



tebubio

Facilitators of Life Sciences Research

Advancing In Vivo Drug Delivery with Certest Pharma's Smart Lipids & Smarter Targeting

Dr Javier Gimenez Warren – CTO at Certest Pharma



Our Team Today



Speaker

Javier Gimenez Warren , PhD
CTO at Certest Pharma



Q&A Moderator

Erica Cirri, PhD
Project Manager, RNA Specialist



Session Moderator

Diana Perrier
Digital Campaign Manager

Webinar Agenda

1. | Tebubio at a glance
2. | Speaker Introduction
3. | Certest Pharma presentation

Webinar Agenda

1. | Tebubio at a glance
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We facilitate Life Sciences Research everyday and contribute to a brighter future



We are Pan-European

- Founded in 1953
- Family-owned
- 100+ Employees
- Local offices across Europe



We Act for Life Sciences

- Innovation is in our DNA
- Contract Research Services Lab
- Part of EU Life Sciences ecosystems



We Care

- Ethical, compliant and transparent sourcing (from OEMs only)
- Animal welfare policy
- Corporate Social Responsibility (ISO 14001 / ISO 9001, Decarbonation Program)

With Tebubio, advance your Research Projects faster

Thanks to our Holistic Range of Solutions



Order advanced biological solutions



Outsource and Accelerate research



Streamline your ordering process

A large portfolio

Access to **over 1,300,000 standard** references and **non-catalogue** ones.

From trusted & ethical suppliers

Get solutions from **reputable global suppliers**, carefully selected for their **relevance, ethical** and **legal** compliance (e.g. Animal Welfare).

Dedicated scientific support

Our **Scientific Team** guides you to source, select and use solutions.

Based in Europe

Our **Teams** and **Contract Research Services Lab** are in Europe.

Team committed to success

A **PhD project manager** ensures the success of your project from A to Z.

Strong expertise in Life sciences

- **mRNA** production & delivery
- **Cell line** engineering & **protein** production
- **Cellular studies**
- **Biomarkers** & Biostatistics analysis

Reliable Supply Chain Management

- **IATA**
- **Human/Animal Biological Solutions**
- **Sourcing outside** existing suppliers
- **Warehousing** services

Order from a single source

Consolidate your orders with us.

Tailored agreements

From specific **one-off terms** to **procure-to-pay**, supported by **e-procurement** solutions.

Tebubio CRS : Facilitators of Life Sciences Research

What do you want to talk about?



RNA based therapeutic
discovery

Production | Delivery | Expression



in vitro modeling

Organoids | Microfluidics | 2&3D
Models



Biomarker mapping

Target identification | Profiling |
Quantification



Data analysis

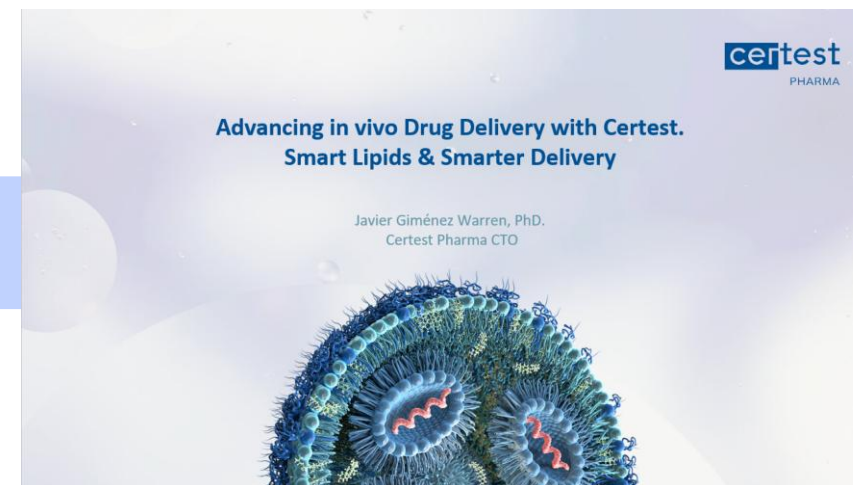
Biostatistics | NGS | Custom

Tebubio & Certest Pharma: A Strategic Partnership for in vivo Success

A seamless transition from Discovery to In vivo Delivery



X



Webinar Agenda

1. | Tebubio at a glance
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3. | Certest Pharma presentation

Our Speaker



Speaker

Javier Gimenez Warren , PhD

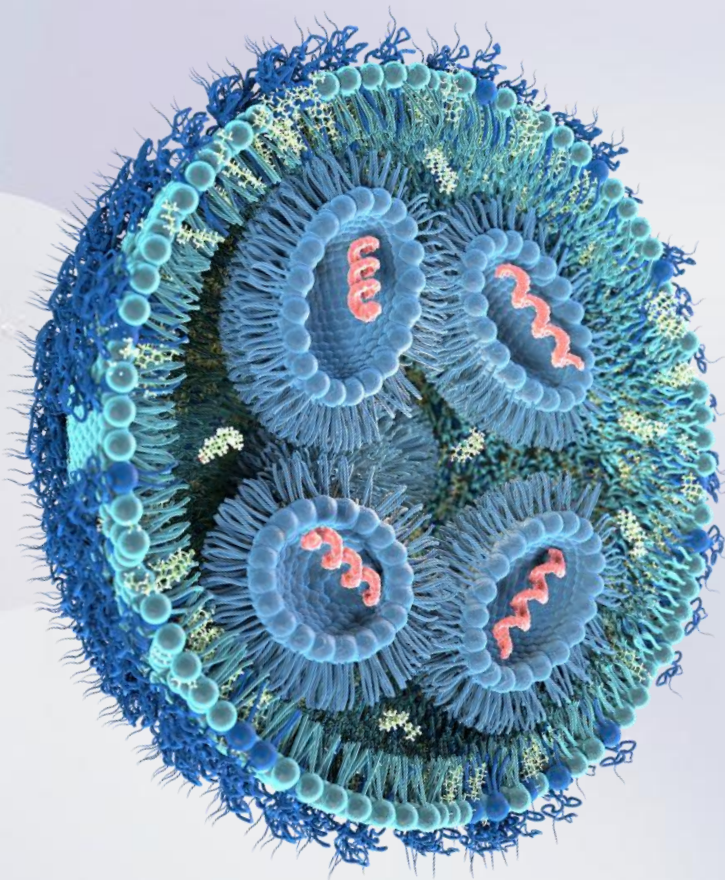
CTO at Certest Pharma

- Dr. Javier Giménez Warren holds a PhD in organic chemistry and has over 15 years of experience in synthetic chemistry applied to biotechnology. He has contributed to the development of oncology therapies and the design of innovative vaccine models.
- Currently serving as the Chief Technical Officer (CTO) at Certest Pharma, he leads the lipid department. Since joining in 2021, he has filed four patents for lipid families used in lipid nanoparticles (LNPs) with outstanding results.
- In addition to his role at Certest Pharma, Javier collaborates with the European Pharmacopoeia as an expert, contributing to the drafting of monographs for RNA-based vaccines.

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End-to-End IP from discovery to market



1,500+ Proprietary Ionizable Lipids

As the new benchmark for efficient nucleic acid delivery



Optimized Thermostable LNP Formulations

Stability and efficacy of lyophilized LNPs and naked oligonucleotides, as well as liquid formulations



Precision Targeting for Enhanced Delivery

Ensure a precise delivery to specific cells



RNA and Oligonucleotide modifications

Tailored modifications to improve stability, specificity, and functionality

INDEX

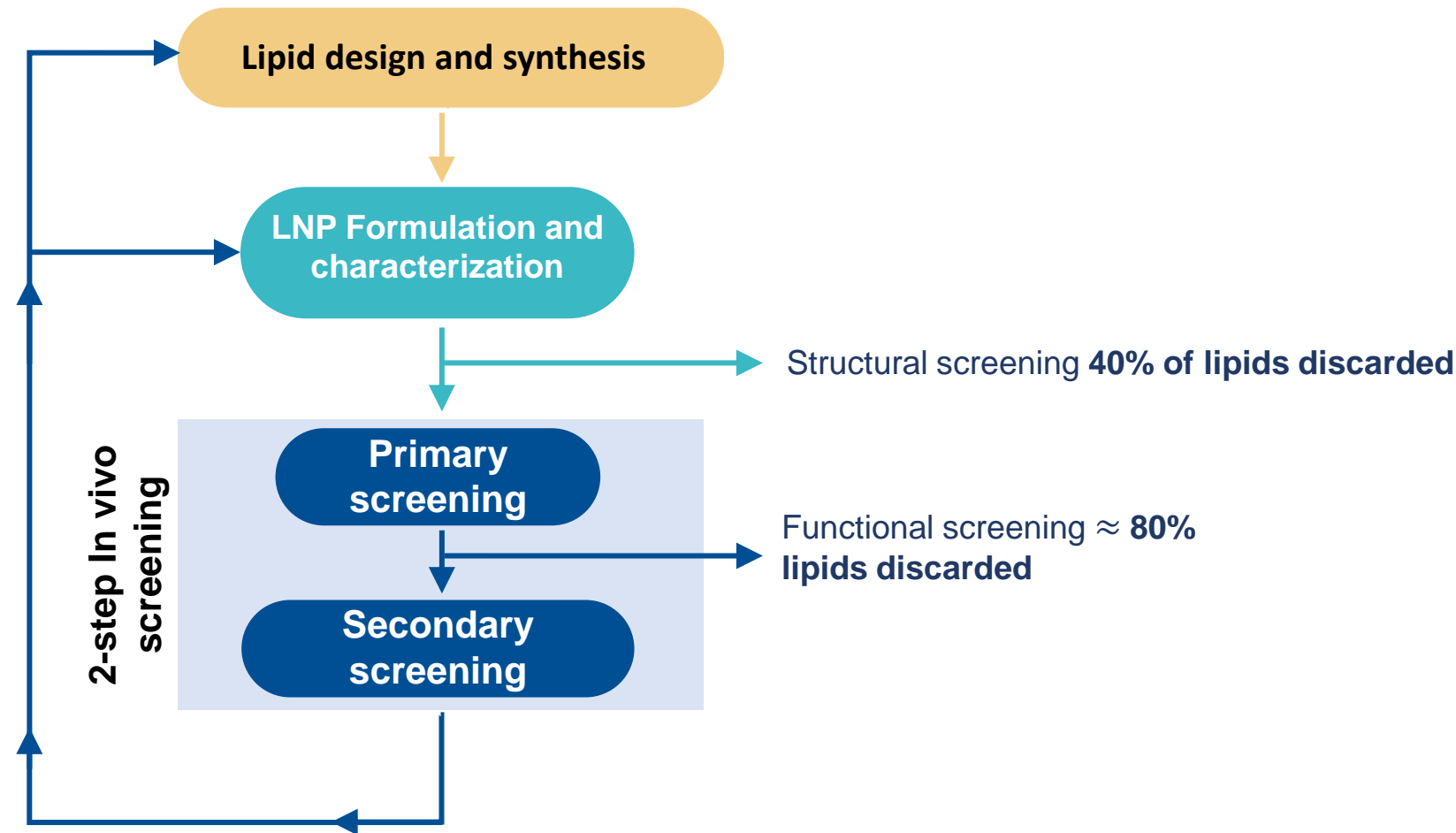
- 1. Proprietary Ionizable Lipids**
2. Thermostable LNP Formulations
3. Targeting
4. Partnership

Machine Learning

- 14,000 descriptors per lipid
- Structural and functional results on LNPs

Screening of new ionizable lipids

- Workflow based on *in vivo* results
- 1500+ lipids tested *in vivo*

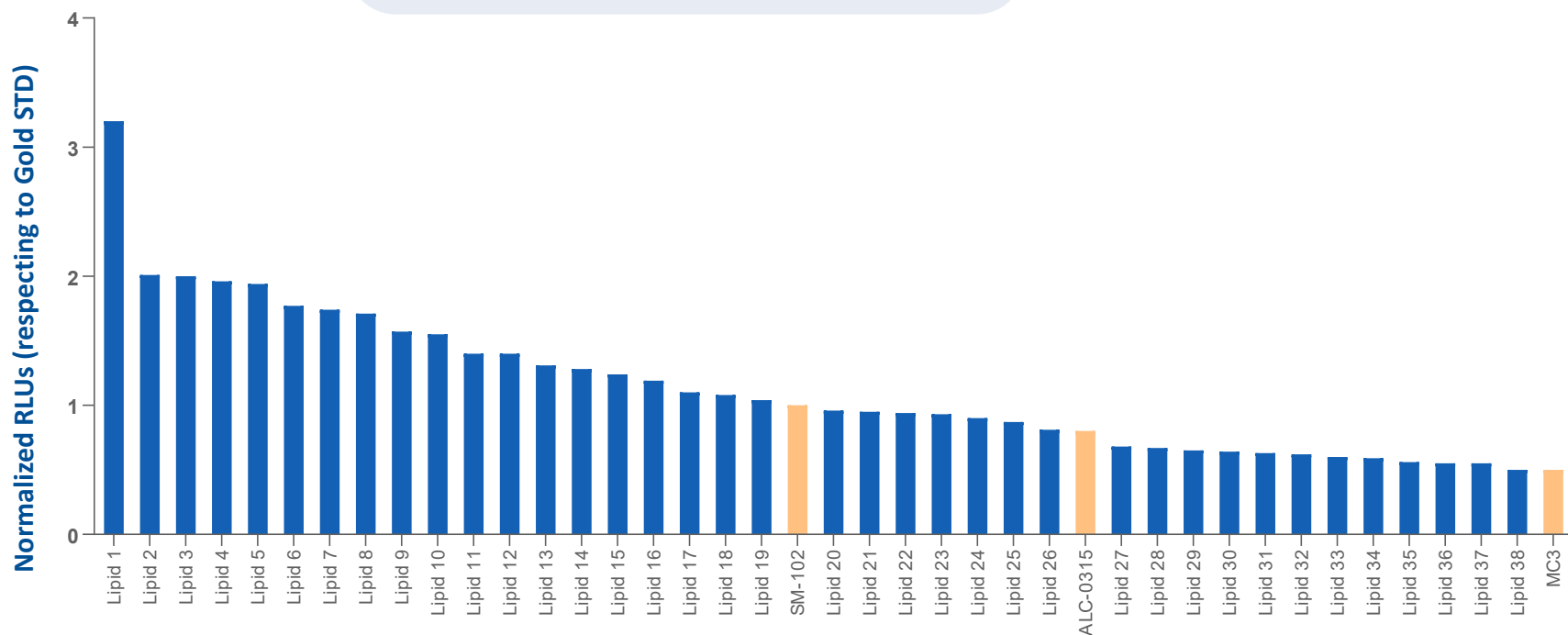


Certest Pharma Ionizable Lipids



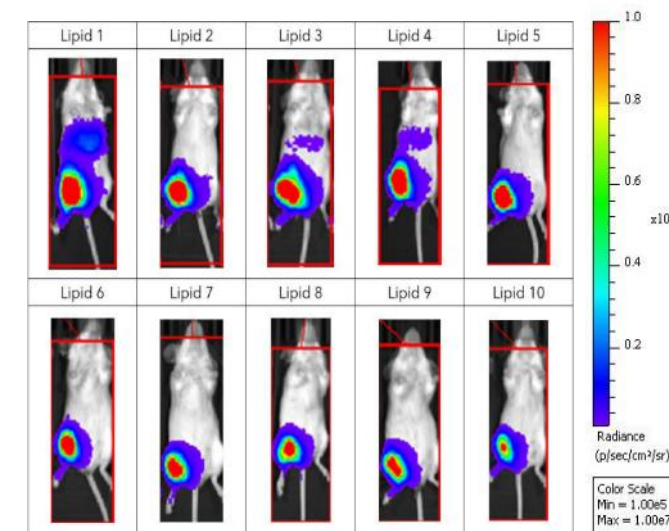
Outstanding *in vivo* results vs gold standard

mRNA PROTEIN EXPRESSION



Semi-rational design

- Machine learning guided
- 1500+ lipids tested *in vivo**



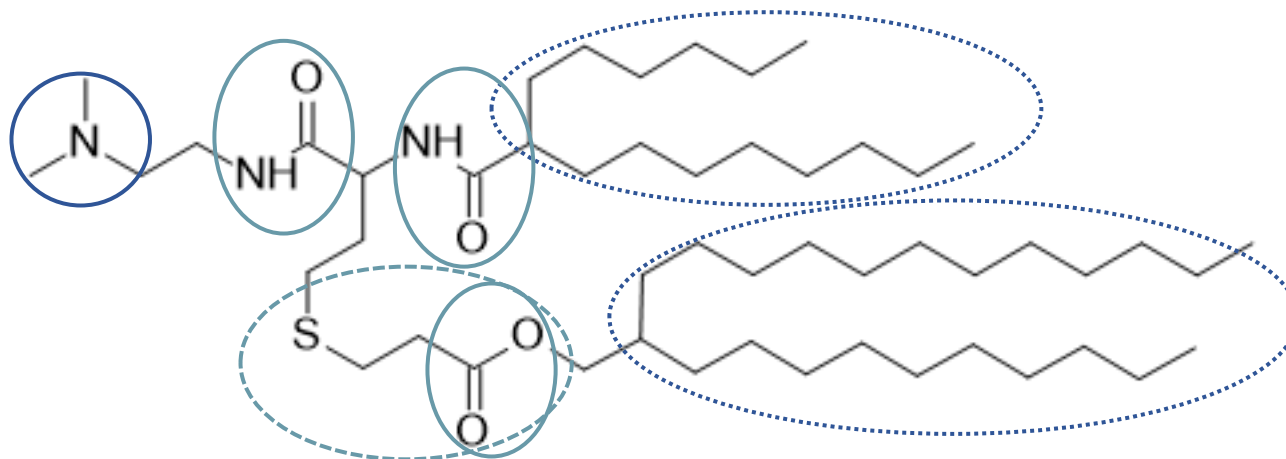
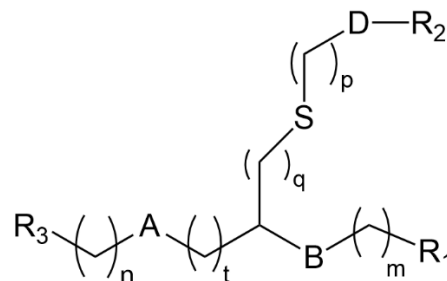
Proprietary lipid structure

certest



GMP
Available

WO2024/110381



CP-LC-0741

Ionizable head

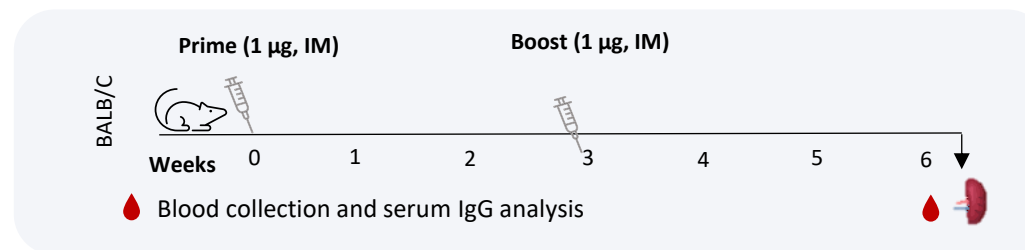
Branched tails

Biodegradable groups

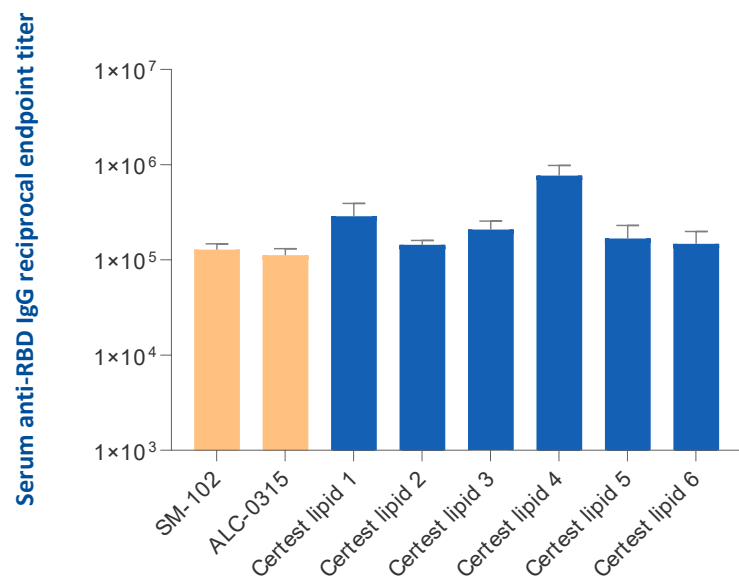
Superior biodegradability

“Multicomponent Thiolactone-Based Ionizable Lipid Screening Platform for an Efficient and Tunable mRNA Delivery to the Lungs”. DOI: 10.1101/2024.10.09.617396

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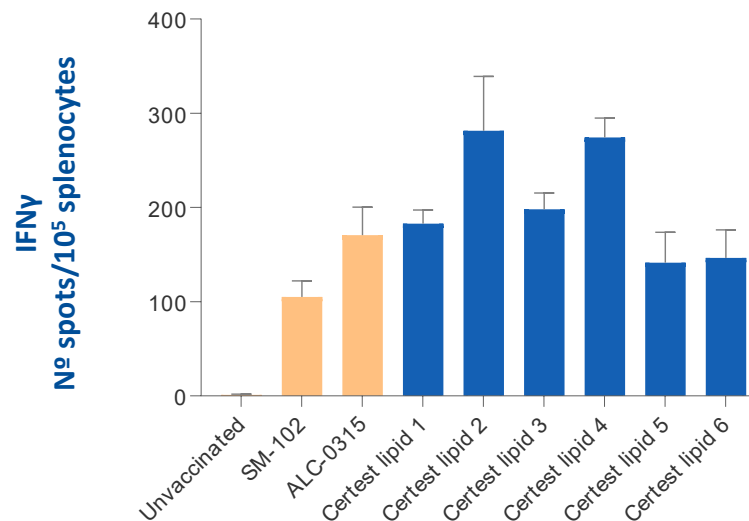


ANTIBODY RESPONSE

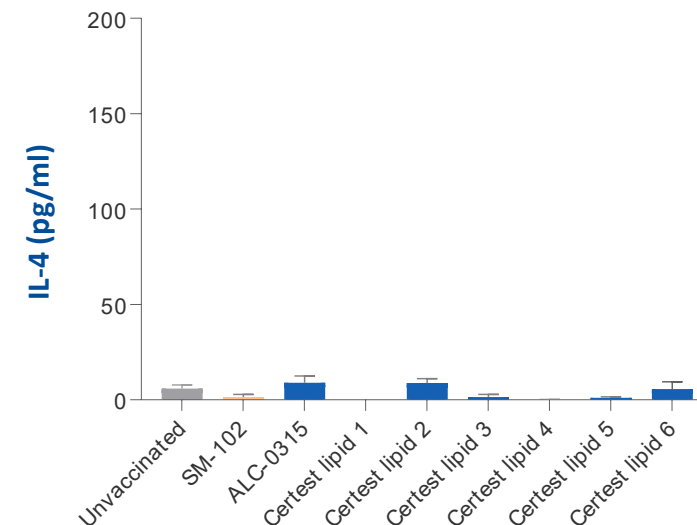


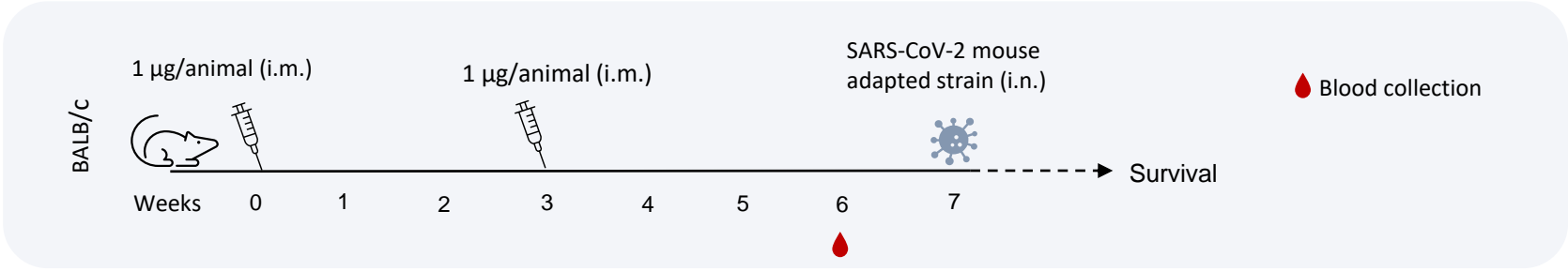
T-CELL RESPONSE

Th1



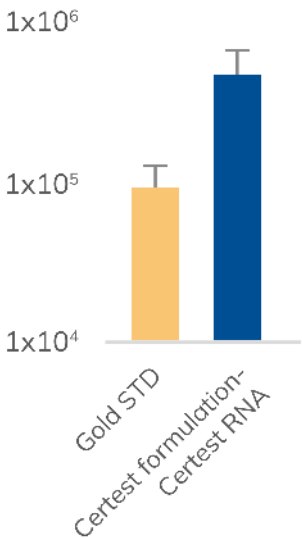
Th2



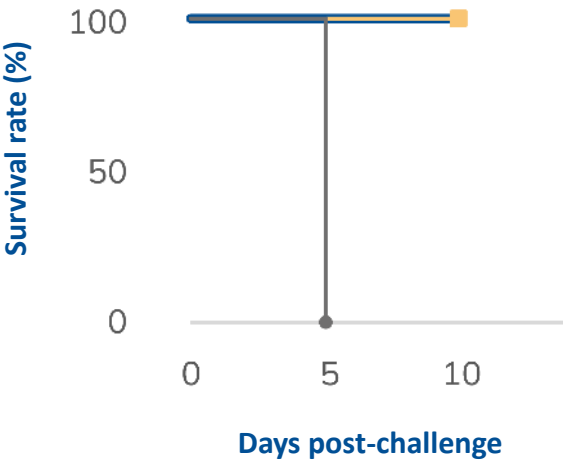


ANTI-RBD IgG (week 6)

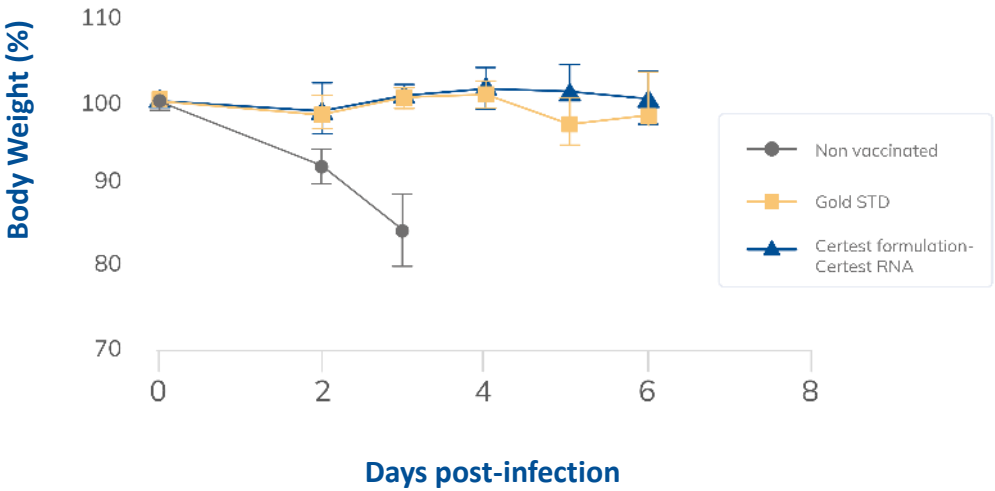
Reciprocal endpoint titer



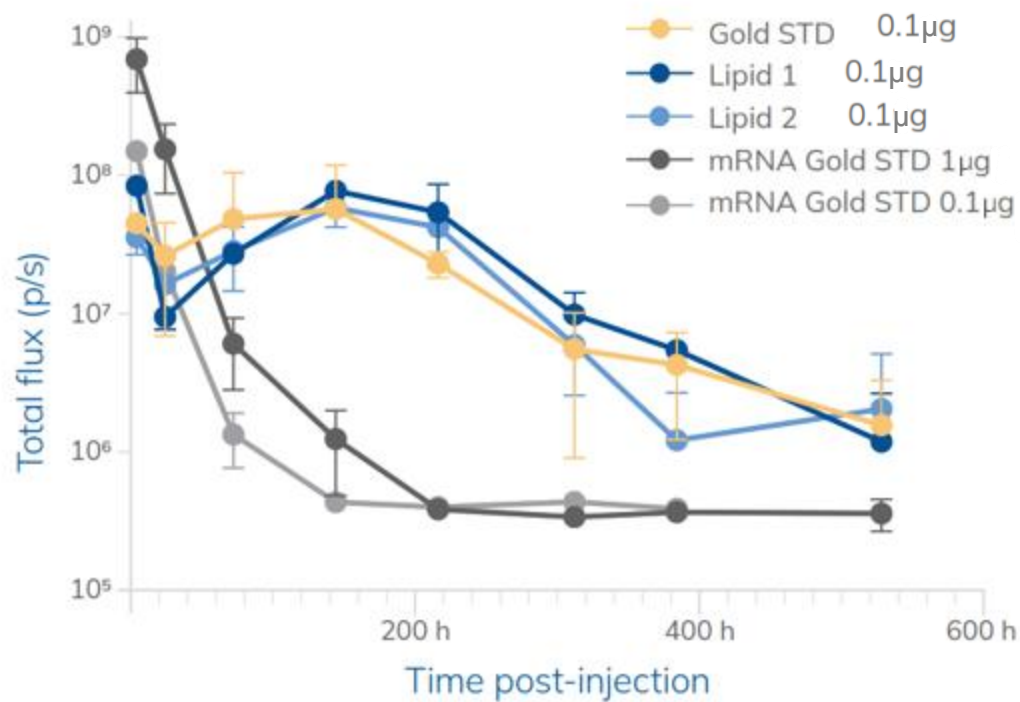
SURVIVAL RATE



WEIGHT LOSS

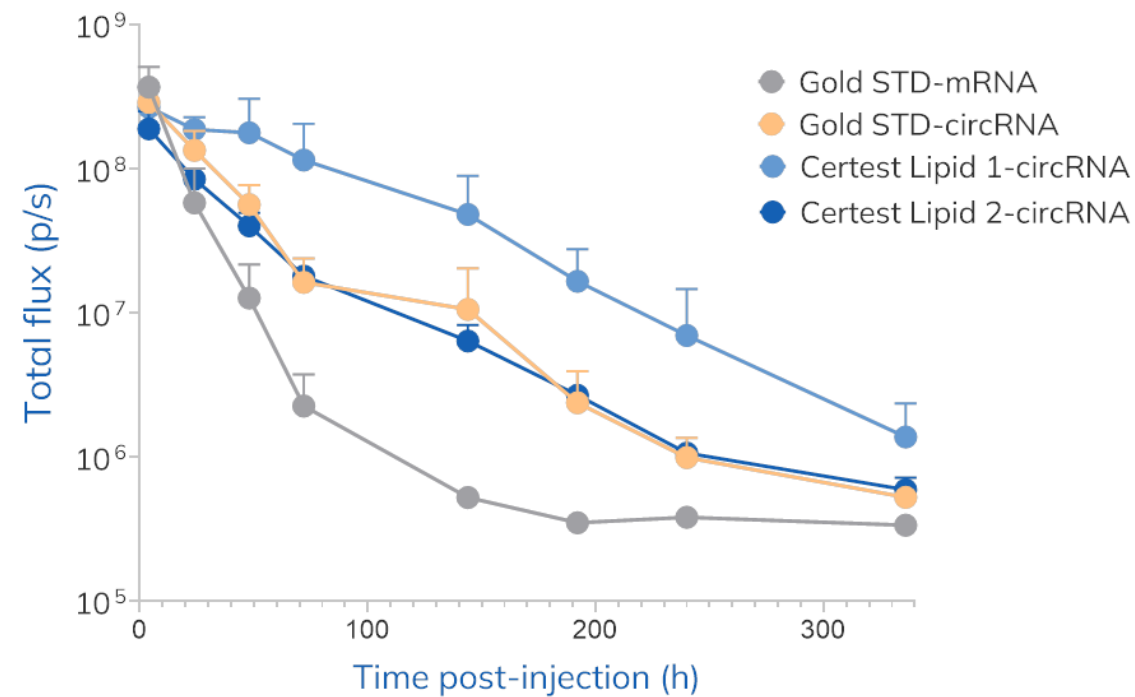


saRNA



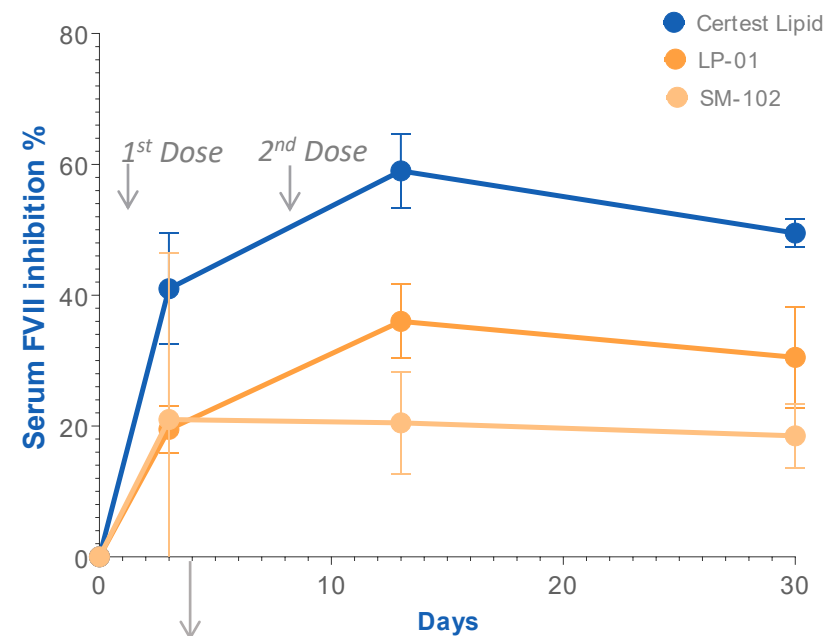
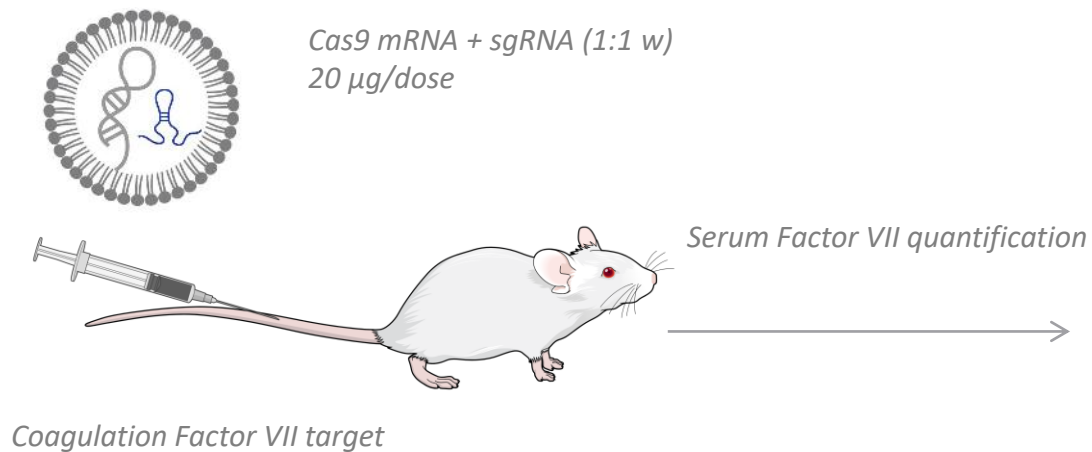
I.M. injection

circRNA

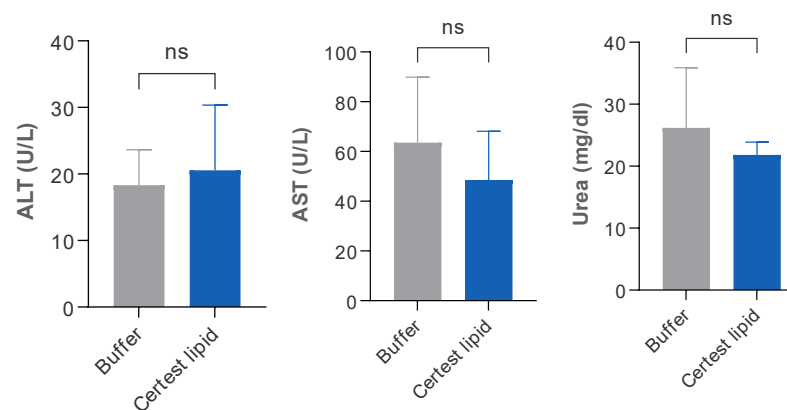


I.M. injection, 1 µg circRNA/mouse

Enhanced CRISPR/Cas gen editing

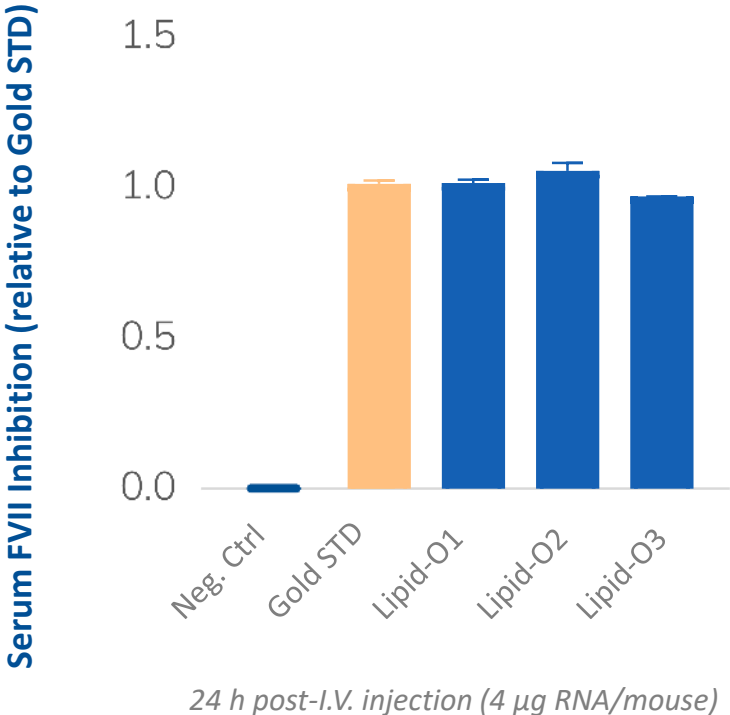


Serum biochemical analysis

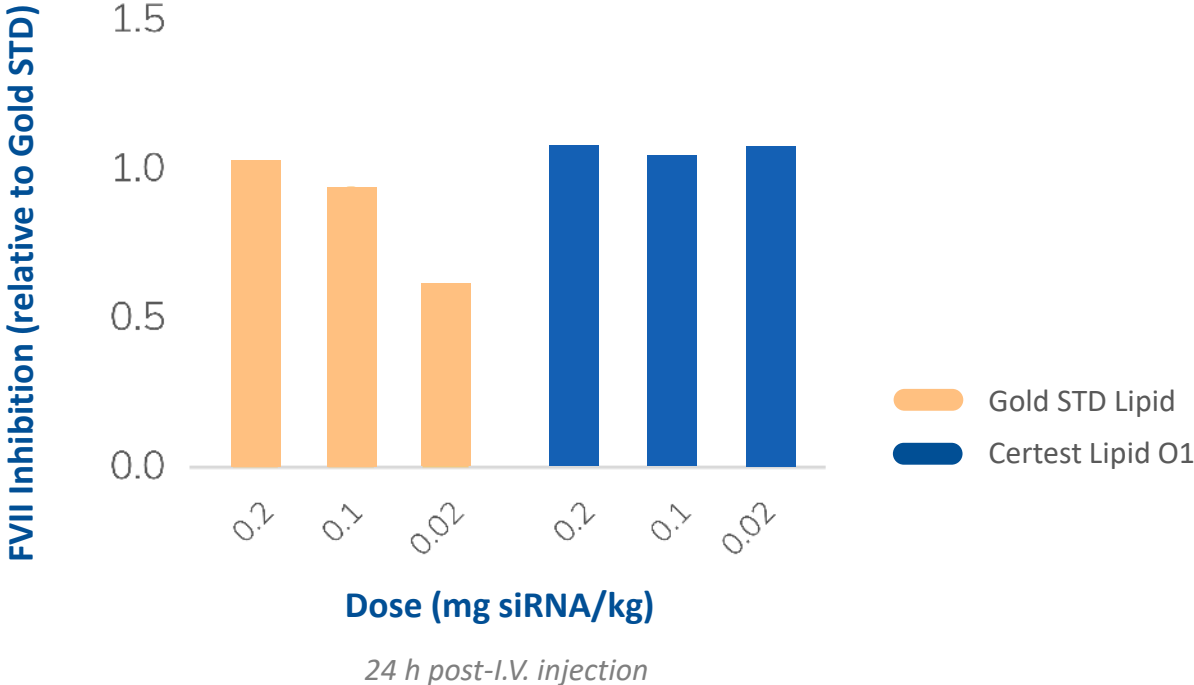


Certest's ionizable lipid dramatically outperforms market-leading competitors in CRISPR/Cas delivery efficiency and exhibits a favorable safety profile

PROTEIN EXPRESSION INHIBITION
BY OLIGONUCLEOTIDES

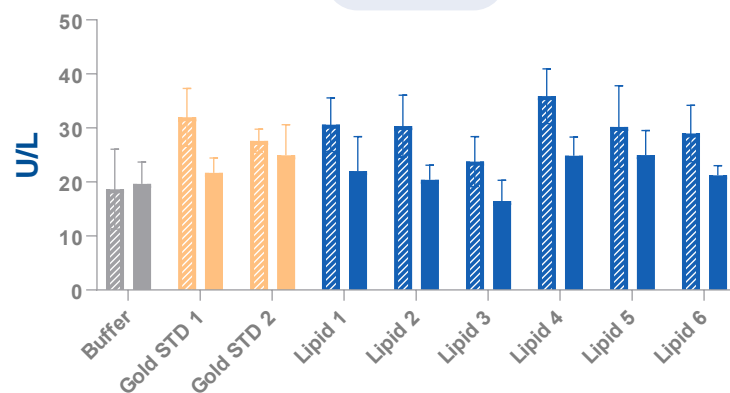


PROTEIN EXPRESSION INHIBITION
WITH DECREASING DOSES

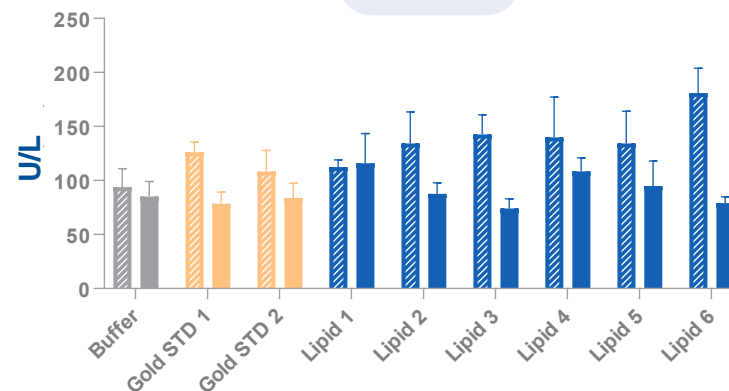


In vivo safety profile

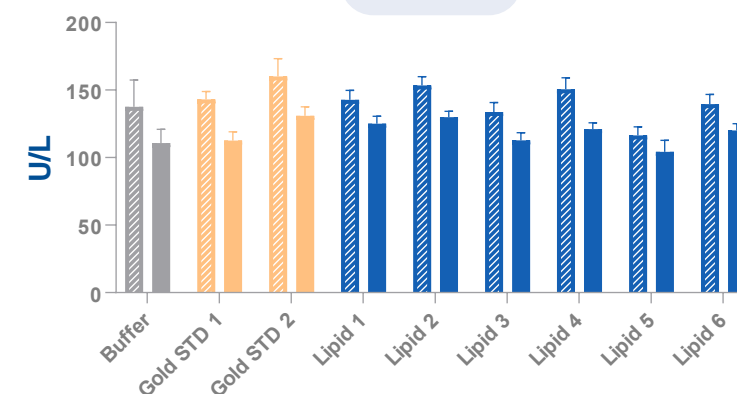
ALT



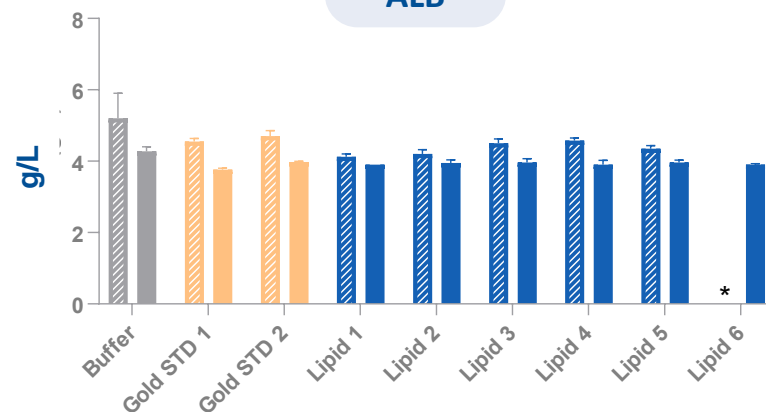
AST



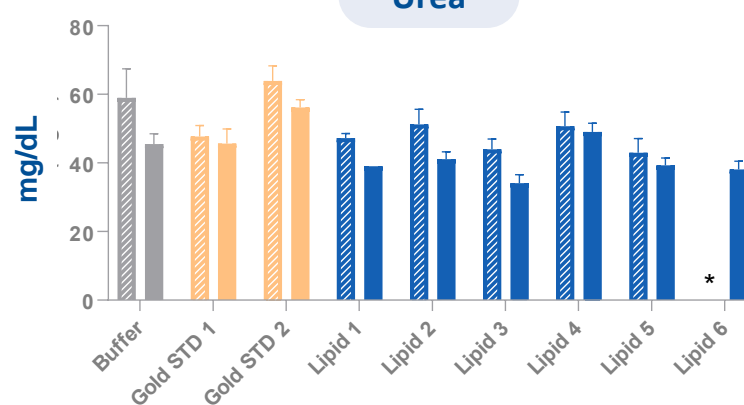
ALP



ALB



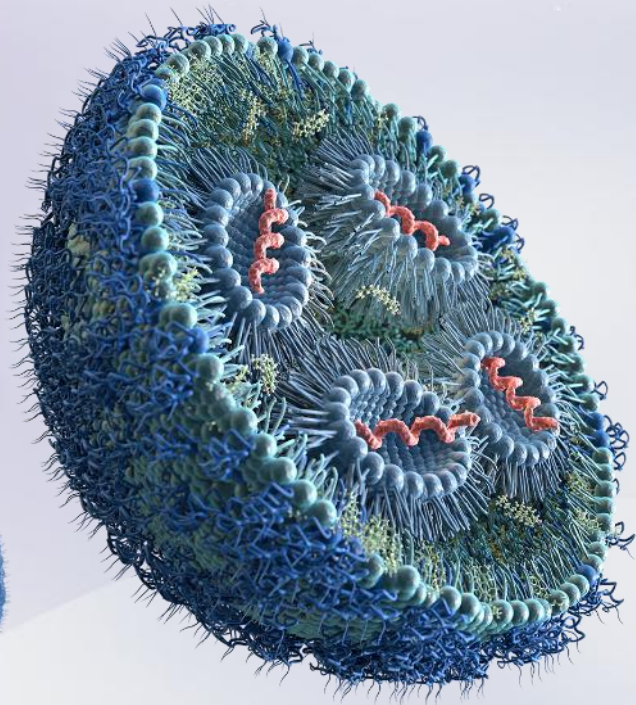
Urea



■ PBS
 ■ Gold STD
 ■ Certest lipids
 ▨ 24 h
 ■ 48 h



Dose: 50 µg RNA/mouse. Serum biochemical analysis 24 and 48 h post-i.v. injection



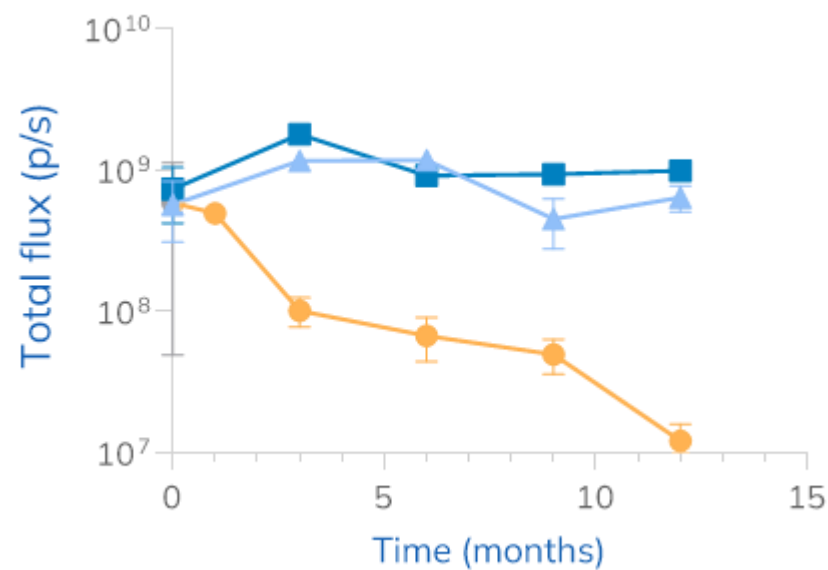
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- 2. Thermostable LNP Formulations**
3. Targeting
4. Partnership

Enhancement of thermal stability. Freeze-drying

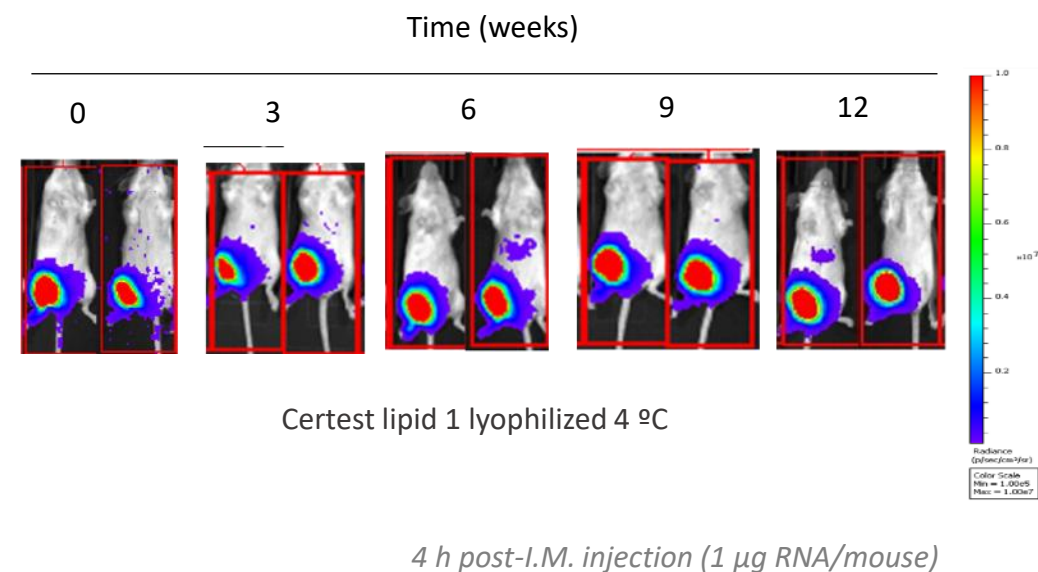
STABILITY AFTER 1 YEAR

(ongoing experiment)



- Gold STD aqueous 4 °C
- ▲ Certest lipid 1 lyophilized 4 °C
- Certest lipid 2 lyophilized 4 °C

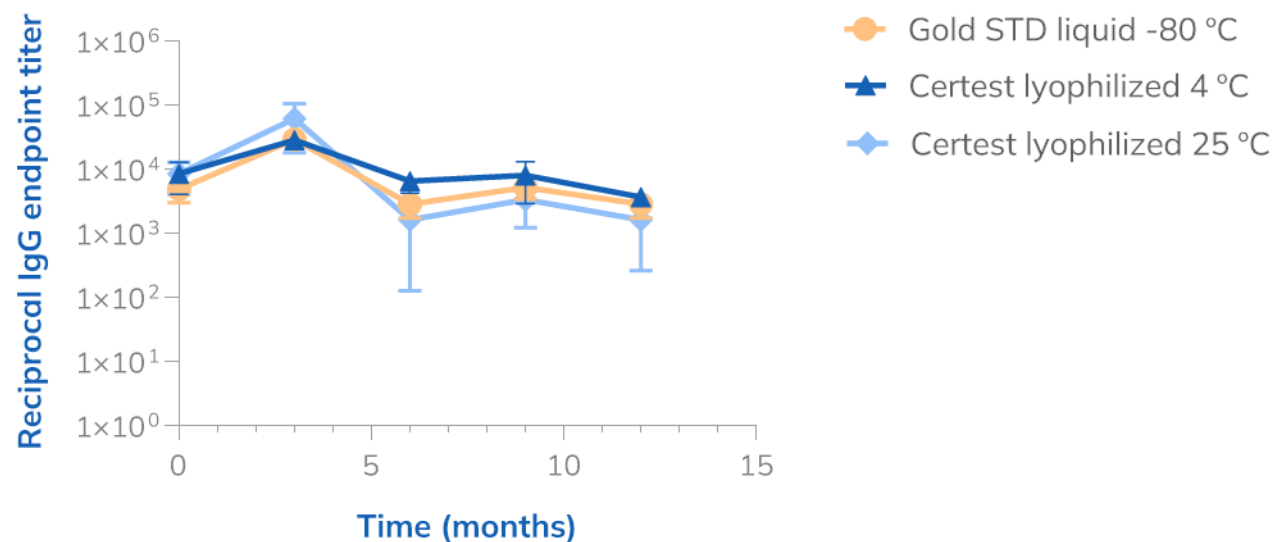
IN VIVO LUMINESCENCE



Stability results of immune response

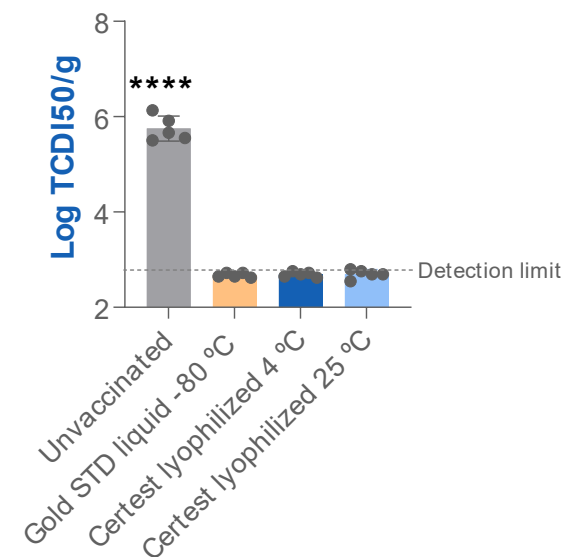
ANTIBODY RESPONSE

Day 21 after single I.M. injection, 1 μ g mRNA/mouse

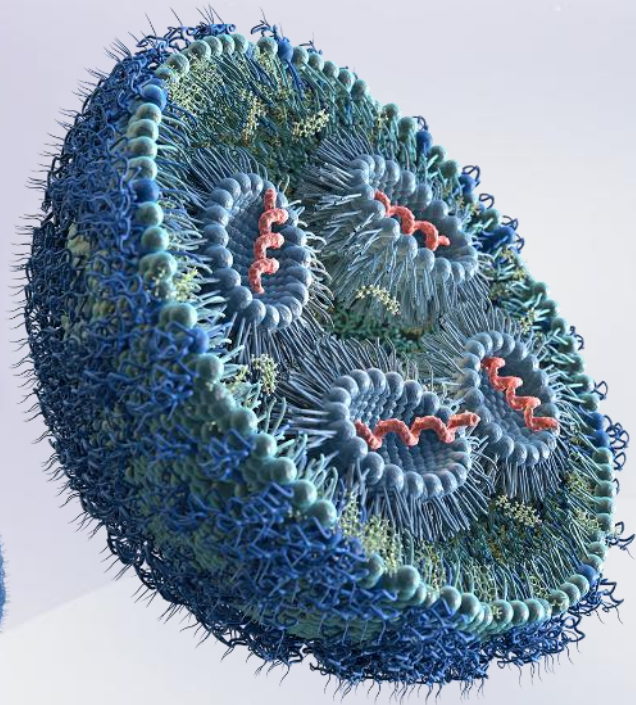


VACCINE EFFICACY AFTER 12 MONTHS

Day 3 post-SARS-CoV-2 challenge after prime-boost I.M. injection, 1 μ g mRNA/mouse



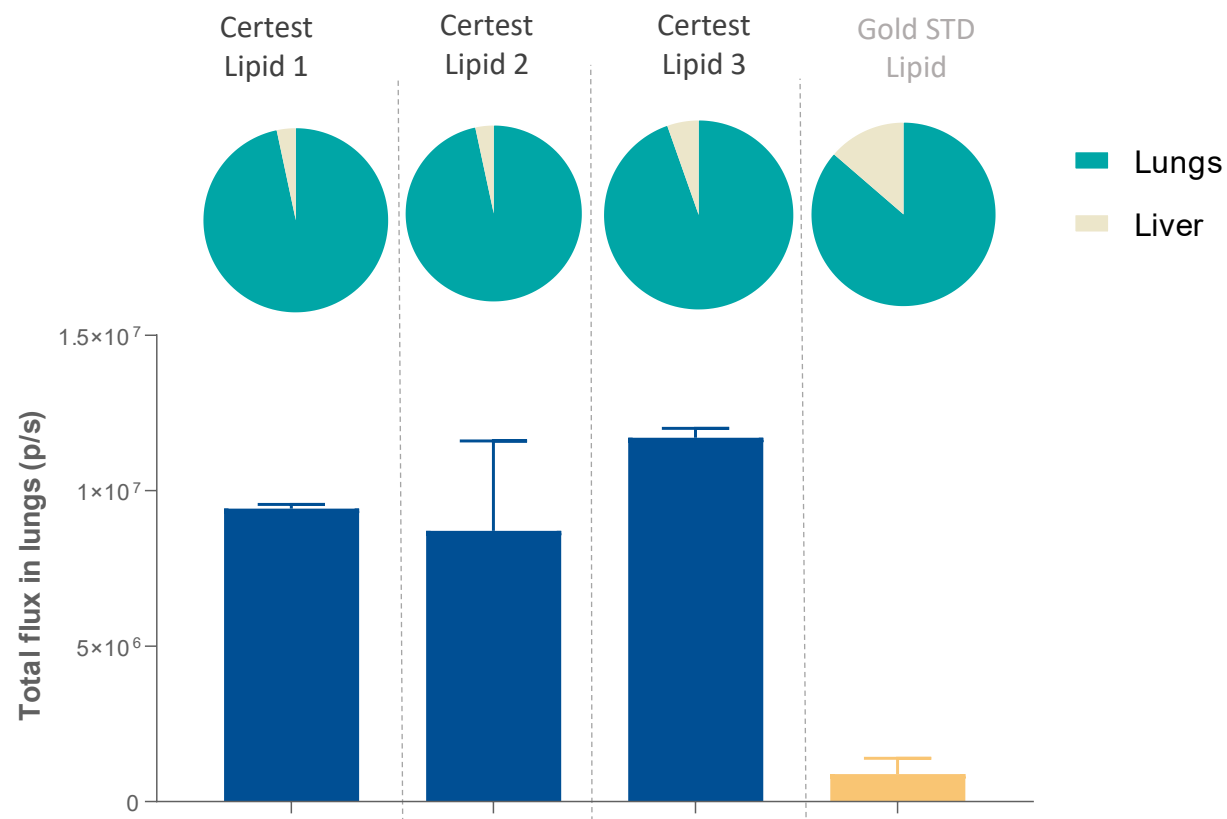
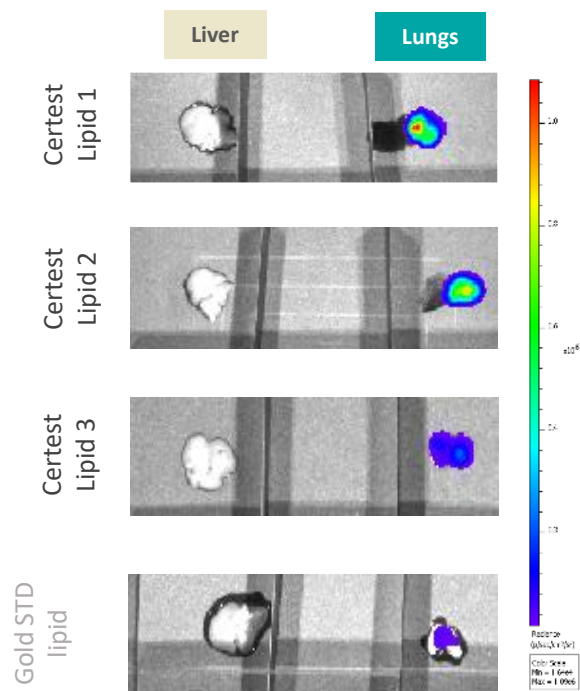
Certest Lyophilized vaccines retain their immunogenicity and efficacy after **12 months of storage** at temperatures up to **25°C**



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Inhaled and intranasal 4 component LNP formulations



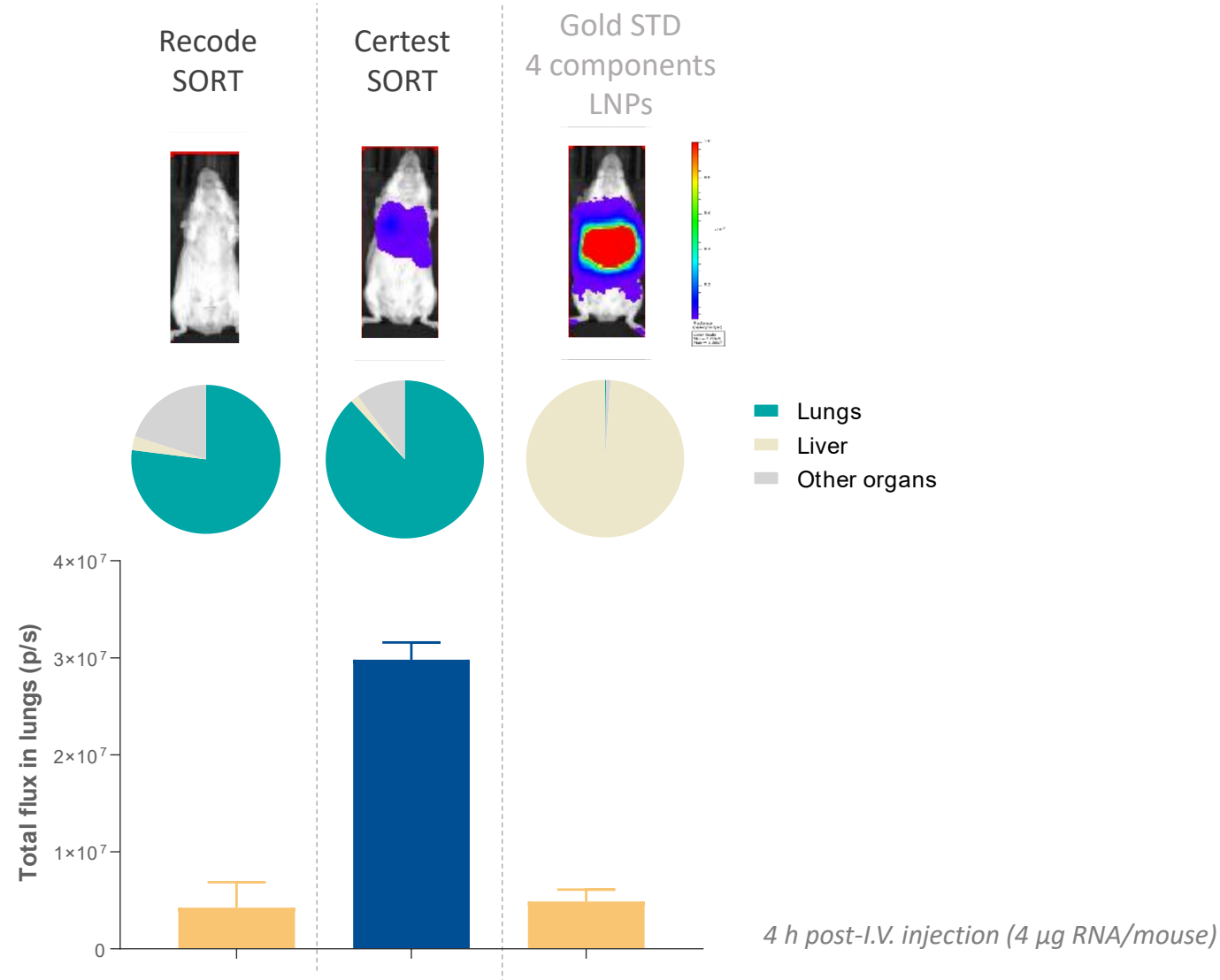
Tissue selectivity

Expression intensity

Improving 5 component LNPs for lung delivery

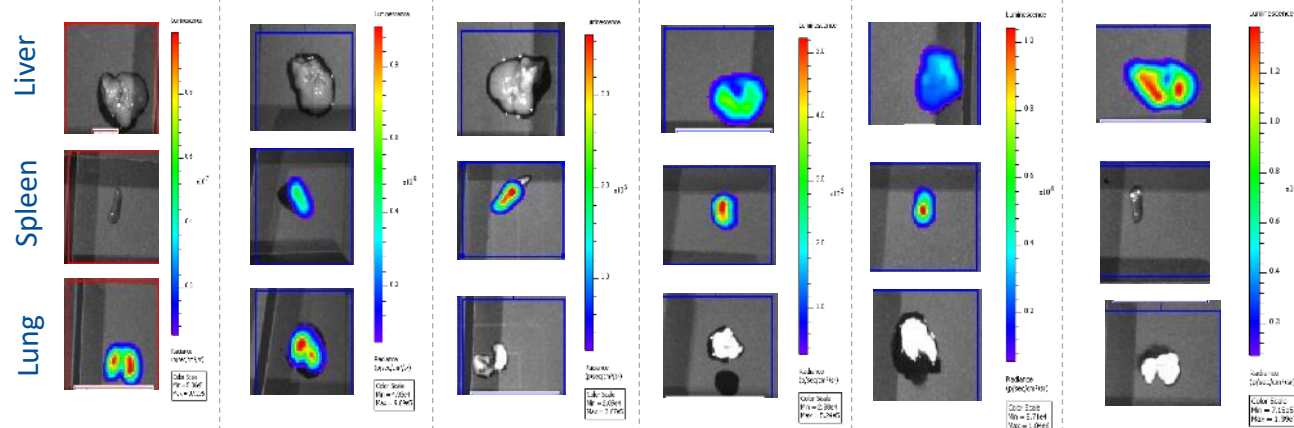
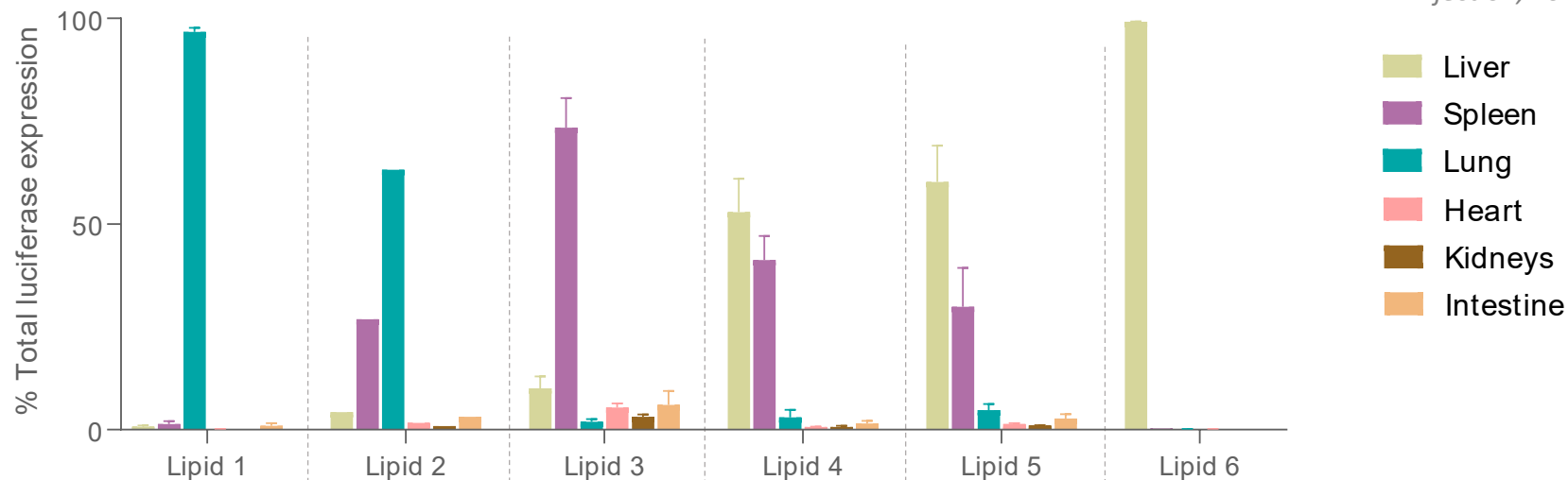
Tissue selectivity

Expression intensity



In vivo TISSUE SELECTIVITY

I.V. injection, 10 μ g mRNA/mouse



Tissue targeting by just choosing the right Certest ionizable lipid

Extrahepatic delivery

Lung and Spleen delivery

certest



Certest Seq + spleen1

Certest spleen 1

Certest spleen 2

Certest spleen 3

Gold STD

■ Spleen
■ Liver
■ Other organs



Certest lungs 1

Certest lungs 2

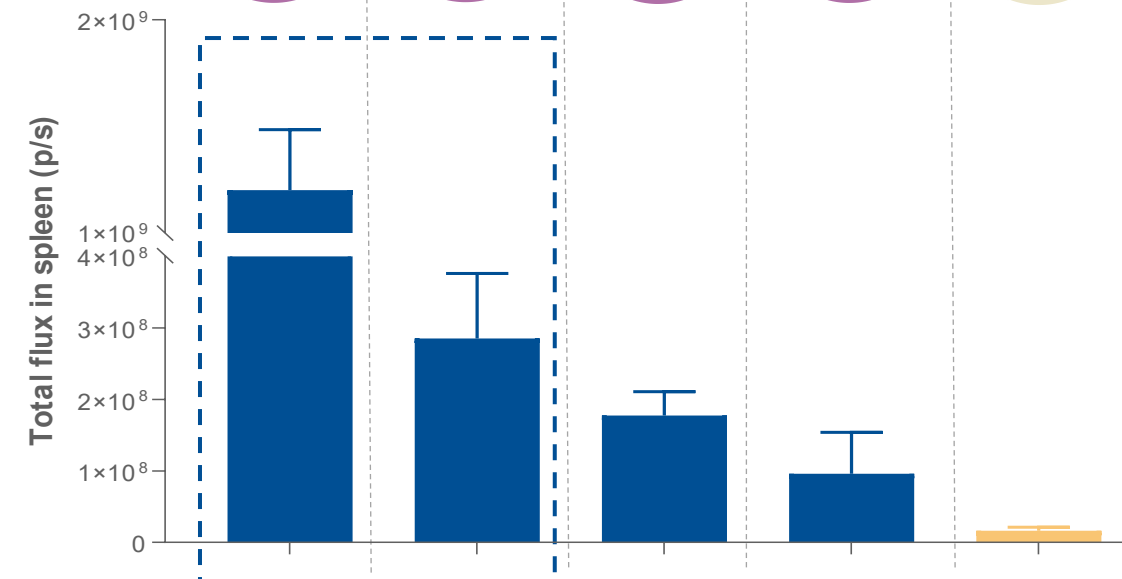
Certest lungs 3

Gold STD

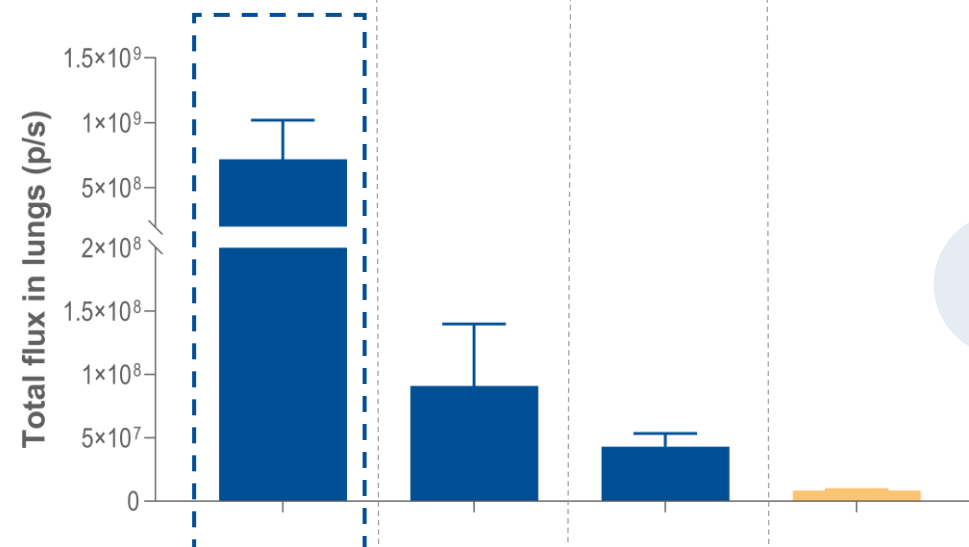
■ Lungs
■ Liver
■ Other organs

Tissue selectivity

Expression intensity



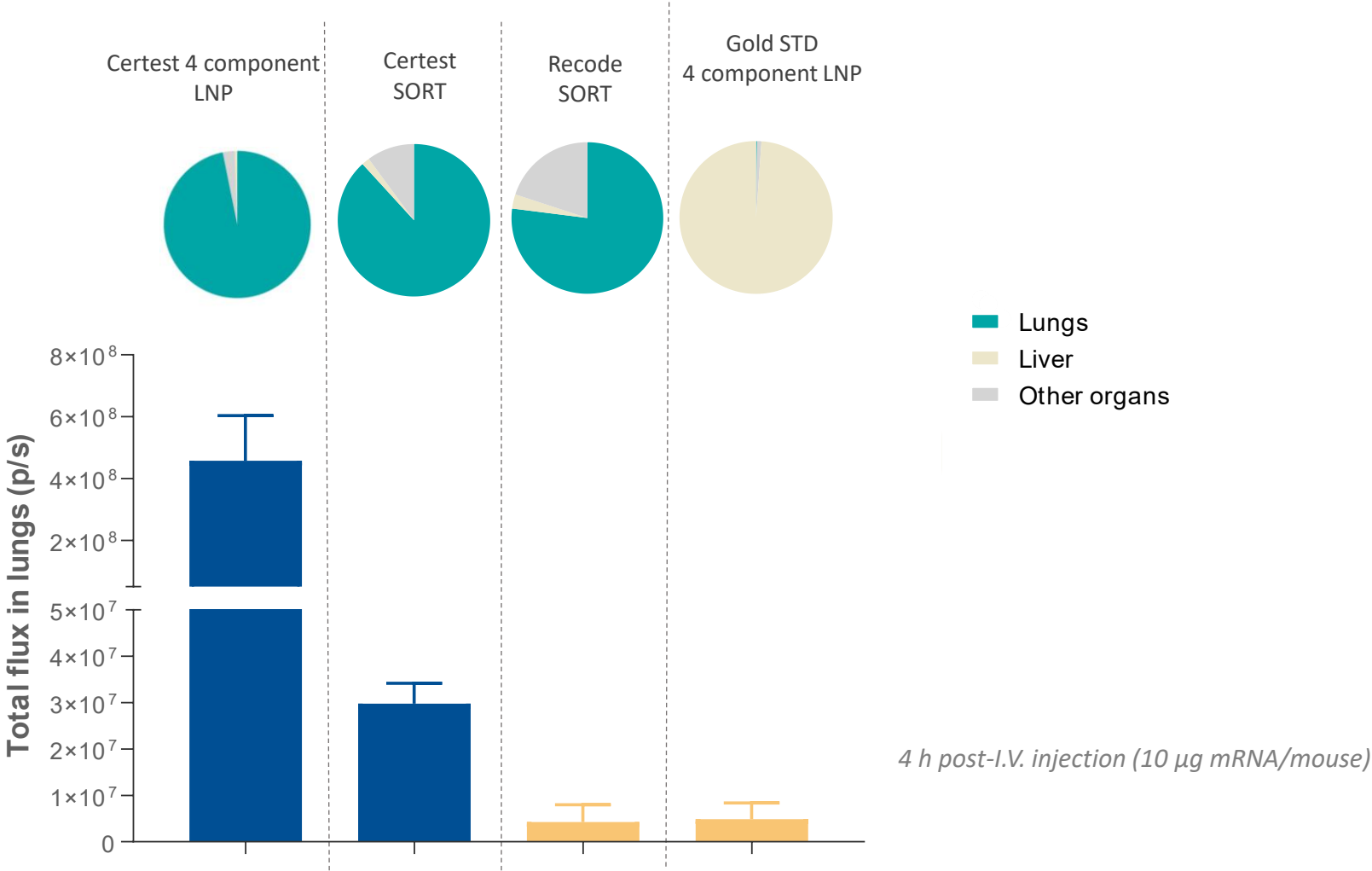
Cytometry assays show expression in T-cells



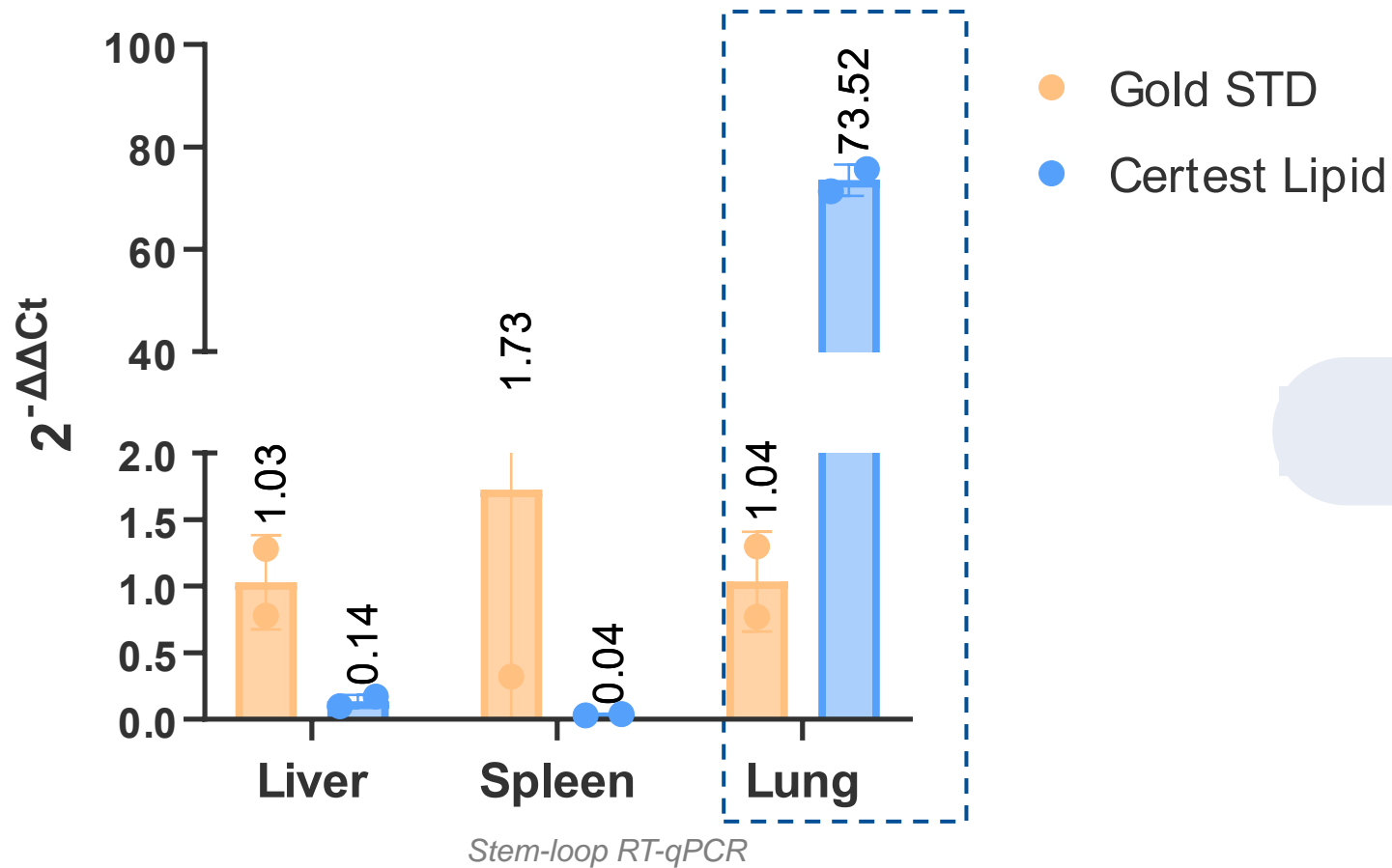
Improving 5 component LNPs for lung delivery

Tissue selectivity

Expression intensity



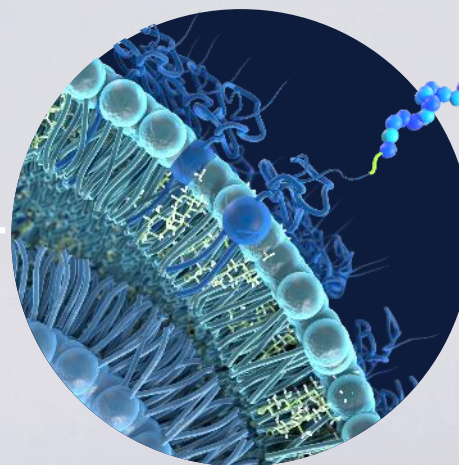
70% higher siRNA delivery to the lungs



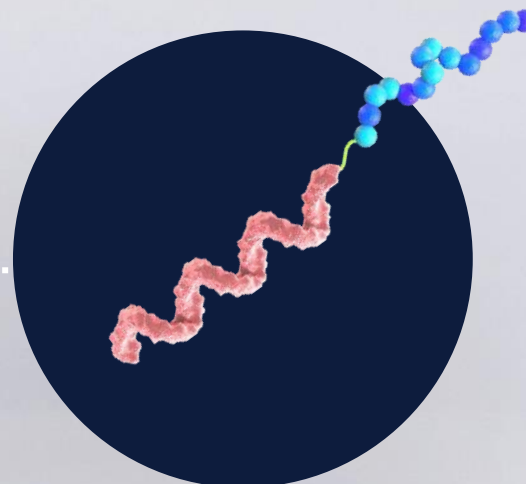
Selective delivery to minimize secondary effects

Active Targeting for enhanced delivery

Precision Targeting for Enhanced Delivery



Peptide-conjugated LNPs



Peptide-conjugated
Oligonucleotides

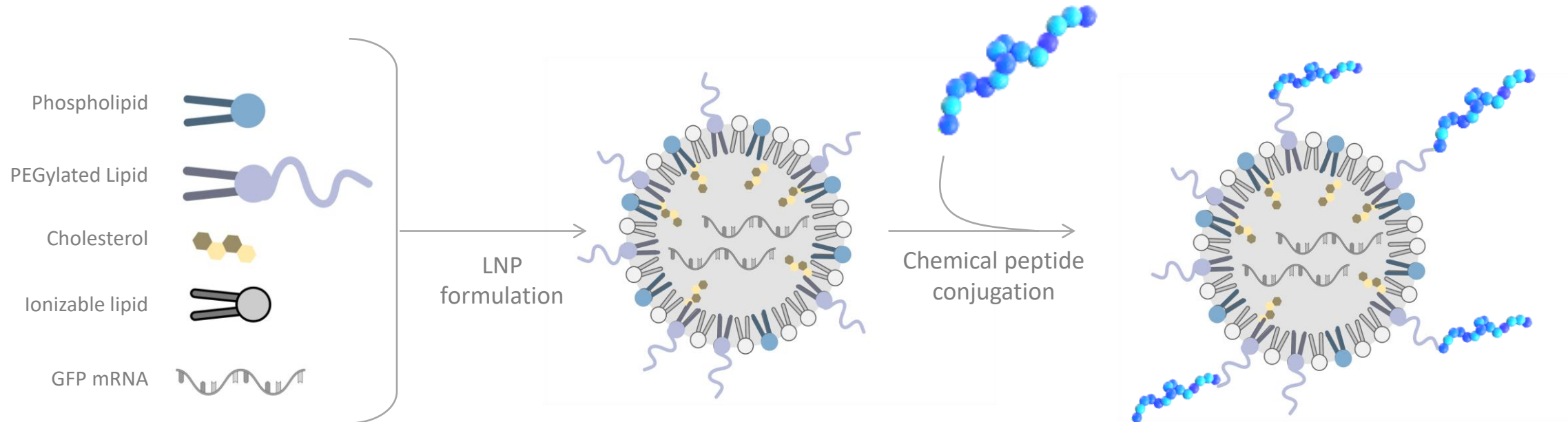
Active Targeting projects



Personalized
solutions designed
for your project

- 1 Target identification
- 2 Peptide design
- 3 Peptide synthesis
- 4 LNP or oligo conjugation
- 5 *In vitro* & *in vivo* Evaluation

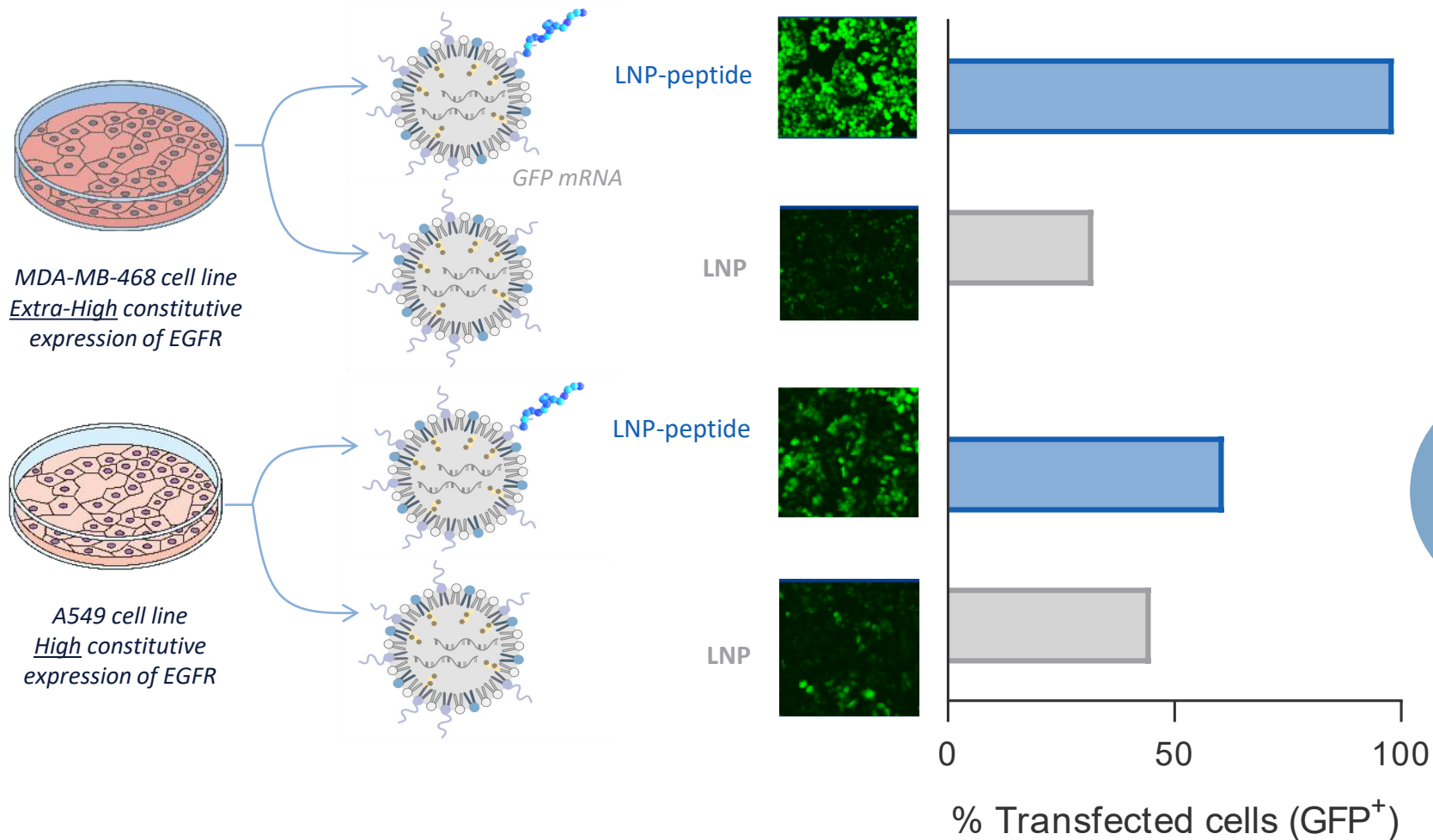
LNP conjugation technology



High level of peptide conjugation efficiency

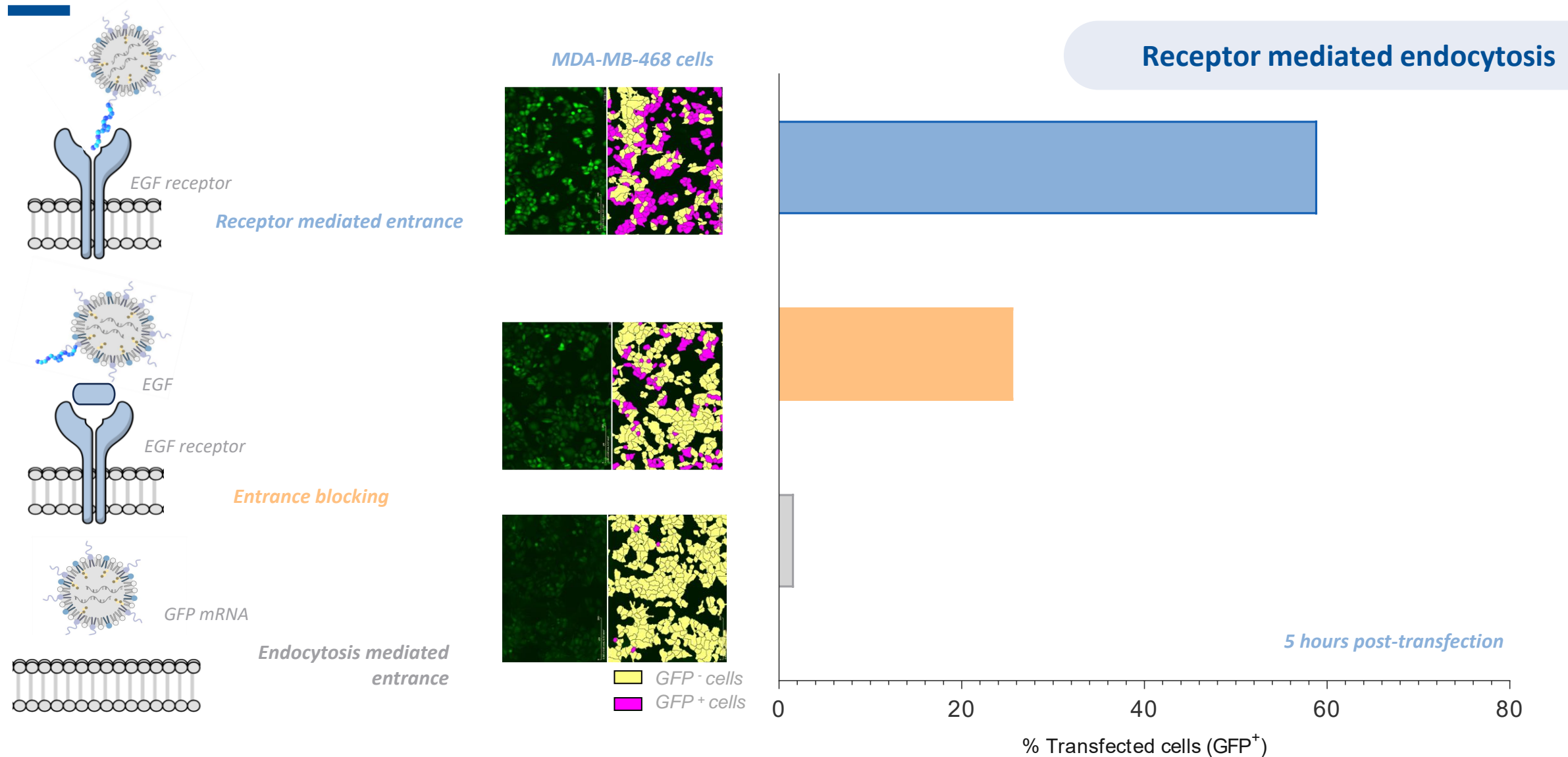
LNP conjugation technology preserving LNP quality properties

LNP peptide-conjugated targeting

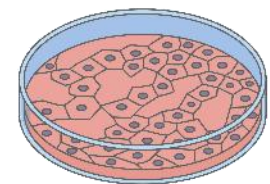


Certest's active targeting technology enables efficient cellular entry and high RNA expression in target cells

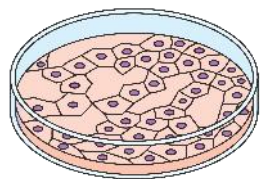
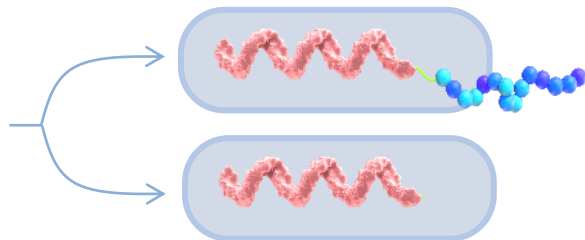
LNP peptide-conjugated targeting



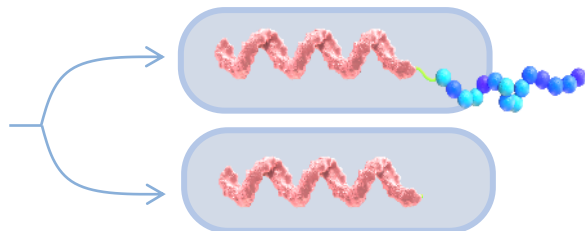
Oligonucleotide peptide-conjugated targeting



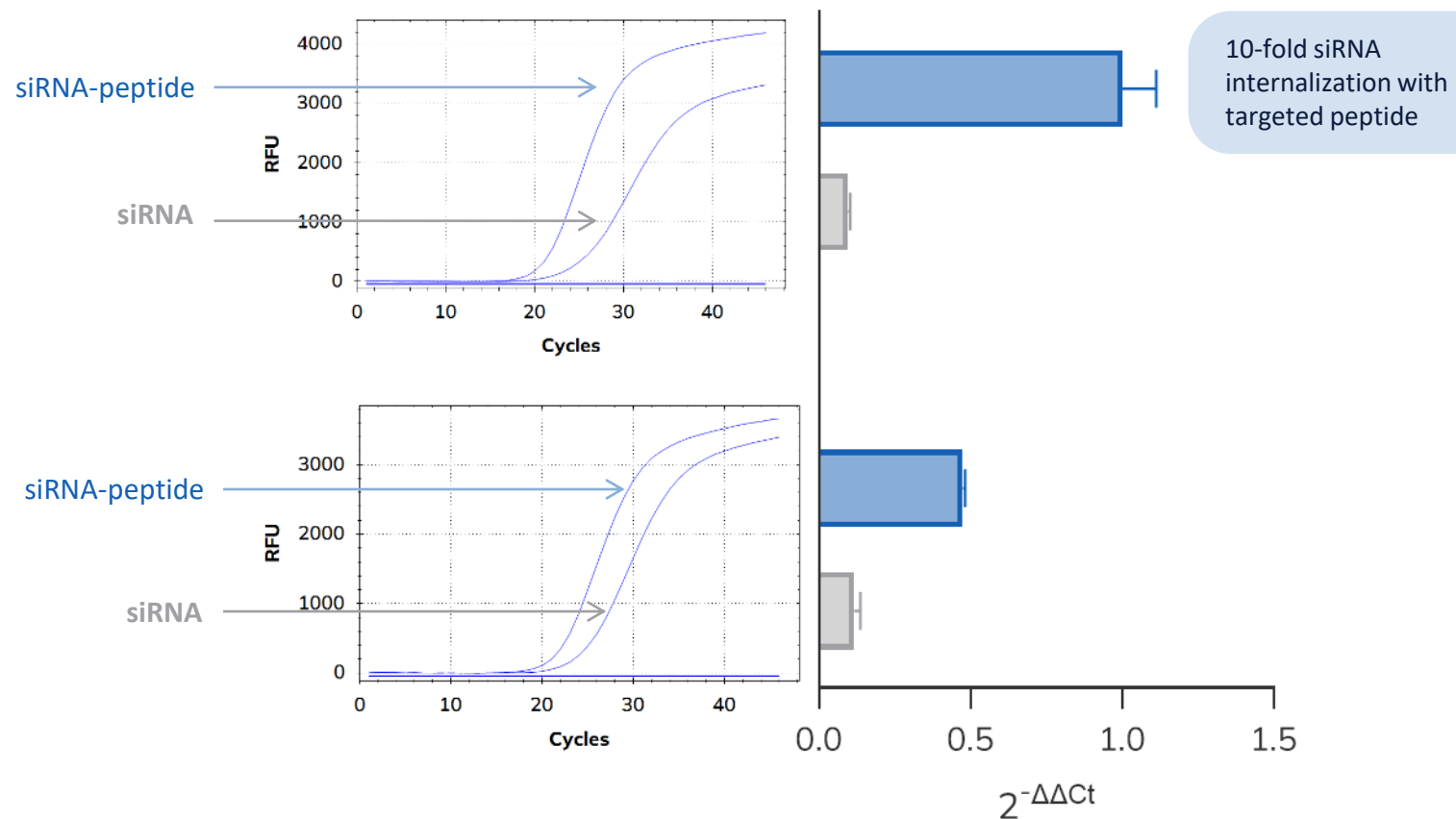
A549 cell line
High constitutive
expression of EGFR

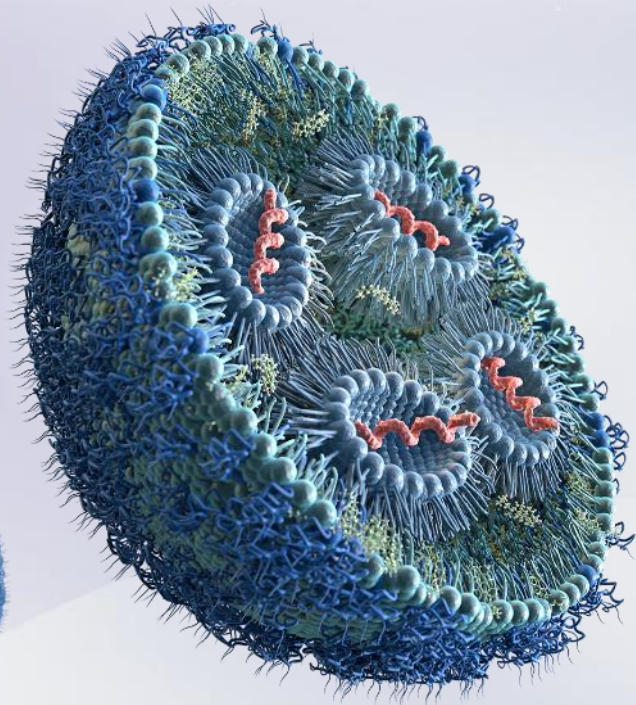


HEK293T cell line
Low constitutive
expression of EGFR



Stem-loop qPCR internalized siRNA quantification





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- mRNA UTRs & mRNA codon optimization algorithms
- Ionizable lipids
- PEG-alternatives
- Thermostable lyophilized LNPs
- Targeting lipids
- Peptide-conjugated Targeted LNPs
- Peptide-conjugated Targeted Oligonucleotides

Licenses, co-Developments and Services

End-to-End IP

Tailored programs for Generic Drug Development

Thank you



[*https://pharma.certest.es*](https://pharma.certest.es)



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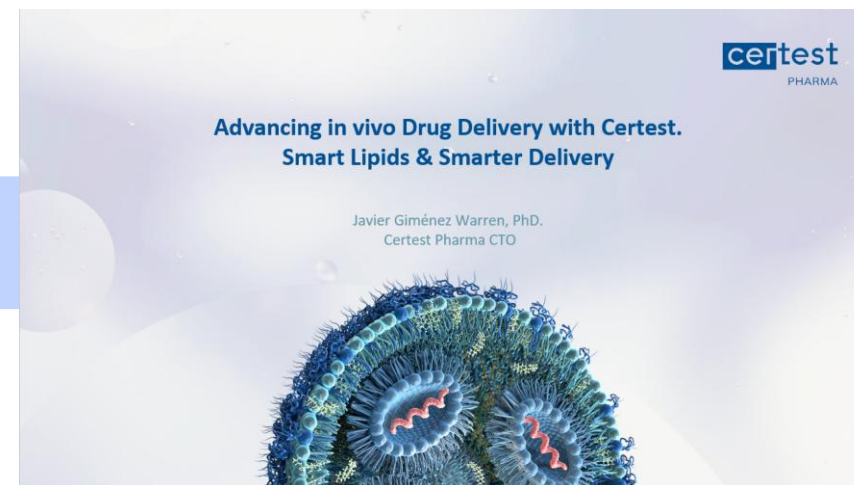
[*pharma@certest.es*](mailto:pharma@certest.es)

Tebubio & Certest Pharma: A Strategic Partnership for in vivo Success

Take home message



X



A seamless transition from Discovery to In vivo Delivery



tebubio

Facilitators of Life Sciences Research