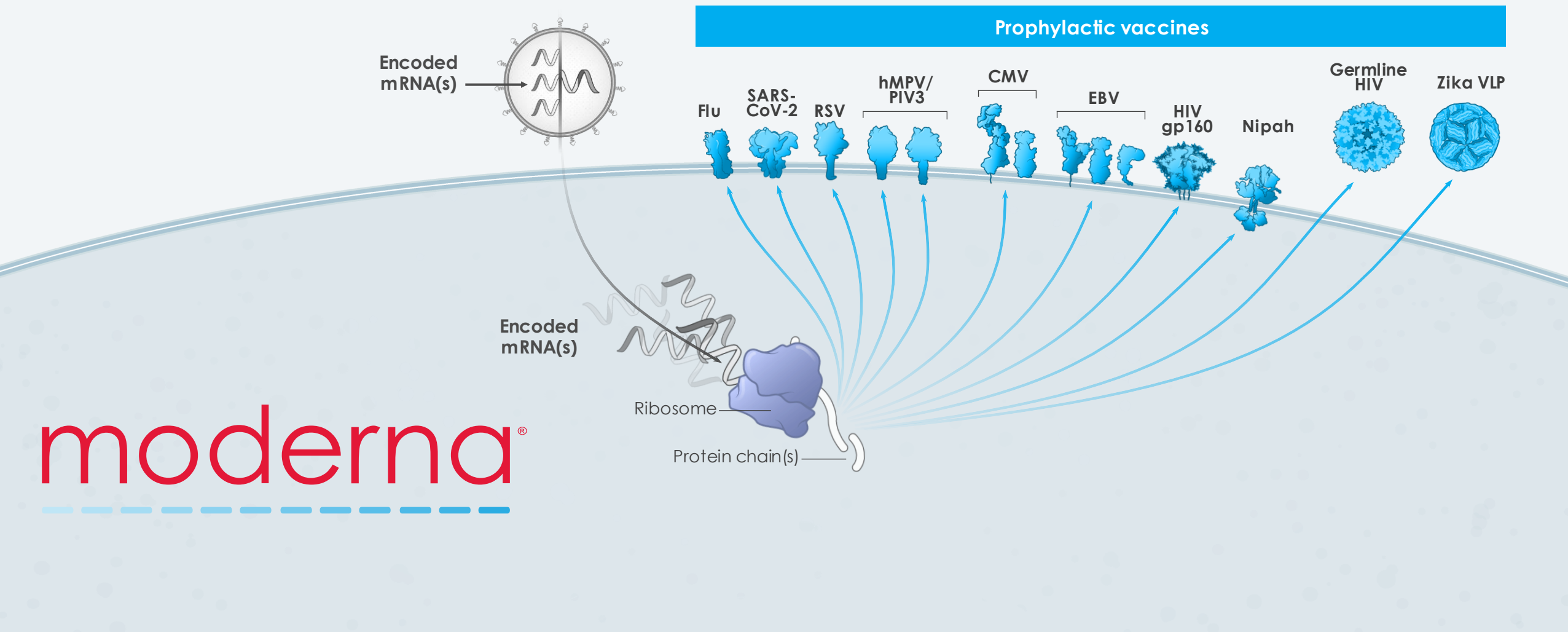




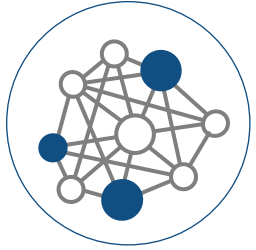
Second Annual Vaccines Day

Wednesday, April 14th, 2021

Forward-looking statements and disclaimer

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including statements regarding: the Company's investments to accelerate the development of its mRNA vaccine pipeline; the safety profile and tolerability of the Company's vaccines and the potential of these vaccine candidates to trigger an immune response (including vaccines for RSV (mRNA-1345) and CMV (mRNA-1647)); the Company's ability to develop vaccines with complex antigens and combination vaccines, and the speed and flexibility of the Company's development platform; the size and potential future growth of the market for vaccines; the Company's development of a vaccine (mRNA-1273) to protect against the SARS-CoV-2 virus; the ability of mRNA-1273 to protect against COVID-19 over time; the Company's ability to develop vaccines against variants of the SARS-CoV-2 virus and the protection conferred by those variant-specific vaccines; plans for adolescent and pediatric clinical studies of the Moderna COVID-19 Vaccine and its potential administration in those populations; the need for booster vaccines against the SARS-CoV-2 virus and its variants; the Company's production and supply of its COVID-19 vaccine to the U.S. government and other customers and the anticipated timing for those deliveries; the estimated medical costs associated with respiratory viruses; the lack of association between administration of mRNA-1273 and cerebral venous sinus thrombosis or thrombotic events; the Company's development and clinical trial plans for various vaccines, including against hMPV/PIV3 (mRNA-1653), Zika (mRNA-1893), Nipah virus (mRNA-1215), Epstein-Barr virus (mRNA-1189) and CMV (mRNA-1647); the Company's plans to develop vaccine candidates against HIV (mRNA-1644 and mRNA-1574) and coordination efforts with third parties and strategic partners and to launch clinical trials for those vaccine candidates; the Company's development of vaccine candidates against seasonal influenza and the timing for clinical trials of those vaccine candidates; and the Company's plans to increase ethnic diversity and representation in clinical trials. In some cases, forward-looking statements can be identified by terminology such as "will," "may," "should," "could," "expects," "intends," "plans," "aims," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. The forward-looking statements in this presentation are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond Moderna's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. These risks, uncertainties, and other factors include, among others: the fact that there has never been a commercial product utilizing mRNA technology approved for use; the fact that the rapid response technology in use by Moderna is still being developed and implemented; the safety, tolerability and efficacy profile of the Moderna COVID-19 Vaccine observed to date may change adversely in ongoing analyses of trial data or subsequent to commercialization; the Moderna COVID-19 Vaccine may prove less effective against variants of the SARS-CoV-2 virus, or the Company may be unsuccessful in developing future versions of its vaccine against these variants; despite having ongoing interactions with the FDA or other regulatory agencies, the FDA or such other regulatory agencies may not agree with the Company's regulatory approval strategies, components of our filings, such as clinical trial designs, conduct and methodologies, or the sufficiency of data submitted; Moderna may encounter delays in meeting manufacturing or supply timelines or disruptions in its distribution plans for the Moderna COVID-19 Vaccine; whether and when any biologics license applications and/or additional emergency use authorization applications may be filed in various jurisdictions and ultimately approved by regulatory authorities; potential adverse impacts due to the global COVID-19 pandemic such as delays in regulatory review, manufacturing and clinical trials, supply chain interruptions, adverse effects on healthcare systems and disruption of the global economy; and those other risks and uncertainties described under the heading "Risk Factors" in Moderna's most recent Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (SEC) and in subsequent filings made by Moderna with the SEC, which are available on the SEC's website at www.sec.gov. Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this presentation in the event of new information, future developments or otherwise. These forward-looking statements are based on Moderna's current expectations and speak only as of the date hereof.

We believed mRNA would disrupt the traditional vaccine market



High **biological fidelity**

Ability to do **complex antigens**

Ability to do **combinations**

High Efficacy



Speed

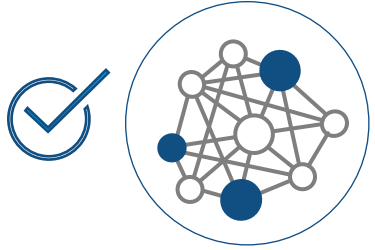
mRNA is a platform – ability to go from sequence to the clinic to approved products in record time



**Flexible
manufacturing**

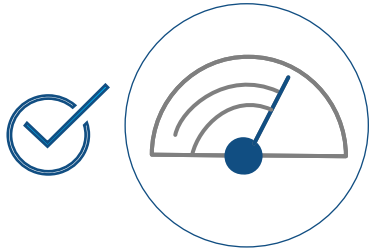
No need for dedicated plants – ability to go from mRNA vaccines to mRNA therapeutics using the same process
Cell-free manufacturing process

Now we know mRNA will disrupt the traditional vaccine market



High Efficacy

High **biological fidelity**
Ability to do **complex antigens**
Ability to do **combinations**



Speed

mRNA is a platform – ability to go from sequence to the clinic to approved products in record time



Flexible manufacturing

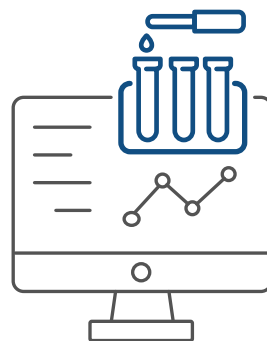
No need for dedicated plants – ability to go from mRNA vaccines to mRNA therapeutics using the same process
Cell-free manufacturing process

Now we **KNOW**
mRNA vaccines
can achieve all
three

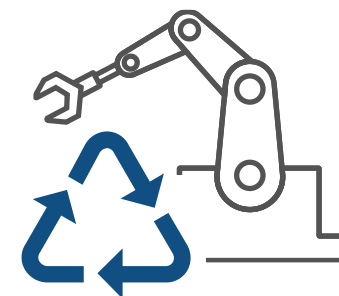
Where do we go next?

We believe our mRNA vaccines will have a significant impact on human health

Largest first-in class vaccine portfolio



We do it fully digitally and embed AI in how we run the company



We design and develop best-in-class vaccines while growing sustainably



We believe this is a large commercial opportunity

1

The vaccine market is large and growing (current market is ~\$35B (2020)¹)

2

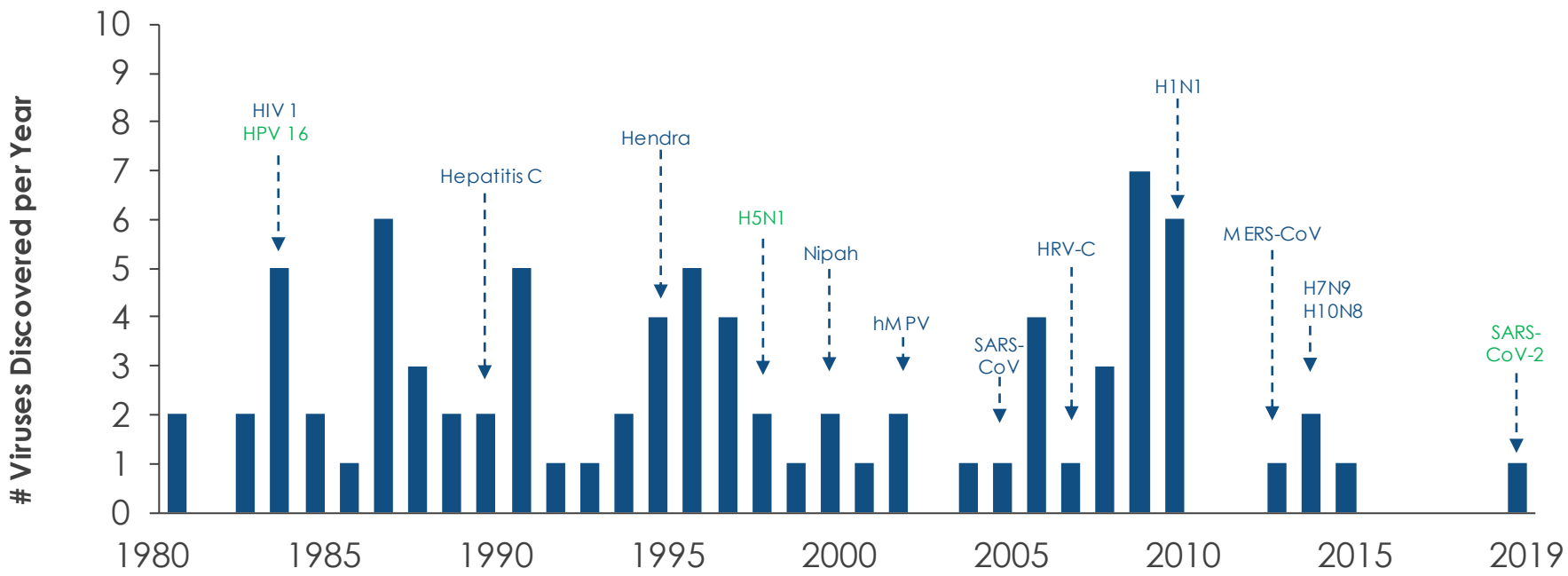
New vaccines against viruses for which there are no vaccines on the market

3

New vaccines to materially improve efficacy and/or safety of currently approved vaccines

80+ new viruses discovered since 1980... but vaccines on the market against only 3 of these viruses

Novel Viruses Discovered, (1980 - 2019)



Commercial market (2021 estimates) or annual direct medical costs exceeds **>\$100B** for these viruses

DISCOVERED BEFORE 1980

Select viruses:	Yellow fever (1901)	PIV3 (1950s)	VZV (1954)	EBV (1964)	Lassa (1969)
	Rubella (1941)	Chikungunya (1952)	RSV (1956)	Hepatitis B (1965)	Ebola (1976)
	Dengue (1943)	Zika (1952)	CMV (1956-1957)	Marburg (1967)	

Sources: Institute of Medicine (US) Forum on Microbial Threats (2009); Medscape Medical News (2008); Lederburg, J. *Emerging Infectious Diseases from the Global to the Local Perspective: A Summary of a Workshop of the Forum on Emerging Infections* (2001); National Institutes of Health (US) Biological Sciences Curriculum Study (2007); Holshue, M. et al. *NEJM* (2020); Bush, L. *Emerging and Re-emerging Infectious Diseases* (2015); Gibbs, A.J. *Virology* (2009); CDC Zika Overview; CDC Ebola About; Plotkin, S.A. *Clinical Infectious Diseases* (2004); Woolhouse, M. et al. *Phil Trans R Soc* (2012); WHO H7N9 China Update (2018); Tapparel, C. et al. *Virology* (2013); Hepatitis B Foundation. *History Page*; Ho, M. *Med Microbiol Immunol* (2008); Nature. *Dengue Viruses Page*; Brauburger, K. et al. *Viruses* (2012); FDA approved vaccine list; CDC RSV Overview; Hendrickson, K.J. *Clinical Microbiology Reviews* (2003); Andersson, J. *Herpes* (2000); WHO Chikungunya Overview; CDC Varicella Overview; CDC Lassa Fever Overview; Xu, Y. et al. *Infect Genet Evol* (2015).

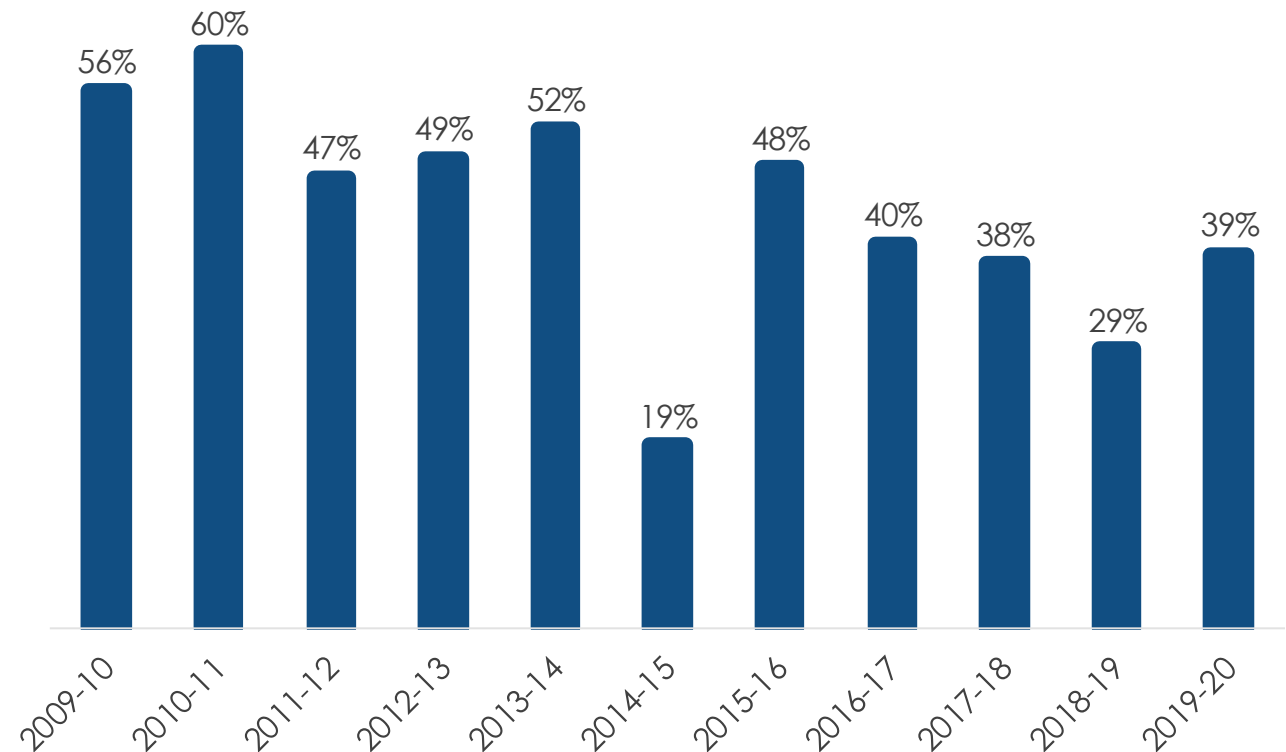
We believe we can improve upon vaccines that underserve the market with low efficacy

Influenza vaccines

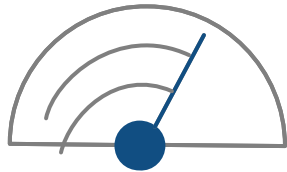
Currently approved vaccines are ~40-60% effective and face significant challenges from strain mismatch¹

High-risk groups would benefit from higher efficacy

Influenza Vaccine Effectiveness²



We believe our mRNA platform has competitive advantages



Speed

Accelerated research and development timelines

Received authorization for our COVID-19 vaccine in 11 months



Capital Efficiency

We are making up to 1 billion doses of our Moderna COVID-19 vaccine

Simultaneously advancing 9 mRNA vaccine programs

Largest first in class vaccine development pipeline in the industry

9 vaccine programs for major unmet needs

Program		ID #	Preclinical development	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
COVID-19 vaccine		mRNA-1273 mRNA-1273.351/-211 mRNA-1283		mRNA-1283	mRNA-1273.351/-211			Worldwide BARDA funded
Cytomegalovirus (CMV) vaccine		mRNA-1647						Worldwide
hMPV/PIV3 vaccine		mRNA-1653						Worldwide
Zika vaccine		mRNA-1893						Worldwide BARDA funded
Respiratory syncytial virus (RSV) vaccine		mRNA-1345						Worldwide
Epstein-Barr virus (EBV) vaccine		mRNA-1189						Worldwide
Flu vaccine		mRNA-1010 mRNA-1020 mRNA-1030						Worldwide
Nipah vaccine		mRNA-1215						Worldwide NIH funded
HIV vaccine		mRNA-1644 mRNA-1574						Worldwide IAVI/BMGF/NIAID and others funded
Influenza H7N9 vaccine		mRNA-1851						Worldwide Advancing subject to funding

Today's speakers from Moderna



Stéphane Bancel
Chief Executive Officer



Stephen Hoge, M.D.
President



**Melanie Ivarsson,
Ph.D., M.B.A.**
Chief Development
Officer



**Corinne M. Le
Goff, Pharm.D.,
M.B.A.**
Chief Commercial
Officer



**Jacqueline Miller,
M.D.**
Senior Vice President,
Therapeutic Area Head,
Infectious Diseases



**Lori Panther, M.D.,
M.P.H.**
Vice President,
Clinical Development,
Infectious Diseases



Tal Zaks, M.D., Ph.D.
Chief Medical Officer

Agenda

8:00 - 8:10 AM	Introduction of mRNA Vaccine Platform	Stéphane Bancel, CEO
8:10 - 8:20 AM	Overview of Clinical Experience with Moderna's COVID-19 Vaccine	Tal Zaks, M.D., Ph.D., CMO
8:20 - 8:45 AM	Commercial Update on Moderna's COVID-19 vaccine	Corinne Le Goff, Pharm.D., M.B.A., CCO
8:45 - 9:30 AM	Infectious Disease Vaccine Strategy	Stephen Hoge, M.D., President
9:30 - 10:45 AM	Vaccines Against Respiratory Diseases	Jacqueline Miller, M.D., SVP Sir Jeremy Farrar, OBE FMedSci FRS, Director of Wellcome Professor Miles P Davenport, University of New South Wales, Head, Infection Analytics Program, Kirby Institute Benjamin Cowling, BSc, PhD, FFPH, Division of Epidemiology and Biostatistics, School of Public Health, The University of Hong Kong
10:45 - 10:50 AM	Coffee Break	
10:50 - 11:50 AM	Public Health Vaccines	Jacqueline Miller, M.D., SVP William Schief, Ph.D., Director for Vaccine Design at the International Aids Vaccine Initiative (IAVI)
11:50 - 12:30 PM	Vaccines Against Complex Antigens	Jacqueline Miller M.D., SVP Lori Panther, M.D., M.P.H., VP Melanie Ivarsson, Ph.D., M.B.A, CDO
12:30 - 12:45 PM	Commercial Vaccines Business Model	Corinne Le Goff, Pharm.D., M.B.A., CCO
12:45 - 1:00 PM	Conclusion	Stéphane Bancel, CEO
1:00 - 1:30 PM	Q&A	



Overview of Clinical Experience with Moderna's COVID-19 Vaccine

Tal Zaks, M.D., Ph.D.

Chief Medical Officer

Moderna COVID-19 Vaccine: Authorized Use & Safety Information

Authorized Use in the United States:

The Moderna COVID-19 Vaccine has not been approved or licensed by the US Food and Drug Administration (FDA), but has been authorized for emergency use by FDA, under an Emergency Use Authorization (EUA), to prevent Coronavirus Disease 2019 (COVID-19) for use in individuals 18 years of age and older. There is no FDA-approved vaccine to prevent COVID-19.

The EUA for the Moderna COVID-19 Vaccine is in effect for the duration of the COVID-19 EUA declaration justifying emergency use of the product, unless the declaration is terminated or the authorization is revoked sooner.

Important Safety Information:

- Do not administer the Moderna COVID-19 Vaccine to individuals with a known history of severe allergic reaction (e.g., anaphylaxis) to any component of the Moderna COVID-19 Vaccine.
- Appropriate medical treatment to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of the Moderna COVID-19 Vaccine. Monitor Moderna COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention guidelines (<https://www.cdc.gov/vaccines/covid-19/>).
- Immunocompromised persons, including individuals receiving immunosuppressive therapy, may have a diminished response to the Moderna COVID-19 Vaccine.
- The Moderna COVID-19 Vaccine may not protect all vaccine recipients.
- Adverse reactions reported in a clinical trial following administration of the Moderna COVID-19 Vaccine include pain at the injection site, fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting, axillary swelling/tenderness, fever, swelling at the injection site, and erythema at the injection site. Additional adverse reactions, some of which may be serious, may become apparent with more widespread use of the Moderna COVID-19 Vaccine. Severe allergic reactions, including anaphylaxis, have been reported following administration of the Moderna COVID-19 Vaccine during mass vaccination outside of clinical trials.
- Available data on Moderna COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy. Data are not available to assess the effects of Moderna COVID-19 Vaccine on the breastfed infant or on milk production/excretion.
- There are no data available on the interchangeability of the Moderna COVID-19 Vaccine with other COVID-19 vaccines to complete the vaccination series. Individuals who have received one dose of Moderna COVID-19 Vaccine should receive a second dose of Moderna COVID-19 Vaccine to complete the vaccination series.
- Additional adverse reactions, some of which may be serious, may become apparent with more widespread use of the Moderna COVID-19 Vaccine.
- Vaccination providers must complete and submit reports to VAERS online at <https://vaers.hhs.gov/reportevent.html>. For further assistance with reporting to VAERS, call 1-800-822-7967. The reports should include the words " Moderna COVID- 19 Vaccine EUA " in the description section of the report.

Safety profile allowed for accelerated clinical development

✓ Phase 2 study planning started after early Phase 1 safety data became available

✓ Phase 1 safety and immunogenicity were the basis for the Phase 3 dose selection of 100 µg

Vaccine safety profile known 6 weeks post second-dose

Phase 1
started

March 16th

Phase 2
started

May 29th

Phase 3
started

July 27th

COVID-19 Vaccine (mRNA-1273) saw similar reactogenicity in clinical trials

Phase 1: Reactogenicity at the 100 µg dose level (n=45)¹

- Most reported systemic adverse reactions following second vaccination were **fatigue** (80%), **chills** (80%), **headache** (60%) and **myalgia** (53%)
- The most common local adverse reaction was **pain after injection** (100%)
- Adverse reactions were transient and mild or moderate in severity

Phase 3: Reactogenicity at the 100 µg dose level (n=30,406)²

- Solicited systemic adverse events were most commonly **headache, fatigue and myalgia**
- Most common solicited adverse reactions (ARs) after the two-dose series was **injection site pain** (86.0%)
- The majority of local solicited ARs occurred within the first one to two days after injection and generally persisted for a median of one to two days

Reactogenicity profiles of mRNA vaccines in v-safe monitoring are consistent with what was observed in clinical trials (CDC)³

Real-world evidence of the Moderna COVID-19 vaccine is consistent with the clinical trials

Moderna Vaccinations in the U.S. (CDC)¹



>85
million

Moderna COVID-19 vaccines administered

CDC and Prevention V-safe Surveillance System (December 14, 2020, to February 28, 2021)²

Solicited local & systemic reactions 0 to 7 days after vaccination	Dose 1 (%) (n=1,984,194)	Dose 2 (%) (n=949,497)
Pain	71.4%	78.3%
Redness	7.4%	19.2%
Swelling	13.6%	26.2%
Itching	6.8%	16.2%
Fatigue	32.5%	60.0%
Headache	26.9%	53.2%
Myalgia	21.3%	51.4%
Chills	10.3%	40.0%
Fever	10.0%	37.6%
Joint pain	9.8%	31.5%
Nausea	8.1%	20.2%

AR's less than 10%: Vomiting, Diarrhea, Abdominal pain, rash outside of injection site

Statement on CVST and thrombotic events

A comprehensive assessment of the totality of the available safety data for mRNA-1273 after over 64.5 million doses administered globally does not suggest an association with CVST or thrombotic events*

"To date, V AERS has received no reports of CVST with thrombocytopenia among persons who received either of the two mRNA-based COVID-19 vaccines." (CDC)³

CVST: Cerebral venous sinus thrombosis

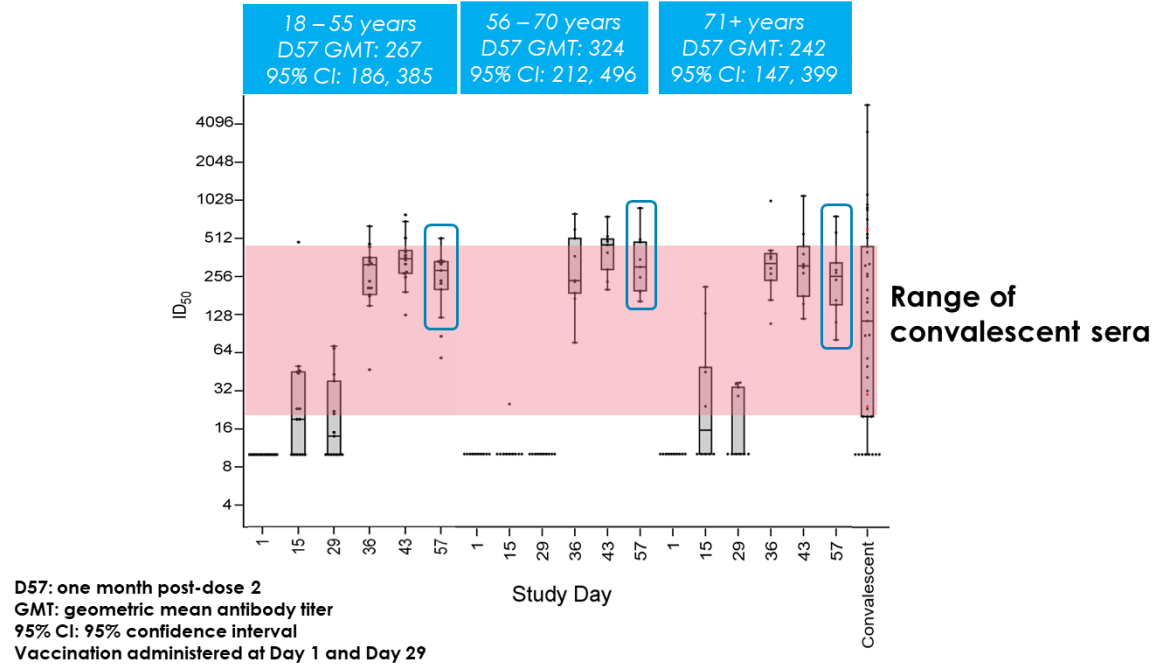
* Analyses performed using data through March 22, 2021. Number of vaccinations was derived from the CDC website, ECDC website, and inferred for other countries based on distribution and the proportion of doses distributed administered in EX-US settings

(1) CDC, COVID-19 Vaccinations in the United States, <https://covid.cdc.gov/covid-data-tracker/#vaccinations>
(2) Chapin-Bardales J, Gee J, Myers T, et al., "Reactogenicity Following Receipt of mRNA-Based COVID-19 Vaccines," JAMA (05 Apr. 2021), <https://jamanetwork.com/journals/jama/fullarticle/2778441?guestAccessKey=faeccfe9-4d32-4467-a7ce-1fd8370a50bd>
(3) CDC, <https://emergency.cdc.gov/han/2021/han00442.asp>

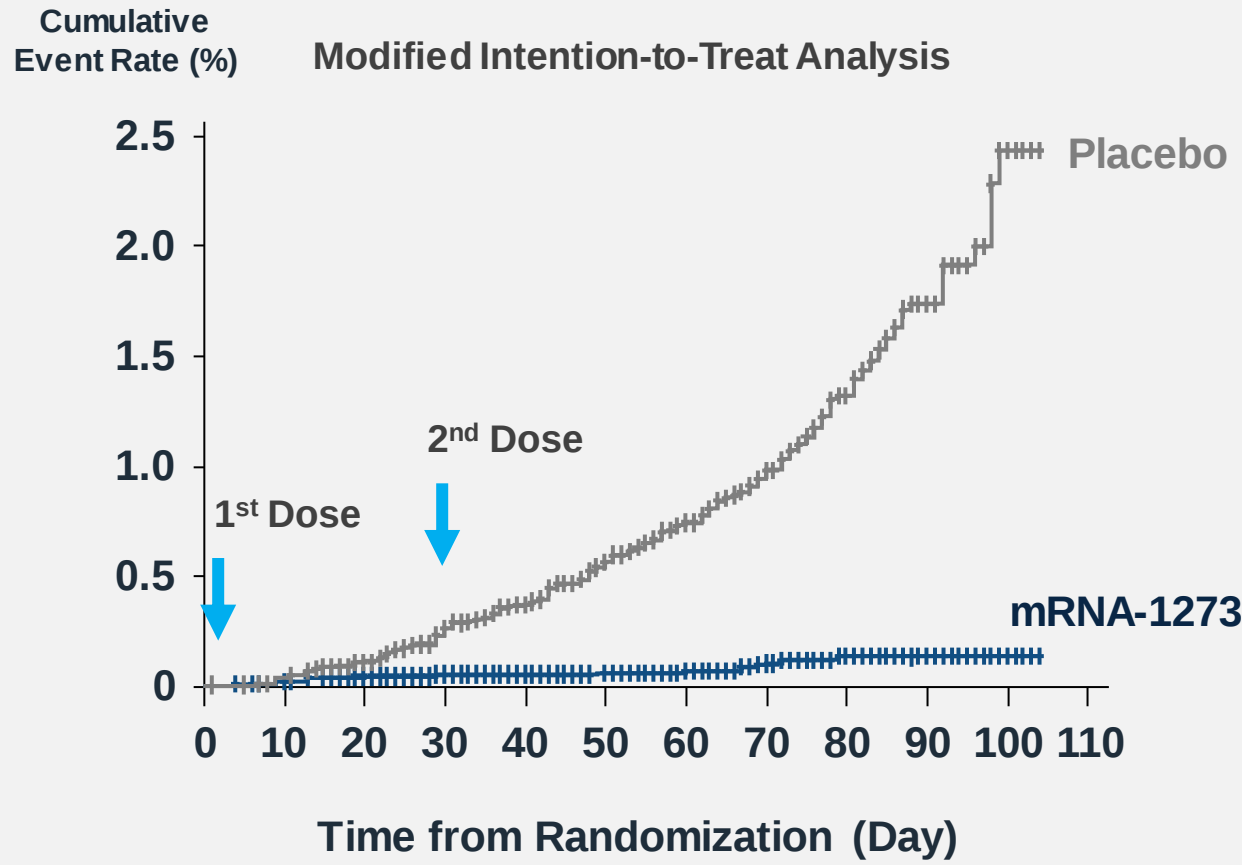
Neutralizing antibodies are correlated to strong efficacy

Phase 1: Neutralizing antibody titers were above convalescent sera¹

Pseudovirus neutralization assay titers (ID₅₀)- 100 µg at Day 1 and Day 29



Phase 3 Vaccine: Efficacy from the Primary Efficacy Analysis²: 94.1%





Commercial Update on Moderna's COVID-19 Vaccine

Corinne M. Le Goff, PharmD, MBA

Chief Commercial Officer

Our COVID-19 vaccine is reaching across the globe

Signed deals

 Signed APAs

- **United States** (300 million doses with option for additional 200 million doses)
- **European Union** (310 million doses with option for additional 150 million doses in 2022)
- **Japan** (50 million doses)
- **Canada** (44 million doses)
- **South Korea** (40 million doses)
- **Philippines** (20 million doses)
- **United Kingdom** (17 million doses)
- **Switzerland** (13.5 million doses)
- **Colombia** (10 million doses)
- **Israel** (6 million doses)
- **Taiwan** (5 million doses)
- **Qatar**
- **Singapore**



We have independent supply chains for US and international markets

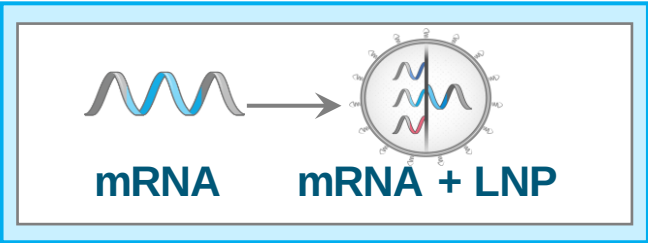


Independent supply chains

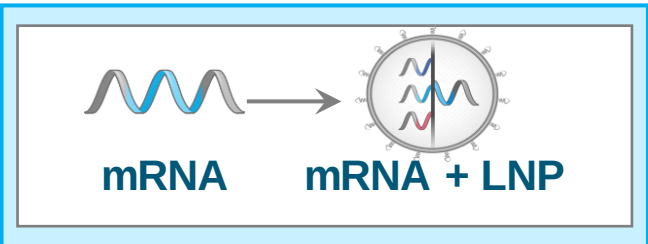
Manufacturing scale up to supply 700 million to 1 billion doses in 2021



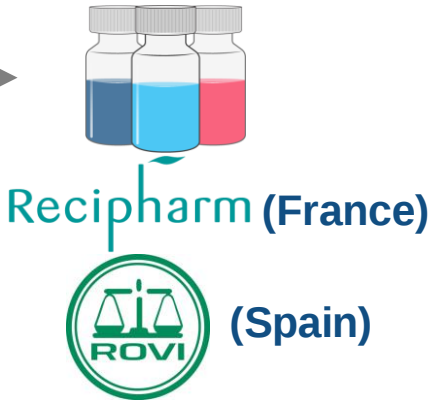
moderna + **Lonza** (US)
Pharma & Biotech



Catalent
Baxter



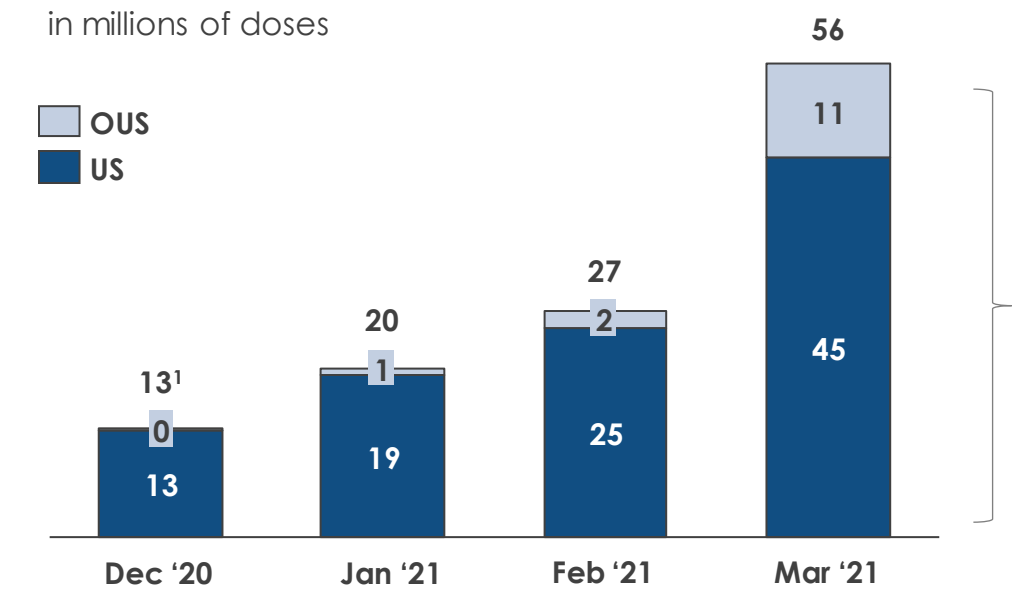
Lonza (Switzerland)
Pharma & Biotech



To date approximately 132 million doses of our COVID-19 vaccine have been delivered to the US and around the world

Moderna COVID-19 Vaccine Deliveries

(only deliveries that meet revenue recognition criteria)
in millions of doses



International scale-up is approximately one quarter behind U.S.



Region	1Q deliveries	1Q Average Selling Price (\$)
US	88	\$15.4 ²
OUS	14	\$22 - 37 (volume-based pricing)

¹Does not include an additional 4 million doses delivered to BARDA, which were not accounted for as product sales

²Average selling price to the U.S. Government does not reflect approximately ~\$1B in received and expected reimbursements under the BARDA Agreement for clinical development and technical scale-up of mRNA-1273

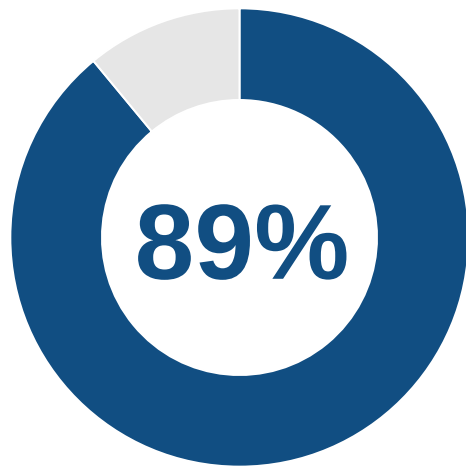
We are proud and humbled to be in the position of helping return life to normal



>1 million consumer social media posts mentioning #moderna



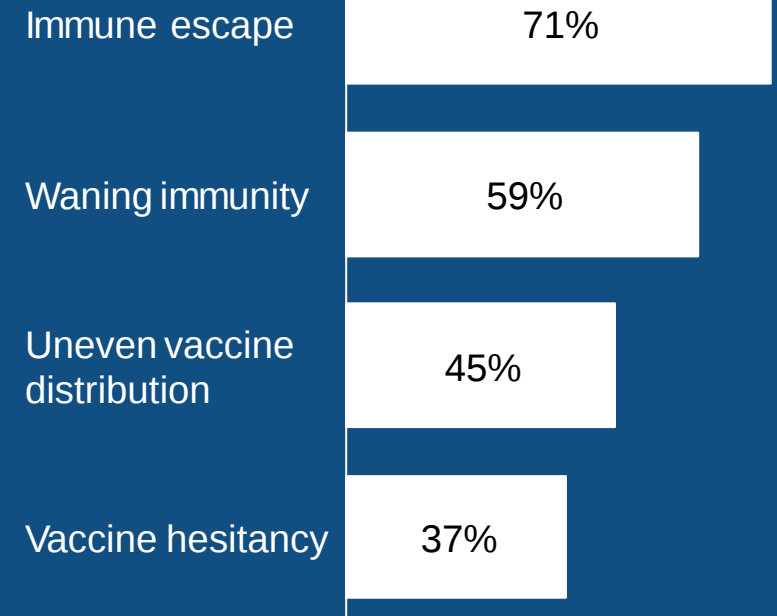
Expert immunologists expect SARS-CoV-2 to become an endemic virus



of immunologists surveyed consider it likely or very likely that COVID-19 will become endemic

Top driving factors

Respondents who selected each factor



Moderna is well positioned to address variants of concern

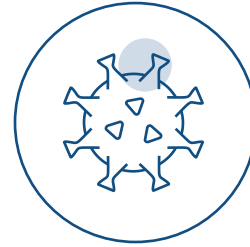
Moderna advantages to address variants



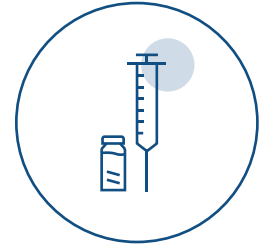
Rapid
development



Rapid response
manufacturing



Potential for
multivalent
boosters

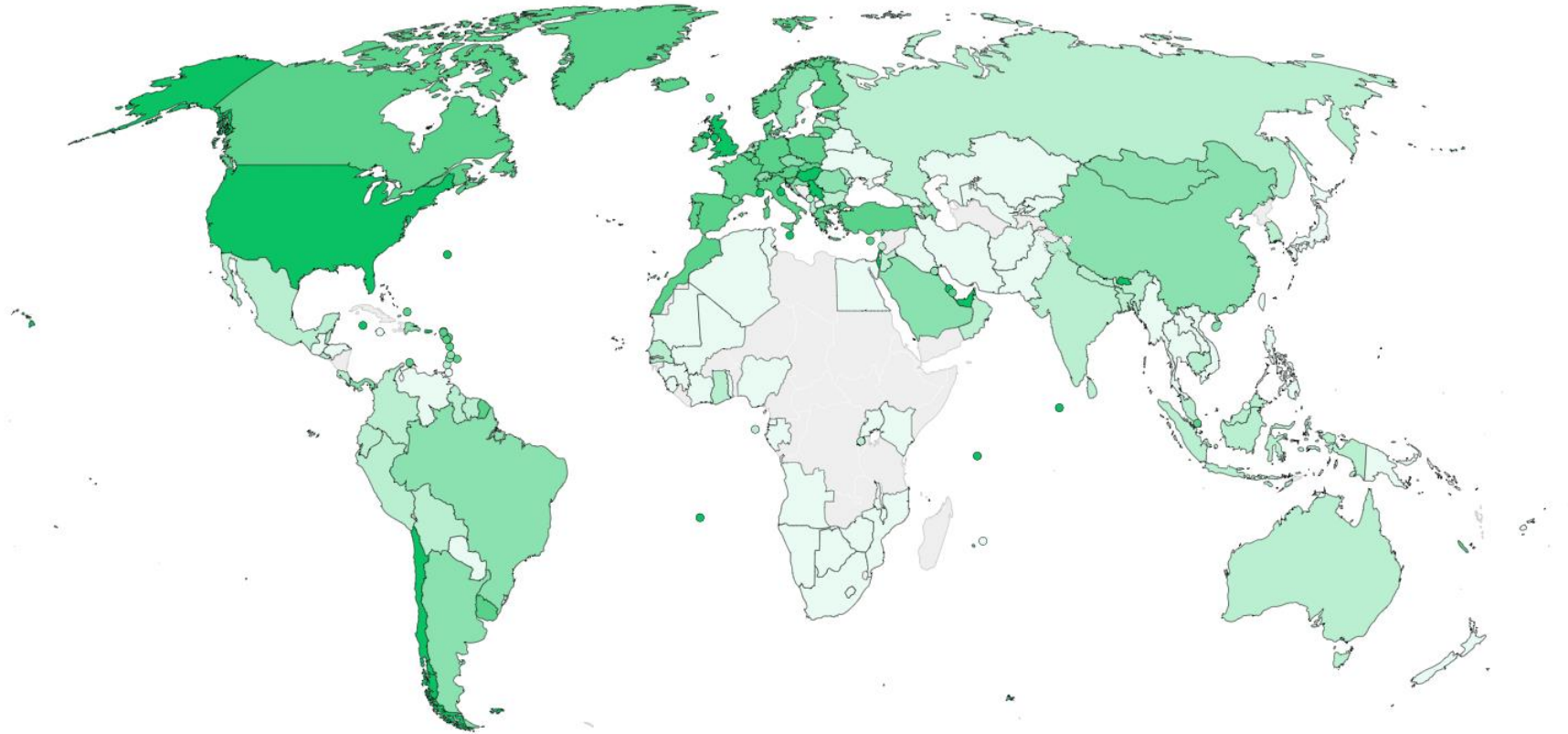


Potential for
heterologous
boosters

COVID-19 vaccination campaigns in 2022

World Map of Vaccinations
More than 797 million doses have been administered—enough to vaccinate 5.2% of the global population

no data 1 5 10 20% of population covered

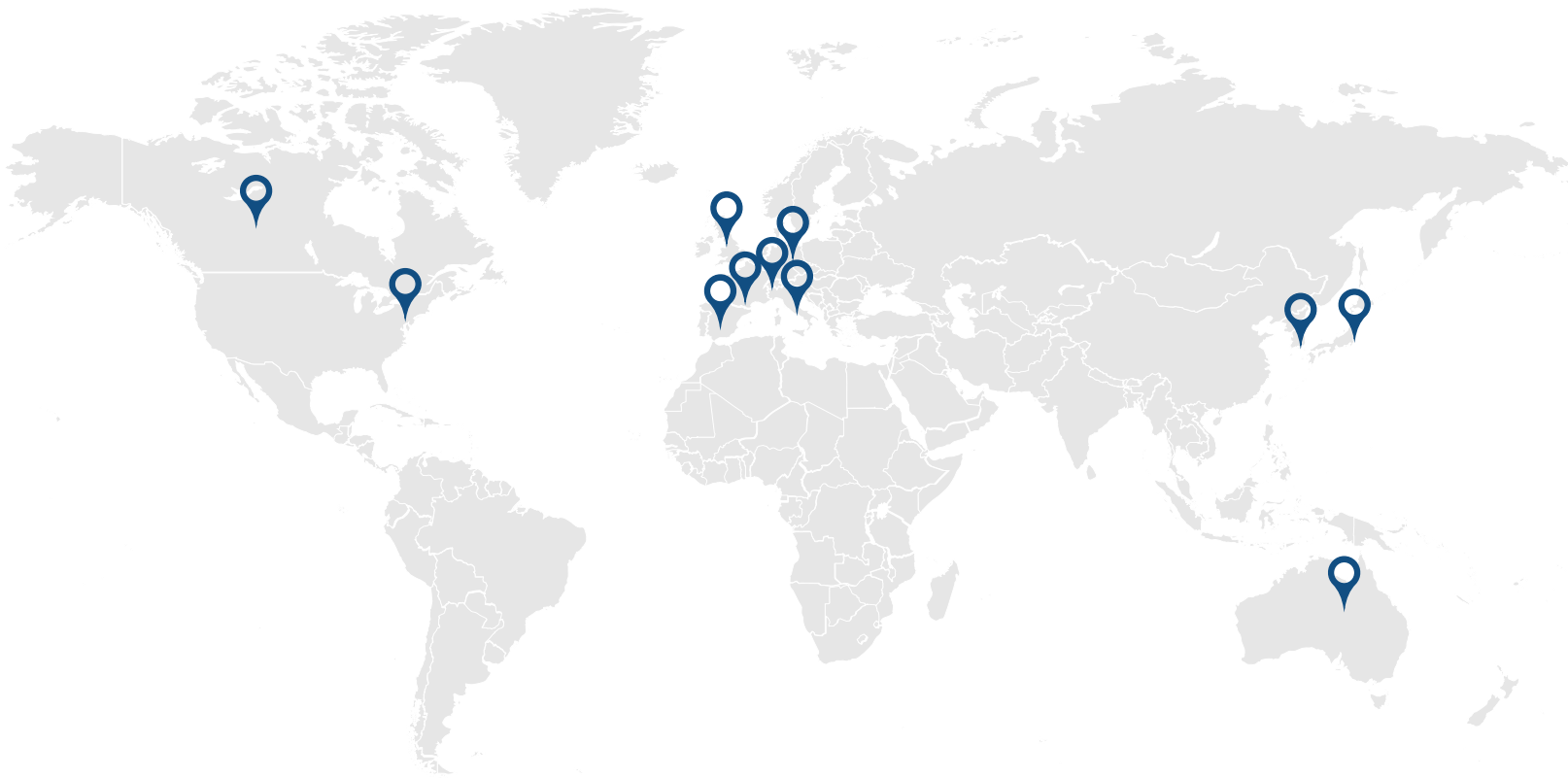


COVID-19 vaccines in 2022 will be driven by:

- Continuing ramp up on 18+ vaccination campaigns
- Expanding into <18 populations
- In countries that have already achieved high vaccine coverage, a shift to boosters in 2022

We are expanding our commercial geographic footprint

To maximize commercial opportunities, and to increase population impact



Direct presence in strategic markets – Already 8 subsidiaries, and 3 more planned to open in 2021 in JAPAC

Partners and distributors in Israel, Eastern Europe, LATAM, Asia

Vaccines: A clear value proposition

Beyond healthcare costs and impact on labor productivity, infectious diseases can have enormous broader social, economic, political, psychological and ethical consequences



COVID-19 total estimated societal cost: **\$20-25 trillion¹**

Even if the entire world population of 7.8 billion people is vaccinated with two doses at an average of \$20 per dose, **the total cost would be about ~1.3% of the cost of the pandemic**



Infectious Disease Vaccines Strategy

Stephen Hoge, M.D.

President

How did we get here?

Idea of mRNA vaccines has been around since early 1990's, but none of the approaches tried prior to 2013 translated into clinical success

1990's

Discovery of **mRNA-LNP** vaccines changed the story...

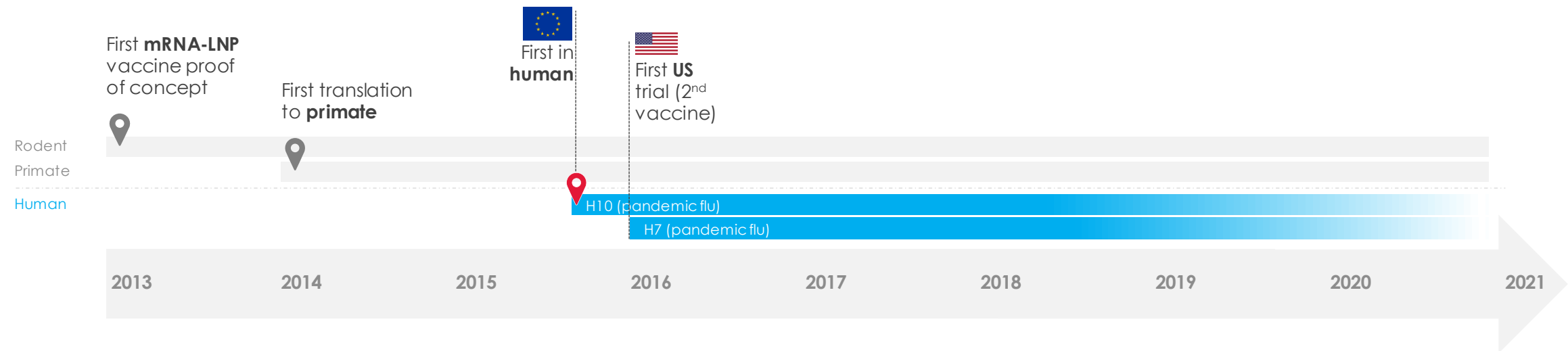
2013

...and since then **all successful examples** use the approach

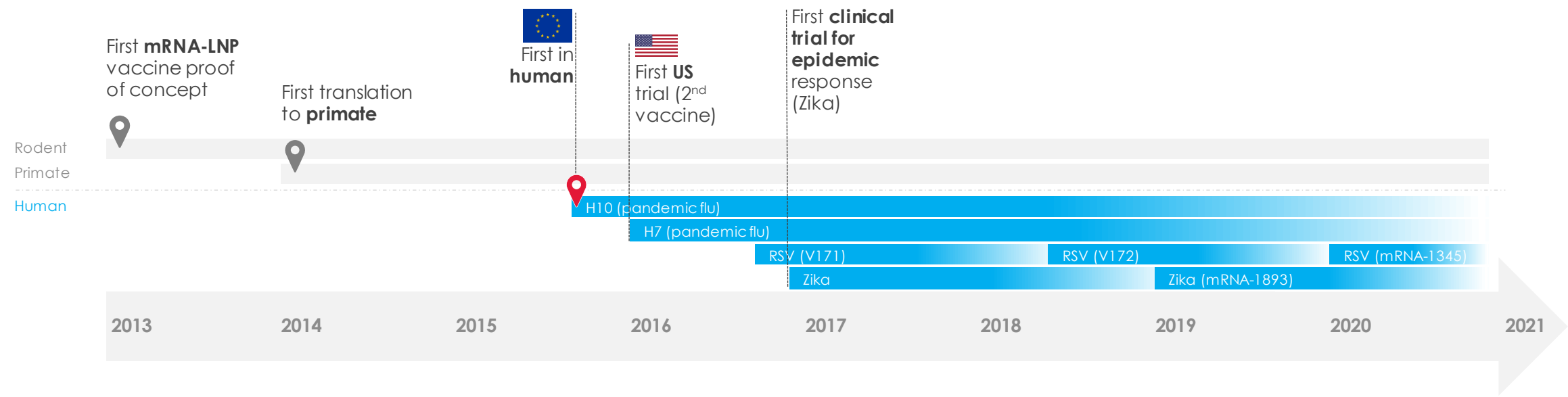
How did we get here?



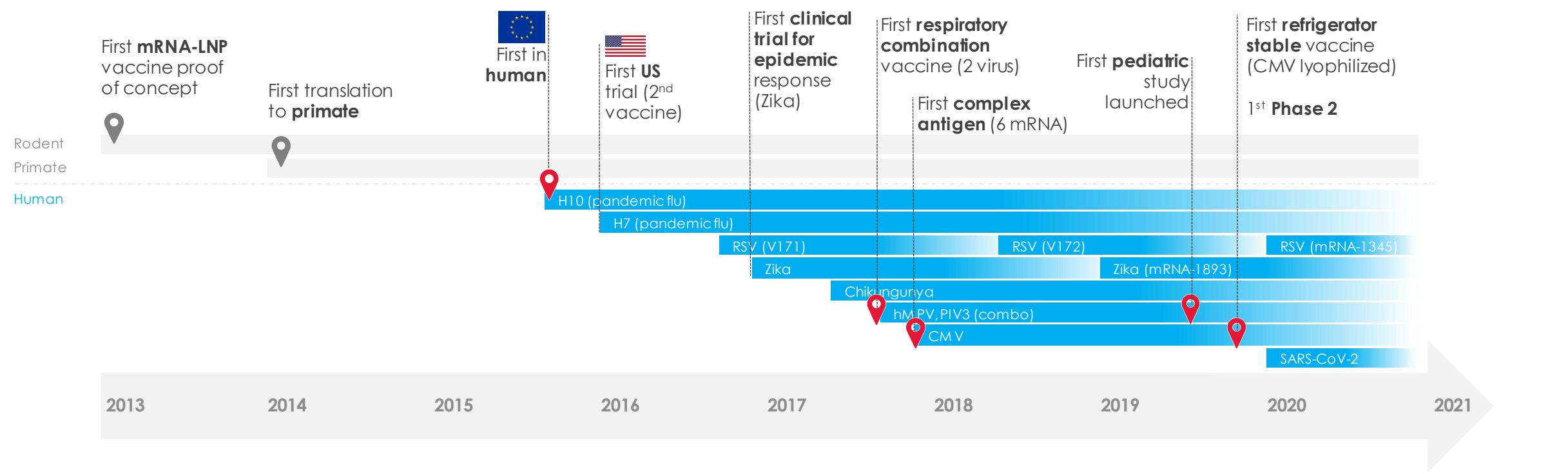
How did we get here?



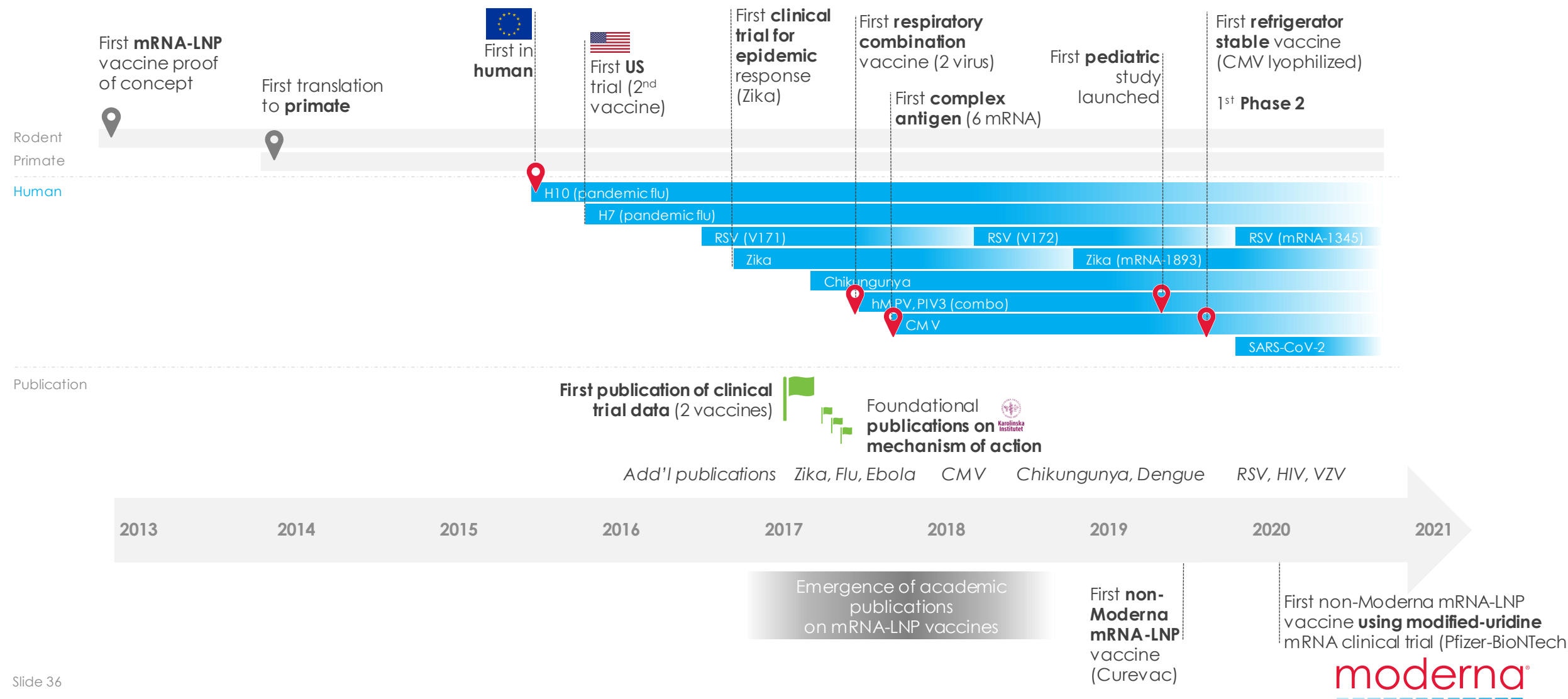
How did we get here?



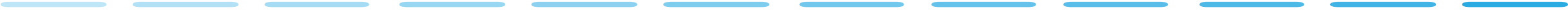
How did we get here?



How did we get here?



Our vaccine strategy



Where will mRNA-LNP vaccines make the biggest impact on human health?

Combination vaccines

Complex antigen vaccines

Speed (rapid development)

Capital **efficiency**

Our vaccine strategy

Where will mRNA-LNP vaccines make the biggest impact on human health?

1

Respiratory combination vaccines



- Combinations
- Complex antigens
- Rapid development
- Capital efficiency

Our vaccine strategy

Where will mRNA-LNP vaccines make the biggest impact on human health?

1 Respiratory combination vaccines



2 Complex antigens



- Combinations
- Complex antigens
- Rapid development
- Capital efficiency

Our vaccine strategy

Where will mRNA-LNP vaccines make the biggest impact on human health?

1 Respiratory combination vaccines



2 Complex antigens



3 Vaccines against public health threats



- Combinations
- Complex antigens
- Rapid development
- Capital efficiency

Our vaccine strategy

Where will mRNA-LNP vaccines make the biggest impact on human health?

1 Respiratory combination vaccines



2 Complex antigens



3 Vaccines against public health threats



Combinations

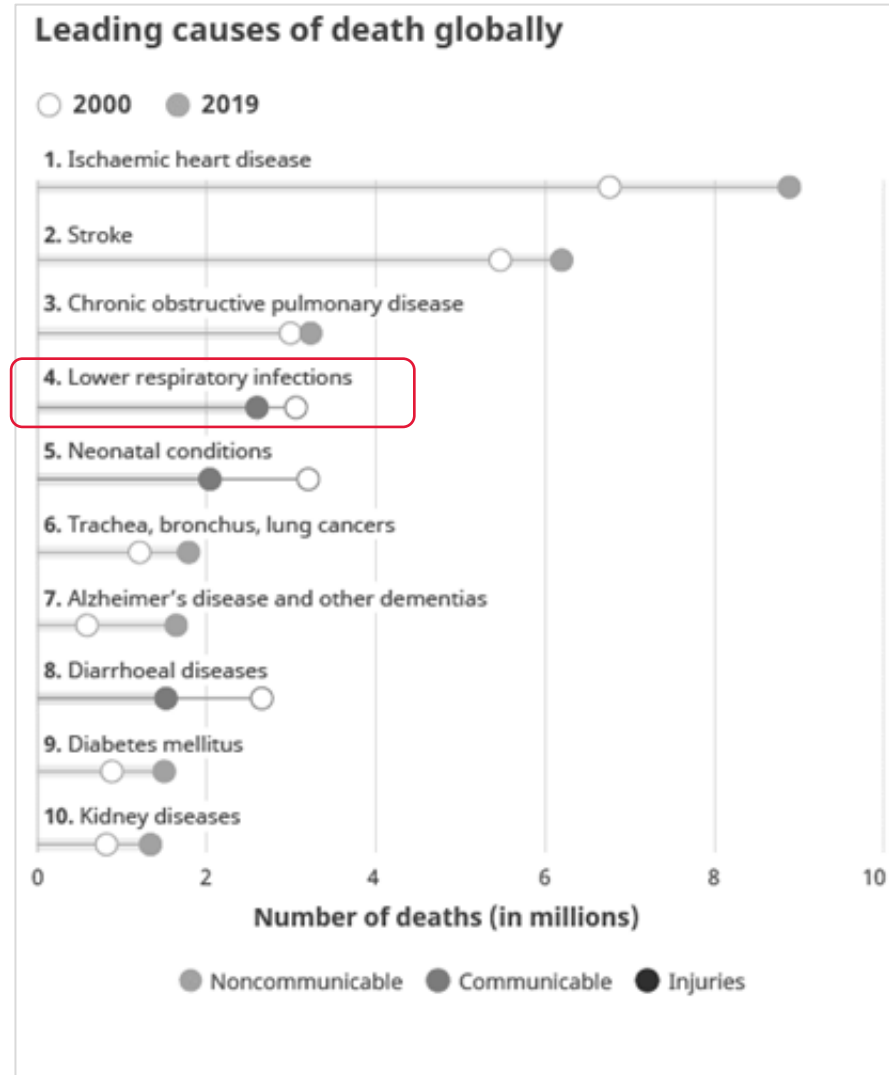
Complex antigens

Rapid development

Capital efficiency

Our vaccine strategy

1 Respiratory combination vaccines

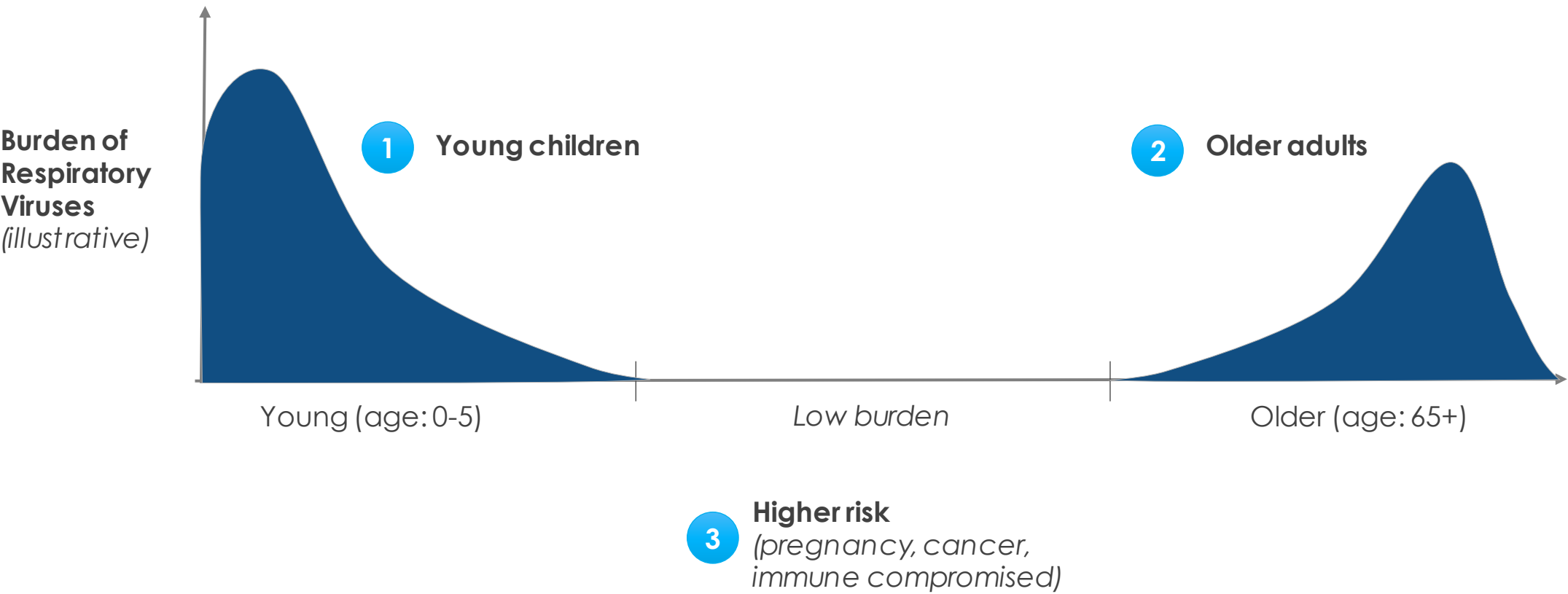


Respiratory infections are **a top cause of death** globally (3 million deaths) with approximately 1/3rd from tuberculosis

Approximately **1 million deaths annually** in high & upper middle-income countries

Respiratory infections **kill more people than colorectal cancer** in high income countries

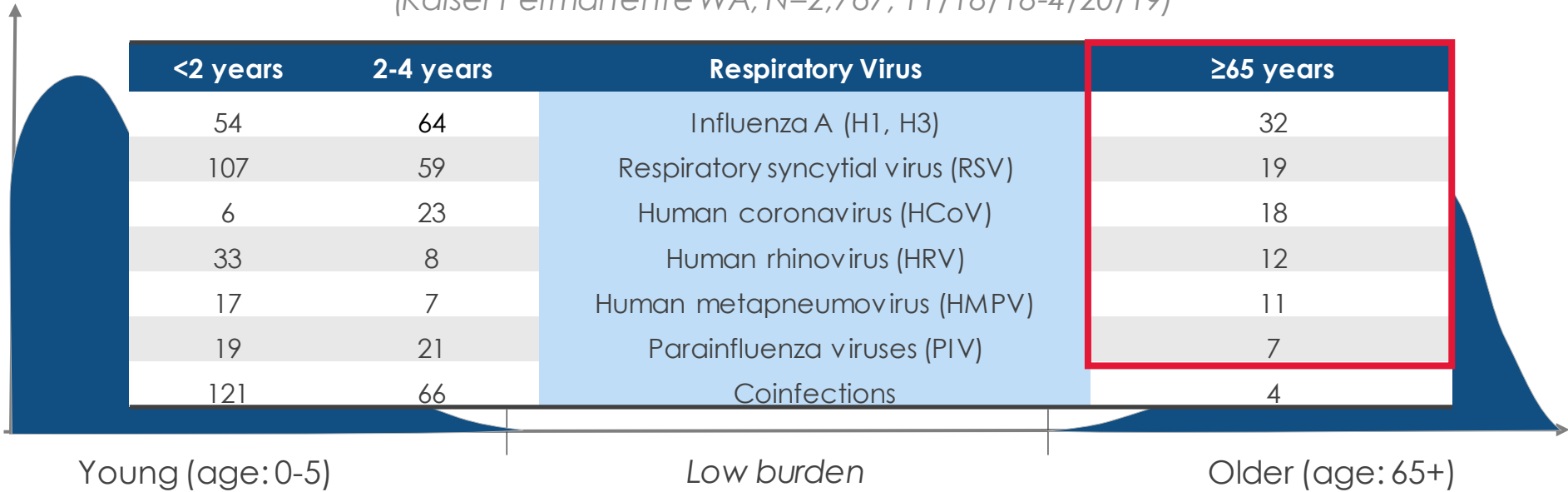
Respiratory virus disease burden is greatest in the young and the old



Respiratory virus disease burden is greatest in the young and the old

Within Season Outpatient Acute Respiratory Infection
Attack Rate per 1,000
(Kaiser Permanente WA, N=2,767, 11/18/18-4/20/19)

Burden of
Respiratory
Viruses
(illustrative)



Top respiratory viruses drive >\$15 billion of annual cost just in the 65+ US population (excl. COVID-19)

US adults age 65+

Respiratory Virus	Within Season Outpatient (Attack Rate per 1,000)	Annual Inpatient (Attack Rate per 1,000)	Inpatient Mortality	US Estimated Annual Cost
Influenza (all)	32	4.3	3-4%	\$5.6 bn
Respiratory syncytial virus (RSV)	19	1.9	5.2%	\$1.5 bn
Human coronavirus (HCoV) excl. SARS-CoV-2	18	2.6	7.3%	\$1.4 bn
Human rhinovirus (HRV)	12	5.9	3.2%	\$4.0 bn
Human metapneumovirus (HMPV)	11	1.6	3.9%	\$1.3 bn
Parainfluenza viruses (PIV)	7	1.5	4.9%	\$1.1 bn
Subtotal	94	17.8	3-7%	~\$15 bn

+

SARS-CoV-2 will add to these totals

Global implications

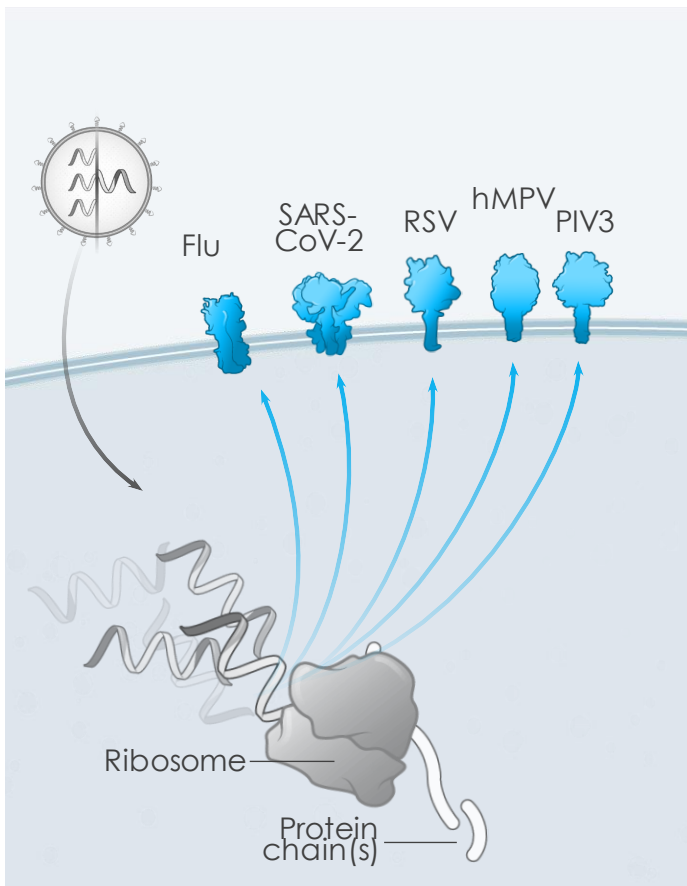
Estimated **\$20-40 billion of annual cost globally** from these viruses in 65+ adults

Approximately **19 million disability adjusted life-years (DALY)** lost in 2019 alone

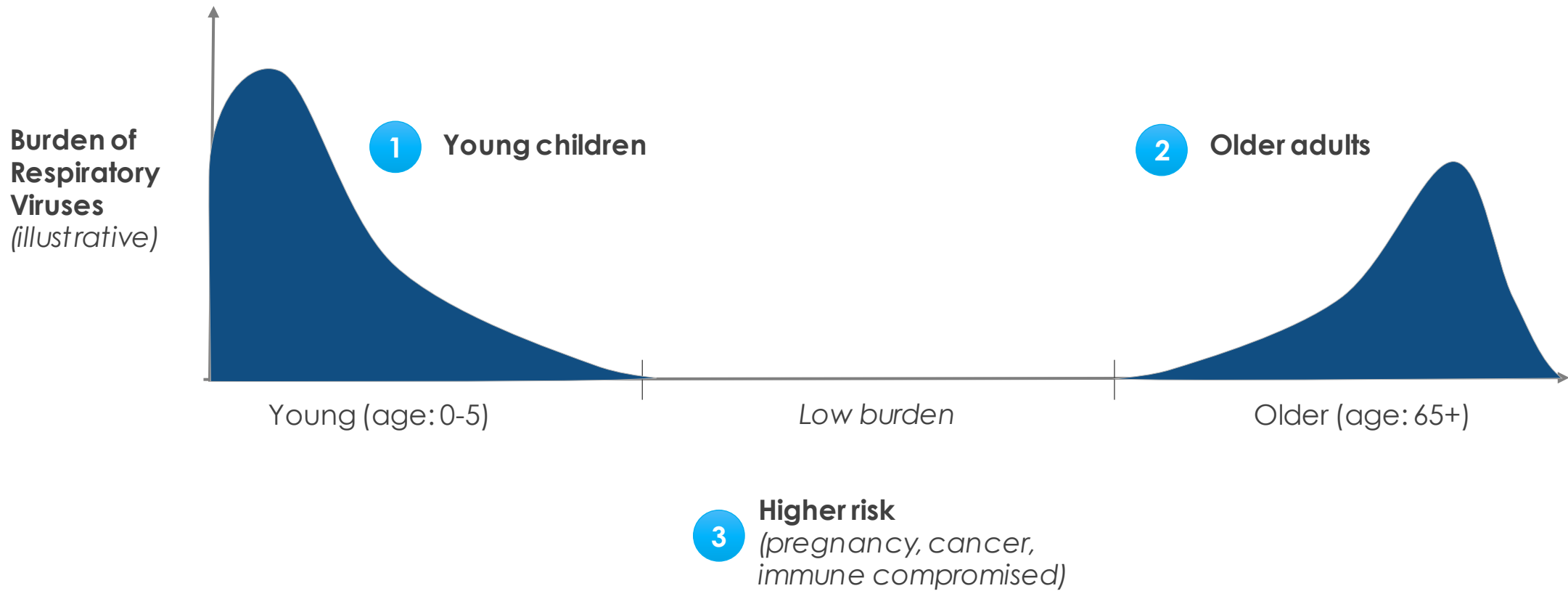
Moderna respiratory vaccine portfolio

Top respiratory viruses	Moderna programs (disclosed)	Clinical data against pathogen
• Influenza	mRNA-1851, -1010/20/30	✓
• Resp. syncytial virus (RSV)	mRNA-1345	✓
• Metapneumovirus (HMPV)	mRNA-1653	✓
• Parainfluenza virus(PIV)	mRNA-1653	✓
• SARS-CoV-2	mRNA-1273, -1283	✓
• Endemic human coronavirus		
• Rhinovirus (HRV)		

Current programs target pathogens responsible for ~\$10bn of annual cost in US 65+ alone, before SARS-CoV-2



Older adults is just the beginning of potential impact



Our vaccine strategy

1 Respiratory
combination
vaccines



2 Complex
antigens

3 Vaccines
against public
health threats



Diseases of high unmet need due to complex antigens

CMV

mRNA-1647



- Leading cause of **birth defects** (20,000 congenital CMV cases annually in the US alone)
- Major driver of **immune dysfunction with aging**
- Significant cause of **disease in transplant** populations

EBV

mRNA-1189

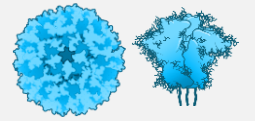


- >160K deaths attributed to EBV-related **malignancies** (2017)
- Major driver of **Multiple Sclerosis risk** (10-15x increase)

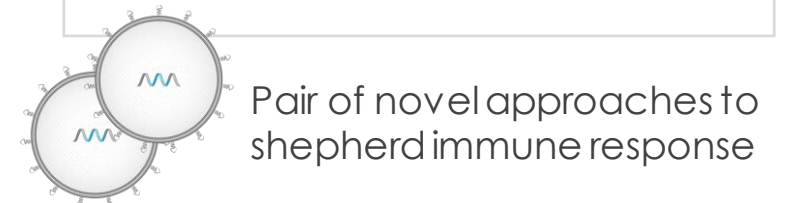
HIV

mRNA-1644

mRNA-1574



- Cause of AIDS, resulting in approximately **700,000 deaths worldwide** annually (2019)
- In collaboration with IAVI, NIAID, and Gates Foundation



Our vaccine strategy

1 Respiratory
combination
vaccines



2 Complex
antigens



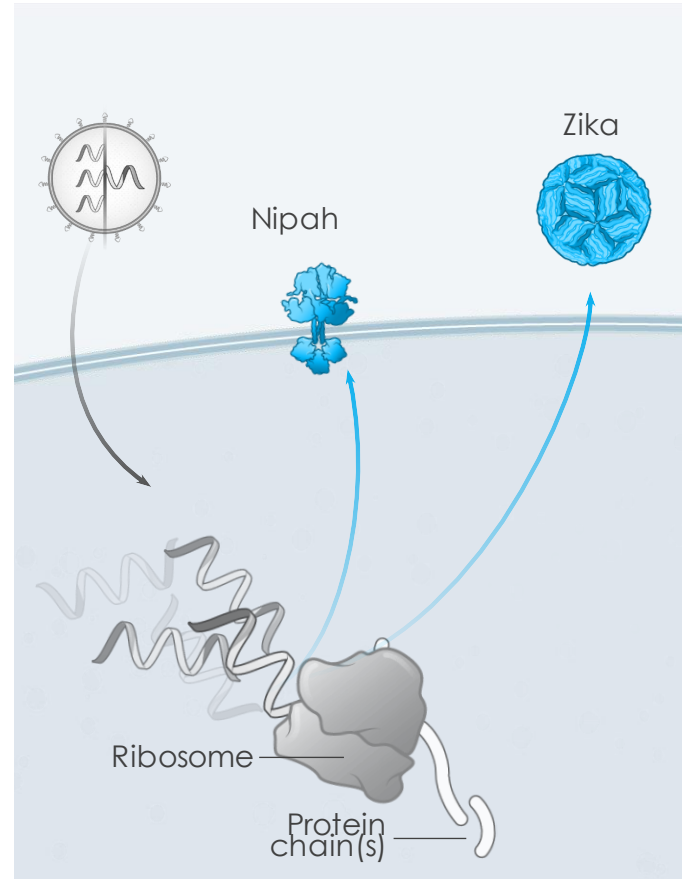
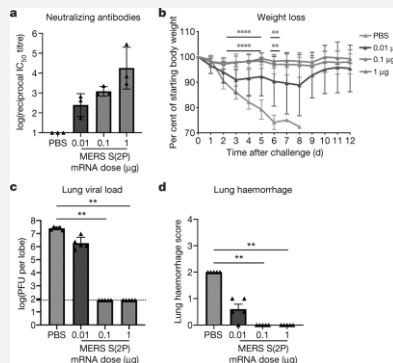
3 Vaccines
against public
health threats



Public health threats

Vaccines against pathogens of public health concern are **critical to health security**

Prior MERS vaccine work accelerated global response to SARS-CoV-2



Two development programs

- **Zika** (mRNA-1893) – Major arthropod (mosquito) driven epidemic in 2016; planning for Phase 2
- **Nipah** (mRNA-1215) – Outbreak potential with 40 to 75% risk of death; expected to enter Phase 1

Our vaccine strategy

Where will mRNA-LNP vaccines make the biggest impact on human health?

1 Respiratory combination vaccines



2 Complex antigens



3 Vaccines against public health threats



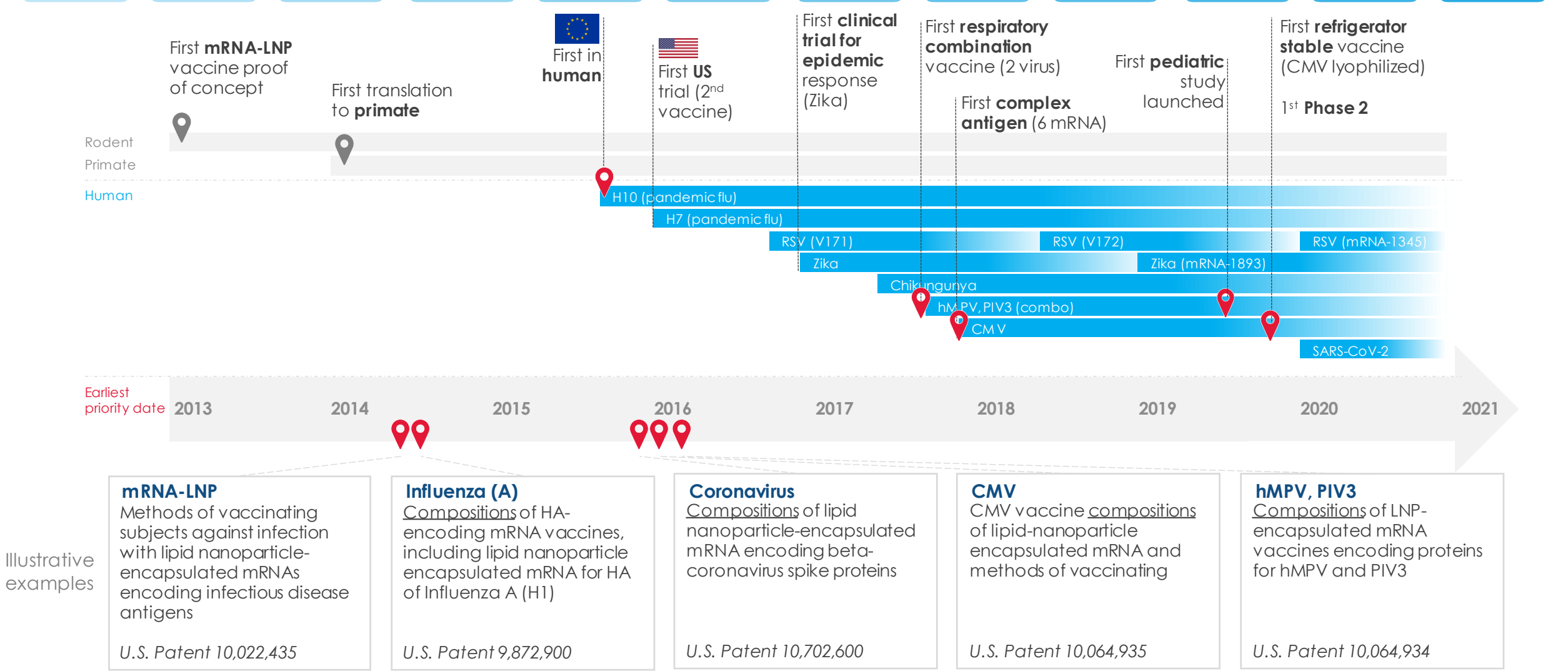
Combinations

Complex antigens

Rapid development

Capital efficiency

Over 275 issued patents, including many covering vaccines



Our vaccine strategy

R&D
Strategy

1

Respiratory combination vaccines



2

Complex antigens



3

Vaccines against public health threats



Portfolio

2

Phase 3 programs

Nine

Programs with positive clinical data

+5

More first-in-human expected in 2021

Foundations

Creator of mRNA-LNP vaccines

Strong technical and manufacturing

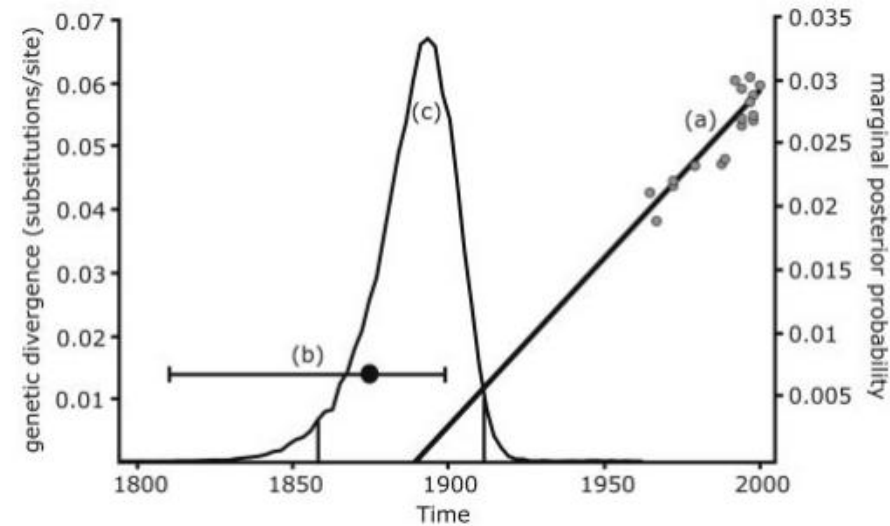
Broadest clinical & preclinical experience

200+ issued patents, including extensive coverage of vaccines

How are we thinking about the evolution of COVID-19?

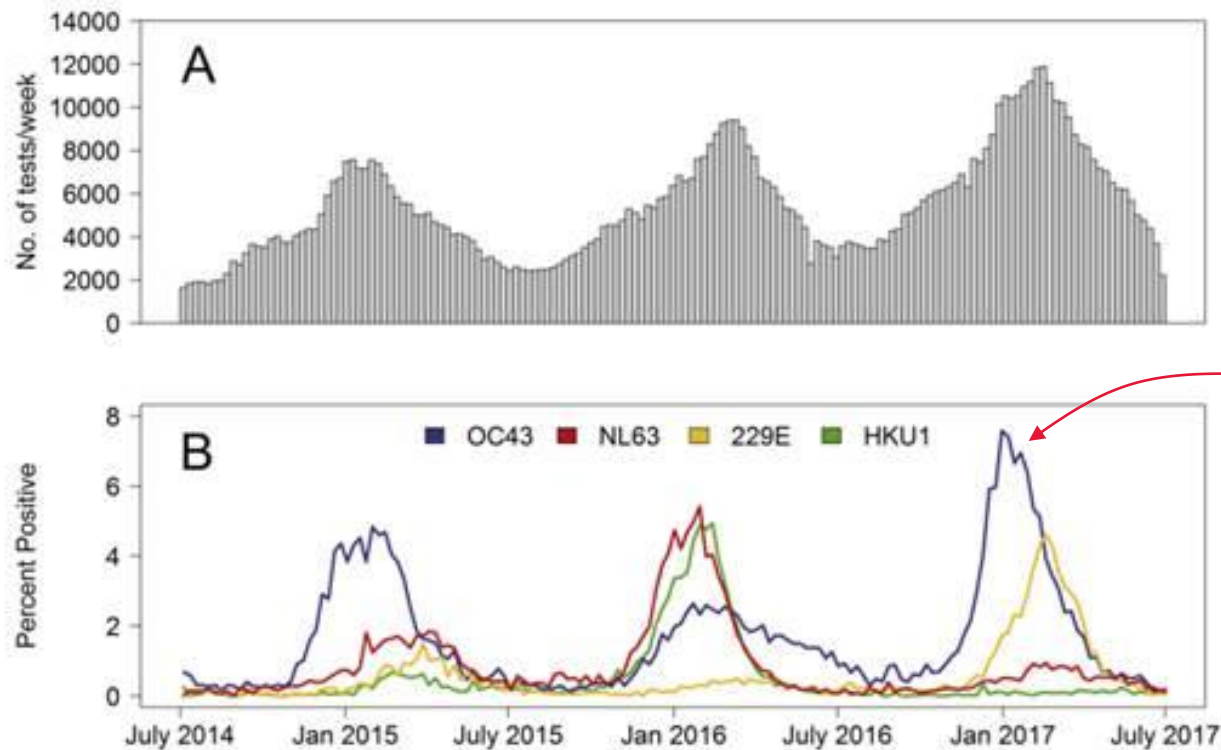
What can we learn from the past?

A pandemic originated in Central Asia during 1889-1890, around the time that a bovine coronavirus jumped to humans and likely became the first **HCoV-OC43 strain**



What can we learn from the past?

130 years later, OC43 still causes 3-5% of acute respiratory infections annually

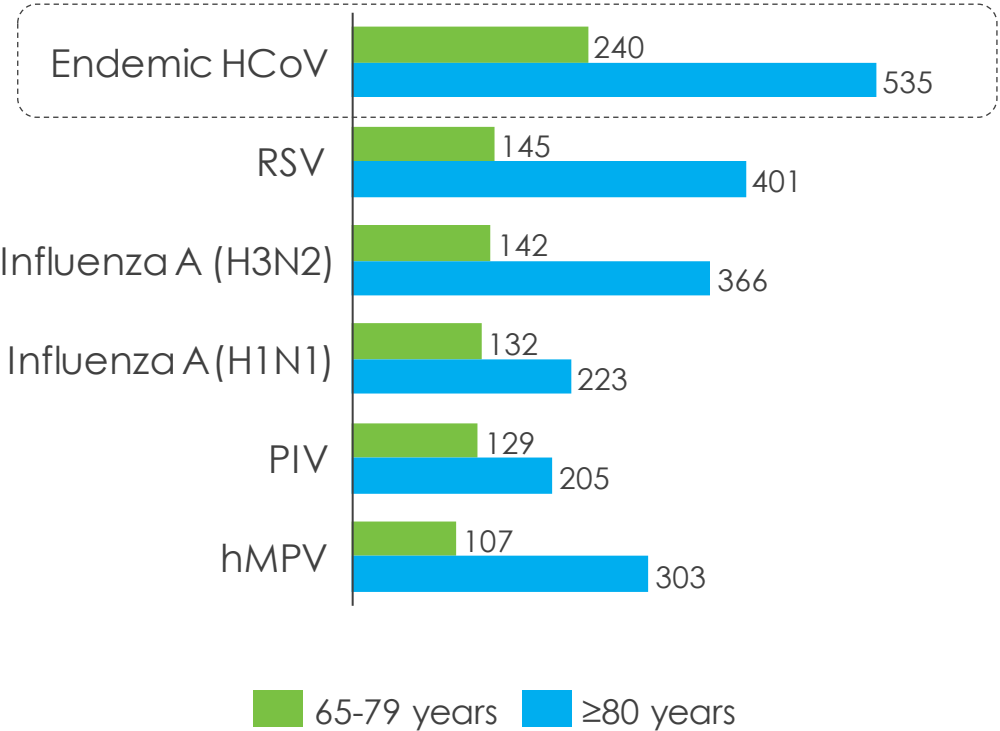


Seasonal epidemics seen in young children and older adults (65+)

Endemic coronaviruses cause significant annual disease

Incidence of Community-onset Respiratory Viruses Associated with Hospitalization per 100,000 Persons

NYC, 10/2018 – 9/2019



Estimated impact in 65+ across OECD markets...

Over 1 million outpatient visits

Approximately 350,000 hospitalizations

Approximately 20,000 deaths

\$3-4 billion of direct medical expenses

~50% driven by OC43
(131 years later)

What can we learn from the past?

Human coronaviruses cause seasonal disease in young and old

Reinfections happen at varying rates (1-3 years)

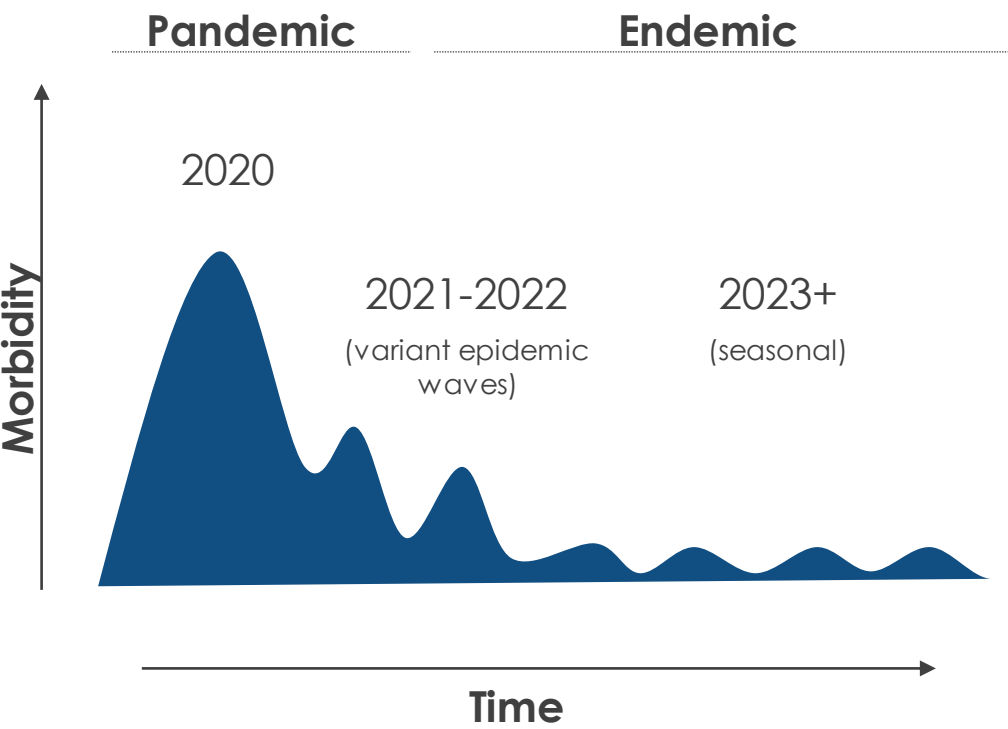
Disease can often be mild or asymptomatic, but can also be lethal in older seropositive adults

Open questions:

- When (*not if*) reinfections will happen (and role of variants)
- When will more severe disease re-emerge in high-risk seropositive populations
- Will the endemic SARS-CoV-2 mortality rate be similar to endemic hCoV

How we currently think SARS-CoV-2 will evolve

ILLUSTRATIVE



Stage	Focus for vaccines
Pandemic <i>Initial waves</i>	• Heavy focus on protecting high-risk populations • Mostly ancestral virus vaccine
Variant epidemics <i>Reinfection waves</i>	• Focus to suppressing transmission of variants • Speed & adaptability are critical
Endemic <i>Seasonal</i>	• Multi-valent approaches with broadest immunity • Focus on toddlers and seasonal protection against waning immunity in high-risk (e.g., 65+)

Our strategy for combating COVID-19

Stay ahead
of SARS-
CoV-2

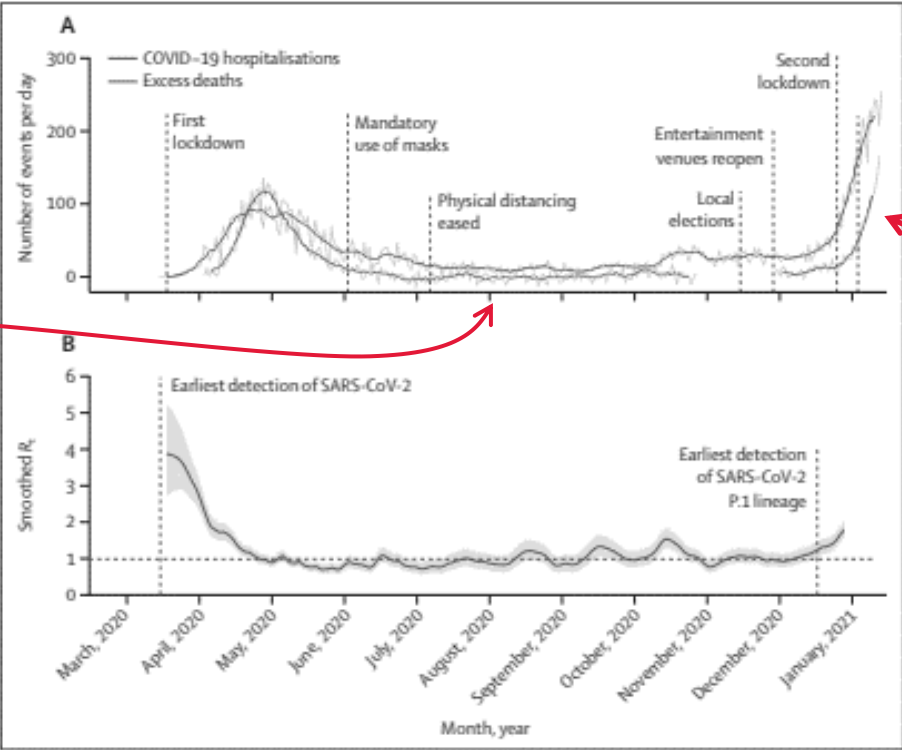
- 1 Closely monitor **emerging variants** and **waning immunity**
- 2 Rapidly move to **update vaccine** for VOC with breakthrough potential
- 3 Partner with governments to **ensure access** to the most *up-to-date* boosters

...with Coronaviruses the question is 'when' not 'if'

Our strategy for combating COVID-19

1

Closely monitor **emerging variants** and **waning immunity**



Data has suggested
~75% sero-positivity
after first wave

Second wave appears to
start 8–9 months later
with a new strain (P.1)

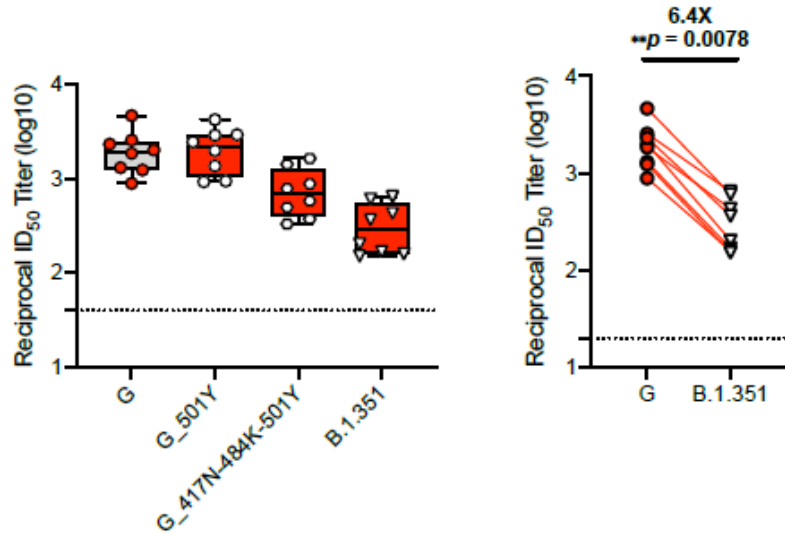
Our strategy for combating COVID-19

1

Closely monitor **emerging variants** and **waning immunity**

Decreased neutralization with B.1.351

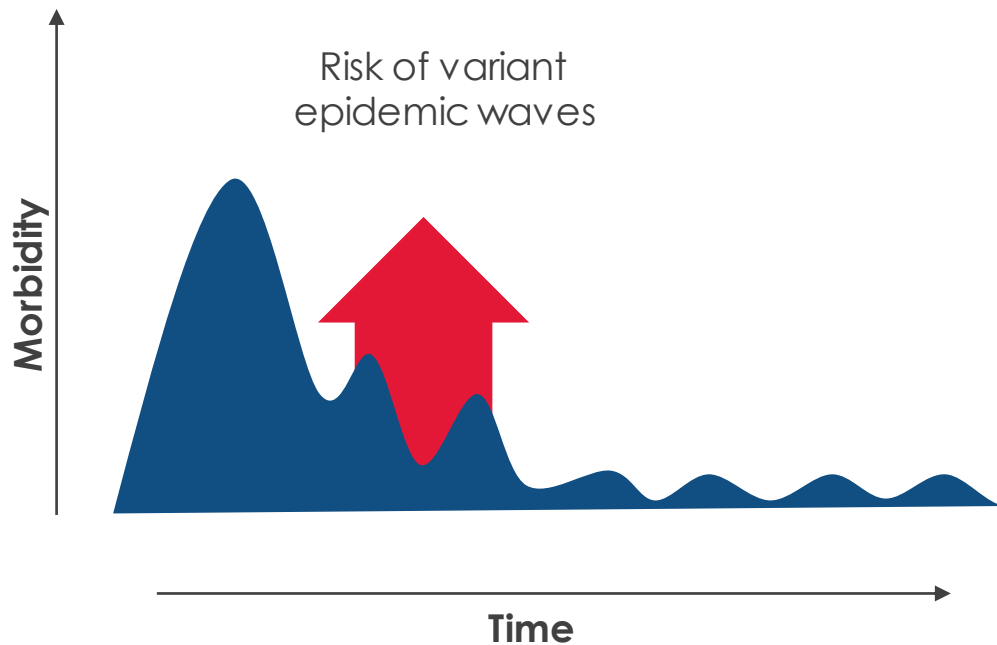
Phase 1 vaccine Human Serum



- Variant first identified in South Africa (B.1.351) is associated with increased transmission, higher viral burden, and possibly increased mortality in infected persons¹
- All vaccines based on Wuhan-sequence have reported reduced neutralizing activity against B.1.351
- Sera from individuals vaccinated with mRNA-based vaccines had a ~6-fold reduction in neutralizing activity against a B.1.351-matched pseudovirion relative to a Wuhan-matched pseudovirion²

Our strategy for combating COVID-19

1 Closely monitor **emerging variants** and **waning immunity**



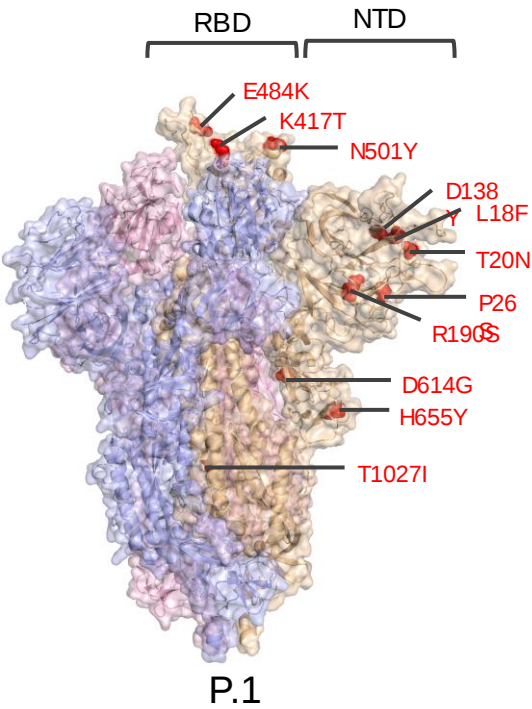
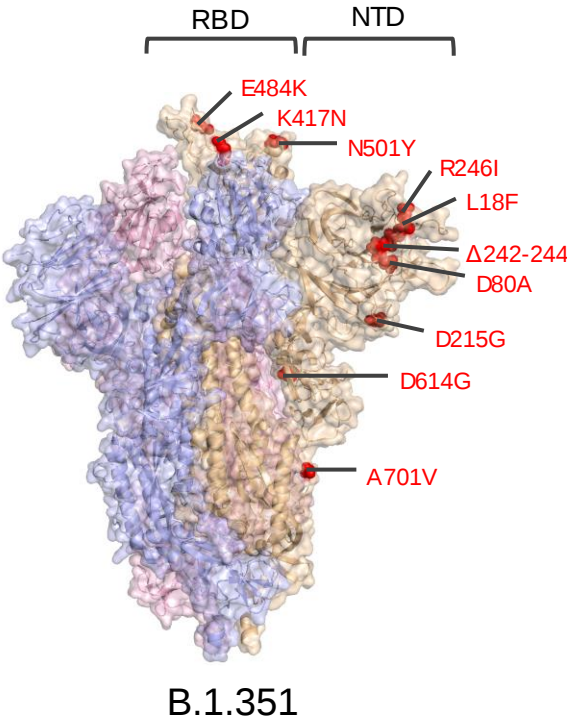
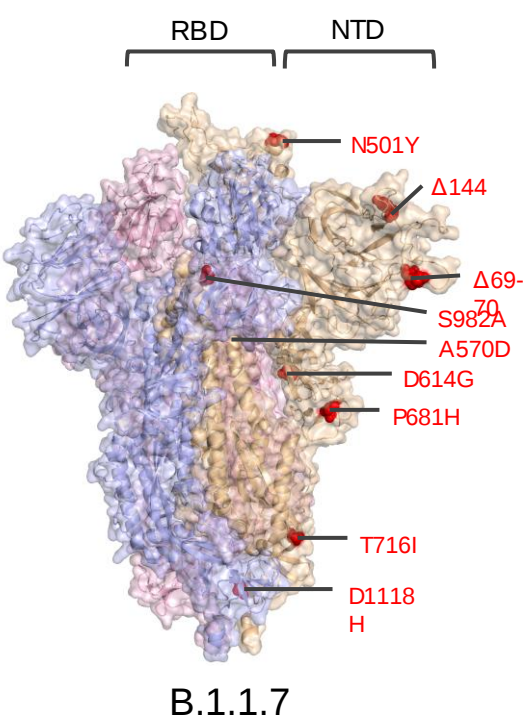
- Lower neutralizing titers suggest a risk of earlier waning immunity
- Increased transmissibility of VOC could increase the exposure risks in high-risk populations
- Immune pressure and selection just beginning

Our strategy for combating COVID-19

2

Rapidly move to **update vaccine** for VOC with breakthrough potential

RBD: Receptor binding domain
NTD: N-terminal domain

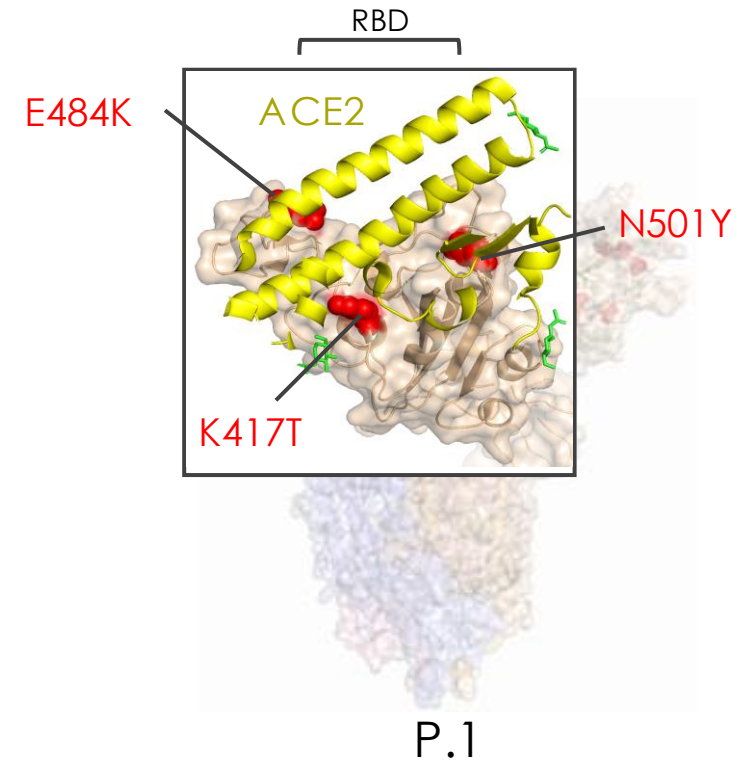
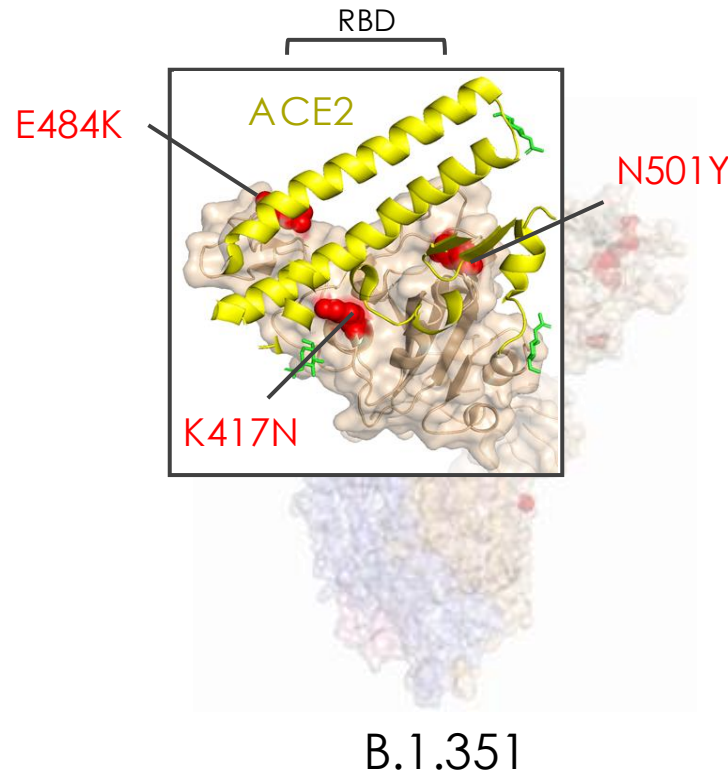
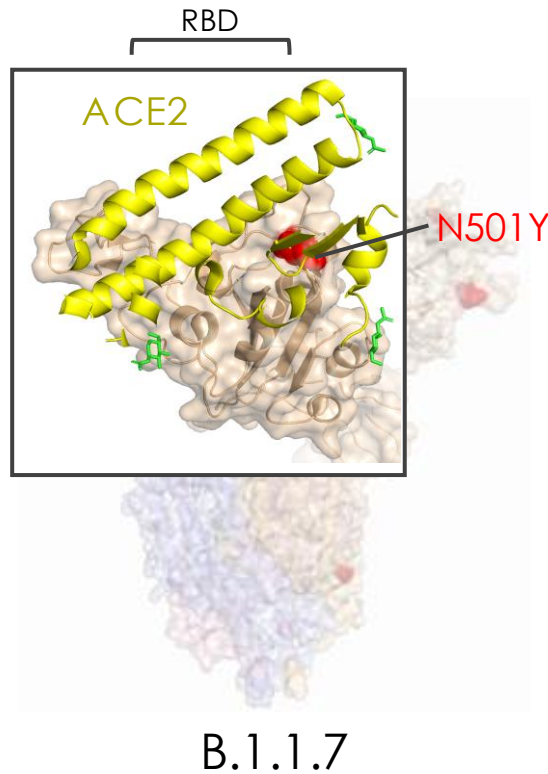


Our strategy for combating COVID-19

2

Rapidly move to **update vaccine** for VOC with breakthrough potential

RBD: Receptor binding domain

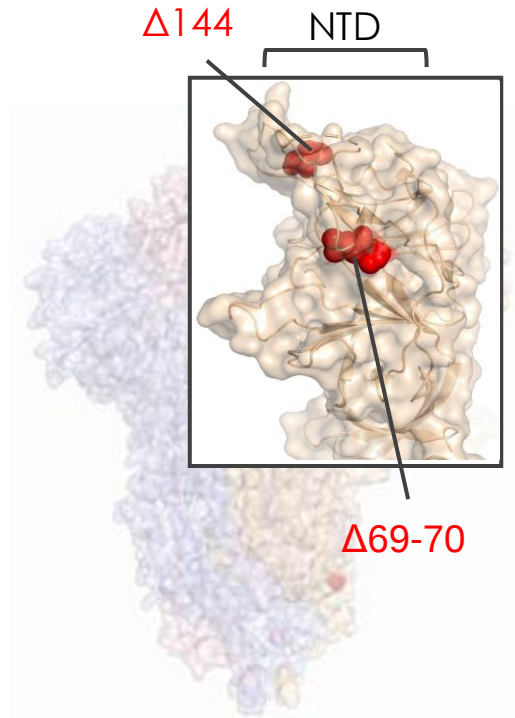


Our strategy for combating COVID-19

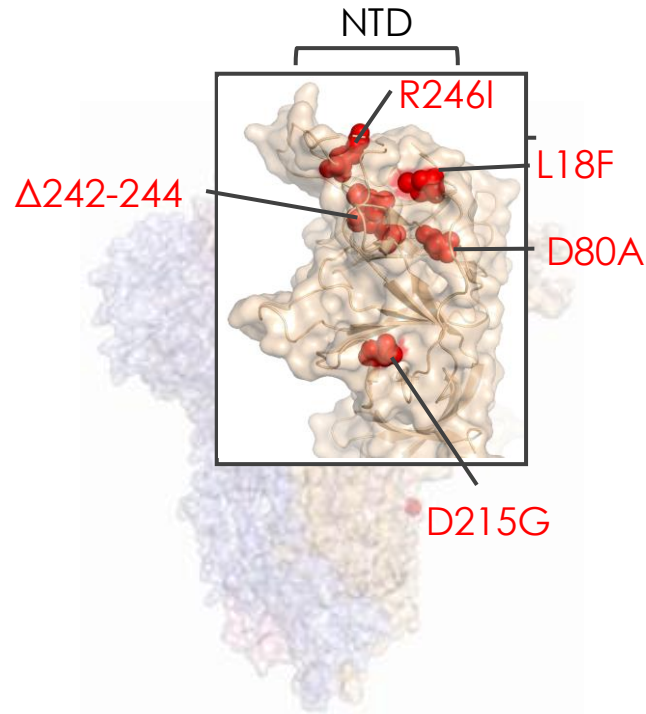
2

Rapidly move to **update vaccine** for VOC with breakthrough potential

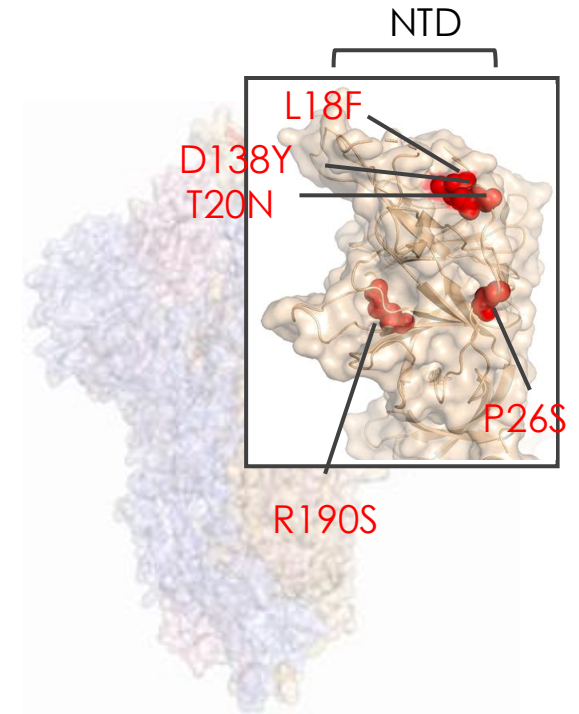
NTD: N-terminal domain



B.1.1.7



B.1.351



P.1

Our strategy for combating COVID-19

2

Rapidly move to **update vaccine** for VOC with breakthrough potential

Phase 2 trial underway to evaluate **three boosting strategies** against VOC

I

mRNA-1273.351: Variant-specific booster candidate based on the B.1.351 (variant first identified in the Republic of South Africa)

- 20 µg of mRNA-1273.351 (N=20)
- 50 µg of mRNA-1273.351 (N=20)

II

mRNA-1273.211: Multivalent booster candidate which combines mRNA-1273 and mRNA-1273.351 in a single vaccine

- 50 µg of mRNA-1273.211 (N=20)

III

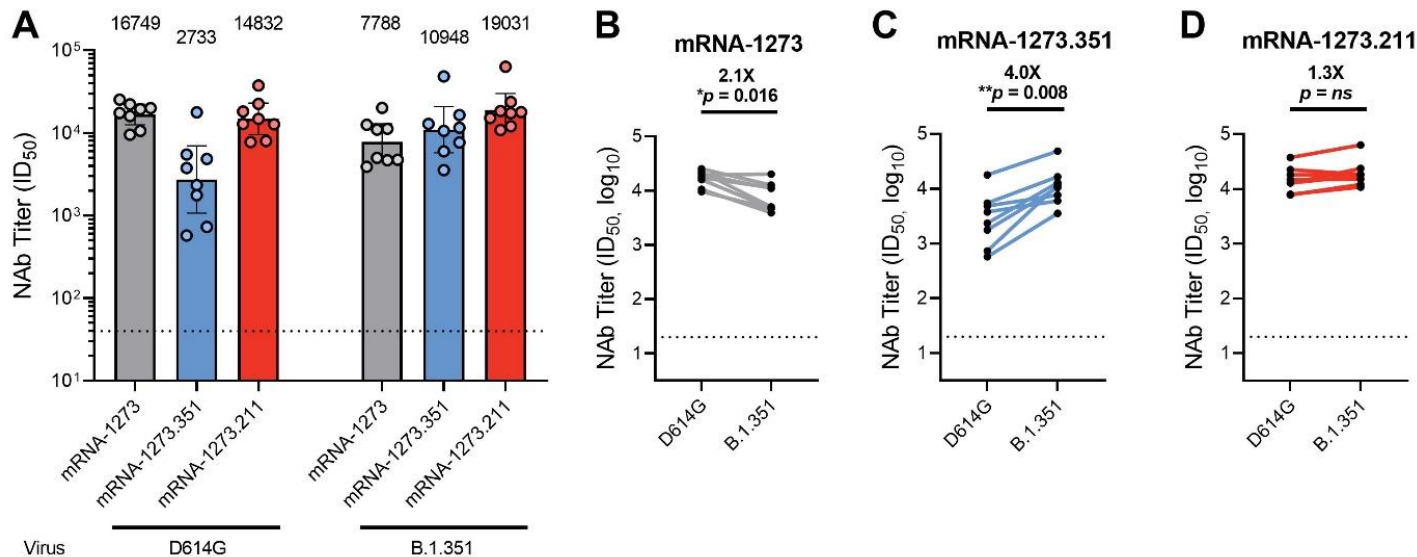
mRNA-1273: Moderna COVID-19 Vaccine

- 50 µg of mRNA-1273

Our strategy for combating COVID-19

2

Rapidly move to **update vaccine** for VOC with breakthrough potential

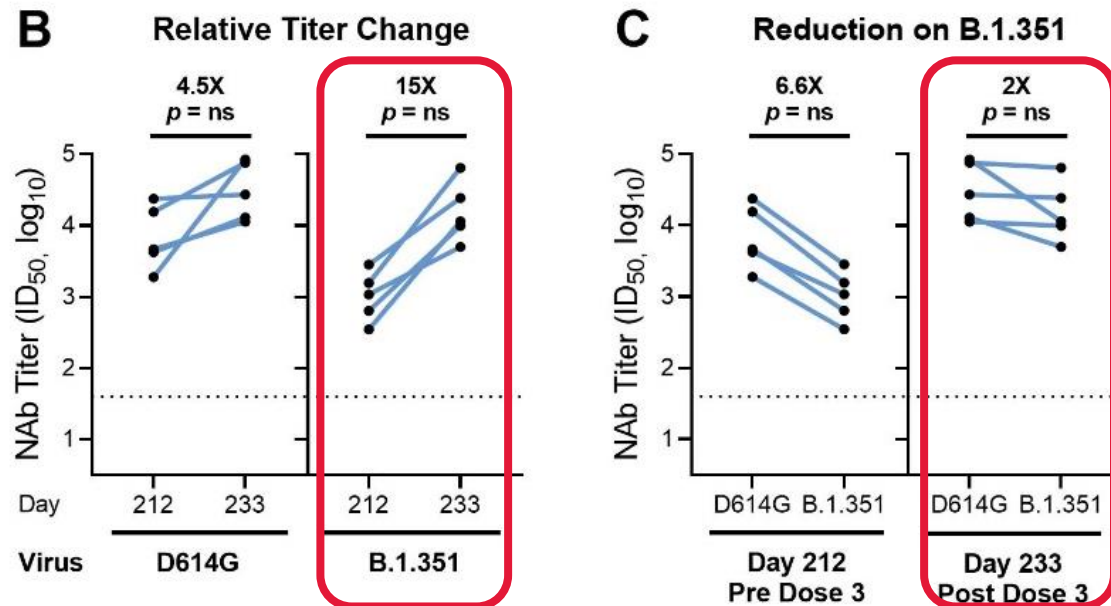


- Preclinical data confirms **improved neutralizing titers against B.1.351** with mRNA-1273.351 vaccine candidate (primary series)
- **Multi-valent vaccine (.211)** including antigens from B.1.351 and ancestral strains provided the broadest neutralizing immunity

Our strategy for combating COVID-19

2

Rapidly move to **update vaccine** for VOC with breakthrough potential



- Boost at 6 months with B.1.351 vaccine booster **closed neutralizing titer gap** for VOC
- Following B.1.351 boost, neutralizing titers were comparable between ancestral strain (Wuhan) and new variant

Our strategy for combating COVID-19

Stay ahead of
SARS-CoV-2

1

Closely monitor **emerging variants** and **waning immunity**

- Two VOC (B.1.351 and P.1) pose risk of earlier waning immunity in high-risk populations

2

Rapidly move to **update vaccine** for VOC with breakthrough potential

- Addition of B.1.351 strain to vaccine provides good coverage against current VOC
- Multi-valent vaccines provide broadest neutralizing protection
- Three strategies being evaluated in Phase 2 (initial dosing complete)
- Scale-up for commercial manufacturing already underway

3

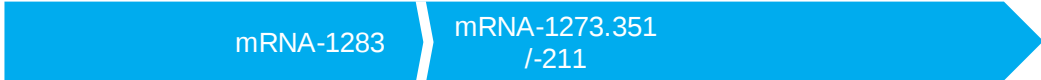
Partner with governments to **ensure access** to the most *up-to-date* boosters



COVID-19 Overview

Jacqueline Miller, M.D.

Senior Vice President, Infectious Diseases, Moderna

Program		ID #	Pre-clinical	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
COVID-19 vaccine		mRNA-1273						Worldwide <i>BARDA funded</i>
hMPV/PIV3 vaccine		mRNA-1653						Worldwide
Respiratory syncytial virus (RSV) vaccine		mRNA-1345						Worldwide
Flu vaccine		mRNA-1010 mRNA-1020 mRNA-1030						Worldwide

COVE: Moderna COVID-19 Vaccine Efficacy and Safety Study Update

Phase 3 COVE Study Overview

- ✓ Placebo controlled
- ✓ ~30,000 participants enrolled
- ✓ Participants received 100 µg or placebo
- ✓ Study objectives to demonstrate efficacy, safety and immunogenicity of mRNA-1273



Phase 3 COVE Study Updates

- ✓ Demonstrated mRNA-1273 is well-tolerated with 94.1% vaccine efficacy against COVID-19 in the primary efficacy analysis
- ✓ 84% of the placebo participants have crossed over to the active arm
- ✓ Updated cases show continued strong efficacy, including greater than 90% against cases of COVID-19 and greater than 95% against severe cases of COVID-19, with approximately 6 months median follow-up post dose 2

We will be sharing updated data from our Phase 3 COVE study throughout the year

✓ Efficacy against asymptomatic infection

✓ Genotyping data

✓ Durability data

✓ Correlate(s) of protection

Expecting multiple data points from the Phase 3 COVE Study

April 2021



Moderna COVID-19 Vaccine Population Expansion Studies

TeenCOVE

- Phase 2/3 study in adolescents ages 12-17 fully enrolled
- 3,000 participants enrolled in the U.S.
- Participants to receive placebo or 100 µg

Japan study¹

- Placebo-controlled, Phase 1/2 study (TAK-919), led by Takeda, is fully enrolled
- 200 participants aged 20 years and older

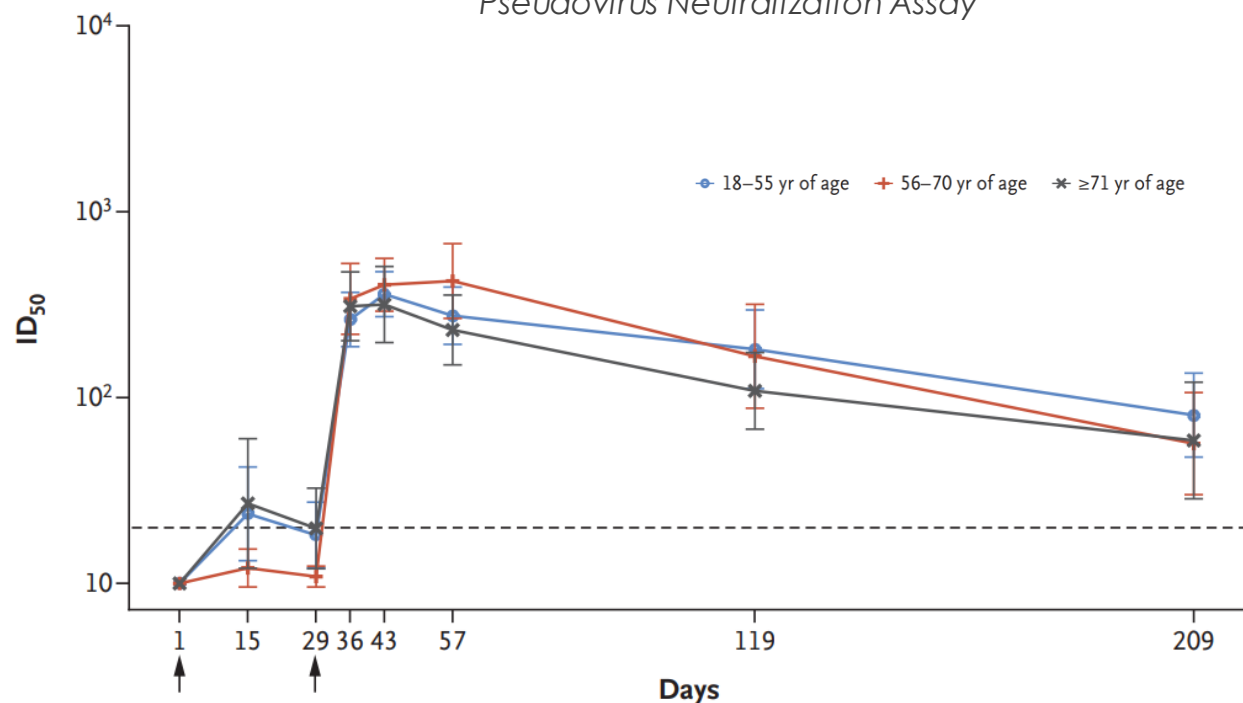
KidCOVE

- Phase 2/3 study in pediatric population ages 6 months-11 years currently enrolling
- Expected to enroll 6,750 healthy pediatric participants in the U.S. and Canada
- Dose escalation study
 - Ages 2-11 to receive placebo, 50 µg or 100 µg
 - Ages six months–2 to receive placebo, 25 µg, 50 µg or 100 µg
 - Interim analysis to determine which dose will be used in Part 2

Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for Covid-19

Time Course of SARS-CoV-2 Antibody Binding and Neutralization Responses after mRNA-1273 Vaccination

Pseudovirus Neutralization Assay



All the participants received 100 µg of mRNA-1273 on days 1 and 29, indicated by arrows. The numbers of participants in each age group with data available at day 209 are as follows: 18 to 55 years, 15 participants; 56 to 70 years, 9 participants; and 71 years or older, 9 participants. The titers shown are the 50% inhibitory dilution (ID₅₀) titer on pseudovirus neutralization assay on days 1, 15, 29, 36, 43, 57, 119, and 209. Lines show geometric mean titers for each age group; I bars indicate 95% confidence intervals. The dashed line indicates the limit of detection for each assay

- Antibodies persist in all age strata for at least 6 months after vaccination
- Ongoing studies are monitoring immune responses beyond 6 months as well as determining the effect of a booster dose to extend the duration and breadth of activity against emerging viral variants

Next generation COVID-19 Vaccine (mRNA-1283)

- mRNA-1283 encodes for the portions of the SARS-CoV-2 spike protein critical for neutralization, **specifically the Receptor Binding Domain (RBD) and N-terminal Domain (NTD)**
- The encoded mRNA-1283 antigen is being developed as a potentially refrigerator-stable mRNA vaccine that will **facilitate distribution** and administration by healthcare providers
- Phase 1 study in healthy volunteers **ongoing**

*Next generation COVID-19
vaccine candidate*



Potentially refrigerator-stable

Sir Jeremy Farrar OBE FMedSci FRS

Director of Wellcome



Before joining Wellcome in October 2013, Jeremy Farrar was Director of the Oxford University Clinical Research Unit in Vietnam for 18 years. His research interests were infectious diseases and global health, with a focus on emerging infections. He has published more than 600 articles, mentored many dozens of students and fellows, and served as Chair on several advisory boards for governments and global organisations.

In 2018 he was awarded the President Jimmy and Rosalynn Carter Humanitarian of the Year Award. He is a Fellow of the Academy of Medical Sciences UK, the National Academies USA, the European Molecular Biology Organisation and a Fellow of The Royal Society. Jeremy was knighted in the Queen's 2019 New Year Honours for services to global health.

SARS-CoV2

A very predictable 2020
to a
less predictable 2021-2022

Jeremy Farrar

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T: [@jeremyfarrar](https://twitter.com/jeremyfarrar)

Conflicts of interest

Wellcome Trust

Wellcome

Information in following slides are from a third-party source. While Moderna believes such information is reliable, we have not independently verified any third-party information, and make no guarantee, express or implied, as to the accuracy and completeness of it.



1980 – 1995

University College London

Edinburgh

Melbourne

Oxford & UCSF

1995 – 2013

Viet Nam



196X – 1979

Singapore

Malaysia

Aden Yemen

Cyprus

New Zealand

Libya

UK







VIET NAM



UK



The 'new' global health

Endemic infections

Non-communicable diseases

Drug resistance

1999-2019



SARS-COV2
MERS-CoV
H7N9, H5N1, H1N1, H3
Ebola
EV71 & EV68
Resistant Malaria
Chikungunya
Hepatitis E
Cholera
Salmonella
Zika
Dengue
Yellow Fever
SARS-CoV1
Nipah



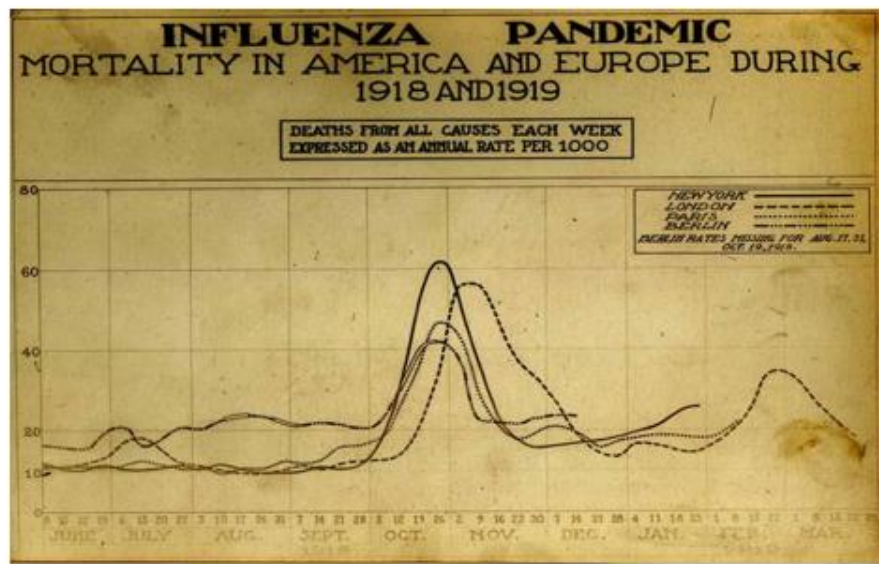
The world has changed and will change more
Environment, People, Wildlife, Nutrition, Migration, Technology, Society
(Convergence)



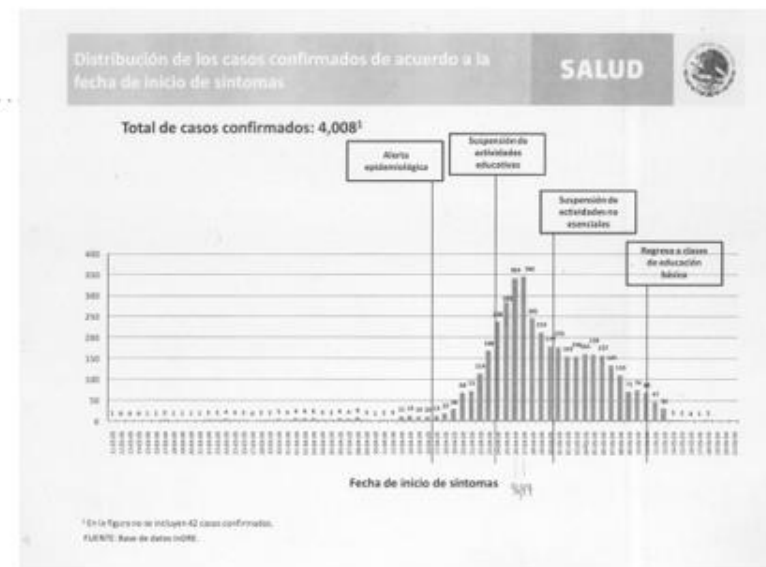
1976

2014

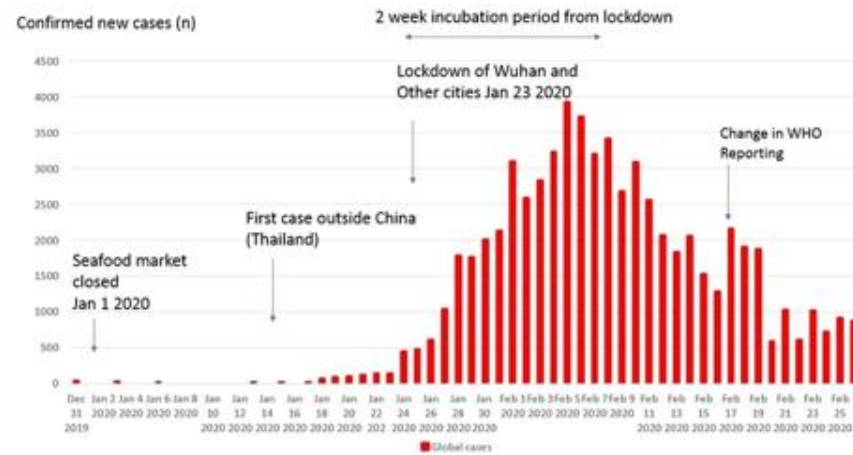




1918
London, Paris, New York, Berlin



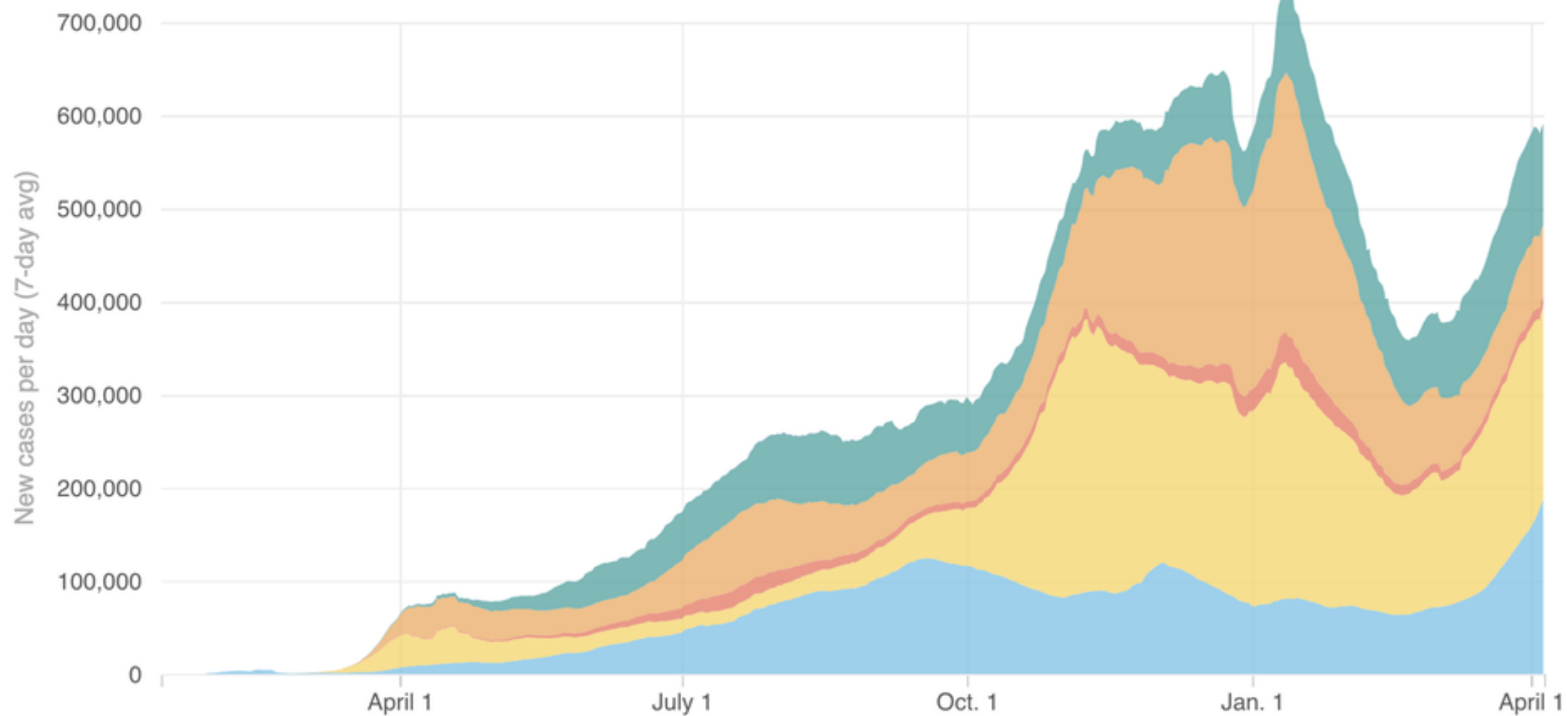
2009
Mexico

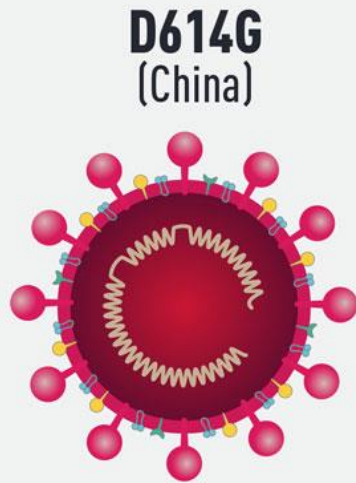


Date from December 31 2019 to 2020 Data sources: PROMEDmail, WHO, media reports

2020
Wuhan

Asia Europe Africa North America South America Oceania





D614G
(China)

Variant of Concern
(country where first detected)

**Total Characteristic
Mutations**

**Mutations in the S gene
receptor binding domain**

**Possible
functional changes**

B.1.1.7
(United Kingdom)



18

N501Y

- More efficient transmission
- Reduced antibody binding and immune protection

B.1.351
(South Africa)



8

**N501Y,
E484K,
K417N**

- Reduced vaccine efficacy against B1.351 and P.1

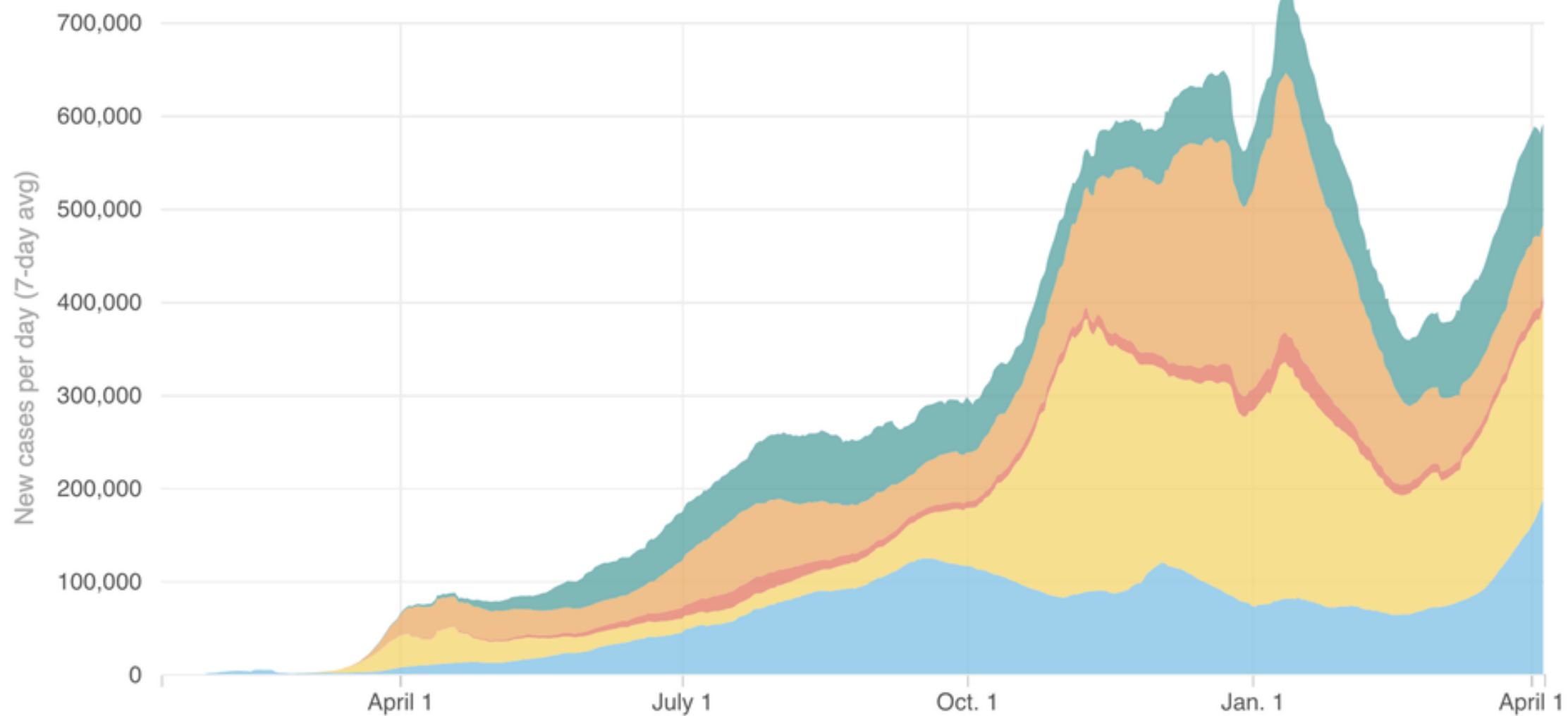
P.1
(Brazil)



21

**N501Y,
E484K**

Asia Europe Africa North America South America Oceania



Health @21st Century



Convergence

Speed

Innovation

Scale



Platforms

Blurring of definitions

Distribution and access



EDITORIAL

The Ebola Emergency — Immediate Action, Ongoing Strategy

Jeremy Farrar & Peter Piot

N Engl J Med 2014; 371:1545-1546

"First, in today's world, it's important to recognize that if certain conditions are met — biologic shifts in a pathogen, changes in the interactions between humans and our environment, fragile health systems, international indifference, high population mobility, customs and culture, urbanisation, and a lack of trust in authorities — what might once have been a limited outbreak can become a massive, potentially uncontrollable epidemic.

the development of diagnostic tools, therapies, and vaccines for these relatively rare but inevitable and potentially devastating epidemic diseases must be prioritized during interepidemic periods, with an accepted, preapproved, and ethical mechanism for accelerating development and testing such interventions when epidemic situations arise. We believe that in this epidemic, we are reaching the limit of what classic containment can achieve.

Despite great improvement over the past decade, there is still a need for better surveillance, sharing of data in real time, and rapid action based on the available information. But we cannot think that surveillance alone will bring such events under control. We have become better at picking these things up; we now must also learn to act more effectively."

SARS-CoV2

A very predictable 2020
to a
less predictable 2021-2022

Jeremy Farrar

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Conflicts of interest

Wellcome Trust

Wellcome

Professor Miles P Davenport

*Head, Infection Analytics Program
Kirby Institute, University of New South Wales*



Miles Davenport is Professor of Medicine and Head of the Infection Analytics Program at the Kirby Institute for Infection and Immunity at UNSW Sydney. He graduated in medicine from the University of Sydney and completed his DPhil at the University of Oxford in immunology before retraining in mathematical biology. He leads a team of applied mathematicians who use statistical analysis and modelling to understand host-pathogen interactions in infection and immunity. This involves collaboration with a wide variety of experimental and clinical scientists both in Australia and internationally.

Major areas of investigation include understanding HIV latency, malaria immunity and treatment, and neonatal immune development. He is a past-President of the Australasian Society for Immunology and is supported by an NHMRC (Australia) Investigator grant.

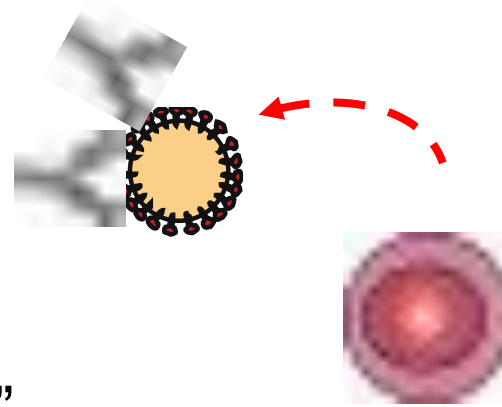
Predicting protection from SARS-CoV-2

Information in following slides are from a third-party source. While Moderna believes such information is reliable, we have not independently verified any third-party information, and make no guarantee, express or implied, as to the accuracy and completeness of it.

Professor Miles P Davenport

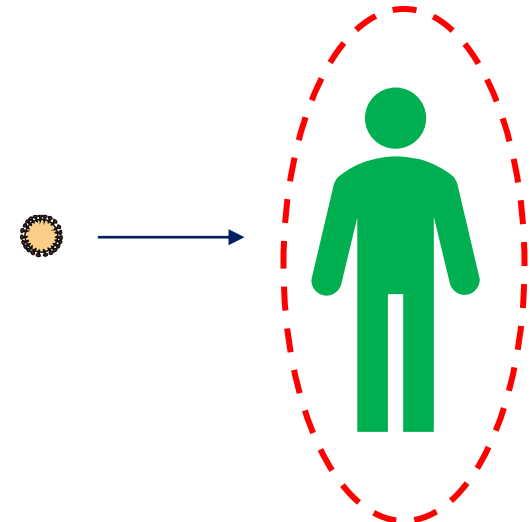
Measuring vaccine protection.

PHASE 1: Safety
(10's)

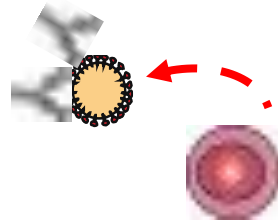


PHASE 2: “Immunogenicity”
(10's – 100's)

PHASE 3: Protective efficacy.
(1,000's - 10,000's)



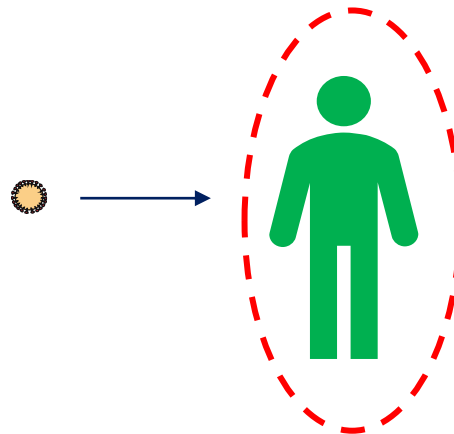
Measuring vaccine protection.



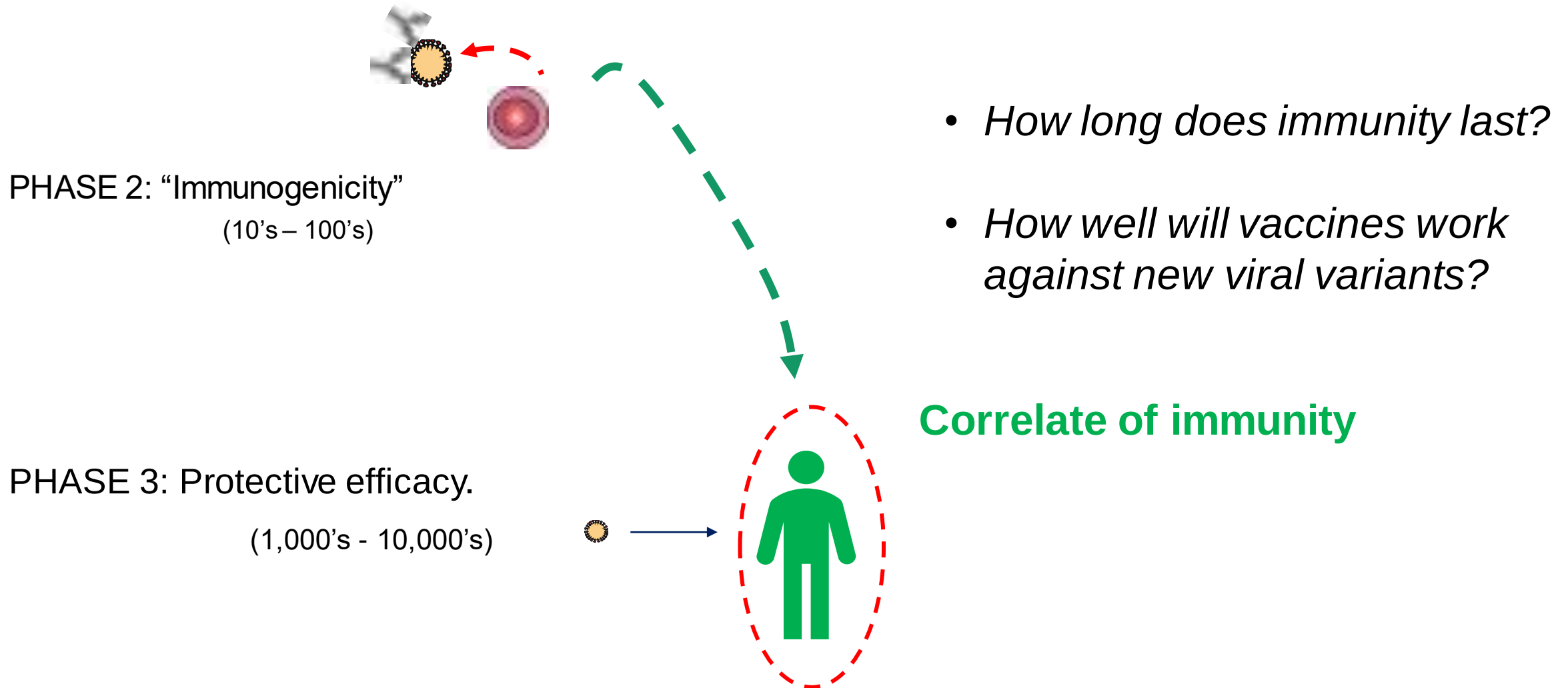
PHASE 2: “Immunogenicity”
(10’s – 100’s)

- *How long does immunity last?*
- *How well will vaccines work against new viral variants?*

PHASE 3: Protective efficacy.
(1,000’s - 10,000’s)

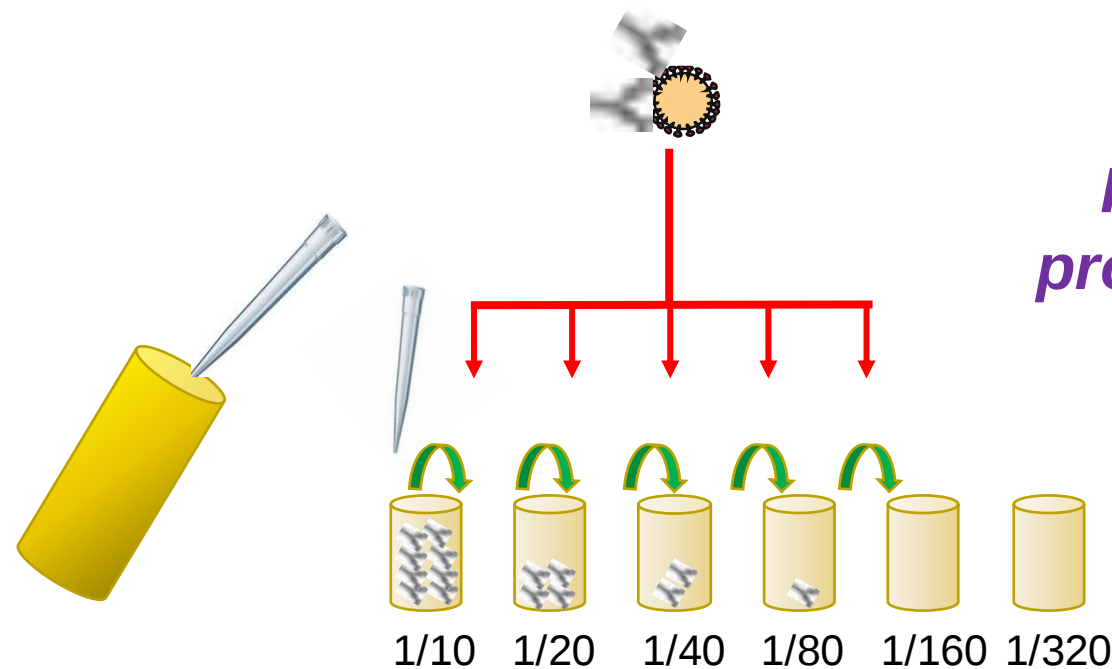


Measuring vaccine protection.



SARS-CoV-2 Neutralization titer

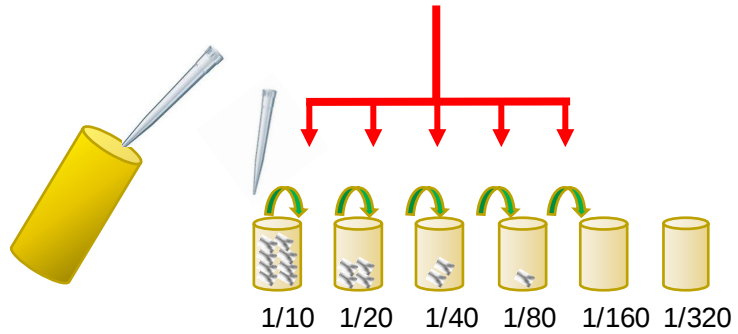
What dilution of serum neutralizes the virus in an assay?



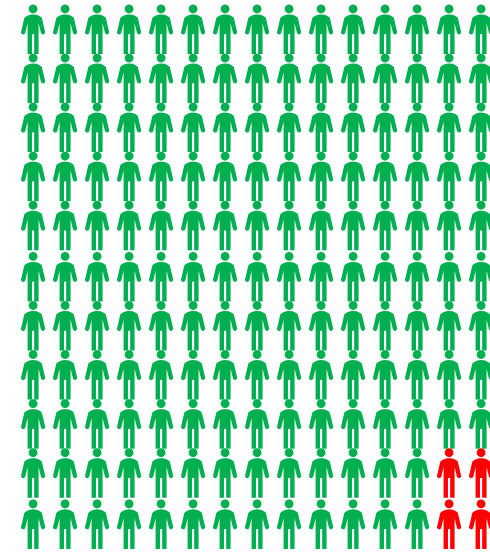
How does this predict protection from infection?

Available data

Neutralization

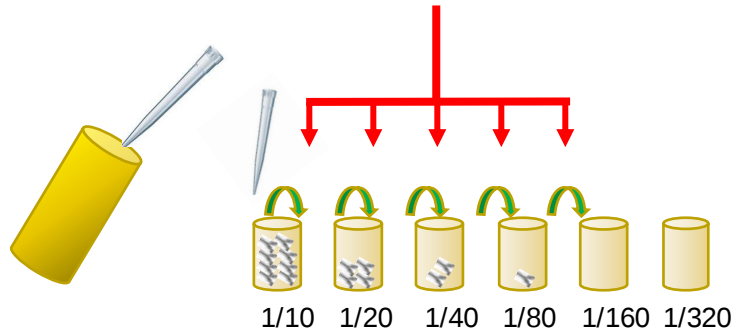


Efficacy



Available data

Neutralization

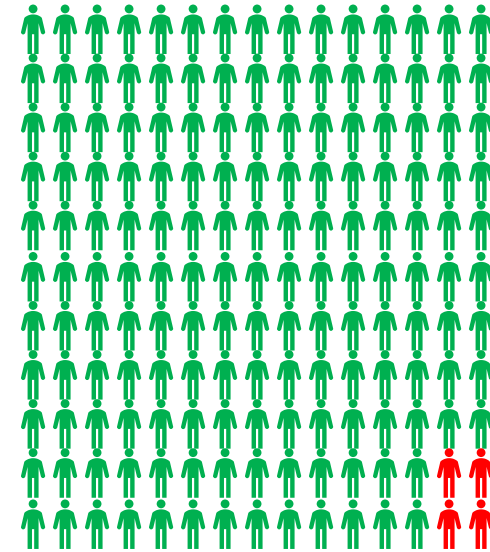


Quite different ways of measuring neutralization.

(standardize vaccine level to convalescent serum level)

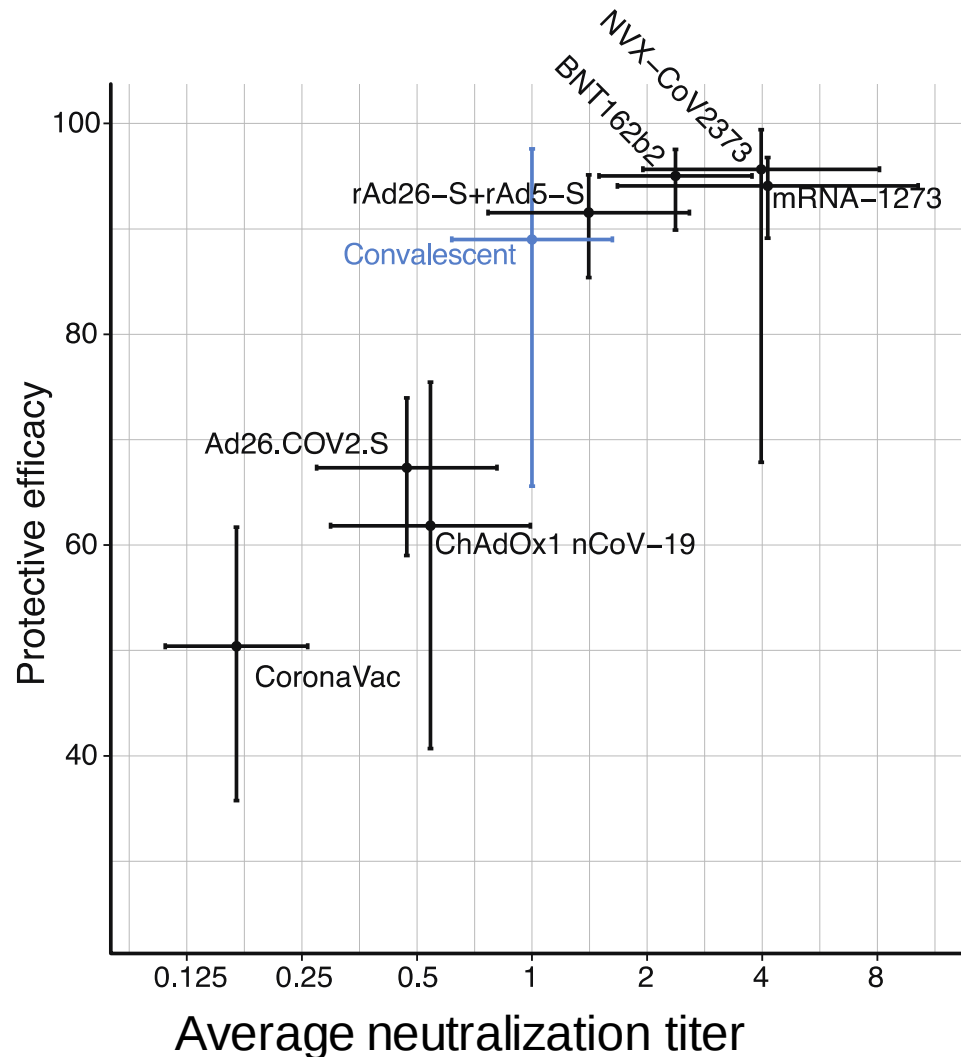
(different definition of convalescent)

Efficacy



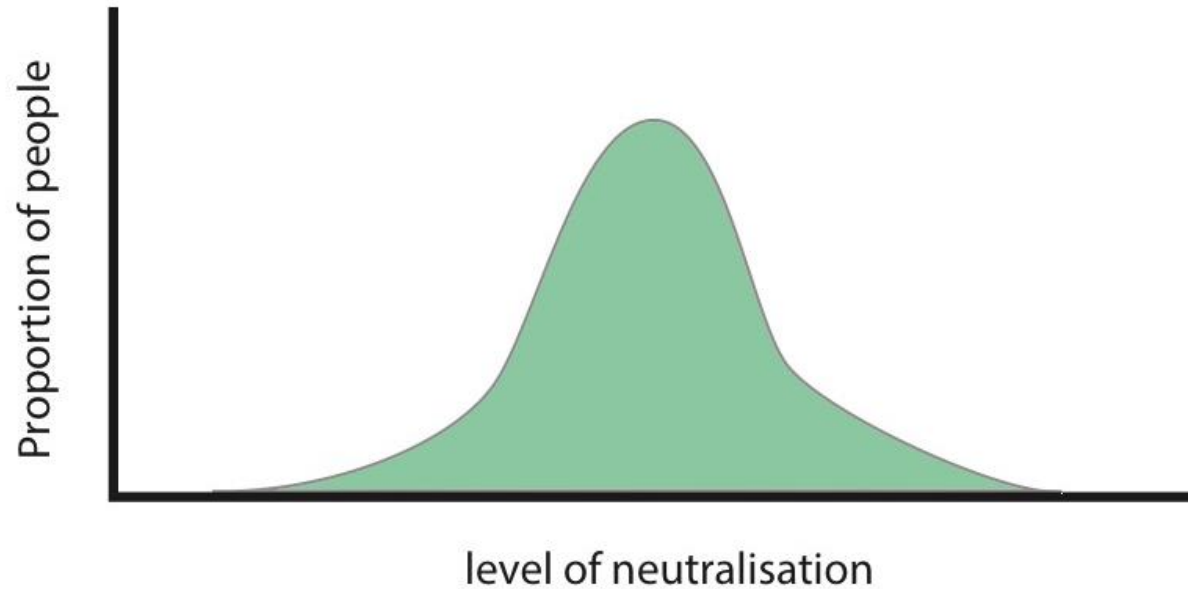
Slightly different ways of measuring 'protection'.

Does neutralization titer predict protection?

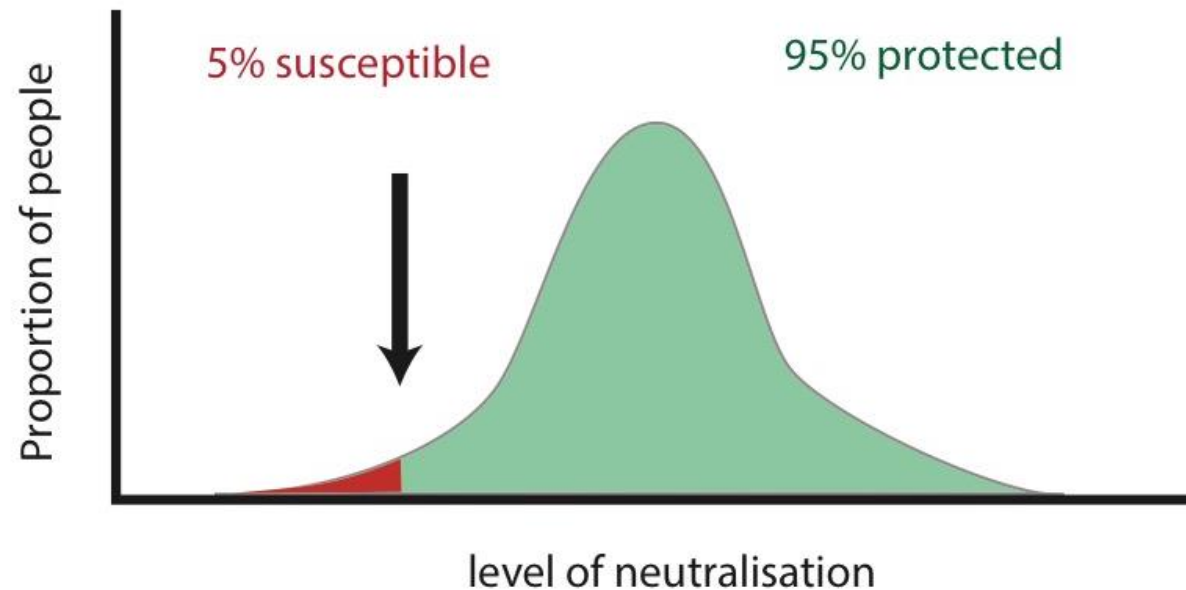


- Which immune responses predict protection? ✓
- How large a response is needed for protection?

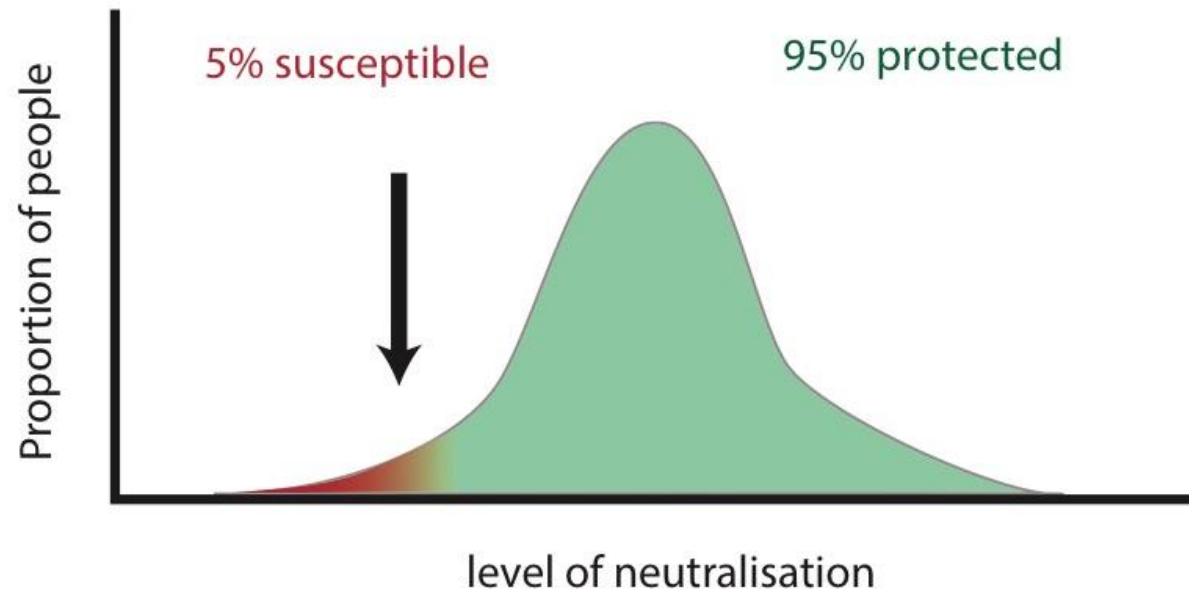
How much neutralization is needed for protection?



How much neutralization is needed for protection?



How much neutralization is needed for protection?

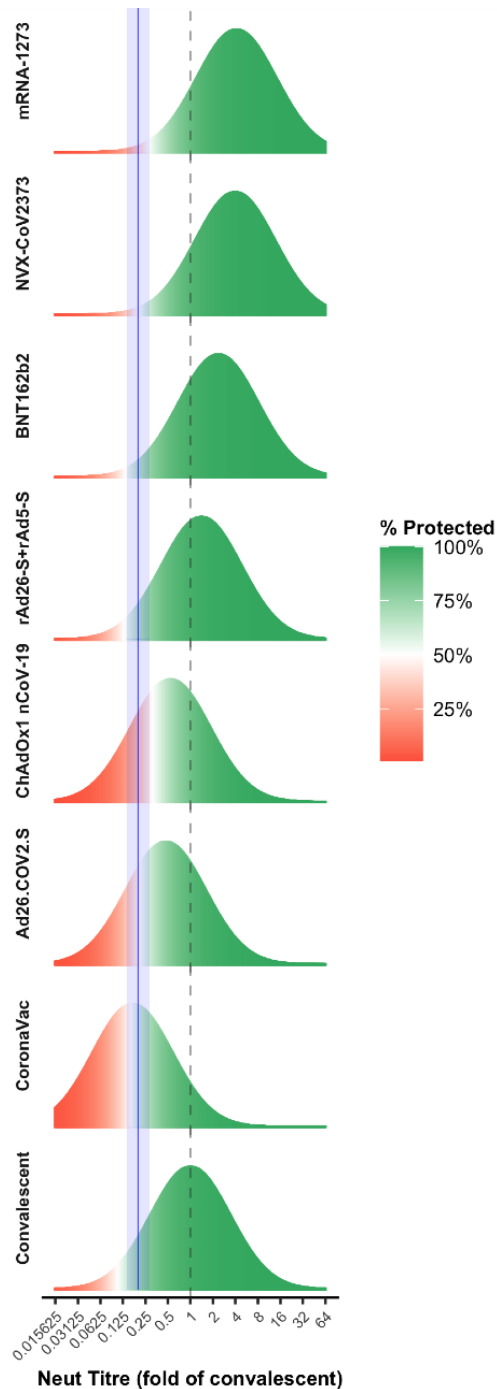


50% protective level

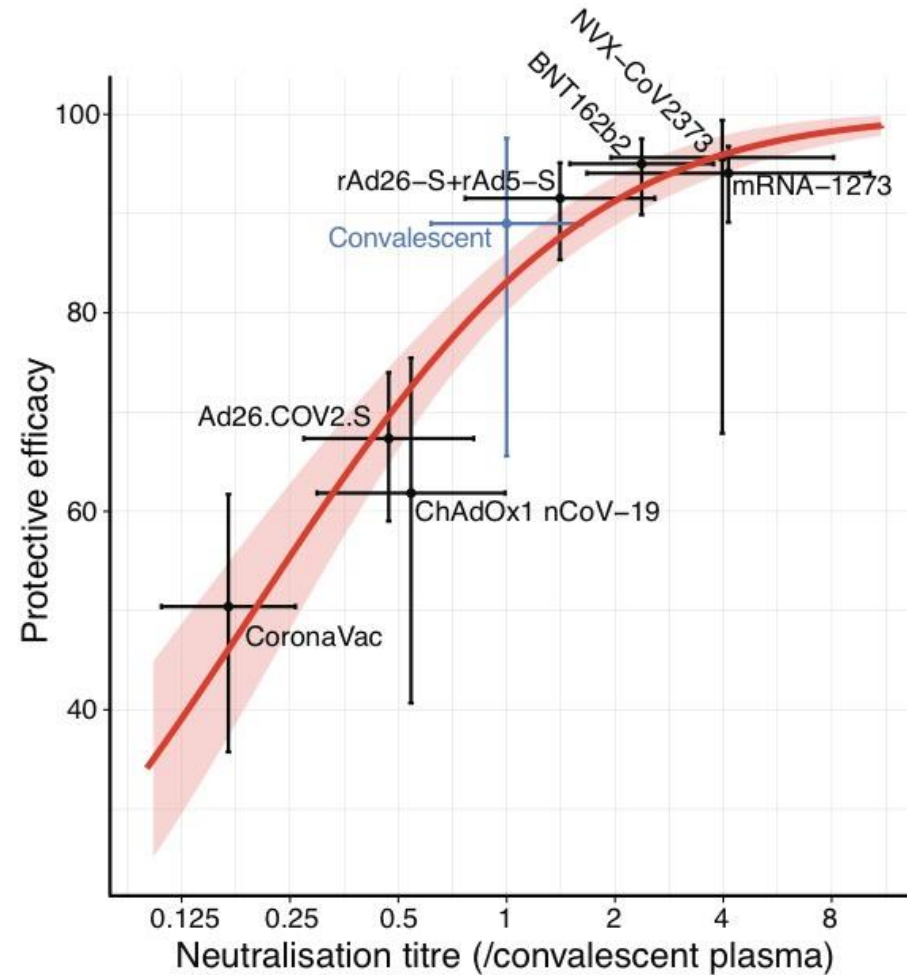
Seven vaccines +
convalescent subjects.

Estimate 50% protective titer:

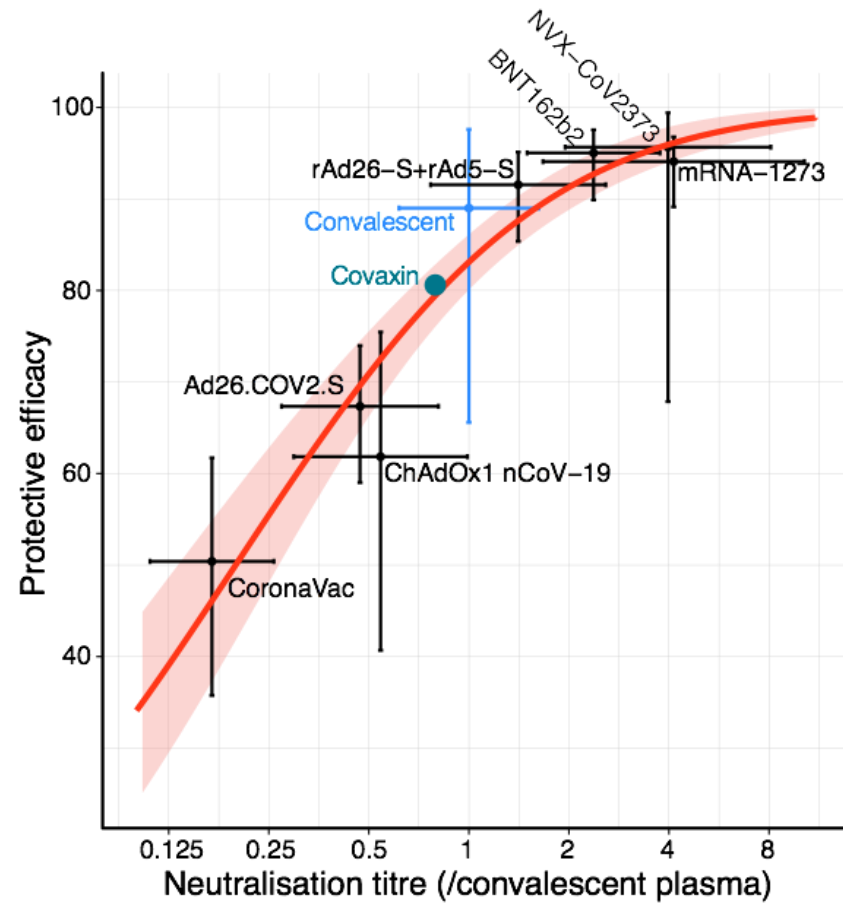
*A level of **20%** of the 'normal' convalescent
titer provides 50% protection*



Relationship between neutralization and protection.



Can we predict the efficacy of a new vaccine?

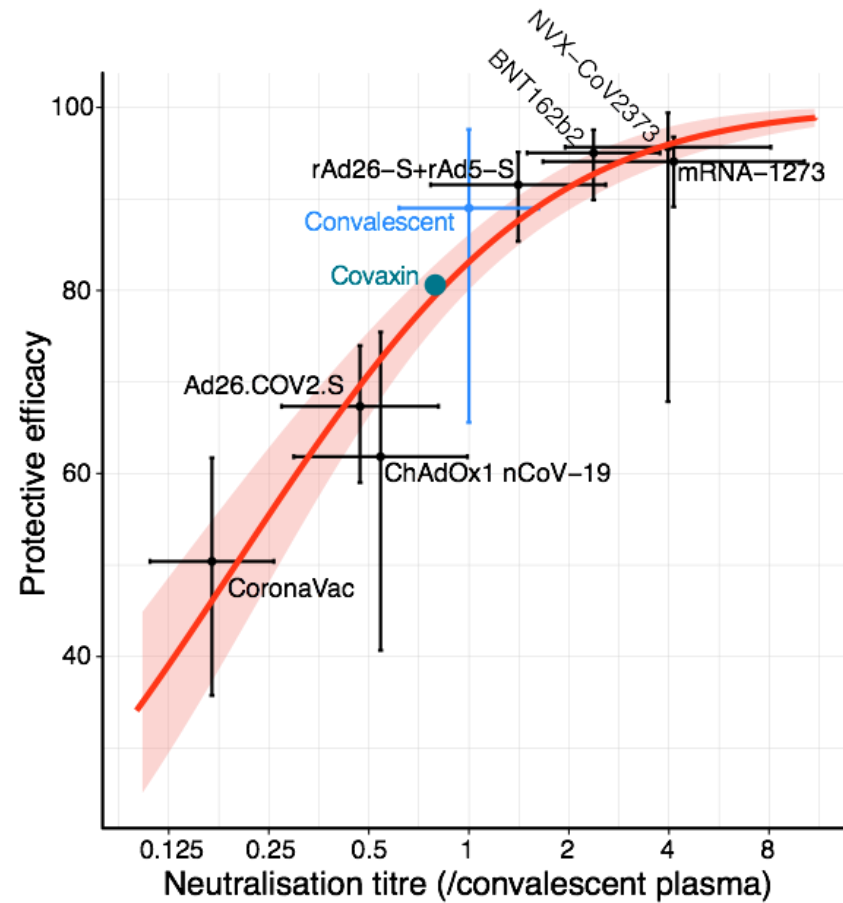


Bharat Biotech Announces Phase 3 Results of COVAXIN®: India's First COVID-19 Vaccine Demonstrates Interim Clinical Efficacy of 81%

- Data from 25,800 participants, received vaccine or placebo in a 1:1 ratio showed that the vaccine candidate was well tolerated.
- COVAXIN® demonstrated 81% interim efficacy in preventing COVID-19 in those without prior infection after the second dose.
- Clinical trial to continue through to final analysis at 130 confirmed cases in order to gather further data and to evaluate the efficacy of COVAXIN in additional secondary study endpoints.

Hyderabad, India, 03, March, 2021: Bharat Biotech, a global leader in vaccine innovation, developing vaccines for infectious diseases, today announced the first interim analysis of its BBV152 (COVAXIN®). The whole virion inactivated COVID-19 vaccine candidate demonstrated an interim vaccine efficacy of 81% in its Phase 3 clinical trial. The trials involved 25,800 subjects, the largest ever conducted in India, in partnership with the Indian Council of Medical Research.

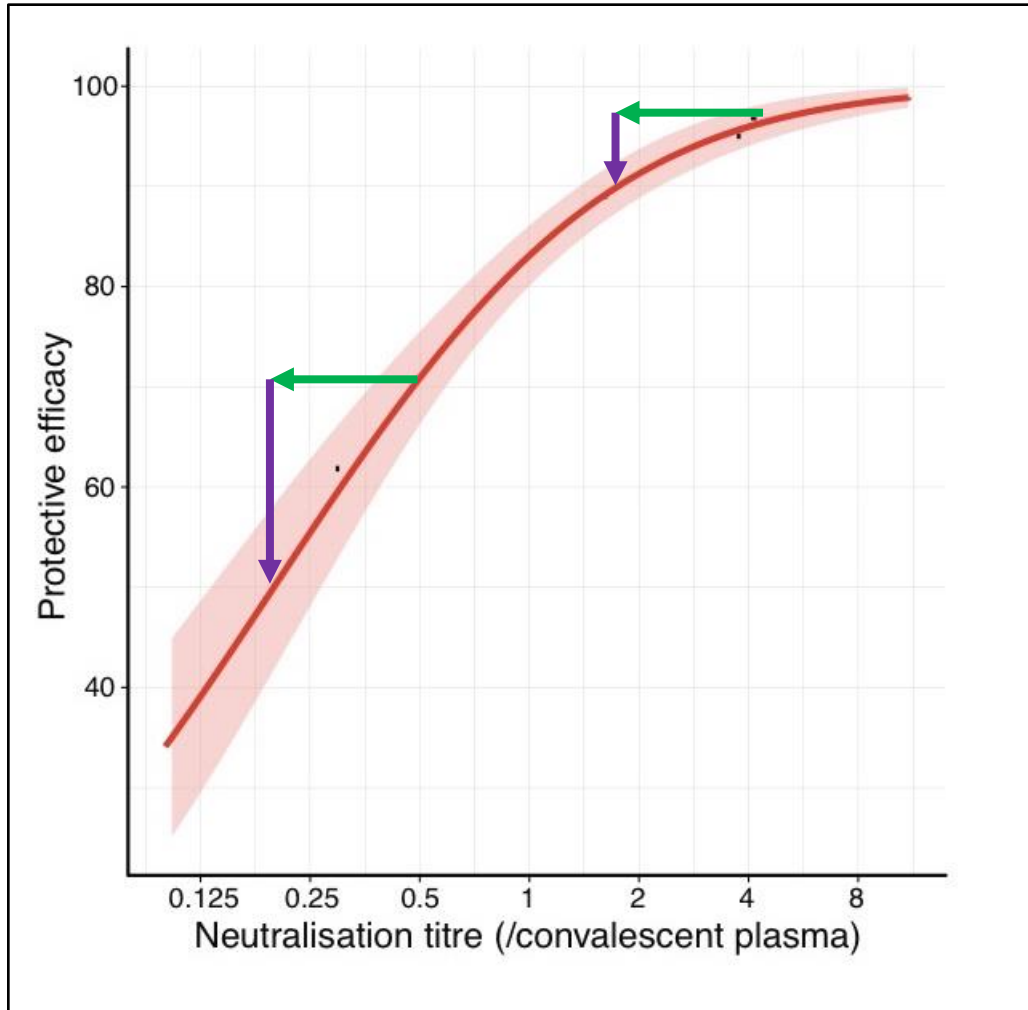
Can we predict the efficacy of a new vaccine?



Model prediction: 79.4% (76.0% - 82.8%)

Observed efficacy: 80.6%

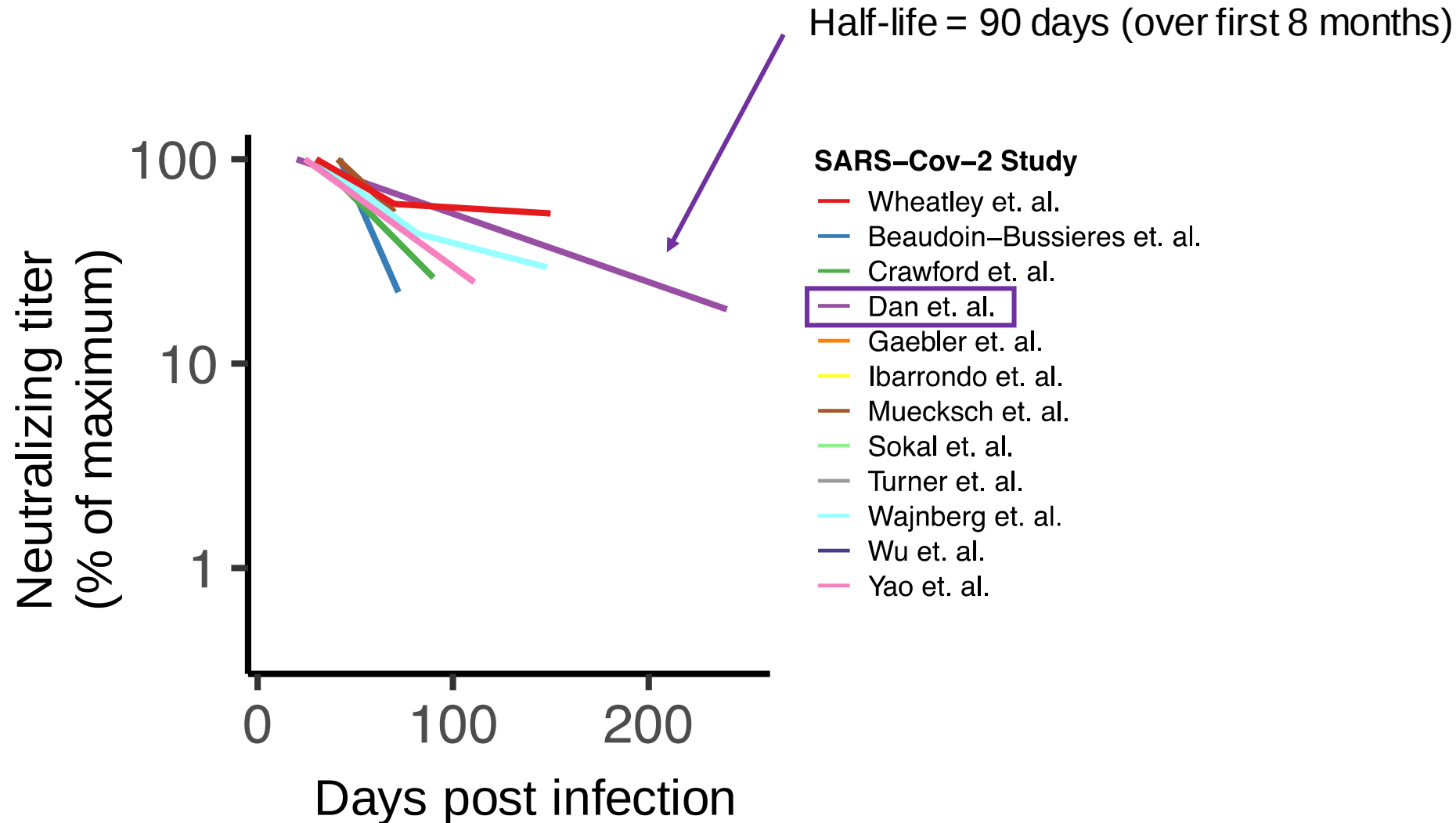
What does this relationship tell us?



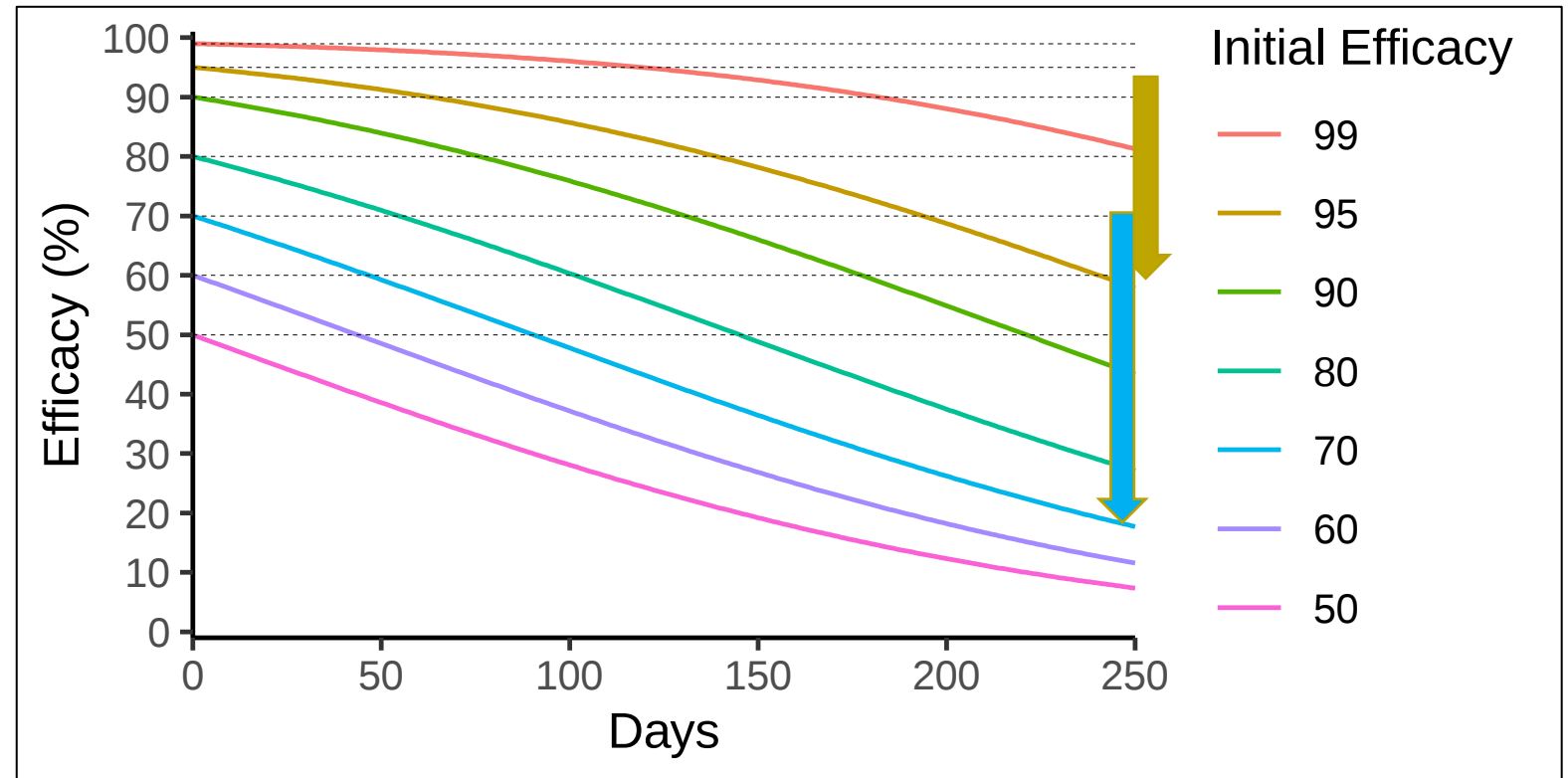
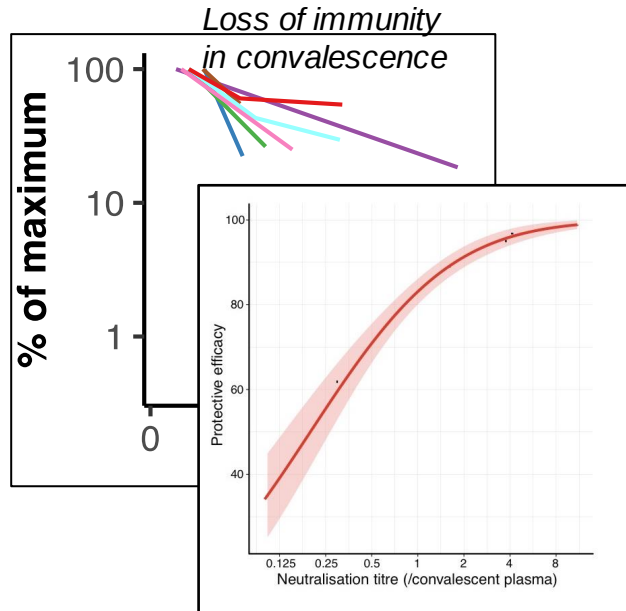
Waning immunity

What is the decrease in neutralization over time?

Neutralizing antibody decay in convalescence.



Protective efficacy over time?

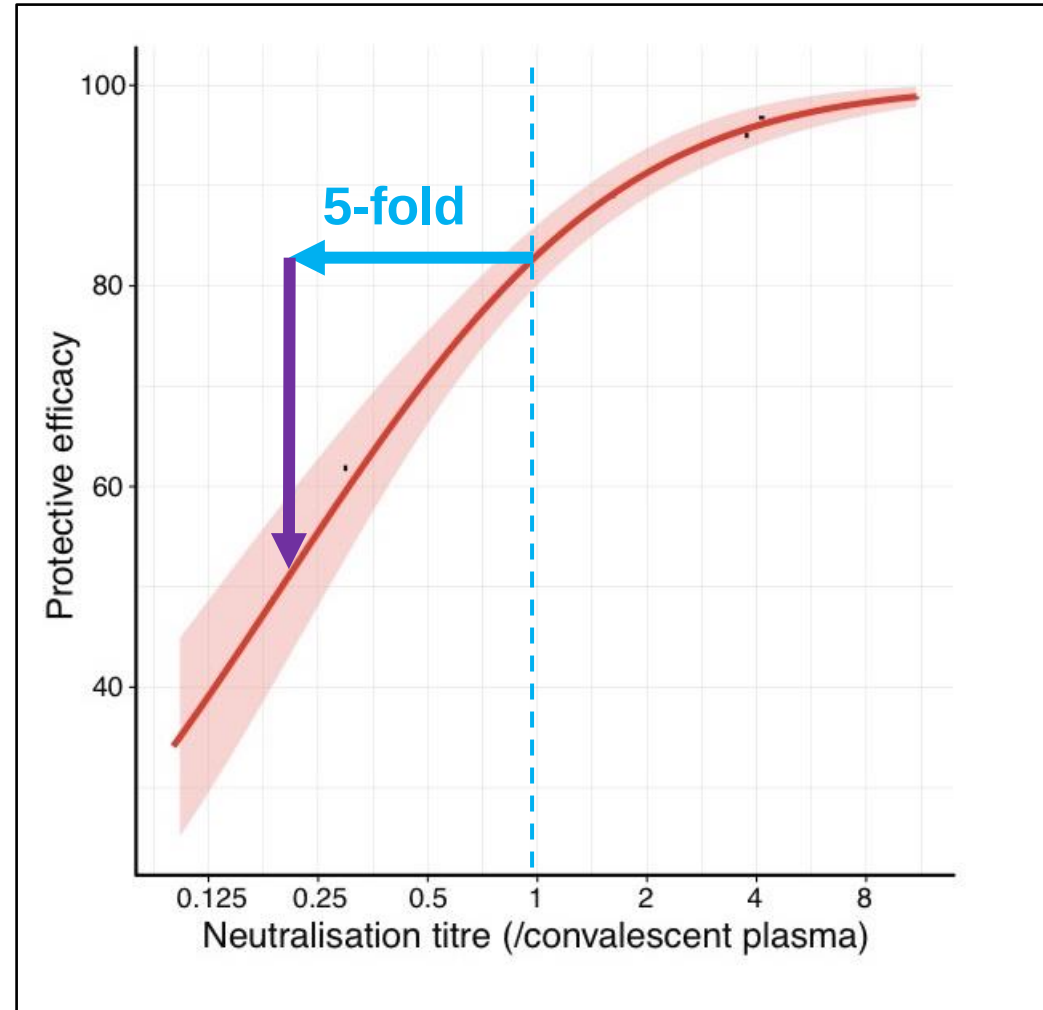


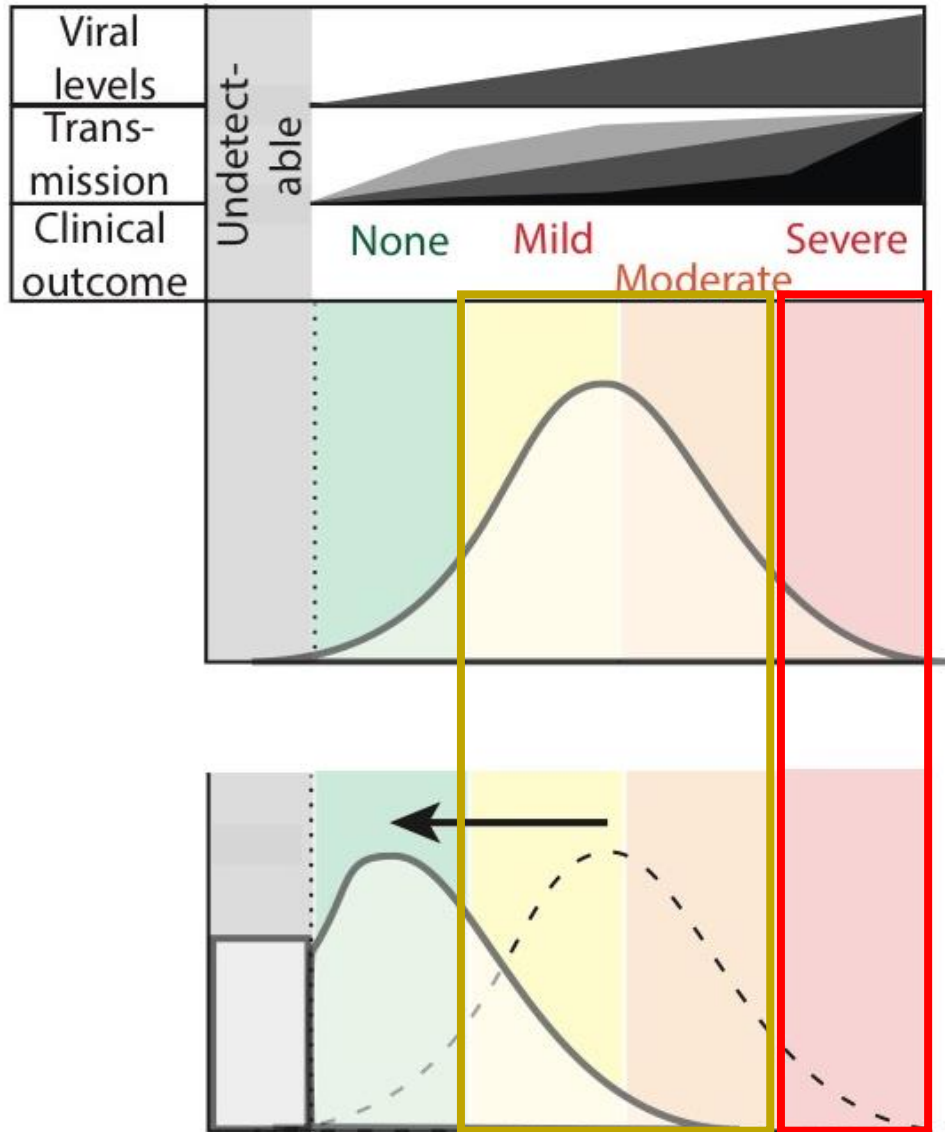
Variants of concern.

B1.1.7 (UK).

B1.351 (Sth Africa)

P1 (Brazil)





Preventing severe disease.

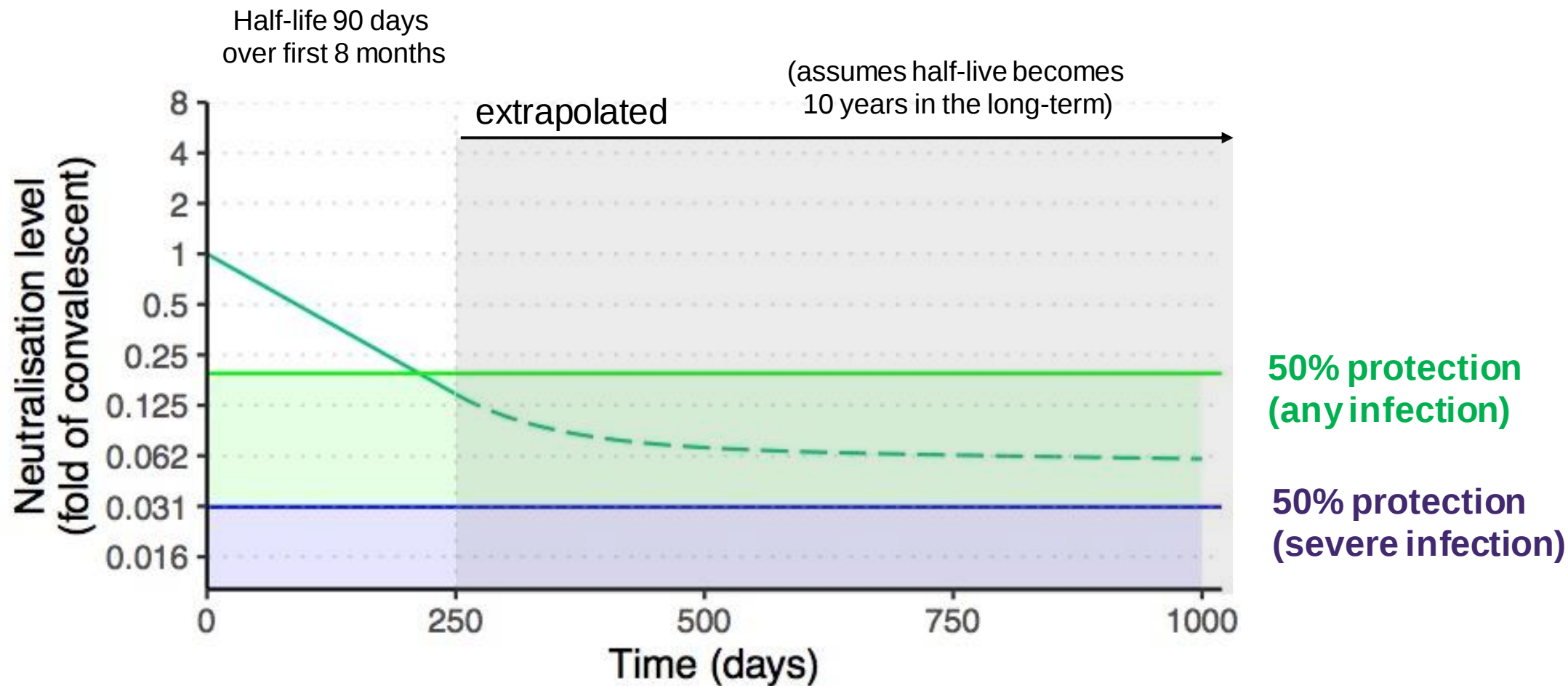
Distribution of viral levels and outcomes in unprotected infection

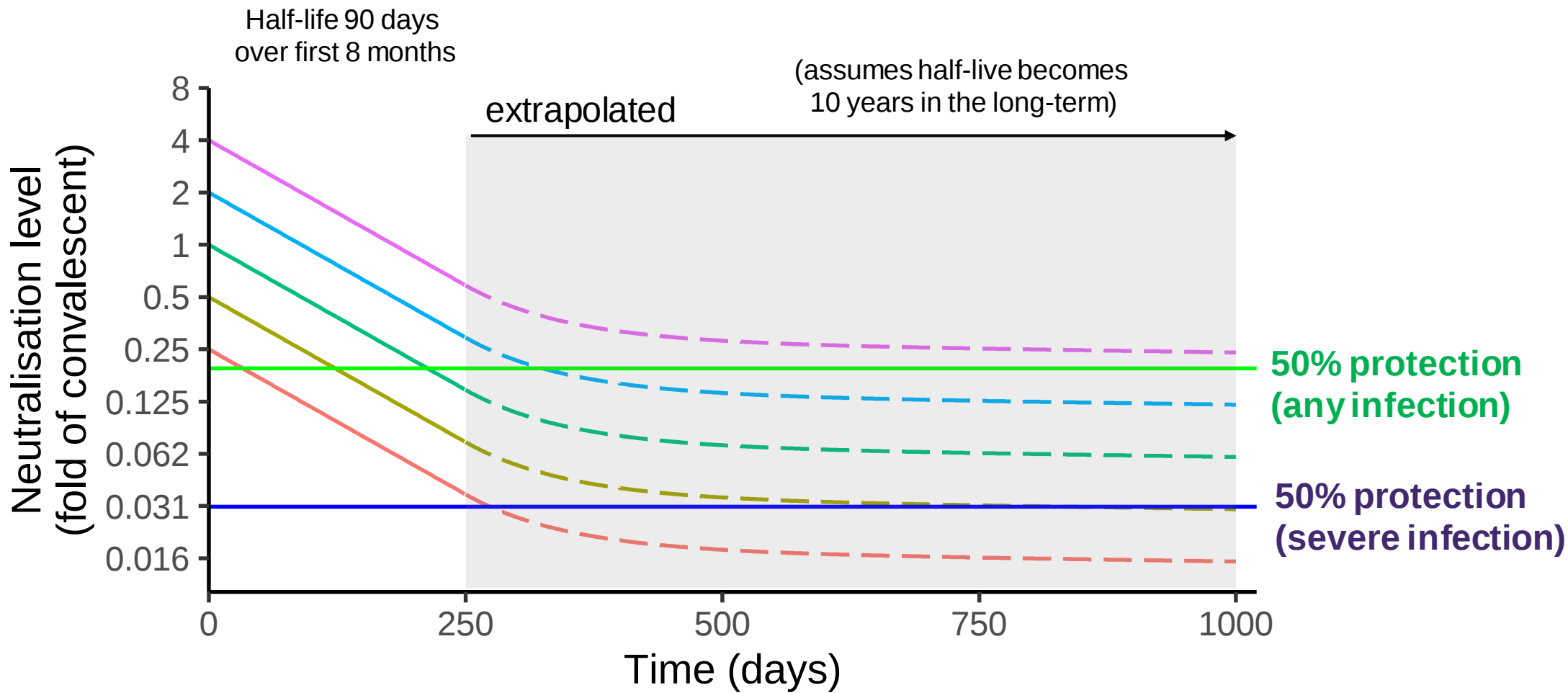
Preventing severe disease.

50% protection from mild (any) infection:
=> 20% of convalescent titer

50% protection from *SEVERE* infection*:
=> 3% of convalescent titer

*less than 100 severe cases seen in studies





Caveats

Vaccination studies:

- Different tests for neutralization.
- Different convalescent controls.
- Different definitions of 'protection'.
- Very little data available on protection from severe infection.
- Very little data on durability of neutralization available.

Predictions of future efficacy:

- Assumes neutralization the only / major source of protection (or that any other sources correlated).
- Assumes relationship between neutralization and protection is constant over time.
- Uses decay of convalescent titer to predict vaccine decay.

Implications:

If the relationship between neutralization and protection from '*any infection*' is maintained over time and against variants:

- may need revaccination within a year.
- may need variant-specific vaccines.

BUT: Protection from severe infection should be considerably more robust.

Predicting protection from SARS-CoV-2

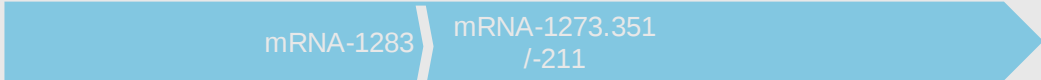
Professor Miles P Davenport



RSV Overview

Jacqueline Miller, M.D.

Senior Vice President, Infectious Diseases, Moderna

Program		ID #	Pre-clinical	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
COVID-19 vaccine		mRNA-1273						Worldwide BARDA funded
hMPV/PIV3 vaccine		mRNA-1653						Worldwide
Respiratory syncytial virus (RSV) vaccine		mRNA-1345						Worldwide
Flu vaccine		mRNA-1010 mRNA-1020 mRNA-1030						Worldwide

RSV is the leading cause of respiratory illness in young children and older adults (65+) are at high risk for severe RSV infections

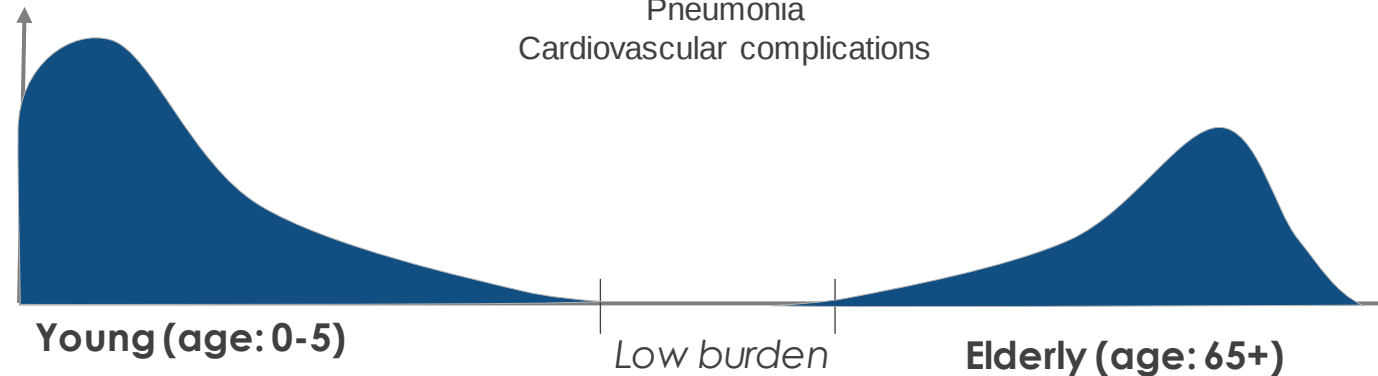
Disease burden in pediatrics

- Hospitalization rate in children <5 years old in the U.S.: ~3:1000¹
- Annually over 2 million medically attended RSV infections in children <5 years old in the U.S., more than 86,000 are hospitalized²
- Pediatric RSV results in an estimated ~\$2 billion in annual medical costs in the U.S.
- Almost all children will have had an RSV infection by their second birthday³

Disease burden in older adults

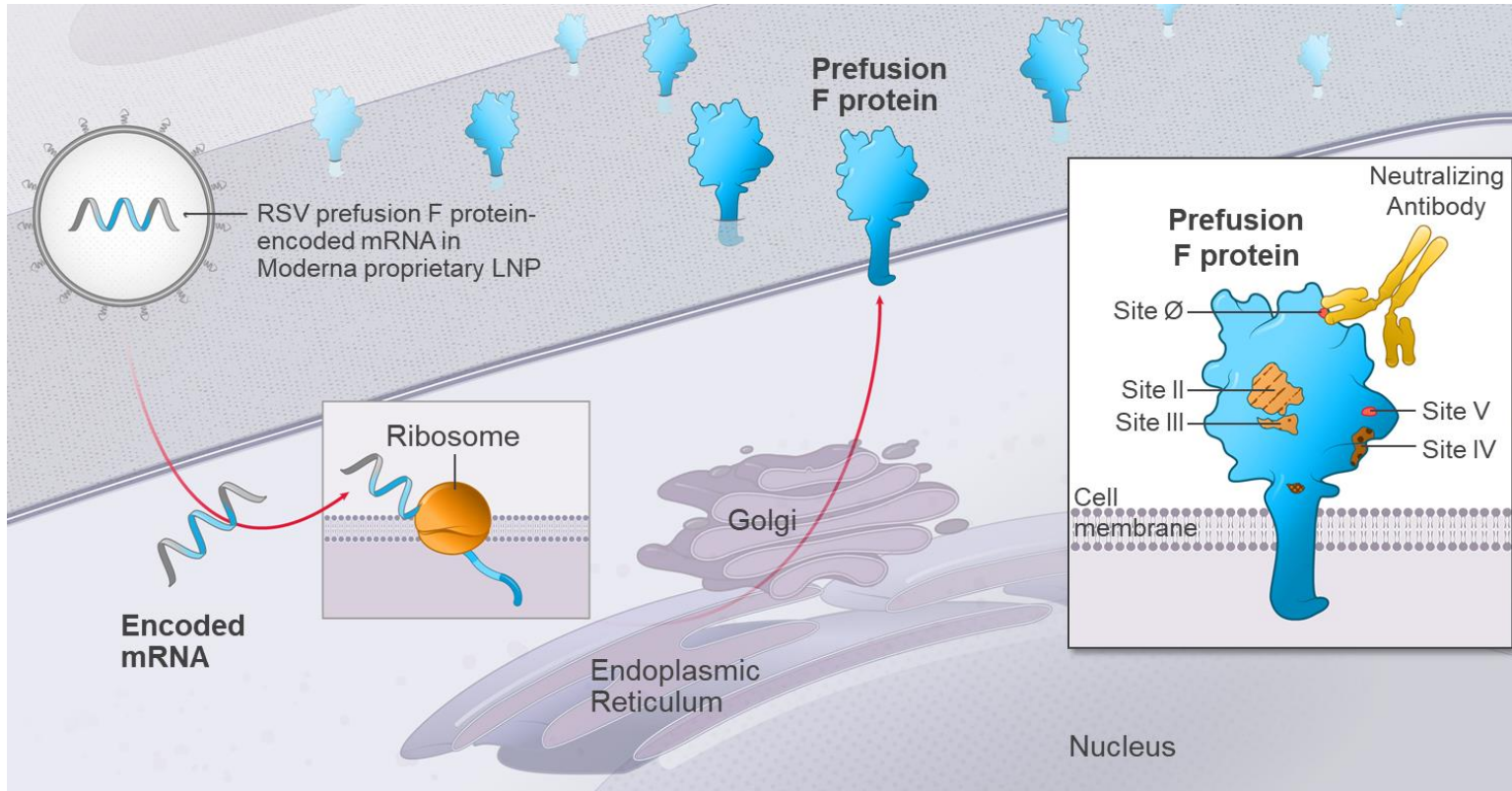
- There are ~177,000 hospitalizations in adults 65+ due to RSV in the U.S. each year, and ~14,000 deaths⁴
- Globally it is estimated that there are ~1.5 million episodes of acute respiratory tract infection and ~336,000 hospitalizations related to RSV each year⁵
- RSV in older adults results in an estimated >\$3 billion in annual medical costs in the U.S. each year

Burden of
RSV
(illustrative)



(1) Rha, Brian, et al. "Respiratory Syncytial Virus-Associated Hospitalizations Among Young Children: 2015-2016," *Pediatrics* (Jul. 2020), <https://pubmed.ncbi.nlm.nih.gov/32546583/>
(2) Eiland, Lea. "Respiratory Syncytial Virus: Diagnosis, Treatment and Prevention," *J Pediatr Pharmacol Ther.* (Apr-Jun 2009), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3461981/>
(3) Respiratory Syncytial Virus Infection (RSV), CDC, <https://www.cdc.gov/rsv/about/symptoms.html>
(4) RSV in Older Adults and Adults with Chronic Medical Conditions, CDC, <https://www.cdc.gov/rsv/high-risk/older-adults.html>
(5) Shi, Ting, et al. "Global Disease Burden Estimates of Respiratory Syncytial Virus," *J Infect Dis.* (07 Oct 2020), <https://pubmed.ncbi.nlm.nih.gov/30880339/>

RSV vaccine (mRNA-1345) encodes for a stabilized prefusion F glycoprotein



- Prefusion F elicits a superior neutralizing antibody response compared to the post-fusion protein
- RSV uses same LNP as Moderna COVID-19 Vaccine

RSV vaccine (mRNA-1345) Phase 1 ongoing in pediatric and adult populations

Key Objectives

- The primary objectives of this study are to evaluate the tolerability and reactogenicity of mRNA-1345 in younger adults, older adults and children

Primary endpoints

- Safety

Secondary endpoints

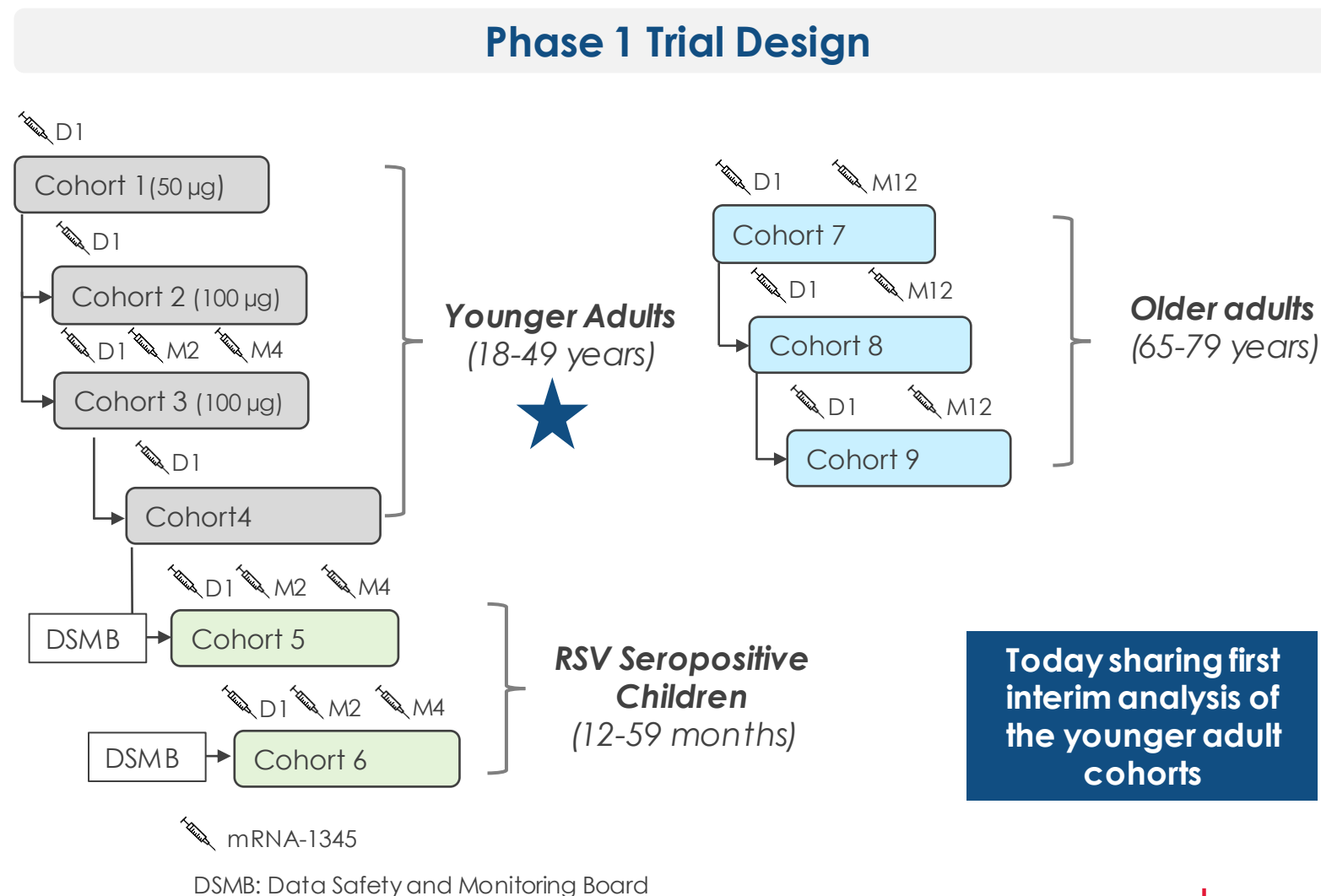
- Neutralizing antibody titers against RSV

Trial progress

- All 4 younger adult cohorts are fully enrolled
- Older adult dosing is ongoing

Interim data

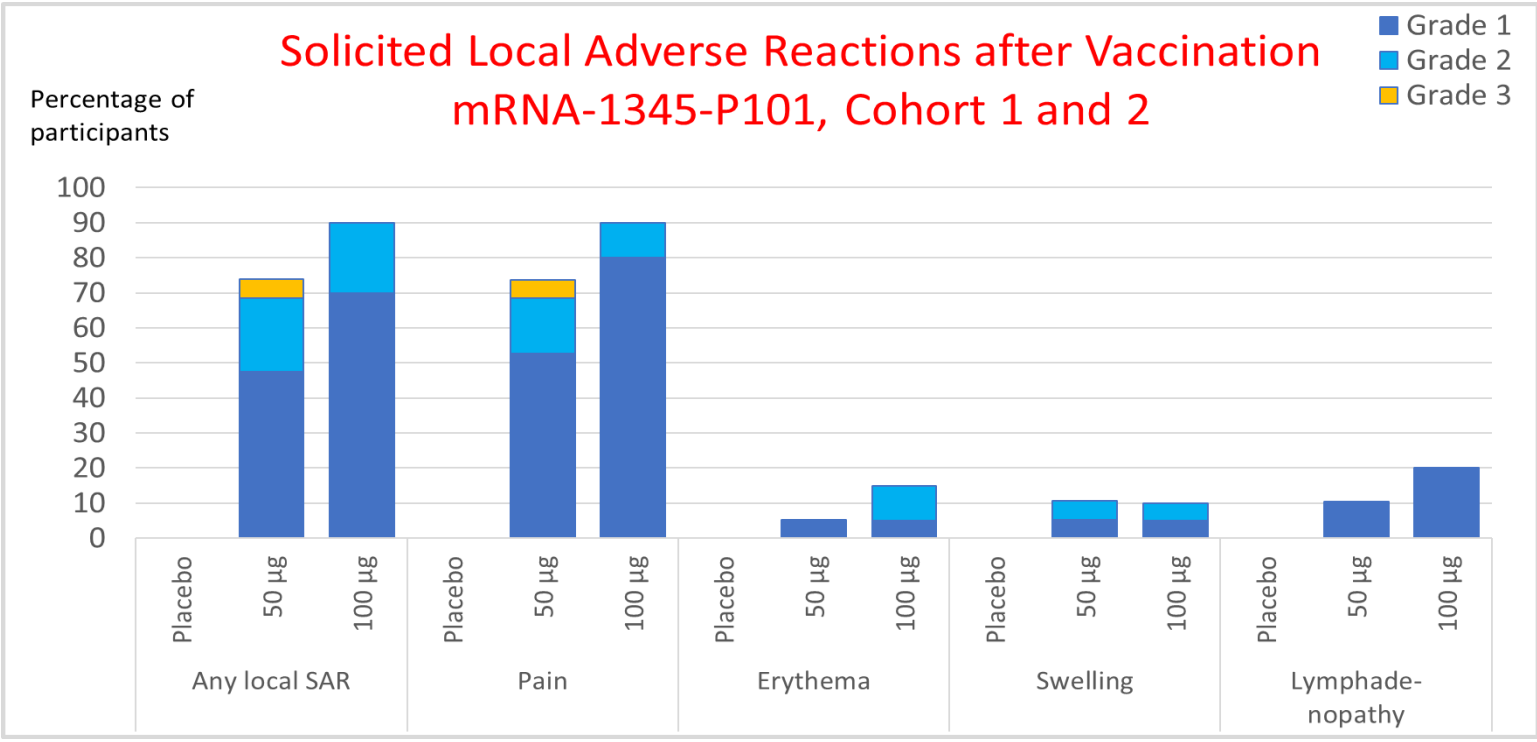
- Safety and immunogenicity of Cohorts 1 and 2 through Month 1 post vaccination



Today sharing first interim analysis of the younger adult cohorts

Solicited local adverse reactions after vaccination

A single mRNA-1345 vaccination of 50 or 100 µg was generally well-tolerated in adults 18-49 years of age

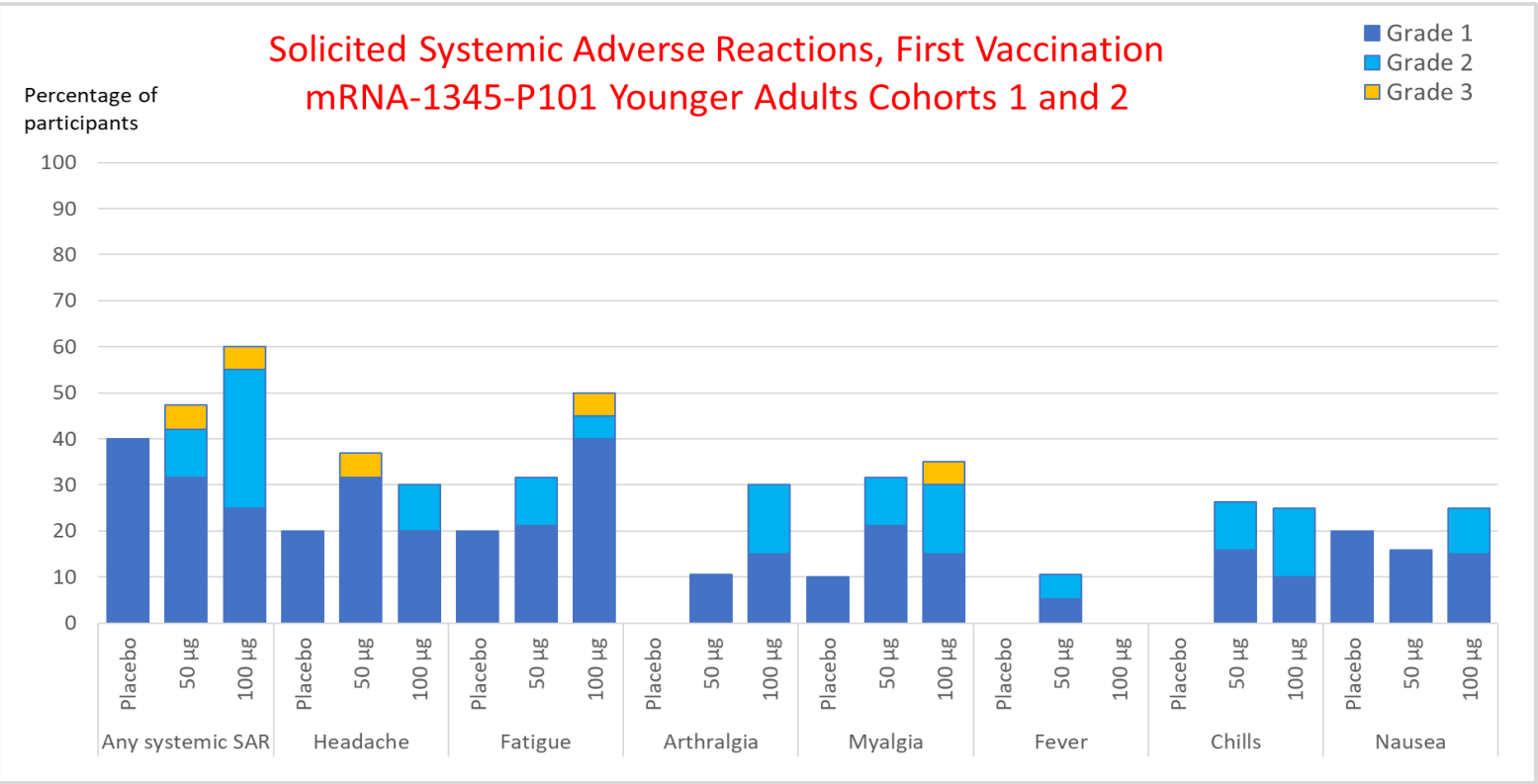


- The most common local solicited adverse reaction was injection site pain, reported by at least 73.7% of participants in mRNA-1345 groups
- The most common systemic solicited adverse reaction were headache, fatigue and myalgia
- The majority of solicited adverse reactions occurred within 1-3 days after vaccination and resolved after 1-4 days
- There were no deaths, no SAEs, no study discontinuations due to AEs, and no AEs that led to a study pause

Interim data through 1 month post vaccination, Solicited Safetyset
N = 10 for placebo, 19 for 50 µg and 20 for 100 µg

Solicited systemic adverse reactions after vaccination

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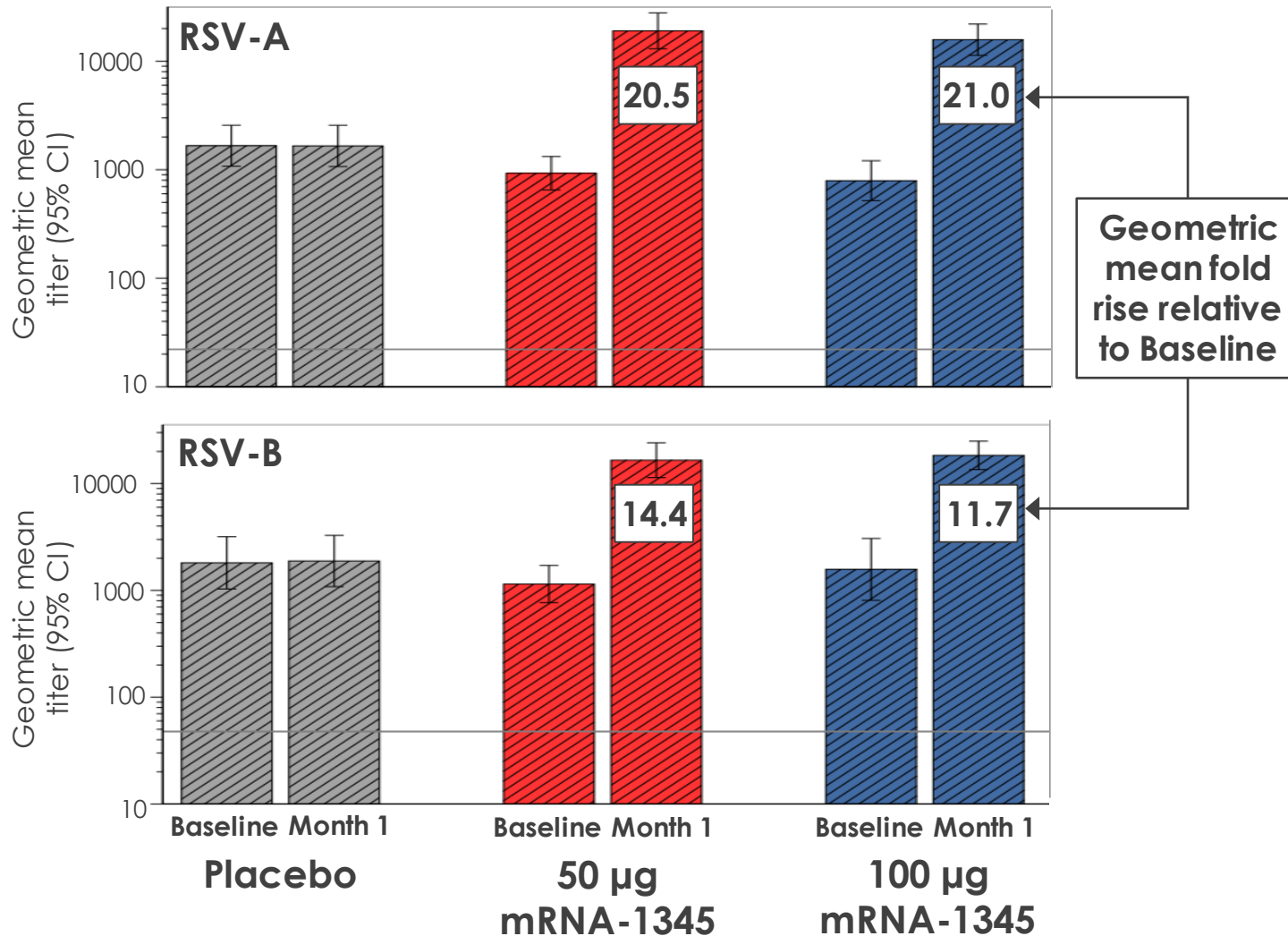


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mRNA-1345 boosts RSV neutralizing antibodies in younger adults

RSV Neutralizing Antibody



- Neutralizing antibodies were confirmed to be present at baseline in all subjects, as expected
- A single mRNA-1345 vaccination of 50 or 100 µg boosted neutralizing antibody titers against RSV with no apparent dose response
- At Month 1, the geometric mean fold rise in neutralizing antibody relative to baseline was at least 20.5 for RSV-A and at least 11.7 for RSV-B

Interim data, Per-Protocol analysis set
N = 10 for placebo, 18 for 50 µg and 19 for 100 µg

Increased immunogenicity of RSV mRNA vaccines achieved through technology advances

Geometric Mean Fold Rise (95% CI) in RSV-A Neutralizing Antibody Titer at Month 1 Relative to Baseline;

Younger Adults 18-49 Years

Treatment	mRNA-1777 ¹	mRNA-1345 ²
Placebo	1.2 (0.9, 1.6)	1.0 (0.9, 1.1)
25 µg mRNA	1.6 (1.3, 1.9)	
50 µg mRNA		20.5 (13.6, 30.9)
100 µg mRNA	2.7 (2.1, 3.4)	21.0 (13.9, 31.8)
200 µg mRNA	3.9 (3.1, 4.9)	

- mRNA-1777 and mRNA-1345 both encode prefusion RSV-F
- Changes include:
 - Optimization of the protein sequence
 - Optimization of the codon usage
 - Same LNP technology as mRNA-1273

(1) Aliprantis, Antonios, "A phase 1, randomized, placebo-controlled study to evaluate the safety and immunogenicity of an mRNA-based RSV prefusion F protein vaccine in healthy younger and older adults," *Hum Vaccin Immunother.* (29 Oct. 2020), <https://doi.org/10.1080/21645515.2020.1829899>

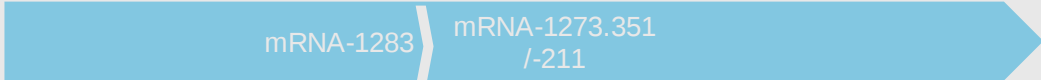
(2) mRNA-1345 Phase 1 interim analysis, Cohorts 1 and 2, Per Protocol set



hMPV/PIV3 Overview

Jacqueline Miller, M.D.

Senior Vice President, Infectious Diseases, Moderna

Program		ID #	Pre-clinical	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
COVID-19 vaccine		mRNA-1273						Worldwide BARDA funded
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Flu vaccine		mRNA-1010 mRNA-1020 mRNA-1030						Worldwide

Human metapneumovirus (hMPV) and parainfluenza virus type 3 (PIV3) represent an unmet need in young children

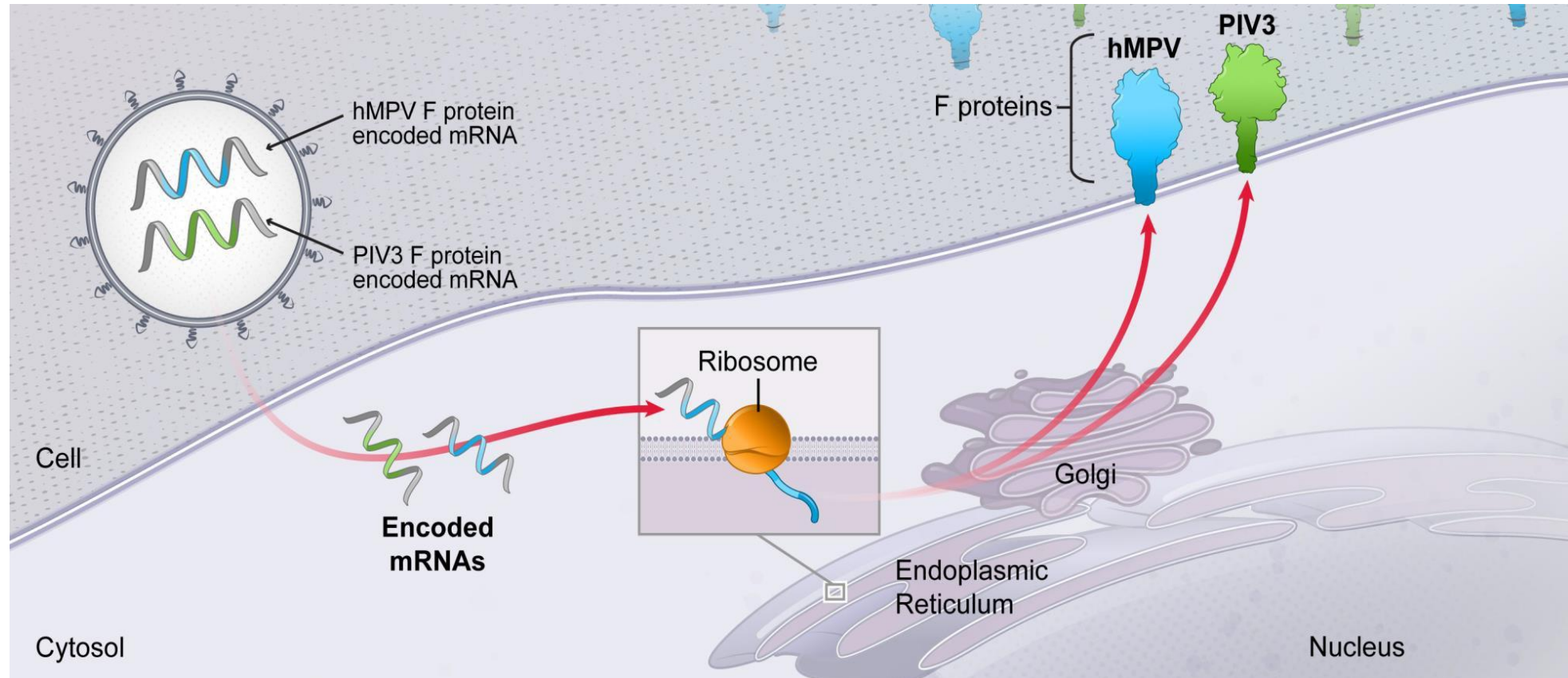
hMPV and PIV3 are RNA viruses that are important causes of respiratory tract infections, particularly in children

- Increasing rates of diagnosis and association with hospitalization for respiratory illness
- Most hMPV or PIV3-associated hospitalizations in children occur under 2 years old
- Hospitalization rates in children < 5 years old in the U.S.¹:
 - hMPV: 1.2 per 1,000
 - PIV3: 0.5 per 1,000

hMPV and PIV3 infection sequelae

High fever
Otitis media
Thick nasal discharge
Breathing difficulties, coughing
Croup
Pneumonia
Bronchiolitis

hMPV/PIV3 vaccine (mRNA-1653) combines mRNAs encoding antigens from two different viruses



hMPV/PIV3 (mRNA-1653) Phase 1b trial is ongoing in children

Key objective

- To evaluate the safety and immunogenicity of mRNA-1653 when administered to adults and to children 12-59 months of age with serologic evidence of prior exposure to hMPV and PIV3

Primary endpoints

- Safety

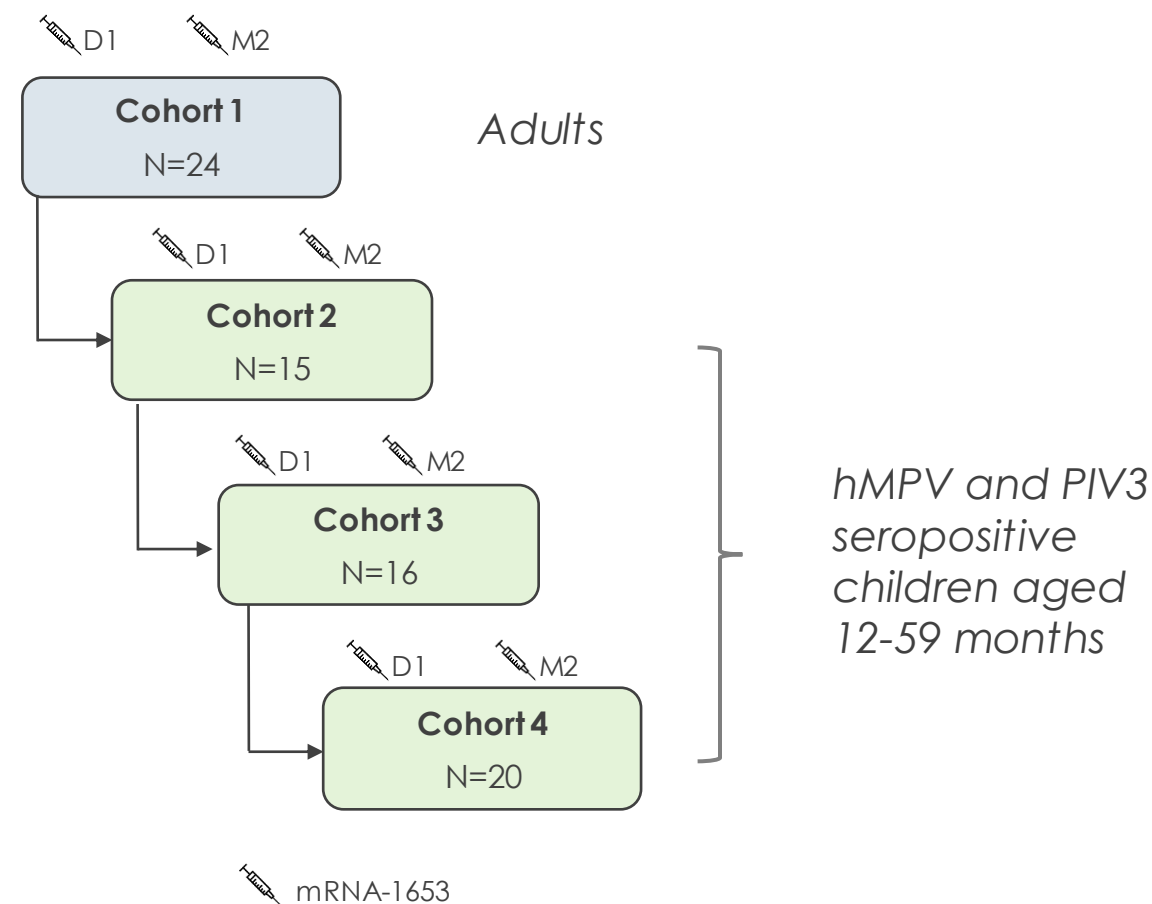
Secondary endpoints

- Neutralizing antibodies against hMPV and PIV3

Trial progress

- Positive Phase 1 interim analysis data reported in 2019
- Phase 1b enrolling – Cohort 1 and 2 fully enrolled

Phase 1 trial design



hMPV, PIV3 and RSV seropositivity rates in children have dropped ~50% during COVID pandemic*

Seropositivity rate in children aged 12-36 months,
as measured by microneutralization assay

Sample collection date (number of samples)	hMPV	PIV3	RSV
Feb-Mar 2020 (n=39)	68%	63%	93%
Aug-Dec 2020 (n=20)	35%	35%	50%

* Data are exploratory and not the output of a formal study.

Benjamin Cowling, BSc, PhD, FFPH

Professor and Division Head, Division of Epidemiology and Biostatistics, School of Public Health, The University of Hong Kong



Professor Benjamin Cowling joined the School of Public Health (SPH) at HKU in 2004. Prior to moving to Hong Kong, he graduated with a PhD in medical statistics at the University of Warwick (UK) in 2003, and spent a year as a postdoc at Imperial College London (UK). Professor Cowling has been the Head of the Division of Epidemiology and Biostatistics since 2013. He is responsible for teaching the introductory module in epidemiology on the MPH curriculum, and is the chairman of the Departmental Research Postgraduate Committee. Prof Cowling is a co-director of the WHO Collaborating Centre for Infectious Disease Epidemiology and Control at HKU SPH.

Prof Cowling's primary research focus is in infectious disease epidemiology. In recent years he has designed and implemented large field studies of influenza transmission in the community and the effectiveness and impact of control measures. His latest research has focused on the modes of respiratory virus transmission, influenza vaccination effectiveness, and immunity to infections at the individual and population level. He has strong links with China CDC, and the NIGMS-funded Harvard Center for Communicable Disease Dynamics.

Professor Cowling is a fellow of the Royal Statistical Society and a Fellow of the UK Faculty of Public Health. He is the Editor-in-Chief of Influenza and Other Respiratory Viruses, and an Associate Editor of Emerging Infectious Diseases.

Epidemiology and control of influenza – the need for next-generation vaccines

Ben Cowling

School of Public Health, The University of Hong Kong

14 April 2021

Information in following slides are from a third-party source. While Moderna believes such information is reliable, we have not independently verified any third-party information, and make no guarantee, express or implied, as to the accuracy and completeness of it.

Influenza

- One of the most common acute infections; around 20-25% of children and 10-15% of adults are infected with influenza virus each year
- Most infections are mild and self-limiting, a small fraction lead to severe disease. Figure on right is wrong (common misconception). Fever in <50% of infections.

IS IT A COLD OR THE FLU?



Influenza is a leading cause of respiratory deaths worldwide

- Influenza can cause mild to severe respiratory illness which can result in hospitalization or death
- Older adults and young children are at high risk of seasonal flu complications
- Globally about 3-5 million severe cases of flu each year, and 290-650,000 flu-related respiratory deaths¹
- About 8% of the US population experiences symptoms from flu each year in the US
 - Fever, cough, sore throat, nasal congestion, fatigue, vomiting/diarrhea (more common in children)
 - Pneumonia (viral and/or bacterial), ear infections, sinus infections, exacerbation of chronic conditions

Estimated Range of Annual Burden of Flu in the U.S. from 2010-2020³



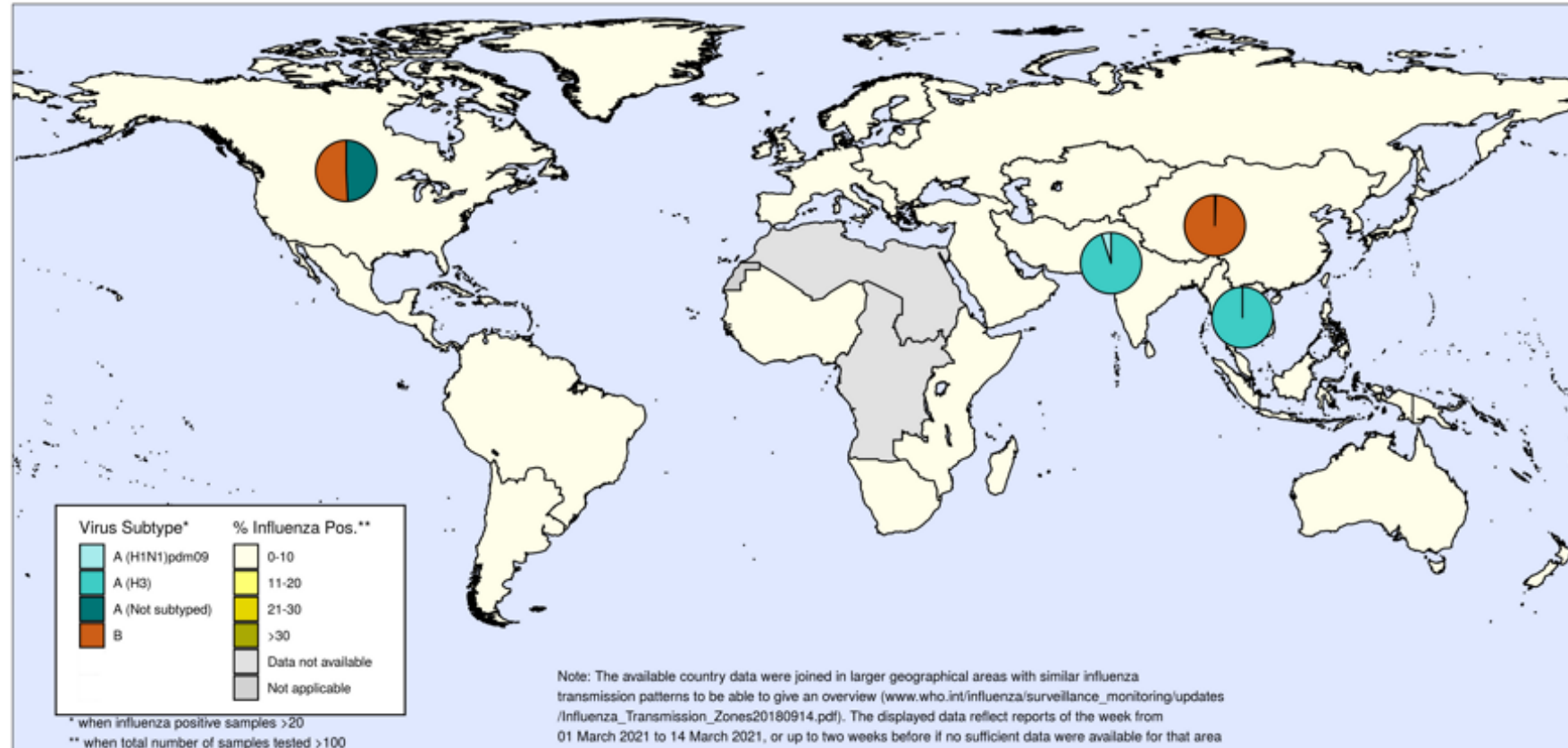
*The top range of these burden estimates are from the 2017-2018 flu season. These are preliminary and may change as data are finalized.

Iuliano et al. 2018 Lancet
Rolfes et al. 2018 IORV

Near-disappearance of influenza in 2020/21

Percentage of respiratory specimens that tested positive for influenza
By influenza transmission zone

Map generated on 26 March 2021

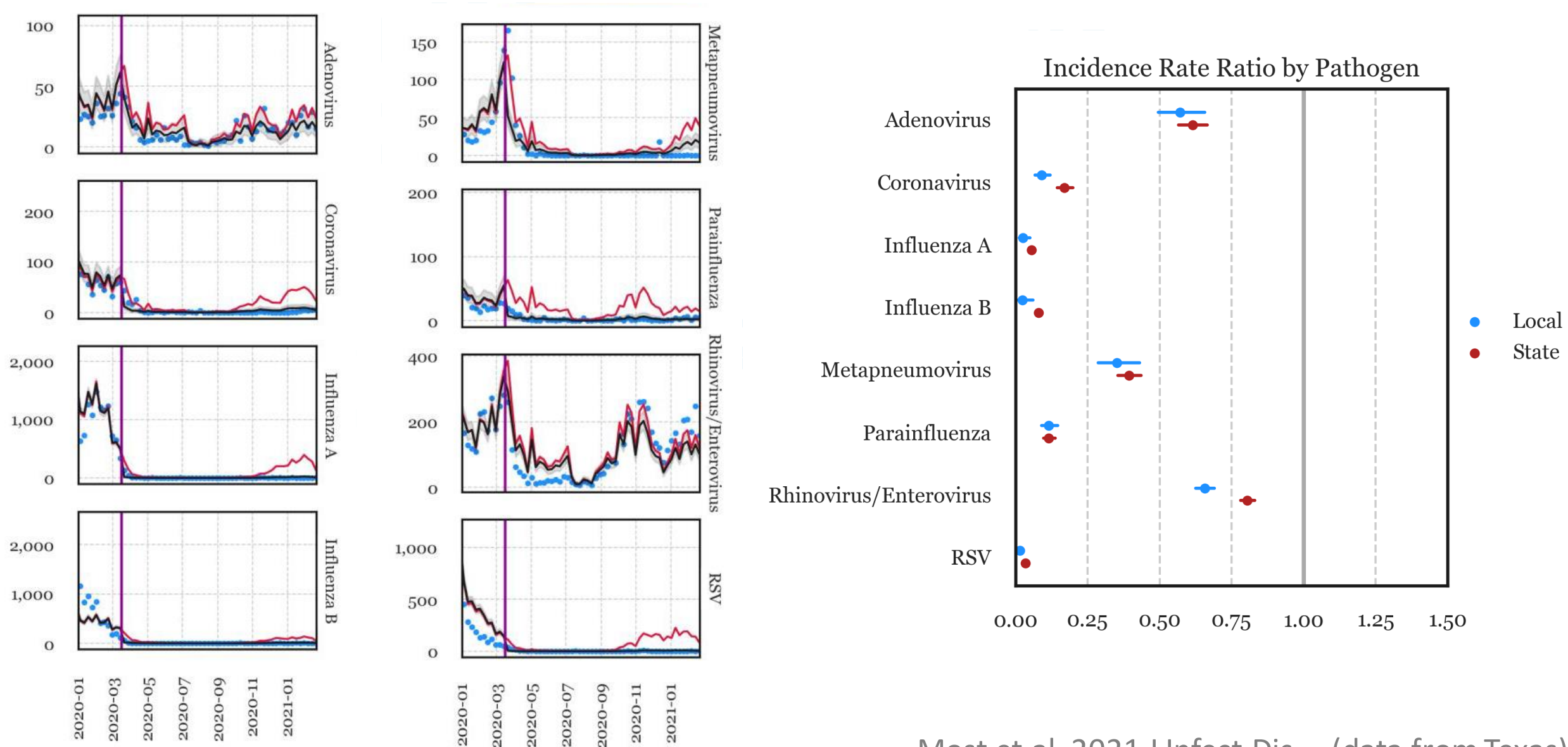


The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data source: Global Influenza Surveillance and Response System (GISRS), FluNet (www.who.int/fluNet)
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Disappearance of most other respiratory viruses



Influenza will be back

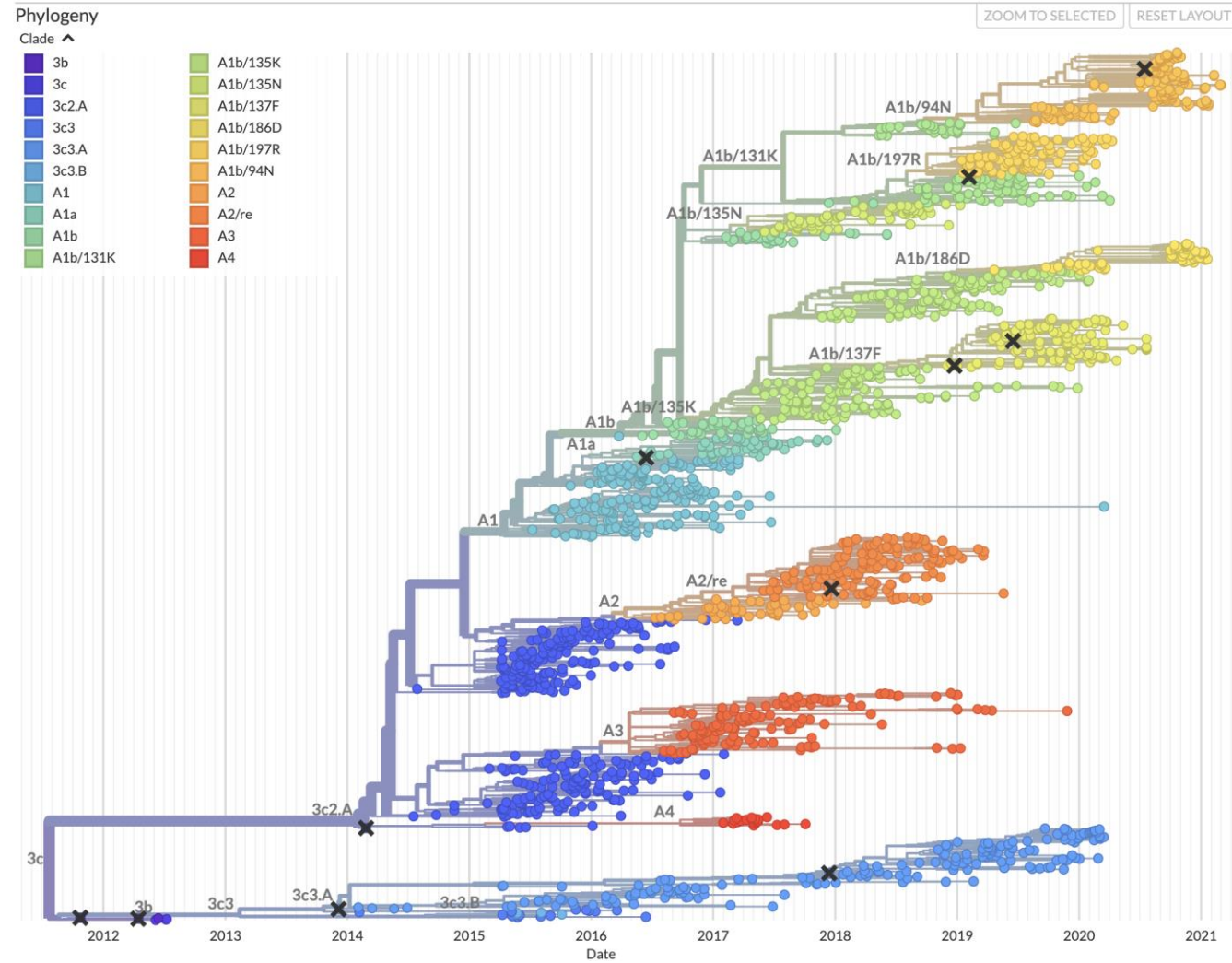
- Influenza has not disappeared from the world, but social distancing measures for COVID-19 have successfully suppressed influenza transmission in many parts of the world for now
- No winter influenza epidemic in 2020/21 winter -> drop in population immunity and a risk of a larger epidemic in winter 2021/22

Real-time tracking of influenza A/H3N2 evolution using data from GISAID



Built with [nextstrain/seasonal-flu](#). Maintained by [Jover Lee](#), [Richard Neher](#) and [Trevor Bedford](#). Enabled by data from [GISAID](#).

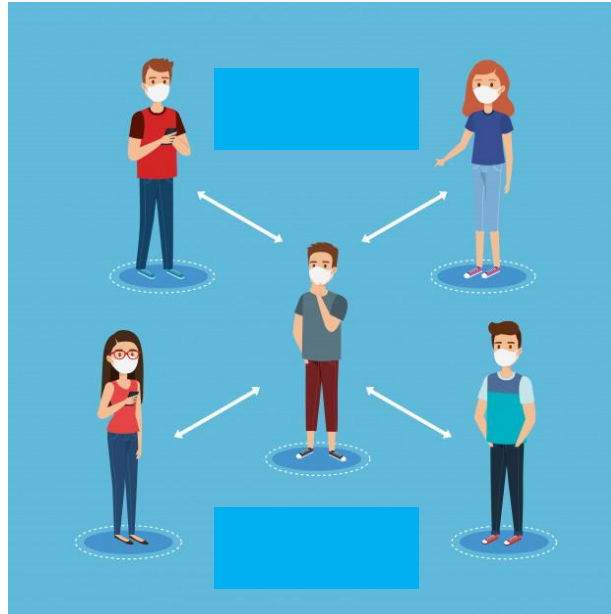
Showing 2001 of 2001 genomes sampled between Oct 2011 and Mar 2021. Filtered to [Nov 2007 to Mar 2021](#)



Strategies to reduce the impact of seasonal (and pandemic) influenza



Vaccines



Non-pharmaceutical
interventions
(face masks, social distancing ...)



Medications
including antivirals

Existing influenza vaccine technologies

Table 1. Characteristics of Currently Licensed Influenza Vaccines.

Vaccine Type	Origin	Characteristics and Uses
Live Attenuated (FluMist™)	Embryonated hens' eggs	Quadrivalent (QIV), cold-adapted viruses administered intra-nasally (IN). Available for children/adolescents 2-17 year olds (yo)
Inactivated split-virion (egg-based) (examples: Agrippal™, Fluzone™, Fluvirin™, Fluarix™, FluLaval™, Influvac™)	Embryonated hens' eggs	Trivalent (TIV) or QIV formulations. Viruses chemically-inactivated and detergent split. Administered intramuscularly (IM) or intra-dermally (ID). Varies with the product: available for all ages >6 months (ages 18-64yo for the ID formulation) at 15µg/strain dose. A 60µg/strain high-dose targeted for those ≥65yo (TIV only)
Inactivated split-virion and sub-unit (tissue culture-based) (examples: Flucelvax™, Preflucel™)	Madin Darby Kidney (MDCK) or Vero cells	TIV or QIV formulations. Viruses inactivated and detergent split as above. Partial purification of HA & NA proteins in subunit vaccines. 15µg/strain dose IM. Available for all ages >6 months (and 4-64yo for subunit).
Inactivated split-virion + Adjuvant (FluAd™)	Embryonated hens' eggs	TIV formulation. Viruses inactivated and detergent split as above. MF59 added as an adjuvant. 15µg/strain standard dose IM. Targeted for those ≥65yo
Inactivated split-virion + virosomes (Inflexal V™)	Embryonated hens' eggs	TIV inactivated and detergent split as above formulated as 'virosomes' with. 15µg/strain standard dose IM. Available for those ≥4yo
Recombinant hemagglutinin (HA) protein (FluBlok™)	Baculovirus transfected insect cells (<i>Spodoptera frugiperda</i>)	QIV formulation with recombinant HA proteins only. 45µg/strain dose IM. Available for those ≥18yo

Table 1 illustrates the general types of influenza vaccines licensed in different jurisdictions around the world and their most important characteristics but is not meant to be exhaustive. Not all vaccines are available in all jurisdictions. Some are available as trivalent formulations (TIV: 2xA and 1xB viruses/antigens) while others are available as quadrivalents (QIV: 2xA and 2xB viruses/antigens).

Egg adaptations

“The majority of influenza vaccines are produced in embryonated eggs, but mutations occur as human influenza A(H3N2) viruses adapt to grow in eggs. This can alter virus antigenicity.”

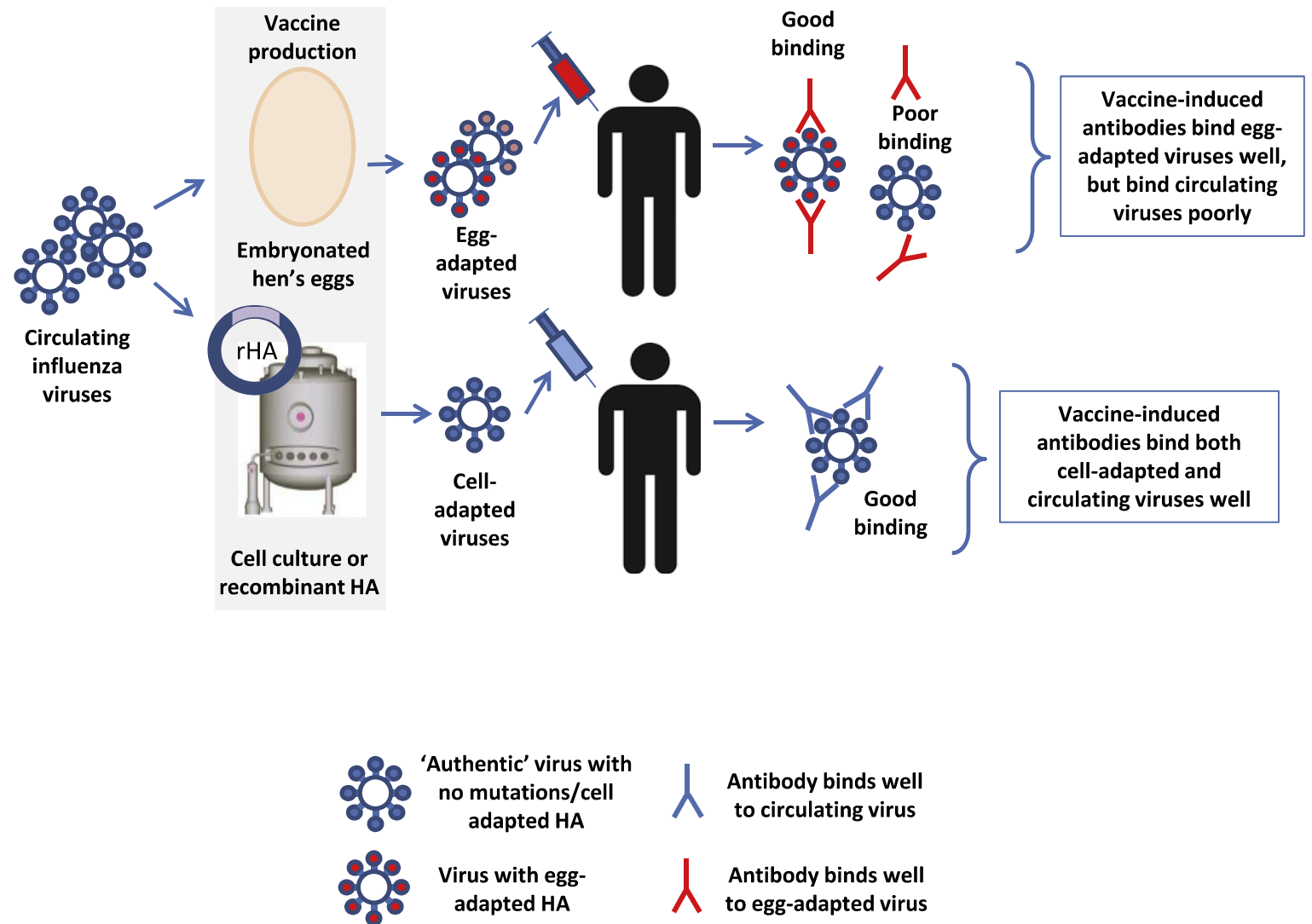


Figure 1. The Consequences of Egg Adaptation on Influenza Vaccines

The vast majority of influenza vaccines are manufactured in embryonated hens' eggs (upper panel). During passage in eggs, human influenza viruses acquire egg-adaptation mutations in the hemagglutinin that can alter virus antigenicity. As a consequence, egg-based vaccines may induce antibodies that bind the vaccine virus well but bind circulating viruses poorly. Potentially, cell-grown influenza virus or recombinant HA vaccines (lower panel), in which egg-adaptation mutations are absent, induce antibodies that bind both vaccine viruses and circulating viruses well.

A number of serologic assays are used to monitor immune responses to influenza vaccination. The HI assay is the most widely used.

Some regulatory agencies have established licensure criteria based on the HI response.

Table 2. Serologic Assays Used to Assess Influenza Vaccine Responses.

Assay	Biologic Reagents Used	Read-Out
Hemagglutination Inhibition Assay (HI)	Source of antigen – Either live or whole inactivated virus grown in embryonated hens' eggs or in tissue culture – Detergent-split antigens from virus grown in embryonated hens' eggs or in tissue culture – ≥ 1 recombinant proteins generated in different expression systems – Virus-like particles bearing ≥ 1 viral protein generated by different platforms Red blood cells (RBC) from different species: – chicken or turkey – horse – guinea pig – human – other Receptor-destroying enzyme (RDE) derived from <i>Vibrio cholerae</i> culture supernatant	Subjective based on degree and timing of RBC agglutination in 96-well plate
Microneutralization Assay (MN)	Live virus – grown in embryonated hens' eggs – grown in tissue culture Mammalian cell lines – MDCK-II (ATCC CCL-34); MDCK-I; serum free MDCK; MDCK clone CB4; MDCK-Siat cells; LLC-MK2; and HepG2 cells [Meijer 2006]	Readouts vary in degree of objectivity (ie: visual inspection of plaques, immunofluorescence, etc)
Single Radial Hemolysis Assay (SRH)	RBC from different species: – chicken or turkey – horse – guinea pig – other Source of Complement – typically rabbit – other species Agarose derived from seaweed	Semi-objective: area of hemolysis typically read by eye using light-box and calipers (note: hemolysis not always symmetrical or clear-cut)
Enzyme-linked Immunosorbent Assays (ELISA) for IgG, IgG subtypes, IgA, etc.	Source of antigen (as per HI assay above)	Objective: optical density (OD) or immunofluorescence read by machine

Inactivated influenza vaccines have moderate effectiveness

	Vaccine type	Pooled VE (%)	Pooled standard error	VE estimates (n)	p value for heterogeneity	I^2
Type B	Seasonal	54% (46–61)	0.083	36	<0.0001	61.3
H3N2	Seasonal	33% (26–39)	0.050	34	0.005	44.4
H1N1pdm09	Seasonal	61% (57–65)	0.048	29	0.783	0.0
H1N1pdm09	Monovalent	73% (61–81)	0.188	10	0.217	31.4
H1N1 (pre-2009)	Seasonal	67% (29–85)	0.397	5	0.093	57.6

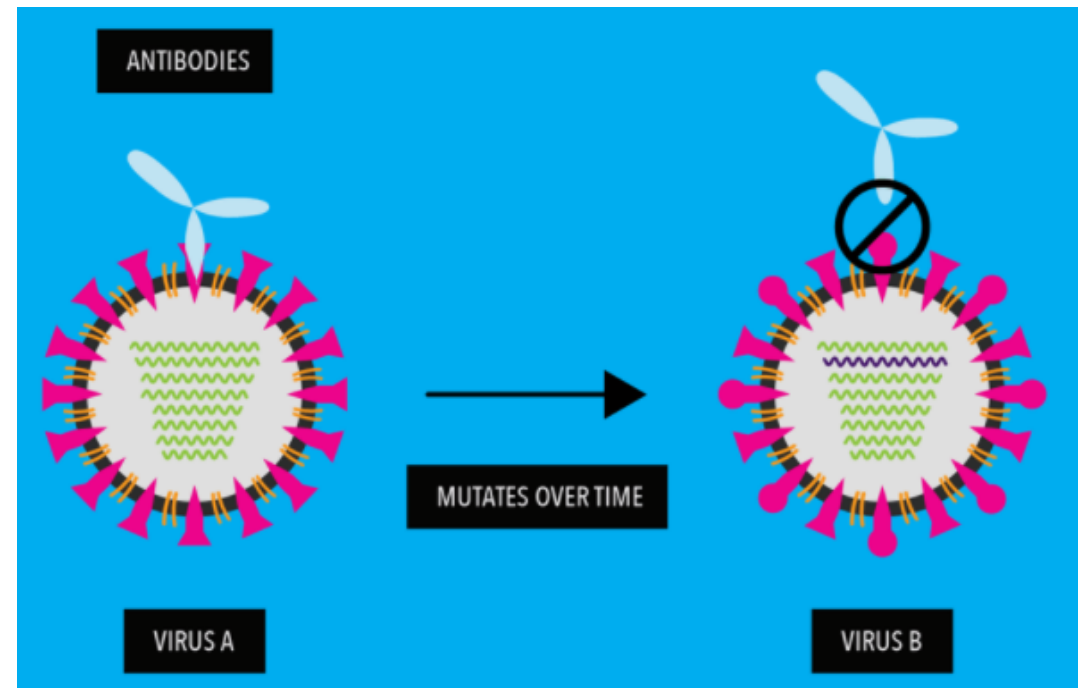
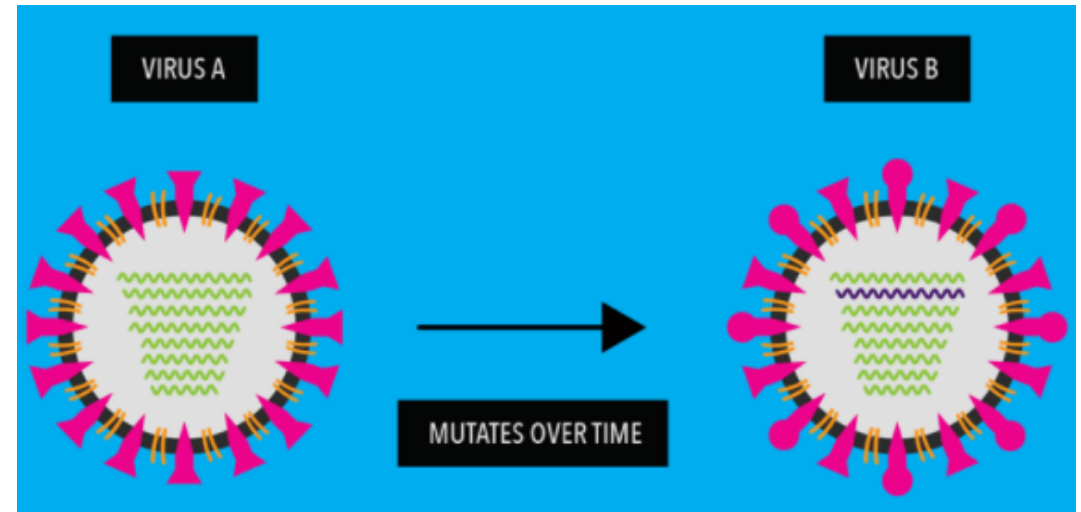
Data in parentheses are 95% CIs. VE=vaccine effectiveness.

Table 2: Pooled VE by type and subtype in studies without age restriction

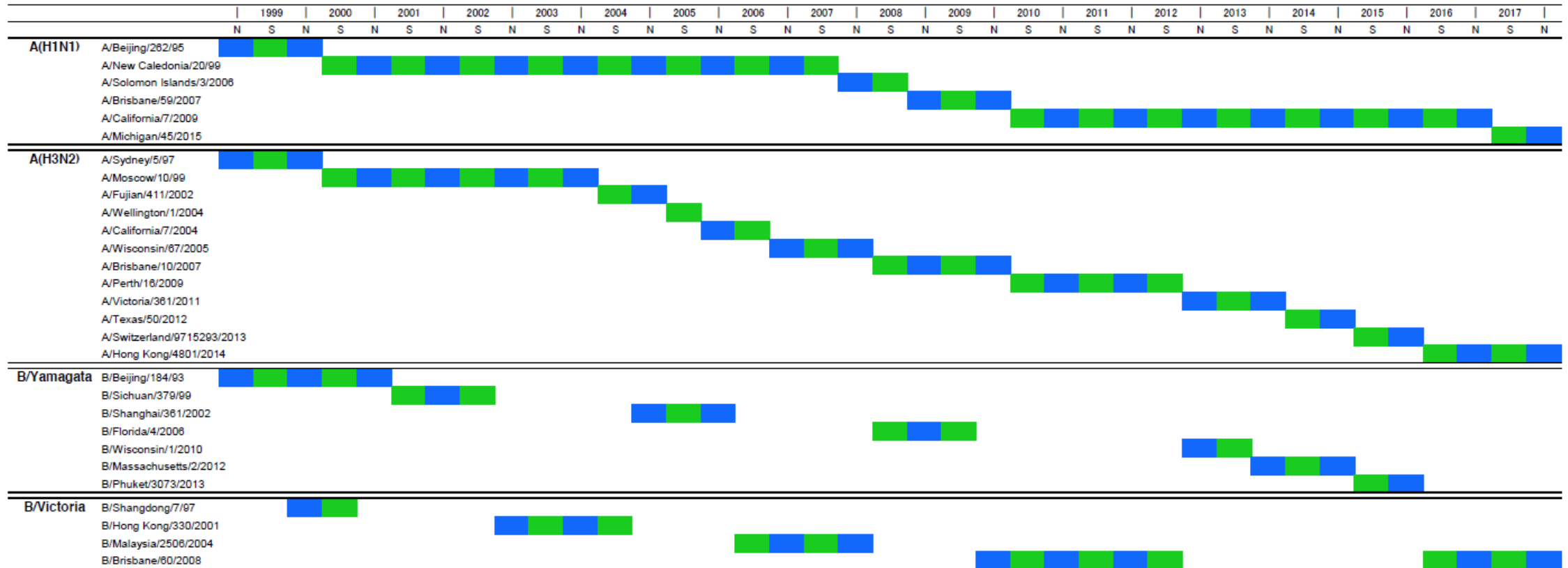
VE lower for A(H3N2) than for A(H1N1) or B
Some evidence that VE declines with age

Frequent antigenic drift of circulating strains ...

- As a virus replicates, its genes undergo random “copying errors” (i.e. genetic mutations)
- Over time, these genetic copying errors can, among other changes to the virus, lead to alterations in the virus’ surface proteins or antigens
- In influenza viruses, genetic mutations accumulate and cause its antigens to “drift”—meaning the surface of the mutated virus looks different than the original virus



... necessitates frequent updates of vaccine strains



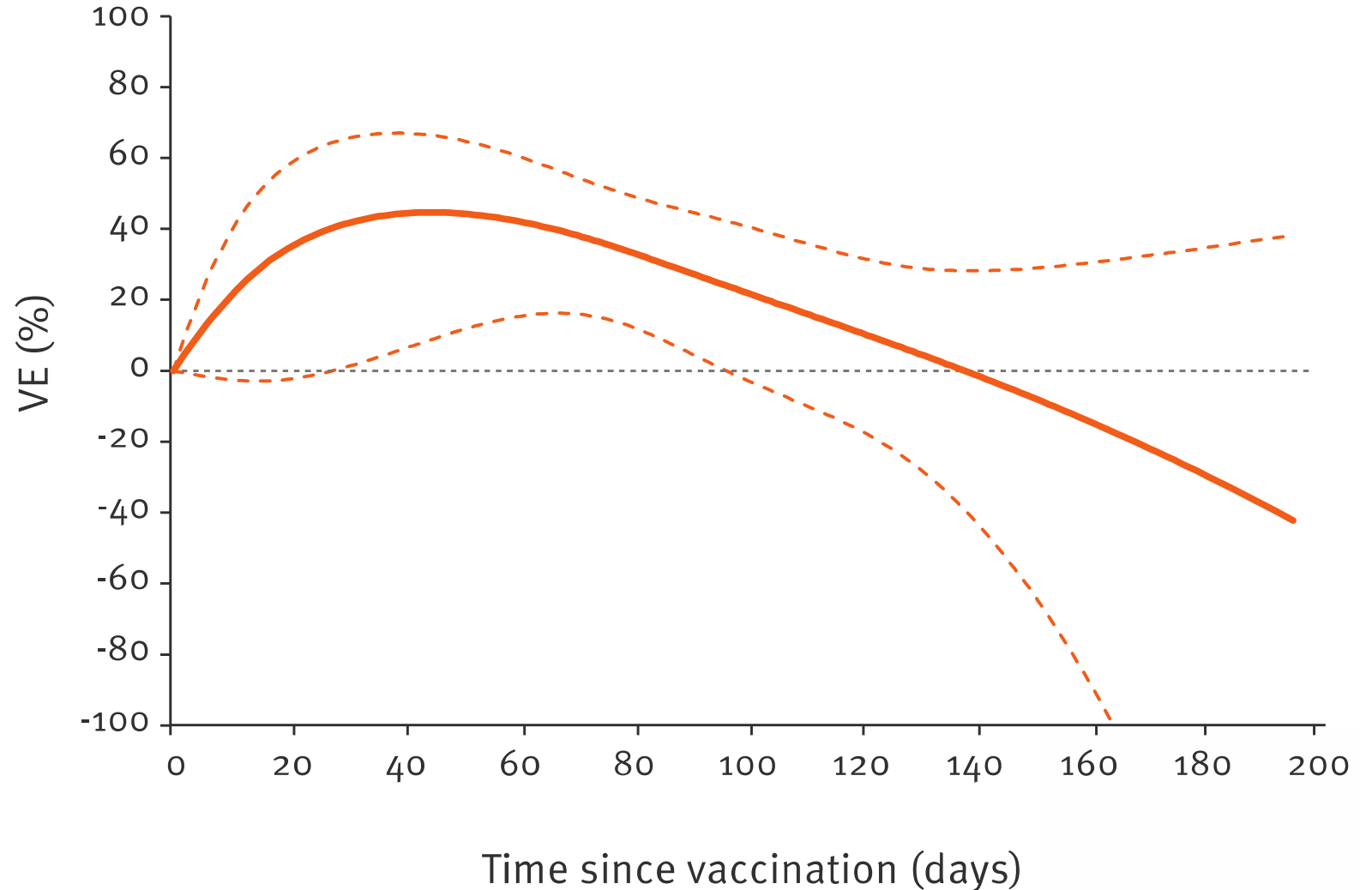
The vaccine compositions recommended by WHO for trivalent influenza vaccines to be used in NH influenza seasons from 1998-99 through 2017-18 (blue) and those for SH influenza seasons from 1999 through 2017 (green). There were 26 changes in 19 years.

Potential waning over time in vaccine effectiveness

Influenza vaccination effectiveness by time since vaccination, adults 65+y, I-MOVE study

Two issues:

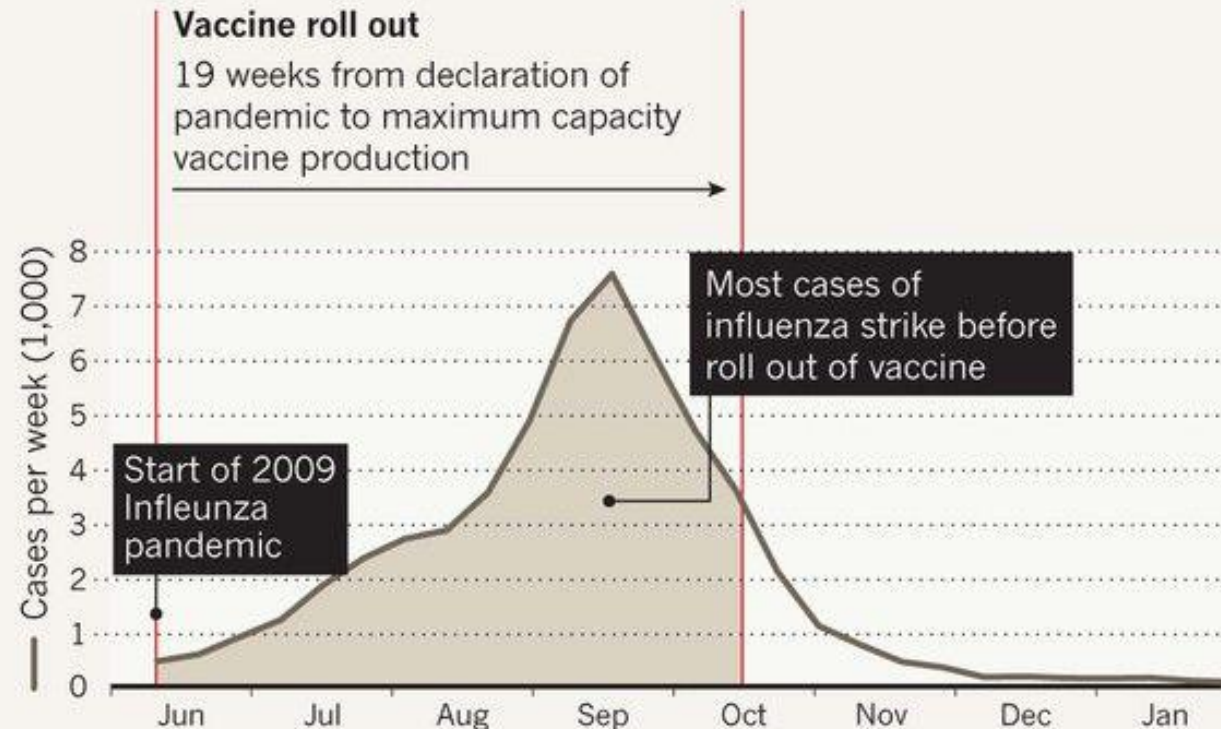
1. poor to moderate effectiveness
2. protection may not be year-round



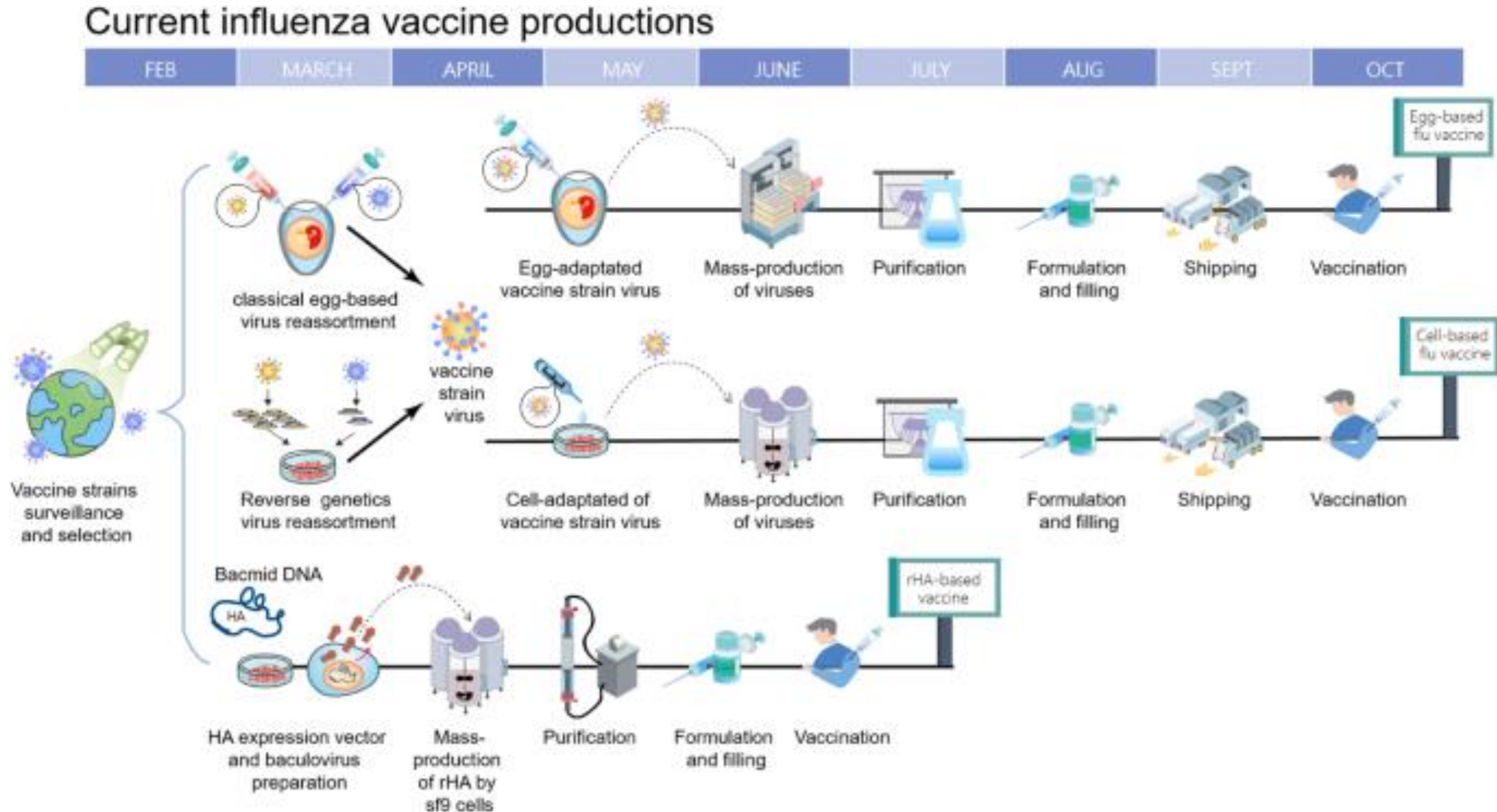
Delays in availability when strains updated

LATE TO THE PANDEMIC

Influenza vaccine doses became available in large quantity only after the 2009 pandemic had peaked. Data shown are from a northern hemisphere country that had in place a significant pandemic preparedness program.



Long lead time for vaccine strain selection



Limitations of existing vaccines

- **Punctuated antigenic changes (particularly in HA)** result in escape from the previously induced immunity and necessitate reformulation of the seasonal influenza virus vaccine
- **Formulation of influenza vaccines decided up to 9 months before vaccines intended to be used**
 - Largely due to the use of chicken egg-based vaccine production technologies
- **Egg-based vaccine production also has the potential to cause unintended antigenic changes to the vaccine virus**
- **Current inactivated vaccines result in relatively weak (and sometimes mis-directed) immune responses**

Opportunities for new vaccines

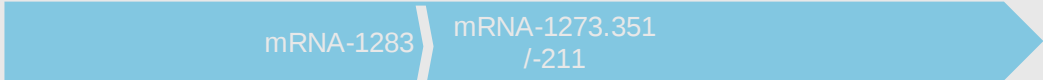
- **Would like influenza vaccines which have improved efficacy (and provide protection for longer)**
- **Would like influenza vaccines that can be manufactured more quickly so that the long lead time for strain selection can be shortened, and vaccine strains can be “better matched” to circulating strains**
- **Particularly useful for influenza pandemic preparedness to have alternative vaccine technologies – and note that some influenza viruses do not grow well in eggs**



Flu Vaccine Overview

Jacqueline Miller, M.D.

Senior Vice President, Infectious Diseases, Moderna

Program		ID #	Pre-clinical	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
COVID-19 vaccine		mRNA-1273						Worldwide <i>BARDA funded</i>
hMPV/PIV3 vaccine		mRNA-1653						Worldwide
Respiratory syncytial virus (RSV) vaccine		mRNA-1345						Worldwide
Flu vaccine		mRNA-1010 mRNA-1020 mRNA-1030						Worldwide

We plan to start a Phase 1 flu vaccine trial in 2021

Flu development candidates (DCs)

mRNA-1010

mRNA-1020

mRNA-1030

*Nominated 3 DCs
Plan to start Phase 1 in 2021*

- **Flu is an underserved medical need**
 - The WHO estimates globally about 3-5 million severe cases of flu each year, and 290-650,000 flu-related respiratory deaths¹
 - About 8% of the US population experiences symptoms from flu each year in the US²
- **Influenza virus “drift” leads to challenges**
 - Genetic mutations accumulate and cause its antigens to “drift”—meaning the surface of the mutated virus looks different than the original virus
- **Currently approved vaccines are ~40-60% effective and face significant challenges from strain mismatch³**
 - Formulation of influenza vaccines decided nine months before vaccines intended to be used
 - Egg-based vaccine production also has the potential to cause unintended antigenic change to the vaccine virus

(1) World Health Organization. Influenza (Seasonal). WHO. 2018. [https://www.who.int/news-room/fact-sheets/detail/influenza-\(seasonal\)](https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal))

(2) Centers for Disease Control and Prevention. Disease burden of influenza. Available at: <https://www.cdc.gov/flu/about/burden/index.htm>

(3) Centers for Disease Control and Prevention. Vaccine Effectiveness: How Well Do the Flu Vaccines Work? <https://www.cdc.gov/flu/vaccines-work/vaccineeffect.htm>.

Agenda

8:00 - 8:10 AM	Introduction of mRNA Vaccine Platform	Stéphane Bancel, CEO
8:10 - 8:20 AM	Overview of Clinical Experience with Moderna's COVID-19 Vaccine	Tal Zaks, M.D., Ph.D., CMO
8:20 - 8:45 AM	Commercial Update on Moderna's COVID-19 vaccine	Corinne Le Goff, Pharm.D., M.B.A., CCO
8:45 - 9:30 AM	Infectious Disease Vaccine Strategy	Stephen Hoge, M.D., President
9:30 - 10:45 AM	Vaccines Against Respiratory Diseases	Jacqueline Miller, M.D., SVP Sir Jeremy Farrar, OBE FMedSci FRS, Director of Wellcome Professor Miles P Davenport, University of New South Wales, Head, Infection Analytics Program, Kirby Institute Benjamin Cowling, BSc, PhD, FFPH, Division of Epidemiology and Biostatistics, School of Public Health, The University of Hong Kong
10:45 - 10:50 AM	Coffee Break	
10:50 - 11:50 AM	Public Health Vaccines	Jacqueline Miller, M.D., SVP William Schief, Ph.D., Director for Vaccine Design at the International Aids Vaccine Initiative (IAVI)
11:50 - 12:30 PM	Vaccines Against Complex Antigens	Jacqueline Miller M.D., SVP Lori Panther, M.D., M.P.H., VP Melanie Ivarsson, Ph.D., M.B.A, CDO
12:30 - 12:45 PM	Commercial Vaccines Business Model	Corinne Le Goff, Pharm.D., M.B.A., CCO
12:45 - 1:00 PM	Conclusion	Stéphane Bancel, CEO
1:00 - 1:30 PM	Q&A	



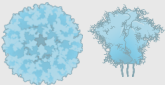
Public Health Vaccines

Jacqueline Miller, M.D.

Senior Vice President, Infectious Diseases, Moderna

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Zika vaccine (mRNA-1893)
Nipah vaccine (mRNA-1215)

Program		ID #	Pre-clinical	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
Zika vaccine		mRNA-1893						Worldwide <i>BARDA funded</i>
Nipah vaccine		mRNA-1215						Worldwide <i>NIH funded</i>
HIV vaccine		mRNA-1644 mRNA-1574						Worldwide <i>IAVI/BMGF/NIAD and others funded</i>

Public-private partnerships in public health programs

Partnerships help prepare and advance programs capable of responding to future pandemics

- Zika vaccine (mRNA-1893) partnered with BARDA
- Nipah vaccine (mRNA-1215) partnered with the NIH

Prioritizing diseases for research and development in emergency contexts



COVID-19

Crimean-Congo haemorrhagic fever

Ebola virus disease and Marburg virus disease

Lassa fever

Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS)

Nipah and henipaviral diseases

Rift Valley fever

Zika

Moderna's Zika Virus (ZIKV) and Nipah Virus (NiV) vaccine programs are important for future pandemic preparedness

Zika virus (ZIKV) was declared a public health emergency by the WHO in 2016 due to an outbreak in the Americas

Nipah virus has symptoms ranging from asymptomatic infection to acute respiratory distress and encephalitis, with a case fatality rate of 40-75%



G. J. Nabel, E. A. Zerhouni, "Once and future epidemics: Zika virus emerging," *Sci. Transl. Med* (16 Mar. 2016), <https://stm.sciencemag.org/content/scitransmed/8/330/330ed2.full.pdf>
Luby, Stephen. "The pandemic potential of Nipah virus," *Antiviral Research* (Oct. 2013), <https://doi.org/10.1016/j.antiviral.2013.07.011>

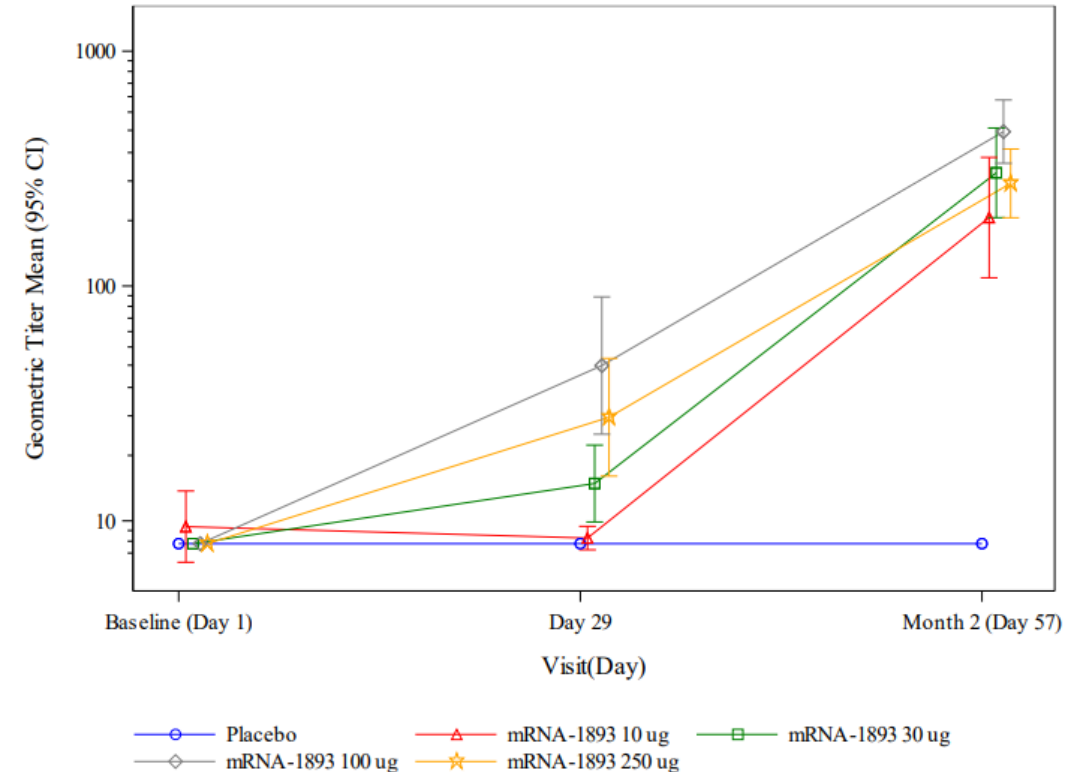
Zika vaccine (mRNA-1893) positive Phase 1 results

Phase 1 Clinical Trial Summary

- mRNA-1893 was well tolerated at all dose levels (10, 30, 100 and 250 µg)
- All dose levels induce a strong neutralizing ZIKV-specific antibody response in both flavivirus infection naive participants and in participants with pre-existing flavivirus antibodies (such as Zika, Yellow Fever and Dengue)
- Notably, the 100 µg dose level is sufficient to seroconvert (PRNT) baseline flavivirus seronegative subjects following only a single vaccine administration

Anti-ZIKV Neutralizing Antibodies in Seronegative Participants

Immunogenicity (PRNT₅₀), Per-Protocol Set

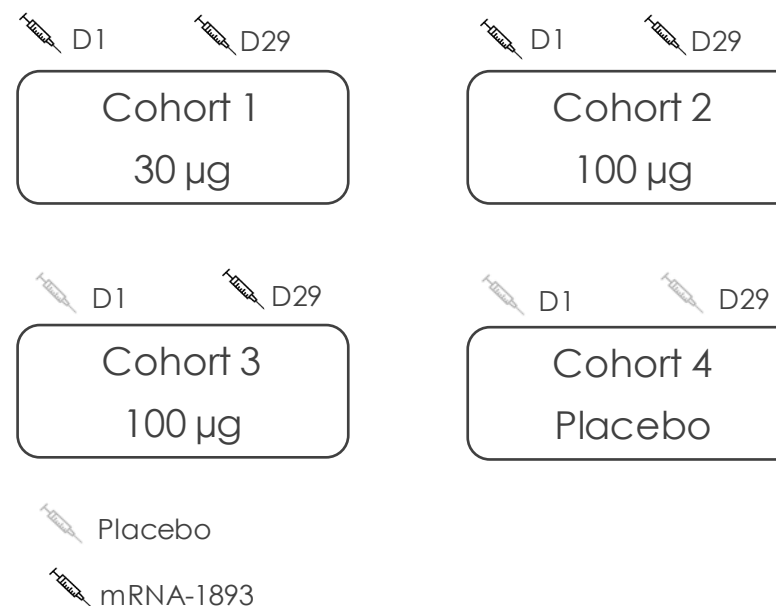


Zika Phase 2 expected to start in Summer 2021

Phase 2 Study Overview (N=800)

- Randomized, placebo-controlled study to be conducted in the U.S. (including Puerto Rico)
- Each cohort to have 100 baseline flavivirus seronegative participants and 100 baseline seropositive participants
- **Primary objectives:**
 - Evaluate the safety, tolerability and reactogenicity of mRNA-1893 compared to placebo
 - Evaluate the immunogenicity of 2 dose levels of mRNA-1893 (1-dose or 2-dose schedule) compared to placebo

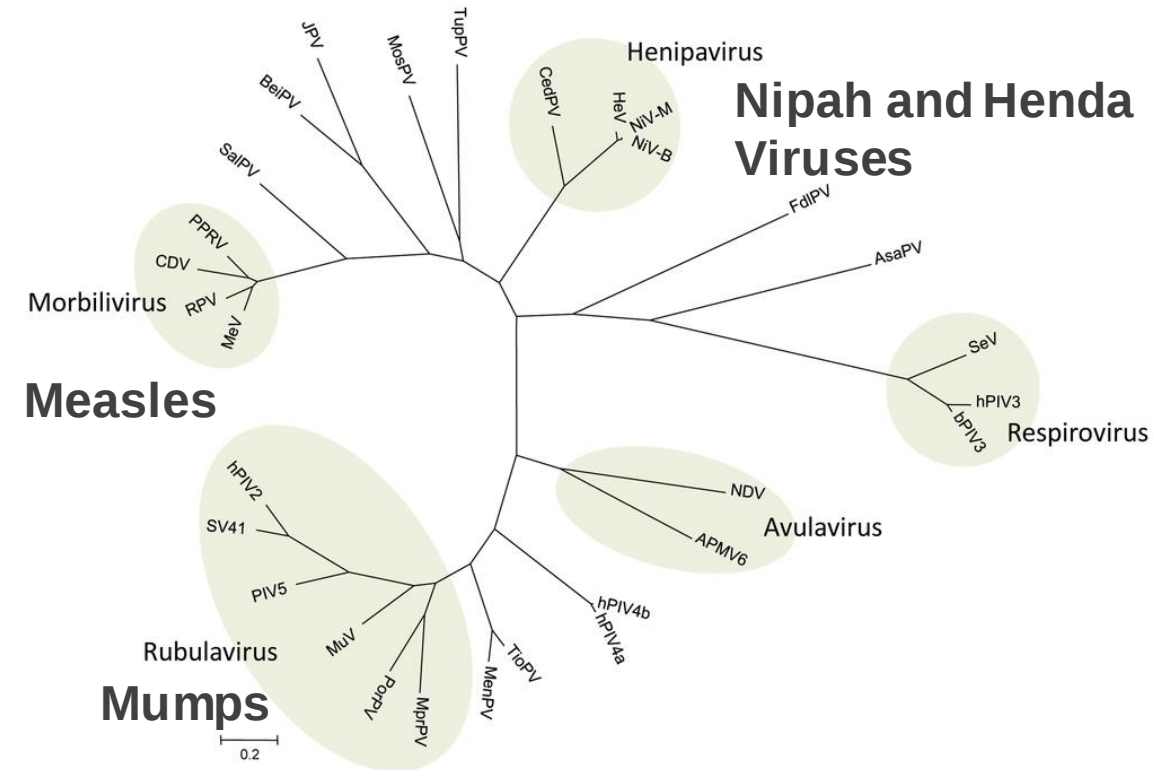
Phase 2 Study Design



Nipah vaccine (mRNA-1215) Phase 1 testing is for pandemic preparedness

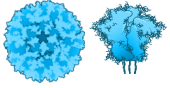
Nipah virus is closely related to some of the most common human pathogens

- Aim to define **general solution for vaccine antigen design** and to develop approaches for platform manufacturing
- Clinical testing can help determine whether having **successful antigen designs for viruses within a given family** might facilitate rapid development of vaccines against similar viruses
- NIH to sponsor Phase 1 study



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HIV vaccine (mRNA-1644)

Program		ID #	Pre-clinical	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
Zika vaccine		mRNA-1893						Worldwide <i>BARDA funded</i>
Nipah vaccine		mRNA-1215						Worldwide <i>NIH funded</i>
HIV vaccine		mRNA-1644 mRNA-1574						Worldwide <i>IAVI/BMGF/NIAID and others funded</i>

We plan to test two different HIV vaccine approaches in the clinic

1

Moderna/IAVI/Scripps/BMGF/NIAID/PEPFAR/US AID HIV Vaccine Collaboration (mRNA-1644)

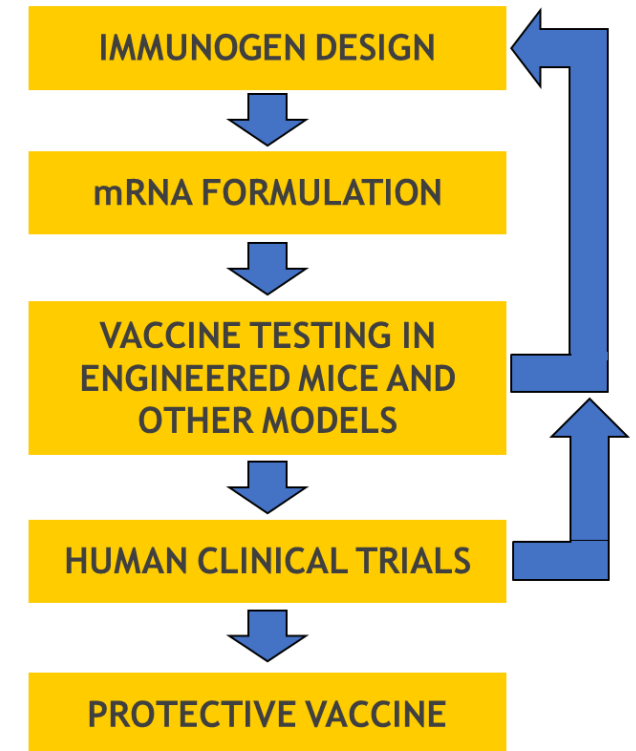
- Nomination of mRNA-1644 to test a novel HIV vaccine strategy in humans for eliciting broadly Neutralizing HIV-1 Antibodies (bnAbs)
- Validation of novel approaches/antigens thru iterative human testing
- Multiple novel antigens for Germline targeting/immuno-focusing

2

Moderna/Scripps/CHAUD/NIAID/IAVI/BMGF HIV Vaccine Collaboration (mRNA-1574)

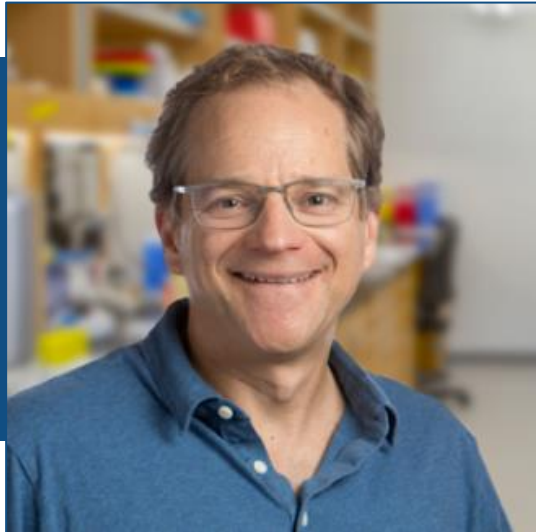
- Nomination of mRNA-1574 to test novel HIV trimer designs in humans
- Multiple native-like HIV trimer antigens

Iterative Vaccine Design/Test Cycle



William Schief, Ph.D.

*Professor, Immunology and Microbiology, Scripps
Executive Director, Vaccine Design, IAVI*



William Schief is a Professor in the Immunology and Microbial Science Department at Scripps Research in La Jolla, CA, Executive Director for Vaccine Design at IAVI, and an Associate Member of the Ragon Institute of MGH, MIT and Harvard.

William received a B.S. in Applied Mathematics from Yale University and a Ph.D. in Physics from the University of Washington. Dr. Schief's work focuses on computation-guided and structure-based design of immunogens and immunization regimens, with the goal of inducing broadly neutralizing antibodies against HIV and other pathogens that have frustrated traditional vaccine design strategies.



Vaccines Against Complex Antigens

Lori Panther, M.D., M.P.H.

Vice President, Infectious Diseases, Moderna

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Cytomegalovirus (mRNA-1647)

Program	ID #	Pre-clinical	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
Cytomegalovirus (CMV) vaccine	 mRNA-1647						Worldwide
Epstein-Barr virus (EBV) vaccine	 mRNA-1189						Worldwide

Cytomegalovirus (CMV) Overview

**Most common
cause of congenital
infection worldwide**

**>\$1B in annual
healthcare costs**

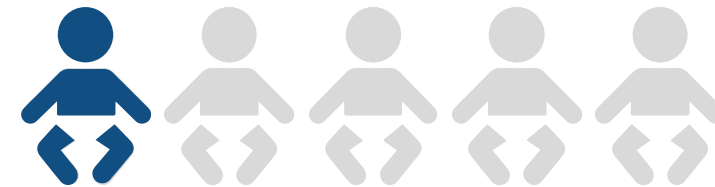
Sequalae include:

- At birth: microcephaly, chorioretinitis, seizures, sensorineural hearing loss
- Long term: cognitive impairment, cerebral palsy, seizure disorder, sensorineural hearing loss



1 in 200

babies are born with a congenital CMV infection
(CMV infection is present at birth)



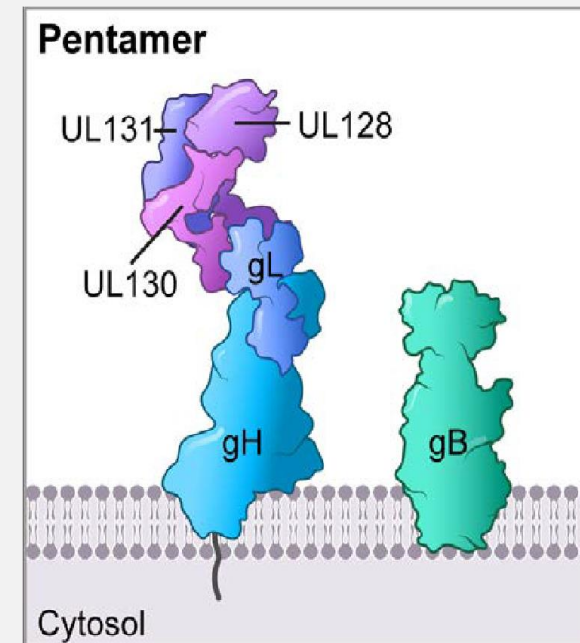
1 in 5

will have severe, life-altering health problems

Moderna's approach to a CMV Vaccine

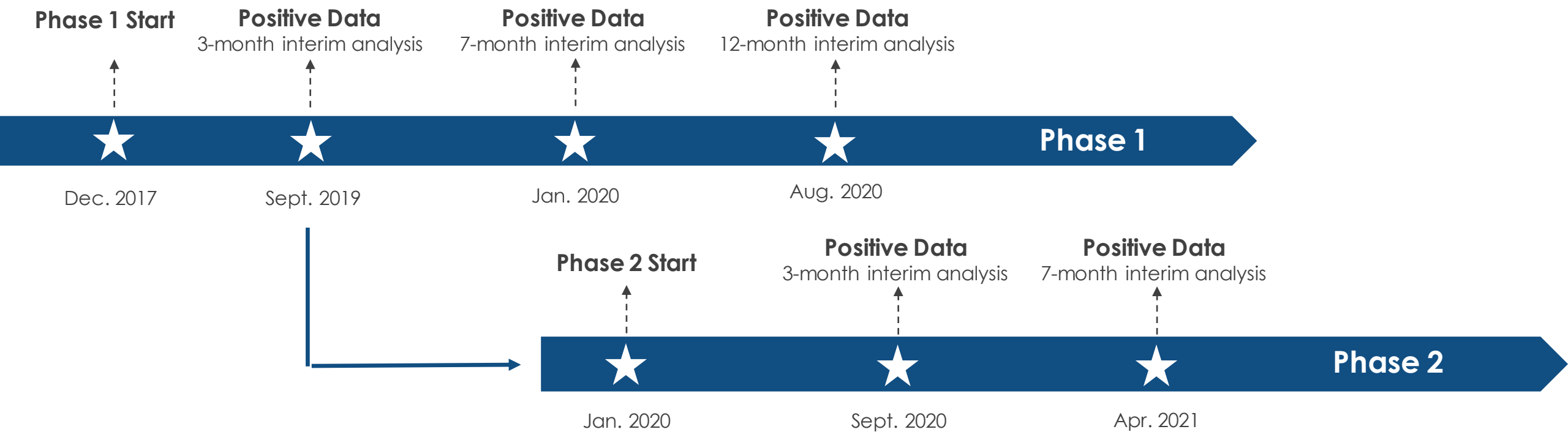
- Comprises six mRNAs encoding the CMV pentamer complex and gB antigens together into one vaccine
- Phase 1 and 2 studies demonstrate functional antigen-specific responses that support the vaccine's potential to prevent CMV infection
- We believe a vaccine that protects women from CMV infection should protect against congenital CMV infection

CMV vaccine (mRNA-1647) includes 6 mRNAs
5 encode the pentamer, 6th encodes gB antigen



CMV vaccine (mRNA-1647) clinical development

Phase 3 pivotal efficacy trial expected to start in 2021



CMV vaccine (mRNA-1647) Phase 1 data summary (12-month IA)

- **Generally well-tolerated, no vaccine-related serious adverse events (SAEs)**
- **Neutralizing antibody (nAb) response, CMV-seronegative group:**
 - At 1 month after the 3rd vaccination, nAb geometric mean titers (GMTs) against epithelial cell infection (measuring pentamer response) ranged 2.8-fold to 17-fold higher than the CMV-seropositive baseline GMT benchmark, and nAb GMTs against fibroblast infection (measuring gB response) ranged 0.8-fold to 5.0-fold higher than the CMV-seropositive baseline GMT benchmark
- **Neutralizing antibody titers in the CMV-positive group:**
 - At 1 month after the 3rd vaccination, the ratio of nAb titers compared to baseline (geometric mean ratios, or GMRs) against epithelial cell infection ranged 13.4-40.8 and against fibroblast infection ranged 4.0-7.1
- **Early evidence of immune persistence out to 12 months (6 months after the 3rd vaccination)**

Key changes to mRNA-1647 in Phase 2 clinical trial

Improved Potency

- Improved ratio of mRNA components to increase potency

Improved Tolerability

- Optimized the manufacturing process to improve tolerability

Lyophilization

- Phase 2 utilizes the intended Phase 3 and commercial formulation



Liquid, Single-Dose Vial,
-20°C storage ≥ 6 months shelf-life



Lyophilized, Single-Dose (0.5mL),
5°C storage ≥ 18 months shelf-life

CMV vaccine (mRNA-1647) Phase 2 trial overview

Key objective

- To assess the safety and immunogenicity of mRNA-1647 vaccine in its Phase 3 presentation-to select a dose level to progress into Phase 3 development

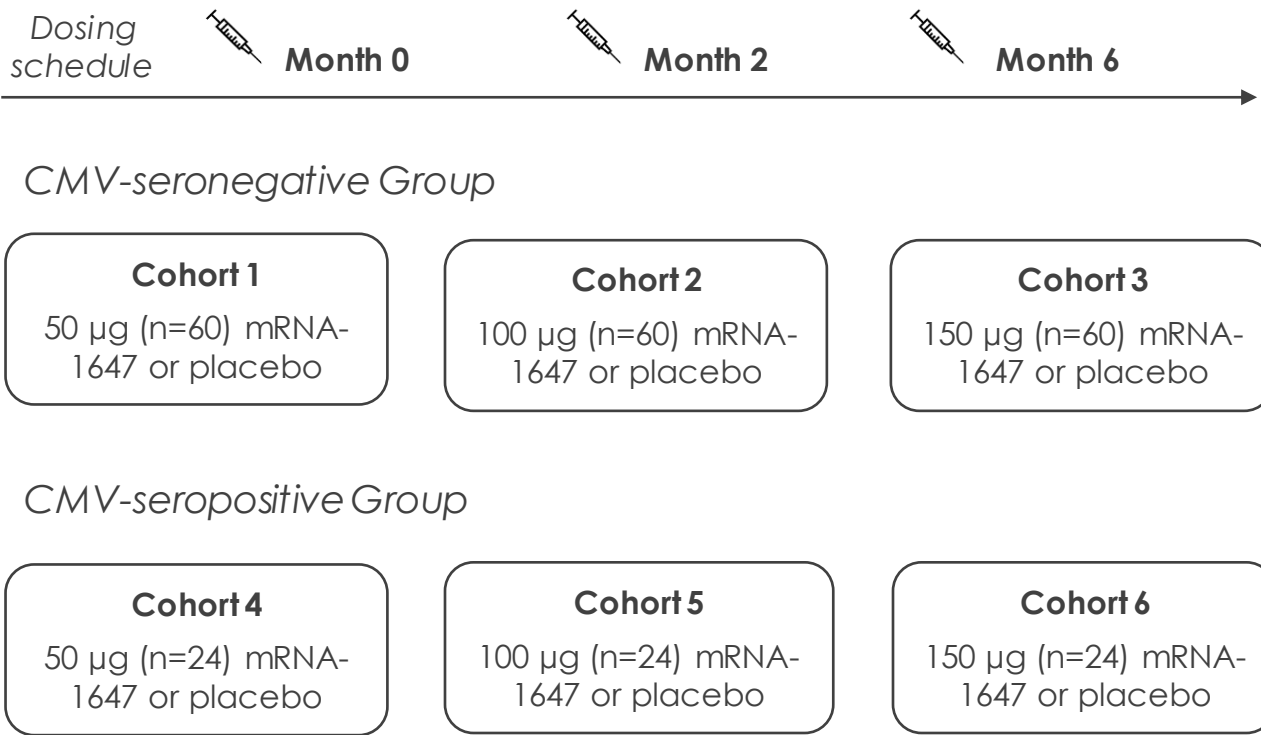
Primary endpoints

- Defined safety parameters
- Pentamer-specific and gB-specific neutralizing antibody responses as measured by epithelial cell and fibroblast assays

Secondary endpoints

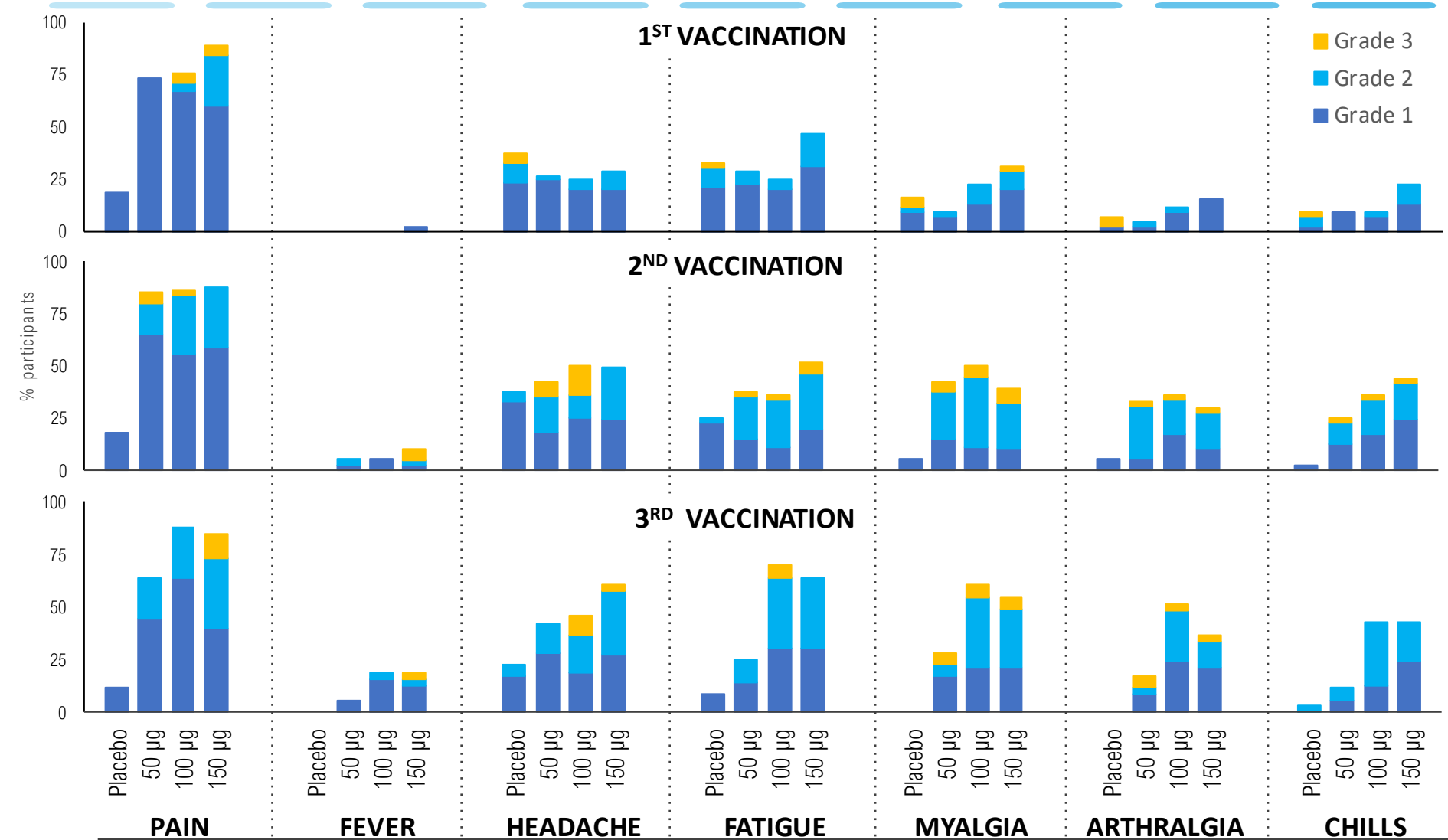
- Pentamer-specific and gB-specific binding IgG responses as measured by ELISA

Participants enrolled in a 3:1 ratio of mRNA-1647: placebo



Most Common Solicited Adverse Reactions (ARs) after Each Vaccination

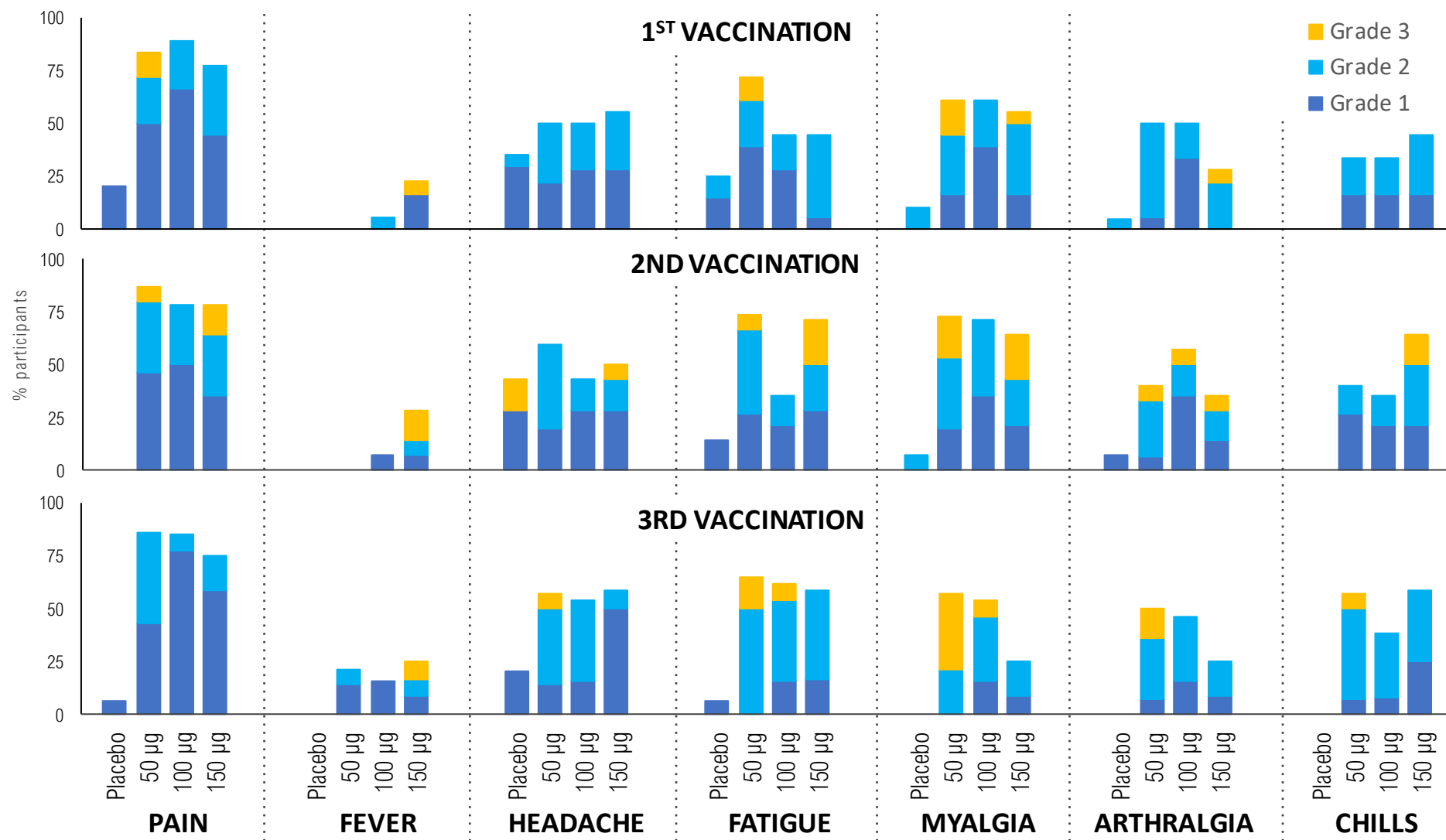
CMV-seronegative group



- No treatment-related SAEs
- No study pause rules were met
- Injection site pain was the most commonly reported solicited local adverse reaction
- The most common solicited systemic ARs were headache, fatigue, myalgia, arthralgia, and chills

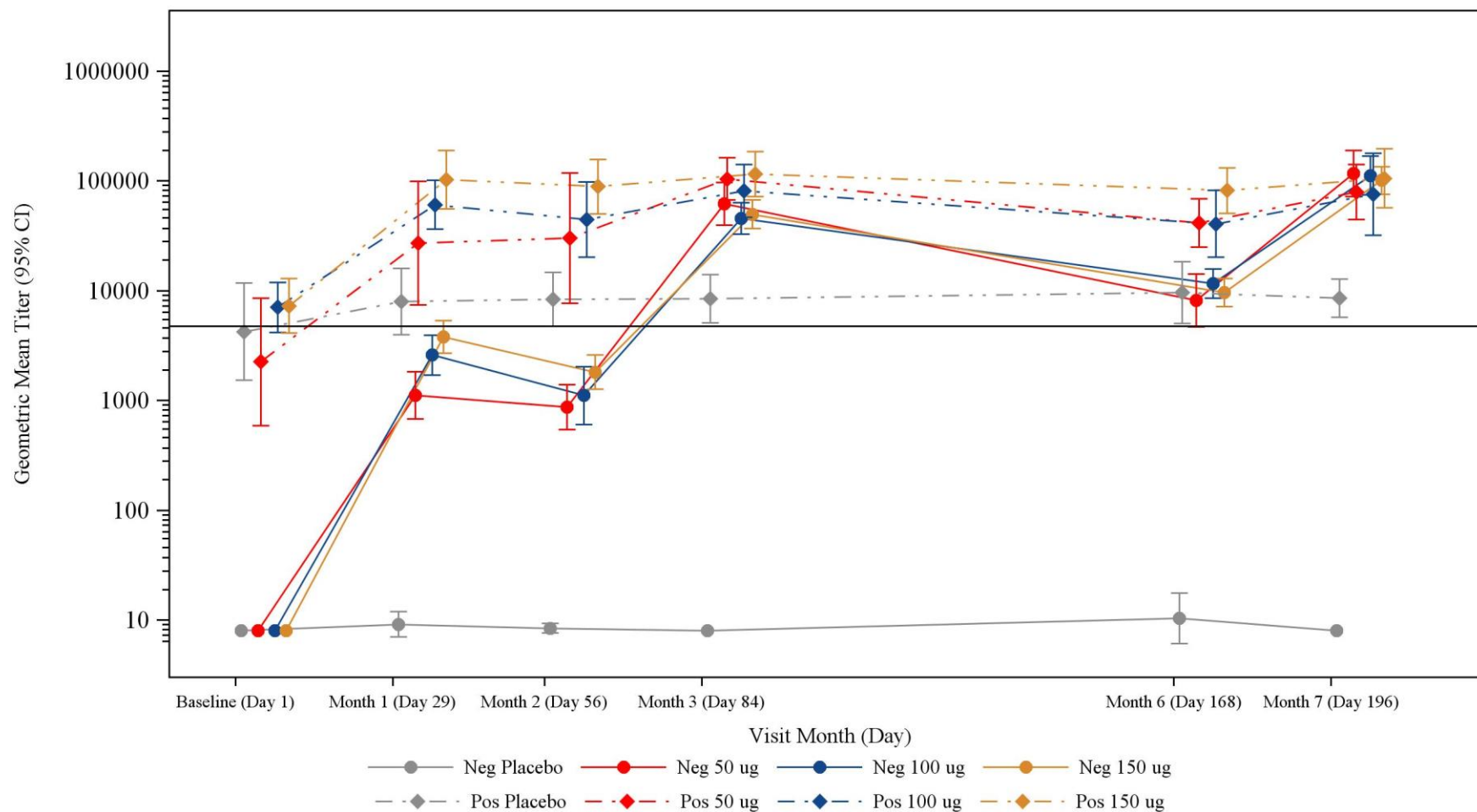
Most Common Solicited Adverse Reactions (ARs) after Each Vaccination

CMV-seropositive group



- No treatment-related SAEs
- No study pause rules were met
- Injection site pain was the most commonly reported solicited local adverse reaction
- The most common solicited systemic ARs were headache, fatigue, myalgia, arthralgia, and chills

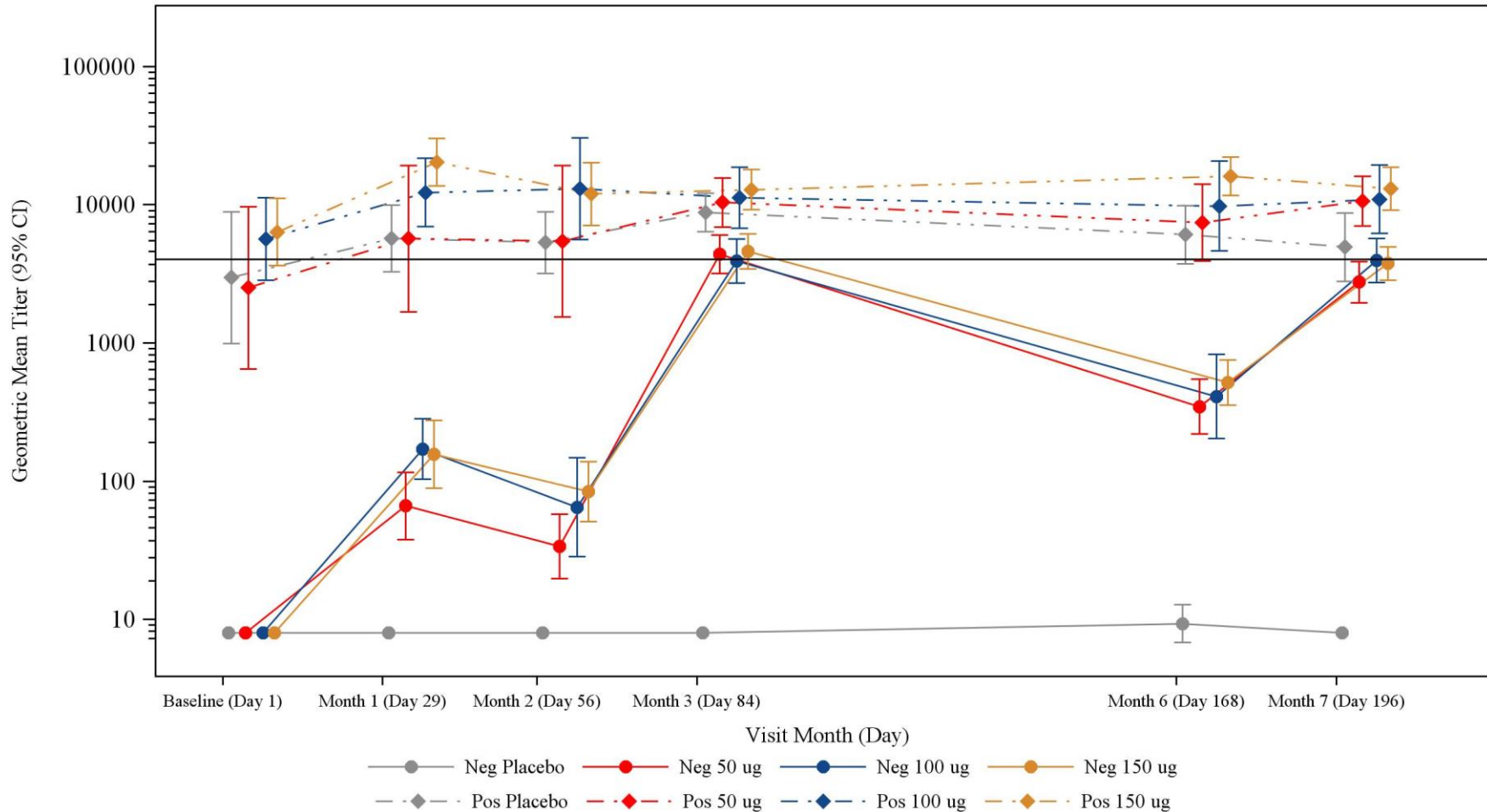
Neutralizing antibody titers against epithelial cell infection through Month 7



Neutralizing antibodies against epithelial cell infection:

- Increased in a dose-related manner after the 1st vaccination in both seronegative and seropositive participants
- Increased further after the 2nd vaccination and again after the 3rd vaccination to GMTs exceeding the seropositive benchmark GMTs in all treatment groups by over 20-fold

Neutralizing antibody titers against fibroblast cell infection through Month 7



Neutralizing antibodies against fibroblast infection:

- Increased after the 2nd vaccination to GMTs approaching or exceeding the seropositive benchmark GMT in all treatment groups
- After the 3rd vaccination, GMTs in the 100 μ g and 150 μ g treatment groups were comparable to GMTs after the 2nd vaccination

Phase 2 seven-month interim analysis conclusion

- **mRNA-1647 CMV vaccine was generally well tolerated:**
 - The most common solicited local AR was injection site pain
 - The most common solicited systemic ARs were headache, fatigue, myalgia, arthralgia, and chills.
 - In general, solicited AR frequency and severity after the 3rd vaccination were similar to or lower compared to the 2nd vaccination
- **In CMV-seronegative participants in mRNA-1647 treatment groups after the 3rd vaccination:**
 - Neutralizing antibody (nAb) GMTs against epithelial cell infection were at least 20-fold higher than the CMV-seropositive baseline GMT benchmark
 - nAb GMTs against fibroblast infection approximated the CMV-seropositive baseline GMT benchmark
- **In CMV positive participants in mRNA-1647 treatment groups after the 3rd vaccination:**
 - nAb GMTs against epithelial cell infection increased to at least 6.8-fold over baseline
 - nAb GMTs against fibroblast infection increased to approximately 2-fold over baseline

Pivotal Phase 3 CMV trial to start in 2021

Based on the Phase 2 interim analysis,
the **Phase 3 pivotal trial will test the
100 µg dose level**

Primary endpoint: prevention of
primary CMV infection in
seronegative females 16-40 years old





Leveraging COVID-19 Trial Experience to Our CMV Phase 3 Trial

Melanie Ivarsson, Ph.D., M.B.A.
Chief Development Officer

Moderna's COVID-19 vaccine trials in 2020 accelerated clinical operations development

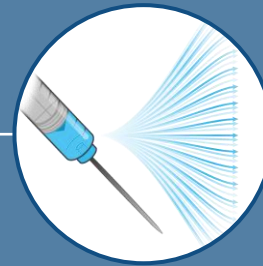
- ✓ In 2020, over 31,000 participants enrolled in our COVID-19 vaccine trials
- ✓ Phase 3 COVE study conducted in 100 locations across the United States
- ✓ Strengthened partnerships with the NIH, BARDA, OWS and PPD

First patient dosed
in NIH-led
Phase 1 study



March 16th

First patient
dosed in
Phase 2 study



May 29th

Pivotal
Phase 3 COVE
study begins



July 27th

Committed to ensuring diversity & inclusion in the COVE study

- ✓ Slowed enrollment in the COVE study to ensure the representation
- ✓ Included more than 11,000 participants from communities of color, representing 37% of the study population

Pivotal
Phase 3 COVE
study begins



July 27th

Announced a slowing
of enrollment to ensure
the representation of
communities of color



September

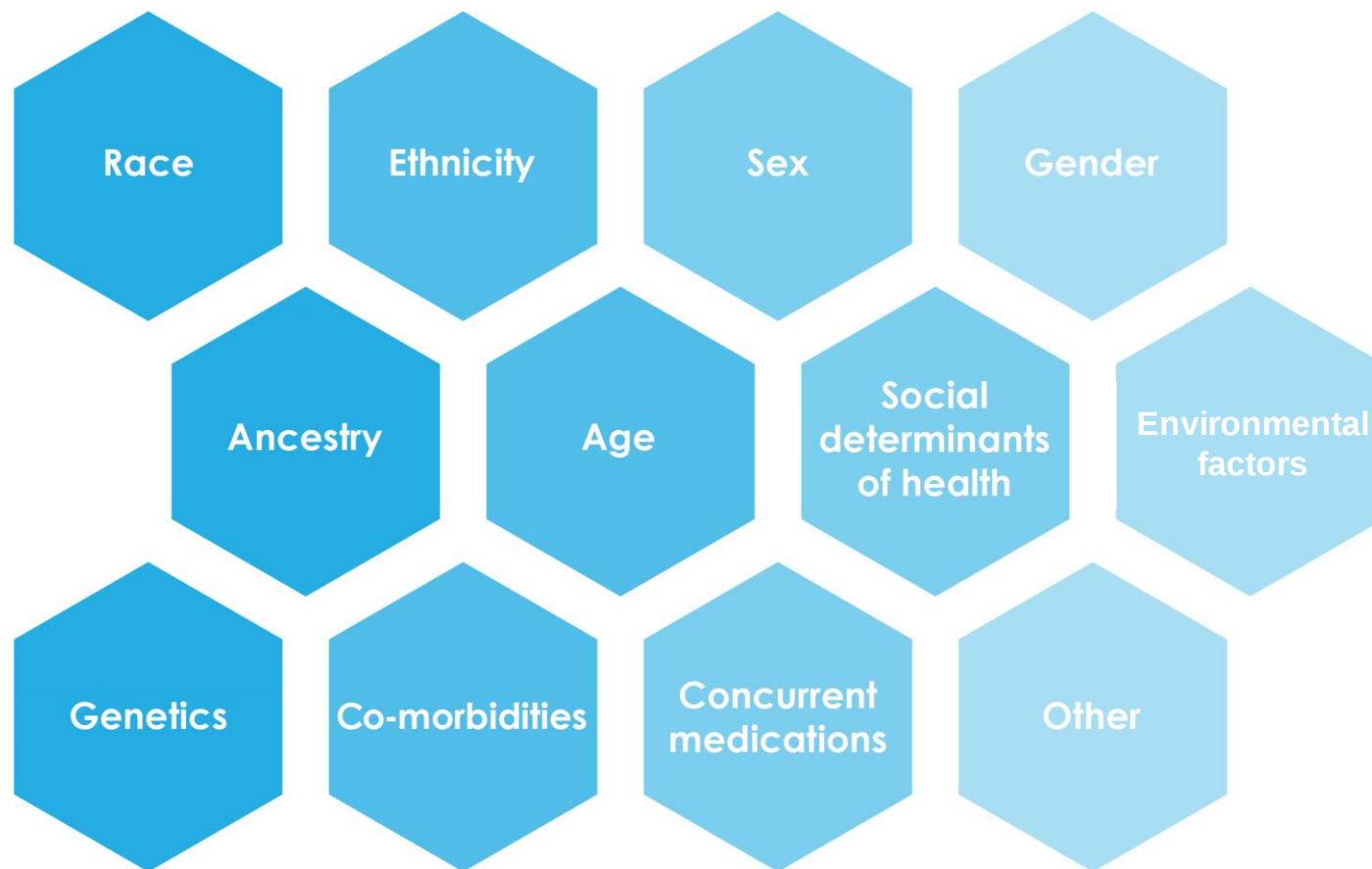
Enrollment completed
of Phase 3 study



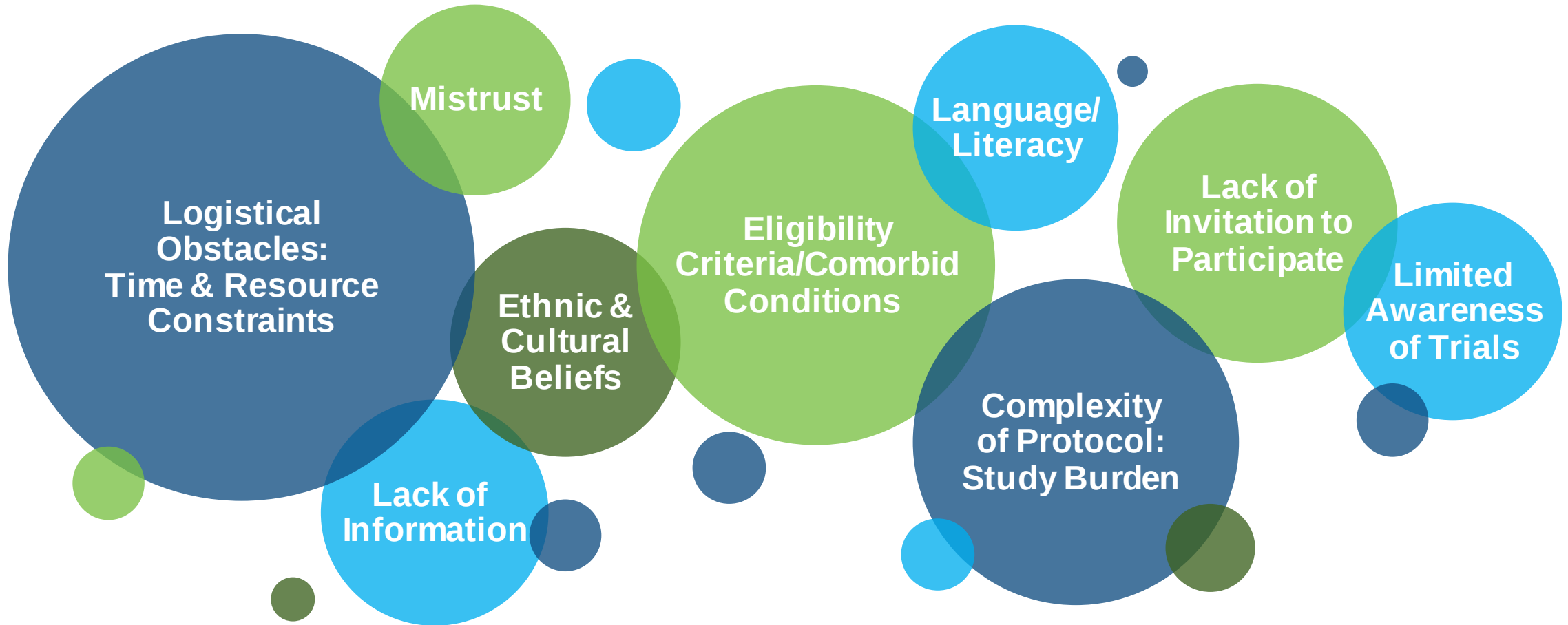
Oct. 22nd

Purpose of Diversity & Inclusion in Clinical Research

- Diversity exists across many dimensions
- Diversity is context-specific
- The importance of each factor may vary depending upon the disease/ condition and the population at risk



Barriers to diversity in clinical trials



We worked to ensure diversity in the COVE trial

Education: Ourselves & Stakeholders

Listen
We created an Advisory Committee of experts and we listened to them



Start the Conversation
Dr Fauci and Dr Adams spoke at our PI meeting about the ‘why’ importance of diversity



Educate
The CoVPN CE team conducted implicit bias training & the CEAL team provided expertise



Transparency: Intent & Information

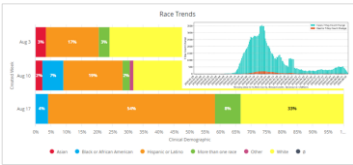
Be Transparent
Be explicit about intent; published data on progress; published protocol on our website



Create Tools
Tailored our Patient Information sheets and translated materials for different populations



Use Data
We provided each site with their ethnic enrollment trends and epi weekly, and monitored enrollment daily



Help: Partner with Experts

Partner
Seek experts and those with specific experience



Innovate
Be creative; new solutions are needed



Motivate
OWS leadership motivated through visiting and listening to the sites



The population in the COVE Study is representative of the US population at-risk for COVID-19 infection

COVE Study Participants	Count
White, non-Hispanic	19,060
Hispanic or Latinx	6,247
Black or African American	3,114*
Asian	1,365
Others	871^
Total	30,406+

* Includes 251 participants who identify as both Black and Hispanic/Latinx

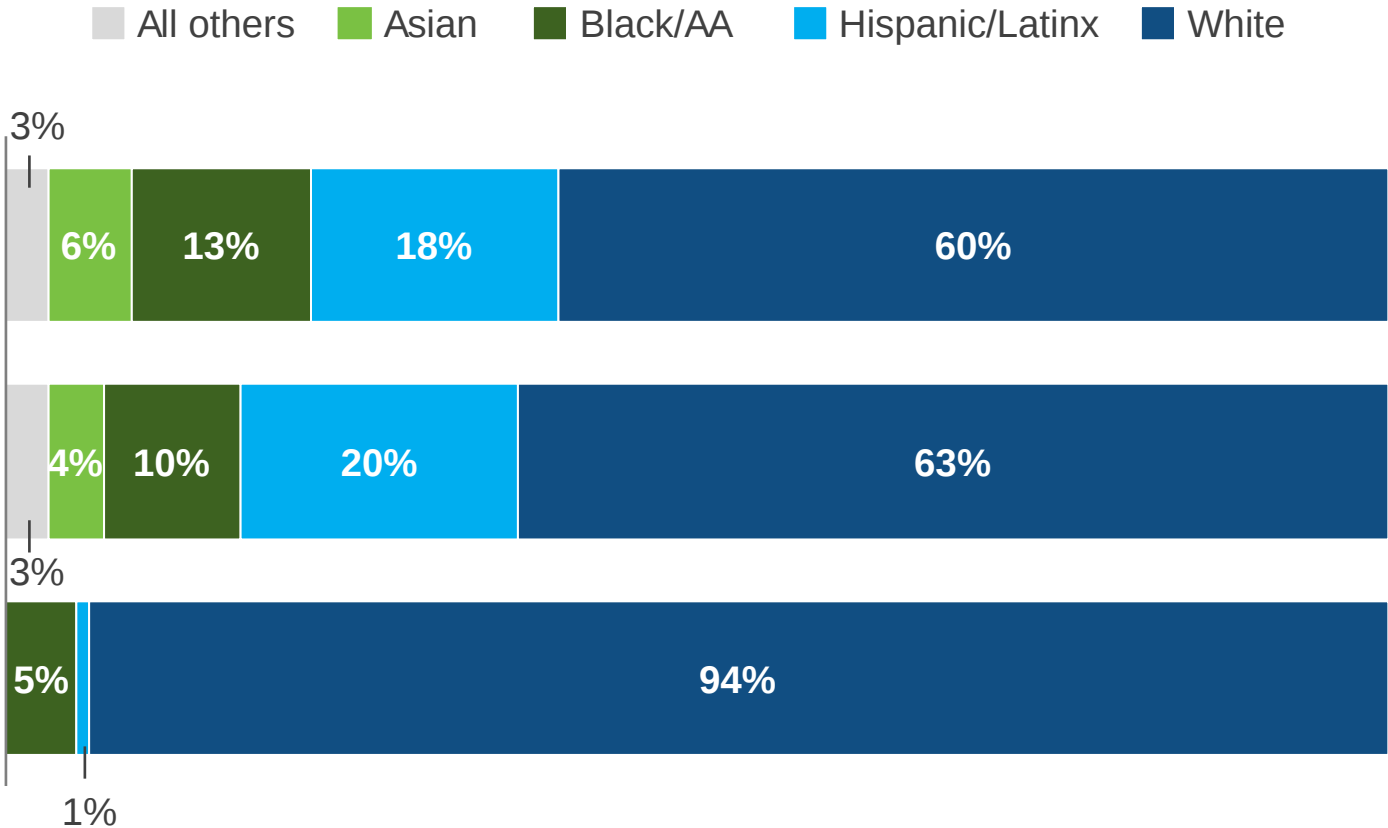
^Including 148 American Indian or Alaska Native

+ Final Enrollment 30,423 (Oct 22, 2020)

US population 2020¹



Estimate of Clinical Trial Participants pre-COVID²



(1) US Census Bureau, <https://www.census.gov/content/dam/Census/library/publications/2020/demo/p25-1144.pdf>
(2) ACRP, Representation in Clinical Trials: A Review on Reaching Underrepresented Populations in Research, <https://acrpn.net.org/2020/08/10/representation-in-clinical-trials-a-review-on-reaching-underrepresented-populations-in-research/>; FDA, 2015-2019 for Approved Drugs Snapshots Summary Report, <https://www.fda.gov/media/143592/download> (providing race distribution data in clinical trials for approved products)

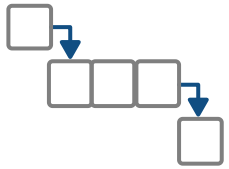
The population in the COVE Study is representative of the US population at-risk for COVID-19 infection



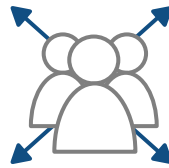
Diseases don't discriminate – neither should clinical research

Moderna is committed to **increasing diversity** in our clinical trials by identifying the **barriers that currently impede inclusion**, and implementing approaches to more efficiently **identify, engage, recruit, and retain** study participants from racial/ethnic **minority communities and vulnerable populations.**

Companies don't run clinical trials, people do



We are investing in a talented clinical development organization



Our team has deep vaccine development experience



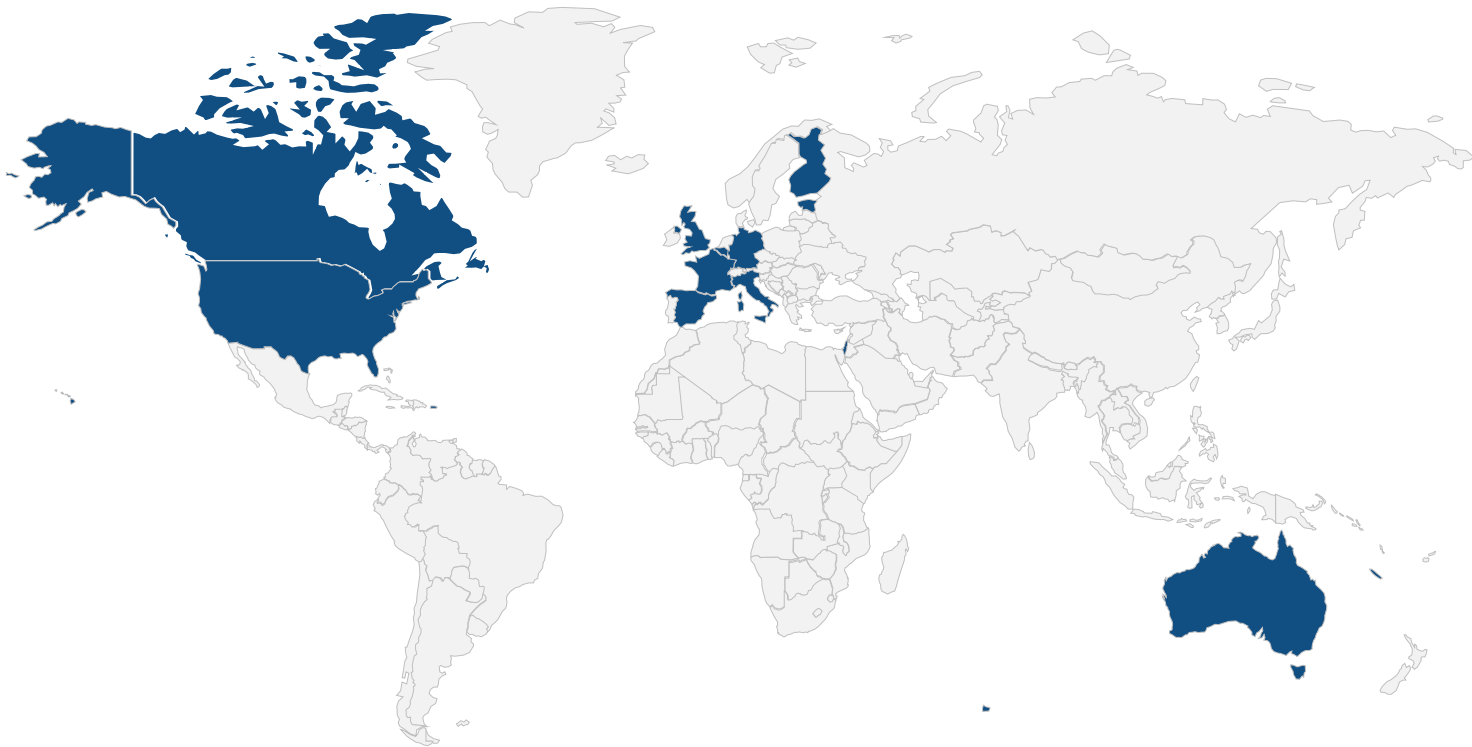
Our team has led 7 different vaccines to approval



We are building new innovative capabilities

Phase 3 CMV trial expects to enroll ~8,000 participants

- ~150 sites across the U.S., Europe and APAC
- Pivotal Phase 3 trial will test the 100 µg dose level
- Expected enrollment of ~8000 participants
- Expected to start in 2021



CMV Trial Participants – US Demographic Composition	Target
White, non-Hispanic	58%
Hispanic or Latinx	23%
Black or African American	12%
Asian	4%
Others	3%
White	58%
Persons of Color	42%



Epstein-Barr Virus Vaccine (mRNA-1189)

Jacqueline Miller, M.D.

Senior Vice President, Infectious Diseases, Moderna

Program	ID #	Pre-clinical	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
Cytomegalovirus (CMV) vaccine	 mRNA-1647						Worldwide
Epstein-Barr virus (EBV) vaccine	 mRNA-1189						Worldwide

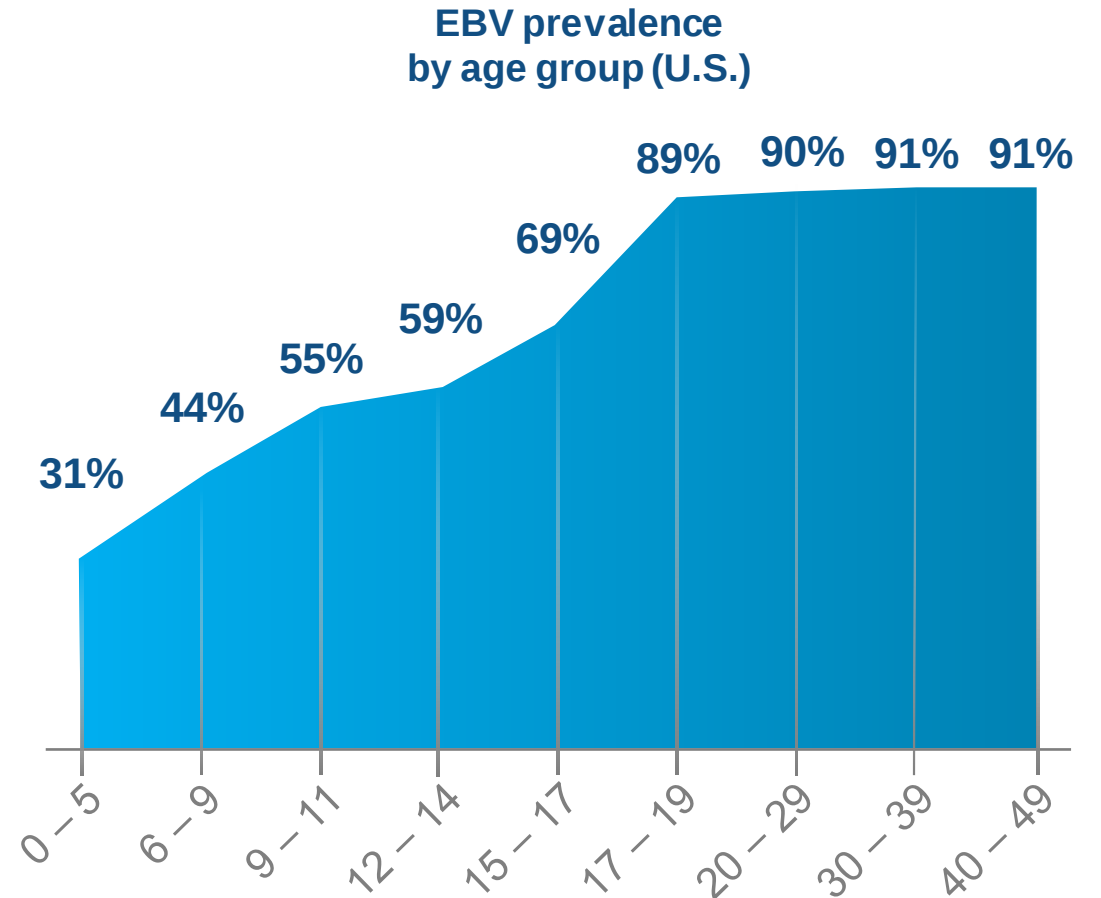
Epstein-Barr virus (EBV) is a major cause of infectious mononucleosis (IM)

Overview

- EBV is a member of the herpesvirus family that includes CMV, is spread through bodily fluids (e.g., saliva) and contracted primarily by young children and adolescents

Disease burden

- EBV is a major cause of infectious mononucleosis (IM) in the U.S., accounting for over 90% of the ~1+ million cases annually¹



Direct and indirect costs of EBV-linked IM exceed \$1 billion

IM Overview

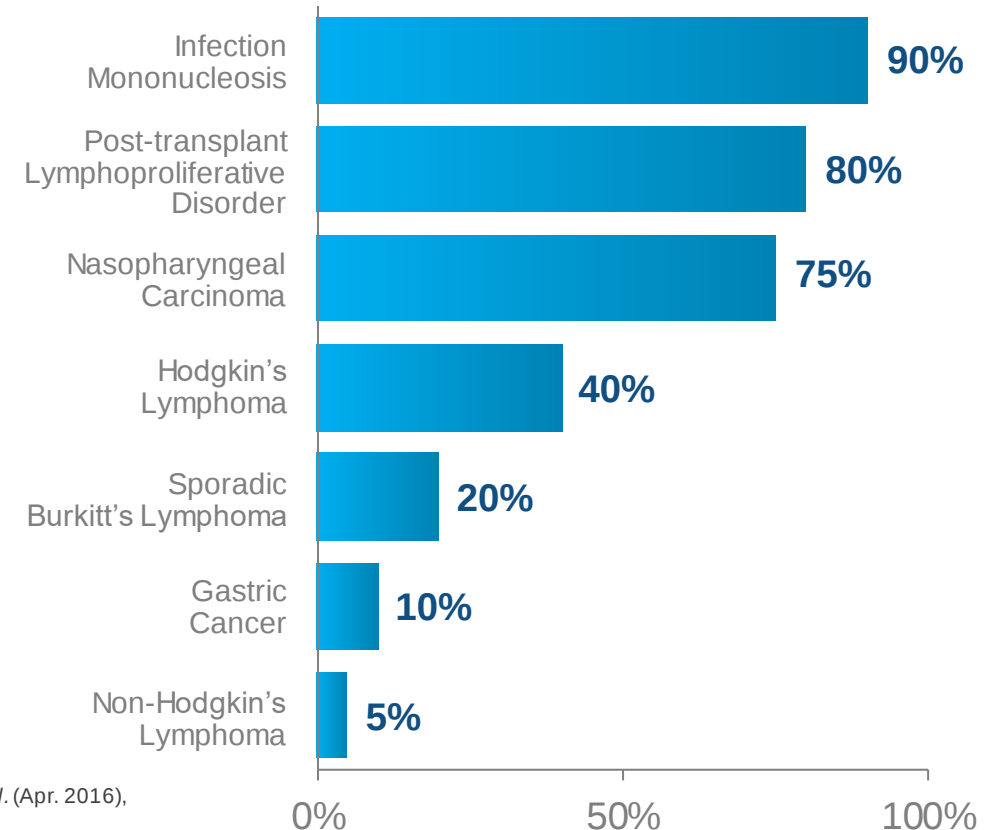
- IM can debilitate patients for weeks to months, can lead to hospitalization and (rarely) splenic rupture
- Estimated worldwide direct costs of EBV-linked IM to reach \$500 million annually and indirect costs to exceed \$1 billion
- Vaccine to prevent IM in seronegative adolescents could be a significant commercial opportunity, analogous to meningitis vaccines
- No approved EBV vaccine

EBV infection sequelae ¹	
Adolescents and young adults	<i>Infectious Mononucleosis</i> • Sore throat • Lymphadenopathy • Fever • Body aches • Fatigue
Lifetime associated risks	Increased risk of developing cancer and multiple sclerosis

80% of PTLD (post-transplant lymphoproliferative disease) cases can be attributed to EBV

- EBV infection is also associated with certain lymphoproliferative disorders, cancers and autoimmune diseases
- IM and EBV infection are associated with increased risk of developing multiple sclerosis (MS) by ~10-15 fold¹

Association of Epstein-Barr Virus by Indication in the United States²



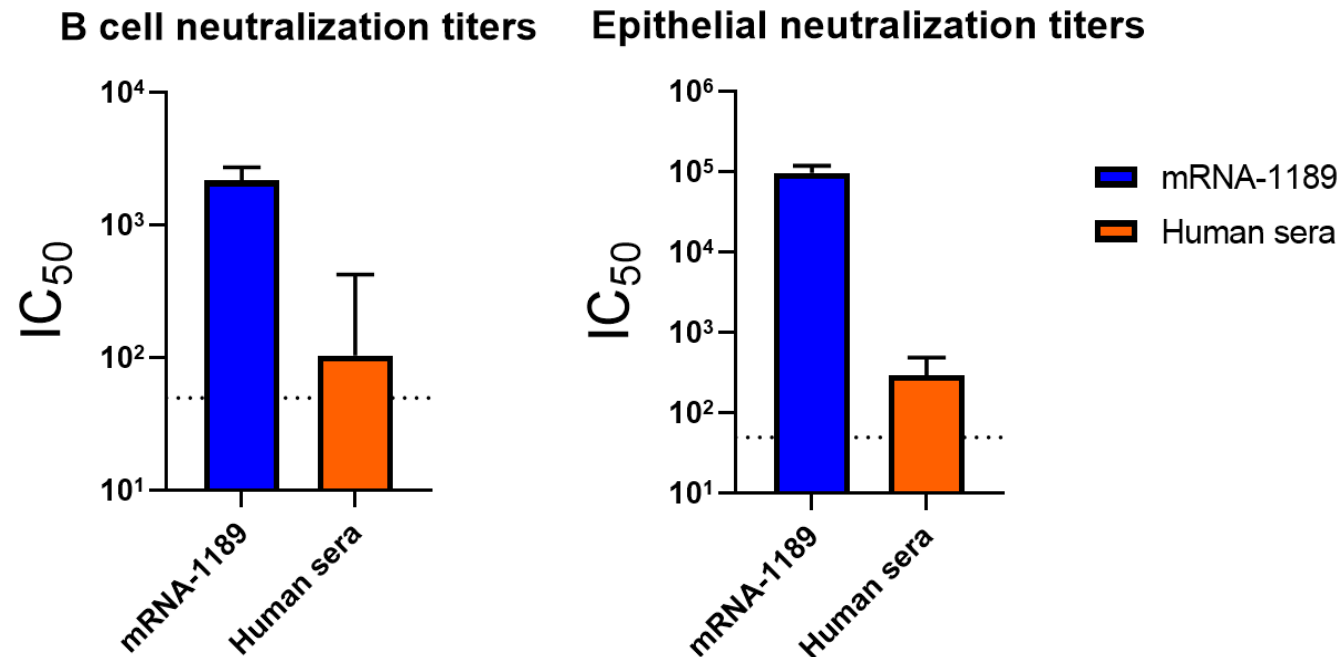
(1) Ascherio, Alberto, et al. "Epidemiology of Multiple Sclerosis: From Risk Factors to Prevention-An Update," *Semin Neurol.* (Apr. 2016), <https://doi.org/10.1055/s-0036-1579693>

(2) Gequelin, Lucian, et al. "Epstein-Barr virus: general factors, virus-related diseases and measurement of viral load after transplant," *Rev Bras Hematol Hemoter* (2011), <https://doi.org/10.5581/1516-8484.20110103>

(3) Khan, Gulfaraz, et al. "Global burden of deaths from Epstein-Barr virus attributable malignancies 1990-2010," *Infect Agent Cancer* (2014), <https://doi.org/10.1186/1750-9378-9-38>

We aim to start a Phase 1 EBV vaccine study in 2021

mRNA-1189 induces a robust immune response in preclinical animal studies



Results shown here represent eight animals per group and demonstrate high levels of neutralizing antibodies against B and epithelial cells, and at levels significantly higher than those observed in naturally-infected human sera

Naïve Balb/c mice were given two doses of a vaccine comprised of EBV antigens approximately three weeks apart. Neutralizing antibodies against B cell or epithelial cell infection were measured two weeks after the second dose using GFP-labeled virus. Neutralizing antibodies in a set of eight convalescent human sera were measured for comparison.

Dotted lines represent lower limit of detection.



Commercial vaccines business model

Corinne M. Le Goff, PharmD, MBA

Chief Commercial Officer

Our innovative business model

The attributes of the Moderna mRNA technology platform translates to a disruptive go-to-market approach

Speed



- Accelerated development
- Rapid iteration cycles

- Fast to market
- Most updated vaccines
- Competitive advantage

De-risked



- Established safety & efficacy profile of mRNA+LNP construct

- Allows for early investments for fast uptake post registration

Agile



- Adaptability

- Low fixed costs & flexible resource allocation model
- Lean organization
- Digitally enabled

We are building a go-to-market approach for variants and combos



New strain readiness

- We have **candidates in trials to address variants**:
 - Monovalent booster against B.1.351
 - Multivalent booster
- Our **rapid development cycles** will enable us to be fast to market and drive competitive advantage
- As a commercial organization, **we are preparing to meet the demand** and maintain our speed to market

Value-based approach and innovative pricing

- Based on a 2-dose efficacy of 90%, COVID-19 vaccine use during a pandemic between \$460-\$540 per 2-dose series was found cost-effective at \$50K/ QALY for the overall population (adults 18+)
- We are **incorporating cost-effectiveness** into our value-based approach for the endemic market

Our platform is de-risked, and we are engaging consumers early to build trust and educate



mRNA vaccines technology

- **We are confident in our mechanism of action** and ability to target a variety of diseases, including complex antigens that were not previously targeted
- **We are investing early to educate and build trust** in our platform, and raise disease awareness

aboutmrna.com

moderna[®]

Our bodies can create
their own defense.

mRNA, also called messenger RNA, is being investigated across many of our greatest health challenges. Keep reading to find out more about how mRNA delivers the instructions your body needs to potentially prevent, treat, or cure a disease.

Capitalize on Moderna household name to raise awareness in CMV

Our ambition is to eliminate CMV

- We have an opportunity to speak to the millions of consumers that trust us today, and address vaccine hesitancy by reinforcing consumers' trust in us through transparency, and our commitment to health education
- Now is the time to raise awareness about CMV, a complex antigen disease which has not been previously targeted and is mostly unknown

91%
OF WOMEN



DO NOT
KNOW
ABOUT CMV

Today



91%
OF WOMEN



DO NOT
KNOW
ABOUT CMV

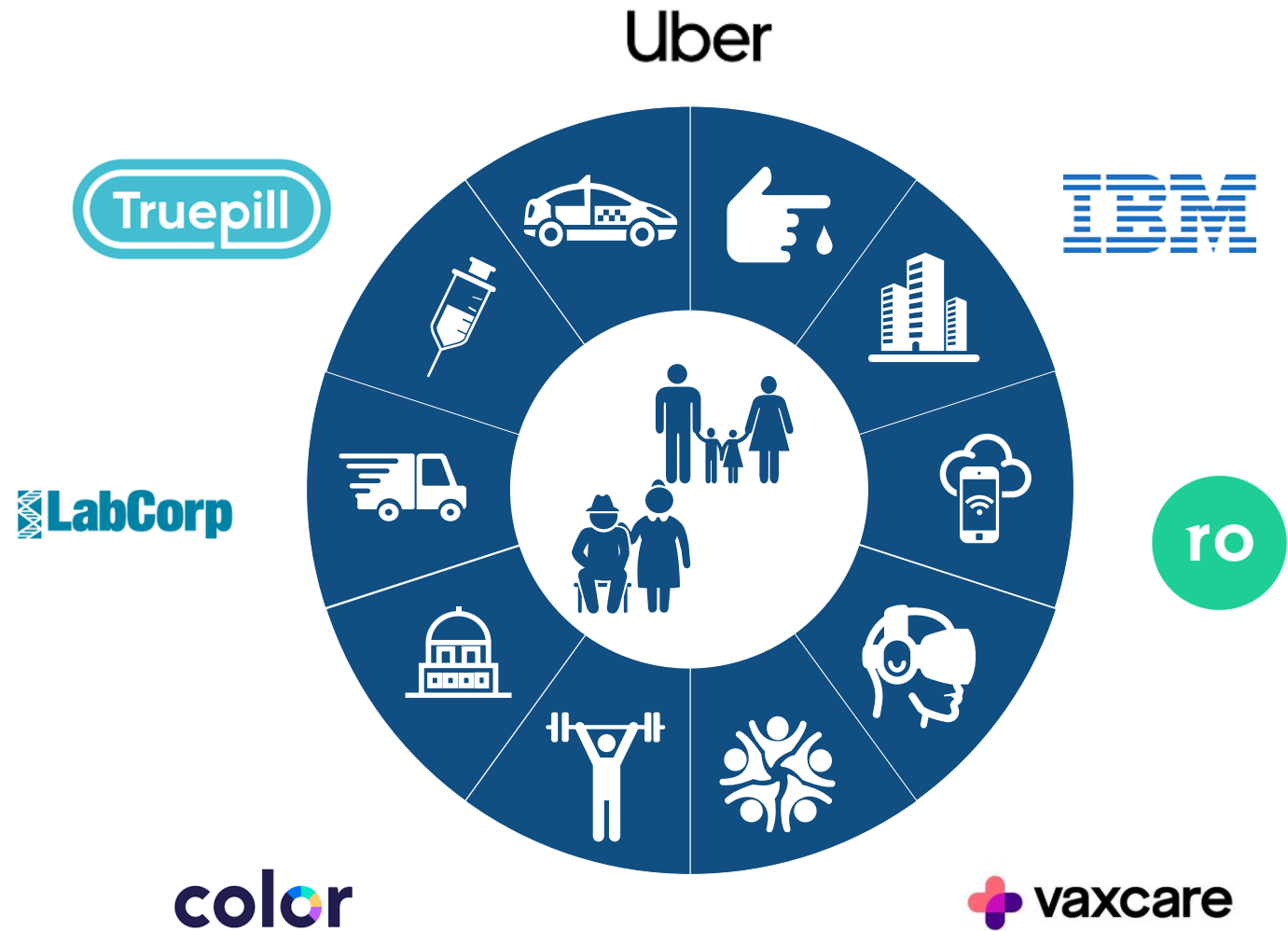
At launch



B2C model in CMV

- Consumers play a massive role in vaccination decisions
- We are engaging in direct-to-consumer education and awareness-building
- We are learning from consumers, curating ideas from communities

We are establishing a coalition of partners in the US to extend our direct-to-consumer reach



We are commercializing through a lean, agile, and digital-first approach

Digital-first go-to-market

- Small team
- Data and analytics to gain deep consumer insights
- Digital-first, scalable approaches to customer engagement:
 - Direct-to-consumer education
 - Webinar-based education sessions with customers and stakeholders
 - Targeted engagement of communities with high unmet need
 - Collaboration with our coalition of partners



Digital engagement in COVID-19



Engaging women on CMV



Engage



Educate +
Engage

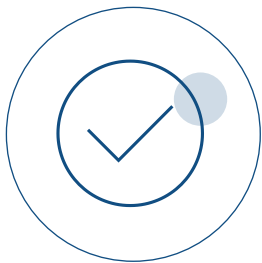


Build

At Moderna, our people make all the difference



We are leveraging the decades of experience our commercial team has in vaccines and biopharma



We are questioning the status quo to bring innovative solutions to complex commercialization issues in a rapidly shifting environment to better serve global population health needs

Fueled by our recent success in COVID-19, we are **engaging the best minds and attracting the best talent** to our organization to achieve our vision



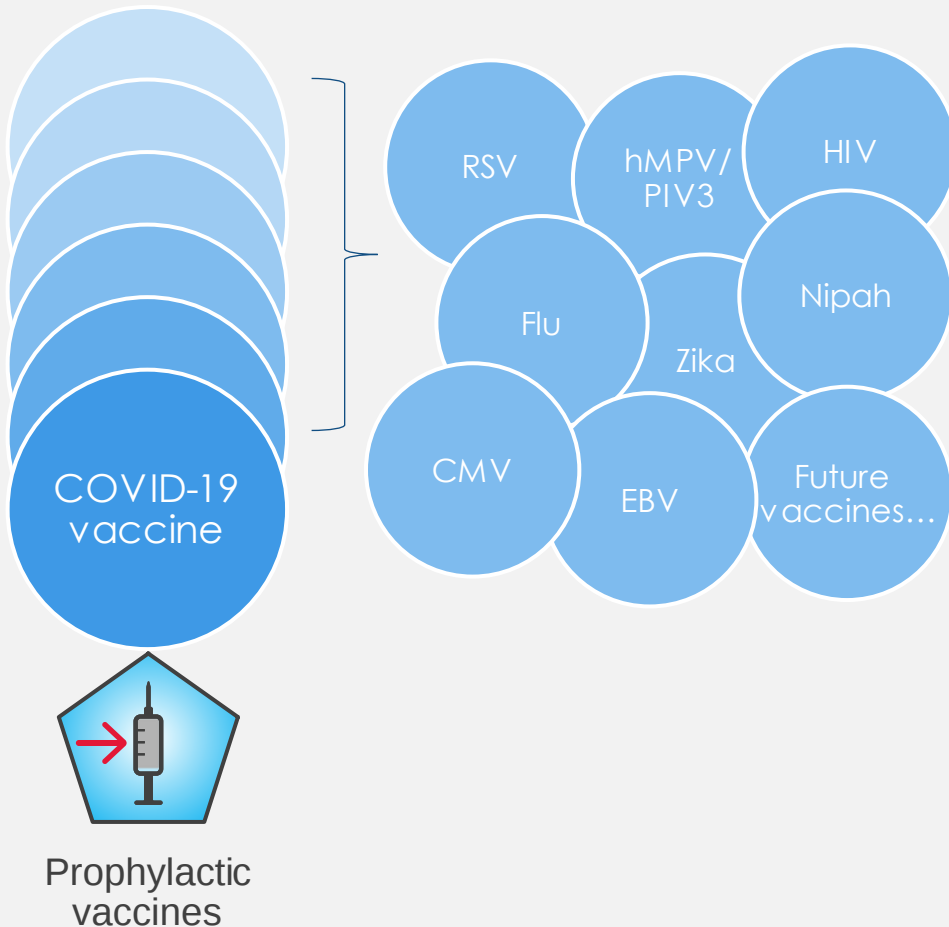
Conclusion

Stéphane Bancel

Chief Executive Officer

Moderna could become the best vaccine company

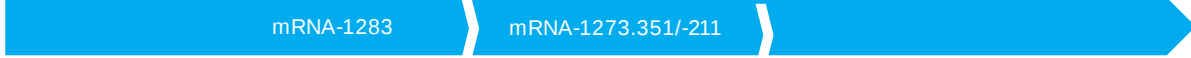
Multiple first-in class vaccine candidates



- ✓ Same **LNP** formulation
- ✓ Same **mRNA** nucleotides
- ✓ Same mRNA & LNP **manufacturing** processes
- ✓ Same **commercial** infrastructure

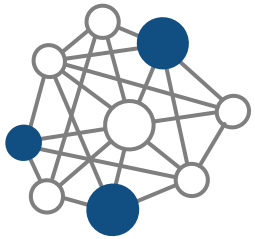
Largest first in class vaccine development pipeline in the industry

9 vaccine programs for major unmet needs

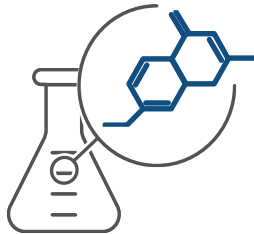
Program		ID #	Preclinical development	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
COVID-19 vaccine		mRNA-1273 mRNA-1273.351/-211 mRNA-1283						Worldwide BARDA funded
Cytomegalovirus (CMV) vaccine		mRNA-1647						Worldwide
hMPV/PIV3 vaccine		mRNA-1653						Worldwide
Zika vaccine		mRNA-1893						Worldwide BARDA funded
Respiratory syncytial virus (RSV) vaccine		mRNA-1345						Worldwide
Epstein-Barr virus (EBV) vaccine		mRNA-1189						Worldwide
Flu vaccine		mRNA-1010 mRNA-1020 mRNA-1030						Worldwide
Nipah vaccine		mRNA-1215						Worldwide NIH funded
HIV vaccine		mRNA-1644 mRNA-1574						Worldwide IAVI/BMGF/NIAID and others funded
Influenza H7N9 vaccine		mRNA-1851						Worldwide Advancing subject to funding

Given our conviction and our cash balance, we have a large appetite to invest

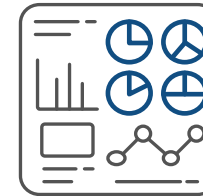
mRNA Science



Infectious Disease Research



Clinical Development



Long-term Studies



Long-term vision for our respiratory vaccines franchise

Long-term vision to provide a convenient annual, single dose boost against as many respiratory viruses as possible

- **COVID-19:** We will continue to bring variant booster shots until COVID-19 is under control
- **Flu:** High efficacy flu vaccine would address an underserved market
- **Combinations:** Increase convenience through combination vaccines: Flu + COVID variant + RSV...?

Vaccines requiring complex antigens and against highly prevalent infections

Vaccines against complex antigens

CMV
vaccine

EBV
vaccine



We are going to **invest in education** during Phase 3



Goal is to **eradicate the virus and the disease burden**

While we build what could be the best vaccine company, we also aim to transform medicine...again...with mRNA therapeutics

2021 will be an inflection year for Moderna

**2020 was the year of
COVID-19 vaccine
development**

11 months from sequence
design to regulatory
authorization

**2021 could be the year of
proof-of-concept in
therapeutics**

Seven clinical proof-of-
concept trials

Positive preliminary Phase 1 data reported in PCV and IL-12

5 oncology trials currently in the clinic

Select programs

Personalized cancer vaccine (mRNA-4157)



- mRNA-4157 in combination with Merck's Keytruda is well tolerated
- In HPV(-) Head and Neck Squamous Cell Carcinoma (HNSCC) patients ORR is 50% (5/10) and mPFS is 9.7 months, compares favorably to published ORR and mPFS of 14.6% and 2.0 months respectively, for Keytruda monotherapy
- Expansion of HNSCC ongoing

IL-12 (MEDI-1191)



- Phase 1 data presented at ESMO TAT conference
- MEDI-1191 is well tolerated (without >Grade 3 AE, DLT or SAEs)
- Monotherapy efficacy in IO refractory melanoma patient and a response in HNSCC
- Phase 1 ongoing

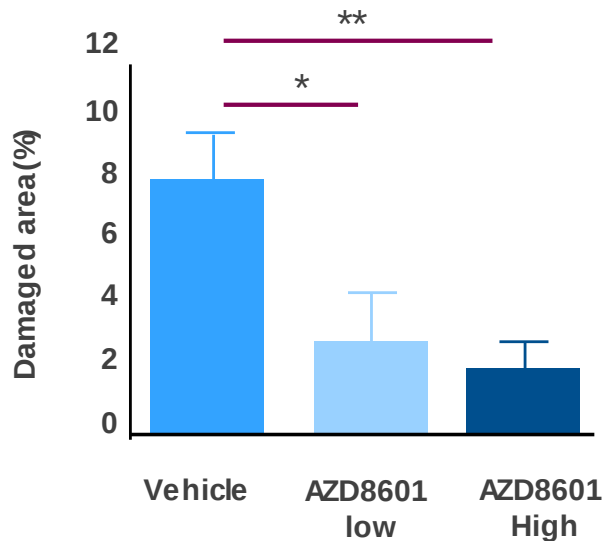
Localized regenerative therapeutics

AZD-8601 is ongoing in a Phase 2 study

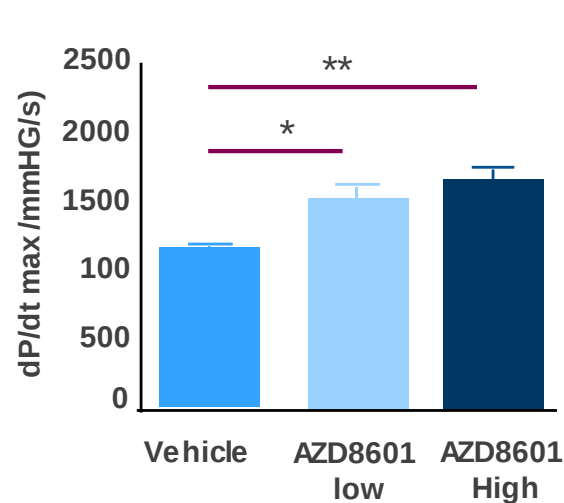
Single cardiac administration improves cardiac function two months after myocardial infarction in the pig *in vivo*¹

Positive Phase 1 data²

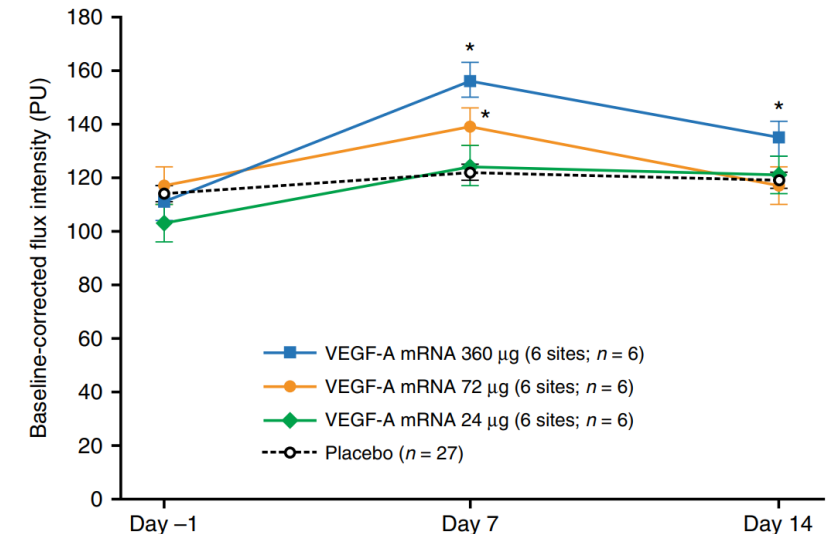
Reduces heart damage



Improves heart function



Enhanced basal skin blood flow



(1) Carlsson, Leif, et al. "Biocompatible, Purified VEGF-A mRNA Improves Cardiac Function after Intracardiac Injection 1 Week Post-myocardial Infarction in Swine," *Molecular Therapy* (26 Apr. 2018), <https://doi.org/10.1016/j.omtm.2018.04.003>

(2) Gam Li-Ming, et al. "Intradermal delivery of modified mRNA encoding VEGF-A in patients with type 2 diabetes," *Nature Communications* (20 Feb. 2019), <https://doi.org/10.1038/s41467-019-08852-4>

We expanded into the autoimmune therapeutic area in 2020

2 autoimmune candidates in IND-enabling studies; share same LNP as our Chikungunya antibody program (mRNA-1944)

PD-L1 (mRNA-6981)

- First indication intended to be autoimmune hepatitis, a compelling unmet need

IL-2 (mRNA-6231)

- IL-2 based therapeutics are being clinically evaluated for a wide range of autoimmune conditions
- First intended subcutaneous administration

Rare diseases are a significant opportunity for Moderna

4 programs for rare diseases within the systemic intracellular therapeutics modality

Select programs

PA (mRNA-6981)

- Phase 1/2 sites are being initiated to enter the clinic in 2021
- We will be looking for biomarkers as early indicators for therapeutic impact

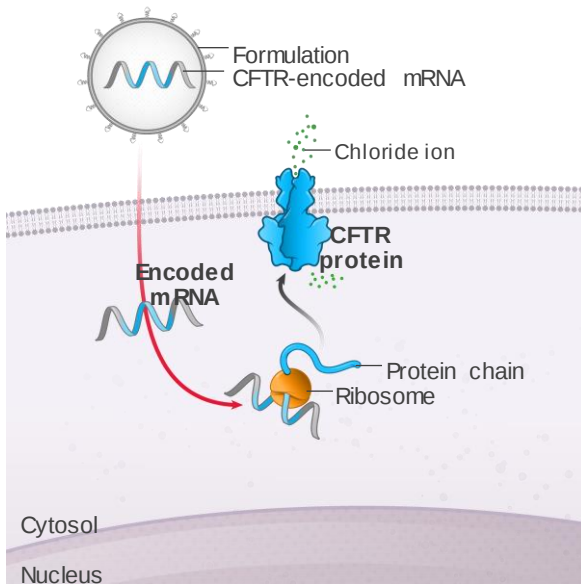
MMA (mRNA-3705)

- Working on filing new IND and CTA applications for our next generation MMA candidate

Future modalities are being worked on, like delivery to the lungs

1st partnership with Vertex to apply mRNA to the lungs

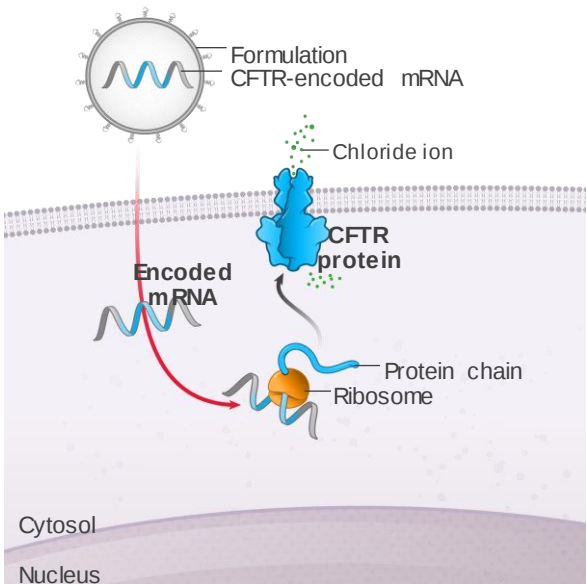
mRNA for CFTR



What if we could use our mRNA + LNPs to do gene editing ?

2nd partnerships with Vertex to do gene editing in the lungs

mRNA for CFTR

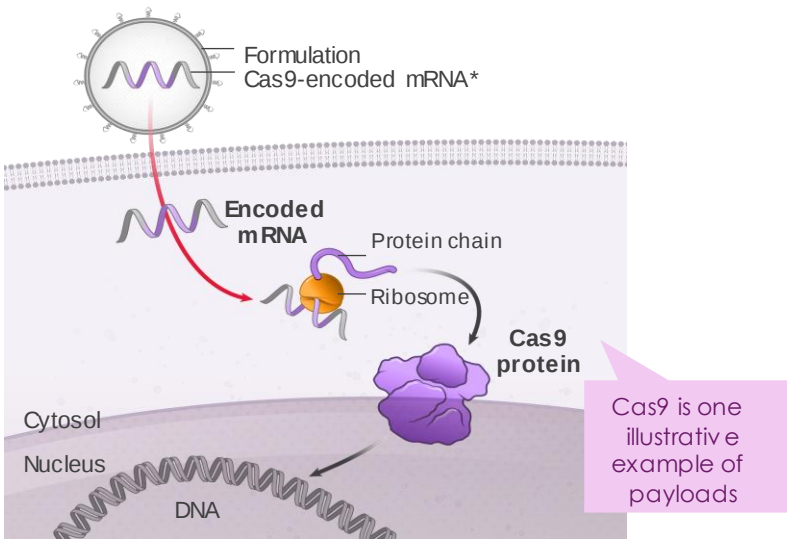


Two parallel approaches
to addressing the unmet
need in Cystic Fibrosis

*(Approximately 10% of Cystic
Fibrosis patients are not
addressable with a CFTR
modulator)*



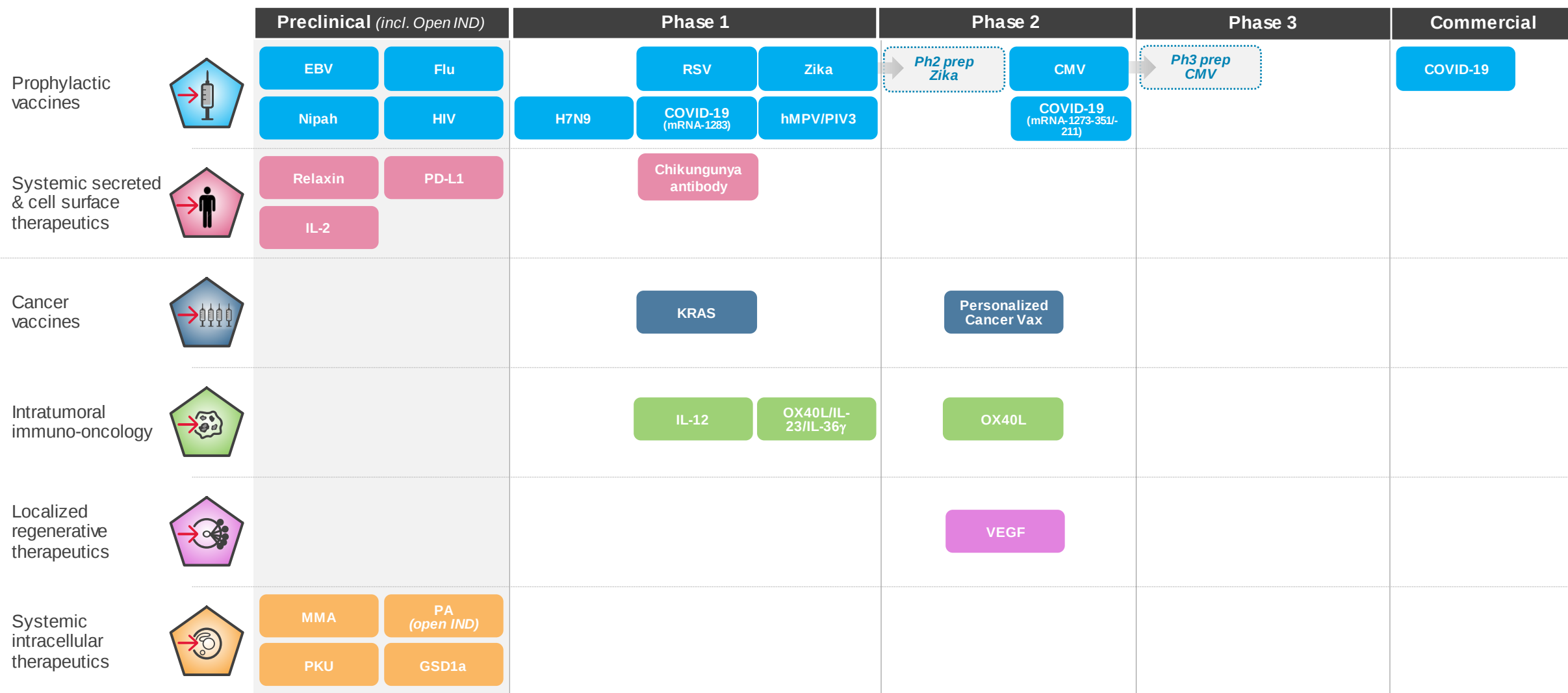
mRNA for gene editing

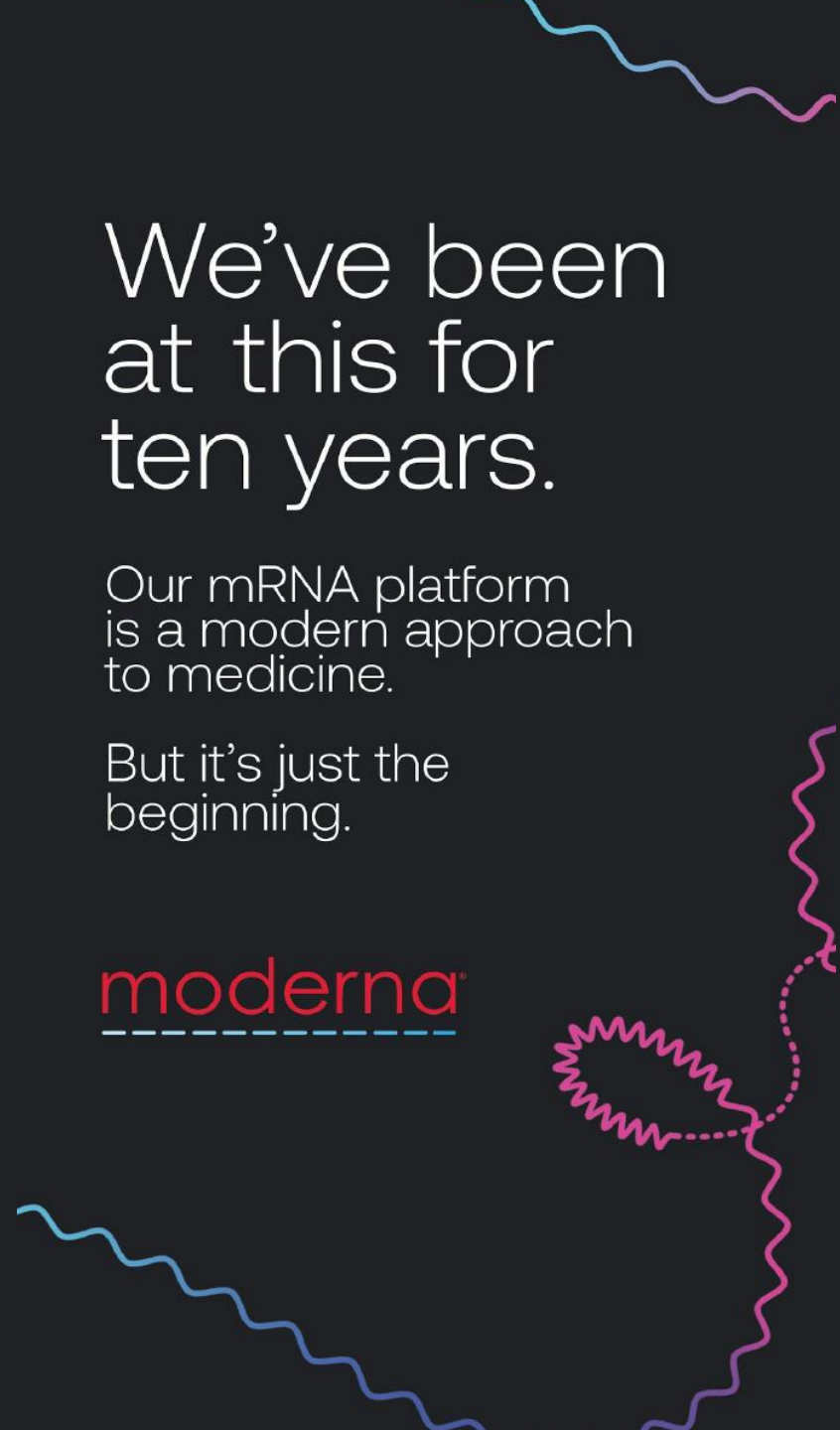


Moderna's Development pipeline

April 2021

Core modalities



The background features several decorative wavy lines. A blue line starts at the top left and curves towards the bottom left. A pink line starts at the top right and curves towards the bottom right. Another pink line forms a circular shape on the right side. A dotted pink line also curves on the right side.

We've been at this for ten years.

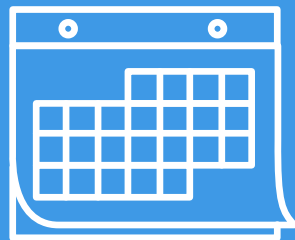
Our mRNA platform
is a modern approach
to medicine.

But it's just the
beginning.

moderna[®]



Q&A



Save the Date Events in 2021



Science Day

May 27th



R&D Day

September 9th