Advancing RNA medicine. Together.

A reducible carbamate ionizable lipid library tailored towards intramuscular and systemic therapeutic applications

Dr. Bram Bogaert - Business Development Manager

Flanders Vaccine 2024

About us

Founded 2013
Series A 2016
Series B 2022

Team Members
75+

Locations
Belgium & USA

Driving discovery and solving challenges for partners across LNP formulation and RNA chemistry to enable delivery of cost-effective, differentiated and efficacious RNA therapeutics

Corporate Headquarters
GMP manufacturing facility
Niel, Belgium

Discovery Facility
Zwijnaarde, Belgium

Business Development
Boston, USA

Experienced Leadership Team with Deep Expertise in RNA drug development

Bernard Sagaert

CEO

Sterigenics A Sotera Health company · VIATRIS

Ronald Openshaw

CFO

SIMBEC-ORION · plethora SOLUTIONS · Jefferies

Stefaan De Koker

VP Technology & Innovation

UNIVERSITEIT GENT · VIB

Phil Challis

SVP Manufacturing

ucb · Lonza · OXURION

Philip Van der Auwera

VP HR

BDO · PRODATA

Florence Lambolez

Director Pharmacology

iTEOS THERAPEUTICS · La Jolla Institute FOR IMMUNOLOGY

Tony de Fougerolles

Chairman of the Board (Founding CSO Moderna)

moderna · Alnylam PHARMACEUTICALS · Ablynx

Marijn Dekkers

Board member (ex-CEO Bayer, ex-CEO Thermo Fisher)

Novalis Capital Partners · BAYER · ThermoFisher SCIENTIFIC

Kenneth Chien

Board member (Co-founder Moderna)

moderna · EQT · Swedish Research Council

John de Koning

Board member

ONWARD EMPOWERING MOVEMENT · EQT · VarmX

Kenneth Wils

Board member

PMV · flanders.bio · animab

Phil Chase

Board member (CEO Adimab)

ADIMAB · Alnylam PHARMACEUTICALS

etherna: full end to end capabilities for RNA medicine development

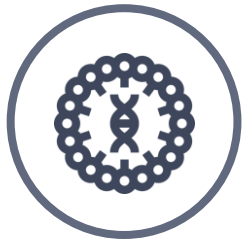
mRNA Chemistry	Lipid Chemistry	Formulation	Analytical	Preclinical	CMC	Regulatory
mRNA design	Lipid design	Customized LNP formulation	Biophysical characterization	*in vitro/ex vivo* pharmacology	Scale up manufacturing	CMC support
Sequence engineering	Lipid synthesis	High-throughput screening	QC analytical development	*in vivo* pharmacology	cGMP capabilities	(pre) IND/CTA review
Codon/UTR optimization	SAR analysis	LNP characterization	Assay validation	Toxicology	Purification optimization	Tech Transfer
Research – GMP production		Tailored LNP biodistribution		Immunology		IP

Our expertise offers end-to-end capabilities in RNA drug development

etherna positioned to be the BioPhama partner of choice for RNA medicine discovery and development collaborations

etherna: mRNA LNP expert

mRNA
Maximized expression
Specific payloads



LNP
Maximized expression
Tailored biodistribution & immunogenicity

Process technologies
Ultrapure mRNA
Improved tolerability
cGMP capabilities

Partner: disease biology expert

Disease biology
Target selection
Indication selection
Disease models
Biomarkers

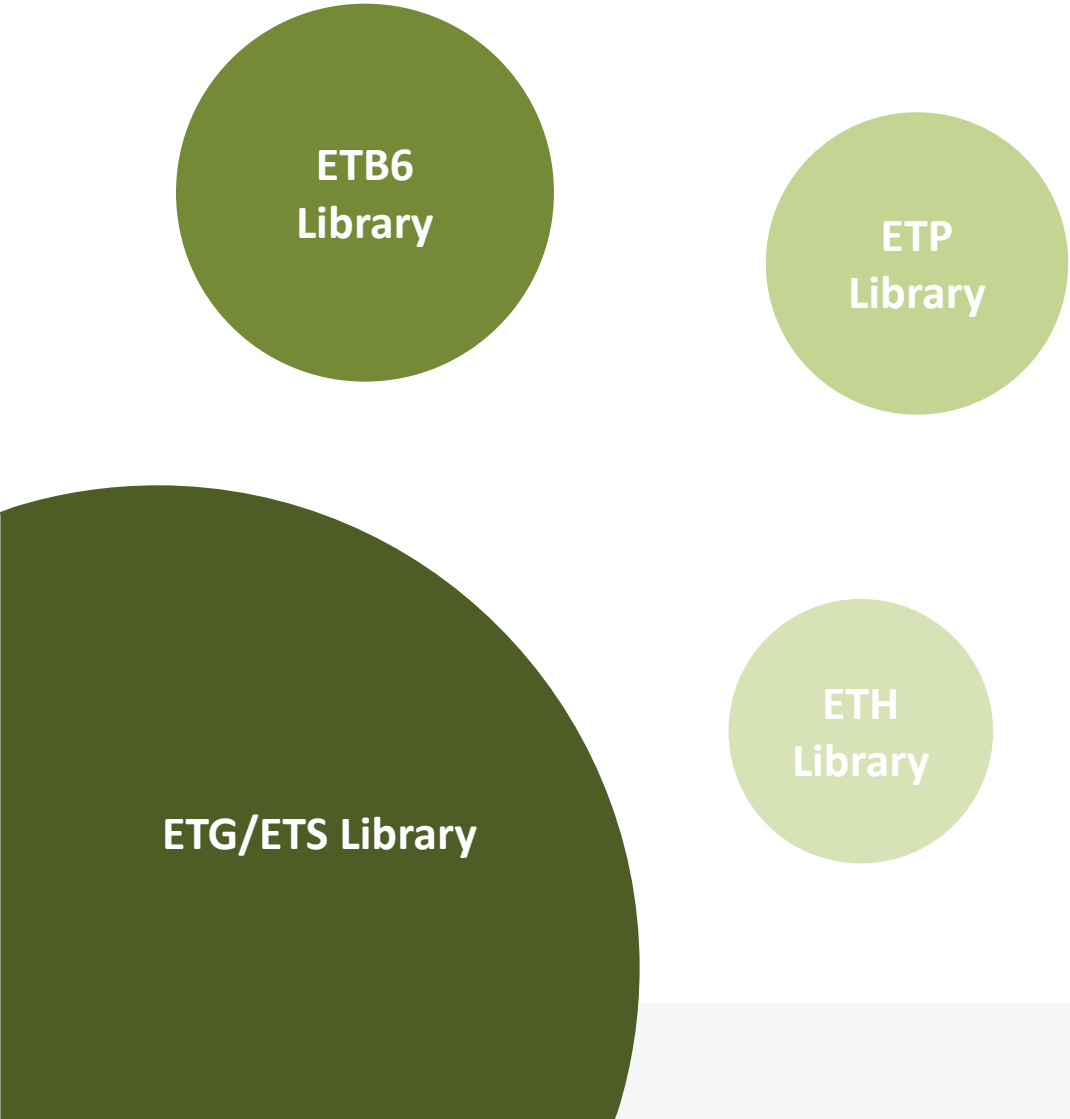
Clinical expertise
Treatment protocol
Patient selection

RNA partnership combines etherna's technology platform with almirall's therapeutic expertise to advance oncology / dermatology programs

- Multi-target alliance to discover and develop new mRNA-based therapies for severe skin diseases, including non-melanoma skin cancer
- Collaboration leverages etherna's proprietary mRNA and LNP technology with Almirall's expertise in the dermatology space
- etherna received upfront and tech access payments, and is eligible to receive >$300 million in development and commercial milestones as well as tiered royalties
- etherna and Almirall will work collaboratively on the research activities, while Almirall will lead clinical development and commercialization

LNP Platforms

State-of-the-art LNP libraries tailored for specific applications



ETG/ETS Library
- Enhanced potency *in vivo/ex vivo*
- Contains bio-reducible linker to increase degradability
- Immune-stimulatory lipids for vaccine applications
- Immune-silent lipids for protein replacement & gene editing
- Extrahepatic delivery to bone marrow and spleen

ETB6 Library
- Enhanced LNP stability
- Lipids with anti-inflammatory properties
- Extrahepatic delivery to monocytes/macrophages

ETP Library
- High immune cell tropism
- Enhanced LNP stability and potency

ETH Library
- Enhanced payload encapsulation

4 libraries with chemically diverse ionizable lipids
Rapidly expanding LNP portfolio **> 2500 ionizable lipids**

Example therapeutic applications of our customized LNP platforms

Prophylactic & therapeutic vaccination

iVAX-cLNP

Enhanced immune responses

Autoimmune disease

Tol-cLNP

Induced immune tolerance against auto-antigen

Oncology

iTu-cLNP

Maximized local expression in tumor tissue

Liver diseases, secreted factors

eLi-cLNP

High expression in liver

Inflammatory diseases & Oncology

M-cLNP

Selective expression in macrophages/monocytes

Hematological disorders and CAR-applications

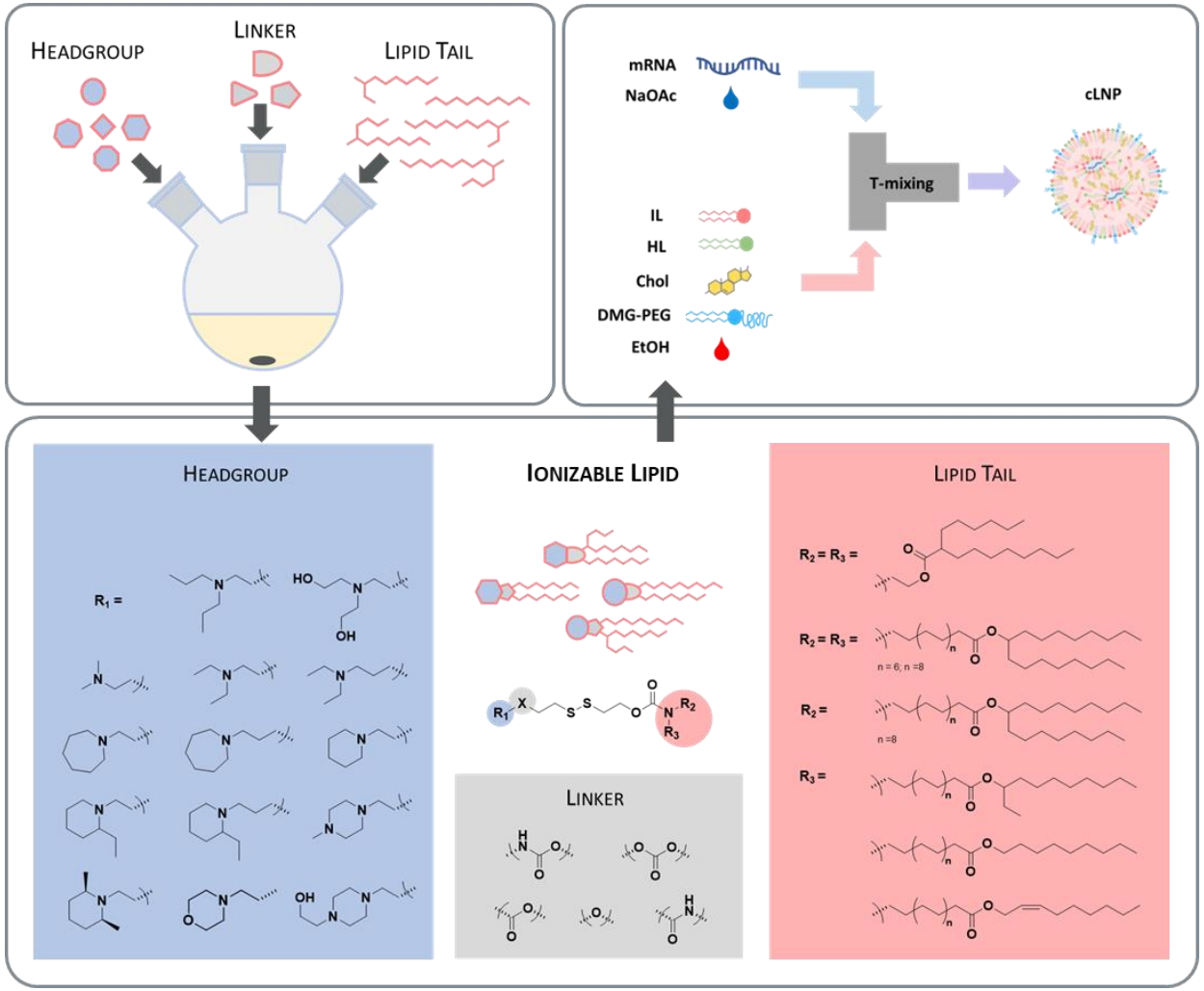
Extrahep-cLNP

High expression in bone marrow HSCs, T-cells

Customized LNPs tailored towards partner's needs

etherna cLNPs for prophylactic vaccination enhance immune responses

Reducible carbamate ionizable lipid library



INTRAMUSCULAR PROPHYLACTIC vaccination platform

Background

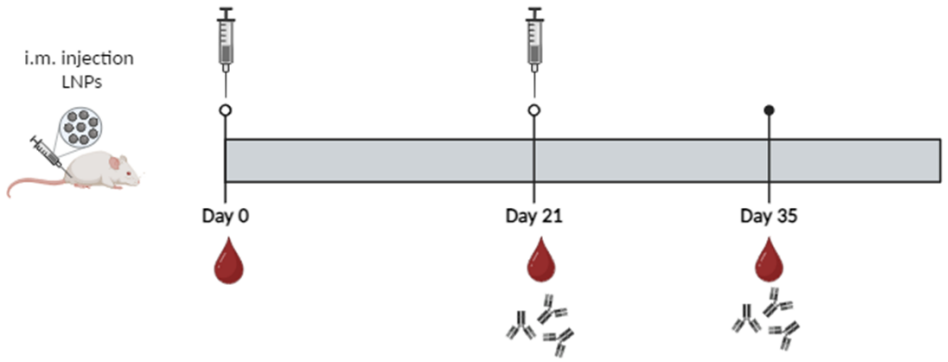
- Ionizable lipid chemistry not only governs mRNA expression but also displays intrinsic adjuvant properties

Our approach

- SAR based optimization of ionizable lipid chemistries for enhanced antibody responses: 75 lipids/LNPs tested – 3 generations
- **iVax-cLNP1:** improved antibody titers to benchmarks; IgG1-biased
- **iVax-cLNP2:** improved Th1 responses; IgG2a-biased

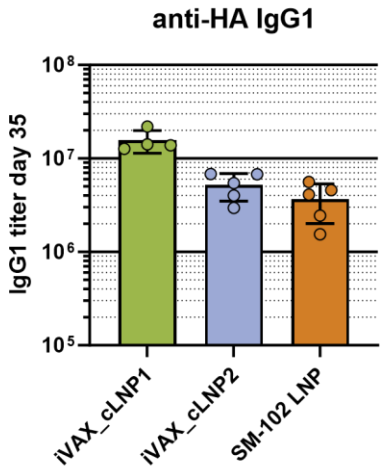
iVax-cLNPs induce strong immune response against HA influenza strain

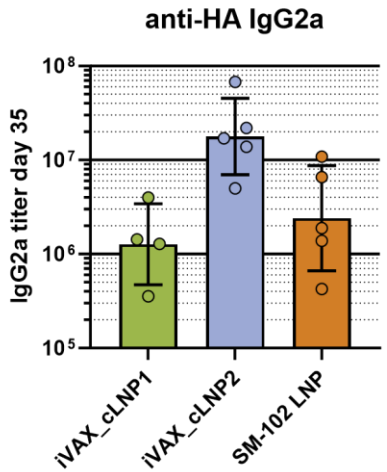
Antigen: influenza viral Hemagglutinin (HA)

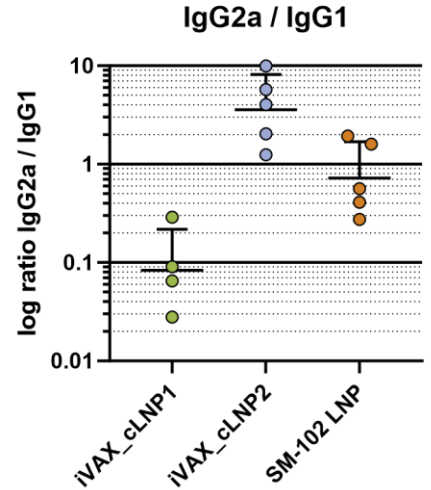


Day 35: blood sampling

IgG1 and IgG2a ELISA







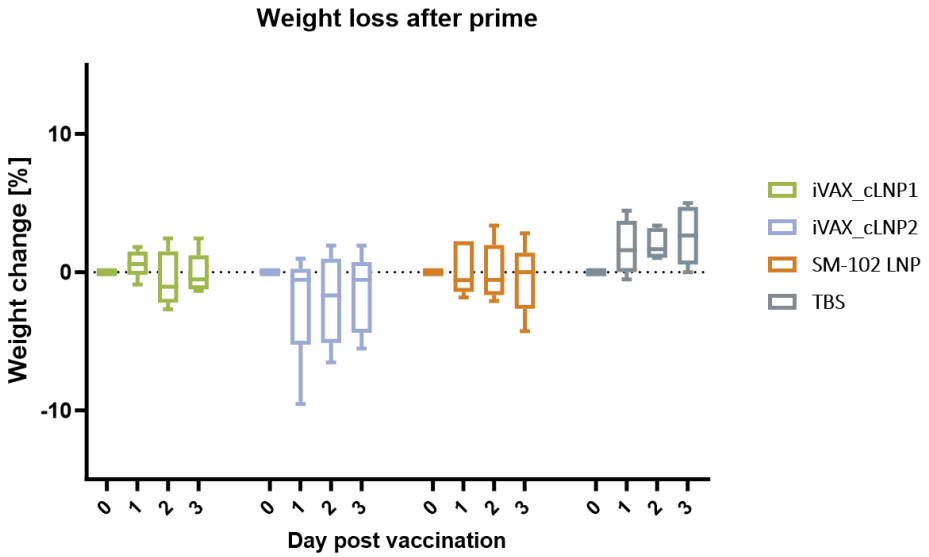
iVax-cLNPs:

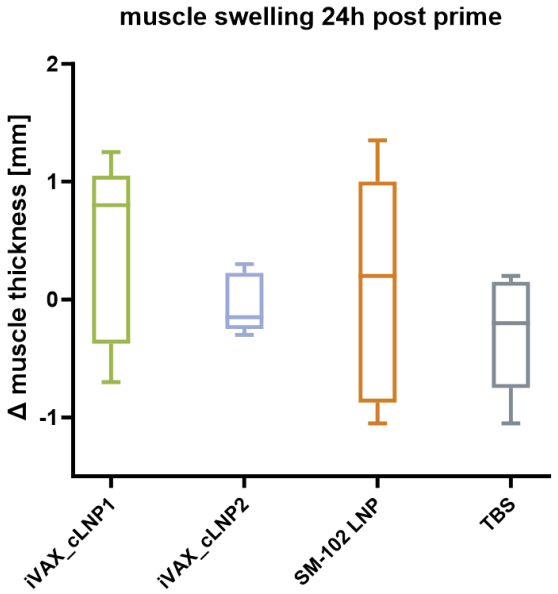
Built-in adjuvant properties

Increased antibody titers compared to Moderna SM-102 LNPs (Spikevax™)

Different IgG1 (iVax-cLNP1) vs IgG2a bias (iVax-cLNP2)

iVax-cLNPs are well-tolerated in rodents





iVax-cLNPs:

Similar reactogenicity profile compared to SM-102

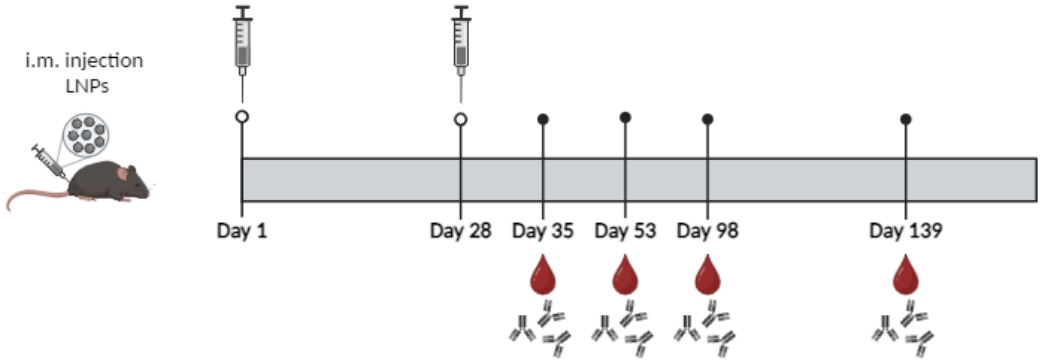
No increase in ALT/AST

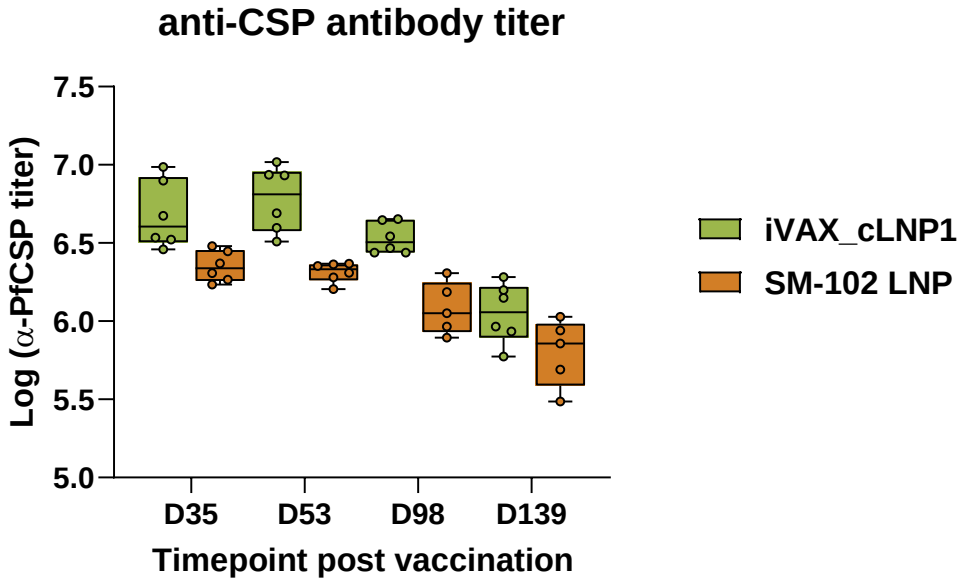
Coming-up: NHP safety & immunogenicity studies – design phase (late 2024- early 2025)

mRNA based malaria vaccine – towards improved activity

Enhanced immune response against CSP

Antigen: *P. Falciparum* derived antigen





Data generated at Institute Pasteur, Paris

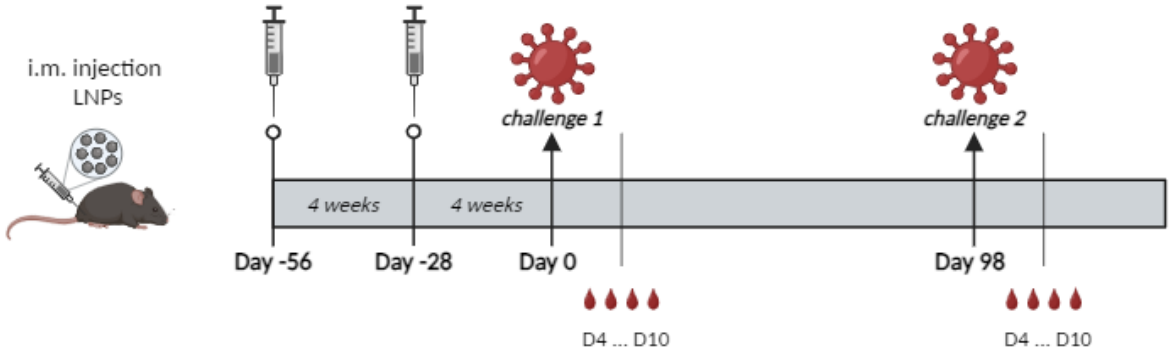
iVax-cLNP 1

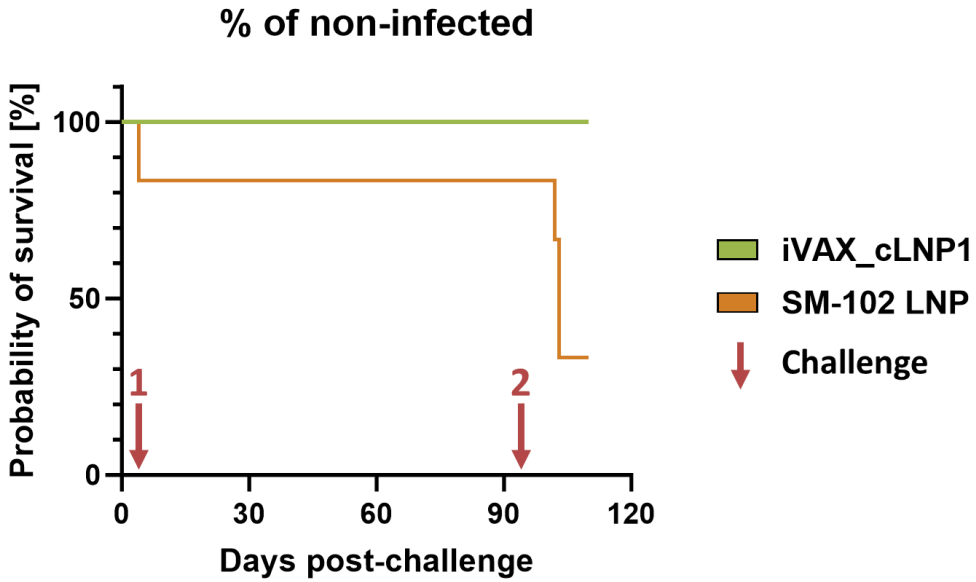
Vaccination of *P. falciparum* circumsporozoite protein (fCSP) mRNA results in superior antibody titers compared to the benchmark SM-102 LNP

mRNA based malaria vaccine – towards improved activity

Enhanced immune response against CSP

Antigen: *P. Falciparum* derived antigen
+ challenge with 5k *Plasmodium berghei*





Data generated at Institute Pasteur, Paris

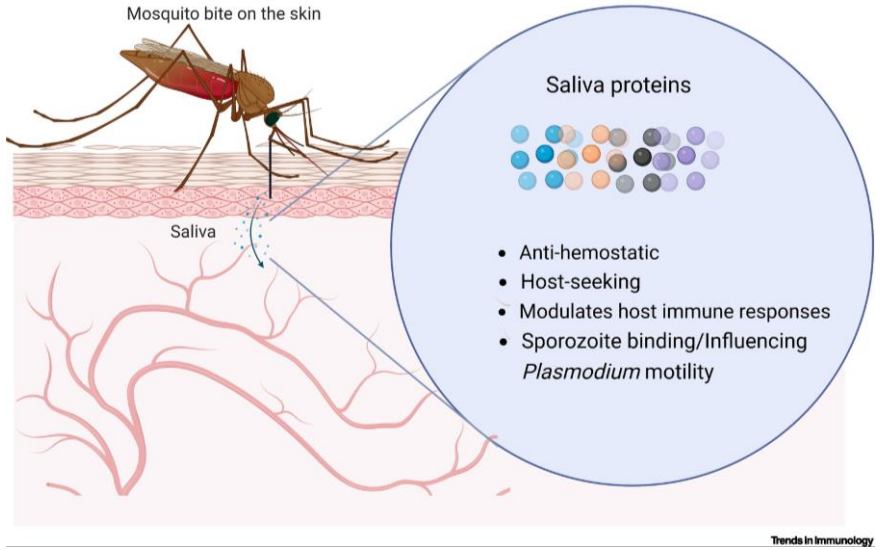
iVax-cLNP 1

Challenge with 5k *Plasmodium berghei* transgenic for fCSP
Superior protection against malaria infection compared to the SM-102

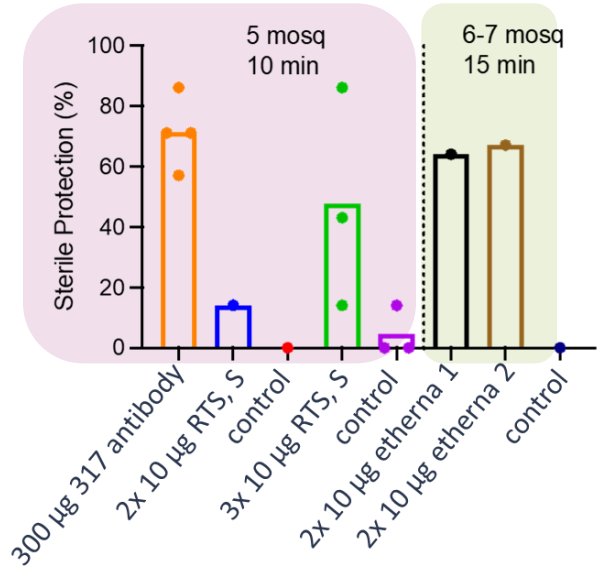
etherna CSP mRNA LNP vaccine induces superior protection

Mosquito bite model

Mosquito bite model



Mosquito bite challenge



Data generated at Institute Pasteur, Paris

NPJ vaccines 2024

etherna CSP mRNA LNP vaccines outperform approved GSK vaccine RTS,S/AS01 vaccine (Mosquirix™) in mosquito bite challenge model (comparison based on published data – Lock et.al. NPJ vaccines 2024)
Next: assessment and optimization of multivalent vaccines ongoing to improve efficacy and duration of protection

The RNA revolution: a wealth of opportunities

Why partner with us?

Broad IP portfolio

- ✓ Ionizable lipids
- ✓ LNP compositions
- ✓ mRNA platforms
- ✓ Immune-modulatory payloads
- ✓ Production Processes

End-to-end capabilities in mRNA drug development

- ✓ Target selection
- ✓ mRNA design
- ✓ LNP formulation
- ✓ Pre-clinical evaluation
- ✓ cGMP mRNA manufacturing
- ✓ Regulatory support

Customized solutions

- ✓ Lipid/ LNP customization tailored to your needs
- ✓ mRNA sequence engineering

Flexible, professional partnership

- ✓ mRNA and LNP or single components
- ✓ Collaborative mindset
- ✓ Partner centered
- ✓ Professional alliance and project management

etherna

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