A Promising Novel Approach to DNA Vaccines

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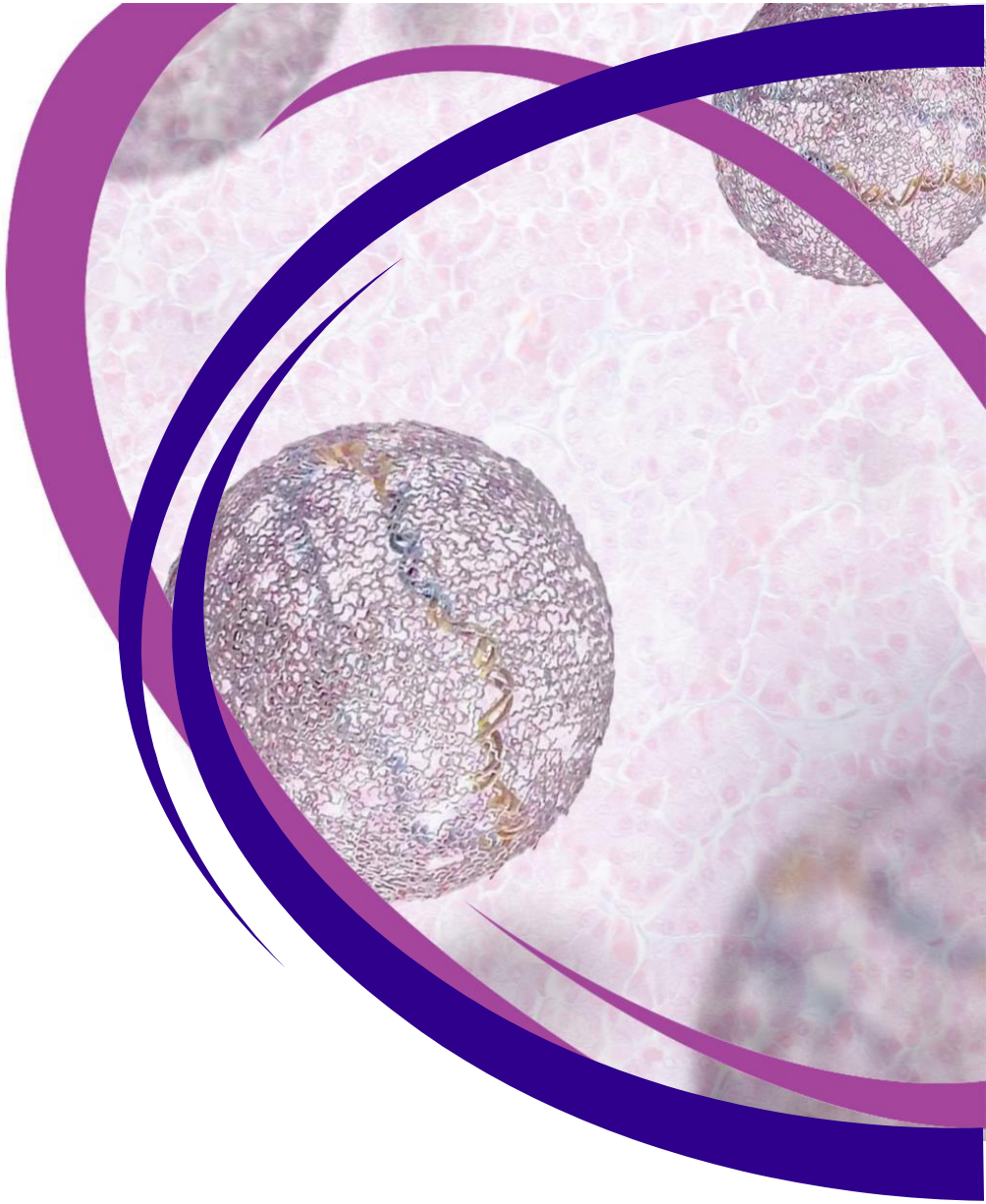

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DNA Vaccines are Well-Suited to Overcome the Limitations of Current mRNA and Protein Vaccines

Current Vaccines & their Limitations

mRNA

- Short duration of antigen expression & immune responses
- Reactogenicity & other safety concerns
- Poor stability at working temperatures

Protein

- Challenges in manufacturing & subunit mixtures
- Weak cytotoxic T-cell responses

Advantages of DNA Vaccines

- Longer duration of antigen expression/ exposure
- Strong T-cell responses (compared to protein vaccines)
- Stability at $\geq 4^{O}$ C
- Flexible manufacturing
- Rapid turnaround for mutating virus

DNA Vaccines Require a DNA Delivery System

Current Delivery Systems Warrant Alternate Approaches

Viral Vectors

- Biological in nature
- High delivery efficiency
- Poor repeatability
- Safety limitations

Electroporation devices

- User compliance
- Tissue damage
- Additional cost

Jet devices

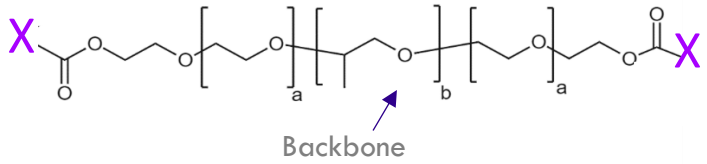
- Injection site reaction
- Cross-contamination risk
- Additional cost
- Training requirement
- Incompatibility with certain vaccines

PlaCCine – A Novel DNA Vaccine Platform Technology

Relies on Synthetic Vectors for DNA Delivery

PlaCCine Vaccines do not Require Virus or Device:

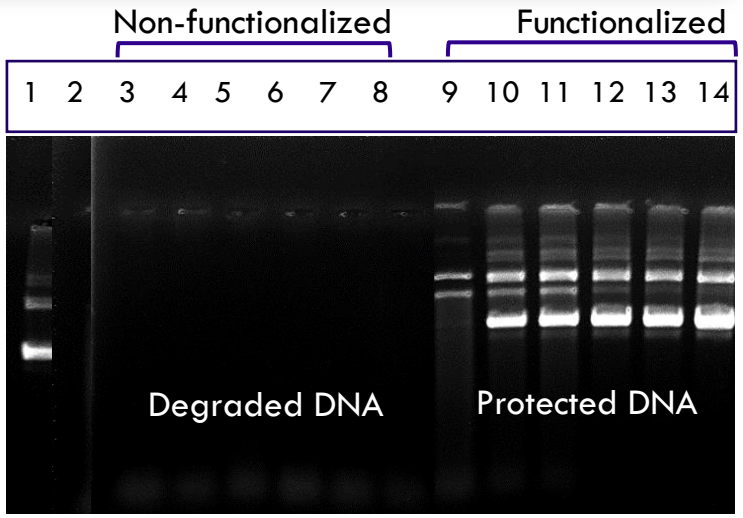
A PlaCCine Synthetic Delivery Systems: covalently-functionalized amphiphilic polymer



X- functional group: same or different

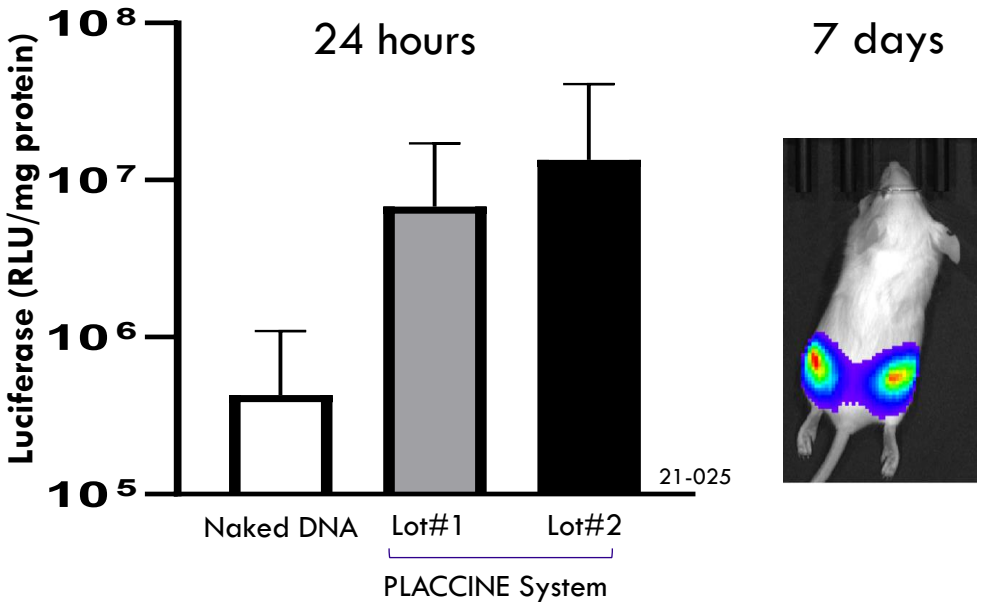
DNA Protection & Enhanced Gene Expression by PlaCCine Delivery System

Protection of DNA Degradation

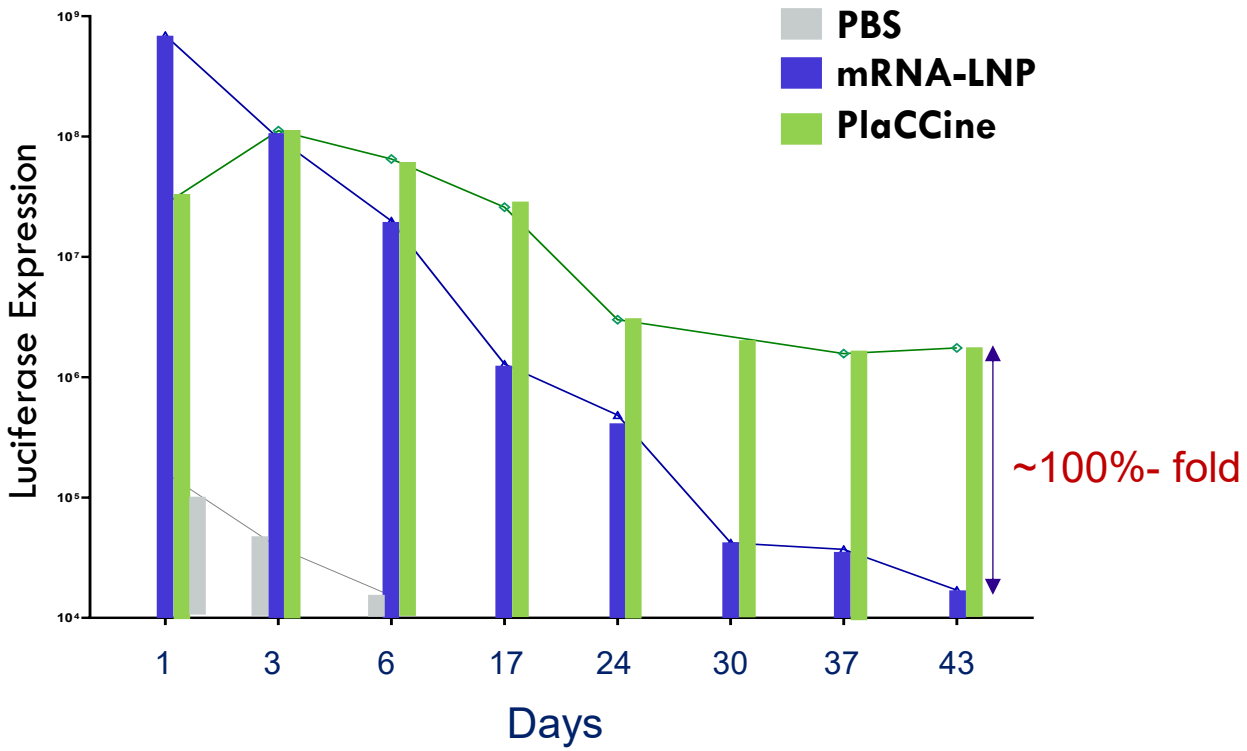


1. naked DNA, no DNAse
2. naked DNA + DNAse
3-8. DNA formulation in increasing concentrations of non-functionalized polymer
9-14. DNA formulated in increasing concentrations of functionalized polymer

Gene Expression: 10-15-fold > Naked DNA



PlaCCine gives more Durable Antigen Expression Compared to mRNA-LNP



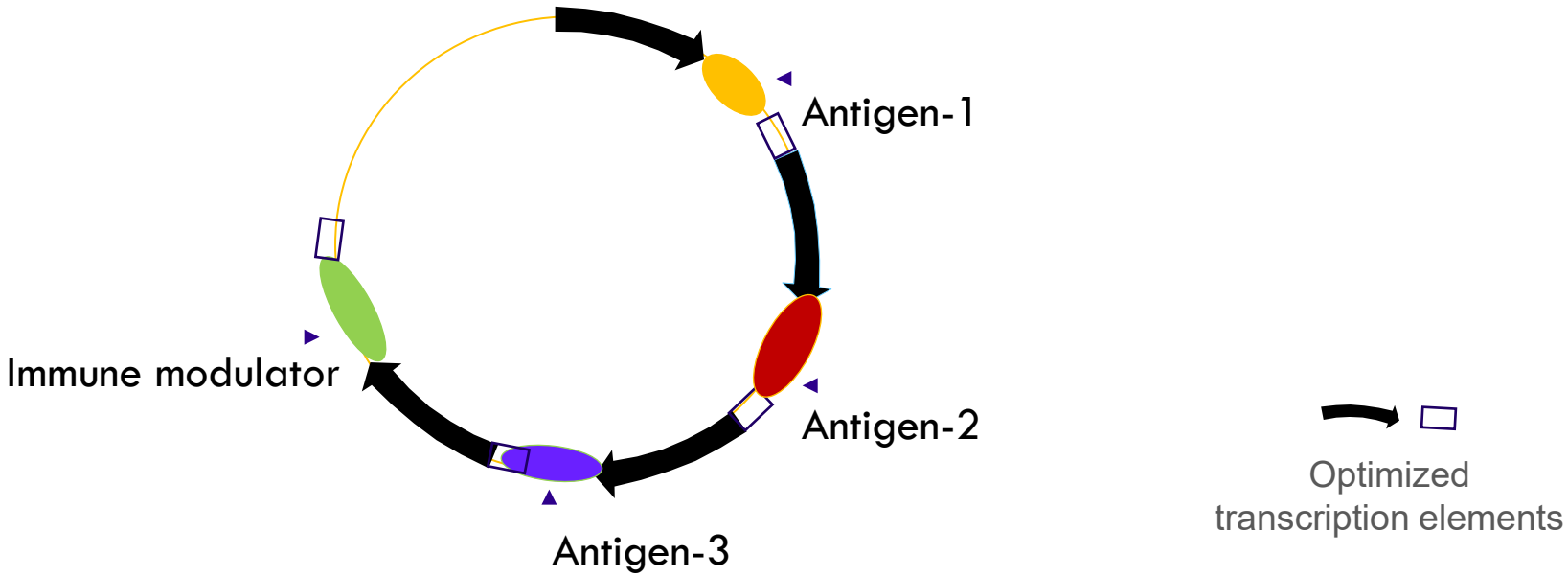
Durable antigen expression- a potential solution to short-lived mRNA vaccines in mice.

Imunon unpublished data

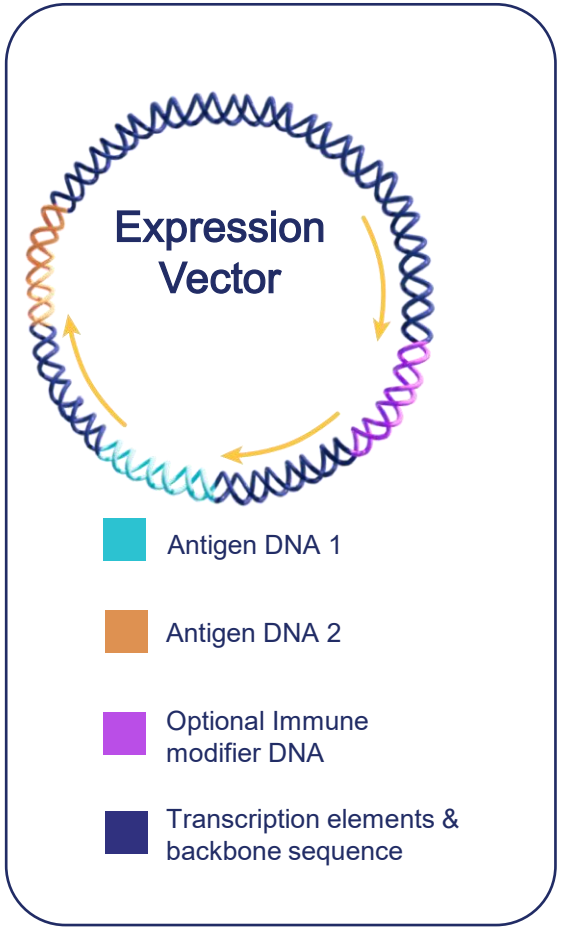
Multivalent Antigen Expression Cassette in an Optimized Backbone

Allows for a Broad-based Antigen Targeting- One or More Pathogens

- A template backbone cassette with optimized transcriptional elements
- Flexible cloning sites for rapid gene incorporation/removal
- Up to four gene sequences have been cloned in the current plasmid cassette



Novel Delivery Systems & Antigen Plasmids Constitute the PlaCCine Technology



Up to 4 genes have been successfully incorporated and expressed

PlaCCine pDNA Construct

PlaCCine Delivery Systems

Synthetic Delivery Systems

- Non-viral
- Non-device

Nanoparticles/Complexes

PlaCCine Vaccines

Intramuscular (IM) Administration

Potential Administration Routes

- Subcutaneous (SC)
- Intradermal (ID)
- Intranasal (IN)

Humoral & Cell Mediated Immune Response

PlaCCine Immunogenicity Demonstrated Against Various Pathogens in Multiple Species

Pathogens

- SARS CoV-2 (multiple variants)
- Influenza
- Marburg
- Lassa
- Monkeypox

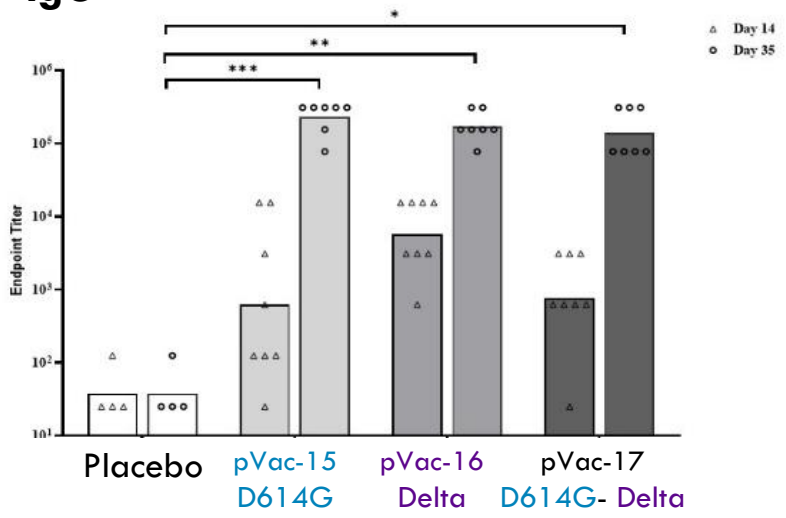
Species

- Mouse
- Rabbit
- Monkey
- Human

PlaCCine Immunogenicity Against SARS CoV-2 Variants- Mice

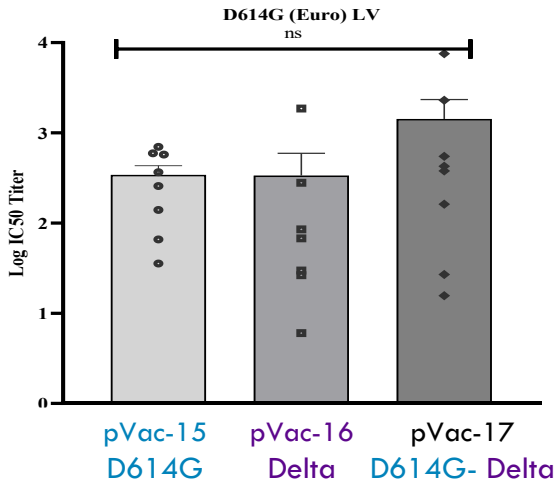
IgG, NAb, and T-cell Responses

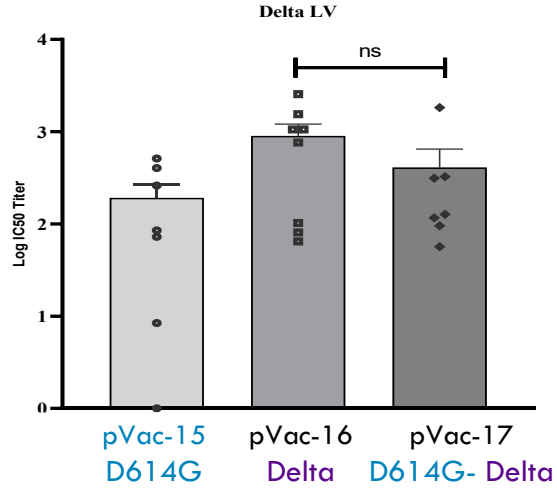
IgG



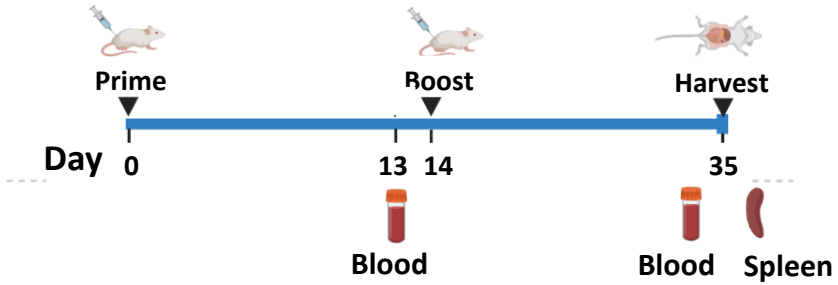
*P< 0.05, **P < 0.01, **** P<0.0001

NAb

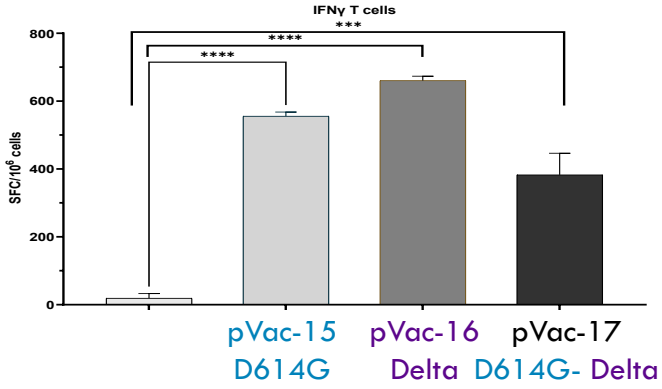




Prime-Boost Vaccination Model



T-cell



Peptide pools were 15 mers overlapping by 11 aa that encompassed the S1 protein from Wuhan Strain.

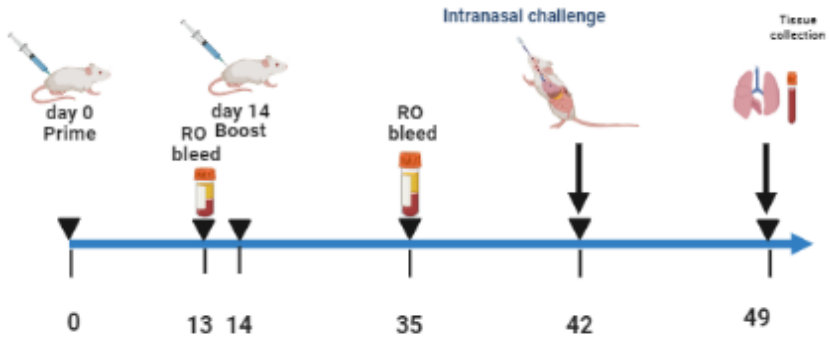
*P< 0.05, **P < 0.01, **** P<0.0001

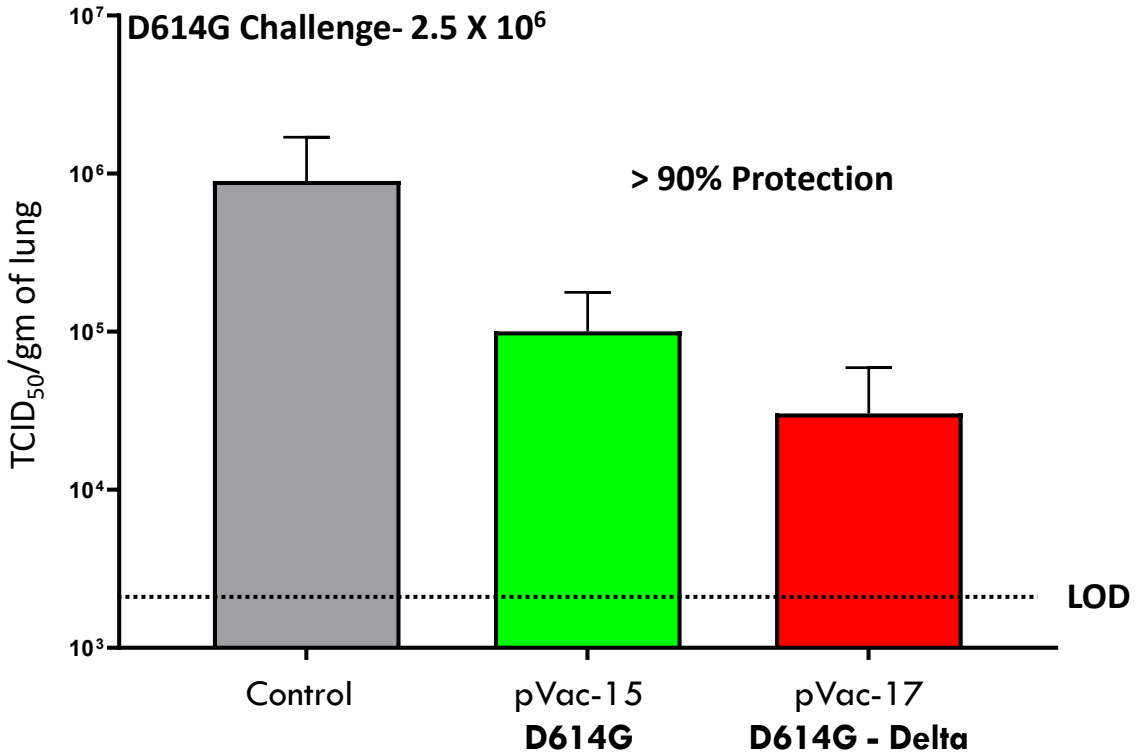
Protection Against SARS-CoV-2- hACE2:K16 Mice

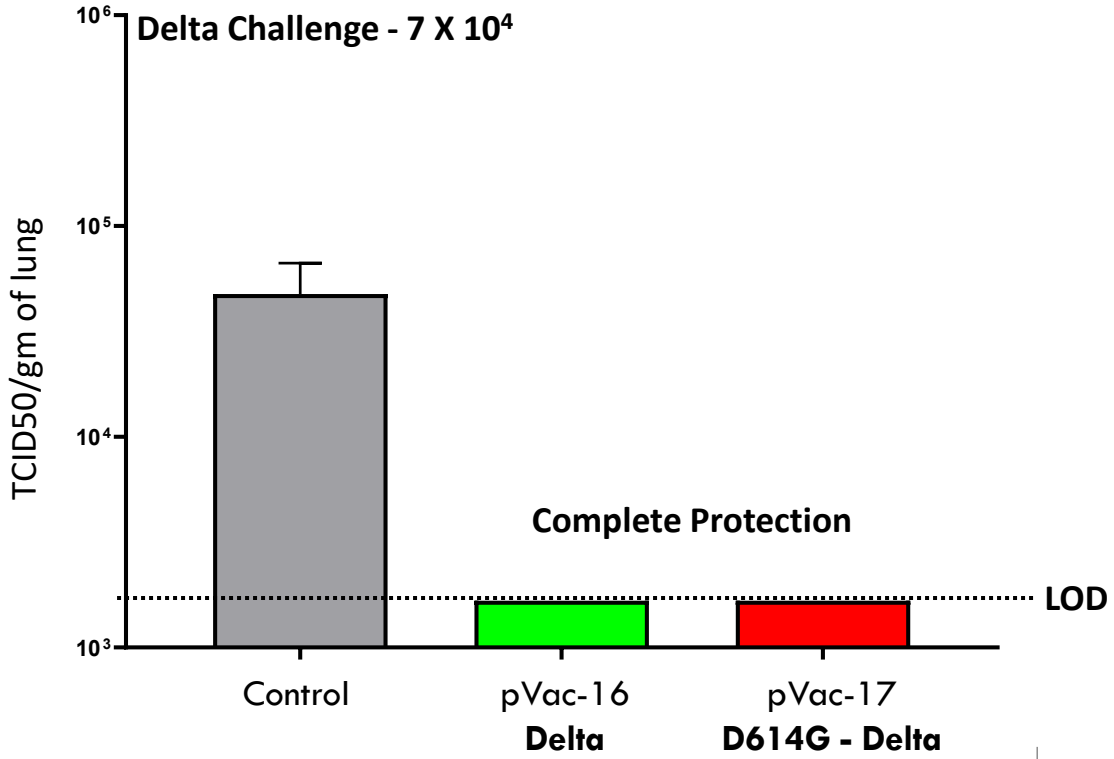
>90% Protection

- Formulation: PlaCCine including an adjuvant
- Dose - 125 µg DNA

7 days post challenge

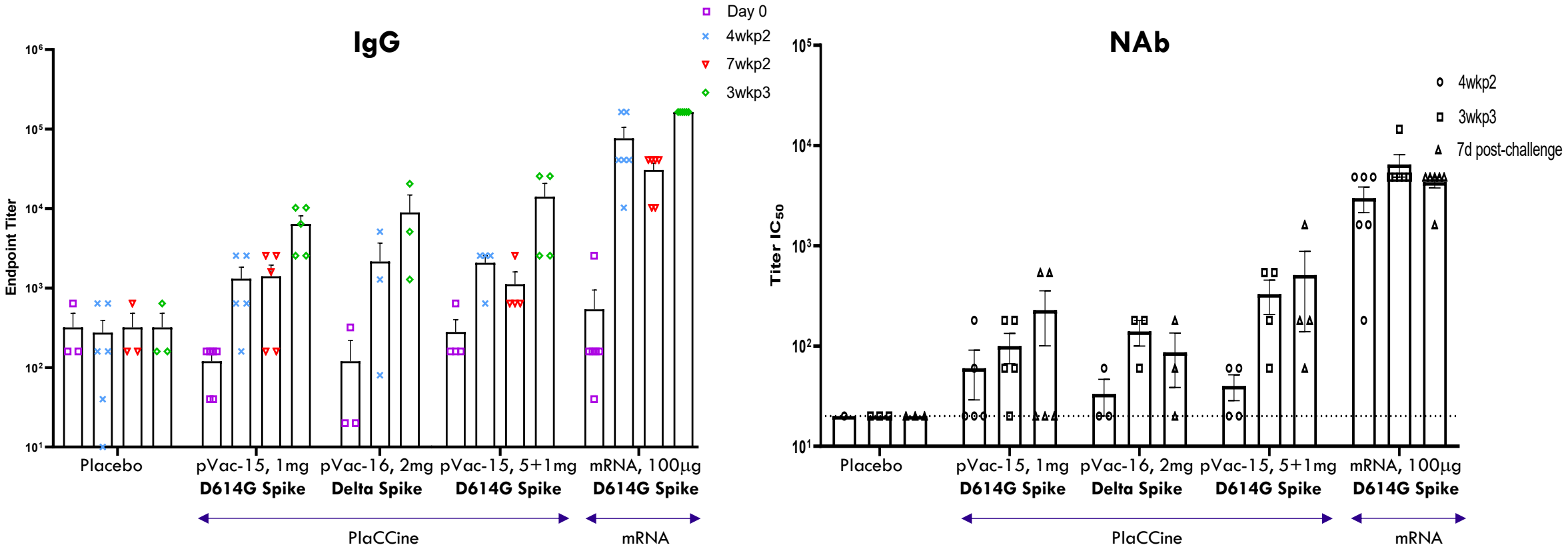






PlaCCine Immunogenicity Against SARS CoV-2 Variants- Cynomolgus Monkeys

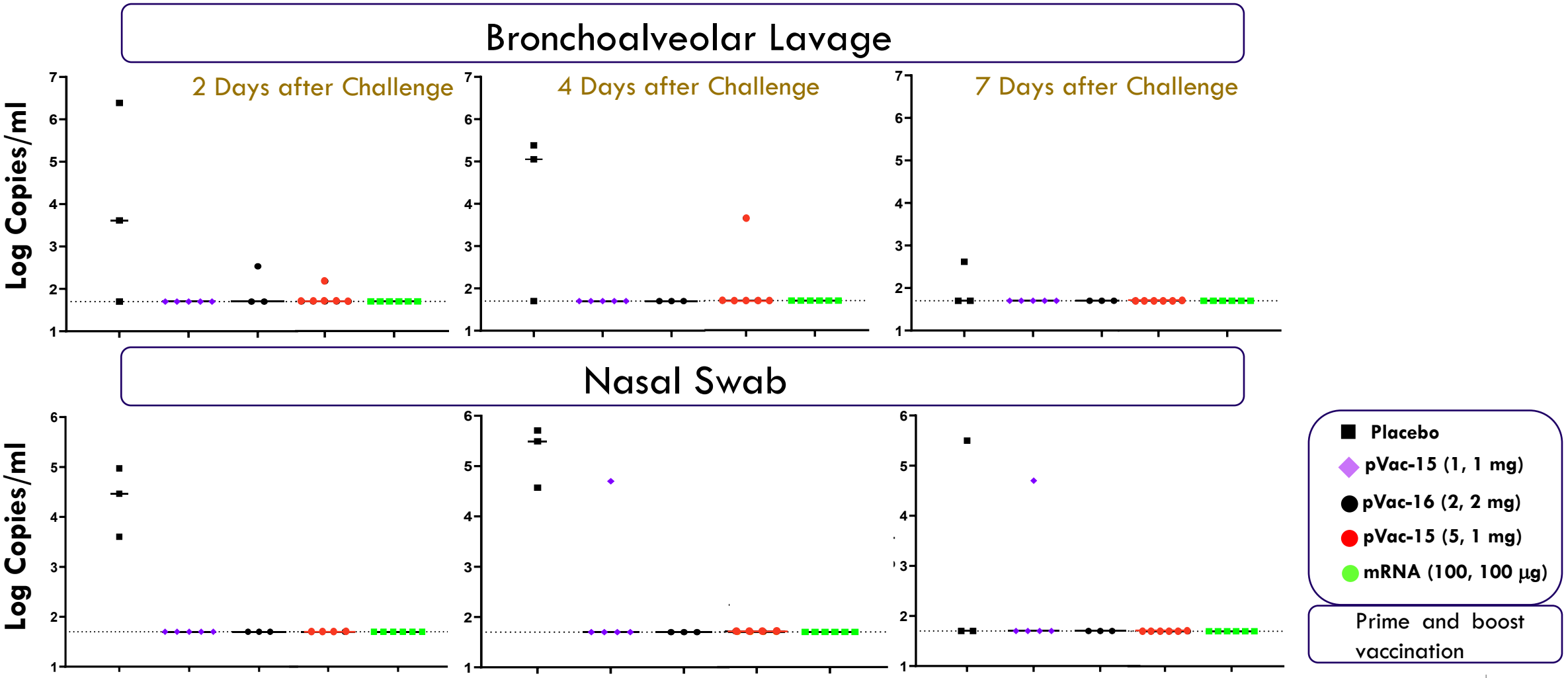
IgG, NAb, and T-cell Responses



PlaCCine Protection Against Viral Challenge in Cynomolgus Monkeys

Comparable Potency to mRNA Vaccines

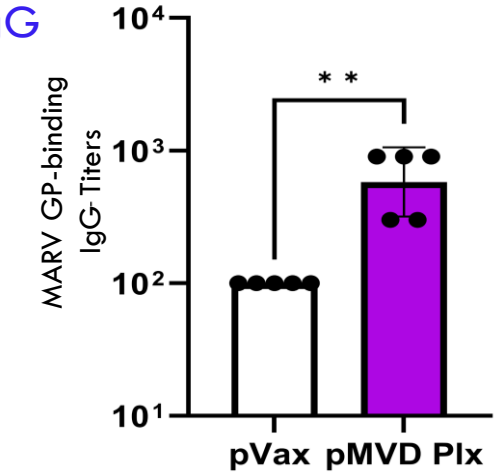
Challenge dose: 1 x 10^6 $TCID_{50}$



PlaCCine Vaccines for **Marburg, Influenza, and Lassa**- Mice

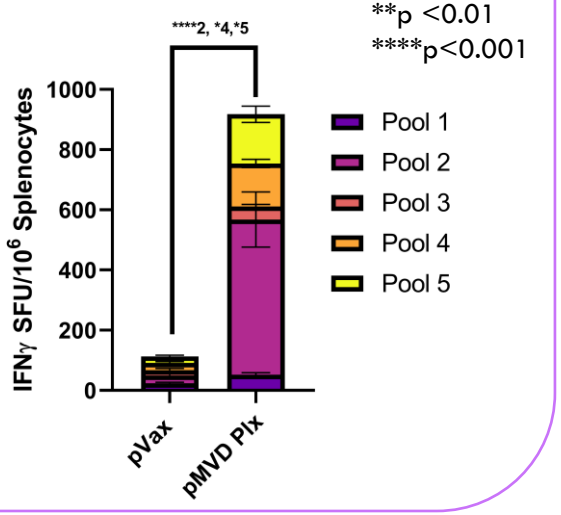
Marburg

IgG



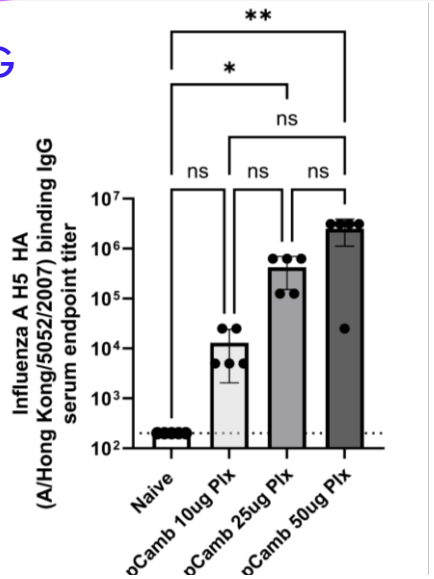
*p <0.05
**p <0.01
****p<0.001

T-cell

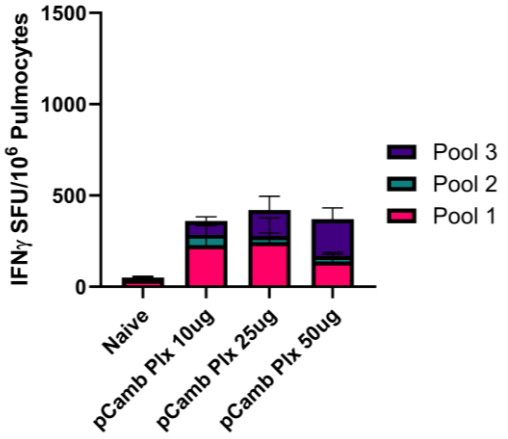


Influenza

IgG

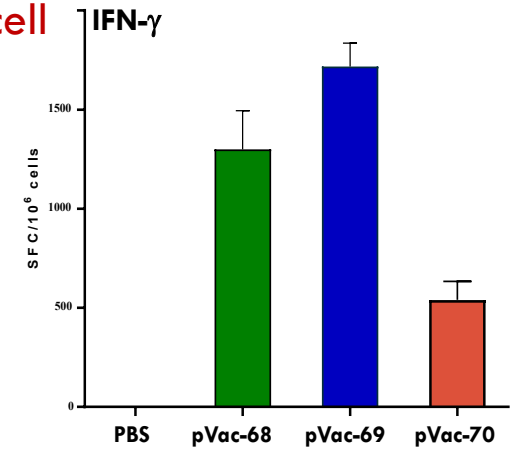


T-cell

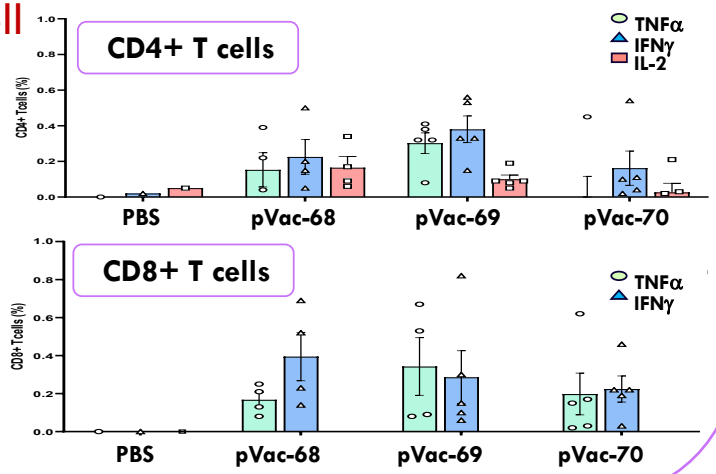


Lassa

T-cell

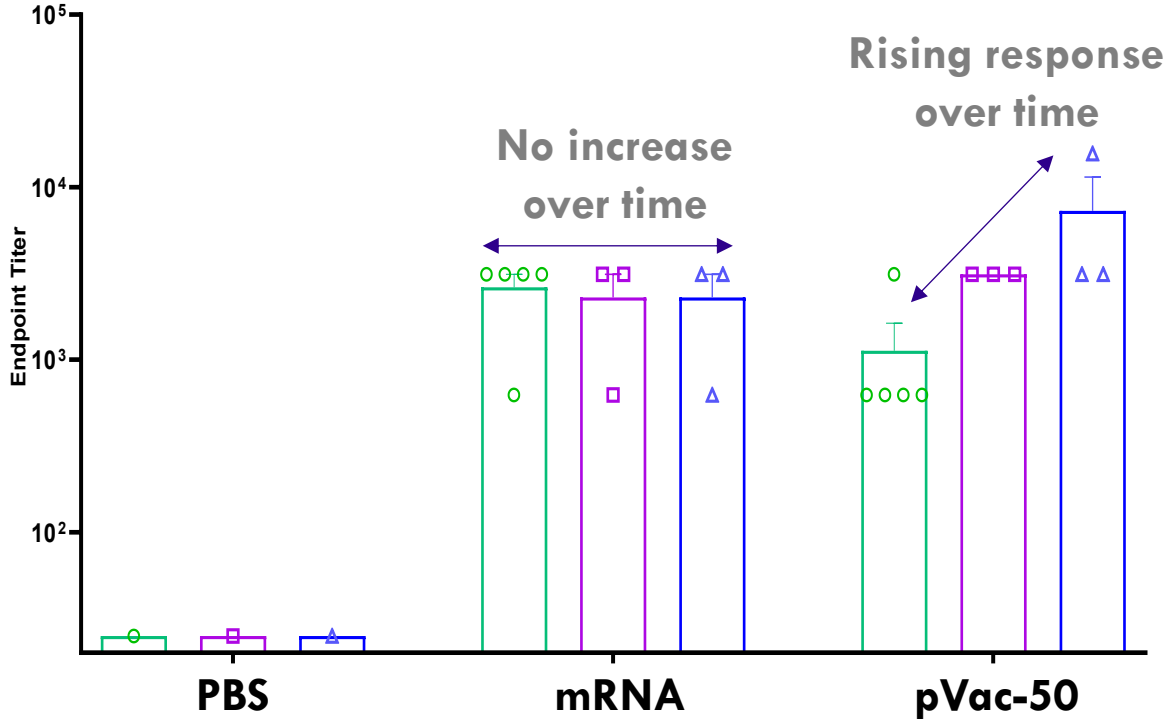


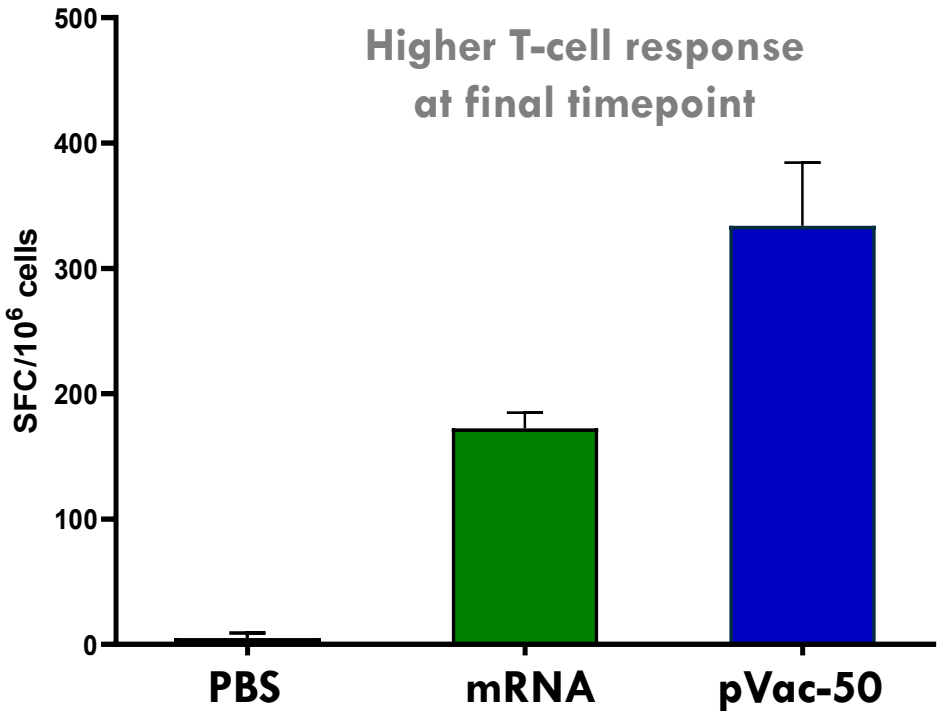
T-cell



PlaCCine Addresses the Limitations of Current Vaccines

Rising Immune Response Kinetic Compared to mRNA-LNP at a Single Dose

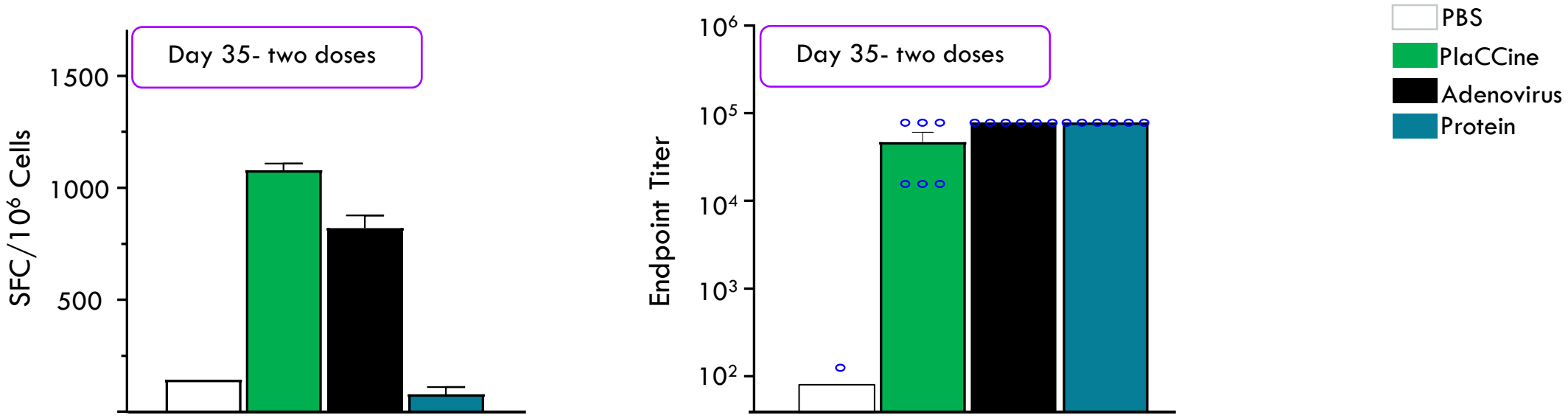




Favorable PlaCCine kinetics is suitable for single dose vaccination

Better T Cell Responses Compared to Viral Vector DNA & Protein Vaccines

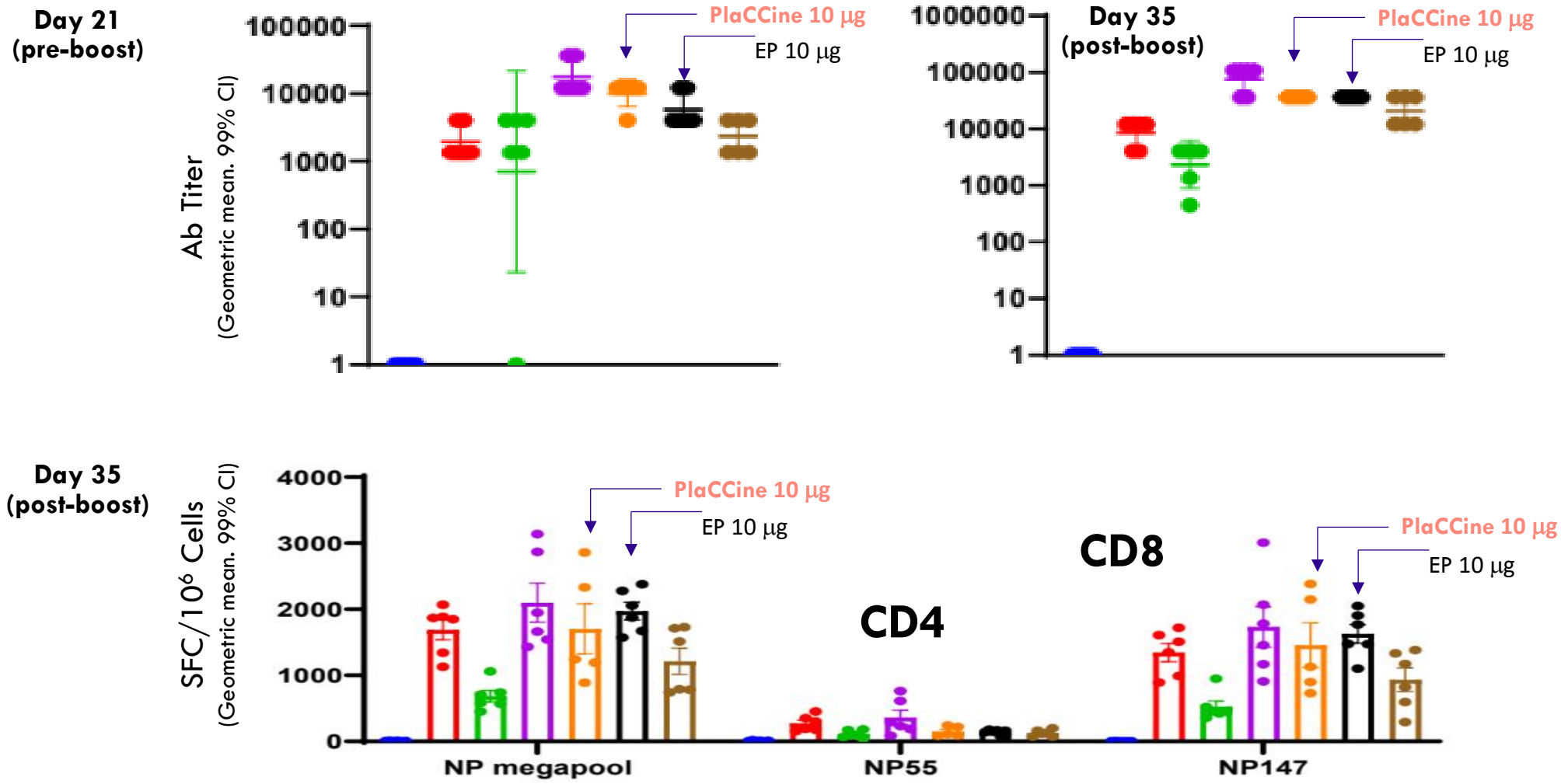
PlaCCine Offers Better Commercial Viability due to Safety Advantage



PlaCCine has safety advantage (no chromosomal integration) over viral DNA vaccines due to and manufacturing speed and flexibility over protein vaccines

Comparable Immune Responses to Electroporated DNA Vaccines

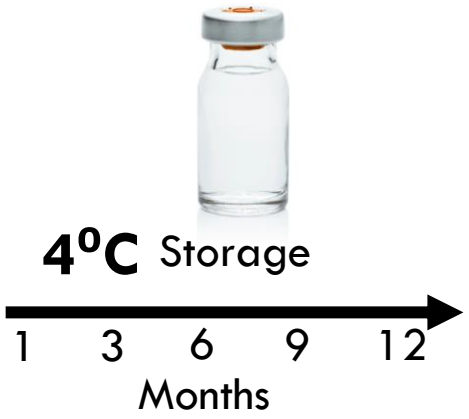
PlaCCine Offers Better Commercial Viability due to User Compliance Advantage

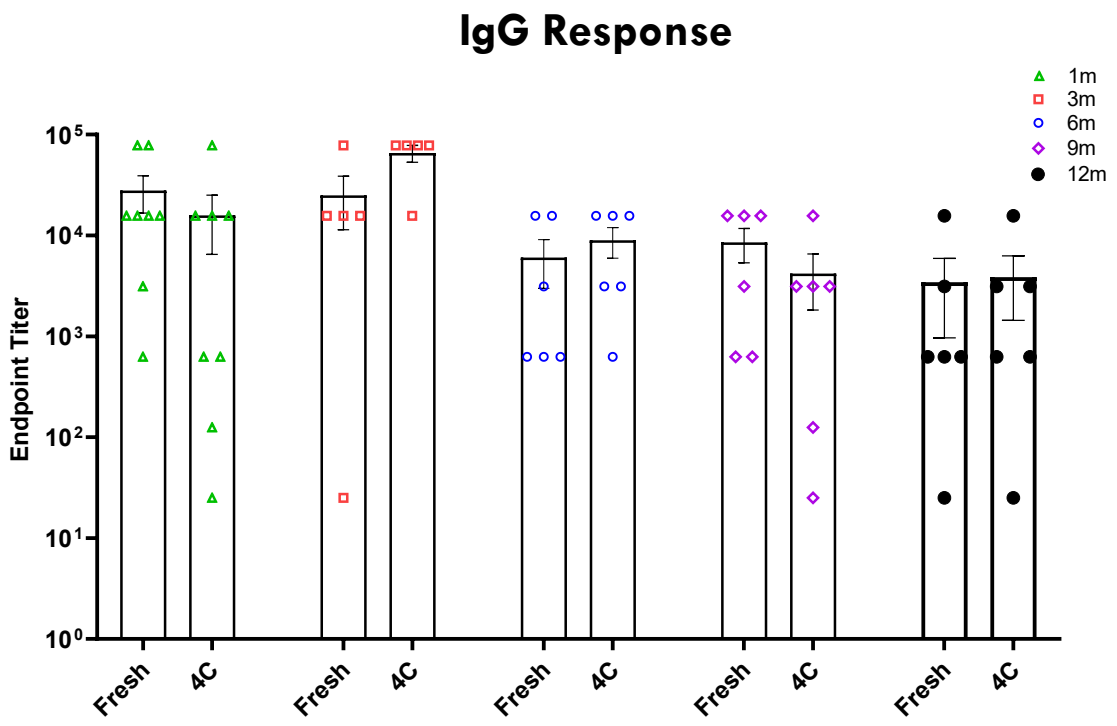


Commercial Advantages of PlaCCine over mRNA Vaccines

Stable at 4° C for at Least 12-Months

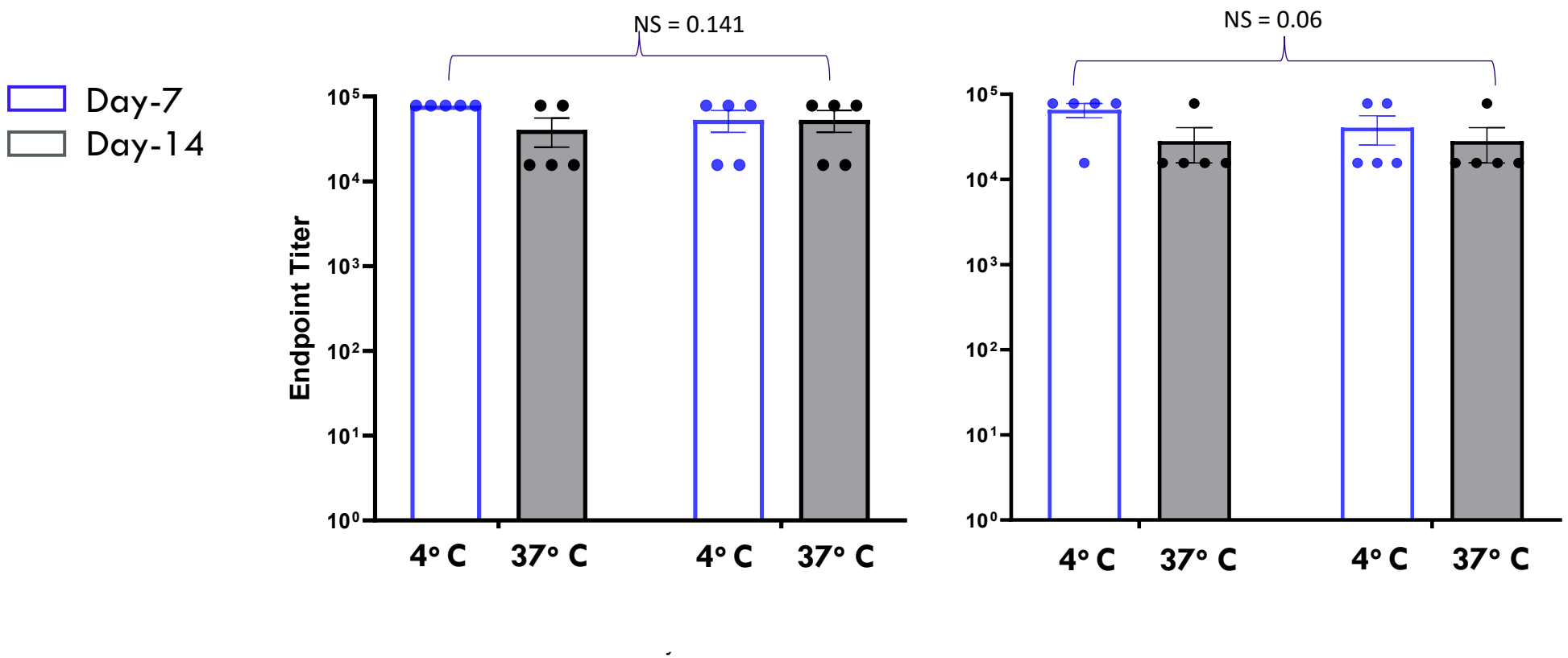
- Vector: pVac-17 (D614G-Delta)
- Formulation: PlaCCine





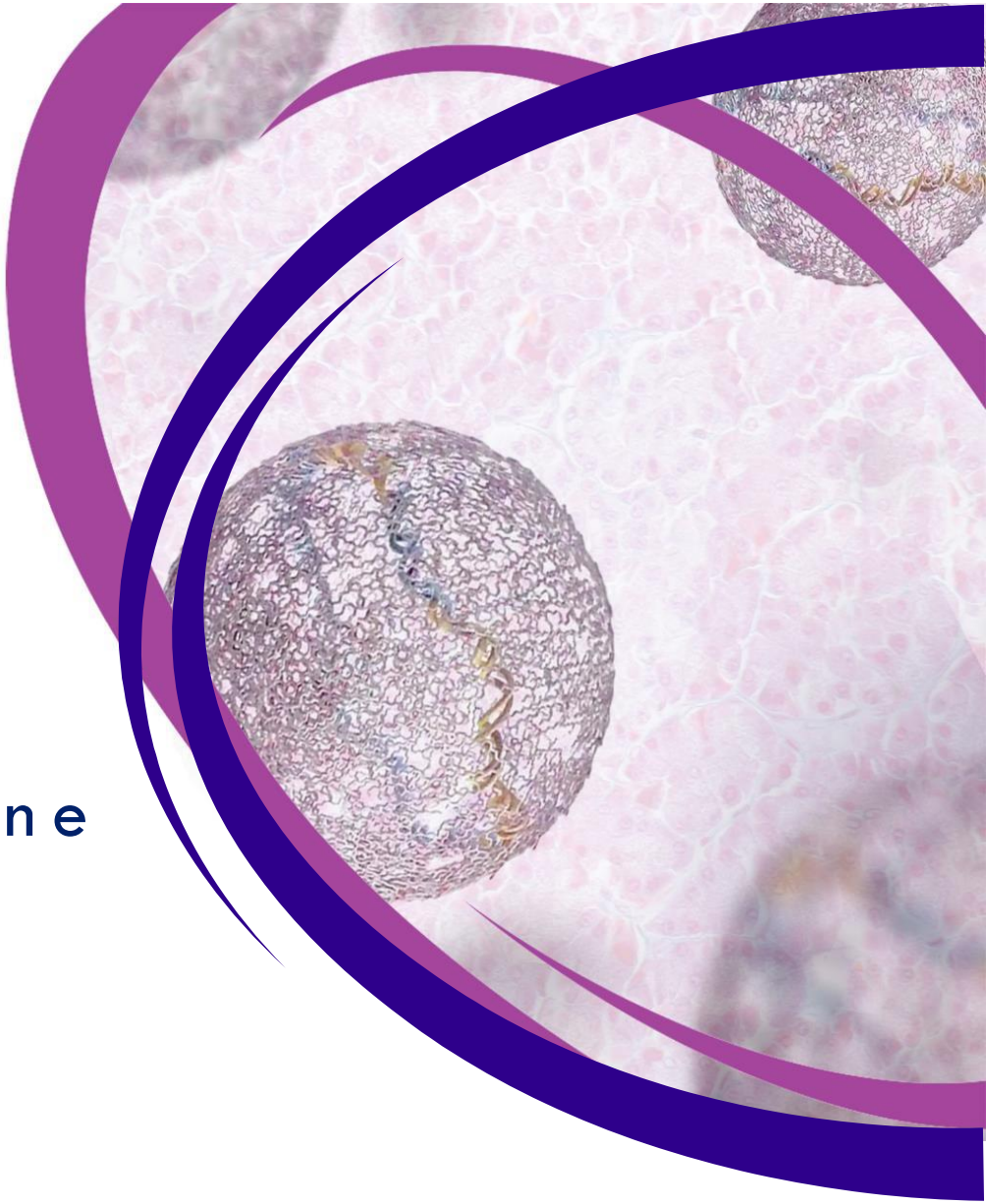
Commercial Advantages of PlaCCine over mRNA Vaccines

Stable at 37° C for at Least 14 Days



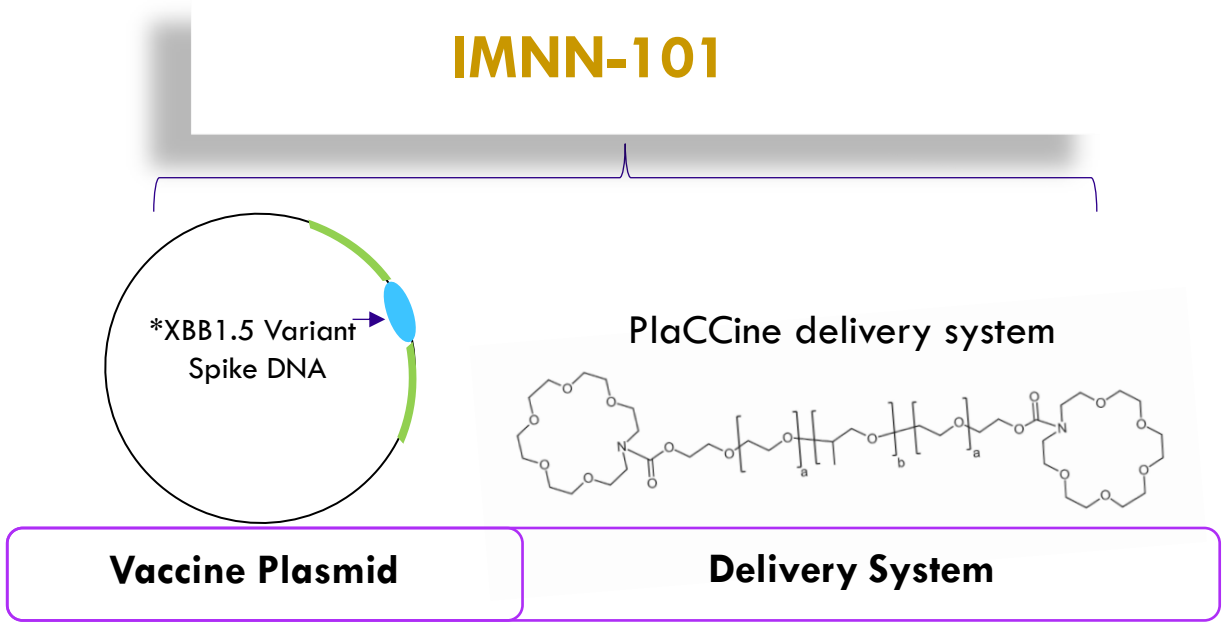
IMNN-101

A Clinical Stage PlaCCine Vaccine

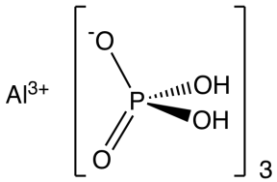


IMNN-101- A COVID-19 Vaccine

First-in-Human PlaCCine Vaccine



* Variant of Concern
(FDA: VRBPAC 2023)

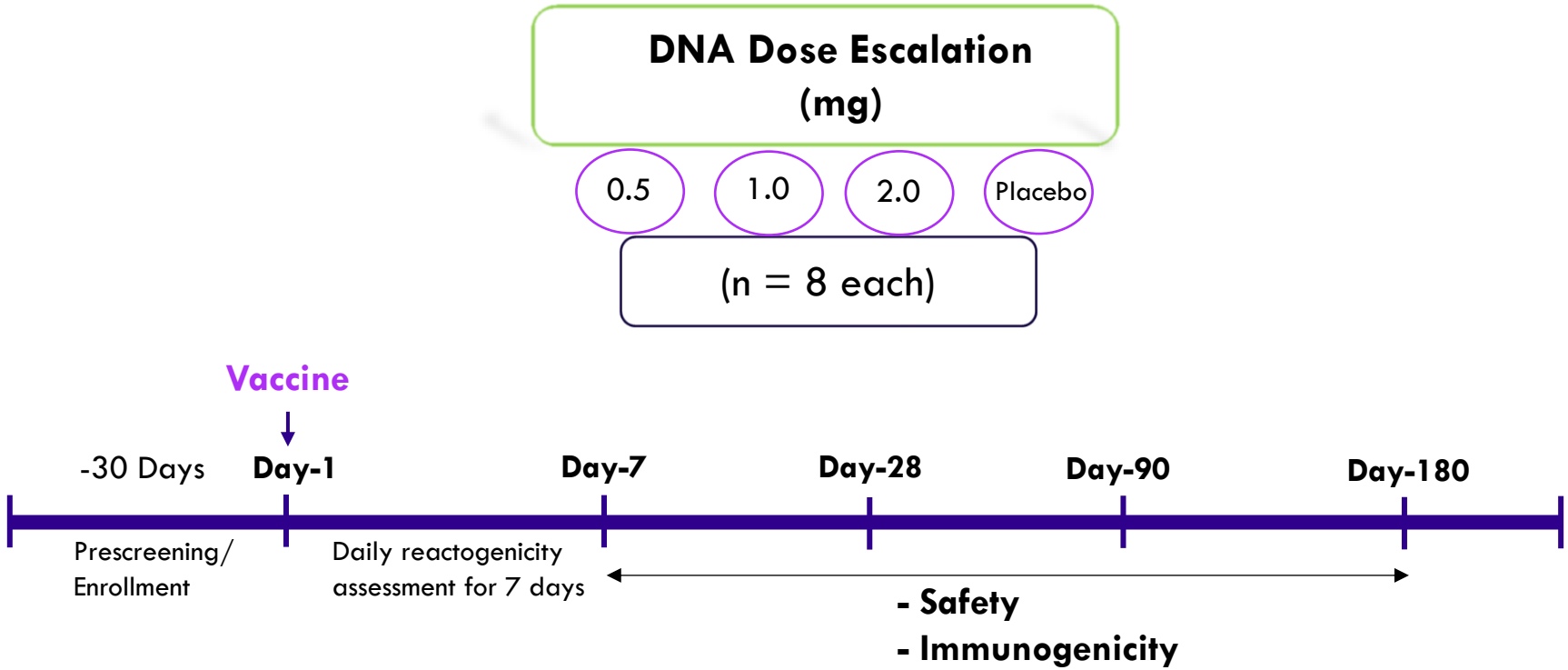


Adjuvant Alum PO4

IMNN-101- Single Dose, Placebo Controlled Phase 1 Trial in Healthy Subjects

NCT06283459

Rapid Dose Escalation for Speedy Completion



Demographic Characteristics of the Study Patients

Baseline Characteristics		All Participants (n = 24)	Dose Group 1 (n = 8)	Dose Group 2 (n = 8)	Dose Group 3 (n = 8)
Age (years)	Mean	47.7	47.9	44.7	50.5
Sex	Male	9 (37.5%)	3 (37.5%)	4 (50%)	2 (25%)
	Female	15 (62.5%)	5 (62.5%)	4 (50%)	6 (75%)
Ethnicity	Hispanic or Latino	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Not Hispanic or Latino	24 (100%)	8 (100%)	8 (100%)	8 (100%)
Race	American Indian or Alaska Native	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Asian	1 (4.2%)	1 (12.5%)	0 (0%)	0 (0%)
	Black or African American	11 (45.8%)	2 (25%)	5 (62.5%)	4 (50%)
	Native Hawaiian or Other Pacific Islander	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	White	12 (50%)	5 (62.5%)	3 (37.5%)	4 (50%)

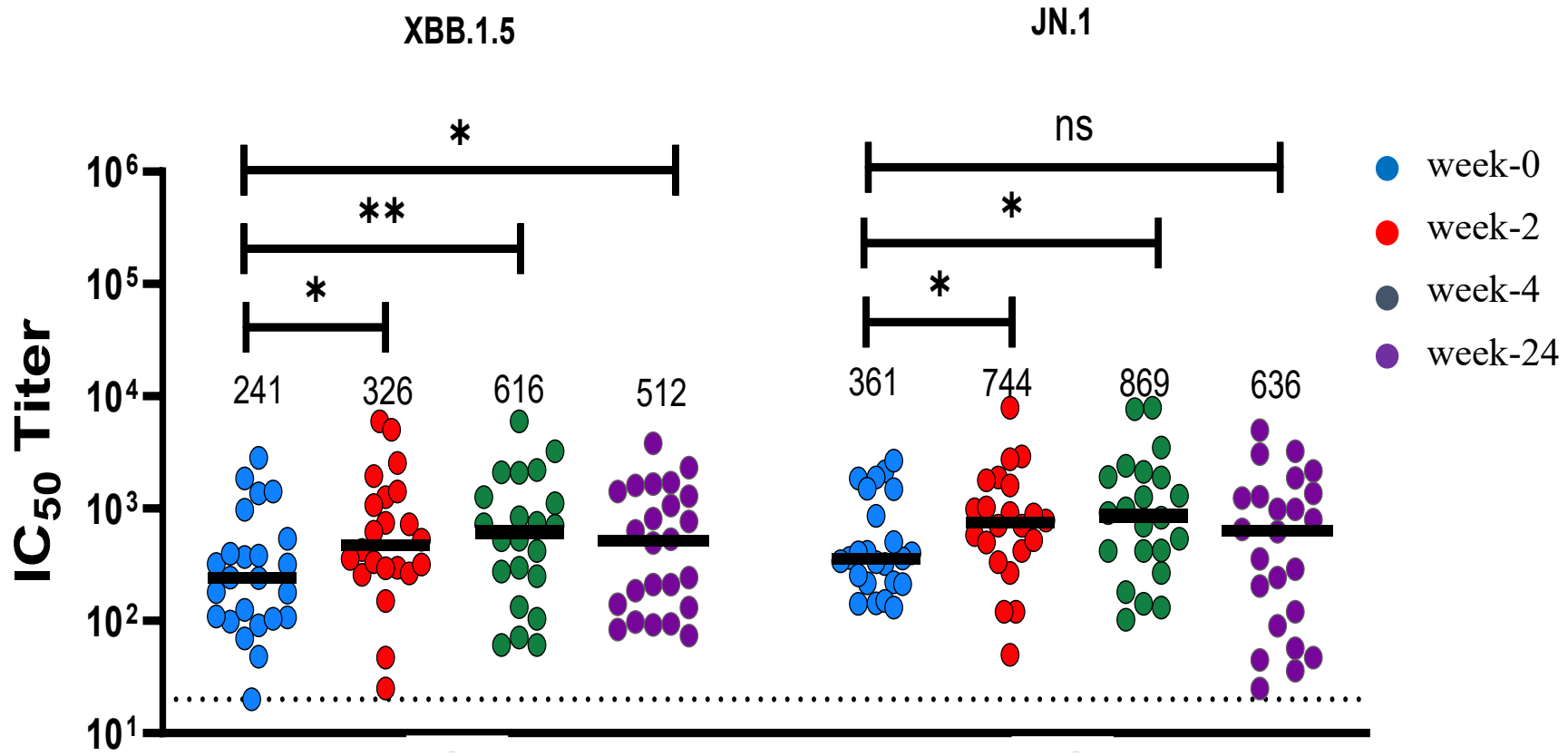
Safety Profile of IMNN-101

Treatment-emergent Adverse Events During 6-Month Follow Up

Body System/Class	TEAE Preferred Term	n (%) (n = 24)	Grade 1	Grade 2	Grades 3 – 5
Ear and labyrinth disorders	Vertigo	**1 (4.2%)**	**1 (4.2%)**	**0 (0%)**	0 (0%)
Infections and infestations	Bronchitis	**1 (4.2%)**	**0 (0%)**	**1 (4.2%)**	0 (0%)
	COVID-19	**3 (12.5%)**	**0 (0%)**	**3 (12.5%)**	0 (0%)
	Viral pharyngitis	**1 (4.2%)**	**1 (4.2%)**	**0 (0%)**	0 (0%)
	Vulvovaginal candidiasis	**1 (4.2%)**	**0 (0%)**	**1 (4.2%)**	0 (0%)
Injury, poisoning and procedural complications	Arthropod bite	**1 (4.2%)**	**0 (0%)**	**1 (4.2%)**	0 (0%)
	Joint dislocation	**1 (4.2%)**	**0 (0%)**	**1 (4.2%)**	0 (0%)
Metabolism and nutrition disorders	Hyperlipidemia	**1 (4.2%)**	**1 (4.2%)**	**0 (0%)**	0 (0%)
Musculoskeletal and connective tissue disorders	Torticollis	**1 (4.2%)**	**0 (0%)**	**1 (4.2%)**	0 (0%)
Psychiatric disorders	Attention deficit hyperactivity disorder	**1 (4.2%)**	**0 (0%)**	**1 (4.2%)**	0 (0%)
	Depression	**1 (4.2%)**	**0 (0%)**	**1 (4.2%)**	0 (0%)
	Panic attack	**1 (4.2%)**	**1 (4.2%)**	**0 (0%)**	0 (0%)

NAb Responses to XBB.1.5/JN.1 Variant following a Single Dose of IMNN-101

Subjects Previously Infected/Vaccinated Multiple Times



The statistical significance between pre-treatment group (week-0) and each of the pot-treatment groups (Week-2, -4, -24) was assessed using Wilcoxon sign rank test *p<0.05, **p<0.01, ns= not significant.

Dose-dependence of the Neutralizing Antibody Responses to XBB.1.5 and JN.1 Variant

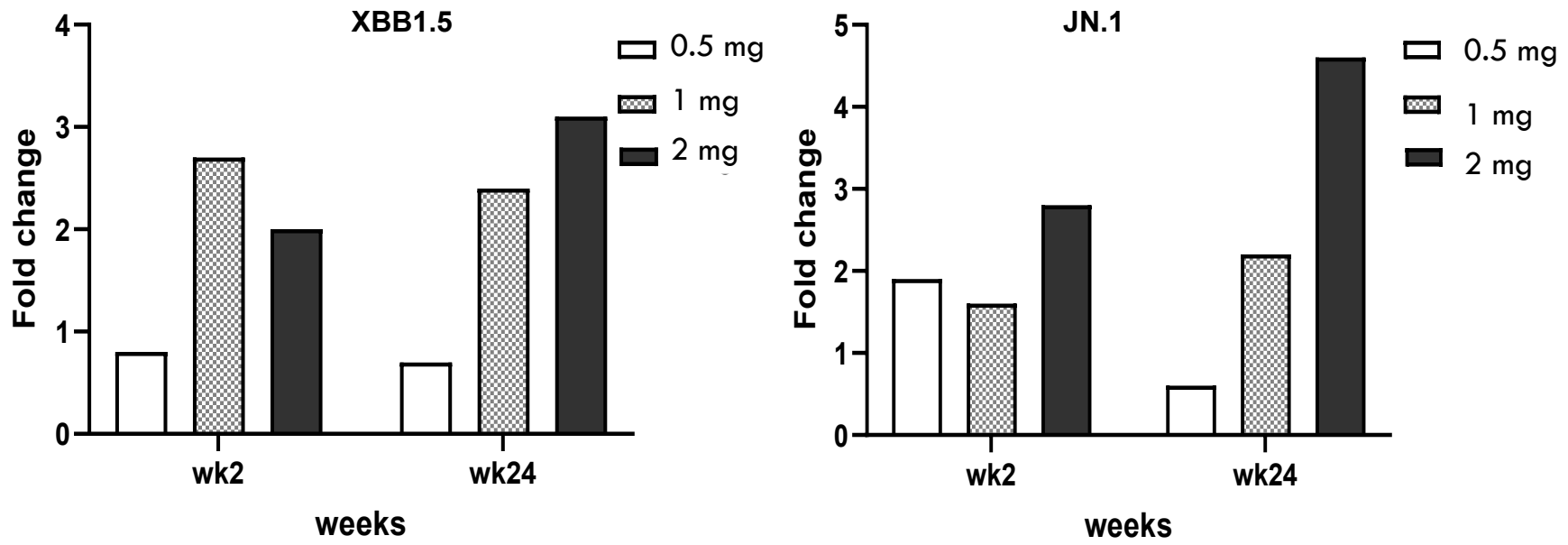


Fig. 2: Fold changes in median NAb titers at different vaccine doses following a single injection of IMNN-101.

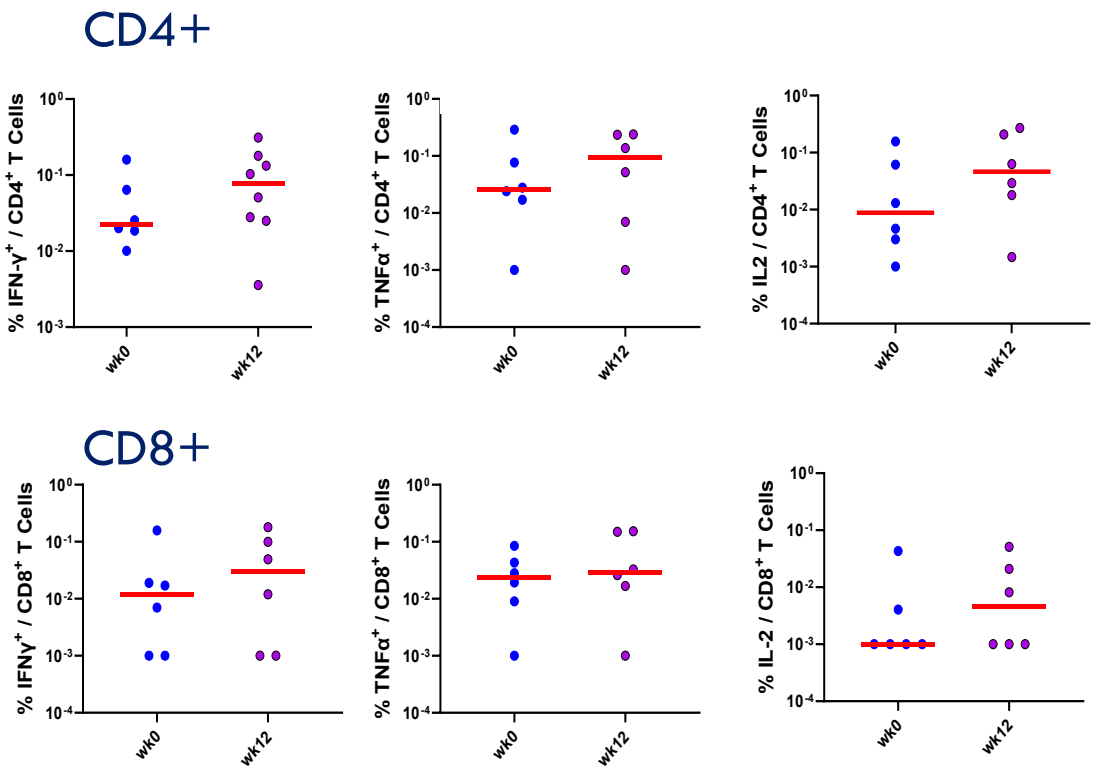
Cellular Immune Responses to XBB.1.5 & JN.1 Following IMNN-101

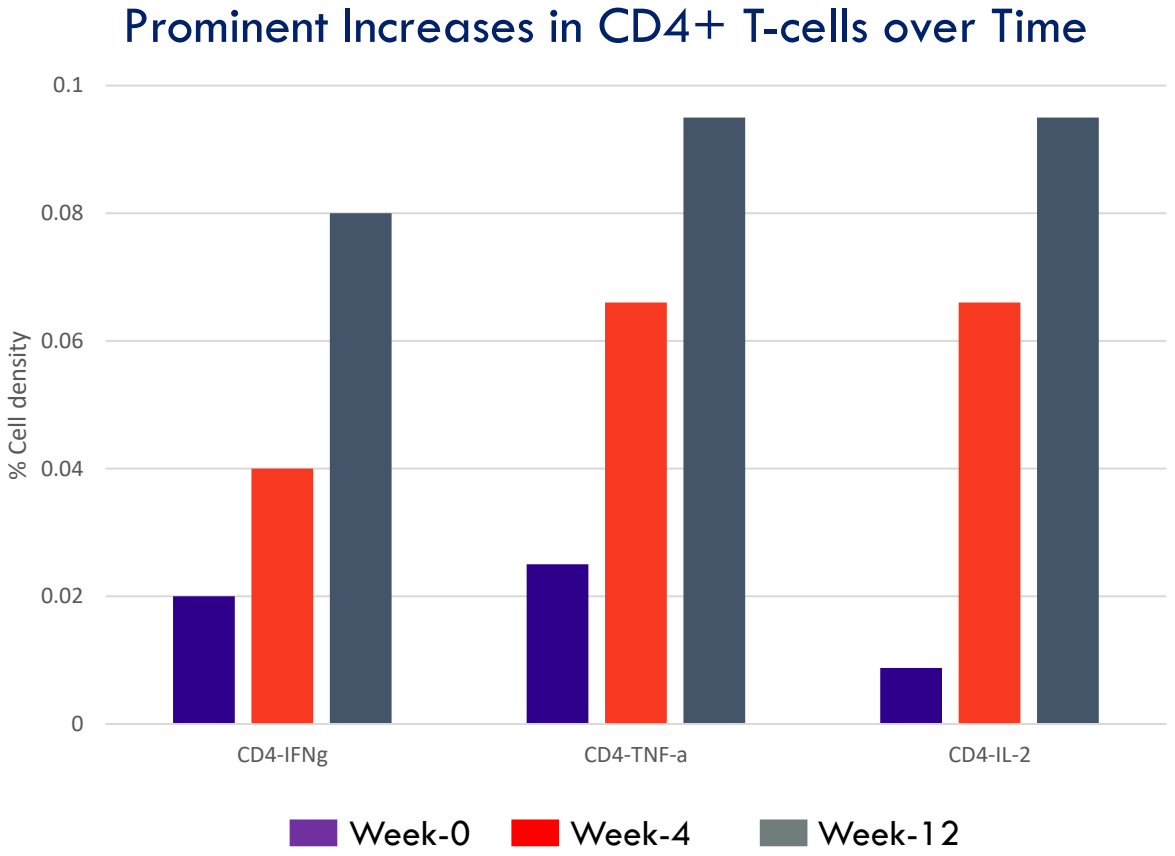
Subjects Previously Infected/Vaccinated Multiple Times

	CD4+ T-cells			CD8+ T-cells		
	% Responders					
	IFN-g	TNF-a	IL-2	IFN- g	TNF-a	IL-2
XBB1.5	53%	47%	68%	63%	63%	32%
JN.1	56%	61%	61%	50%	63%	50%
		Highest Fold-increase from Baseline & Dose				
XBB1.5	6.5	7.4	10.7	49	33	7
Dose	2 mg	2 mg	2 mg	2 mg	1 mg	2 mg
JN.1	4.9	20	20	15	18	21
Dose	2 mg	2 mg	2 mg	2 mg	1mg	2 mg

T-cell Responses to JN.1 Following a Single Dose of IMNN-101

Subjects Previously Infected/Vaccinated Multiple Times





PlaCCine Summary-

- A novel platform for prophylactic vaccines that leverages DNA advantages on:
  - Durability of antigen expression, temperature stability, flexible manufacturing, rapid development
- Safety and immunogenicity demonstrated in healthy human subjects after a single injection.
  - NAb responses lasted for at least 6 months
  - Evidence of cellular immune responses
- IMNN-101 data supports further development of PlaCCine in:
  - Naïve population- would allow for an optimal magnitude of effect
  - Prime and boost vaccination- for an optimal benefit
- Examples of preferred disease targets for future development of PlaCCine vaccines:
  - HIV, Influenza, Zika, Ebola, Hepatitis B & C, Rabies