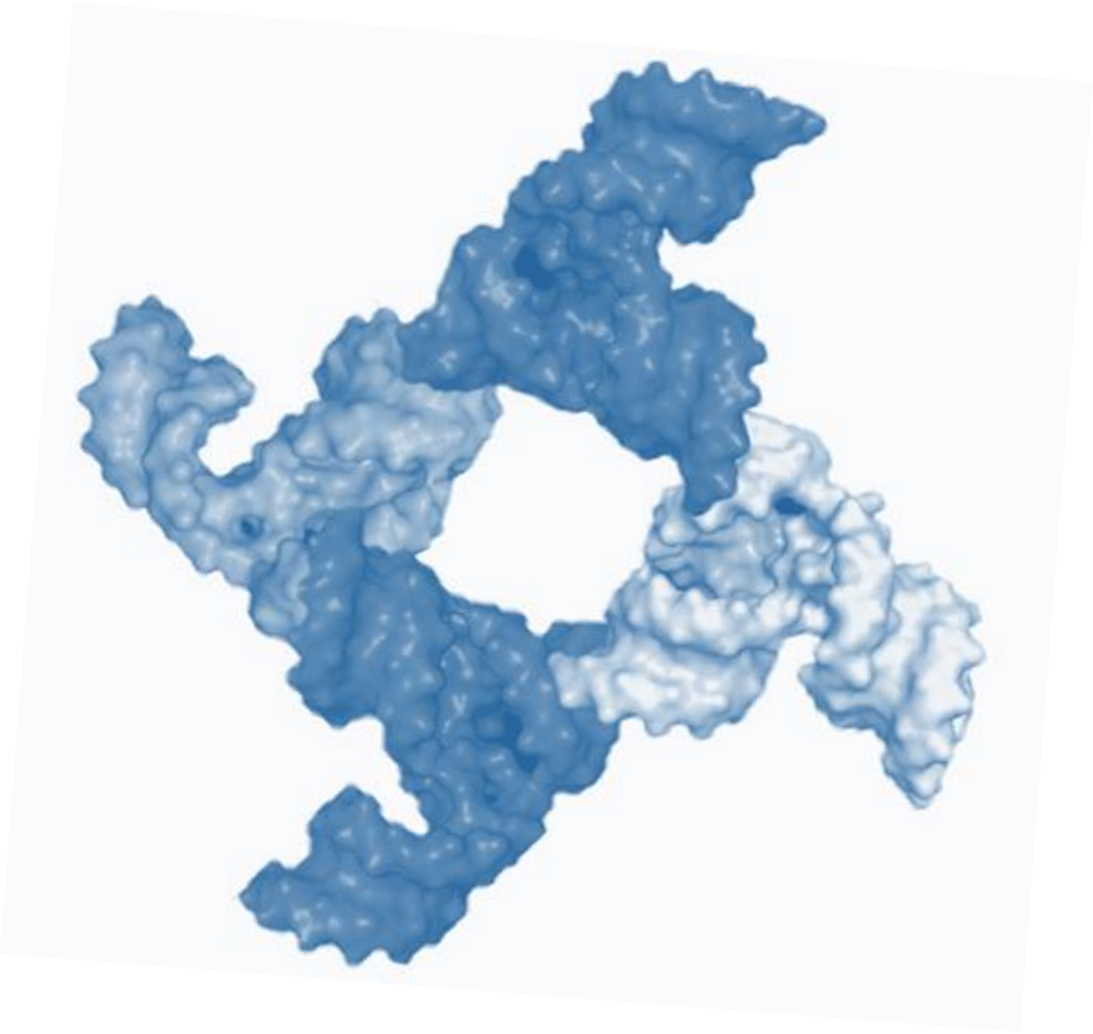
RNA NanoBiotics

RNA Nanotechnology:

Targeted Chemo and Radiotherapy in Cancers



James Carroll, President & CEO

September 2025

RNA NANOBIOTICS EXECUTIVE SUMMARY

RNA NanoBiotics

- Technologies developed in the RNA Nanotechnology Center at Ohio State University (OSU) by Dr. Peixuan Guo - Fellow, National Academy of Inventors
- **All RNA Nanotechnologies for targeted drug delivery and developed drugs patented and fully licensed to RNA NanoBiotics.**

$30 Million+ non-dilutive capital already invested in development.

Additional $2.5M dollars for further technical developments recently granted to OSU.

OSU agreed to a 10% equity investment in lieu of any license or other major up-front fees.

Several existing cancer drug candidates developed to pre-clinical stage and data published papers in top journals. **All the technologies covered by the licensed patents.**

Several papers publishes in 2024 and 2023 (with more pending), describe enhancements to the technologies covered by the licenses.

In discussions with past and potential new academic and commercial collaborators for further radioligand work to use for targeted radiation therapies.

Seeking $5M convertible note with $65M Cap and 20% discount on conversion

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
- 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

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.

SCIENTIFIC ADVISORS

RNA NanoBiotics

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

Christophe Tournerie

MD

Expert in Clinical Trials of Oligonucleotide Drugs

Medical Research Institute, France

Bin Guo

PhD

Associate Professor of Pharmaceutics, Pharmacological and Pharmaceutical Sciences University of Houston College of Pharmacy

Marc Lemaitre

PhD

Oligonucleotide cGMP and FDA Reguatory Expert, Girindus America, Eurogentec, Institute Pasteur

B Mark Evers

MD

Oncologist, Surgeon\University of Kentucky, Director of Markey Cancer Center

URGENT AND UNMET MEDICAL NEEDS

RNA NanoBiotics

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

- 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

- 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**.

PRIMARY CHALLENGES OF CANCER TREATMENT

RNA NanoBiotics

Cancer is a complex and adaptable disease, making effective treatment extremely difficult due to:

Drug Resistance (most critical)
Cancer cells can mutate rapidly

Tumor Heterogeneity
Contain many different types of cancer cells with distinct mutations and behaviors

Metastasis
Behave differently and less responsive

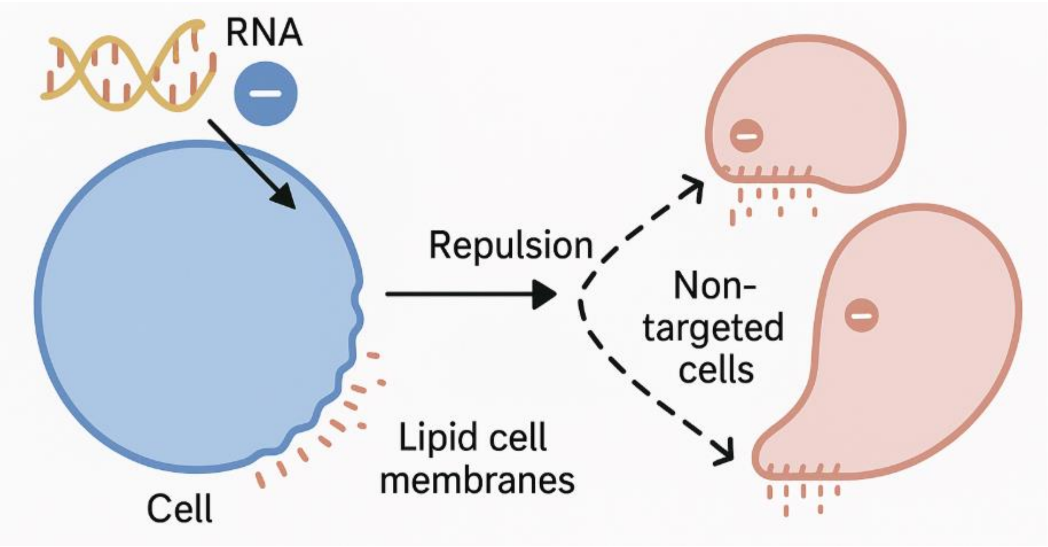
Limited Selectivity
< 1% reaches the tumor, causing off-target toxicity (typical of ADCs)

Immune Evasion
Hide from or suppress the immune system

Cost and Accessibility
Increased development costs

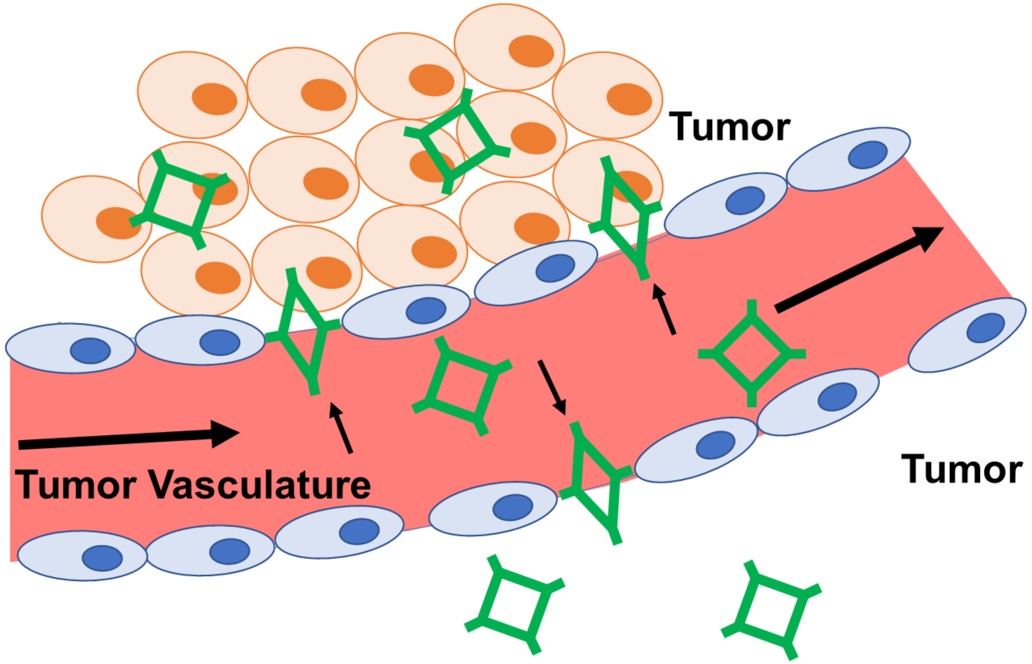
TARGETED RNA DELIVERY TO SOLID TUMORS

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



Xia B. et al & Guo P. *Pharmacological Research.* (2025).

Enhanced tumor targeting and accumulation in solid tumors.

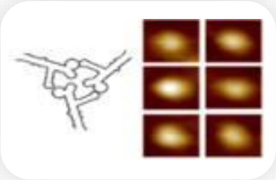


Ghimire C. et al & Guo P. *ACS Nano.* (2020).

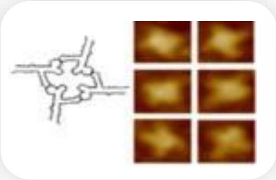
APTAMER ARCHITECTURE

Aptamers fold into unique three-dimensional structures enabling interaction with diverse targets

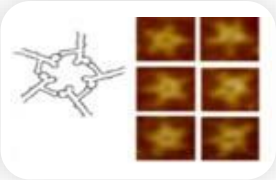
1. Trimer



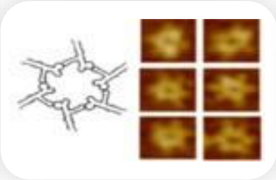
2. Tetramer



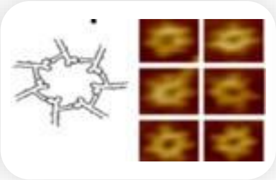
3. Pentamer



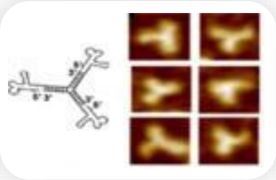
4. Hexamer



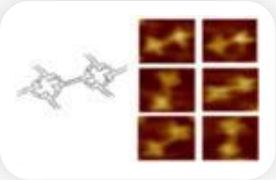
5. Heptamer



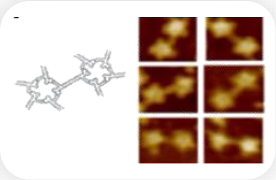
6. 3WJ- pRNA



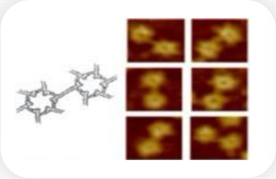
7. Foot-to-foot Tetramer



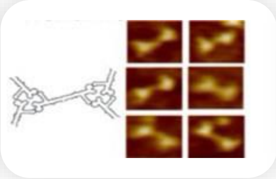
8. Foot-to-foot Pentamer



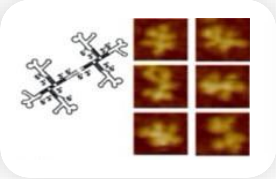
9. Foot- to - foot Hexamer



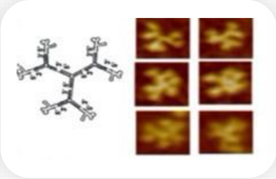
10. Foot- to- foot Trimer



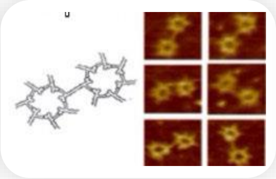
11. Foot- to- foot Tetramer



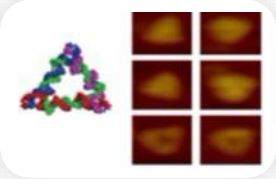
12. Arm - to - arm Dendrimer



13. Foot- to- foot Pentamer



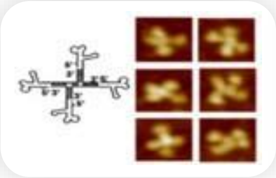
14. Triangle



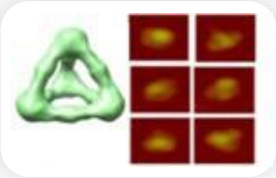
15. Square

16. Pentagon

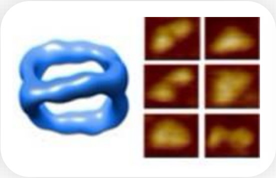
17. X- pRNA



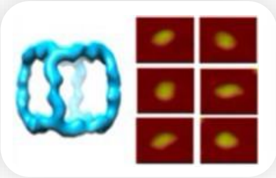
18. Tetrahedron



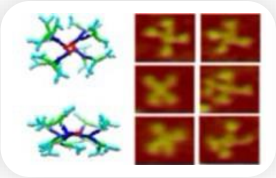
19. Prims



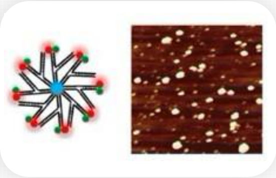
20. Cube



21. Dendrimer



22. Micelle



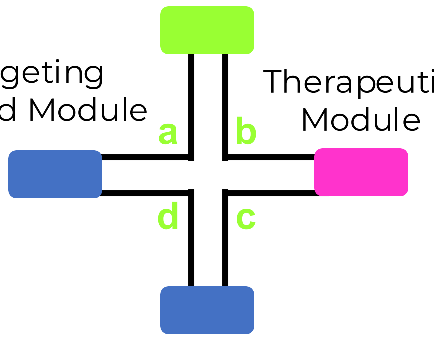
Shu Y, et al, RNA, 2013; Khisamutdinov E, et al, Nucleic Acid Res, 2.14,42:9996-100004; Xu C. et al, Nano Research, 2019: 12:41; Yin H, et al, ACS Nano; 13(1): 706-717

Engineering Drugs Via 4 Way Junction RNA Nanoparticle Targeted Delivery Platform System

RNA NanoBiotics

Four Engineered Modules Combine

Radioisotope Module

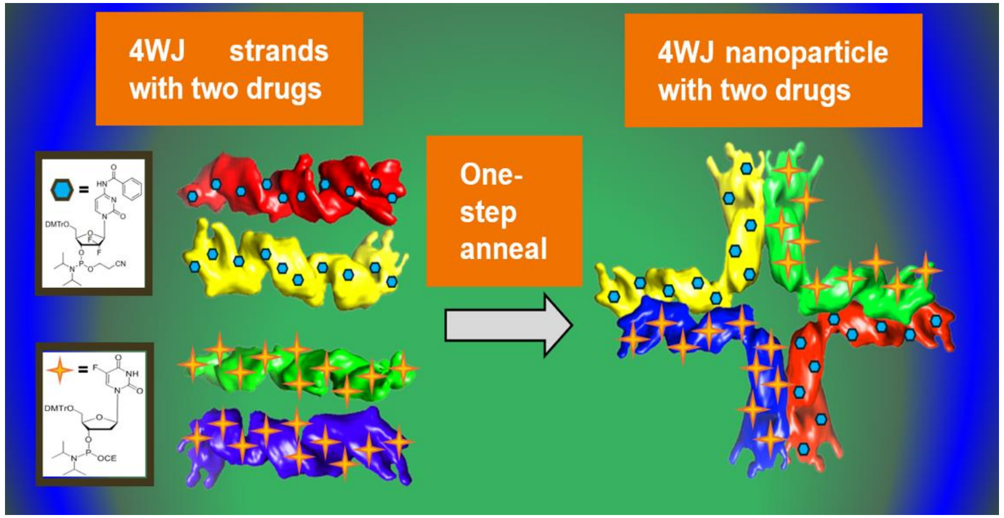


Targeting Ligand Module

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



The Targeting Aptamer Sequence and the SiRNA Drugs are Engineered into the RNA Nanoparticle Backbone

Key Steps:

- Incorporate targeting aptamer sequences into designated arms.
- Engineer therapeutic and optional radioisotope modules.
- Assemble via one-step anneal - no conjugation needed.

ADC's VS 4 Way Junction RNA Nanoparticles

RNA NanoBiotics

	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.

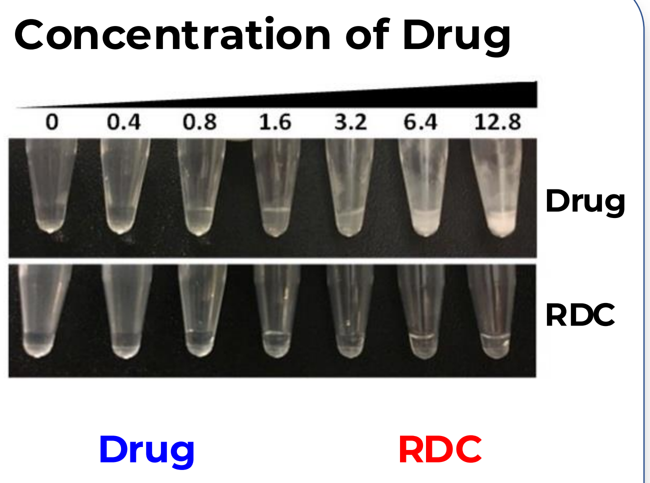
- Tumor Penetration & PK (Size) - Size is decisive: ADCs (~10–15 nm) struggle to penetrate solid tumors, while 4WJs (~5–10 nm) diffuse throughout tumor tissue, improving therapeutic reach.

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

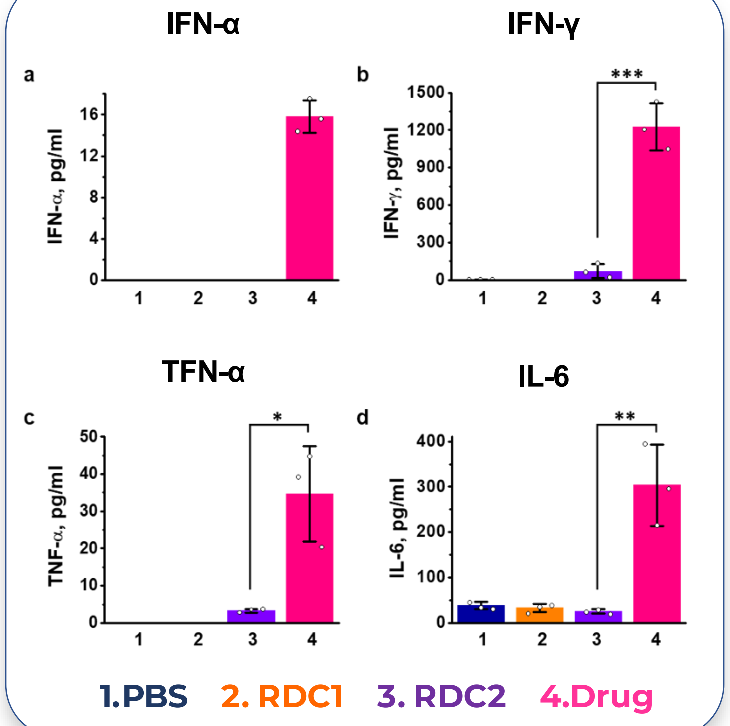
RNA NANOPARTICLE CONJUGATES

Anticancer drug is conjugated to RNA Nanoparticles to target and kill cancer cells while sparing healthy cells.

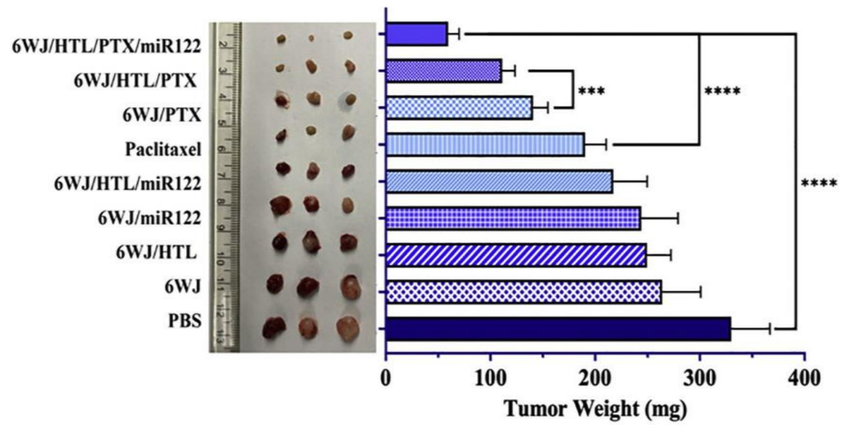
A. Enhanced Drug Solubility



B. Reduced Immunogenicity



C. Enhanced Tumor Suppression



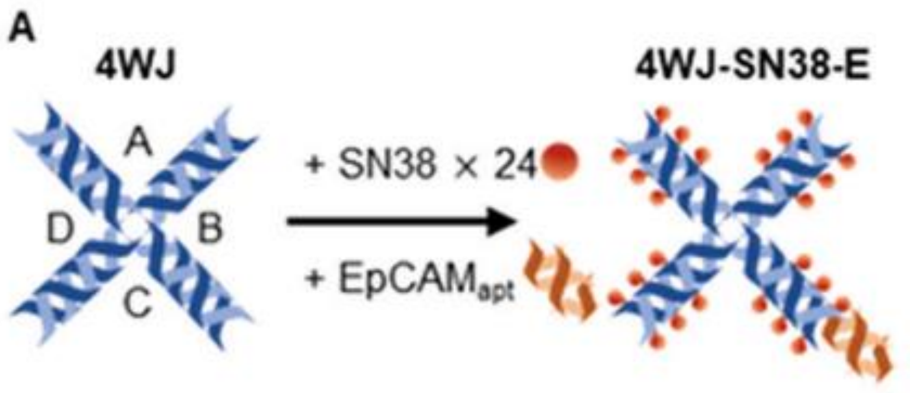
Guo S et.al.& Guo P. Nature Communications, 2020, 11, WO2019156726(A1), Wang H, Ellipli S, Lee W, Li X, Vieweger M, Ho Y, Gu

Guo P. Journal of Controlled Release. 2021

4-WAY-JUNCTION DESIGN & TARGETING APTAMER

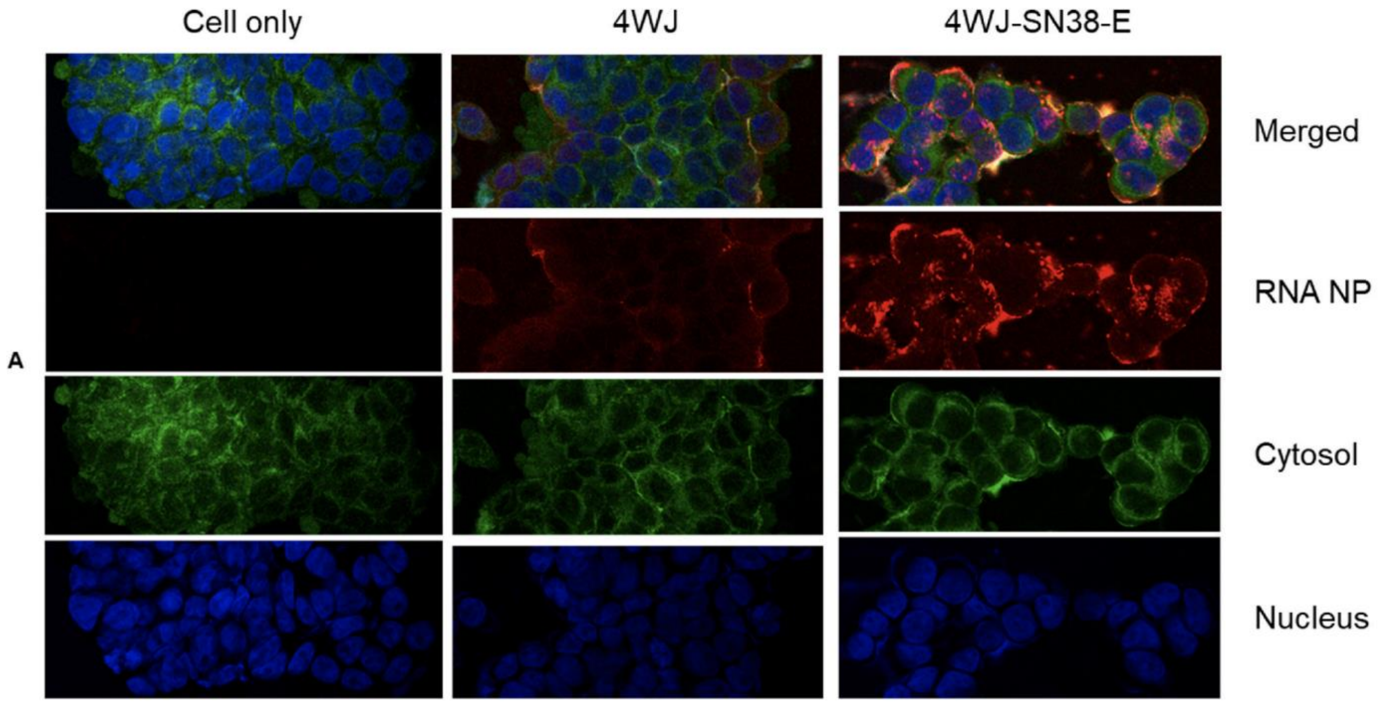
4WJ is comprised of 4 helixes that each contain a core domain to control the structure formation and a payload domain that is used for functionalization

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

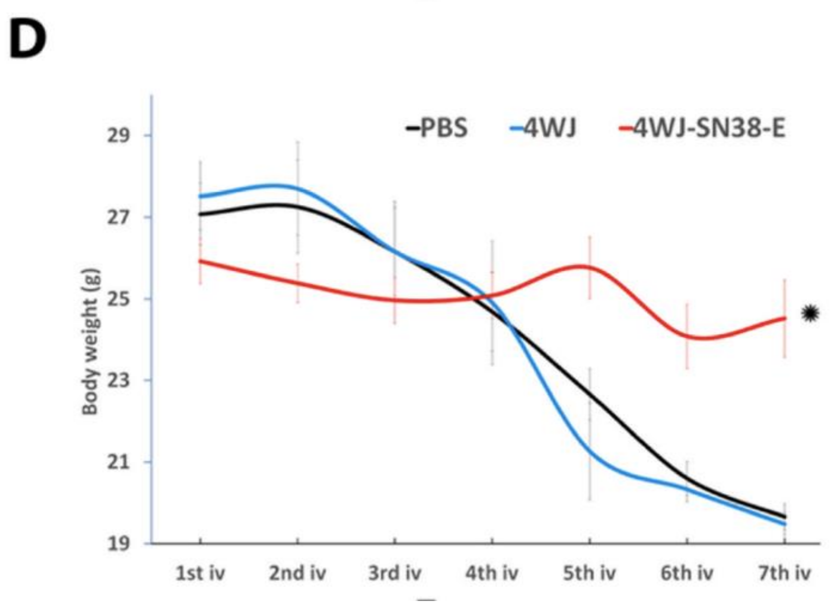
EpCAMapt displaying RNA nanoparticles specifically bind to EpCAM-overexpressed tumor cells and are further internalized into the cells efficiently by receptor-mediated endocytosis



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

4WJ-SN38-EpCAM BIODISTRIBUTION

RNA NanoBiotics

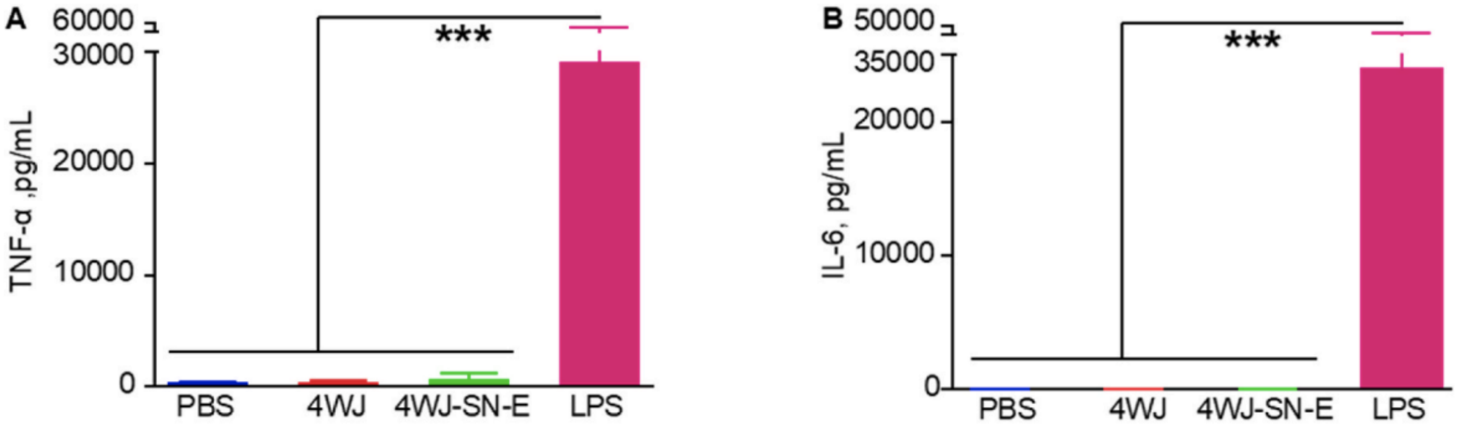


Rapid Renal Clearance:

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

Undetectable Toxicity & Immunogenicity:

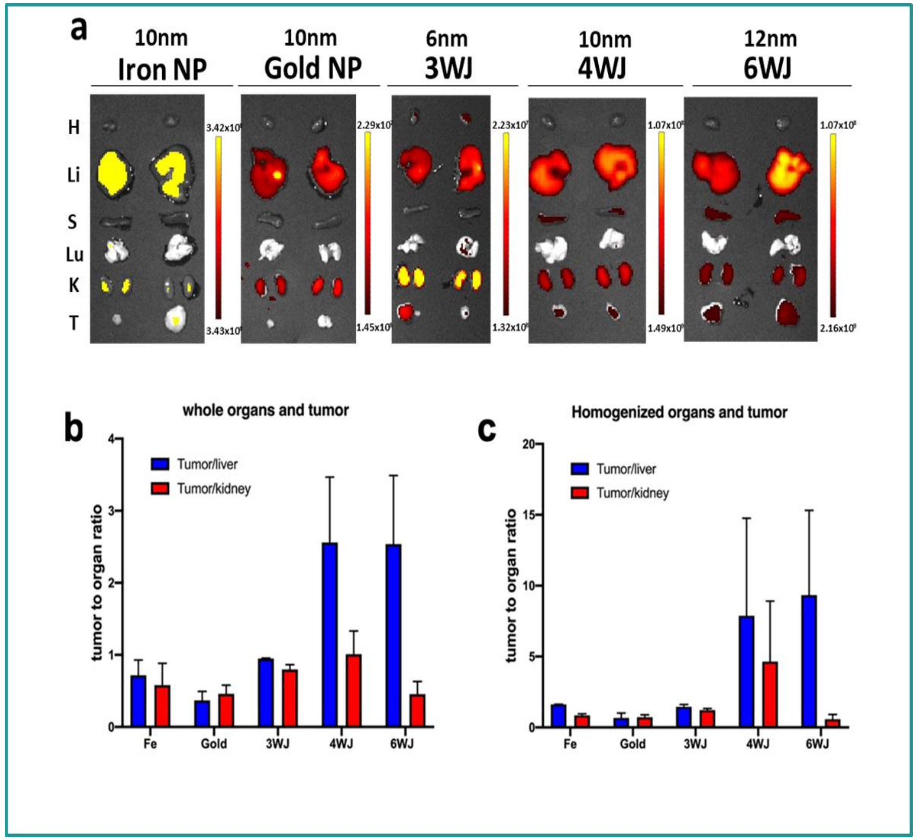
- ELISA shows cytokine levels **comparable to untreated controls**



RNA NANOPARTICLE BIODISTRIBUTION

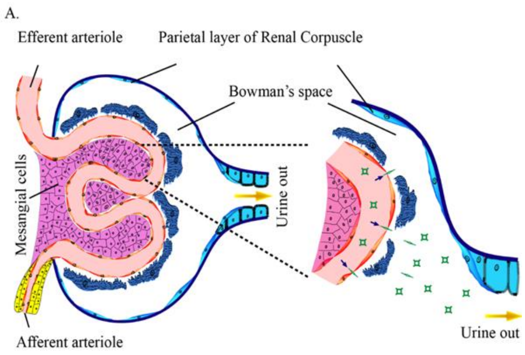
RNA NanoBiotics

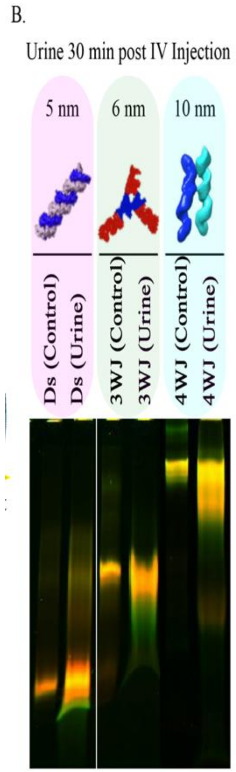
Versatile structure combinations allow for rapid and efficient intra-tumor penetration resulting in spontaneous tumor accumulation.



Ghimire C. et al & Guo P. *ACS Nano.* (2020).

RNA Nanoparticles quickly clear the kidney's 5 nm Glomerular Filtration Barrier and excreted in the urine.





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

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

RNA NANOPARTICLE BIODISTRIBUTION

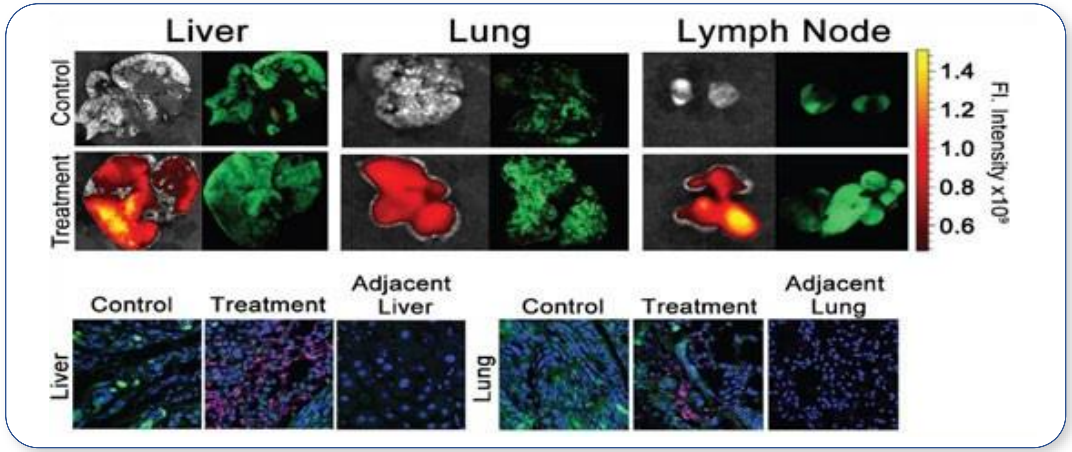
RNA nanoparticles circulate well upon injection

Nanoparticles are cleared within 4 hours in blood

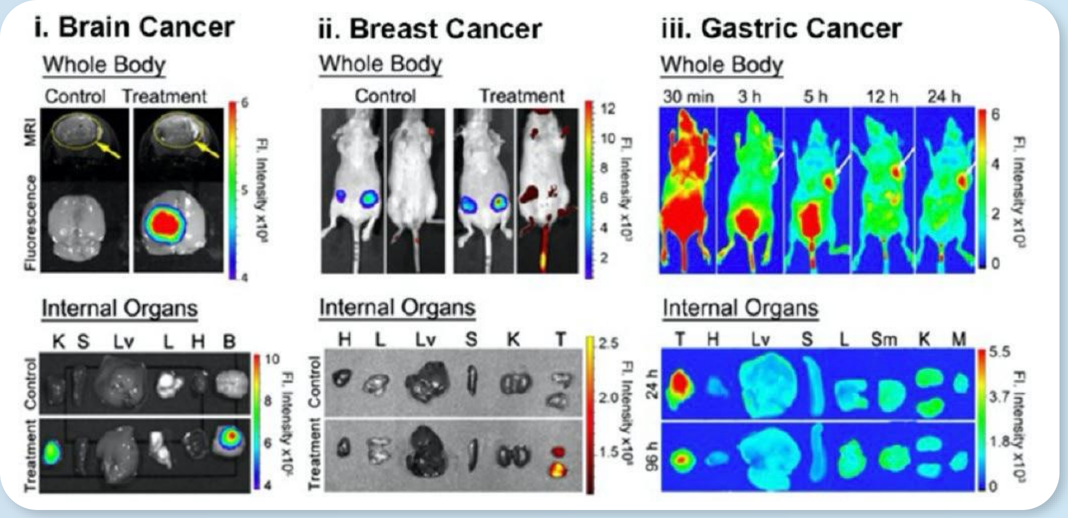
Have high tumor retention for better therapeutics

RNA nanoparticles with ligands tested

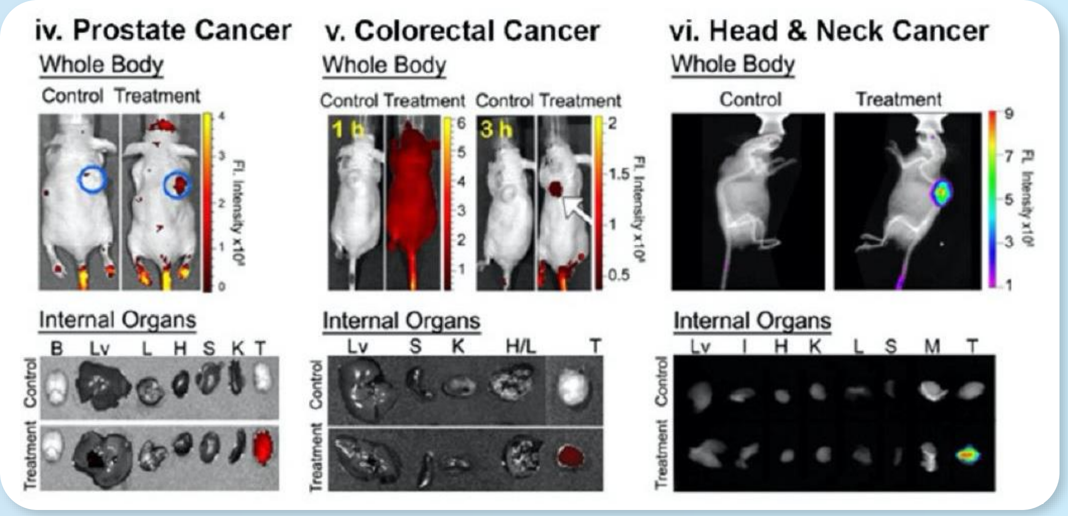
Allows for tumor targeting without accumulation in organs



Colorectal Cancer Metastases to Liver and Lung, Lymph Node



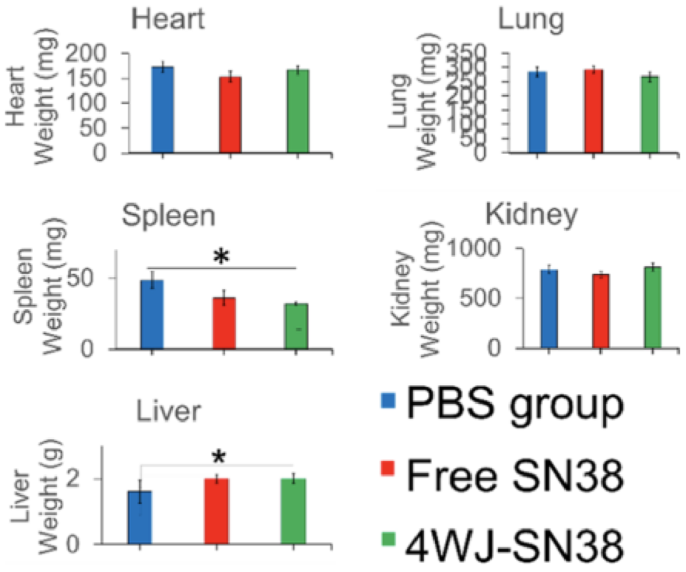
Fast Clearance In Circulation vs Slow Clearance In Tumors

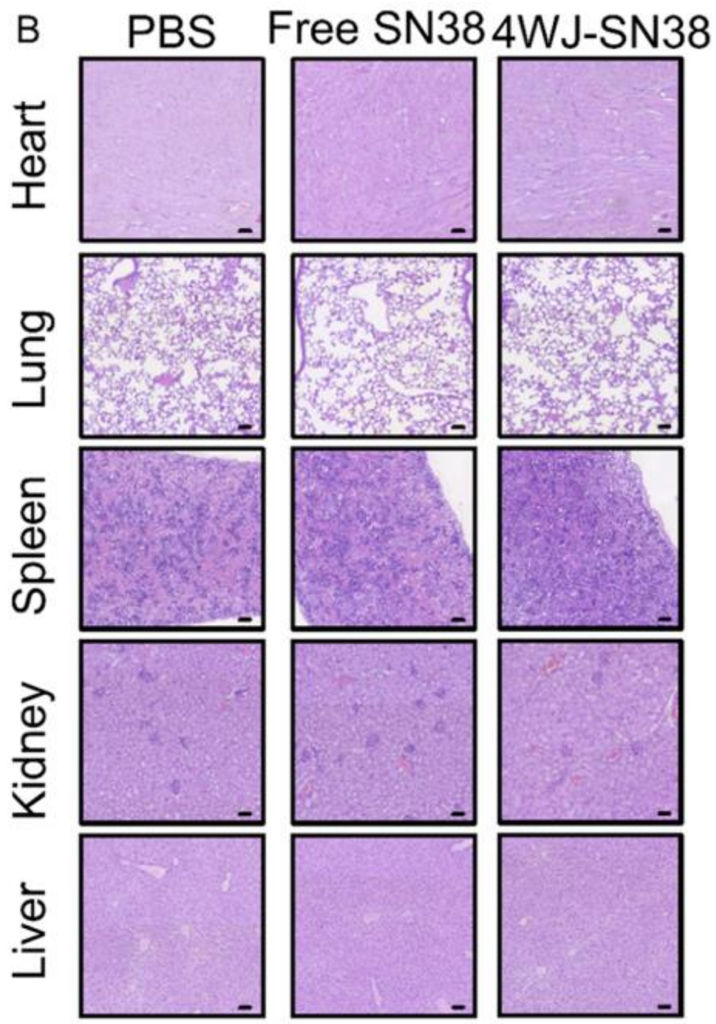


These Benefits Are Critical for Targeted Radiation Therapeutics

PATHOLOGY & SAFETY OF 4WJ-SN38

No significant toxicity, side effects or immune responses.





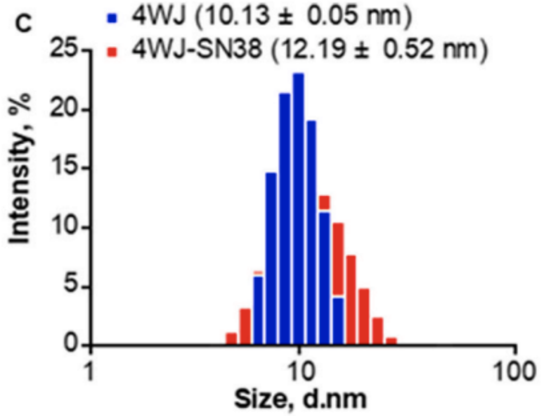
- Repeated IV injections up to 30mg/kg do not result in toxicity
- PK (T ½) 5 to 10 hours vs 0.25-0.76 hr for siRNA itself
- Avoidance of antibody induction (as protein free)

Jin K et al. Guo P. *Mol. Pharmaceutics*. 2024.

4WJ-SN38-EpCAM EFFICACY

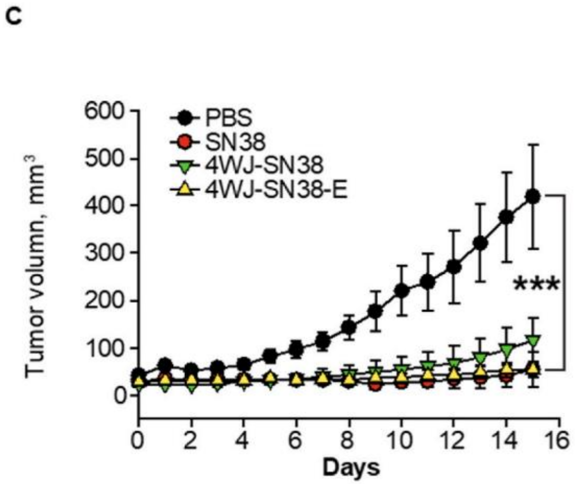
High Tumor Accumulation:

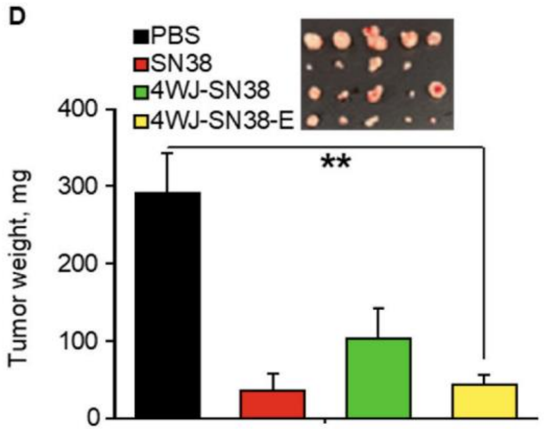
- Small size; Deformable and hydrophilic properties aiding EPR effect-based penetration



No Organ Accumulation:

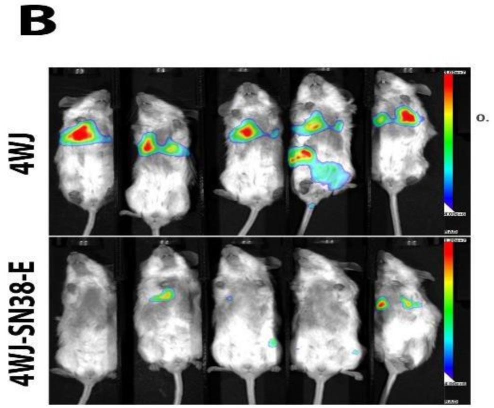
- No visible accumulation in liver, spleen, or lungs

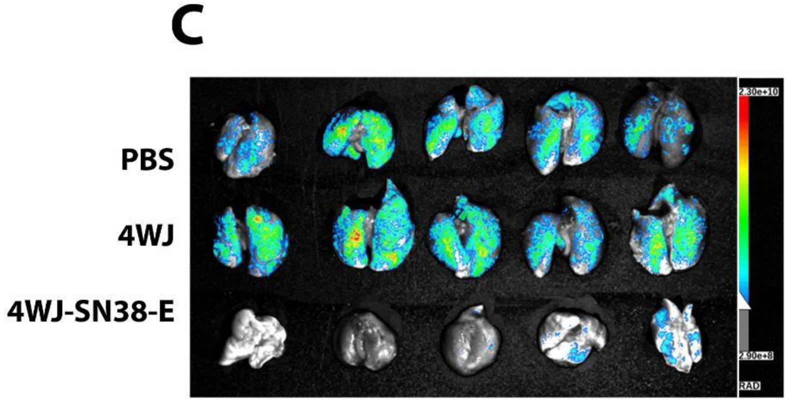




Safe uptake:

- Tumor suppression with-out off-target effects





SYNERGISTIC EFFECT SN38+GEM

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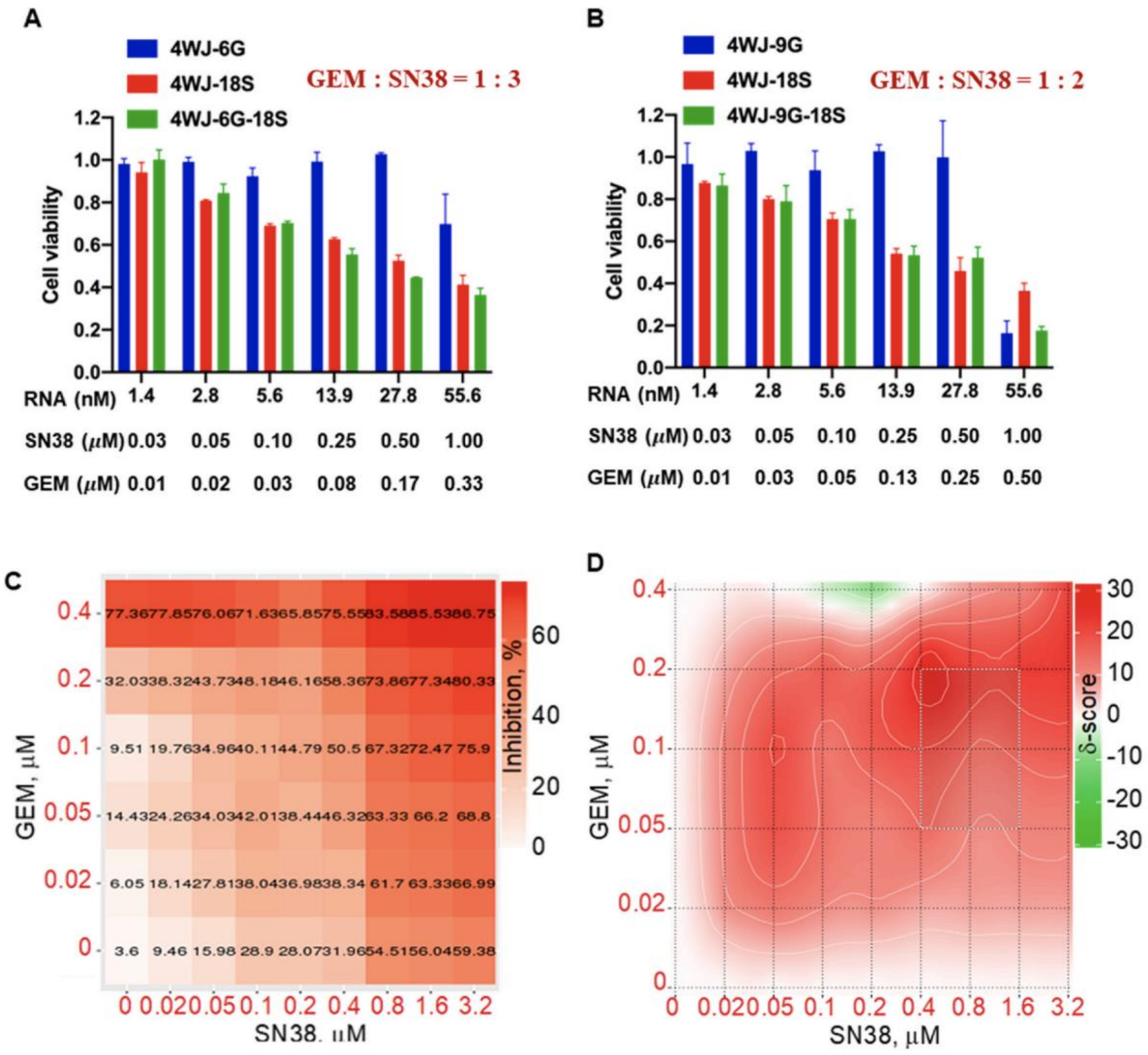


Combination chemotherapy of SN38+GEM:

- 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

PRECLINICAL POC DATASET 4WJ-SN38

RNA NanoBiotics

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	✓

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

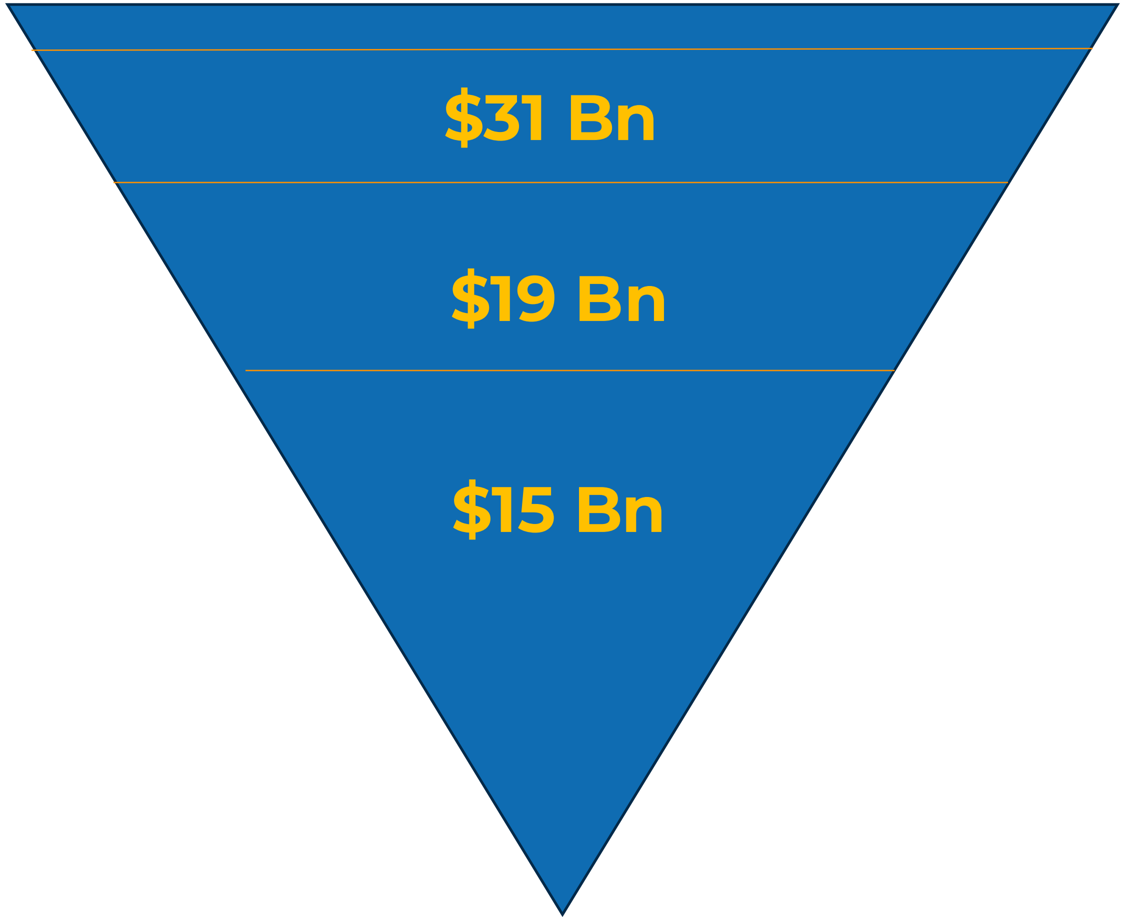
GLOBAL MARKET mCRC Liver/Lung

RNA NanoBiotics

95% (TAM)
CRC EpCAM+ Expression

60% (SAM)
CRC Metastatic disease (mCRC)

77% (SOM)
Liver and/or lung metastases



https://www.researchnester.com/reports/colorectal-cancer-therapeutics-market/436?utm_source

IND SUBMISSION TIMELINES

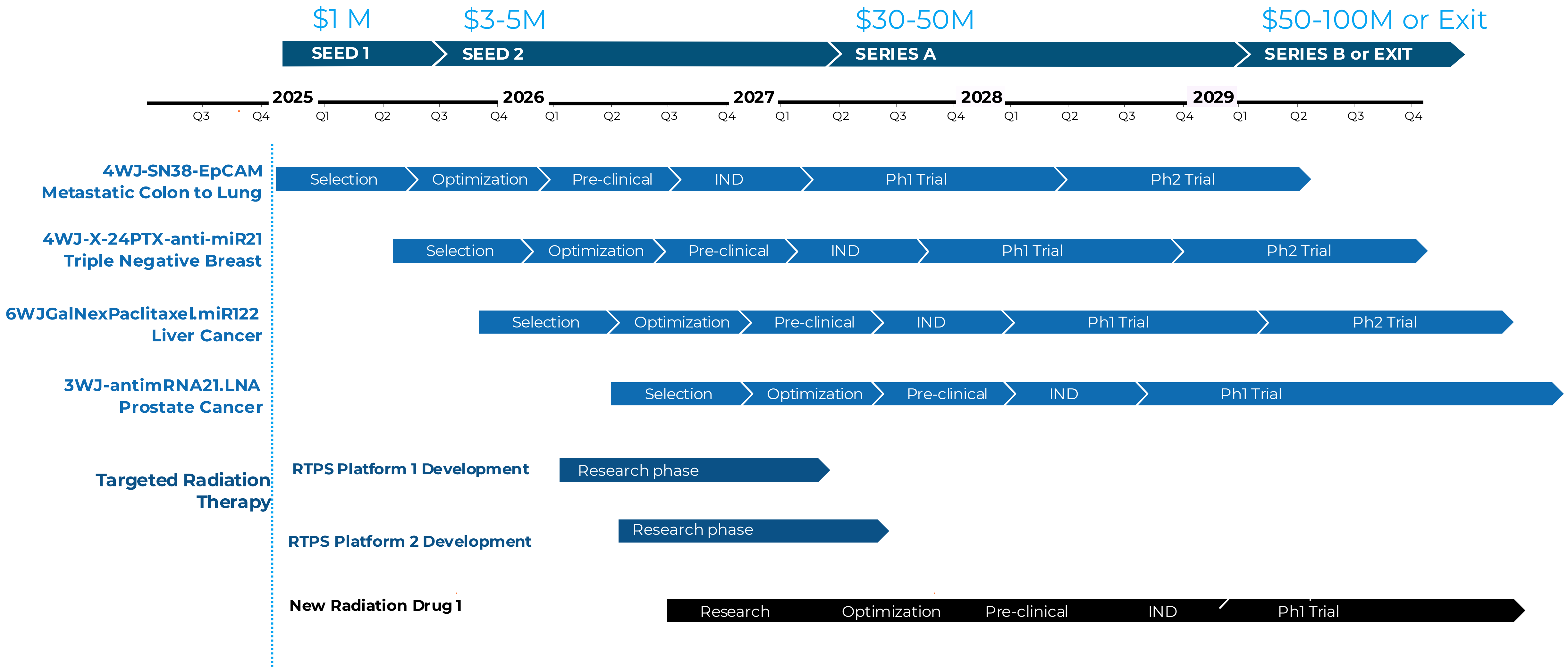
RNA NanoBiotics

	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

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

RNA NANOBIOTICS TIMELINES

RNA NanoBiotics



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

FINANCIAL STRATEGY

Currently Seeking

$5M

Convertible Note with $25M Cap 6% Interest and a 20% discount on conversion

Planned Series A – Mid 2026

$30 M

$65M Pre-money,

Phase II-ready asset

IND-ENABLING PROGRAM

GMP Manufacturing	1,800,000
GLP Studies	1,700,000
Regulatory Support	250,000
Operations	1,250,000
TOTAL	**5,000,000**

QUADRAVANCE THERANOSTIC AGENT

Conjugate Radiolabeling	250,000
QC Methods	250,000
Cell-based Animal Models	250,000
POC Efficacy (GLP tox)	500,000
TOTAL	**1,250,000**

- **Lead Investors: Wharton Alumni Angels, Think Inc., Wilson Sonsini Goodrich & Rosati**
- **Grant applications for company in process**
- **Actively looking for develppment partners**

CURRENT COMPETITORS

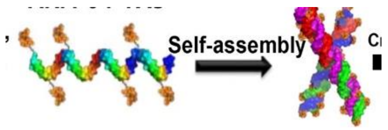
RNA NanoBiotics

Company	Category	Main Challenges
Sixfold Bioscience	Small RNA Hexamer Small RNA Hexamer Therapeutics Delivery	Requires High Mg Concentrations; Very Low TM With Usability; Unfavorable Biodistribution; Accumulates Strongly In The Liver
Sirnanomics	Polypeptide Nanoparticles As The Vehicle For Sirna Delivery	The PNP Carries The Positive Charge With Negatively Charged Double-stranded Sirna, Forming A Nanoparticle For Delivery. Nanoparticles Will Bind To Nonspecific Cells And accumulate In Liver.
AuraSene (Exicure)	Gold (Metal) Nanoparticle	Very Unfavorable Biodistribution And Liver Accumulation
Can-Fite BioPharma Ltd	On Inflammatory, Liver And Metabolic Diseases	Namodenoson, The Phase II Clinical Trial Has Shown Treatment-related Grade 3 Toxicities Accounted For Anemia And Hyponatremia.
Transcode Therapeutics	Targeted RNAi for oncology and imaging	Using conjugated Iron Nanoparticles to keep drugs in circulation

EXIT VALUATION / FUNDING COMPARABLES

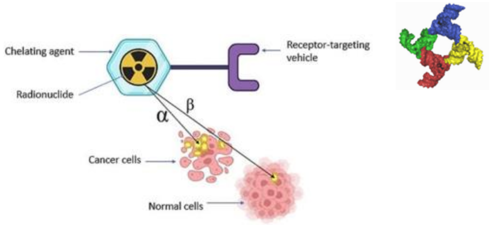
Company	Fundraising	Notes	Valuation
Aktis Oncology	Raised $175M Series B on 9/30/24	Develops precision radio-pharmaceuticals targeting cancers with radiation therapy	Private
RayzeBio	Purchased by BMS In 2023	Targeted Radiation Therapeutics	$4.1 Billion
Entrada Therapeutics	Spun Out of Ohio State University 2018 with a raise of $60M	Endosomal Escape Vehicle Platform	$570 Million
Mariana Oncology	Purchased by Novartis For $1 Billion up front	Targeted Radiation Therapeutics	$1 Billion plus
City Therapeutics	Raised $135M Initial Round 10/8/24	Targeted RNAi Technology Licensed from Ohio State University	Private
Alpha 9 Oncology	Raised $175M Oversubscribed Series C 10.23.24	Targeted Radiation Therapy for Oncology	Private
Ratio Therapeutics	Ratio Will work with Novartis to research and select SSTR-2 oncology drug to treat soft tissue sarcoma	Novartis takes responsibility for all additional drug development	$745M deal for one drug

RNA NANOTECHNOLOGY PLATFORM DESIGNS



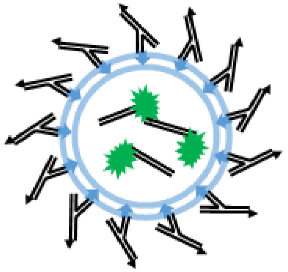
Quadravance™ + Click Chemistry

- 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



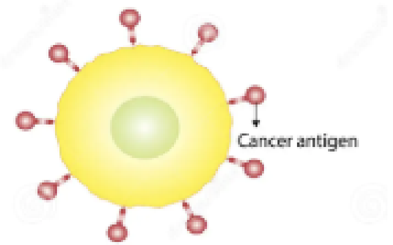
New Radioisotope Linkers & Radiation Therapy

- 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



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



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

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 NANO-PARTICLES FOR TARGETED RADIATION THERAPY

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

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

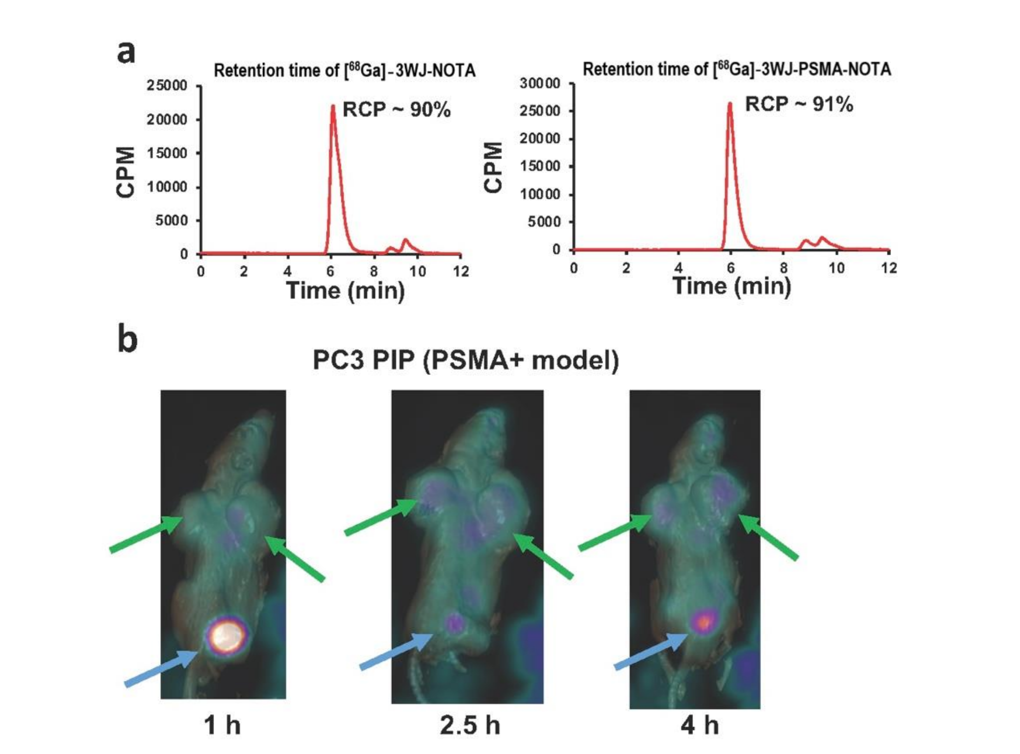
Alpha Emitter Priorities

- ^{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

RNA Naonomed (August 2025), Peixuan Guo et al.



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

Green Arrow - Tumor

Blue Arrow – Bladder (showing excretion)

THANK YOU!

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617-899-6583

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

RNA NanoBiotics