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RNA NanoBiotics

**Executive Summary**

**Development of RNA Nanoparticles for Targeted Cancer Therapy**

**Overview**

RNA NanoBiotics is at the forefront of oncology innovation, transforming the groundbreaking RNA nanoparticle technology developed by Dr. Peixuan Guo at The Ohio State University into a versatile, next-generation therapeutic platform. Our proprietary RNA Nanotechnology Platform is engineered to deliver RNA interference (RNAi), microRNAs, nucleoside analogs, chemotherapeutics, and radioisotopes directly to cancer cells, enhancing treatment efficacy while minimizing systemic toxicity. Crucially, these embedded molecules morph into active therapeutic drugs only after being internalized into target cells, ensuring high specificity and controlled release precisely to the tumor.

**Engineering RNA Nanoparticles: A Modular 4-Way Junction Platform**

To address the limitations of conventional cancer therapies, RNA NanoBiotics has built a modular engineering platform that transforms how therapeutic agents are delivered.  
  
At the core is a patented 4-way junction (4WJ) RNA architecture developed at The Ohio State University. This structure self-assembles into a thermostable scaffold, where each of the four arms can be independently functionalized. The result is a plug-and-play nanoparticle design that can be rapidly adapted to different cancers and therapeutic approaches.

Key programmable modules of the 4WJ platform can include:

• Targeting Ligand Module

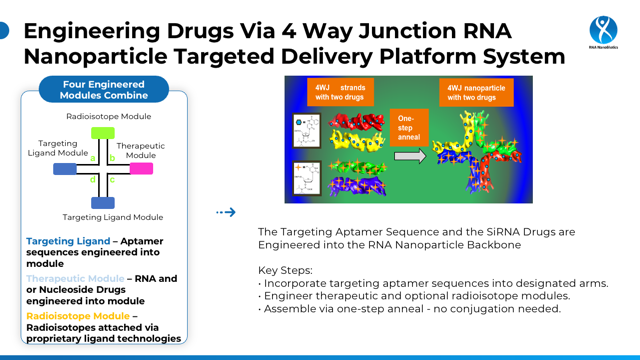
Any aptamer sequence can be engineered into the scaffold, allowing specific recognition of tumor antigens (e.g., EpCAM, EGFR) and receptor-mediated uptake.

• Therapeutic Payload Module

Chemotherapeutics (e.g., SN38, paclitaxel) or RNA drugs (siRNA, antisense, microRNA, RNAi) can be loaded directly, improving solubility (e.g., paclitaxel >30,000-fold) and enabling co-delivery of RNAs with conventional drugs for synergistic combination therapy.

• Radiolabeling Module

Chelator arms support both diagnostic isotopes (⁶⁸Ga, ¹⁸F) and therapeutic α/β-emitters (²¹²Pb, ²²⁵Ac, ²¹¹At, ¹⁷⁷Lu), creating a true theranostic pathway within the same chemistry framework.



**Why this matters:**

• Allows specific combination drug payloads to be engineered for the specific cancers.  
• Demonstrated tumor regression in preclinical models with clean safety (no weight loss, no organ pathology, cytokine levels comparable to controls).  
• One-step annealing assembly supports reproducible, scalable manufacturing.  
• A single GMP/regulatory backbone supports chemotherapy, RNAi, and radiotherapeutic programs, enabling pipeline breadth from one platform.

**Antibody Drug Conjugates (ADCs) vs 4WJ RNA Nanoparticles**



**Comprehensive Comparison:**

|  |  |  |
| --- | --- | --- |
| Category | ADCs | 4WJ RNA Nanoparticles |
| Engineering Simplicity | Requires antibody discovery, optimization, and conjugation. Complex biology and chemistry. | Purely chemical; change RNA sequences as needed. No biological production required. | |
| Manufacturing Platform | Cell culture + protein purification + conjugation. Expensive and heterogeneous. | Produced on nucleic acid synthesizers. No biological systems required. Consistent and scalable. |
| Payload Diversity | Primarily cytotoxic small molecules. Limited combination flexibility. | Delivers RNAi, microRNA, chemotherapeutics, modified nucleosides, and radioisotopes simultaneously. |
| Payload Capacity | 2–8 drugs per antibody (DAR distribution, often averages ~3–4). | Carries up to ~24 drugs in defined stoichiometry. |
| Tumor Targeting & Uptake | Antibodies bind with high affinity but face binding‑site barrier near vasculature. | Spontaneously targets cancer cells plus aptamer‑guided targeting. Efficient cell entry. |
| Safety / Toxicity | Payload leakage and off‑target retention can cause systemic toxicity. | Negatively charged; avoids normal cells/organs. Lower toxicity and wider therapeutic index. |
| Clearance & Retention | Clears slowly via liver/spleen; risk of prolonged background exposure. | Passes intact through ~5 nm kidney filters. Rapid renal clearance of unbound particles while tumor‑bound drug remains. |
| Tumor Penetration & PK (Size) | Large (~150 kDa, ~10–15 nm). Long circulation (days–weeks). Limited deep penetration. | Smaller (~tens of kDa, ~5–10 nm). Short circulation (hours). Diffuses rapidly into tumor tissue. |
| Development Speed | Typically >1 year to reach tox material due to antibody generation and optimization. | 3–9 months to tox batches using modular, sequence‑defined design. |
| Combination Therapy | Variable DAR prevents precise ratio control. Not suited for rational synergy design. | Exact strand ratios (e.g., 1:1:1). Enables fixed‑ratio combinations for synergy and resistance prevention. |
| Manufacturing & COGS | Complex biologic + conjugation. High cost of goods and lot variability. | Sequence‑defined oligo synthesis and assembly. Reproducible, scalable, lower COGS trajectory. |
| Theranostics | Radiolabeled antibodies possible but slow tissue kinetics. High background radiation. | Direct chelator integration. Same scaffold for PET and therapy. Rapid uptake and clearance. |
| Immunogenicity | Potential immune responses to antibody backbone. Repeated dosing can be limited. | Minimal immunogenicity with modified nucleosides. Safe for repeated dosing. |
| Bifunctional Equivalent | Bispecific antibodies require complex dual binding domain engineering. | Simply place two aptamers on separate arms of the 4WJ → bispecific equivalent. |

**Why Each Point Matters:**

* 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.

* Manufacturing Platform

ADCs require costly biologic production, while 4WJs are produced entirely via chemical synthesis on oligo synthesizers, improving scalability and cost predictability.

* Payload Diversity

Unlike ADCs, which mainly deliver toxins, 4WJs can combine RNA, small molecules, and isotopes. This diversity supports both combination therapies and theranostics.

* Payload Capacity

4WJs can carry far more payloads—up to 24 vs 2–8 for ADCs—enabling higher therapeutic delivery per unit and fewer administrations.

* Tumor Targeting & Uptake

Antibodies often get stuck at the tumor edge. 4WJs both target cancer cells via aptamers and spontaneously accumulate in tumors, ensuring broader delivery.

* Safety / Toxicity

ADCs risk payload leakage and systemic toxicity. 4WJs’ negative charge prevents entry into healthy cells, creating a safer therapeutic window.

* Clearance & Retention

Fast renal clearance of unbound 4WJs prevents prolonged off‑target exposure. Tumor‑bound particles remain effective—critical for radiation safety.

* 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.

* Development Speed

Faster preclinical cycles: 3–9 months for 4WJs vs >1 year for ADCs, earlier proof‑of‑concept and quicker investor value inflection.

* Combination Therapy

ADCs cannot fix precise ratios of multiple drugs. 4WJs enable exact stoichiometry, making rationally designed drug combinations possible.

* Manufacturing & COGS

4WJs’ chemical synthesis and modular design make them cheaper and more reproducible at scale, compared to ADCs’ complex biologic manufacturing.

* Theranostics

4WJs integrate isotopes directly for both imaging and therapy, with rapid uptake and clearance. This makes them an ideal platform for precision theranostics.

* Immunogenicity

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

* Bispecific Antibody Applications

Bifunctional antibody equivalence delivers the functionality of bispecific antibodies, but engineered in weeks at a fraction of the cost.

**RNA Nanotechnology Platform**

We are pioneering a transformative RNA nanotechnology platform that overcomes the limitations of traditional cancer therapies. Our patented RNA four-way junction (4WJ) nanoparticles deliver an unprecedented combination of high drug payload, precise tumor targeting, and exceptional safety.

Preclinical data demonstrate robust tumor regression and metastasis suppression in multiple cancer models with no toxicity, weight loss, or off-target effects. The 4WJ platform is modular, enabling rapid functionalization with additional drugs, RNAi agents, or targeting ligands, making it ideally suited for multi-drug resistant cancers.

With scalable CMC-ready production and compelling proof-of-concept efficacy and safety data, this RNA nanoparticle platform represents a new generation of precision therapeutics poised for first-in-human trials. We invite visionary investors to join us at the forefront of oncology innovation - delivering safer, smarter, and more effective treatments to patients who need them most.

**Key Innovations**

* RNA Nanocarrier Design: Utilizes a proprietary design **4WJ RNA scaffold** that enables precise, programmable assembly, modular drug loading, and rapid renal clearance to minimize off-target effects.
* Conjugation: The platform enables **high-payload** delivery while maintaining nanoparticle stability and tumor targeting capability.
* Tumor-Specific Targeting: Aptamer- and radio-targeting ensures **selective accumulation** in tumor tissues while sparing normal cells.

**Lead Clinical Candidate – 4WJ-SN38-EpCAMapt**

**Targeting Metastatic Colon Cancer to the Lung and Liver which is the leading cause of cancer death in men <50 years.**

**Preclinical Efficacy**

* Tumor Volume Reduction: Up to **90% reduction** in tumor size in colorectal cancer xenograft models at **2 mg/kg** SN38 dosing.
* Targeting Advantage: EpCAM-targeted nanoparticles showed a **20.4% greater tumor weight reduction** than non-targeted controls.
* Apoptotic Activity: Induced **31.6% apoptosis** in HT29 colorectal cancer cells in vitro, comparable to free SN38.

**Safety and Tolerability**

* **No observable toxicity** in mice at therapeutic doses: no weight loss, no organ histopathology changes, and no elevated cytokine levels.
* **Hemocompatibility** confirmed: <5% hemolysis, no complement activation, and no coagulopathy.
* Immunogenicity: **No significant TNF-α or IL-6 elevation** in treated PBMCs or mouse serum.
* Renal clearance and fast systemic elimination mitigate long-term tissue accumulation.

**Preclinical Proof of Concept Achieved**

RNA NanoBiotics’ data meets or exceeds all preclinical benchmarks for efficacy, targeting specificity, and systemic safety, thus establishing **clear proof-of-concept** for the SN38-RNA nanoparticle system. These findings justify advancement toward formal IND-enabling studies.

**Lead Potential Improved Clinical Candidate – 4WJ-SN38-GEM-EpCAMapt**

Data shows broader application of the drug with the incorporation of Gemcitibine (GEM) into the nanoparticle structure. The structure of the drug would not be altered and the GEM would be incorporated into the synthesis of the nanoparticles. We would also have the potential to incorporate an RNAi drug such as BCCL2/BCL-XL, Survivin (BIRC5), or TOP1.

**Second Clinical Candidate - 4WJ-EGFRapta-Paclitaxel-anti-miR21**

**Targeting Triple Negative Breast Cancer which is notably the most aggressive breast cancer subtype with a low survival rate.**

**Preclinical Efficacy**

* **Cellular activity (MDA-MB-231, EGFR+):** Targeted 4WJ-X-24PTX-EGFRapt bound cells strongly and was more cytotoxic than controls; apoptosis at 24 h was **45.1%** (vs 37.3% non-targeted 4WJ-X-24PTX, 24.6% free PTX, 8.3% aptamer alone). Growth inhibition notable at ≥250 nM.
* **Biodistribution:** After i.v. dosing, targeted RNA nanoparticles **preferentially accumulated in tumor** with low signal in liver/other organs (8 h post-injection).
* **Tumor growth inhibition (orthotopic TNBC xenograft):** Dosed at **8 mg/kg PTX-equivalent** every 2 days ×5, the 4WJ-X-24PTX nanoparticles (±EGFR aptamer) **significantly slowed tumor growth** vs PBS and free PTX (Cremophor/EtOH). Representative tumor images and stats are shown, with stronger inhibition for the targeted version.

**Safety and Tolerability**

* **General tolerability:** Treatments were **well tolerated** over two weeks; **no notable body-weight loss** and **no histologic organ damage** on post-treatment pathology.
* **Immunostimulation:** At **5 mg/kg PTX-equivalent i.v.**, 4WJ-X-24PTX induced **negligible TNF-α, IL-6, IFN-α, IFN-γ** compared with elevated cytokines from Cremophor-formulated PTX; a 25-chemokine panel showed no significant broad elevations (a few chemokines mildly increased vs PBS).
* **Acute toxicity margin:** Compared against the **LD50 of free PTX (~12 mg/kg)**, mice receiving 4WJ-X-24PTX at study doses had **no fatalities**, consistent with improved tolerability when PTX is carried by RNA nanoparticles.

**Systemic delivery of anti-miR-21:**

**Preclinical Efficacy**

* **Tumor targeting:** Anti-miR-21 3WJ nanoparticles conjugated with a folate aptamer preferentially accumulated in TNBC tumors after i.v. injection, with minimal uptake in normal tissues.
* **Gene silencing:** Significant downregulation of miR-21 in tumor tissue after treatment, confirmed by qPCR.
* **Molecular effects:** Increased expression of miR-21 target genes **PDCD4** and **PTEN**, consistent with successful miR-21 inhibition.
* **Tumor growth inhibition:** Repeated systemic dosing (5 mg/kg oligo-equivalent, twice weekly × 4 weeks) **slowed tumor growth** significantly compared to scrambled-miRNA controls.
* **In vitro apoptosis:** Treated MDA-MB-231 cells showed increased apoptosis and reduced proliferation.

**Safety & Tolerability**

* **No acute toxicity:** Mice tolerated the regimen well, with **no significant body-weight loss** during treatment.
* **Histopathology:** Major organs (heart, liver, spleen, lung, kidney) appeared normal by H&E staining after treatment.
* **Cytokine profile:** Anti-miR-21 nanoparticles caused **negligible induction of inflammatory cytokines** (IL-6, TNF-α, IFN-α, IFN-γ) compared to PBS controls.
* **No hematological toxicity:** Blood counts remained within normal ranges after repeated dosing.

**Preclinical Proof of Concept Achieved**

RNA NanoBiotics’ data meets or exceeds all preclinical benchmarks for efficacy, targeting specificity, and systemic safety, thus establishing **clear proof-of-concept** for the EGFRapt nanoparticle system. These findings justify advancement toward formal IND-enabling studies.

**Additional Drug Candidates with Animal Data**

* **Third Clinical Candidate – 4WJ-GalNex-PTX-miR122-HtLs**

Targeting Liver Cancer

* **Fourth Clinical Candidate -4WJ-anti-mRNA21-LNA-PSMAapt**

Targeting Prostate Cancer

**RNA Nanoparticles for use in Theranostics/Targeted Radiation Therapy**

Recent work from *RNA NanoMed* (Aug 2025) provides a compelling **proof-of-concept** for using modular SF5 three-way junction (3WJ) RNA nanoparticles as **targeted radiotherapeutic agents**. The 3WJ Nanoparticles can be quickly converted to 4WJ and chemical and localization behavior is the same. These nanoparticles demonstrate **rapid tumor accumulation** within 1–4 hours, minimal off-target retention, and a “plug-and-play” design where the targeting ligand and chelator strand can be swapped without altering the core architecture. This makes it possible to seamlessly substitute therapeutic alpha or beta emitters (e.g., ²¹²Pb, ²²⁵Ac, ¹⁷⁷Lu) for the diagnostic ⁶⁸Ga used in the study, enabling a **true theranostic pipeline** across multiple cancer indications.

The commercial potential is substantial: the global targeted radiotherapy market is projected to exceed **$15 billion by 2030**, driven by expanding indications, earlier-stage treatment, and strong reimbursement for high-value precision oncology drugs. By extending this platform from diagnostics into therapy, each new ligand–isotope pairing becomes a differentiated asset with billion-dollar addressable markets, leveraging the same GMP manufacturing backbone and regulatory dossier.

* **²¹²Pb → TCMC on the 4WJ chelator strand**  
  Swap the current NOTA strand for **TCMC** (Pb²⁺ chelator) and keep everything else (ligand strand, core) the same. ²¹²Pb’s ~10.6 h half‑life aligns with the NP’s **1–4 h tumor uptake window** and rapid background washout, so you’ll get useful tumor dose with low normal‑organ dose. This is the cleanest drop‑in.   
  *(The paper explicitly contemplates ²¹²Pb among intended therapy nuclides.)*
* **²²⁵Ac → DOTA (or macropa) on the 4WJ chelator strand**  
  Also a straight chelator‑strand substitution. Practically, you’ll plan for **daughter recoil** and may want multivalency/dendrimer variants to help with payload and potential daughter retention, but it’s still architecturally a swap.
* Potential Theranostic Applications
  + Designs include dual-use payloads, such as:
    - Therapeutic isotopes (Astatine-211, Actinium-225)
    - Diagnostic isotopes (Gallium-68, Fluorine-18 for PET/CT imaging)

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| Cancer Type | Targetable Surface Markers | Applicable Radioisotopes | Why It’s a Fit |
| Prostate Cancer | PSMA, EpCAM | Actinium-225, Lutetium-177 | Already proven in radioligand therapies; RNA platform can improve targeting/safety |
| Neuroendocrine Tumors (NETs) | SSTR2 (somatostatin receptor) | Lutetium-177, Actinium-225 | Alpha-emitters could overcome resistance to current Lutathera®-based therapies |
| Colorectal Cancer (CRC) | EpCAM | Astatine-211, Lutetium-177 | EpCAM aptamers enable high-precision targeting of liver/lung metastases |
| Pancreatic Cancer | Mesothelin, EpCAM | Actinium-225, Astatine-211 | Hard-to-penetrate tumor; small, stable RNA particles improve delivery |
| Ovarian Cancer | FRα, EpCAM | Astatine-211, Lutetium-177 | Suitable for residual disease and intraperitoneal delivery |
| Glioblastoma (GBM) | CD133, EGFRvIII | Astatine-211, Actinium-225 | Exosomes or small RNA carriers may cross the BBB better than antibodies |
| Multiple Myeloma | BCMA, CD38 | Actinium-225, Lutetium-177 | Novel route for alpha-emitting therapies targeting marrow-resident tumor cells |
| Breast Cancer (TNBC) | EpCAM, MUC1 | Astatine-211 | No hormone targets in TNBC—RNA-guided radiation offers a non-toxic alternative |
| Lung Cancer | EGFR, EpCAM | Astatine-211, Actinium-225 | Can target both primary NSCLC and CRC lung metastases |
| Liver Cancer (HCC) | GPC3, EpCAM | Astatine-211, Lutetium-177 | High unmet need; radioRNA may bypass resistance to kinase inhibitors |

**Other Licensing or Partnering Technologies Within IP Portfolio**

**Strategic Platform Applications**

1. **RNA‑Ligand Displaying Exosomes for Targeted Therapeutics**

RNA nanoparticles are displayed on the surface of exosomes. Designed to target specific cell types (e.g., cancer cells) by combining an RNA targeting aptamer (or RNA nanoparticle) with an exosome vector that carries therapeutic or diagnostic payloads.

* Surface-displayed RNA nanoparticles: Exosomes are engineered so that the RNA nanoparticle (including targeting moieties) is presented on their membrane, facilitating specific cell binding and uptake.
* Therapeutic or diagnostic function inside exosome: The exosome itself can include a “functional moiety” e.g. therapeutic cargo such as siRNA, miRNA, or imaging compound.
* Multifunctional platform: Supports treating cancer, infections, and diagnostic imaging using a unified exosome-RNA nanoparticle delivery system.

This application extends the RNA nanotechnology IP into the realm of extracellular vesicle-based delivery, combining the modularity and targeting of RNA nanostructures with the natural delivery advantages of exosomes. Key benefits:

* Hybrid platform potential: Merges two validated delivery modalities—engineered exosomes and RNA nanoparticles—for added targeting, stability, and payload versatility.
* Differentiation: Distinct from current ADCs or lipid nanoparticles, leveraging exosome immune stealth and cell compatibility.
* Extension opportunities: Can be licensed or co-developed in areas such as cancer, infectious disease, and diagnostic imaging.

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| Cancer Type | Known Aptamer Targets | Platform Cargo Potential |
| Colorectal (mCRC) | EpCAM | SN38, miRNA, siRNA, radiotherapeutics |
| Breast (TNBC) | EpCAM, MUC1 | SN38, siRNA, checkpoint inhibitor RNA |
| Ovarian | EpCAM, FRα | siRRM2, SN38, miRNA |
| Liver (HCC) | ASGR1, EpCAM | miR34, siRNA |
| Prostate | PSMA | siRNA, radiotherapeutics |
| Lung | EGFR, EpCAM | Chemotherapeutics, siRNA |
| Brain (GBM) | EGFRvIII, CD133 | siRNA, radiotherapeutics |
| Pancreatic | Mesothelin, EpCAM | miRNA, chemo |
| Multiple Myeloma | BCMA, CD38, SLAMF7 | siRNA, miRNA, immunomodulatory RNA, BiTE RNA |

1. **Cell Therapy Applications**

RNA nanoparticles functionalized with aptamers that bind to immune cells (e.g., CD4, CD8, CD28, 4-1BB).These particles can:

* + Deliver activation signals to T cells or NK cells (immune stimulation)
  + Deliver gene-modulating RNAs (e.g., siRNA, miRNA) to reprogram immune responses
  + Target CAR-T cells post-infusion to regulate their activity or persistence

Exosome-RNA Nanoparticle Hybrids

1. The RNA-decorated exosome platform (US20190024085A1) can be adapted to:
   * Deliver co-stimulatory signals to immune cells in vivo
   * Package and direct immunoregulatory RNAs to myeloid or lymphoid cells
   * Potentially carry CAR constructs or guide RNAs for transient gene editing or expression

Cell-Specific Aptamer Targeting

* RNA aptamers can be engineered to bind:
  + T cell markers (CD3, CD4, CD8)
  + Myeloid markers (CD11b, CD14)
  + Stem cell markers (CD133, Sca-1)
* This enables RNA-particle–guided programming of immune cells in vivo—without viral vectors or electroporation.

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| Cancer Type | Immune Targets / Pathways | RNA Platform Application |
| Acute Lymphoblastic Leukemia (ALL) | CD19, CD22 (CAR-T targets) | In vivo CAR mRNA delivery or checkpoint knockdown (PD-1, CTLA-4) |
| Diffuse Large B-Cell Lymphoma (DLBCL) | CD19, CD20 | RNA nanoparticle support for CAR-T enhancement or immune evasion |
| Multiple Myeloma | BCMA, SLAMF7, CD38 | In vivo delivery of anti-BCMA CAR constructs or immune modulators |
| Non–Small Cell Lung Cancer (NSCLC) | PD-L1, EGFR | siRNA delivery to tumor or TME; checkpoint modulation in T cells |
| Triple-Negative Breast Cancer (TNBC) | EpCAM, MUC1 | Combination of RNA-targeted drug + immune checkpoint knockdown |
| Ovarian Cancer | FRα, EpCAM | Dendritic cell RNA vaccines or T cell modulator delivery |
| Colorectal Cancer (mCRC) | EpCAM, CEACAM5 | Tumor-associated antigen delivery to DCs for vaccination; TAM reprogramming |
| Prostate Cancer | PSMA | NK cell activation or T cell stimulation via RNA payloads |
| Glioblastoma (GBM) | EGFRvIII, CD133 | Delivery to tumor-infiltrating lymphocytes (TILs); checkpoint silencing |
| Melanoma | gp100, MART-1, PD-1/PD-L1 axis | mRNA vaccines or immune checkpoint RNA delivery to T/NK cells |
| Pancreatic Cancer | Mesothelin, CD40, PD-L1 | Macrophage/monocyte reprogramming or RNA-activated DC therapy |

1. **Bispecific Applications**

**Multi-arm RNA nanoparticles** (e.g., 3WJ, 4WJ, 6WJ structures) can be engineered to simultaneously:

* Display a **tumor-targeting aptamer** (e.g., EpCAM, PSMA)
* Display an **immune cell–binding aptamer** (e.g., CD3 for T cells, CD28, 4-1BB, CD16 for NK cells)

This creates a **bispecific bridge** between cancer cells and immune effectors—mimicking the mechanism of bispecific antibodies or BiTEs (bispecific T-cell engagers).

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| Cancer Type | Tumor Target (Aptamer) | Immune Target (Aptamer) | Clinical Opportunity |
| Colorectal Cancer (mCRC) | EpCAM | CD3, CD28, 4-1BB | Recruit T cells to liver/lung mets; improve response to immunologically “cold” tumors |
| Ovarian Cancer | FRα, EpCAM | CD3, CD28 | Target chemo resistant cells in peritoneum; engage immune effectors |
| Triple-Negative Breast Cancer (TNBC) | EpCAM, MUC1 | CD3, CD16 | No hormone targets—BiTE-style RNA can recruit T or NK cells |
| Multiple Myeloma | BCMA, CD38, SLAMF7 | CD3, CD16 | Novel immune engagement strategy vs marrow-resident tumors |
| Prostate Cancer | PSMA | CD3, CD28, 4-1BB | Use in metastatic CRPC with T cell or NK cell recruitment |
| Lung Cancer (NSCLC) | EGFR, CEACAM5 | CD3, 4-1BB | Combine with immune checkpoint silencing (siPD-1, siTGF-β) |
| Glioblastoma (GBM) | EGFRvIII, CD133 | CD3 | Cross blood–brain barrier; engage T cells at tumor site |
| Pancreatic Cancer | Mesothelin, EpCAM | CD3, CD28 | Target dense TME and stimulate immune infiltration |
| Melanoma | gp100, MART-1 | CD3, PD-1 | Combine antigen targeting with immune checkpoint interference |
| Liver Cancer (HCC) | ASGR1, GPC3, EpCAM | CD3, NKp46 | Use in immunotherapy-refractory or virus-associated HCC |
| Non-Hodgkin Lymphoma (NHL) | CD19, CD20 | CD3 | RNA BiTEs mimic approved therapies with simpler manufacturing |
| Acute Myeloid Leukemia (AML) | CD33, CD123 | CD3 | Experimental—engage T cells directly via RNA bispecific scaffold |

**Conclusion**

Multiple nanoparticle platforms pioneered by RNA NanoBiotics represents a transformative approach to targeted cancer chemotherapy. With a strong body of preclinical data supporting safety, specificity, and efficacy, the platform is well-positioned for clinical translation as a first-in-class RNA-based therapeutic delivery system for solid tumors.

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Full List of Dr. Peixuan Guo Publications:

[**https://rnanano.osu.edu/Guo/publications.html**](https://rnanano.osu.edu/Guo/publications.html)