ICOSAVAX

The world needs better vaccines.
We're striving to create them.

CORPORATE OVERVIEW | AUGUST 2022

Forward looking statements

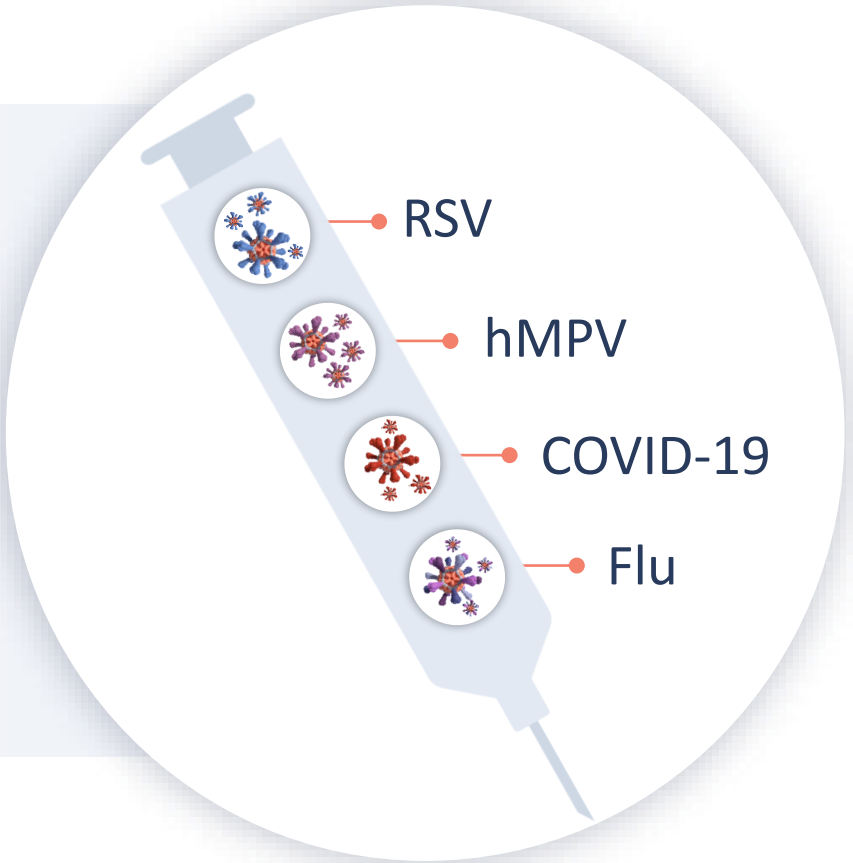
Statements contained in this presentation regarding matters that are not historical facts are forward-looking statements. The forward-looking statements are based on the company's current beliefs and expectations and include, but are not limited to: the company's goal to progress its preclinical and clinical programs, the timing of company milestone achievement, the company's cash balance and the company's expectations regarding the prophylactic and commercial potential of its vaccine product candidates and its platform technology. Actual results may differ from those set forth in this presentation due to the risks and uncertainties inherent in the company's business, including, without limitation: the early stage of the company's development efforts; the company's novel and unproven technology and the uncertainties associated with the development of the company's novel candidates and their potential use as part of a pan-respiratory vaccine; potential delays in the commencement, enrollment, and completion of, and receipt of data from, clinical trials and preclinical studies; the company's dependence on third parties in connection with manufacturing, research, and preclinical and clinical testing; unexpected adverse side effects or inadequate immunogenicity or efficacy of the company's product candidates that may limit their development, regulatory approval, and/or commercialization as monovalent or combination or pan-respiratory vaccines; the possibility of disappointing results in later clinical trials despite promising results in earlier preclinical research or clinical trials; the potential for challenges in the manufacturing and scale up process, including without limitation challenges that reduce drug product stability or potency; competing approaches limiting the commercial value of the company's vaccine candidates and the company's VLP platform technology; regulatory developments in the United States and other countries; the company's ability to obtain and maintain intellectual property protection for its product candidates and maintain its rights under intellectual property licenses; the company's ability to fund its operating plans with its current cash, cash equivalents, and investments; the company's ability to maintain undisrupted business operations during the COVID-19 pandemic, including with respect to clinical trials, manufacturing, and supply chain; and other risks described in the company's prior filings with the Securities and Exchange Commission (SEC), including under the heading "Risk Factors" in the company's quarterly report on Form 10-Q for the quarter ended March 31, 2022 and any subsequent filings with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and the company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

What if a **SINGLE VACCINE** could protect you from multiple viral respiratory infections?

AND LAST BEYOND A SINGLE SEASON

AND COVER EMERGING VARIANTS

AND LIMIT UNWANTED SIDE EFFECTS



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AND significantly reduce hospitalization and death?

U.S. hospitalizations and deaths per year (older adults)

RSV

Annual estimates, older adults 65+

~177,000
hospitalizations

~14,000
deaths

Economic burden:
Estimated at $1.5-3B in direct medical costs for ages 60+

hMPV

Data support similar morbidity and mortality to that seen with RSV or Flu

COVID-19

Data set: August 2020-March 2022, older adults 60+

~2.5 million
hospitalizations

Total deaths as of March 9, 2022, Older adults 65+

~712,000
deaths

Economic burden:
~$28B in preventable COVID-19 hospitalizations costs among unvaccinated adults (18+)^

Flu

2019-2020 flu season, older adults 65+

~171,000
hospitalizations

~12,000
deaths

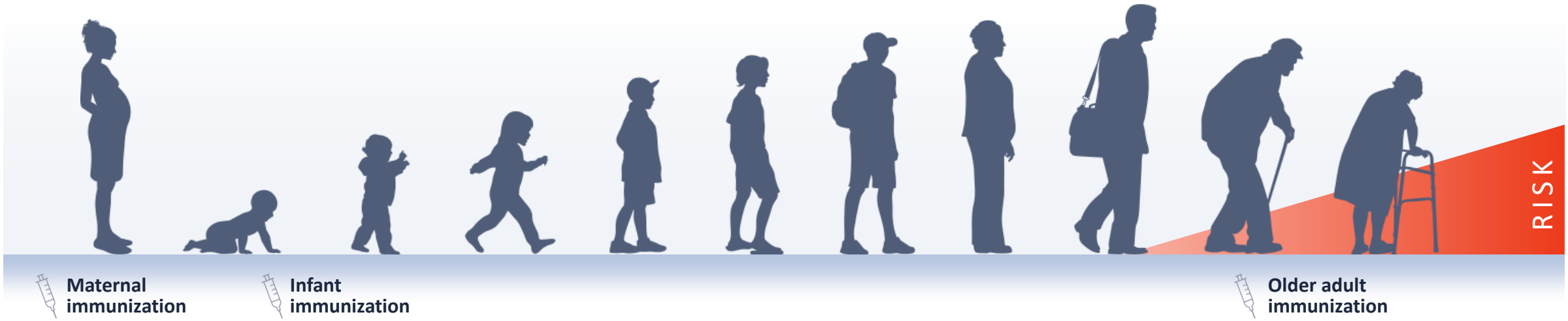
Economic burden:
~$3.2B in direct medical costs, adults 65+ drove ~40% of this (~$1.3B)

^ Extrapolated from six months data to an annualized figure.

CDC, RSV Trends and Surveillance; CDC Health Alert network, alert CDCHAN-00443; Sieling et al 2021, *Influenza Other Respiratory Viruses*; CDC COVID Data Tracker for hospitalizations and deaths; CDC Burden of flu, 2019-2020 flu season; Herring et al 2022, *Vaccine*; Peterson-KFF Health System Tracker, Unvaccinated COVID-19 hospitalizations cost billions of dollars; Putri et al 2018, *Vaccine*

Especially in the MORE VULNERABLE OLDER ADULT POPULATION

WANING IMMUNITY WITH TIME
CREATES RISK FOR INFECTION AND HOSPITALIZATION



PROTECTING THE WORLD'S >600 MILLION* OLDER ADULTS
CAN HELP THEM ACHIEVE THEIR FULL LIFESPAN

*Aged 65+.
Adapted from B. Graham, NIH, ResViNet 2017 presentation.
NIH News Releases 28 Mar 2016, World's older population grows dramatically

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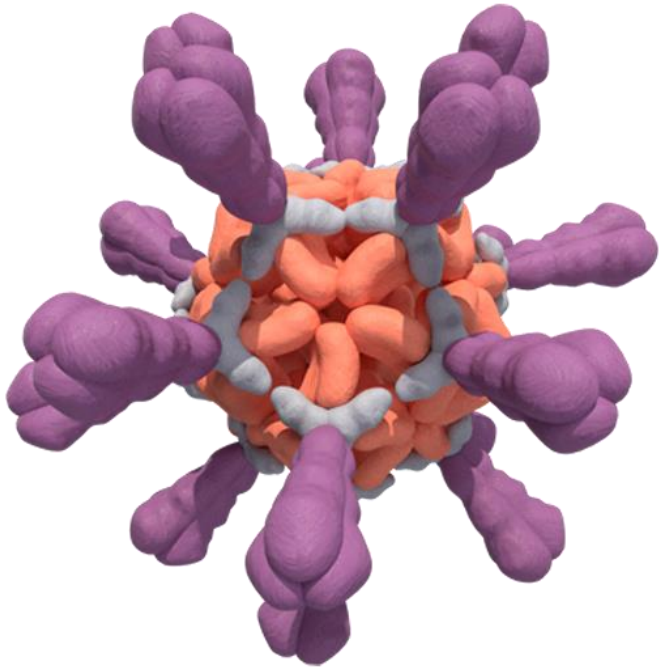
We’re aiming to do just that—with a new approach focused on VIRUS-LIKE PARTICLES (VLPs)

From technology born out of a collaboration between the Gates Foundation and the University of Washington’s Institute for Protein Design, Icosavax emerged with a vision to create better vaccines

Our vaccines are intentionally designed to mimic the structure of viruses



TO EMPOWER BETTER IMMUNE RESPONSE

VLPs may offer one or more of these POTENTIAL BENEFITS

When compared to existing modalities,
WE BELIEVE OUR VLP TECHNOLOGY HAS THE POTENTIAL TO IMPROVE UPON:

Magnitude of response

to counter immunosenescence that can occur in the elderly

Breadth of coverage

greater degree of protection against related viral strains and mutations; less customization for variants

Durability

longer antibody persistence and requiring fewer boosters

Tolerability/reactogenicity

lower incidence of side effects and greater acceptability

Manufacturing

high productivity and scalability with process efficiencies, storage flexibility and stability

Combinability

ability to combine multiple VLPs in one vaccine

VLPs have MULTIPLE POTENTIAL BENEFITS (cont'd)

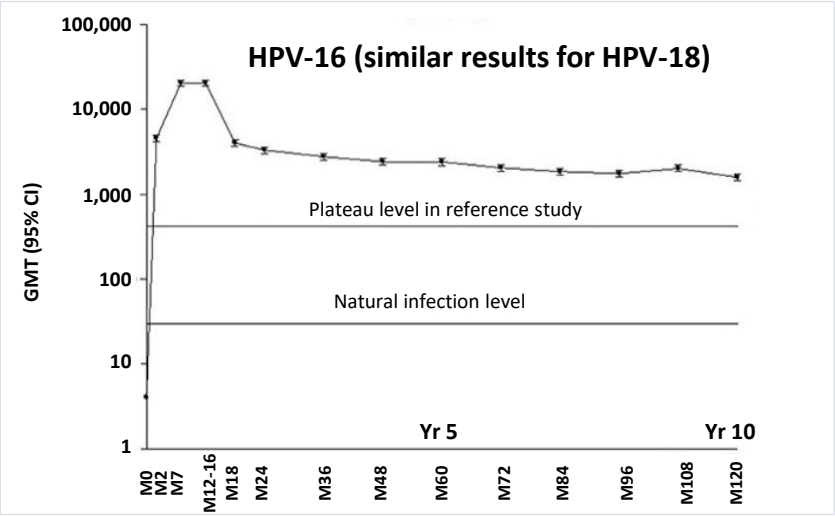
POTENTIALLY HIGHER MAGNITUDE OF RESPONSE (COVID-19)

TECHNOLOGY TYPE		FOLD CHANGE YA NTs/HCS*	EFFICACY (%) ORIGINAL STRAIN*
VLP†	SK Bioscience	~6	TBD
	Bavarian Nordic	~12	TBD
Soluble protein/micelle		~4	96
mRNA		~3-4	94-95
Ad vector		~1	62-90

Clinical studies evaluating the VLP approaches have shown the highest fold change over Human Convalescent Sera (HCS) controls, a measure associated with protection in vaccines assessed for efficacy to date.

†Initial Ph 1 result with IVX-411 was comparable to or below HCS immune response, and an investigation is underway.

POTENTIALLY MORE DURABLE (HPV EXAMPLE)



CERVARIX 10 YEAR IMMUNE RESPONSE

3 doses induced high and sustained antibody levels against HPV-16, 18, 31, and 45 for at least 10 years after initial vaccination in 10-14 y.o. adolescent girls

POTENTIALLY GREATER BREADTH OF COVERAGE

Cervarix HPV VLP vaccine

- In a 4 year follow-up to a pivotal Phase 3 trial of Cervarix, an HPV vaccine targeting HPV types 16 and 18, the vaccine showed strong cross-protective efficacy against 4 additional oncogenic HPV types not expressed by the vaccine

Norovirus VLP vaccine candidate

- HIL-214 is a bivalent VLP formulation of GI.1 and GII.4 norovirus strains
- Post-hoc analysis of the Ph2b trial showed vaccine efficacy against GII.2, a genotype not present in vaccine

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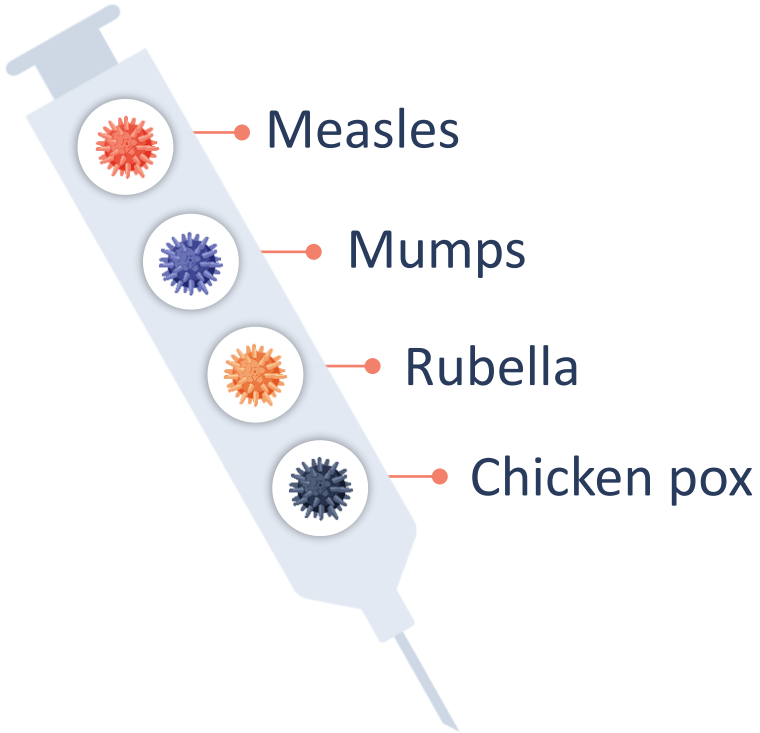
* Not a head-to-head analysis. Results are from separate studies conducted by third parties, presented for illustrative purposes only. YA = young adults; NTs = neutralizing titers; HCS = human convalescent sera.
Sources: Gobeil et al 2021, medRxiv preprint; COVAX compilation of published vaccine data; Schwarz et al 2019, *Hum Vaccines Immunother*; company press releases.

VLPs may also allow for COMBINATION VACCINES for older adults

PEDIATRICS

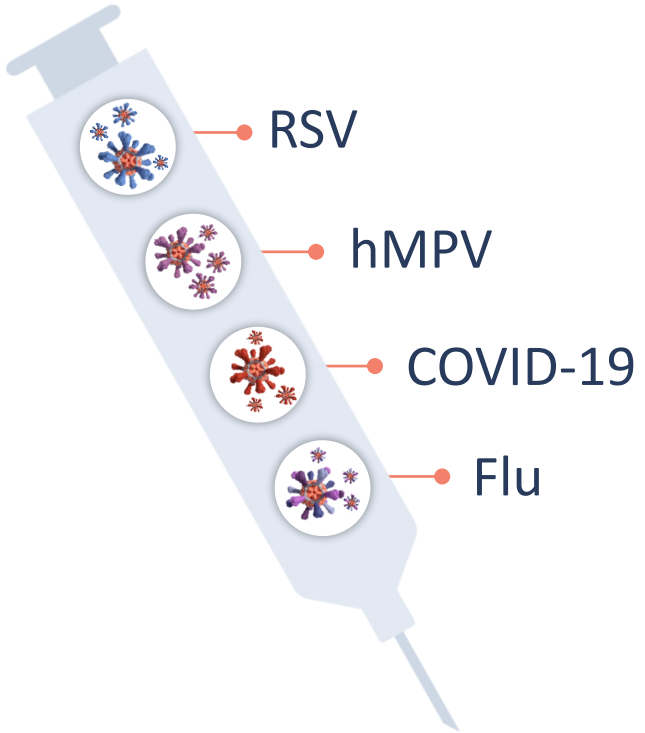
Combination vaccines have been available for years – up to 6 in 1 shot

MMRV



OLDER ADULTS

The time has come for combination vaccines for older adults - VLPs are an ideal modality to succeed with this vision as naturally occurring VLPs have already been utilized as combination vaccines



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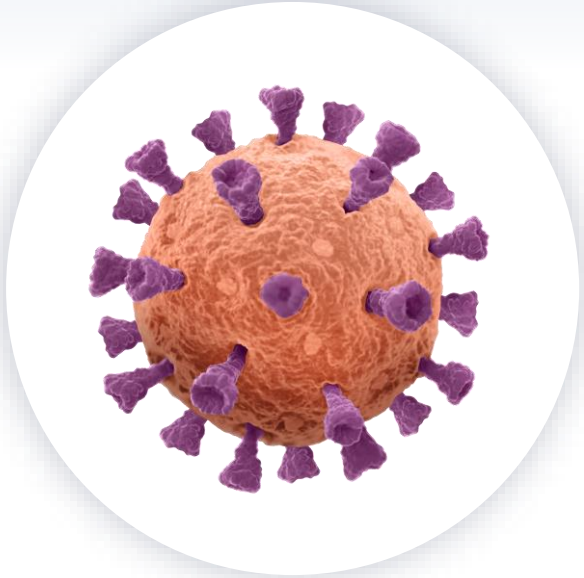
Unlike soluble antigens, VLPs mimic the STRUCTURE of real viruses

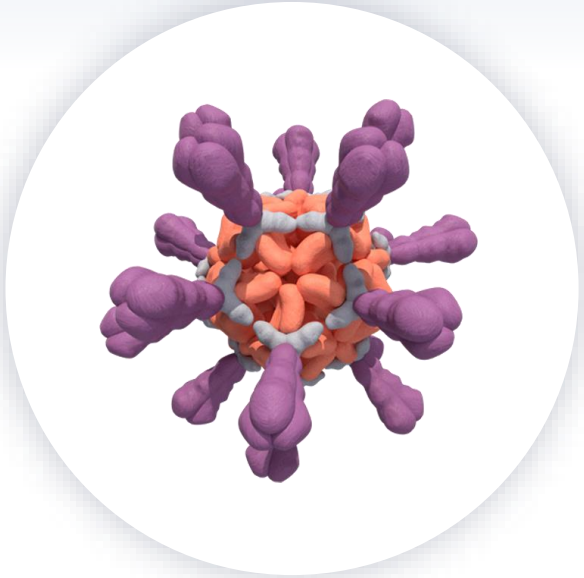
Natural virus



Soluble antigen

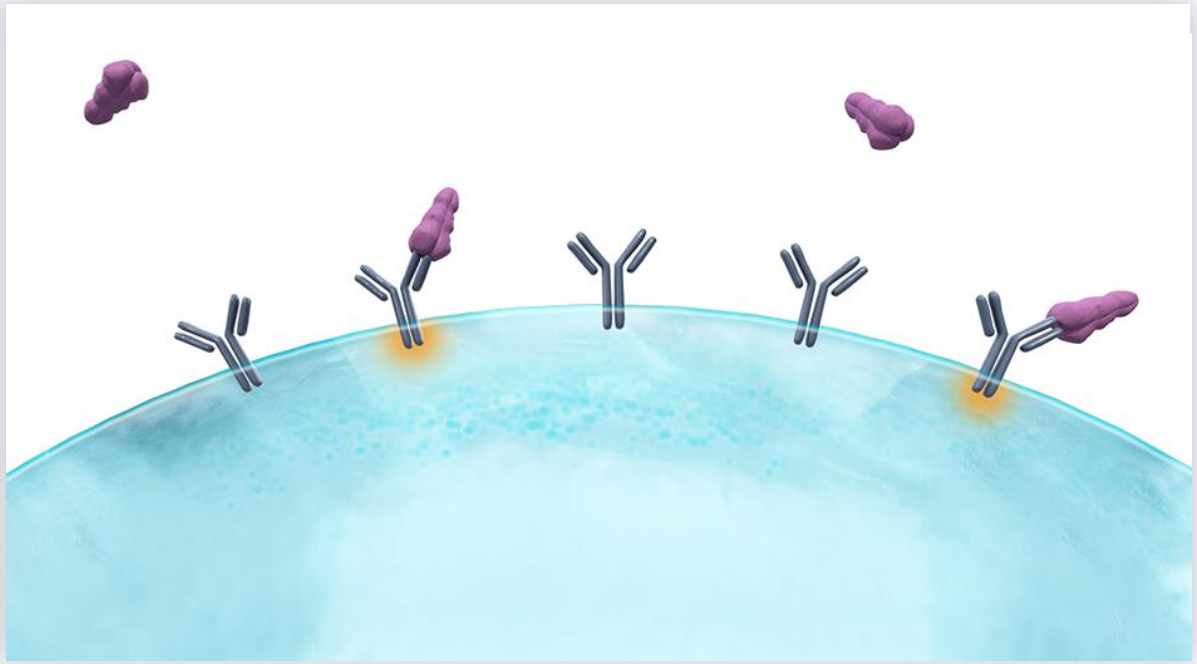
Traditionally manufactured or mRNA-derived

VLP-based antigen



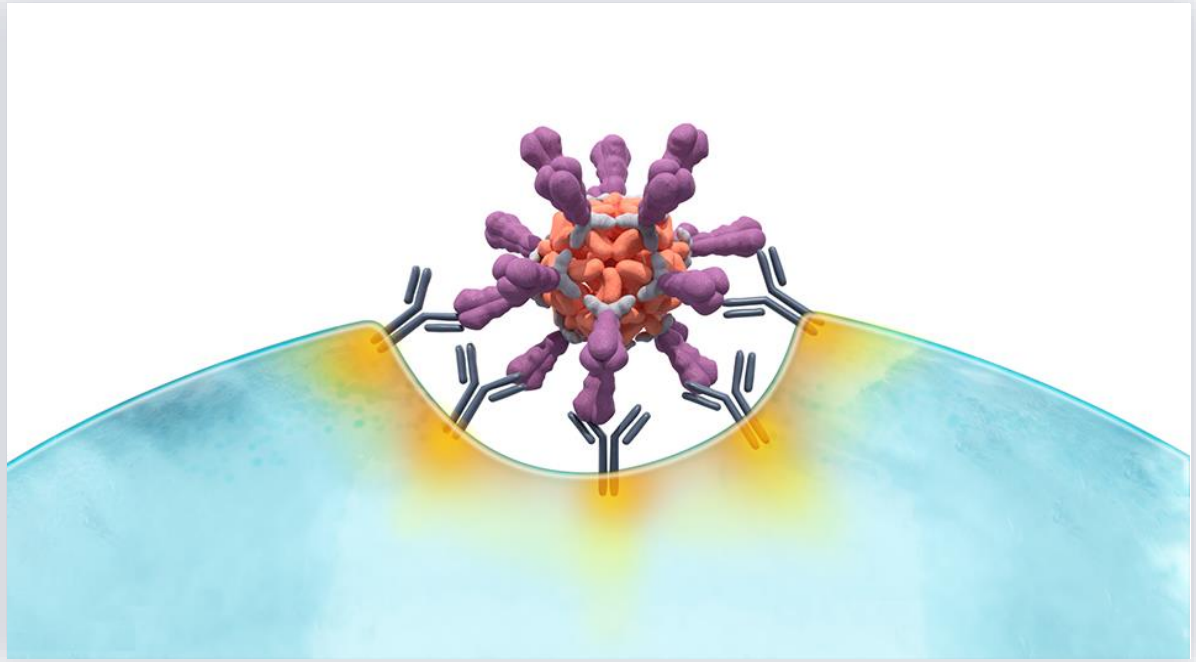
Because the body “sees” VLPs as viruses, the result may be a SUPERIOR IMMUNE RESPONSE

Soluble antigen
(traditionally manufactured or mRNA-derived)



Weaker activation signals and lower levels of antibodies lead to a weaker immune response.

VLP-based antigen



Multivalent antigen display enables cross-linking of B-cell receptors in the lymph nodes, potentially leading to a stronger, more durable immune response.

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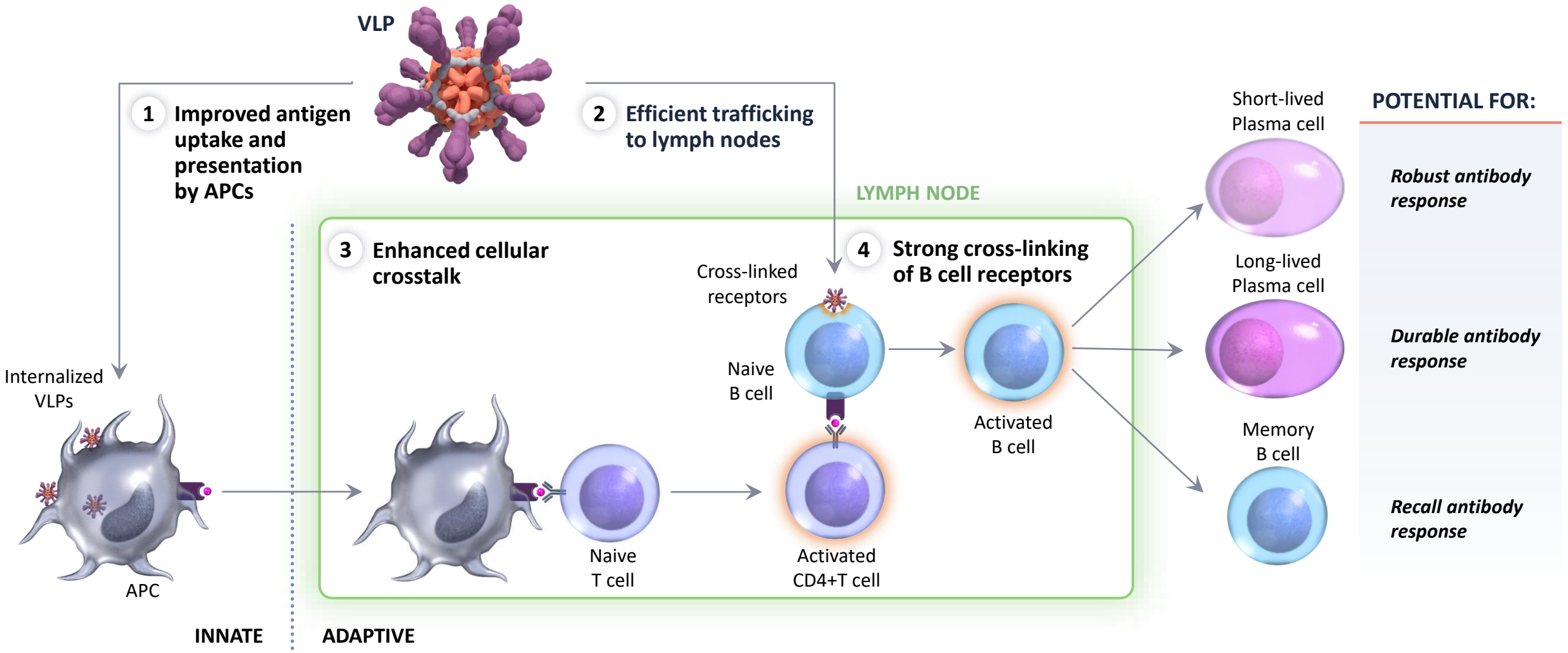
Adapted from B. Graham, NIH, ResViNet 2017 presentation

MULTIPLE MECHANISMS may underpin the anticipated robust immune response to VLPs



Adapted from Gomes et al 2017, *Vaccines*

VLPs have already been PROVEN safe and effective as vaccines; Icosavax candidates now in the clinic

NATURALLY OCCURRING VLPs ARE UTILIZED IN VACCINES
that have been in market and established for years

1st publication about VLP

1973

1981

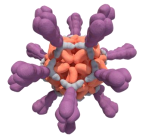
1st VLP based vaccine licensed for humans Hepatitis B virus (HBV)

Human Papillomavirus (HPV) vaccine: Cervarix and Gardasil

2007

2011

Hepatitis E vaccine (licensed in China)



Icosavax VLP-based vaccine candidates in the clinic

2022

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Gomes et al 2018; Rappuoli and Serruto 2019; Sherwood et al 2020; Gara et al 2015; PATH Single-Dose HPV Vaccine Evaluation Consortium, 2019

Our VLPs are produced via a PROPRIETARY, 2-COMPONENT, COMPUTATIONALLY-DESIGNED system

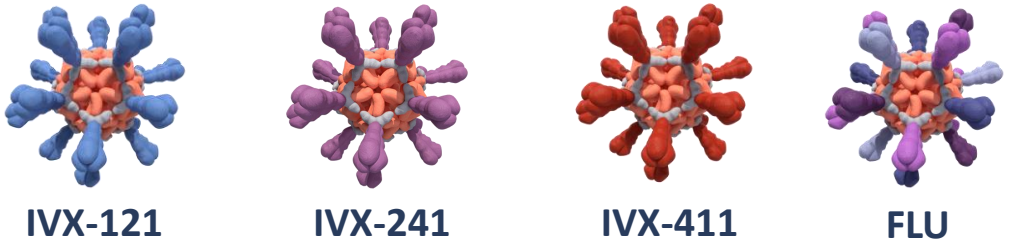
Component A
(antigen-specific)

- Trimeric protein genetically fused to target antigen
- Antigen properly folds to display neutralizing epitopes before assembly into VLP
- New antigen design capabilities allow us to prepare for future threats

Component B
(common)

- Can be used across multiple vaccine candidates

VLPs



- Self-assemble when components A and B are combined
- Icosahedral symmetry and particle size mimics viral properties to potentially enhance immunogenicity
- VLPs can have one antigen target per VLP or multiple different antigens on a single VLP

Our intentionally designed VLPs offer multiple potential MANUFACTURING advantages

Highly productive, flexible scalable system using standard recombinant protein (eg, mAb) production/purification methods

- Supply chain and capacity already exists globally
- Typical single-use bioreactor suite could produce ~100 million–2 billion doses/year*
- Can flex to respond to a pandemic

Process efficiencies across the platform

- Component B common across all VLP candidates to date
- Component A processes leverage common purification methods, expression systems, etc.

Opportunities to build and store inventory

- Provides flexibility to manufacture and stock combination vaccines at commercial scale and quickly switch to respond to pandemics

Anticipating competitive cost of goods at commercial scale

- Relative to established protein-based vaccines

Would slot into standard distribution chain

- Easy technology to commercialize
- Stability at 2-8° C

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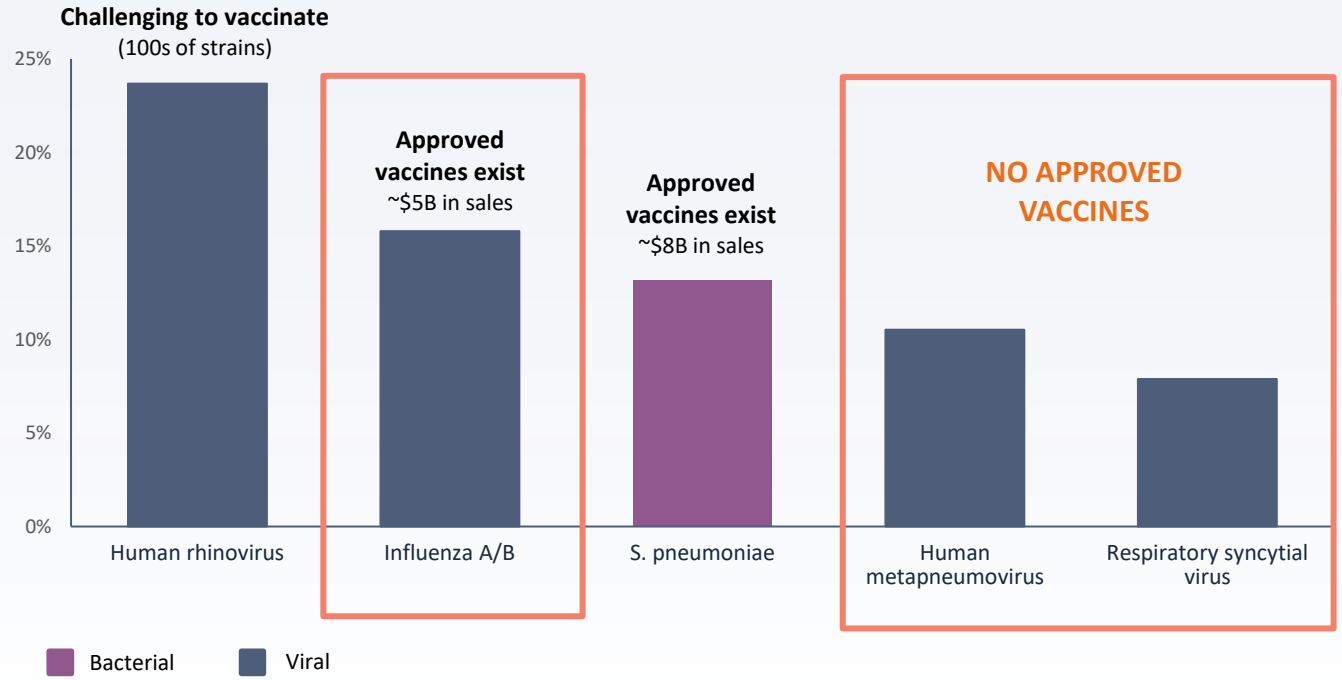
*Depending on dosage level and monovalent vs combination vaccine.

We are pursuing major UNMET NEEDS with our VLP technology

Respiratory vaccines are an emerging market: There are no approved vaccines for RSV or hMPV, and there are opportunities to improve protection from flu vaccines

Top 5 pathogens detected in adults hospitalized with community-acquired pneumonia
(EPIC Study; pre-COVID-19)



RSV/ hMPV

- A vaccine against RSV would be expected to be recommended by policy makers such as ACIP, particularly in older adults, which could drive rapid coverage and uptake and faster growth to peak sales
- Analysts project an RSV vaccine market of ~$10 billion by 2030; we believe hMPV will be similar

COVID-19

- 2021 COVID-19 vaccine sales were ~$60 billion
- Multiple industry sources have estimated that a $10+ billion/year opportunity will persist in the endemic stage (ex: 2025)
  - IQVIA, Global Data, equity analysts

FLU

- Despite their commercial success, existing vaccines have historically had sub-par efficacy (~14%-50% over the last 10 years)

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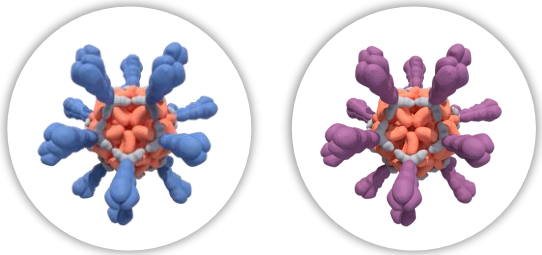
Jain S et al 2017, *Clin Chest Med*; GBD 2015 LRI Collaborators; *Lancet Infect Dis* 2017; Walsh et al 2008, *Arch Internal Med*; World Heath Organization; SVB Leerink May 2021

We are currently progressing MULTIPLE ASSETS in the clinic

TARGET INDICATION	ANTIGEN	LEAD CANDIDATE SELECTION	IND-ENABLING STUDIES	PHASE 1	PHASE 2	PHASE 3	NEXT ANTICIPATED MILESTONE	COMMERCIAL RIGHTS
RSV/hMPV Bivalent*	RSV Monovalent	IVX-121					Ph. 1/1b topline data complete; advance to IVX-A12	ICOSAVAX
	RSV/hMPV Bivalent	IVX-A12					IND submission & initiate Ph. 1 H2 2022	ICOSAVAX
COVID-19	Bivalent RBD						Candidate development^	ICOSAVAX
Flu	Flu Quadrivalent						Candidate development	ICOSAVAX

* Icosavax does not plan to pursue the IVX-121 RSV monovalent candidate as a standalone candidate for RSV in older adults, and plans to transition development to the IVX-A12 bivalent RSV/hMPV candidate following Phase 1.
^ Icosavax has worldwide nonexclusive rights with exception of South Korea (which is not included in the licensed territory), which will convert to exclusive rights in North America and Europe (including Switzerland and United Kingdom) starting in 2025, with non-exclusivity maintained elsewhere. No plan to further advance IVX-411 following completion of the recent investigation and decision to focus development on a bi-valent strategy.



RSV/hMPV Bivalent Vaccine Candidate (IVX-A12)

Our first combination vaccine candidate—IVX-A12—targets BOTH RSV and hMPV

RSV and hMPV are related *Pneumoviridae* and have overlapping seasonal circulation

Both viruses are common with high re-infection rates

The goal for both is to target the F protein (responsible for viral cell entry)

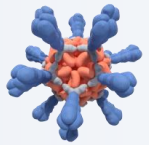
RSV

- Found in 8% of US adults hospitalized for pneumonia where pathogen detected
- 16% likelihood of ICU admission, 5% likelihood of death
- Symptoms: Cough, fatigue, dyspnea, congestion, wheezing, fever

hMPV

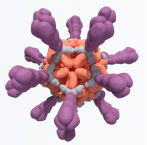
- Found in 11% of US adults hospitalized for pneumonia where pathogen detected
- 17% likelihood of ICU admission, 4% likelihood of death
- Symptoms: Cough, wheezing, dyspnea, congestion, fatigue

IVX-121
RSV

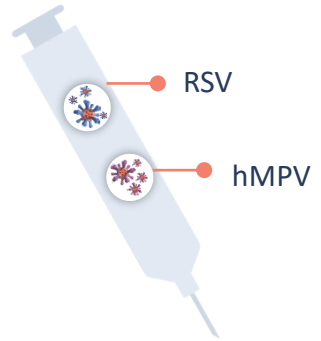


+

IVX-241
hMPV



IVX-A12



RSV/hMPV bivalent vaccine candidate

Clinical precedent for use of VLPs for combination vaccines targeting related pathogens (e.g., human papillomavirus, norovirus)

Icosavax utilizing prefusion stabilized F antigens for display on VLP

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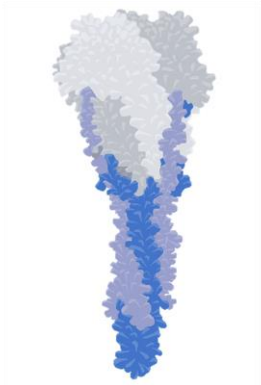
Jain et al 2015; Widmer et al 2012; Walsh et al 2008; T Shi et al 2019

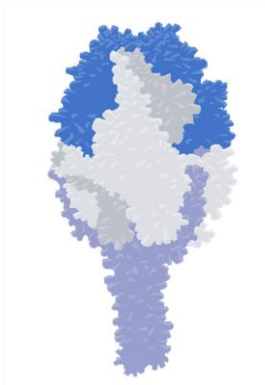
IVX-121 for RSV: Prefusion RSV-F protein may lead to higher neutralizing antibody titers

Postfusion F protein



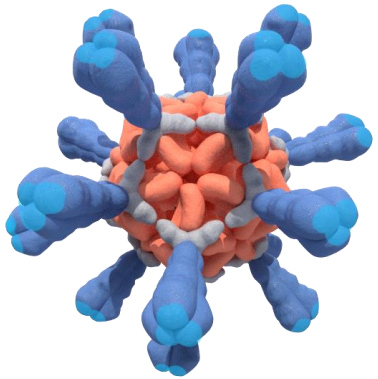
Postfusion protein subunit vaccines

Prefusion F protein



Prefusion stabilized protein subunit vaccines (e.g., DS-Cav1)

IVX-121



VLP with multivalent display of stabilized prefusion proteins

COMPANIES & TECHNOLOGIES:

Postfusion F protein		Prefusion F protein			IVX-121
Subunit	Particle	Proof of concept Subunit (Ph1)	Recombinant vector or mRNA	Subunit	VLP
sanofi pasteur	NOVAVAX	NIH National Institutes of Health	janssen	gsk	ICOSAVAX
			mRNA moderna	Pfizer	
Older Adults Neutralizing Titer Geometric Fold Rise (GMFR) ~2-4x		**DS-Cav1 Adult Neutralizing Titer GMFR ~7-10x**			

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Graham et al 2015; Ruckwardt et al 2021

IVX-121 for RSV: Ph 1/1b topline interim data was presented in June 2022

PHASE 1

- First-in-human dose escalation
- Healthy young adults (YA), aged 18–45 yrs
- 6 treatment groups: 3 dosage levels IVX-121 (25, 75, 250 µg) +/- alum adjuvant
- N = 90 (dosing complete)

Allows comparison to NIH DS-Cav1 Phase 1 data in YA, as representative of stabilized prefusion F-based vaccines

PHASE 1B

- Healthy older adults (OA), aged 60–75 yrs
- 6 treatment groups: 3 dosage levels IVX-121 (25, 75, 250 µg) +/- alum adjuvant
- N = 130 (dosing complete)

Assessment of safety and immunogenicity in OA and potential to counter immunosenescence

PHASE 1B EXTENSION

Preliminary; subject to change

- Subset of Ph 1b OA cohort
- Up to 12 months follow-up
- Revaccination at 12 months after initial Ph 1b dose

Assessment of long term safety and durability and responses to additional dose of IVX-121 in OA

Following the Phase 1/1b trial, we plan to combine IVX-121 with IVX-241 (our hMPV candidate) for further clinical development as IVX-A12 combination candidate

Positive IVX-121 Phase 1/1b topline interim results

- **Initial indication of the company's differentiated VLP platform technology**
  - High RSV-A and RSV-B neutralizing antibody titers seen even at lowest dose tested
- **Positive topline data from the Phase 1/1b trial of IVX-121 suggest a competitive initial profile in RSV**
  - Similarly robust responses in older versus young adults, favorable tolerability, suitability for combination
  - Opportunities to further differentiate RSV profile; durability to be assessed in Phase 1b extension out to 12 months
- **Proceeding to combination with proprietary hMPV VLP in a differentiated bivalent vaccine candidate IVX-A12 (RSV/hMPV) for older adults**
  - Tolerability profile at maximum dose tested in Phase 1 (250 µg) and immunogenicity down to 25 µg gives room for multivalent combinations

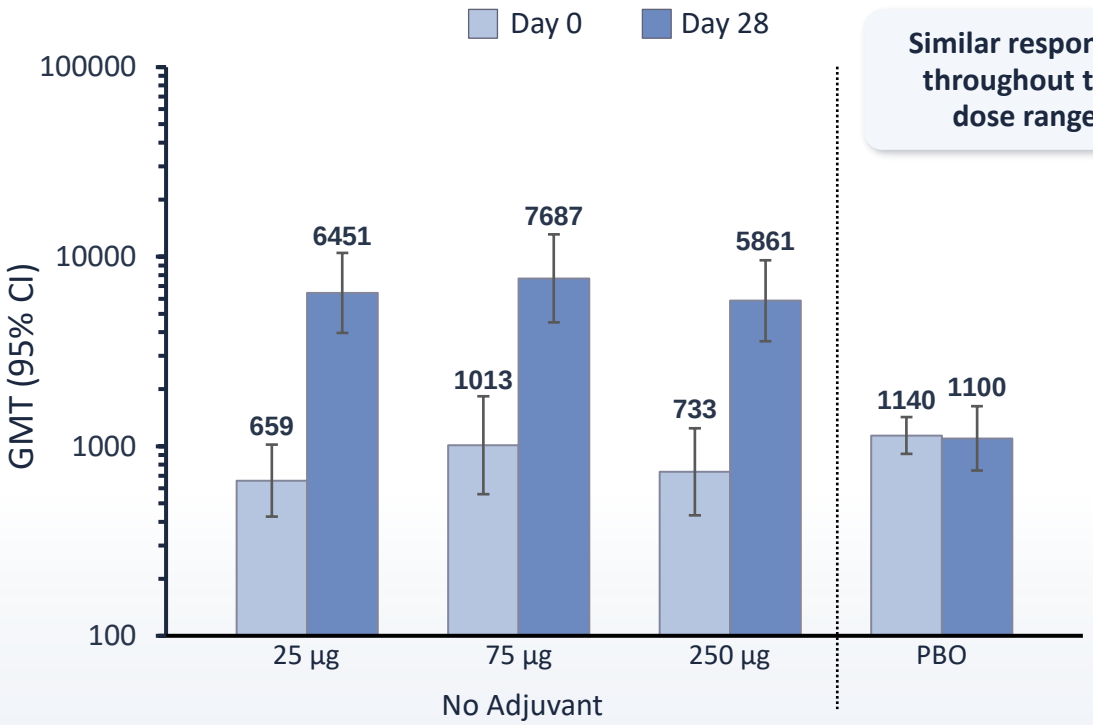
NEXT STEP: IVX-A12 (RSV/hMPV) on track for IND submission and anticipated start of Phase 1 trial in 2H'22

Topline immunogenicity data: RSV-A nAb (unadjuvanted)

GMT expressed in IU/mL – Viroclinics Live nAb Assay

PH1 Young Adult Subjects (ages 18-45) n=90

Day 0 and Day 28 Results

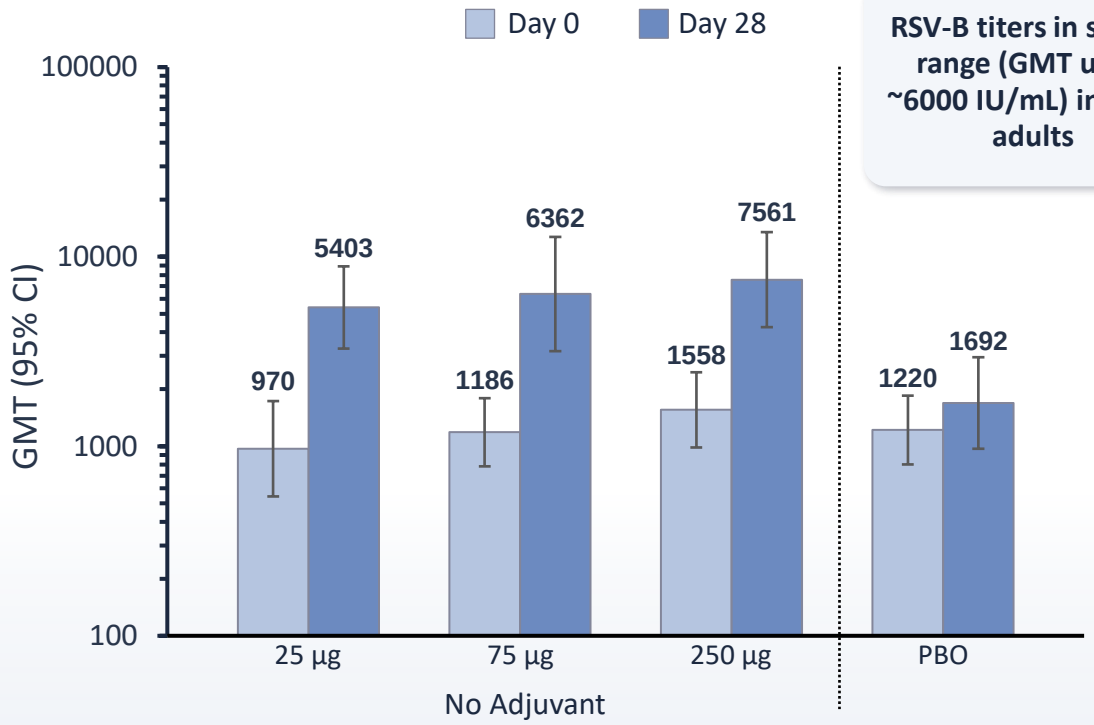


N=	14	13	14	14	14	13	6	6
GMFR	8- to 10-fold						1.0	

Similar responses throughout the dose range

PH1b Older Adult Subjects (ages 60-75) n=130

Day 0 and Day 28 Results



N=	17	19	18	18	18	18	19	19
GMFR	5- to 6-fold						1.4	

RSV-B titers in similar range (GMT up to ~6000 IU/mL) in older adults

Geometric mean titers (in IU/mL) of unadjuvanted IVX-121 are comparable in young and older adults

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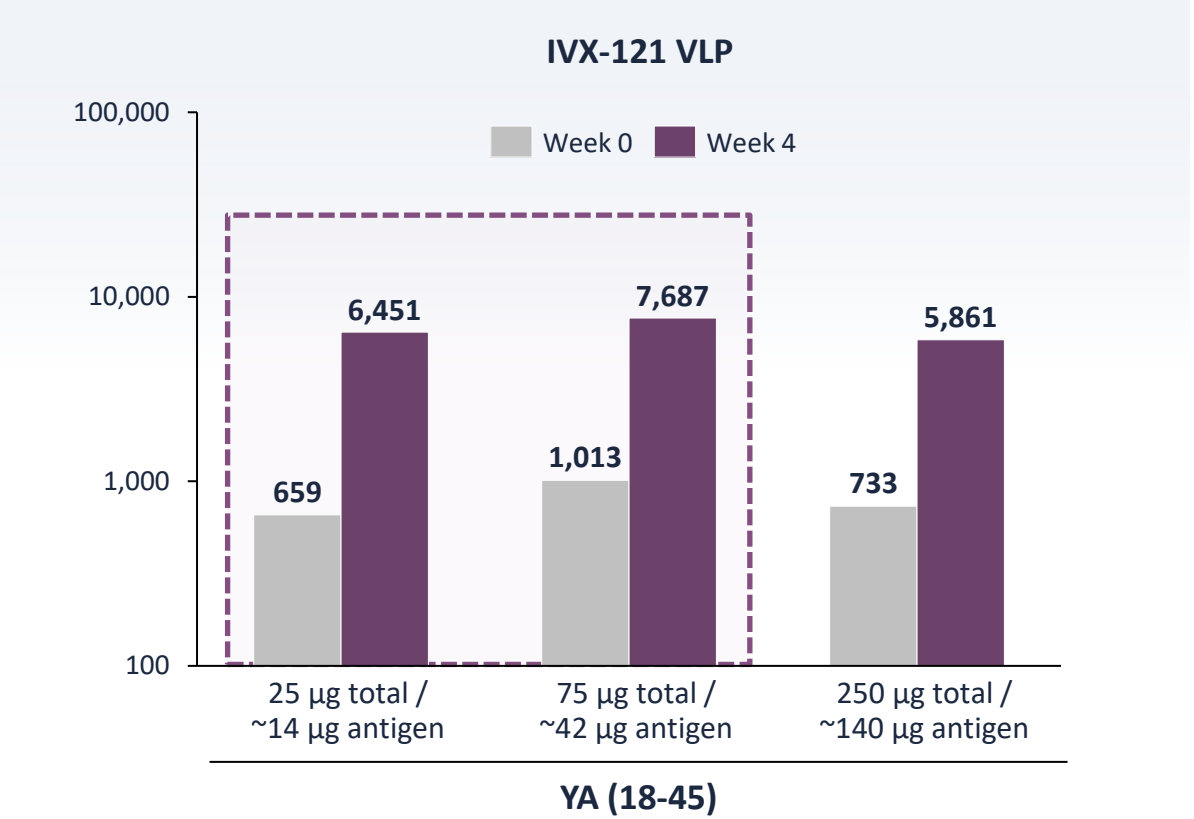
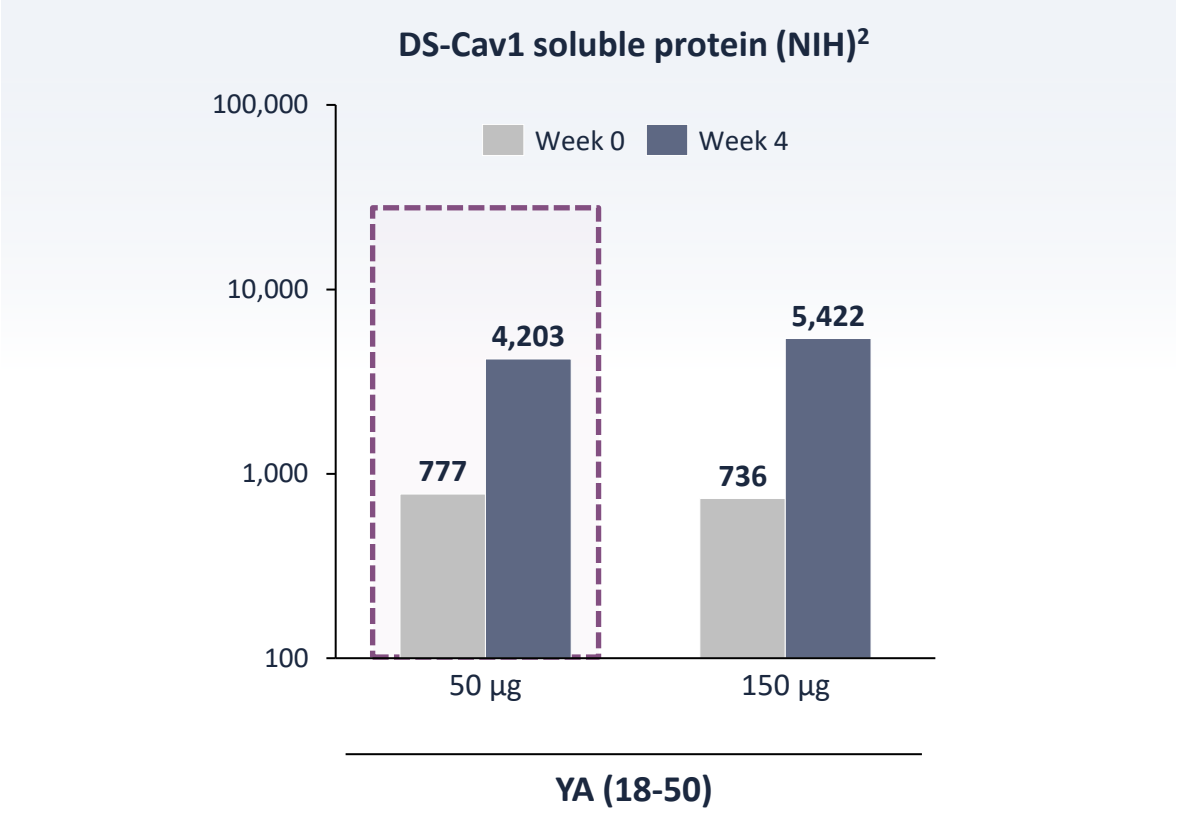
GMT: Geometric mean titer; LLoQ = 9.9; GMFR: Geometric Mean Fold Rise (Day 28) from Baseline. Assays Conducted by Viroclinics

At comparable or lower antigen dose equivalents, IVX-121 elicits high RSV-A NAb titers relative to those previously shown for DS-Cav1 antigen

YA immunogenicity, ~1 month post dose (unadjuvanted): RSV-A neutralization assays (IU/mL)[1]





Robust initial immunogenicity at lower dose levels of VLP enables advancement of multivalent vaccine vision

****Data shown side by side for illustrative purposes only; not a head-to-head comparison and there could be assay and laboratory differences across trials****

[1] NAb assays conducted at different labs, using the World Health Organization (WHO) International Standard for antiserum to RSV-A (NIBSC code: 16/284), for conversions to WHO International Units/mL (IU/mL); [2] DS-Cav1 doses range from 50-500 µg (Ruckwardt et al 2021), doses comparable to IVX-121 are shown

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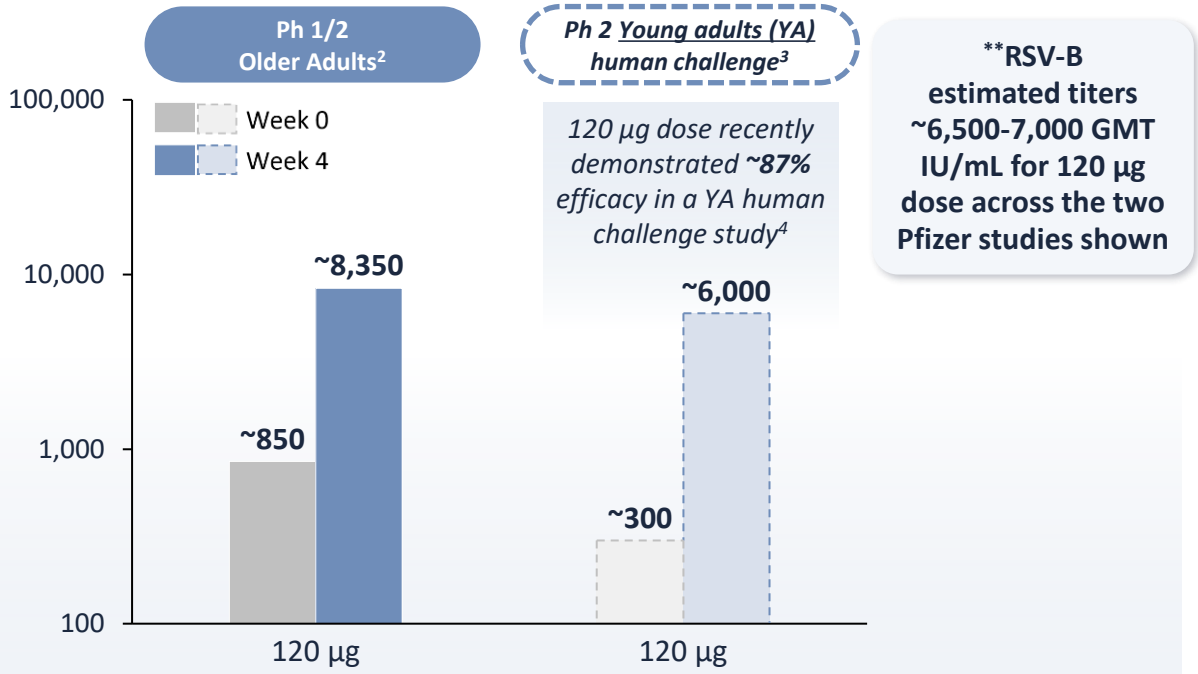
IVX-121 neutralizing antibody titers are in the estimated range of a leading RSV candidate in Phase 3 for older adults

Immunogenicity, ~1 month post dose (unadjuvanted): RSV-A neutralization assays (IU/mL)[1]

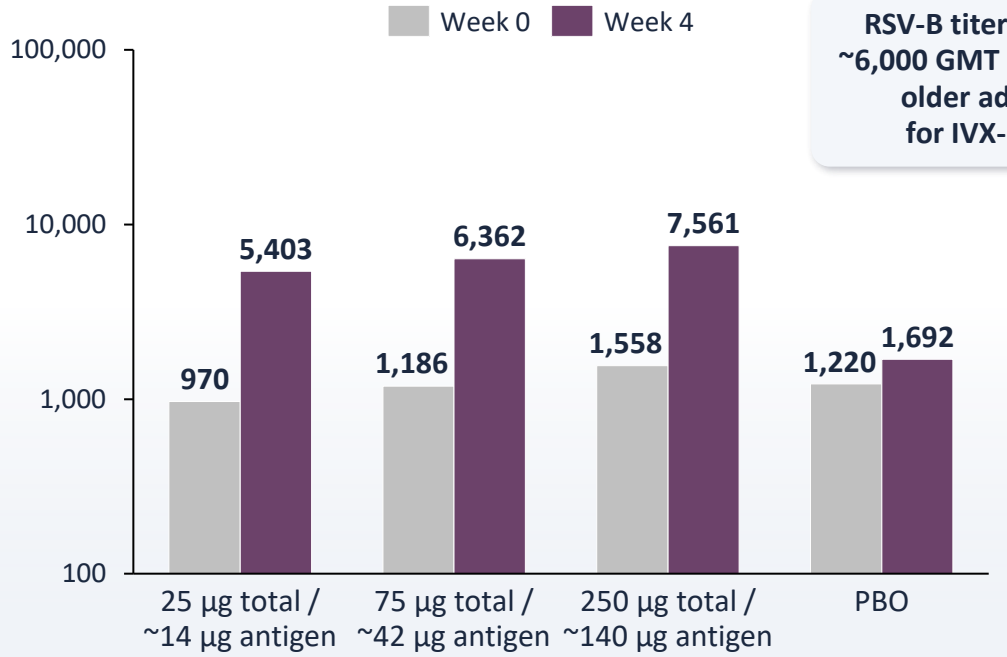
RSVpreF soluble protein (Pfizer; estimated titers)



*120 µg dose recently demonstrated **~87%** efficacy in a YA human challenge study[4]*

****RSV-B estimated titers ~6,500-7,000 GMT IU/mL for 120 µg dose across the two Pfizer studies shown**

IVX-121 VLP (Older Adults)



RSV-B titers up to ~6,000 GMT IU/mL in older adults for IVX-121

IVX-121 durability profile to be assessed in Phase 1b extension out to 12 months

****Data shown side by side for illustrative purposes only; not a head-to-head comparison and there could be assay and laboratory differences across trials****

[1] NAb assays conducted at different labs, using the World Health Organization (WHO) International Standard for antiserum to RSV/A (NIBSC code: 16/284), for conversions to WHO International Units/mL (IU/mL); [2] Based on Ph 1/2 OA expanded cohort in Falsey et al 2021, data are approximate estimates derived from reported graphs and IU/mL conversion factors; [3] Beate Schmoele-Thoma et al 2022; [4] Final RSVpreF formulation selected for OA (120 µg no adj, Baber et al 2022)

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Favorable IVX-121 tolerability data in Phase 1/1b study

	RSV vaccines – OA				Shingles vaccine	Quadrivalent influenza vaccines – OA[1]				IVX-121
	RSVpreF3 (w/ AS01) (GSK)	Ad26.RSV. preF + preF (Janssen)	RSVpreF[2] (Pfizer)	mRNA-1345 (Moderna)	Shingrix (w/ AS01) (GSK)	Fluzone (Sanofi)	Flublok (Sanofi)	Afluria (Sequirus)	mRNA-1010[3] (Moderna)	25-250 µg - OA N=111
Solicited systemic AEs	–	41%	49%	50 - 79%[5]	66%	25%	25%	20%	48% - 77%	11-33%
Grade 3+ solicited systemic AEs	*'Grade 3 AE rates were generally low'*	2%	0 - 7%[4]	–	11%	0.4%	1%	–	0% - 16%	0%
SAEs	*'Low reporting of SAEs'*	5%	5 - 19%	3%	1%	0%	3%	2%[6]	0%	0%
Vaccine-related SAEs	0%	0%	0%	0%	0%	0%	0%	0%[6]	0%	0%
Vaccine-related deaths	0%	0%	0%	–	0%	0%	0%	0%[6]	–	0%
Age Group	65-80	65+	65-85	65-79	50+	65+	50+	65+	65+	60-75
Study Phase	1/2	2b	1/2	1	3	3	3	3	2	1b

IVX-121 Phase 1/1b safety data support advancement of multivalent vaccine vision

****Data shown side by side for illustrative purposes only; not a head-to-head comparison and there could be assay and laboratory differences across trials****

Data are based on: IDWeek2020 (GSK), ReSViNET 2021 (Janssen), Falsey et al 2021 (Pfizer), Jordan et al 2020 (Bavarian Nordic), Moderna Vaccines day 2022 (Moderna), Lal et al, 2015 (Shingrix), Treanor et al 2017 (Afluria), FDA influenza package inserts (Shingrix, Fluzone, Flublok, Afluria); [1] Non-exhaustive, representative set of quadrivalent flu vaccines recommended for 2021-2022 flu season; [2] Ranges represents 60 µg – 240 µg doses +/- alum; [3] Ranges represent 25 µg - 100 µg doses; [4] 'Solicited severe systemic events' interpreted as Grade 3+ AEs; [5] Range represents data post 1 dose (12.5 µg - 200 µg); [6] Data available only for combined safety population (YA and OA), 65+ population represents ~50% of Afluria cohort

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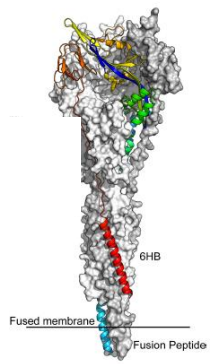
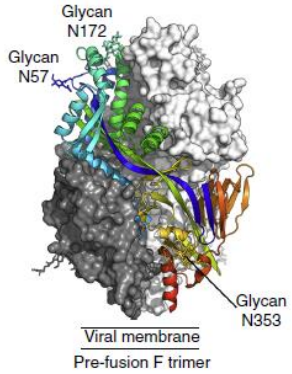
IVX-241 for hMPV: Prefusion stabilized F hMPV antigen selected

Postfusion F Protein

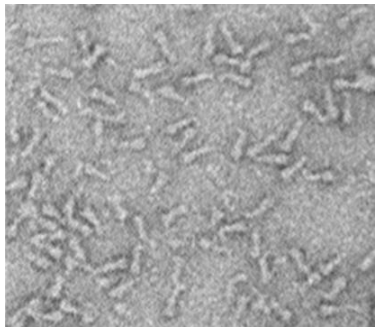


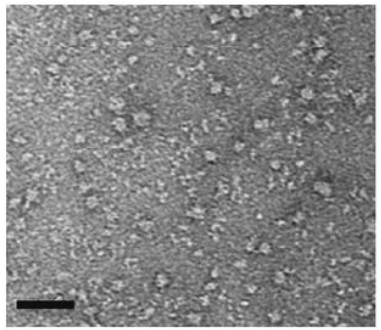
Mas et al., 2016

Prefusion F Protein



Battles et al., 2017





- Similar to RSV, the critical hMPV F protein target undergoes a conformational change upon fusing to the cell membrane
- Prefusion F protein has been shown in the mouse model to have ~6X neutralizing antibody titers against hMPV compared to postfusion F antigen

ICOSAVAX HAS EXCLUSIVELY LICENSED RIGHTS to the prefusion stabilized F antigen incorporated into IVX-241
(except for one mRNA license that can be granted)

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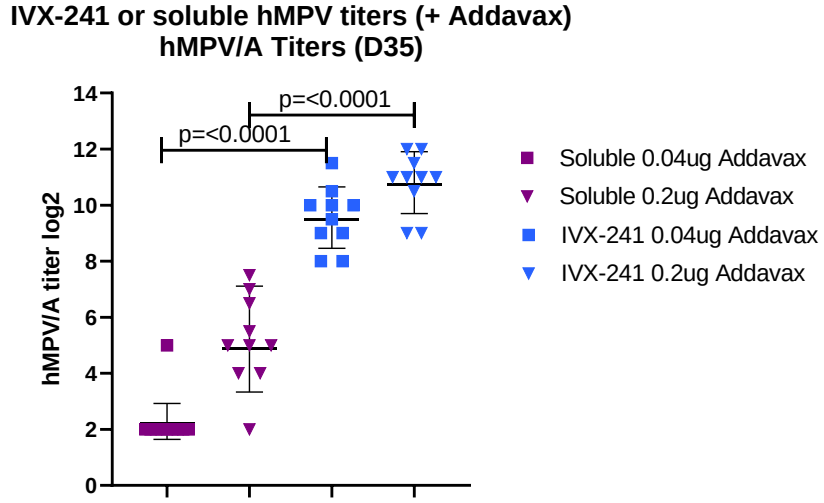
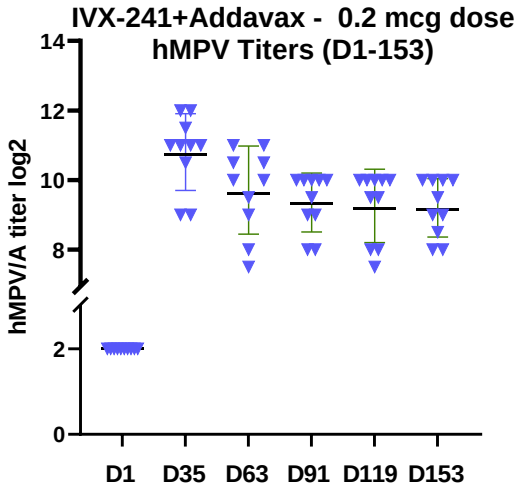
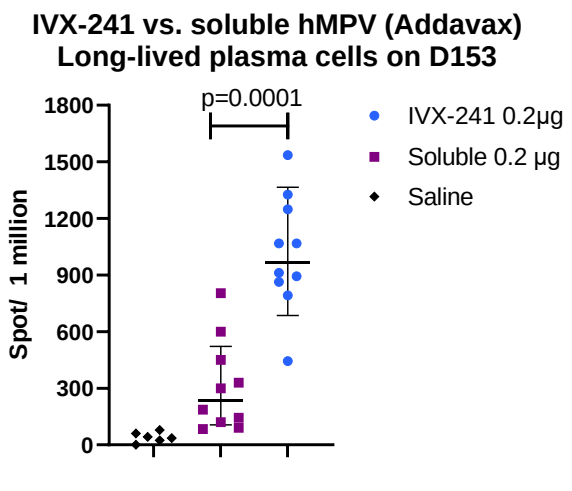
Mas et al 2016, *PLOS Pathogens*; Battles et al 2017, *Nat Commun*; Hsieh et al 2022, *Nat Commun*

IVX-241 for hMPV: Preclinical data show VLP-induced enhancement of immunogenicity and durable immune response



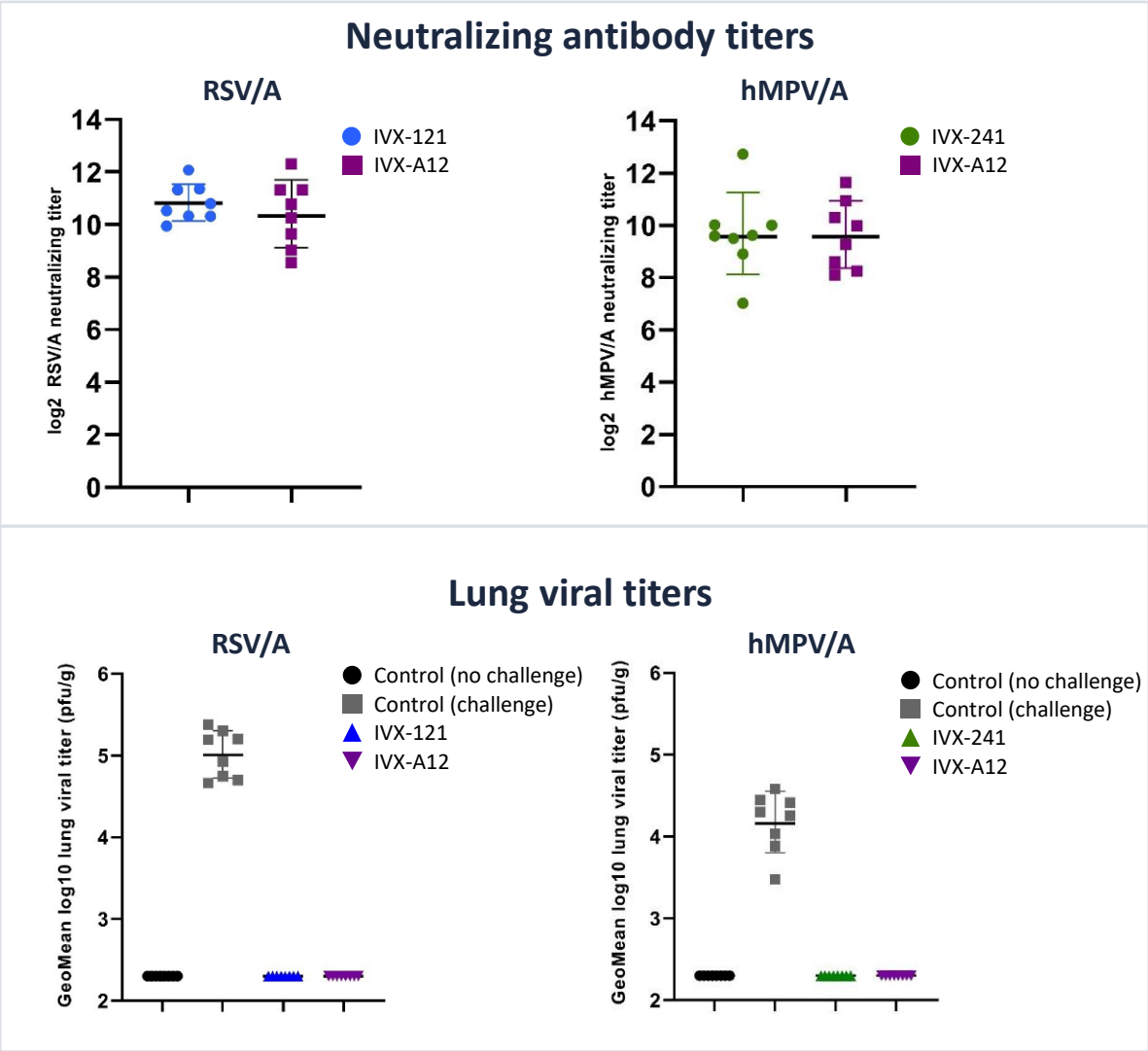




- Naive BALB/c mice dosed on day 1 and day 21
  - Soluble hMPV given at a dose equivalent to quantity of protein on VLP
- hMPV/A neutralizing antibody titers assessed through Day 153 (D153) post dose
  - IVX-241+Addavax induced hMPV/A titers >4 log2 higher than with soluble hMPV +Addavax
  - NAb titers remain stable between days 63 and 153
- Assessment of long-lived plasma cells (LLPC) induction at D153
  - IVX-241 induced significantly higher number of LLPCs than soluble antigen

IVX-241, the hMPV VLP in IVX-A12, led to potent and durable induction of hMPV nAbs in this preclinical study

IVX-A12 for RSV/hMPV: Preclinical proof of concept of protection against BOTH viral causes of pneumonia



Preclinical study showed strong nAb titers induced against both RSV and hMPV, without immune interference

- In a live virus challenge model, cotton rats were administered two doses of adjuvanted IVX-121, IVX-241, or IVX-A12 and subsequently challenged with RSV/A or hMPV/A*

Monovalent and bivalent formulations similarly blocked viral replication post challenge

- In lung tissue, both monovalent (IVX-121, IVX-241) and bivalent (IVX-A12) formulations reduced viral titers to below the lower limit of quantitation**

In preclinical studies, RSV and hMPV two-component VLPs were combined to generate a bivalent immunogen with robust nAb response and blocking of viral replication

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* Two doses of IVX-121, IVX-241, or IVX-A12 (1 ug of each VLP) formulated with Addavax (oil-in-water adjuvant) were administered on day 0 and day 21, with RSV/A or hMPV/A challenge two weeks post 2nd administration;
** Lung tissue samples tested 5 days post challenge

IVX-A12 Ph 1 and 2 trials will plan to assess safety and immunologic non-interference

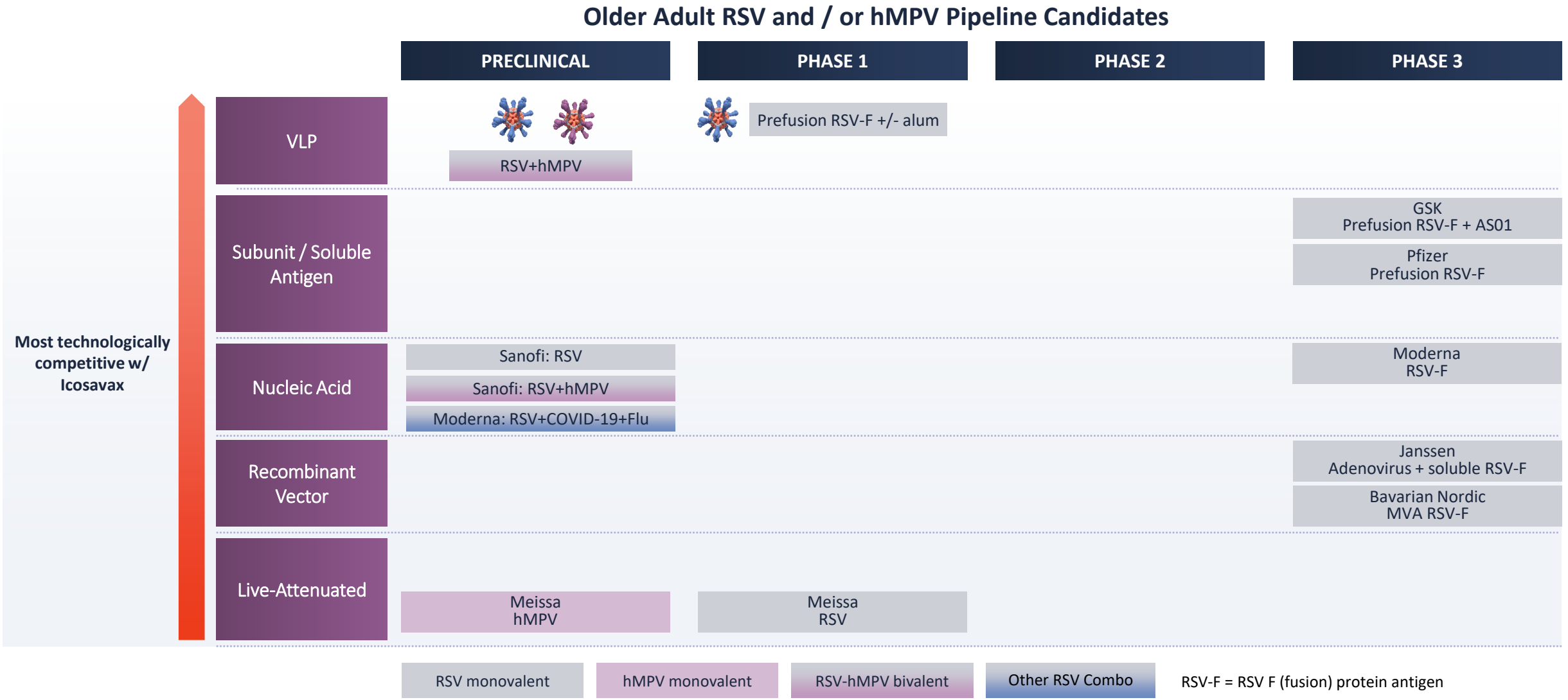
PHASE 1	PHASE 2A	PHASE 2A DURATION
• Safety and immunogenicity of bivalent (RSV/hMPV) formulations • Healthy young and older adults • Constant RSV dosage level + multiple hMPV dosage levels • Single dose +/- adjuvant	• Safety and immunologic non-interference between VLPs; dosage and formulation selection • Healthy older adults • Multiple RSV and hMPV bivalent ratios	• Long-term safety and duration of immunogenicity (multi-year) • Healthy older adults

PRELIMINARY STUDY DESIGNS; SUBJECT TO CHANGE.

THESE STUDIES WILL HELP US OPTIMIZE OUR BIVALENT FORMULATION AND INFORM CLINICAL ENDPOINTS to be used for a potential POC Phase 2b efficacy study

Icosavax is the only company pursuing RSV and hMPV with the VLP modality; combination candidate planned to advance to Phase 1 in H2 2022

Older Adult RSV and / or hMPV Pipeline Candidates

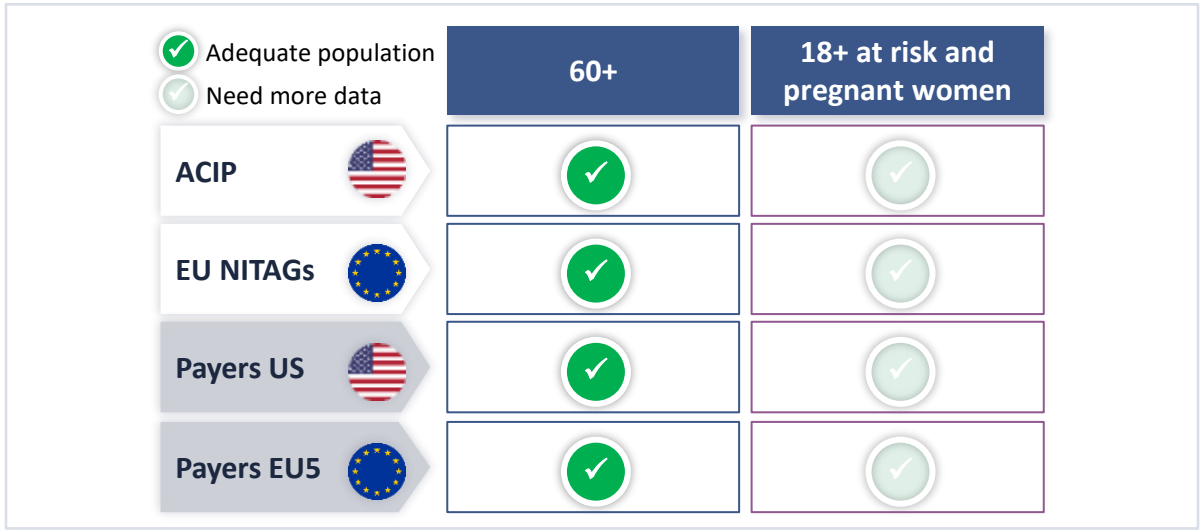


RSV-F = RSV F (fusion) protein antigen

A vaccine against RSV has the potential to be recommended by policy makers, which could drive rapid coverage and uptake; a combination RSV/hMPV vaccine may be preferred by vaccinators

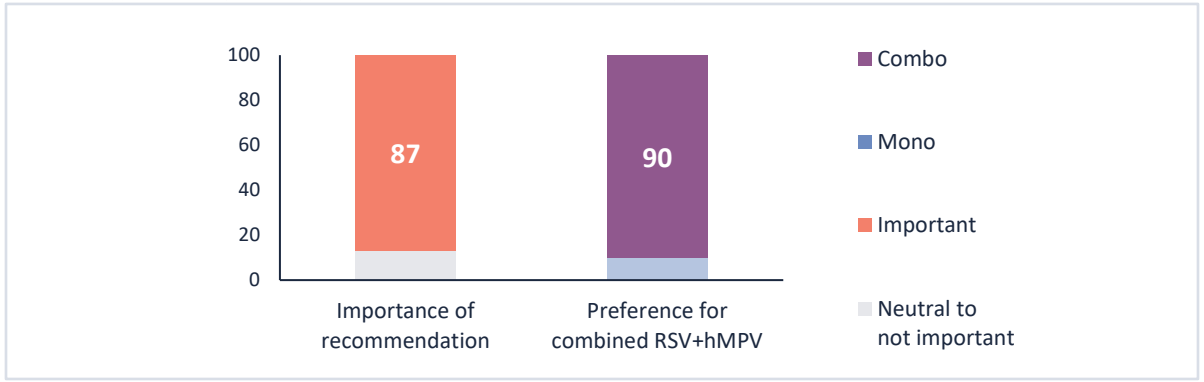
POLICY MAKERS AND PAYORS:

Anticipated recommendations for a RSV vaccine in adults



VACCINATORS:

Impact of policy recommendations and preference for combo vaccines



Primary and quantitative research*

- US and EU payors and policy makers; US vaccinators (physicians, pharmacists)

Findings support our hypotheses

- Once launched, any effective^ RSV vaccine targeting the older adult population could be included in policy guidelines (eg, ACIP) and on formularies
  - Applies to both monovalent and combination vaccines
- Policy recommendations drive immediate vaccine utilization
- Efficacy was the major driver of preference share
- If efficacy "equal" (within 25%), policy makers and vaccinators strongly preferred combination vaccines (more illness prevented w/ fewer vaccinations)

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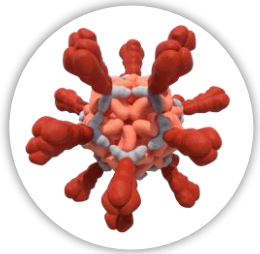
* Conducted by Research Partnership; ^ Minimal efficacy for inclusion in policy recommendations likely to be 50% reduction in severe infection due to pathogen of interest



COVID-19
Vaccine Candidate (IVX-411)

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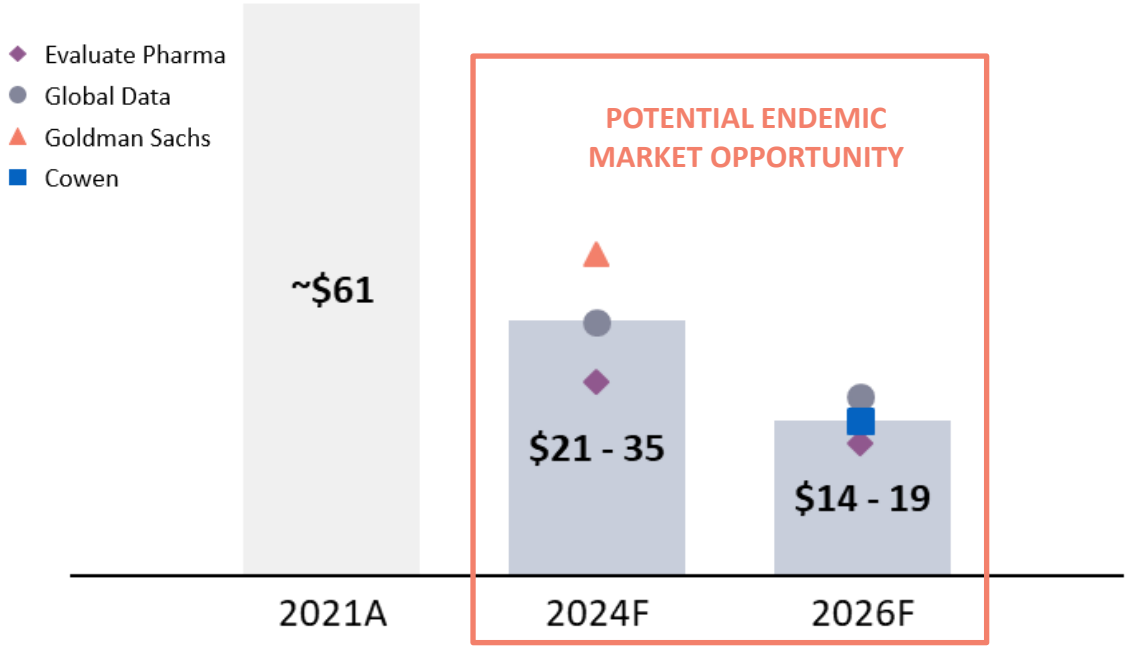
There is value beyond the pandemic – future endemic landscape offers an opportunity

Est. global sales forecasts for COVID-19 vaccines in 2024 and 2026

Bn USD



Emergence of variant strains, reactogenicity and limited durability of current approaches have created gaps/need for additional vaccine modalities

Expectations are for vaccines to shift from prime-boost regimens to regular boosters as SARS-CoV-2 becomes endemic

- 4th dose already authorized for immunocompromised and senior populations
- Likely general population will also continue to need/demand boosters

Share of current vaccines expected to decrease over time as additional technologies enter

- Offerings with lower reactogenicity and longer duration likely to win, and these are potential benefits of a VLP approach

Future market likely to shift toward combinations

- Combo vaccines likely to be preferred choice, and combinability is an expected benefit of VLP technology

WE BELIEVE THERE IS A SIGNIFICANT OPPORTUNITY FOR A VLP VACCINE IN THE COVID-19 MARKET

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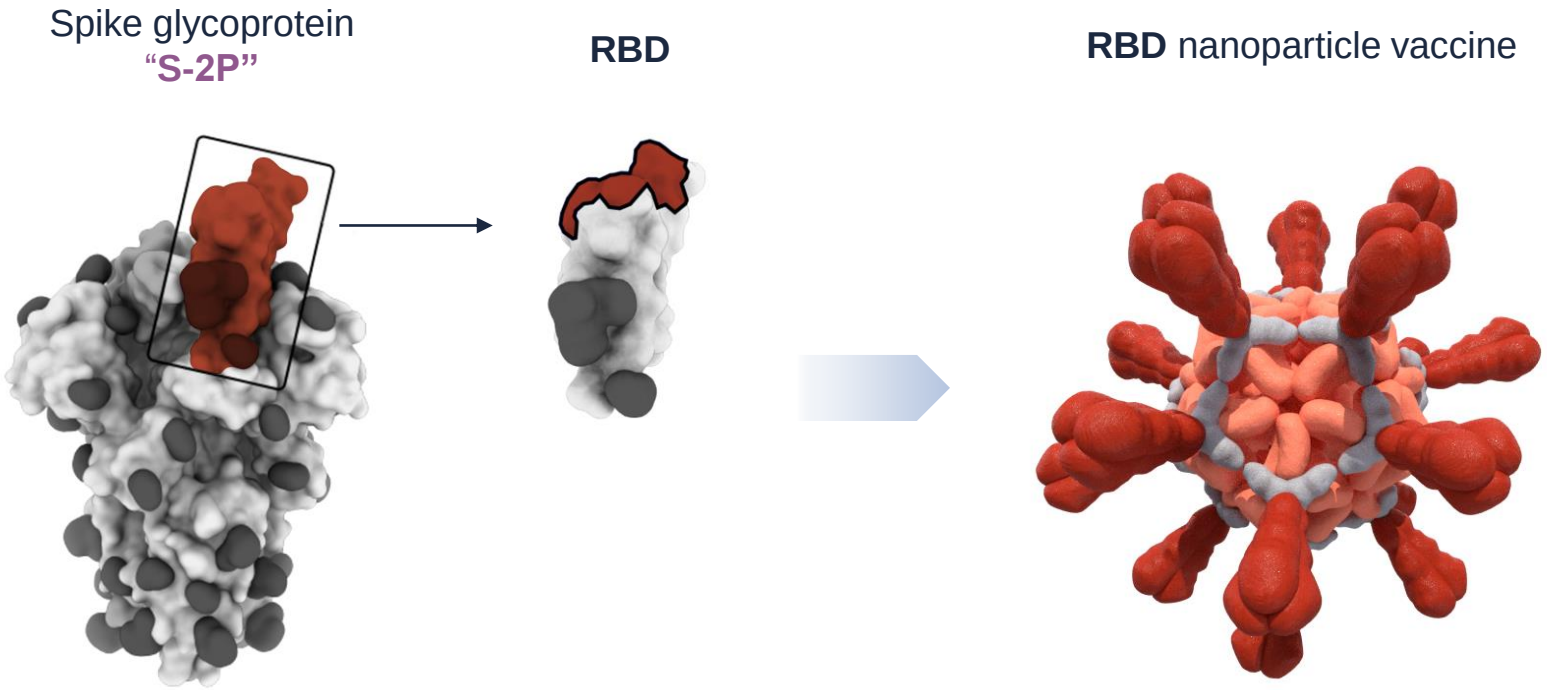
Forecast estimates extrapolated from: Goldman Sachs Pfizer initiating coverage 17Dec2021, Global Data Pharma COVID-19 Sales and Forecasts 2022 (does not include NVX-CoV-2373), Evaluate Pharma consensus forecasts, 2022 (does not include NVX-CoV-2373), Cowen Therapeutic Categories Outlook March 2022; Statista 2021

IVX-411 utilized a non-engineered receptor binding domain (RBD) antigen for SARS-CoV-2



- RBD: Critical functional domain of spike protein responsible for interaction with ACE2 receptor
- ~90% of neutralizing antibodies generated following infection in humans bind RBD; multiple epitopes lowers the likelihood of virus escape through mutation

COVID-19 PROVIDES OPTIONALITY within our combination vaccine vision

Piccoli et al 2020, *Cell*; Walls AC & Fiala B et al 2020, *Cell*

IVX-411 Investigation: Summary & Next Steps

- **An RBD VLP produced by the Institute for Protein Design was shown to stimulate robust and durable neutralizing antibody responses and protection in non-human primates***
  - This RBD VLP became the initial basis of Icosavax's COVID-19 program, with a molecule known as IVX-411
- **In March 2022, Icosavax announced results from its IVX-411 Phase 1/2 clinical study with immunogenicity inconsistent with expectations given the preclinical data**
  - A comprehensive investigation was launched, including review of antigen stability and characterization (drug substance intermediate, drug substance, drug product), and *in vivo* potency
- **Investigation results confirmed the hypothesis that reduced potency observed for IVX-411 was antigen-specific (i.e. not platform related)**
  - RBD antigen component (Component A) of IVX-411 is unstable over time at 2-8°C
  - *In vivo* assessment demonstrates this translates to a loss of potency of IVX-411 clinical lot, consistent with Phase 1/2 results
  - No corresponding instability trend has been seen to date with IVX-121 (RSV) and IVX-241 (hMPV) engineered antigen components or with fully-assembled VLPs at 2-8°C
  - Recent positive results from IVX-121 Phase 1 study confirm potency of RSV-F antigen on Icosavax two-component VLP platform
- **Next steps:**
  - Focusing on a bi-valent strategy for COVID-19 candidate displaying computationally engineered RBD antigens; provides optionality as a potential future component of combination vaccines

The RBD antigen component in IVX-411 is unstable;
investigation results indicate that instability is specific to IVX-411 and not other Icosavax programs

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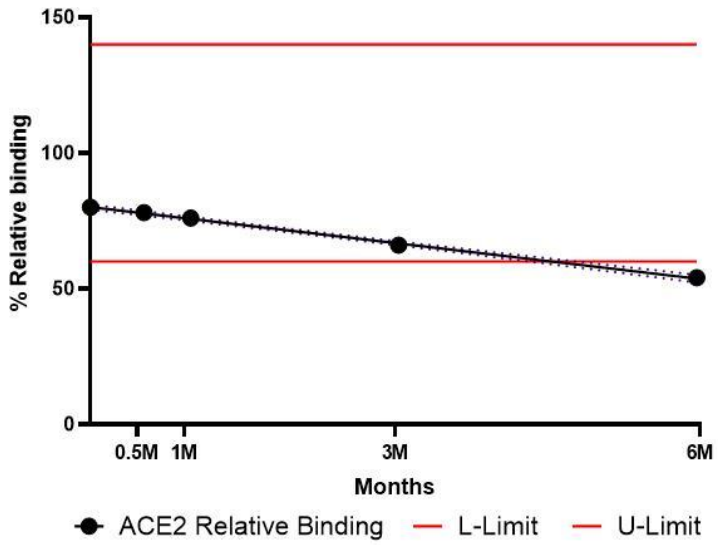
*Arunachalam et al 2021, Nature

Instability of IVX-411 over time is related to the non-engineered RBD antigen component; no corresponding instability trend is seen with the antigen component of IVX-121 at 2-8°C

CompA-RBD

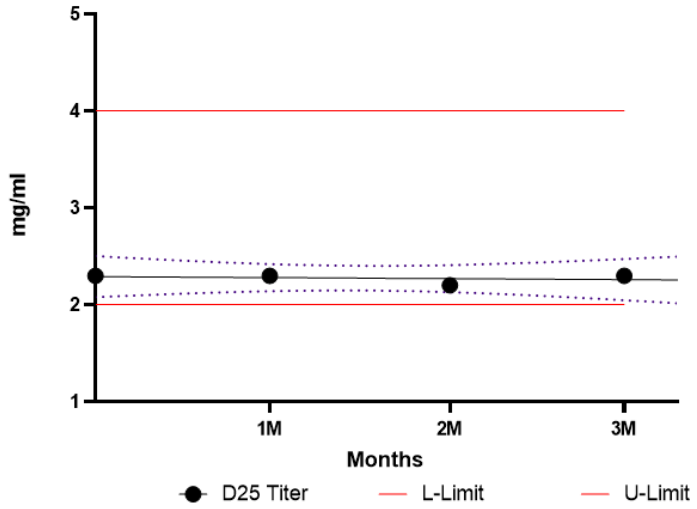
(IVX-411 Antigenic Component)



Strong trend for decrease in RBD CompA stability over time

CompA-RSV

(IVX-121 Antigenic Component)

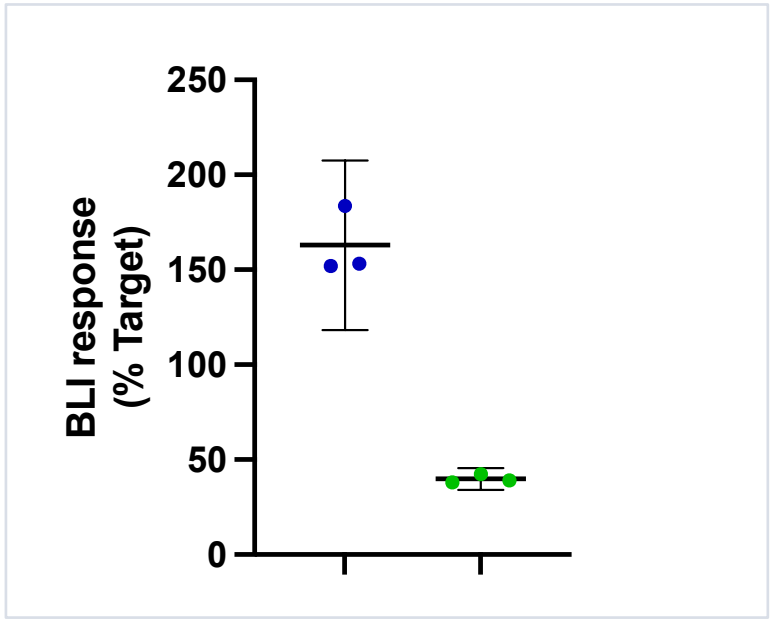


No trend for change in RSV CompA stability over time

Results show antigenic instability at 2-8°C of the RBD incorporated into IVX-411 (COVID-19)
Data to date indicate that this antigenic instability is not observed in other Icosavax vaccine candidates and is not platform related

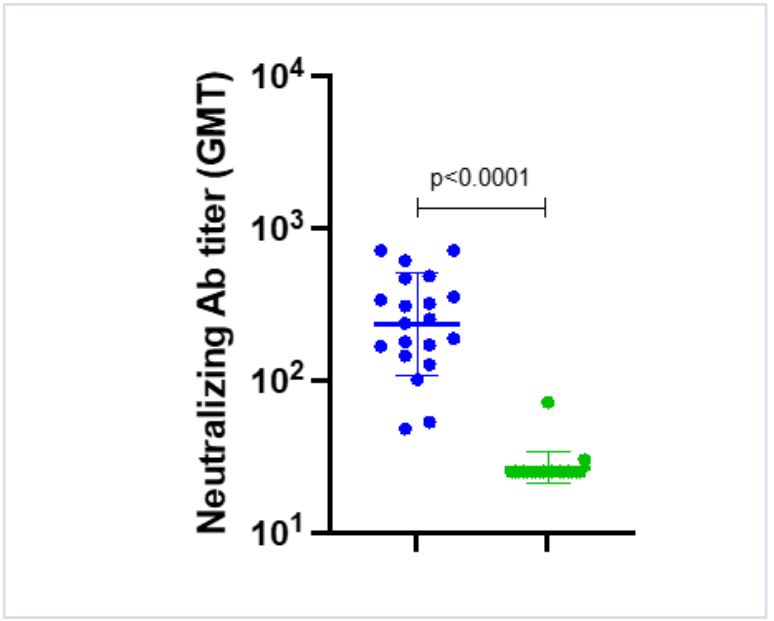
In vitro and *in vivo* analysis of IVX-411 demonstrates loss of antigen structure and potency over time at 2-8 °C

Potency: ACE2-Fc binding



- IPD lab-scale VLPs utilized for NHP study (<-65 °C)
- Icosavax clinical lot (GMP Drug Product, 2-8 °C)

Pseudoviral nAbs

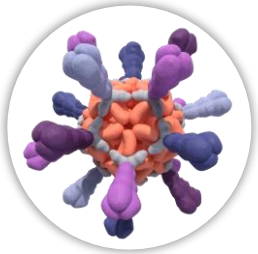


- Six different structural probes used to evaluate distinct regions on the antigen surface - similar trends observed with all structural probes evaluated

- Groups of 20 mice each were injected once with 10 ng of IVX-411 formulated with AddaVax – sera tested in pseudoviral neutralization test

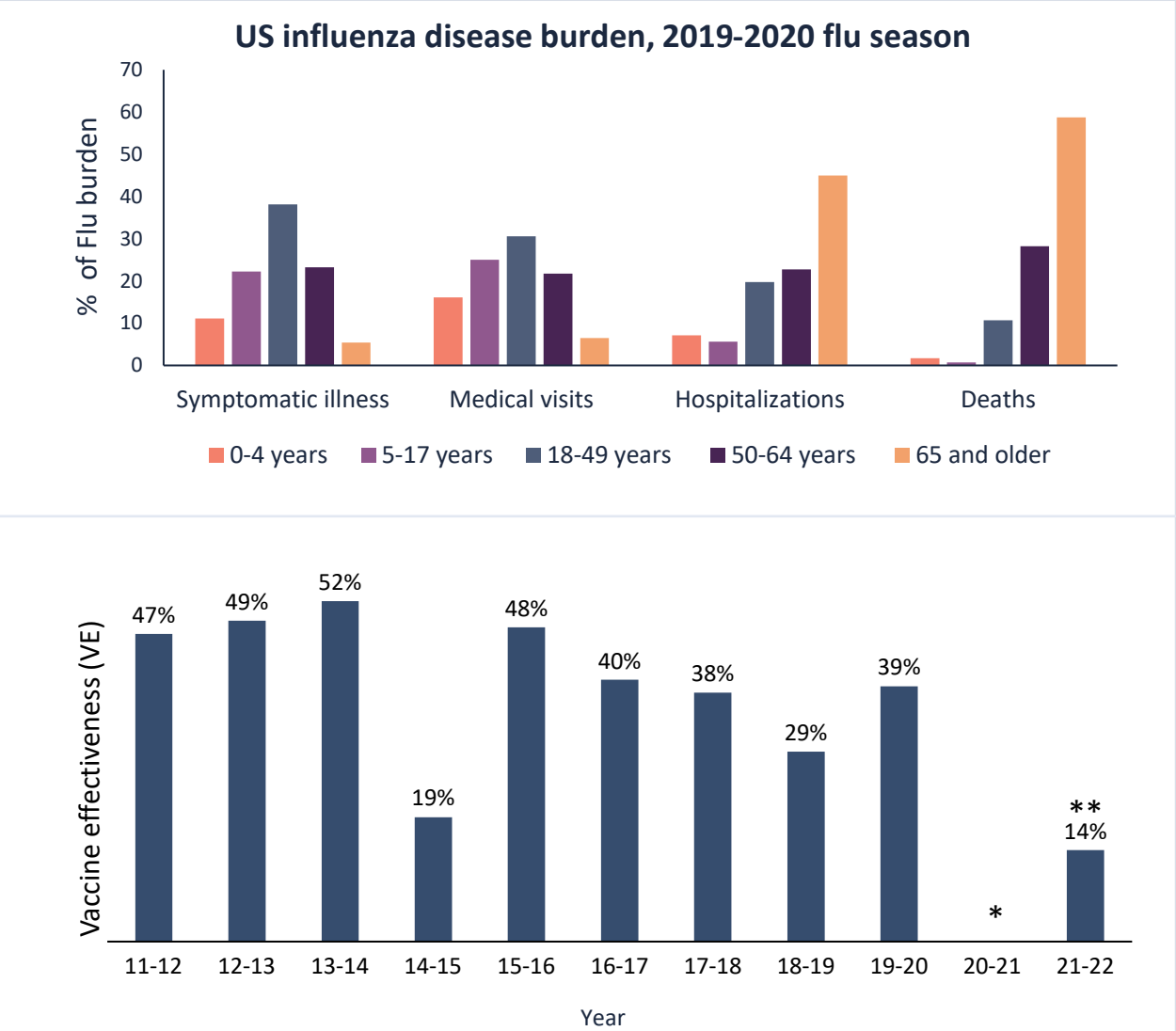
Modified potency method (BLI) can detect loss of antigen structure on VLP, with loss of signal following storage at 2-8 °C

***In vivo* assessment at low-dosages in mice demonstrates a corresponding loss of potency of clinical lot of IVX-411, consistent with IVX-411 Phase 1/2 results**



Flu Program

There is an unmet need for an influenza vaccine with improved efficacy, particularly in the older adult population



- Despite numerous marketed vaccines, influenza causes ~380K hospitalizations and ~20K deaths/year in the US—the majority in people over 65
- Existing vaccines have suboptimal efficacy (~14% - 50% over the last 10 years) and need to be updated every season
  - Vaccines designed to target a narrow subset of predicted strains; mispredictions common
  - Egg-adapted mutations can occur during manufacturing of egg-based vaccines
  - Antigenic variation drives loss of vaccine efficacy from season to season

* 2020-2021 flu vaccine effectiveness was not estimated due to low flu virus circulation during the 2020-2021 flu season;
** Interim vaccine effectiveness estimates, as of March 2022
Source: CDC flu seasonal burden and seasonal flu vaccine effectiveness studies

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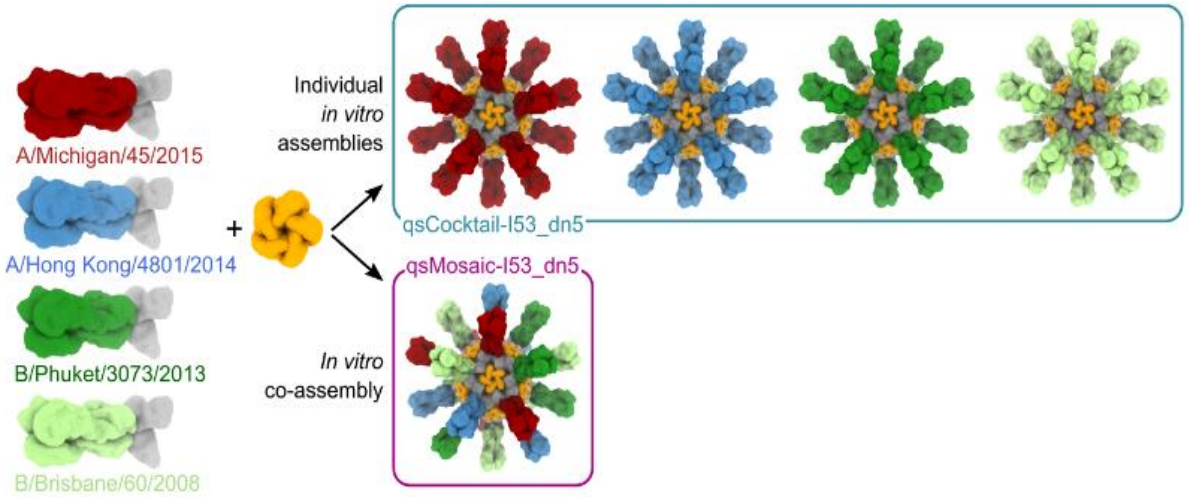
Flu program initiated – another strategic component of our vision

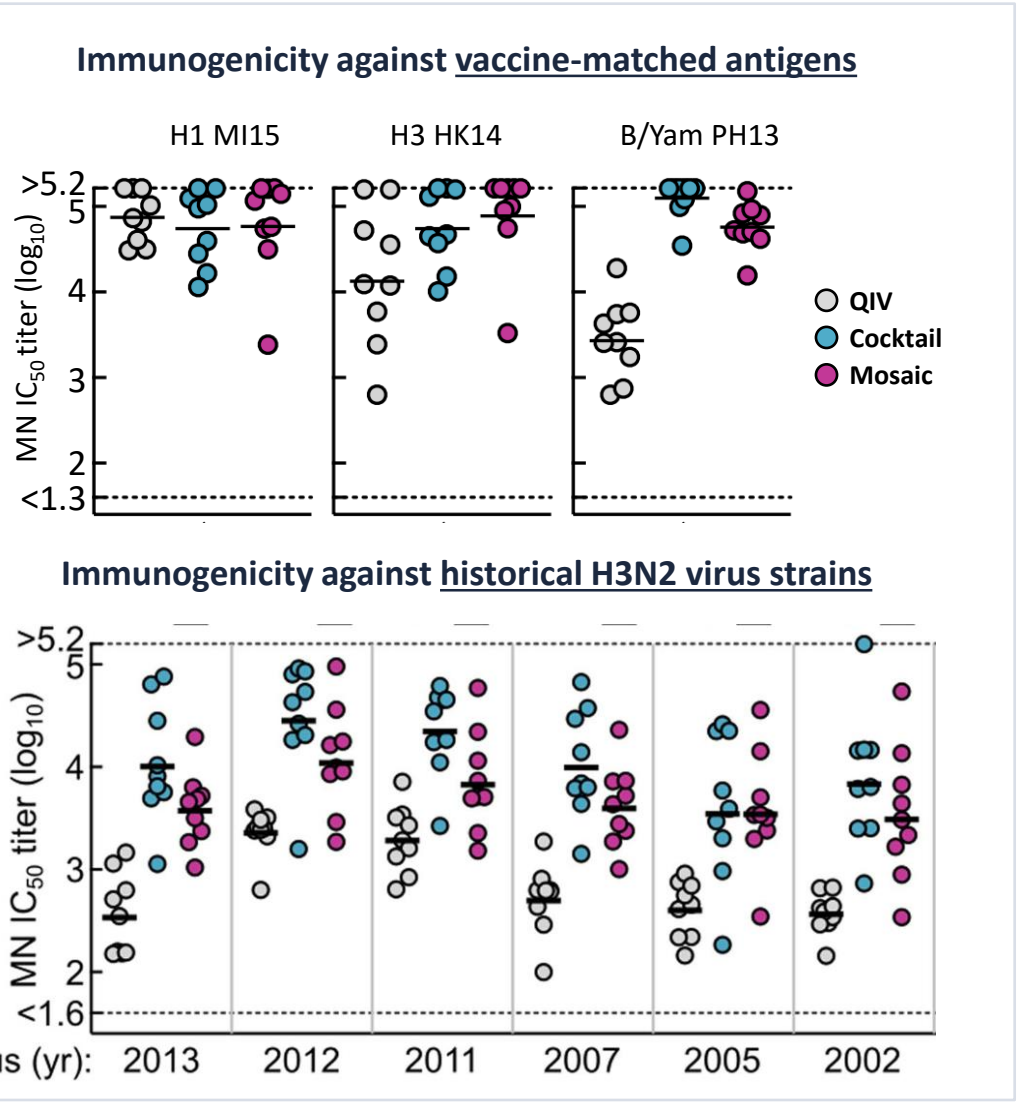
- Initial preclinical evaluation by NIH of a <u>precursor</u> VLP molecule utilized hemagglutinin (HA) protein from 4 flu strains onto VLPs either as a mixture of 4 different VLPs (cocktail) or on a single VLP presenting all 4 HA proteins (mosaic)
- The mosaic approach was selected for the initial proof-of-concept clinical study (NCT04896086) by NIH
  - Phase 1 study of the mosaic candidate initiated Q2 2021 in younger adults (18-50 y.o.), with Flucelvax used as active comparator; n= ~40 participants
  - Unadjuvanted



We have obtained a license from the UW and NIH and have begun candidate development

WE PLAN TO BUILD A RAPID PRODUCTION SYSTEM CAPABLE OF SUPPORTING SEASONAL FLU, which we expect to also enhance our pandemic response capabilities

UW/NIH data (precursor molecule): VLP display of antigens provided higher neutralizing titers and broader strain response



- In mice, ferrets (data shown) and non-human primates, precursor VLP vaccine candidates induced robust neutralizing antibody responses to both vaccine-matched antigens as well as to related virus strains
  - H3N2 is a particularly challenging strain for multiple commercial vaccines, including the commercial QIV comparison vaccine tested
  - VLPs also elicited better protection than QIV against several influenza strains in both mice and ferrets (data not shown)
- In these studies, presentation of influenza antigens on VLPs show potential to increase efficacy by protecting against seasonal variation

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Adapted from Boyoglu-Barnum et al 2021, *Nature*

In summary: Why Icosavax?

Leadership

EXECUTIVE TEAM

Adam Simpson
Chief Executive Officer

PVP BIOLOGICS
Cypher Genomics
MERITAGE PHARMA, INC.
verus Pharmaceuticals

Doug Holtzman, Ph.D. MPH
Chief Scientific Officer

Takeda
BILL & MELINDA GATES foundation
Ironwood
MILLENNIUM PHARMACEUTICALS, INC

Niranjan Kanesa-thasan, M.D. MTMH
Chief Medical Officer

NOVARTIS
gsk
WRAIR
Acambis

Tom Russo
Chief Financial Officer

MERCK
GILEAD
BAIRD
assemblybio

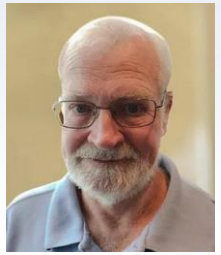
Cassia Cearley, Ph.D.
Chief Business Officer

APTINYX
naurex
Takeda
LEK

Elizabeth Bekiroğlu
General Counsel

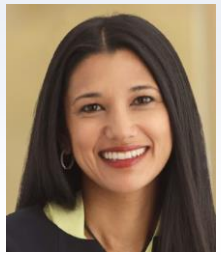
Seagen
emergent
ONCOTHYREON
FENWICK

Charles Richardson, Ph.D.
SVP, Technical Operations



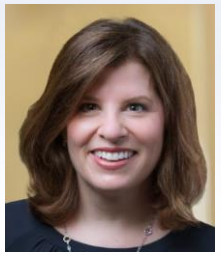
Takeda
LIGOCYTE
corixa

Ami Shah Brown, Ph.D., MPH
SVP, Regulatory Affairs



INOVIO
CIR
SABIN VACCINE INSTITUTE

Lori Stewart
VP, People and Culture



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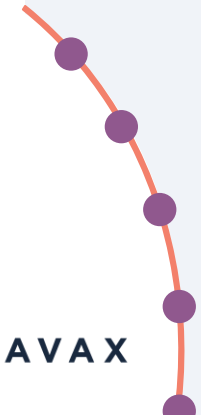
Key highlights



Developing VLP-based vaccines and combinations, with vision of pan-respiratory vaccines for older adults

Unique modality intentionally designed to mimic the structure of viruses to empower better immune response

VLPs have multiple potential benefits—and offer multiple manufacturing advantages and attractive commercial opportunities in major areas of unmet need

RSV vaccine candidate IVX-121 recently reported **positive topline interim data from Phase 1/1b**; first combination candidate and lead program, **IVX-A12 for RSV/hMPV** planned to enter Phase 1 later this year

COVID-19 development to focus on bi-valent strategy utilizing structurally engineered RBD antigens; provides optionality as a potential future component of combination vaccines

Emerging flu program in preclinical development

Continuing to expand capabilities, including new research team bringing state-of-the-art antigen design, optimizing speed in manufacturing, etc.

Experienced team with extensive expertise in protein design and vaccine development supported by leading healthcare investors and distinguished Scientific Advisory Board

Novel VLP technology with multiple near-term value inflection points

CANDIDATE	INDICATION	ACHIEVED MILESTONES 2021/2022	UPCOMING MILESTONES
IVX-121	**RSV**	✓ DP release; CTA approval ✓ Ph 1/1b topline interim data ✓ Advancing to IVX-A12 bivalent RSV/hMPV candidate	• Phase 1b extension, 6 mo. data **[early '23]** • Phase 1b extension, 12 mo. data **[mid '23]**
IVX-A12	**RSV/hMPV**	✓ hMPV candidate selection ✓ Pre-IND meeting	• IND submission **[H2'22]** • Phase 1 initiation **[H2'22]** • Phase 1 topline data **[mid '23*]** • Phase 2a initiation **[H2'23*]**
SARS-CoV-2 candidate	**COVID-19**	✓ DP release; CTN approval ✓ IVX-411 Phase 1/2 top-line interim data ✓ End-to-end drug product investigation	• Bivalent candidate selection **[2023]**
Flu Program	**Influenza**	✓ Exercised option for patent license from UW and HHS	• Candidate selection **[2023]**

Cash balance $244 million (as of 6/30/2022^) currently expected to fund operations through at least 2024

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*Dependent on initiating Phase 1 study of IVX-A12 in H2'22; ^ Cash and cash equivalents, restricted cash, and short-term investments

Appendix

High neutralizing antibody (nAb) titers may be key to better protection

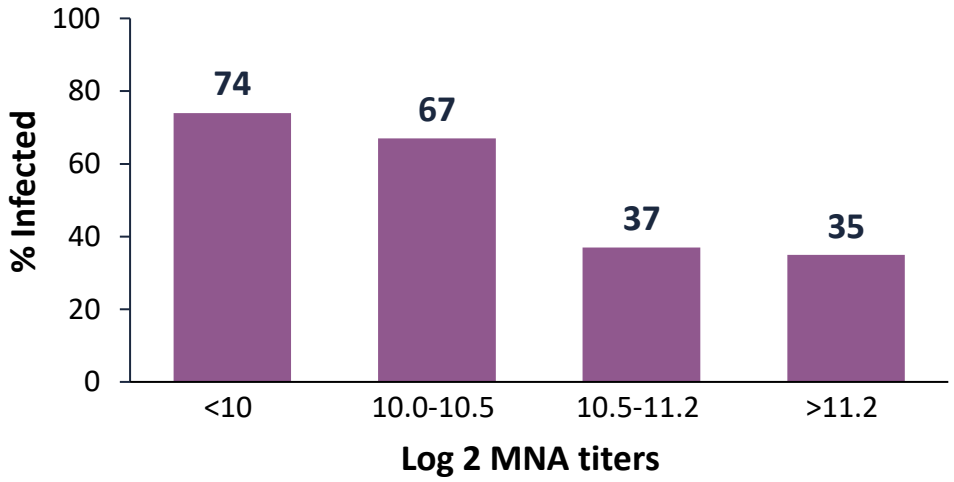
RSV: Increase in neutralization titers highly correlated with decrease in ARI odds ratio

GEOMETRIC MEAN NAB TITER (GMT LOG_2)	OR OF ARI^
<9.01	2.92
11.1-12.0	0.86
>13.0	0.22

Every log_2 increase in nAb titer correlates with reduced risk of disease

Phase 2 Sanofi study of a postfusion RSV vaccine in high-risk elderly; followed subjects for 2 years and tracked RSV infection (PCR).

hMPV: Higher serum neutralizing antibody levels protected against infection



Small study of infected adults and age-matched uninfected control subjects.

Every log_2 improvement in nAb titers believed to LEAD TO A CLINICALLY RELEVANT IMPROVEMENT IN DISEASE OUTCOME

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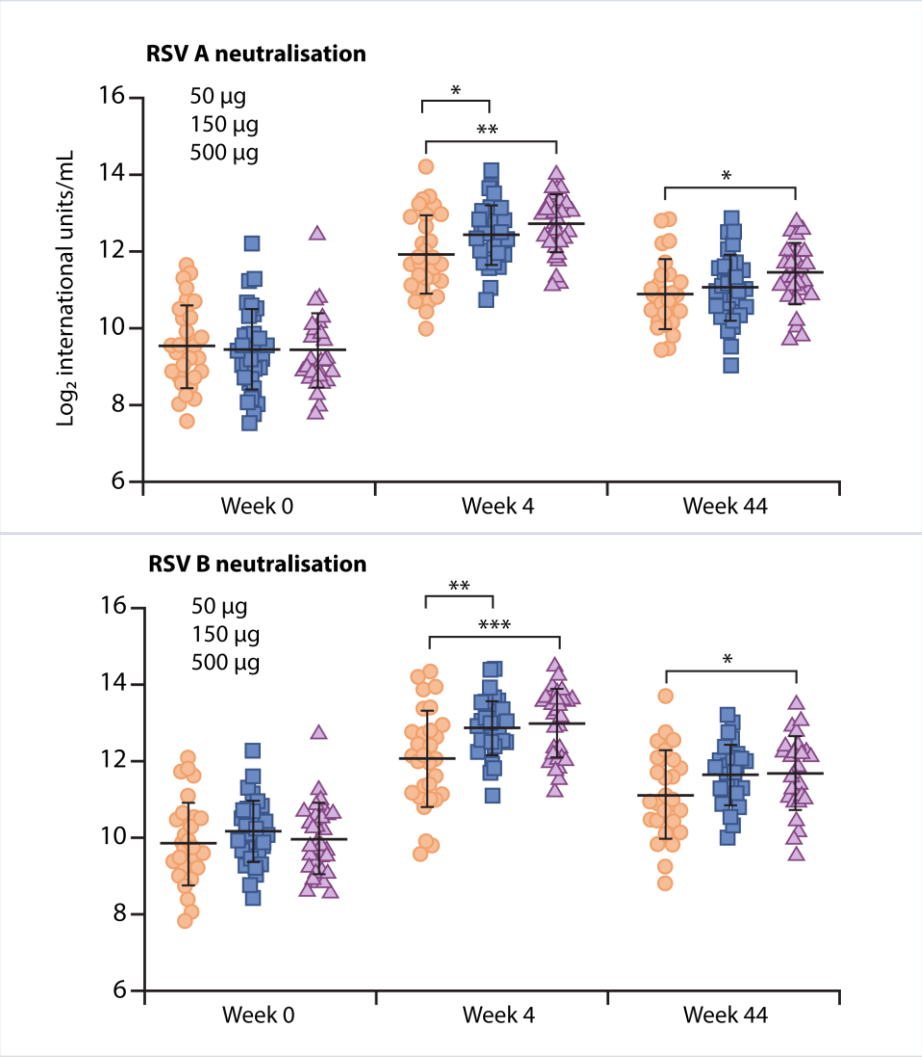
^ OR = odds ratio; defines the relative risk of acute respiratory infection (ARI) for individuals with a specific level of neutralizing antibody

Falsey, ResViNet, Malaga 2017 (data adapted for table on left); data from Falsey et al 2008, *J Infect Dis*; Walsh et al 2004; Falsey et al 2010

IVX-121 for RSV: Clinical data support DS-Cav1 as improved prefusion F antigen



- NIH DS-Cav1 Phase 1 study explored long-term immunogenicity and dosing in young adults (N=95)
  - Reference point for Phase 1 portion of IVX-121 study
- 50, 150, 500 µg +/- alum adjuvant
  - Transient dose effect at week 4, marginal at week 44
  - Effect of alum adjuvant minimal in this population
- Neutralizing antibody responses to RSV A and RSV B of similar magnitude, with both significantly higher than baseline
  - RSV A nAb highly correlated with RSV B nAb
  - RSV A up to ~5-10x above baseline at week 4 (~5-7x at comparable antigen dose equivalents to IVX-121) and ~3–4x above baseline at week 44; opportunity to improve on antibody persistence
- Second dose at 12 weeks did not affect long-term immunogenicity; following interim, switched to single dose

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Ruckwardt et al 2021; *Lancet Respiratory Dis*; ****p<0·0001, ***p<0·001, **p<0·01, and *p<0·05; Alum adjuvanted and non-adjuvanted data combined in figure

Key takeaways from IVX-411 Phase 1/2 topline data readout

Study met primary safety and immunogenicity objectives:

- Phase 1 in primary setting (n = 84). 2 doses, 28 days apart: 5, 25, 125 µg IVX-411 dosage levels +/- adjuvant
- Phase 2 in booster setting (n = 84). 1 dose, 3-6 months after completion of primary regimen: 5, 25, 125 µg IVX-411 +/- adjuvant

IVX-411 was generally safe and well tolerated

- Frequency of observed solicited and unsolicited adverse events (AEs) comparable with placebo
- Mild to moderate reactogenicity, none severe nor dose-limiting. No related serious AEs or AEs of special interest

Immunogenicity shown in primary and booster vaccination

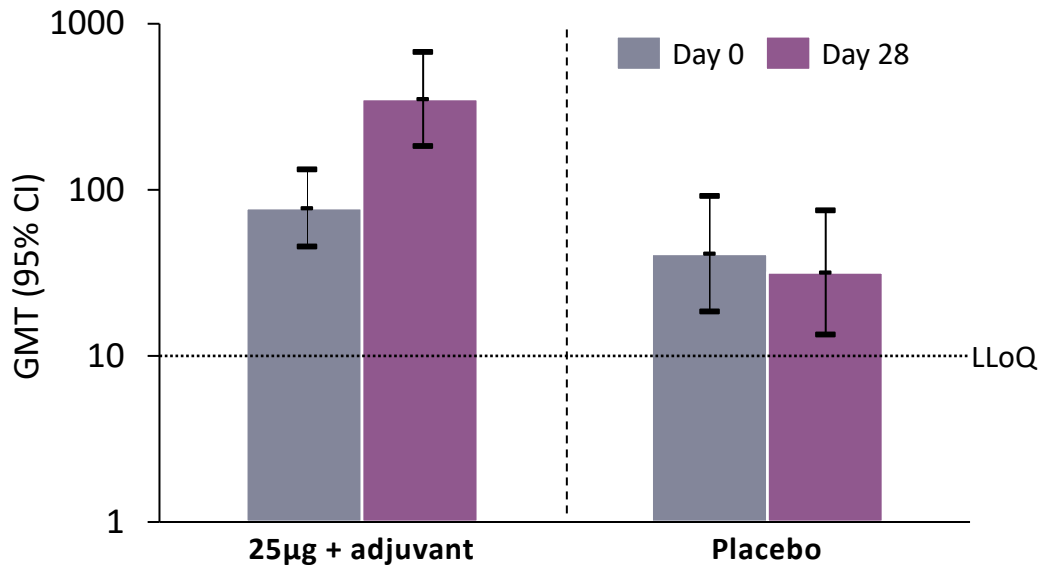
- Primary: Magnitude of nAb and IgG antibody titers for Wild-Type (WT) comparable to or below the Human Convalescent Sera (HCS) levels and above placebo in primary vaccination. High rates of seroconversion in adjuvanted groups
- Booster: Heterologous boosting after mRNA (3/4) and adeno (1/4) primary vaccination induced up to 5x rise from baseline for WT
- Variants: Immune responses seen across all variants of concern (beta, delta, omicron) in primary and booster vaccination context

IMMUNOGENICITY INCONSISTENT WITH EXPECTATIONS for RBD-VLP based on available preclinical data and VLP technology platforms

IVX-411 exhibited a booster immunogenicity effect against both wild-type and Omicron strains

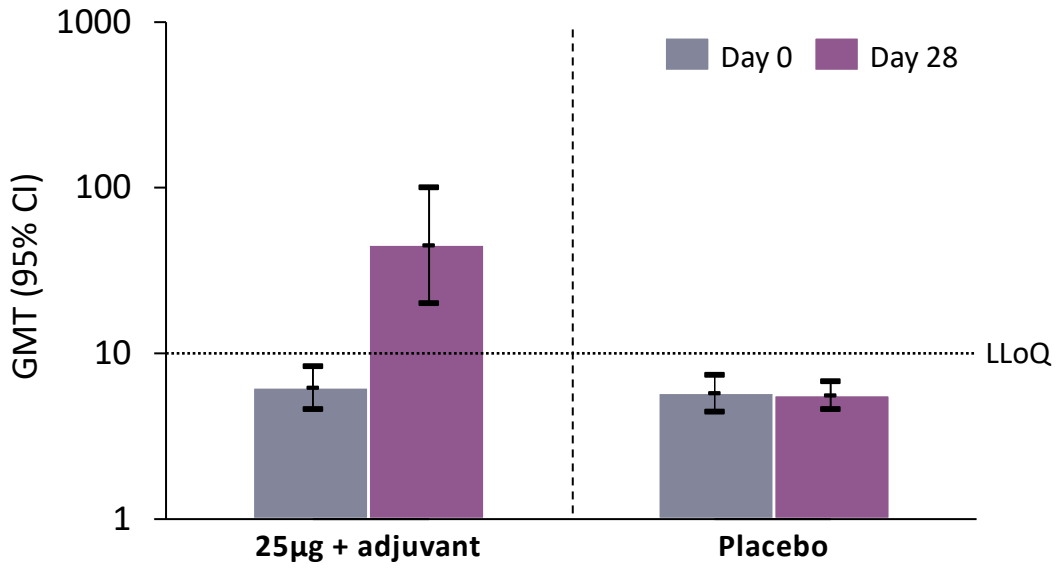
IVX-411 Phase 1/2 Trial

Wild Type



N	11	11	12	12
FOLD-RISE VS BL	-	5	-	1

Omicron



N	11	11	12	12
FOLD-RISE VS BL	-	7	-	1

ADMINISTRATION OF IVX-411 3-6 MONTHS FOLLOWING IMMUNIZATION WITH LICENSED MRNA OR ADENOVIRAL VECTOR BASED VACCINES resulted in a fold-rise of up to 5x or 7x vs. baseline for wild-type and Omicron strains, respectively

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One of six IVX-411 dosage levels tested is shown; laboratory titers are reported for comparison; day 28 fold-rise vs baseline shown; seroresponse is a 4-fold or greater increase in titers from baseline (Day 0)

Data from comparable SK Bio VLP technology suggests possible lack of potency with IVX-411

	SK BIO UNADJUVANTED GBP510, SERORESPONSE RATE*	ICOSAVAX UNADJUVANTED IVX-411, SERORESPONSE RATE**
Primary 2-dose regimen (assay)	Up to 51% (PBNA) Up to 78% (PRNT)	Up to 17% (MNT)
Heterologous booster regimen (assay)	N/A^	Up to 64% (MNT)

- SK Bio and Icosavax licensed the same VLP technology in the COVID-19 field from University of Washington with very similar RBD antigens incorporated into their candidate vaccines: GBP510 and IVX-411 respectively
- When adjuvanted, GBP510 induced up to 6-fold rise in nAb titers vs. HCS^^; IVX-411 fold rise was ≤ 1
- The precise formulations and manufacturing processes are likely different between the candidate vaccines
- An investigation into the potential causes of the apparent lack of clinical potency has been initiated

ROOT CAUSE INVESTIGATION FOR LOW POTENCY UNDERWAY, including antigen stability and characterization and in vivo potency

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*SK Bio data source: Joon Young Song et al 2022 – medRxiv preprint; ** Icosavax seroresponse defined as ≥4 fold rise in Nab levels relative to baseline; ^ SK Bio heterologous booster trial is in combination with AS03 adjuvant; ^^ SK Bio used NIBSC HCS panel with low, mid, and high NAb titers, SK Bio used pseudovirion NT (PBNA) and plaque reduction (PRNT) assays while Icosavax used microneutralization (MNT) assay