

**Vaccines and Related Biological Products  
Advisory Committee October 14-15, 2021 Meeting  
Presentation Meeting**

Individuals using assistive technology may not be able to fully access the information contained in this file. For assistance, please send an e-mail to: [ocod@fda.hhs.gov](mailto:ocod@fda.hhs.gov) and include 508 Accommodation and the title of the document in the subject line of your e-mail.

# Emergency Use Authorization (EUA) Amendment for a Booster Dose for the Janssen COVID-19 Vaccine (Ad26.COV2.S)

Janssen Pharmaceutical Companies of Johnson & Johnson

Vaccines and Related Biological Products Advisory Committee  
October 15, 2021

# Emergency Use Authorization (EUA) Amendment for a Booster Dose for the Janssen COVID-19 Vaccine (Ad26.COV2.S)

Penny M. Heaton, MD

Global Therapeutic Area Head Vaccines

Janssen Pharmaceutical Companies of Johnson & Johnson



# Ad26.COV2.S Development Strategy, Durable Efficacy and Breadth of Immune Response

- Initial Phase 3 study evaluated single-dose regimen for pandemic response, globally
- Single dose demonstrated durable protection
  - In the US, efficacy is 74% against severe disease and 70% against all symptomatic disease
  - Efficacy persisted for > 6 months
- Unique immunoprofile with antibody titers that peak later and persist; durable cellular immunity with persistent responses

*Findings underscore promise of Ad26.COV2.S vaccine and opportunity to use booster dose to further increase protection against COVID-19*

# Clinical Program Supports Booster Dose is Safe, Increases Protection, Including Against Symptomatic COVID-19

## **Booster dose is safe and well-tolerated**

- Similar reactogenicity for first dose and booster dose
- No differences in unsolicited Adverse Events between first dose and booster dose
- No new trends among Adverse Events of Special Interest

## **Booster dose at 2 months provided 94% protection against symptomatic COVID-19 (US)**

- Increase from 70% in single-dose study
- Complete protection against severe/critical COVID-19 globally

## **Booster dose at 6 months provided 12-fold increase in antibodies**

- More potent than at 2 months

## **Booster dose increased antibodies against all variants tested, including Delta**

## **Seeking Emergency Use Authorization for homologous booster dose**

- For all individuals in US who received single-dose primary regimen
- May be given at least 2 months after primary regimen; data may suggest boosting at 6 months provides stronger immunologic response

# Outline of Today's Presentation

## Single-dose Primary Regimen Provides Durable Protection

- Efficacy from COV3001: single-dose primary regimen study
- Real-World Evidence Study of Janssen vaccine
- Immunogenicity: up to 8-9 months

## Boosting Substantially Increases Protection

- Efficacy from COV3009: booster 2 months after single-dose primary regimen
- Immunogenicity: booster 2-6 months after single-dose primary regimen

## Janssen Vaccine Favorable Safety

- Single-dose regimen, as observed in COV3001
- Safety profile after booster administered
- Update on post-authorization experience

## Conclusion

# Efficacy and Immunogenicity of the Single-Dose Primary Regimen

Johan Van Hoof, MD

Managing Director Janssen Vaccines and Prevention, BV  
Janssen Pharmaceutical Companies of Johnson & Johnson



# COV3001 (Single-dose) Final Analysis of Double-Blind Period\*

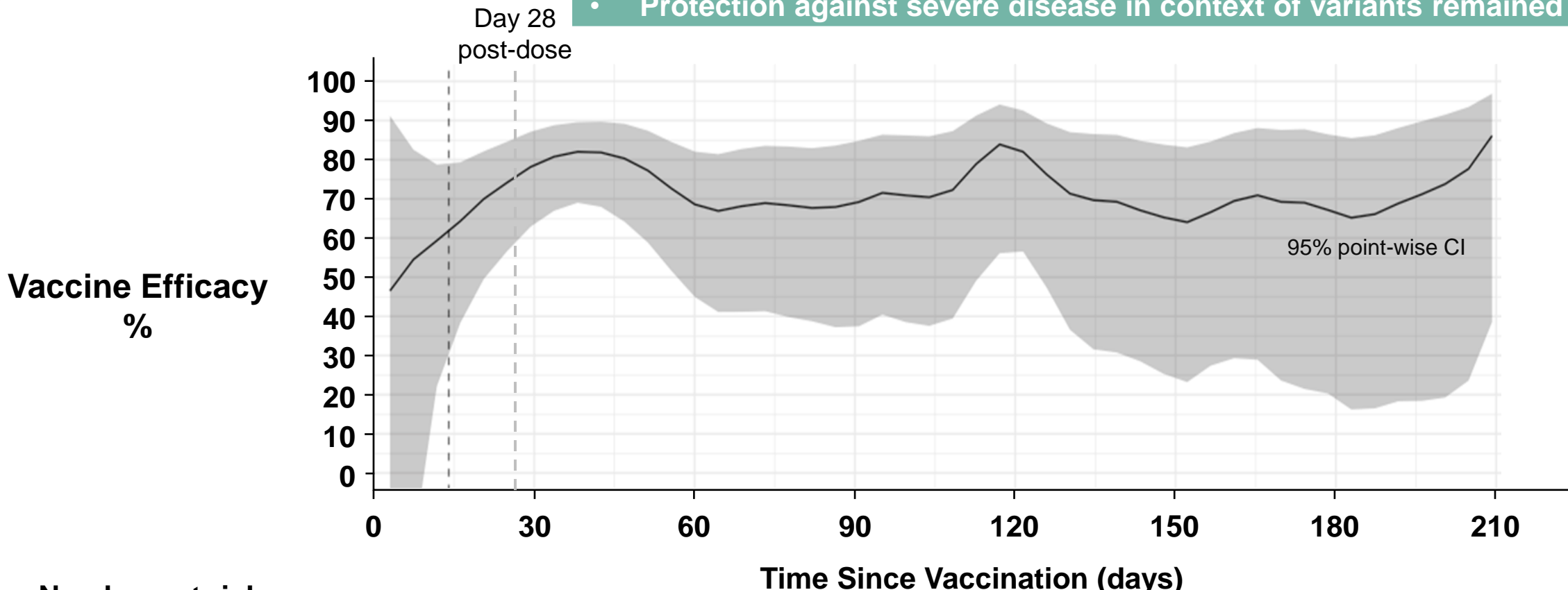
- Following EUA, study protocol amended to unblind participants, allow participants in placebo arm to receive Janssen vaccine
- Regional differences in duration of double-blind period
- Median follow up: 4 months
  - 23% of participants had follow up of  $\geq 6$  months
- SARS-CoV-2 incidence highly variable in time and between regions
- New lineages emerged, became dominant in most countries where study was conducted





# COV3001: Persistent VE Against Severe COVID-19

- 75% VE against severe/critical COVID-19 >Day 28
- Protection against severe disease in context of variants remained strong



**Numbers at risk**

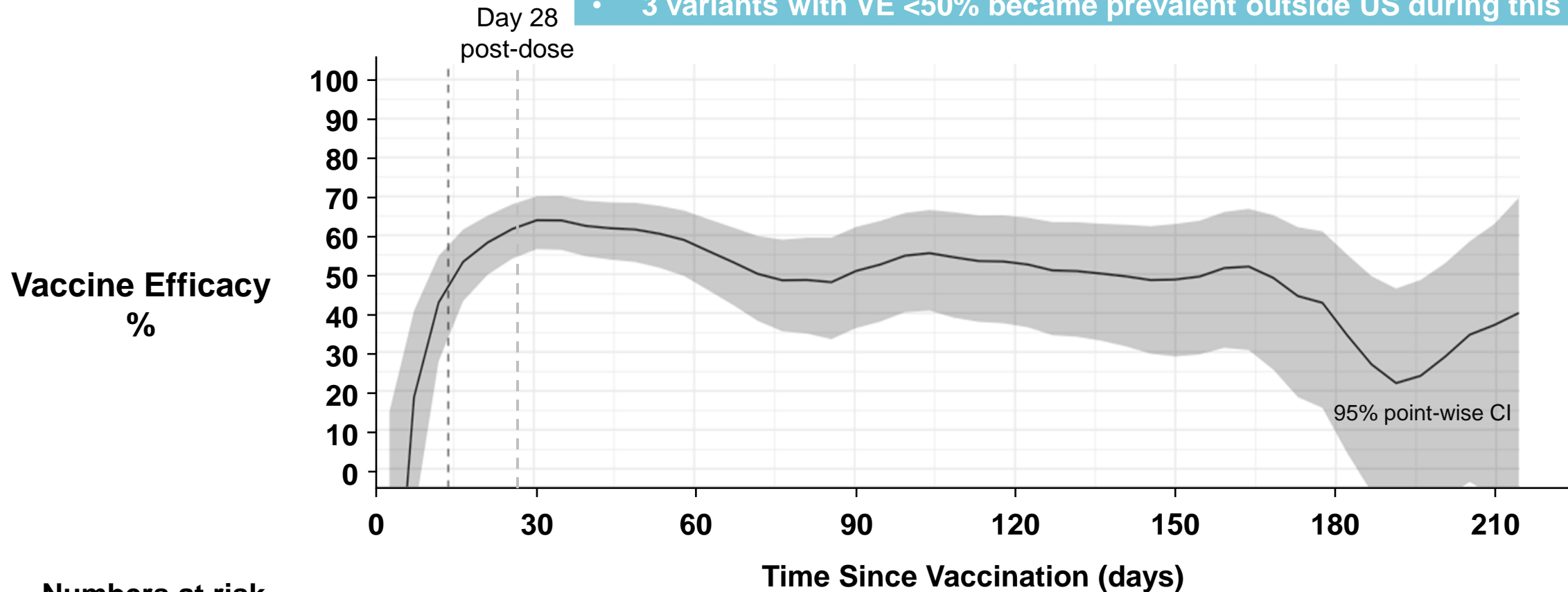
	0	30	60	90	120	150	180	210
<b>Ad26.COV2.S</b>	19562	19230	17764	15591	10284	5432	4045	1307
<b>Placebo</b>	19589	19134	17521	15202	9815	5046	3796	1260



Baseline-seronegative participants, per-protocol (PP) analysis set; based on hazard ratio of severe/critical COVID-19

# COV3001: VE for Symptomatic COVID-19

- 53% VE against symptomatic COVID-19 >Day 28
- 3 variants with VE <50% became prevalent outside US during this period



## Numbers at risk

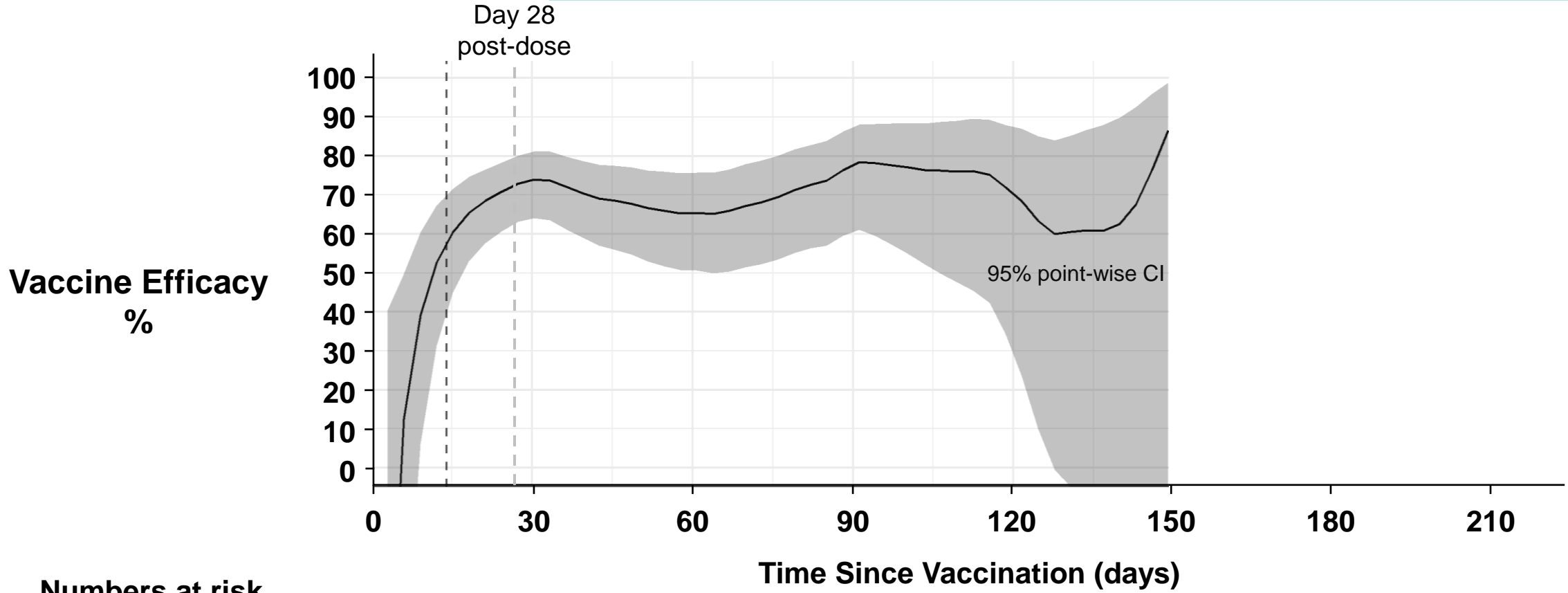
Ad26.COV2.S	19562	19111	17540	15290	10033	5256	3887	1193
Placebo	19589	18902	17052	14622	9328	4745	3531	1098

3001



# COV3001: United States VE for Symptomatic COVID-19

- US: 70% VE against symptomatic COVID-19 >Day 28
- Gamma, lambda, mu and delta not prevalent in US during this period



**Numbers at risk**

	0	30	60	90	120	150	180	210
<b>Ad26.COV2.S</b>	9153	8797	17553	6130	3180	1180	446	153
<b>Placebo</b>	9119	8605	7127	5665	2700	944	385	162



# Real-World Evidence (RWE) Study of Single-Dose Janssen Vaccine

Sebastian Schneeweiss, MD, ScD

Science Lead  
Aetion, Inc

Professor of Medicine and Epidemiology  
Harvard Medical School



# Janssen-Aetion Real-World Evidence Cohort Study of Single-Dose Janssen Vaccine

## CONTEXT

- **COV3001 RCT** demonstrated robust efficacy for single dose Ad26.COVS vaccine, **but no data on Delta in US**
- Published **RWE studies** (1-9) report range of vaccine effectiveness estimates for Ad26.COVS
  - **Hospitalizations/ER (60%-91%):** CDC (60%-84%, US), Janssen-Aetion study (81%, US), Sisonke (67%-84%, South Africa), Dutch Ministry of Health RWE (91%)
- Varying methodologies, sample sizes, follow-up times

## OBJECTIVE of Janssen-Aetion RWE Study

- **Assess vaccine effectiveness over time in US clinical practice with focus on Delta Variant\* (March through August 31, 2021)**

1.Moline et al; 2. Thompson et al; 3. Grannis et al; 4. Self et al; 5. Bekker et al (in prep); 6. de Gier et al; 7. Corchado-Garcia et al; 8.CDC-ICATT study (ACIP meeting, Sep 2021), 9. Polinski et al

\* No sequencing data available for analyses, delta variant period based on time period of CDC sequenced data

# Janssen-Aetion Real-World Evidence Cohort Study of Single-Dose Janssen Vaccine

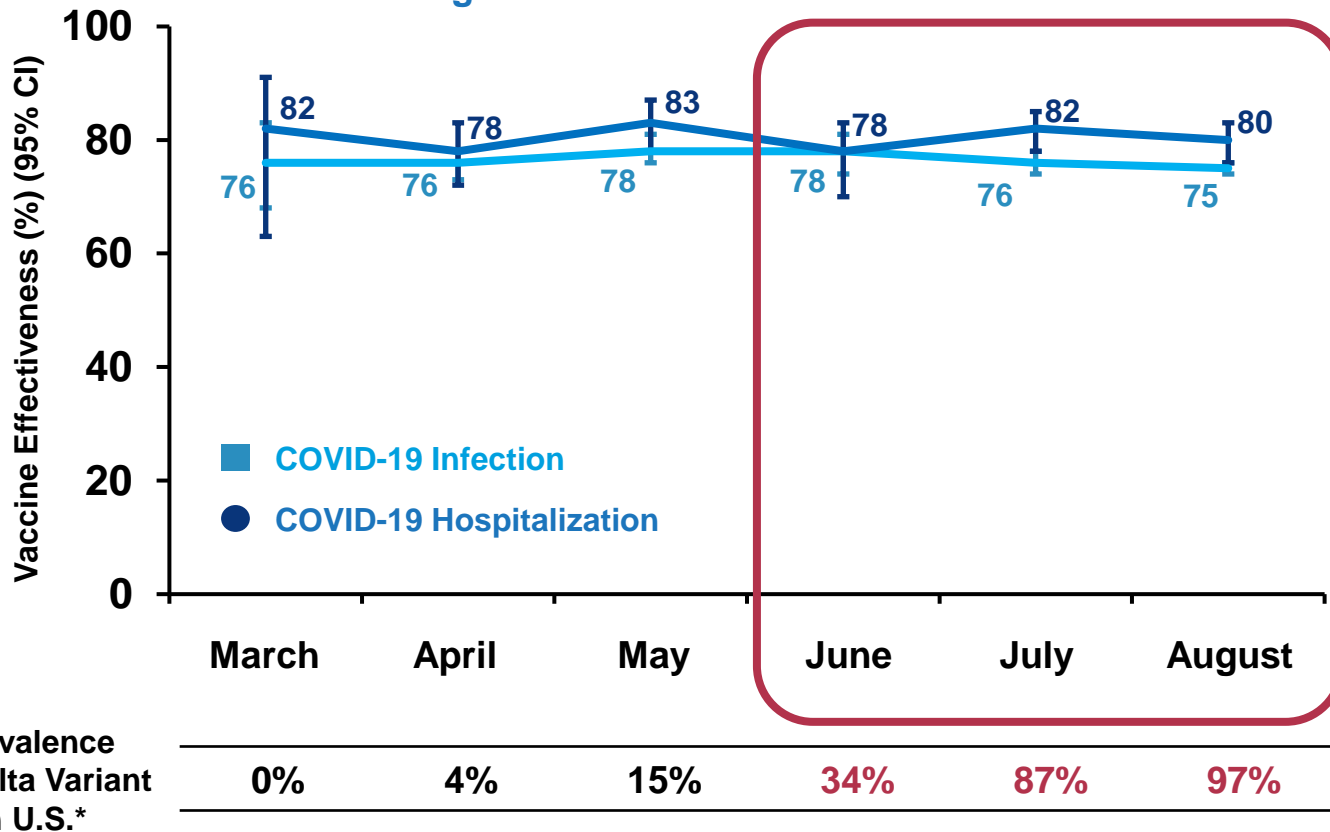
## Janssen-Aetion RWE Study\*

- **Study Design:** Longitudinal cohort study of **422,034** Janssen-vaccinated subjects versus **1,645,397** unvaccinated subjects
- **Data Source:** HealthVerity data – validated, **longitudinal, de-identified** patient-level **medical and pharmacy claims** (including Medicaid participants) and **laboratory data** for ~160M lives
- **Cohort Balance:** Exact-matched by **day, 3-digit ZIP, sex, age** group, comorbidity index; further propensity score-matched on **17 predictors of COVID-19 severity\*\***
- Vaccine effectiveness estimates corrected for **vaccination status misclassification** in healthcare claims data\*\*\*

\*Polinski et al. . <https://www.medrxiv.org/content/10.1101/2021.09.10.21263385v1> - analysis till July 31, 2021; updated analysis till Aug 31<sup>st</sup>, 2021 presented here \*\*COPD, CF, HIV, HTN, Liver Disease, Malignancies, Asthma, Cerebrovascular disease, CKD, Mod-Severe Asthma, PF, Obesity, Serious Heart conditions, Sickle-Cell Disease, Thalassemia, T1DM, T2DM; \*\*\*Assumed 40% under-recording of vaccinations (comparing CDC to HealthVerity vaccination percentages) and applied a correction factor to vaccine effectiveness estimates using standard methods for correcting exposure misclassification. This was confirmed in a linkage study between claims data and the Louisiana State vaccination registry

# Month-Over-Month and Kaplan-Meier Plot Demonstrate Good and Durable Vaccine Effectiveness of Single-Dose Vaccine During July-August 2021, When Delta Dominant in US

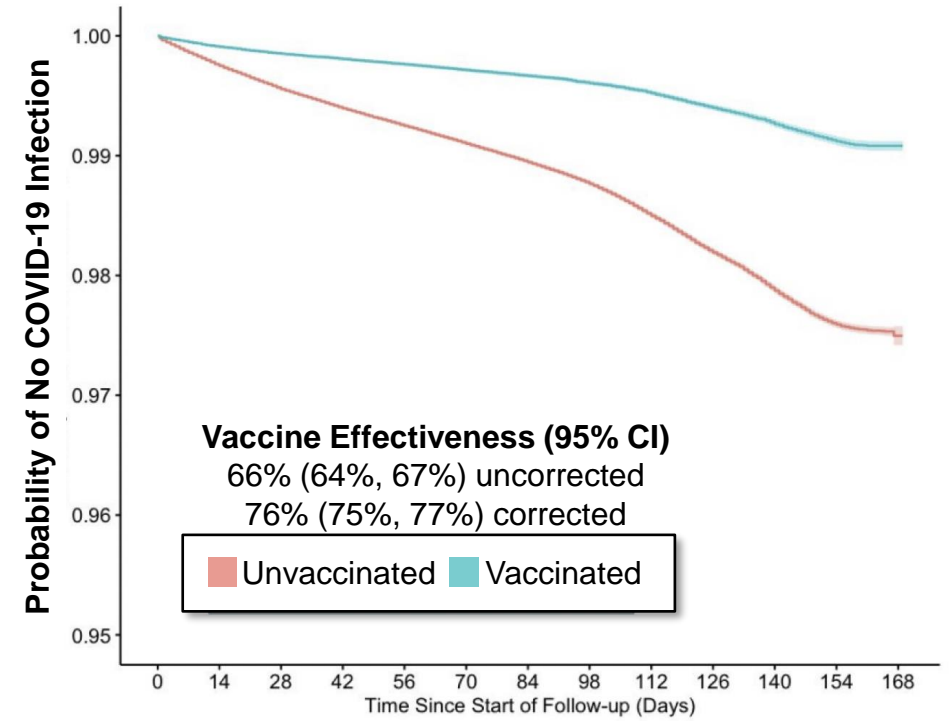
Stable month-over-month vaccine effectiveness including when Delta emerged to when it became dominant



Prevalence of Delta Variant in U.S.\*

March	April	May	June	July	August
0%	4%	15%	34%	87%	97%

Time-to-event analyses show stable vaccine effectiveness during 183 days after vaccination



Covid-19 Infections

Median follow-up = 129 days; Schoenfeld residuals show proportional hazards throughout 183 days of follow-up (p=0.53); Uncorrected vaccine effectiveness was equally stable over 183 days

\*www.nextstrain.org; \*\*Corrected vaccine effectiveness estimates are presented in this slide – Month-over-Month uncorrected vaccine effectiveness estimates are 64%-69% for Covid-19 infections and 68%-75% for Covid-19 related Hospitalization

# Key Takeaways from Janssen-Aetion RWE Study

- RWE demonstrates **single-dose Ad26.COV2.S has good vaccine effectiveness in US clinical practice – consistent with COV3001 RCT data (US)**
- **Single dose vaccine offers good and durable protection over calendar time**, in the pre-Delta and during Delta time periods
- **Given vaccine effectiveness against hospitalization and infection, opportunity to improve the protection via booster dose** especially against emerging variants



# Kinetics and Durability of Ad26.COVS Induced Immune Responses

Dan Barouch, M.D., Ph.D.

Professor of Medicine

Harvard Medical School

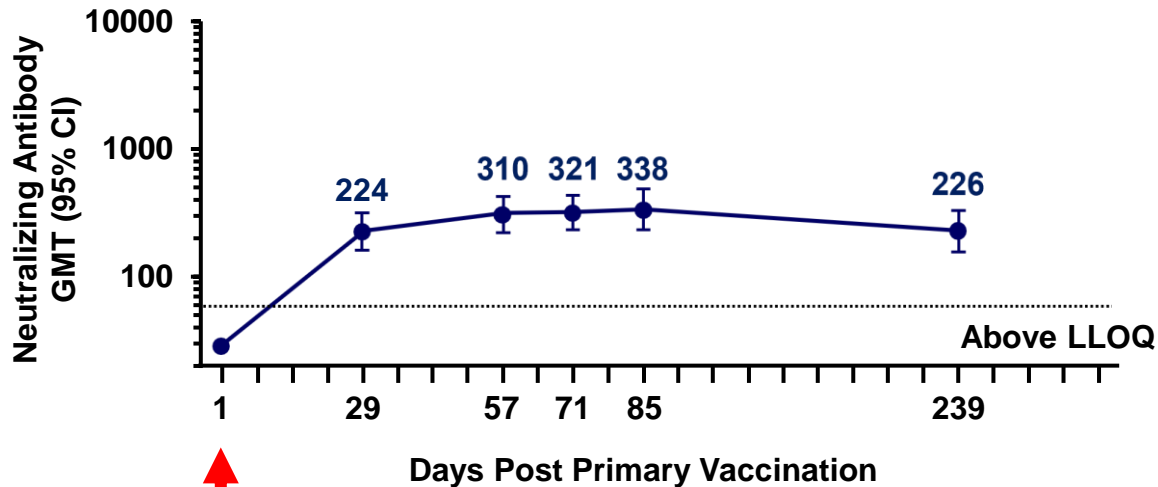
Director, Center for Virology and Vaccine Research

Beth Israel Deaconess Medical Center



# Janssen COV1001: Humoral Immune Responses Persist Over Time, Following a Single Dose (18-55 and $\geq 65$ years)

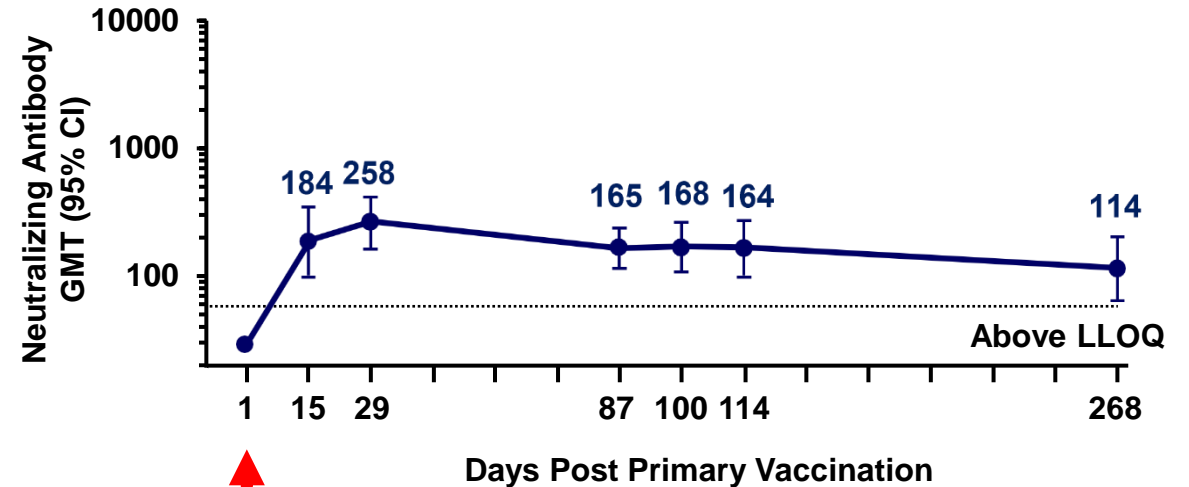
18-55 Years, N=25



Primary vaccination  
 $5 \times 10^{10}$ vp

<b>N</b>	25	24	25	24	24	22
<b>% Responders</b>	96					
<b>% Detectable antibodies</b>		100	100	100		95

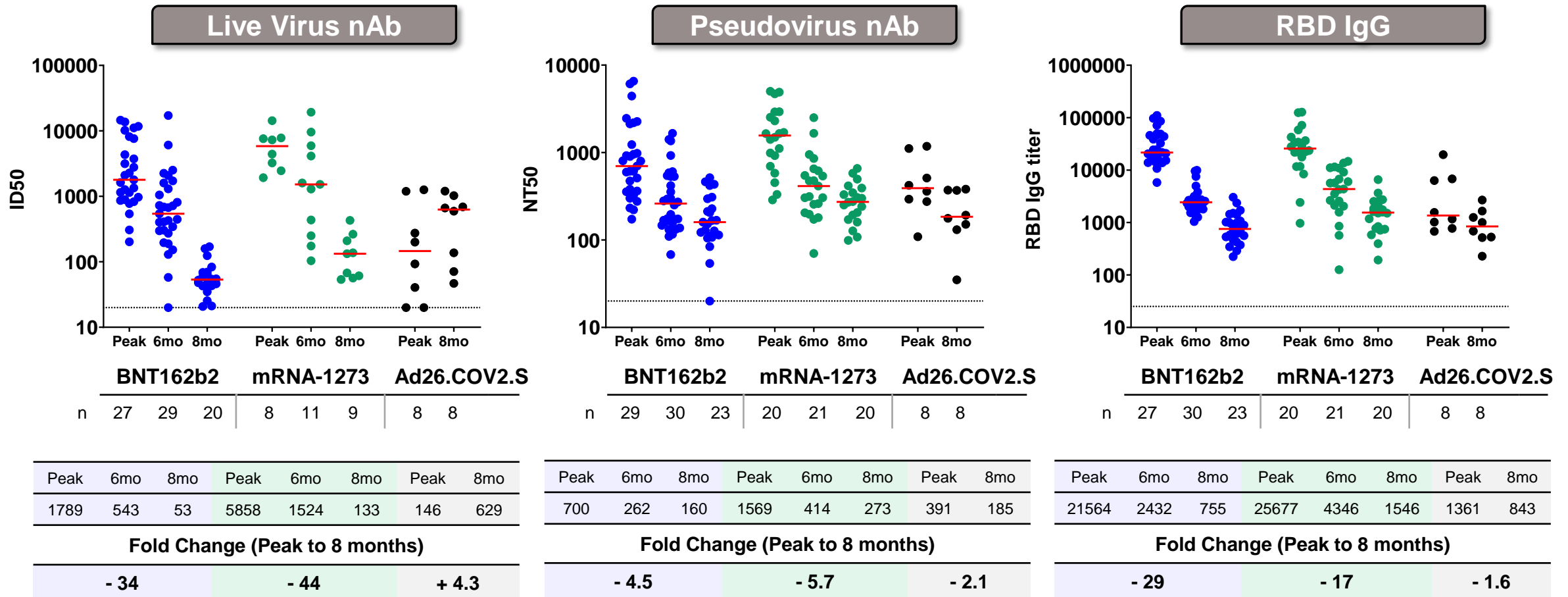
$\geq 65$  Years, N=24



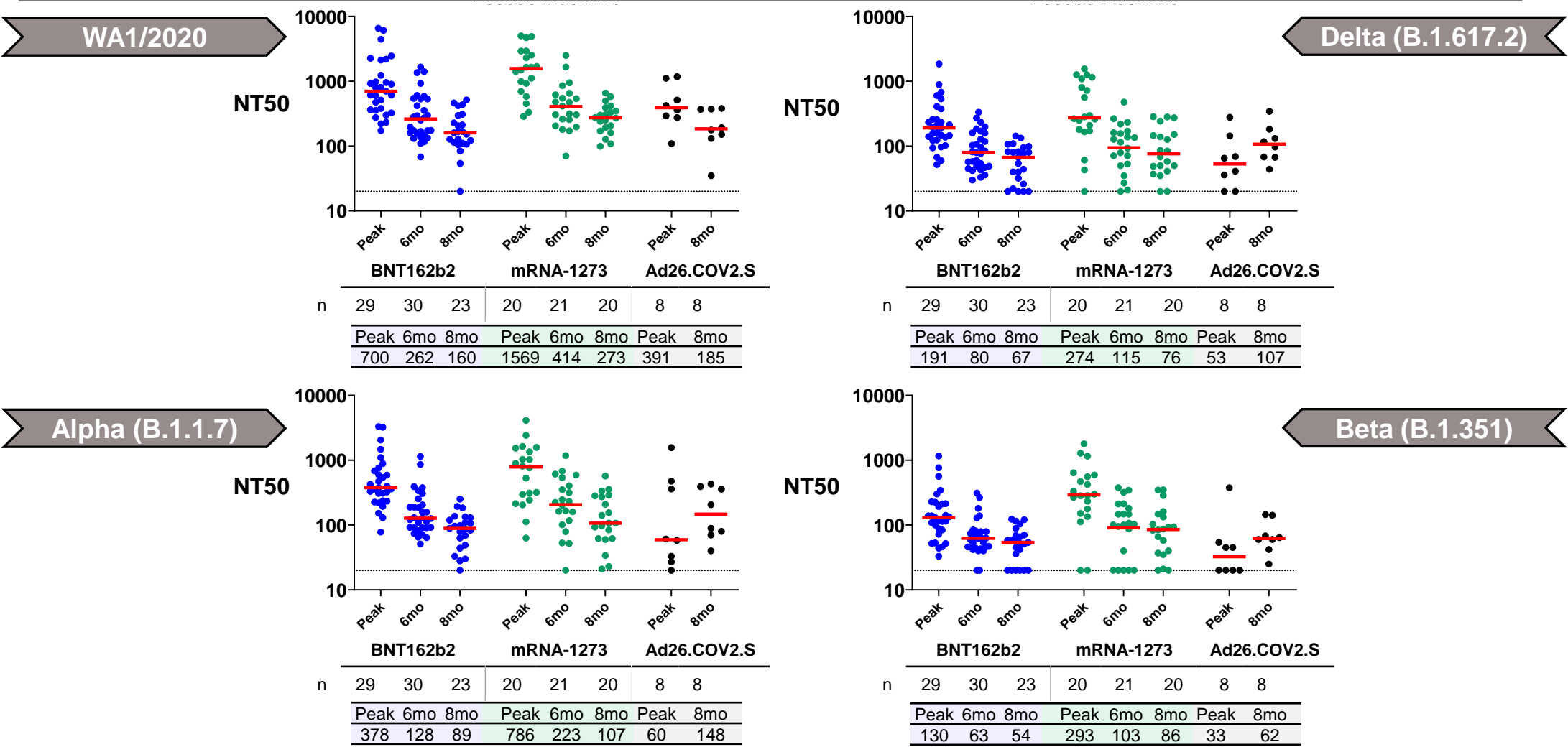
Primary vaccination  
 $5 \times 10^{10}$ vp

<b>N</b>	24	11	25	21	22	22	19
<b>% Responders</b>	100 96						
<b>% Detectable antibodies</b>				90	86	81	68

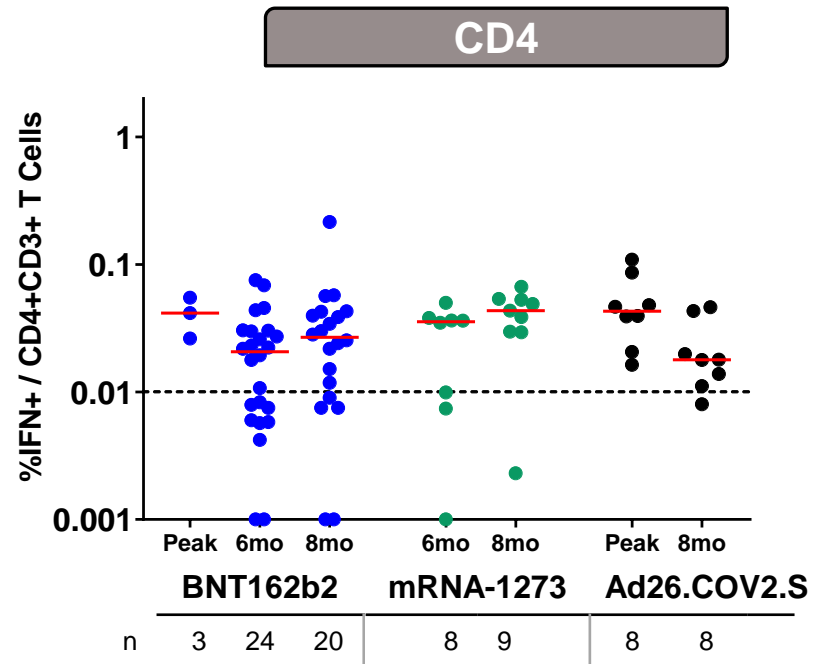
# Ad26.COV2.S Induces Durable Antibody Responses



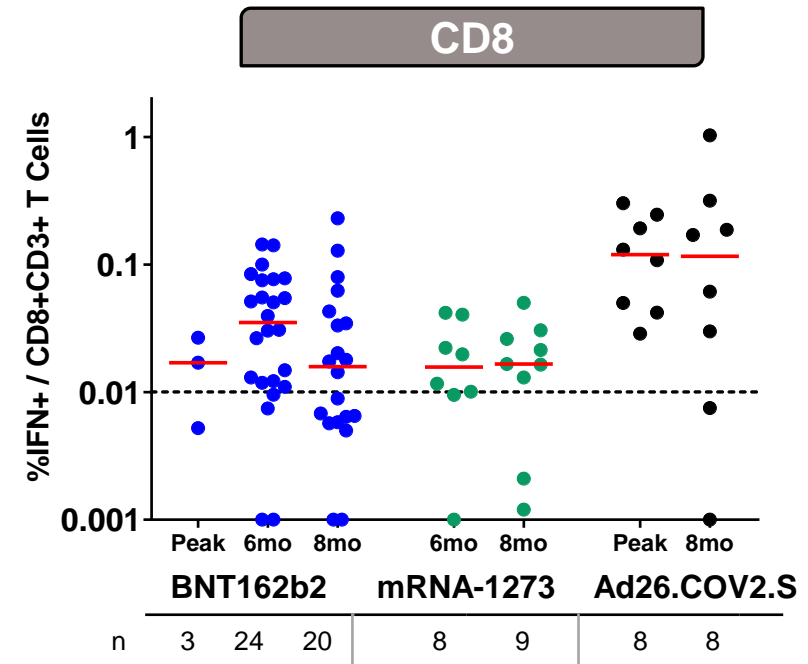
# Ad26.COVS Induces Durable Neutralizing Antibody Responses Against SARS-CoV-2 Variants



# Ad26.COV2.S Induces Durable CD8 T Cell Responses



Peak	6mo	8mo	Peak	6mo	8mo	Peak	8mo
0.042	0.021	0.027	N/A	0.036	0.043	0.043	0.018



Peak	6mo	8mo	Peak	6mo	8mo	Peak	8mo
0.017	0.035	0.016	N/A	0.16	0.17	0.12	0.12

# Ad26.COV2.S Induces a Distinct and Complex Immunologic Profile with Robust Durability

---

- Ad26.COV2.S elicits a diversity of immune responses
  - Neutralizing and Fc functional antibodies
  - CD4 and CD8 T cell responses
- Humoral and cellular immune responses are remarkably durable for  $\geq 8$  months, consistent with the observed durability of protective efficacy
- Multiple immune responses, including both antibodies and CD8 T cells, likely contribute to protection with Ad26.COV2.S
  - Robust protection against beta variant in South Africa despite minimal neutralizing antibody responses to beta variant
  - In nonhuman primates, CD8 depletion partially abrogated protection of natural immunity against SARS-CoV-2 challenge

# Efficacy of Booster After Single-Dose Primary Regimen of Ad26.COV2.S

Johan Van Hoof, MD

Managing Director Janssen Vaccines and Prevention, BV  
Janssen Pharmaceutical Companies of Johnson & Johnson



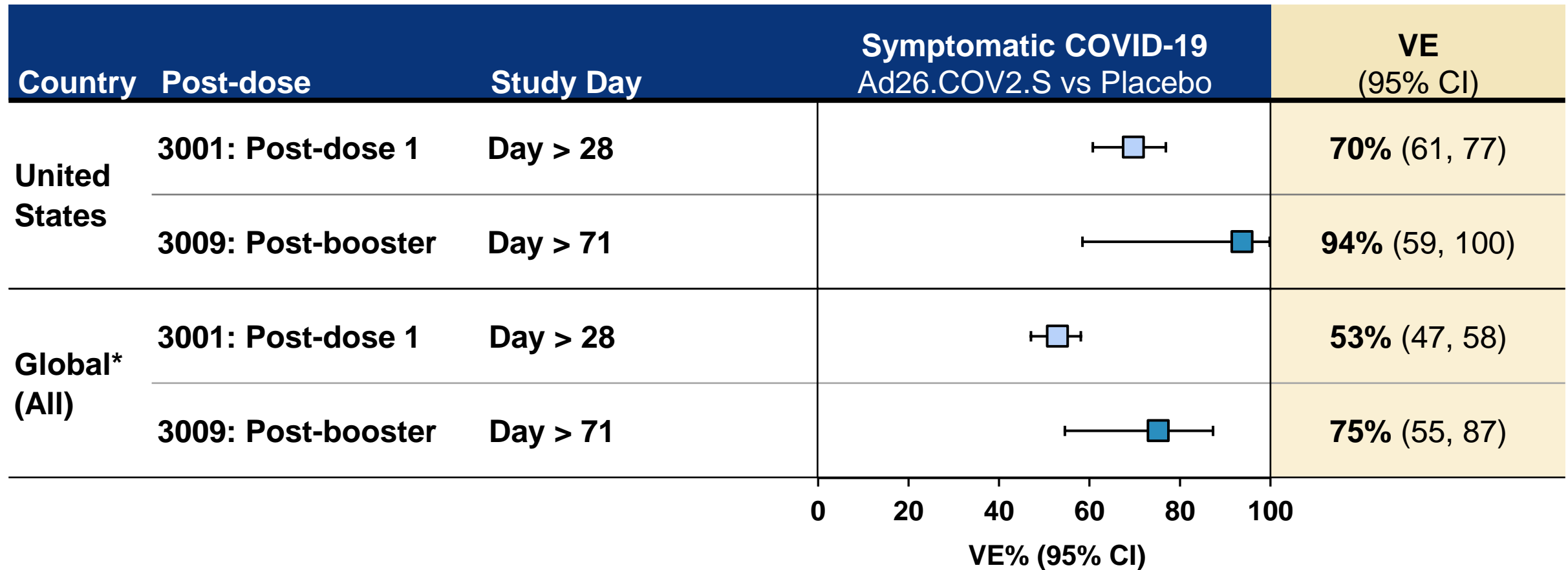
# COV3009: Evaluated Efficacy of Ad26 Following Administration of Booster 2 Months After First Shot

- Large (N=31,300), global, randomized placebo-controlled trial conducted in 9 countries, 3 continents
- Study allowed unblinding following EUA
  - Participants on placebo offered vaccine
- 53% received booster dose during double-blind period
  - 25%\* evaluable for efficacy  $\geq$  60 years
- Median follow-up after booster dose: 36 days (0 to 172 days)
  - 29% (n > 4245) of participants had follow up  $\geq$  2 months





# COV3001 and COV3009: US and Global VE Against Symptomatic COVID-19 for Single Dose vs Booster after 2 Months



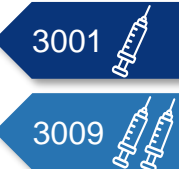
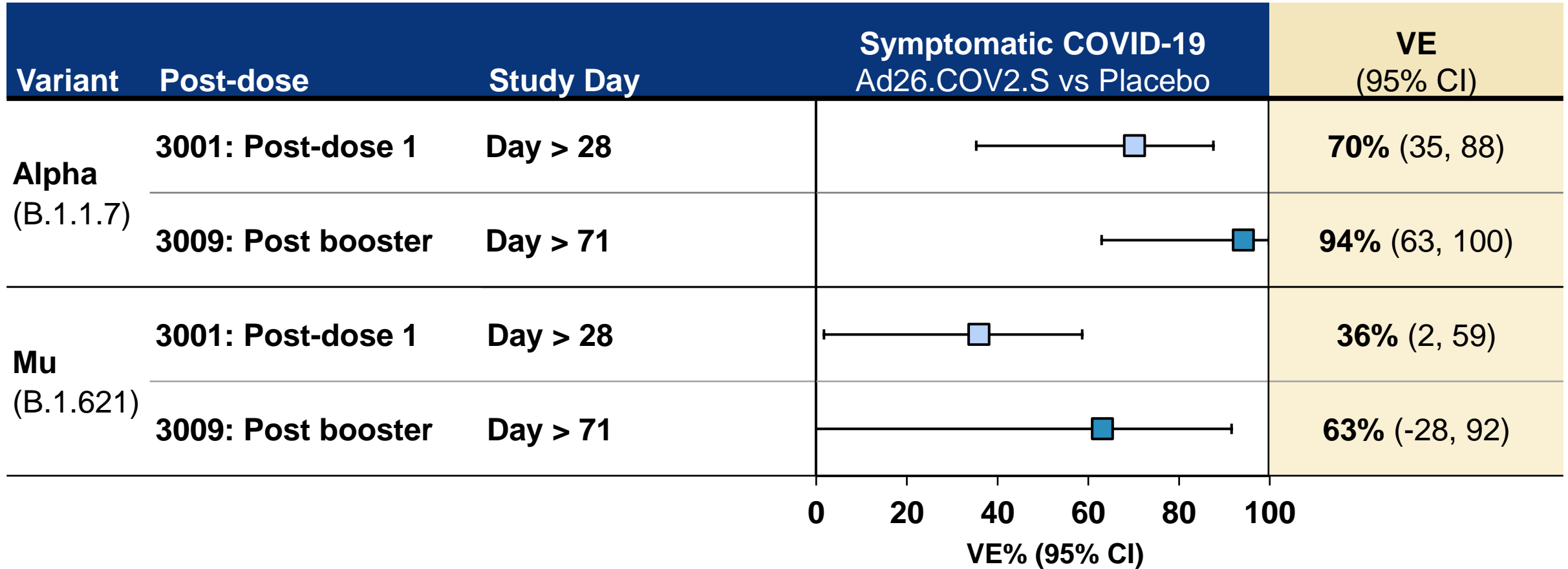
3001 Final analysis cutoff date: July 9, 2021 (all), June 16, 2021 (US)

3009 Final analysis cutoff date: June 24, 2021 (all), June 9, 2021 (US)

\*Primary endpoint for 3001 and 3009 (VE moderate to severe = VE symptomatic)

3001 3009 

# COV3001 and COV3009: Booster Dose Increases VE Against Symptomatic COVID-19 Caused by Variants



# COV3009: Protection Against Severe Outcomes

<i>PP At Risk Set</i> <i>Global</i>	> Day 71 (> 14 Days Post-Booster)		
	<b>Ad26.COVS</b> (N = 6,024)	<b>Placebo</b> (N = 5,615)	<b>VE %</b> (95% CI)
<b>Severe COVID-19</b>	<b>0</b>	<b>8</b>	<b>100%</b> (33, 100)
<b>COVID-19-related hospitalization</b>	<b>0</b>	<b>5</b>	<i>N/A</i>
<b>COVID-19-related death</b>	<b>0</b>	<b>1</b>	<i>N/A</i>





# Immunogenicity Following Booster Dose of Ad26.COVS.S

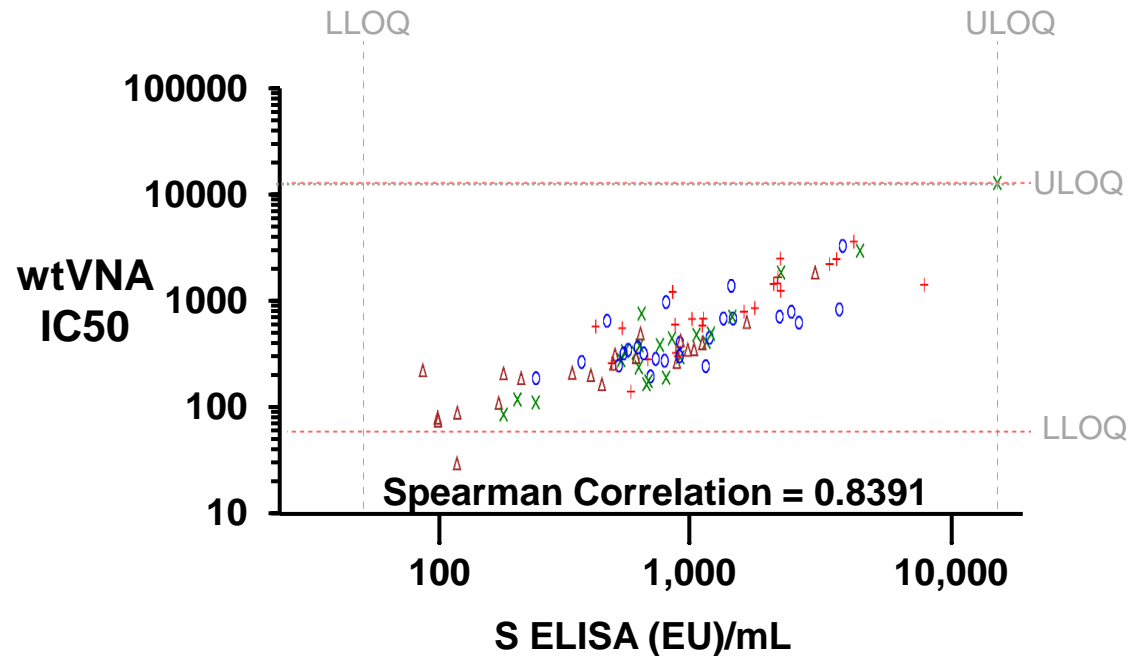
# Clinical Immunogenicity Studies Supporting Ad26.COVS Booster Dose

Booster Timing	Age (yrs)	Sample Size		
		S ELISA	wtVNA	psVNA
2 months	18-55	181	99*	5 (Original, Alpha, Beta, Gamma, Delta, Epsilon, Kappa)
	≥ 65	79	65	-
3 months	18-55	27	22	-
	≥ 65	101	40	-
6 months	18-55	29	-	17 (B1, Alpha, Beta, Gamma, Delta, Lambda)

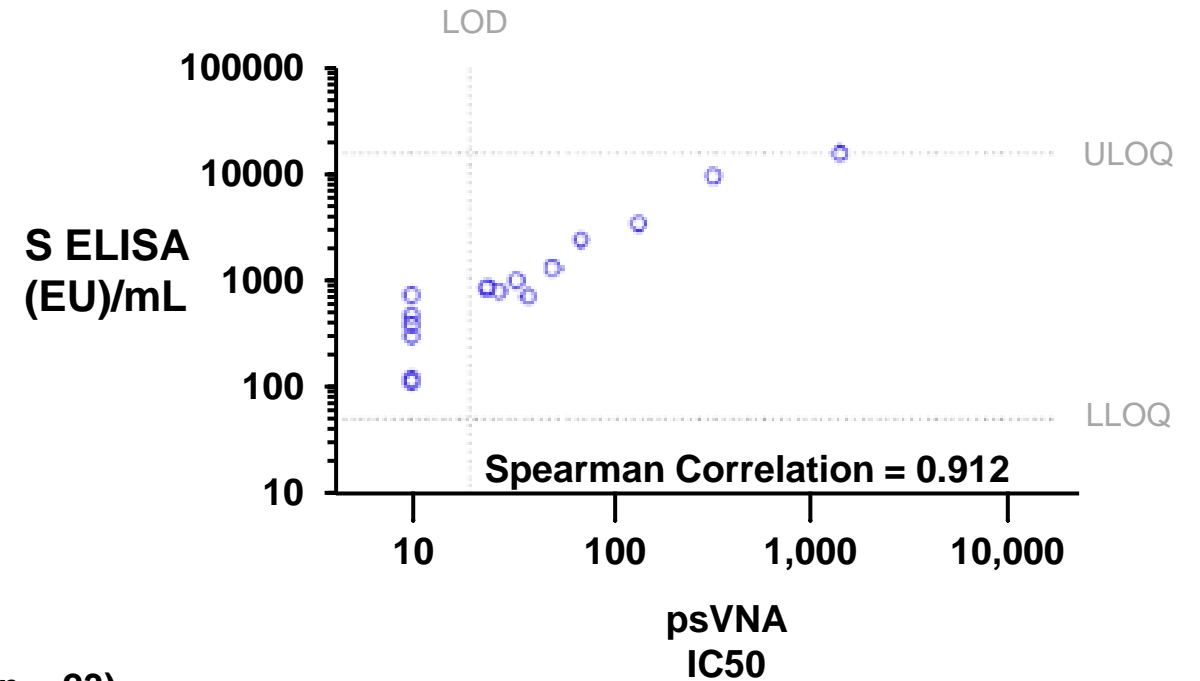
\*Variant wtVNA N=6 (Alpha, Beta); Data originates from studies COV1001, COV1002, COV2001; Sample size depicted are at baseline

# Humoral Immune Responses as Measured by ELISA, wtVNA and psVNA Highly Correlated

wtVNA vs S ELISA Day 239  
(18-55)



S ELISA vs psVNA Day 183  
(18-55)



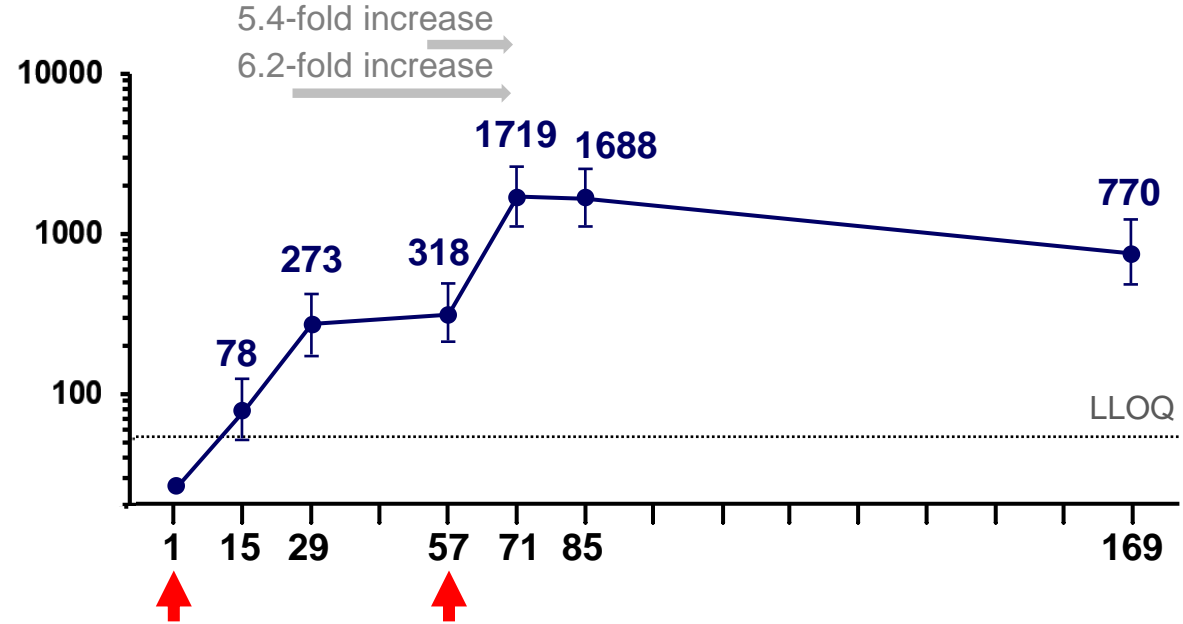
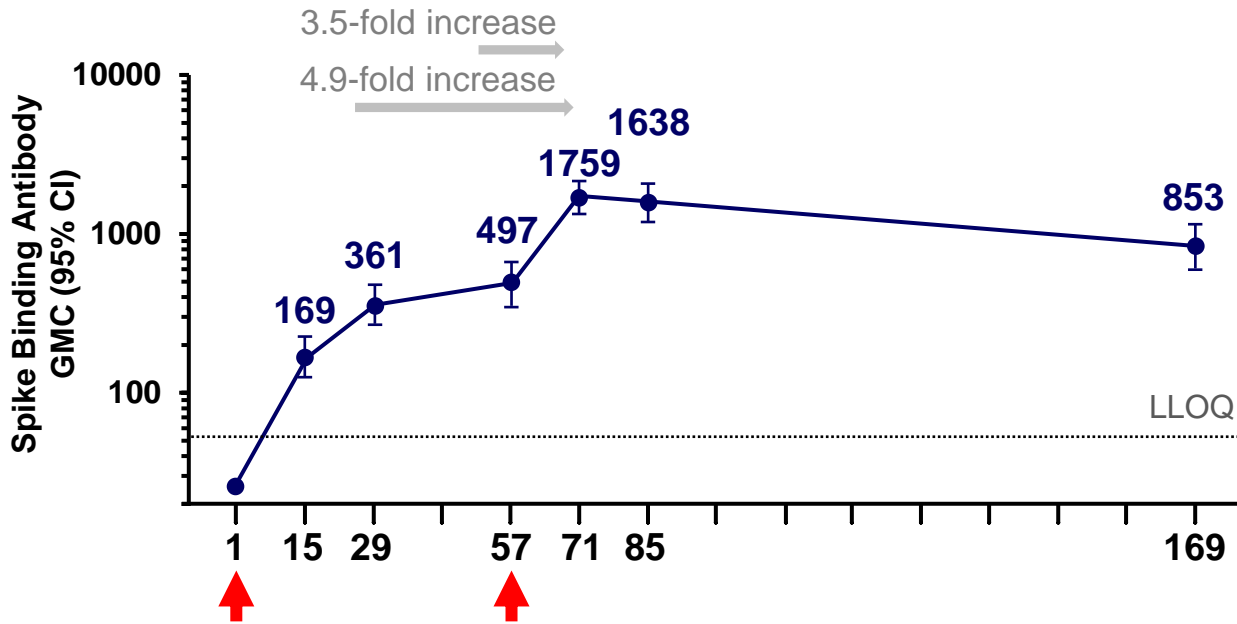
- ✕ Ad26 1e11, Placebo (n = 22)    + Ad26 1e11, Ad26 1e11 (n = 23)
- △ Ad26 5e10, Placebo (n = 22)    ○ Ad26 5e10, Ad26 5e10 (n = 24)

- Ad26 5e10, Ad26 5e10 (n = 17)

# COV2001: Boost at 2 Months Increases Antibody Titers by 3.5- to 6.2-fold

18-55 Years, N=52

≥ 65 Years, N=29

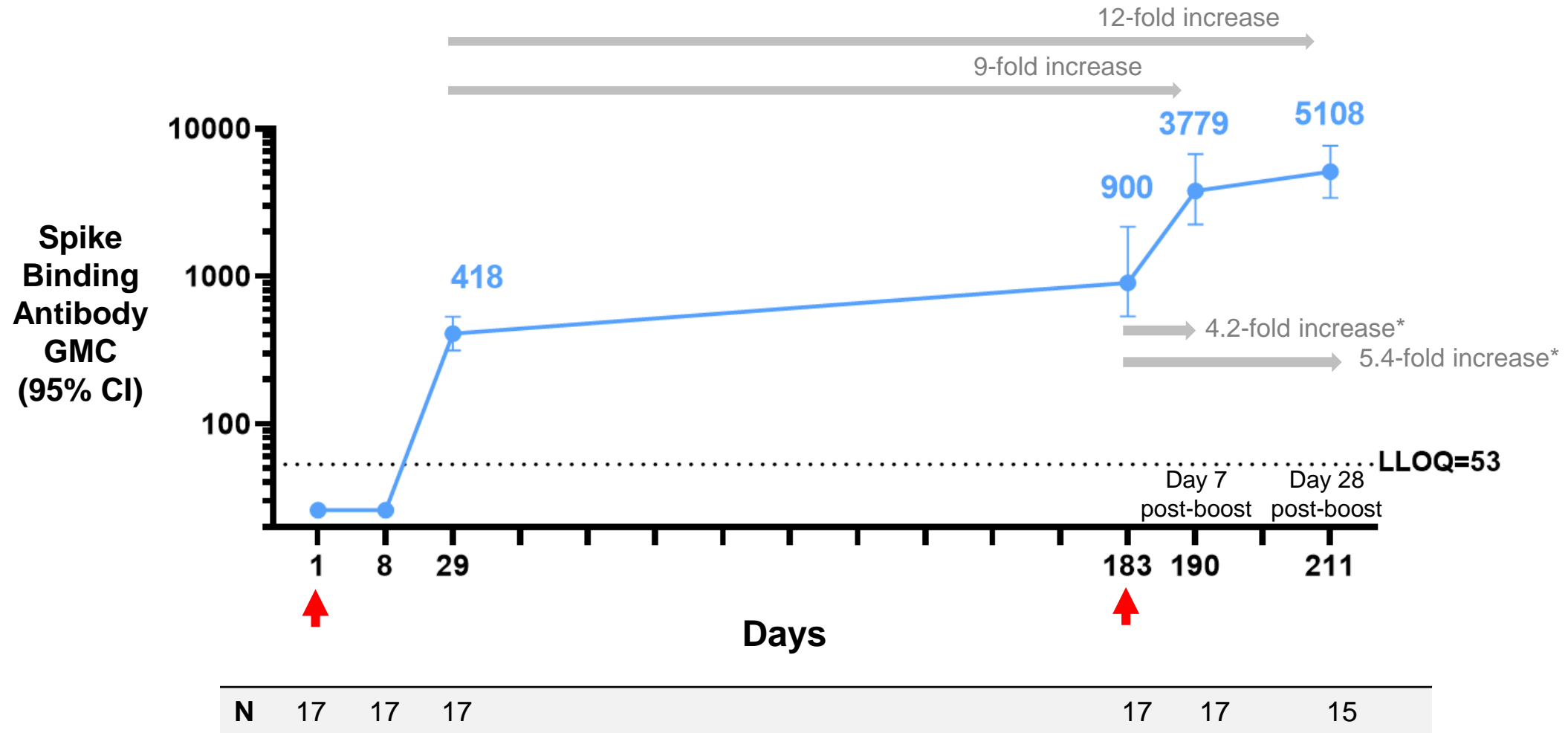


N	52	52	54	54	53	52	50
% responders		86	96	96	100	100	98
% seropositive		89	98	98	100	100	100

N	29	28	29	29	29	28	27
% responders		64	93	97	100	100	96
% seropositive		64	93	97	100	100	96

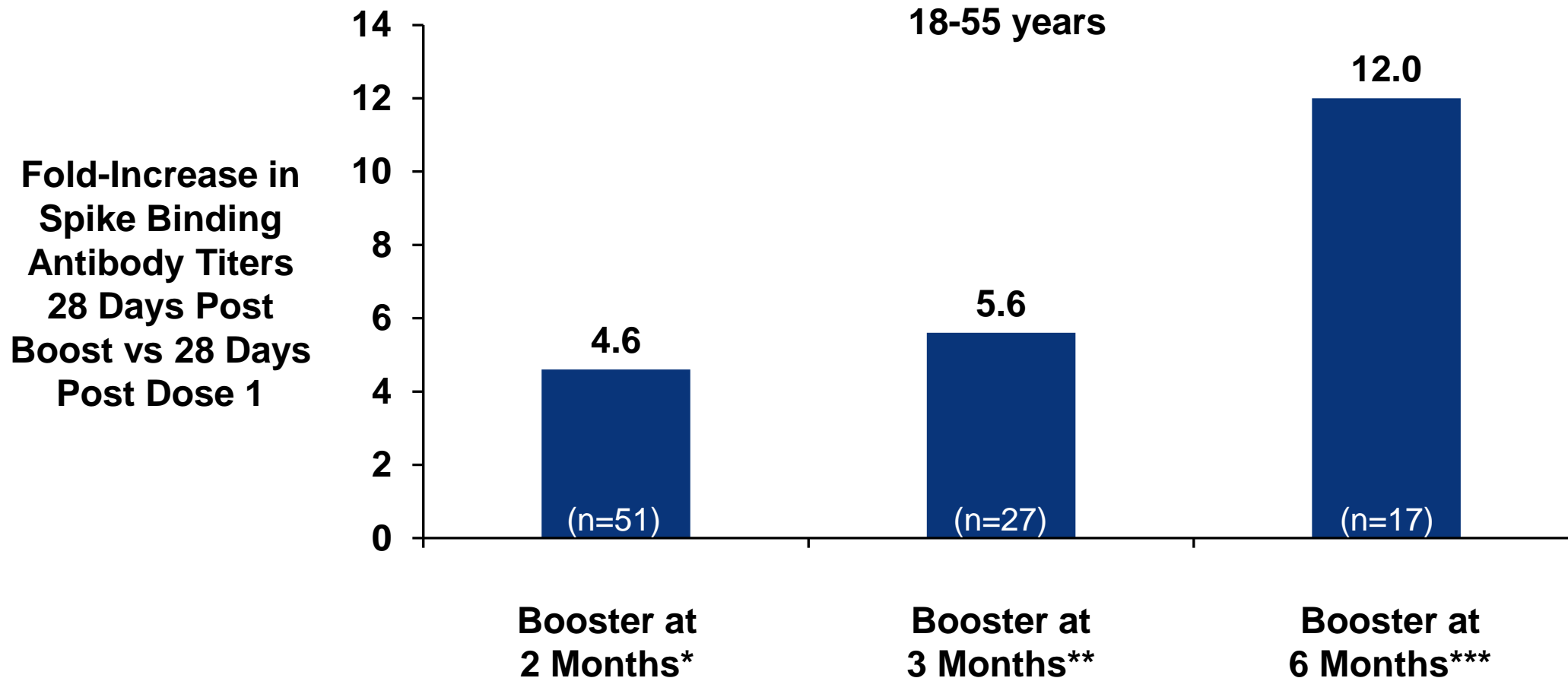
LLOQ = lower limit of quantification

# COV1001: Boost at 6 Months Increases Antibody Titters by 9- to 12-fold





# COV1001 and COV2001: Benefit of Booster Dose Higher When Given at 6 Months or Later



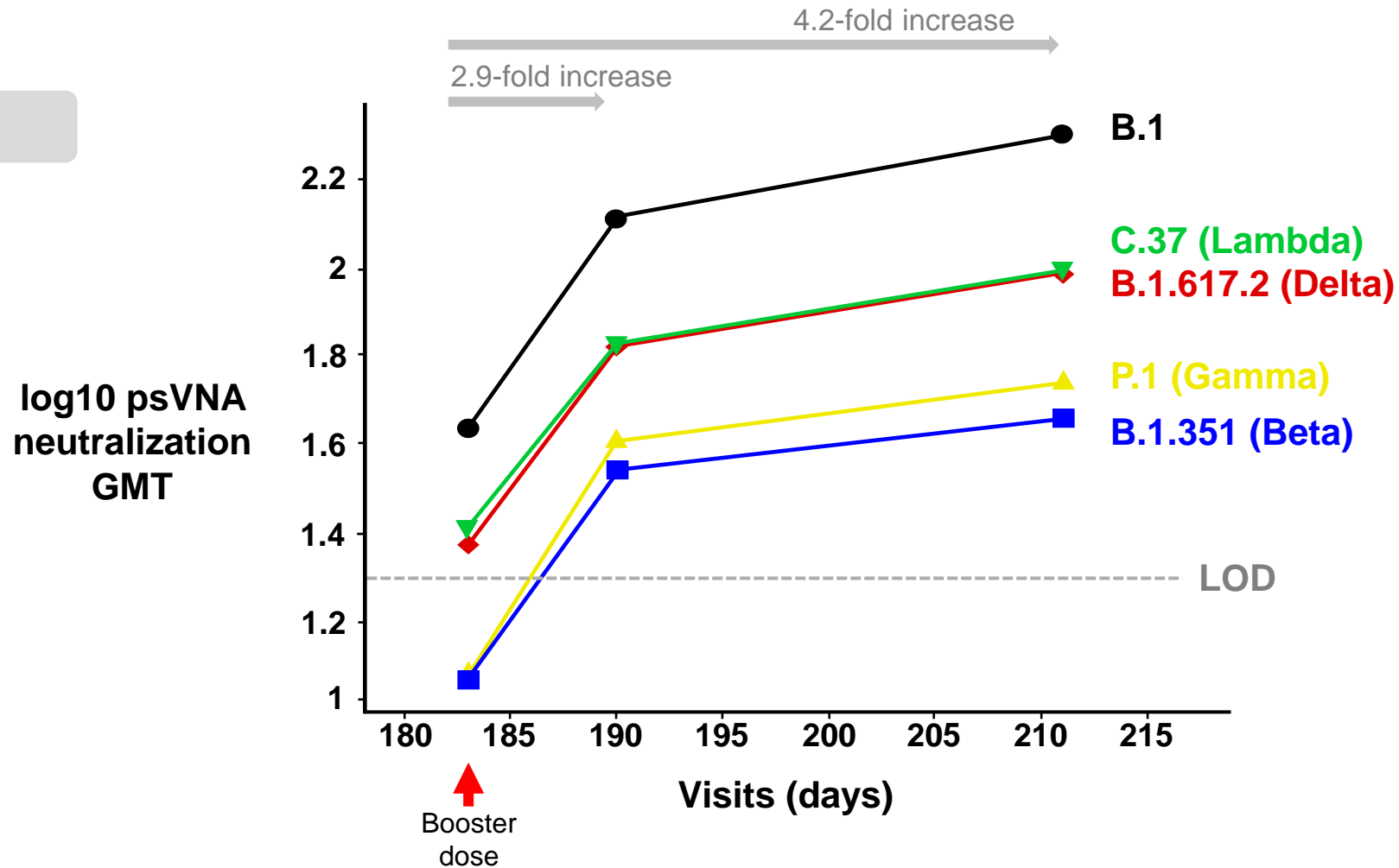
\*Data from COV2001 Group 1

\*\*Data from COV2001 Group 9 / post-dose 1, data from parallel group

\*\*\* Data from COV1001 Cohort 2a

# COV1001: Booster 6 Months After Single-Dose Primary Regimen Proportionally Increases nAb Levels Against Variants of Concern

18-55 Years



Estimated log<sub>10</sub> GMT per visit per strain where titers at LOD of 20 used as values < 20, assuming Gaussian distribution for underlying log<sub>10</sub> titers and calculated in Tobit model with subject, visit, strain and two-way interactions as factors

# Ad26.COV2.S Booster Dose Enhances Immune Response and Individual Protection

- Booster dose at 2 months provided robust anamnestic immune responses
  - More potent when booster administered at 6 months
- Booster dose increased nAbs against variant strains
- Enhanced immune response congruent with higher observed vaccine efficacy in COV3009

# Safety Results of Ad26.COVS Booster

**Macaya Douoguih, MD, MPH**

Head of Clinical Development & Medical Affairs, Vaccines  
Janssen Pharmaceutical Companies of Johnson & Johnson



# Outline for Safety Presentation

- Cumulative exposure to booster dose
- Reactogenicity of booster at 2 months (COV3009)
- Reactogenicity of booster at 6 months (COV1001 & COV2008)
- Safety profile of booster dose at 2 months (COV3009)
- Adverse events of interest / special interest
- Post-authorization safety

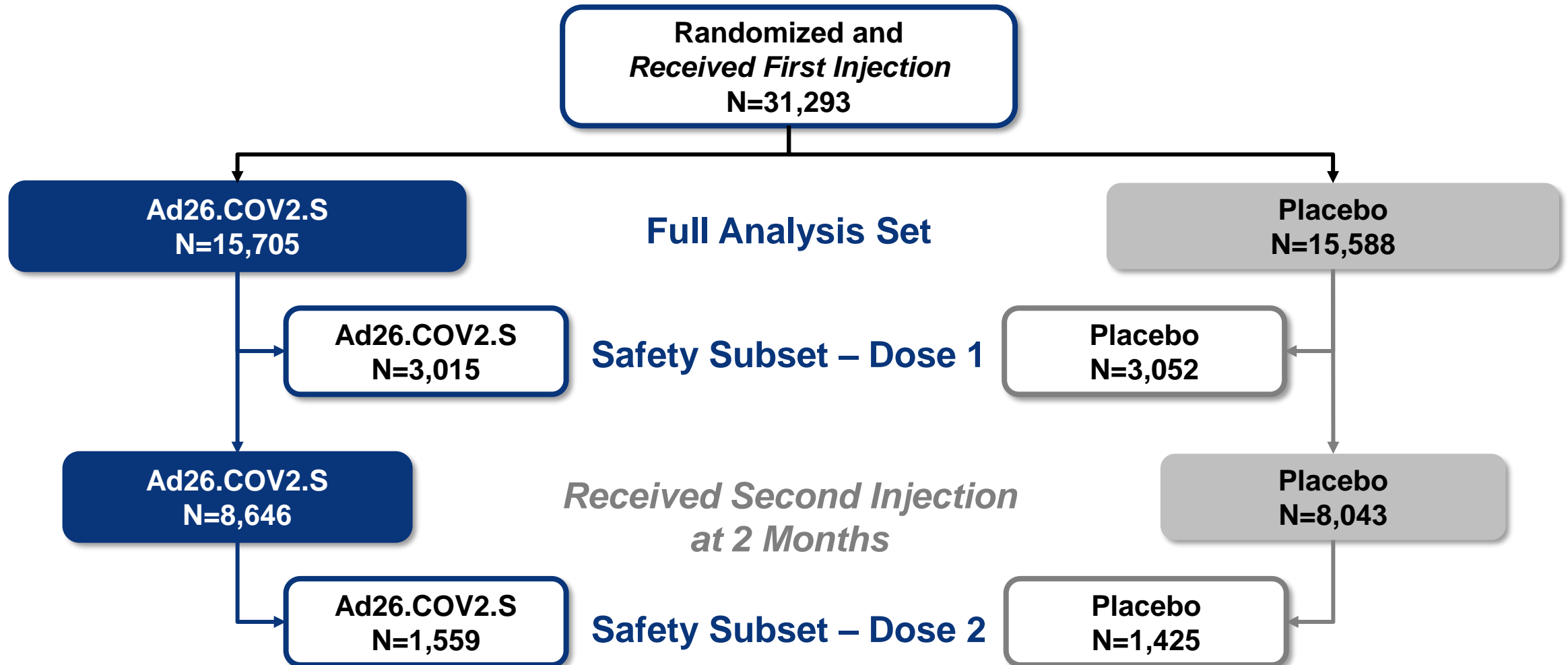
# Cumulative Exposure to Ad26.COVS Booster After Single-Dose Primary Regimen

Study (Dose Level)	Interval Between Primary Regimen and Booster		
	2 months	3 months	≥ 6 months
COV1001 (5 x 10 <sup>10</sup> )	190	77*	19
COV1002 (5 x 10 <sup>10</sup> )	91	0	0
COV2001 (5 x 10 <sup>10</sup> )	137	51	0
COV2008 (5 x 10 <sup>10</sup> )	0	0	127** (blinded)
COV3009 (5 x 10 <sup>10</sup> )	8,655	0	0
<b>Total by Interval</b>	<b>9,073</b>	<b>128</b>	<b>19</b>
<b>Overall Total</b>		<b>9,220</b>	

\*Some participants received second dose with 3-month rather than scheduled 2-month interval because of a study pause

\*\*370 participants received booster in 3:3:1 ratio at dose level of 5 x 10<sup>10</sup>, 2.5 x 10<sup>10</sup>, or 1 x 10<sup>10</sup>. Dose-level data remain blinded

# COV3009: Safety Analysis Sets





# **Reactogenicity of Booster Dose at 2 Months**

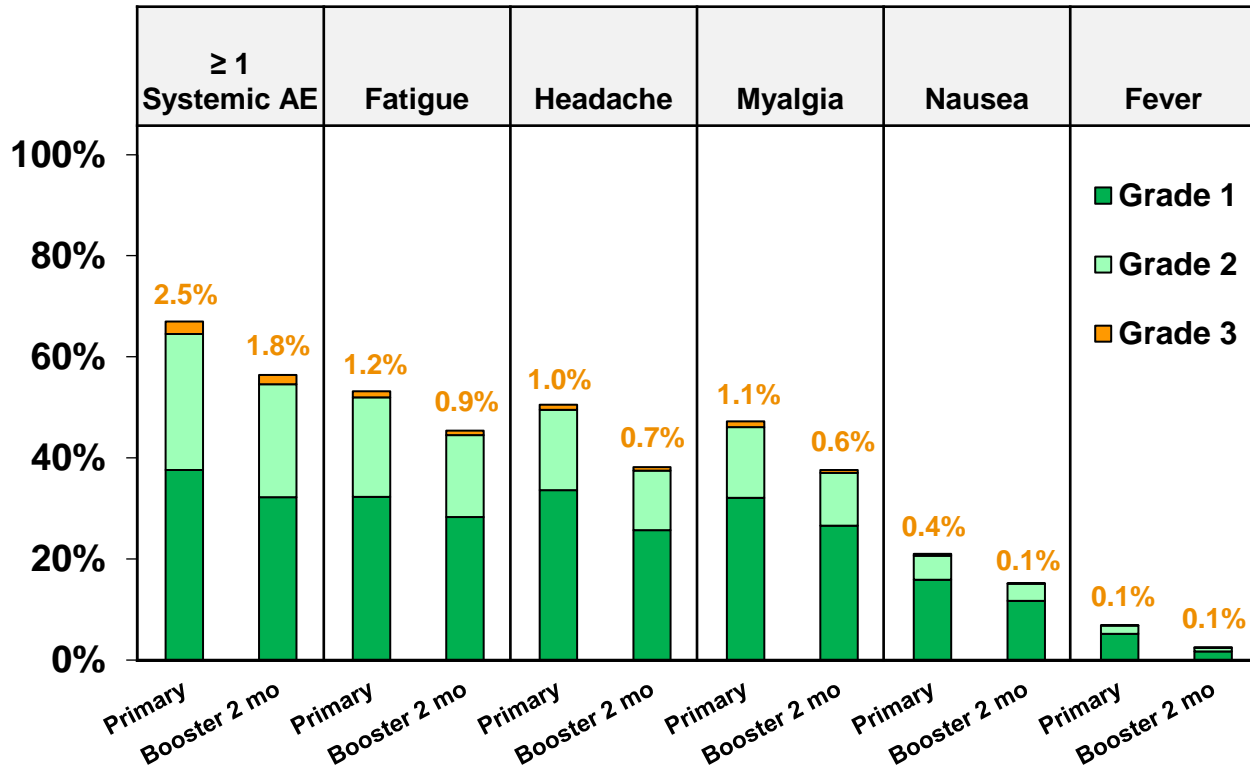
**Study COV3009**



# COV3009: Lower Systemic Reactogenicity with Booster at 2 Months after Primary Dose

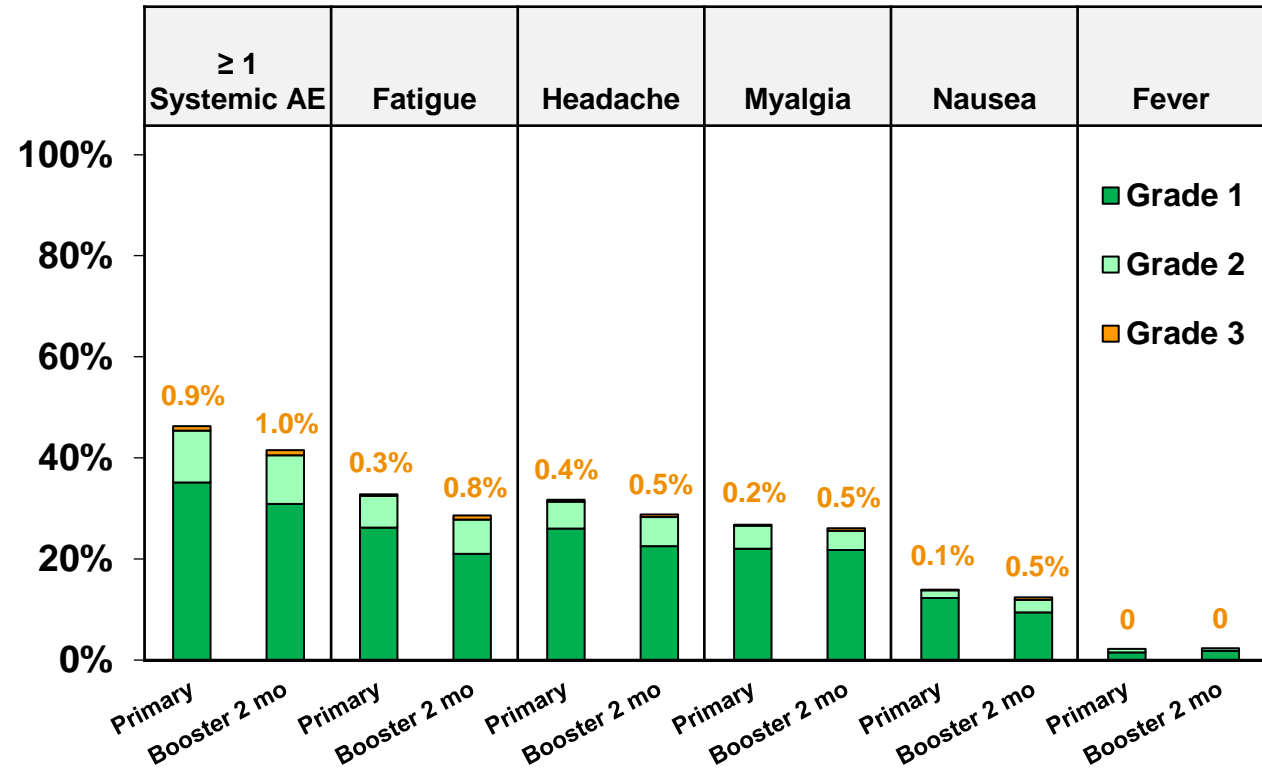
## 18-59 Years

Primary N = 1,784; Booster N = 1,164



## ≥ 60 Years

Primary N = 1,231; Booster N = 395



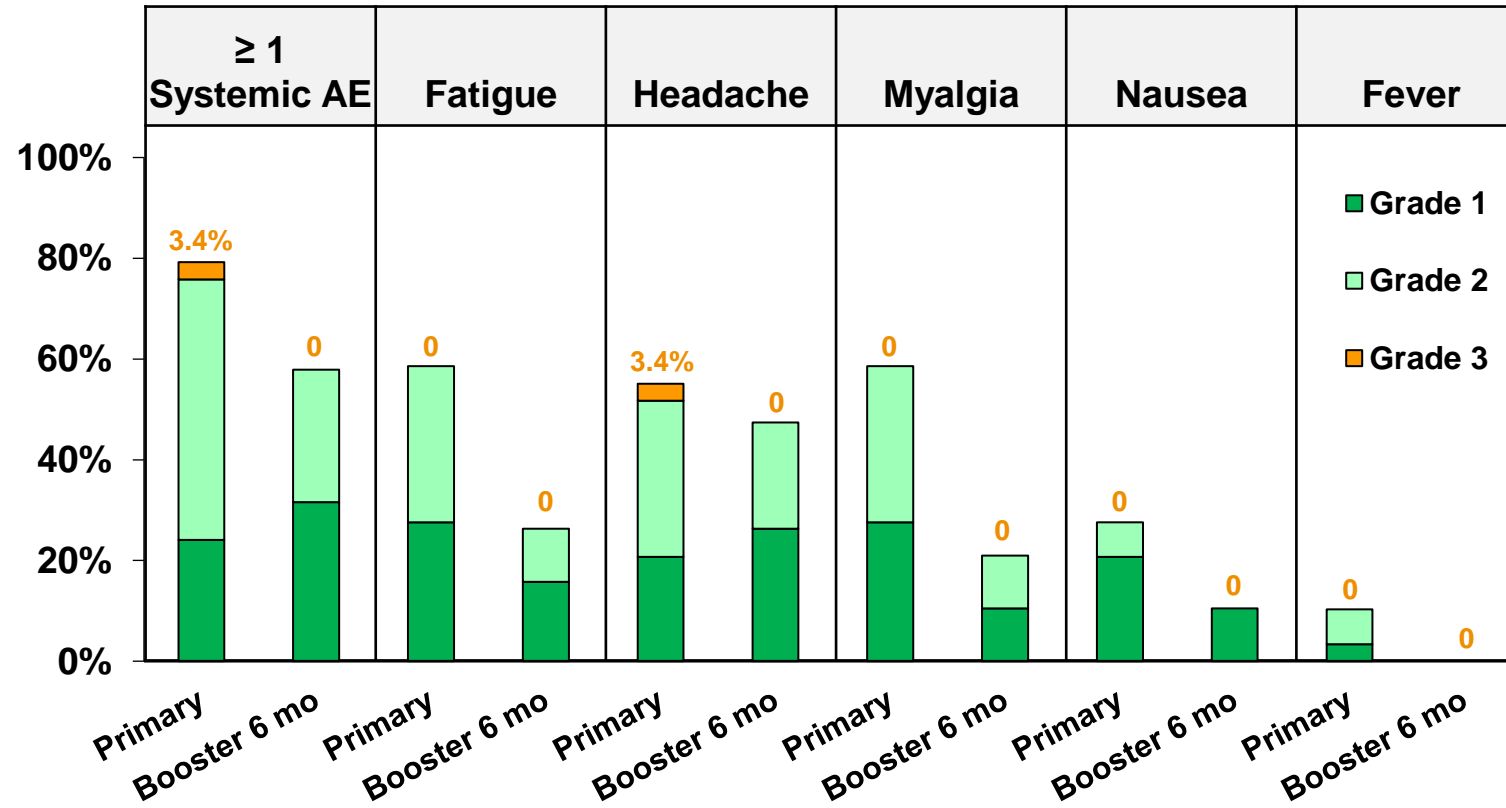


# **Reactogenicity of Booster Dose at 6 Months**

**Study COV1001 and Study COV2008**

# COV1001: Systemic Reactogenicity of Booster at 6 Months vs Primary Dose

**COV1001: 18-55 Years**  
*Primary N = 29; Booster N = 19*



# COV2008: Preliminary Blinded Systemic Reactogenicity of Booster at $\geq 6$ Months

- Ongoing randomized double-blind study of participants enrolled in Study 3001 where three Ad26.COV2.S booster dose levels are being evaluated  $\geq 6$  months following primary vaccination with Ad26.COV2.S
- 127 estimated to have received  $5 \times 10^{10}$  vp
  - Blinded 7-day safety data available on 83 participants (N~32  $\geq 60$  years)
- Dose-level data remain blinded; however, no Grade 3 systemic reactogenicity events have been reported



# **Unsolicited Adverse Events**

**Study COV3009**

# COV3009: Similar Rates of Unsolicited AEs Between Groups

	Ad26.COV2.S		Placebo	
<b>Safety Subset – Dose 1</b>	<b>N = 3,015</b>		<b>N = 3,052</b>	
Any AE	454	15.1%	332	10.9%
<b>Safety Subset – Dose 2</b>	<b>N = 1,559</b>		<b>N = 1,425</b>	
Any AE	159	10.2%	120	8.4%
<b>Full Analysis Set (FAS)</b>	<b>N = 15,705</b>		<b>N = 15,588</b>	
Any MAAE	1033	6.6%	1003	6.4%
Any SAE	104	0.7%	136	0.9%
Non-COVID-19-related	98	0.6%	104	0.7%
Any death*	4	< 0.1%	13	0.1%
COVID-19-related	0	0	6	< 0.1%

\*Reported through June 25, 2021





# **Adverse Events of Interest/Special Interest**

**Study COV3009**

# COV3009: Potential Cases of Thrombosis with Thrombocytopenia Syndrome (TTS)

- Two cases of thrombosis with thrombocytopenia during follow-up
  - **Ad26.COV2.S:** DVT with thrombocytopenia on Day 100 post-vaccination
  - **Placebo:** DVT (Day 27) and PE (Day 29) with thrombocytopenia
  - **Neither case definitive TTS based on CDC criteria**
    - Tier 1: thrombosis in unusual location with thrombocytopenia; anti-PF4 supportive
    - Tier 2: thrombosis with thrombocytopenia in more common site with positive anti-platelet 4 antibody





# Potential TTS Events After Second Dose of Another Adenoviral COVID-19 Vaccine

- Medicines and Healthcare products Regulatory Agency (MHRA) post-marketing surveillance in United Kingdom (Yellow Card scheme)
- AstraZeneca COVID-19 vaccine doses administered in UK as of September 29, 2021
  - Dose 1: 24.9 million
  - Dose 2: 24.0 million
- Estimated rate of blood clots with concurrent low platelets
  - Dose 1 (or unknown): **15.1** cases per million (375 cases)
  - Dose 2: **1.9** cases per million (24 cases)
- Overall case fatality rate: 17% (66 deaths after first dose, 6 deaths after second dose)
- MHRA interpretation: *“no indication of an increased risk of these events after the second dose in any age group”*

# COV3009: No Increase in Other Adverse Events of Interest with Booster Dose

Adverse Event of Interest	Within 28 Days of Primary Dose		Within 28 Days of Booster Dose	
	Ad26.COV2.S (N=15,705)	Placebo (N=15,588)	Ad26.COV2.S (N=8,646)	Placebo (N=8,043)
<b>Embolic and thrombotic events (SMQ)</b>	2 (< 0.1%)	6 (0.1%)	3 (< 0.1%)	3 (< 0.1%)
<b>Convulsions/seizures</b>	0	0	0	0
<b>Tinnitus</b>	4 (< 0.1%)	2 (< 0.1%)	2 (< 0.1%)	2 (< 0.1%)
<b>Guillain-Barre Syndrome</b>	0	0	0	0
<b>Facial paralysis</b>	1 (< 0.1%)	2 (< 0.1%)	1 (< 0.1%)	0
<b>Arthritis</b>	24 (0.2%)	12 (0.1%)	4 (< 0.1%)	5 (0.1%)





# Post-Authorization Safety

# Global Exposure of Ad26.COV2.S as of Aug 31, 2021

- Total number of Ad26.COV2.S vaccines administered: 33,584,049
  - US: 14,358,641
  - EEA: 13,585,015
  - Rest of World: 5,640,393

# Post-Authorization Safety

Since EUA, three major events have been added to US Prescribing Information and fact sheets based primarily on post-authorization spontaneous reports

- Thrombosis with thrombocytopenia
  - Warnings and Precautions and Adverse Reactions during post-authorization use sections
- Guillain-Barre Syndrome
  - Warnings and Precautions and Adverse Reactions during post-authorization use sections
- Capillary Leak Syndrome
  - Adverse Reactions during post-authorization use section

# Reported Post-Authorization Cases of Thrombosis with Thrombocytopenia Globally

- 193 post-authorization reports globally
  - US: 133    EEA: 54    Rest of World: 6
- 73 cases meeting CDC Tier 1 or 2 criteria (**2.1 per million doses**)

<b>CDC Criteria for TTS</b>	Tier 1	68
	Tier 2	5
<b>Sex</b>	Female	50
	Male	23
<b>Age (years)</b> Mean: 45.6 Median: 45 Range: 18 to 87	18 to 35	16
	36 to 50	32
	51 to 64	17
	≥ 65	7
	Not reported	1

- Mean (median) time to onset of event: 14 (11) days
- Of 73 cases meeting CDC Tier 1 or 2 criteria, 12 reported fatal outcome

# Reported Post-Authorization Cases of Guillain-Barre Syndrome Globally

- 252 post-authorization reports (**7.5 per million doses**)
  - US: 162    EEA: 69    Rest of World: 21

<b>Sex</b>	Female	90
	Male	158
	Not reported	7
<b>Age (years)</b> Mean: 53.1 Median: 55 Range: 22 to 87	18 to 35	24
	36 to 50	68
	51 to 64	106
	≥ 65	39
	Adult/Not reported	18

- Mean (median) time to onset of event: 36 (14) days
- 1 report of fatal outcome
- Estimated background rate of GBS: 1-5 cases per million<sup>1-4</sup>

\*Demographic table above includes 2 cases from placebo-controlled studies and 1 report from open-label study COV3012

1. Gubernot et al, 2021; 2. Li et al, 2021; 3. Klein et al, 2010; 4. EMA-ACCESS, 2021

# Reported Post-Authorization Cases of Capillary Leak Syndrome (CLS) Globally

- 7 post-authorization reports, all spontaneous (**0.2 per million doses**)
  - US: 2    EEA: 5:    Rest of World: 0

<b>Sex</b>	Female	4
	Male	3
<b>Age (years)</b> Mean: 62.1 Median: 55 Range: 50 to 92	18 to 35	0
	36 to 50	1
	51 to 64	3
	≥ 65	3

- Mean (median) time to onset of event: 1.3 (1) days
- Outcome reported in 6 cases: fatal (4), not resolved (1), resolving (1)



# Ongoing Post-Authorization Safety Evaluation of Ad26.COV2.S

- Events added as important potential risks in Pharmacovigilance Plan
  - Venous thromboembolism
  - Immune thrombocytopenia
- Events being evaluated by Sponsor as part of pharmacovigilance activities
  - Myocarditis / pericarditis, cardiomyopathy, acute hepatic failure, acute disseminated encephalomyelitis, transverse myelitis, autoimmune disorders, vasculitis
- Totality of post-authorization safety and efficacy data to date continue to support a positive benefit-risk

# Conclusions on Safety of Homologous Boost of Ad26.COV2.S

- Similar reactogenicity and safety profile for homologous boost at 2 or 6 months vs single-dose primary regimen
  - Local AEs similar regardless of booster timing
  - Systemic AEs lower with booster at 6 months than 2 months
- No new safety signals for AEs, SAEs, or AEs of interest with booster
- Global surveillance suggests rare TTS events with viral vector vaccine are less frequent with second dose than first dose
- Ongoing and planned post-approval studies will be revised to incorporate follow-up of booster in addition to primary doses

# Conclusion

**Johan Van Hoof, MD**

Managing Director Janssen Vaccines and Prevention, BV  
Janssen Pharmaceutical Companies of Johnson & Johnson



# Totality of Data Support Safety, Efficacy of Homologous Booster Dose of Ad26.COVS



## Immunogenicity

### Humoral responses persisted after a single-dose of Janssen vaccine

- Distinct immunologic profile
- Base of protection includes nAbs, functional antibodies, cell-mediated immune response



## Vaccine Efficacy

### Administration of booster dose results in greater protection against COVID-19

- At 2 months, 2.5 fold titer increase after booster translates into 20-25% higher efficacy
- Efficacy against symptomatic infection boosted to 94% in US



## Safety

### Booster dose safe and well tolerated

- Large amount of randomized safety data, >9,000 exposures



## Boost

Homologous booster dose with Ad26.COVS preferred over heterologous boost

# Homologous Boost with Ad26.COVS Helps Further Protect Individuals from COVID-19

- Optimize immune responses
- Increase protection against symptomatic infection
- Prepare for future variants of concern
- Potentially help to reduce transmission

## Proposed dosing

- *A booster dose is recommended at 6 months or later, based on the strength of the immune responses, although a booster dose may be administered as early as 2 months*
- *The need for a booster dose and/or its timing will depend on the local/epidemiological situation and the needs of individuals/specific populations*

# Emergency Use Authorization (EUA) Amendment for a Booster Dose for the Janssen COVID-19 Vaccine (Ad26.COV2.S)

Janssen Pharmaceutical Companies of Johnson & Johnson

Vaccines and Related Biological Products Advisory Committee  
October 15, 2021