

Multi-Omics & Physics-Informed AI De Novo Drug Candidate Automated Design Core Patent Licensing Proposal

Next-Generation Macrocyclic Peptide & Biologics In Silico Generation Platform
Integrating Dynamic Clinical Mutation Profiles and Real-Time Physicochemical Energy
Feedback

3 ~ 6 Months

Lead discovery timeframe
compression
(>80% R&D cost & time reduction)

Steric Clash ≈ 0

Real-time potential energy gradients
guaranteeing physical synthesizability

Undruggable PPI

Targeting dynamic cryptic pockets
& clinical resistance (e.g., K-RAS G12D)

Tink Innovation

CEO: [Sung-Chu Kang](#) | Business Development & IP
Division

Contact: staping@naver.com

Headquarters: Seoul, Republic of Korea

IP Status: KR Patent Filed (Priority Secured) | PCT
Prep in Progress

Executive Summary & Table of Contents

Strategic Purpose & Proposal Overview

Tink Innovation respectfully submits this Technology Transfer Proposal to global pharmaceutical leaders for out-licensing, patent buyout, or collaborative development of our proprietary invention: *"System and Method for Automatically Designing De Novo Drug Candidates Using Generative Artificial Intelligence Based on Multi-Omics Mutational Profiles and Physicochemical Potential Feedback."*

The core patent has been **officially filed with the Korean Intellectual Property Office (KIPO)**, establishing our global priority date. We are currently preparing the **PCT international patent application**, offering an extraordinary ground-floor entry window for global biotech partners.

KEY VALUE PROPOSITIONS

- **Compression of Discovery Cycles:** Reduces target-to-lead discovery timelines from 4–6 years to just 3–6 months while slashing early R&D costs by over 80%.
- **Elimination of Steric Clashes:** Solves AI unphysical artifacts by dynamically injecting physicochemical force gradients into every reverse denoising step.
- **Multi-Objective Co-Optimization:** Simultaneously optimizes target affinity, conformational stability, and membrane/BBB permeability in a single pipeline.

DEVELOPMENT STAGE & DEAL SCOPE

- **Current Readiness:** In Silico algorithm architecture, thermodynamic potential formulation, and computational PoC completed (Pre-Wet Lab Stage).
- **Flexible Partnership Models:**
 - ① Global Patent Buyout / Full Assignment
 - ② Field-Exclusive Licensing (e.g., Oncology, CNS)
 - ③ Co-Development with Big Pharma Wet-Lab Validation

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Global Drug Discovery Bottlenecks & Paradigm Shift

The Structural Crisis in Traditional HTS and 1st-Generation Computational Screening

Bringing a novel drug to market currently demands 10–15 years and exceeds \$2.6 billion, yet Phase II/III clinical failure rates remain stubbornly above 90%. Traditional High-Throughput Screening (HTS) and early machine learning models have failed to resolve fundamental thermodynamic and biological barriers.

BOTTLENECK 1: SPACE BOUNDS

Chemical Library Limitation

HTS relies on pre-synthesized compounds, exploring less than 10⁻⁵⁰% of theoretical chemical space (10⁶⁰) and failing to yield novel chemotypes.

BOTTLENECK 2: STATIC TARGETS

Neglect of Clinical Mutations

Standard 3D prediction models (e.g., AlphaFold) target static wild-type proteins, losing binding affinity when point mutations or resistance emerge in oncology patients.

BOTTLENECK 3: PHYSICAL FLAWS

Steric Clash & PK Failure

Pure deep learning hallucinations ignore Lennard-Jones repulsions, outputting molecules with atomic clashes or fatal bioavailability (poor BBB/membrane permeability).

Comparative Benchmark: Traditional HTS vs. 1st-Gen AI vs. Tink Innovation

Metric / Parameter	Traditional HTS	1st-Gen Structure AI	Tink Innovation Platform
Discovery Cycle	4 – 6 Years	1 – 2 Years	3 – 6 Months (>80% Reduction)
Scaffold Generation	Chemical Modification of Library	Docking against fixed PDB	De Novo Generation from Ground State
Mutation Responsiveness	Static In Vitro Assays	Fixed Wild-Type Structure	Multi-Omics Dynamic Ensemble Integrated
Physical Rigor	Empirical Retrosynthesis	Virtual Score Only (Clashes Frequent)	Real-Time Potential Energy Gradient Feedback
PK / Permeability	High Late-Stage Attrition	Sequential Post-Hoc ADME Filtering	Single-Pipeline Co-Optimization via Encoders

 **Market Opportunity:** Tink Innovation’s patented system is engineered to crack high-value, flat-surface protein-protein interactions (PPI) and historically **"Undruggable" targets (e.g., K-RAS, Myc, β-catenin)** by generating physically validated macrocyclic peptides with intrinsic drug-likeness.

Core Technology: Multi-Omics & Physics-Informed AI

The patented system operates via a closed-loop architecture consisting of (1) Multi-Omics Profiler, (2) Physics-Informed Generative Diffusion Engine, (3) Multi-Objective Optimization Module, and (4) Synthesizability Output Interface.

System Architecture & Algorithmic Workflow

- 01 Multi-Omics Profiling & Dynamic Conformational Ensemble Extraction**
Extracts tumor-specific point mutations (e.g., K-RAS G12D/V) from TCGA, CCLE, and patient biopsy data, generating dynamic 4D ensembles ($S = \{s_1, s_2, \dots, s_k\}$) via molecular dynamics (MD) simulations.
- 02 Physics-Informed Reverse Denoising Process**
During each reverse diffusion timestep ($t \in [0, 1]$) over 3D coordinates (X_t) and residue features (H_t), calculates analytical physicochemical potential gradients ($-\nabla_{X_t} E_{\text{total}}$) to guide generative trajectories.
- 03 Multi-Objective Pareto Selection Engine**
Filters candidates through a joint loss function evaluating binding free energy (ΔG_{bind}), folding stability (ΔG_{stab}), membrane permeability (P_{app}), and MHC-I/II immunogenicity scores.

[Mathematical Model 1] Real-Time Physicochemical Total Potential Energy (E_{total})

$$E_{\text{total}}(X, H) = E_{\text{vdw}}(X) + E_{\text{elec}}(X) + \Delta G_{\text{solv}}(X, H) + E_{\text{strain}}(X)$$

• Van der Waals (E_{vdw}) & Electrostatics (E_{elec})

Lennard-Jones 12-6 potential applies infinite repulsive forces upon atomic overlap, **mathematically eliminating steric clashes**, while Coulombic forces establish optimal hydrogen-bonding networks.

• Solvation Free Energy (ΔG_{solv}) & Torsional Strain (E_{strain})

Calculates implicit aqueous/tumor desolvation penalties and enforces Ramachandran-compliant dihedral angle bounds, ensuring **high thermodynamic stability and native foldability**.

Multi-Objective Optimization & Competitive Edge

Unlike single-metric generative tools that maximize in silico binding at the expense of drug-likeness, Tink Innovation's patent integrates proprietary modules for **conformational rigidity** and **membrane permeability**.

CLAIM 2 MECHANISM

Macrocyclic Peptide Scaffold Rigidity Control

- Specializes in 8–30 amino acid macrocyclic peptides.
- Evaluates head-to-tail / side-chain cyclization feasibility during intermediate diffusion steps.
- Locks the 3D backbone into rigid bioactive conformations, conferring extreme proteolytic resistance against serum proteases and minimizing entropic binding penalties.

CLAIM 3 MECHANISM

Permeability-Inducing Side-Chain Dynamic Encoder

- Dynamically orientates polar vs. hydrophobic side-chains based on environmental dielectric constants.
- "Chameleon-like" Conformation:** Presents a hydrophilic surface in systemic circulation and rotates hydrophobic moments outwards when entering lipid bilayers, maximizing passive cell/BBB permeability.

Technological Comparison: Tink Innovation vs. Leading Global AI Drug Platforms

Evaluation Dimension	Structure Prediction (e.g., AlphaFold-based)	Sequence LLM Models (e.g., ProtGPT2-based)	Tink Innovation Patent System
Physics Integration	Post-hoc molecular mechanics filter (High Latency)	None (Pure statistical pattern matching)	Real-Time Potential Energy Gradient Backpropagation
Resistance Profiling	Static reference crystal PDB only	Limited mutation generalization	Dynamic Multi-Omics Ensemble Conditional Layer
Modality Optimization	Predominantly small molecules	Linear peptides / proteins	Macrocyclic Peptides & De Novo Scaffolds
Permeability Optimization	Empirical $\text{ext}\{\text{LogP}\}$ post-filtering	Unpredictable in vivo kinetics	Active Chameleon Side-Chain Spatial Re-alignment

In Silico Proof of Concept: K-RAS G12D Validation

Validation on Undruggable Oncogenic Target: K-RAS G12D (PDB ID: 6X0A)

To validate the algorithmic efficacy of the patented system, we conducted computational simulations targeting the dynamic pocket of **K-RAS G12D** (a notorious oncogenic driver in pancreatic and colorectal cancers) generating 10–15 mer macrocyclic peptides under strict comparative controls.

[Patent Specification Table 1] In Silico Performance & Physicochemical Benchmark

Evaluation Metrics	Control Group A (Static PDB AI Model)	Control Group B (Affinity-Only Deep Learning)	Tink Innovation System (Multi-Omics + Physics-Informed)
Target Binding Free Energy (\$\Delta G_{\text{bind}}\$)	-7.2 kcal/mol	-9.8 kcal/mol	-13.5 kcal/mol (Marked affinity enhancement)
Thermodynamic Stability (\$\Delta G_{\text{stab}}\$)	-12.4 kcal/mol	-15.1 kcal/mol	-28.9 kcal/mol (~2x more stable fold)
Apparent Permeability (\$P_{\text{app}}\$)	\$1.2 \times 10^{-7} \text{ cm/s}\$	\$3.5 \times 10^{-7} \text{ cm/s}\$	\$2.4 \times 10^{-5} \text{ cm/s}\$ (68.5-fold improvement)
Steric Clash Frequency (Atomic Overlaps)	14.2 clashes / struct	8.6 clashes / struct	\$\leq 0.1\$ clash / struct (Unphysical flaws eliminated)
Cross-Variant Retention (G12V / G12R)	32.5%	41.0%	92.4% (High resistance resilience)

1. Guaranteed Synthesizability

By driving atomic collisions below 0.1 per structure, the system ensures that generated candidates correspond to valid local energy minima that can be directly synthesized by standard solid-phase peptide synthesis (SPPS).

2. Clinical Resistance Immunity

Retaining 92.4% binding affinity across secondary resistance mutations demonstrates that the platform extracts fundamental conserved binding pharmacophores rather than overfitting to static crystalline artifacts.

Patent Portfolio & Global IP Strategy

The patent estate is constructed with a robust, multi-layered claim architecture encompassing system architecture, macrocyclic scaffolds, permeability encoders, and automated computational methods.

Intellectual Property Metadata

Invention Title:

System and Method for Automatically Designing De Novo Drug Candidates Using Generative AI Based on Multi-Omics Mutational Profiles and Physicochemical Potential Feedback

Assignee / Owner:

Tink Innovation (팅크이노베이션) [CEO: Seong-Chu Kang]

Filing Status:

KR PATENT APPLICATION FILED (PRIORITY SECURED)

PCT INTERNATIONAL APPLICATION IN PREPARATION

IPC Classifications:

G16B 15/00 (Molecular Structural Prediction), G16B 40/00 (Biostatistical AI Algorithms), C07K 7/00

Patent Claims Structure & Global Protection Scope

Claim Number	Scope Category	Protected Technical Features & Defensible Perimeter
Claim 1 (Independent)	SYSTEM APPARATUS	- Multi-omics profiling engine for dynamic 3D conformational ensembles - Reverse diffusion module with real-time analytical potential energy gradient injection - Pareto multi-objective optimization engine balancing affinity, stability, and permeability
Claim 2 (Dependent)	MACROCYCLIC SCAFFOLD	- Constrained 8–30 residue macrocyclic peptide modality design - Automated N/C-terminal cyclization verification and backbone conformational rigidity control
Claim 3 (Dependent)	PERMEABILITY ENCODER	- Dynamic side-chain spatial rotation controlling amphiphilic dipole moments - Autonomous cellular membrane and blood-brain barrier (BBB) penetration optimization
Claim 4 (Independent)	COMPUTATIONAL METHOD	Stepwise execution: (a) Omics ensemble extraction → (b) Reverse diffusion coordinate correction via potential gradients → (c) Joint fitness screening of optimized sequences

 **Global PCT Expansion Opportunity:** Securing the Korean priority filing enables the acquiring partner to **directly participate in PCT national phase entries** across Tier-1 patent jurisdictions including the US (USPTO), Europe (EPO), Japan (JPO), and China (CNIPA).

Technology Readiness (TRL) & Wet-Lab Roadmap

Current Maturity: TRL 3 (Analytical Formulation & In Silico PoC Validated)

The core mathematical models, neural network architectures, and computational simulations (In Silico) are fully established and benchmarked. Physical synthesis and biological assay experiments (Wet-Lab) have not been conducted internally, creating a highly advantageous, de-risked valuation entry point for a global partner to lead the experimental validation phase.

4-Phase Co-Development & Commercialization Roadmap

Ph 1

[Completed] Priority Patent Filing & In Silico Model Architecture (TRL 3)

- Mathematical energy formulation & KIPO filing completed | • K-RAS G12D simulated PoC showing ≤0.1 clash score

Ph 2

[M+1 ~ M+3] PCT International Filing & Partner Target Ingestion (TRL 4)

- Formalize PCT national entries | • Ingest partner's proprietary target proteins (e.g., oncology, CNS, immunology)

Ph 3

[M+4 ~ M+9] SPPS Synthesis & In Vitro Experimental Validation (TRL 5)

- Solid-phase synthesis of top 10–20 generated peptides | • Surface Plasmon Resonance (SPR), BLI, and Caco-2 permeability assays

Ph 4

[M+10 ~ M+18] In Vivo PK/PD Characterization & Preclinical IND Enabling (TRL 6)

- In vivo xenograft efficacy, serum stability, mouse PK/PD profiles | • Preclinical IND filing dossier generation

TINK INNOVATION RESPONSIBILITIES

- Target-specific AI fine-tuning & candidate generation
- Patent prosecution support & priority filings
- In Silico structural analysis & multi-objective screening

GLOBAL PHARMA PARTNER RESPONSIBILITIES

- Designation of high-priority therapeutic targets
- Wet-lab chemical synthesis & in vitro / in vivo assays
- Preclinical/clinical development & global commercialization

Commercialization Deal Structures & Licensing Models

Tink Innovation proposes three flexible transaction frameworks tailored to the partner's internal R&D strategy, capital allocation, and corporate IP structure.

OPTION A: CO-DEVELOPMENT & MILESTONE LICENSING

Target-Specific Collaborative R&D & Commercial Royalties

Pharma partner designates 3–5 strategic targets. Tink Innovation deploys the AI engine to generate optimized hits; partner funds experimental validation. Remuneration via upfront technology access, milestone payments, and commercial royalties.

Upfront + Milestones + Royalty

OPTION B: FULL PATENT ASSIGNMENT (ASSET BUYOUT)

Complete 100% Transfer of Patent Rights & Algorithmic IP

Full worldwide ownership transfer of the filed Korean patent and PCT application rights to the partner. Enables the partner to internalize the entire AI drug discovery technology into their proprietary platform infrastructure.

Lump-Sum Asset Buyout

OPTION C: FIELD-EXCLUSIVE COMMERCIAL LICENSE

Therapeutic Field Exclusivity (e.g., Oncology, Rare Diseases)

Grants worldwide exclusive rights restricted to specific therapeutic domains (e.g., solid tumors or neurodegeneration), allowing specialized biotech to monopolize their core market while reducing initial capital commitments.

Field-Exclusive License

Deal Parameter	Option A (Co-Development)	Option B (Full Buyout)	Option C (Field License)
Strategic Value	De-risks early R&D with shared milestones	Total IP monopoly & internal platform integration	Targeted domain leadership at reduced upfront
IP Ownership	Platform (Tink/Joint) / Matter (Partner)	100% Partner Single Ownership	Platform (Tink) / Field Rights (Partner)
Ideal Partner	Large Pharma scaling disease pipelines	Biopharma building in-house AI powerhouse	Specialized therapeutic biotech leaders

Corporate Profile & Transaction Process

Company Overview (Tink Innovation)

Company Name:	Tink Innovation (팅크이노베이션)
Representative / CEO:	Sung-Chu Kang (강성추)
Headquarters:	Seoul, Republic of Korea
Core Mandate:	AI-driven De Novo drug discovery IP generation & global licensing
Official Inquiry:	staping@naver.com

Strategic Partner Advantages

- **First-Mover Global Rights:** Early participation in PCT filings allows co-applicant designation and territorial customization.
- **Custom In Silico Profiling:** Tailored screening runs on partner-designated target proteins prior to definitive closing.
- **High Valuation Upside:** Attractive pre-wet lab terms offering maximum ROI upon experimental validation.

Transaction Workflow & Next Steps

STEP Inquiry & Standard Mutual Non-Disclosure Agreement (NDA / CDA)

- 1 • Submit expression of interest to staping@naver.com; execute bilateral CDA to protect technical proprietary data.

STEP Technical Data Room Access & Deep-Dive Video Conference

- 2 • Detailed review of full patent claims, mathematical formulations, and algorithmic code architecture.

STEP Structure Selection (Option A / B / C) & Term Sheet Execution

- 3 • Alignment on financial terms, target definitions, milestone schedules, and IP ownership boundaries.

STEP Definitive Agreement Closing & Global PCT Filing Kickoff

- 4 • Execution of final license/assignment agreement and commencement of joint validation roadmap.

"Transforming Drug Discovery with Physics-Informed Generative AI"

Tink Innovation is ready to partner with global industry pioneers to conquer historically undruggable disease targets. We welcome discussions regarding technology out-licensing and co-development partnerships.

Direct Contact: SungChu Kang, CEO, Tink Innovation | **E-mail:** staping@naver.com