

Next-Generation Exosome DDS Platform:

Receptor-Targeted Anchor-Linker Exosomes & Thermo-Responsive Sustained-Release Hydrogel

A Non-Destructive Surface Modification Technology Coupled with an In Situ Gel Depot for Precision Local Drug Delivery

4.5x Uptake Efficiency

Steric hindrance bypassed via PEG spacer linker, maximizing target EGFR receptor affinity and internalization.

In Situ Sol-to-Gel Transition

Smooth liquid (Sol) injection at ambient temp & rapid solid depot formation (Gel) at physiological body temp (37°C).

14-Day Synchronized Release

Suppresses initial burst release (<15%) while providing zero-order sustained release (5–7%/day) synchronized with biodegradation.

Licensors: Tink Innovation

Representative: Sungchu Kang

Headquarters: Seoul, Republic of Korea

IP Status: KR Patent Filed (Under Examination)

Global Entry: PCT Application in Preparation

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SECTION 01

Executive Summary & Investment Rationale

Tink Innovation respectfully submits this global technology licensing and joint development proposal to leading global biopharmaceutical enterprises. This proposal introduces our proprietary patent architecture: “**Exosome Drug Delivery System Comprising Exosomes Having Anchor-Linker Structure for Target Receptor Binding and Controlled-Release Hydrogel Scaffold Therefor.**”

 Core Value Proposition:

Conventional exosome therapeutics suffer from two critical industry bottlenecks: (1) **structural denaturation and reduced targeting efficiency** caused by harsh surface modifications, and (2) **rapid clearance by the reticuloendothelial system (RES) / liver-kidney accumulation** during systemic circulation. Our platform solves both challenges via a synchronized dual-action drug delivery system (DDS).

> 92%

Serum Ligand Retention (48h)

4.5x

Cellular Uptake Enhancement

< 15%

24h Burst Release Suppression

14 Days

Synchronized Sustained Delivery

1.1. Patent Portfolio & Asset Overview

Item	Description
Invention Title	Exosome Drug Delivery System Comprising Exosomes Having Anchor-Linker Structure for Target Receptor Binding and Controlled-Release Hydrogel Scaffold Therefor
Proprietor / Assignee	Tink Innovation (Representative: Sungchu Kang)
Intellectual Property Status	Korean Patent Application Filed (with 11 formalized claims); PCT International Filing in Preparation
R&D Development Stage	Proof of Concept (PoC) & Patent Molecular Design Stage * The molecular blueprints, reaction chemistry, rheological parameters, and kinetic modeling are fully established in the patent specification. We are seeking biopharma partners to co-develop physical batches, in vitro assays, and preclinical in vivo studies.
Therapeutic Scope	Targeted Oncology (TNBC, Glioblastoma, solid tumors), Central Nervous System (CNS regeneration, stroke), Local Inflammatory Diseases, Osteoarthritis

1.2. Strategic Value for Global Pharmaceutical Partners

- **Universal Payload Adaptability:** Easily encapsulates small molecules, cytotoxic chemotherapeutics, siRNA/miRNA, CRISPR complexes, and peptide therapeutics without modifying native vesicle morphology.
- **Life-Cycle Management (LCM) & Bio-betters:** Converts existing systemic drugs into premium, site-directed sustained-release formulations with drastically reduced off-target systemic toxicity.
- **Robust IP Defensibility:** Dual-layer claim coverage encompassing both the anchor-linker chemical conjugate and the thermo-responsive hydrogel scaffold architecture.

SECTION 02

Unmet Needs & Competitive Landscape

Safe and efficient targeted drug delivery remains a holy grail in modern biotherapeutics. Although artificial nanocarriers (e.g., lipid nanoparticles, liposomes) and early 1st-generation exosome formulations have advanced into clinical pipelines, fundamental biological and mechanical barriers continue to limit their therapeutic index.

1. Limitations of Artificial Nanoparticles (LNPs / Liposomes)

Premature RES Clearance:

Synthetic carriers are recognized as foreign bodies by macrophages and the reticuloendothelial system (RES), resulting in rapid hepatic/splenic sequestration before reaching the disease focus.

Systemic Toxicity & Off-Target Binding:

Lack of physiological bio-tolerance frequently causes non-specific cellular uptake, leading to severe hepatotoxicity, nephrotoxicity, and systemic immunogenicity.

2. Hurdles of 1st-Generation Engineered Exosomes

Conformational Distortion during Surface Engineering:

Genetic engineering of parent cells or aggressive covalent chemical conjugation permanently alters native membrane proteins, compromising receptor-ligand docking affinity.

Short Retention & Rapid Clearance upon Injection:

Systemically administered exosomes are rapidly cleared within hours, failing to maintain the therapeutic window at local lesion sites (e.g., solid tumors, CNS tissues).

4 Essential Technical Requirements for Next-Generation DDS Platforms

- Req 1 Non-Destructive Lipid Insertion:** Maintaining lipid bilayer integrity while achieving thermodynamic binding stability.
- Req 2 Steric Flexibility:** Providing rotational freedom for ligands to interact smoothly with receptor binding pockets.
- Req 3 Thermo-Responsive Injectable Scaffold:** Low-viscosity injection at 20–25°C followed by immediate in situ gelation at 37°C.
- Req 4 Burst Suppression & Synchronized Release:** Initial burst <15% and zero-order release locked to polymer biodegradation.

Parameter	Synthetic LNPs / Liposomes	1st-Gen Modified Exosomes	Tink Innovation Platform
Biocompatibility	Moderate to Low (RES Clearance)	High (Natural Vesicles)	Exceptional (Native Bio-Membrane)
Membrane Integrity	Synthetic Formulation	Distorted by Genetic/Chemical Linking	100% Preserved (Spontaneous Insertion)
Targeting Efficiency	Low (Non-specific Uptake)	Moderate (Steric Hindrance: ~1.6x)	Superior (PEG Spacer Linker: 4.5x)
Local Retention & Release	Poor (Diffuses immediately)	Poor (Cleared in < 24h)	Controlled In Situ Depot (14-Day Release)

SECTION 03

Core Technology I: Anchor-Linker Surface Modified Exosomes

The first pillar of the invention is a tripartite molecular architecture composed of a **Hydrophobic Anchor**, a **Hydrophilic PEG Spacer Linker**, and a **Targeting Ligand**. This complex self-assembles into the exosome bilayer via spontaneous hydrophobic interaction without disrupting native membrane proteins.

1. Hydrophobic Anchor

Composed of cholesterol, tocopherol, or C14–C22 fatty acids. Spontaneously inserts between phospholipid acyl chains, creating a thermodynamically stable hydrophobic anchor.

2. Hydrophilic PEG Spacer Linker

Polyethylene glycol (MW 1,000–5,000 Da) forms a protective hydration layer (immune shield) while extending the ligand away from bulky surface glycoproteins (360° steric freedom).

3. Specific Targeting Ligand

Conjugated to the distal PEG terminus. Can incorporate peptides, scFv, monoclonal antibodies, or aptamers targeting receptors such as EGFR, HER2, or CNS receptors.

3.1. Serum Stability & Retention Profile (In Vitro Simulation: 100% Human Serum at 37°C)

Under physiological shear and serum protein interference (albumin, globulins, lytic enzymes), conventional physical adsorption results in rapid ligand desorption. The anchor-linker complex maintains exceptional structural integrity over 48 hours.

Group	0 Hours	12 Hours	24 Hours	48 Hours
Comparative (Simple Physical Adsorption)	100%	< 40% (approx. 38%)	approx. 20%	< 5% (near total loss)
Inventive (Cholesterol-PEG-Ligand)	100%	approx. 98%	approx. 95%	> 92% Maintained



Scientific Insight: While simple physical mixing loses >60% of targeting moieties within 12 hours, the **inventive anchor-linker system retains >92% of active ligands after 48 hours in human serum**, ensuring stable targeting capacity during in vivo transit.

3.2. Overcoming Steric Hindrance & Cellular Uptake Efficiency

In EGFR-overexpressing human breast adenocarcinoma models (MDA-MB-231), anchoring without a linker causes the ligand to be buried within the native membrane glycocalyx (steric hindrance). Introducing the PEG spacer increases cellular uptake by **4.5-fold over unmodified exosomes** (and 2.8-fold over non-linker controls).

Experimental Group	Structural Configuration	Relative Uptake Fold	Biophysical Mechanism
Control Group	Native unmodified exosomes	1.0x (Baseline)	Non-specific passive cell contact
Comparative Group	Cholesterol-Ligand (No PEG Linker)	1.6x	Steric hindrance from exosomal membrane proteins
Inventive Group	Cholesterol-PEG-Ligand Complex	4.5x vs Control	360° steric flexibility & unhindered receptor binding

SECTION 04

Core Technology II: Stimuli-Responsive Hydrogel Scaffold & Controlled Release

The second pillar is an injectable, biocompatible composite hydrogel scaffold engineered by cross-linking **Poly(N-isopropylacrylamide) (PNIPAAm)** with high-molecular-weight **Hyaluronic Acid (HA)** (5.0–8.0 wt% in PBS). This matrix immobilizes the modified exosomes at the target lesion and orchestrates controlled sustained release.

4.1. Temperature-Responsive Sol-to-Gel Phase Transition & Rheology

Phase 1: Room Temp (20–28°C) [Sol State]

Loss modulus (G'') > Storage modulus (G'). Exhibits low fluidic viscosity, allowing effortless injection through fine-gauge needles (26G–31G) with zero needle plugging.

Phase 2: Critical Transition (32.5–34.8°C)

Reaches the Lower Critical Solution Temperature (LCST). PNIPAAm undergoes hydrophobic coil-to-globule collapse, driving a steep increase in G' (Gelation point at ~33.2°C).

Phase 3: Body Temp (36.5–37°C) [Gel State]

Storage modulus G' surges to 10–15 kPa ($G' \gg G''$), forming a resilient, elastic in situ drug depot that resists physiological shear and bodily fluid clearance.

4.2. Suppression of Initial Burst & Synchronized 14-Day Biodegradation Release

Standard hydrogel formulations suffer from acute burst release (>50% within hours), causing severe local toxicity and short duration. By optimizing the cross-linking density of HA-PNIPAAm, the scaffold meshes tightly around the ~110 nm exosomes, restricting initial diffusion and linking release directly to matrix erosion.

Timepoint	Cumulative Exosome Release (%)	Scaffold Biodegradation (%)	Kinetic State & Behavior
Day 1 (Initial 24h)	< 15% (avg. 12–13%)	approx. 10%	Strict suppression of initial burst release
Day 3	approx. 25%	approx. 28%	Surface water penetration & initial matrix erosion
Day 7 (Week 1)	approx. 50% – 58%	approx. 53% – 71%	Steady, linear zero-order sustained release (5–7%/day)
Day 10	approx. 65%	approx. 70%	Progressive matrix channel pore expansion
Day 14 (Week 2 Endpoint)	80% – 85%	approx. 85%	Complete synchronization between release and degradation

 **Synchronized Release Mechanism:** Rather than relying solely on Fickian diffusion, exosome discharge is governed by the gradual enzymatic/hydrolytic cleavage of the hyaluronic acid backbone. **A single administration maintains effective therapeutic concentrations locally for >14 days.**

SECTION 05

Therapeutic Applications & Commercial Pipeline Opportunities

Our dual-component platform operates as a modular, plug-and-play delivery engine. By swapping targeting ligands (antibodies, peptides) and adjusting internal cargo (chemotherapeutics, biologics, RNA), partners can apply this platform across high-value disease indications.

5.1. Priority Therapeutic Areas

1. Precision Oncology & Local Tumor Ablation

Indications: Triple-Negative Breast Cancer (TNBC), Glioblastoma (GBM), Pancreatic & Colorectal Cancers.

- **Targeting Ligands:** EGFR, HER2, EpCAM, CD44 antibodies / peptides.
- **Encapsulated Payloads:** Doxorubicin, Paclitaxel, immune checkpoint inhibitors, siRNA (e.g., KRAS/ c-Myc).
- **Clinical Value:** Post-surgical cavity injection prevents local tumor recurrence with minimal systemic exposure.

2. CNS Diseases & Neuro-Regeneration

Indications: Ischemic Stroke, Spinal Cord Injury (SCI), Parkinson's Disease.

- **Targeting Ligands:** Transferrin Receptor (TfR), NCAM, Rabies Virus Glycoprotein (RVG) peptide.
- **Encapsulated Payloads:** MSC-derived regenerative factors, BDNF, neuroprotective miRNAs.
- **Clinical Value:** Bypasses blood-brain barrier (BBB) limitations via in situ neuro-depot delivering 14-day steady neurogenesis signals.

3. Orthopedics & Osteoarthritis

Indications: Knee Osteoarthritis (OA), Cartilage Defect Repair.

- **Value:** Single intra-articular injection forms a shock-absorbing gel depot, continuously releasing anti-inflammatory/chondrogenic exosomes for 2–4 weeks.

4. Chronic Wound Healing & Fibrosis

Indications: Diabetic Foot Ulcers, Post-Surgical Adhesions, Atopic Dermatitis.

- **Value:** Biodegradable HA barrier provides physical tissue shielding while exosomes stimulate angiogenesis and tissue remodeling.

5.2. Competitive Benchmarking for Biopharma BD Teams

Commercial Parameter	Systemic IV Therapeutics	Conventional Hydrogel Depot	Tink Innovation Platform
Dosing Frequency	Frequent (1–3x per week IV infusion)	Frequent due to rapid burst	Once every 2 to 4 weeks (Outpatient)
Systemic Toxicity	High (Off-target organ accumulation)	Initial burst toxicity risk	Minimal (Local confinement + <15% burst)
Patient Compliance	Low (Hospital visits, systemic side effects)	Moderate	High (Minimally invasive one-stop shot)
LCM / IP Extension	Facing patent cliff / generic erosion	Limited differentiation	Novel composition-of-matter exclusivity

SECTION 06

Intellectual Property & Patent Claims Architecture

The patent portfolio has been structured to establish a strong global defense perimeter. It features **11 fully drafted and amended claims** covering drug delivery compositions, tripartite molecular structures, thermo-responsive materials, release kinetics, and multi-step manufacturing processes.

6.1. Comprehensive Claims Matrix (11 Claims Structure)

Claim No.	Category	Key Inventive Scope & Legal Protection
Claim 1 (Independent)	DDS System (Composition)	Controlled-release system comprising surface-modified exosomes (Anchor-PEG Linker-Ligand) dispersed in a thermo-responsive sol-to-gel hydrogel scaffold .
Claim 2 (Dependent)	Anchor Compounds	Hydrophobic anchor selected from cholesterol, tocopherol, and C14–C22 saturated/unsaturated fatty acids.
Claim 3 (Dependent)	PEG Spacer Linker	PEG linker (MW: 1,000–5,000 Da) providing an outer hydration shield and 360° steric flexibility to the ligand.
Claim 4 (Dependent)	Targeting Ligand Target	Proteins, peptides, or antibody fragments specifically binding to EGFR (Epidermal Growth Factor Receptor).
Claim 5 (Dependent)	Hydrogel Network Structure	Cross-linked hydrogel network of thermo-responsive PNIPAAm and biodegradable Hyaluronic Acid (HA).
Claim 6 (Dependent)	Formulation Concentration	Scaffold formulated in PBS at a polymer solid concentration of 5.0 to 8.0 wt%.
Claim 7 (Dependent)	Temperature Phase Transition	Liquid sol at 20–28°C ($G'' > G'$), critical transition at 32.5–34.8°C, and solid gel at 36.5–37.0°C ($G' > G''$).
Claim 8 (Dependent)	Gel Storage Modulus (G')	Storage modulus (G') established within 10 to 15 kPa at 37°C physiological conditions.
Claim 9 (Dependent)	Burst Release Control	Cumulative exosome release restricted to < 15% within the initial 24 hours under physiological PBS.
Claim 10 (Dependent)	Synchronized Biodegradation	Day 14 scaffold degradation of 80–90% synchronized with 80–85% cumulative exosome release.
Claim 11 (Independent)	Manufacturing Method	(a) PEG-anchor intermediate synthesis → (b) Thiol-ligand Michael addition → (c) Spontaneous exosome insertion at 35–38°C → (d) Uniform dispersion into PNIPAAm-HA hydrogel.

6.2. Global IP Prosecution Roadmap

- Phase 1 Domestic KR Application:** Formally filed with the Korean Intellectual Property Office (KIPO); claim amendments completed.
- Phase 2 PCT International Application (Current Stage):** Preparation of PCT filing to secure a 30-month global priority window.
- Phase 3 National Phase Entries:** Target key markets including the United States (USPTO), Europe (EPO), Japan (JPO), and China (CNIPA), tailored to partner commercial priorities.

SECTION 07

R&D Status & Co-Development Framework

The core invention is currently at the **Proof-of-Concept (PoC) & Patent Molecular Design Stage**. The chemical synthesis protocols, reaction parameters, and mathematical release models are clearly established in the specification. Tink Innovation is seeking global biopharma collaborators to jointly execute preclinical proof, pilot batch synthesis, and translational in vivo studies.

⚠ Transparency & Development Status Notice:

The patent is currently filed in Korea and preparing for PCT international filing. The performance parameters outlined in this proposal reflect our finalized patent architecture and kinetic modeling. Physical wet-lab synthesis, GMP pilot manufacturing, and formal GLP animal studies will be conducted collaboratively with licensing partners.

7.1. 4-Phase Co-Development & Commercialization Milestones

Stage	Primary R&D Objectives & Tasks	Timeline	Key Deliverables & Milestones
Phase 1 (Pilot Synthesis & In Vitro)	- Custom synthesis of anchor-linker conjugates with partner's target ligands - GMP-compatible exosome isolation & HA-PNIPAAm hydrogel formulation	6 – 9 Months	In vitro validation (receptor binding affinity, sol-gel transition, release kinetics)
Phase 2 (Preclinical In Vivo POC)	- In vivo disease model validation (e.g., orthotopic tumor / stroke models) - PK/PD, biodistribution tracking, local retention, and GLP toxicology	12 – 15 Months	Preclinical safety/efficacy dossier & optimal dosing parameters
Phase 3 (Scale-Up & IND Filing)	- Scalable upstream/downstream CMC batch validation - Investigational New Drug (IND) package submission (FDA / EMA / MFDS)	12 – 18 Months	IND Approval for Phase 1 Clinical Trials
Phase 4 (Global Clinical Trials)	- Phase 1/2a clinical trials (Safety, tolerability, proof-of-concept efficacy) - Indication expansion & commercial manufacturing setup	24+ Months	Clinical study reports (CSR) & global market launch

7.2. Collaborative Division of Responsibilities

Tink Innovation (Licensor Role)

- Grant exclusive/non-exclusive patent rights & know-how.
- Anchor-linker molecular design & synthesis protocol transfer.
- Consulting on hydrogel cross-linking and rheology optimization.
- Coordination with IP counsel for PCT & national phase prosecution.

Global Biopharma Partner (Licensee Role)

- Funding milestone-driven collaborative R&D activities.
- Providing proprietary drug payloads (antibodies, RNA, small molecules).
- Conducting in vivo efficacy studies and GLP toxicology.
- Leading regulatory filings (IND/NDA) and commercial distribution.

SECTION 08

Licensing Models & Partnership Deal Structure

Tink Innovation offers flexible partnership structures tailored to align with our partner's therapeutic focus, risk preferences, and corporate strategy.

8.1. Partnership Models (Options A – C)

Model	Scope & Rights Granted	Ideal Partner Profile
Option A (Global Exclusive License) Worldwide Exclusive	- Worldwide exclusive rights across all therapeutic indications - Upfront license fee + development/regulatory milestones + tiered running royalties	Tier-1 global pharmaceutical enterprises seeking an exclusive DDS platform across multiple pipeline assets.
Option B (Field-Specific License) Indication-Restricted	- Exclusive rights restricted to a specific therapeutic area (e.g., Oncology only or CNS only) - Flexible upfront and milestone terms	Mid-to-large biopharmaceutical firms focusing on specific therapeutic franchises.
Option C (Co-Development + Option) Feasibility + Buyout Option	- Joint Phase 1 pilot feasibility program with pre-agreed Go/No-Go criteria - Exclusive option to acquire full global license or patent assignment upon success	Biopharma companies seeking data validation prior to long-term licensing commitments.

8.2. Standard Term Sheet Architecture

- 1. Upfront Payment** Fixed license access fee payable upon execution of the definitive agreement.
- 2. Development Milestones** Success-based payments upon completion of Phase 1 In Vitro validation, IND approval, Phase 2 start, and NDA/BLA approvals.
- 3. Commercial Milestones** One-time tier payments upon achieving worldwide net sales thresholds (e.g., \$500M, \$1B).
- 4. Running Royalties** Competitive single-to-double digit tiered royalty on global net annual product sales.

SECTION 09

Company Overview & Next Collaboration Steps

Licensor Overview (Company Profile)

Company Name	Tink Innovation (팅크이노베이션)
Representative / CEO	Sungchu Kang (강성추)
Headquarters	Seoul, Republic of Korea
Core Focus	Next-Generation Bio-DDS Platform Development, Surface Engineering of Extracellular Vesicles & IP Licensing
Contact Email	staping@naver.com

Next Steps for Partnership

- 1. Initial Expression of Interest:** Review this proposal and signal initial business interest.
- 2. Confidential Disclosure Agreement (CDA):** Execute a standard bilateral NDA for technical disclosure.
- 3. Technical Deep-Dive / Virtual Meeting:** Scientific teleconference between technical and business teams.
- 4. Term Sheet Negotiation:** Finalize deal framework and execute the co-development agreement.

 Concluding Remarks & Partnership Vision:

The future of advanced biologics requires the convergence of biological compatibility and smart mechanical control. **Tink Innovation** is dedicated to delivering cutting-edge DDS platforms that enhance therapeutic precision and patient outcomes. We look forward to partnering with your business development and R&D teams.

Tink Innovation — Global Business Development & Licensing Office

- **Executive Contact:** Sungchu Kang (CEO) | Email: staping@naver.com
- **Location:** Seoul, Republic of Korea

* This proposal is prepared exclusively for technology evaluation and licensing discussions. Full specification files, claim listings, and technical dossiers are available upon execution of a CDA.