



RNA NanoBiotics

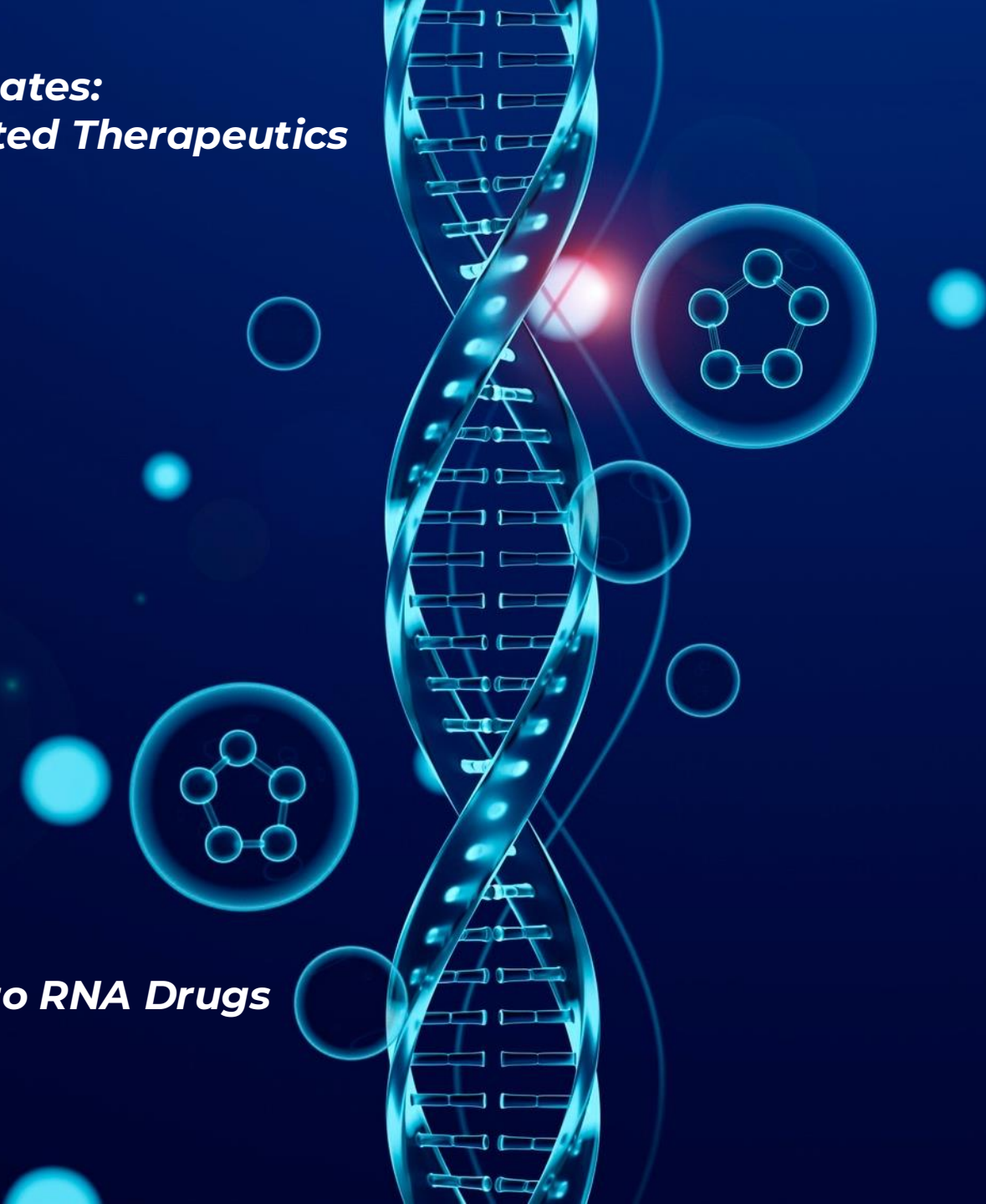
*Beyond Antibody Drug Conjugates:  
The Next-Generation Of Targeted Therapeutics*

# RNA Nanotechnology for Targeted Multi-therapeutic Treatments of Cancers

*The RNA Nanoparticles Morph into RNA Drugs*

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MARCH, 20 | 2025



# RNA NANOBOTICS OVERVIEW



- Technologies developed in the RNA Nanotechnology Center at Ohio State University (OSU), University of Kentucky and University of Cincinnati by Dr. Peixuan Guo and Colleagues over 25 years with an investment of over \$30 Million....**Ongoing research at OSU adds to drug candidate portfolio and tech**
- All related technologies related to RNA Nanoparticle and associated technologies for targeted drug delivery of the drugs and drugs themselves licensed to the company in one license from the three universities.
- Current Focus is on the Quadavance™ (4 Way Junction) RNA Nanoparticle Platform System for oncology applications
- Current lead drug candidate: metastatic colon cancer prevalent in the lung with target IND Filing Q4 2026

**Simplified Manufacturing Strategies via Automated Nucleic Acid Synthesis Techniques.**

**Chem Genes, USA based manufacture, can produce GMP materials for Clinical Studies**

Sponsored Research Agreement with OSU to Optimize the Lead Drug Candidate and Conduct CMC to Facilitate IND Filing in Q4 2026

Over 50 published papers with several publishes in 2025, 2024 and 2023 (more pending), describe enhancements to the technologies covered by the licenses.

Intention to broaden focus on the use of Radioisotopes, Nucleoside and RNA drugs in the therapeutic combinations

# EXCLUSIVE WW IP LICENSES ON PATENT FAMILIES COVERING ALL RNA NANOPARTICLES AND DRUGS



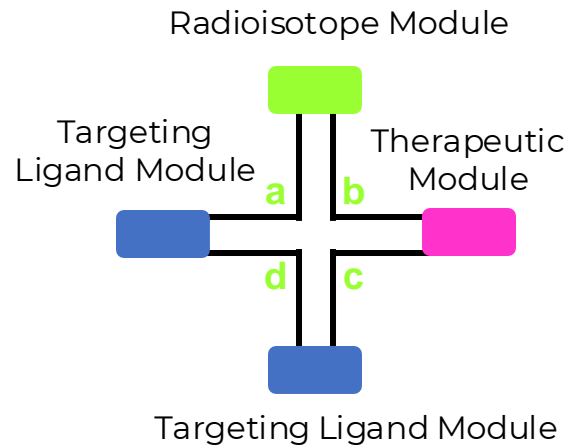
- 9+ Key Patent Families licensed From Ohio State University, University of Kentucky
- More applications further covering RNAi delivery chemistries and nucleoside drugs
- Patents licensed also include Targeted RNA Exosome technologies which offers alternative drug delivery approaches
- Ohio State University obtained a 10% ownership position in RNA Nanobiotics via transaction
- Patents cover all RNA Nanoparticle designs, use of any targeting aptamer, any RNA drug, Chemo drugs carried, use in targeted imaging and radiation therapy, and delivery of modified nucleoside drugs
- Patents also cover a variety of manufacturing techniques for RNA Nanoparticles

**Note: Ongoing Research at Ohio State University is adding to drug, technology and patent portfolio!**

**\$2.5 Million grant awarded for KRAS derived lung cancer therapies using RNA Nanoparticles awarded to OSU in October**

# The Quadravance™ (4 Way Junction) RNA Nanoparticle Targeted Delivery Platform System

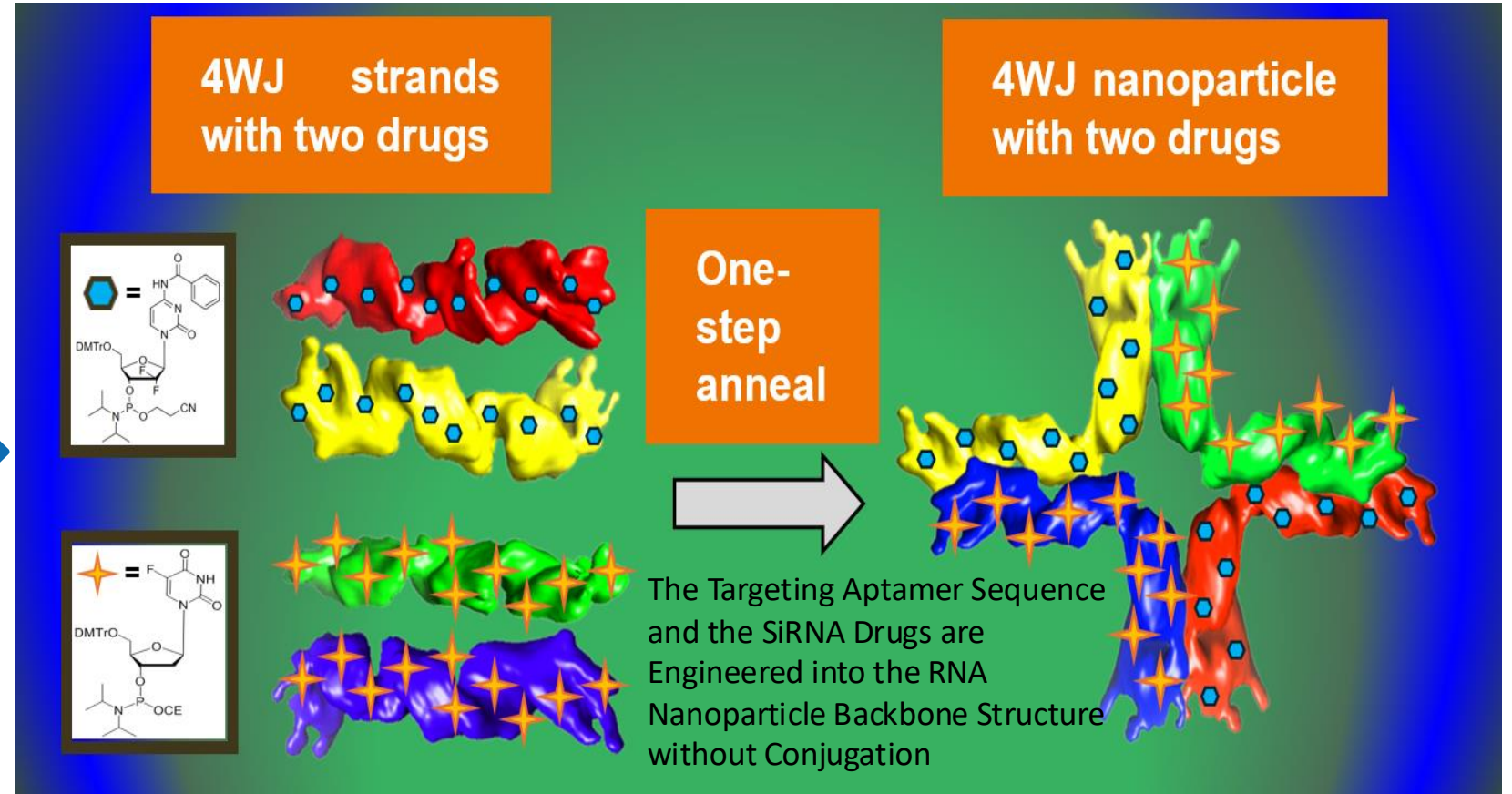
## Four Engineered Modules Combine



**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



Two papers by Kai Jin et al & P Guo, Mol Therapy, Sep 2024

# THE QUADRAVANCE™ TARGETED DELIVERY SYSTEM

*Beyond Antibody Drug Conjugates: The Next-Generation of Targeted Therapeutics*

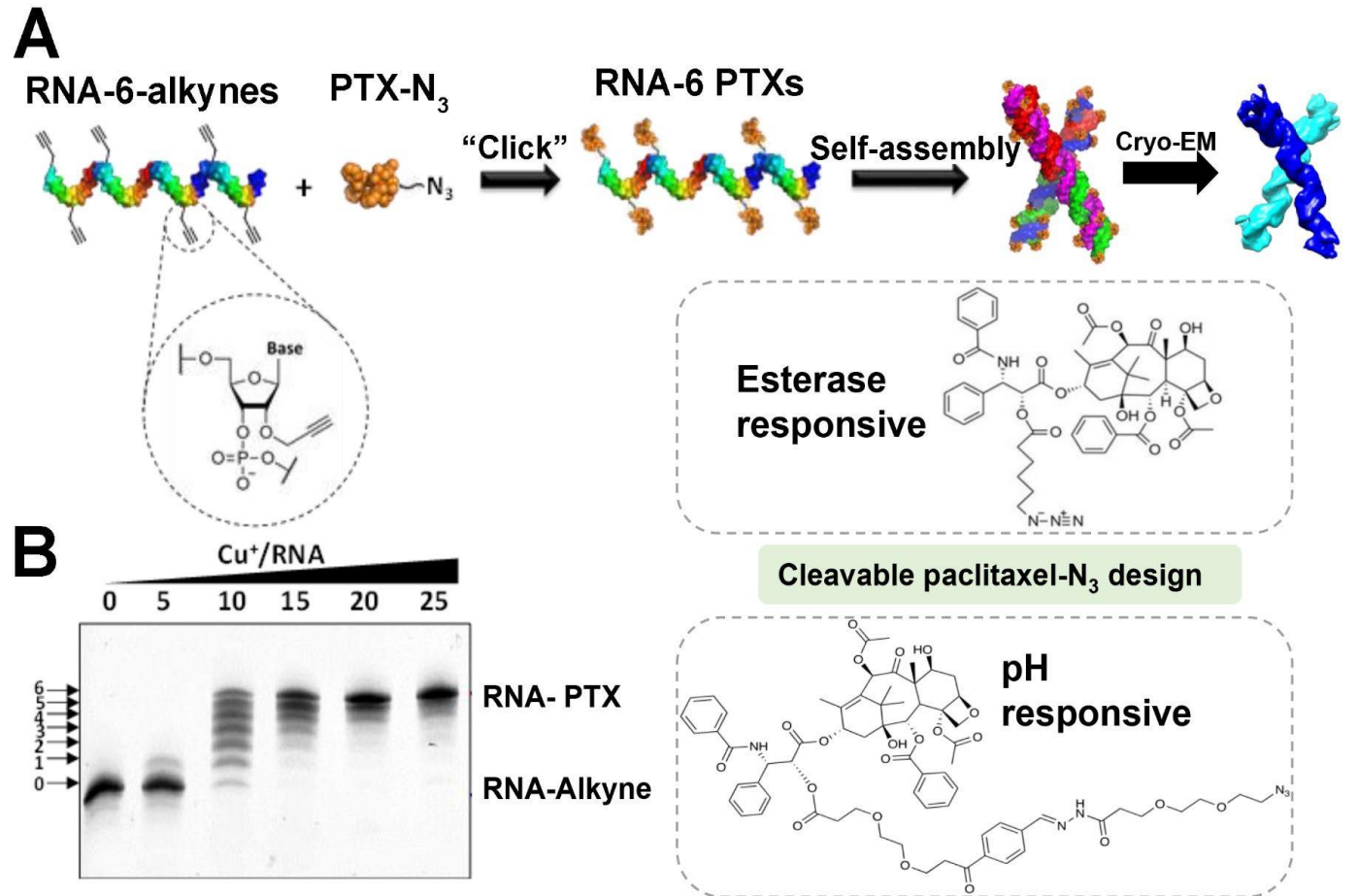
## Advantages of Quadravance™ Over Antibody Drug Conjugates (ADCs)

- Easy Engineering as no biological production needed since system is chemical: just change RNA Sequences
- Manufactured entirely with NA synthesizers – no biological development
- Simultaneously deliver precise therapeutic and synergistic stoichiometries of drugs including: RNAi, microRNA, chemotherapeutics (taxol etc.), modified nucleosides (GEM etc.), and radioisotopes
- Carries 24 drugs compared to 2 for ADCs
- Spontaneously targets to cancer cells in addition to targeted entry into cells
- No toxicity as it is negatively charged so do not enter normal cells or healthy organs
- Pass intact through the 5nm Kidney Filters
- No immunogenicity

Li X, Jin K, Cheng TC, Liao YC, Lee WJ, Bhullar A, Chen LC, Rychahou P, Phelps M, Ho YS, Guo P. RNA four-way junction (4WJ) for spontaneous cancer-targeting, effective tumor-regression, metastasis suppression, fast renal excretion and undetectable toxicity. *Biomaterials*, 2024 Mar [[link](#)] [[PDF](#)]

## Conjugation of RNA-Paclitaxel (PTX) And Construction of 4WJ-24 PTX Nanoparticles With Esterase Responsive Labile Bond

- A. Schematic of RNA-6 PTX chemical conjugation.
- B. Conjugating 4 PTX to one RNA strand evaluated by denaturing PAGE.



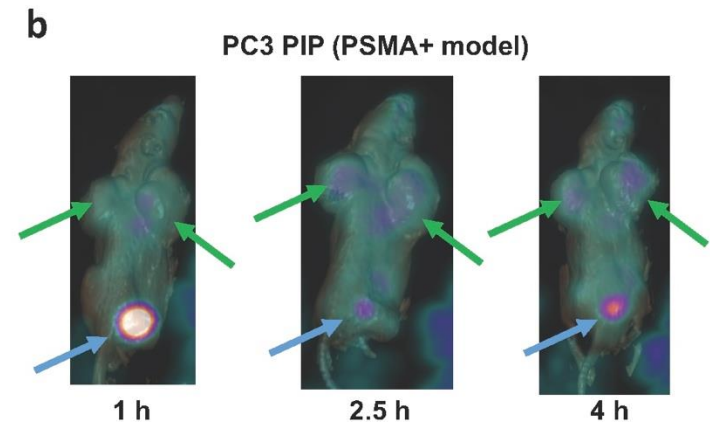
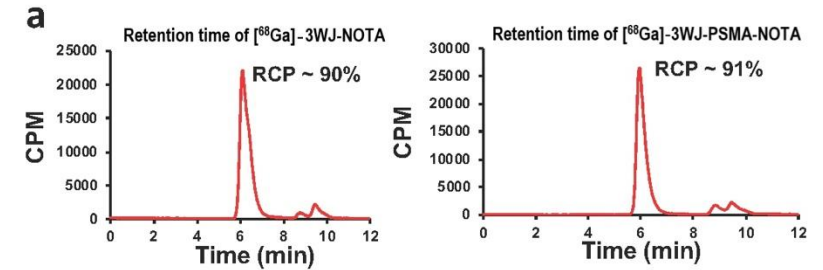
# TARGETED RADIATION THERAPY + APPLICATIONS



## Incorporating Alpha Emitting Radioisotopes into the Targeted RNA Nanoparticles:

- **Quadravance™ Nanoparticles** are designed to have an arm dedicated to carrying radioisotopes with proprietary linker technologies.
- The 4WJ Particle can quickly clear the 5nm kidney glomerular filtration barrier so radiation quickly clears from the body into the urine unless taken up by cancer cells
- **Astatine-211** and **Actinium-225** have become a radioisotopes of choice for targeted therapy due to their high energy and both can be incorporated.

Related Publication: Li X, Jin K, Liao YC, Lee WJ, Chen LC, Cheng TC, Ho YS, **Guo P**. RNA Nanotechnology for Codelivering High-Payload Nucleoside Analogs to Cancer with a Synergetic Effect. Mol. Pharmaceutics, 2024 Oct [[link](#)][[PDF](#)]

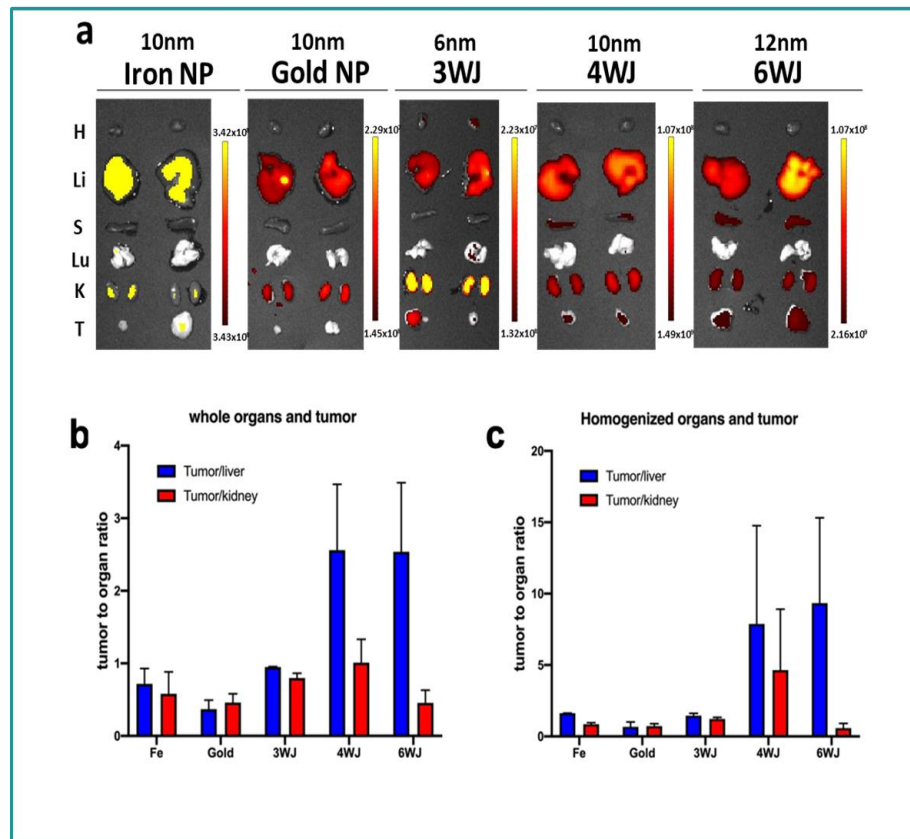


## RNA Nanoparticle with Gallium-68 Radioisotope for Medical Imaging

- **Green Arrow - Tumor**
- **Blue Arrow – Bladder (showing excretion)**

# Rubbery and Amoeba Properties of RNA Nanoparticles Lead to Fast Renal Excretion

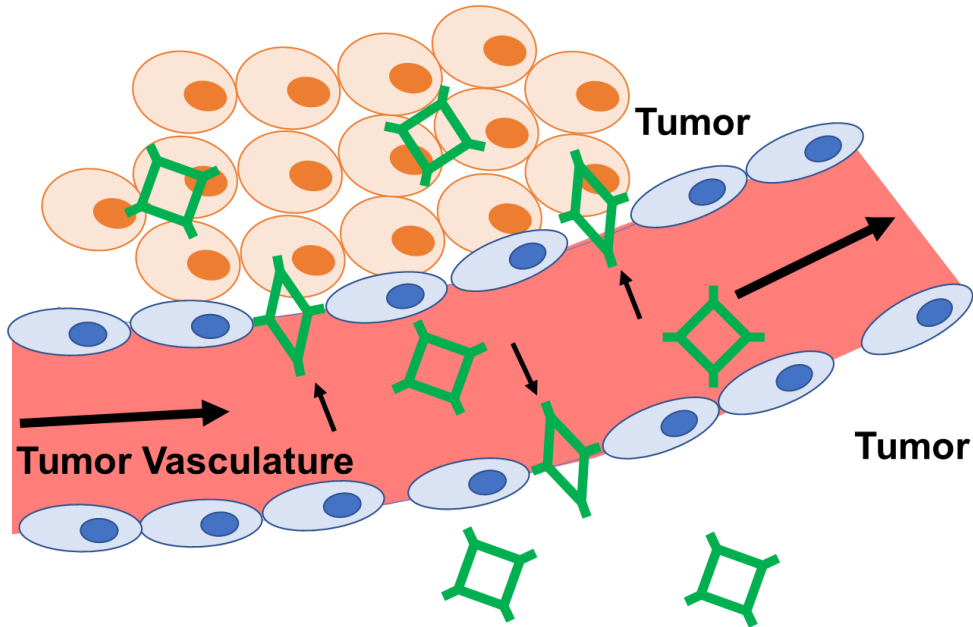
The rubbery property of RNA nanoparticles make them more efficiently target to tumor by comparing the retention time in tumor, kidney and liver with iron and gold nanoparticles with the same size





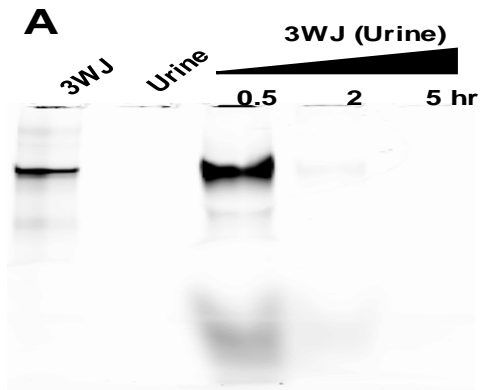
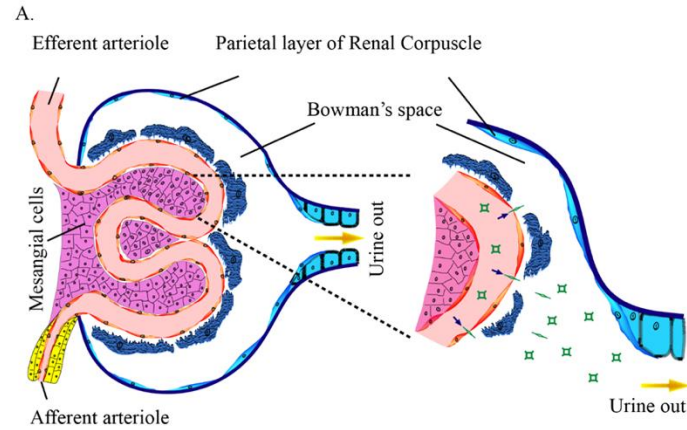
# The Rubbery Properties Benefits

## The Rubbery Property of RNA Nanoparticles Enhanced Tumor Accumulation **even without Aptamers**

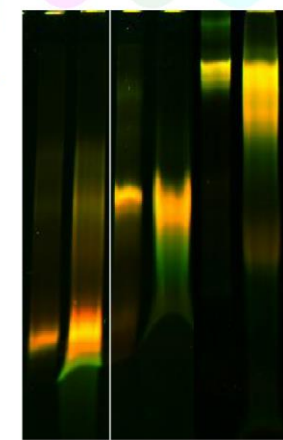
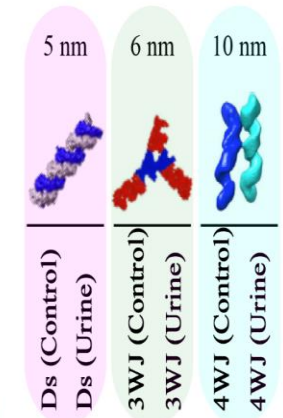


Ghimire C. et al & Guo P. *ACS Nano*. (2020).

## Rubbery and amoeba property of RNA leads to **fast renal excretion**



B. Urine 30 min post IV Injection



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

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

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

# KEY BENEFIT OF APPROACH IS FAST CLEARANCE IN CIRCULATION & ORGANS, BUT LOW CLEARANCE IN TUMORS

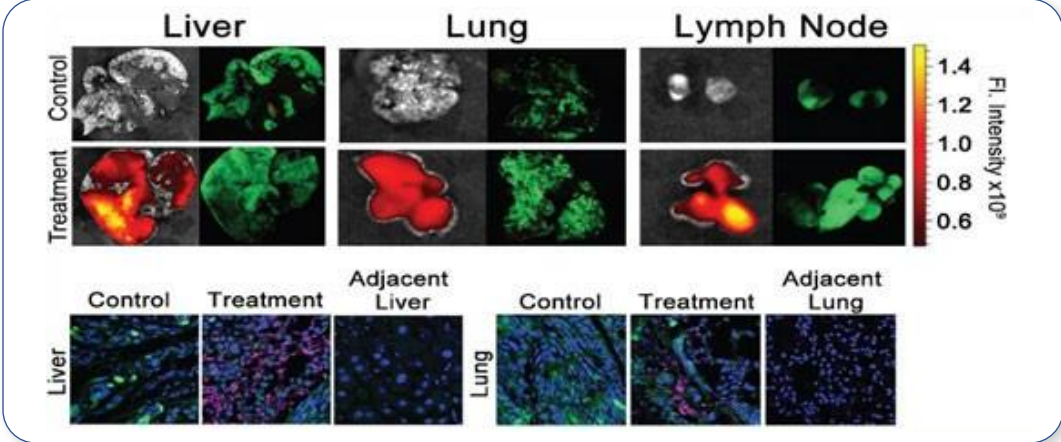
RNA nanoparticles circulate well upon injection

Nanoparticles are cleared within 4 hours in blood

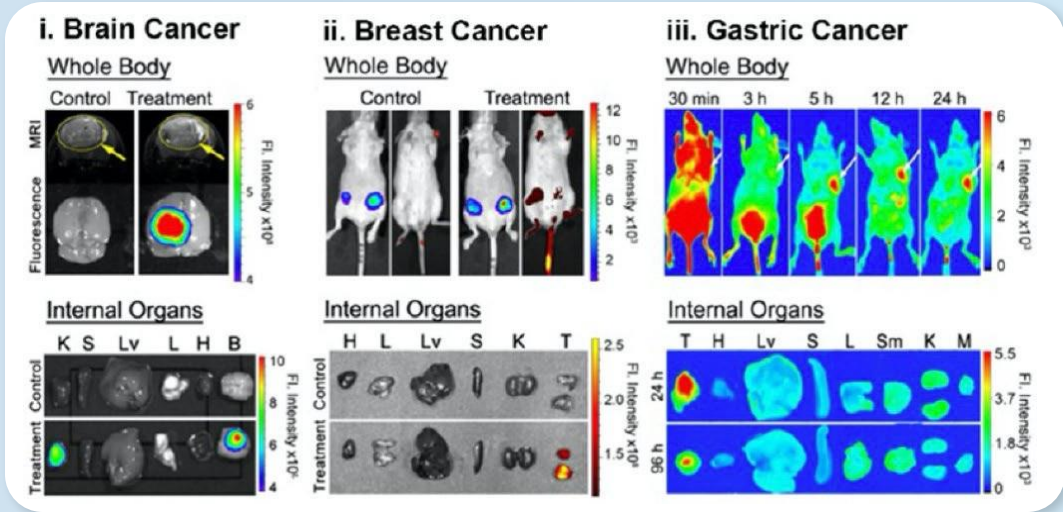
Have high tumor retention for better therapeutics

RNA nanoparticles with ligands tested

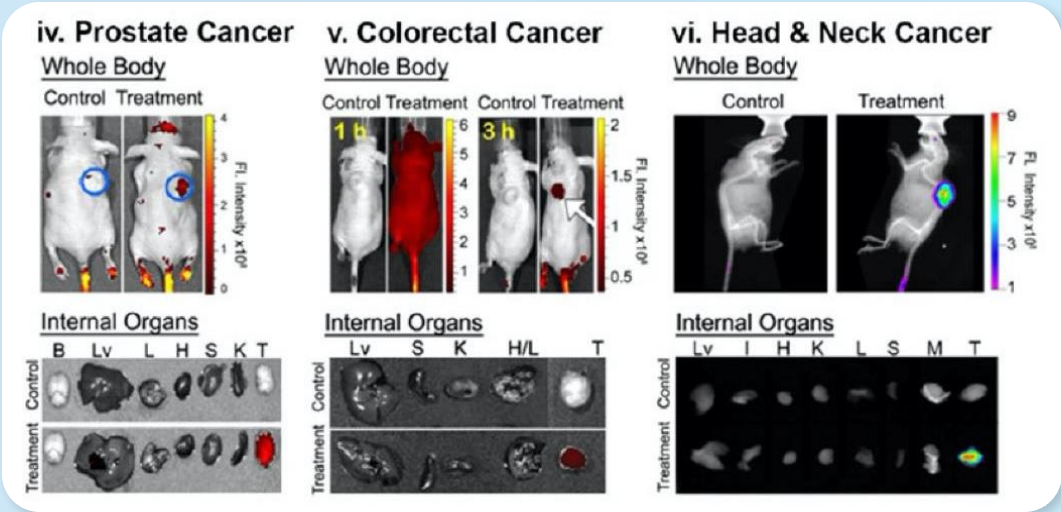
Allows for tumor targeting without accumulation in organs



Colorectal Cancer Metastases to Liver and Lung, Lymph Node



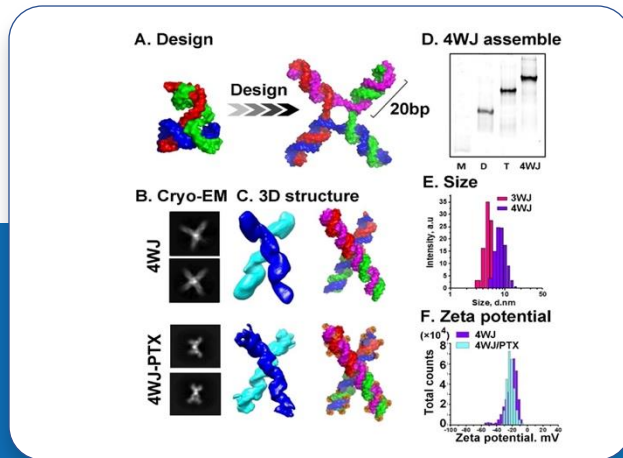
Fast Clearance In Circulation vs Slow Clearance In Tumors



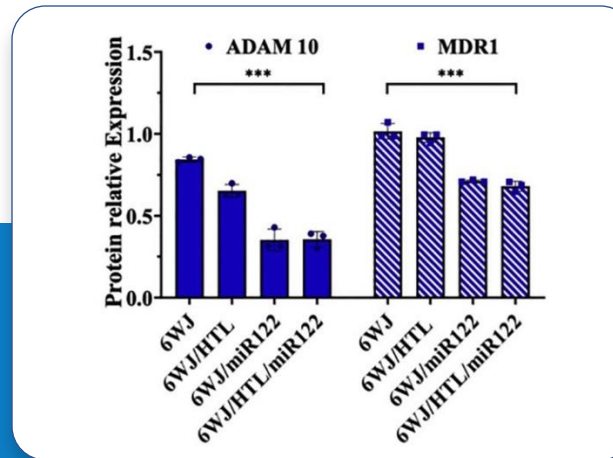
These Benefits Are Critical for Targeted Radiation Therapeutics

# RNA NANOPARTICLES TARGETED DELIVER COMBINATION RNAi and TAXOL THERAPEUTICS with SYNERGISTIC EFFECT

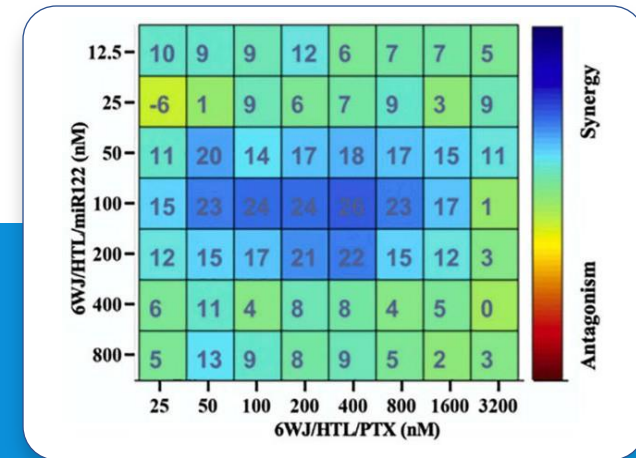
## Multifunctional RNA Nanoparticle



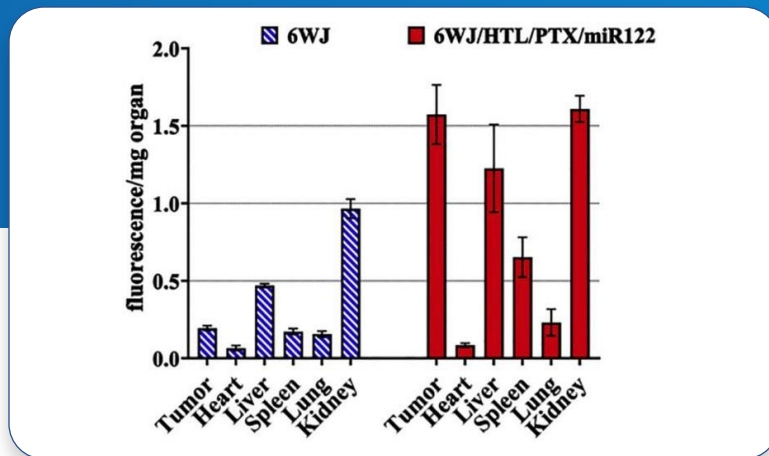
## Protein knockdown by miR122



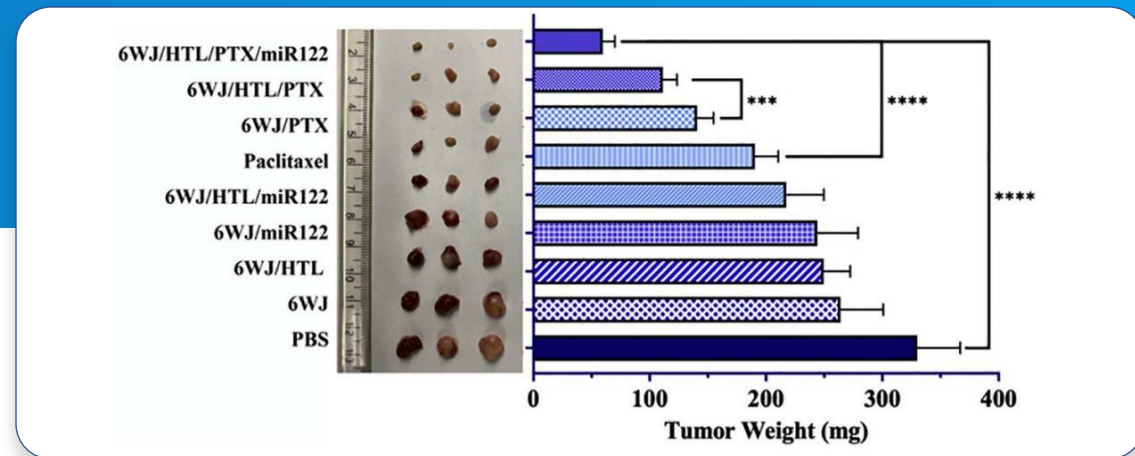
## Synergistic effect



## Tumor accumulation



## Tumor inhibition



# CURRENT POTENTIAL DRUG DEVELOPMENT PIPELINE-FOCUSED ON NANOPARTICLES

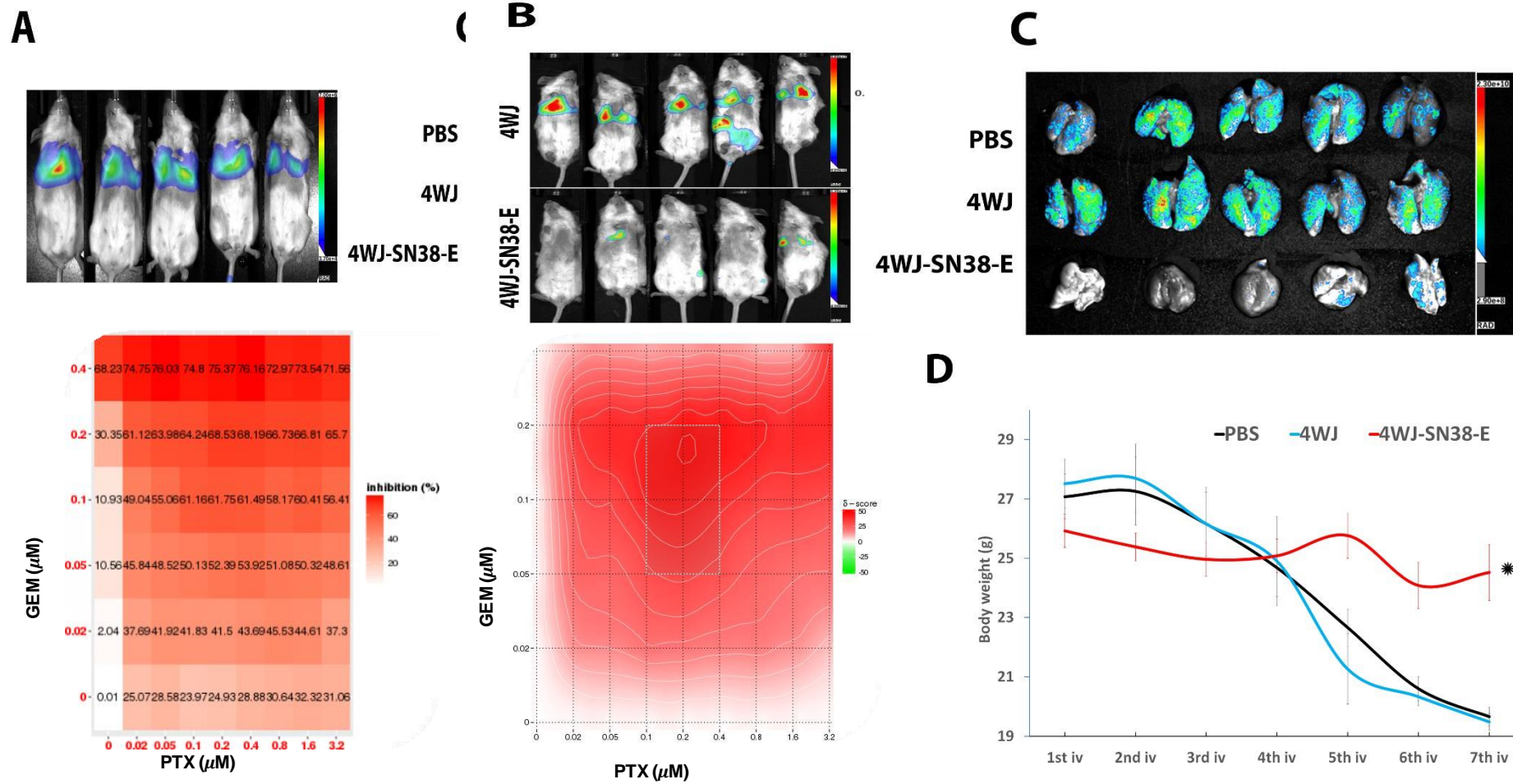


## Drug Candidates for IND Submission and Phase I Trial

	Drug Name	Cancer Target	Drug Combination	Animal Data	Planned IND
1	4WJ-SN38-EpCAM	KRAS Colon/Lung	SN38 Gem	Mouse	2026
2	4WJ-FUDR-GEM	Triple Negative Breast Cancer	Taxol chemo and Floxuridine, Gemcitabene Nucleoside	Mouse	2027
3	4WJ-miR34	Liver Cancer	Micro RNA	Mouse	2027
4	4WJ-siRNA(RRM2)	Ovarian Cancer	siRNA	Mouse	2028
6	Folate-4WJ-Exosome/Survivin	Prostate and Breast Cancer	Survivin protein chemo	Mouse	2028
7	Folate-4WJ-Exosome/miR122	Liver Cancer	Micro RNA	Mouse	2028
8	EGFA-4WJ-Paclitaxel	Breast Cancer and Lung Cancer	Taxol chemo	Mouse	2029

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

# LEAD DRUG CANDIDATE: SN38 GEM FOR TREATING COLON CANCER LUNG METASTASIS

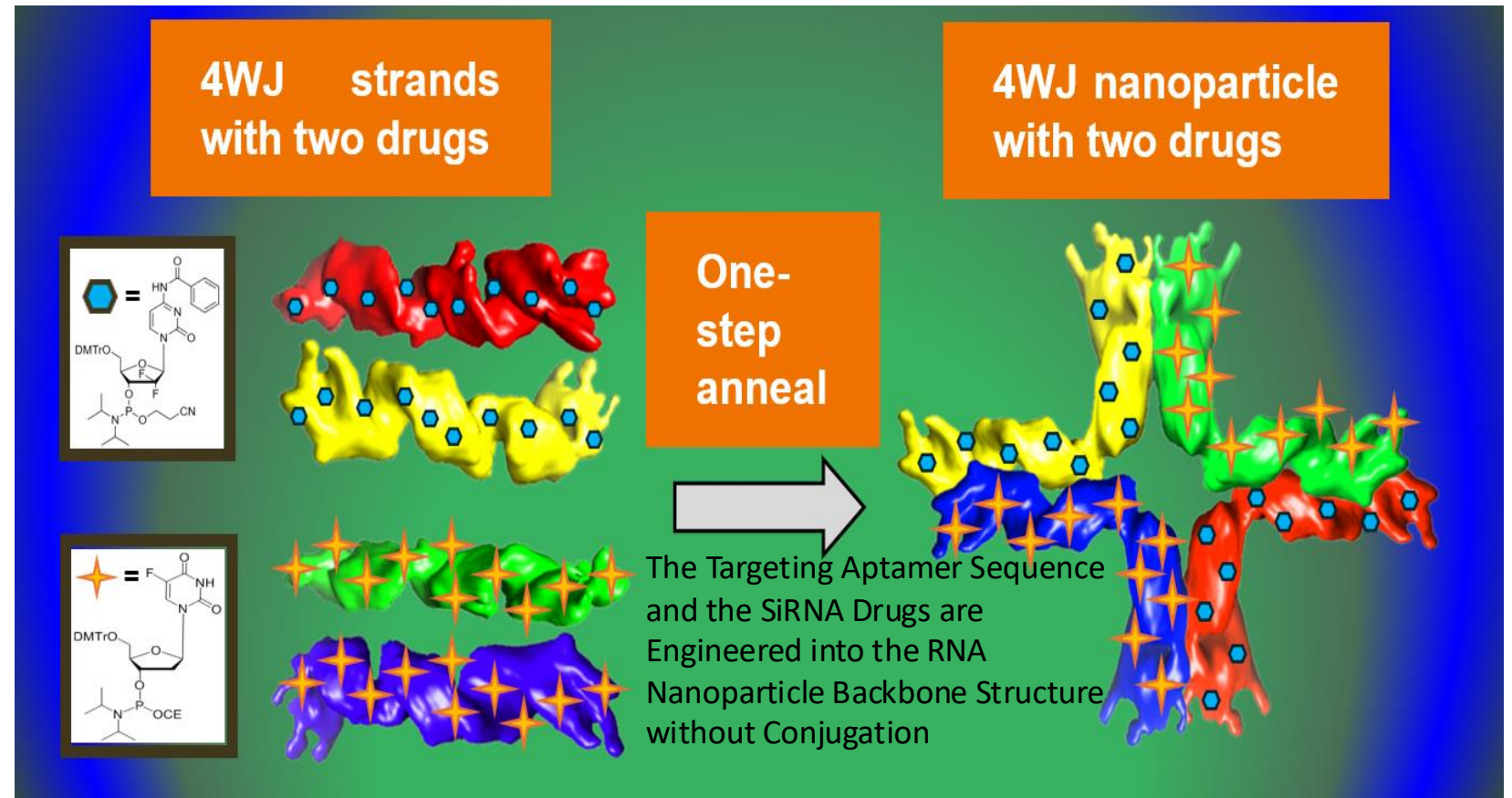


SN38 & SiRNA for the treatment of Orthotopic Colon Cancer Lung Metastasis Kai Jin et al. & Guo P. *Bioaterials*, 2024

# Lead Drug Candidate Manufactured Without Additional Attachment Chemistry Post Nanoparticle Synthesis

## DRUG MANUFACTURE

- ChemGenes located in USA Can Manufacture the drugs Under GMP for phase 1 and 2 Clinical trials
- Drug optimization and CMC be completed under a sponsored research at Ohio State University
- IND Filing Planned for Q4 2026
  - Early non GMP CMC work conducted and published
  - cGMP study work can be initiated with funding



**Two papers by Kai Jin et al & P Guo, Mol Therapy, Sep 2024**

# PATHOLOGY AND SAFETY OF RNA NANOBIOTIC'S QUADRAVANCE™ PLATFORM



Key paper just published on the safety of Quadravance™ System:

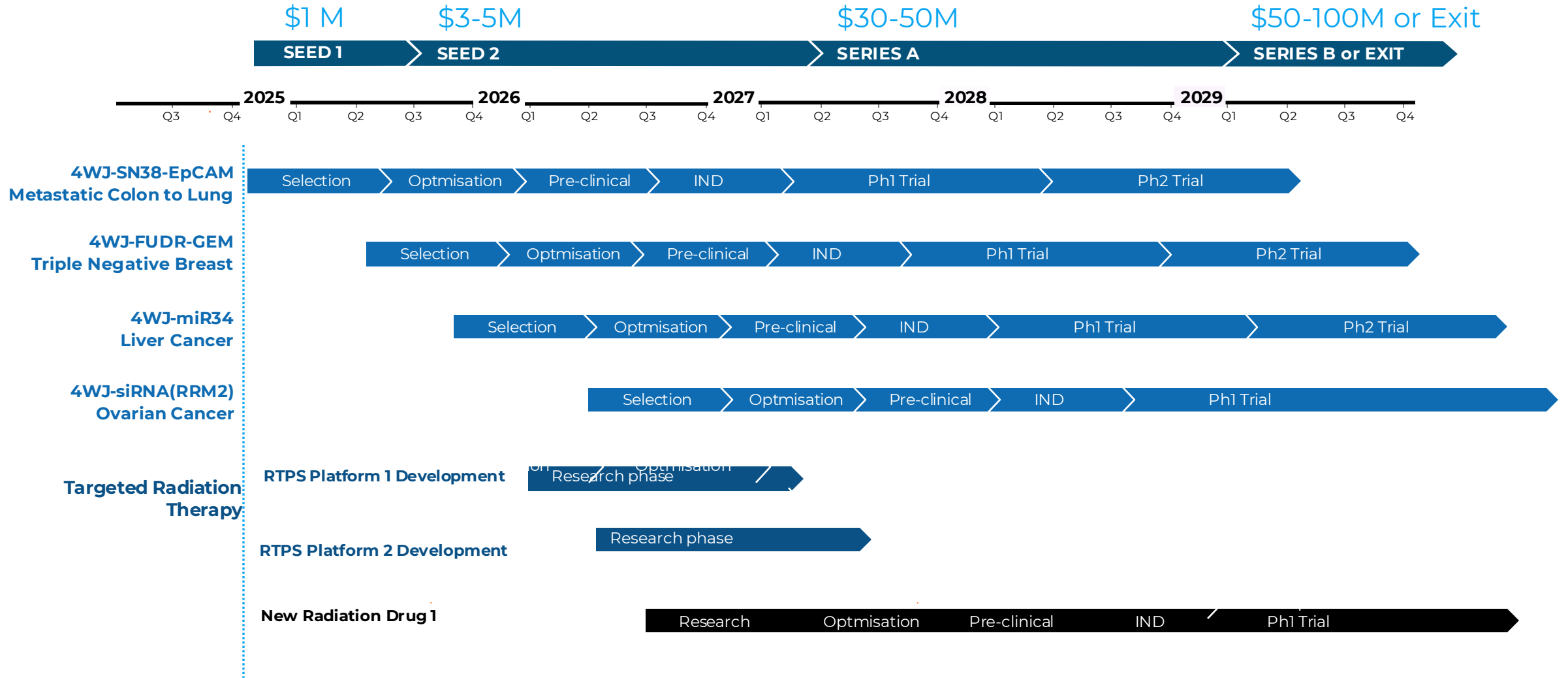
**Jin K, Liao YC, Cheng TC, Li X, Lee WJ, Pi F, Jasinski D, Chen LC, Phelps M, Ho YS, Guo P. In Vitro and In Vivo Evaluation of the Pathology and Safety Aspects of Three- and Four-Way Junction RNA Nanoparticles. Mol. Pharmaceutics, 2024 Jan [\[link\]](#) [\[PDF\]](#)**

- Studies on in vitro and in vivo hemolysis, platelet aggregation, compliment activation, plasma coagulation, Interferon induction, cytokine induction, organ weight, H&A staining, serum biochemistry, and hematology revealed:  
**No significant toxicity, side effects or immune responses.**

Other Data Shows:

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

# R&D PLAN AND CURRENT PIPELINE



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



# FOUNDER AND THE INVENTOR



**James Carroll**  
President and CEO

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



**Peixuan Guo, PhD**  
Inventor 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
- Fellow of the National Academy of Inventors (NAI), 2022

# SCIENTIFIC ADVISORS



## Fengmei Pi

**PhD**

GenScript, Head of RNA Biology Former Chief Science Officer at ExonanoRNA, PhD, University of Kentucky, Advisor - Dr. Peixuan Guo



## Bin Guo

**PhD**

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



## Marc Lemaitre

**PhD**

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



## B Mark Evers

**MD**

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

# Other Nanoparticle Delivery Platform Examples



The RNA NanoBiotics Platform has indirect competition from several platforms.

Only RNA Nanoparticles: morph into RNA Drugs within cells or clear the 5nm Glomeruli Kidney Filters and...

Targeted to cancer cells via amoeba like properties and aptamers engineered into nanoparticles

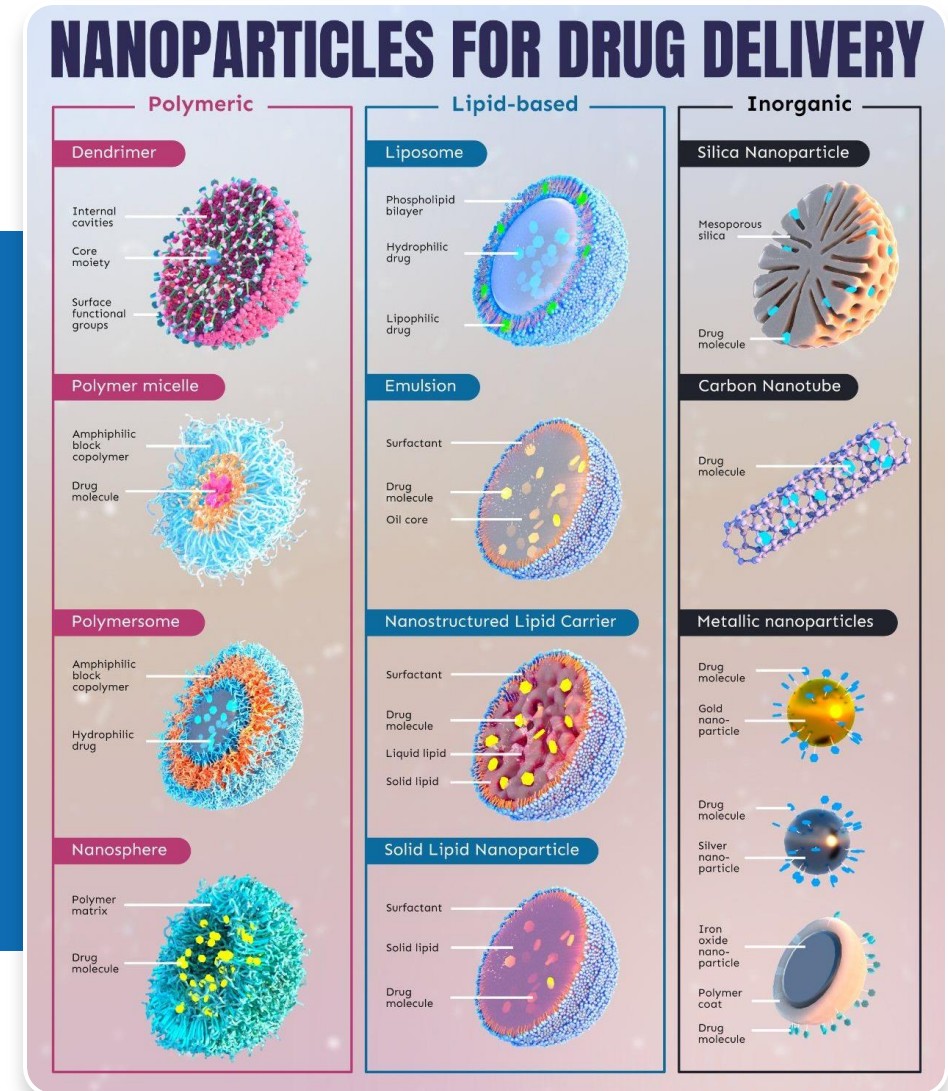
RNAi and miRNA Drugs are engineered into the nanoparticle sequences

Modified Nucleoside Drugs can be engineered into the Nanoparticles at specific molecular ratios.

Radioisotopes can be added into the structures post Nanoparticle assembly

Multiple drug classes can be co-loaded into the Targeted RNA Nanoparticles at particular molar ratios for max synergistic effect

**RNA NanoBiotics could be the Platform Company to consolidate additional RNA Therapies Technologies**



# EXIT VALUATION / FUNDING COMPARABLES



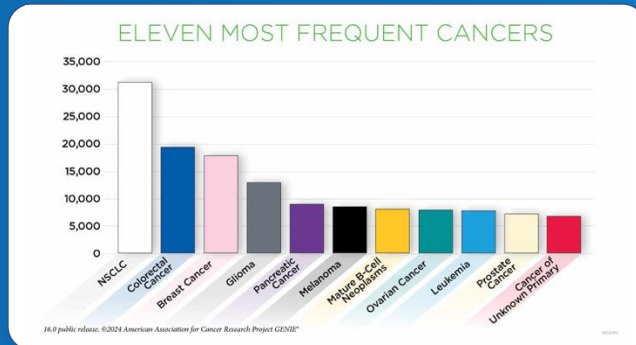
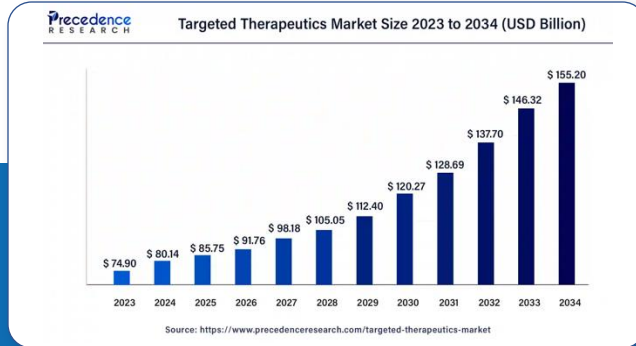
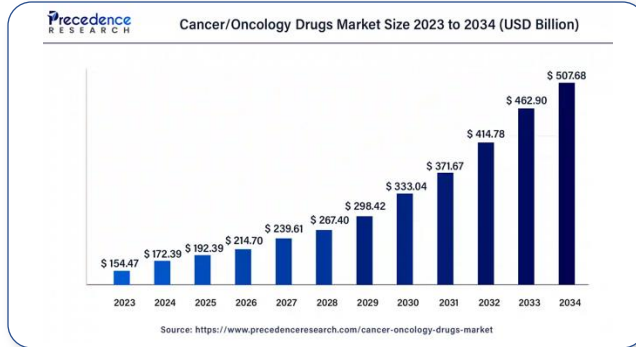
Company	Fundraising	Notes	Valuation
<b>Aktis Oncology</b>	Raised \$175M Series B on 9/30/24	Develops precision radio-pharmaceuticals targeting cancers with radiation therapy	Private
<b>RayzeBio</b>	Purchased by BMS In 2023	Targeted Radiation Therapeutics	\$4.1 Billion
<b>Entrada Therapeutics</b>	Spun Out of Ohio State University 2018 with a raise of \$60M	Endosomal Escape Vehicle Platform	\$570 Million
<b>Mariana Oncology</b>	Purchased by Novartis For \$1 Billion up front	Targeted Radiation Therapeutics	\$1 Billion plus
<b>City Therapeutics</b>	Raised \$135M Initial Round 10/8/24	Targeted RNAi Technology Licensed from Ohio State University	Private
<b>Alpha 9 Oncology</b>	Raised \$175M Oversubscribed Series C 10.23.24	Targeted Radiation Therapy for Oncology	Private
<b>Ratio Therapeutics</b>	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

# COMPETITORS



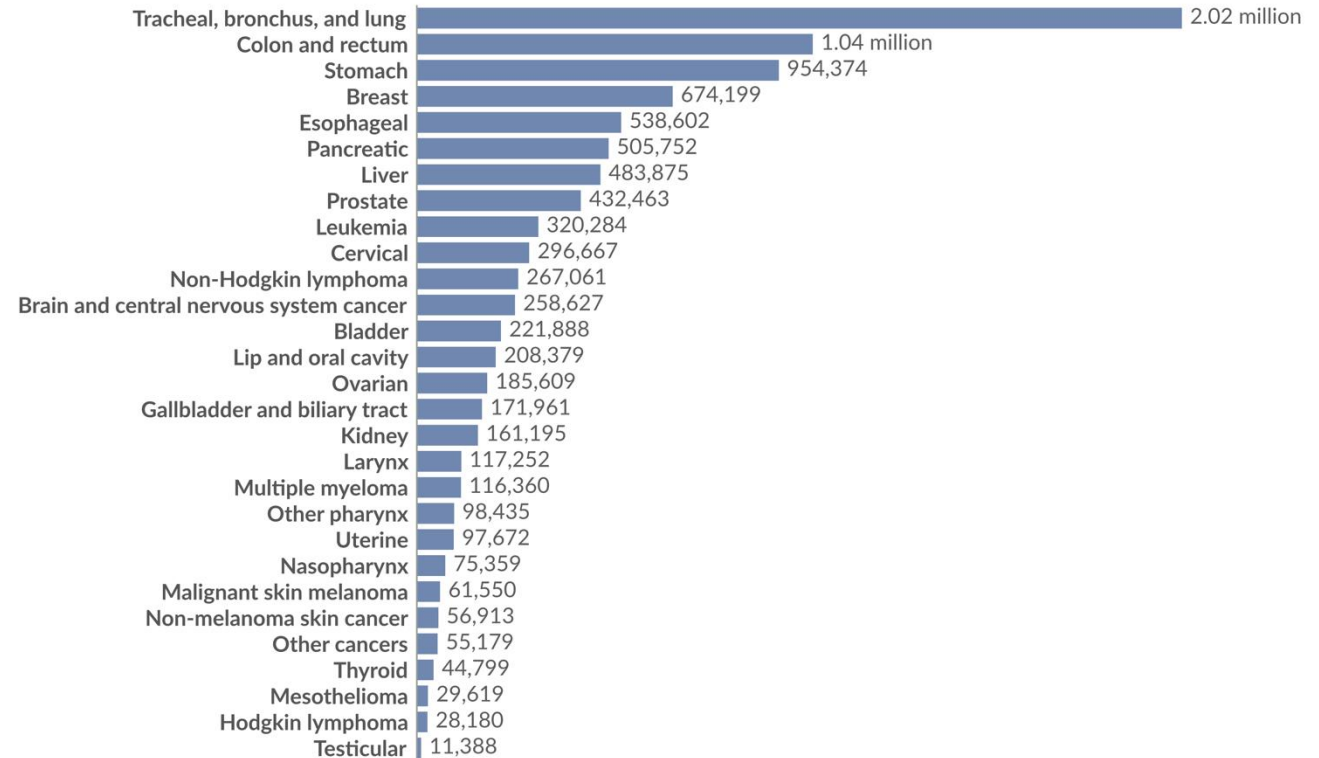
Company	Category	Main Challenges
<b>Sixfold Bioscience</b>	Small RNA Hexamer Small RNA Hexamer Therapeutics Delivery	Requires High Mg Concentrations; Very Low TM With Usability; Unfavorable Biodistribution; Accumulates Strongly In The Liver
<b>Sirnanomics</b>	Polypeptide Nanoparticles As The Vehicle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

# CANCER OCCURRENCE AND THERAPEUTICS MARKET SIZES



## Cancer deaths by type, World, 2021

Total annual number of deaths from cancers<sup>1</sup> across all ages and both sexes, broken down by type.



Data source: IHME, Global Burden of Disease (2024)

OurWorldinData.org/cancer | CC BY

1. **Cancer:** Cancer describes a group of diseases in which abnormal cells in the body begin to grow and multiply uncontrollably. These cells can form lumps of tissue called tumors, which can interfere with normal bodily functions. Cancerous cells have the potential to spread to other parts of the body (this process is called "metastasis"), disrupting normal processes and causing serious health problems.

# THANK YOU!

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**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>



**RNA NanoBiotics**