Aramis Biotechnologies

Aramis Scientific Horizon

2025-06-12

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Welcome and Corporate Introduction

Agenda

Welcome and corporate introduction

Mr. Frédéric Ors, Chief Executive Officer

Presentation of the major breakthroughs on the bioproduction platform

Dr. Marc-André D'Aoust, Chief Scientific Officer

Presentation of the major breakthroughs of the seasonal influenza vaccine candidate

Dr. D'Aoust & Dr. Brian Ward, Chief Medical Officer

Summary and next steps

Mr. Ors

Global leader in plant-based bioproduction

Leading a green revolution in biotechnology across multiple markets

Accelerated commercial demonstration & strategic partnerships

Platform vision

Proven

Speed, productivity, versatility

Safety in 28,000 subjects

Commercial scale & Regulatory approval

Commercial focus

Next gen vaccine technology

Mimicking the virus mimics natural immunity

Long-lasting and effective protection

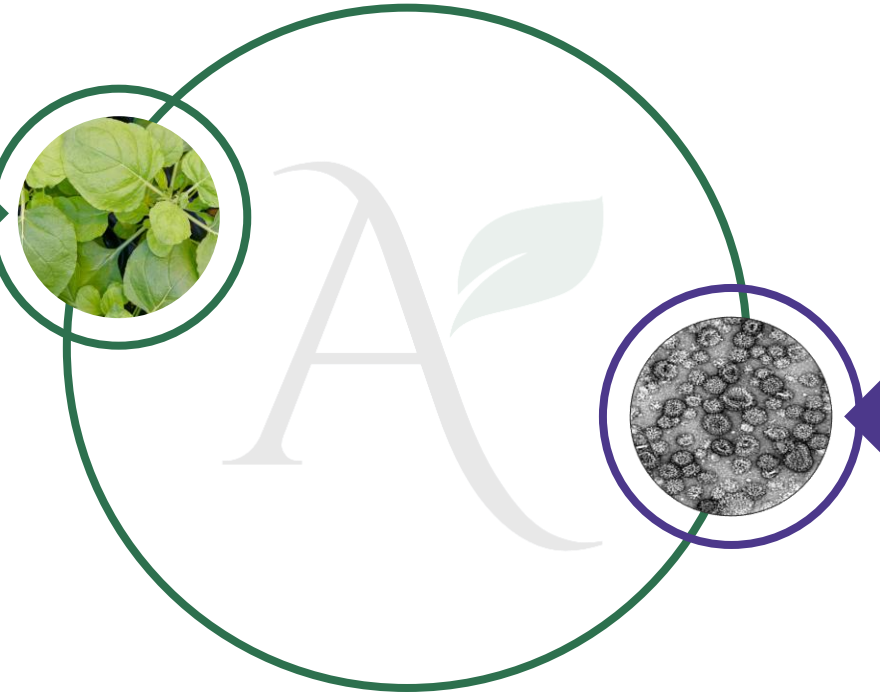
Phase 3 clinical studies

Aramis

Research & Development priorities

Platform

- Facilitate commercialization by reducing production scale
- Worldwide applicability with various products



Product

- Preserving structural mimicking of the virus, regardless of the strains
- Immunity and duration of protection

Major breakthroughs Platform

Benefits of plants as a manufacturing platform

Nicotiana benthamiana

Flexibility	Efficient production of vaccines, biotherapeutics and small molecules
Large production scale	Scaled up to >100 million vaccine doses per year
Response speed	Response time comparable to the fastest platforms for pandemic response
Precision	Recombinant technology eliminates the risk of mutation
Safety	No live agent and no animal products - No viral contamination NOT tobacco

Process for plant-based vaccine production

ARAMIS

Master Vectors Bank	Plant growth	Vacuum Infiltration	Expression	Harvest and extraction	Clarification
Viral gene synthesized from sequences of targeted viruses	*N. benthamiana* plants grown in controlled environment	Genetic material introduced into plants through vacuum infiltration of a bacterial vector	6-9 days in growth chambers for protein expression and VLP assembly VLPs mimic structure of virus but are non-infectious	Plant leaves are harvested and content is extracted	First step purification to stabilize extract before shipping to CDMO

CDMOs

Purification	Fill & Pack
VLPs purified to obtain drug substance Very similar process compared to other vaccine products	Drug product is filled and packaged

VLP = virus-like particles

Objectives for bioproduction platform optimization

Plant-based vaccine bioproduction technology is efficient, fast, flexible, safe and allows for large-scale production

The work to improve the acquired manufacturing platform had 2 objectives

Improvement Objectives	*Impact*
Increasing the yields of manufacturing and purification processes	• Reduced cost per dose • Reduced scale of commercial process • Reduction in the size of the commercial plant
Elimination of the plant growth step in greenhouses – transition to closed production system	• Increased reproducibility • Increased robustness to environmental conditions • Reduced environmental footprint

Improvement to expression vectors

Areas of development

1. **Increasing the influenza VLP content of plants**

   Translates into increased yields through the entire process

2. **Improving the quality of biomass at harvest**

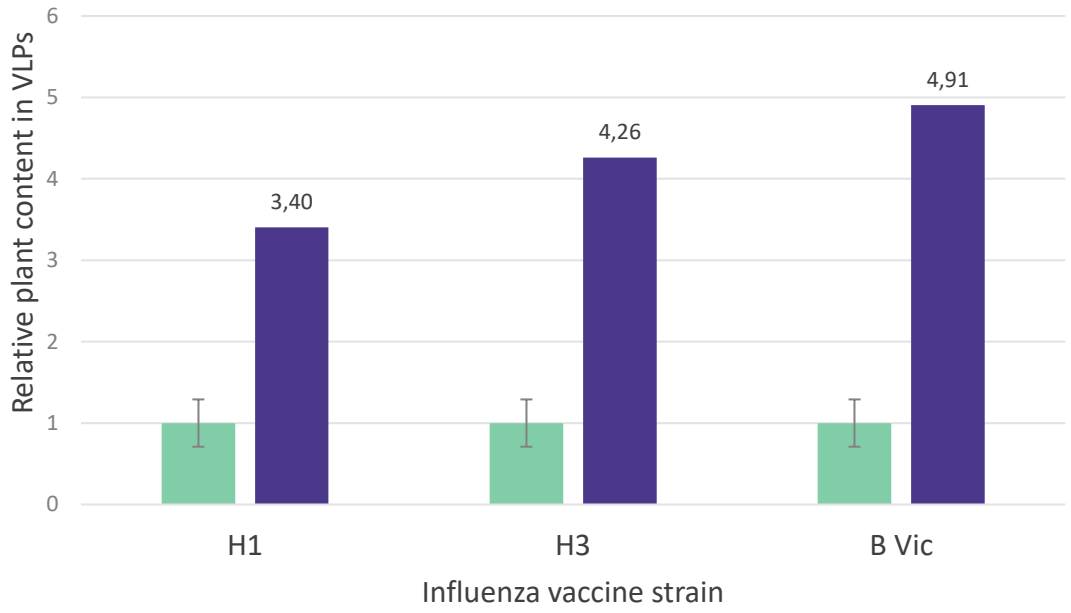
   Improves the efficiency of the purification process

- The incorporated concepts come from the advancement of knowledge on the expression of complex proteins in plants
  - Learnings from the Covifenz® development project applied to influenza VLPs
  - Recent advances in fundamental knowledge in the field of plant defense reactions

- Evaluations carried out on the production of influenza VLPs for the 3 strains making up the recombinant seasonal vaccine for the 2025-2026 season in the Northern Hemisphere
  - an A/Wisconsin/67/2022 (H1N1)pdm09-like virus
  - an A/District of Columbia/27/2023 (H3N2)-like virus
  - a B/Austria/1359417/2021 (B/Victoria lineage)-like virus

Optimisations have greatly increased the efficiency of the manufacturing and purification processes

Level of VLP accumulation in plants



Phase 3 lot production (Medicago)

Optimised vectors (Aramis)

Increased final yield of the optimized process*

VLPs H1: 4.1 times

VLPs H3: 4.4 times

VLPs B Victoria: 19 times

* Increase from Medicago's Phase 3 clinical batch yields

Closed Plant Production System (CPPS)

Significant benefits for pharmaceutical production

Environmental parameters control

Reproductive/robust production

Exportable to all countries in the world

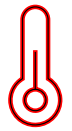
Reduced environmental impact

High level of automation - without human contact

Provides the opportunity to establish the commercial production unit at our current location

15X reduction in the weight of substrate used

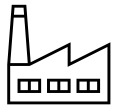
100X reduction in water used



10X reduction in CO_2 injection

Increased phytosanitary control

Reduction of plastic waste



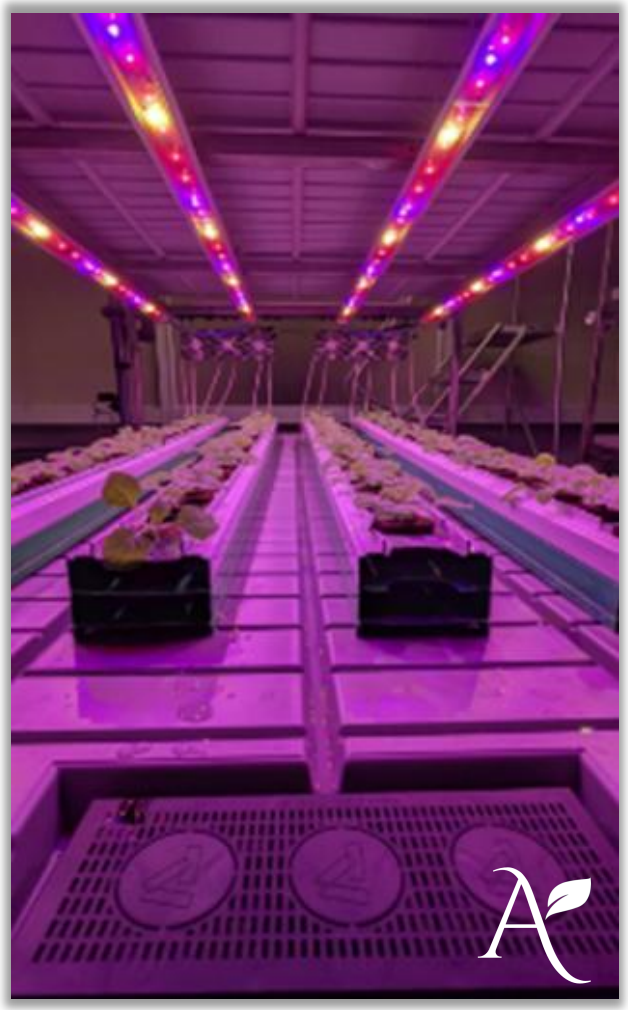
Reduction of the soil footprint by density (1.7 X), stacking (3 to 10 X) and yield in g/plant (1.3 X)

Adaptation of CPPS for vaccine bioproduction

- Conditions developed for horticultural crops were not suitable for the growth of *N. benthamiana* to produce VLPs

- Several conditions had to be optimized to ensure a productivity equivalent to that of plants grown in greenhouses
  - Intensity and quality of the lighting
  - Air circulation
  - Substrate and fertilization
  - Plant spacing

- Today, improvements allowed to obtain yields similar to the best yields observed with plants grown in greenhouses



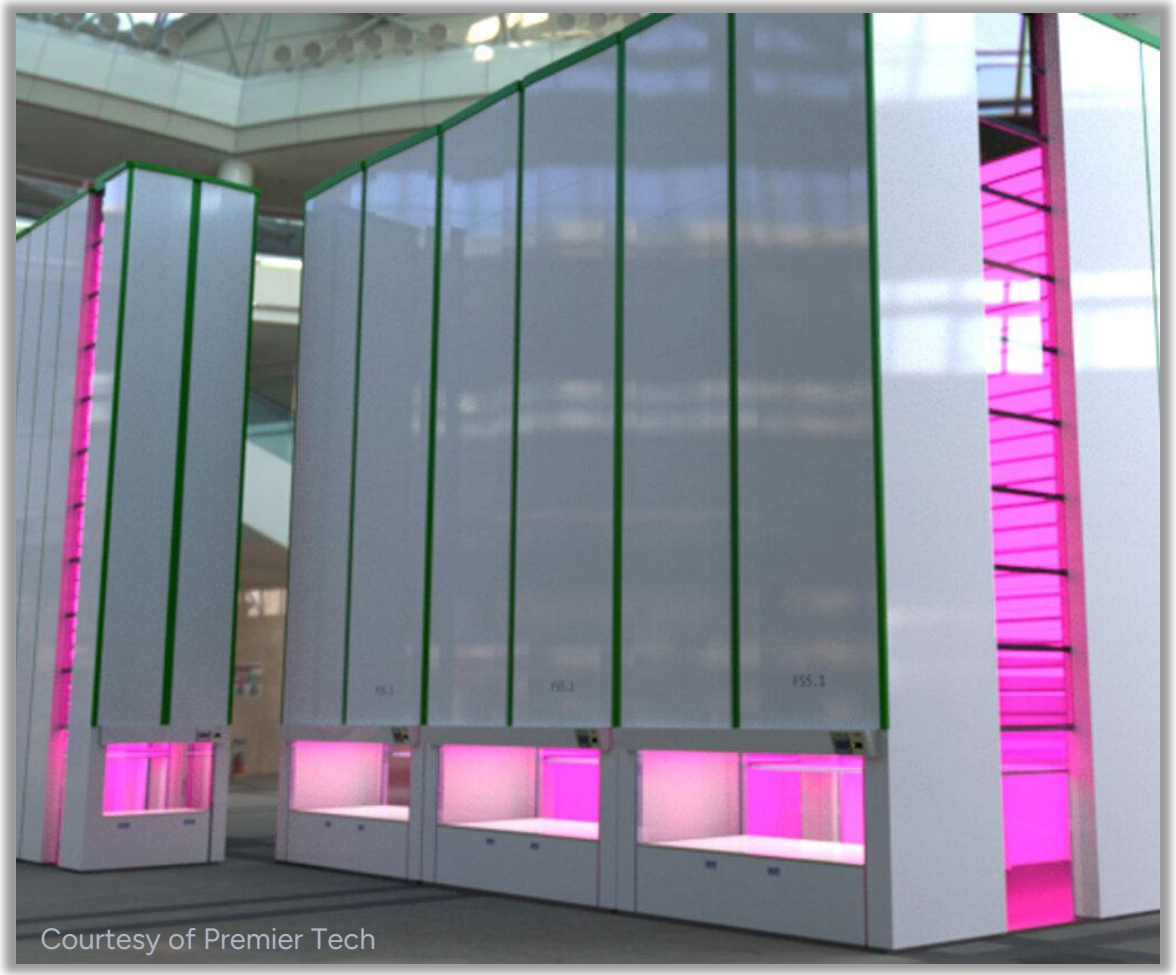
Improvements to the bioproduction platform have allowed to:

Increase the combined expression and purification yields of influenza VLPs between 4X and 19X depending on the HA strains

- Reduction of the vaccine production cost (capital and operations)
- Eliminating scale-up issues for commercial production

Plan a transition to vertical cultivation (CPPS) for plant production

- Increased control of growing conditions
- Increased production robustness
- Reduced environmental impact

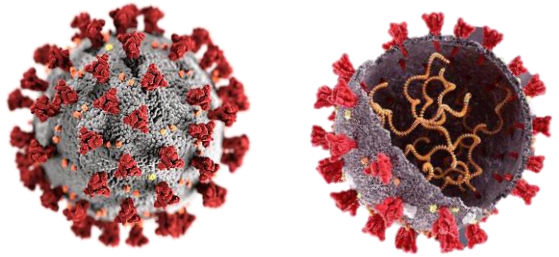

Courtesy of Premier Tech

Major breakthroughs Product

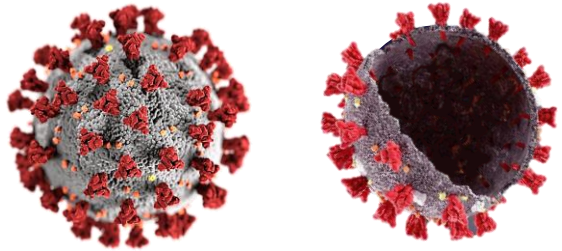
VLP vaccines

Virus-like particles (VLPs) are products used for vaccination that look like viruses on the outside, but are not infectious because they do not contain genetic material

SARS-CoV-2 virus

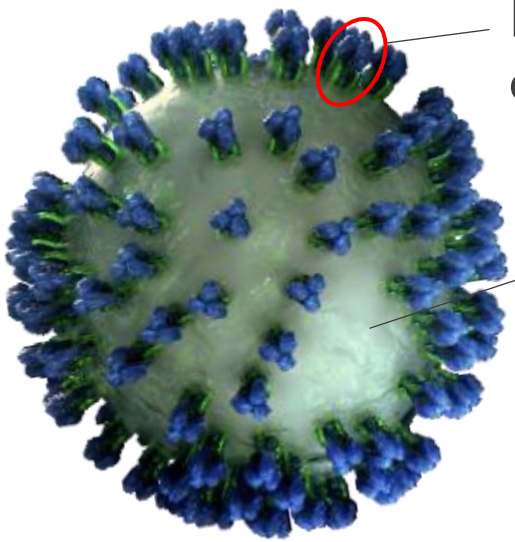


SARS-CoV-2 VLP



VLPs are among the most effective vaccine technologies on the market today (e.g. hepatitis B, human papillomavirus).
There is currently no VLP vaccine for influenza

Our Influenza VLP vaccine candidate



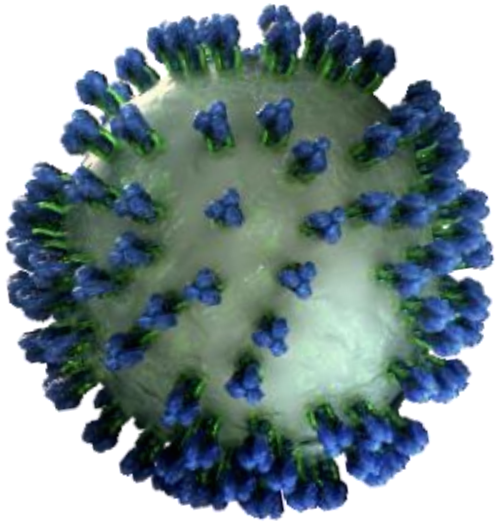
Characteristics of Influenza VLPs

- Nanoparticles (~100 nm)
- Multiplicity of antigens
- Antigen density
- Abundant glycosylation
- Organized antigen presentation

The characteristics of Influenza VLPs can ensure

- A fast and long-lasting immune response
- High production of antibodies and T cells
- Epitope presentation promoting neutralizing antibodies production

Objectives for Influenza VLP optimization

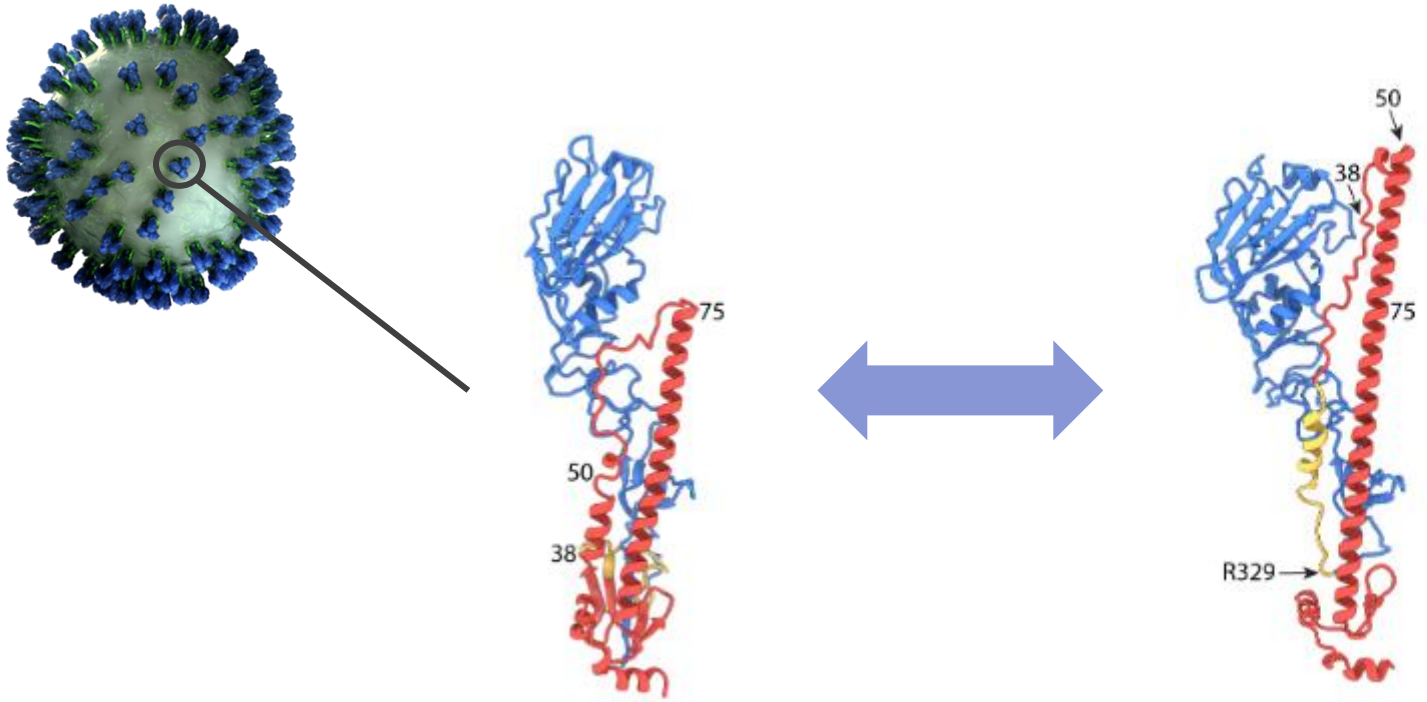


The work to improve the influenza vaccine had 2 objectives

Improvement Objectives	*Impact*
HA stabilisation in pre-fusion conformation by protein engineering	• Promotes neutralizing antibodies production against the circulating virus
Process adaptation to optimize Influenza VLPs characteristics	• Improves VLP integrity • Increases antibody and T cells responses

Optimisation objectives

- Stabilisation of hemagglutinin (HA) in pre-fusion conformation



Pre-fusion (monomer)

Post-fusion (monomer)

Certain conditions can induce a change in the HA conformation, resulting in a change in epitope presentation to the immune system

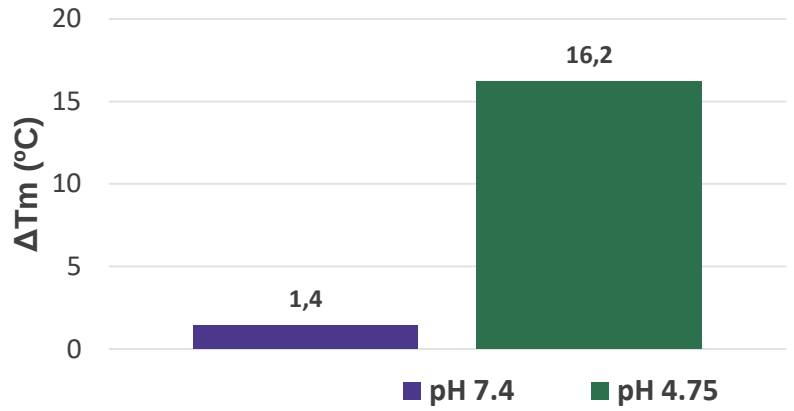
Pre-fusion HA stabilization optimizes HA presentation to the VLP surface

HA representations extracted from: Eva Garcia-Moro, Jie Zhang, Lesley J Calder et al. (2022) Proc Natl Acad Sci U S A. 8;119(33): e2208011119. doi: 10.1073/pnas.2208011119

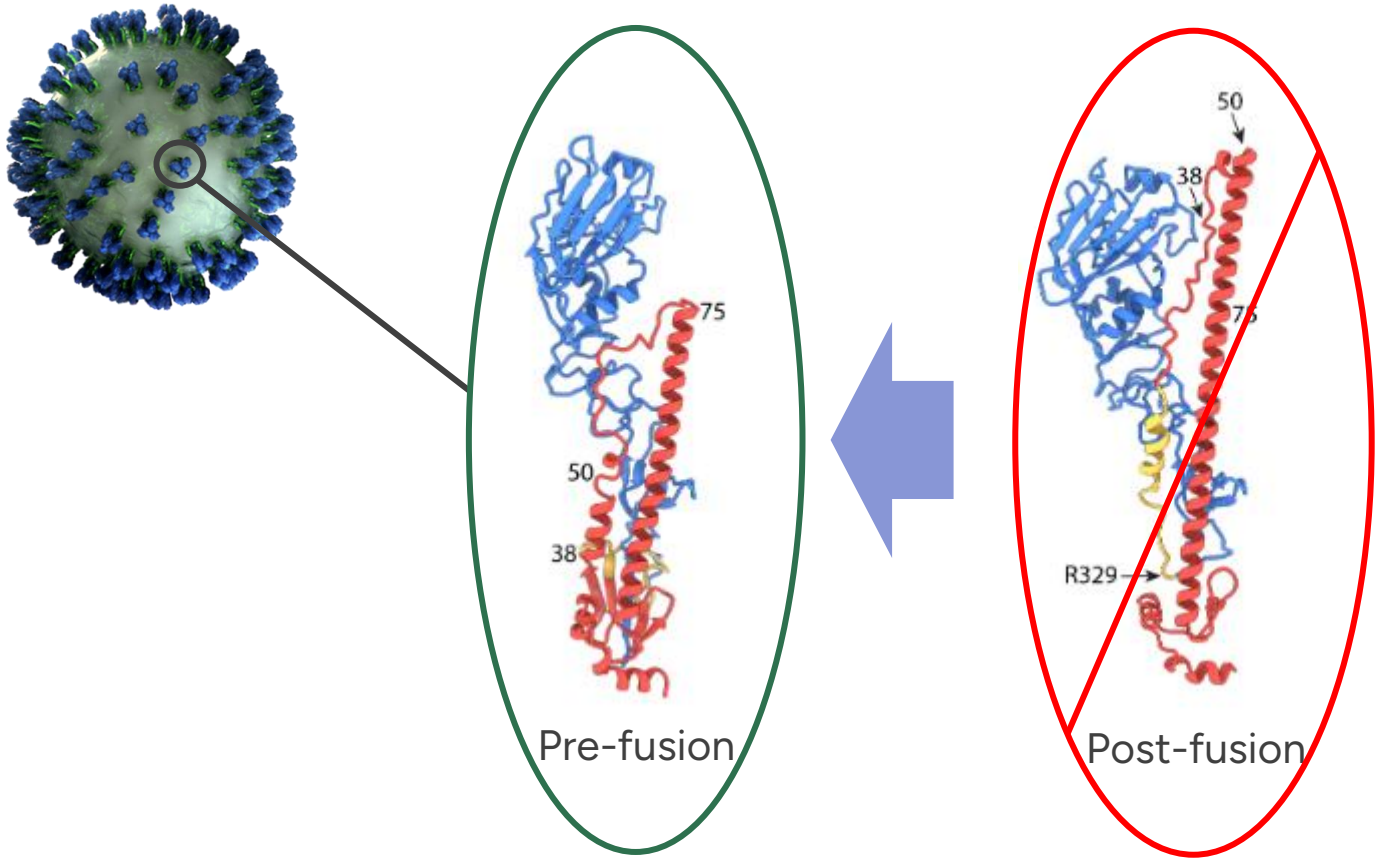
Optimisation of HA epitope presentation

A patent application has been filed for this technology

HA sequence engineering increased its resistance to conformational change, stabilizing it in pre-fusion conformation



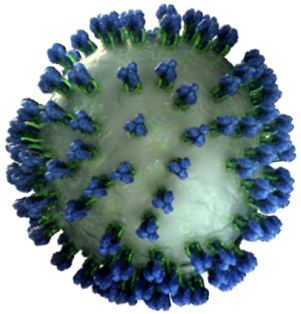
Increased melting temperature* of H3 A/District of Columbia/27/2023 stabilized in pre-fusion compared to native H3 at pH 7.4 and 4.5



HA engineering allowed to stabilize the pre-fusion form, promoting the production of neutralizing antibodies against the circulating virus

* This measurement is performed by differential scanning fluorometry (DSF).

Optimisation of VLPs characteristics



Our observations on the Medicago product indicated that the purification process altered the integrity of the VLPs

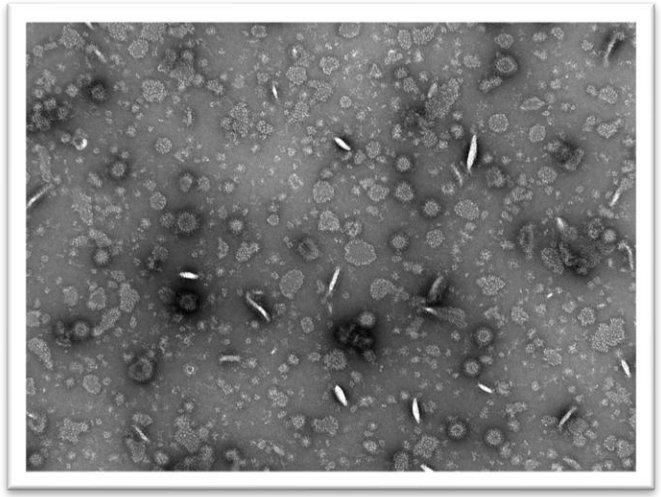
- HA shedding from the surface of VLPs
- Loss of HA density on the surface of VLPs

… leading to a loss of product effectiveness in inducing a strong and lasting immune response

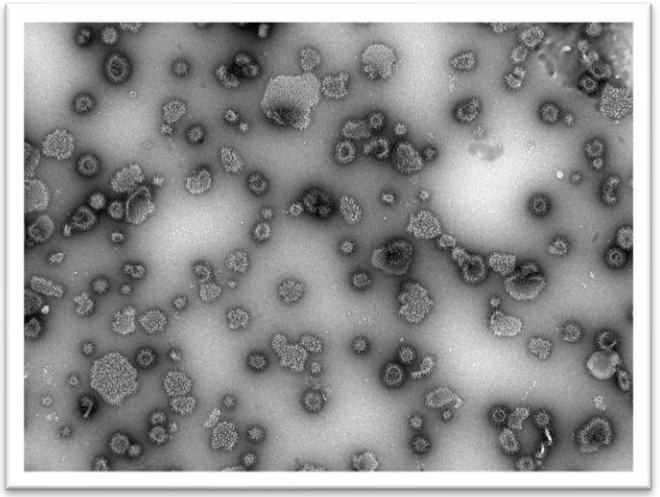
Adaptation of the VLP purification process

Following the identification of the causes of the loss of integrity of the VLPs, the purification and formulation process were adapted **to optimize influenza VLPs characteristics and stability**.

Non-optimized process

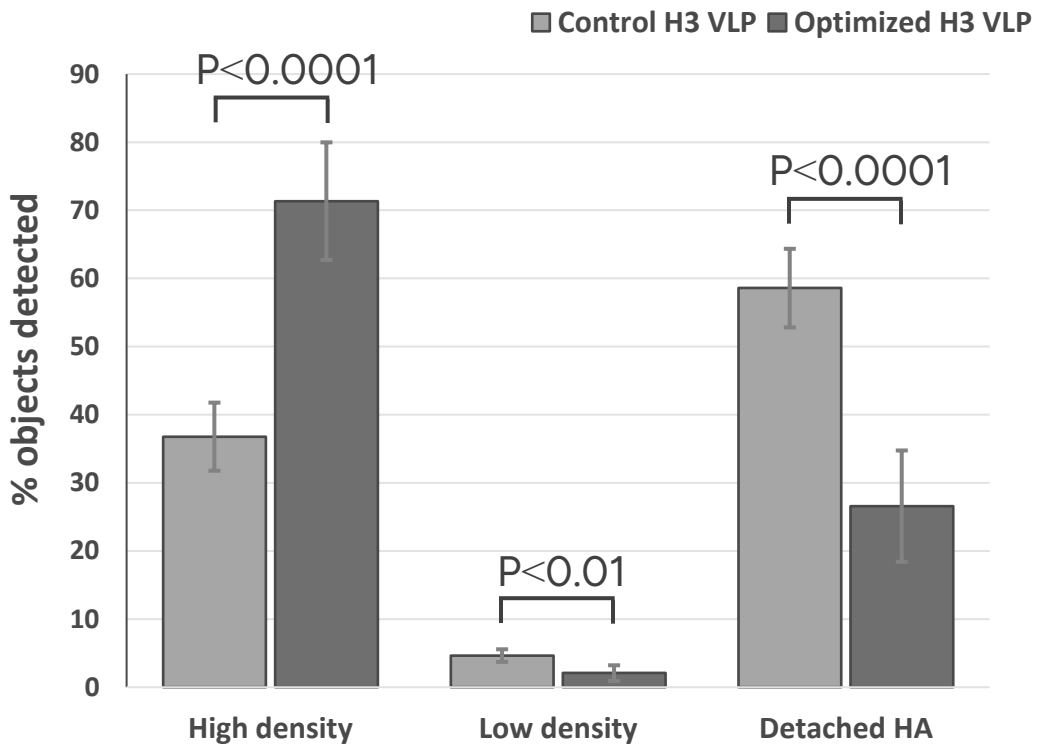


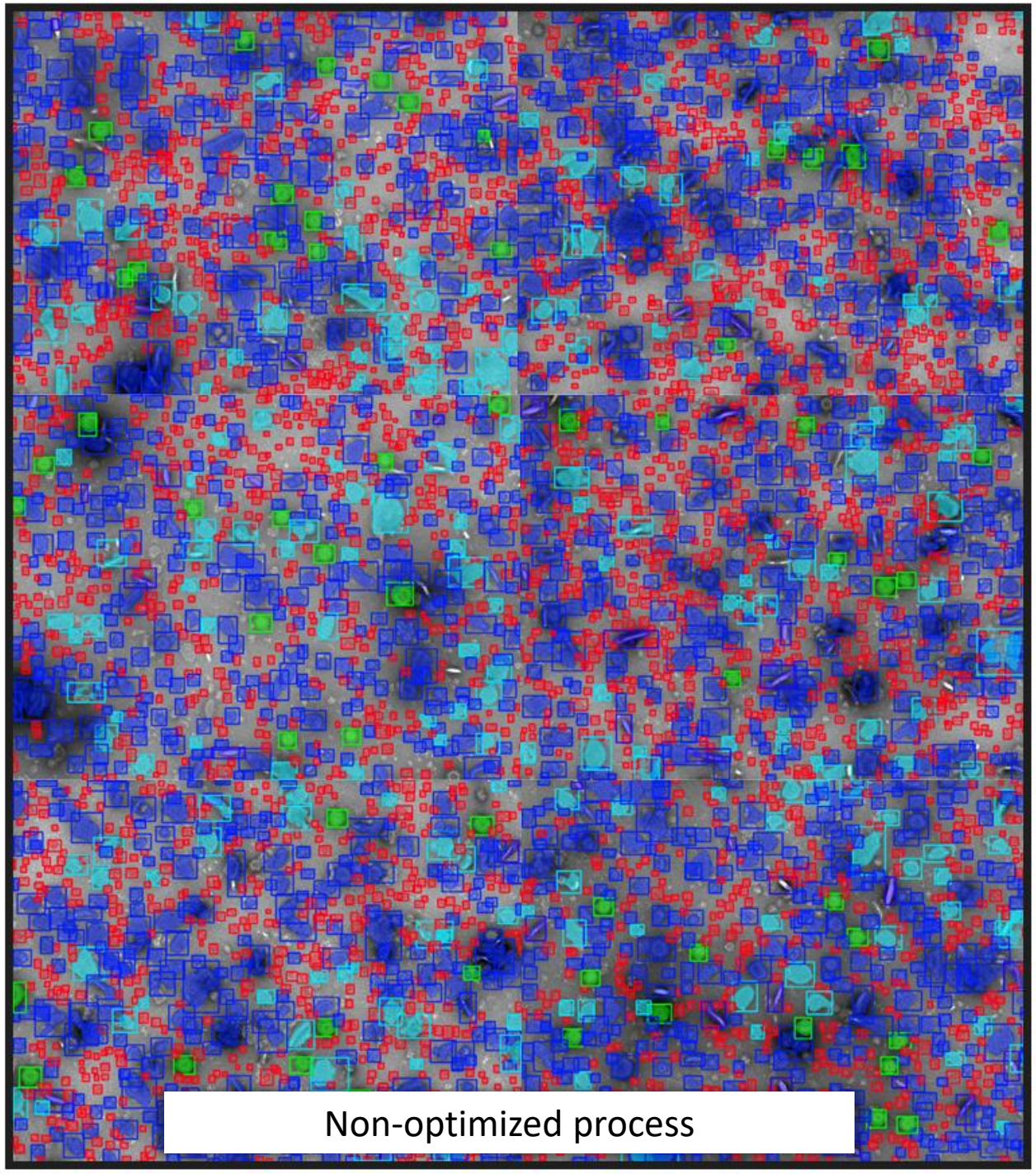
Optimized process

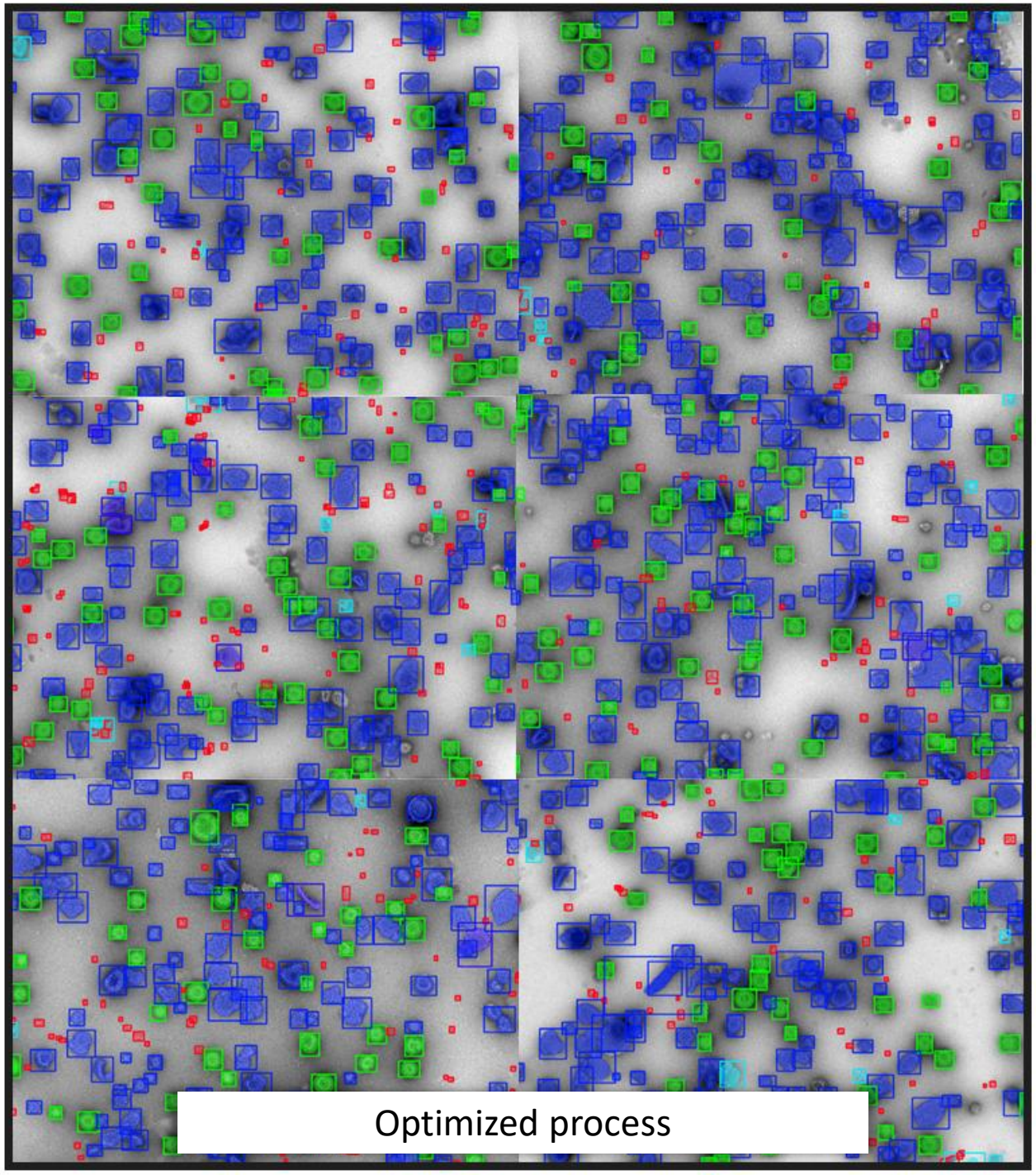


Development of an algorithm for particle characterization

- Machine learning model training for object detection from electron microscopy images
  - Particle types
  - HA density
  - HA detached from VLPs
- Enables the quantification and characterization of particles in the product




Non-optimized process


Optimized process

Animal study design

Study objectives

- Compare immunogenicity of optimized VLPs to VLPs from the original process
- Compare immunogenicity of optimized VLPs to current commercial vaccine

Study design (mouse)

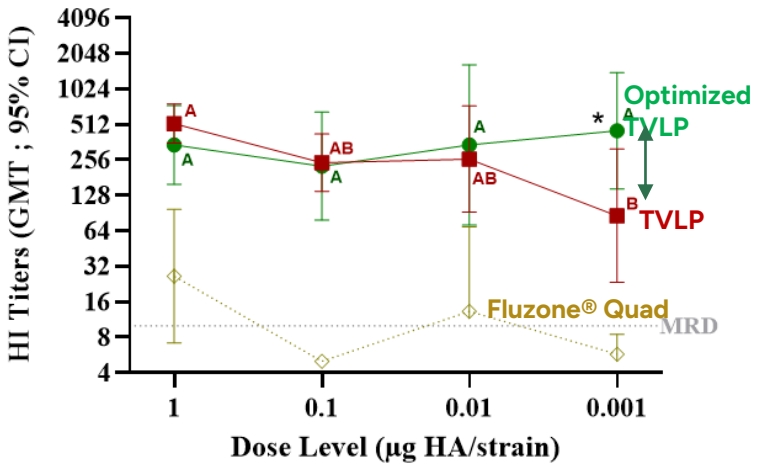
- 5 mice / group
- 4 dose levels (1 μg, 0.1 μg, 0.01 μg and 0.001 μg)
- 2 immunizations: Days 0, 21
- Comparator: inactivated vaccine
- 3 blood samples: Days 0, 21, 49 (28 days post-immunization)
- HI and MN titer analyses on Days 0 & 49 and IgG on Days 0, 21, 49

HI: Hemagglutination Inhibition; MN: microneutralization

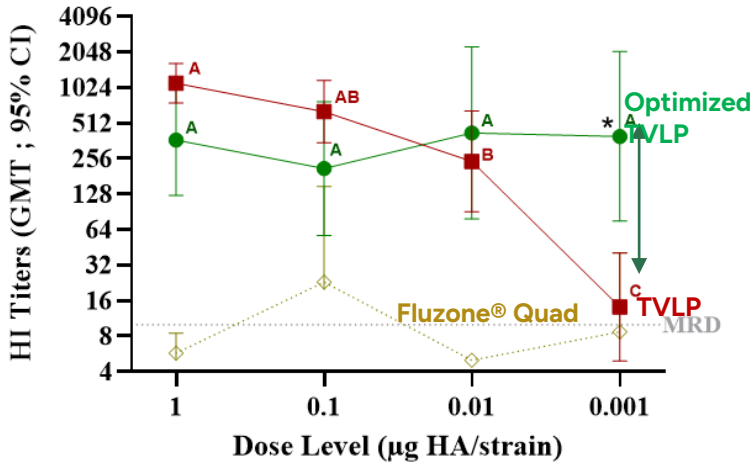
Titration of the vaccine candidate and VLPs comparison to the commercial vaccine (HI titres*)

*The HI response is accepted as a "correlate of protection" for influenza

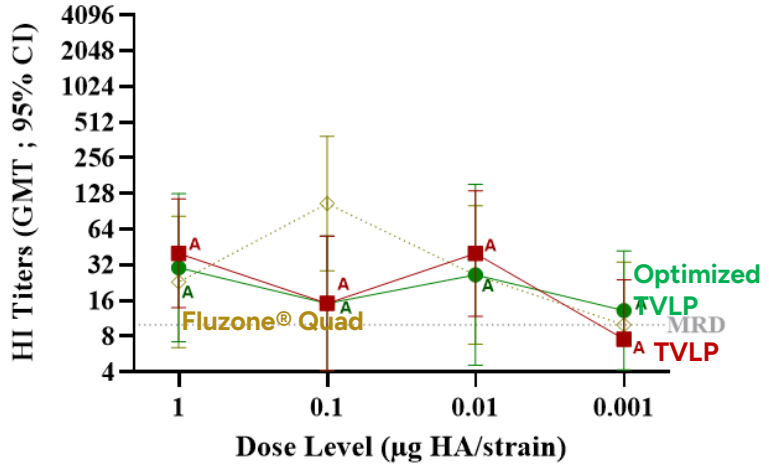
H1/Wisconsin
Reagent: A/Wisconsin/67/2022 (H1N1)pdm09
(IRR FR1857) Cell-based



H3/District of Columbia
Réactif: A/District of Columbia/27/2023
(IRR FR-1896) Cell-based



B/Austria
Réactif: B/Michigan/01/2021
(IRR FR-1800) Cell-based



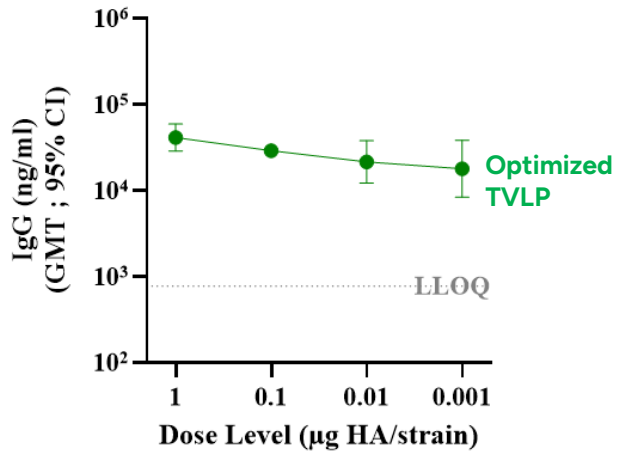
- The "equivalent" of 15 µg/strain per dose in a 70-kg person is 0.005 µg in a 25-g mouse
- Optimized TVLPs (at 0.001 µg) induce a higher HI response than non-optimized TVLP for 2 of the 3 strains
- Optimized TVLPs (all doses) induce a higher HI response than Fluzone® for 2 of the 3 strains
- Both optimized TVLPs and Fluzone® induce low responses for B/Austria. However, the B VLPs are immunogenic (next slide)

TVLP: trivalent vaccine candidate (H1, H3 et B/Vic)

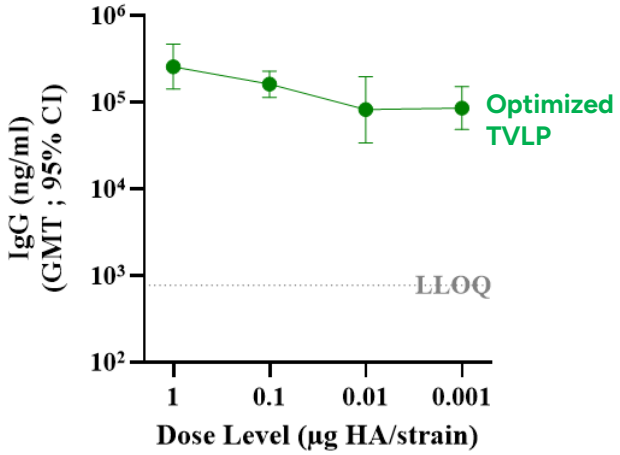
Titration of the vaccine candidate (HA-specific IgG)

IgG titres

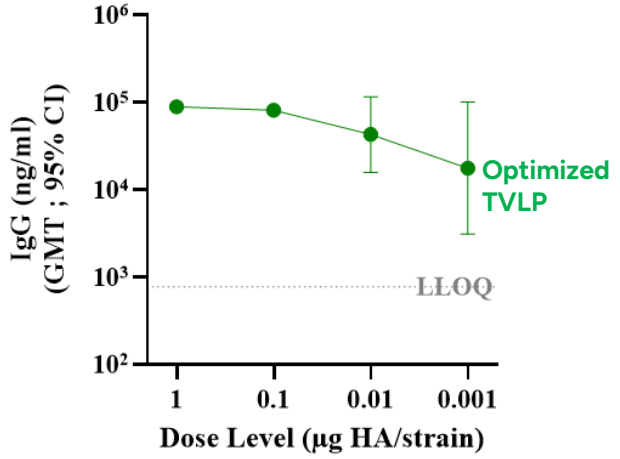
H1/Wisconsin
Reagent: A/Wisconsin/67/2022 (IA-H1-W22tp)



H3/District of Columbia
Reagent: A/District of Columbia/27/2023 (IT-003-00448ΔTMp)



B/Austria
Reagent: B/Austria/1359417/2021 (IB-HA-A21WP)



- In contrast to HI titres, HA-specific IgG titers responses are similar for the optimized H1, H3, and B VLPs
- Therefore, the low HI response for the B strain with the optimized TVLP is not due to a "response deficit" but rather reflects a deficiency in the HI response for the B strain in mice. Rats, on the other hand, generate a good HI response against the optimized B VLPs

Phase 1/2 clinical study in preparation for Q1 2026

Phase 1/2 study aims to evaluate the **immunogenicity** and **safety** of **optimized** TVLP versus commercial vaccines in adults ≥18 years of age

- Design: Randomized, blinded, active-comparator-controlled study, dosage, immunogenicity, safety and tolerability
- Age groups: 18 to 64 years old and ≥65 years old
- Dose: Single dose, intramuscular
- Comparators (inactivated vaccines): 15 µg/strain (18-64 years) and 60 µg/strain (≥65 years)
- Number of subjects: 750
- Analyses: serology and cellular response
- Follow-up: 6 months

Improvements in the TVLP influenza vaccine candidate

- Stabilization of the HA antigens in the pre-fusion conformation should improve functional antibody production against the targeted viruses

- Higher density of stabilized HA antigens on the plant-made VLPs should induce a pattern of response 'typical' for other VLP vaccines including:
  - Rapid and long-lasting immune responses
  - Strong induction of both antibodies and T cells
  - Presentation of the HA antigen in a way that promotes functional antibody responses

- Several of these predicted advantages have been observed with the optimized VLPs in mice and rats. The full impact of these improvements will be evaluated in the planned Phase 1/2 study.

Acknowledgements

Our research partners

- Research Institute of the McGill University Health Centre
- Université Laval
- Université de Montréal

Our scientific advisors

The Aramis Biotechnologies teams

Summary and next steps

Major advances in the first 12 months

Multiplied productivity

Reduces and eliminates the need for scaling-up for commercialization

Closed system

Makes the process exportable worldwide, "greener" and applicable in other markets

Optimized product

For a new generation of vaccine with improved immune potential and duration of protection

Next 12 months

Commercial acceleration & exploitation of the platform's potential

Phase 2 results, strategic partnerships and commercial expansion of the facility

A colossal amount of work by the team

1 clinical GMP factory

70 000 plants
150 optimization experiments
600 expression vectors
3 600 agrobacteria batches
4 000 extracts tested
75 small-scale lots
25 analytical tests developed
8 GMP development lots
519 approved quality Documents
54 equipment validations
5576 completed trainings
4 preclinical studies
600 vaccine candidates administered

Aramis Biotechnologies' clinical GMP plant

Thank you!

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