UPDATE ON NOVAVAX INVESTIGATIONAL NanoFlu VACCINE AND COVID-19-INFLUENZA COMBINATION VACCINE DEVELOPMENT

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APRIL 20, 2022 | NOVAVAX

SAFE HARBOR STATEMENT

Certain information, particularly information relating to the future of Novavax, its operating plans and prospects, its partnerships, the ongoing development of NVX-CoV2373, including Novavax' plans to initiate a pediatric study in Q2 2022, NanoFlu, its COVID-seasonal influenza investigational vaccine candidate, COVID-NanoFlu combination vaccine, including Novavax' plans to initiate a Phase 2 clinical trial for COVID-NanoFlu combination vaccine, Omicron-specific vaccine, and other Novavax vaccine product candidates, the timing of results from clinical trials, the potential impact of Novavax and NVX-CoV2373 in addressing vaccine access, controlling the pandemic and protecting populations, including the potential for a booster dose of NVX-CoV2373 to provide protection against COVID-19 (including variants), and the efficacy, safety, and intended utilization of NVX-CoV2373, the scope, timing, and outcome of future regulatory filings and actions, including Novavax' plans to supplement global regulatory filings with the pediatric data and pediatric investigations plans agreed to by regulatory authorities, the global market opportunities for NVX-CoV2373, the readiness of our global supply chain and future availability of NVX-CoV2373 at a global scale and the commercialization and expected delivery of NVX-CoV2373, and key upcoming milestones constitute forward-looking statements.

Forward-looking statements may generally contain words such as "believe," "may," "could," "will," "possible," "can," "estimate," "continue," "ongoing," "consider," "anticipate," "intend," "seek," "indicate," "plan," "project," "expect," "should," "would," "aim," or "assume" or variations of such words or other words with similar meanings. Novavax cautions that these forward-looking statements are subject to numerous assumptions, risks and uncertainties that change over time and may cause actual results to differ materially from the results discussed in the forward-looking statements.

These risks and uncertainties include, without limitation, challenges satisfying, alone or together with partners, various safety, efficacy, and product characterization requirements, including those related to process qualification and assay validation, necessary to satisfy applicable regulatory authorities; difficulty obtaining scarce raw materials and supplies; resource constraints, including manufacturing capacity, including human capital and manufacturing capacity, on the ability of Novavax to pursue planned regulatory pathways; challenges meeting contractual requirements under agreements with multiple commercial, governmental, and other entities; and those other risk factors identified in the "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of Novavax' Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the Securities and Exchange Commission, which are available at www.sec.gov and www.novavax.com.

Forward-looking statements are based on current expectations and assumptions and currently available data and are neither predictions nor guarantees of future events or performance.

Current results may not be predictive of future results.

You should not place considerable reliance on forward-looking statements which speak only as of the date hereof.

The Company does not undertake to update or revise any forward-looking statements after they are made, whether as a result of new information, future events, or otherwise, except as required by applicable law.

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OVERVIEW

NanoFlu (qNIV) Vaccine Program Development

COVID-Influenza Combination (CIC) Vaccine Development

NanoFlu* (qNIV) VACCINE DEVELOPMENT

*NanoFlu identifies a recombinant hemagglutinin (HA) protein nanoparticle influenza vaccine candidate produced by Novavax. This investigational candidate was evaluated during a controlled phase 3 trial conducted during the 2019-2020 influenza season.

CHARACTERISTICS OF CURRENTLY LICENSED INFLUENZA VACCINES

VACCINE TYPE	Characteristics Addressed			
	EGG-ADAPTIVE CHANGES	ANTIGENIC DRIFT	IMMUNOSENESCENCE	
			ANTIBODIES	T-CELLS
Standard Inactivated[1,2,3,4,5]	✗	✗	✗	✗
High-dose inactivated[1,3,4,5]	✗	✗	✓	✗
MF-59 Adjuvanted[4,5,6,7]	✗	✓	✓	?
Cell-derived inactivated[5,8]	?	✗	✗	✗
Recombinant[2,3,4]	✓	✓	✓	✗
NanoFlu (qNIV)[9,10] [recombinant + adjuvanted]	✓	✓	✓	✓

NanoFlu (qNIV) has been shown to induce BOTH broadly cross-reactive antibodies AND potent polyfunctional CD4+ T-cell responses AND avoids egg-adaptive antigenic changes

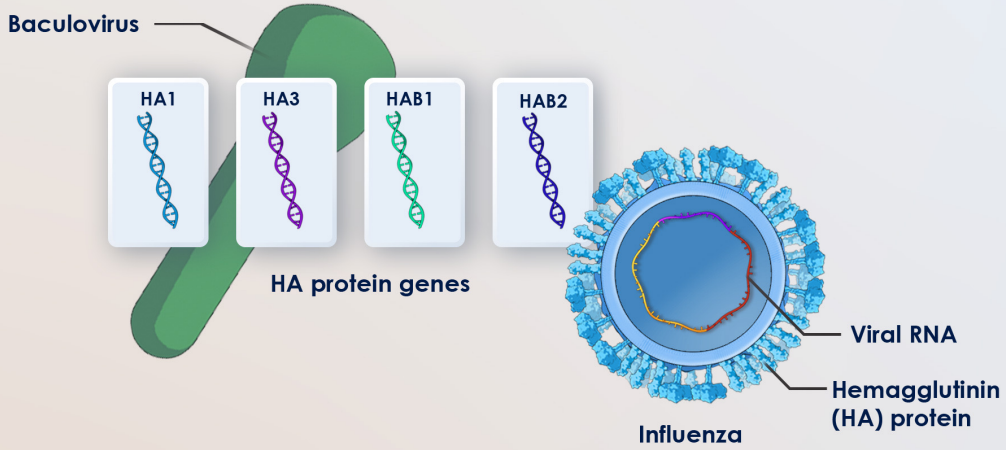
These are product characteristics only and no head-to-head studies have been done and are not meant to imply clinical efficacy.

1. Diaz-Granados 2015; 2. Dunkle, 2017; 3. Zost, 2017; 4. Cowling 2019; 5. Izurieta 2019; 6. Frey 2014; 7. Mannino 2012; 8. Gouma 2020; 9. Shinde 2018; 10. Shinde 2020

NanoFlu (qNIV) Investigational Vaccine Design

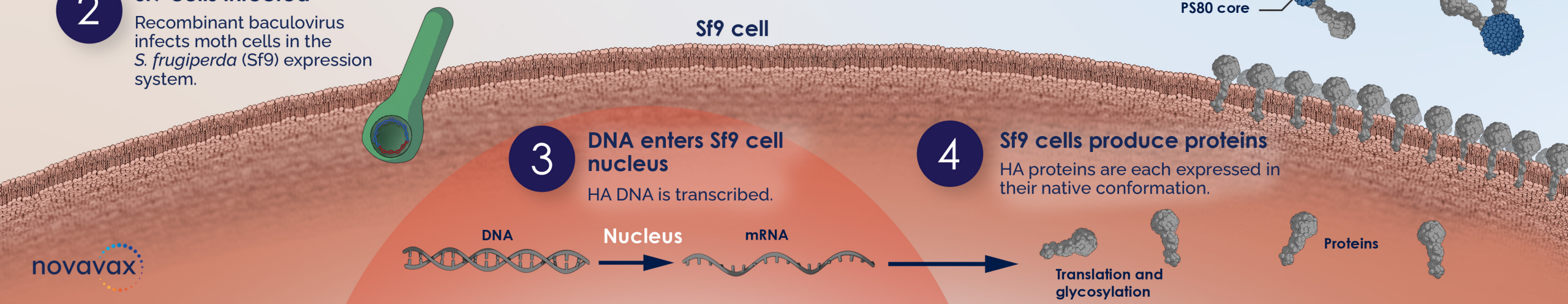
1 Genes inserted into insect virus

Four Influenza Hemagglutinin (HA1, HA3, HAB1, HAB2) genes are engineered into baculovirus for independent expression.



2 Sf9 cells infected

Recombinant baculovirus infects moth cells in the *S. frugiperda* (Sf9) expression system.



3 DNA enters Sf9 cell nucleus

HA DNA is transcribed.

4 Sf9 cells produce proteins

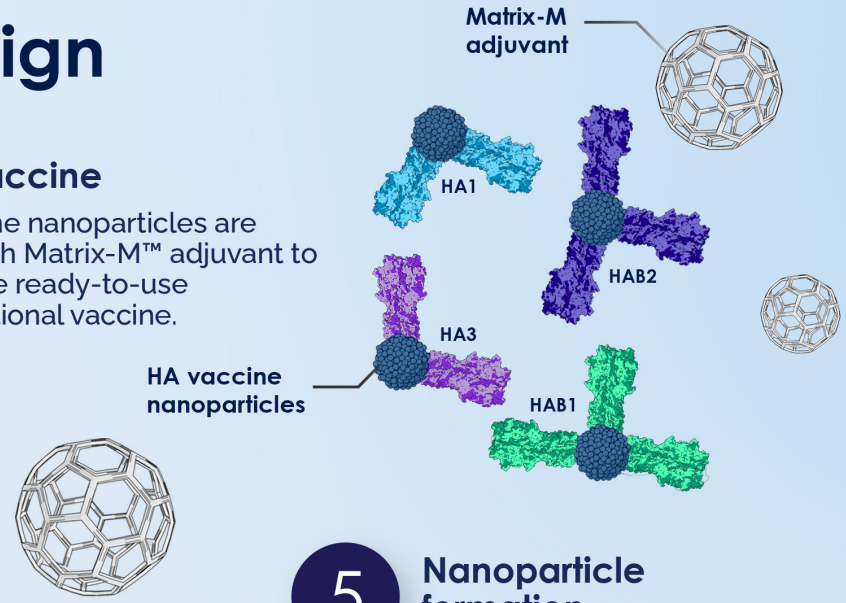
HA proteins are each expressed in their native conformation.

5 Nanoparticle formation

Proteins are harvested. Vaccine nanoparticles assemble as proteins arranged around a Polysorbate 80 (PS80) core.

6 Final vaccine

HA vaccine nanoparticles are mixed with Matrix-M™ adjuvant to create the ready-to-use investigational vaccine.



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COR-GL-FLU-0001 04/2022

PHASE 3: A NON-INFERIORITY IMMUNOGENICITY TRIAL

AIMS

- Demonstrate immunologic non-inferiority to licensed influenza vaccine (Fluzone Quadrivalent) on 4 homologous strains
- Establish pivotal clinical trial dataset to support filing of BLA via accelerated approval path

DESIGN

- 2650 adults ≥65 years of age, across 19 US sites
- Randomized to 1:1 to either NanoFlu or Fluzone Quadrivalent
- Stratified by receipt of prior year seasonal influenza vaccine
- Single dose of test vaccine on Day 0

Day 0 Trial Treatment Injection					
Treatment Group	Vaccine	HA Dose per Strain, µg ($H1N1/H3N2/B_V/B_Y$)	Matrix-M1 Adjuvant Dose, µg	Formulation	**Subjects Per Group**
A	NanoFlu (qNIV)	60, 60, 60, 60	75	Co-form	1325
B	Fluzone Quad [standard dose]	15, 15, 15, 15	N/A	N/A	1325
				Total Trial Subjects	2650

Primary objectives:

- Demonstrate non-inferior immunogenicity of NanoFlu vs. Fluzone Quadrivalent:
  - Day 0 and 28 egg-propagated virus HAI titers against the 4 homologous strains
- Describe the safety profile of both vaccines

PHASE 3 SUMMARY: PRIMARY ENDPOINT MET

- Primary **immunogenicity** endpoint met on all homologous strains assessed with egg-adapted HAI antibody responses
  - GMT ratio and seroconversion difference success criteria met for non-inferiority
- NanoFlu: **24—66%** higher **wild-type** HAI antibody responses vs Fluzone quadrivalent against 4 homologous strains
- NanoFlu: **34—46%** higher **wild-type** HAI antibody responses vs Fluzone quadrivalent against 6 A/H3N2 drift strains
- Wild-type microneutralization antibody responses confirmed wild-type HAI antibody responses

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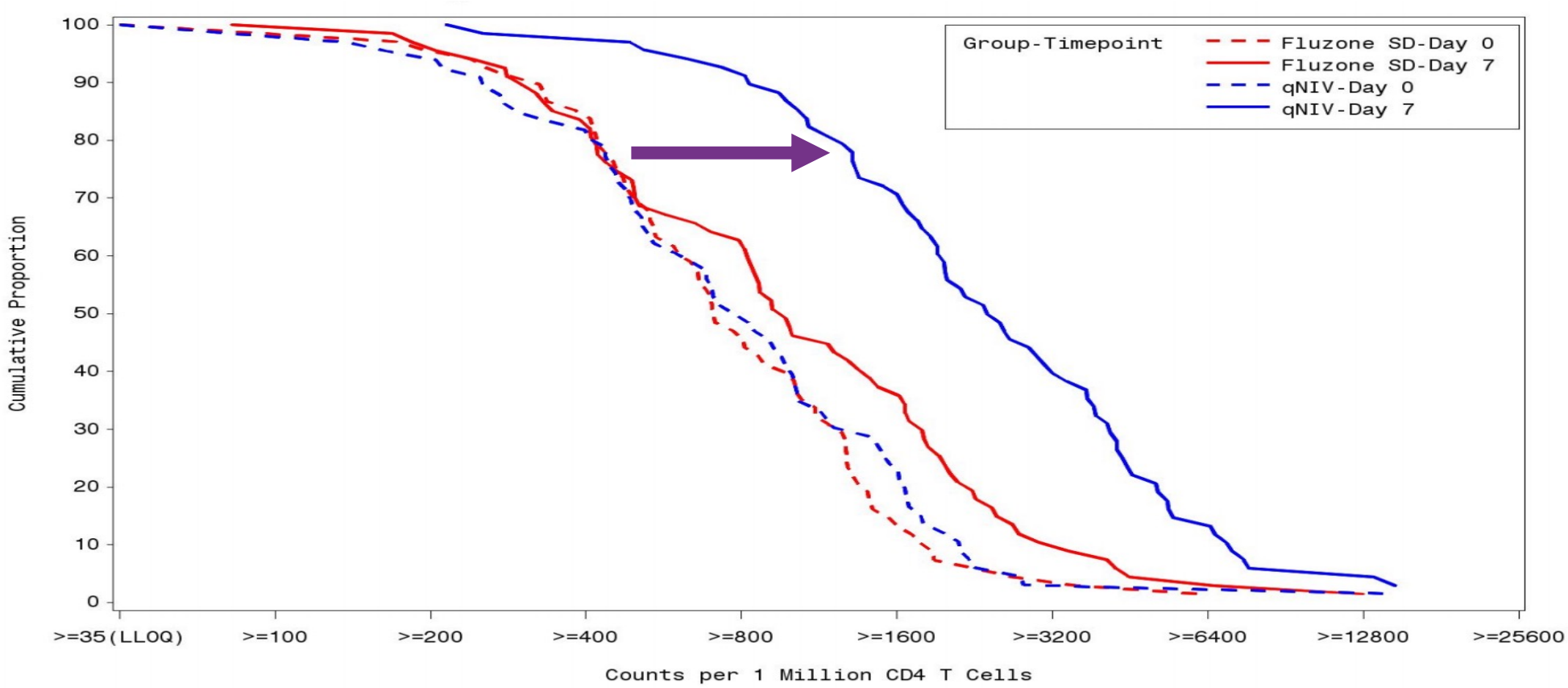
Shinde et al. Lancet ID. 2021. DOI: 10.1016/S1473-3099(21)00192-4

PHASE 3 CMI: POTENT INDUCTION OF POLYFUNCTIONAL CD4+ T CELL RESPONSES

RCD plot of Day 0 and 7 counts of double cytokine+ effector CD4+ T cells against A/Kansas (H3N2)

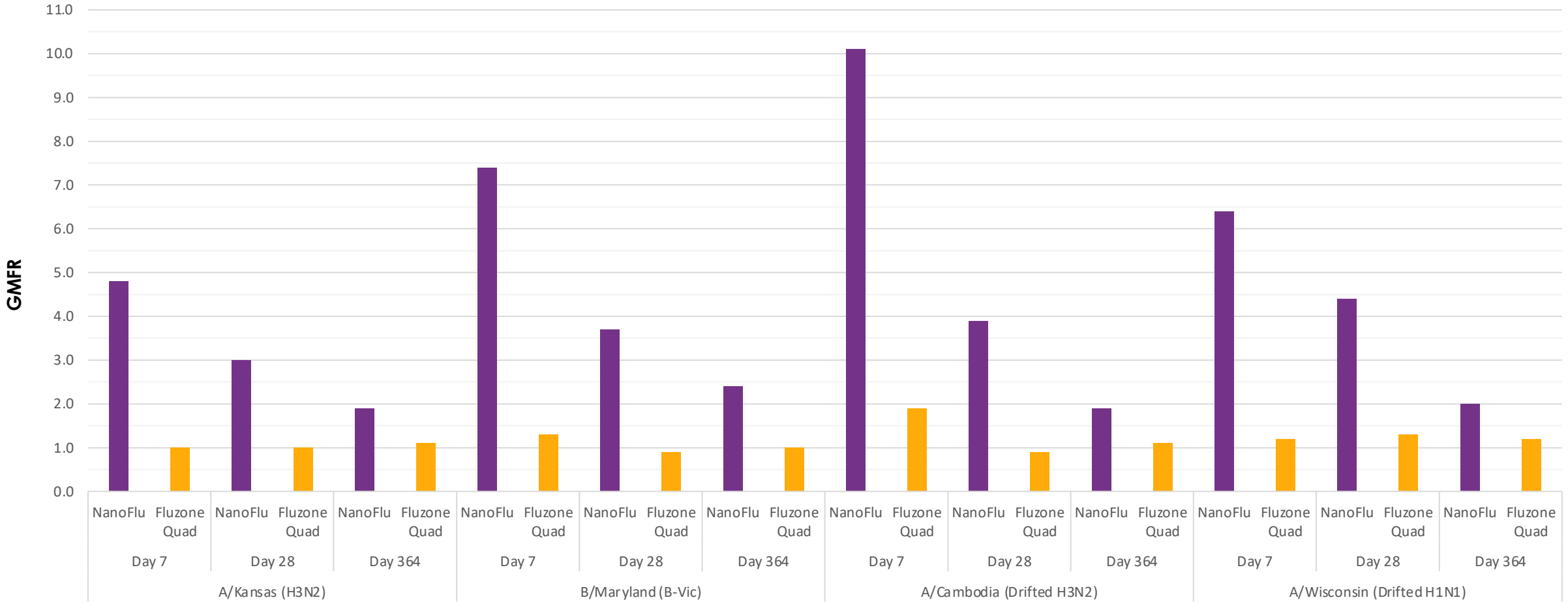


- qNIV **right shifted** distribution
- Virtually all qNIV participants became "**CMI responders**," including those with low baseline
- Similar pattern of CMI responses seen for triple and quadruple cytokine+ responses, and against B/Maryland (B-Vic)

Shinde et al. Lancet ID. 2021. DOI: 10.1016/S1473-3099(21)00192-4

PHASE 3 CMI: KINETICS OF EFFECTOR CD4+ T CELL RESPONSES OVER 1 YEAR

Day 7, 28, 364 geometric mean fold rise (GMFRs) relative to Day 0, of double cytokine+ effector CD4+ T cells against A/Kansas (H3N2), B/Marylan(B-Vic), A/Cambodia (drifted H3N2), or A/Wisconsin (drifted H1N1)



qNIV induced **higher fold-rises** of CD4+ T cells as compared to Fluzone against **homologous and drifted strains** and these responses **remained elevated at 1 year**

Fluzone (Sanofi Pasteur Limited / Sanofi Pasteur Limitée)

PHASE 3: SUMMARY AND CONCLUSIONS

Primary endpoint met:

- **Demonstrated immunologic non-inferiority** to Fluzone Quad (egg-adapted HAI antibody responses)

Statistically significant higher wild-type HAI antibody responses compared to Fluzone Quadrivalent:

- 24—66% improved Day 28 GMTs against **homologous strains**
- 34—46% improved Day 28 GMTs against multiple **drifted A/H3N2 strains**

Wild-type neutralizing antibody responses corroborated wild-type HAI antibody responses, including against drift strains

Potent induction of polyfunctional CD4+ T-cell responses, with persistence one year later

- Virtually all NanoFlu subjects became "CMI responders", including, notably, those with low baseline CMI

COVID-INFLUENZA COMBINATION (CIC) VACCINE DEVELOPMENT

RATIONALE FOR A COVID-INFLUENZA COMBINATION VACCINE

RECURRENT BOOSTERS OF A SARS-COV-2 VACCINE MAY BE NEEDED IN FUTURE

- Ongoing potential for **emergence of variants** escaping natural/vaccine immunity
- Continued **SARS-CoV-2 circulation**, potentially in a **seasonally recurrent** pattern
- **Waning of neutralizing antibody responses** in the 4 to 12 months following vaccination or infection

THERE IS AN ONGOING NEED FOR ANNUAL SEASONAL INFLUENZA VACCINATION

- Despite little influenza transmission during the COVID-19 pandemic in 2020 and 2021, **influenza transmission likely to rebound in 2022** and beyond with reopening of society
- Continued **urgent public health need** to develop **more effective** seasonal influenza vaccines

ADDRESS TWO MAJOR PUBLIC HEALTH PROBLEMS WITH ONE POTENTIAL VACCINE SOLUTION

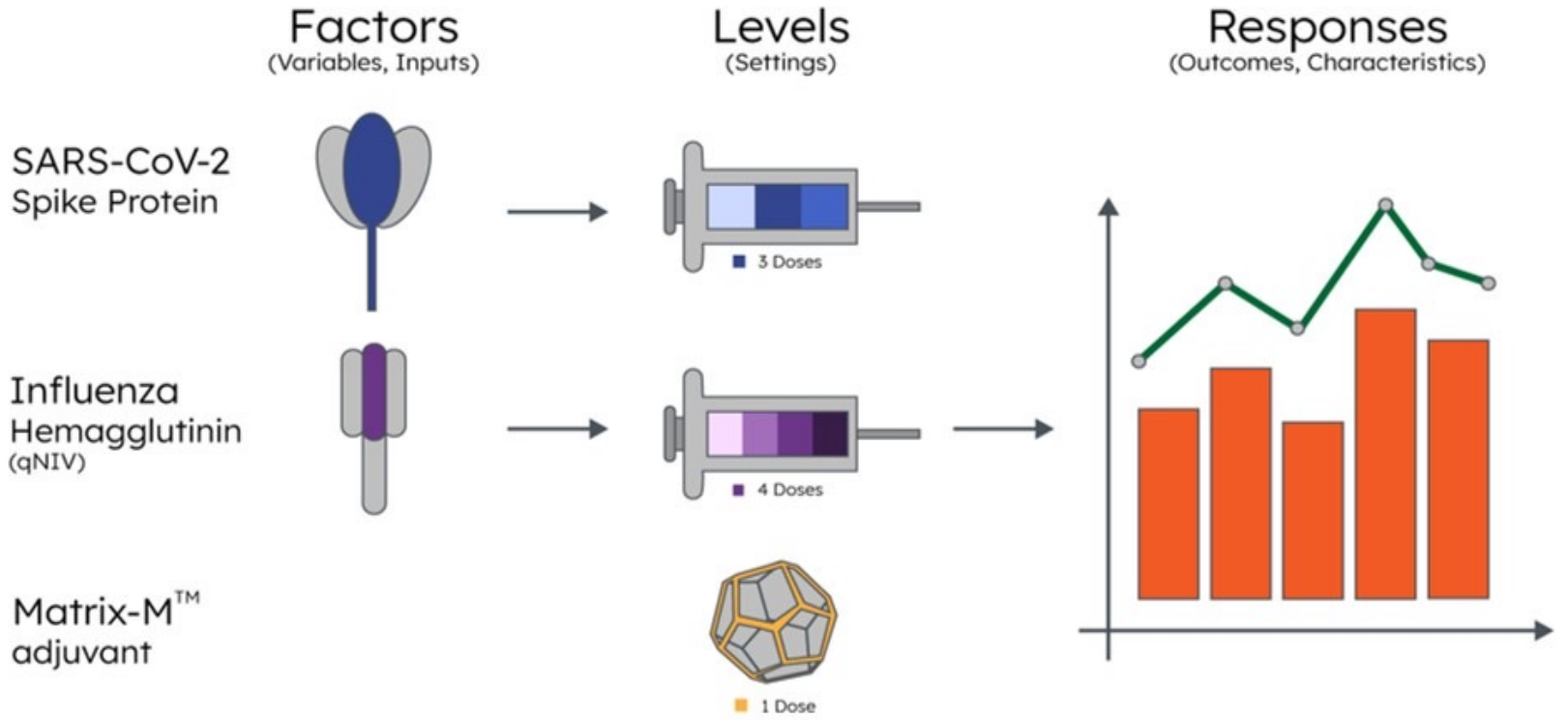
Development of **combination vaccine anticipates future need** to annually immunize against both SARS-CoV-2 and influenza virus in advance of the winter transmission season

A NOVEL DOSE FINDING STUDY DESIGN USING A DESIGN OF EXPERIMENTS (DoE) APPROACH

Phase I/II Study

The study will evaluate **dose ranges** for both **Spike** and **Hemagglutinin** antigens, using a **Design of experiments (DoE)** approach with **14 treatments groups**

Key **antibody** and **cell-mediated immunity responses** will be used to select one or more doses to advance into further development



Control Groups			
	NanoFlu Only	rHA 60µg	75µg
	NVX-CoV2373 Only	rS 5µg	50µg

Participants are administered the reference formulation of a single vaccine, at the dose level evaluated in previous Phase III trials

NOVEL DOSE FINDING STUDY DESIGN USING A DESIGN OF EXPERIMENTS (DOE) APPROACH

Phase I/II Study

OBJECTIVES

- Assess **safety and reactogenicity** of various COVID-19 Influenza combination (CIC) vaccine formulations
- Assess **immunogenicity** of various CIC formulations
- Optimize HA and rS **dose selection** for combo vaccine

DESIGN

- **640** adults aged **50 – 70 years**, **seropositive** by infection or vaccination ≥ 8 week prior
- **2 doses** of various CIC formulations, **56 days apart**
  - **rS dose range** 2.5-22.5 µg/dose
  - **HA dose range** 5-60 µg/strain/dose
  - **Matrix-M adjuvant dose**: 50 µg/dose
- Safety and reactogenicity: through Day **70** and 182
- Immunogenicity (Anti-S IgG and HAI): Day **0, 28**, 56, 70
- Cell mediated immune (CMI) responses: Day 0, 7, 63

Study Design							
Vaccine Group	N	Day 0			Day 56 (± 4 days)		
		HA Dose per Strain, µg	rS, µg	Matrix-M, µg	HA Dose per Strain, µg	rS, µg	Matrix-M, µg
ICC vaccine formulations							
A	40	60	22.5	50	60	22.5	50
B	40	10	7.5	50	10	7.5	50
C	40	60	22.5	50	60	22.5	50
D	40	10	7.5	50	10	7.5	50
E	40	10	22.5	50	10	22.5	50
F	40	35	7.5	50	35	7.5	50
G	40	5	22.5	50	5	22.5	50
H	40	60	2.5	50	60	2.5	50
I	40	5	7.5	50	5	7.5	50
J	40	5	2.5	50	5	2.5	50
K	40	35	22.5	50	35	22.5	50
L	40	35	2.5	50	35	2.5	50
M	40	60	7.5	50	60	7.5	50
N	40	60	2.5	50	60	2.5	50
qNIV with Matrix-M adjuvant reference formulation							
O[1]	40	60	0	75	0	5	50
SARS-CoV-2 rS with Matrix-M adjuvant reference							
P	40	0	5	50	0	5	50
Total	**640**						

Note: [1] Participants from treatment Vaccine Group O will receive an additional dose of 5µg SARS-CoV-2 rS with 50µg Matrix-M1 at Day 70; HA = hemagglutinin; rS = recombinant spike protein; qNIV = quadrivalent hemagglutinin nanoparticle influenza vaccine

PRELIMINARY RESULTS OF PHASE 1/2 CIC VACCINE TRIAL

BASELINE CHARACTERISTICS, REACTOGENICITY AND SAFETY RESULTS

Treatment groups were comparable at baseline

- Median age **59 years**
- 62% male / 38% female
- **100%** had received **prior primary series** EUA COVID-19 vaccine; **median 10.7 weeks prior** to Day 0
- ~0.2% had been previously infected with SARS-CoV-2

CIC formulations were well tolerated with:

- **Comparable** reactogenicity **to standalone reference** rS (NVX-CoV2373) and HA (qNIV) formulations
- Most common solicited **local** AEs were pain and tenderness
- Most common solicited **systemic** AEs were fatigue, headache, malaise, muscle pain; fever was rare
- **Generally Grade 0, 1 or 2**. Grade 3 rare. No Grade 4.
- Solicited local and systemic AEs **did not vary** substantially **by rS dose** level
- Slightly higher solicited local AEs by increasing HA dose level
- Comparable reactogenicity between dose 1 and dose 2

Safety through Day 70:

- CIC formulations demonstrated **comparable** rates of unsolicited AEs **to standalone reference** rS and HA formulations
- Severe unsolicited AEs were rare; and none assessed as related to vaccine
- Serious AEs (SAEs) were rare; and none assessed as related to vaccine
- No reports of adverse event of special interest (AESIs)

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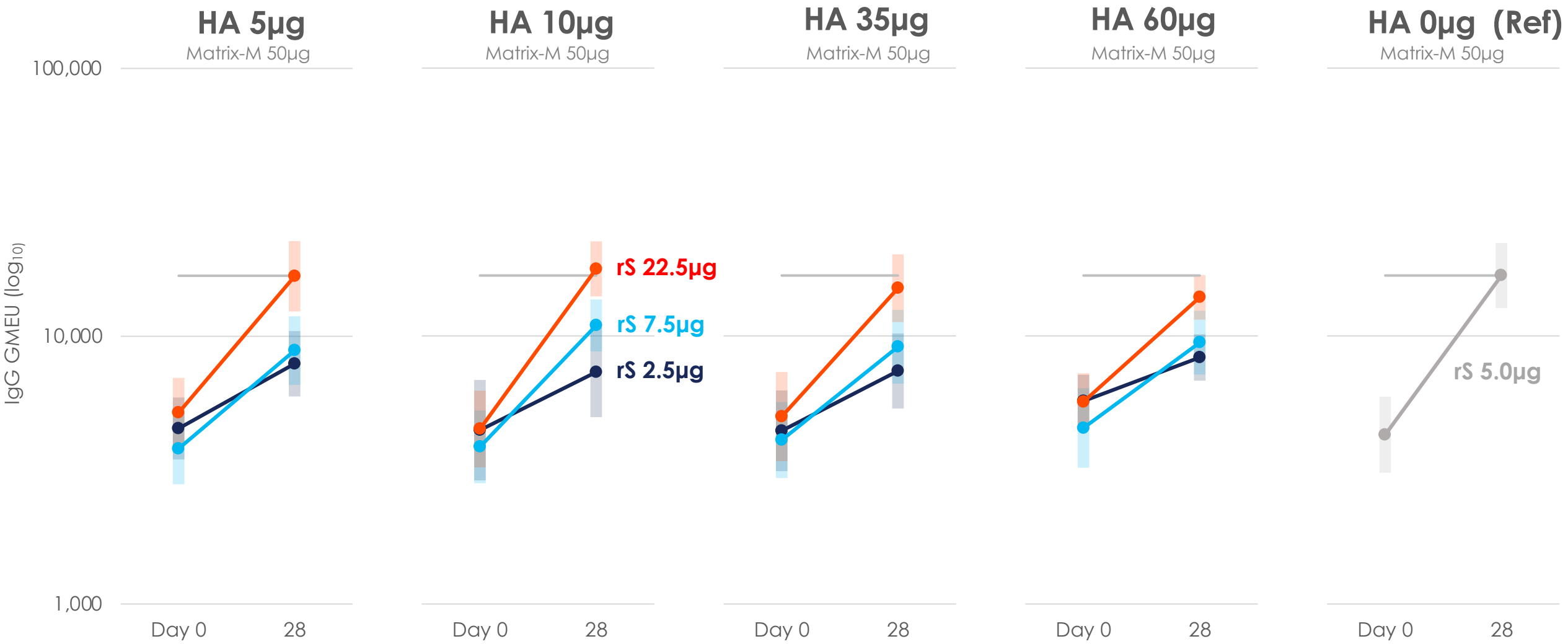
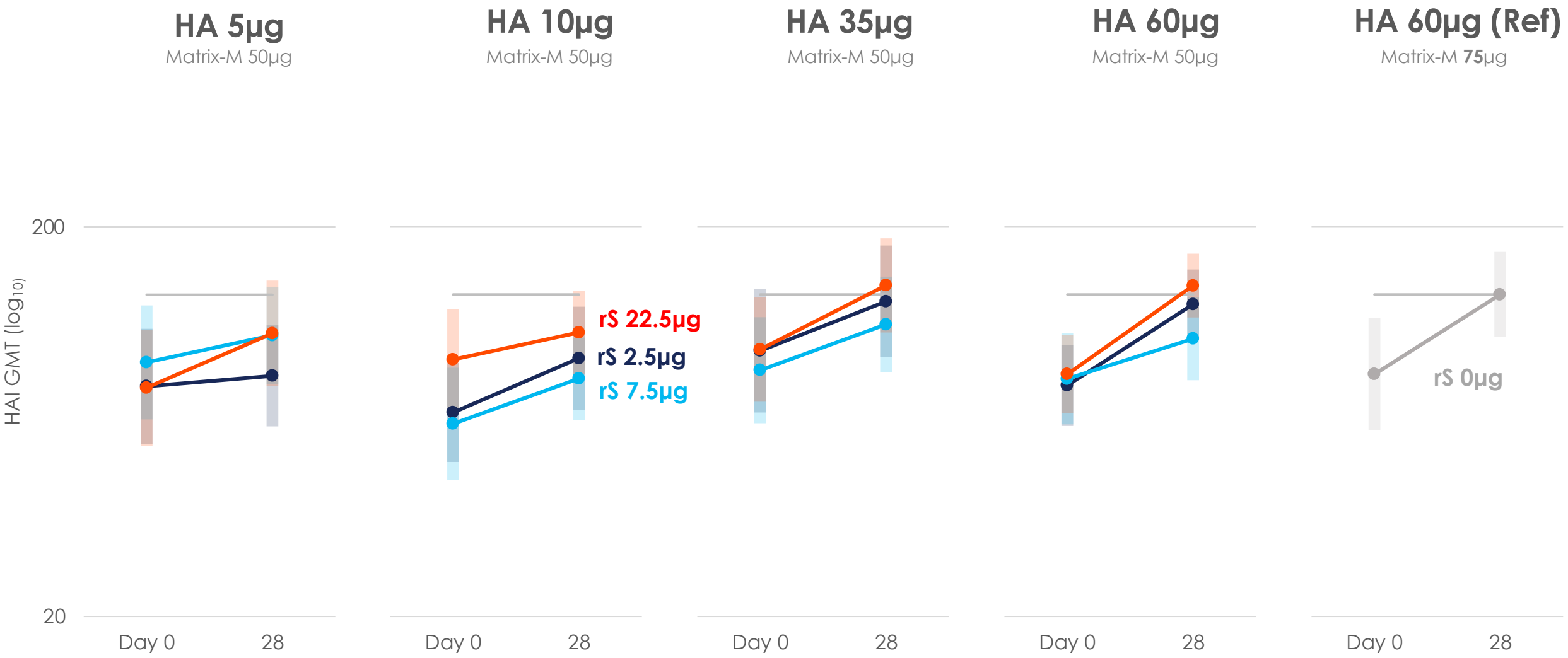
ANTI-S IgG DOSE RESPONSE WITH INCREASING rS DOSE ACROSS ALL LEVELS OF HA DOSE

Anti-Spike IgG antibody geometric mean ELISA units (GMEU) by dose and visit



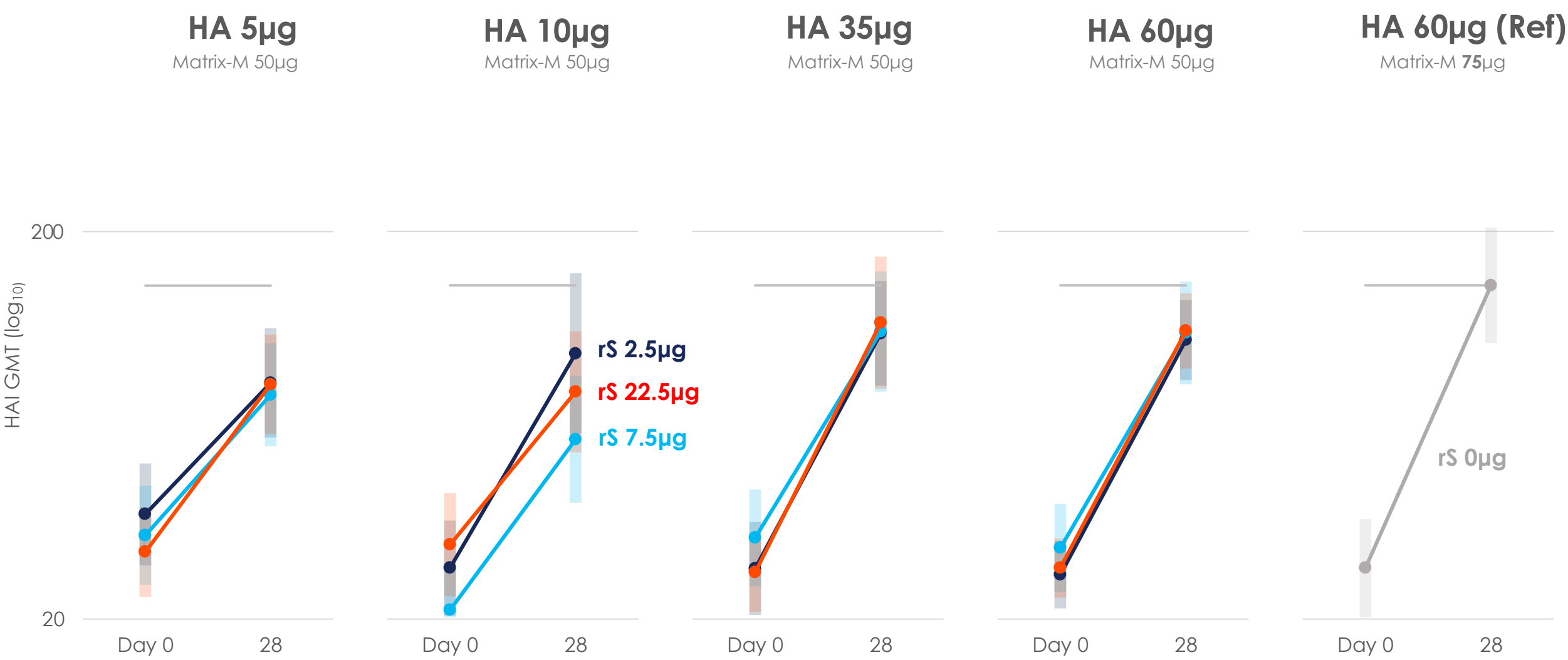
PEAK INFLUENZA HAI ANTIBODY DOSE RESPONSE WITH INTERMEDIATE LEVELS OF HA DOSE

Hemagglutination inhibition (HAI) antibody geometric mean titers (GMT) by dose and visit – A/Brisbane H1N1



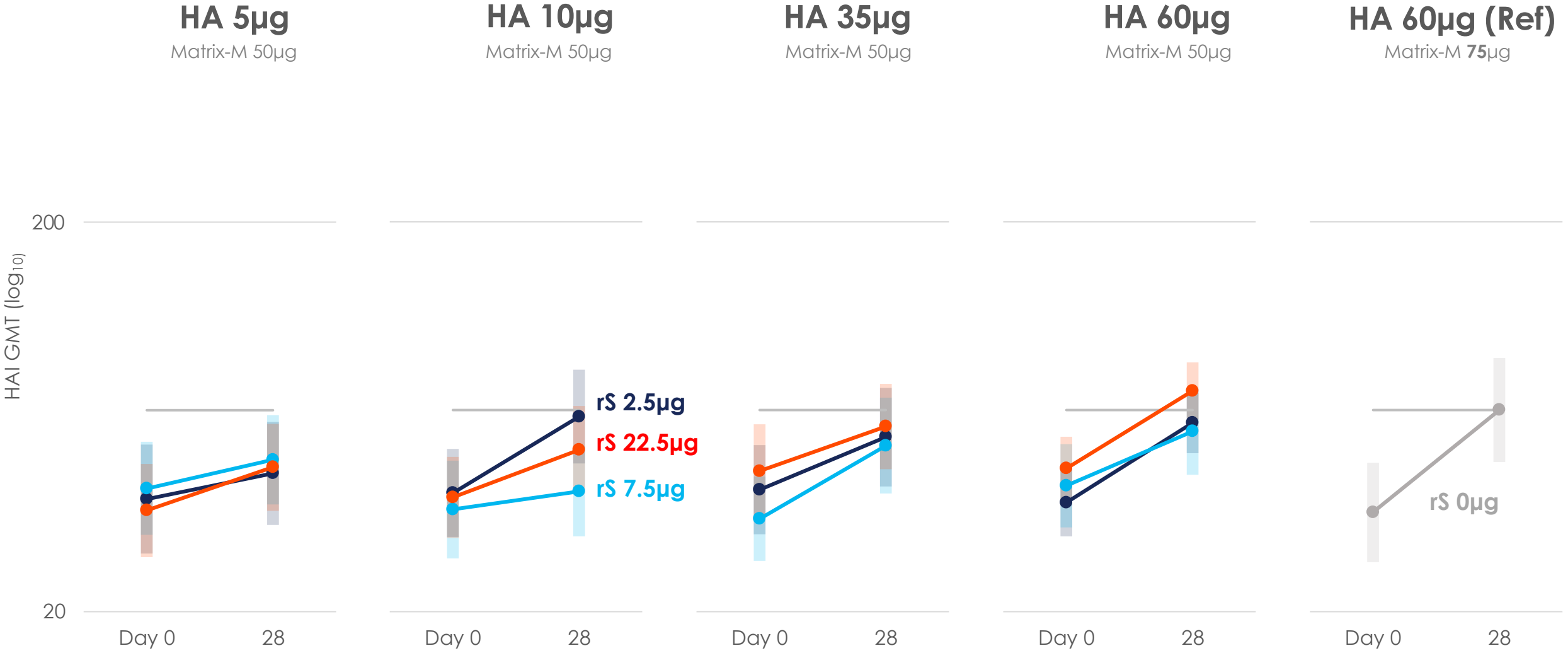
PEAK INFLUENZA HAI ANTIBODY DOSE RESPONSE WITH INTERMEDIATE LEVELS OF HA DOSE

Hemagglutination inhibition (HAI) antibody geometric mean titers (GMT) by dose and visit – A/Kansas H3N2



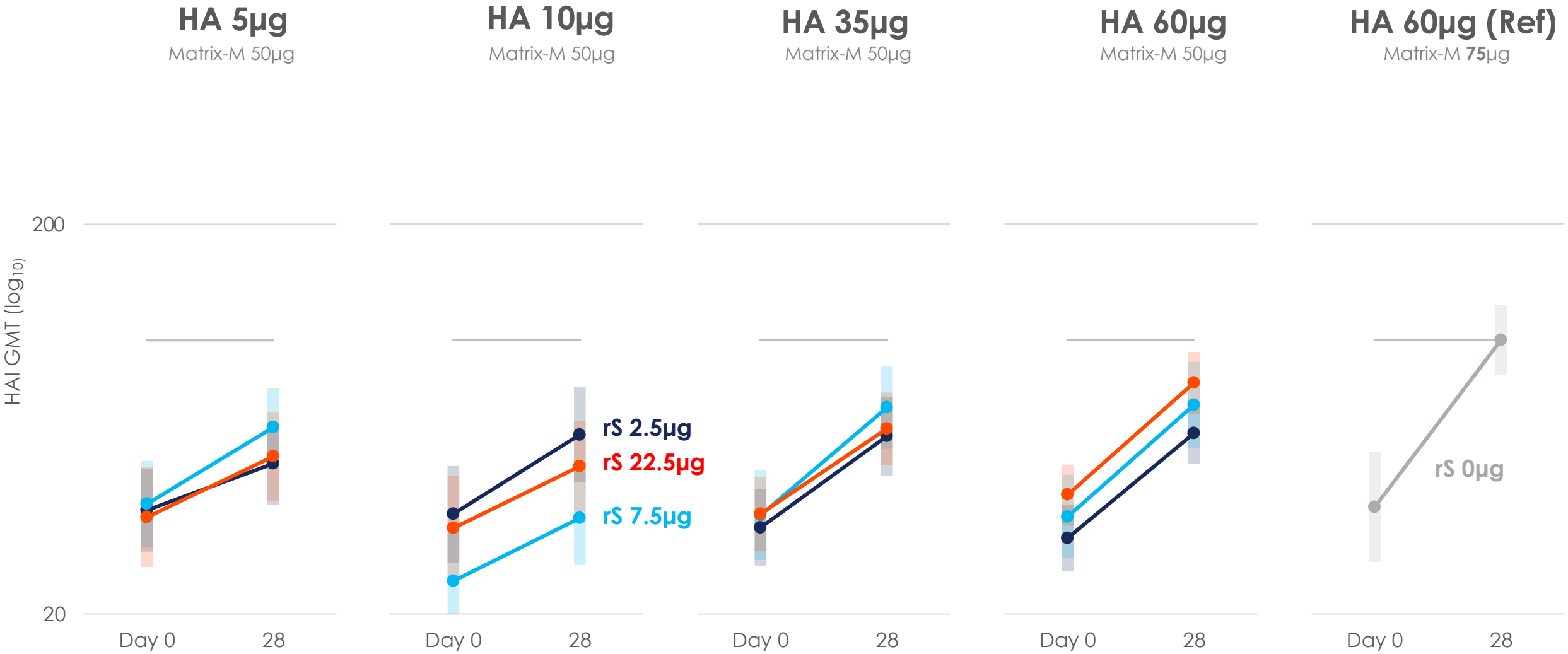
PEAK INFLUENZA HAI ANTIBODY DOSE RESPONSE WITH INCREASING LEVELS OF HA DOSE

Hemagglutination inhibition (HAI) antibody geometric mean titers (GMT) by dose and visit – B/Maryland (Vic)



PEAK INFLUENZA HAI ANTIBODY DOSE RESPONSE WITH INTERMEDIATE LEVELS OF HA DOSE

Hemagglutination inhibition (HAI) antibody geometric mean titers (GMT) by dose and visit – B/Phuket (Yam)



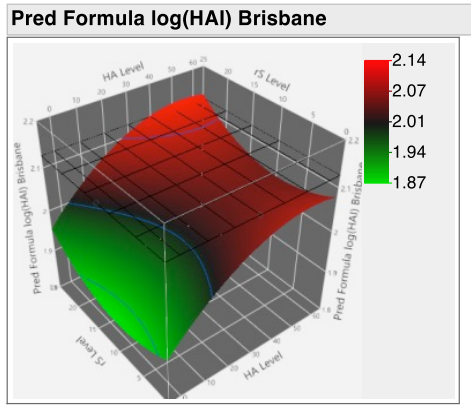
MODELING CAN PREDICT AN OPTIMAL DOSE OF rS AND HA

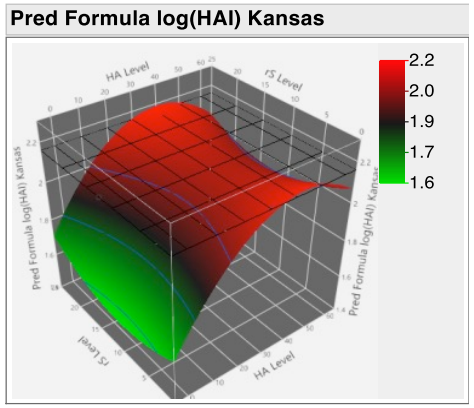
Design of experiments (DoE) response surface modeling methods

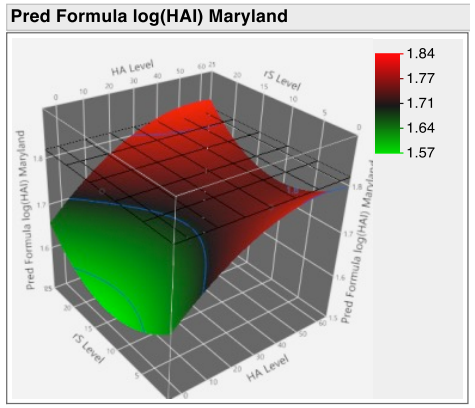
3 separate multiple **regression modeling approaches** were employed. Each approach:

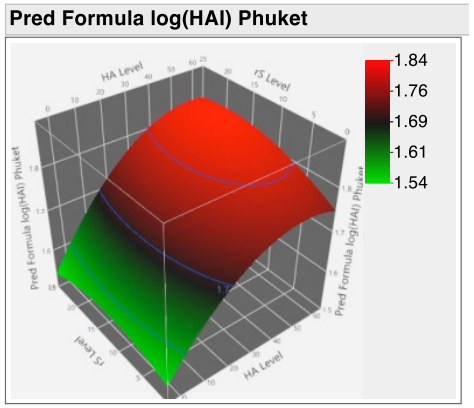
- Constructed **5 separate second order models** (ie, main rS and HA dose effects, quadratic of rS and HA dose, and interaction terms)
  - **One model each** for the Day 28 (post-first dose) **antibody response to each strain**: SARS-CoV-2 IgG and each of the 4 homologous flu strain HAI responses
- Considered different **covariates**: age, sex, BMI, baseline IgG or HAI, time since EUA COVID-19 vaccine, and EUA vaccine brand
- Produced an **antibody response "surface"** for each antibody measure**;** imagine a 3-D shape, could be a hill, a valley, a saddle, etc.
- Used **different methods for dose optimization**, which involved **simultaneously varying the rS and HA dose** values and observing where that puts us on each of the 5 antibody response surfaces, **to find an optimal dose level of rS and HA** that **maximize antibody responses to each antigen** and matches reference standalone vaccine responses (red region)

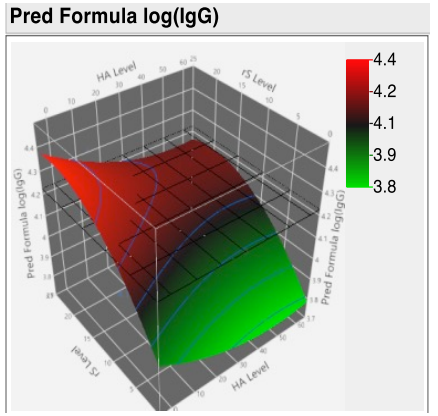
Multiple combinations of HA and rS dose levels that represents an **optimal** or desirable formulation can be considered for further development











MODELING CAN PREDICT AN OPTIMAL DOSE OF rS AND HA

Design of experiments (DoE) response surface modeling for dose optimization

- We used these models to **predict the impact of every permutation of combinations of HA dose and rS dose** on the IgG and HAI response, and then **compared the predicted responses versus reference** standalone HA and rS responses
- As an example, **selected output** is shown below for permutations of combinations of **rS 25µg with HA dose level ranging from 24-34µg** that produce optimal HAI and IgG responses comparable to the reference standalone
- Across a range of sample dose levels shown, responses closely match or exceed reference values for H1N1, H3N2, B-Vic, IgG

HA dose (µg)	rS dose (µg)	Predicted A/Bris H1N1	Reference A/Bris H1N1	Predicted A/Kans H3N2	Reference A/Kans H3N2	Predicted B/MD B-Vic	Reference B/MD B-Vic	Predicted B/Phu B-Yam	Reference B/Phu B-Yam	Predicted IgG	Reference IgG
24	**25**	126.7	133.9	134.2	145.1	62.4	65.8	61.7	100.8	15,778	16,818
25	**25**	127.5	133.9	136.5	145.1	62.8	65.8	62.3	100.8	15,693	16,818
26	**25**	128.3	133.9	138.7	145.1	63.2	65.8	62.8	100.8	15,606	16,818
27	**25**	129.1	133.9	140.8	145.1	63.6	65.8	63.3	100.8	15,518	16,818
28	**25**	129.8	133.9	142.7	145.1	64.0	65.8	63.9	100.8	15,428	16,818
29	**25**	130.6	133.9	144.6	145.1	64.4	65.8	64.4	100.8	15,337	16,818
30	**25**	131.3	133.9	146.3	145.1	64.7	65.8	64.9	100.8	15,244	16,818
31	**25**	132.0	133.9	147.9	145.1	65.1	65.8	65.4	100.8	15,150	16,818
32	**25**	132.7	133.9	149.3	145.1	65.4	65.8	65.9	100.8	15,055	16,818
33	**25**	133.4	133.9	150.6	145.1	65.8	65.8	66.3	100.8	14,958	16,818
34	**25**	134.0	133.9	151.7	145.1	66.1	65.8	66.8	100.8	14,859	16,818

USING MODELING TO PREDICT AN OPTIMAL DOSE OF rS AND HA

Design of experiments (DoE) response surface modeling for dose optimization

The **3 different modeling approaches broadly converged** on a similar set of results with regards to optimal dose combinations, increasing the **robustness of the overall interpretation** and conclusions:

- Both rS and HA antigens as a combined formulation **modestly interfere** with each other, **however, interference can be overcome with dose adjustment**
- **Higher rS** dose levels (>20µg) can **overcome the interference of HA** dose, and can **match** (standalone) **reference** rS vaccine responses
- **Intermediate dose levels of HA** (24-40µg per strain) can **overcome the interference of rS** dose, and can **match** (standalone) **reference** HA responses for H3N2, H1N1, B-Vic strains; but modestly lower for B-Yam strain

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PRELIMINARY FINDINGS AND NEXT STEPS

- The **first study** to demonstrate that a **COVID-Influenza combination vaccine** is **feasible, well-tolerated, and immunogenic**, and these data warrant continued development

- A **novel DoE modeling**-based approach to dose finding/optimization is a **powerful tool** that may allow:
  - Granular resolution of immune responses across a response surface, and
  - Fine-tuned dose selection

- **Various CIC formulations** may **induce antibody responses comparable** to the **standalone** qNIV and COVID-19 vaccine formulations (for H1N1, H3N2, B-Vic, and rS)
  - Higher rS dose needed in CIC than standalone rS
  - Lower dose of HA needed in CIC than standalone HA
  - Implies up to **50% reduction in total antigen** content in the CIC formulation compared to the sum of standalone rS and HA components – potentially dose sparing

PRELIMINARY FINDINGS AND NEXT STEPS

- This study evaluated **CIC formulations with 50µg of Matrix-M** adjuvant, which was **lower than the 75µg Matrix-M** previously used in the **standalone** qNIV
  - A higher Matrix-M adjuvant dose of 75µg in CIC might further enhance antibody responses, and lead to further dose sparing. To be evaluated in future trial.

- **Additional immunogenicity data are expected** on microneutralization antibody and CMI responses, as well as 2nd dose and durability of antibody responses

- Data from this study will inform a **planned Phase 2** dose confirmation study which will:
  - Confirm the combination vaccine dose/formulation
  - Assess lower doses of standalone qNIV

THANK YOU

CONTRIBUTORS

VIVEK SHINDE, WAYNE WOO, SHARON LIU, SUSAN NEAL, JOYCE PLESTED, TIM VINCENT, MINGZHU ZHU, SHANE CLONEY-CLARK, IKSUNG CHO, LOU FRIES, FILIP DUBOVSKY, GREG GLENN

BACKUPS

Matrix-M™ Adjuvant Production Process

Saponins, from the *Quillaja saponaria* tree, help generate a robust immune response

1 Trees are pruned and bark is harvested

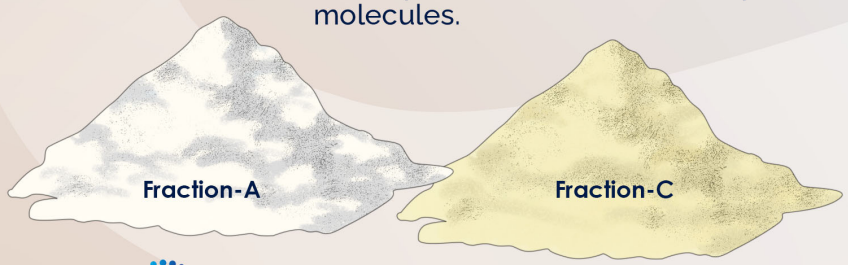
Saponins are found in the tree's bark. Bark is harvested sustainably, without felling the whole tree.

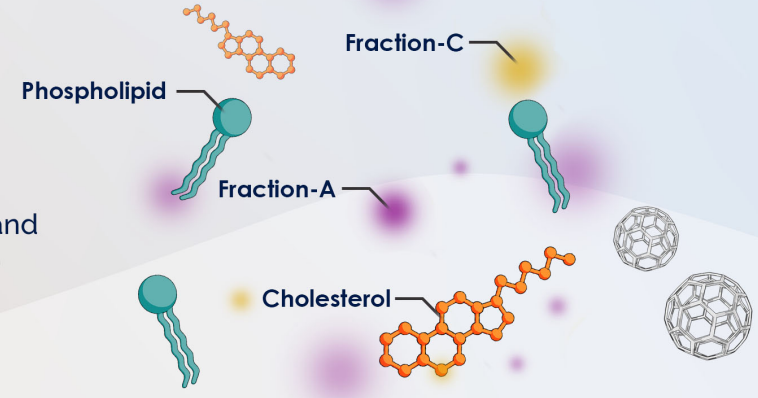
Quillaja saponaria bark

Quillaja saponaria (Soapbark) tree

2 Bark is processed

Bark extract is processed into Fraction-A and Fraction-C, then freeze-dried (lyophilized). These powders contain "raw" saponin molecules.



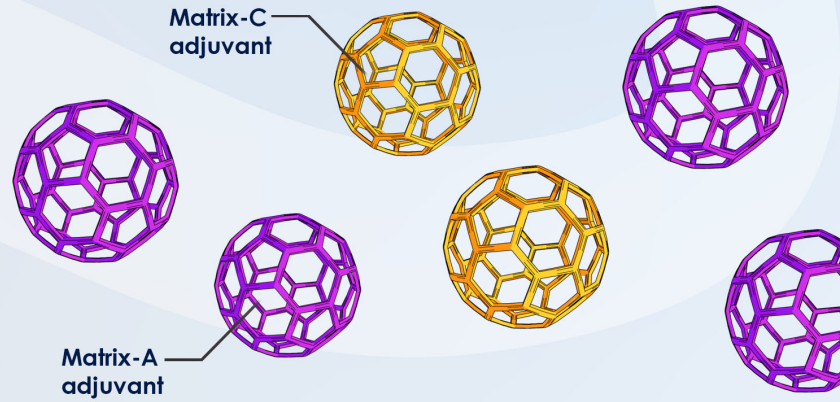


3 Liquid formulation prepared

Fraction-A and Fraction-C, as liquids, are formulated with phospholipids and cholesterol, producing distinctive nanostructures.

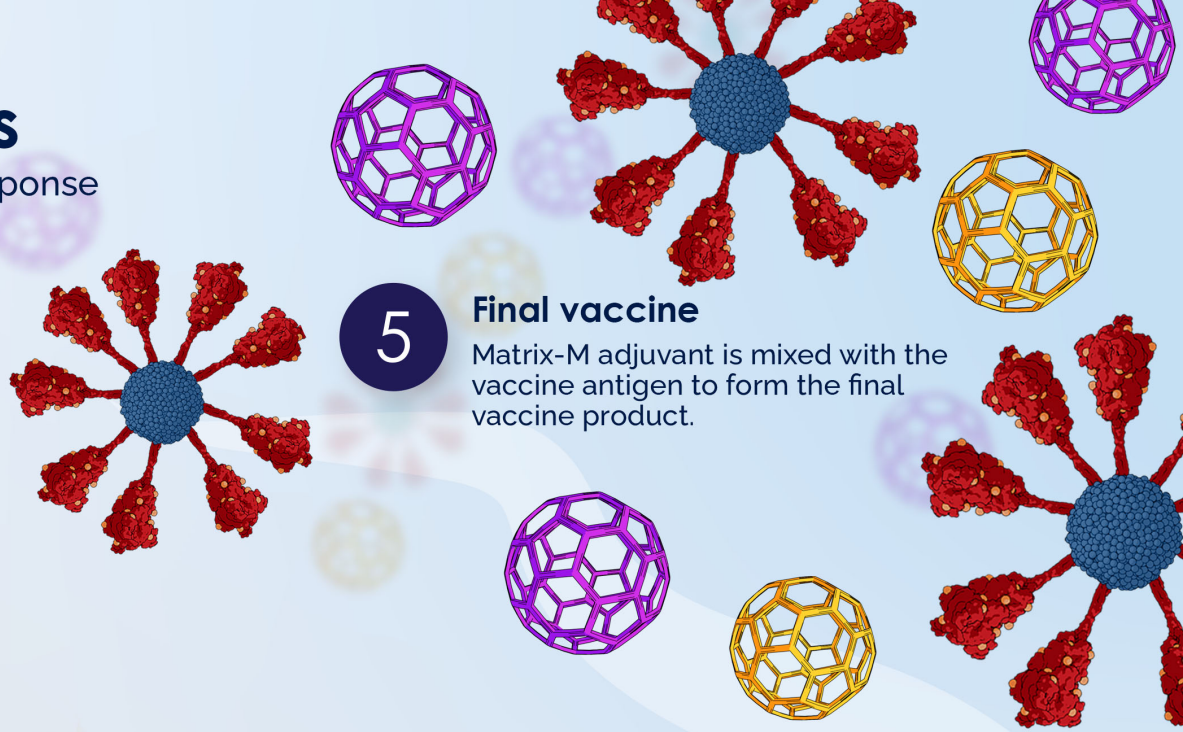
4 Matrix-M adjuvant formation

Matrix-A and Matrix-C components are mixed to form Matrix-M adjuvant.



5 Final vaccine

Matrix-M adjuvant is mixed with the vaccine antigen to form the final vaccine product.



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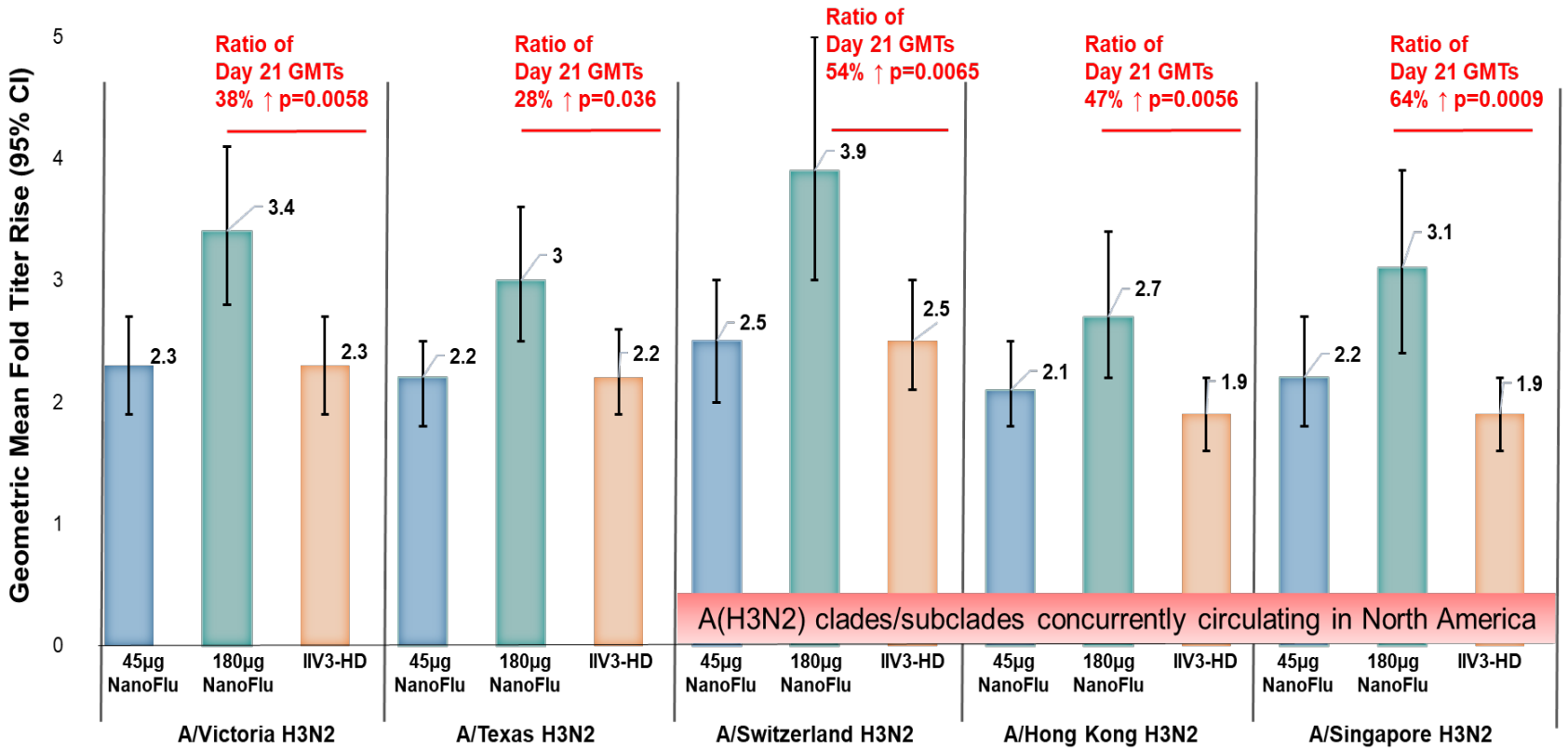
PHASE 1: NanoFlu (tNIV) INDUCED HIGHER WILD-TYPE HAI ANTIBODY RESPONSES (GMFRs) VS. FLUZONE-HIGH DOSE (IIV3-HD) AGAINST 5 GENERATIONS OF ANTIGENICALLY DRIFTED A(H3N2) STRAINS



Phase 1 design:
330 US adults aged ≥60 years
Randomized 1:1:1

- tNIV: 15µg each HA (45µg total) + 50µg Matrix-M, or
- tNIV: 60µg each HA (180µg total) + 50µg Matrix-M, or
- Fluzone High Dose: 60µg each HA (180µg total)

Objectives/endpoints:

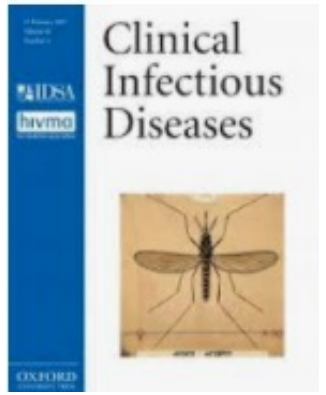
- Day 21 wild-type HAI antibody responses against homologous and drift strains
- Safety profile through 1 year

Shinde et al. NEJM 2018. DOI: 10.1056/NEJMc1803554

Fluzone (Sanofi Pasteur Limited / Sanofi Pasteur Limitée)

PHASE 2: SUMMARY

- Demonstration of an "**adjuvant effect**"
  - Matrix-M adjuvant resulted in significant enhancement of immune responses when compared to unadjuvanted formulation
- **Higher** wild-type HAI antibody responses against **homologous A/H3N2 and drifted A/H3N2 strains** as compared to Fluzone HD
- **Similar** wild-type HAI antibody responses against **homologous and drifted strains** as compared to Flublok
- **Potent** induction of **polyfunctional CD4+ T cell responses**, which were higher than both Fluzone HD and Flublok
- **Well-tolerated**, with acceptable safety profile



Phase 2 Design:
1375 adults aged ≥65 years
Randomized to 1 of 7 groups
- NanoFlu: bedside mix
- NanoFlu: co-formulated
- NanoFlu: increased adjuvant dose (75µg Matrix-M)
- NanoFlu: increased B antigen dose
- NanoFlu: antigen only (no Matrix)
- Fluzone HD
- Flublok

Objectives/endpoints:
- Primary: demonstrate "adjuvant effect"
- Day 28 wild-type HAI antibody responses against homologous and drift strains
- Safety profile through 1 year
- Exploratory: CD4+ T cell responses

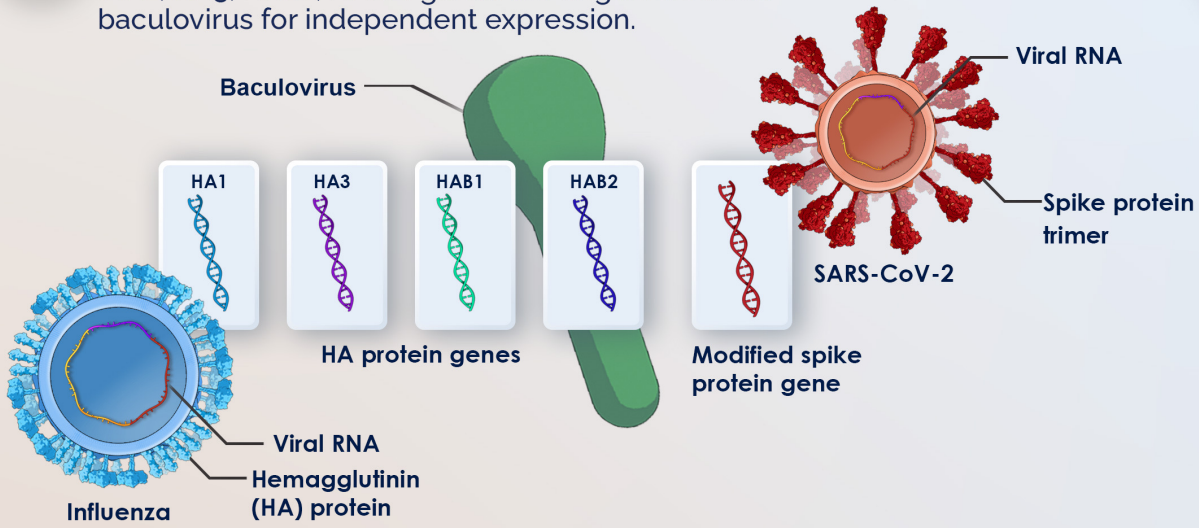
Shinde et al. Clin Infect Dis. 2020. DOI: 10.1093/cid/ciaa1673

Fluzone (Sanofi Pasteur Limited / Sanofi Pasteur Limitée); Flublok (Protein Sciences Corporation)

COVID-Influenza Combination (CIC) Investigational Vaccine Design

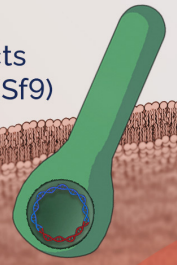
1 Genes inserted into insect virus

SARS-CoV-2 spike and four Influenza Hemagglutinin (HA1, HA3, HAB1, HAB2) genes are engineered into baculovirus for independent expression.



2 Sf9 cells infected

Recombinant baculovirus infects moth cells in the *S. frugiperda* (Sf9) expression system.



3 DNA enters Sf9 cell nucleus

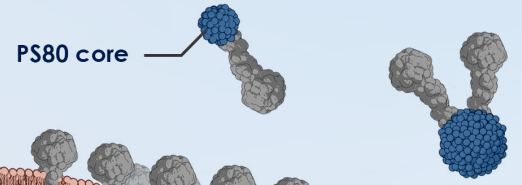
Spike and HA DNA is transcribed.

4 Sf9 cells produce proteins

Proteins are each expressed in their native conformation.

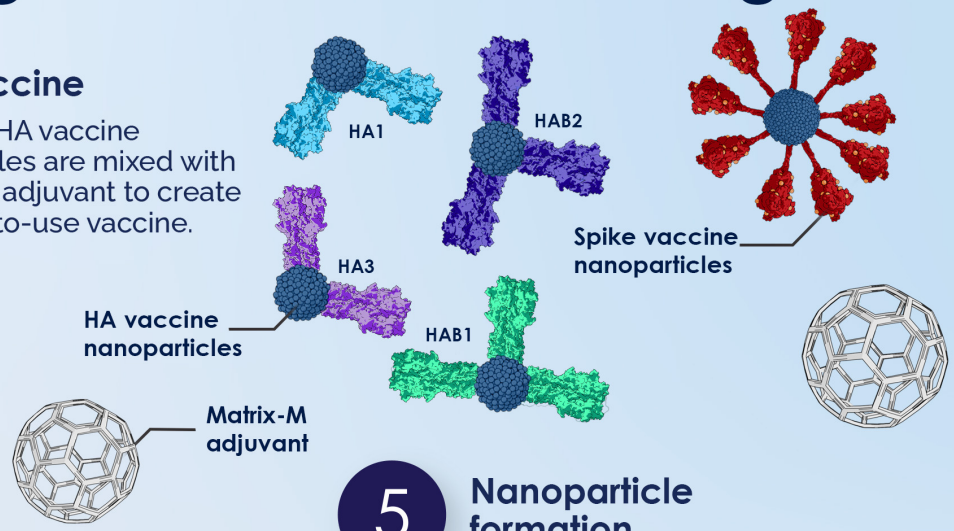
5 Nanoparticle formation

Proteins are harvested. Vaccine nanoparticles assemble as proteins arranged around a Polysorbate 80 (PS80) core.



6 Final vaccine

Spike and HA vaccine nanoparticles are mixed with Matrix-M™ adjuvant to create the ready-to-use vaccine.



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Matrix-M™ Adjuvant Mechanism of Action

1 Matrix-M-adjuvanted vaccine is injected into the muscle

Matrix-M adjuvant

NVX-CoV2373 vaccine

2 Recruitment and activation of innate immune cells

Dendritic cells

Monocytes/ Macrophages

Neutrophils

Natural killer cells

Cytokines are released

3 Rapid delivery and activation in lymph node

Skin

Muscle

4 Effective antigen presentation

Antigen presenting cell

Vaccine spike

B-cell

MHCII

TCR

CD4+ T-cell

B-cell proliferation

Cytokines

5 Long-lasting memory response

Plasma cells

Memory B-cells

High affinity antibodies

CD4+ Th2 T-cell

CD4+ Th1 T-cell

Antigen-specific effector and memory T-cells

novavax

COR-GL-ALL-0009 03/2022

Magnusson, et al., 2018. DOI: 10.1007/s12026-018-8991-x
Tian, et al., 2021. DOI: 10.1038/s41467-020-20653-8
Reimer, et al., 2012. DOI: 10.1371/journal.pone.0041451
Lövgren-Bengtsson, et al., 2016. DOI: 10.1016/j.vaccine.2016.02.033

PHASE 3 IMMUNOGENICITY: ENHANCED RESPONSES AGAINST HOMOLOGOUS AND DRIFTED A/H3N2 AND B-VICTORIA STRAINS

Day 28 wild-type HAI vs wildtype Neutralizing antibody (NanoFlu / Fluzone)

	HAI: Wild-type				Microneutralization: Wild-type			
	NanoFlu	Fluzone Quad	D28 GMT Ratio		NanoFlu	Fluzone Quad	D28 GMT Ratio	
Strain	D28 GMT	D28 GMT	(NanoFlu / Fluzone)	95% CI	D28 GMT	D28 GMT	(NanoFlu / Fluzone)	95% CI
A/Brisbane/02/2018 (H1N1) pdm09 (Homologous)	76.6	62.7	1.24	(1.17, 1.32)	797.8	719.6	1.12	(1.01, 1.25)
A/Kansas/14/2017 (H3N2) (Homologous)	153.6	90.7	1.66	(1.53, 1.79)	1244.6	694.8	1.78	(1.57, 2.03)
B/Maryland/15/2016 (Homologous)	62.8	47.2	1.32	(1.26, 1.39)	500.8	325.3	1.52	(1.40, 1.66)
B/Phuket/3073/2013 (Homologous)	118.3	78.4	1.47	(1.40, 1.55)	183.6	139.2	1.38	(1.26, 1.52)
A/California ("Drifted" H3N2; Clade 3C2a1b-131K)	115.0	80.6	1.41	(1.33, 1.50)				
A/Cardiff ("Drifted" H3N2; Clade 3C2a1b-135N)	63.9	45.4	1.34	(1.27, 1.43)				
A/Netherlands ("Drifted" H3N2; Clade 3C3a)	102.3	74.7	1.38	(1.30, 1.46)				
A/So. Aus. ("Drifted" H3N2; Clade 3C2a1b-131K)	98.1	70.4	1.36	(1.28, 1.44)	168.8	111.1	1.53	(1.31, 1.79)
A/Idaho ("Drifted" H3N2– Clade 3C3a)	202.5	136.8	1.46	(1.37, 1.56)				
A/Tokyo ("Drifted" H3N2– Clade 3C2a2)	78.0	54.5	1.39	(1.31, 1.48)				
A/Hong Kong ("Drifted" H3N2"-2019)					192.6	107.2	1.61	(1.35, 1.90)
A/Wisconsin ("Drifted" H1N1-2019)					78.3	70.3	1.11	(0.99, 1.24)
B/Washington ("Drifted B-Victoria)	88.2	71.4	1.23	(1.18, 1.28)	390.9	233.6	1.67	(1.50, 1.87)
B/Colorado (B/Maryland-like homologous strain)					185.7	142.9	1.37	(1.21, 1.55)

Shinde et al. Lancet ID. 2021. DOI: 10.1016/S1473-3099(21)00192-4

Fluzone (Sanofi Pasteur Limited / Sanofi Pasteur Limitée)

COVID-INFLUENZA COMBINATION VACCINE DEVELOPMENT

KEY MILESTONES

MAY 2021
Announced positive preclinical data*

JUNE 2021
Announced data from co-administration sub-study**

SEPTEMBER 2021
Initiated phase I/II clinical trial of COVID-NanoFlu Combination Vaccine

Clinical Proof of Concept

- UK Phase III co-administration sub-study completed
- Demonstrated viability of simultaneous COVID-19 and influenza vaccination

Preclinical Development

- Hemagglutination inhibition (HAI) and ACE2 titers were **comparable between individual and combination vaccines** (hamster and ferrets)
- Maintained **clinical and virologic protection** against experimental challenge with SARS-CoV-2 (hamster model)
- Induced antibodies against SARS-CoV-2 neutralizing epitopes common between USA-WA1 (original strain) and Beta (B.1.351) variant

Clinical Development

- Phase I/II trial in Australia initiated and fully enrolled
  - Safety, immunogenicity, and dose finding

novavax

Source: *Massare et al. 2021; DOI: 10.1101/2021.05.05.442782 ,**Toback et al. 2021; DOI: 10.1101/2021.06.09.21258556

PHASE 3 IMMUNOGENICITY: PRIMARY ENDPOINT MET ON ALL HOMOLOGOUS STRAINS

Day 28 egg-based or wild-type HAI GMTs and GMT ratios (NanoFlu / Fluzone)

Assay	Strain	NanoFlu D28 GMT	Fluzone Quad D28 GMT	D28 GMT Ratio (NanoFlu / Fluzone)	95% CI
HAI: EGG	A/Brisbane/02/2018 (H1N1) pdm09 (Homologous)	49.3	45.0	1.09	(1.03, 1.15)
	A/Kansas/14/2017 (H3N2) (Homologous)	151.5	126.8	1.19	(1.11, 1.27)
	B/Maryland/15/2016 (Vic) (Homologous)	110.7	106.3	1.03	(0.99, 1.07)
	B/Phuket/3073/2013 (Yam) (Homologous)	168.5	133.9	1.23	(1.16, 1.29)
HAI: WT	A/Brisbane/02/2018 (H1N1) pdm09 (Homologous)	76.6	62.7	1.24	(1.17, 1.32)
	A/Kansas/14/2017 (H3N2) (Homologous)	**153.6**	**90.7**	**1.66**	**(1.53, 1.79)**
	B/Maryland/15/2016 (Vic) (Homologous)	62.8	47.2	1.32	(1.26, 1.39)
	B/Phuket/3073/2013 (Yam) (Homologous)	118.3	78.4	1.47	(1.40, 1.55)

Success criteria: All 95% CI lower bounds are ≥ 0.67

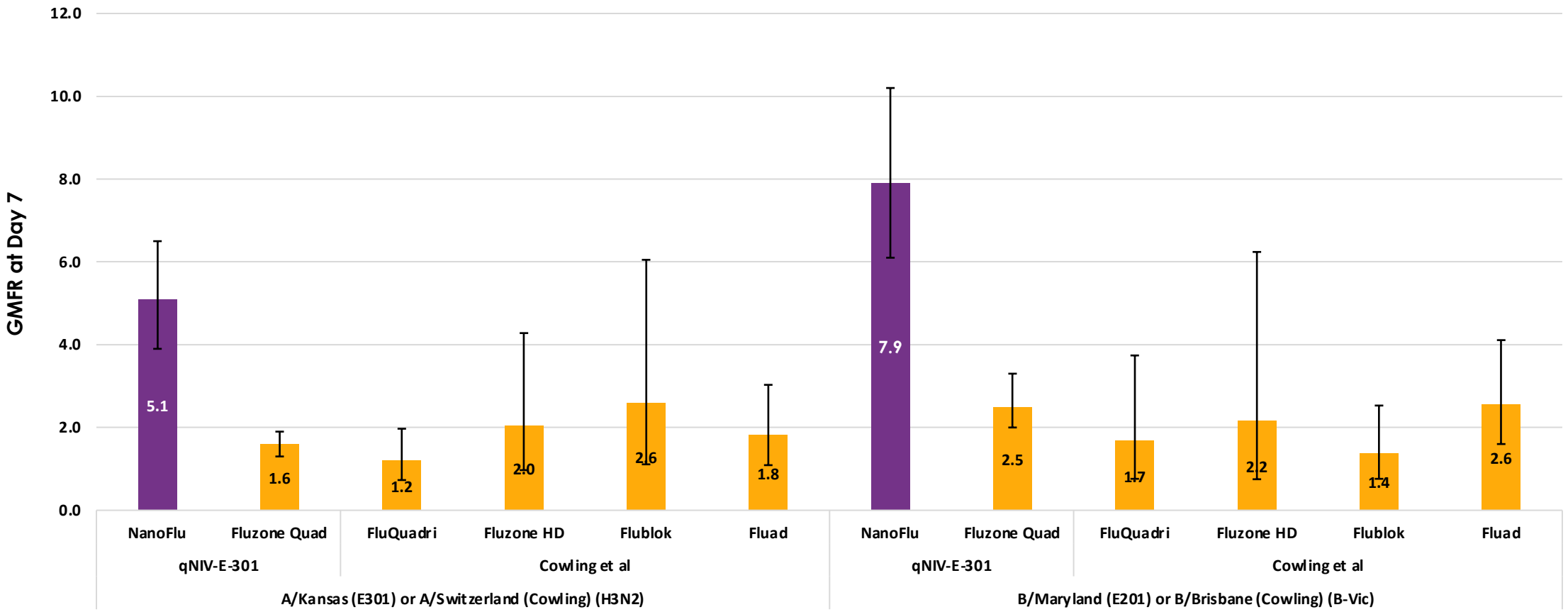
- GMT ratio success criteria met for non-inferiority
- NanoFlu: **3—23%** increased using egg-based HAI
- NanoFlu: **24—66%** increased using wild-type HAI, a more biologically and clinically relevant measure

Shinde et al. Lancet ID. 2021; DOI: 10.1016/S1473-3099(21)00192-4

Fluzone (Sanofi Pasteur Limited / Sanofi Pasteur Limitée)

PHASE 3 CMI: COMPARISON TO ENHANCED INFLUENZA VACCINES IN UNIV OF HK STUDY

Day 7 / 0 geometric mean fold rise (GMFRs) of IFN-γ cytokine+ total CD4+ T cells against A/H3N2 or B-Victoria strain



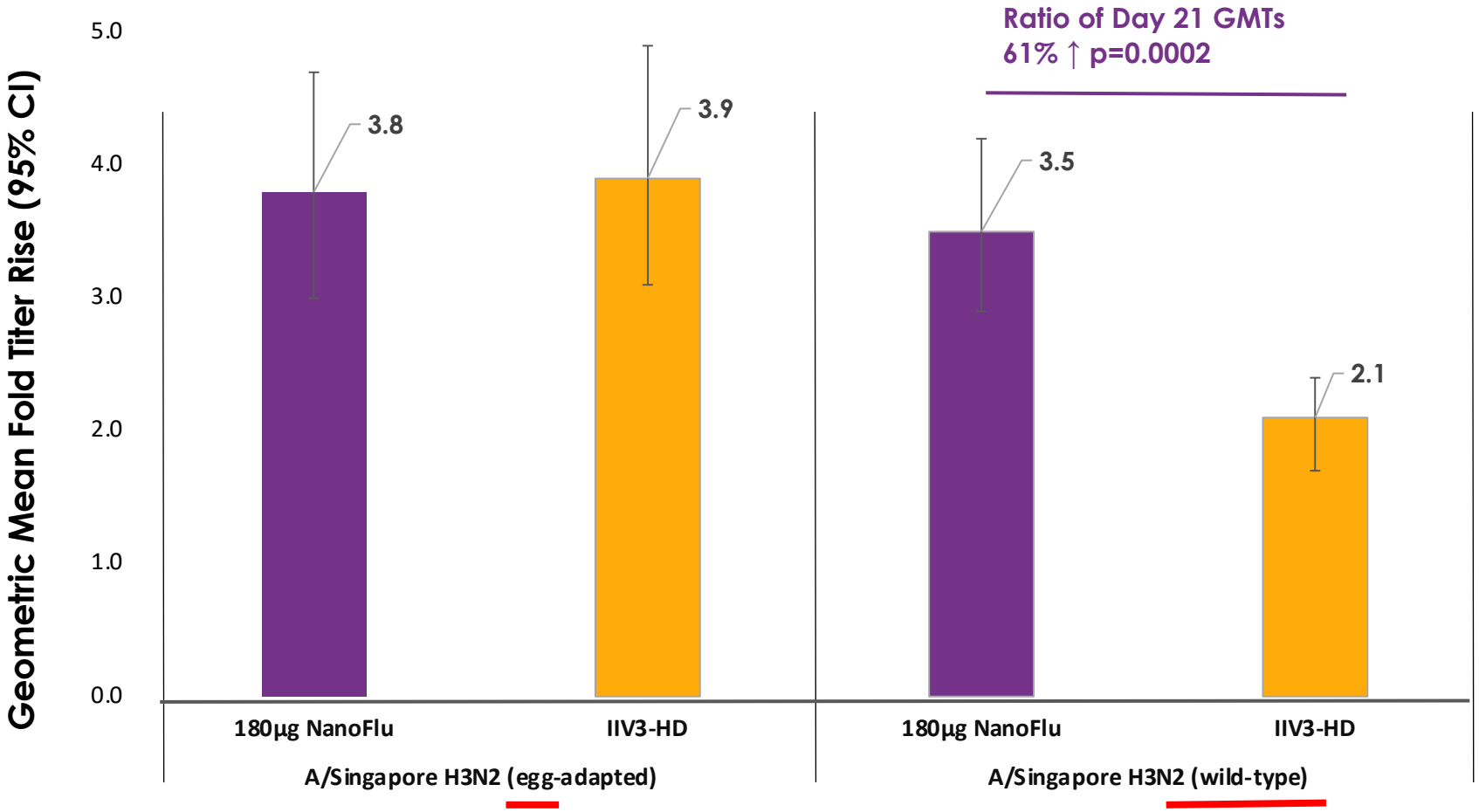
NanoFlu induced substantially higher fold-rises of IFN-γ+ CD4+ T cells as compared to Fluzone HD, Flublok, or FLUAD based on comparable literature estimates

Cowling 2019; DOI: 10.1093/cid/ciz103

Fluzone (Sanofi Pasteur Limited / Sanofi Pasteur Limitée);
Flublok (Protein Sciences Corporation)
FLUAD (Seqirus, Inc.)

PHASE 1: EGG-ADAPTED REAGENTS MAY GIVE A MISLEADING RESULT

Microneutralization antibody responses (GMFRs) against egg-adapted vs. wild-type A/Singapore A/H3N2 virus



NanoFlu induced improved neutralization responses against *wild-type* vs. egg-adapted A/Singapore H3N2 viruses underscoring the problem of egg-adaptive mutations

Neutralization antibody responses against wild-type circulating viruses are more clinically relevant

PHASE 3 SAFETY DATA THROUGH DAY 365

NanoFlu well tolerated

	Through Day 365	
	NanoFlu	**Fluzone Quad (SD)**
N	1333	1319
	Counts (%) of Subjects with Events	
Any treatment emergent adverse event (TEAE)	783 (58.7)	697 (52.8)
Any Solicited TEAE	551 (41.3)	420 (31.8)
Local solicited	372 (27.9)	243 (18.4)
Severe local solicited	8 (0.6)	2 (0.2)
Systemic Solicited	369 (27.7)	292 (22.1)
Severe systemic solicited	15 (1.1)	11 (0.8)
Unsolicited TEAE	469 (35.2)	466 (35.3)
Severe unsolicited	75 (5.6)	59 (4.5)
Severe & related unsolicited	10 (0.8)	2 (0.2)
Medically-attended unsolicited	353 (26.5)	354 (26.8)
Serious adverse events (SAEs)*	81 (6.1)	78 (5.9)

**No SAEs in either treatment group were assessed by study investigators as related to vaccine at either timepoint.*

Shinde et al. Lancet ID. 2021; DOI: 10.1016/S1473-3099(21)00192-4