



**Innovative Engineering Synthetic  
Adjuvants and Delivery Platforms  
to Enhance Global Health  
Accessibility and Affordability**

**Accessible | Available | Efficacious**

**Jay Evans, PhD.  
Chief Scientific Officer  
Inimmune Corporation**

# Agenda



- Introduction
- SPI/Inimmune Partnership highlights
- Novel TLR4 (INI-2002) Based Adjuvant Systems
  - T4Q: INI-2002 + QS-21 adjuvant system
  - T4Q<sub>GH</sub>: INI-2002 + QS-21GH adjuvant system
  - T4AH: INI-2002 + Alum adjuvant system
  - T4SE: INI-2002 + squalene emulsion
- Expanded synthetic adjuvant portfolio
  - INI-4001: best in class fully synthetic TLR7/8 adjuvant
  - TRAC-478 emulsion: combination adjuvant system

# The Inimmune Difference: Global leaders in innate immune modulator development



\$180M NIH grants, contracts, and collaborations for pre-clinical R&D

Next generation innate immune modulators targeting TLR4 or TLR7/8 to initiate and direct the immune response

Reprogram the Immune Response

Disease Modifying Allergy Therapy

Activate Exhausted Immune Cells

Broad Oncology Immunotherapy

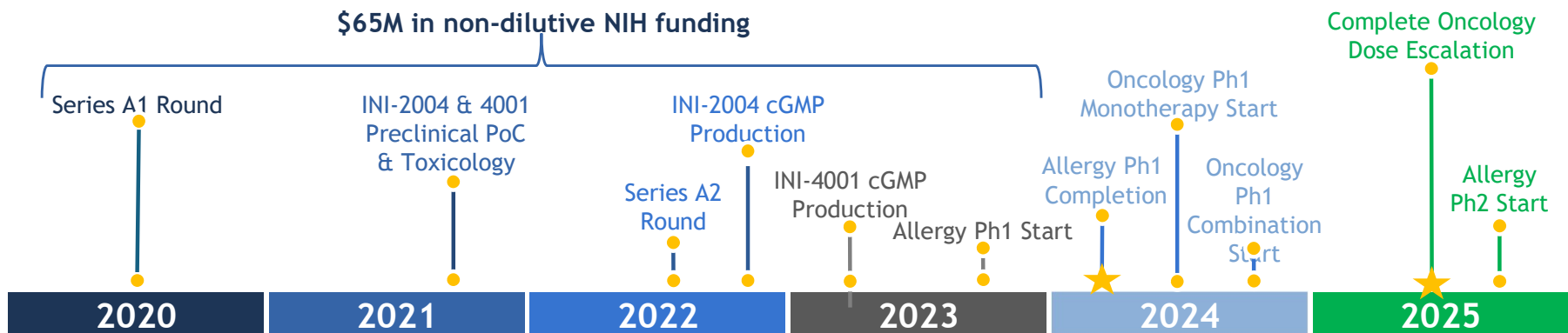
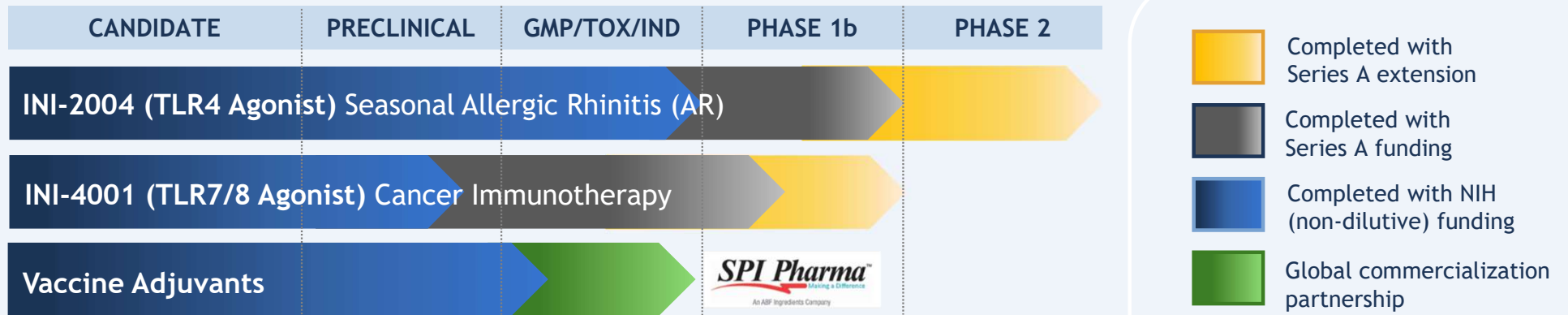
Stimulate Vaccine Immune Response

Adjuvants to Enhance Efficacy and Safety



- Over 20 years of experience in immuno-modulatory drug discovery and development
- Strong external funding and IP generation >\$180 M in NIH Contracts for pre-clinical R&D and 20 patents in the past 10 years
- Expertise from discovery through clinical implementation

# Deep Immunotherapy Pipeline with Two Clinical Stage Assets



# Stronger Solutions, Built Together

Efficacious, Affordable, Scalable, Stable Adjuvant Systems



## **SPI is a global adjuvant player**

Global Supplier of alum adjuvants

Local presence in all regions

Strong Regulatory Expertise

## **Q-Vant are saponin experts**

End-to-end Supply Chain

Sustainable and secure supply

Different Grades of QS-21

## **Inimmune are immunomodulator experts**

Next-Generation Immunomodulators

Synthetic TLR4 Agonists

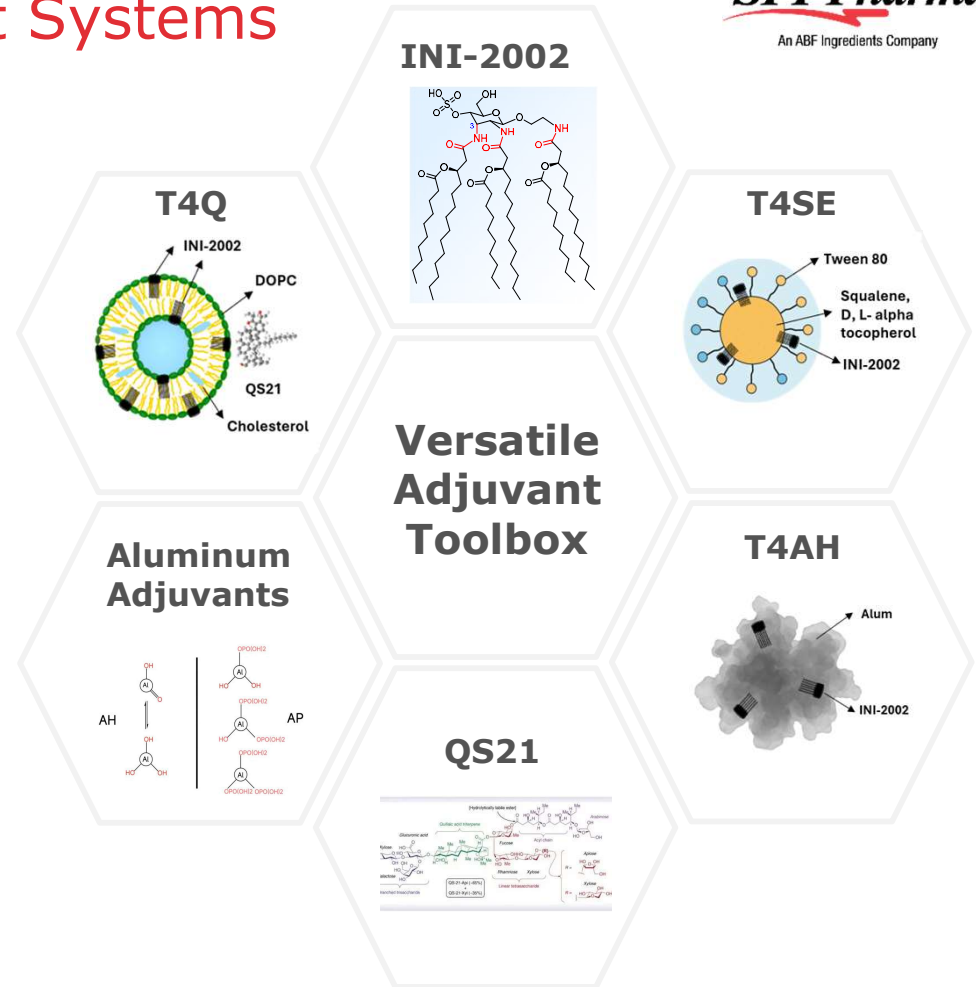
Advanced Adjuvant Systems

*Together we enable flexible adjuvant design for human and veterinary vaccines.*

# A New Class of Accessible Adjuvant Systems



*We leverage our strengths to create innovative adjuvant systems available and make them accessible to vaccine developers.*

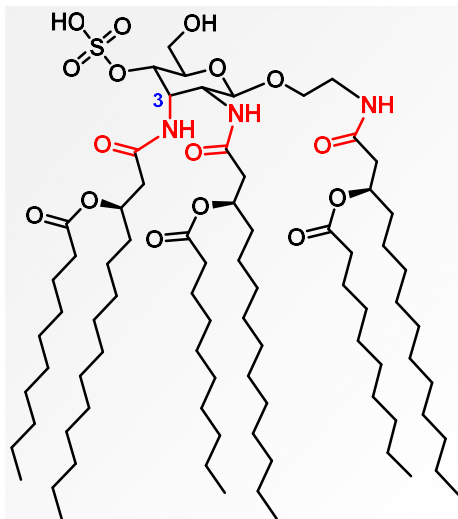


# INI-2002: Fully Synthetic TLR4 Agonist

Designed for Scalable Vaccine Manufacturing

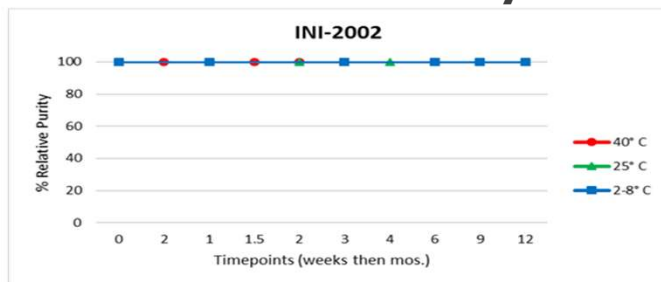


## INI-2002

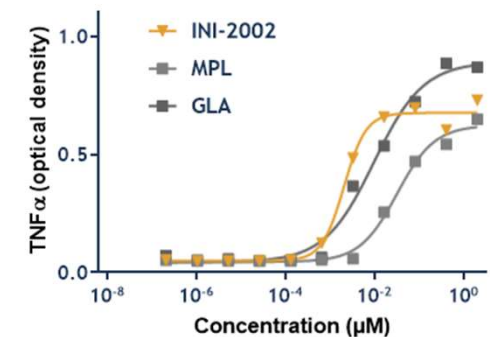
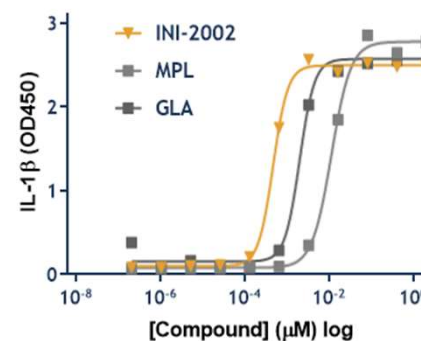


- *Fully Synthetic • Consistent • Scalable*
- *cGMP Manufacturing multi-kilo lots*
- Thermostable Stable → Enables Global Distribution
- Strong IP Protection
- Meets or Exceeds Industry-Standard TLR4 Agonists

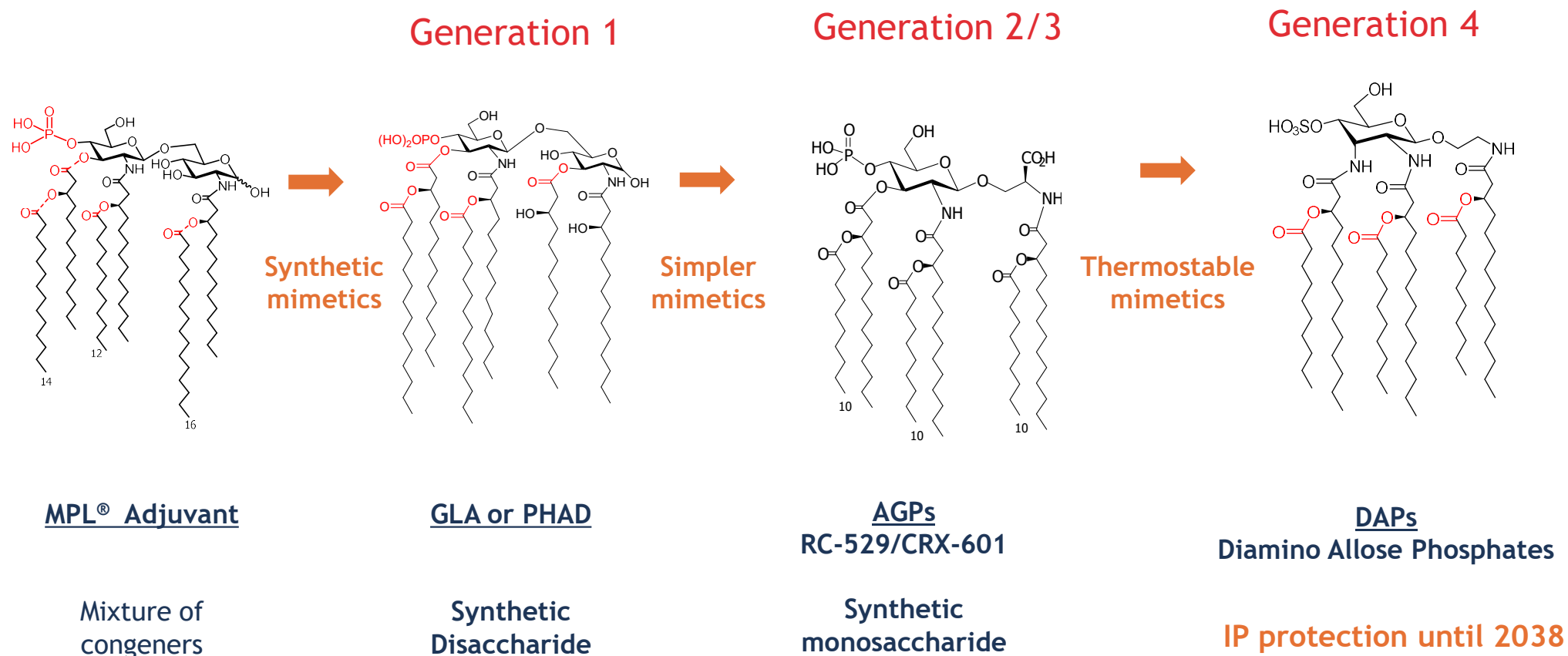
## Thermostability



## Human PBMC Potency Comparison



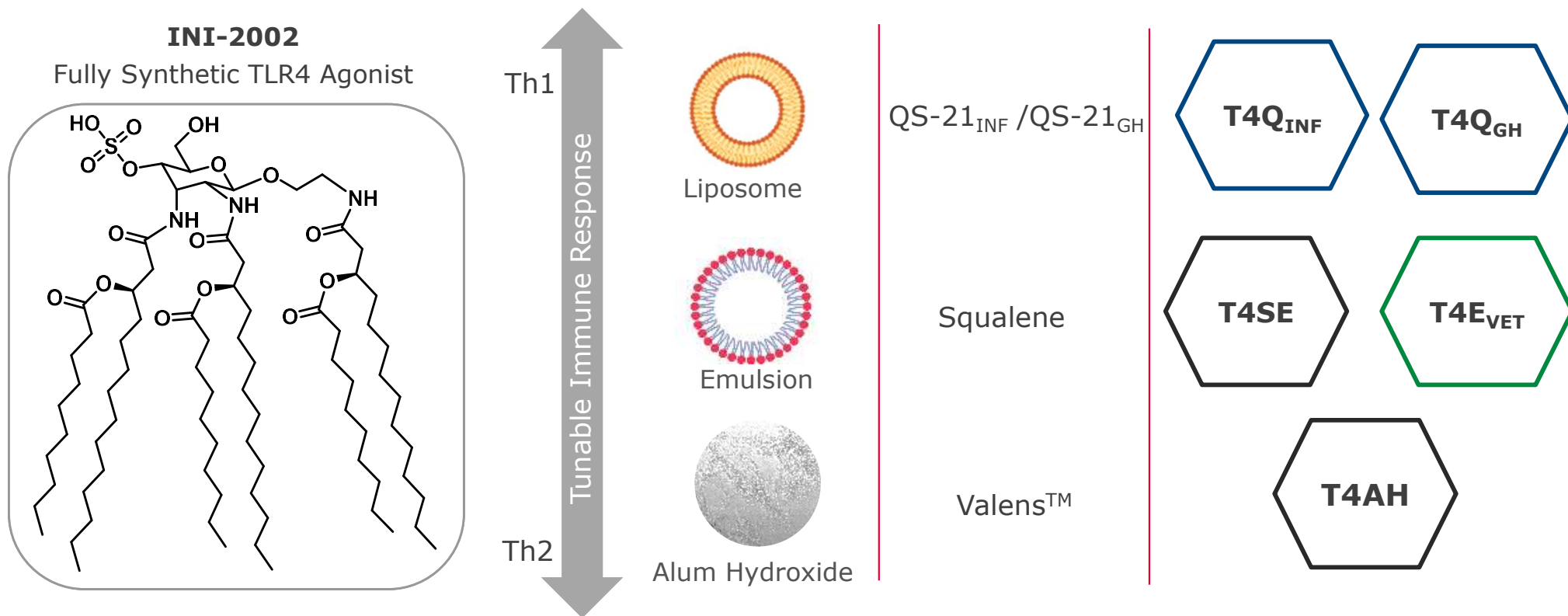
# DAPs (Diamino Allose Phosphates): Synthetic TLR4 agonists



# INI-2002 Enables a Versatile Adjuvant Platform



From individual systems to a flexible platform



# Sustainable and Secure Saponin Supply at Global Scale



Q-VANT  
Approach



*Our technology allows us to obtain QS-21 from any quillaja plant material including biomass, leaves, plantlets, cell cultures. In this way Q-VANT can supply to billions of doses in a 100% sustainable manner.*

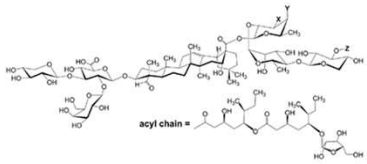
## QSap™ Technology

Reliable, scalable, cost-effective QS-21 supply

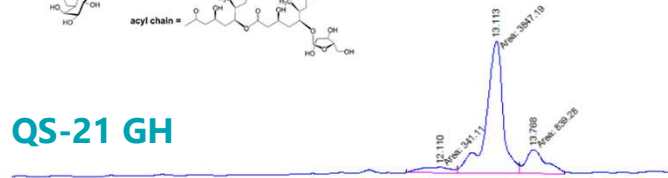
- **QS-21 INFINITY:** High purity (>95%)
- **QS-21 GH:** Cost-optimized solution for global health
- **QSap™** Veterinary-grade saponin



# QSap™ Technology: Supply for Global Health



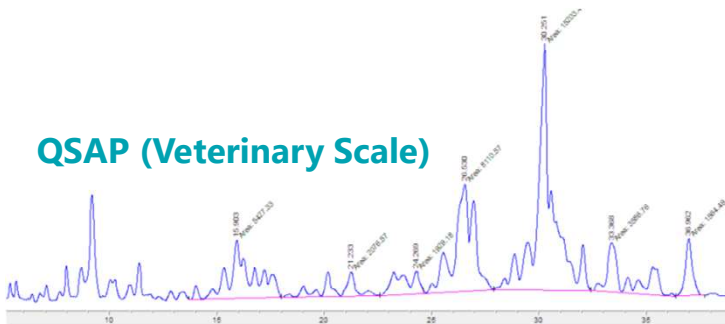
QS-21 GH



QS-21 INFINITY



QSAP (Veterinary Scale)



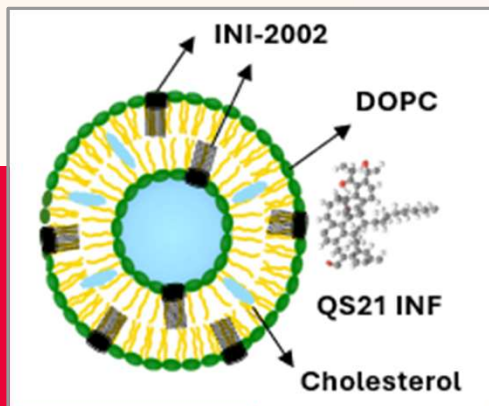
- **Sustainable:** No bark extraction required
- **Affordable:** QS-21 GH for global health
- **GMP-ready:** Production begins 2026
- **Compatible:** Works with TLR4-based adjuvants
- **Potent:** Drives strong humoral and cellular immunity
- **Integral:** Core component of T4Q<sub>GH</sub> Adjuvant System



# T4Q: A High-Performance Adjuvant System for Next Generation Vaccines



T4Q Liposomal System



## Why T4Q?

- Fully synthetic TLR4 agonist (INI-2002) + QS-21
- Synergistic, Th1-biased immunity
- Human vaccine applications
- cGMP manufactured
- Thermostable

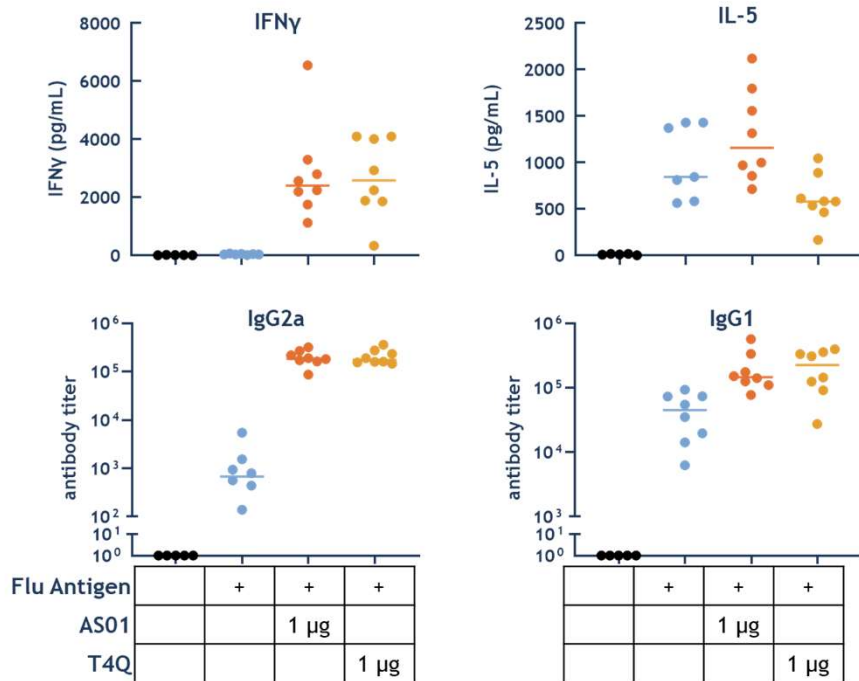
Potent • Synergistic • Available Adjuvant System

# T4Q Stable, Drives Strong Immune Responses

Demonstrates performance comparable to ASO1®

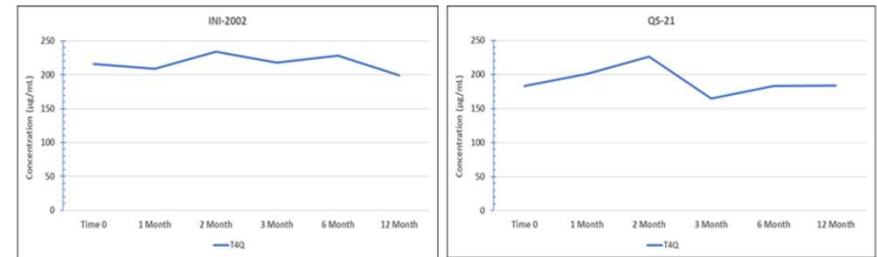


## Strong Th1-Biased Immune Response

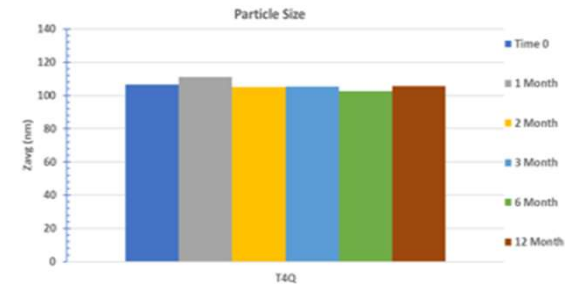


- Th1-biased response comparable to ASO1®
- Enhances both cellular (IFN $\gamma$ ) and humoral responses

## Chemical Stability



## Colloidal Stability



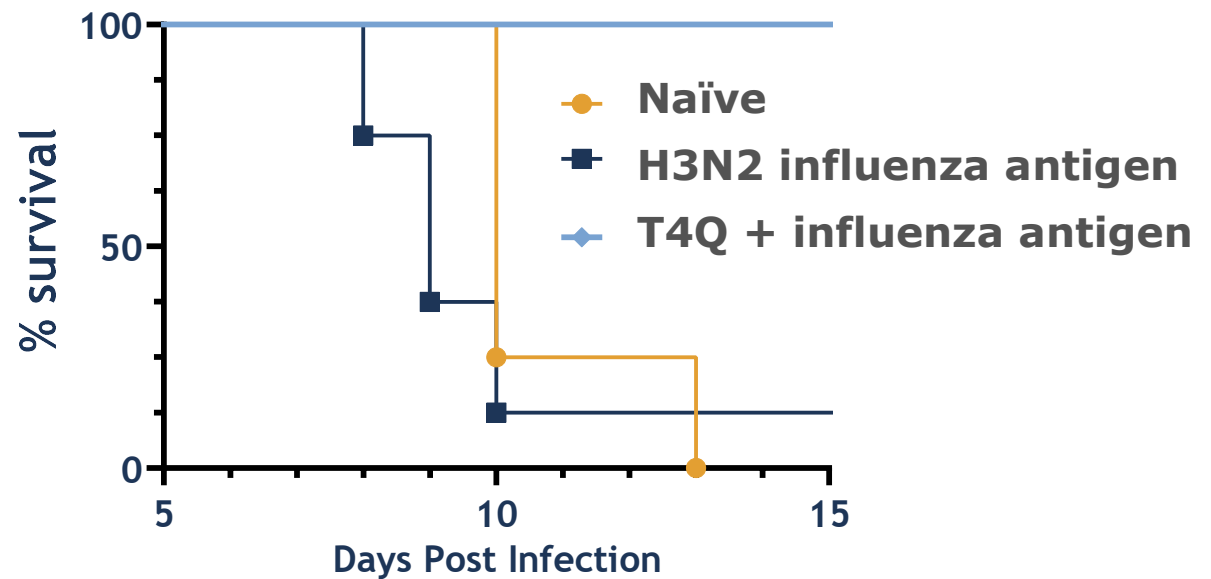
- Robust chemical stability at 2–8°C
- Stable colloidal properties
- Lyophilized for flexible storage and handling

# T4Q + split H3N2 influenza antigen protects mice from heterologous influenza challenge

## Drifted mouse influenza challenge

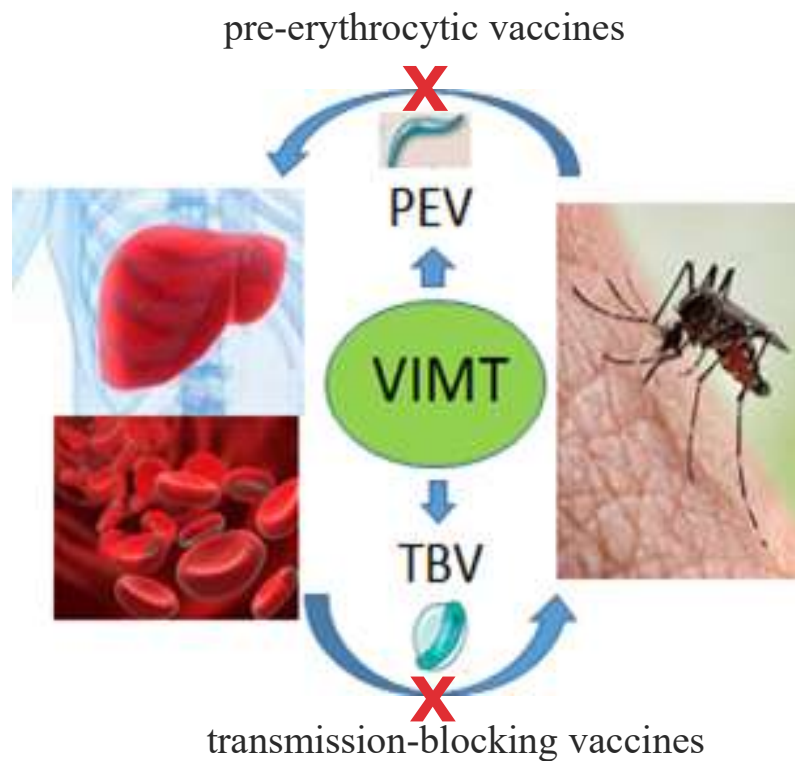
Antigen: Detergent split  
A/Victoria/2009 (H3N2)

Challenge virus: Mouse adapted  
A/Hong Kong/1968 (H3N2)



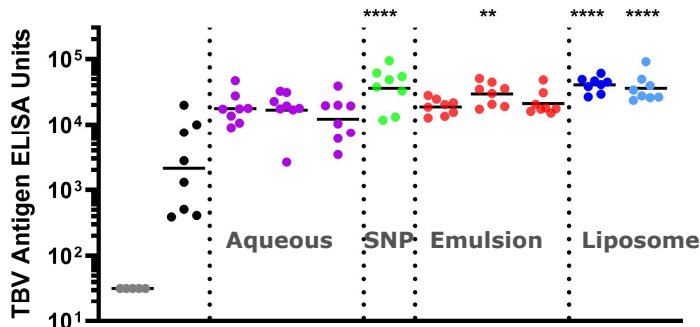
T4Q adjuvanted influenza vaccination resulted in 100% protection from lethal influenza challenge in a heavily drifted H3N2 murine challenge model. Cross-protection is T-cell mediated.

# T4Q Adjuvanted Multi-stage Vaccines for Interruption of Malaria Transmission (VIMT)

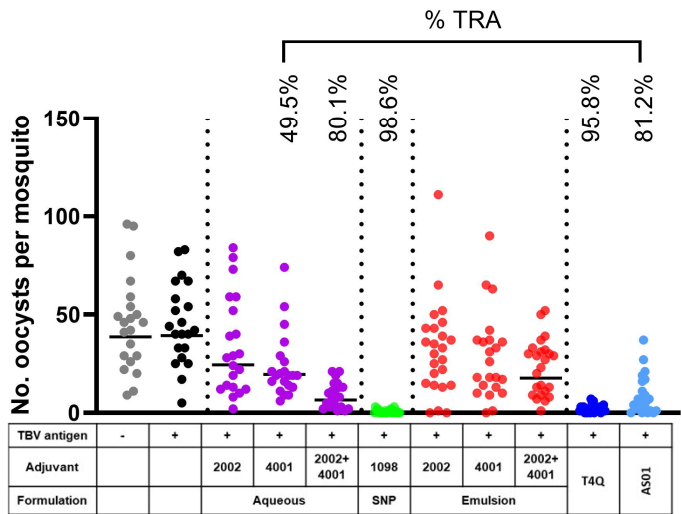


VIMT regimen targets different stages of malaria life cycle

# Multi-stage T4Q adjuvanted transmission blocking vaccine



UM-1098/SNP (Green) and T4Q (Dk. Blue) drive significantly higher TBV-specific antibody titers compared to antigen only and at the same level as the AS01 benchmark (Lt. Blue).



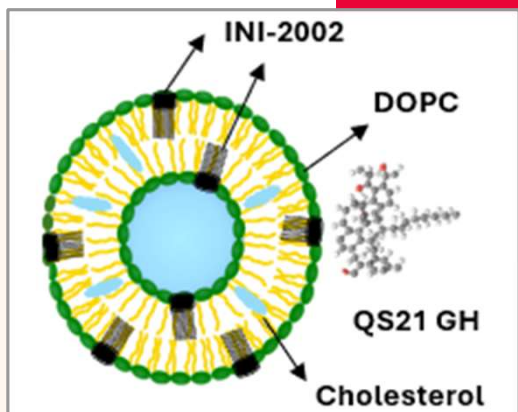
Anti-TBV specific antibodies elicited by UM-1098/SNP (Green) and T4Q (Dk. Blue) induce superior functional activity (%TRA) than all the other groups including the benchmark, AS01 (Lt. Blue) in membrane feeding assay.

\*INI-4001 is a novel synthetic TLR7/8 ligand

\*UM-1098 is a novel synthetic Mincle ligand targeting Th17 immunity.

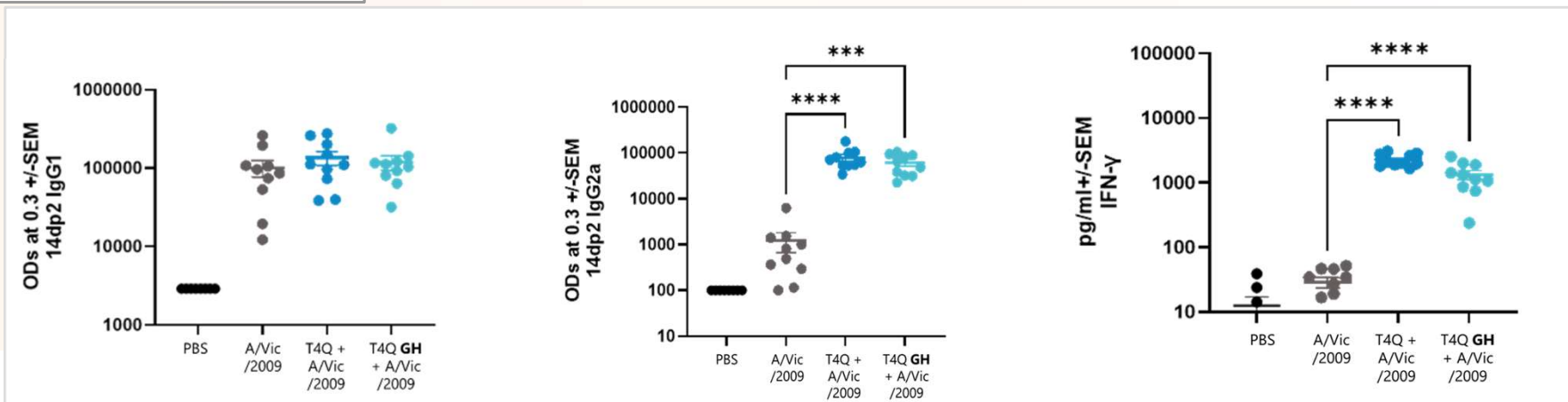
# T4Q<sub>GH</sub>: A Next-Generation Adjuvant System Designed as a Cost-Effective Solution for Global Health

T4Q<sub>GH</sub> Liposomal System



## Why T4Q<sub>GH</sub>?

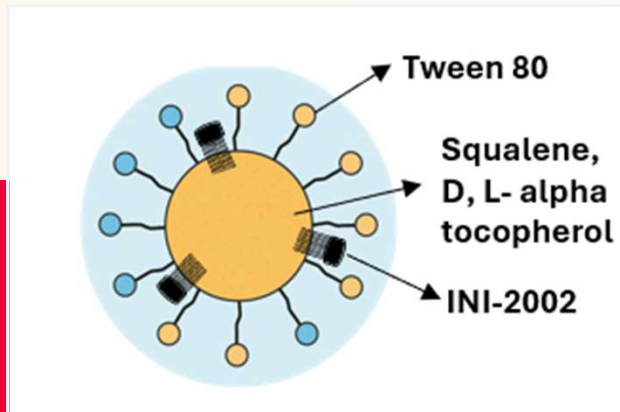
- Cost-optimized for global health
- Synergistic, Th1-biased immunity
- Ready for human and veterinary applications
- Comparable to T4Q and AS01®



# T4SE: A TLR4-Emulsion Adjuvant System



T4SE Emulsion System

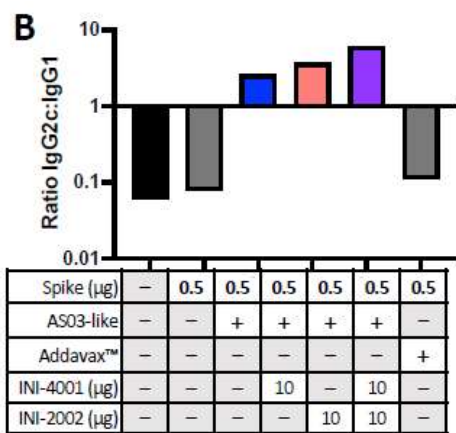
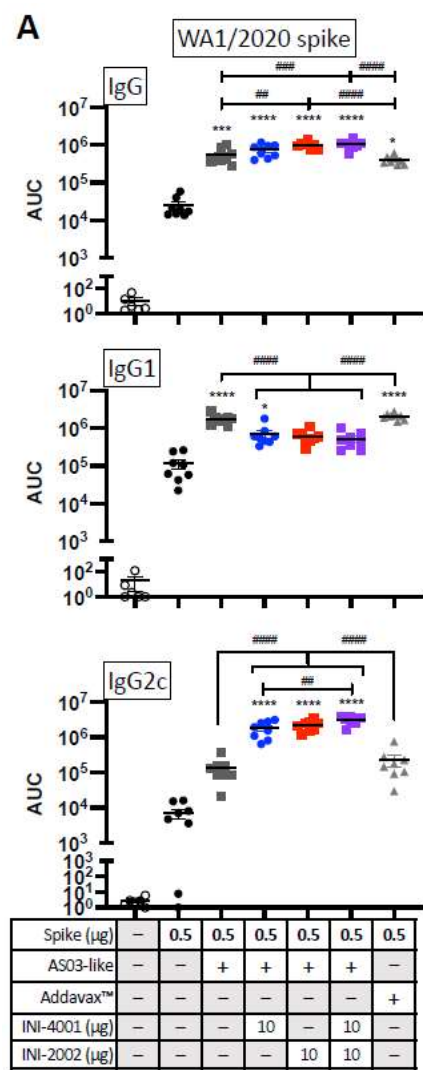


## Why T4SE?

- Stable squalene-based emulsion formulation
- Synergistic activation of innate and adaptive immunity
- Drives strong, broad immune responses
- Human and veterinary vaccine applications
- Scalable, cGMP-ready manufacturing (engineering lot Q2, 2026)
- Lower squalene dose for improved safety/reactogenicity

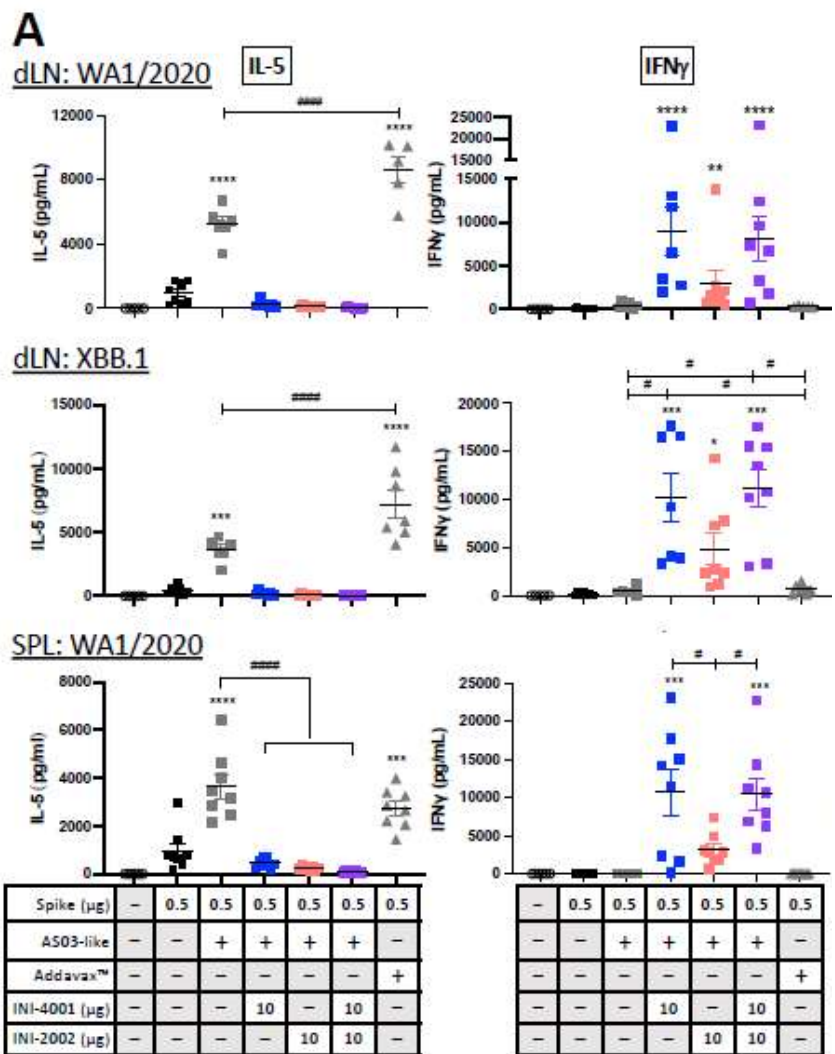
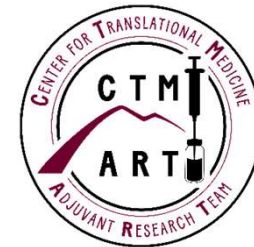
*Well-established emulsion platform with enhanced TLR4 activation.*

## Addition of synthetic TLR ligands significantly improves class switch response to IgG2c humoral immunity in mice



C57BL/6J mice were vaccinated 2 times (21-day interval) with FL Spike antigen from WA-1.

Serum was harvested on day 42

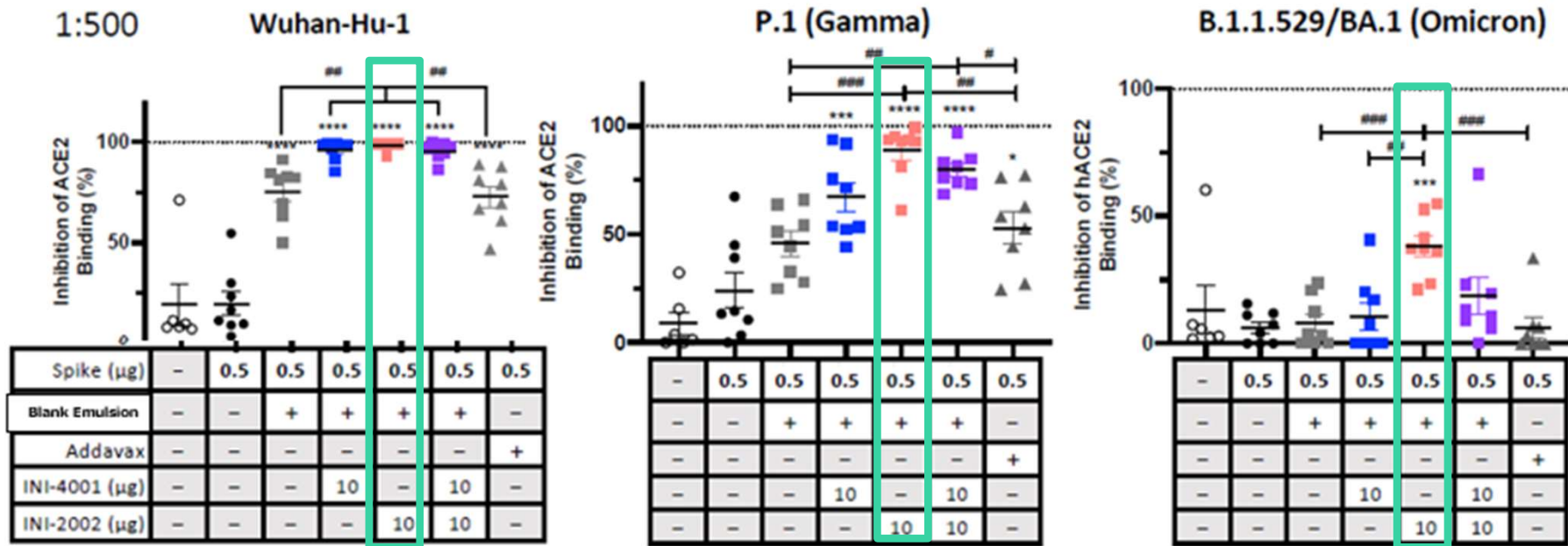


TLR adjuvants significantly enhance Th1 cellular immunity in mice to Wuhan or Omicron Variants

# T4SE Drives Broad and Cross-Protective Immune Responses

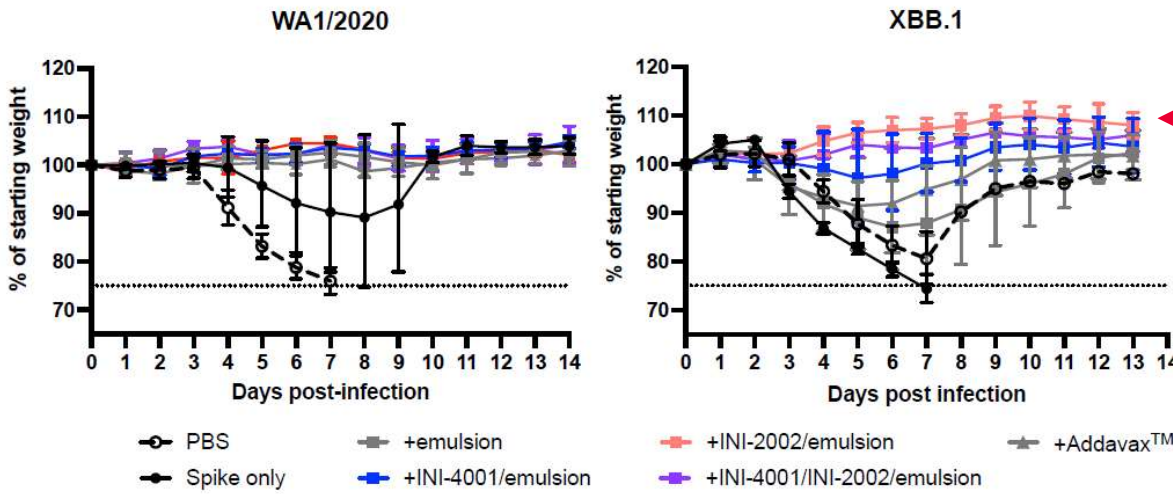


## Cross-Variant Immune Response

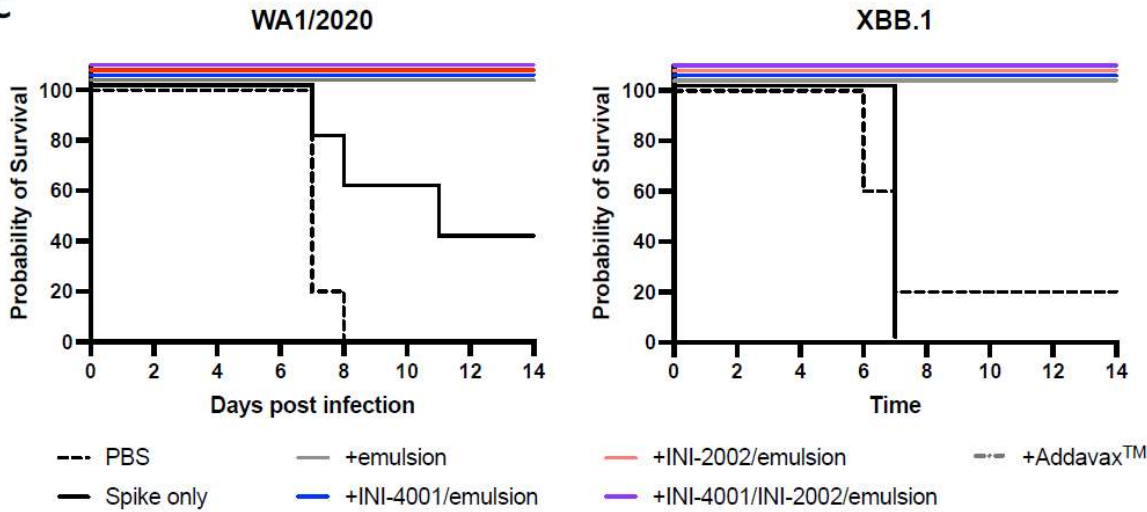


- Enhances Th1 cellular immunity across variants (Wuhan, Gamma, Omicron)
  - Provides cross-protection against multiple viral strains
- (Data generated by the University of Montana (UM-CTM))*

B



C



Wuhan Spike + INI-2002 vaccine protects mice from Omicron XBB.1 Challenge



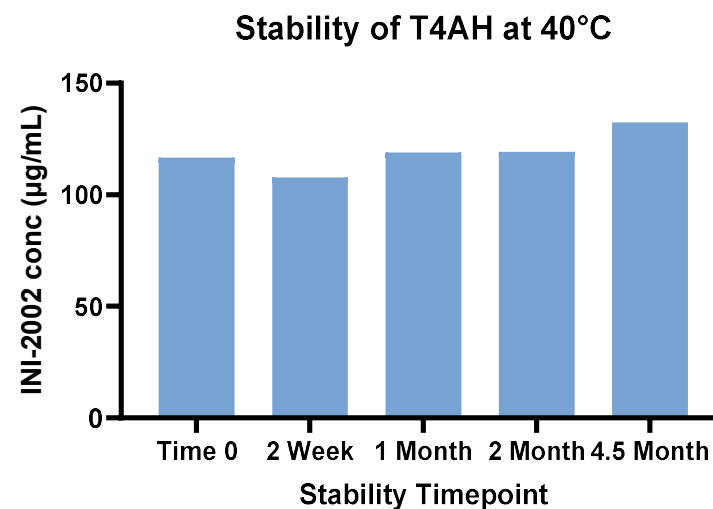
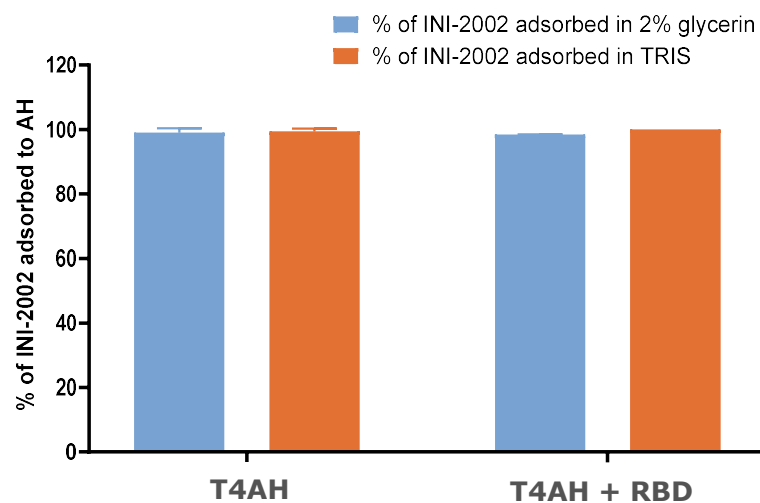
## ***T4AH Adjuvant System***

- Synthetic INI-2002 adsorbed on alum
- Highly thermostable
- Enhances TLR4-driven cellular immunity
- Human and veterinary vaccine applications
- Scalable, cGMP-ready manufacturing
- Strong IP protection



# T4AH Adjuvant System: INI-2002 adsorbed to Alum for AS04-like performance with improved stability

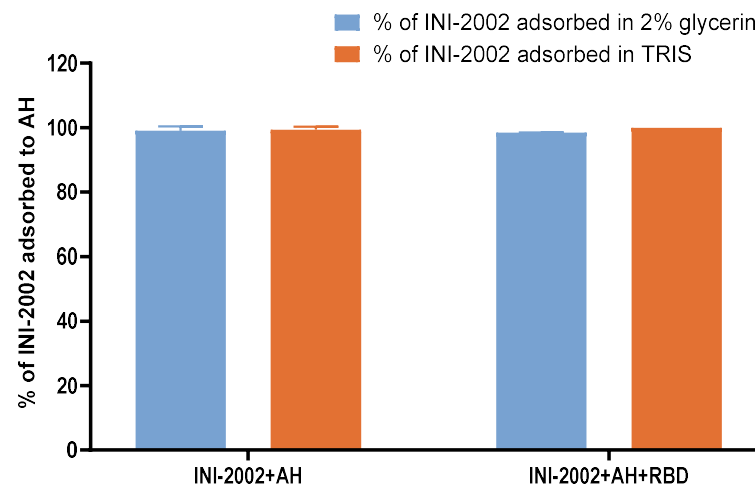
- T4AH is an AS04-like adjuvant formulation
- Manufacturing process is readily scalable for commercial use
- T4AH exhibits excellent chemical stability at 40 °C
- Internal preclinical data shows it's comparable to AS04\*
- Adjuvant patent protection can provide exclusivity through 2039



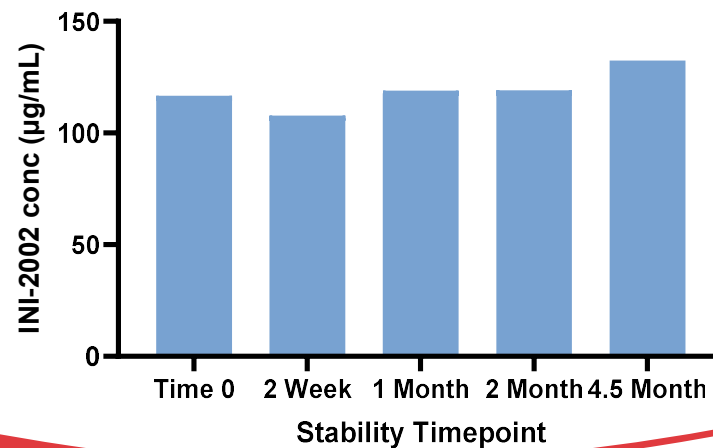
## T4AH – Stability

Test	Specification
Assay INI-2002 Adsorbed (Total)	80-120 ug/mL
Assay INI-2002 Unadsorbed	0-20 ug/mL
Aluminum	0.8-1.2 mg/mL
pH	6.0-7.0
Osmolality	225-350 mmol/kg

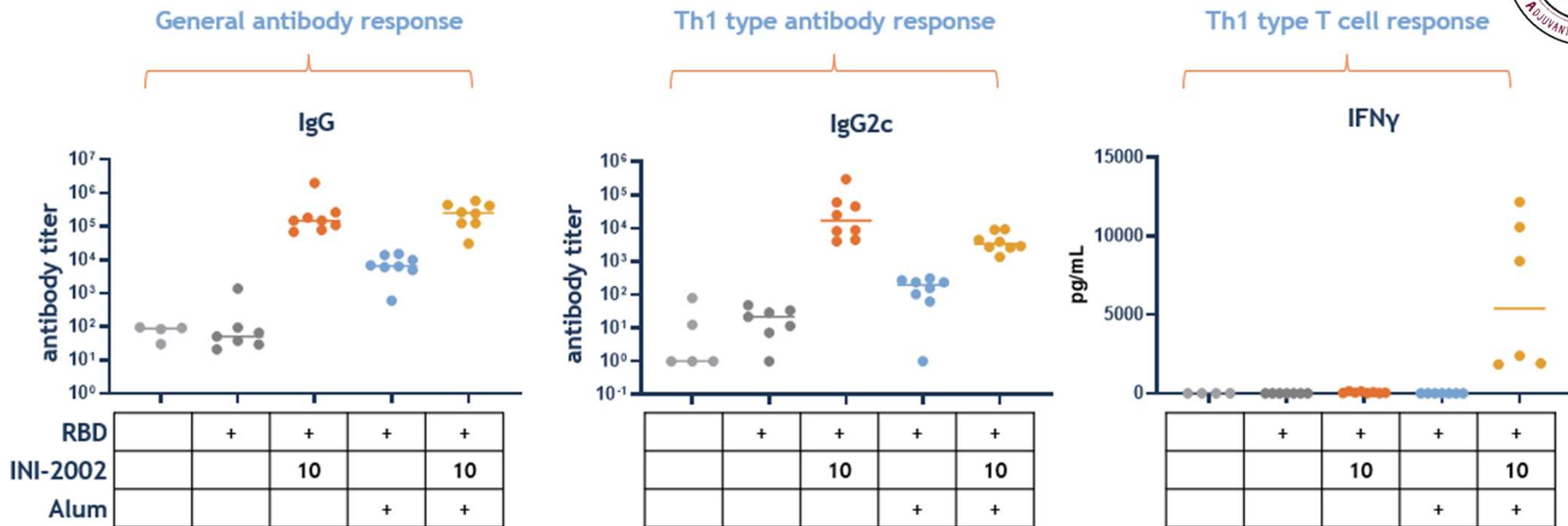
- Excellent INI-2002 adsorbed stability across all temperatures, projected >24 months.
- Low unadsorbed INI-2002 maintained at <20 ug/mL
- Osmolality and pH remain stable.



Stability of T4AH at 40°C

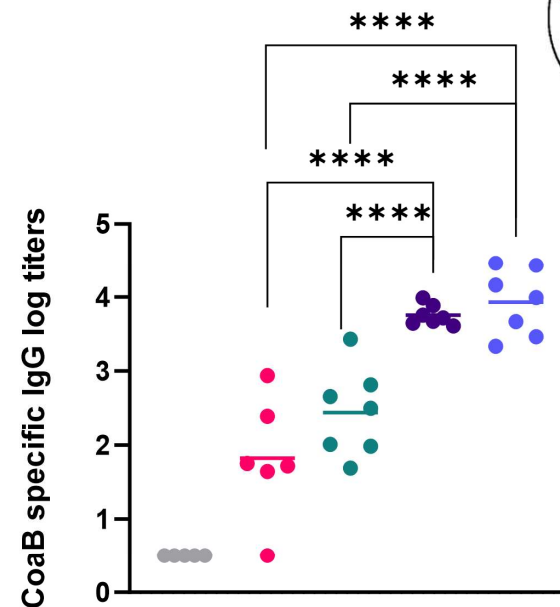
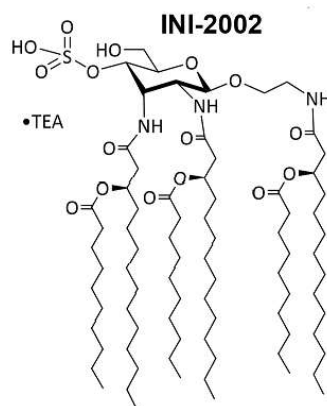
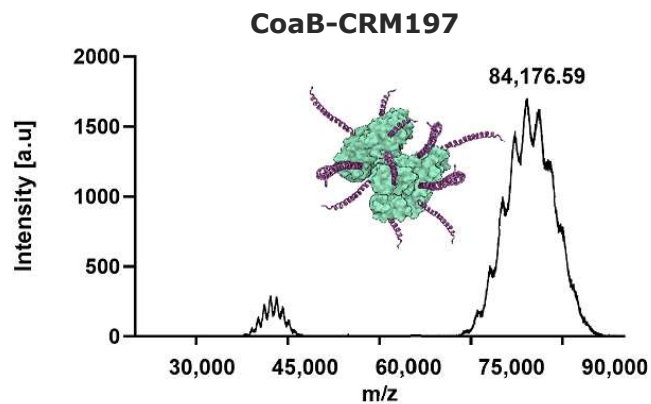


# BALB/c mice vaccinated with T4AH plus an RBD antigen exhibit a robust immune response



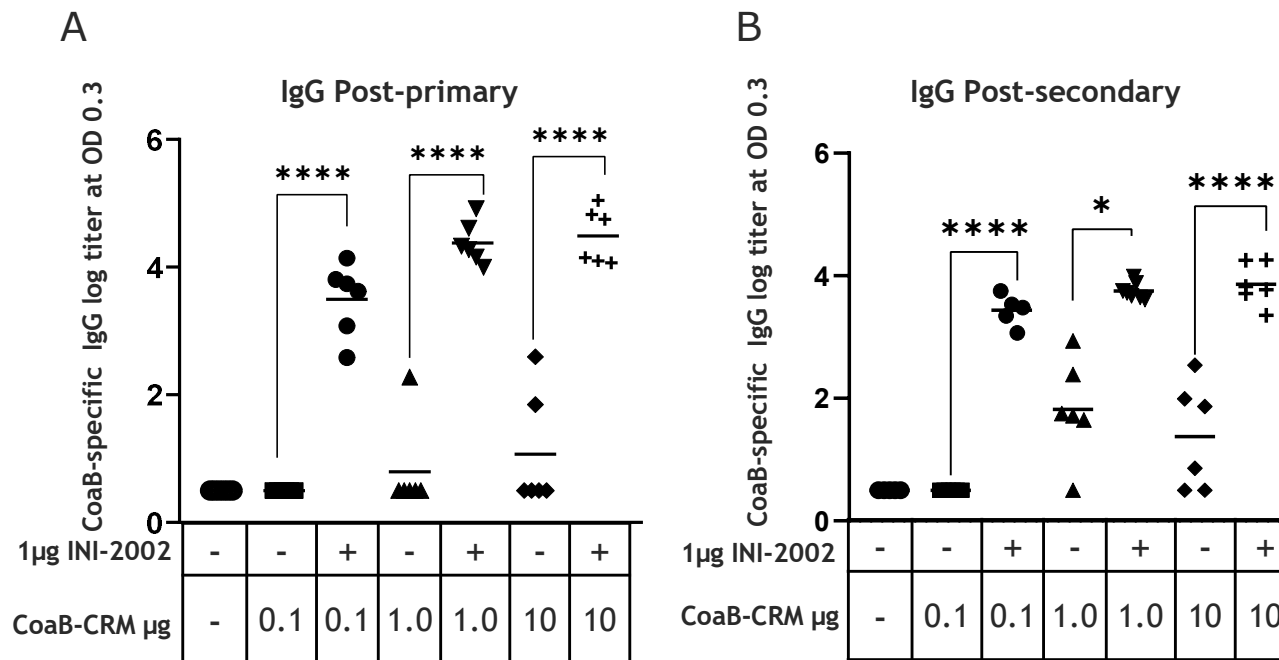
Combination Adjuvant T4AH generates a Th1 biased T cell response

# T4AH plus CRM-conjugate vaccine exhibits a robust immune response



CoaB-CRM ( $\mu\text{g}$ )	-	1	1	1	1
INI-2002 ( $\mu\text{g}$ )	-	-	-	1	1
Alum ( $\mu\text{g}$ )	-	-	3	-	3

# INI-2002 enables single-dose vaccination and significant antigen dose-sparing





## Adjuvant Systems Tailored to Application Needs

	T4Q	T4Q <sub>GH</sub>	T4E <sub>VET</sub>	T4SE	T4AH
<b>Platform</b>	Liposome (QS21 INFINITY)	Liposome (QS21 GH)	Emulsion (Veterinary Saponin)	Emulsion (squalene)	Alum
<b>Immune bias</b>	Th1	Th1	Th1	Th1 (broad)	Th1/Th17
<b>Use case</b>	Advanced human vaccines	Scalable human vaccines	Veterinary vaccines	Broad/ global vaccines	Established & scalable vaccines
<b>Strength</b>	Max potency	Balanced potency & cost	Cost-effective, scalable immunity	Broad, cross-protective response	T cell enablement
<b>cGMP ready</b>	cGMP manufactured	cGMP-ready	In development	cGMP-ready	cGMP-ready
<b>Cost/dose</b>	>\$3.5	<\$1.5	<\$0.1	<\$0.5	<\$0.5

Flexible • Scalable • Available • Cost-Effective Adjuvant Systems for Global Access

*Powered by fully synthetic INI-2002, also available as standalone for custom adjuvant systems.*


*\* INI-2002 API (cGMP) can also be purchased as a bulk vaccine ingredient (RT Stable).*

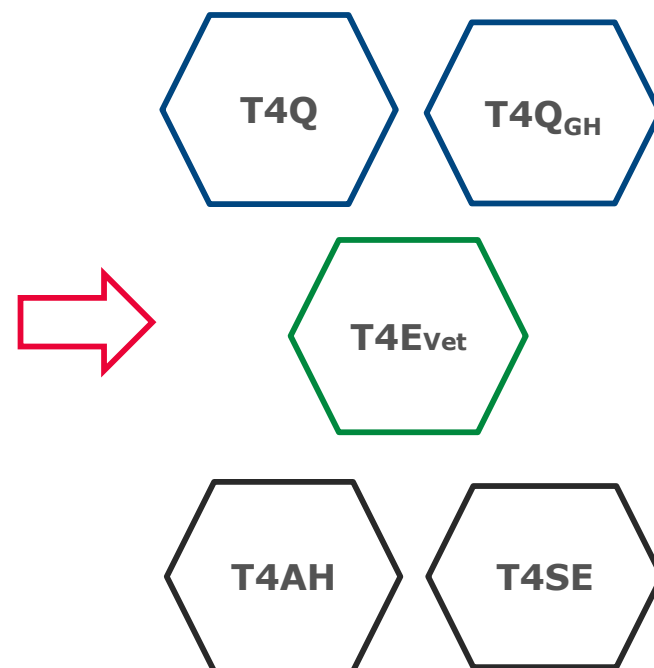
# From Components to Integrated Adjuvant Systems

Combining proven adjuvants with a fully synthetic immune activation platform

**SPI Pharma™**  
**Valens™**  
Aluminium Hydroxide

**Q-VANT**  
BIOSCIENCES™  
Sustainable Saponins

**Inimmune**  
**INI-2002**  
Synthetic TLR4 Agonist



*Tailored adjuvant systems for human and veterinary vaccines*



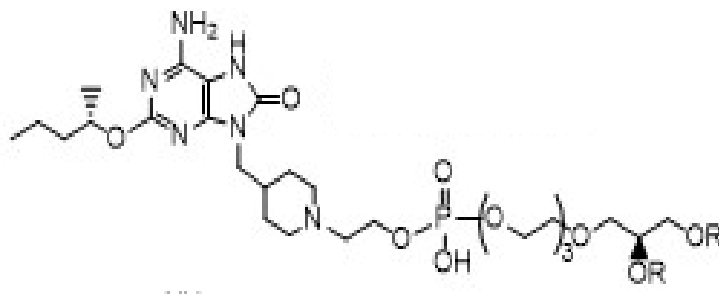
## **Inimmune Expanded Adjuvant Portfolio**



# TLR7/8 Adjuvant Discovery and Development

10-Year NIH Funded Adjuvant Discovery and Development Program  
(>\$25 M invested)

## INI-4001 Adjuvant

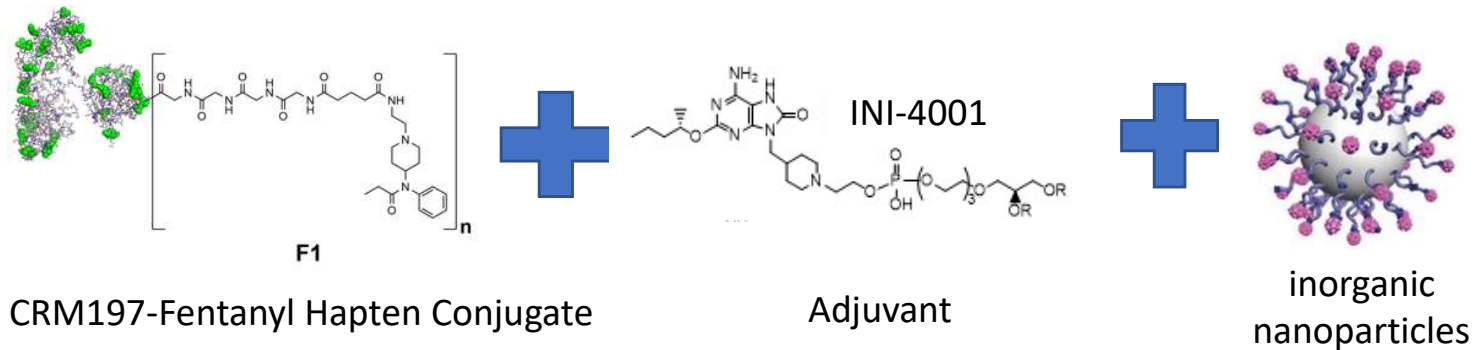


# Development of an adjuvanted fentanyl vaccine for the treatment of opioid use disorder and reduction of fatal overdoses

- Vaccination against fentanyl, and other small molecule drugs of abuse, is being investigated as a strategy to prevent overdose deaths in individuals with opioid use disorder (OUD)
- Using the principle of linked recognition, a small molecule drug hapten is linked to a carrier protein to drive antibody responses against the drug hapten. An adjuvant is required to increase antibody concentrations to a protective level
- Inimmune is developing an INI-4001 + alum adjuvanted vaccine against fentanyl using the fentanyl hapten F1 conjugated to the carrier protein CRM<sub>197</sub>



# Anti-Fentanyl Vaccine

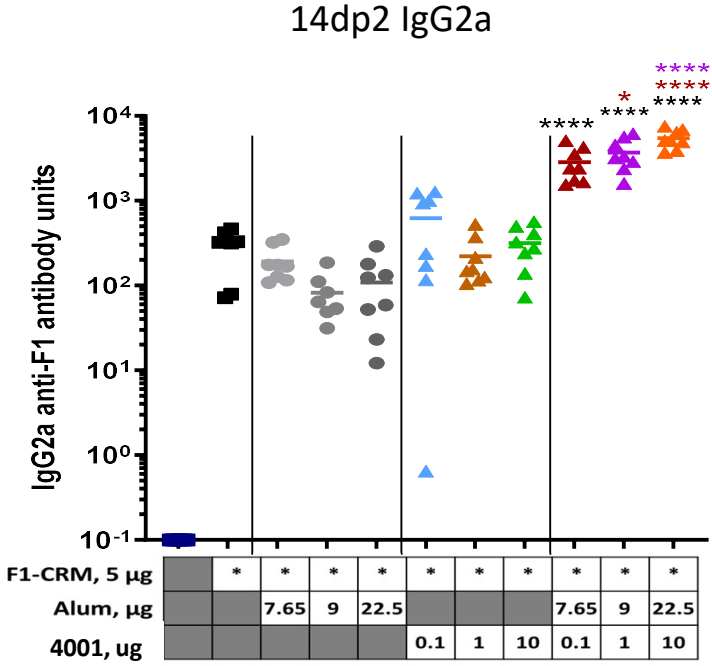
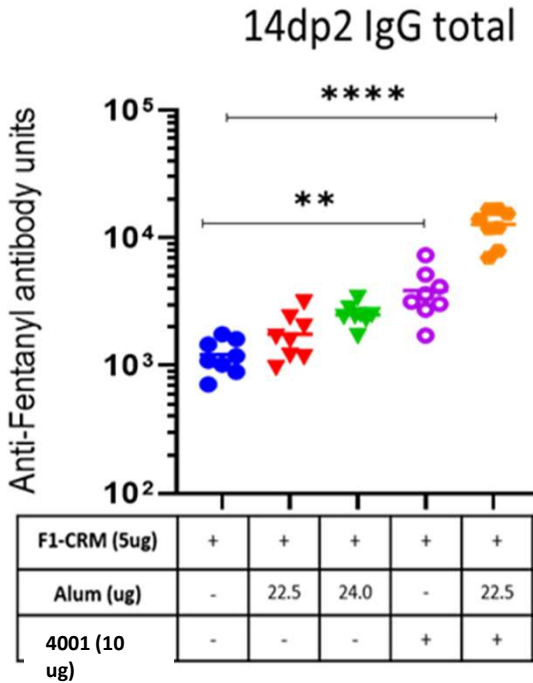


**Hapten-** F1-Gly4 Fentanyl hapten discovered by Dr. Marco Pravetoni (University of Minnesota)

**Adjuvant-** Toll Like Receptor 7/8 ligand discovered by UM Vaccine Research Team

**Inorganic Nanoparticle-** Aluminum Salts, optimized to co-adsorb conjugate and adjuvant

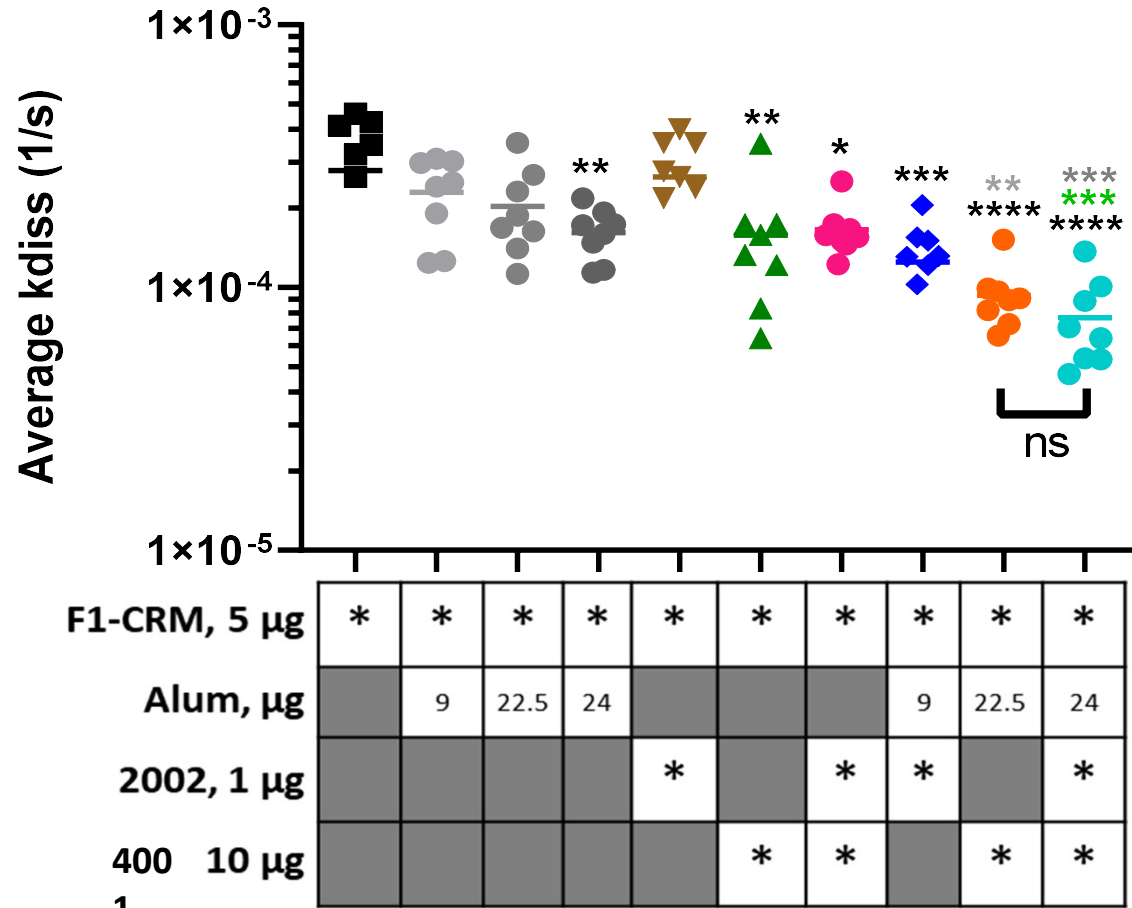
# Lead Fentanyl Vaccine Candidate



Miller et al, NPJ Vaccines 8, 97 (2023)  
 Crouse et al, NPJ Vaccines. 8, 107 2023.

- Vaccine was well tolerated in mice and rats.
- Anti-Fentanyl antibody titer increases with the addition of alum or synthetic TLR7/8 adjuvant.
- Adjuvant alters antibody isotype (IgG2a), believed to be important for anti-fentanyl response.

# INI-4001 adjuvant increases antibody affinity to fentanyl



No response was detected in the naïve group

- Higher affinity antibodies are produced when both adjuvants are used together (50-fold increase).

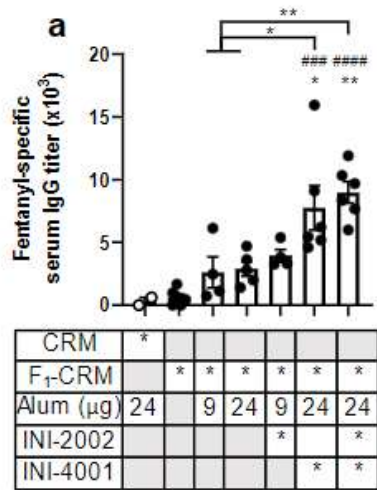
Increased Antibody Affinity

Miller et al, NPJ Vaccines 8, 97 (2023)  
Crouse et al, NPJ Vaccines. 8, 107 2023.

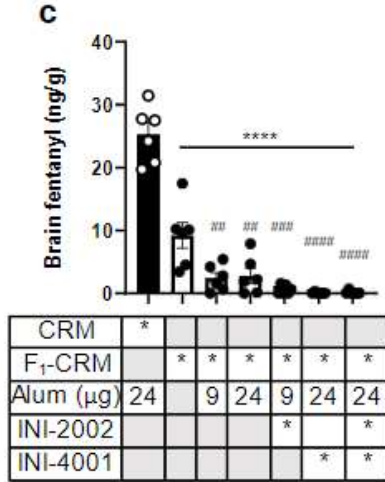
# Vaccine Protects Rats from Fentanyl Challenge



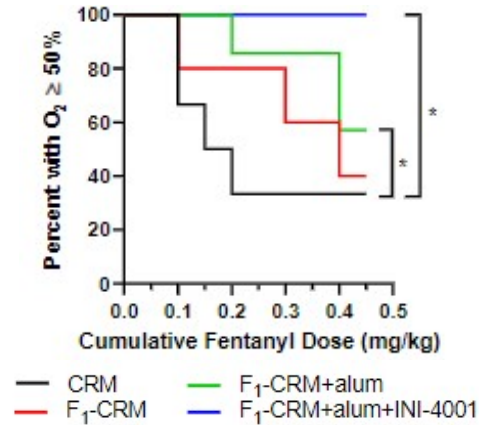
Anti-Fentanyl  
Antibody Titers



Brain Fentanyl Levels  
After Challenge



% below 50% O<sub>2</sub>  
After Challenge



- No adverse events noted in fentanyl vaccine studies (safety)
- Lead vaccine candidate induces high levels of anti-fentanyl antibodies in rats
- Vaccine protects rats from lethal cumulative fentanyl dose
- Vaccine improves oxygen saturation levels following fentanyl challenge
- Response is highly specific to fentanyl (no impact on other opioid pain meds)



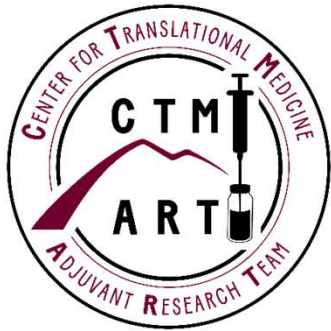
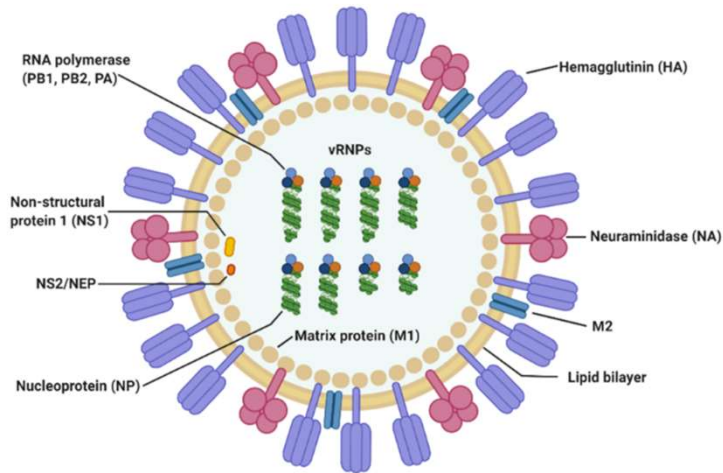
**TRAC-478 Emulsion: A next-generation combination adjuvant system**

# TRAC-478 is a TLR4 (INI-2002) + TLR7/8 (INI-4001) agonist combination adjuvant system

- TRAC-478 is a fully synthetic combination (INI-2002 + INI-4001) adjuvant system.
- Readily formulated as aqueous, alum adsorbed, liposomes, or emulsion.
- cGMP TRAC-478 emulsion is available.
- TRAC-478 drives a strong antibody and T-cell response against vaccine antigens.
- NIH CIVICs flu programs selected TRAC-478 to advance through Phase I clinical trial.

# Case Study: Influenza Vaccine Improvements

Can we use adjuvants to improve influenza vaccine efficacy and breadth?



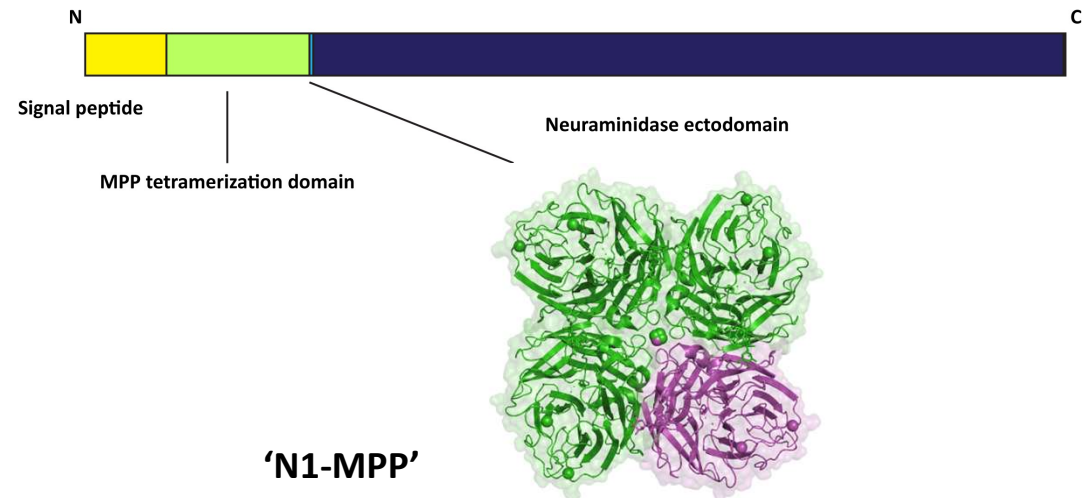
**Mount  
Sinai**

# Adjuvants, antigen, formulations and delivery systems

## Intramuscular delivery:

Adjuvant	Description	Formulation
INI-2002	TLR4 agonist, lipid A mimetic	Aqueous, liposomal, emulsion
INI-4001	TLR7/8 ligand, lipidated oxoadenine	Aqueous, liposomal, emulsion
TRAC-478	Combination: TLR4 and TLR 7/8 agonists	Aqueous, liposomal, emulsion

**Antigen:** Recombinant neuraminidase protein consisting of the globular head domain of the **H1N1 A/Michigan/45/2015 NA** and the measles virus phosphoprotein tetramerization domain

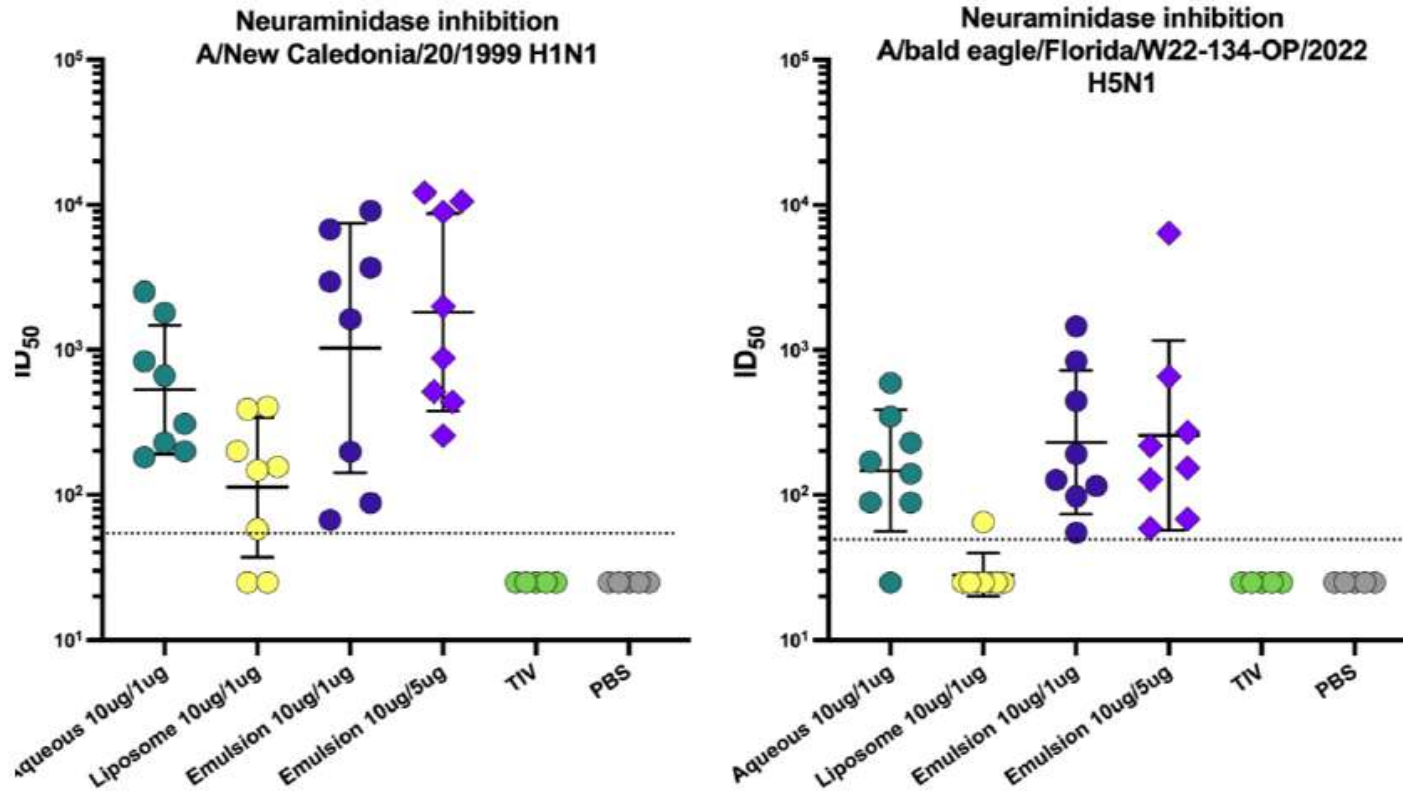


*globular head domain of the H1N1 A/Michigan/45/2015 NA and the measles virus phosphoprotein (MPP) tetramerization domain*

## N1-MMP + TRAC-478 adjuvant induces cross-reactive NA inhibiting antibodies



**Mount  
Sinai**

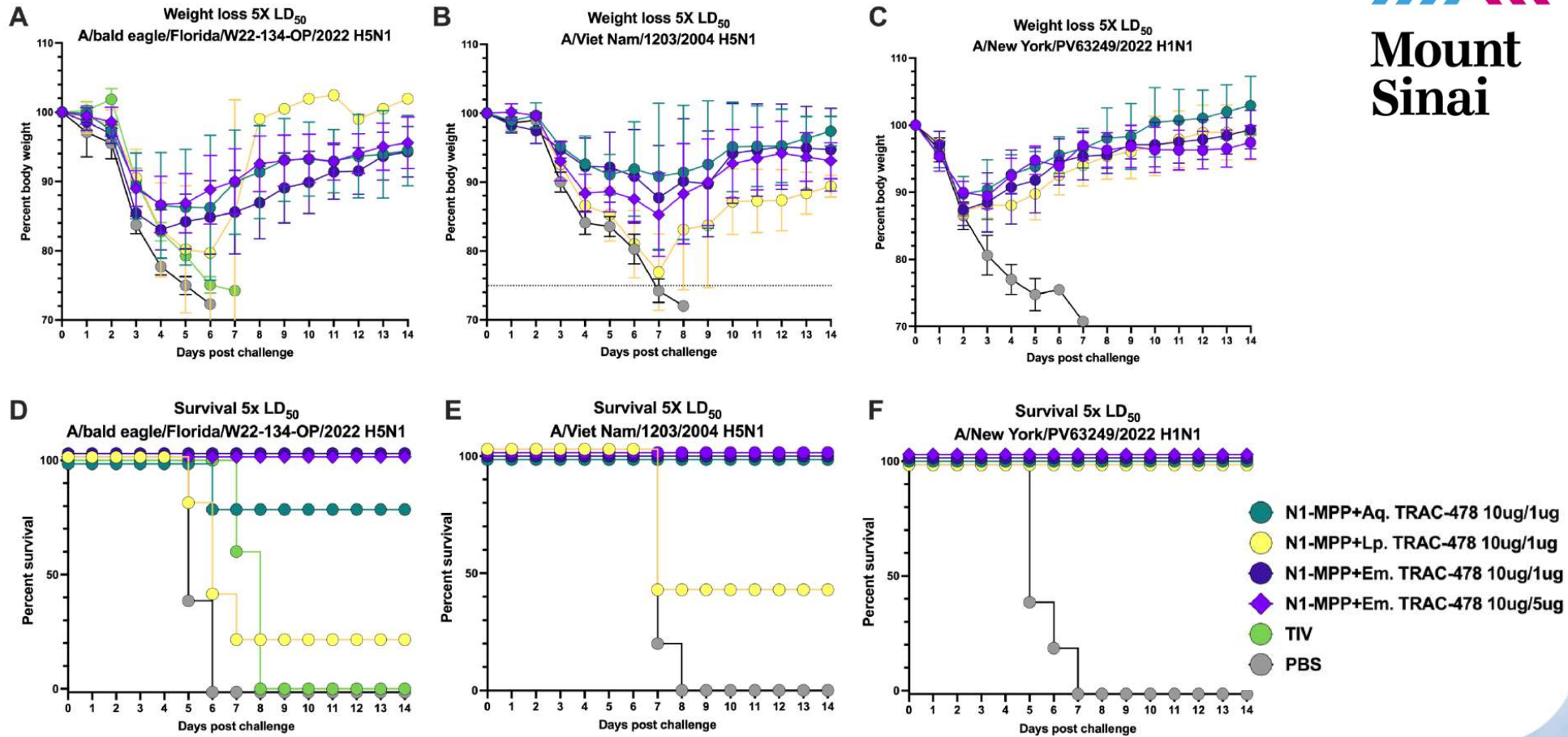


*Vaccine Antigen: N1 from A/Michigan/45/2015*

# N1-MMP + TRAC-478 Provides Cross-Protection to pH1N1 and Avian H5N1



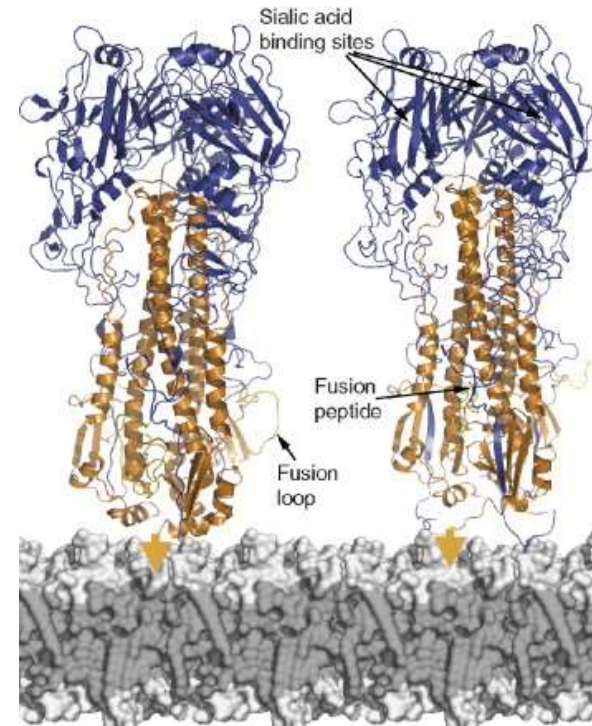
Mount  
Sinai



## H3 trimer + TRAC-478 Liposome Vaccine Studies

### *Intramuscular delivery:*

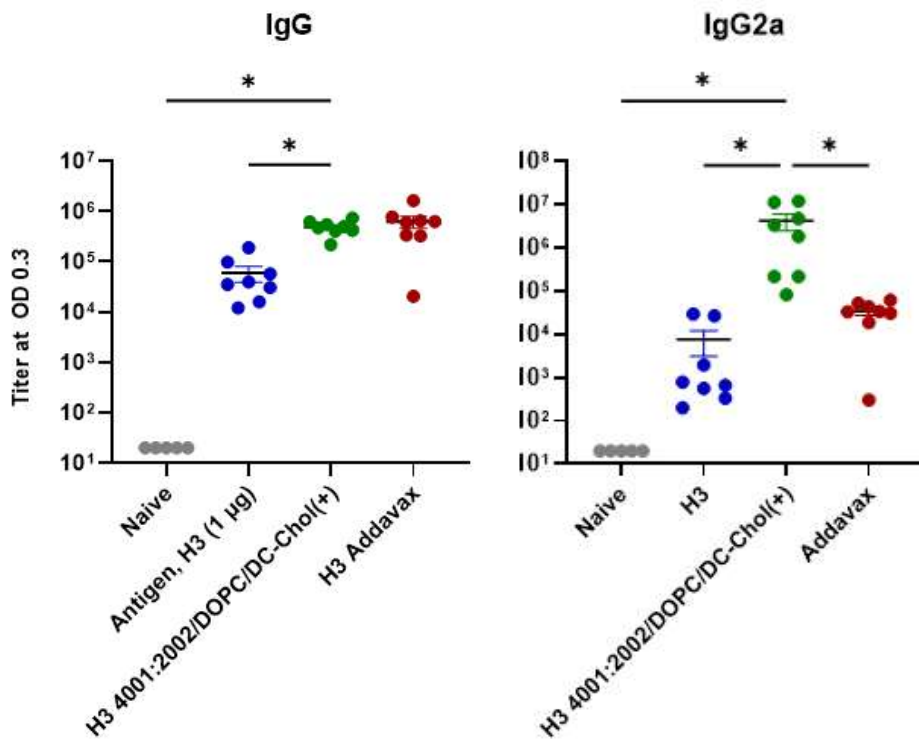
Adjuvant	Description	Formulation
Addavax	Squalene	emulsion
TRAC-478	Combination: TLR4 and TLR 7/8 agonists	liposome



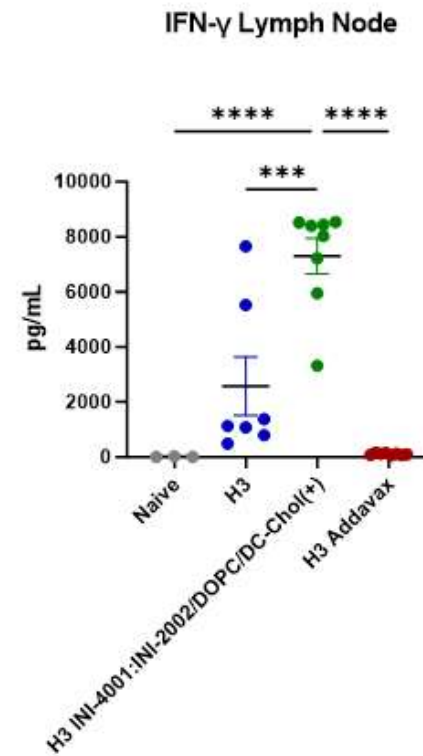
H3 (A/HongKong/4801/2014) (recombinant antigen trimer from Krammer lab)

# H3 trimer + TRAC-478 Enhances IgG2a Humoral Immunity and Th1 Cell-Mediated Responses Following IM Vaccination

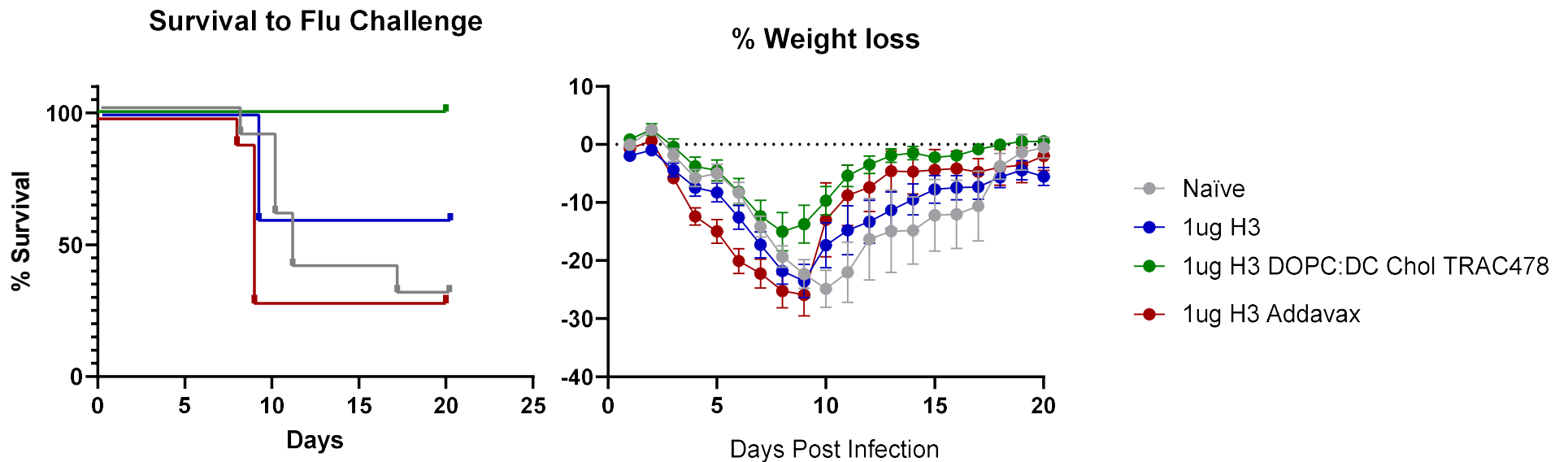
## Humoral Immunity



## Cell-Mediated Immunity



## H3 Trimer + TRAC-478 Vaccination: H3N2 Drifted flu challenge



2014 (A/HongKong/4801/2014) H3 vaccine and 1968 (A/HK/68) challenge virus  
\*no HAI cross reactivity or neutralization between H3N2 strains

# THANK YOU!

Working together to improve lives around the world through trusted, patient-first pharmaceutical solutions.

