aptamer sequences engineered into Arm
- Chemo Drugs: SN38, Taxol, and others
- siRNA Drugs
- microRNA Drugs
- Nucleoside Drugs Like FUDR or GEM
- Radioisotope Chelators

Modular System Simplifies Drug Design: Allows Thousands of Targeted Combination Drug Therapies Including Those Requiring Staggered Drug Delivery/Release

4WJ Modular Platform: Multi-Payload Assets, Differentiated Activation Timing & Regulatory Strategy

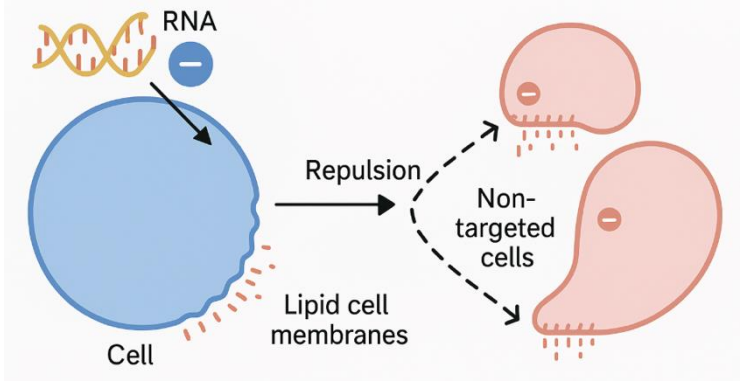
RNA nanobiotics

Distinct payload classes activate on different intracellular timelines-enabling inherent sequential drug exposure within a single nanostructure.

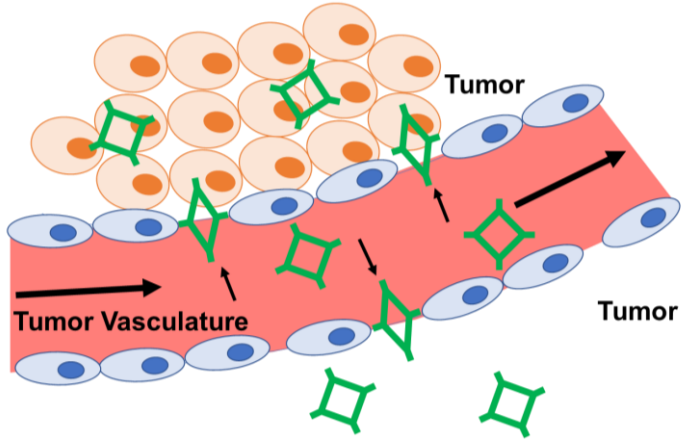
4WJ Arm	Loaded / Demonstrated Assets	Release Mechanism/ Activation Timing	Regulatory Path
Targeting Arm	EpCAM aptamer (CRC Lead), TNBC aptamer, leukemia aptamer…several	Binding only	CMC component internal sequence only changes, if aptamer.
Stability Arm	Chemically stabilized RNA motifs	No release	CMC / PK / tox
Chemotherapeutic Arm	SN-38 (lead), Paclitaxel (Taxol), Cisplatin…	Cleavable linkers -> rapid, early intracellular release	**505(b)(2) if preapproved**
Nucleoside Drug Arm	FUDR, Gemcitabine	RNA degradation-dependent activation -> delayed later intracellular release	**505(b)(2) if preapproved**
siRNA Arm	KRAS and oncogenic drivers	Cytosolic release -> processing-dependent intermediate release	505(b)(1) RNA Sequence Changes
miRNA Arm	Anti-miR-21, tumor suppressor miRNAs	Cytosolic release -> processing-dependent intermediate release	505(b)(1) RNA Sequence Changes
Radiopharma Arm	Gallium (validated) → Pb / Lu / Ac via linker	No release	Radiopharma pathway

Intrinsic 4WJ RNA Nanostructure Properties Enable Precise Deep Tumor Penetration

The amoeboid rubbery property of RNA nanoparticles make them penetrate more efficiently into tumors as they can easily clear the 5nm glomerulus kidney filter intact



The negative charge of RNA prevents entry into non-targeted cells or accumulation in vital organs.



Combined result is greatly enhanced tumor targeting and accumulation in solid tumors as compared to significantly larger ADCs.

Aptamers Also Confer Precise Recognition of Tumor Cells- Ensuring Minimal Uptake by Healthy Tissues

4WJ Cytosolic Delivery Enables Controlled Intracellular Activation and Payload Sequencing

4WJ Nanostructure Behavior
- Stable in circulation → payloads remain intact until cellular uptake

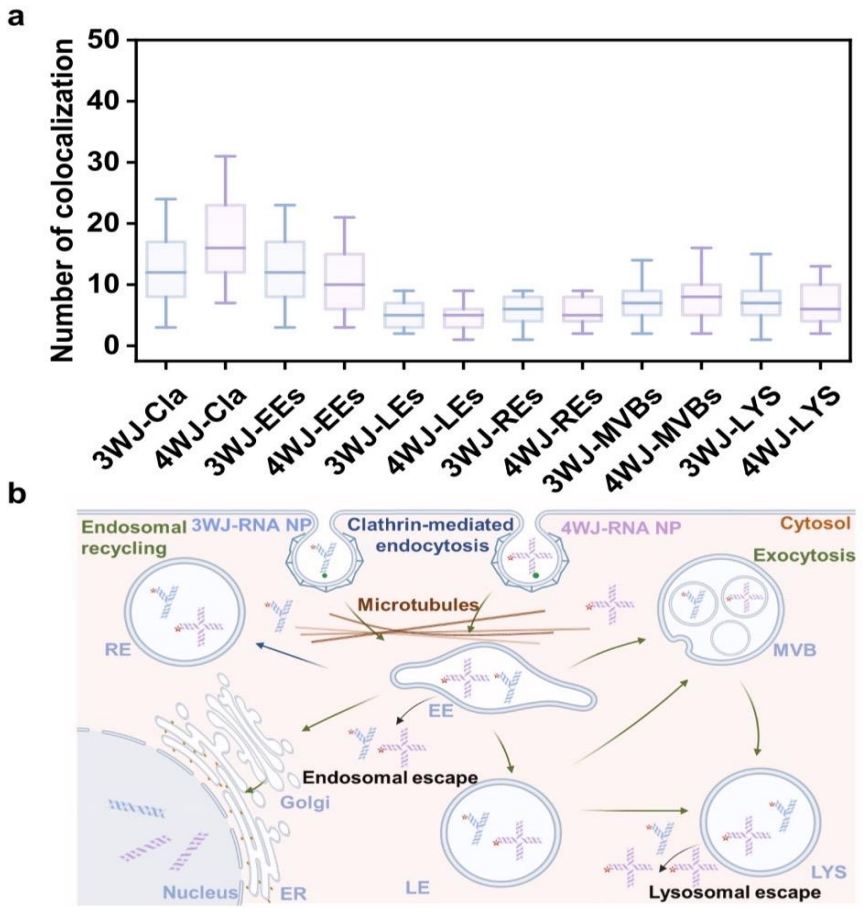
Intracellular Barrier (Industry Limitation)
- Endosomal uptake → ADC/LNP payloads trapped or degraded → reduced activity

4WJ Mechanistic Advantage
- Efficient endosomal escape → cytosolic delivery
- Payload integrity preserved → functional intracellular activity

Observed Outcome (tie directly to your SN-38 data)
- Cytosolic delivery → effective tumor cell kill observed in vivo

Strategic Implication
- Cytosolic delivery preserves payload function
- Enables differential activation across payload classes

Foundation for Clinically relevant sequential combination therapy within a single targeted delivery

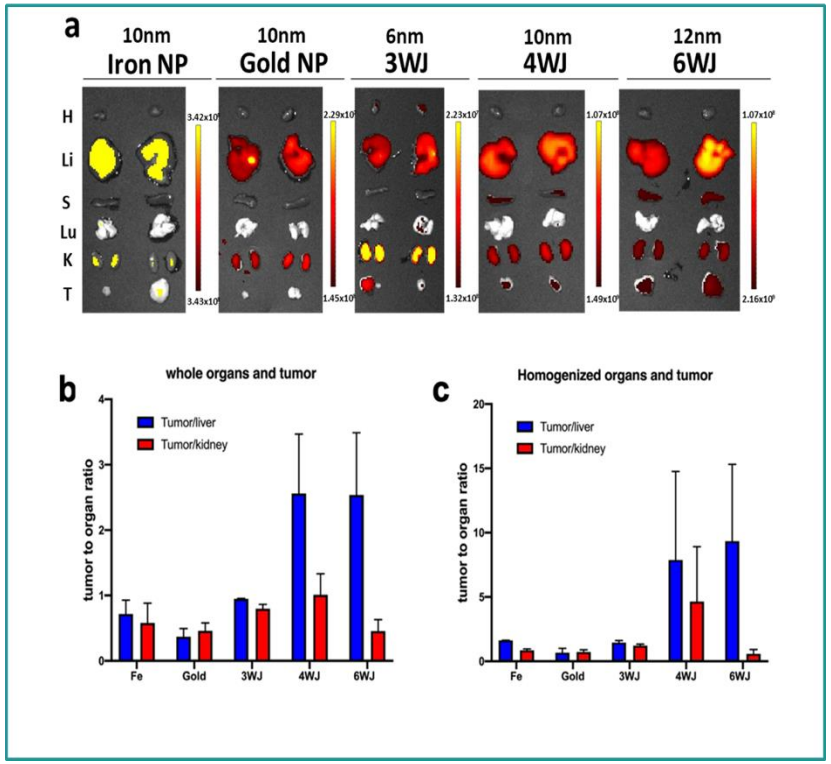


Intracellular delivery fate of RNA NPs. (a) The colocalization number in each cell for 3WJ-RNA NPs and 4WJ-RNA NPs (b) Schematic of the intracellular delivery pathway of RNA NPs. EE-early endosome, LE-late endosome, RE-recycle Endosome, MVB-multivescular bodies, LYS-lysosome

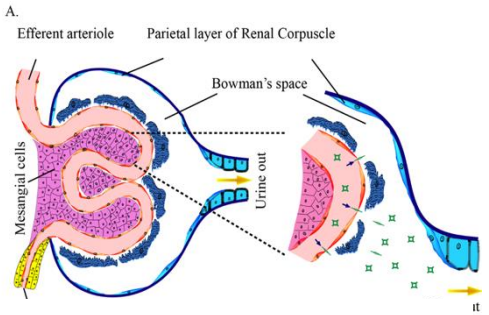
Reference: H. Wang et al., Chemical Engineering Journal 526 (2025) 171092

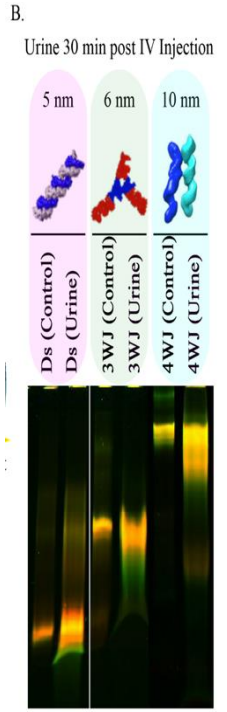
Favorable PK and Safety: Rapid Clearance with Minimal Off-Target Accumulation

Versatile 4WJ structure combinations allow for rapid and efficient intra-tumor penetration without organ accumulation.



RNA Nanoparticles quickly clear non tumor accumulated drug through the kidney's 5 nm Glomerular Filtration Barrier and excreted in the urine al.





Binzel D., et al. & Guo P. *Chemical Reviews 2021*

Li X., et al. & Guo P. *Advanced Drug Delivery Reviews.* 2022

RNA Junction Nanostructures — Consistent Payload-Agnostic Safety Across >15 Independent Studies

Cross-Study Validation
- **Consistent safety across >15 independent studies (in vivo, in vitro, human serum), including external laboratory validation**

Systemic Safety
- **No acute or chronic toxicity in repeat-dose studies at therapeutic and supra-therapeutic exposure**
- **Normal clinical chemistry and hematology**

Low Immunogenicity
- **Minimal immune activation (no significant IL-6, TNF-α, IFN-γ)**

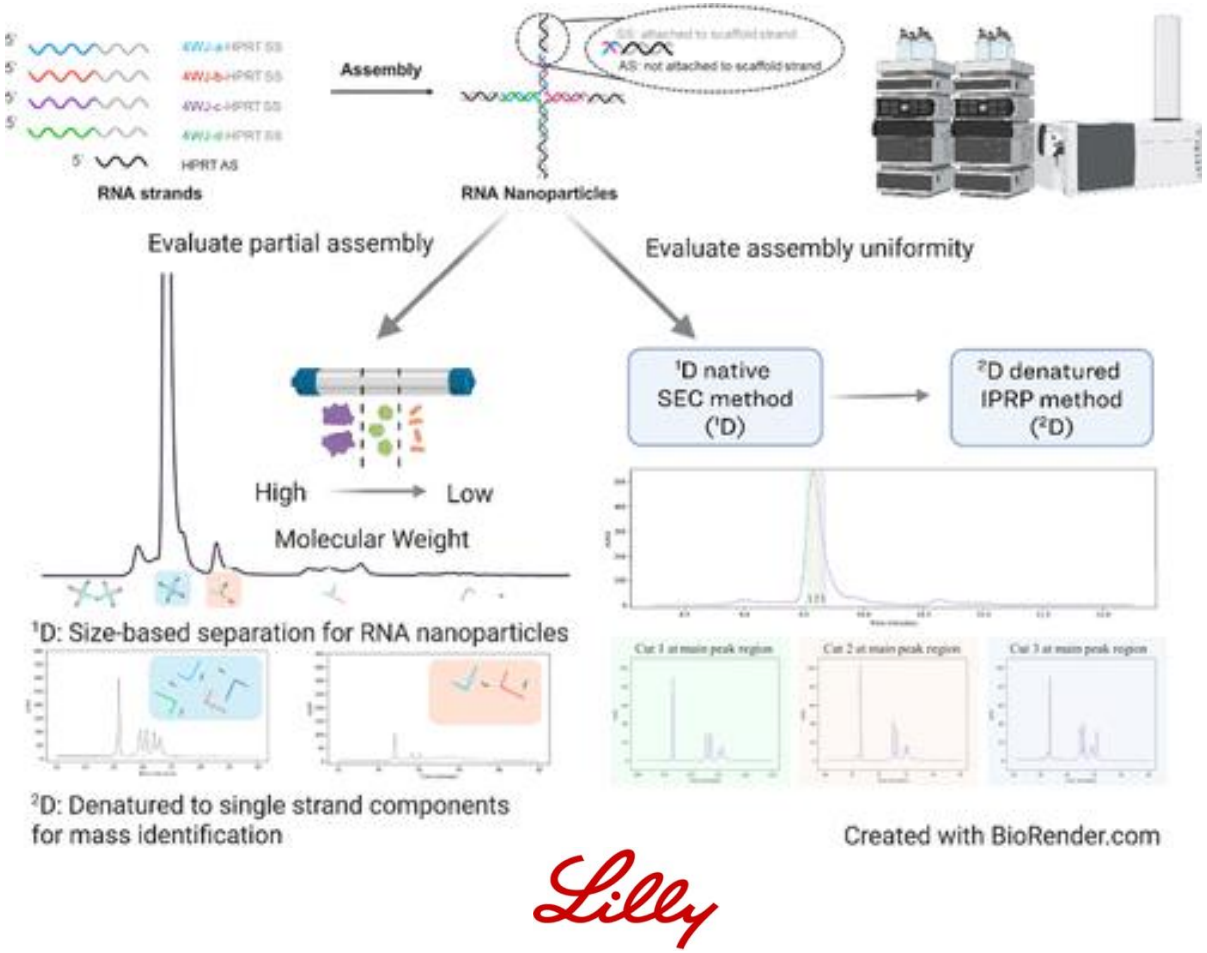
Biodistribution & Clearance
- **Tumor-selective uptake; minimal off-target accumulation**
- **Rapid renal clearance of non-bound nanostructures**

Platform Consistency
- **Safety maintained across multiple payload classes**

Bottom Line
- **Enables repeat dosing and supports multi-payload, staged therapeutic delivery**

Industrial-Grade CMC Validation of 4WJ RNA Nanostructures: Independent Eli Lilly

- Independent validated at Eli Lilly Institute of Genetic Medicine and Lilly Research Laboratories, demonstrating pharma-grade CMC transferability.
- Manufacturing Transferability: standard analytical methods (SEC, IPRP, MALS, and HRMS) support scale up, batch consistency, and release testing.
- Assembly Control: SEC × IPRP 2D-LC confirm fully assembled RNA nanostructures confirming defined stoichiometry and uniformity.
- Formulation Stability: no strand dissociation under formulation conditions, supporting clinical readiness.
- Orthogonal Validation: native SEC-MS confirms intact mass. SEC-MALS shows narrow MW distribution. In vitro knockdown potency unchanged.
- Reproducible, scalable platform suitable for multi-payload therapeutic development.
- cGMP manufacturing capability established (ChemGenes), enabling immediate clinical supply.



Wu et al., ACS Applied Bio Materials, 2025 | Eli Lilly Institute of Genetic Medicine & Lilly Research Laboratories | DOI: 10.1021/acsabm.5c01565

Why EpCAM ADCs Were Limited — and Why RNA Nanostructures Enable Combination Therapy

Limitations of EpCAM ADCs:

- Large antibody size limits tumor penetration
- **Fc receptor interactions drive prolonged circulation and off-target exposure**
- Long serum half-life increases systemic toxicity risk
- Endosomal internalization limits cytosolic payload availability
- Fixed, low payload capacity (drug-to-antibody ratio constraints)
- **Targeting relies solely on antigen binding (single targeting mechanism)**

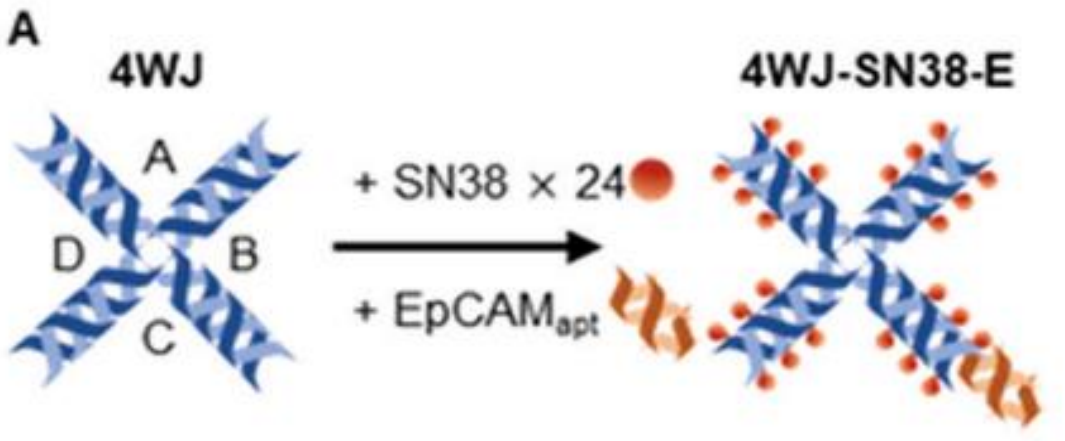
RNA Nanostructure Advantages:

- Small, deformable structures enable deep tumor penetration
- **No Fc receptor interactions; controlled circulation and rapid renal clearance**
- Short systemic exposure reduces off-target toxicity
- Efficient cytosolic delivery enables functional activation of diverse payloads and release timing
- Programmable, high payload stoichiometry
- **Multi-layer targeting: aptamer binding + size + charge-driven tumor uptake**
- Multi-payload capability enables combination and staggered (time-dependent) therapy
- Enables staggered multi-drug activation within the same cell, not achievable with ADCs

RNA nanostructures replace single-mechanism ADC targeting with multi-layer targeting, controlled pharmacokinetics, and functional cytosolic delivery

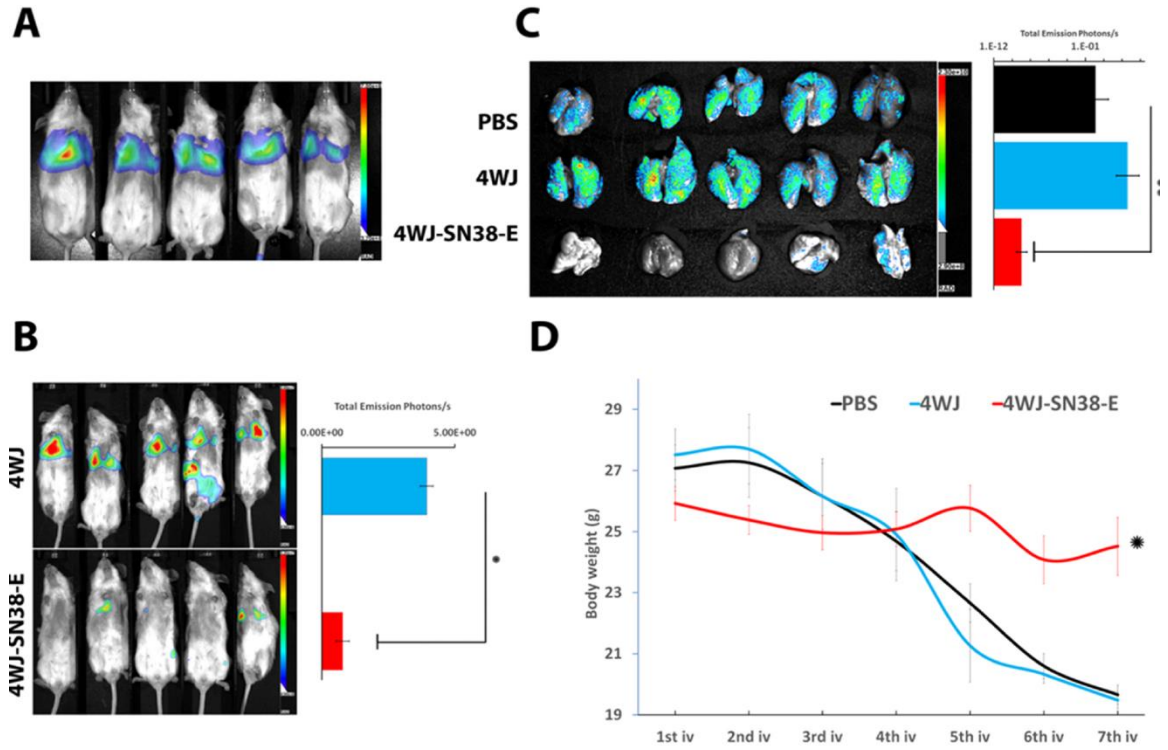
Lead Clinical Candidate - 4WJ-SN38 Design with Targeting EpCAM Aptamer (Single Drug)

SN-38 Pursued Under 505(b)(2), Referencing Irinotecan to Reduce Development Risk, Time and Cost



EpCAM is overexpressed (70-90%) in numerous cancers

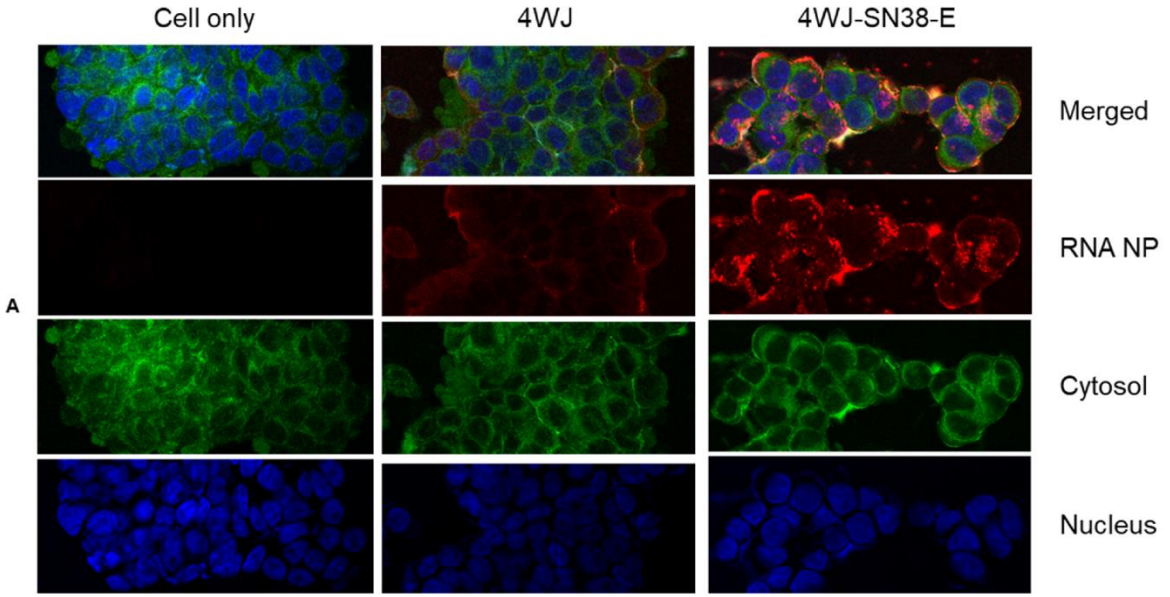
- Dramatic reduction of metastatic lung burden
- In vivo and ex vivo imaging show near-eradication of lesions
- Achieved with excellent tolerability and no weight loss

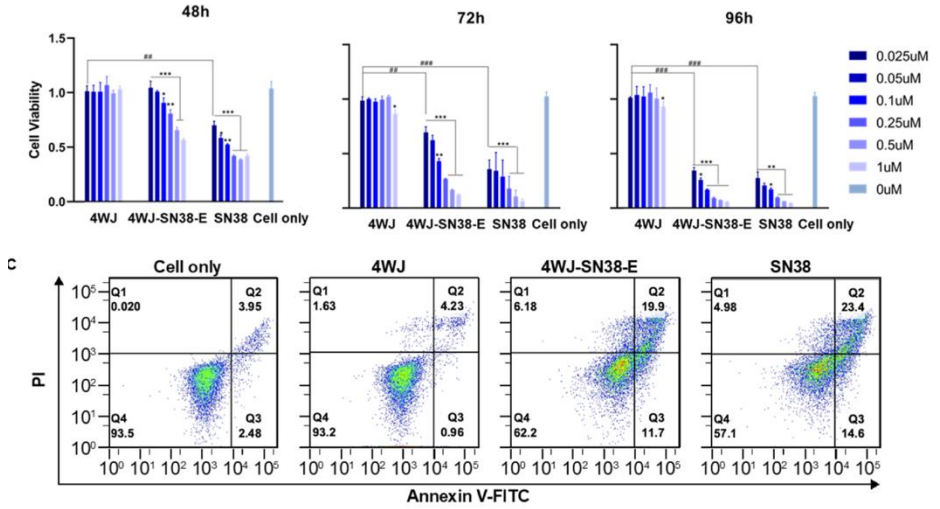


ig. 6. *In vivo* colorectal cancer lung metastasis model inhibition of 4WJ-SN38-E. (A) Lago imaging to confirm metastasis establishment 5 days after IV injection. (E ioluminescence to compare metastasis *in vivo* between 4WJ and 4WJ-SN38-E groups. The mice in the PBS control group were so sick (see D) and cannot survive ti ıe whole body imaging. (C). GFP imaging to compare metastasis *ex vivo* between PBS, 4WJ, and 4WJ-SN38-E groups. (D). Mice weight changes on day 5, 8, 11, 14 7, 20, and 23.

4WJ-SN38-EpCAM In Vitro Efficacy: Tumor Cell Killing & Apoptosis

- Dose-dependent killing of HT-29 colorectal cancer cells
- 4WJ-SN38-EpCAM matches free SN-38 potency by 96 hrs.
- Strong apoptosis induction (~32%), comparable to free SN-38 (~38%)
- Confocal imaging confirms aptamer-mediated internalization



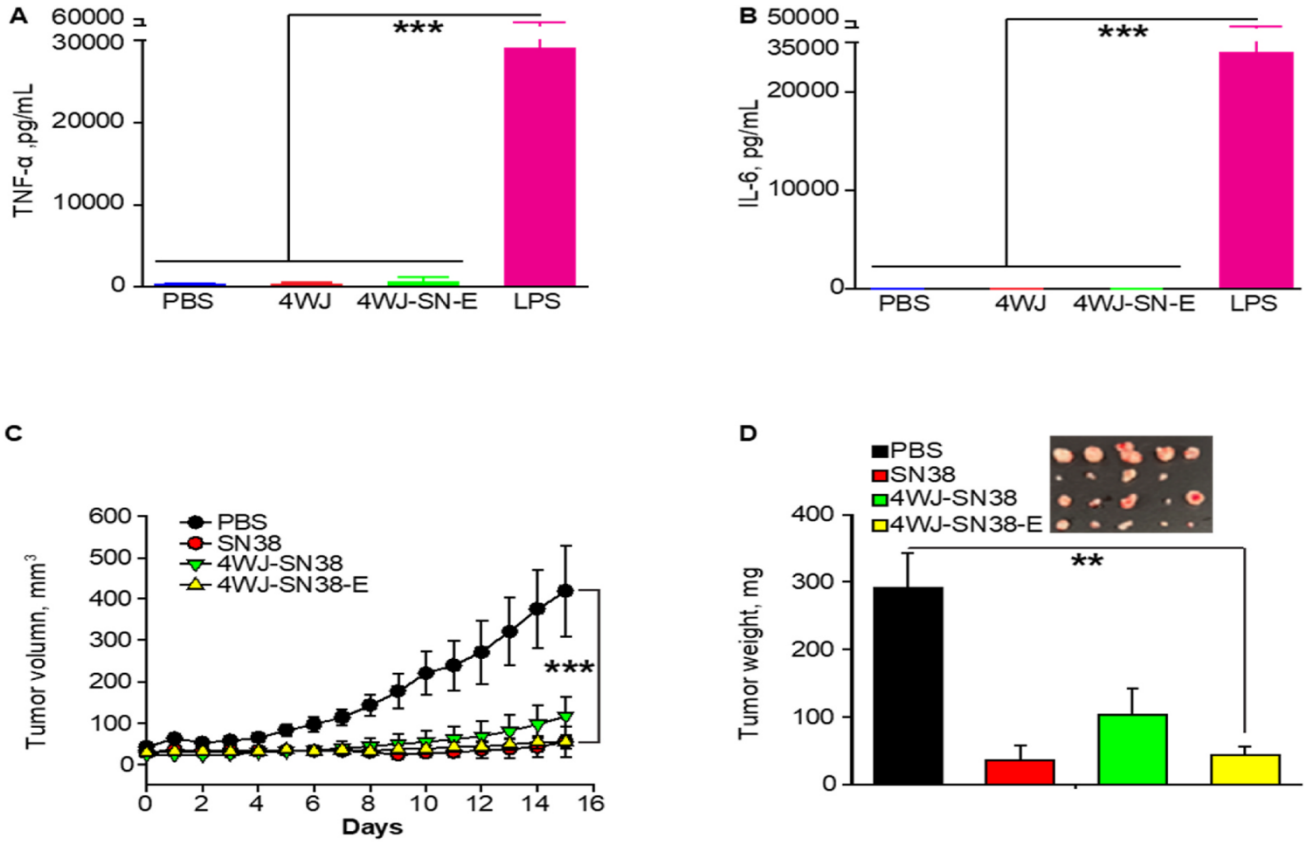


ig. 3. *In vitro* cell binding, internalization, and cancer suppression study of 4WJ-SN38-E RNA nanoparticles. (A) Confocal images of HT29 cells after incubation with BS, 4WJ, and 4WJ-SN38-E, respectively. (Blue: nucleus; Green: Cytosol; Red: RNA nanoparticle). (B) Evaluation of cell viability by MTT assay in HT29 cells ıcubated with RNA nanoparticles and SN38 for 48, 72, and 96 h, respectively. Statistics were calculated by two-tailed unpaired *t*-test presented as mean ± SEM. ignificant results compared to the RNA nanoparticle at a concentration of 0.025 μM are marked with an asterisk (*p < 0.05, **p < 0.01, ***p < 0.001). Significant esults compared to the 4WJ at a concentration of 0.025 μM are marked with an hash (##p < 0.01 and ###p < 0.001). (C) *In vitro* apoptotic effects of RNA anoparticles and SN38 by PI/Annexin V-FITC dual staining and FACS analysis (Q2 = Annexin V-FITC positive & PI positive, indicating late apoptotic and dead cells;)3 = Annexin V-FITC positive & PI negative, indicating early apoptotic cells). (For interpretation of the references to color in this figure legend, the reader is referred) the Web version of this article.)

4WJ-SN38-EpCAM In Vivo CRC Xenograft: Significant Tumor Suppression

4WJ-SN38-EpCAM

- Strong tumor growth suppression vs. PBS and free SN-38
- Targeted 4WJ-SN38-EpCAM achieves deepest tumor suppression
- ~20% additional tumor mass reduction vs. non-targeted 4WJ-SN38

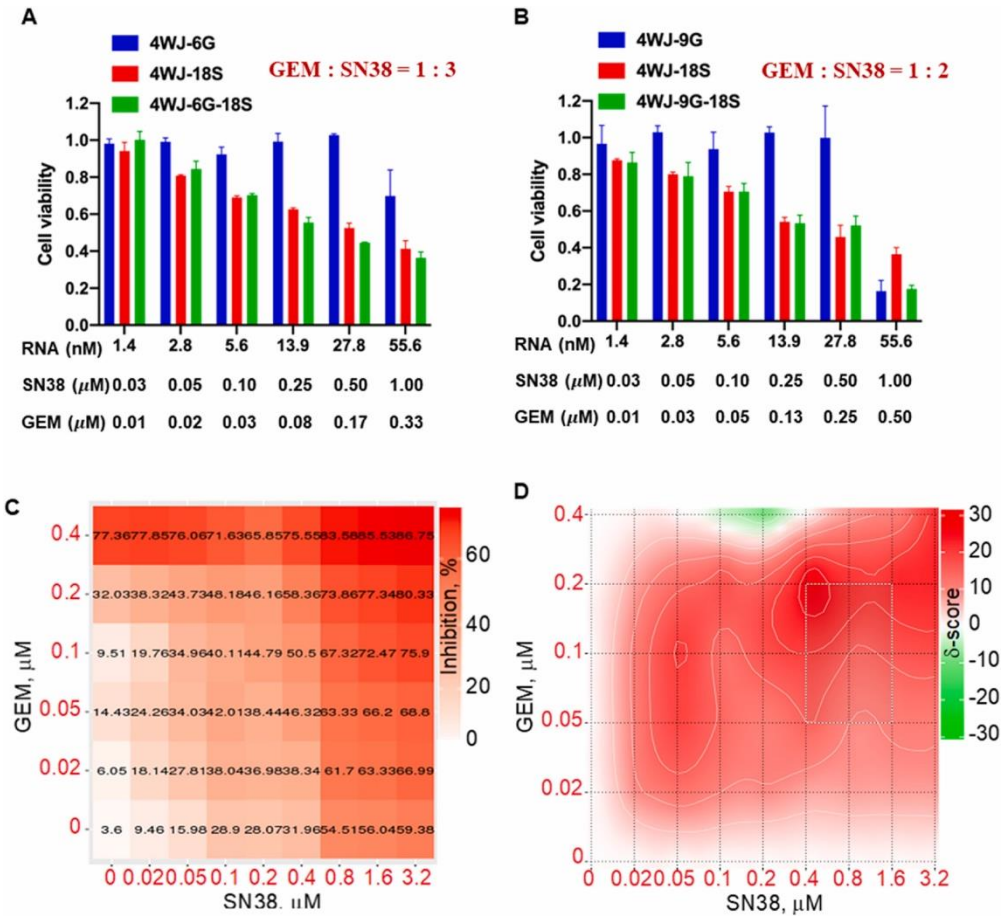


ig. 5. *In vitro* immune response and *in vivo* tumor inhibition of 4WJ-SN38-E RNA nanoparticles. (A,B) Evaluation of TNF-α (A) and IL-6 (B) production afte ıcubating 4WJ-SN38-E with macrophage-like cells by ELISA. (C) Intravenous treatment of nude mice bearing HT29 xenografts with 4WJ-SN38-E and control group very three days for a total of 5 injections (indicated by arrows). Mice tumor size was monitored during the time course of treatments. (D) Comparison of tumc /eight and size at the endpoint (n = 5 biologically independent animals). Statistics were calculated by two-tailed unpaired *t*-test presented as mean ± SEM, **p < .01, ***p < 0.001.

Validated Preclinical Proof-of-Concept: 4WJ EpCAM SN38 Demonstrates Efficacy and Safety

Key Requirement	RNA NanoBiotics Result	Benchmark Met
Drug Loading Efficiency	24 SN38 molecules per 4WJ-RNA nanoparticle	
In Vitro Apoptosis / Cytotoxicity	31.6% apoptosis in HT29 cells (4WJ-SN38-EpCAM)	
In Vivo Tumor Volume Reduction	85–90% tumor volume reduction at 2 mg/kg SN38 (x5 doses)	
Targeting Benefit over Non-Targeted NP	20.4% greater tumor reduction with EpCAM-targeted NPs	
Maximum Tolerated Dose (MTD) Margin	No observable toxicity at effective dose; safe at 2 mg/kg × 5 doses	
Systemic Toxicity (weight, organs)	No weight loss, no histopathologic changes in liver, kidney, spleen, heart, lung	
Cytokine Induction (e.g., TNF-α, IL-6)	No significant TNF-α or IL-6 elevation at 100 nM (comparable to PBS control)	
Hemolysis / Plasma Compatibility	<5% hemolysis, no platelet aggregation, complement activation, or abnormal coagulation	
Biodistribution / Clearance	Tumor-targeted accumulation; fast renal clearance; undetectable off-target accumulation	
RNA Nanoparticle Stability	Stable >12 hrs. in human serum; maintains shape and function	

Follow-On Program: Optimizing SN-38 + Nucleoside Analog (Gemcitabine, FUDR) Dual-Payload Therapy



Preclinical Dual-Payload Synergy

- Published 4WJ data demonstrate synergistic co-delivery of SN-38 and gemcitabine
- Synergy observed across defined SN-38:GEM ratios (1:2–1:3)
- Confirms co-delivery does not compromise individual drug potency

Mechanistically Distinct Activation

- SN-38: esterase-mediated linker cleavage → rapid intracellular release
- Gemcitabine: Incorporated into RNA Structure → release via RNA degradation
- Result: Structurally driven differential activation timing from a single nanostructure

Resulting Activation Profile

- Non-synchronous intracellular activation driven by nanostructure design
- Inherent delay in gemcitabine activation relative to early SN-38 release

Clinical Relevance

- Aligns with clinically established staged administration of SN-38 and gemcitabine
- Sequencing is used to optimize efficacy and reduce antagonism
- The nanostructure reproduces staged intracellular exposure from a single administration
- Known oncology agents with differentiated mechanisms

Extends lead SN-38 program into a follow-on dual-payload candidate using staged intracellular release

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Li X, Guo P. *Biomaterials*. **2023.**

Leadership Team Built for IND Execution

EXECUTIVE TEAM

James Carroll, MBA
CEO/ Financing, Strategy & Partnerships

- 25+ years pharma, diagnostics, biomanufacturing, BD and startup execution
- President, Wharton Alumni Angels
- Led business development, financings, acquisitions and exits across life sciences

Krystle Karoscik, PhD
CTO/ Translational Development & External Execution

- Led >20 early-stage clinical programs
- IND-enabling, clinical/commercialization strategy, and life-science operations
- Coordinates external development vendors and milestone execution

CORPORATE BOARD

Ildiko Csiki, MD, PhD
Board/Oncology Clinical Development

- Cancer drug development and commercialization leader
- Clinical trial design, treatment landscape, patient selection

Cynthia Cai, PhD, MBA
Board/Finance, Governance & Strategic Growth

- 25+ years healthcare/life-science executive and investor experience
- Board governance, equity investment, business development

SCIENTIFIC ADVISOR

Peixuan Guo, PhD
Platform Inventor/RNA Nanotechnology Platforms

- Inventor of foundational 3WJ/4WJ RNA nano-technology based platforms
- National Academy of Inventor Fellow
- Founder of the RNA nanotechnology field

Capital-efficient IND advancement through expert CRO/CDMO partners under internal leadership oversight.

Validated Radiopharmaceutical Arm for Modular Targeted RNA Nanoparticle Therapy

Global targeted radiotherapy market projected to exceed $15B by 2030

Platform Highlights:

- Chelator/payload arm is modular-same chemistry enables substitution of diagnostic and therapeutic isotopes (e.g., ^{68}Ga -> alpha emitters).
- Rapid tumor uptake: 1–4 h; rapid clearance from non-tumor tissues
- Plug-and-play design: swap targeting ligand & chelator strand without altering core
- Chelator arm supports direct substitution of diagnostic and therapeutic isotopes without altering core structure
- Single GMP & regulatory backbone supports multiple products

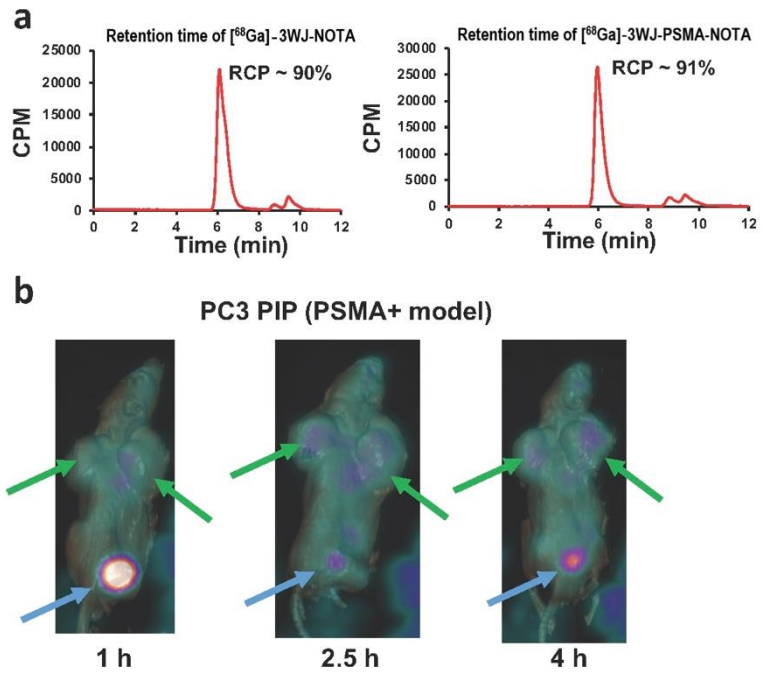
Alpha Emitter Priorities

- ^{212}Pb / TCMC strand – Best PK match; clean drop-in for therapy
- ^{225}Ac / DOTA or macropa strand – Straight substitution; manage daughter recoil

Theranostic Options

- Therapeutic: ^{212}Pb, ^{225}Ac, ^{211}At
- Diagnostic: ^{68}Ga, ^{18}F, ^{64}Cu

RNA NanoMed (Aug 2025) published proof-of-concept



^{68}Ga-Labeled RNA Nanoparticle (3WJ-PSMA-NOTA) for Medical Imaging Proof of Concept

Green Arrow - Tumor

Blue Arrow – Bladder (showing excretion)

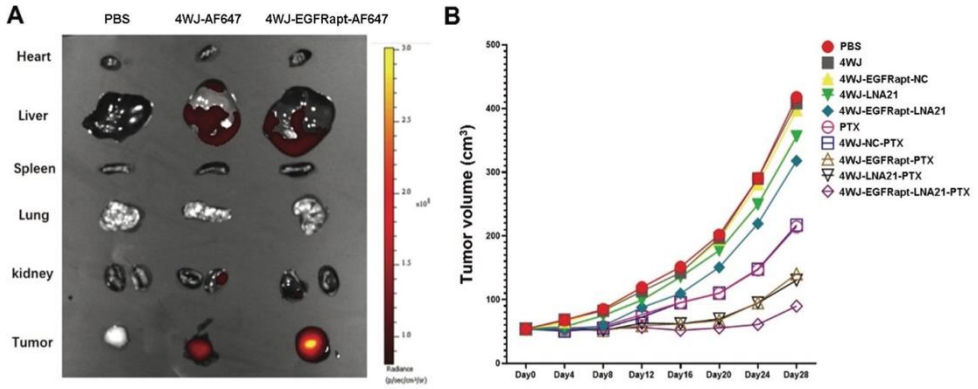
Validated Multi-Mechanism Payload: Chemotherapy + microRNA via Single RNA 4WJ

Therapeutic design

- **Enables coordinated or staged activation based on intracellular release mechanisms**
- **RNA4WJ nanostructure co-delivering paclitaxel (PTX) and anti-miR-21-5p**
- **EGFR-targeted delivery to head & neck squamous cell carcinoma (HNSCC)**
- **Modular multi-payload architecture extendable beyond two payload classes**

Key results

- **Combination therapy demonstrates superior tumor suppression vs single drugs.**
- **Validating simultaneous chemo + RNAi delivery from a single nanostructure.**
- **Validated microRNA therapeutic arm**



In vivo validation of combination chemo–RNA therapy using RNA4WJ nanoparticles.

Panel (A) demonstrates tumor-selective accumulation of targeted RNA4WJ nanoparticles by IVIS imaging following systemic administration.

Panel (B) shows tumor volume reduction over time in HNSCC xenografts, where RNA4WJ nanoparticles with combination loading profiles achieve greater antitumor efficacy than free paclitaxel or single-loaded controls at matched PTX dosing.

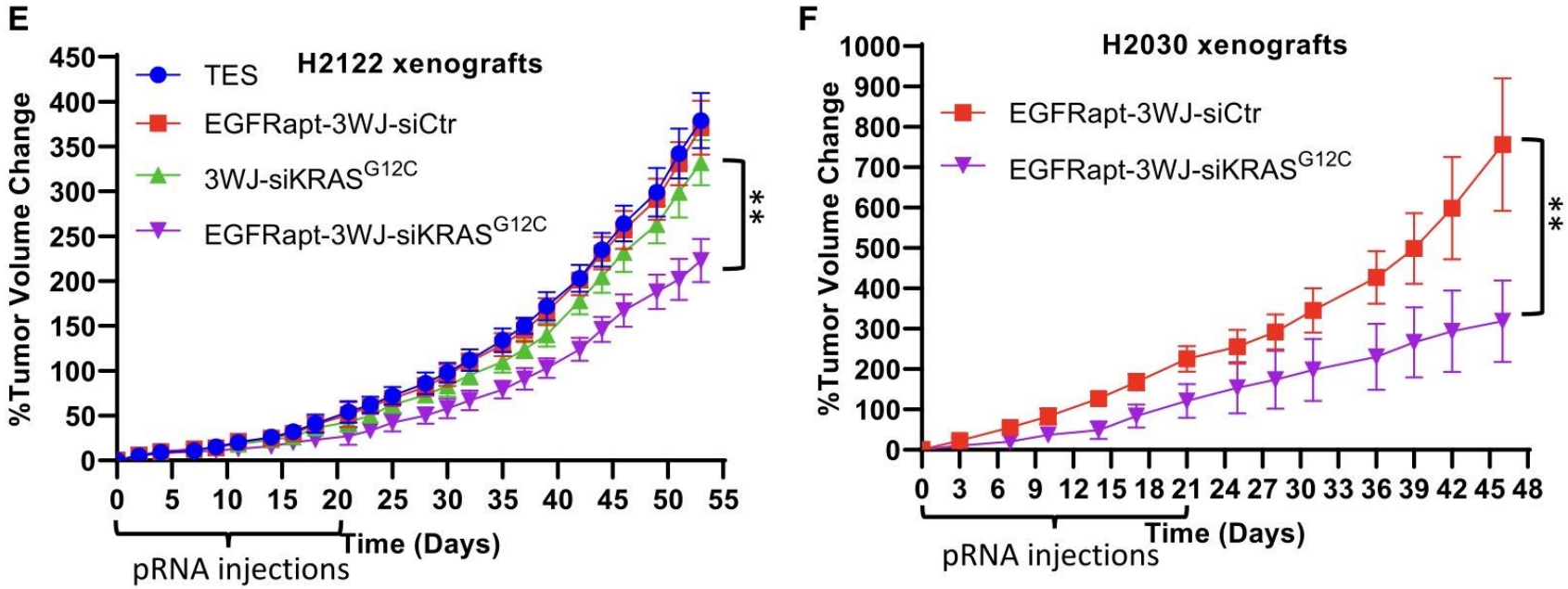
RNA nanostructures enable integrated multi-mechanism therapy (chemo + RNAi) within a single targeted nanostructure.

RNA NanoMed 2025 — RNA4WJ nanoparticles co-delivering paclitaxel and anti-miR-21 in head & neck cancer

Validated siRNA Single Therapeutic Arm: KRAS siRNA Delivery Suppresses NSCLC Tumors In Vivo

EGFR-aptamer–targeted RNA Nanostructures deliver KRASG12C siRNA with tumor-selective uptake and in vivo efficacy.

- Systemic IV delivery of KRASG12C siRNA using pRNA-3WJ nanostructures
- EGFR aptamer–mediated tumor-selective uptake
- Significant suppression of NSCLC tumor growth versus controls

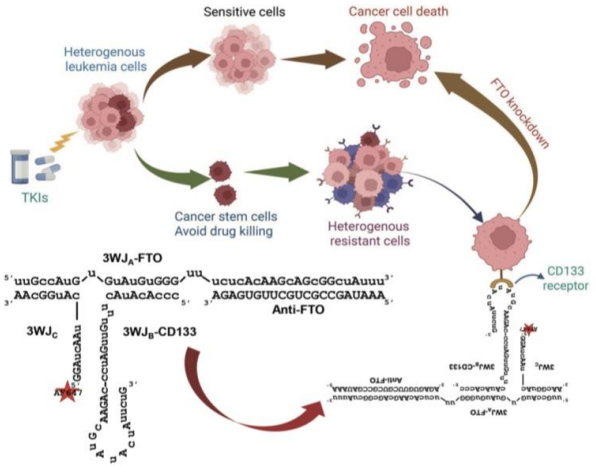


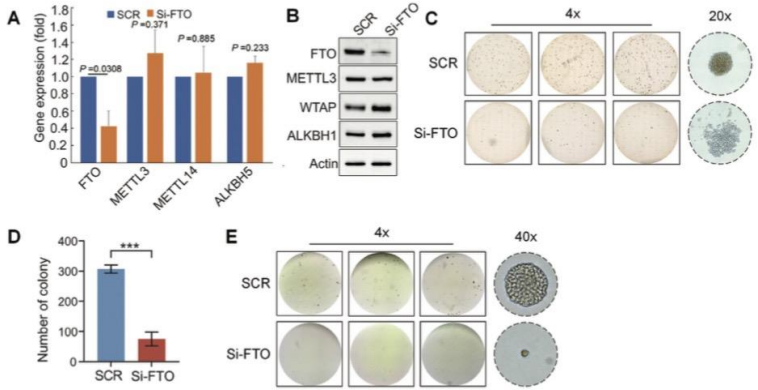
Li et al., Molecular Therapy – Nucleic Acids, 2023. EGFR-aptamer–targeted pRNA-3WJ nanoparticles delivering KRASG12C siRNA suppress NSCLC tumor growth in vivo.

Validated siRNA Arm: CD133-Targeted siRNA Delivery in Liquid Tumors (Leukemia)

CD133-targeted RNA Nanoparticle delivery of siFTO demonstrates functional knockdown and suppression of drug-resistant leukemia cells:

- RNA therapeutic: FTO siRNA (2'-F pyrimidine stabilization; guide strand unmodified) delivered on phi29 pRNA-3WJ scaffold; targeting via CD133 RNA aptamer (B19 > A15 binding).
- Mechanism: CD133-high TKI-resistant K562 cells show markedly higher binding/uptake of CD133-3WJ constructs, enabling gene-specific FTO knockdown without broad disruption of other m6A regulators.
- Functional outcome: CD133 and spheroid growth in nilotinib-resistant cells versus scrambled control—supporting RNAi as a route to override drug-tolerant/stem-like leukemia populations.





(A,B) FTO mRNA and protein knockdown by CD133-targeted siRNA.
(C,D) Colony formation markedly reduced vs control.
(E) Spheroid growth suppressed in resistant K562 cells.

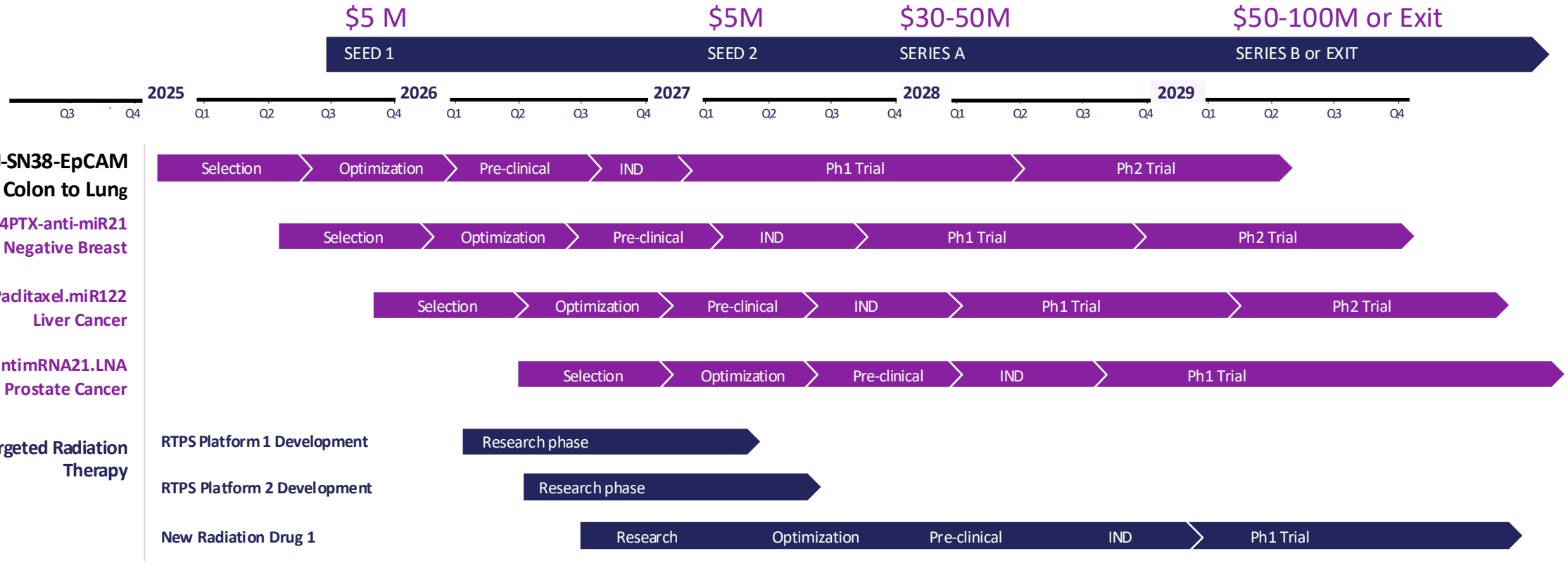
Demonstrates a modular RNAi therapeutic arm complimentary to chemotherapeutic and radiopharmaceutical payloads.

Reference: Bian H, Zhou C, Koyama H, et al. "CD133-Guided RNA Nanoparticle Delivery of FTO siRNA Impairs Leukemia Resistance to Tyrosine Kinase Inhibitor Therapy." RNA NanoMed. Oct 2025;2(1):70–?.

Lead IND in 2026 with Multi-Payload Platform Pipeline Expansion

	Target	Payload	Cancer Type	Ready to Initiate IND Program	Planned IND	505 (b) (2)
1	**EpCAMapt**	**4WJ-SN38**	**mCRC (Liver/Lung Mets)**	✓	**2026**	
1A	EpCAMapt	4WJ-CPTH+Nucleoside (Gemcitabine/FUdR)	mCRC-Liver/Lung, Gastric, pancreatic, ovarian, NSCLC	secondary more potent combination assets	2027	✓
2	**EGFRapt**	**4WJ-X-24PTX-anti-miR21**	**Triple Negative Breast Cancer**	✓	**2027 +**	**505(b)(1)**
2	**EGFRapt**	**4WJ-X-24PTX-anti-miR21**	**Head and Neck Esophageal**	✓	**2027 +**	**505(b)(1)**
3	HTLs	4WJ-GalNex-Paclitaxel.miR122	Liver Cancer	Animal data	2027 +	✓
4	PSMAapt	4WJ-anti-mRNA21-LNA	Prostate Cancer	Animal data	2027 +	**505(b)(1)**

MCC Lead IND 2026 with Scalable Multi-Payload Pipeline Expansion



Modular platform enables rapid expansion across targets, payloads, and indications

Competitive Comparative Platform Attributes (Illustrative)

Based on public literature and internal assessment of modality design characteristics

Modality	Example drug / program	Tumor-specific targeting	Direct cytotoxic payload	Tumor penetration advantage	Clinical translation (CRC)	Multi-Payload Capability	Staggered Release
RNAi / siRNA therapeutics	Patisiran / KRAS siRNA programs						
miRNA therapeutics	MRX34 (miR-34 mimic)						
Antisense oligonucleotides (ASO)	Nusinersen / Imetelstat						
RNA aptamers	Pegaptanib	✅					
RNA–drug conjugates	SN38-RNA nanoparticle (preclinical)		✅				
ADCs (EpCAM / TROP2 / HER2)	Sacituzumab govitecan (Trodelvy)	✅	✅		✅	**Patented Linker for 2**	
Peptide–drug conjugates	Investigational CPT analog conjugates	✅	✅				
SOC Combination therapies	FOLFIRI; IO + chemo		✅		✅		
4WJ-EpCAMapt-SN38 + Gemcitabine	**4WJ-EpCAMapt-SN38**	✅	✅	✅	✅	✅ **3 plus**	✅ **Differentiated**

Strategic Partnering and Exit Landscape – Top Targets

Company	Strategic Fit	Partnering Rationale	Relevant Deals / Why It Matters
Eli Lilly	Oncology focus: next-gen delivery and multi-payload interest.	Independent Lilly-generated CMC data and recent acquisition activity indicate strong relevance to Lilly	CrossBridge Bio ($300M preclinical, 2026), Loxo Oncology ($8B): strong platform-driven acquisitions in targeted oncology
Roche / Genentech	ADC leader; deep oncology presence	Aggressive dealmaker, proven external innovation appetite	Spark ($4.3B, 2019); multiple ADC deals >$1B; Entrada IPO $570M
Pfizer / Seagen	Oncology & ADC strength; RNA interest	Large acquisitions; RNA expertise post-COVID	Seagen ($43B, 2023); Array ($11.4B, 2019); RayzeBio ($4.1B, 2023)
Bayer (Radiopharma)	Radioligand leader (Pluvicto, Xofigo)	Active acquirer/licensor in radiopharma space	Ratio $745M; Aktis $175M raise; Noria/PSMA acquisition
Novartis (Radioligand Therapy)	Oncology powerhouse; radioligand expansion	Open to early partnerships; acquisitive	Mariana $1B upfront (2023); Endocyte $2.1B; AAA $3.9B; Alpha9 $175M

$1M Seed Note to Achieve IND-Enabling Milestones

RNA nanobiotics

Current Strategic Financing Opportunity

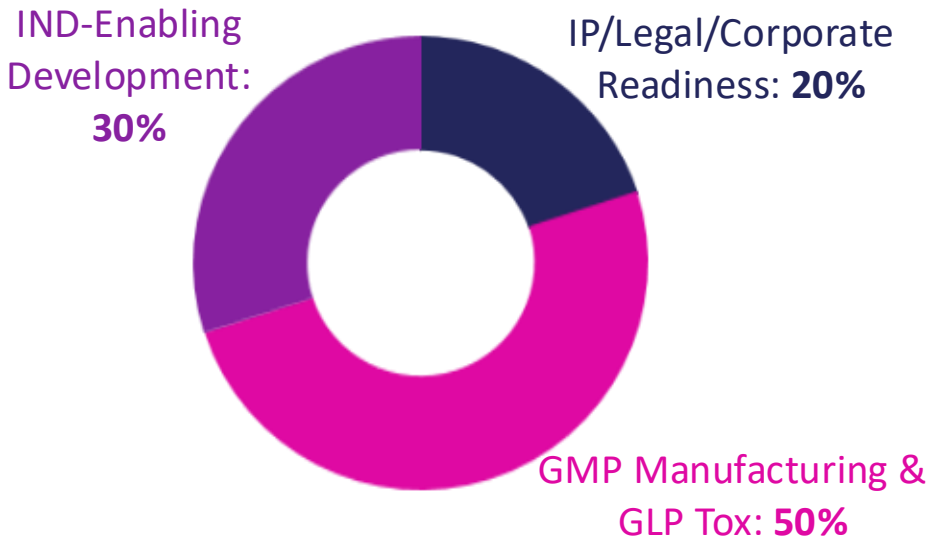
$1.0 Million SEED NOTE:
$24M Cap 20%; Discount; 6% Interest

Targeted Use of Proceeds

- $500K: GMP SN38 Drug production plus GLP tox (Rat)
- $300K : OSU-sponsored IND-enabling development work
- $200K : IP, legal and financing readiness

Expected Outcome: IND-Ready Lead EpCAM-SN38 Program Positioned for Next Institutional Financing

CAPITAL DEPLOYMENT TOWARD IND MILESTONES



Existing support from strategic and angel investors: active outreach to target sector partners

- **Lead Investors: Wharton Alumni Angels, Think Inc.**

Capital Plan to Clinical Inflection and Partnership Positioning (18-24 Months)

Backed by Early Investors including Wharton Alumni Angels, Think Inc., OSIF and Wilson Sonsini

	Seed I ($4.0M) First Half 2026, $4.0M Note $28-32M Cap, 15-20% Discount	**Seed 2 ($4.0M)** End 2026 → 2027 , $4.0M Note $36-40M Cap, 10-15% Discount
Drug Assets)	EpCAM–SN38 -> IND filed	EpCAM-SN38 (lead) + Gemcitabine (combination expansion) -> IND Initiation for additional indications
Clinical Progress	Phase I Initiation (EpCAM-SN38)	Phase 1 Completion (EpCAM-SN38) and expansion into Combination therapy
Operations	Platform, IP, and G&A support	Platform, IP, and G&A support

Clinical entry and combination therapy expansion position the company for strategic partnership or acquisition

RNA nanobiotics

THANK YOU!

James J Carroll, President and CEO

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617-899-6583

Link to Dr. Peixuan Guo publications:
https://rnanano.osu.edu/Guo/publications.html

EXECUTIVE TEAM

James Carroll

President, CEO & Chairman

25+ years of pharma, diagnostics, biomanufacturing, corporate development, strategy and investing.

- President of Wharton Alumni Angels
- Led RNA/DNA Nucleotide drug production and development initiatives at Millipore/Waters
- Led acquisitions, turnarounds, financing and exits
- Experience across Bionostics, Bio-Rad, Repligen, Harvard Medical School (Targeted Radiation Therapy). Remedium Bio, Edulis,

Dr. Krystle Karoscik

Chief Technology Officer

Technology, operations and strategy executive

- Translational research and clinical/commercial strategy
- Led >20 early-stage clinical programs
- Serial entrepreneur in therapeutics and med-tech
- Managing Director of Life Sciences, Wharton Alumni Angels
- Oversees external development, vendors and milestone execution

CORPORATE BOARD

James J Carroll, MBA
Chairman

Experienced life sciences executive with leadership across operations, financing, commercialization, business development, and strategic growth in biotechnology, diagnostics, and medical devices.

Ildiko Csiki, MD, PhD
Board Member

- Oncology drug development and commercialization leader
- Extensive experience in clinical trial design and treatment strategy
- Led strategic initiatives advancing cancer therapies and patient care

Cynthia Cai, PhD, MBA
Board Member

- 25+ years healthcare and life sciences executive/investor experience
- Expertise in governance, equity investing, business development, and growth strategy
- Board roles including: Spectral AI (NASDAQ: MDAI), HAYA Therapeutics, and other emerging companies and institutions

SCIENTIFIC INVENTOR & LEGAL ADVISOR

Peixuan Guo, PhD

Inventor, Advisor & Chair
Scientific Advisory Board

- Sylvan G. Frank Endowed Chair, Ohio State University
- 2021 Innovator Of The Year Ohio State University
- Fellow of the National Academy of Inventors (NAI)
- Director of Center for RNA Nano-biotechnology and Nano-medicine
- President of International Society of RNA Nanotechnology and Nanomedicine
- Founder of RNA nanotechnology field

Jennifer Fang

Partner, Wilson Sonsini
Biotech Corporate Law

- Focus on emerging growth and life science companies
- J.D., University of Pennsylvania Law School
- M.Eng., Biological Engineering, MIT
- B.S., Biology, MIT

SCIENTIFIC ADVISORS

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- **President of International Society of RNA Nanotechnology and Nanomedicine**

Christophe Tournerie

MD

- Expert in Clinical Trials for RNA/DNA Therapeutics
- Medical Research Institute, France

Bin Guo

PhD

- Associate Professor, University of Houston College of Pharmacy

Marc Lemaitre

PhD

- Oligonucleotide cGMP & FDA Regulatory Expert

B. Mark Evers

MD

- Oncologist, Surgeon University of Kentucky, Markey Cancer Center

RNA Junction–Engineered EV Platform

In Vivo TNBC Suppression with Reduced Chemotherapy Dosing

Orthotopic TNBC Xenograft

Treatment: CD44-targeted EV + Survivin siRNA + GEM + PTX

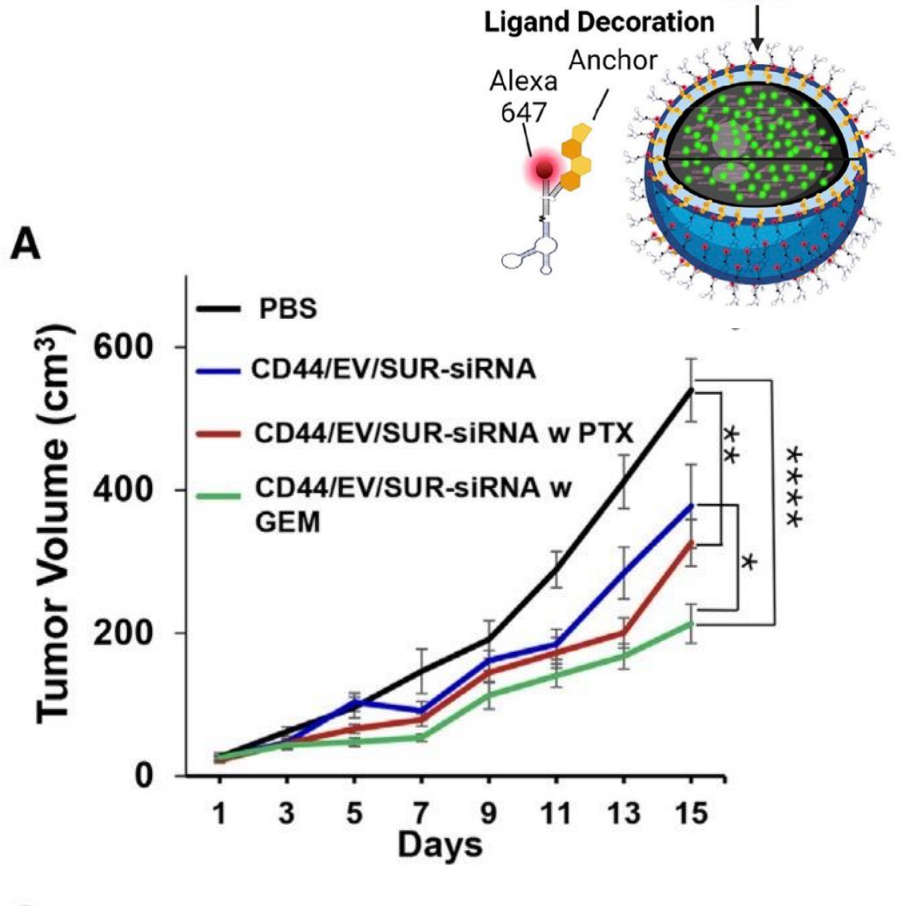
Study Dose Levels:

Gemcitabine: 2.2 mg/kg
(typical mouse dosing 50–100 mg/kg)

Paclitaxel: 5.6 mg/kg
(typical mouse dosing 10–20 mg/kg)

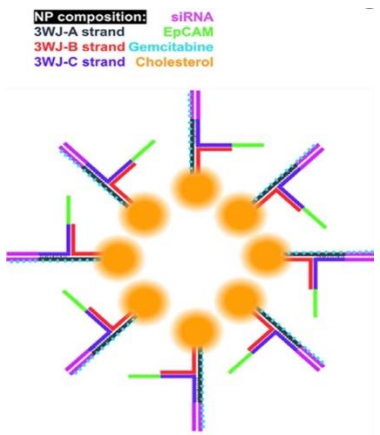
Outcomes:

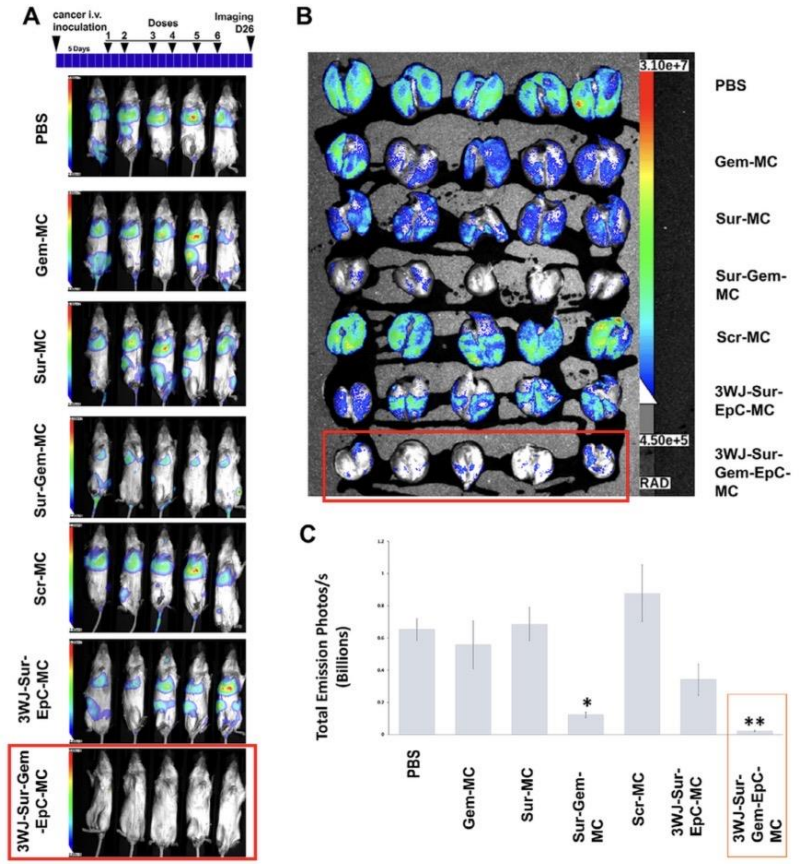
- Significant tumor suppression vs controls
- Efficacy maintained at substantially reduced chemotherapy doses
- Targeted multi-delivery demonstrated synergistic potential



RNA-Micelle Platform for RNAi + Chemotherapy in Metastatic CRC

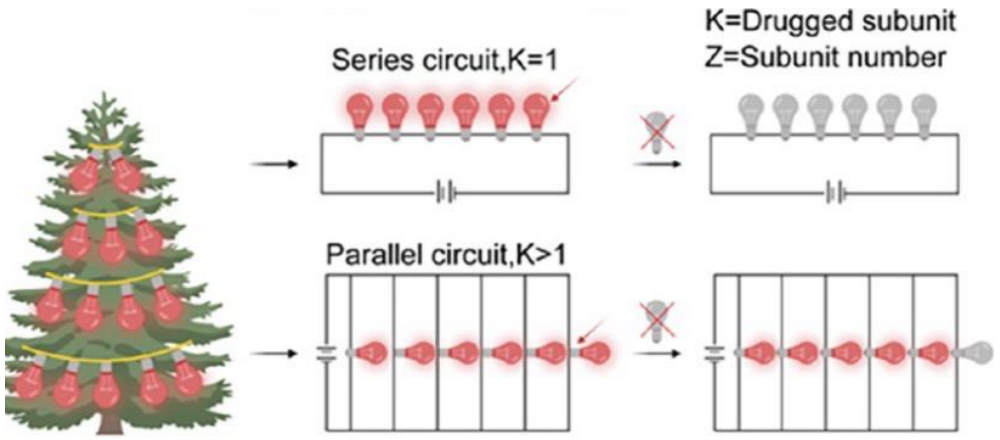
- Distinct RNA delivery architecture: cholesterol-driven self-assembly (separate from 3WJ/4WJ)
- Single RNA vehicle delivers survivin siRNA + high-payload gemcitabine to the same cell
- Intracellular synergy by design: RNAi disables resistance → chemotherapy induces apoptosis
- Represents a complementary RNA platform with a mechanistically distinct approach to metastatic CRC
- Near-complete suppression of CRC lung metastases (Fig. 5A–C)





Jin et al., Advanced Functional Materials (2026) — RNA-Micelle platform for synergistic RNAi + chemotherapy delivery

Overcoming Resistance Requires Multi-Target RNAi



- Chemoresistance is driven by RNA-regulated ABC drug efflux systems
- Efflux requires multiple RNA-controlled components to function:
  - transporter expression (e.g., ABCB1/P-gp)
  - ATP binding and hydrolysis conformational cycling and membrane transport
- Silencing a single RNA target allows rapid biological compensation

Conceptual takeaway: turning off one light does not shut down the system — multiple connections must be silenced simultaneously.

- Cancer signaling networks are redundant and adaptive, not linear
- Silencing a single gene often triggers pathway rerouting or compensation
- Multiple RNAi agents acting in parallel are required to overcome pathway compensation and resistance
- RNA nanostructures enable coordinated delivery of multiple RNAi payloads-addressing resistance mechanisms not tractable with single-agent therapies

*Yudhistira T, Yunker B, Dhir L, Ho YS, Liu S, **Guo P**. Developing Potent Therapeutics for Liver Cancer Chemoresistance via an RNA Nanotech and Series-Circuit-Christmas-Bulb Mechanism Targeting ABC Transporters. Mol. Pharmaceutics, 2025*

Regulatory Implications of RNA Nanostructures

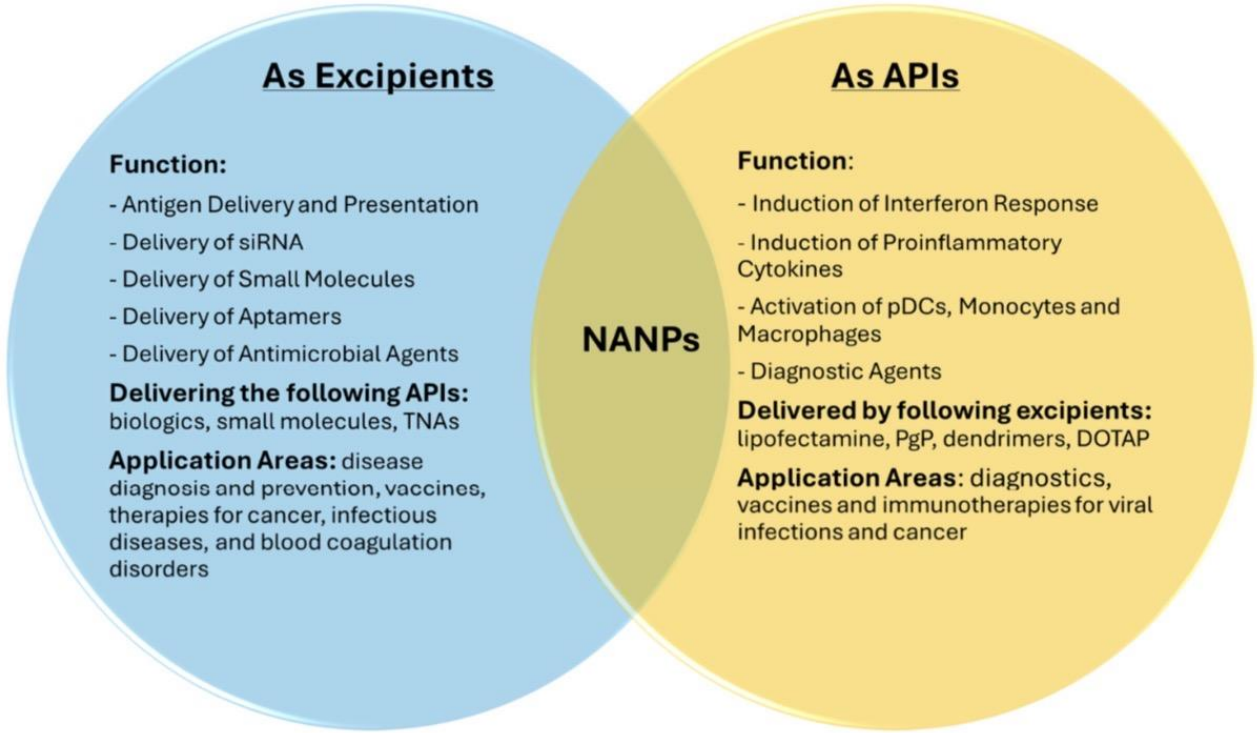
4WJ platform can be an API, an excipient, or both — depending on context

"Nucleic acid nanoparticles can serve as active pharmaceutical ingredients (APIs) and excipients and can even combine both functions simultaneously, depending on their intended therapeutic mechanism of action and formulation context."

— ACS Nano Medicine (Afonin et al.)

"Traditional binary classification as either API or excipient does not fully capture the regulatory reality of nucleic acid nanostructures."

— ACS Nano Medicine Perspective



Implications for RNA NanoBiotics:

- 4WJ scaffold classification is payload- and context-dependent
- Enables 505(b)(2) paths for small molecules and nucleosides
- RNAi / miRNA arms align with established RNA therapeutic frameworks
- Shared platform CMC and toxicology with payload-specific deltas

Reference: Kozlov S. et al. Nucleic Acid Nanoparticles Redefine Traditional Regulatory Terminology. ACS Nano Medicine, 2025.