CURAPATH

certest

PHARMA

Next generation Lipid Nanoparticle (LNPs) formulation with Certest's & Curapath's proprietary excipients

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Technical report

This collaboration aims to create an advanced LNP platform with improved performance and reduced immunogenicity, offering a safer and more efficient option for gene therapy, mRNA vaccines, and other therapeutic modalities. By **combining Curapath's extensive CDMO capabilities with Certest's innovative LNP formulation and lipid technologies**, this partnership opens new possibilities for pharmaceutical companies. With expertise in advanced lipid excipients, LNP formulation, and aseptic manufacturing, Curapath ensures streamlined access to cutting-edge solutions for safer and more effective drug delivery systems.

Certest's Advanced Ionizable Lipids

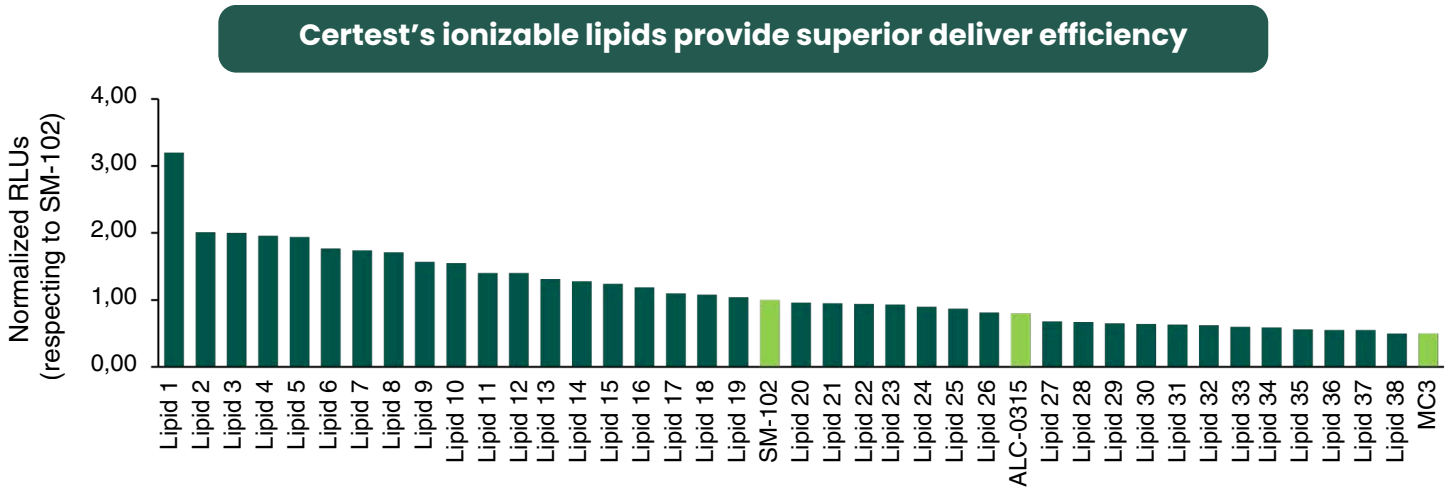

Figure 1. In vivo mRNA expression of LNPs formulated with Certest's ionizable lipids at 4 hours after intramuscular injection of 1 µg of Fluc mRNA/mouse compared to gold standard ionizable lipids.

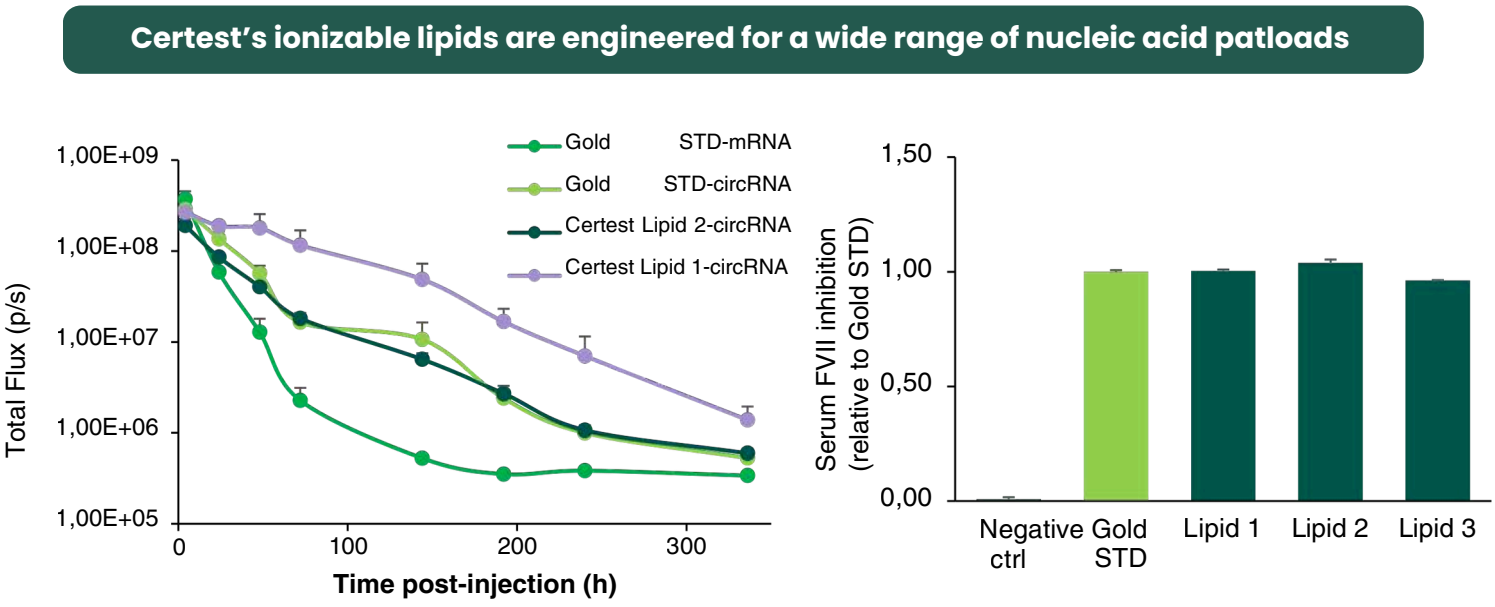

Figure 1. In vivo activity of different nucleic acid payloads encapsulated with Certest's ionizable lipids. (Left) CircRNA vs mRNA time-course expression after intramuscular injection of 1 µg. (Right) Serum inhibition of FVII expression 24 hours after intravenous injection of siRNA.

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Certest's ionizable lipids exhibit an excellent safety profile in preclinical studies

Certest's ionizable lipids show no signs of toxicity after single or repeated administrations.

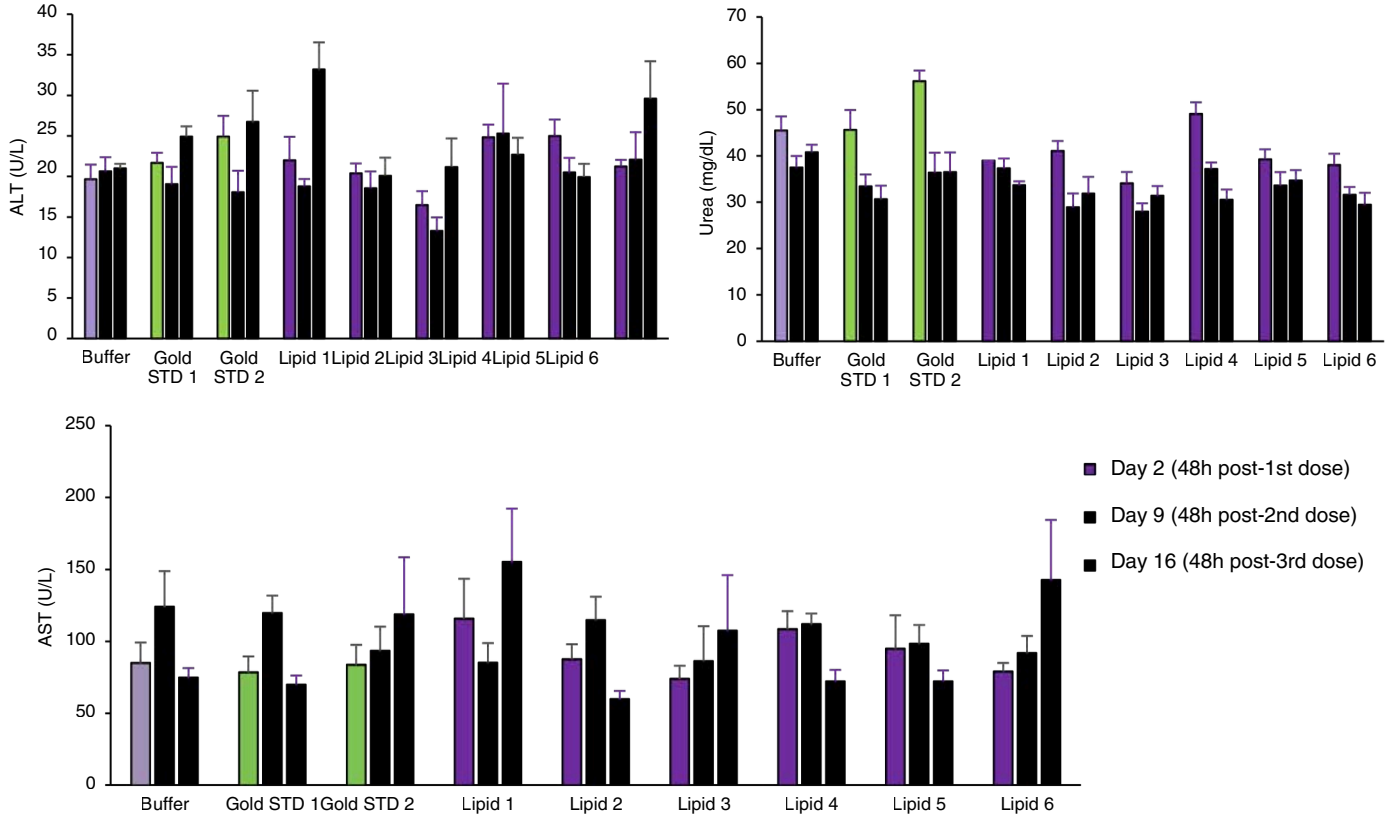

Figure 3. Serum biochemistry analysis of hepatic enzymes following in vivo administration of three weekly doses of 50 µg mRNA per animal, encapsulated with Certest's ionizable lipids.

Certest's ionizable lipid formulations can be successfully lyophilized and stored

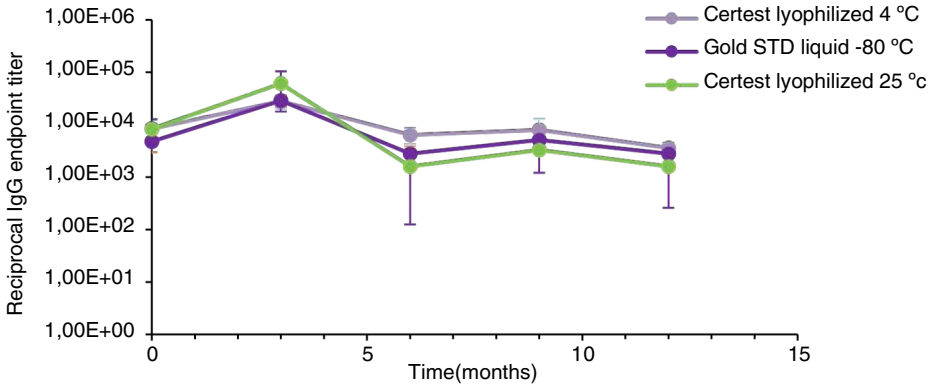

Figure 4. In vivo anti-RBD IgG production 21 days post-single intramuscular administration (1 µg mRNA/mouse) of a lyophilized SARS-CoV-2 vaccine formulated with Certest's ionizable lipids after different storage conditions for up to 1 year. Certest's lyophilized LNPs demonstrate long-term stability at both 4 °C and 25°C, maintaining their physicochemical properties and biological activity.

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Curapath's PEG-Alternative Shielding Lipid

Curapath's shielding lipids are produced with robust & scalable synthesis

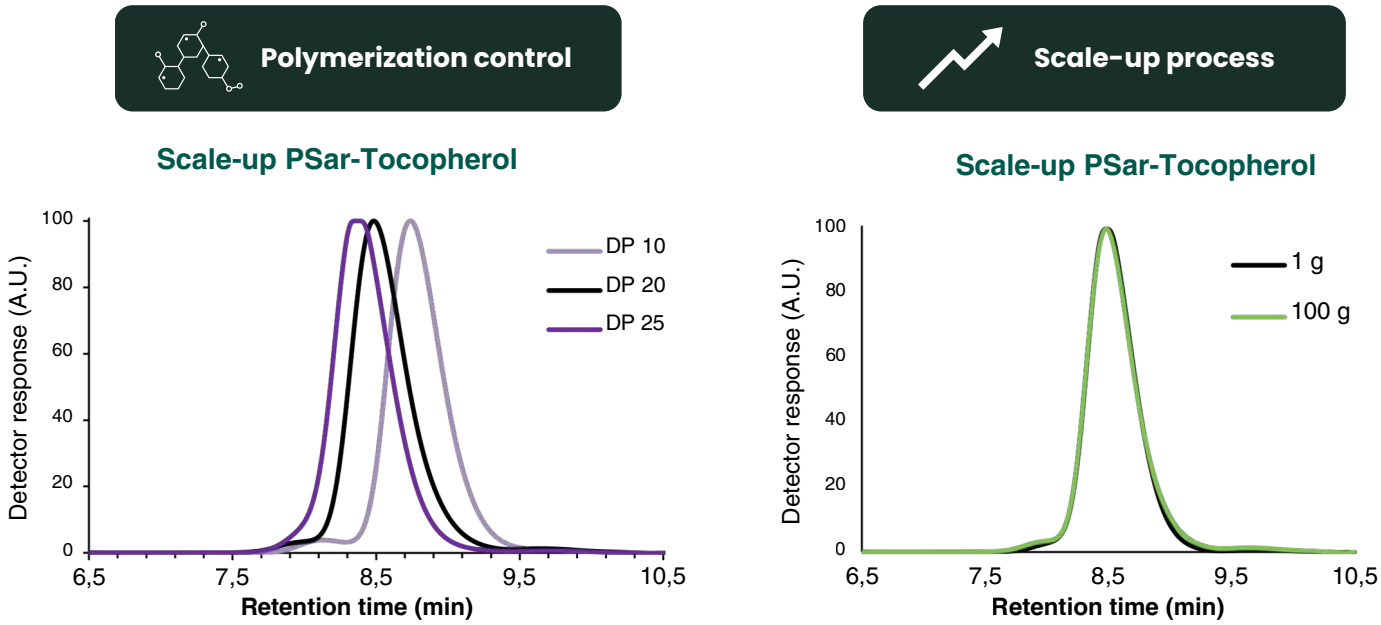

Figure 5. The shielding lipid is designed for reliable, large-scale production, ensuring a consistent and cost-effective supply for high-demand applications. This makes it ideal for scaling from preclinical development to commercial manufacturing. The SEC traces illustrate Curapath's control of polymerization degree and reproducibility upon the scale-up process for the Shielding 1 compound.

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.

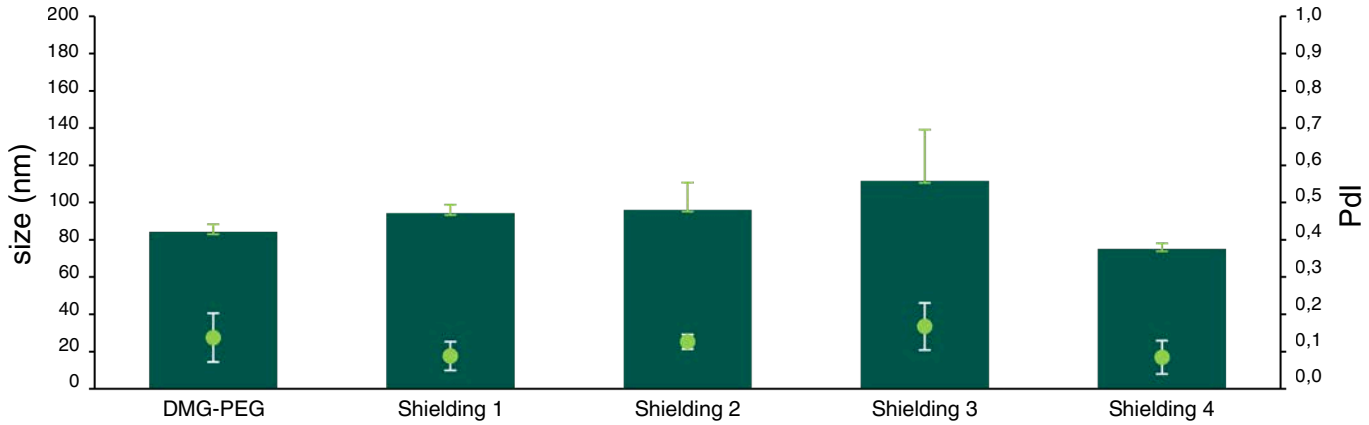

Figure 6. Size and polydispersity of LNP formulations using Curapath's lipids comparable to DMG-PEG LNP shielding formulations.

Technical report

Resilience in Freeze-Thaw Cycles

The shielding lipid maintains nanoparticle integrity even after multiple freeze-thaw cycles.

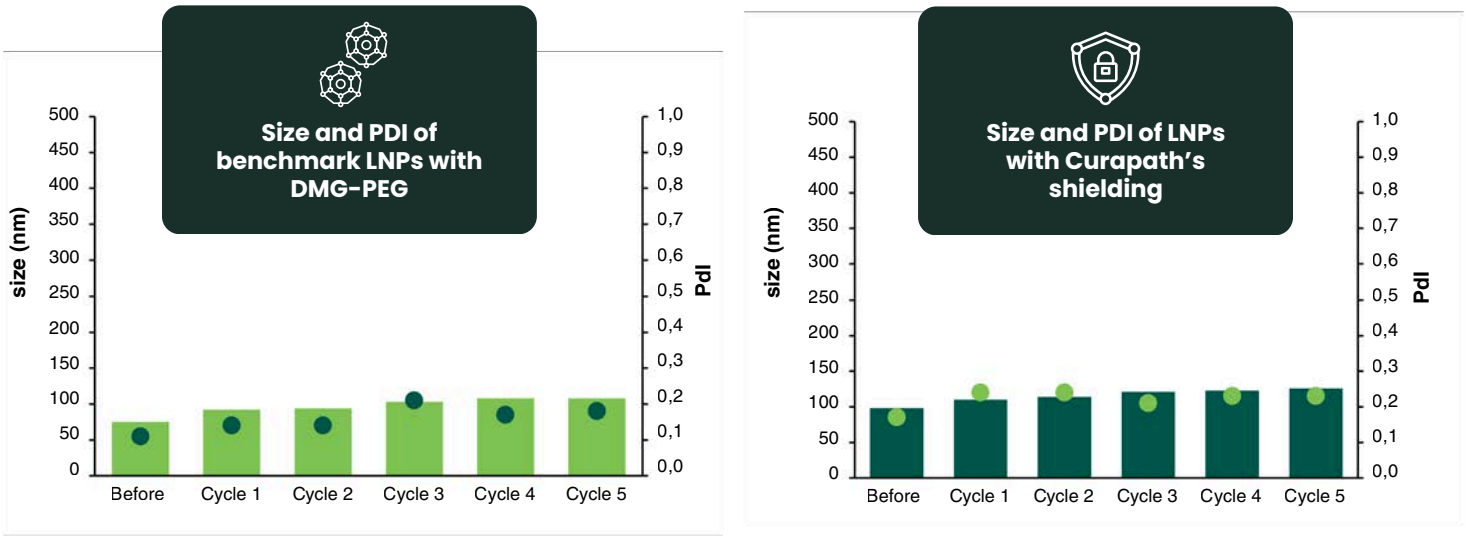

Figure 7. Size (diameter, nm) and polydispersity measurement sof LNPswith DMG-PEG and Curapath's shielding lipids.

Curapath'slipid consistently outperformed PEG-based formulations

By improving transfection efficiency and having comparable bio distribution to PEG, Curapath's lipid proves to be an ideal component to substitute PEG in repeated dosing regimens.

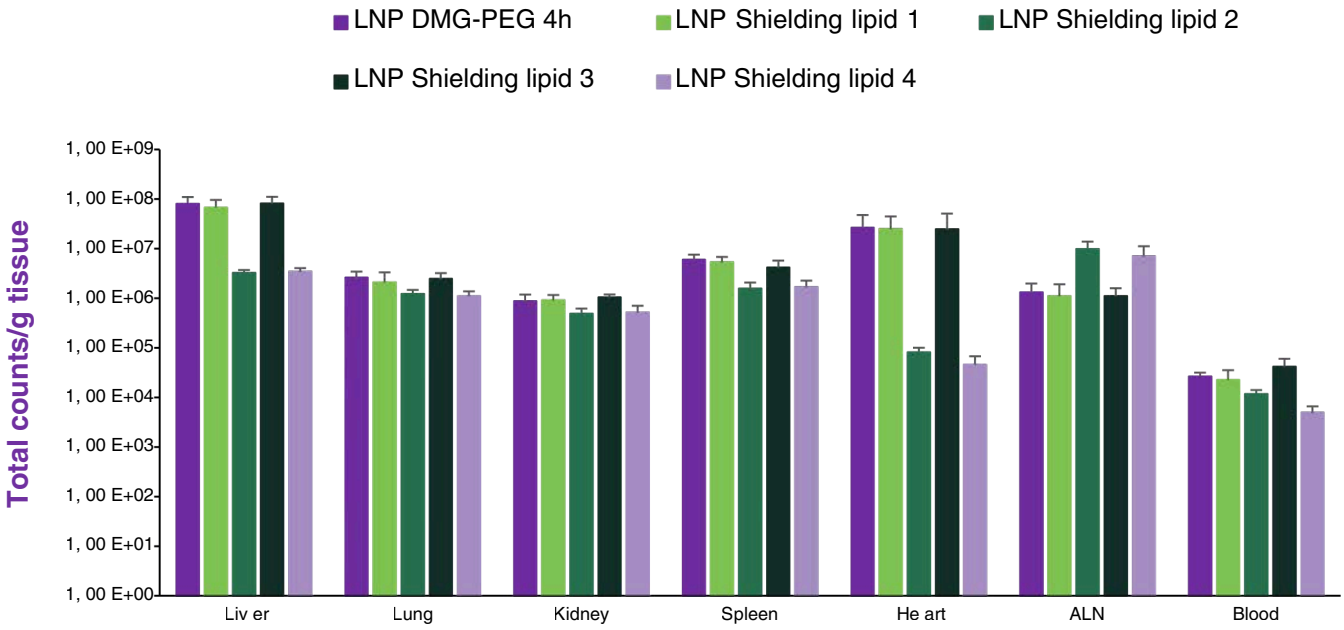

Figure 8. ***In vivo*** transfection efficiency in different organs 4 hours after intravenous administration of LNPs containing different shielding lipids(20µg mRNA/mice).

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The Power of Combination: Joint Formulation with Certest's Ionizable Lipids and Curapath's Shielding Lipids

By combining **Certest's versatile ionizable lipids and Curapath's PEG-alternative shielding lipids**, a synergistic LNP formulation is created, addressing key challenges in current LNP formulations and demonstrating strong potential for enhanced performance:

The joint formulation using Certest's ionizable lipids produces LNPs with a size distribution below 200 nm, facilitating enhanced cellular uptake and optimal stability with nucleic acids encapsulation efficiency over 95%, reducing the lipid-to-payload ratio and optimizing therapeutic efficacy.

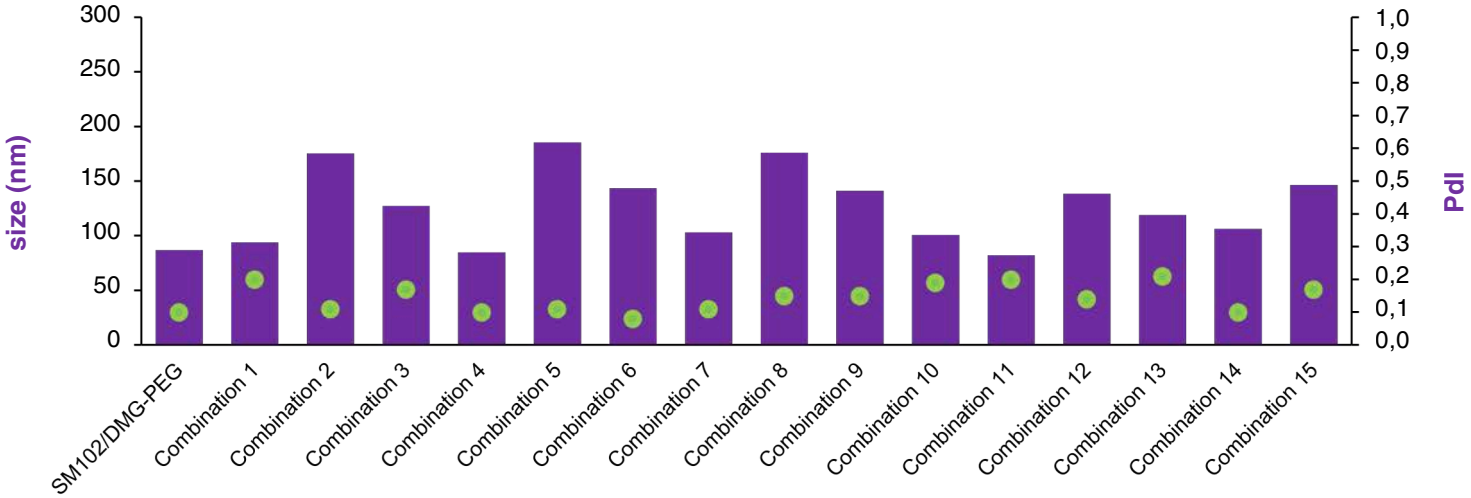

Figure 9. Size and polydispersity of LNP formulations using Curapath's shielding lipids in combination with Certest's ionizable lipids.

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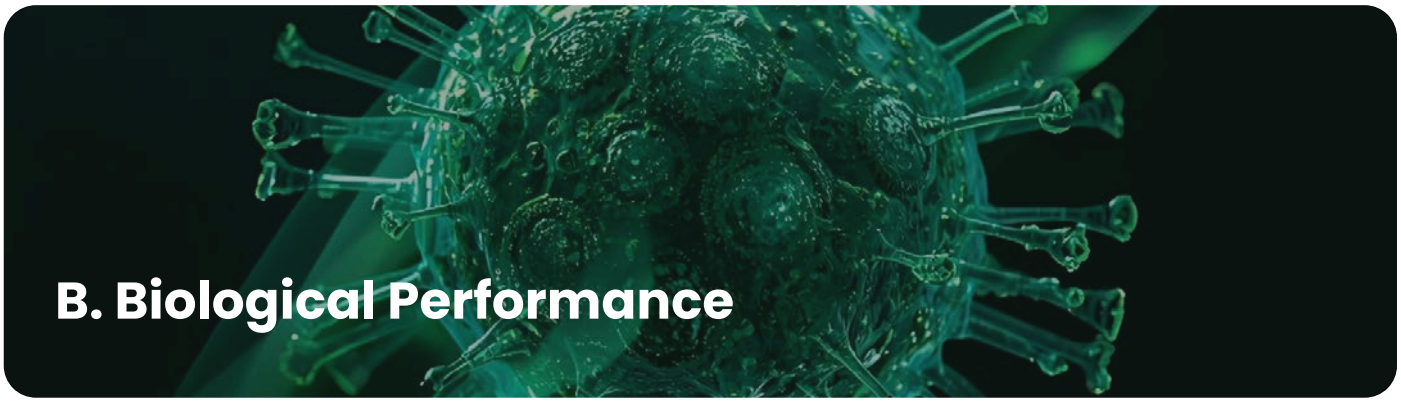

Increased Transfection Efficiency: The combination of Certest's ionizable lipid and Curapath's shielding lipid results in higher transfection rates ***in vitro***.

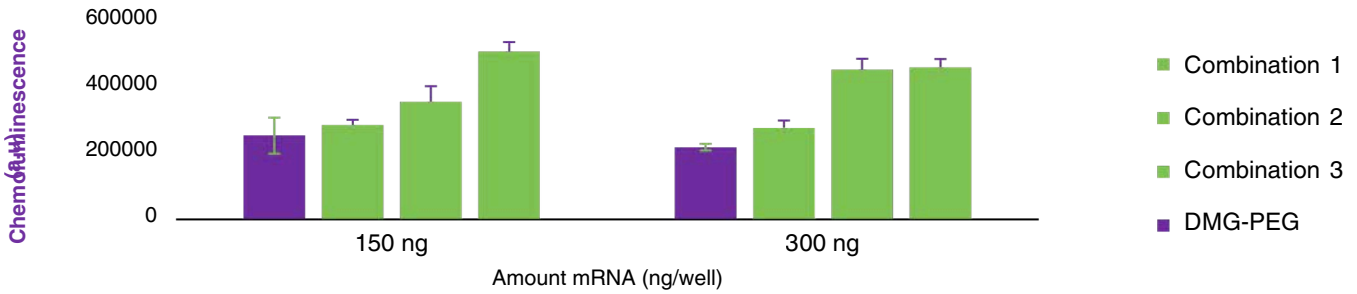

Figure 10. ***In vitro*** transfection of LNPs containing Certest's ionizable lipid with different Curapath's shielding lipids in HEK 293 cellline,after24 hoursofincubation.

Outstanding in vivo performance

The synergistic effects of Certest's and Curapath's technologies result in improved delivery and gene expression ***in vivo***, outperforming current gold standard LNP formulations with SM102 and DMG-PEG.

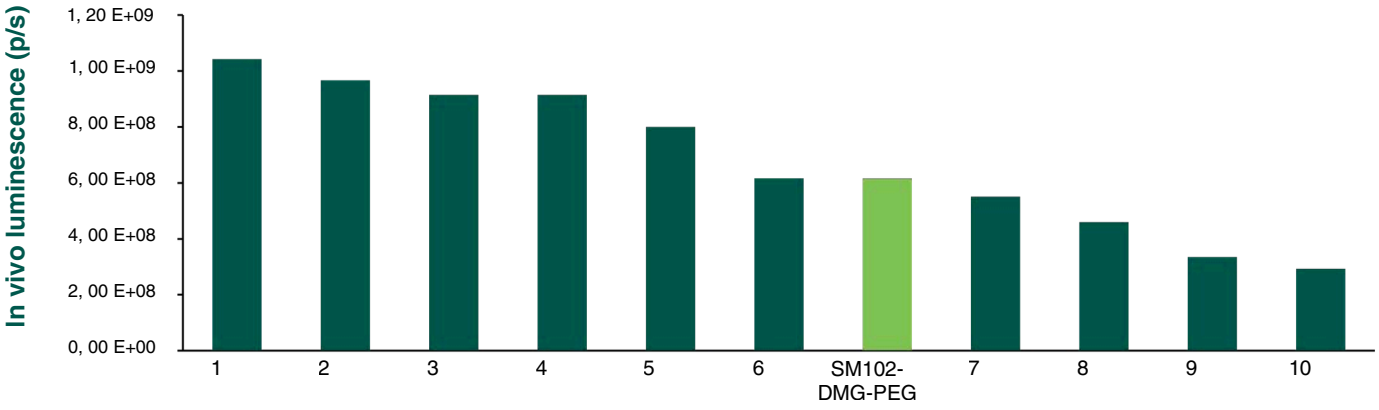

Figure 11. Quantification of ***in vivo*** luminiscence results obtained with a panel of different Certest ionizable lipids formulated with Curapath's Shielding Lipids. Luminescence was measured 4 hours after intramuscular injection of 1 µgofFlucmRNA/mouse.

Technical report

C. Freeze-Thaw and Lyophilization Stability Studies

Developed Lyophilized Formulation

To further enhance stability and enable long-term storage, a lyophilized version of LNP formulations including Certest's ionizable lipids and Curapath's PEG alternatives has been developed by Certest. This formulation retains the LNPs' structural integrity and, importantly, in vivo functionality after reconstitution, underscoring the high stability of these novel LNPs and offering more flexibility in storage and transportation, especially for global distribution in low-resource settings.

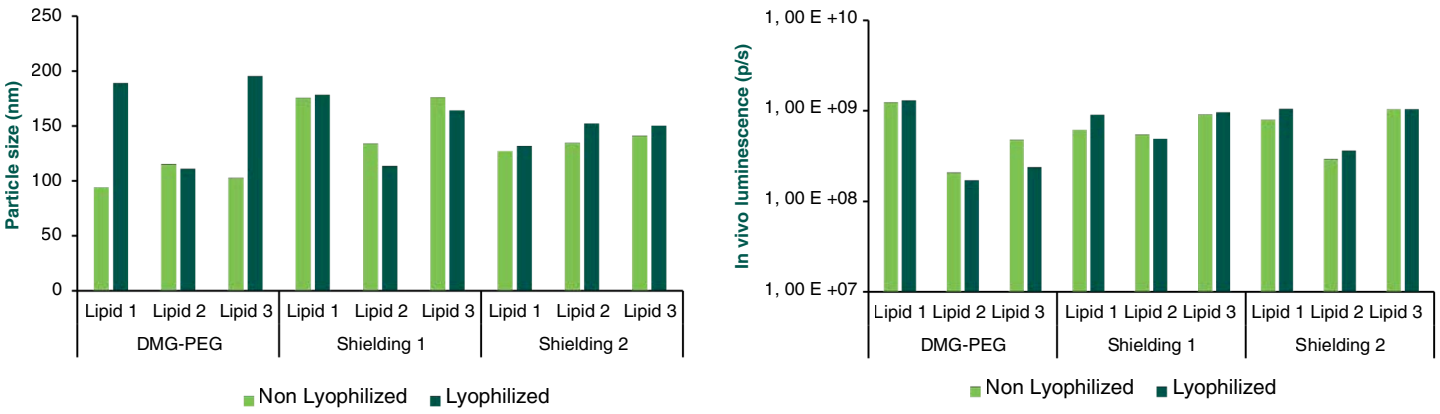

Figure 12. Particle size (left) and in vivo performance (right) of mRNA containing LNPs formulated with 3 different Certest ionizable lipids in combination with DMG-PEG, and 2 different Curapath's shielding lipids. Luminescence was measured 4 hours after intramuscular injection of1 µgofFlucmRNA/mouse

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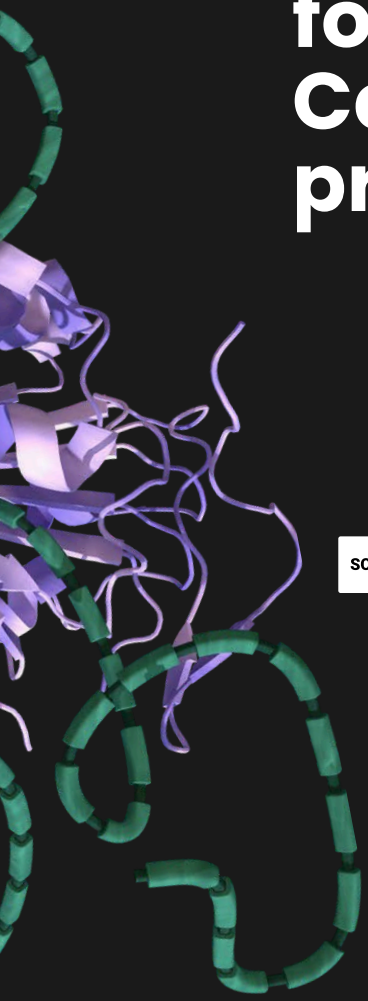

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