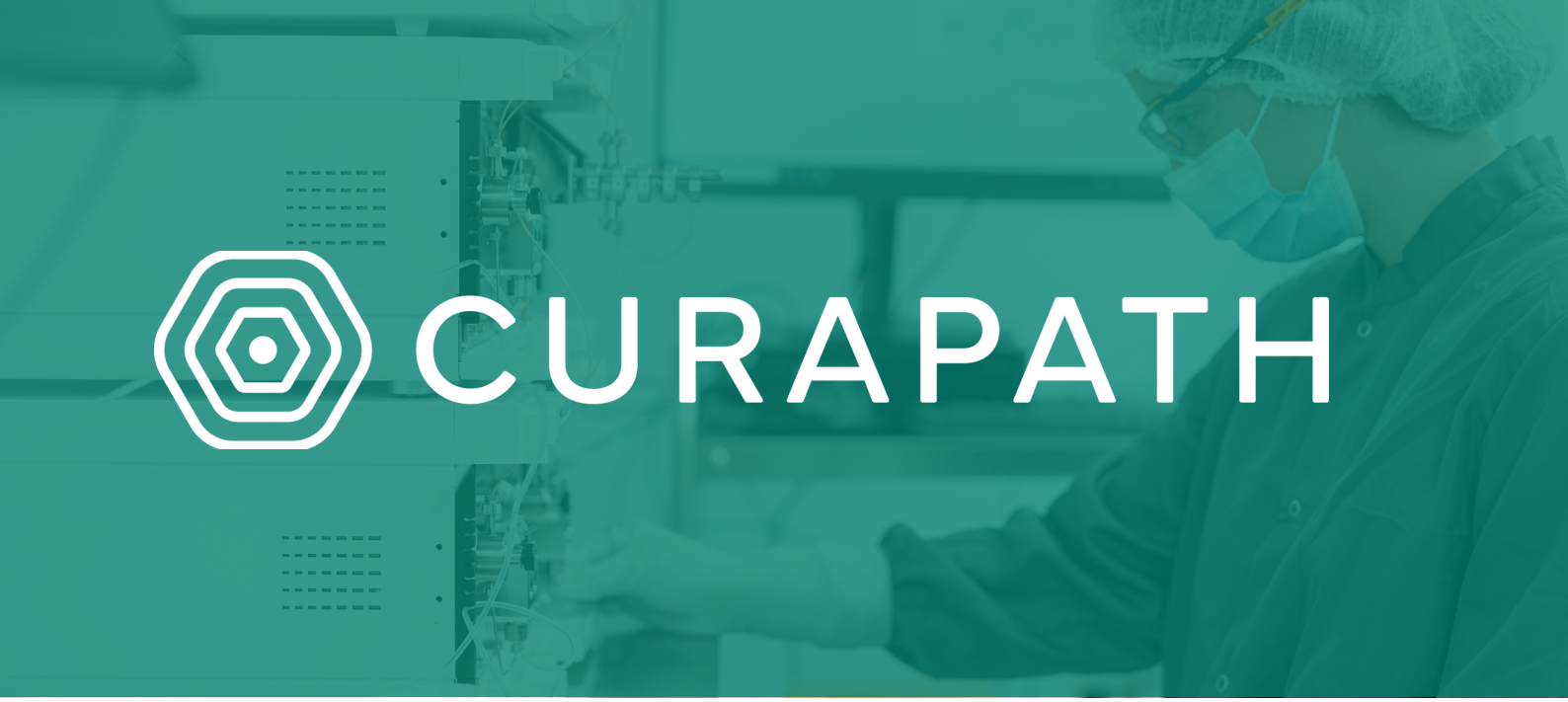
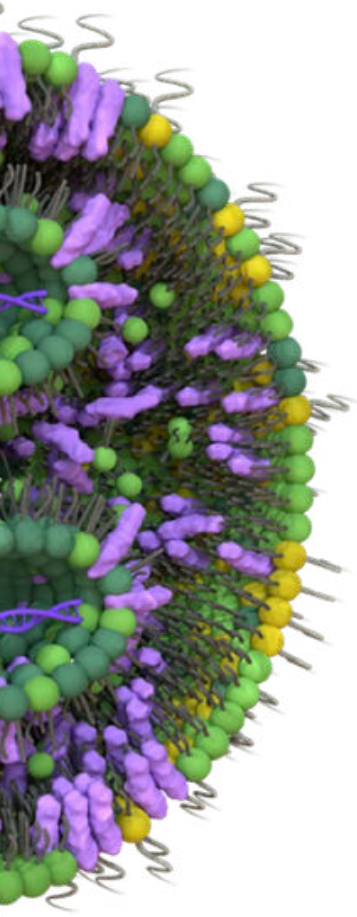


CURAPATH



PEG-Free Shielding Lipids

Product Highlight

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RESOURCES

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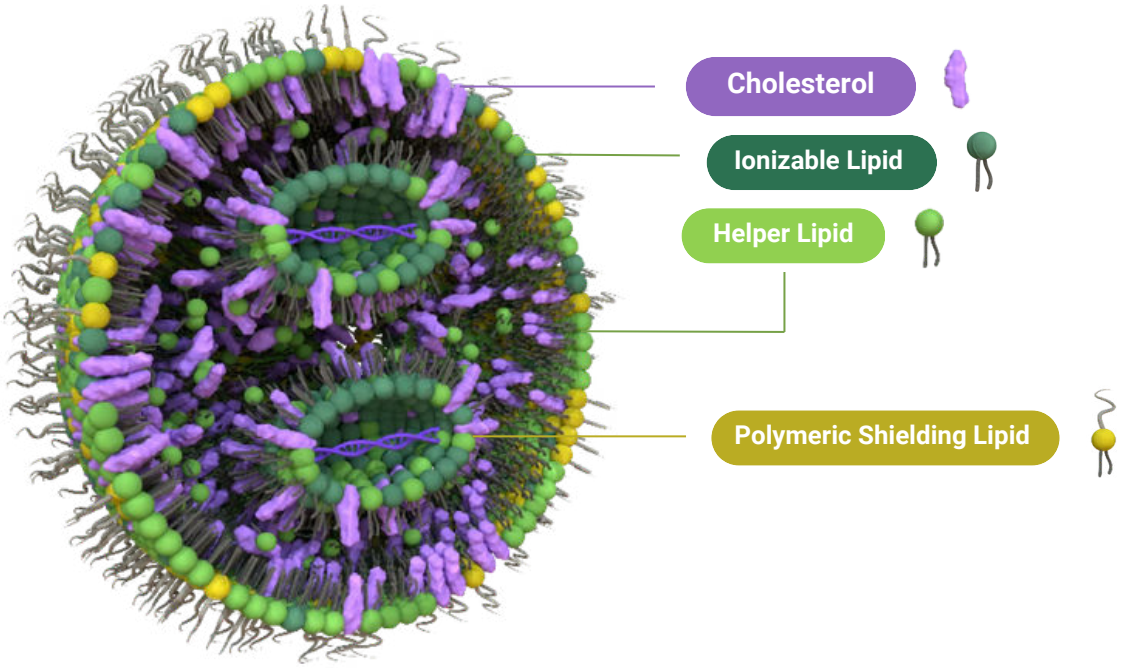
More than a CDMO

Shielding Lipids in LNP Formulations

Shielding lipids are essential structural components of lipid nanoparticles (LNPs) that create a protective, hydrophilic interface between the nanoparticle and the biological environment. By controlling how LNPs interact with proteins and immune cells, these lipids play a central role in determining circulation time, stability, and overall delivery efficiency of nucleic-acid–based therapeutics.



Key Contributions of Shielding Lipids

Hydrated steric protection

Reduces protein adsorption and immune recognition.

Enhanced stability

Prevents aggregation during formulation and storage for consistent.

Prolonged circulation

Enabling longer systemic exposure.

Optimized biodistribution

Improves in vivo performance and delivery efficiency.

Robust manufacturability

Supports reliable self-assembly & reproducible encapsulation.

The PEG Dilemma

Polyethylene glycol (PEG) has long been the gold standard shielding lipid for lipid nanoparticles, enabling extended circulation and improved stability. However, increasing evidence highlights important limitations associated with PEGylation. The so-called “PEG dilemma” reflects the balance between its protective benefits and emerging immunological and performance challenges.

Key Concerns about PEG

Anti-PEG antibodies

Pre-existing antibodies may accelerate clearance and reduce efficacy.

Accelerated blood clearance (ABC effect)

Repeated dosing can trigger faster elimination.

Potential immunogenicity

Hypersensitivity reactions have been reported in some cases.

Reduced cellular uptake

Strong steric shielding may hinder endosomal escape & intracellular delivery.

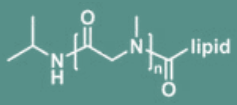
Regulatory & clinical scrutiny

Growing focus on PEG safety in advanced therapeutics.

PEG-Free shielding lipids for gene therapies and RNA vaccines

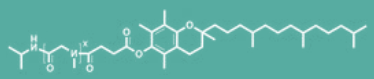
In response to the growing challenges associated with PEGylation, Curapath has developed a comprehensive portfolio of next-generation shielding lipids. Designed to maintain the benefits of steric stabilization while addressing immunogenicity and repeat-dosing concerns, our alternatives provide flexible, high-performance solutions for advanced LNP development.

Portfolio of PEG Alternatives



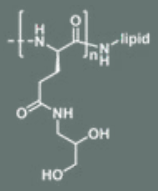
PSar

- Versatile
- Targeteable



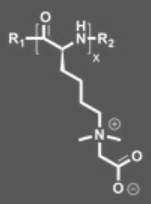
VitE-PSar

- Low bioaccumulation VS PEG
- Increased stability in solution
- Increased performance in LNP formulations Vs PEG



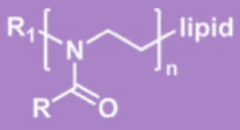
PGA-diol

- Biodegradable
- Increased performance in LNP formulations Vs PEG
- Long-term stability
- Ideal for freeze dryed LNPs



Pbetaines

- Zwitterionic
- Biodegradable



PAOx

- Tunable Platform

Product highlights
Stability

PEG-Free Stability: Curapath's shielding lipid eliminates the need for PEG

In addition to eliminating the need for PEG, Curapath's shielding lipid provides comparable steric stabilization to PEGylated formulations.

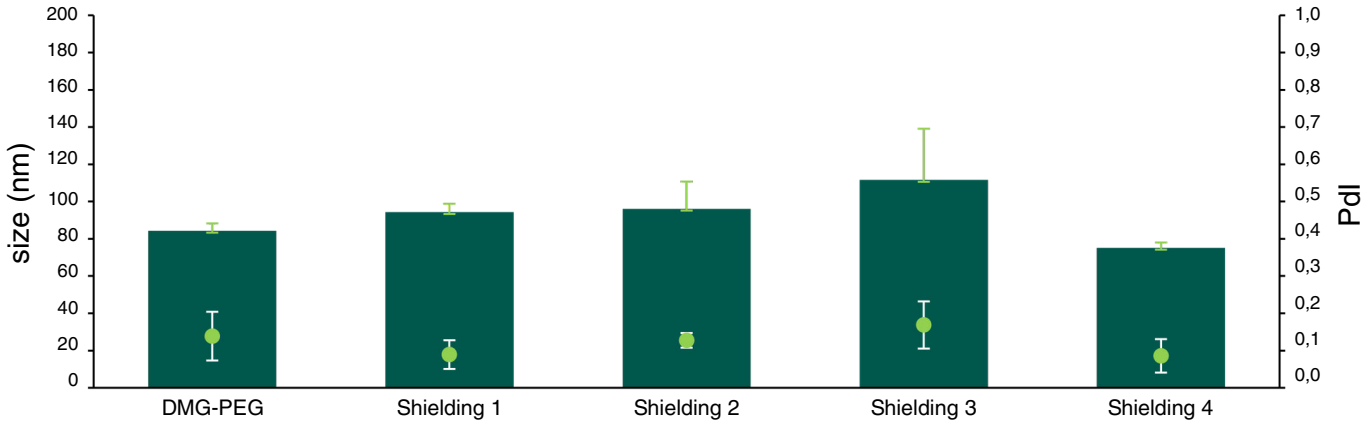


Figure 1. Size and polydispersity of LNP formulations using Curapath's lipids comparable to DMG-PEG LNP shielding formulations.

Curapath's shielding lipid technology enables Stable Lyophilize Formulations

Excellent stability after freeze-drying

Dependable particle size and performance in vivo

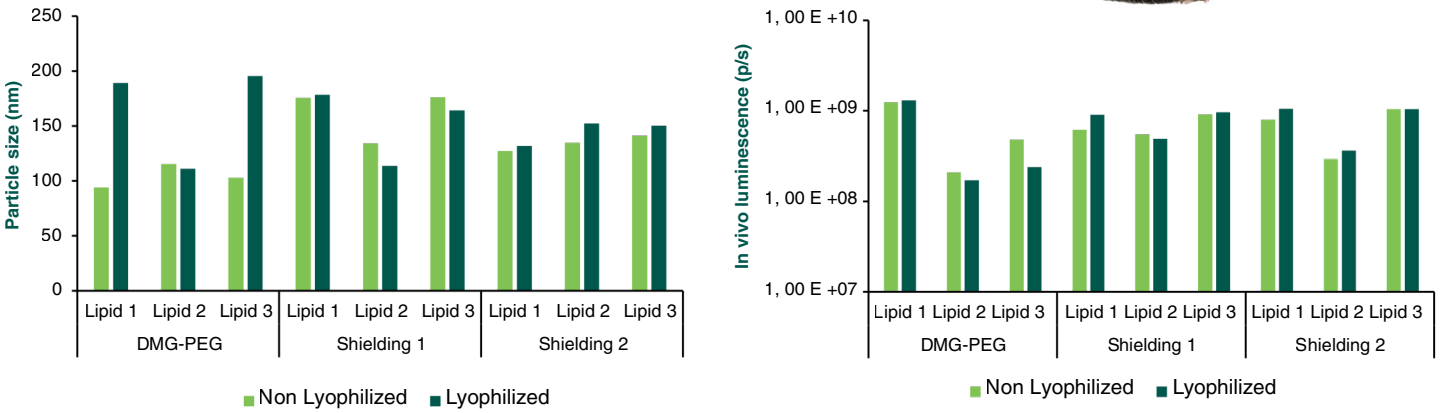


Figure 2. Particle size (left) and in vivo performance (right) of mRNA containing LNPs formulated with 3 different partnered ionizable lipids in combination with DMG-PEG, and 2 different Curapath's shielding lipids. Luminescence was measured 4 hours after intramuscular injection of 1 µg of Fluc mRNA/mouse.

Allows inhalated delivery of LNPs

Product highlights
In vivo performance

Outstanding in vivo Performance vs Gold standards

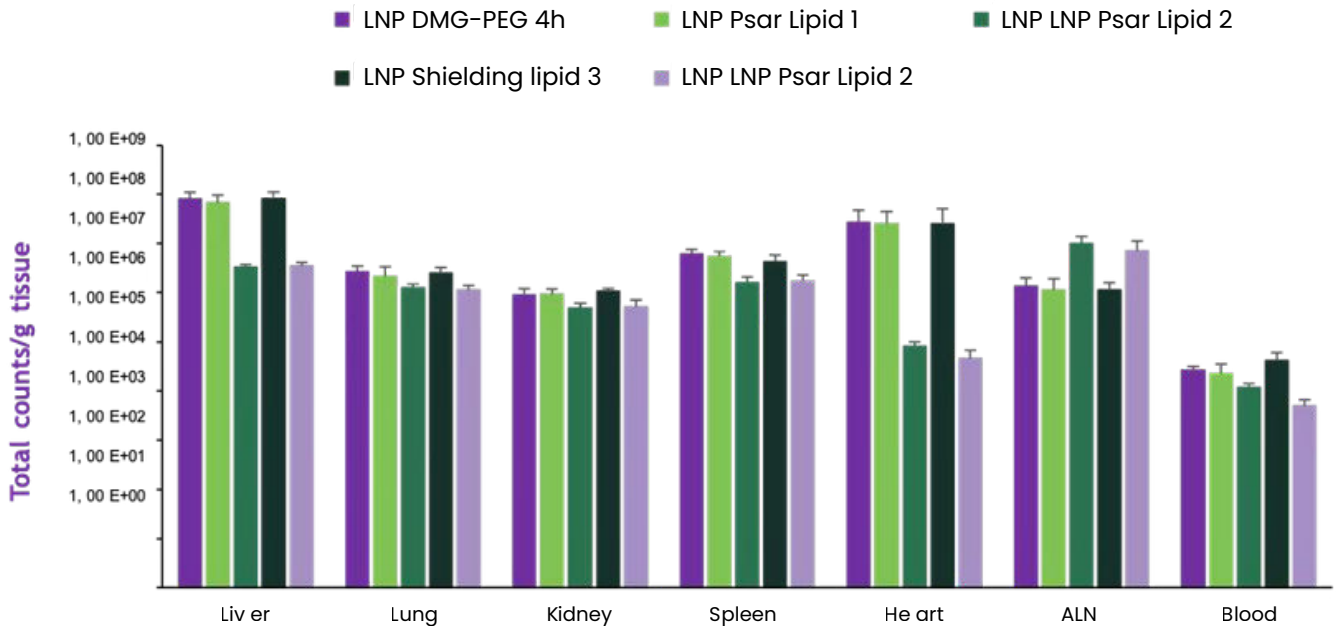


Figure 3. ***In vivo*** transfection efficiency in different organs 4 hours after intravenous administration of LNPs containing different shielding lipids(20µg mRNA/mice).

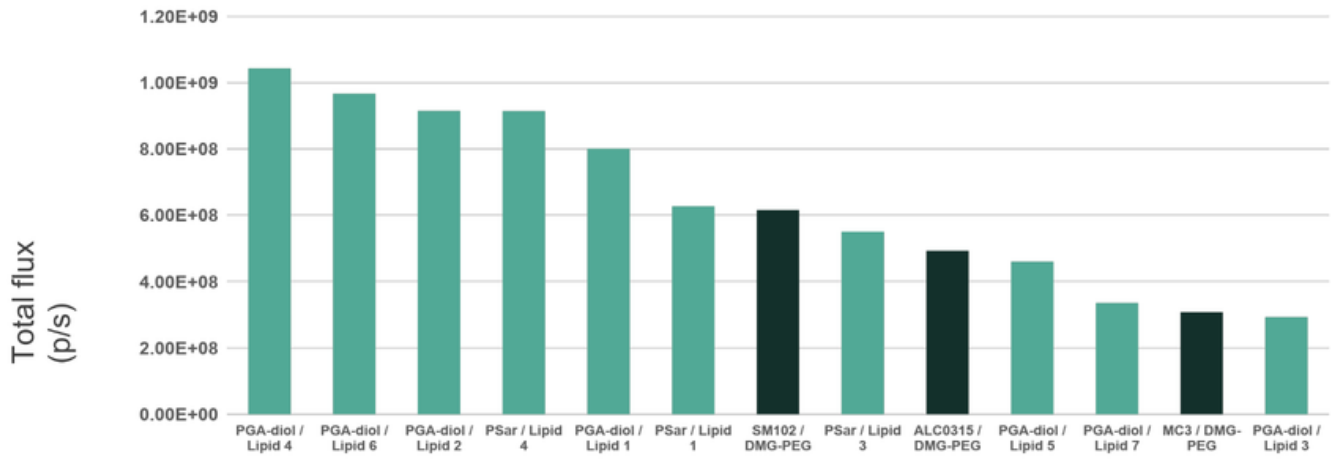


Figure 4. ***In vivo*** mRNA expression of LNPs formulated with Curapath's portfolio of ionizable lipids from strategic partner (Certest pharma) and proprietary Curapath's shielding lipids at 4 hours after intramuscular injection of 1 µg of Fluc mRNA/mouse compared to gold standard formulations.

Comparable biodistribution to PEGylated LNPs

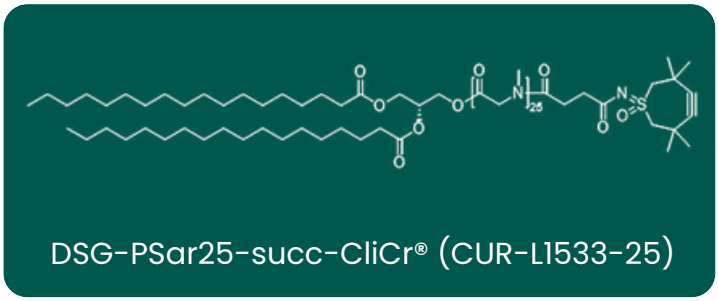
Consistently outperformed PEG in vivo

Ideal to substitute PEG in repeated dosing regimes

Enabling active targeting

By combining our **PEG-free shielding lipids with CliCr®** conjugation technology, **we enable the attachment of your targeting ligand of choice directly onto formulated LNPs**.

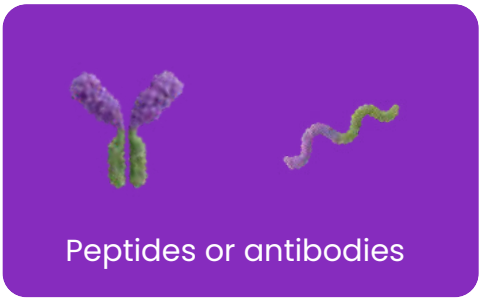
Targeting PEG-free shielding lipid



DSG-PSar25-succ-CliCr® (CUR-L1533-25)

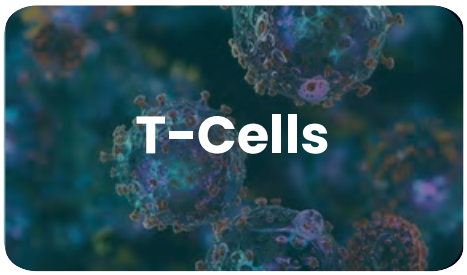
*more options in our catalog

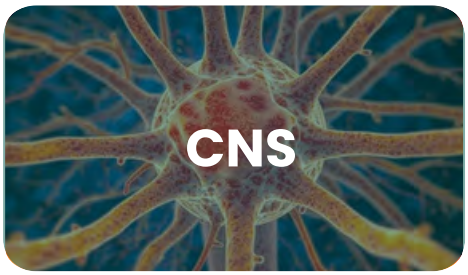
Targeting Ligand



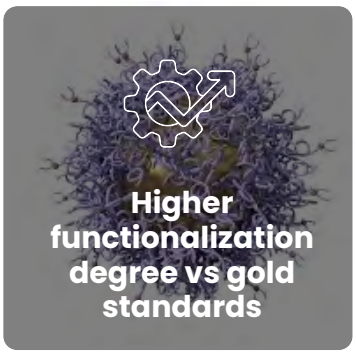
Peptides or antibodies

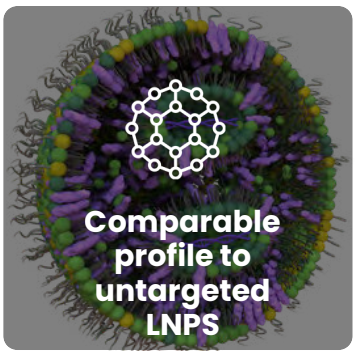
By using **Active Targeting, LNPs** can reach **therapeutic concentrations** in hard to reach **targets like**:

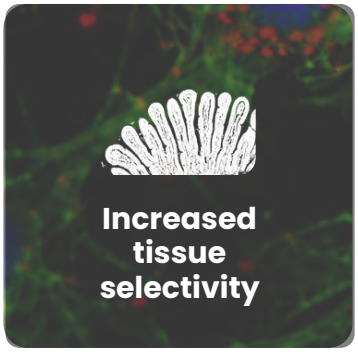




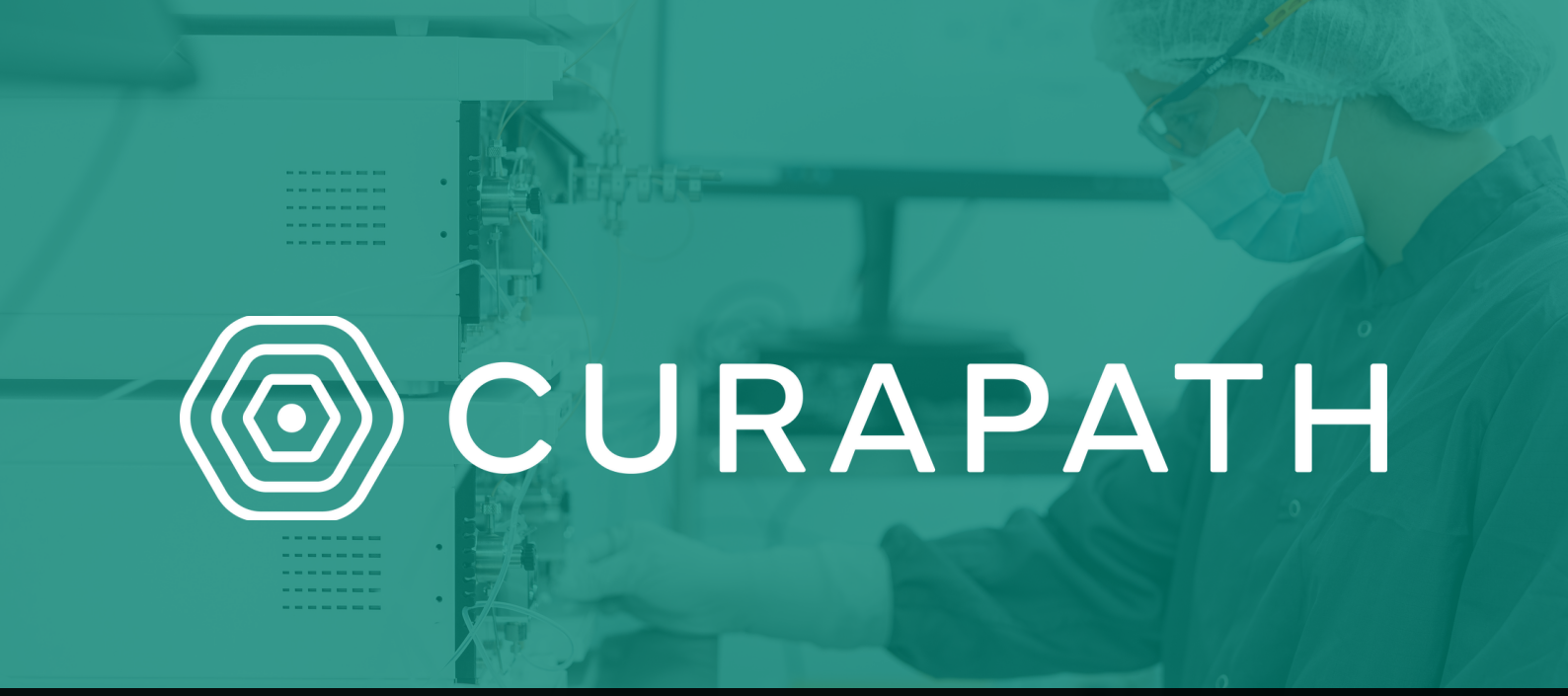
Key Advantages of this apporach







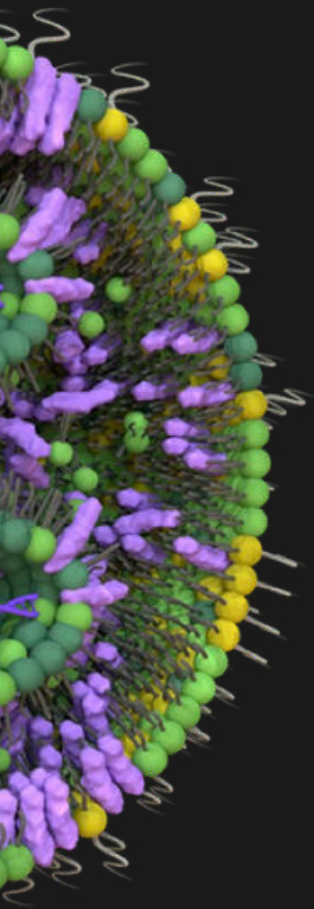
*R&D Grade



CURAPATH

PEG-Free Shielding Lipids

Product Highlight



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