

# **COVID-19: Developing a Vaccine During a Pandemic**

**Dan H. Barouch, M.D., Ph.D.**

**Director, Center for Virology and Vaccine Research**

**Beth Israel Deaconess Medical Center**

**William Bosworth Castle Professor of Medicine**

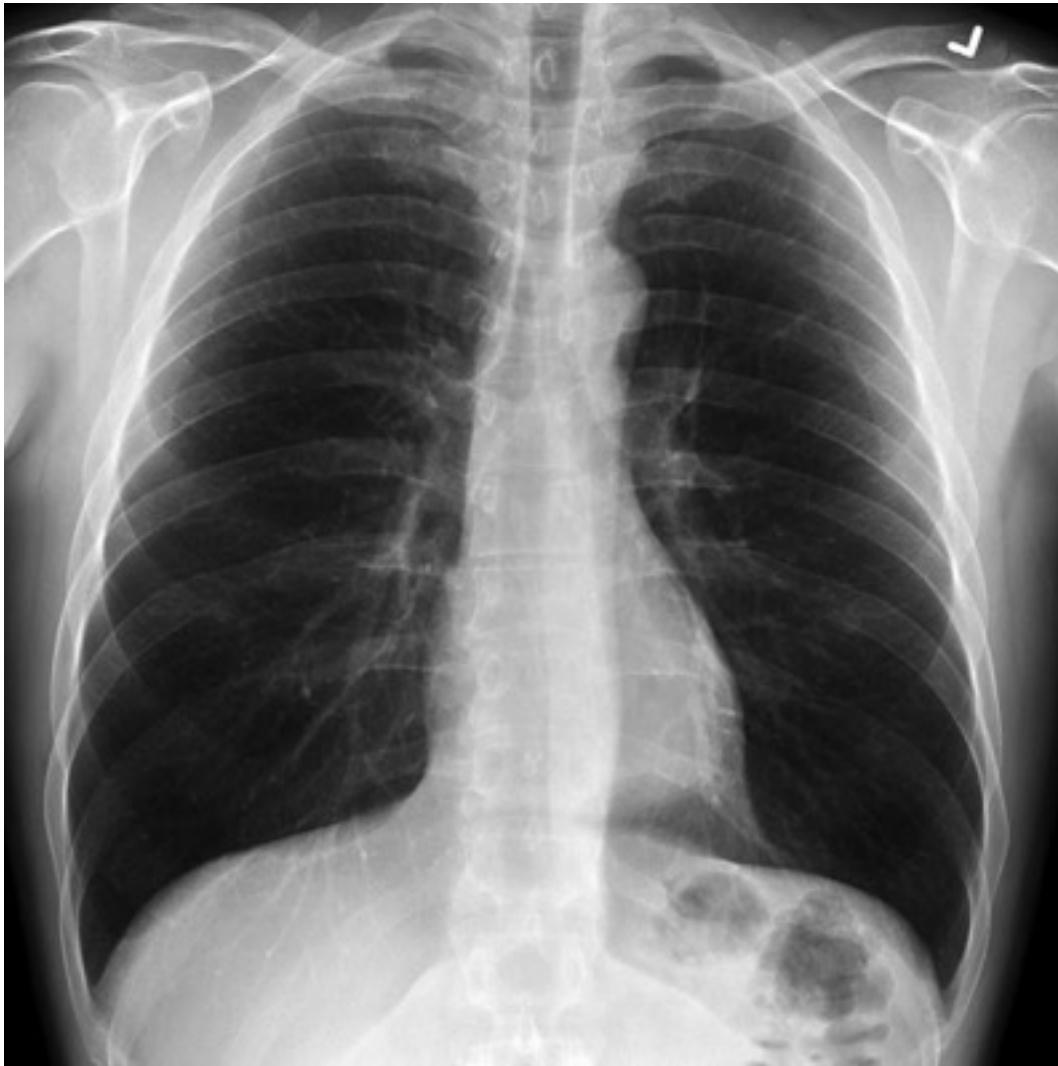
**Harvard Medical School**

**Ragon Institute of MGH, MIT, and Harvard**

**MIT 6.881/20.S948, Cambridge, MA**

**February 17, 2022**

# December 2019: A New Disease

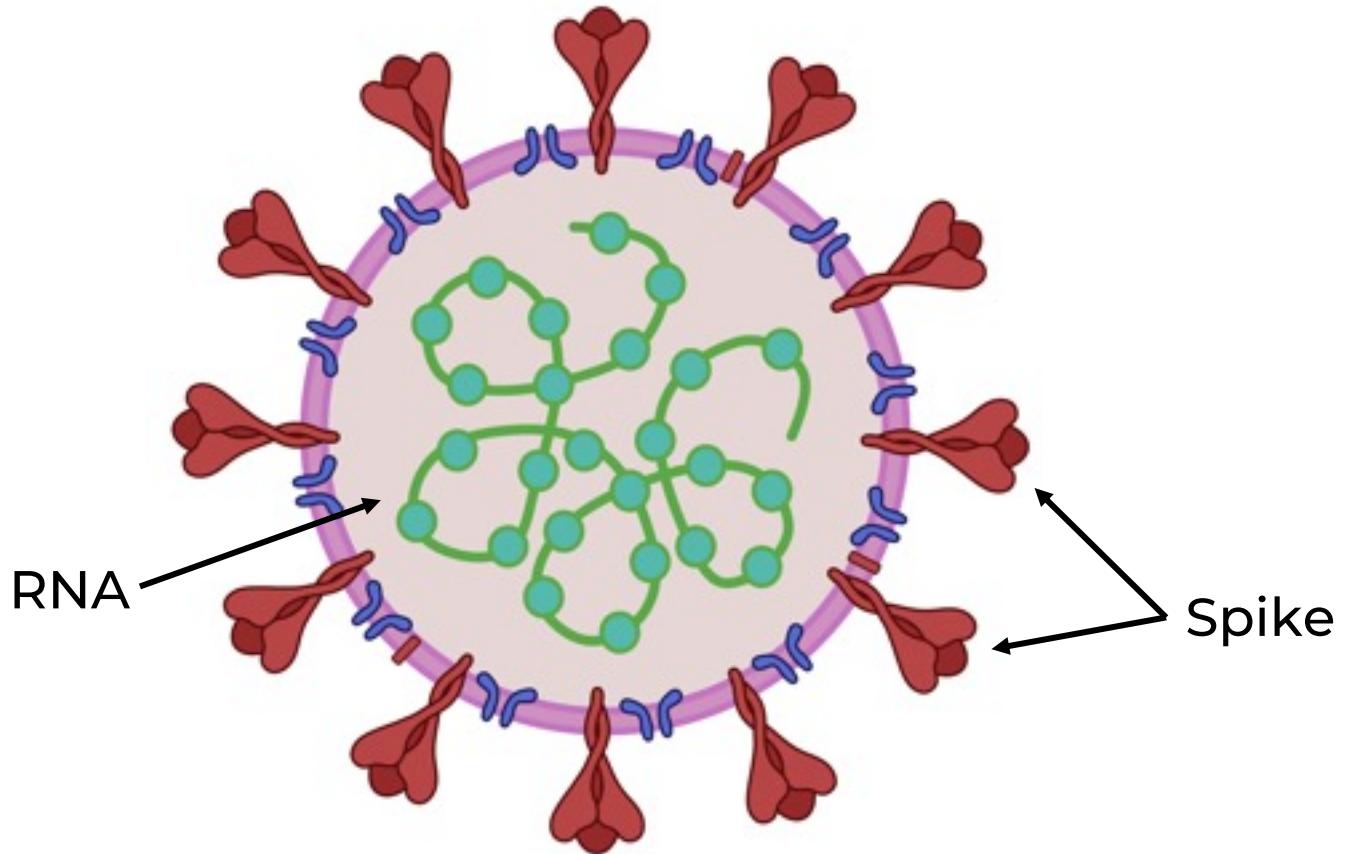


Normal



Pneumonia of Unknown Cause

# January 10, 2020: SARS-CoV-2 Sequenced 41 Cases, 1 Death





Tracking Home

Data Visualizations ▾

Global Map

U.S. Map

Data in Motion

Tracking FAQ



## COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)



Last Updated at (M/D/YYYY)

2/12/2022, 8:21 AM

Cases | Deaths by  
Country/Region/Sovereignty

US

28-Day: 12,567,476 |

65,958

Totals: 77,652,197 | 918,451

France

28-Day: 7,965,786 | 7,823

Totals: 21,646,561 | 135,534

India

28-Day: 5,735,582 | 22,229

Totals: 42,586,544 | 507,981

Brazil

28-Day: 4,366,047 | 16,404

Totals: 27,299,336 | 637,467

Germany

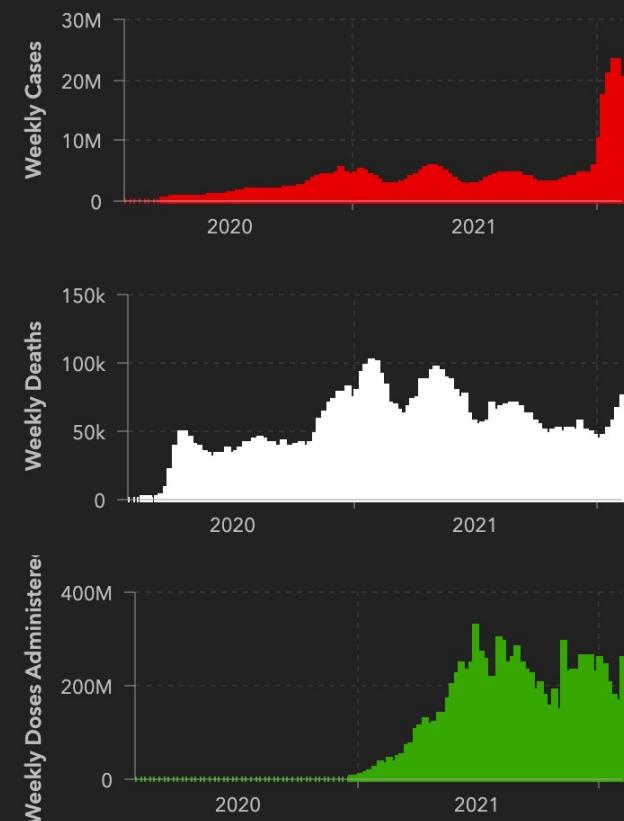
28-Day: 4,330,694 | 4,305

Totals: 12,281,007 | 119,882

Total Cases  
**408,959,299**Total Deaths  
**5,804,310**Total Vaccine Doses Administered  
**10,186,345,353**28-Day Cases  
**84,447,772**28-Day Deaths  
**269,399**28-Day Vaccine Doses Administered  
**747,134,114**

Esri, FAO, NOAA

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# Phase 3 COVID-19 Vaccine Efficacy Trials in the US

• <u>Developer</u>	<u>Platform</u>	<u>Launch</u>	<u>Efficacy</u>
• Pfizer	mRNA	Jul 2020	Nov 2020
• Moderna	mRNA	Jul 2020	Nov 2020
• J&J	Ad26	Sept 2020	Jan 2021
• AstraZeneca	ChAdOx1	Aug 2020	Mar 2021
• Novavax	Protein	Dec 2020	Jun 2021

# **Pfizer, Moderna, JnJ Vaccine Efficacy in Phase 3 Randomized Controlled Trials (US Data; Pre-Omicron)**

**Pfizer (two-shot)** **95%**

**Moderna (two-shot)** **94%**

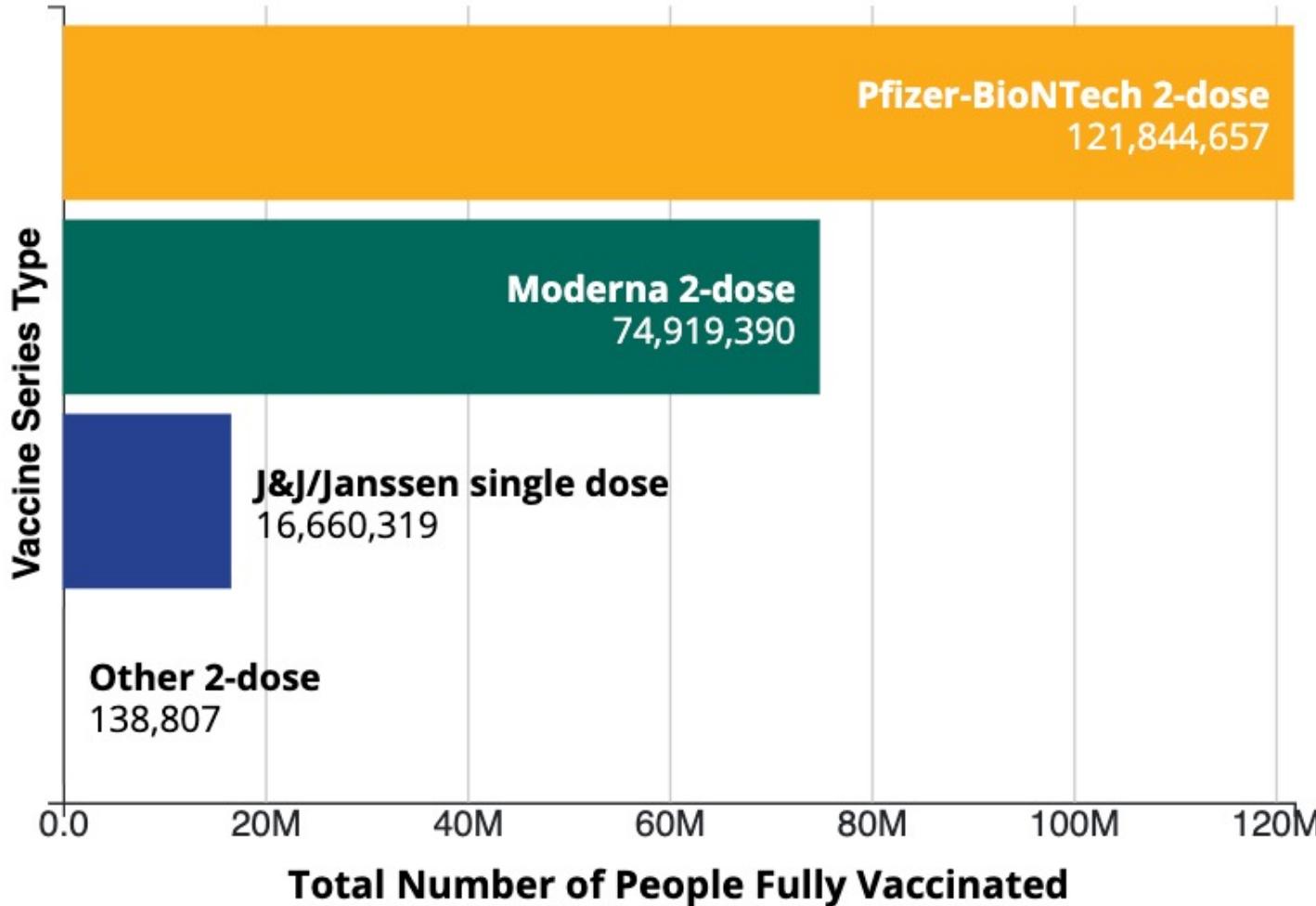
**JnJ (single-shot)** **72%**

**JnJ (two-shot)** **94%**

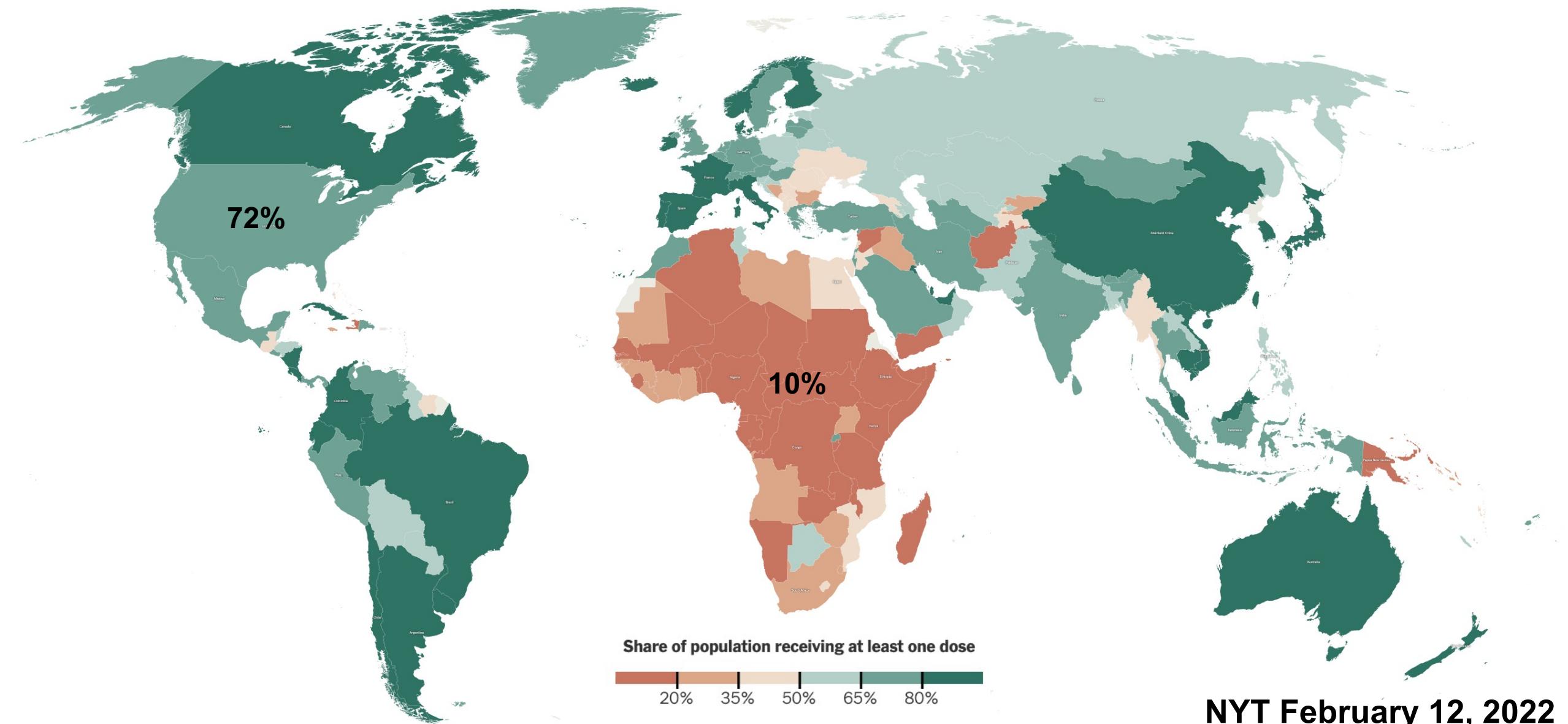
**Note:** JnJ international efficacy 66% (single-shot) and 75% (two-shot) in the context of  $\beta/\mu/\lambda$  variants.

Polack NEJM 2020; Baden NEJM 2020; Sadoff NEJM 2021, 2022; Thomas NEJM 2021; El Sahly NEJM 2021; Hardt medRxiv 2022

# Fully Vaccinated Individuals in the US



# Stark Global Health Disparities in Vaccination Rates



# Limited Use of mRNA Vaccines in Africa

**Pfizer-BioNTech**  
152 COUNTRIES



**Moderna**  
88 COUNTRIES



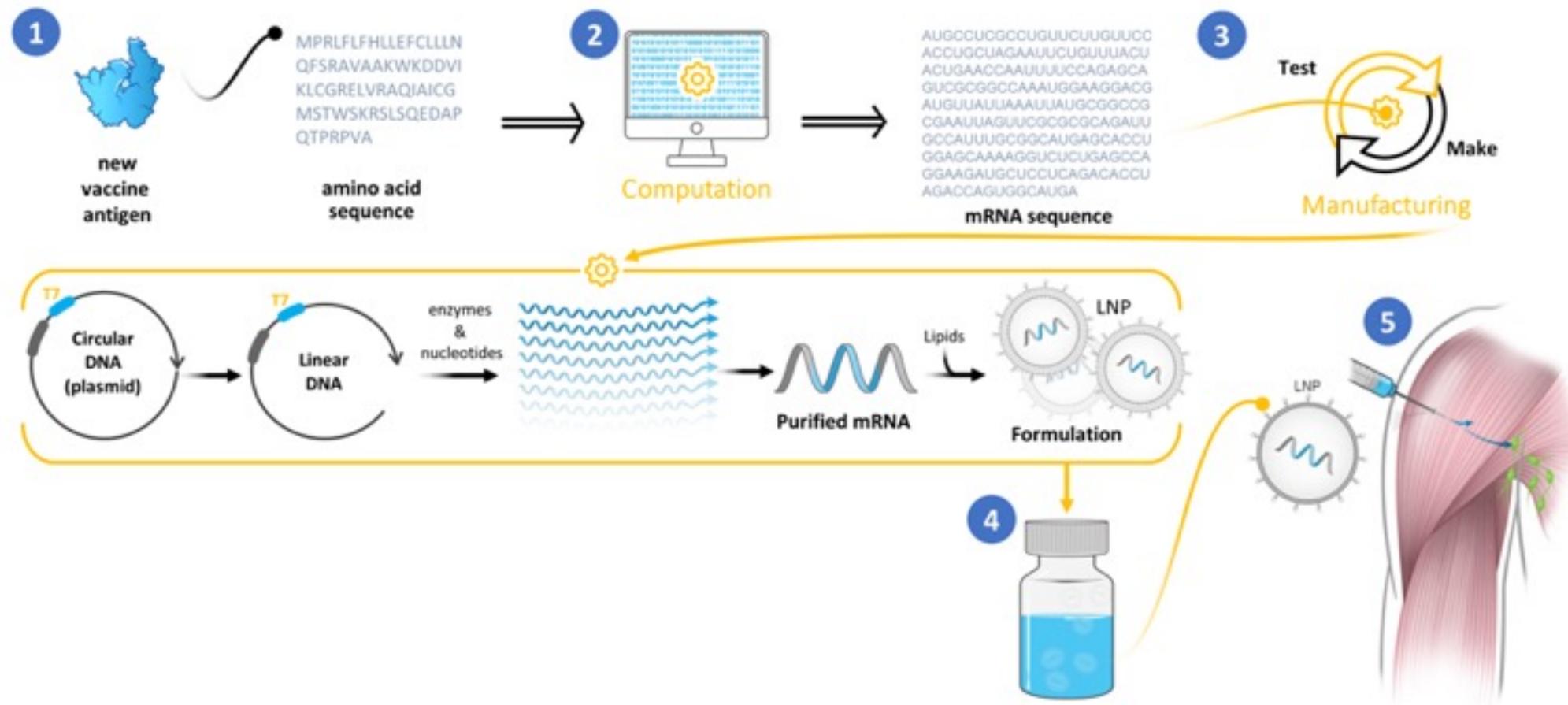
**Oxford-AstraZeneca**  
182 COUNTRIES



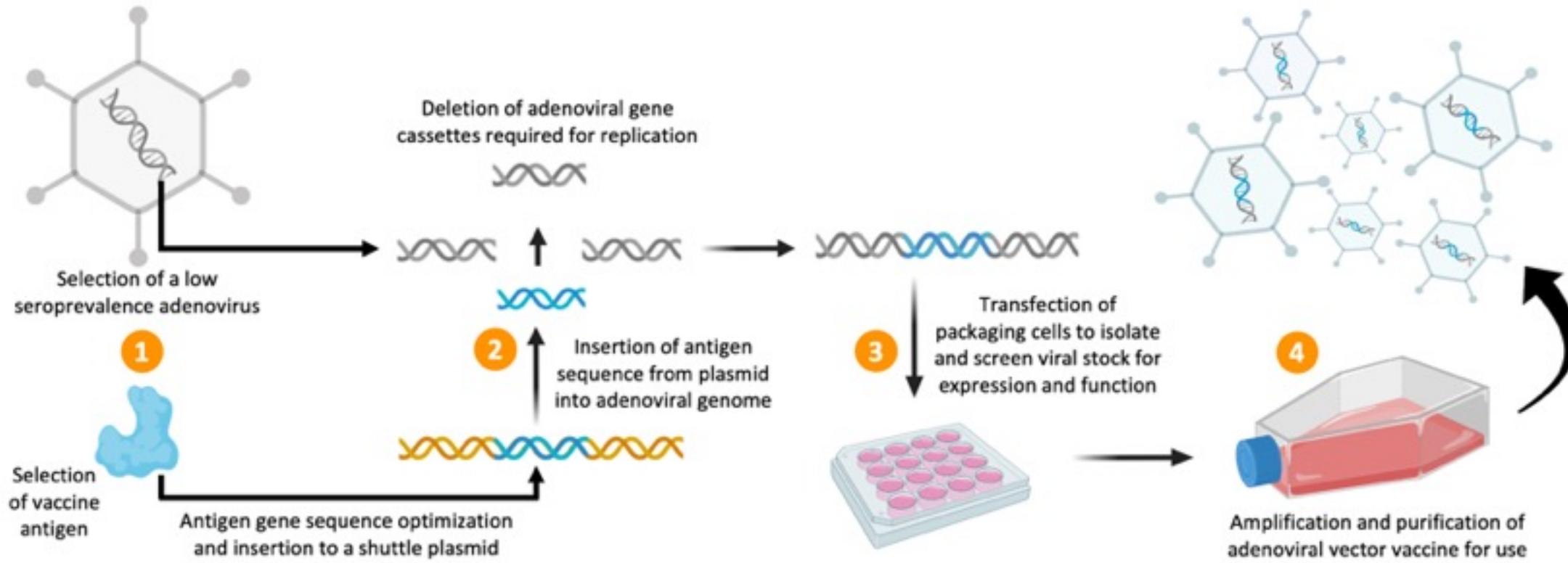
**Johnson & Johnson**  
82 COUNTRIES



# mRNA Vaccines



# Adenovirus Vector Vaccines



# **Why Have Vaccines Not (Yet) Controlled the Pandemic?**

- **Global and local health disparities**
- **Vaccine misinformation and hesitancy**
- **Rapid waning of vaccine protection**
- **Emergence of viral variants**

# The Case for Global Vaccination for COVID-19

- The global health disparities in current COVID-19 vaccination rates show stark inequities between rich and poor countries
  - As rich countries are now rolling out third and even fourth boosts, with plans for additional boosts this spring, many poor countries have yet administered any population-wide vaccines
- Global COVID-19 vaccination is a humanitarian and ethical imperative
- Delta and Omicron originated in areas of the world with limited vaccine coverage; as long as any regions of the world remain poorly vaccinated, new variants will continue to emerge that will re-threaten the entire world

# Cloning, Vectorization, and Selection of Replication-Incompetent Ad26 Vaccine Vectors (2003-2007)

JOURNAL OF VIROLOGY, May 2007, p. 4654–4663  
0022-538X/07/\$08.00+0 doi:10.1128/JVI.02696-06  
Copyright © 2007, American Society for Microbiology. All Rights Reserved.

Vol. 81, No. 9

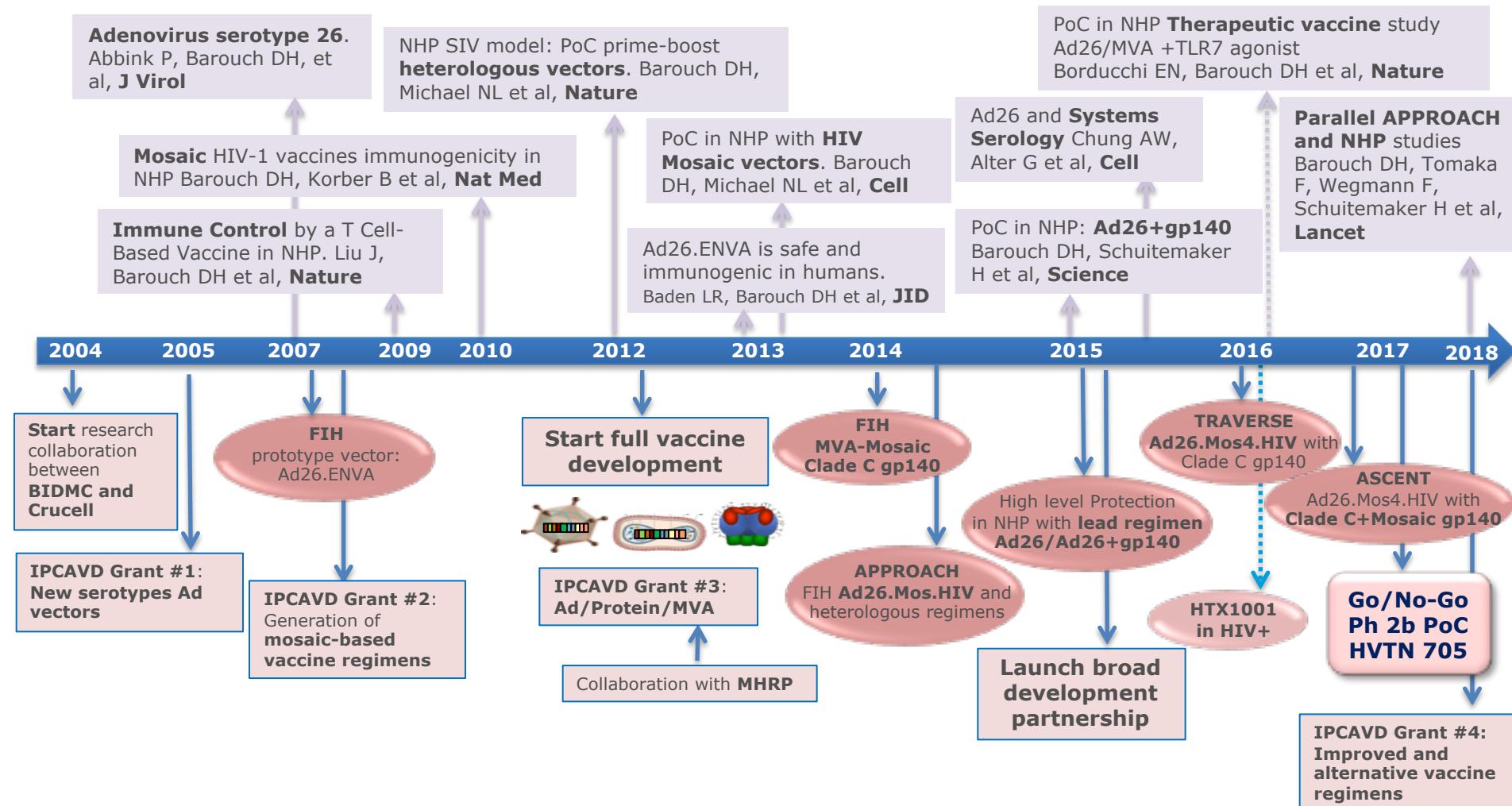
## Comparative Seroprevalence and Immunogenicity of Six Rare Serotype Recombinant Adenovirus Vaccine Vectors from Subgroups B and D<sup>▽</sup>

Peter Abbink,<sup>1</sup> Angelique A. C. Lemckert,<sup>2</sup> Bonnie A. Ewald,<sup>1</sup> Diana M. Lynch,<sup>1</sup> Matthew Denholtz,<sup>1</sup> Shirley Smits,<sup>2</sup> Lennart Holterman,<sup>2</sup> Irma Damen,<sup>2</sup> Ronald Vogels,<sup>2</sup> Anna R. Thorner,<sup>1</sup> Kara L. O'Brien,<sup>1</sup> Angela Carville,<sup>3</sup> Keith G. Mansfield,<sup>3</sup> Jaap Goudsmit,<sup>2</sup> Menzo J. E. Havenga,<sup>2</sup> and Dan H. Barouch<sup>1\*</sup>

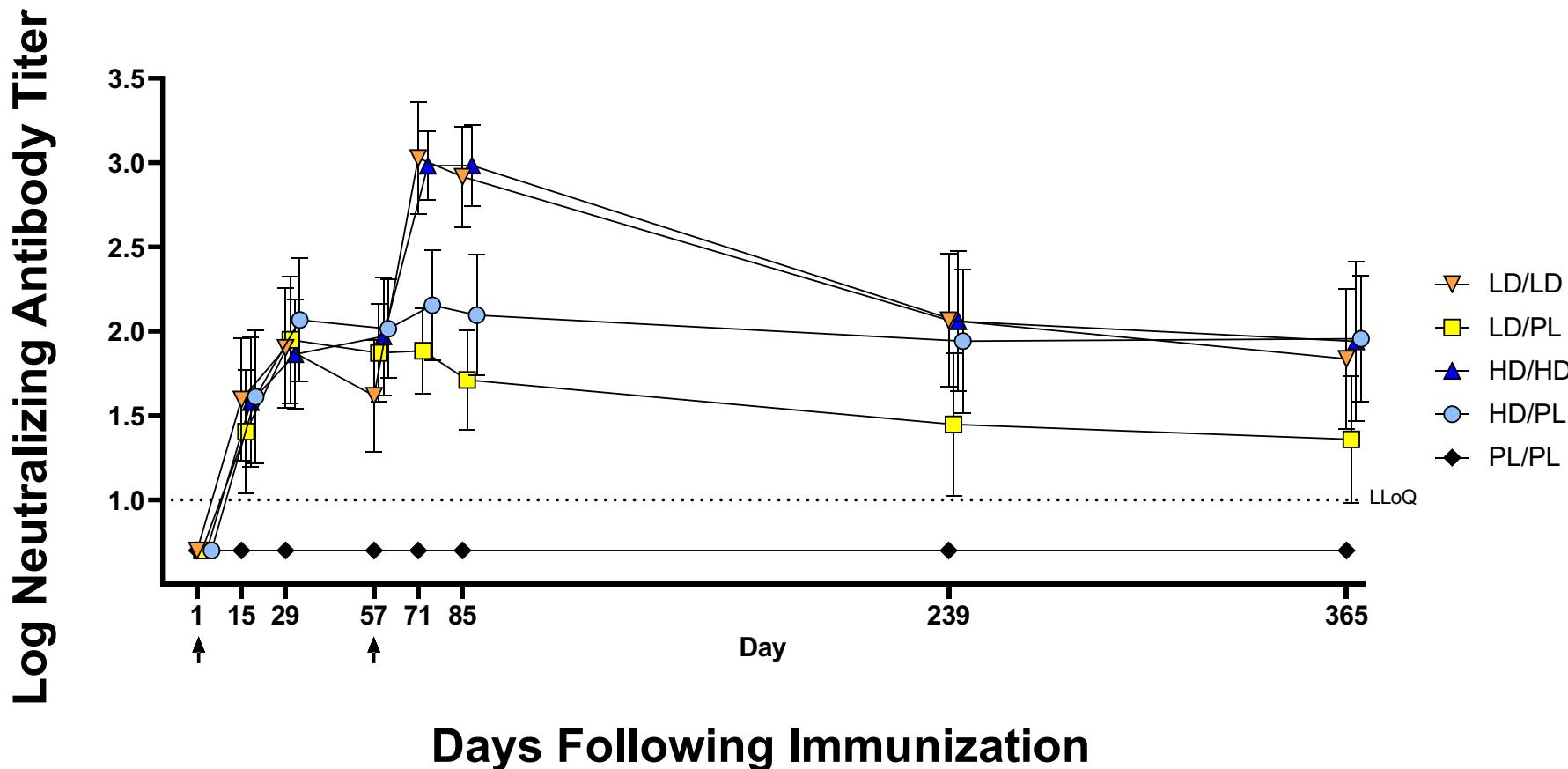
*Division of Viral Pathogenesis, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts 02215<sup>1</sup>; Crucell Holland BV, 2301 CA, Leiden, The Netherlands<sup>2</sup>; New England Primate Research Center, Southborough, Massachusetts 01772<sup>3</sup>*

Received 6 December 2006/Accepted 17 February 2007

# Replication-Incompetent Ad26 Vaccine Vectors: Development as an HIV-1 Vaccine (2004-2021)



# Replication-Incompetent Ad26 Vaccine Vectors: Development as a ZIKV Vaccine (2016-2020)



# Ad26-Based COVID-19 Vaccine: Rationale

- Replication-incompetent Ad26 developed as vaccine vector for multiple pathogens prior to 2020 (HIV, ZIKV, Ebola, RSV)
- Ad26-HIV was the initial development of the Ad26 platform technology
- Ad26-ZIKV demonstrated the potential of a single-shot vaccine and improved responses with a two-shot vaccine
- Ad26-Ebola showed mass production and global distribution feasible without the need for a subzero frozen cold chain
- Ad26-RSV administered to infants down to 4 months of age

# Ad26-Based COVID-19 Vaccine: Timeline

- Jan 10, 2020: Virus sequence released
- Jan 13: Synthetic genes ordered to design vaccine
- Jan 31: Collaboration agreement signed with J&J
- Feb 6: Mice immunized
- Feb 12: Rhesus monkeys immunized
- May 20: Science publications on natural and vaccine immunity in NHPs
- Jul 22: Initiation of phase 1/2 clinical trials
- Jul 30: Nature publication on Ad26 vaccine protection in NHPs
- Sep 21: Initiation of single-shot phase 3 clinical trial (N=45,000)
- Nov 16: Initiation of two-shot phase 3 clinical trial (N=30,000)
- Jan 29, 2021: Interim safety and efficacy data announced
- Feb 27, 2021: FDA emergency use authorization granted
- 2021: J&J produced 500 million vaccines
- 2022: J&J plans for >1 billion vaccines; 70% for low/middle-income countries

Cite as: A. Chandrashekhar *et al.*, *Science*  
10.1126/science.abc4776 (2020).

## SARS-CoV-2 infection protects against rechallenge in rhesus macaques

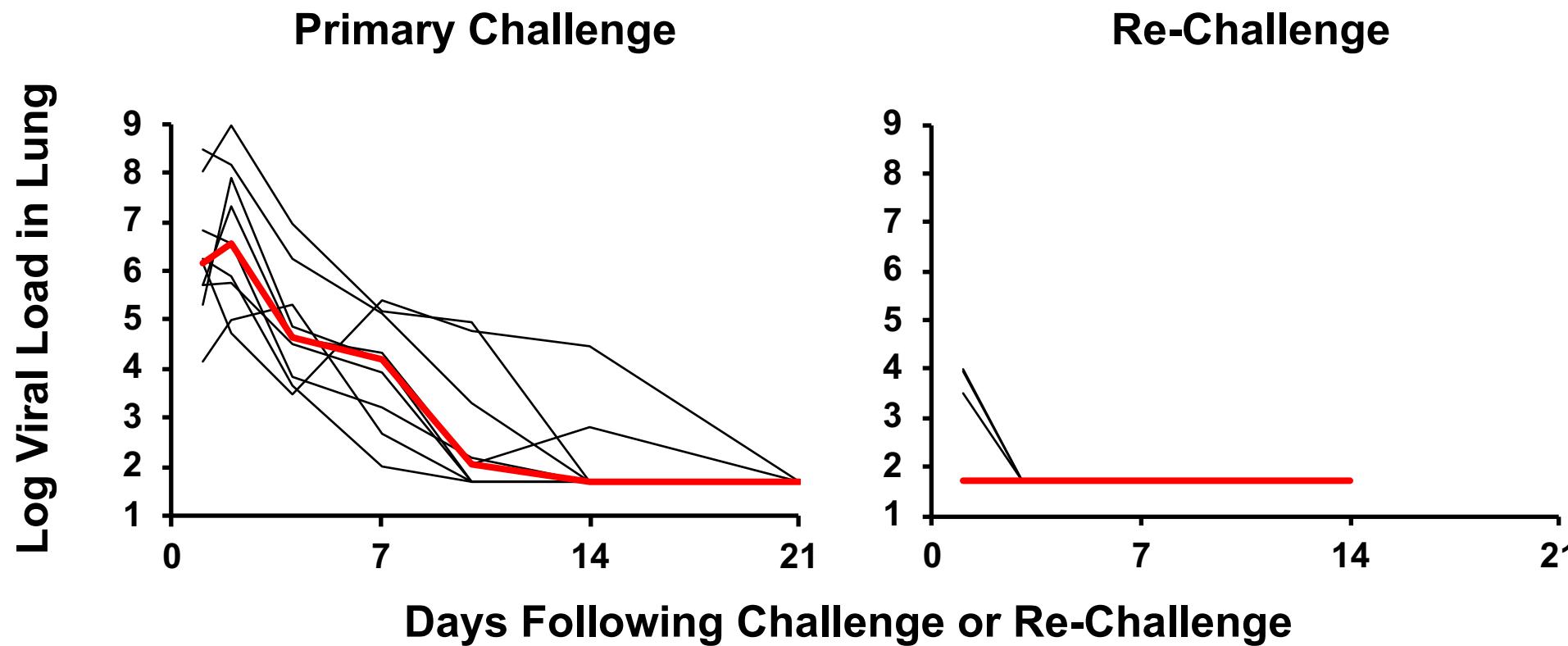
Abishek Chandrashekhar<sup>1\*</sup>, Jinyan Liu<sup>1\*</sup>, Amanda J. Martinot<sup>1,2\*</sup>, Katherine McMahan<sup>1\*</sup>, Noe B. Mercado<sup>1\*</sup>, Lauren Peter<sup>1\*</sup>, Lisa H. Tostanoski<sup>1\*</sup>, Jingyou Yu<sup>1\*</sup>, Zoltan Maliga<sup>3</sup>, Michael Nekorchuk<sup>4</sup>, Kathleen Busman-Sahay<sup>4</sup>, Margaret Terry<sup>4</sup>, Linda M. Wrijil<sup>2</sup>, Sarah Ducat<sup>2</sup>, David R. Martinez<sup>5</sup>, Caroline Atyeo<sup>3,6</sup>, Stephanie Fischinger<sup>6</sup>, John S. Burke<sup>6</sup>, Matthew D. Slein<sup>6</sup>, Laurent Pessaint<sup>7</sup>, Alex Van Ry<sup>7</sup>, Jack Greenhouse<sup>7</sup>, Tammy Taylor<sup>7</sup>, Kelvin Blade<sup>7</sup>, Anthony Cook<sup>7</sup>, Brad Finneyfrock<sup>7</sup>, Renita Brown<sup>7</sup>, Elyse Teow<sup>7</sup>, Jason Velasco<sup>7</sup>, Roland Zahn<sup>8</sup>, Frank Wegmann<sup>8</sup>, Peter Abbink<sup>1</sup>, Esther A. Bondzie<sup>1</sup>, Gabriel Dagotto<sup>1,3</sup>, Makda S. Gebre<sup>1,3</sup>, Xuan He<sup>1</sup>, Catherine Jacob-Dolan<sup>1,3</sup>, Nicole Kordana<sup>1</sup>, Zhenfeng Li<sup>1</sup>, Michelle A. Lifton<sup>1</sup>, Shant H. Mahrokhanian<sup>1</sup>, Lori F. Maxfield<sup>1</sup>, Ramya Nityanandam<sup>1</sup>, Joseph P. Nikolola<sup>1</sup>, Aaron G. Schmidt<sup>6,9</sup>, Andrew D. Miller<sup>10</sup>, Ralph S. Baric<sup>5</sup>, Galit Alter<sup>6,9</sup>, Peter K. Sorger<sup>3</sup>, Jacob D. Estes<sup>4</sup>, Hanne Andersen<sup>7</sup>, Mark G. Lewis<sup>7</sup>, Dan H. Barouch<sup>1,6,9†</sup>

<sup>1</sup>Center for Virology and Vaccine Research, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215, USA. <sup>2</sup>Tufts University Cummings School of Veterinary Medicine, North Grafton, MA 01536, USA. <sup>3</sup>Harvard Medical School, Boston, MA 02115, USA. <sup>4</sup>Oregon Health & Sciences University, Beaverton, OR 97006, USA. <sup>5</sup>University of North Carolina, Chapel Hill, NC 27599, USA. <sup>6</sup>Ragon Institute of MGH, MIT, and Harvard, Cambridge, MA 02139, USA. <sup>7</sup>Bioqual, Rockville, MD 20852, USA. <sup>8</sup>Janssen Vaccines & Prevention BV, Leiden, Netherlands. <sup>9</sup>Massachusetts Consortium on Pathogen Readiness, Boston, MA 02215, USA. <sup>10</sup>Cornell University College of Veterinary Medicine, Ithaca, NY 14853, USA.

\*These authors contributed equally to this work.

†Corresponding author. Email: dbarouch@bidmc.harvard.edu

# SARS-CoV-2 Infection Protects Against Re-Challenge in Rhesus Macaques



**Accelerated Article Preview****Correlates of protection against SARS-CoV-2  
in rhesus macaques**

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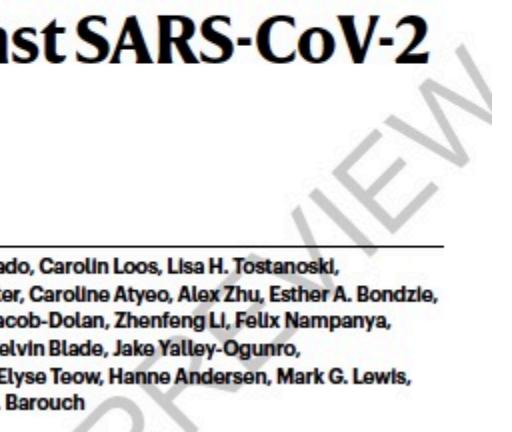
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Accepted: 25 November 2020

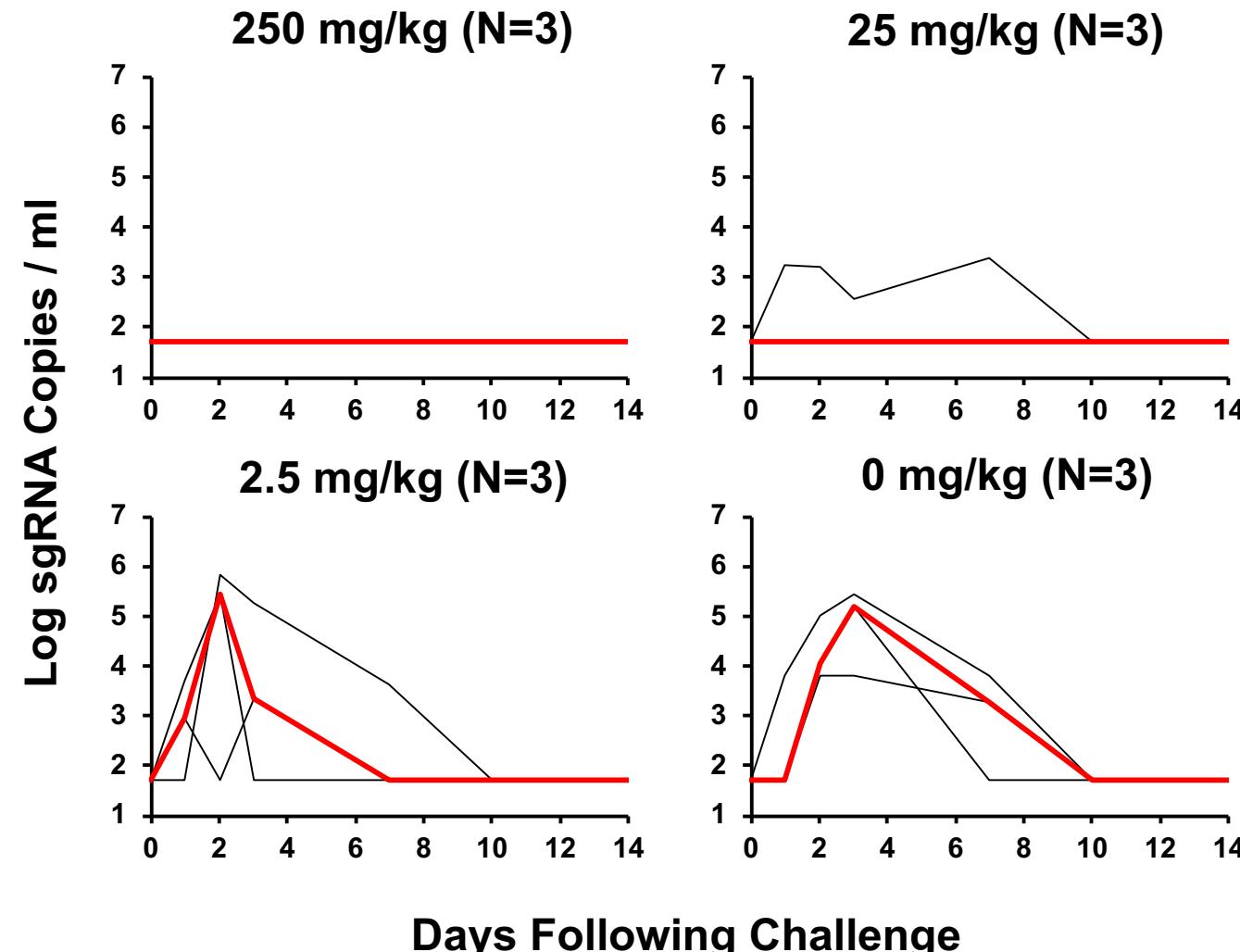
Accelerated Article Preview Published  
online 4 December 2020

Cite this article as: McMahan, K. et al.

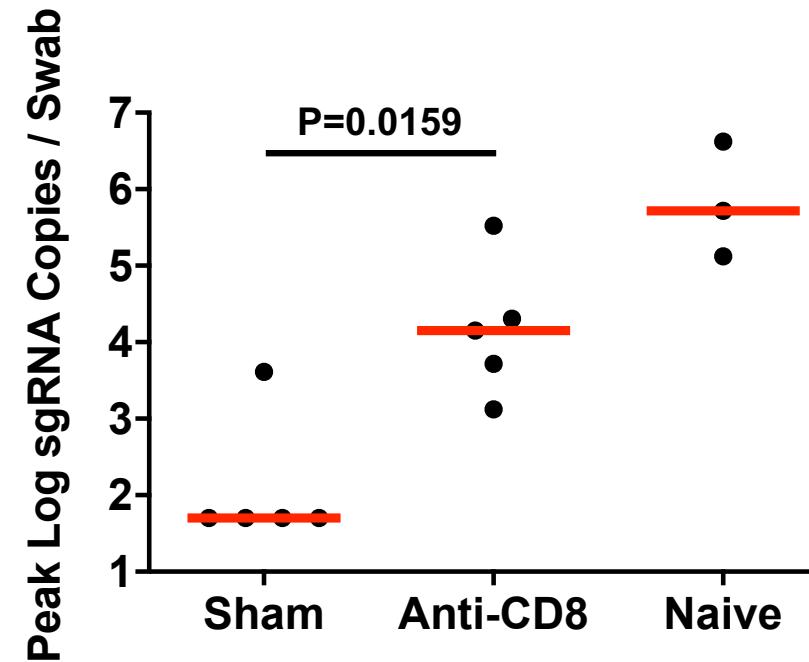
Katherine McMahan, Jingyou Yu, Noe B. Mercado, Carolin Loos, Lisa H. Tostanoski, Abishek Chandrashekhar, Jinyan Liu, Lauren Peter, Caroline Atyeo, Alex Zhu, Esther A. Bondzle, Gabriel Dagotto, Makda S. Gebre, Catherine Jacob-Dolan, Zhenfeng Li, Felix Nampanya, Shivanli Patel, Laurent Pessaint, Alex Van Ry, Kelvin Blade, Jake Valley-Ogunro, Mehtap Cabus, Renita Brown, Anthony Cook, Elyse Teow, Hanne Andersen, Mark G. Lewis, Douglas A. Lauffenburger, Galit Alter & Dan H. Barouch



# Dose-Dependent Adoptive Transfer of Purified IgG Protects Against SARS-CoV-2 in Rhesus Macaques



# CD8 Depletion Partially Abrogates Protection of Natural Immunity Against SARS-CoV-2 in Rhesus Macaques



# Immune Correlates of Protection

- Purified IgG protects macaques against SARS-CoV-2 challenge in a dose-dependent fashion
- CD8 depletion reduced protection against re-challenge in convalescent macaques with waning Ab titers
- These data suggest that Abs alone can protect, but cellular immune responses contribute when Ab titers are borderline or subprotective

**Accelerated Article Preview**

# Single-shot Ad26 vaccine protects against SARS-CoV-2 in rhesus macaques

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Received: 20 June 2020

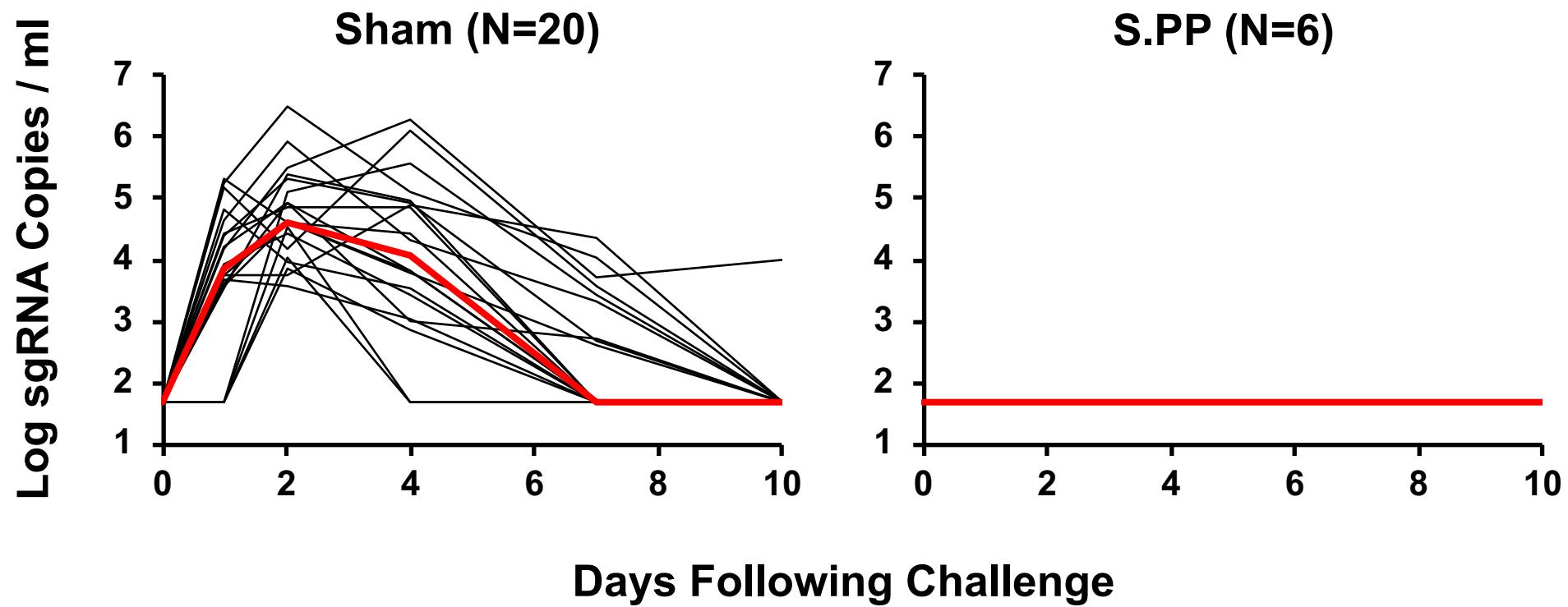
Accepted: 24 July 2020

Accelerated Article Preview Published online 30 July 2020

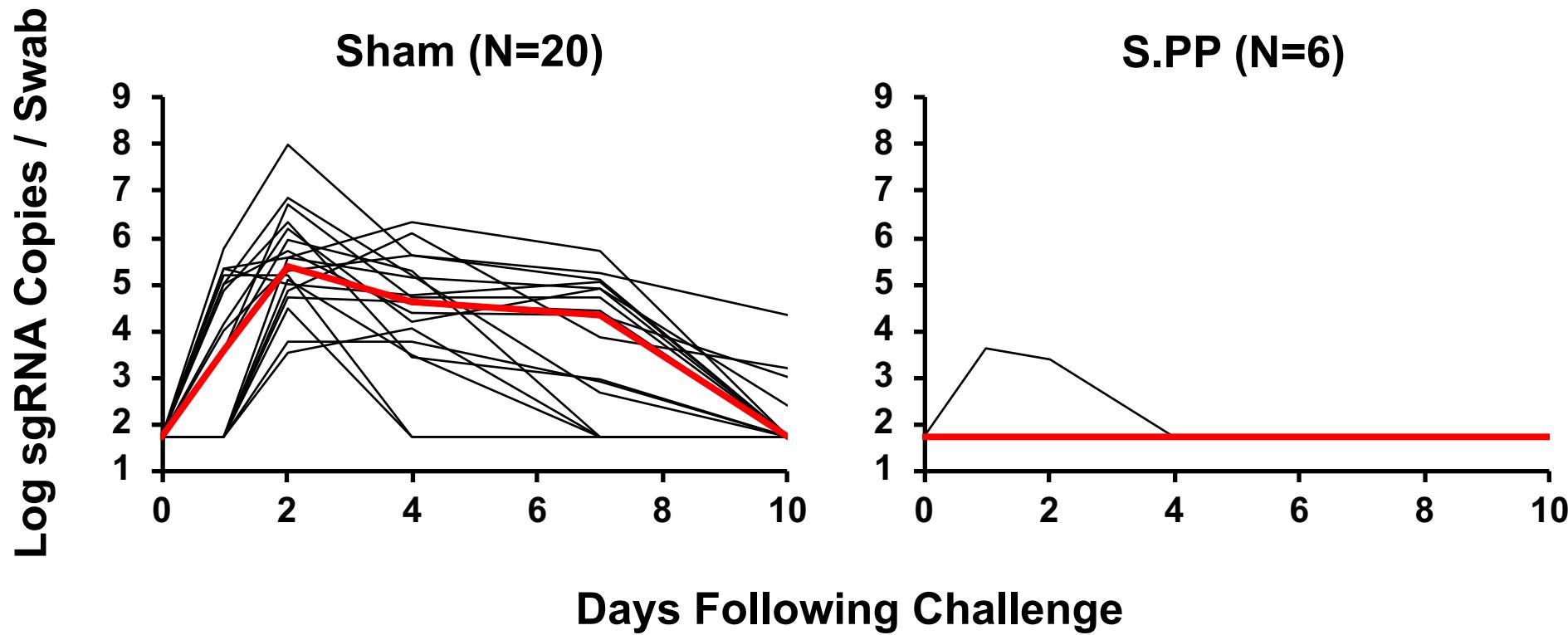
Cite this article as: Mercado, N. B. et al. Single-shot Ad26 vaccine protects against SARS-CoV-2 in rhesus macaques. *Nature* https://doi.org/10.1038/s41586-020-2607-z (2020).

Noe B. Mercado, Roland Zahn, Frank Wegmann, Carolin Loos, Abishek Chandrashekar, Jingyou Yu, Jinyan Liu, Lauren Peter, Katherine McMahan, Lisa H. Tostanoski, Xuan He, David R. Martinez, Lucy Rutten, Rinke Bos, Danielle van Manen, Jort Vellinga, Jerome Custers, Johannes P. Langendijk, Ted Kwaks, Mark J. G. Bakkers, David Zuidgeest, Sietske K. Rosendahl Huber, Caroline Atyeo, Stephanie Fischinger, John S. Burke, Jared Feldman, Blake M. Hauser, Timothy M. Caradonna, Esther A. Bondzie, Gabriel Dagotto, Makda S. Gebre, Emily Hoffman, Catherine Jacob-Dolan, Marinela Kirillova, Zhenfeng Li, Zijin Lin, Shant H. Mahrokhian, Lori F. Maxfield, Felix Nampanya, Ramya Nityanandam, Joseph P. Nkolola, Shivani Patel, John D. Ventura, Kaylee Verrington, Huahua Wan, Laurent Pessaint, Alex Van Ry, Kelvin Blade, Amanda Strasbaugh, Mehtap Cabus, Renita Brown, Anthony Cook, Serge Zouan-changadou, Elyse Teow, Hanne Anderson, Mark G. Lewis, Yongfei Cai, Bing Chen, Aaron G. Schmidt, R. Keith Reeves, Ralph S. Baric, Douglas A. Lauffenburger, Galit Alter, Paul Stoffels, Mathai Mammen, Johan Van Hoof, Hanneke Schuitmaker & Dan H. Barouch

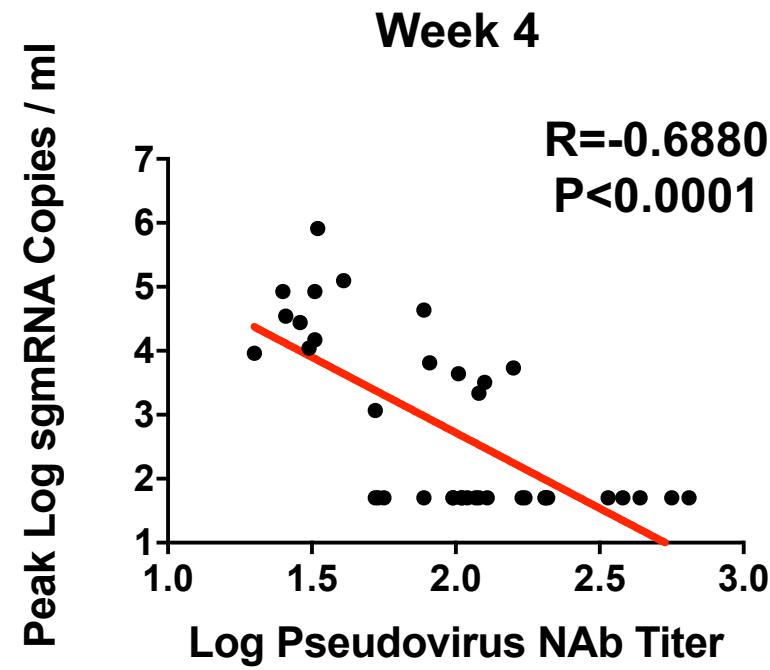
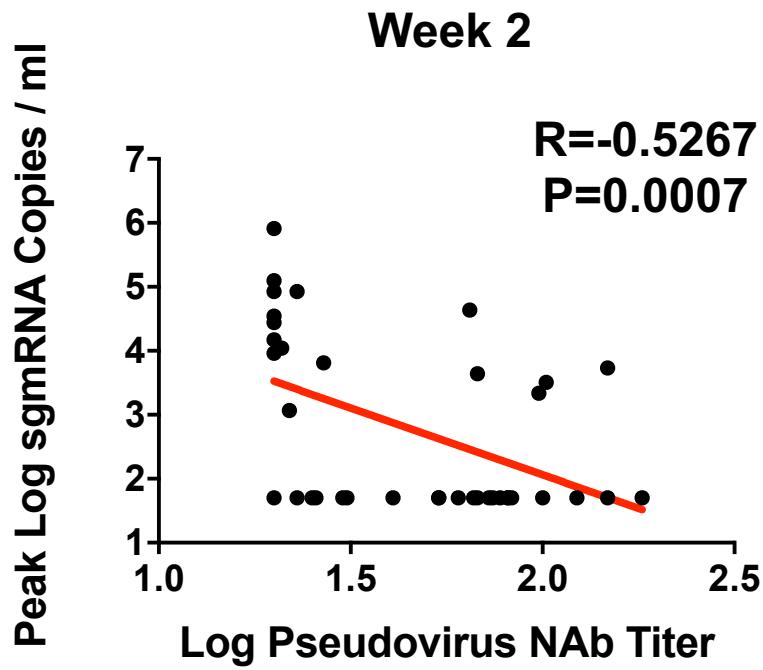
# Viral Loads (BAL)



# Viral Loads (Nasal Swab)



# BAL Immune Correlates: Pseudovirus NAb



ORIGINAL ARTICLE

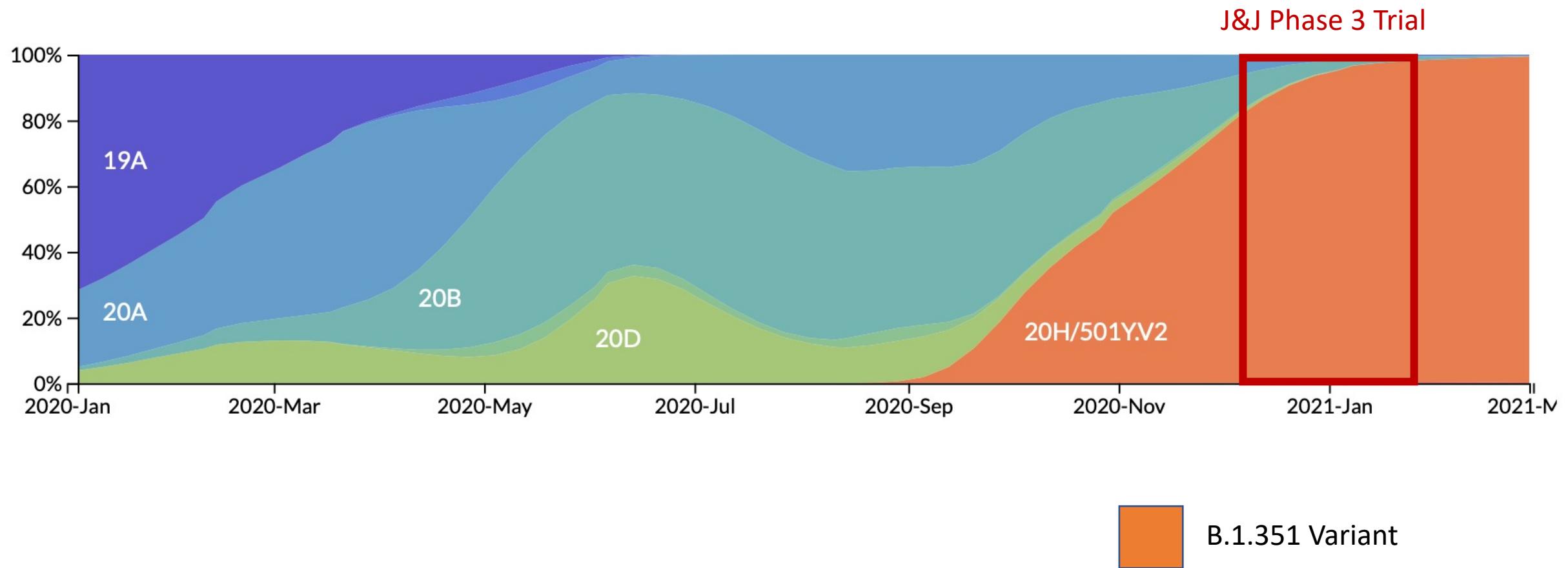
# Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19

J. Sadoff, G. Gray, A. Vandebosch, V. Cárdenas, G. Shukarev, B. Grinsztejn,  
P.A. Goepfert, C. Truyers, H. Fennema, B. Spiessens, K. Offergeld, G. Scheper,  
K.L. Taylor, M.L. Robb, J. Treanor, D.H. Barouch, J. Stoddard, M.F. Ryser,  
M.A. Marovich, K.M. Neuzil, L. Corey, N. Cauwenberghs, T. Tanner, K. Hardt,  
J. Ruiz-Guiñazú, M. Le Gars, H. Schuitemaker, J. Van Hoof, F. Struyf,  
and M. Douoguih, for the ENSEMBLE Study Group\*

# **COV3001: Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial of Single-Shot Ad26.COV2.S**

- Enrollment Sept-Dec 2020: 44,000
- 1:1 vaccine:placebo randomization
- Single-shot vaccine ( $5 \times 10^{10}$  vp)
- United States, South Africa, Argentina, Brazil, Chile, Colombia, Mexico, Peru

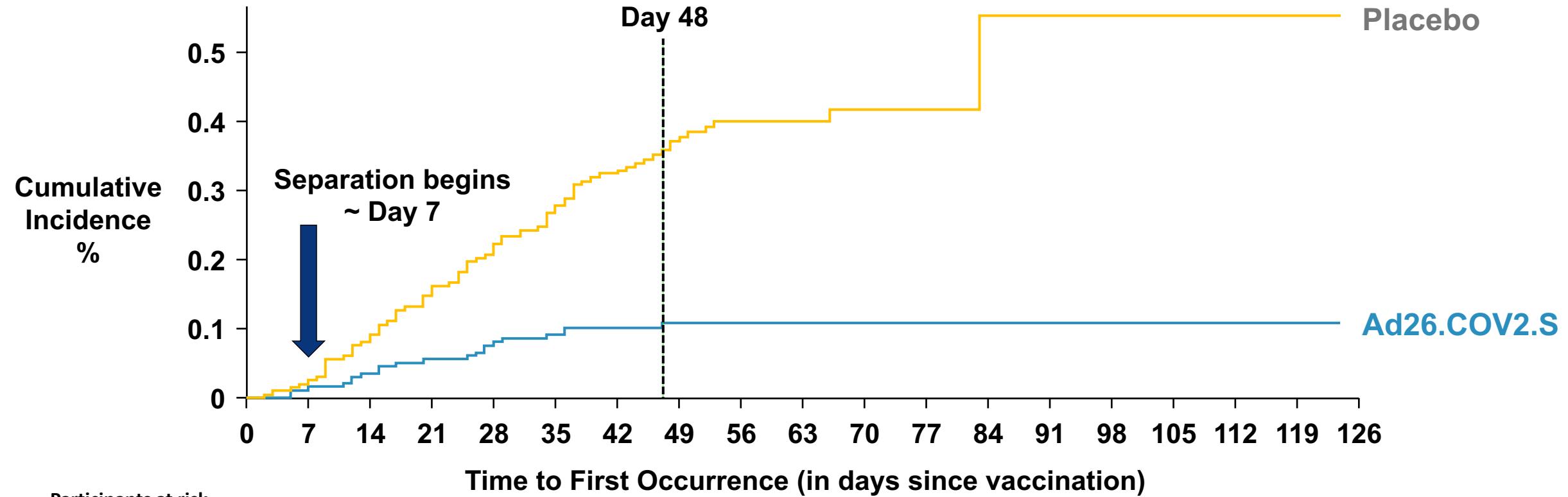
# Emergence of Resistant B.1.351 Variant in South Africa



# COV3001: Interim Results (January 29, 2021)

- Study conducted in multiple countries at peak surge including South Africa with 95% B.1.351 resistant variant
- Protection against any symptomatic infection: 72% (US), 68% (Latin America), 64% (South Africa)
- Protection against severe disease: 85% (global)
- Protection against hospitalization/death: 100% (global)

# Time to First Occurrence of Severe/Critical COVID-19 Demonstrates Early Onset of Protection



## Participants at risk

Ad26.COV2.S	19744	19741	19734	19725	19718	19705	18685	15043	11046	7919	4039	1481	720	490	490	489	146	31	0
Placebo	19822	19817	19799	19779	19760	19725	18682	15088	11069	7939	3995	1485	732	500	497	495	137	29	0

## Number of cases

Ad26.COV2.S	0	3	7	11	16	18	20	21	21	21	21	21	21	21	21	21	21	21	21
Placebo	0	5	18	32	44	55	65	73	76	76	77	77	78	78	78	78	78	78	78

FDA NEWS RELEASE

# FDA Issues Emergency Use Authorization for Third COVID-19 Vaccine

*Action Advances Fight Against COVID-19, Follows Comprehensive Evaluation of Available Safety, Effectiveness and Manufacturing Quality Information by FDA Career Scientists, Input from External Experts*

**For Immediate Release:**

February 27, 2021

Today, the U.S. Food and Drug Administration issued an emergency use authorization (EUA) for the third vaccine for the prevention of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The EUA allows the Janssen COVID-19 Vaccine to be distributed in the U.S for use in individuals 18 years of age and older.

# Joint CDC and FDA Statement on Johnson & Johnson COVID-19 Vaccine

The following statement is attributed to Dr. Anne Schuchat, Principal Deputy Director of the CDC and Dr. Peter Marks, director of the FDA's Center for Biologics Evaluation and Research

## Media Statement

For Immediate Release: Tuesday, April 13, 2021

Contact: [Media Relations](#)  
(404) 639-3286

As of April 12, more than 6.8 million doses of the Johnson & Johnson (Janssen) vaccine have been administered in the U.S. CDC and FDA are reviewing data involving six reported U.S. cases of a rare and severe type of blood clot in individuals after receiving the J&J vaccine. In these cases, a type of blood clot called cerebral venous sinus thrombosis (CVST) was seen in combination with low levels of blood platelets (thrombocytopenia). All six cases occurred among women between the ages of 18 and 48, and symptoms occurred 6 to 13 days after vaccination. Treatment of this specific type of blood clot is different from the treatment that might typically be administered. Usually, an anticoagulant drug called heparin is used to treat blood clots. In this setting, administration of heparin may be dangerous, and alternative treatments need to be given.

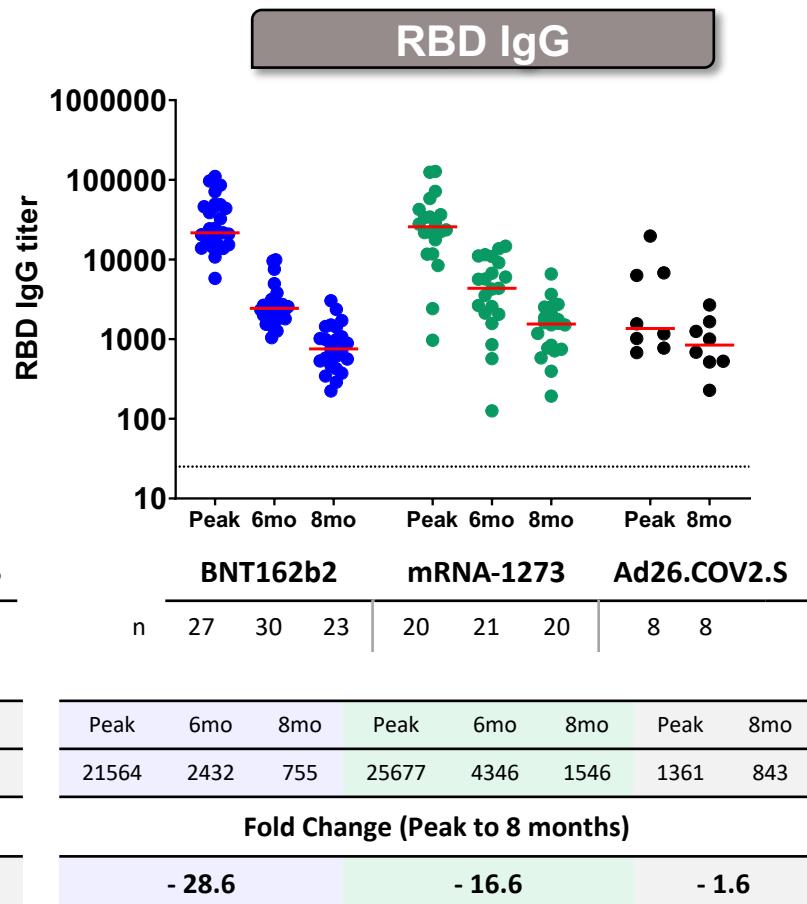
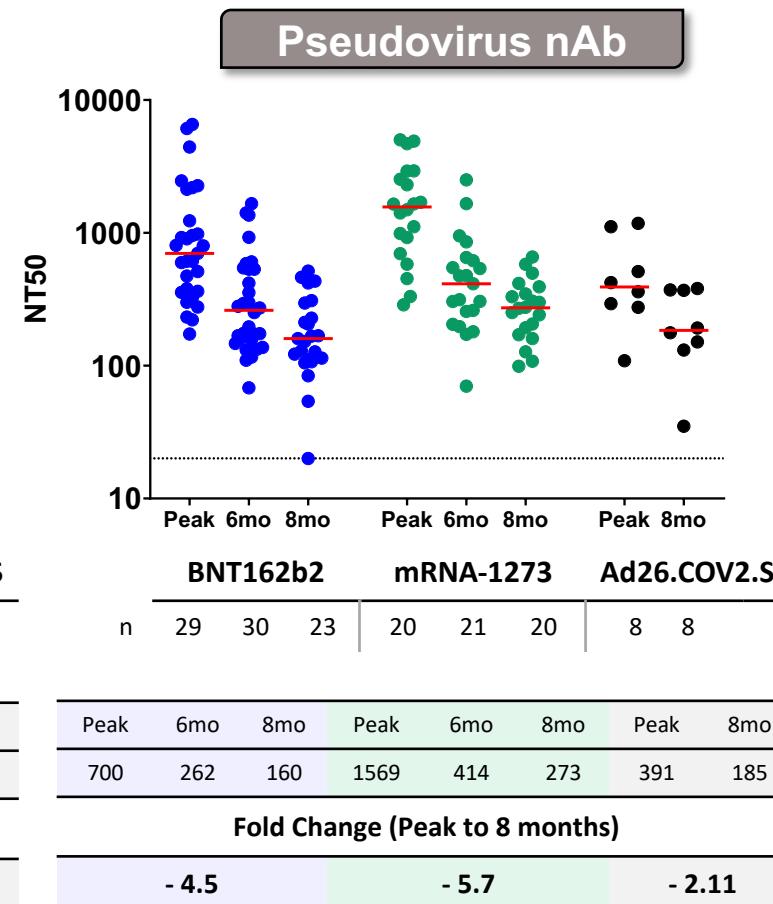
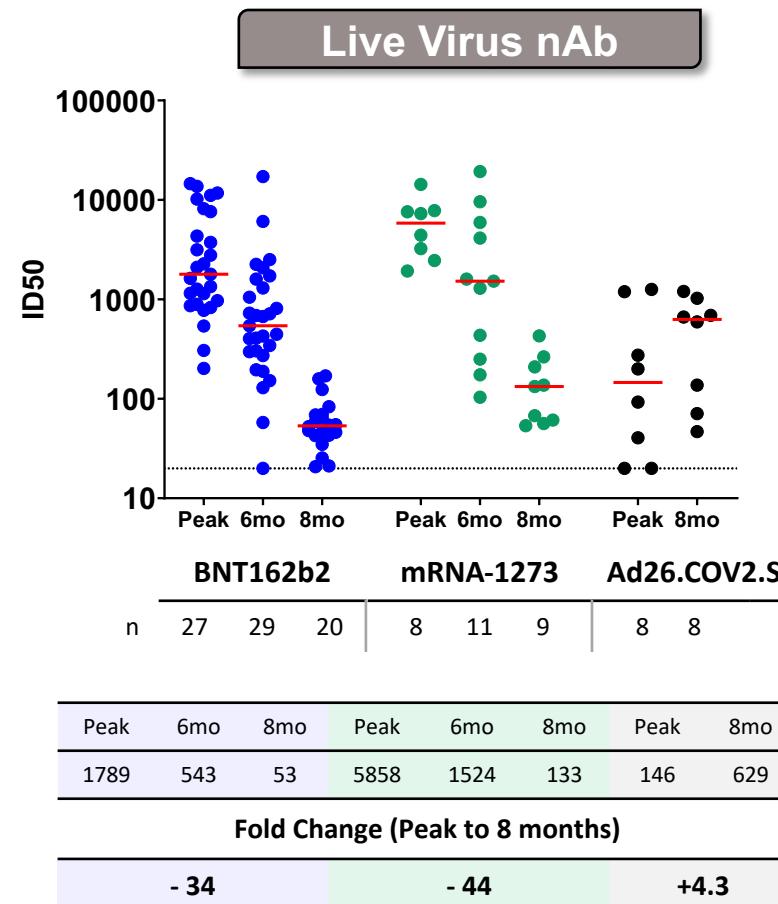
CDC will convene a meeting of the Advisory Committee on Immunization Practices (ACIP) on Wednesday to further review these cases and assess their potential significance. FDA will review that analysis as it also investigates these cases. Until that process is complete, we are recommending a pause in the use of this vaccine out of an abundance of caution. This is important, in part, to ensure that the health care provider community is aware of the potential for these adverse events and can plan for proper recognition and management due to the unique treatment required with this type of blood clot.

*The NEW ENGLAND JOURNAL of MEDICINE*

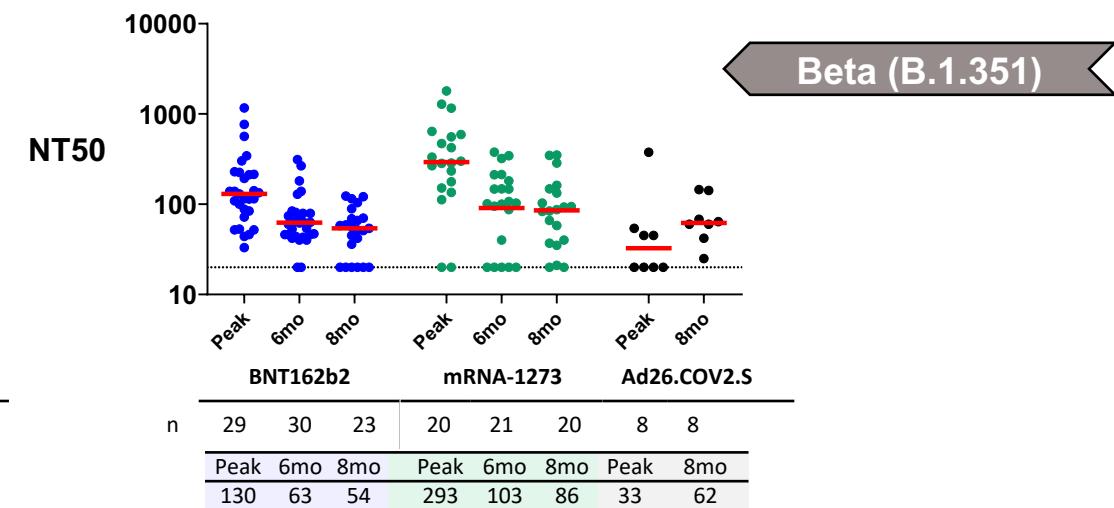
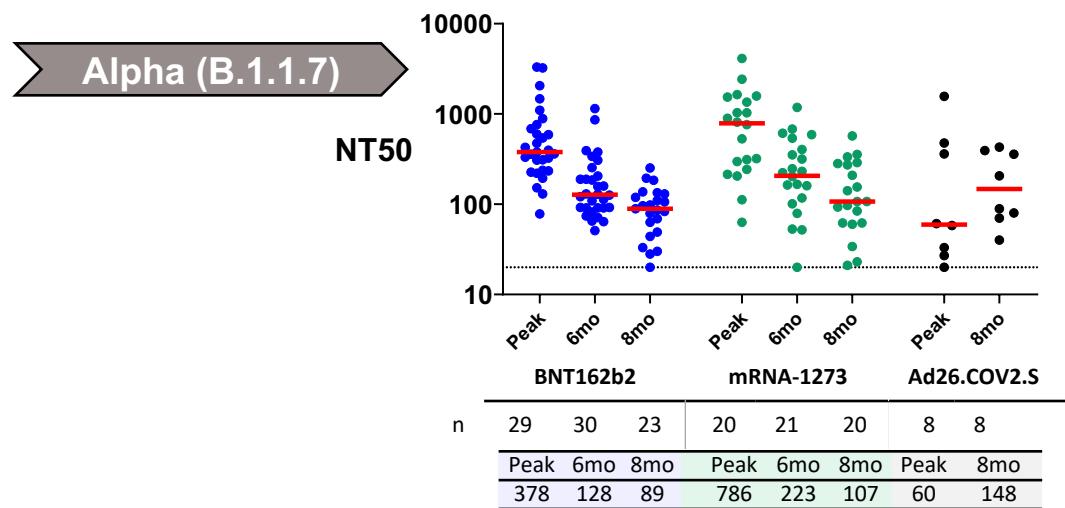
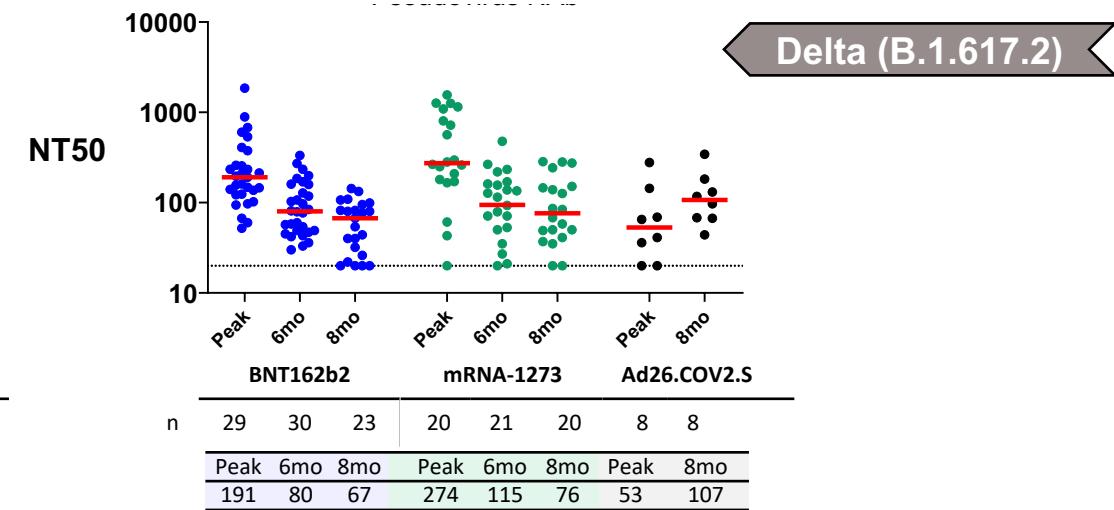
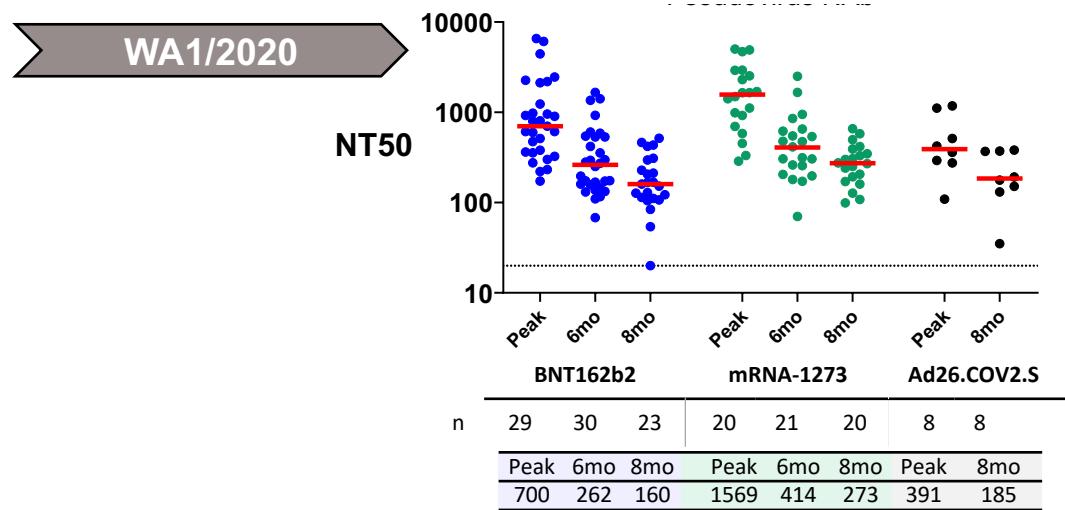
CORRESPONDENCE

**Differential Kinetics of Immune Responses  
Elicited by Covid-19 Vaccines**

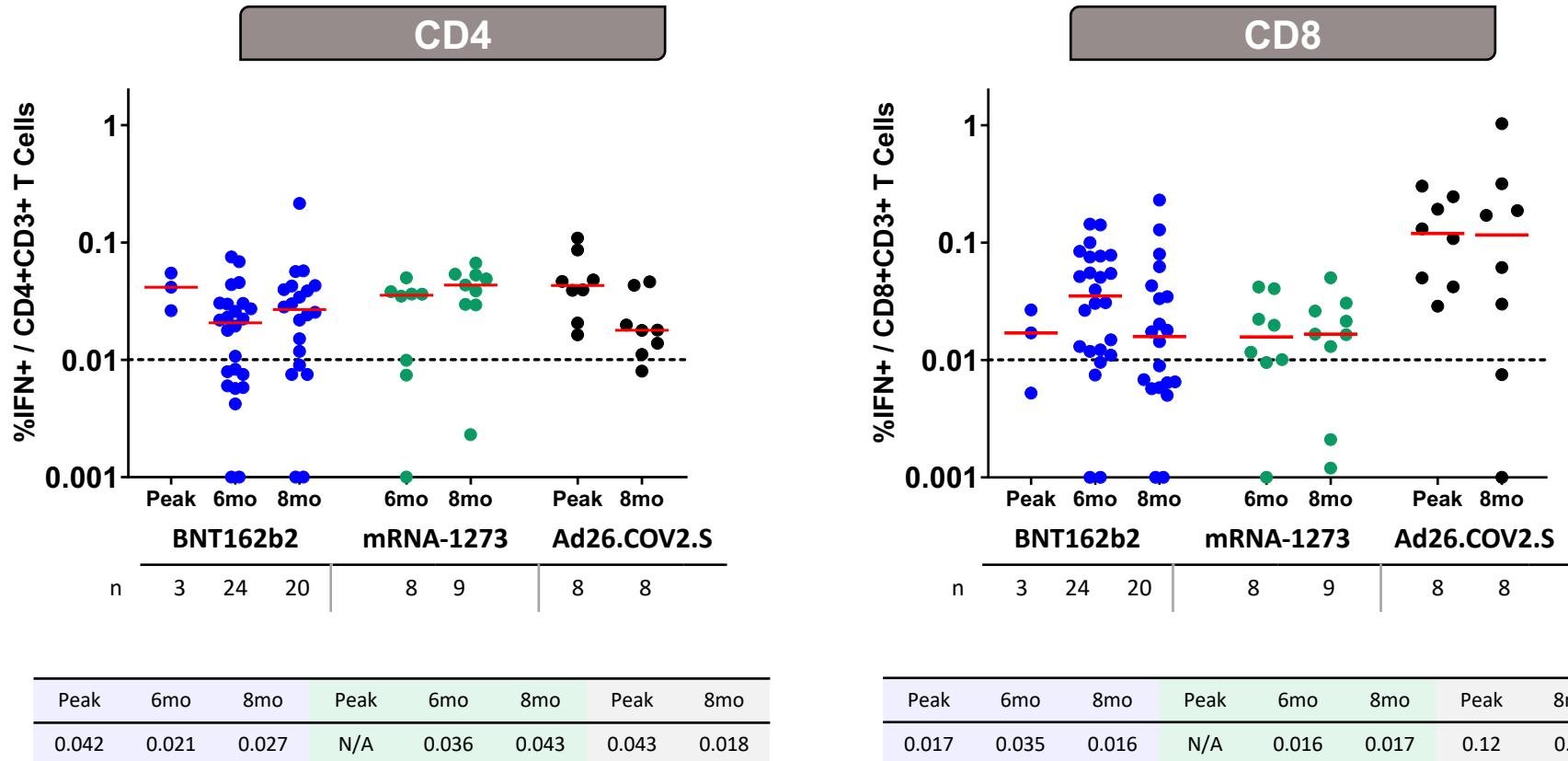
# Ad26.COV2.S Induces Durable Neutralizing and Binding Antibody Responses



# Ad26.COV2.S Induces Durable Neutralizing Antibody Responses Against SARS-CoV-2 Variants



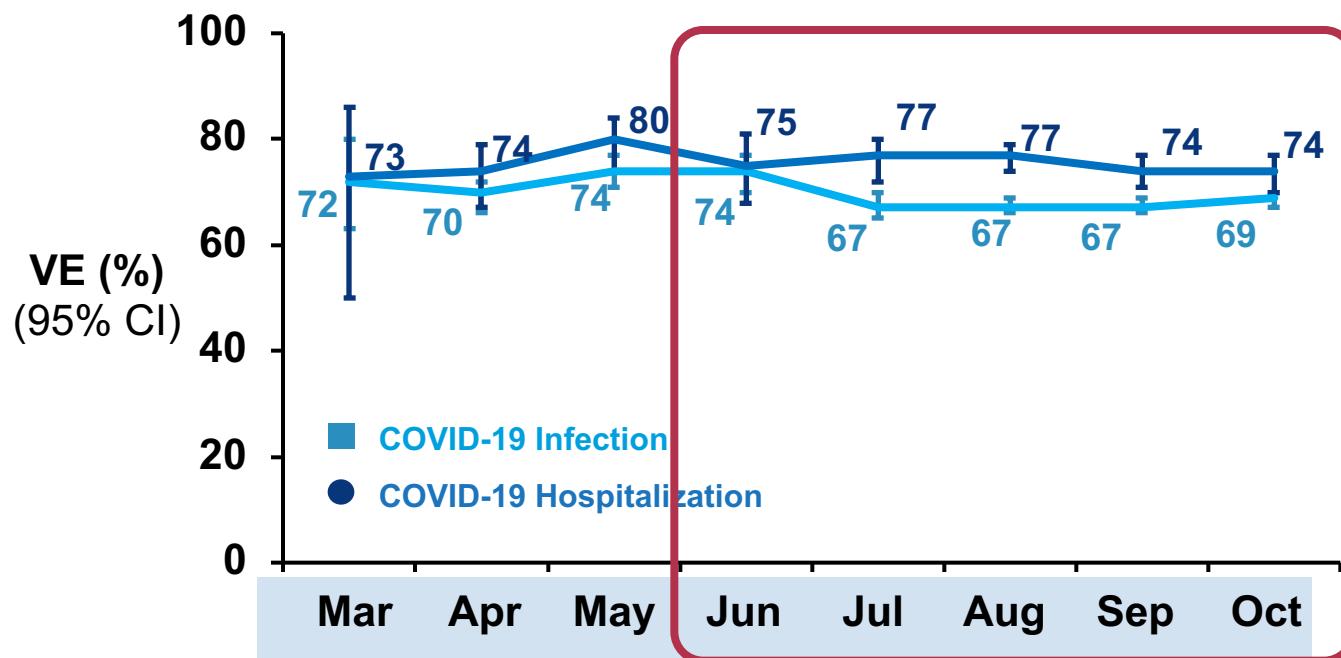
# Ad26.COV2.S Induces Durable CD4+ and CD8+ T Cell Responses



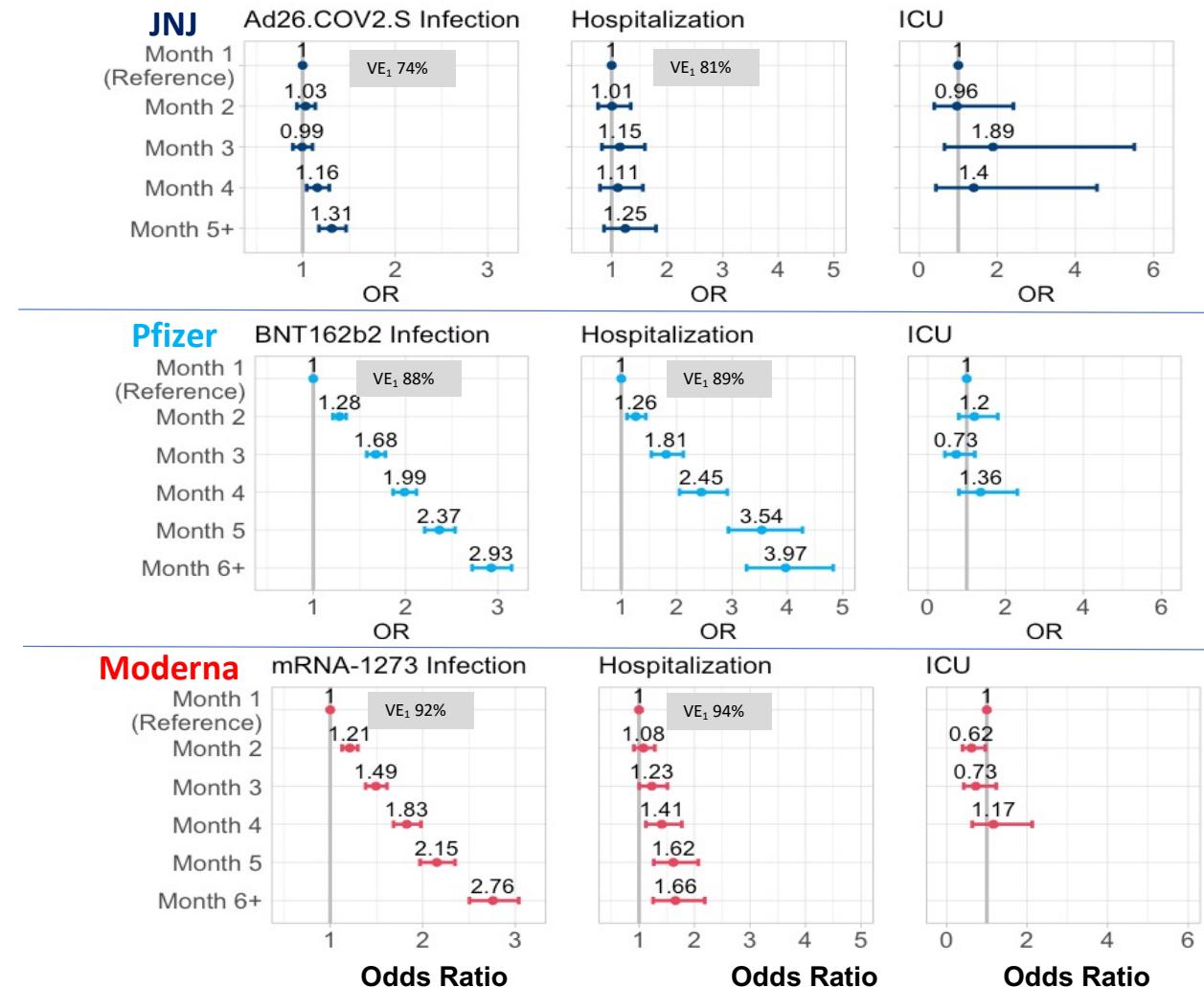
# **Differential Kinetics of Immune Responses with BNT162b2, mRNA-1273, and Ad26.COV2.S Vaccines**

- mRNA vaccines induce high initial antibody titers, but these responses decline sharply by 6 months and even further by 8 months
- Ad26.COV2.S induces lower initial antibody titers, but these responses show minimal decline for 8 months
- By 8 months, antibody responses similar for mRNA and Ad26.COV2.S
- Ad26.COV2.S induces durable CD4+ and CD8+ T cell responses

# Real World Efficacy of Single-Shot Ad26.COV2.S in the United States

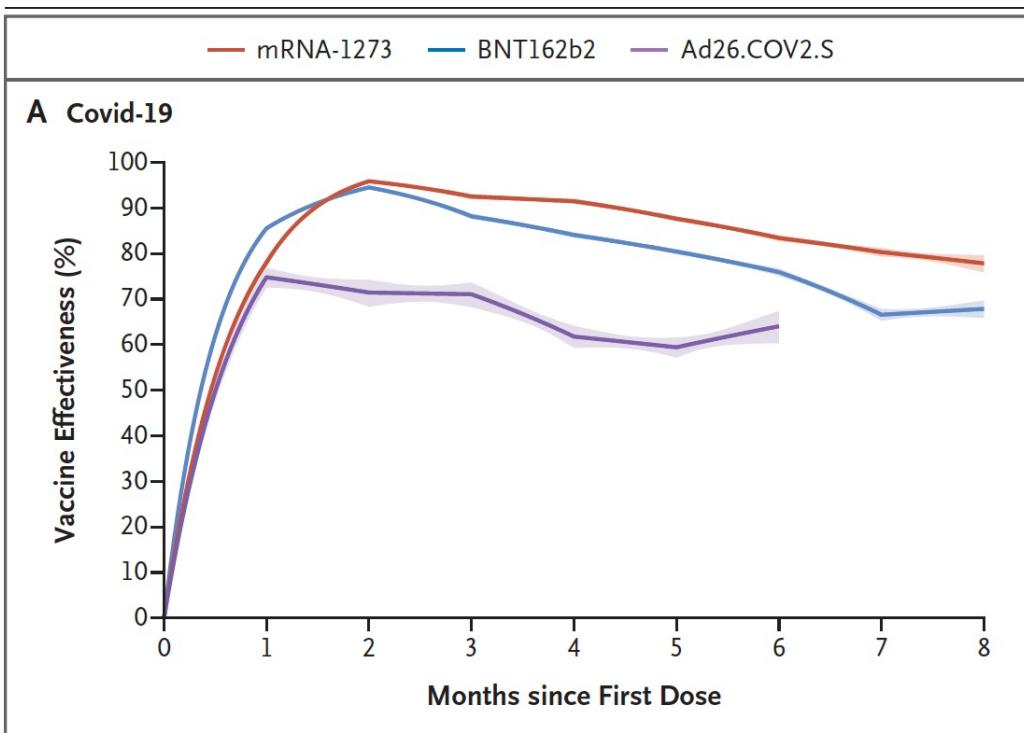


# Durability of Vaccine Efficacy in 17 Million Vaccine Recipients in the United States



# Durability of Vaccine Efficacy in NC and NY

## North Carolina



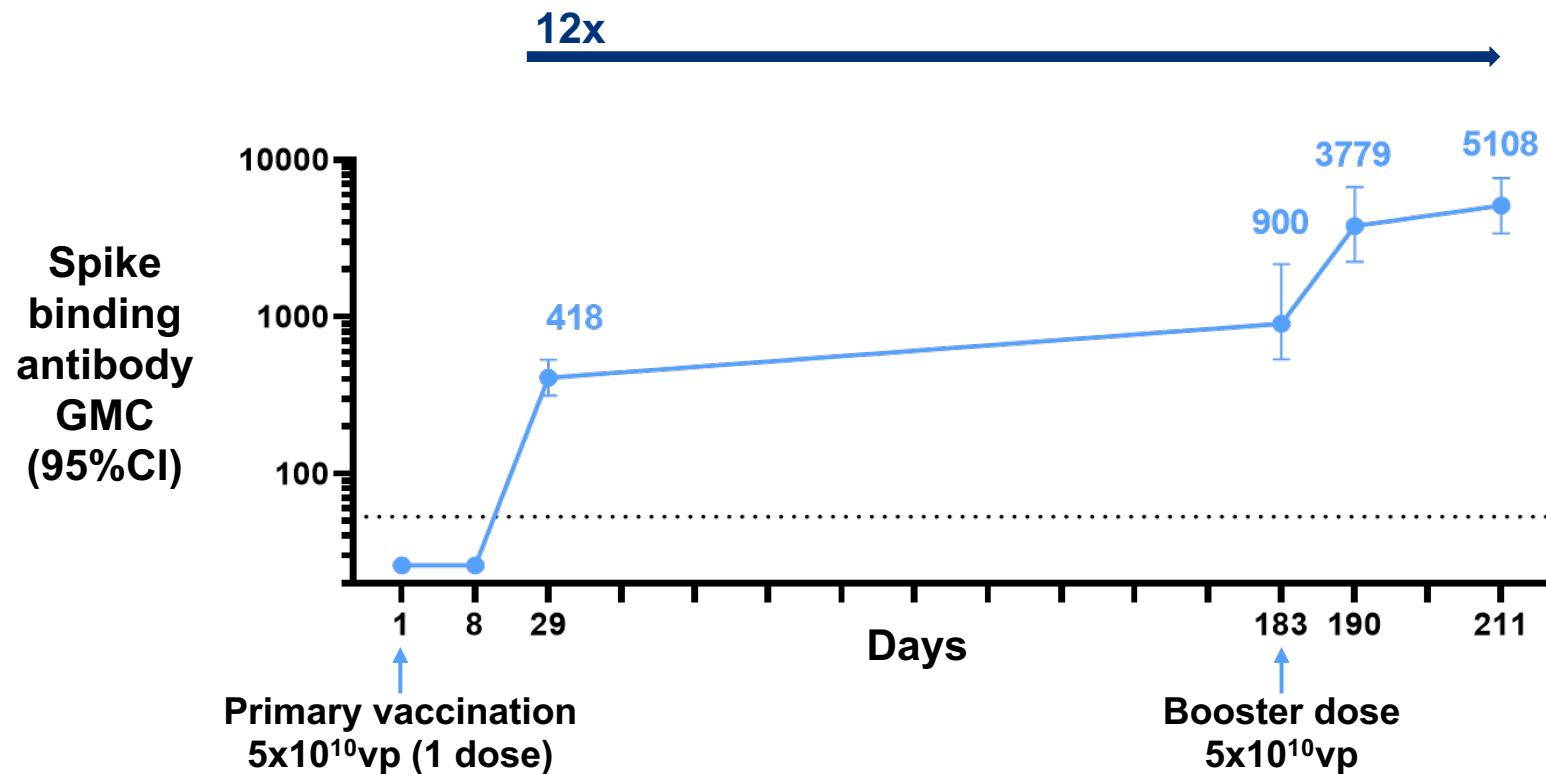
## New York

Cohort	Vaccine Effectiveness (95% CI)		
	Week of May 1, 2021	Week of July 10, 2021	Week of August 28, 2021
<b>Age 50–64 yr</b>			
BNT162b2†	95.0 (94.0 to 96.0)	69.2 (63.8 to 74.6)	74.7 (72.8 to 76.6)
January–February	88.7 (84.9 to 92.4)	67.2 (55.0 to 79.3)	71.1 (66.6 to 75.6)
March	93.0 (90.1 to 95.9)	69.2 (57.6 to 80.8)	72.3 (68.0 to 76.6)
April	97.0 (96.0 to 97.9)	69.7 (63.6 to 75.9)	76.1 (74.0 to 78.2)
mRNA-1273†	97.3 (96.4 to 98.1)	84.7 (80.7 to 88.7)	81.8 (80.0 to 83.5)
January–February	95.9 (93.7 to 98.0)	76.0 (66.3 to 85.7)	74.7 (70.8 to 78.6)
March	96.9 (94.9 to 98.9)	82.2 (73.0 to 91.4)	76.5 (72.4 to 80.7)
April	98.0 (97.1 to 99.0)	89.4 (85.1 to 93.7)	86.8 (84.9 to 88.6)
Ad26.COV2.S†	86.1 (82.5 to 89.6)	70.6 (60.7 to 80.5)	74.7 (71.2 to 78.3)
March	87.8 (81.8 to 93.8)	73.4 (56.8 to 90.1)	68.8 (61.7 to 75.9)
April	85.3 (81.0 to 89.7)	69.4 (57.5 to 81.3)	77.3 (73.3 to 81.3)

# **COV3009: Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial of Two-Shot Ad26.COV2.S**

- Target enrollment: 30,000
- 1:1 vaccine:placebo randomization
- Two-shot vaccine regimen ( $5 \times 10^{10}$  vp; week 0, 8)
- United States, United Kingdom, Belgium, France, Germany, Spain, Columbia, South Africa, Philippines

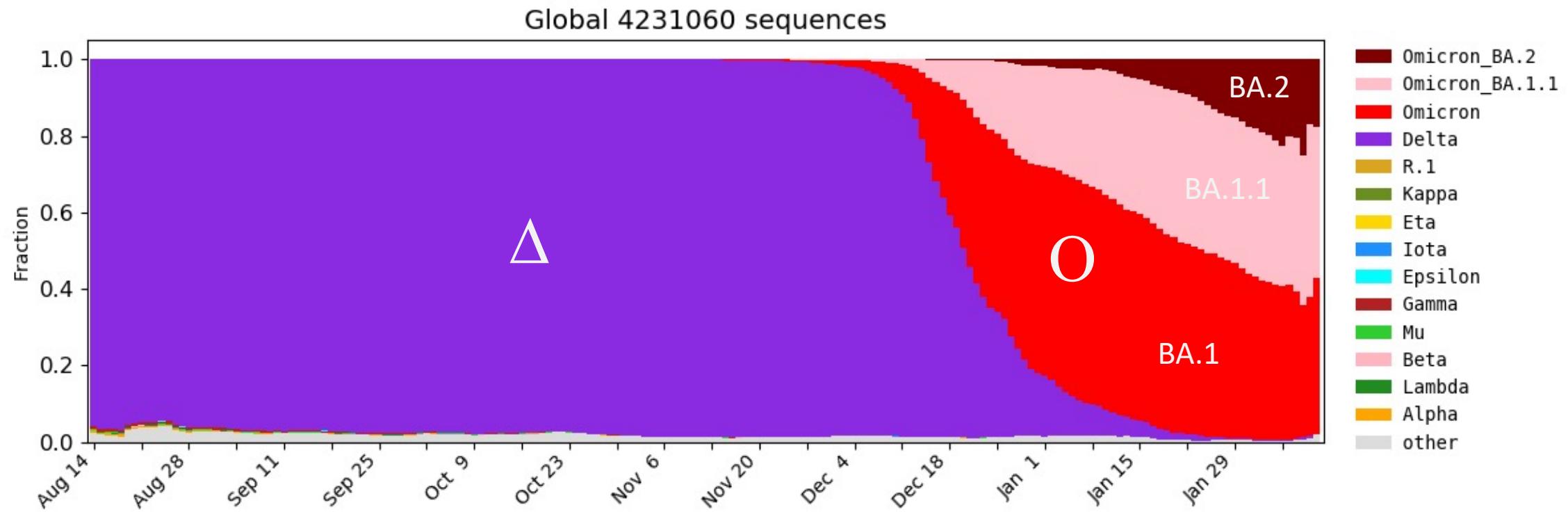
# Immunogenicity of 2-Dose Ad26.COV2.S Vaccine



# COV3009: Interim Results (September 21, 2021)

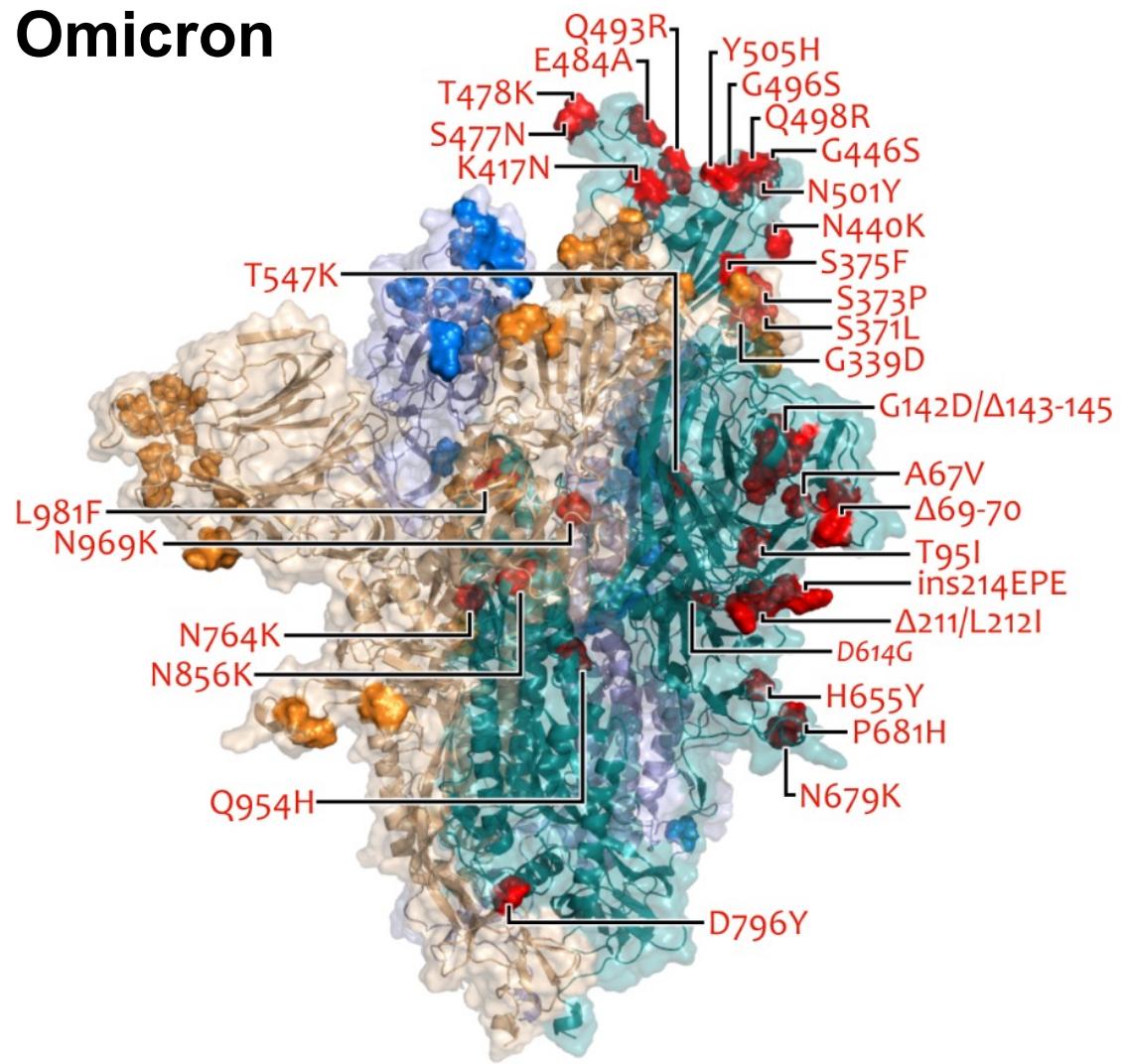
- Efficacy of two-dose Ad26.COV2.S vaccine:
- **94% protection against any symptomatic disease in the US**
- **75% protection against any symptomatic disease globally**
- **100% protection against severe disease globally**

# Transition from SARS-CoV-2 Delta to Omicron

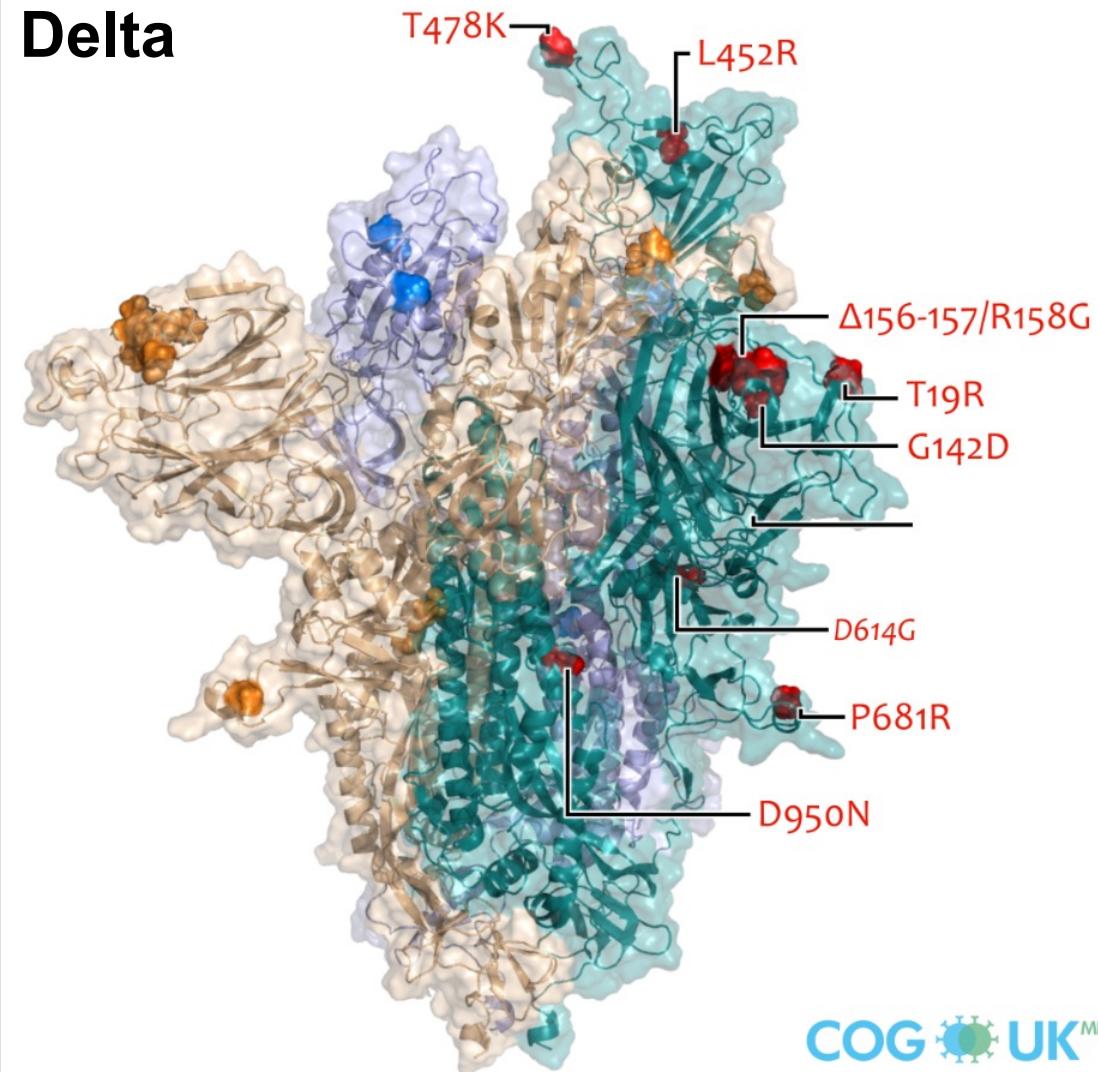


# Heavily Mutated Omicron Spike

Omicron

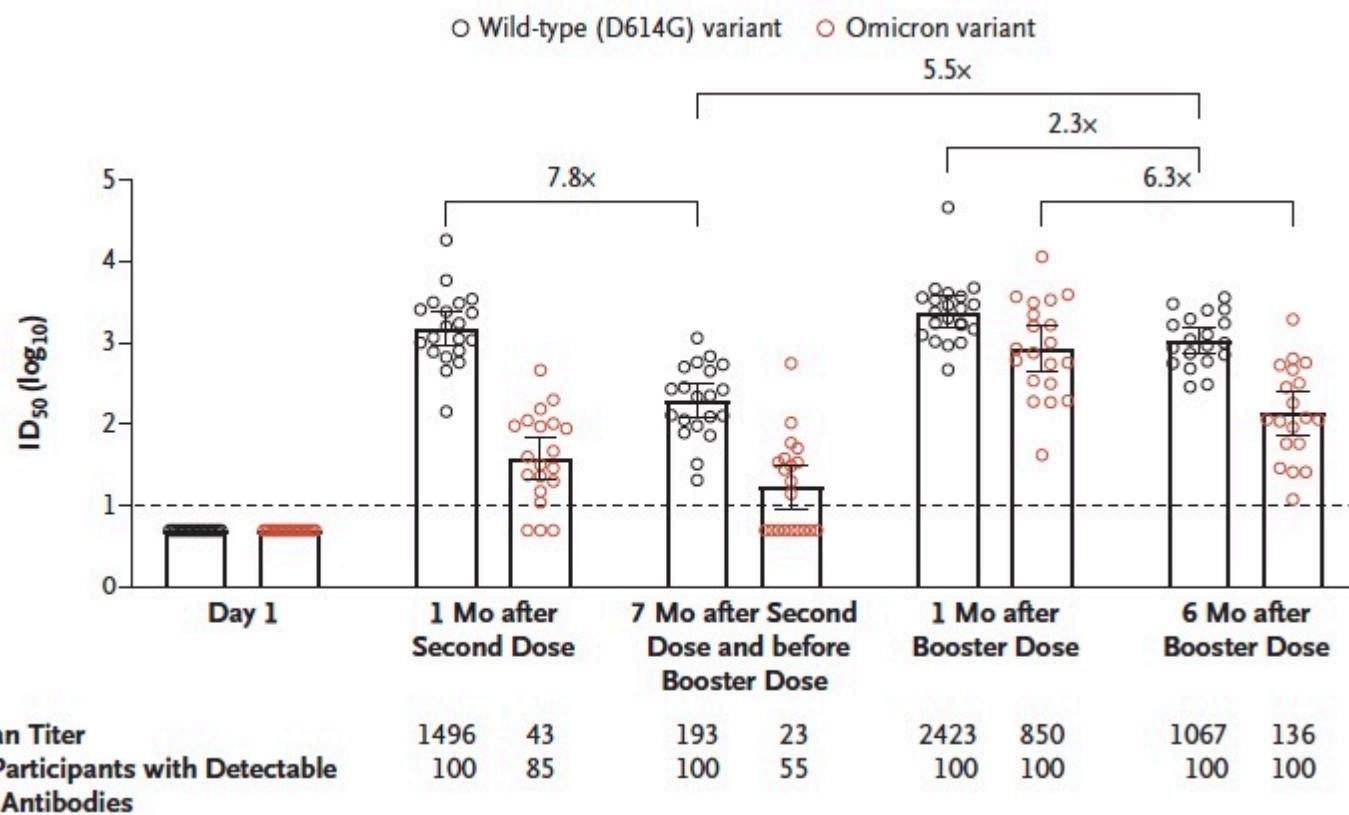


Delta



COG UK<sup>ME</sup>

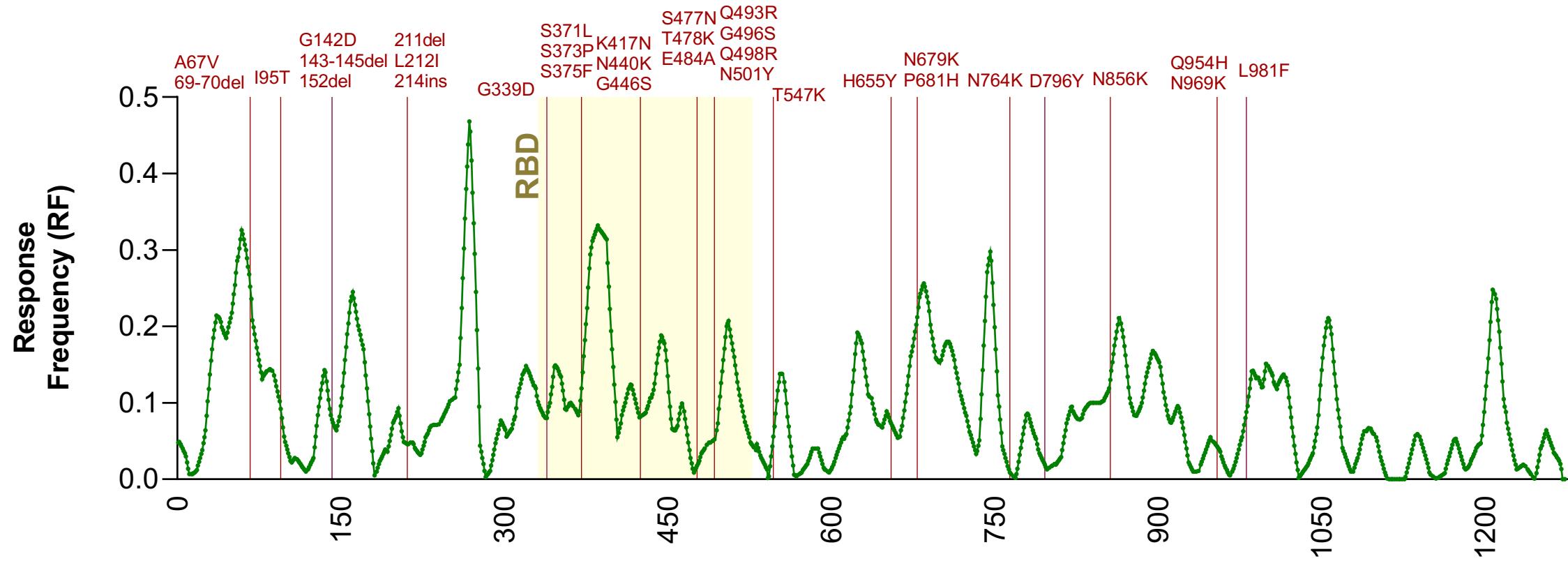
# Omicron NAbs Minimal After Initial mRNA Vaccination, Increase with Boost, and Decline 6.3-Fold by 6 Months



# Vaccine Protection Against Omicron

- Vaccine protection against Omicron infection is modest, even with 3<sup>rd</sup> and 4<sup>th</sup> boosts, and wanes rapidly in early data from UK and Israel
  - In contrast, vaccine protection against Omicron hospitalization in South Africa remains robust, in absence of high titers of neutralizing antibodies
    - 2-shot Pfizer efficacy: 70%
    - 2-shot J&J efficacy: 85%
- These data suggest that immune mechanisms other than neutralizing antibodies may be critical for protection against severe disease
- J&J vaccine well suited for the developing world: high efficacy, durability, low cost, stability, no frozen cold chain, use as either 1- or 2-shot vaccine

# Most CD8 T Cell Epitopes are Unaffected by Omicron



Grifoni et al. 2021 Cell Host & Microbe  
Courtesy Alba Grifoni and Alex Sette

**Accelerated Article Preview**

# Vaccines Elicit Highly Conserved Cellular Immunity to SARS-CoV-2 Omicron

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Received: 28 December 2021

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Accelerated Article Preview

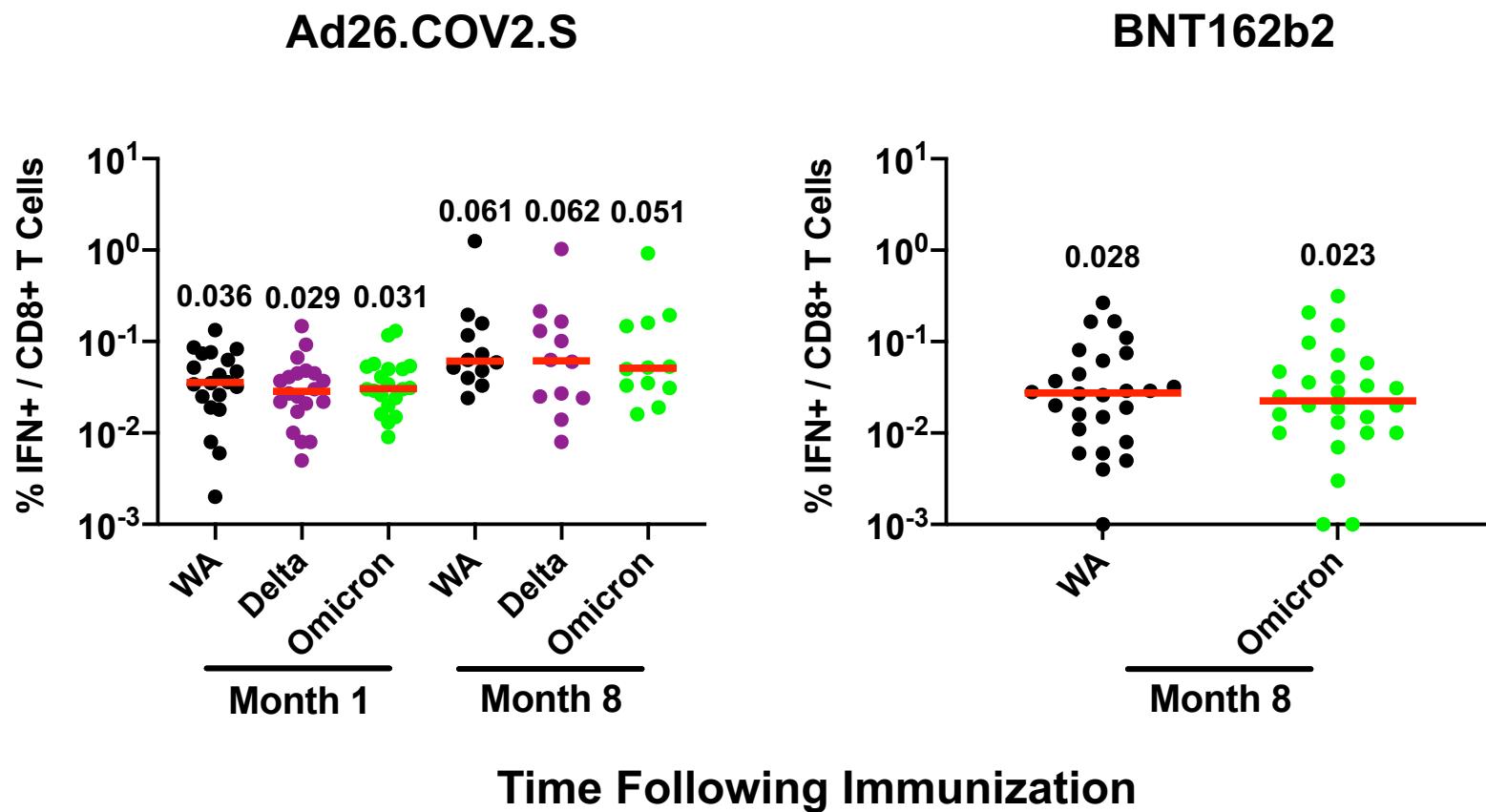
Published online: 31 January 2022

Jinyan Liu, Abishek Chandrashekhar, Daniel Sellers, Julia Barrett, Catherine Jacob-Dolan, Michelle Lifton, Katherine McMahan, Michaela Sciacca, Haley VanWyk, Cindy Wu, Jingyou Yu, Ai-ris Y. Collier & Dan H. Barouch

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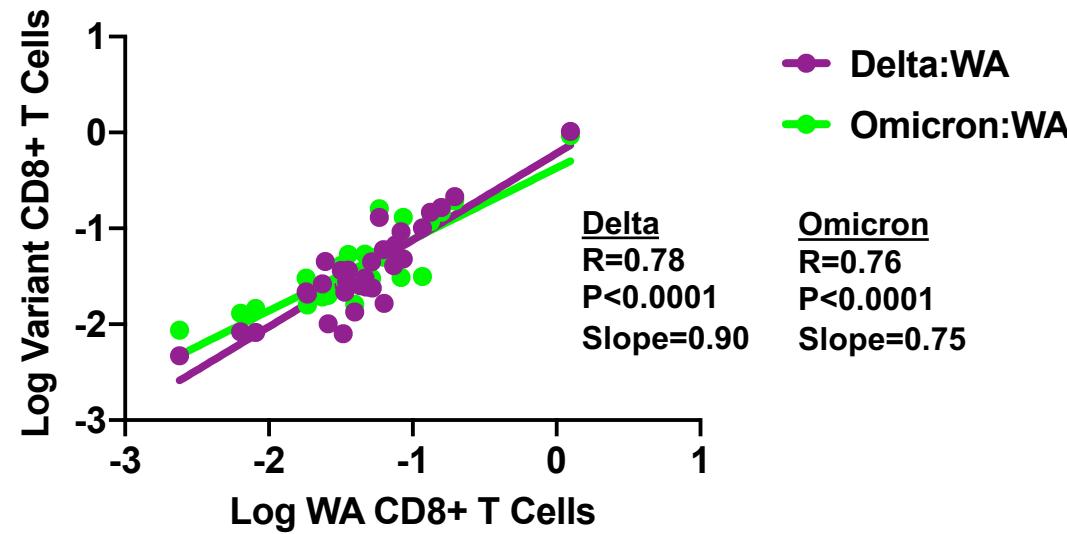
This is a PDF file of a peer-reviewed paper that has been accepted for publication.

# Vaccine-Elicited CD8 T Cell Responses are Highly Cross-Reactive to Omicron

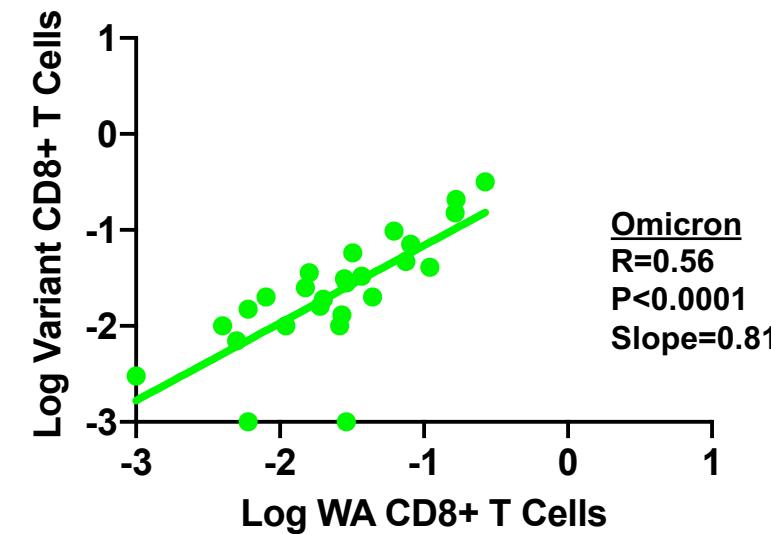


# Vaccine-Elicited CD8 T Cell Responses are Highly Cross-Reactive to Omicron

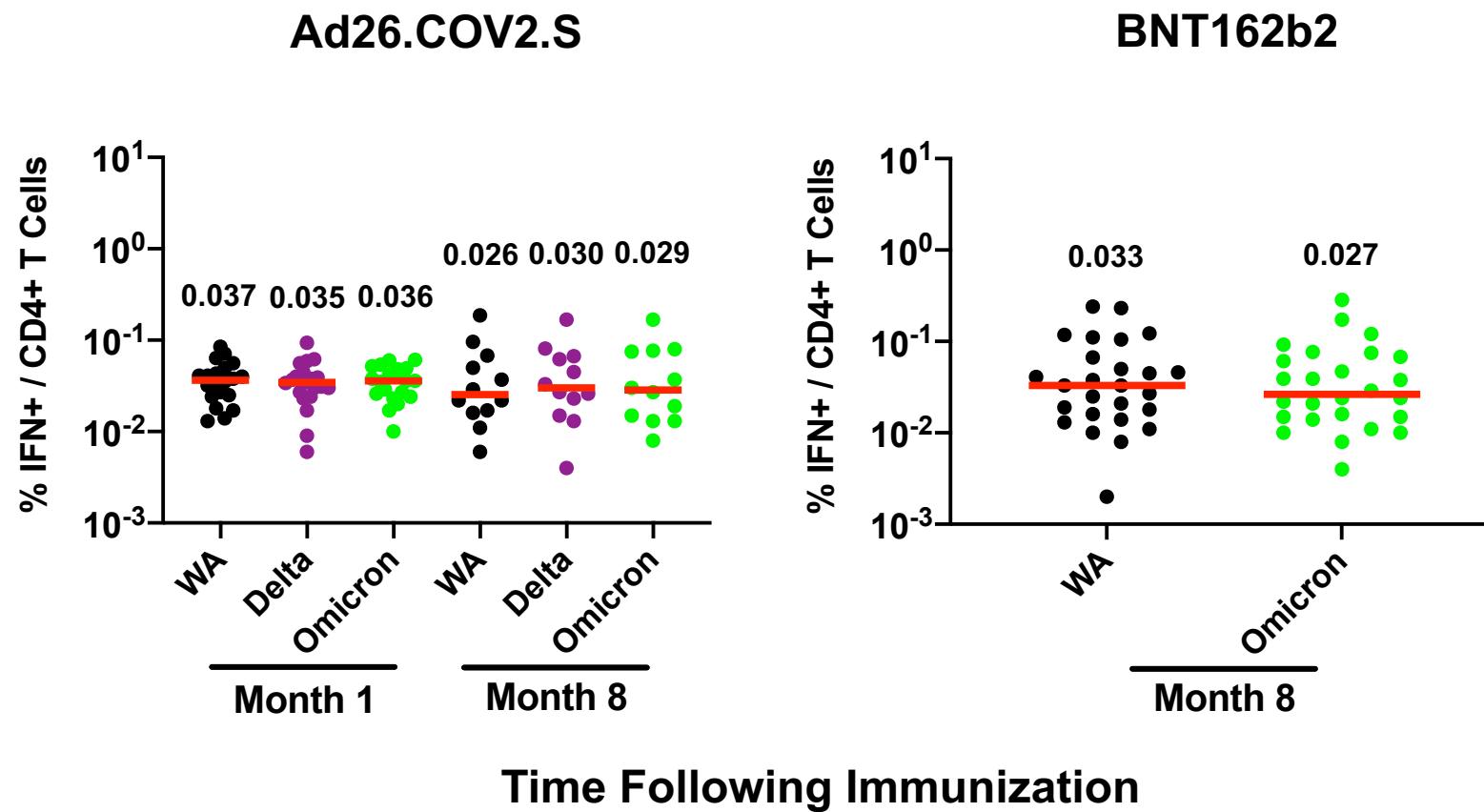
Ad26.COV2.S



BNT162b2

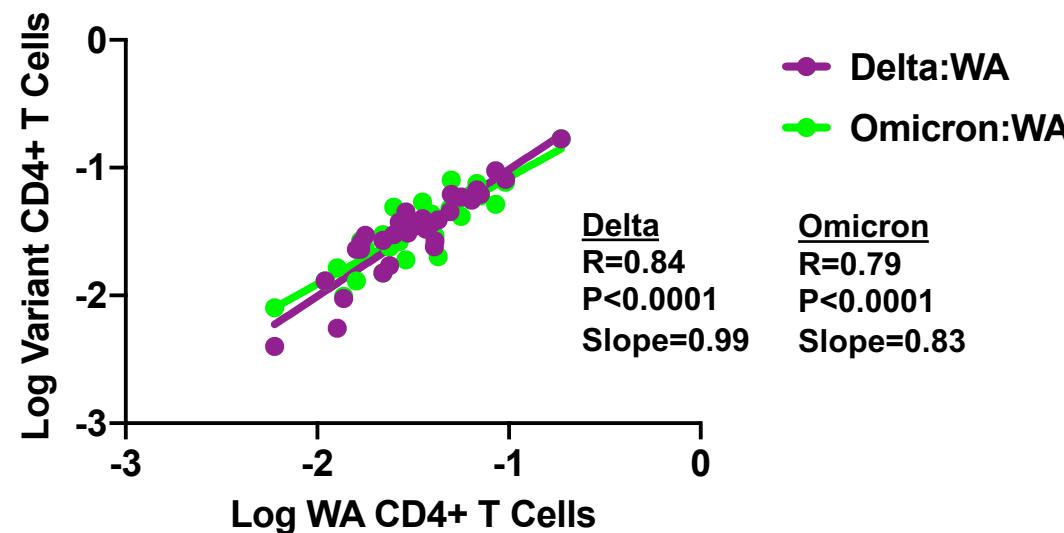


# Vaccine-Elicited CD4 T Cell Responses are Highly Cross-Reactive to Omicron

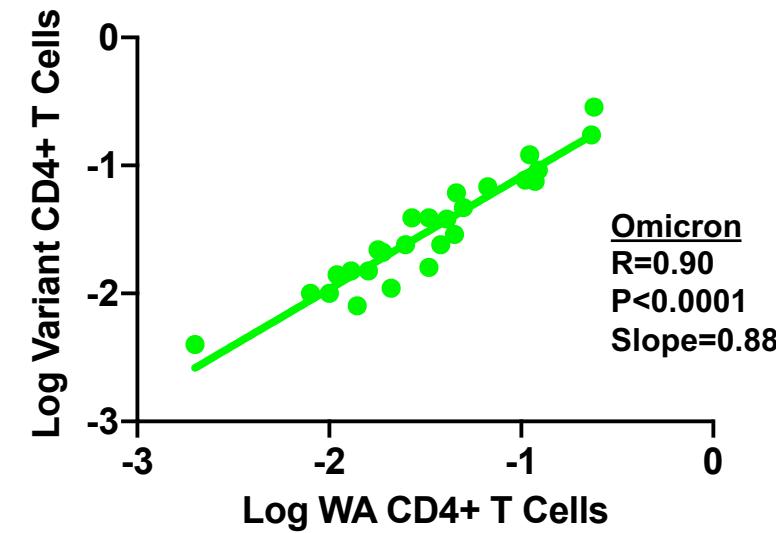


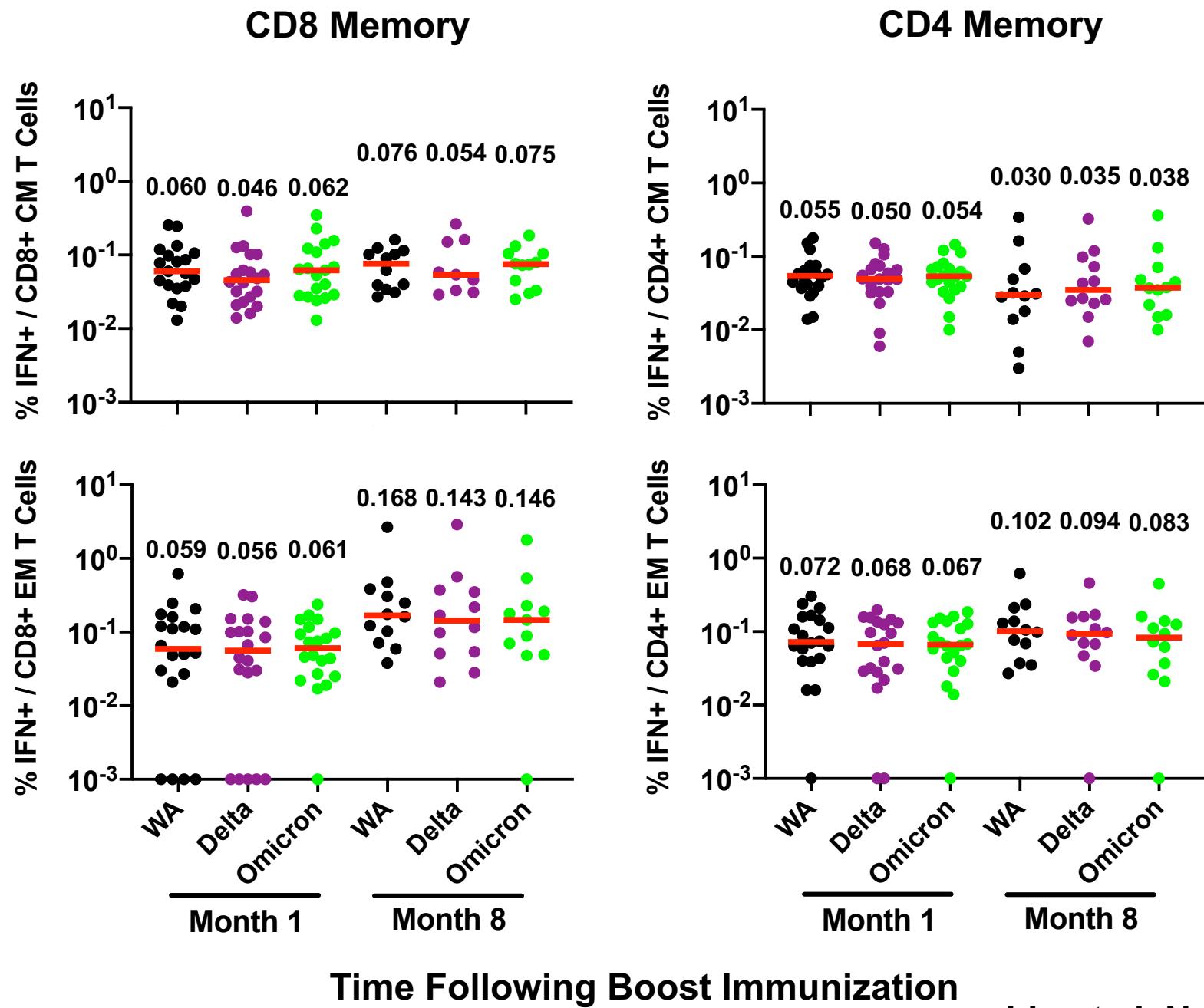
# Vaccine-Elicited CD4 T Cell Responses are Highly Cross-Reactive to Omicron

Ad26.COV2.S



BNT162b2

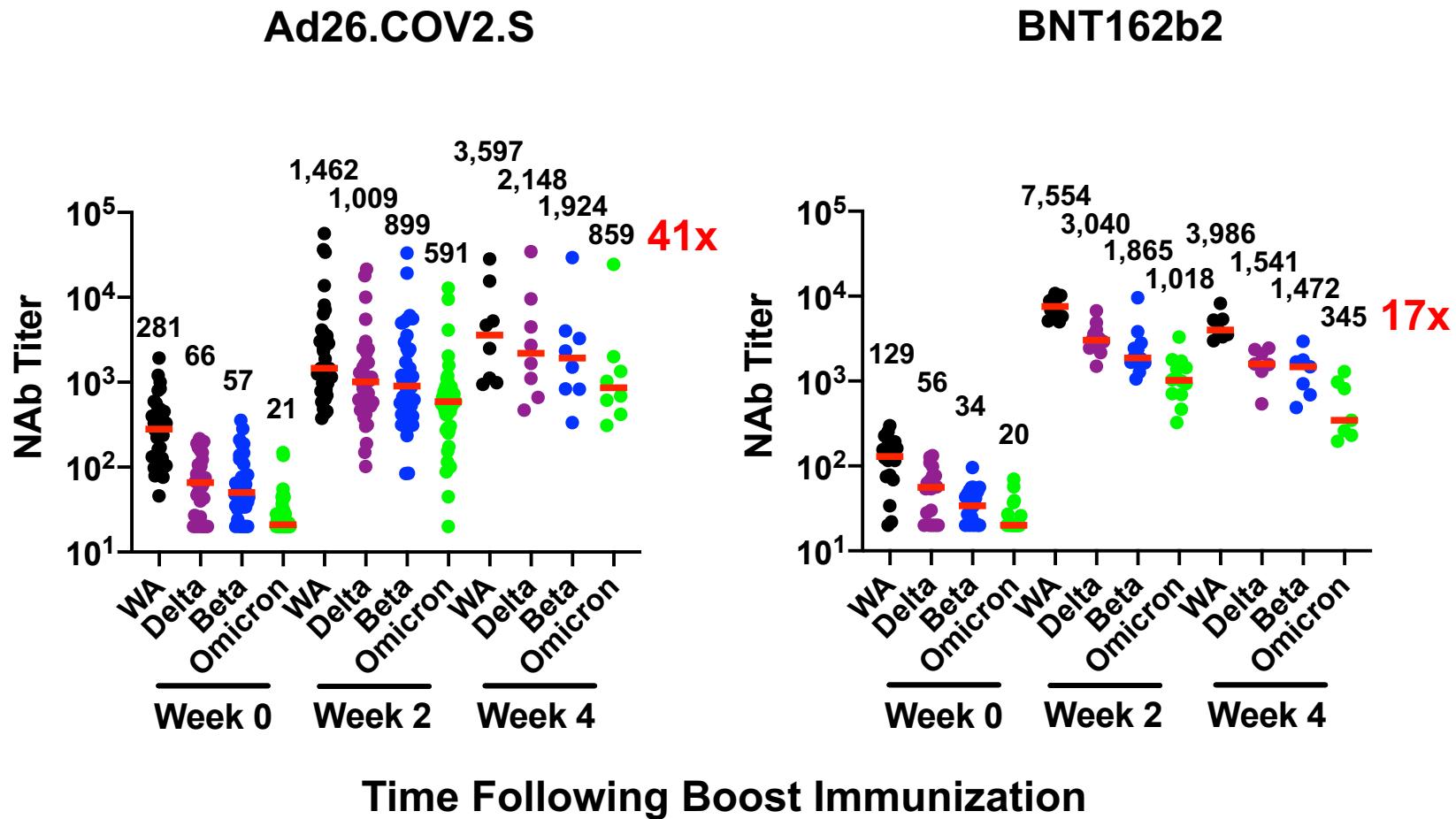




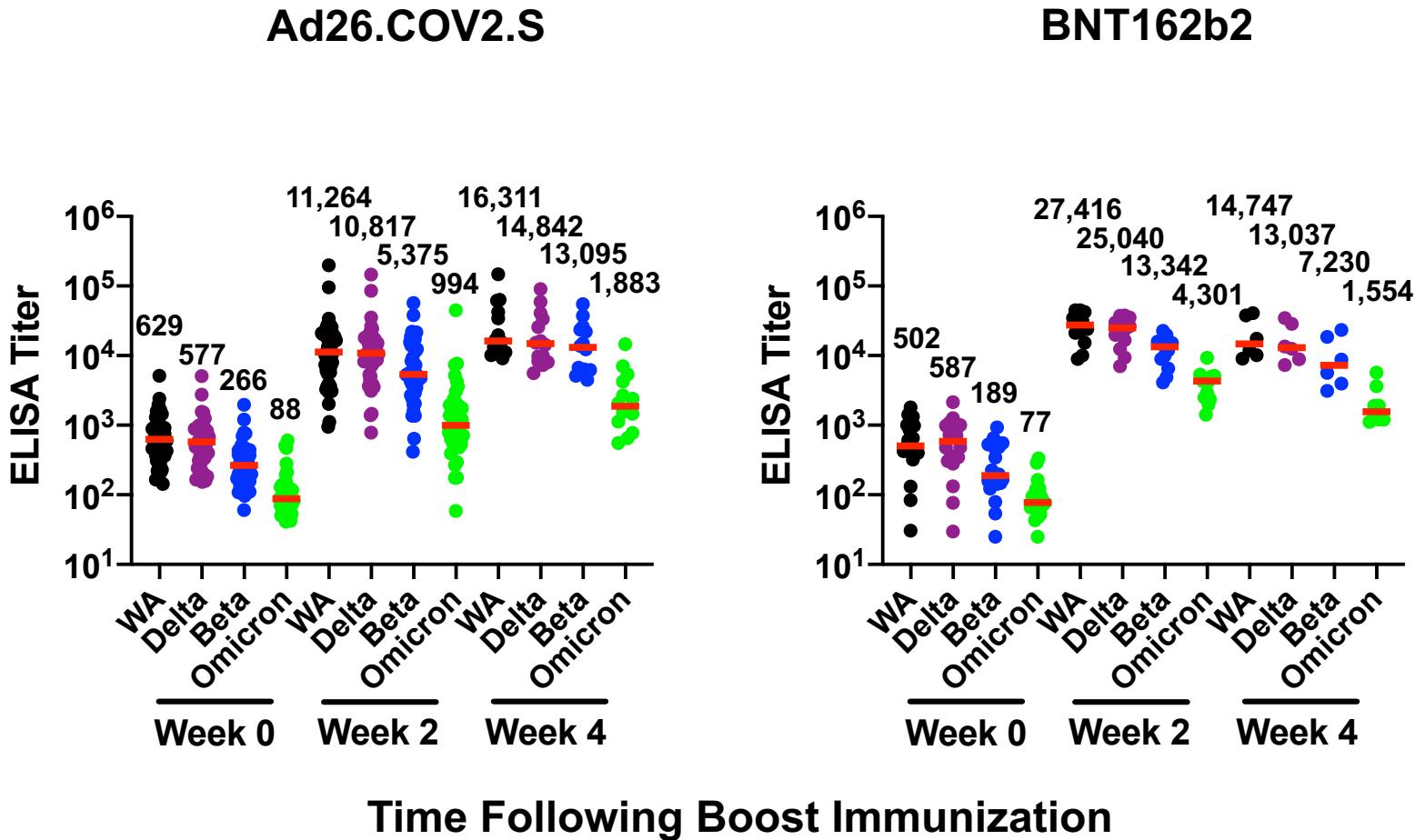
# **Homologous vs Heterologous Boosts to Increase Immunologic Coverage of Omicron**

- **65 individuals who received the BNT162b2 vaccine at least 6 months prior**
- **“Mix-and-match” heterologous boost with Ad26.COV2.S (N=41) or homologous boost with BNT162b2 (N=24)**
- **Evaluation of Omicron-specific antibodies and T cell responses at week 2 and week 4 following boost**
- **Durability studies ongoing**

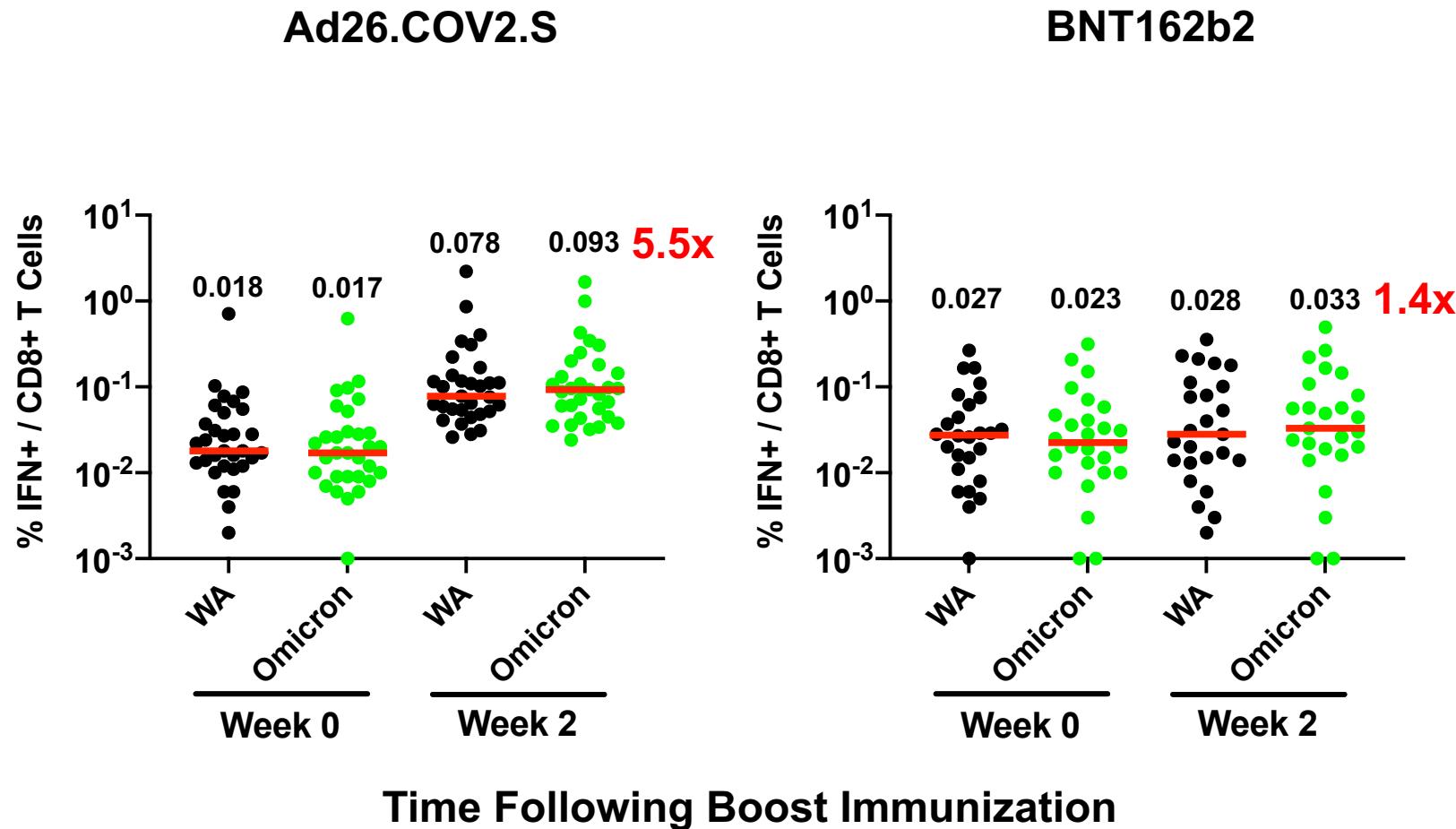
# Omicron-Specific NAb Responses Following Boost



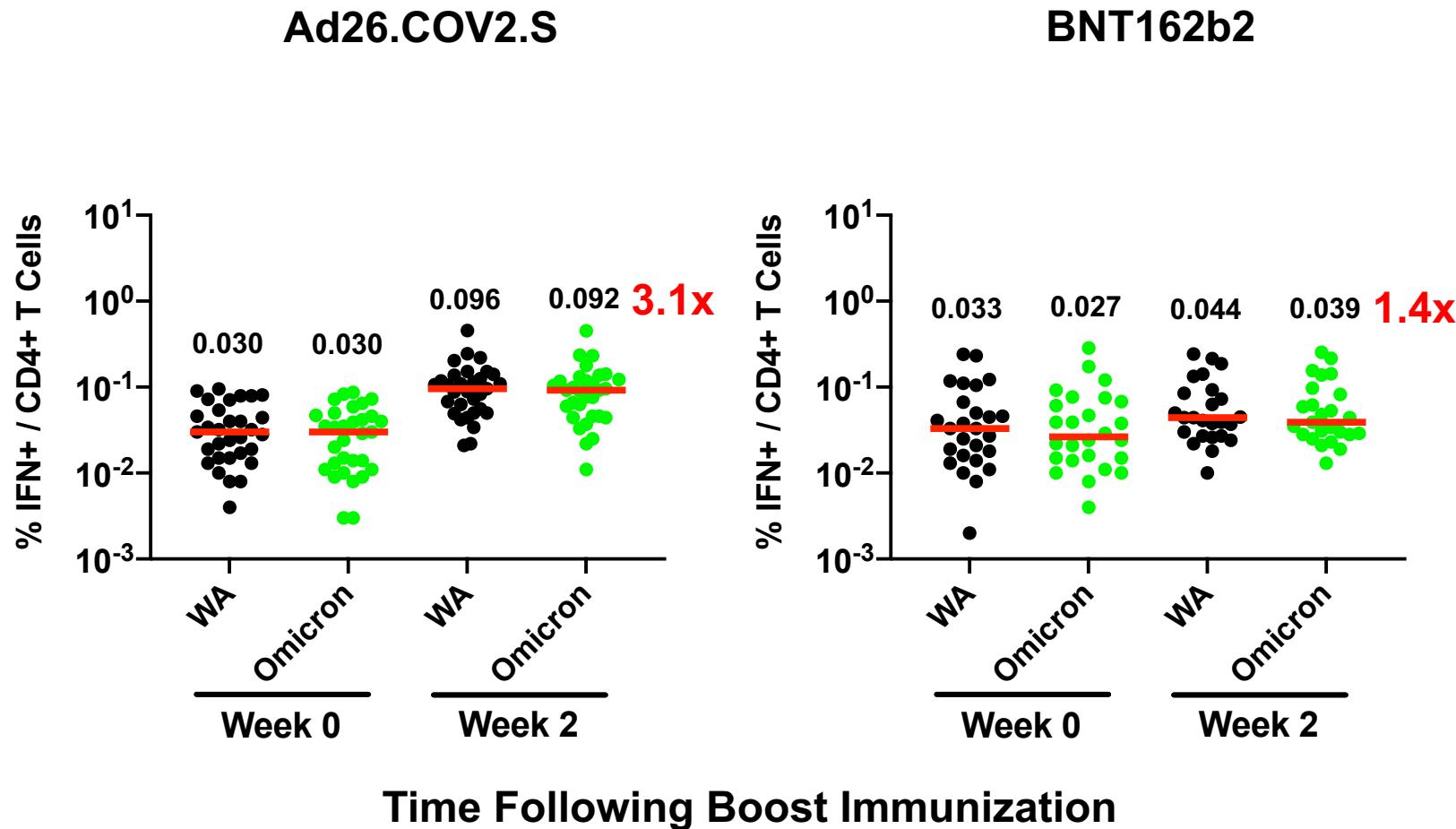
# Omicron-Specific ELISA Responses Following Boost



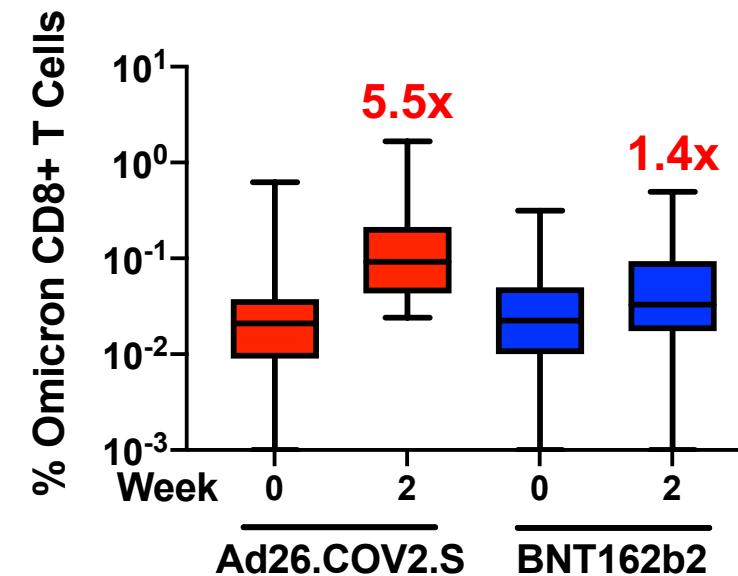
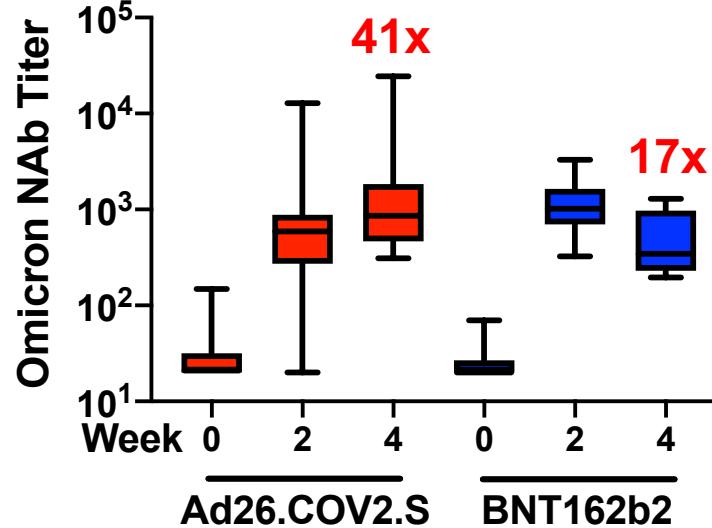
# Omicron-Specific CD8 T Cell Responses Following Boost



# Omicron-Specific CD4 T Cell Responses Following Boost



# Omicron-Specific NAb and CD8 T Cell Responses Following Boost: Summary



# Perspectives

- The rapid development of multiple COVID-19 vaccines is a biomedical triumph but has also exposed stark global health inequities
  - Current vaccines show reduced efficacy against infection with the Omicron variant, but still provide robust efficacy against severe disease
  - Boosts are useful and currently dominate much discussion, but the top priority should be to provide initial vaccines to unvaccinated people
  - A policy of boosting every 3-6 months is likely not a practical or feasible strategy for the developed world and will exacerbate inequity in the developing world; vaccines with improved durability are needed
- **Multiple vaccines need to be deployed as quickly as possible to accelerate the vaccine rollout in all regions of the world**

# **When Will This Pandemic End?**



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