RNA NanoBiotics

RNA Nanotechnology: Targeted Chemo and Radiotherapy in Cancers

James Carroll, President & CEO

Fall 2025

RNA NANOTECHNOLOGY PLATFORM DESIGNS

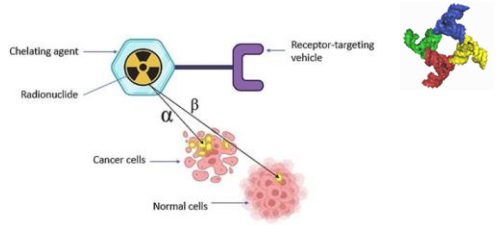
Exclusive Licensed Patent Portfolio Covers All Applications

RNA NanoBiotics

4WJ RNA Nanoparticles + Click Chemistry

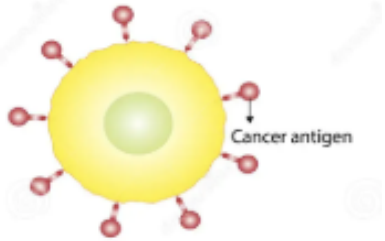
- Enhance its cancer cell targeted delivery efficiency to > 5% , vs traditional nanotechnology <0.7%
- Extraordinary PK profiles and low accumulation to VITAL ORGANS
- Increased solubility of chemical drugs, e.g., Increased Paclitaxel solubility by 32,000 folds

CURRENT FOCUS



4WJ RNA Nanoparticles for Radiation Therapy

- Conjugate chemical drugs to RNA nanoparticles to enhance the solubility and reduce the toxicity, include RNAi drug and an alpha emitting radioisotope in the complex for complete cytotoxicity to cancer cells

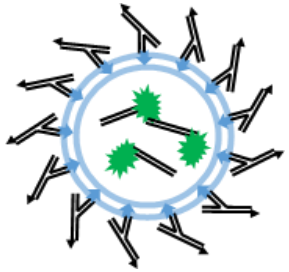


4WJ Cell Therapy

- Ex vivo delivery of regulatory RNAs to T cells or stem cells
- RNA nanoparticles as immune-cell targeting agents (like nanoparticle-guided CAR-T)
- Enhancing tumor infiltration of immune cells via co-administered nanoparticles
- RNAi-based modulation of checkpoint pathways

4WJ Bispecifics

- Dual targeting of two aptamers or ligands to bind to tumor + T cell receptor or two tumor antigens for enhanced specificity
- Therapy + Immune engagement to target tumor antigen and immune stimulant or checkpoint inhibitor RNAi.



RNA/Exosome

- Display RNA on exosome to make it negatively charged, minimize nonspecific binding
- Display aptamer or chemical ligand onto exosomes for efficient targeting
- Delivers siRNA to cell's cytoplasm to escape from endosome trapping

SECONDARY PLATFORM

Engineering 4 Way Junction RNA Nanoparticles for Precision Oncology

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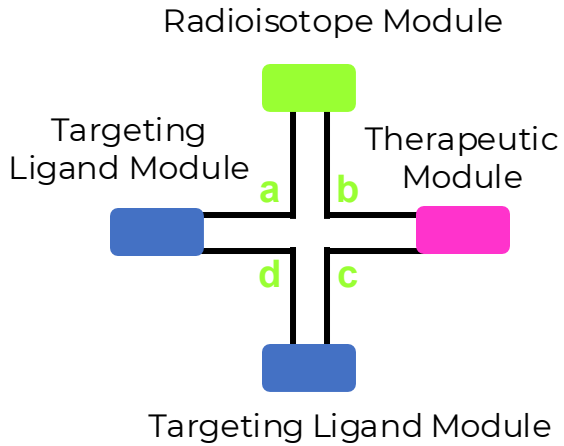
Four Engineered Modules Combine



Targeting Ligand – Aptamer sequences engineered into module

Therapeutic Module – RNA and or Nucleoside Drugs engineered into module

Radioisotope Module – Radioisotopes attached via proprietary ligand technologies

Currently Manual Via OSU Sponsored Research:

- 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
- Chelators selected for radioisotope integration (if used)
- Aptamer surface orientation and density optimized
- Drugs Synthesized. Screened in Cell Culture and on to Animal Testing

AI End-to-End System Architecture

- Target module: Literature + trial mining → aptamer targets.
- Design module: Generative LLM for aptamers + 4WJ scaffolds.
- Simulation module: Folding, docking, DAR prediction.
- Payload module: siRNA + miRNA optimizer.
- Integration module: Multi-objective RL engine.
- Feedback module: Wet lab loop for retraining.
- Drugs Synthesized. Screened in Cell Culture and on to Animal Testing

Cycle time: Weeks instead of months

Engineering RNA Nanoparticles with AI In Silico Tools

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Step 1. Target Cancer Selection

- Inputs: Tumor type, prevalence data, unmet need.
- AI tool: Natural-language mining model (PubMed/clinical trials ingestion)
  that ranks aptamer-accessible biomarkers
- Output: Shortlist of high-prevalence targets + % expression and validated aptamer sequences.

Step 2. Aptamer & Scaffold Generation

- Generative AI: Transformer models fine-tuned on SELEX aptamer libraries propose candidate sequences.
- AI Filter: ViennaRNA / NUPACK / Rosetta-RNA compute folding ΔG, discard unstable junctions.
- Output: Dozens of stable 4WJ scaffold candidates with aptamer(s) positioned.

Step 3. Payload Docking & Chemistry

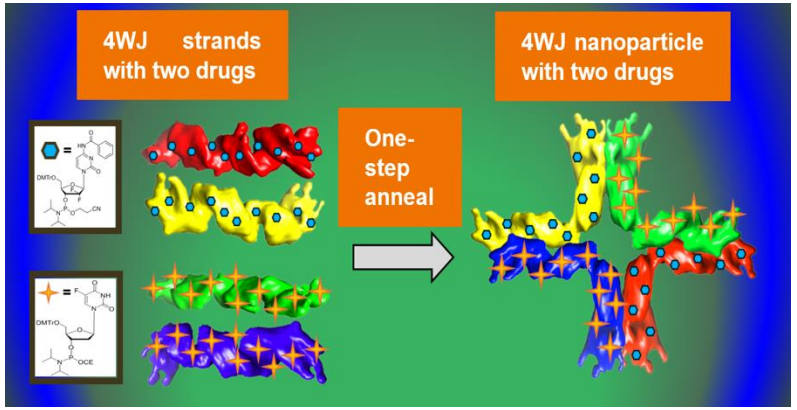
- AI docking (DiffDock, EquiBind): Simulate payload–RNA handle interactions.
- Payload library: Generics (SN-38, paclitaxel, gemcitabine, doxorubicin) + licensed classes (DXd, duocarmycin, PBD).
- Multi-objective optimization: DAR, linker stability, steric fit with aptamer folding.
- Output: Ranked list of compatible payload–handle designs per scaffold.

Step 4. RNAi & microRNA Integration

- siRNA design AI: siRNAoff / GuideScan-AI → screens all ABC transporters (ABCB1, ABCG2, ABCC5) and resistance genes (RRM1, TUBB3, AR-V7).
- microRNA design AI: miRDB + ML predictors → propose tumor-sensitizing mimics/antagomirs (miR-34a, miR-145, miR-200c, anti-miR-21).
- Output: Candidate duplexes scored for potency, off-target risk, manufacturability.

Step 5. Multi-Objective AI Optimizer

- Reinforcement learning engine: Balances aptamer affinity, NP stability, payload DAR, RNAi/miRNA efficacy, and predicted toxicity.
- Reward function: ΔIC50 vs parent drug, tumor vs normal selectivity, manufacturability (oligo length/mods <60 nt).
- Output: Optimized drug designs per cancer type.



EXECUTIVE TEAM

James Carroll

President, CEO and Board Chairman

25+ years in Executive Management, strategy, corporate and business development, and investments

- President of Wharton Alumni Angels
- Led RNA/DNA Nucleotide drug production and development efforts at Millipore/Waters
- Several Acquisitions, Turnarounds and Exits
- ExonanoRNA, Remedium Bio, Edulis, Bionostics, BioRad, Repligen, Harvard Medical School

Dr. Krystle Karoscik

Chief Technology Officer

Technology, Operations and Strategy Executive

- Niche in Translational Research and Clinical & Commercial Strategy
- Serial entrepreneur in therapeutics and med-tech
- Led >20 early-stage clinical programs
- Managing Director of Life Sciences, Wharton Alumni Angels
- VP BoD Penn Club of Boston; Co-Chair of Women in Leadership fostering development in STEM and finance

CORPORATE BOARD

RNA NanoBiotics

James J Carroll, MBA
Chairman

Highly committed business operations, sales, marketing, business development, turnaround management, life science start-up, operations, and finance executive with in-depth understanding of biotechnology, life science instrumentation, in vitro diagnostic, and medical device product development, commercialization, and strategic financing.

Ildiko Csiki, MD, PHD
Board Member

- Pioneered strategic initiatives in drug development, leading to significant advancements in cancer treatment and patient care.
- Spearheaded the development and commercialization of groundbreaking therapies, overseeing research, business development, and licensing.
- Expert in clinical trial design

Cynthia Cai, PhD, MBA
Board Member

- Executive & Investor with 25+ years in healthcare and life sciences, experienced in equity investment, board governance, marketing, and business development.
- Board Member of Spectral AI (NASDAQ: MDAI), Arthrosi Therapeutics, Amberstone Biosciences, Basking Biosciences, HAYA Therapeutics, and the Science History Institute.

Wharton
University of Pennsylvania

SCIENTIFIC AND LEGAL ADVISORS

Peixuan Guo, PhD

Inventor, Advisor and Chairman of Scientific Advisory Board

Professor, Sylvan G. Frank Endowed Chair

Pharmaceutics and Pharmacology, Ohio State University

- 2021 Innovator Of The Year Ohio State University
- Fellow of the National Academy of Inventors (NAI)
- Director of Center for RNA Nanobiotechnology and Nanomedicine
- President of International Society of RNA Nanotechnology and Nanomedicine
- International Society of RNA Nanotechnology and Nanomedicine

Jennifer Fang

Partner, Wilson Sonsini Specialty Biotech Corporate Law

- Focus on Cutting-Edge Life Science Companies
- J.D., University of Pennsylvania Law School, 2009Internet Editor, University of Pennsylvania Journal of International Law
- M.Eng., Biological Engineering, Massachusetts Institute of Technology, 2006
- B.S., Biology, Massachusetts Institute of Technology, 2005

INTRINSIC 4WJ RNA NANOPARTACLE PROPERTIES

ENABLE PRECISE DEAP TUMOR PENETRATION

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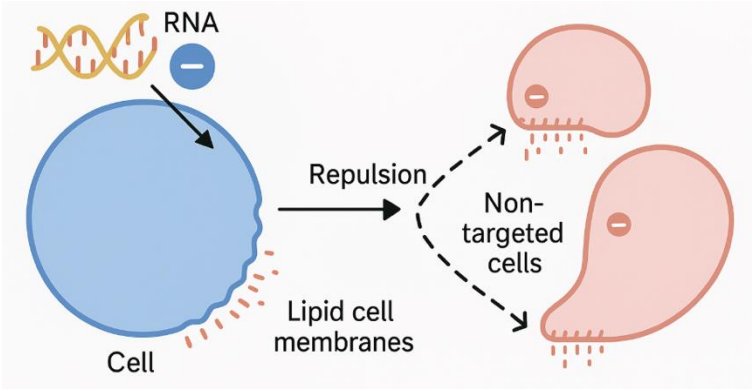

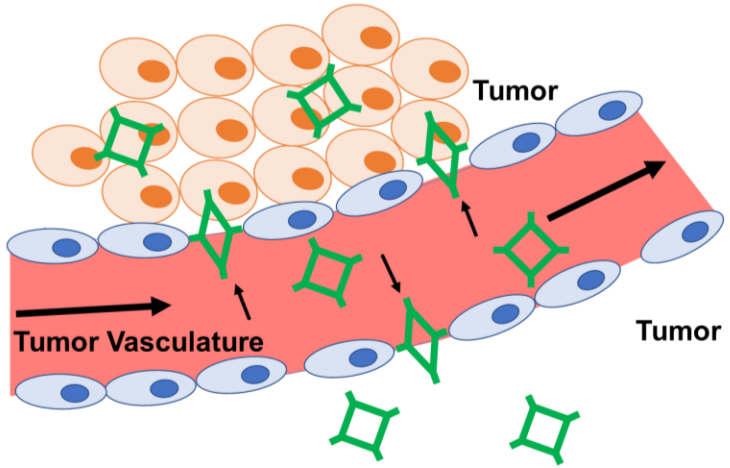

The amoeboid rubbery property of RNA nanoparticles make them penetrate more efficiently into tumors as they can easily clear the 5nm glomerulus kidney filter intact

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

ADC's VS 4WJ RNA Nanoparticles

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	ADCs	4WJ RNA Nanoparticles
Targeting specificity	❌ Off-target risk	✅ Programmable precision
Payload versatility	❌ Limited (mainly cytotoxics)	✅ Multiple payload types (siRNA, miRNA, drugs, imaging)
Size & tumor penetration	❌ Bulky, limited diffusion	✅ Small, tunable, better penetration
Manufacturing	❌ Complex antibody + conjugation	✅ Self-assembling, reproducible
Circulation stability	❌ Risk of premature release	✅ Chemically stabilized RNA
Immunogenicity	❌ Potential immune activation	✅ Low immunogenicity (engineered)
Controlled release	❌ Linker-dependent	✅ Smart release (pH, enzymes, miRNA triggers)
Cost & scalability	❌ Expensive biologics	✅ Low-cost, scalable synthesis

4WJ RNA Nanoparticle Key Advantages

- Engineering Simplicity - 4WJ RNA nanoparticles avoid antibody discovery and conjugation, allowing faster iteration by simply changing RNA sequences. This makes the platform more agile than ADCs.

- Tumor Penetration & PK (Size) - Size is decisive: ADCs (~10-20nm) struggle to penetrate solid tumors, while 4WJs (functionally <5nm and clear glomerulus) diffuse throughout tumor tissue, improving therapeutic reach.

- Immunogenicity - Unlike ADCs, which can trigger immune responses, 4WJs with modified nucleosides show minimal immunogenicity, supporting repeat dosing.

4WJ RNA NANOPARTICLE BIODISTRIBUTION

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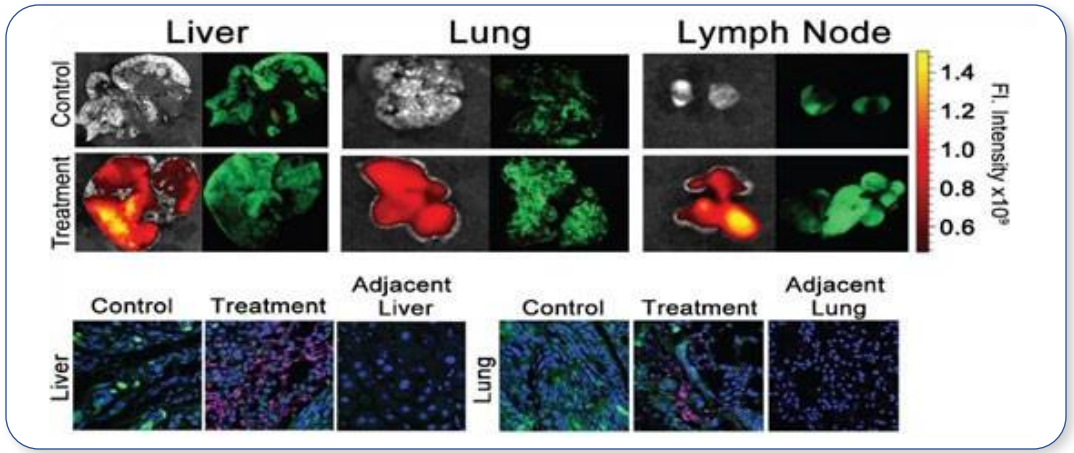
RNA nanoparticles circulate well upon injection

Nanoparticles are cleared within 4 hours in blood

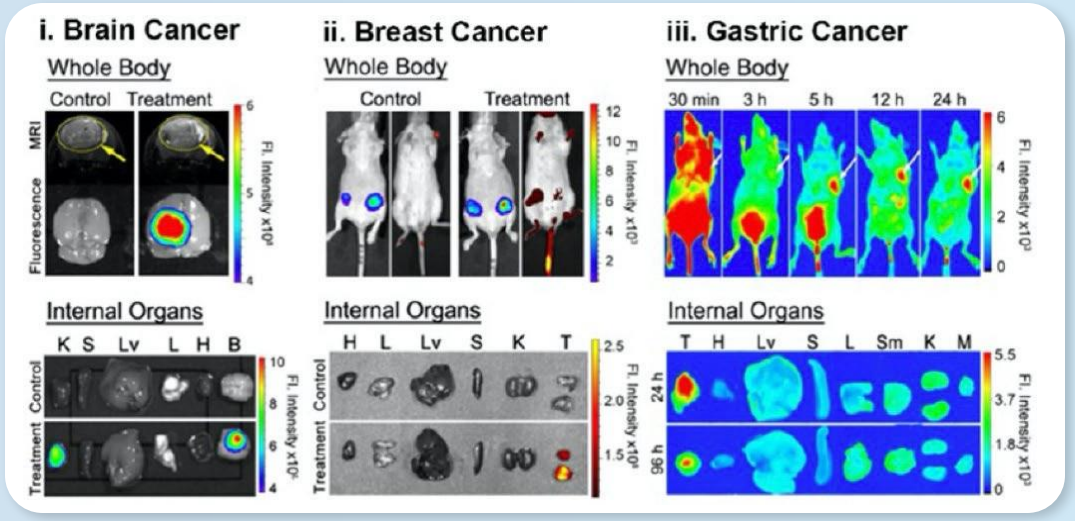
Have high tumor retention for better therapeutics

RNA nanoparticles with ligands tested

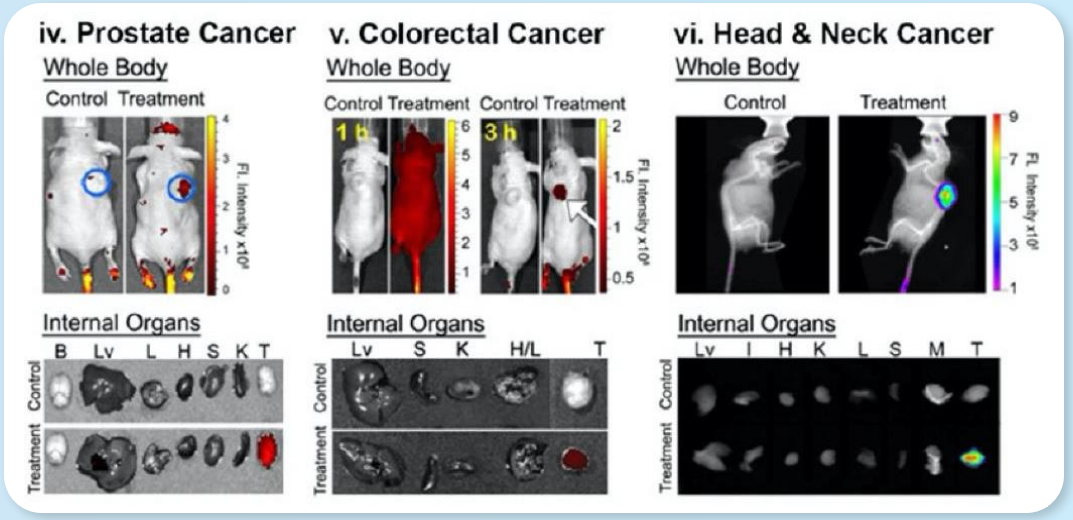
Allows for tumor targeting without accumulation in organs



Colorectal Cancer Metastases to Liver and Lung, Lymph Node



Fast Clearance In Circulation vs Slow Clearance In Tumors



These Benefits Are Critical for Targeted Radiation Therapeutics

4WJ RNA NANOPARTICLES EXIBIT NO ORGAN ACCUMULATION

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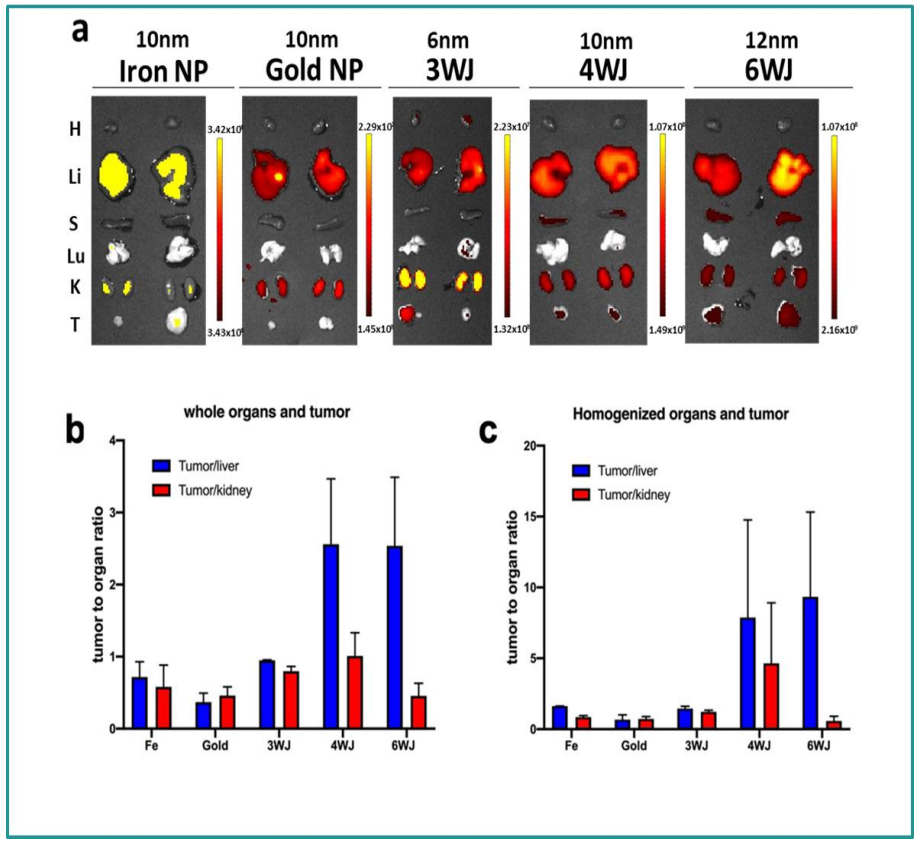
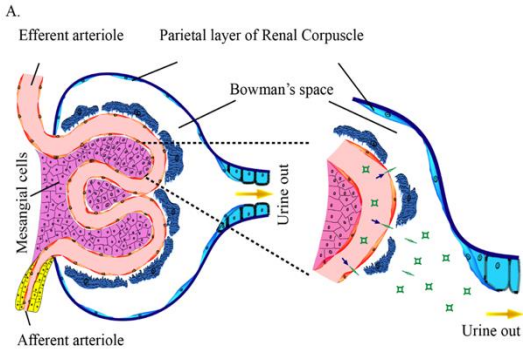
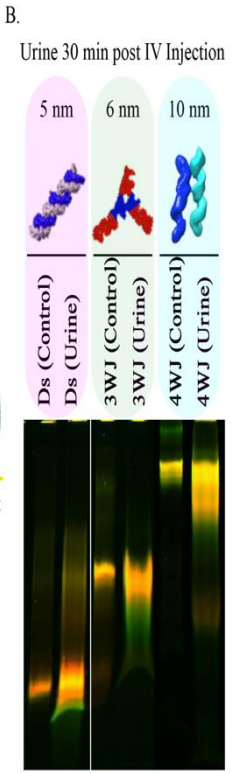
Versatile 4WJ structure combinations allow for rapid and efficient intra-tumor penetration without organ accumulation.



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

4WJ RNA NANOPARTICLE CONJUGATES

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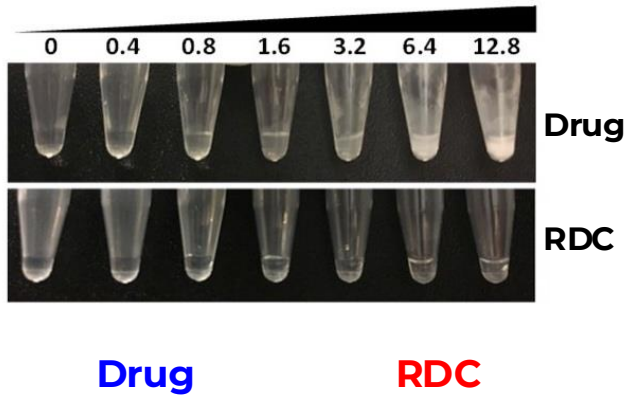
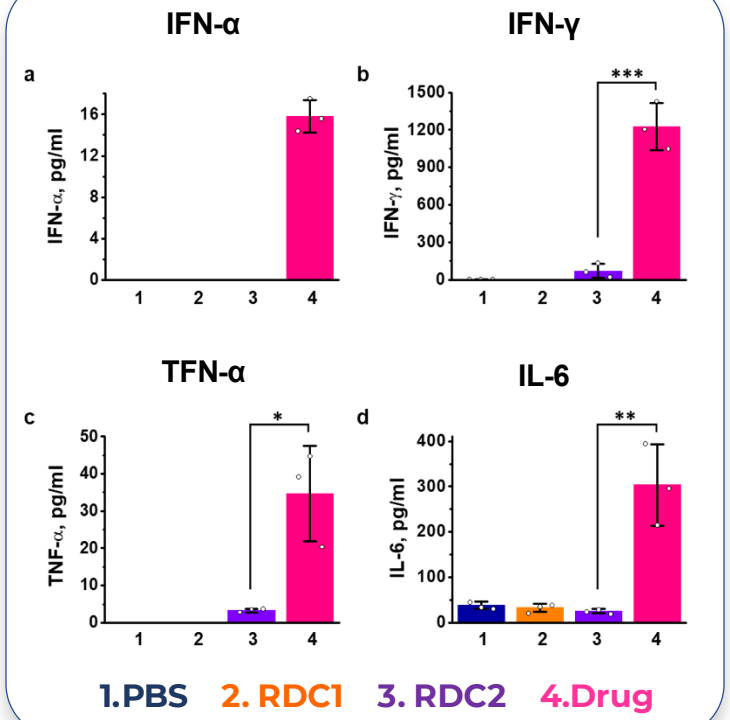
Anticancer drug is conjugated to RNA Nanoparticles to target and kill cancer cells while sparing healthy cells. The linkers are engineered to release drug payloads within the cells only.

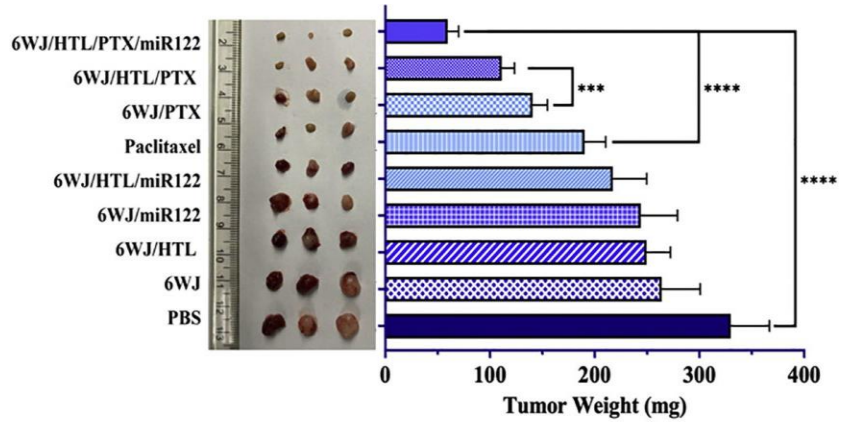
A. Enhanced Drug Solubility



B. Reduced Immunogenicity



C. Enhanced Tumor Suppression



RNA NANO-PARTICLES FOR TARGETED RADIATION THERAPY

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

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RNA NanoMed (Aug 2025) published proof-of-concept for targeted radiotherapeutics using modular RNA nanoparticles

Platform Highlights:

4WJ RNA nanoparticles retain chemical & targeting behavior of 3WJ core

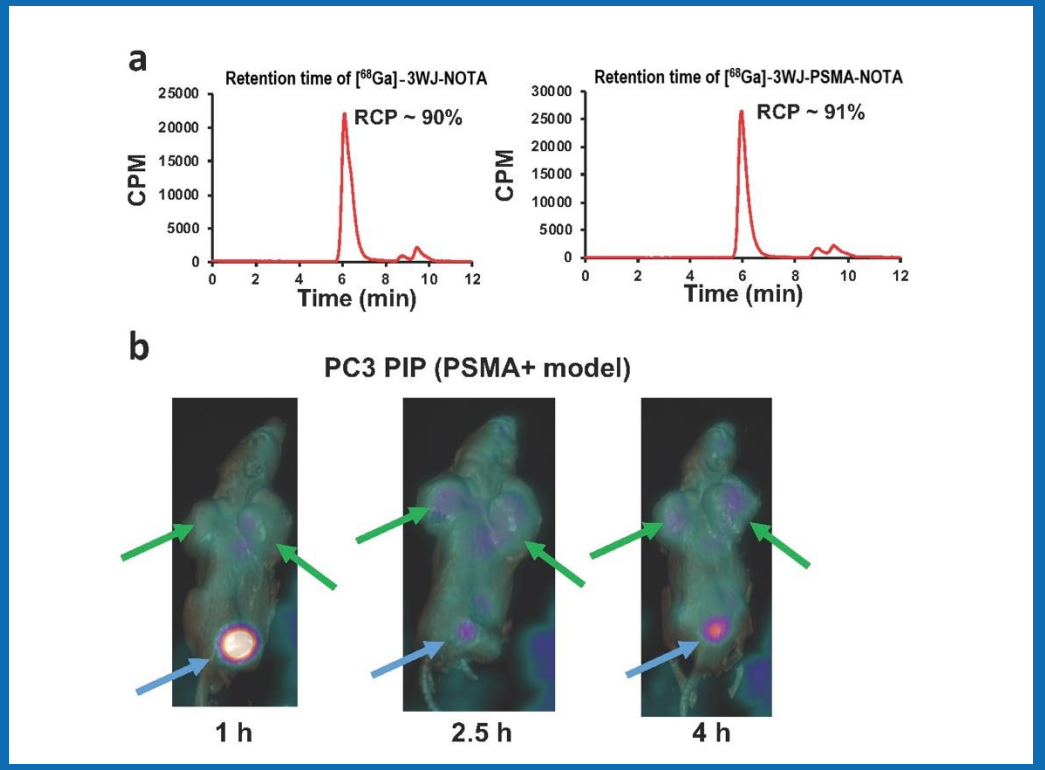
- Rapid tumor uptake: 1–4 h; rapid clearance from non-tumor tissues
- Plug-and-play design: swap targeting ligand & chelator strand without altering core
- Diagnostic ^{68}Ga easily replaced with therapeutic α/β emitters
- Single GMP & regulatory backbone supports multiple products

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



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

Green Arrow - Tumor

Blue Arrow – Bladder (showing excretion)

URGENT AND UNMET MEDICAL NEEDS

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Cancer is the leading cause of death worldwide. For patients diagnosed with metastatic disease, the diagnosis is often a sudden and devastating turn - one that redefines futures, upends families, and begins a race against time.

COLORECTAL CANCER

$12B WW Today Project to $20B 2033

- Leading cause of cancer death in men <50 years
- Fastest-rising cancer in women <50 years
- Most deaths occur after metastasis to the liver and lungs
- 5-year survival rate drops to under 15%.
- Standard care is toxic, non-specific, and ineffective.

TRIPLE NEGATIVE BREAST CANCER

$11B WW Today Project to $20B 2033

- Breast cancer is a leading cause of cancer death in women
- Notably aggressive breast cancer subtype
- High recurrence rate
- Low 5-year survival compared to other subtypes
- Significant lack of targeted therapies

Patients and families aren't waiting for incremental change - they're waiting for a breakthrough. *One that doesn't just delay the inevitable...but*...*redefines the possible*.

CURRENT DRUGS IND SUBMISSION TIMELINES*

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	Target	Payload	Cancer Type	Ready to Initiate IND Program	Planned IND
1	**EpCAMapt**	**4WJ-SN38**	**mCRC – Liver/Lung**	✓	**2026**
1A	Solid tumors	4WJ-SN38-GEM	4T1 - Breast Cancer	(secondary combination asset)	2026
2	**EGFRapt**	**4WJ-X-24PTX-anti-miR21**	**Triple Negative Breast Cancer**	✓	**2027**
3	HTLs	4WJ-GalNex-Paclitaxel.miR122	Liver Cancer	Animal data	2027
4	PSMAapt	4WJ-anti-mRNA21-LNA	Prostate Cancer	Animal data	2029

- **Several Additional Drug Candidates Identified by AI for: Gastric/GEJ, Ovarian, Pancreatic, Endometrial, Lymphoma,…**
- **Drug Potencies May be Enhanced by In-licensed Chemo Agents such as: Exotecans, Duocarmycin prodrugs, PBD dimers,…**

* Priorities/dates may be re-ranked based on new data and review. Platform related work can continue until priority decision.

4WJ-SN38 DESIGN WITH TARGETING EpCAM APTAMER

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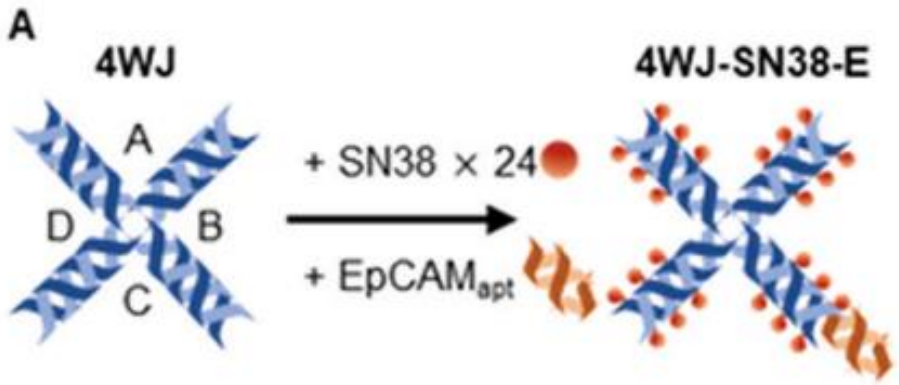
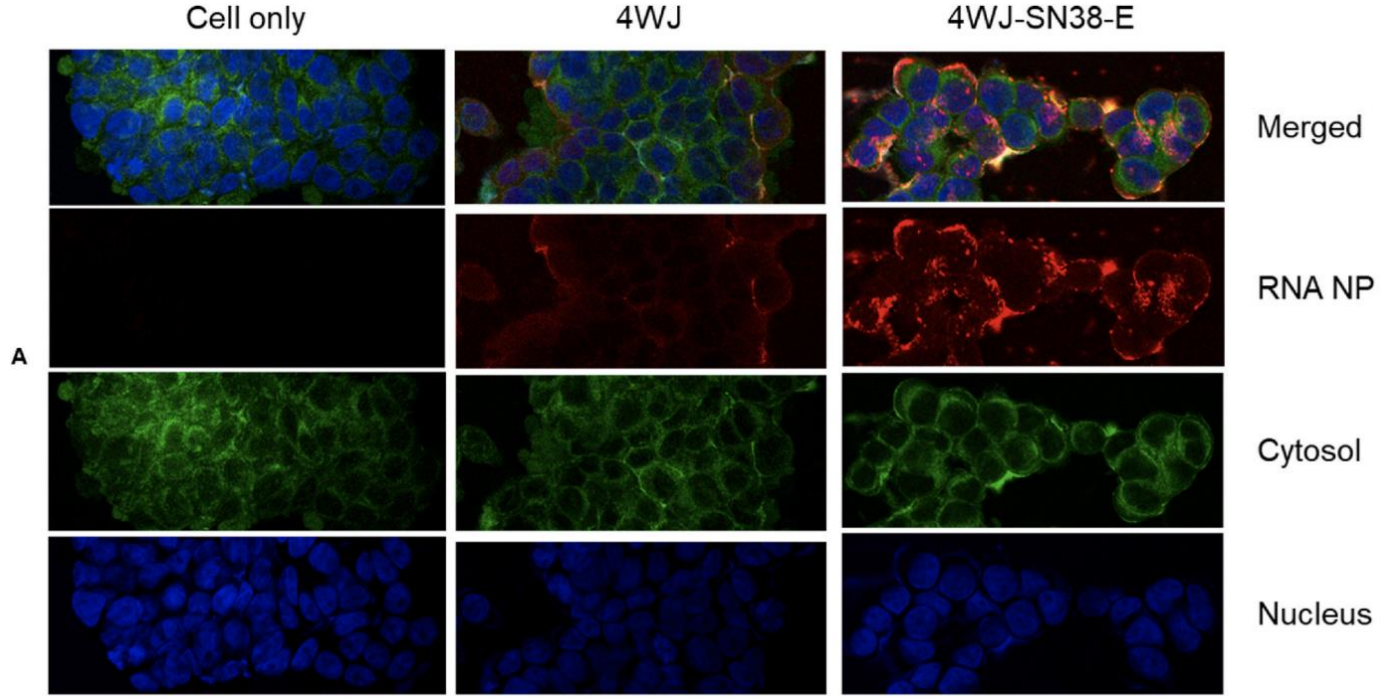
4WJ is comprised of 4 helixes that each contain a core domain to control the structure formation and a payload domain that is used for functionalization

Construction of functionalized thermostable 4WJ RNA nanoparticles with SN38 and EpCAMapt for tumor-specific targeting, covalently bonded via click chemistry.



EpCAM is overexpressed **(70-90%)** in numerous cancers and is a biomarker and cell surface receptor for targeting of RNA nanoparticles

EpCAMapt displaying RNA nanoparticles specifically bind to EpCAM-overexpressed tumor cells and are further internalized into the cells efficiently by receptor-mediated endocytosis



PRECLINICAL POC DATASET 4WJ EpCAM SN38

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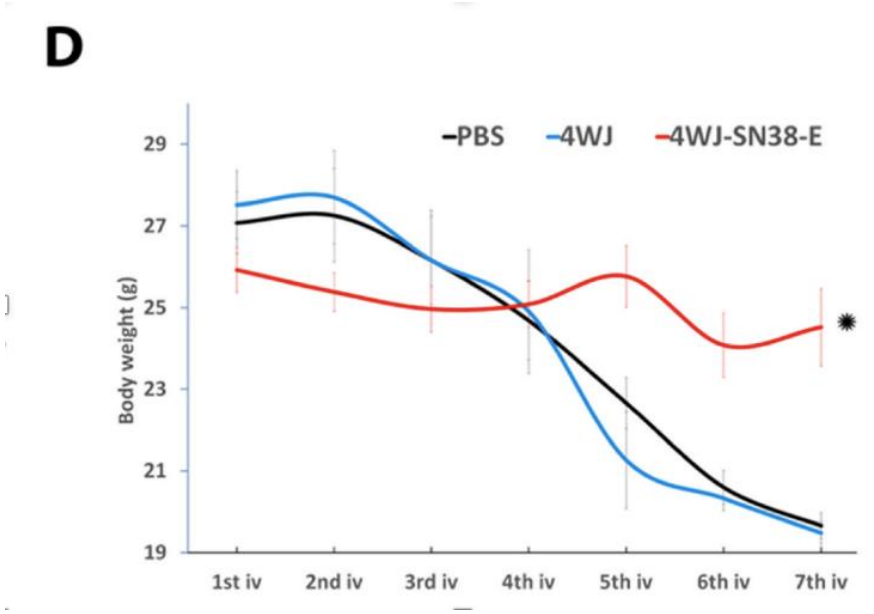
Key Requirement	RNA NanoBiotics Result	Benchmark Met
Drug Loading Efficiency	24 SN38 molecules per 4WJ-RNA nanoparticle	✅
In Vitro Apoptosis / Cytotoxicity	31.6% apoptosis in HT29 cells (4WJ-SN38-EpCAM)	✅
In Vivo Tumor Volume Reduction	85–90% tumor volume reduction at 2 mg/kg SN38 (x5 doses)	✅
Targeting 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	✅

4WJ-SN38-EpCAM UNDETECTED TOXICITY OR IMMUNOGENICITY

RNA NanoBiotics

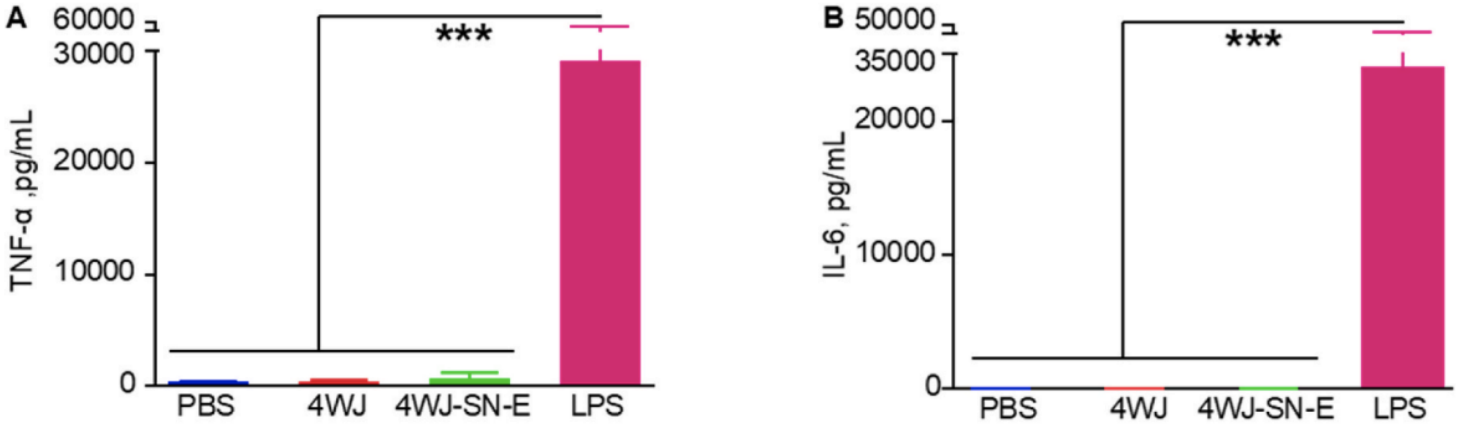
Rapid Renal Clearance:

- Fast clearance documented with **no body weight loss or systemic toxicity**



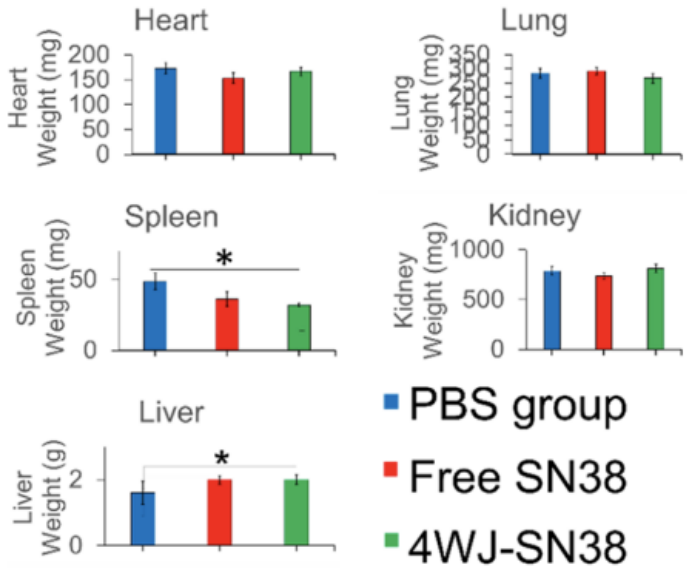
Undetectable Toxicity & Immunogenicity:

- ELISA shows cytokine levels **comparable to untreated controls**

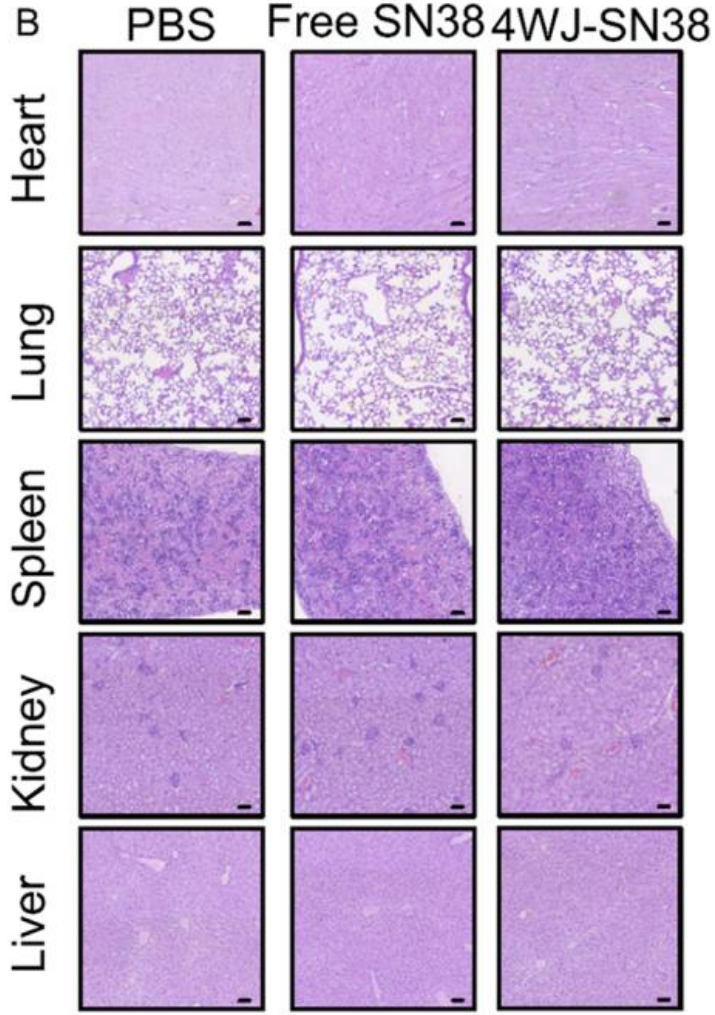


PATHOLOGY & SAFETY OF 4WJ-SN38-EpCAM

No significant toxicity, side effects or immune responses.



- Repeated IV injections up to 30mg/kg do not result in toxicity
- PK (T ½) 5 to 10 hours vs 0.25-0.76 hr for siRNA itself
- Avoidance of antibody induction (as protein free)



4WJ-SN38-EpCAM EFFICACY

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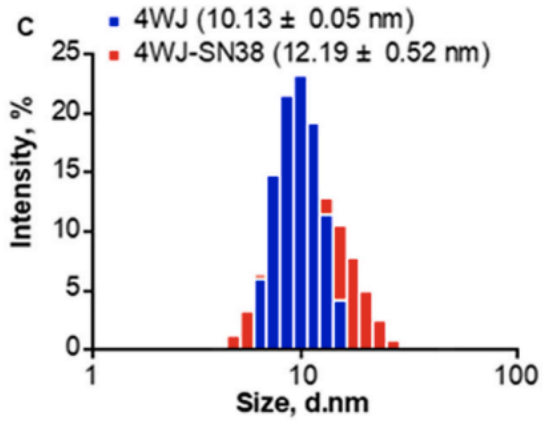
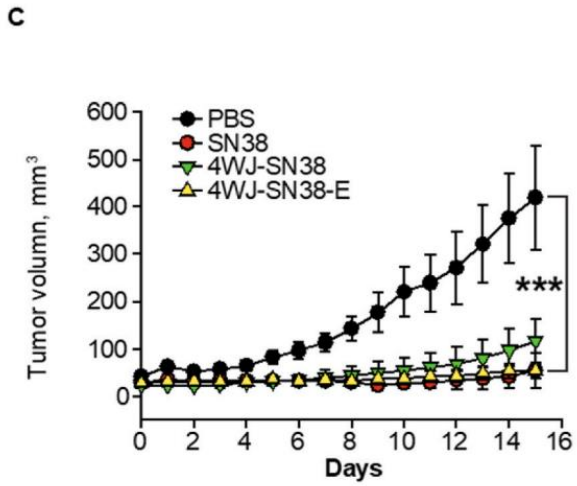
High Tumor Accumulation:

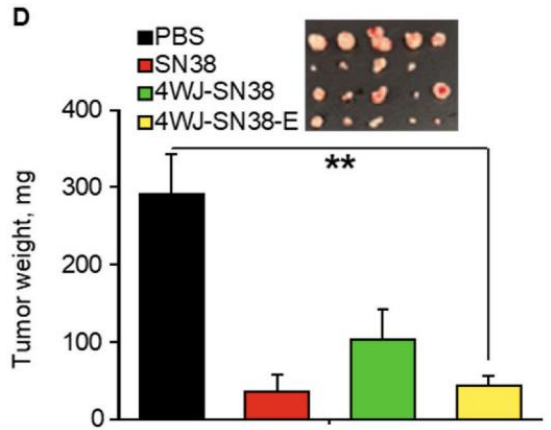
- Small size; Deformable and hydrophilic properties aiding EPR effect-based penetration



No Organ Accumulation:

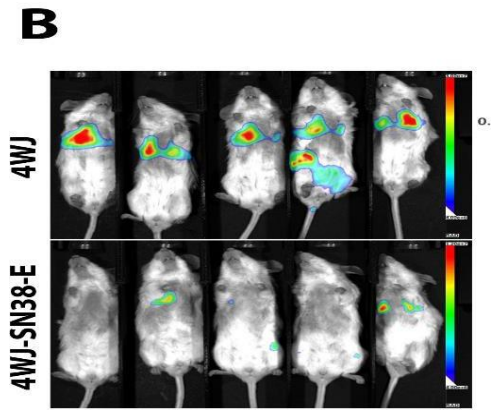
- No visible accumulation in liver, spleen, or lungs

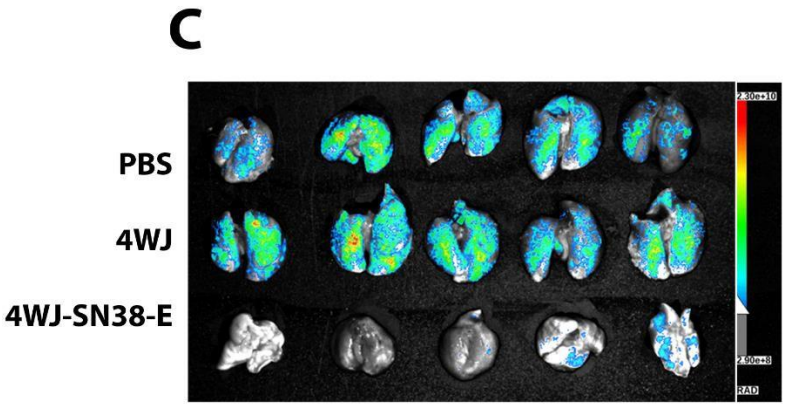




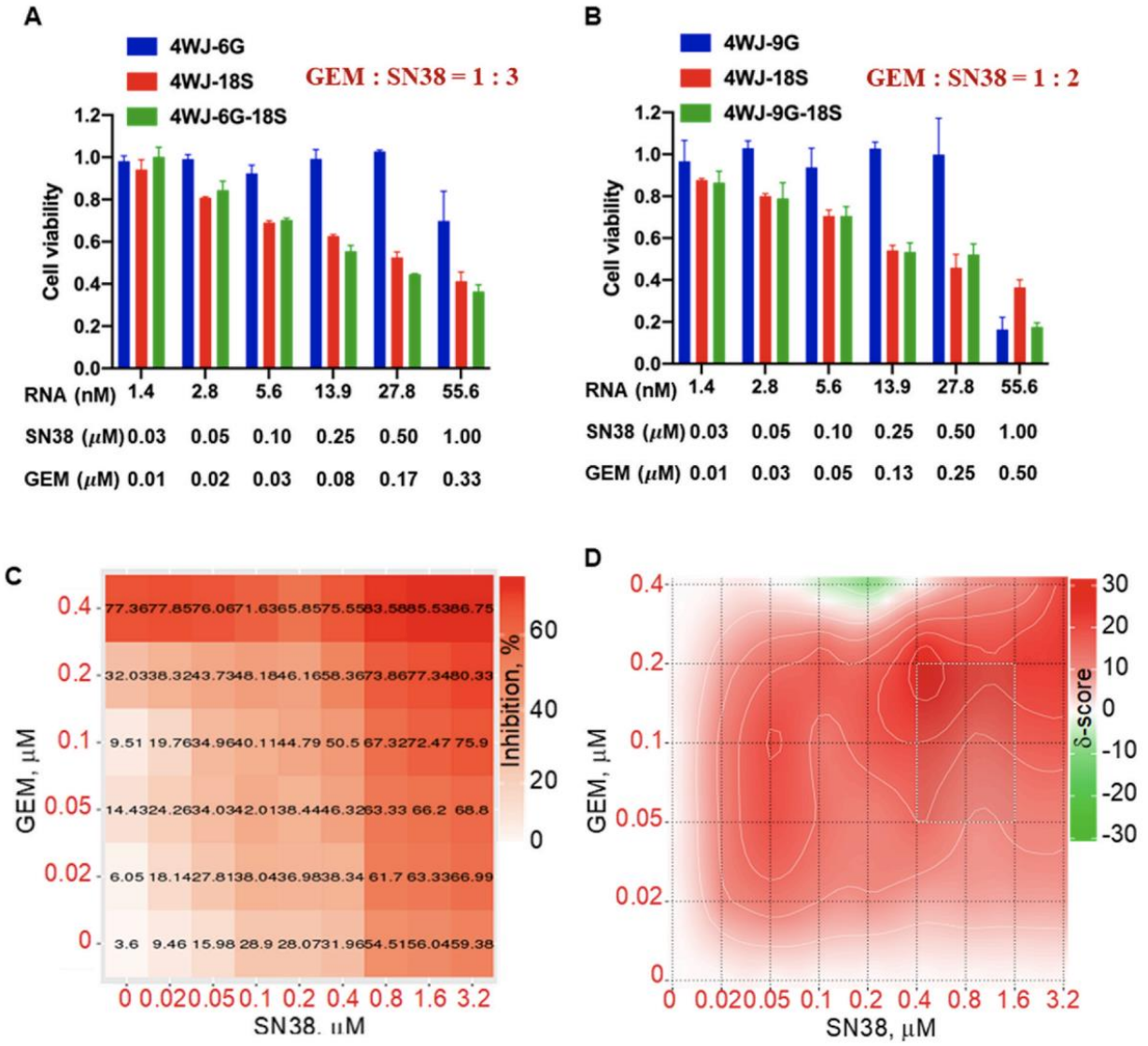
Safe uptake:

- Tumor suppression with-out off-target effects





SYNERGISTIC EFFECT 4WJ SN38+GEM POTENTIAL LEAD 1A



Combination chemotherapy of SN38+GEM:

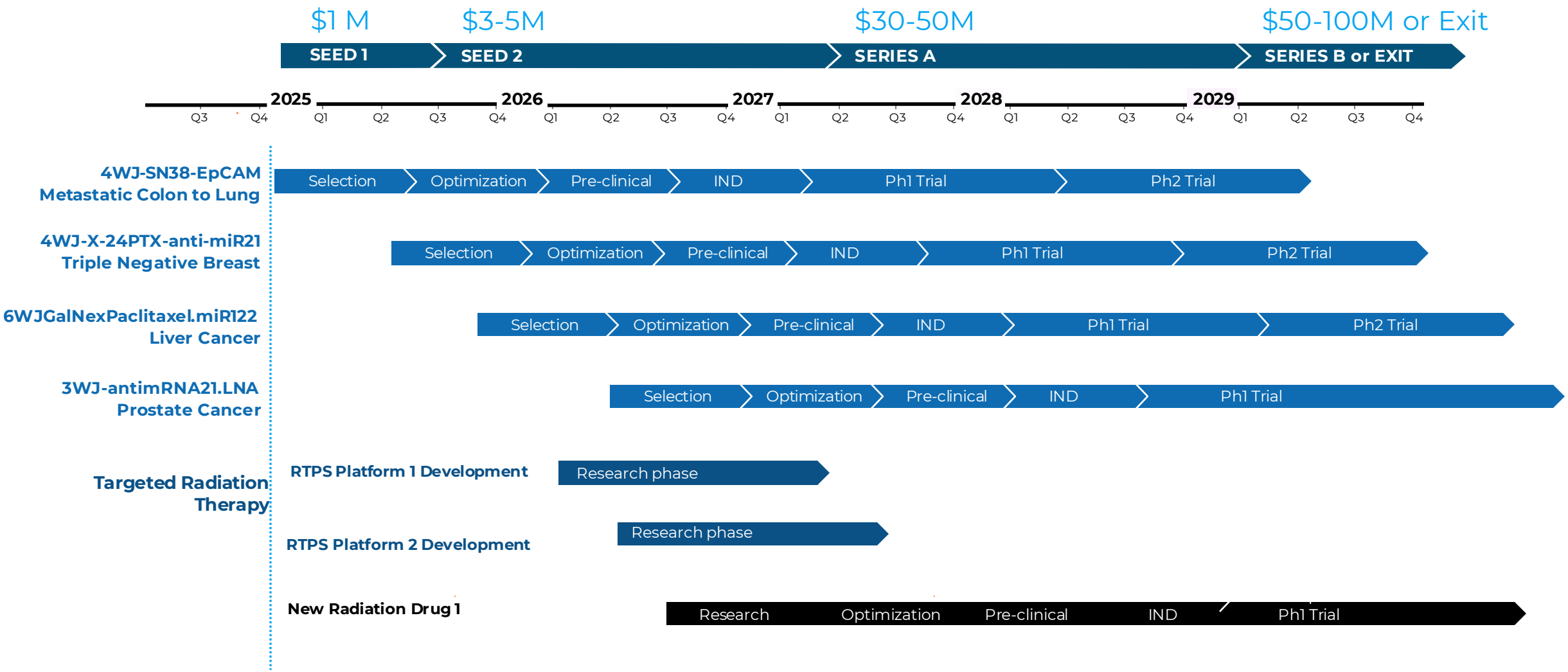
- Cytotoxicty with 1:3 and 1:2 ratios of GEM:SN38

Dose response matrix and HSA. Synergy map, score 11.7 (strong synergy).

Lin X. et al.& Guo P. *Biomaterials*. 2024

RNA NANOBIOTICS DRUG PIPELINE TIMELINES

RNA NanoBiotics



Ongoing Research at OSU may present more advanced drugs that may lead to reprioritization (5+ papers to be published)

Strategic Partnering and Exit Landscape – Top Targets

RNA NanoBiotics

Company	Strategic Fit	Partnering Rationale	Relevant Deals / Why It Matters
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

FINANCIAL STRATEGY

Planned Series A for Clinical plus - $40-$60M (Equity)
Late 2026-2027

RNA NanoBiotics

Category	Q3 2025 → mid-2026 Seed I – $5.0M Note $25M Cap, 20% Discount, 6% Interst	Mid-2026 → end-2026 Seed II – $5.0M Note $38M Cap, 15% Discount, 6% Interst
Drug Assets Readiness (EpCAM–SN38 + TNBC)	Subtotal: $3.2M • $2.4M – EpCAM–SN38 CMC transfer • $0.8M – TNBC CMC prep	Subtotal: $3.0M • $2.5M – EpCAM–SN38 GLP tox + GMP L • EpCAM–SN38 IND filed by end-2026 • $0.5M – TNBC IND-enabling
Platform / AI Development (Radiopharma + synthesis, animals)	Subtotal: $1.0M • Radiopharma in vitro proof • AI software + first hire • Early synthesis vendor setup	Subtotal: $1.2M • Radi in vivo biodistribution + efficacy • AI expansion (1–2 candidates) • Contract synthesis + animals
Overhead & Ops	Subtotal: $0.8M • Salaries, legal, license, G&A,...	Subtotal: $0.8M • Salaries, legal, License, G&A,...
Milestones	• Mid-2026: – EpCAM–SN38 + TNBC in IND-track – Radiopharma chemistry validated – AI platform operational	• End-2026: – EpCAM–SN38 IND filed – TNBC close behind – Radiopharma in vivo proof – AI-designed candidates in animals
Total	$5.0M	$5.0M

- Lead Investors: Wharton Alumni Angels, Think Inc., Wilson Sonsini

ONCOLOGY COMPETITORS: Targeting & Differentiation

RNA NanoBiotics

Company	Platform	Oncology Focus	Radioisotope?	Co-delivery?	Targeting Mechanism
RNA Nanobiotics	**4WJ RNA NPs**	**Solid tumors**	**Yes (opt.)**	**Yes (RNA+chemo)**	**Aptamer-guided (EpCAM etc.)**
Novartis (AAA)	Radioligand	Prostate, NETs	Yes	No	Small-molecule ligands (PSMA, SSTR2)
AstraZeneca (Fusion)	Radioconjugate	Prostate	Yes	No	Peptide ligands to tumor receptors
BMS (RayzeBio)	Actinium RLT	NETs, SCLC, HCC	Yes	No	Peptides/antibodies to tumor receptors
Eli Lilly (POINT)	Radioligand	Prostate	Yes	No	Small-molecule ligand (PSMA)
Telix	Theranostics	Prostate, Kidney	Yes	No	Ligands (PSMA, CAIX, FRα)
Convergent Tx	Radio-Ab	Prostate	Yes	No	Monoclonal antibody (PSMA)
Abdera Tx	Radiopharma	DLL3 SCLC	Yes	No	Antibody (DLL3)
EnGeneIC	EDV™ minicells	Solid tumors	No	Yes (RNA+chemo)	Antibody-decorated minicells
Transcode Tx	RNAi NPs	Oncology (miR-10b)	No	No	Ligand/iron-oxide conjugates
Nanobiotix	Radio-enhancer	Head & neck	No	No	Local intratumoral injection
Sirnaomics	RNAi (PNP, GalNAc)	Skin, cholangio	No	No	GalNAc hepatocyte targeting (not tumors)

THANK YOU!

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