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

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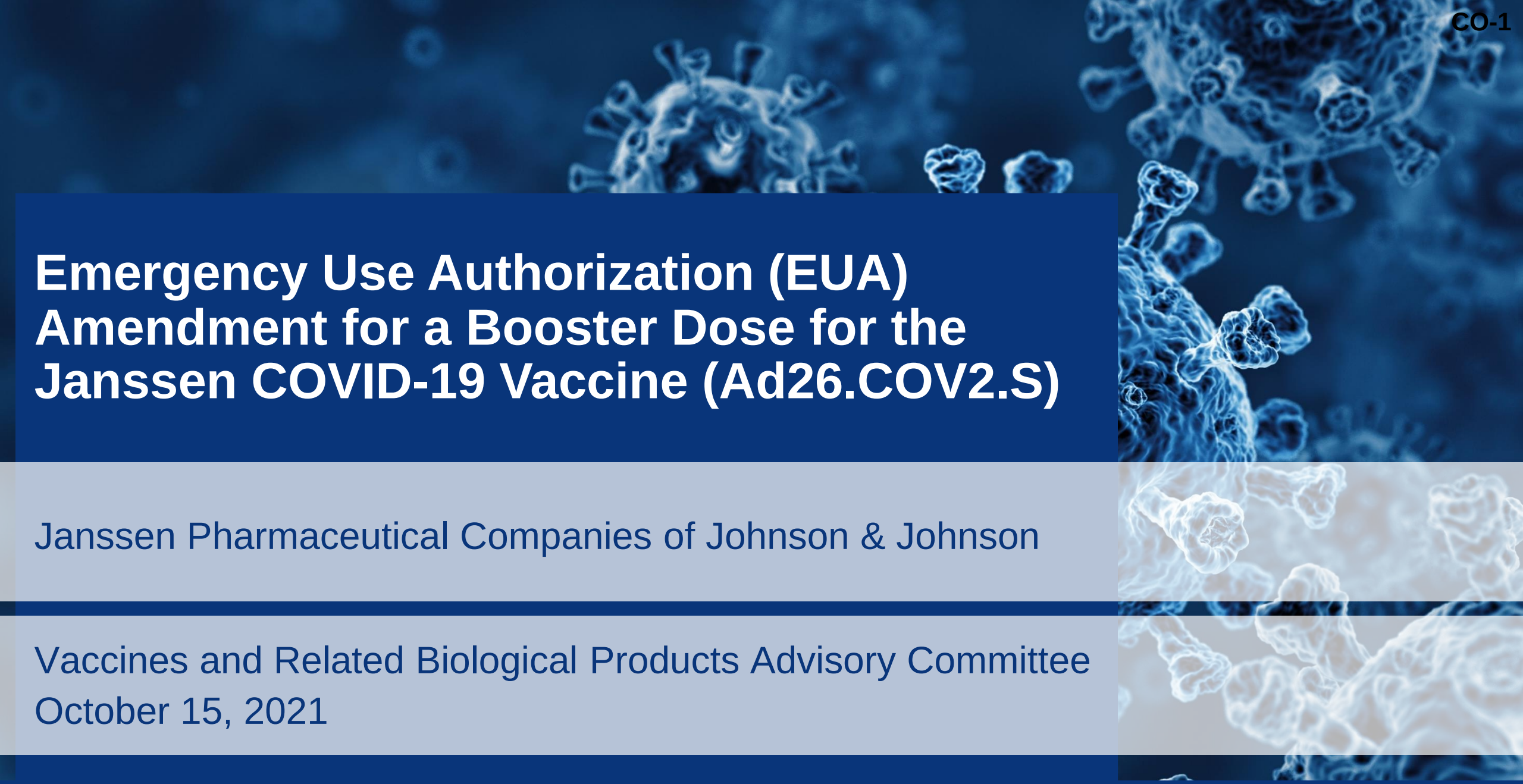


Emergency Use Authorization (EUA) Amendment for a Booster Dose for the Janssen COVID-19 Vaccine (Ad26.COV2.S)

Janssen Pharmaceutical Companies of Johnson & Johnson

Vaccines and Related Biological Products Advisory Committee
October 15, 2021

janssen
PHARMACEUTICAL COMPANIES OF
Johnson & Johnson

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*

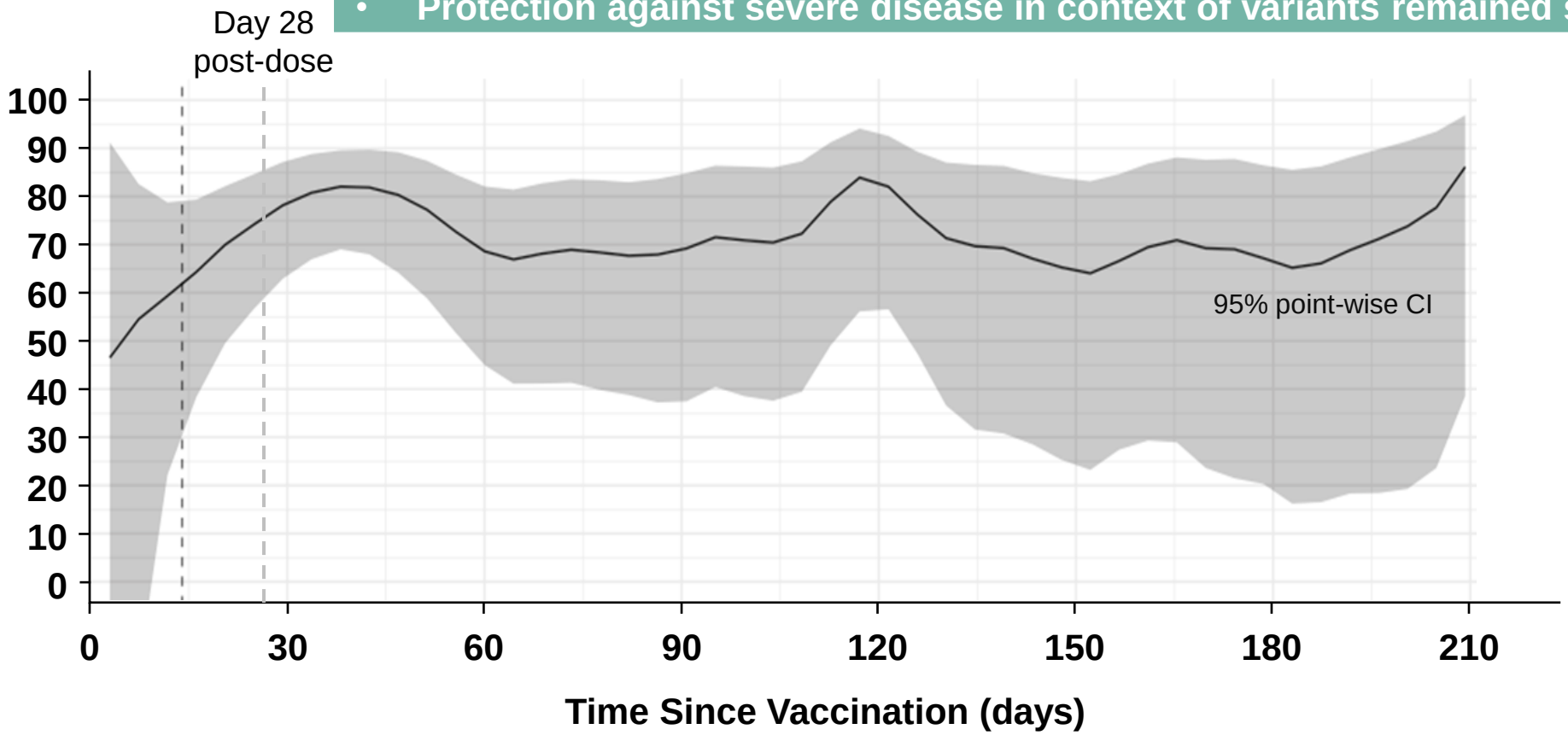
- Following EUA, study protocol amended to unblind participants, allow participants in placebo arm to receive Janssen vaccine
- Regional differences in duration of double-blind period
- Median follow up: 4 months
  - 23% of participants had follow up of ≥ 6 months
- SARS-CoV-2 incidence highly variable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

3001

*Data cut off date of July 9, 2021

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

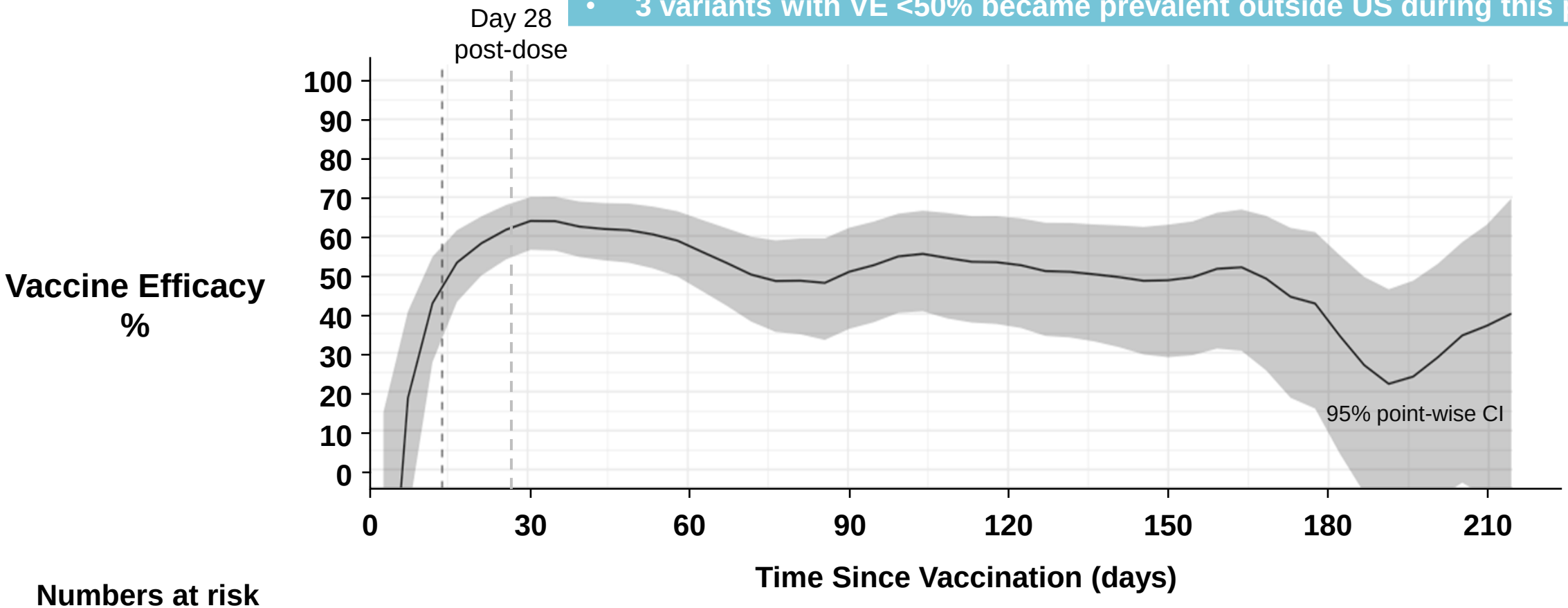
Ad26.COV2.S	19562	19230	17764	15591	10284	5432	4045	1307
Placebo	19589	19134	17521	15202	9815	5046	3796	1260

3001

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



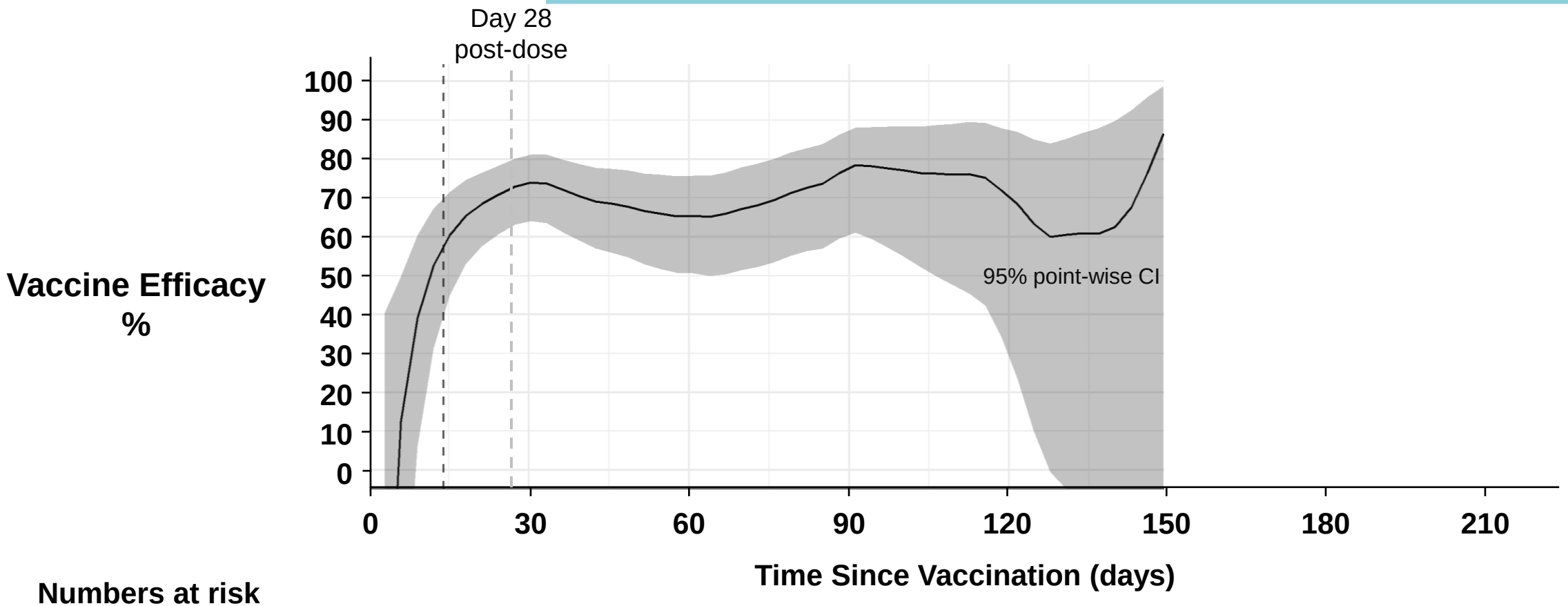
Numbers at risk								
Ad26.COV2.S	19562	19111	17540	15290	10033	5256	3887	1193
Placebo	19589	18902	17052	14622	9328	4745	3531	1098

3001

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

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								
Ad26.COV2.S	9153	8797	17553	6130	3180	1180	446	153
Placebo	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.COV2.S vaccine, **but no data on Delta in US**
- Published **RWE studies** (1-9) report range of vaccine effectiveness estimates for Ad26.COV2.S
  - **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 <u>vaccine effectiveness over time in US clinical practice</u> with focus on <u>Delta Variant*</u> (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

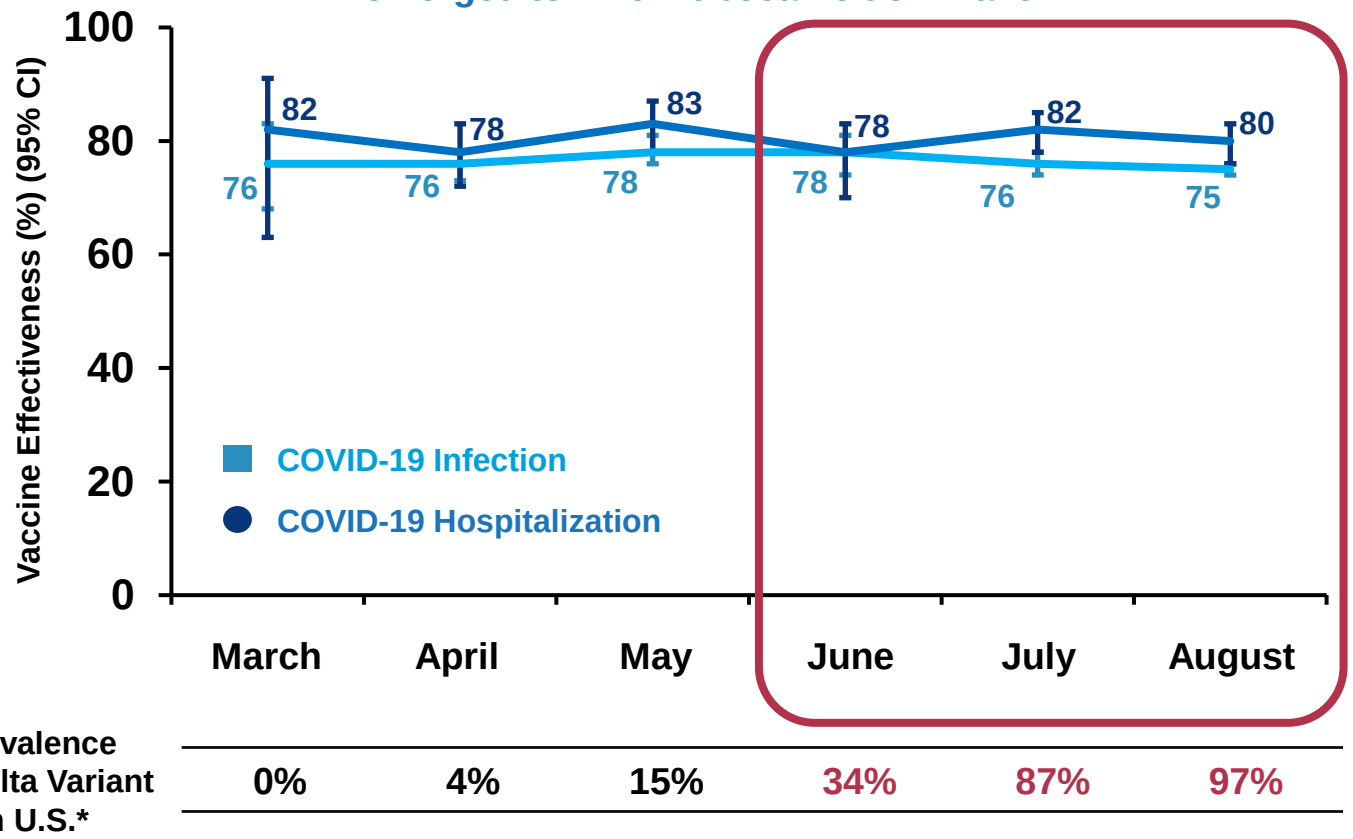
Janssen-Aetion RWE Study*

- **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***

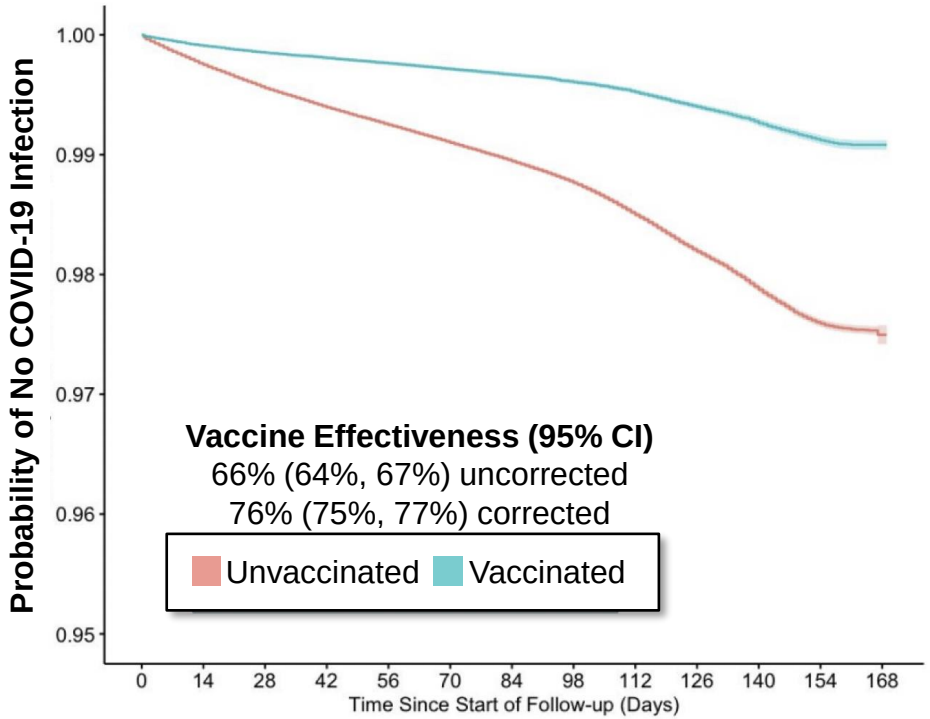
*Polinski et al. . https://www.medrxiv.org/content/10.1101/2021.09.10.21263385v1 - analysis till July 31, 2021; updated analysis till Aug 31st, 2021 presented here **COPD, CF, HIV, HTN, Liver Disease, Malignancies, Asthma, Cerebrovascular disease, CKD, Mod-Severe Asthma, PF, Obesity, Serious Heart conditions, 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



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



Covid-19 Infections

*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

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

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.COV2.S Induced Immune Responses

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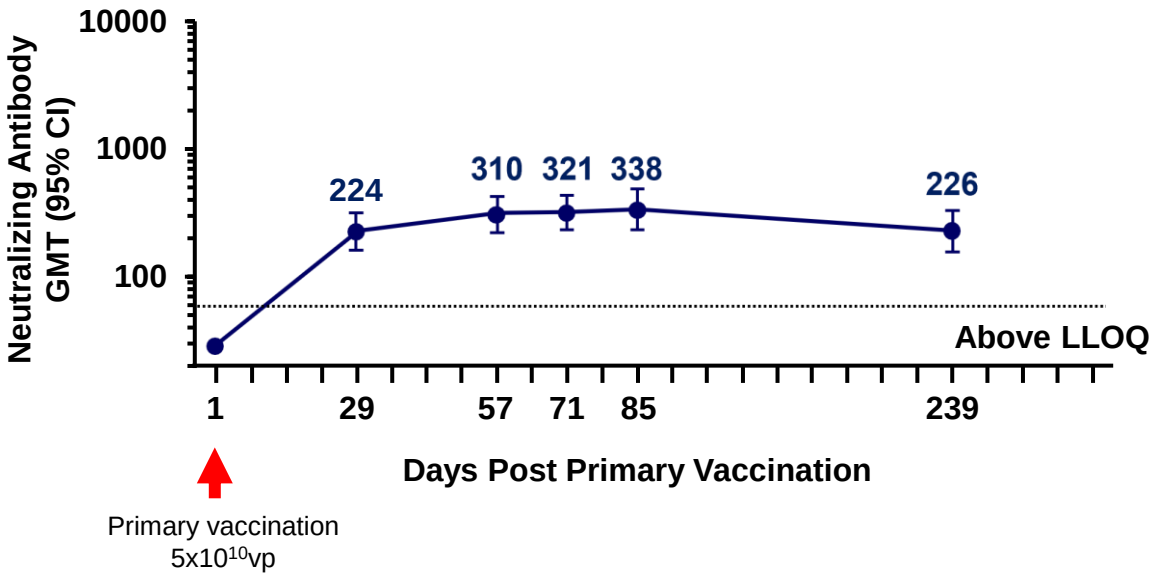
Professor of Medicine
Harvard Medical School
Director, Center for Virology and Vaccine Research
Beth Israel Deaconess Medical Center

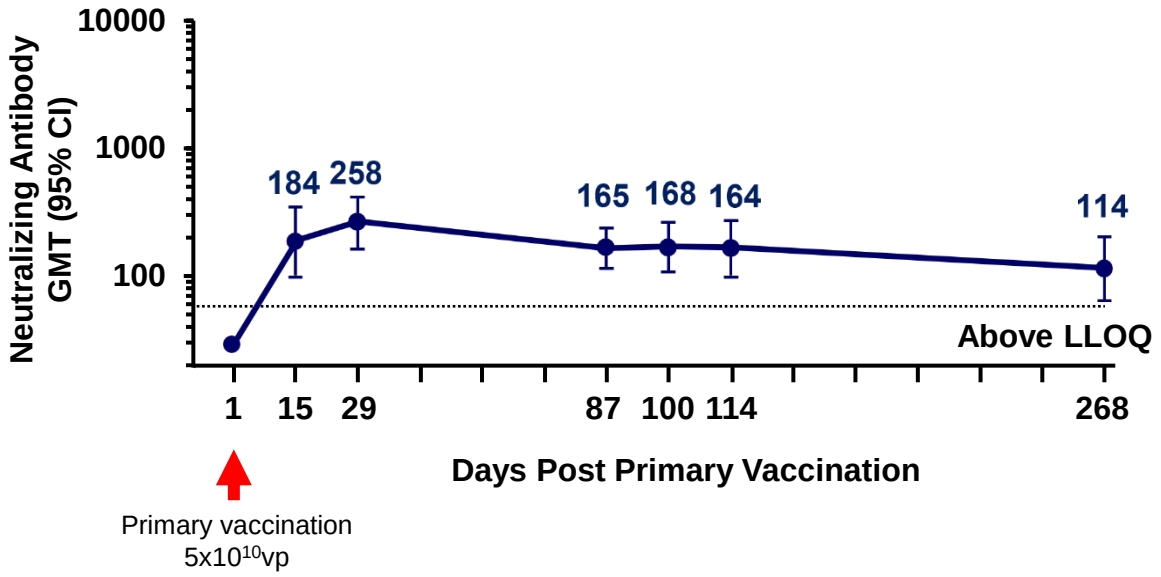
Janssen COV1001: Humoral Immune Responses Persist Over Time, Following a Single Dose (18-55 and ≥ 65 years)

18-55 Years, N=25



N	25	24	25	24	24		22
% Responders		96					
% Detectable antibodies			100	100	100		95

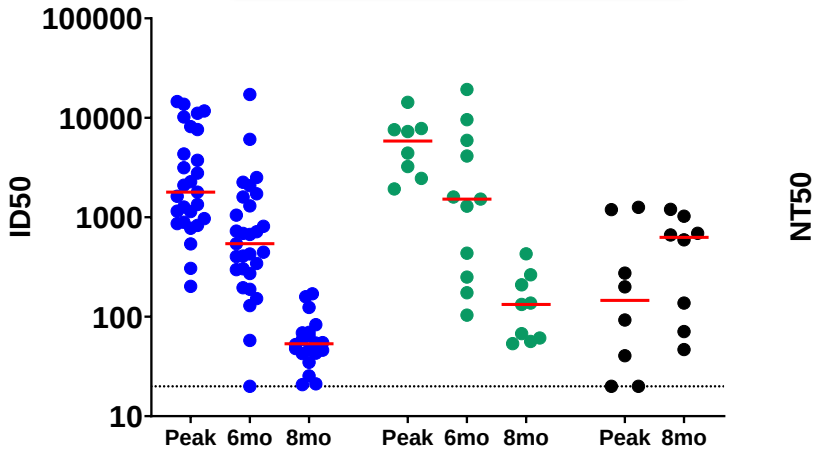
≥ 65 Years, N=24



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

Ad26.COV2.S Induces Durable Antibody Responses

Live Virus nAb

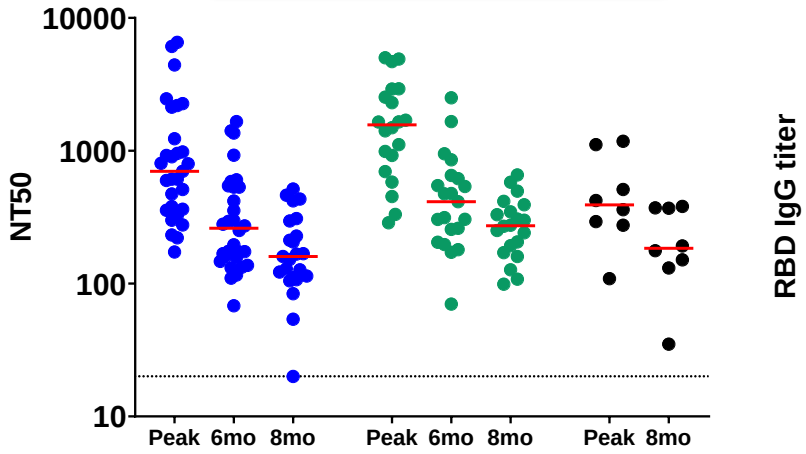


Peak	6mo	8mo	Peak	6mo	8mo	Peak	8mo
1789	543	53	5858	1524	133	146	629

Fold Change (Peak to 8 months)

- 34	**- 44**	**+ 4.3**

Pseudovirus nAb

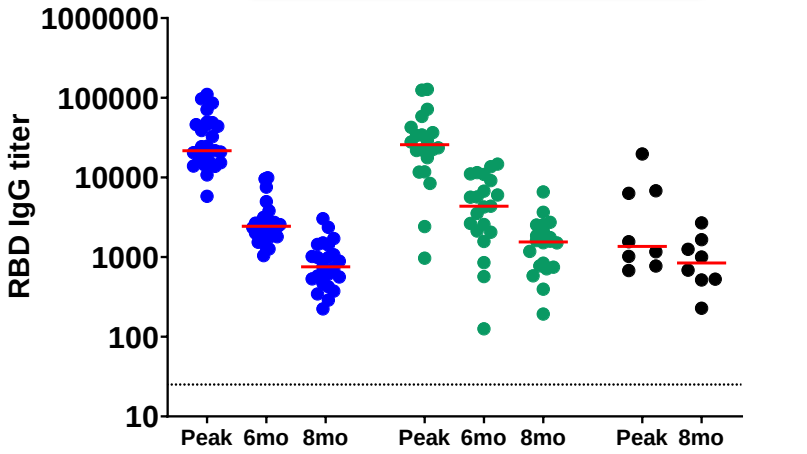


Peak	6mo	8mo	Peak	6mo	8mo	Peak	8mo
700	262	160	1569	414	273	391	185

Fold Change (Peak to 8 months)

- 4.5	**- 5.7**	**- 2.1**

RBD IgG



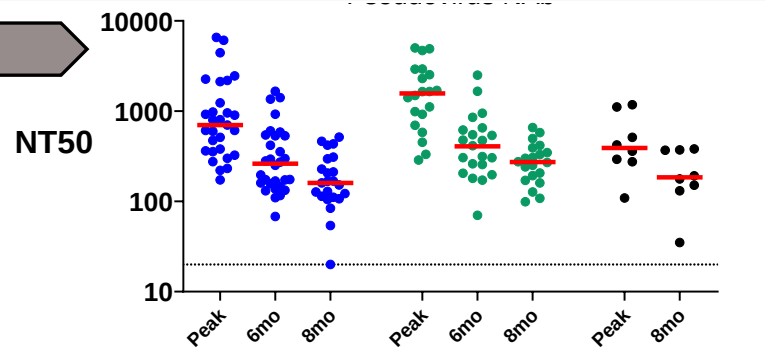
Peak	6mo	8mo	Peak	6mo	8mo	Peak	8mo
21564	2432	755	25677	4346	1546	1361	843

Fold Change (Peak to 8 months)

- 29	**- 17**	**- 1.6**

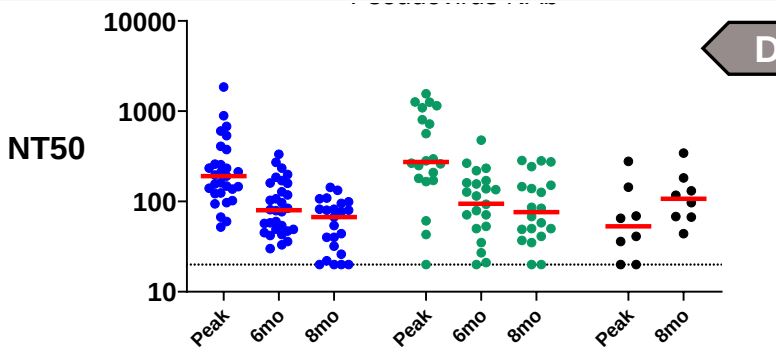
Ad26.COV2.S Induces Durable Neutralizing Antibody Responses Against SARS-CoV-2 Variants

WA1/2020



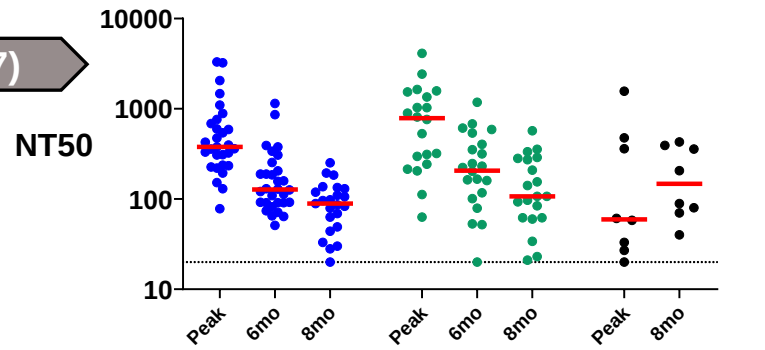
	BNT162b2			mRNA-1273			Ad26.COV2.S	
n	29	30	23	20	21	20	8	8
	Peak	6mo	8mo	Peak	6mo	8mo	Peak	8mo
	700	262	160	1569	414	273	391	185

Delta (B.1.617.2)



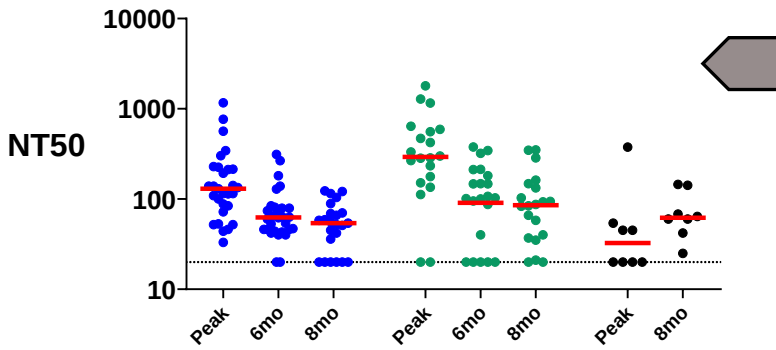
	BNT162b2			mRNA-1273			Ad26.COV2.S	
n	29	30	23	20	21	20	8	8
	Peak	6mo	8mo	Peak	6mo	8mo	Peak	8mo
	191	80	67	274	115	76	53	107

Alpha (B.1.1.7)



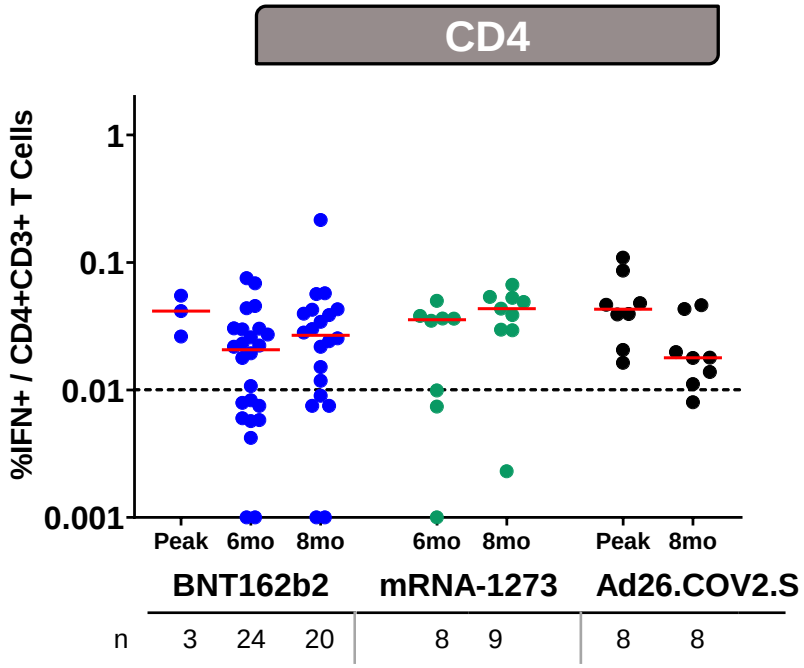
	BNT162b2			mRNA-1273			Ad26.COV2.S	
n	29	30	23	20	21	20	8	8
	Peak	6mo	8mo	Peak	6mo	8mo	Peak	8mo
	378	128	89	786	223	107	60	148

Beta (B.1.351)

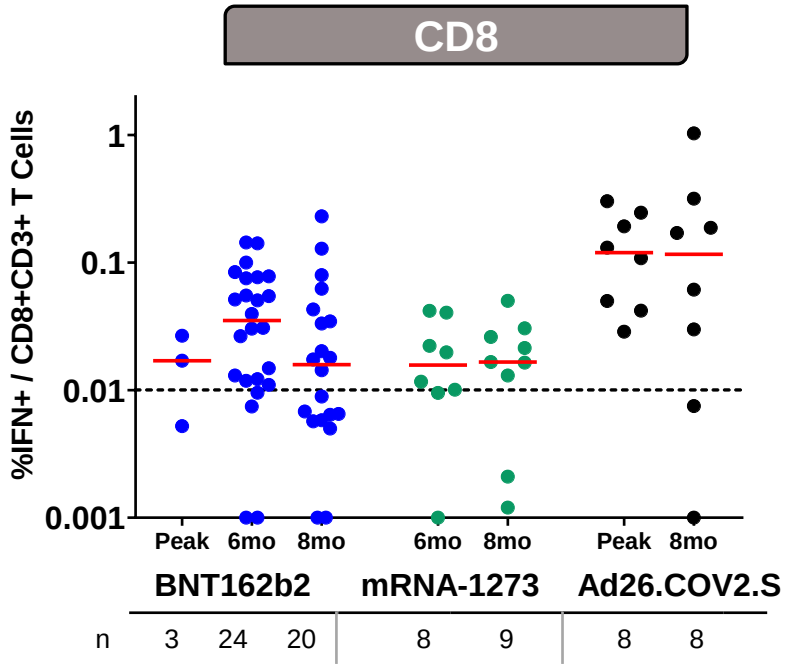


	BNT162b2			mRNA-1273			Ad26.COV2.S	
n	29	30	23	20	21	20	8	8
	Peak	6mo	8mo	Peak	6mo	8mo	Peak	8mo
	130	63	54	293	103	86	33	62

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 ≥ 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

Collier et al. NEJM. October 15, 2021; Barouch et al. NEJM 2021; Alter et al. Nature 2021; McMahan et al. Nature 2021

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

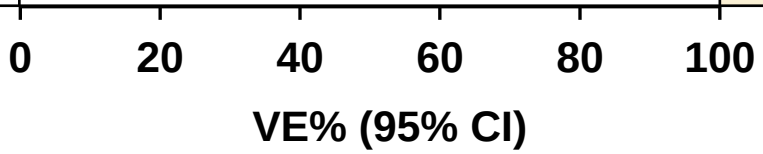
COV3009: Evaluated Efficacy of Ad26 Following Administration of Booster 2 Months After First Shot

- 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 ≥ 60 years
- Median follow-up after booster dose: 36 days (0 to 172 days)
  - 29% (n > 4245) of participants had follow up ≥ 2 months

*Per Protocol data set

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

Country	Post-dose	Study Day	Symptomatic COVID-19 Ad26.COV2.S vs Placebo	VE (95% CI)
United States	3001: Post-dose 1	Day > 28		**70%** (61, 77)
	3009: Post-booster	Day > 71		**94%** (59, 100)
Global* (All)	3001: Post-dose 1	Day > 28		**53%** (47, 58)
	3009: Post-booster	Day > 71		**75%** (55, 87)



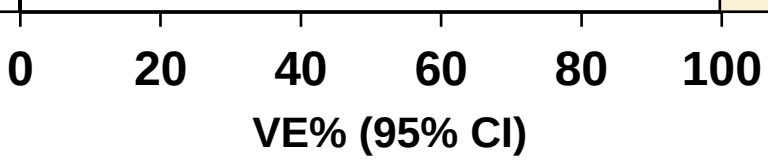
3001

3009

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)

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

Variant	Post-dose	Study Day	Symptomatic COVID-19 Ad26.COV2.S vs Placebo	VE (95% CI)
Alpha (B.1.1.7)	**3001: Post-dose 1**	**Day > 28**		**70%** (35, 88)
	3009: Post booster	**Day > 71**		**94%** (63, 100)
Mu (B.1.621)	**3001: Post-dose 1**	**Day > 28**		**36%** (2, 59)
	3009: Post booster	**Day > 71**		**63%** (-28, 92)



3001

3009

3001 Final analysis cutoff date: July 2021; 3009 Final analysis cutoff date: June 2021

COV3009: Protection Against Severe Outcomes

PP At Risk Set *Global*	> Day 71 (> 14 Days Post-Booster) **Ad26.COV2.S** (N = 6,024)	 **Placebo** (N = 5,615)	 **VE %** (95% CI)
Severe COVID-19	**0**	**8**	**100%** (33, 100)
COVID-19-related hospitalization	**0**	**5**	*N/A*
COVID-19-related death	**0**	**1**	*N/A*

3009 Final analysis cutoff date: June 24, 2021

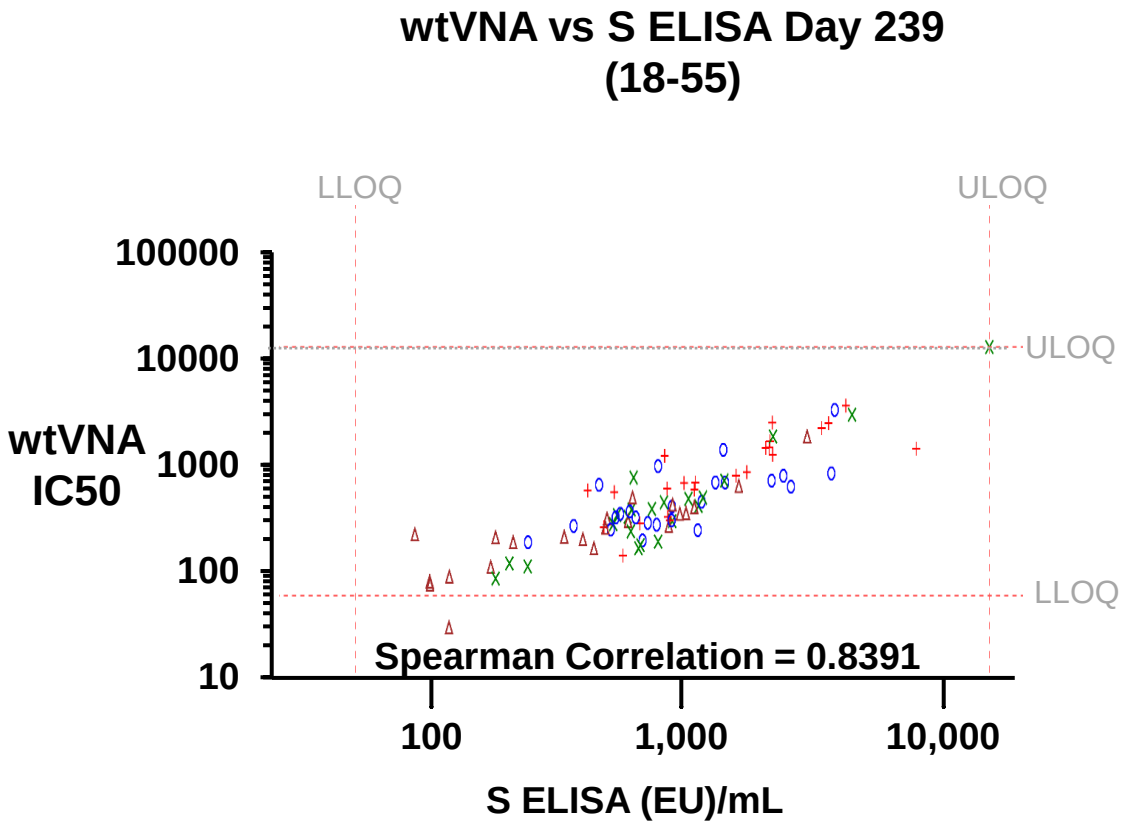
Immunogenicity Following Booster Dose of Ad26.COV2.S

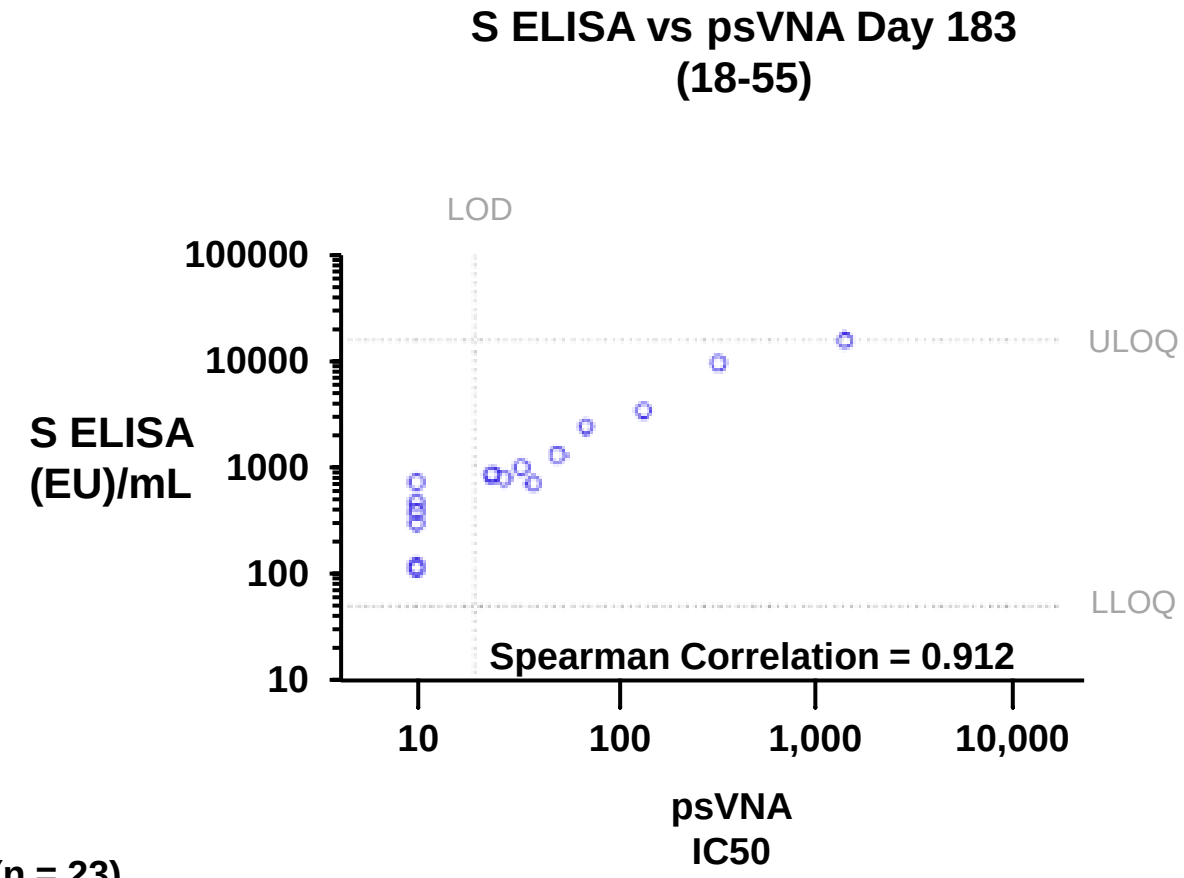
Clinical Immunogenicity Studies Supporting Ad26.COV2.S Booster Dose

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





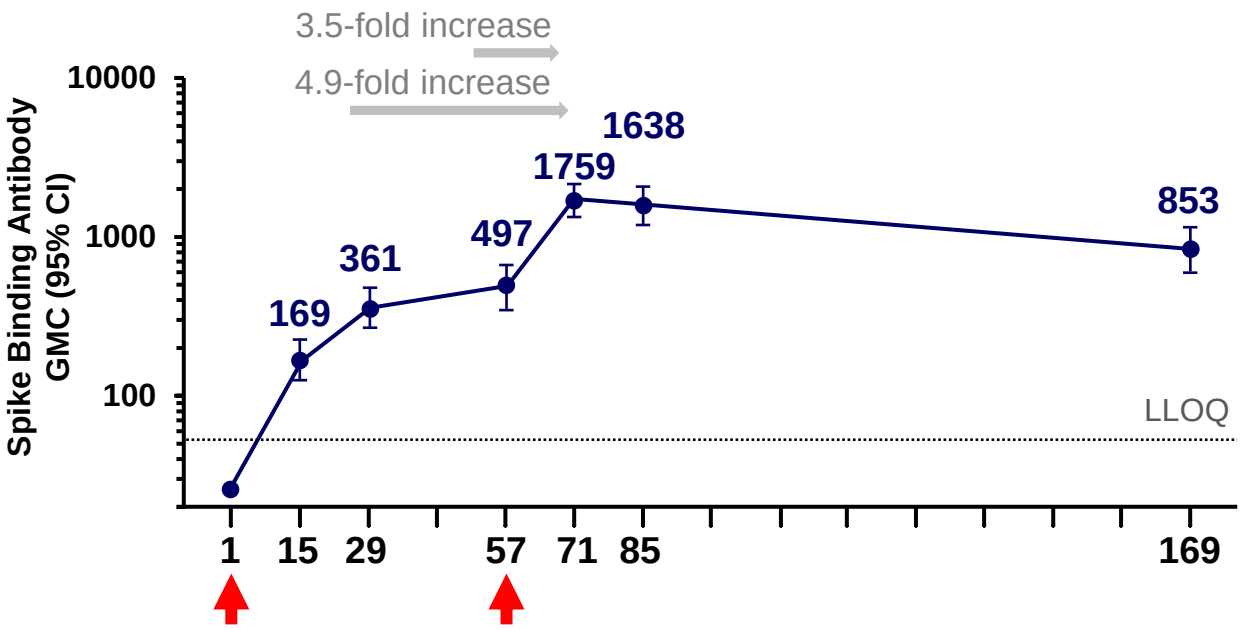
✖ Ad26 1e11, Placebo (n = 22)
✚ Ad26 1e11, Ad26 1e11 (n = 23)
△ Ad26 5e10, Placebo (n = 22)
○ Ad26 5e10, Ad26 5e10 (n = 24)

○ Ad26 5e10, Ad26 5e10 (n = 17)

LLOQ = lower limit of quantification
ULOQ = upper limit of quantification

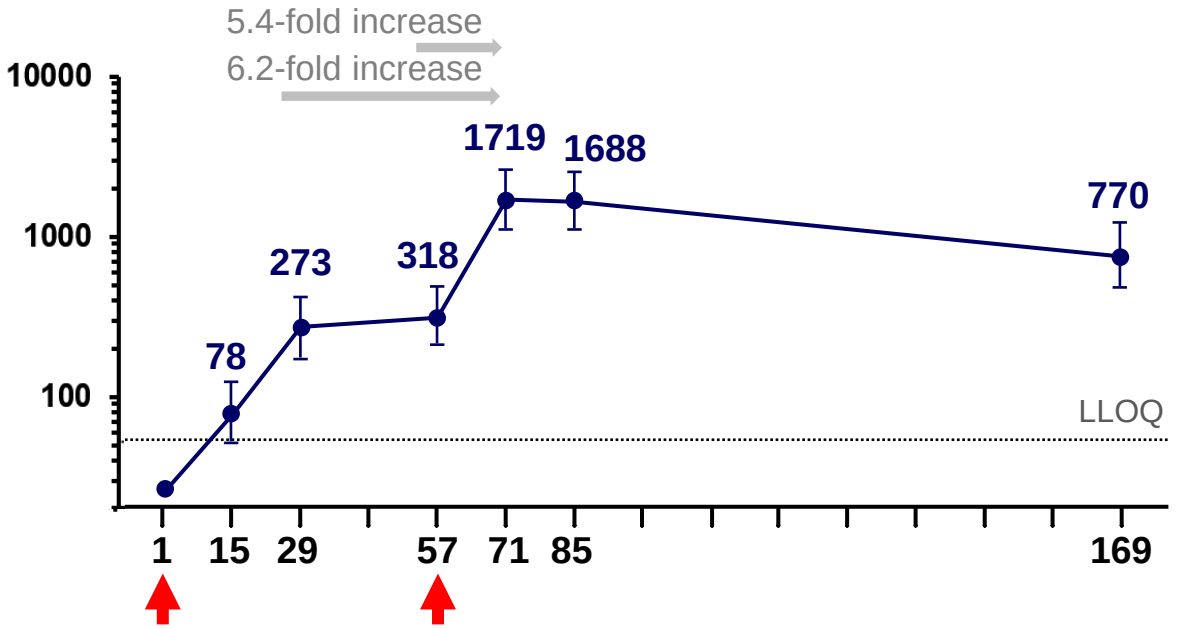
COV2001: Boost at 2 Months Increases Antibody Titers by 3.5- to 6.2-fold

18-55 Years, N=52



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

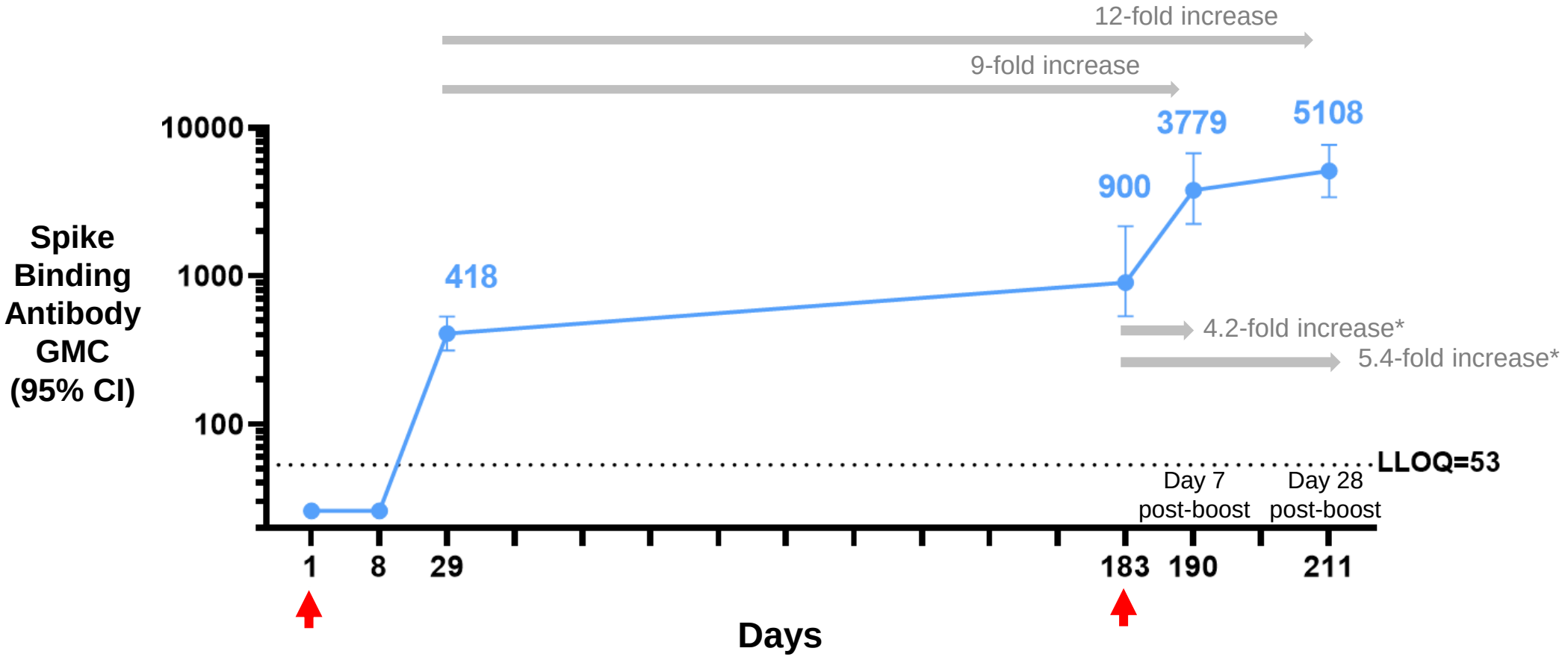
≥ 65 Years, N=29



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

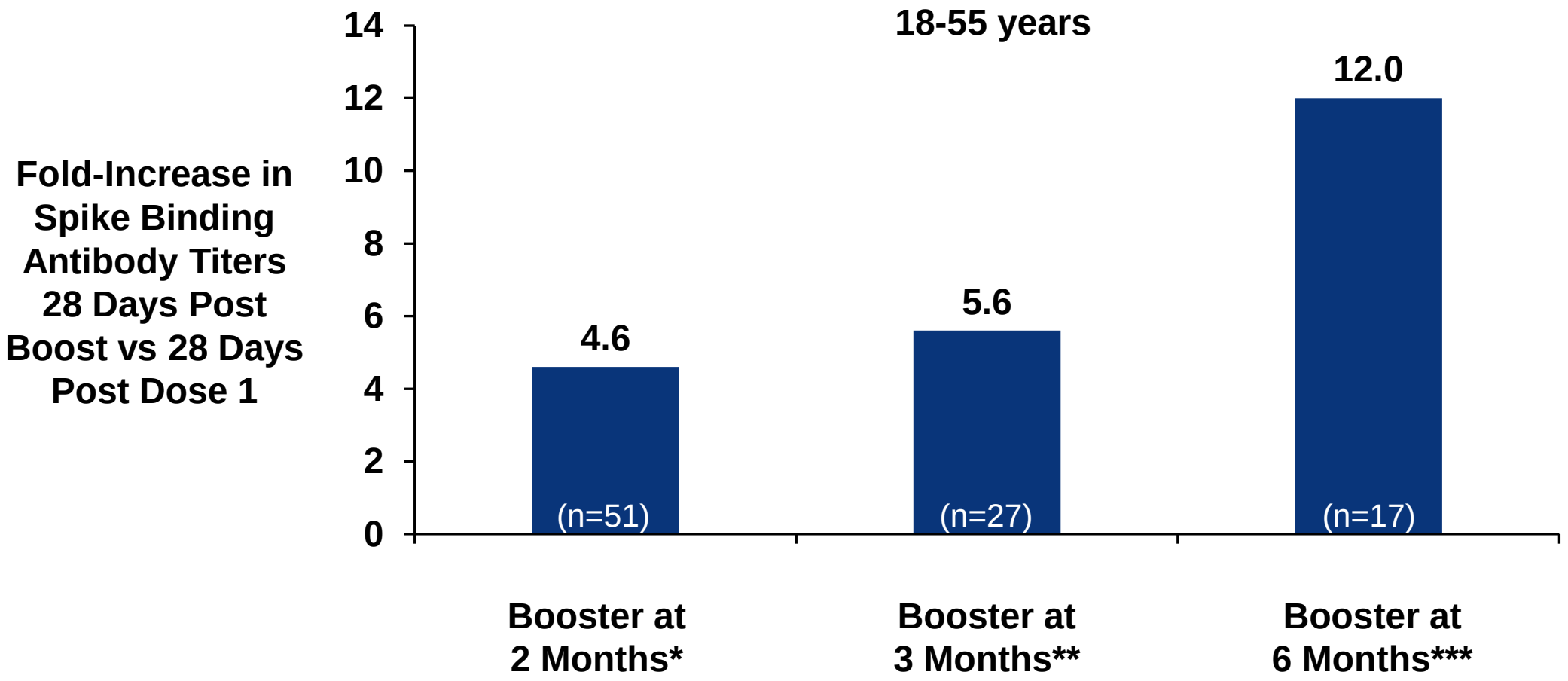
COV1001: Boost at 6 Months Increases Antibody Titers by 9- to 12-fold



Sadoff J, et al. August 26, 2021
Cohort 2a; LLOQ = lower limit of quantification

*GMI: geometric mean increase

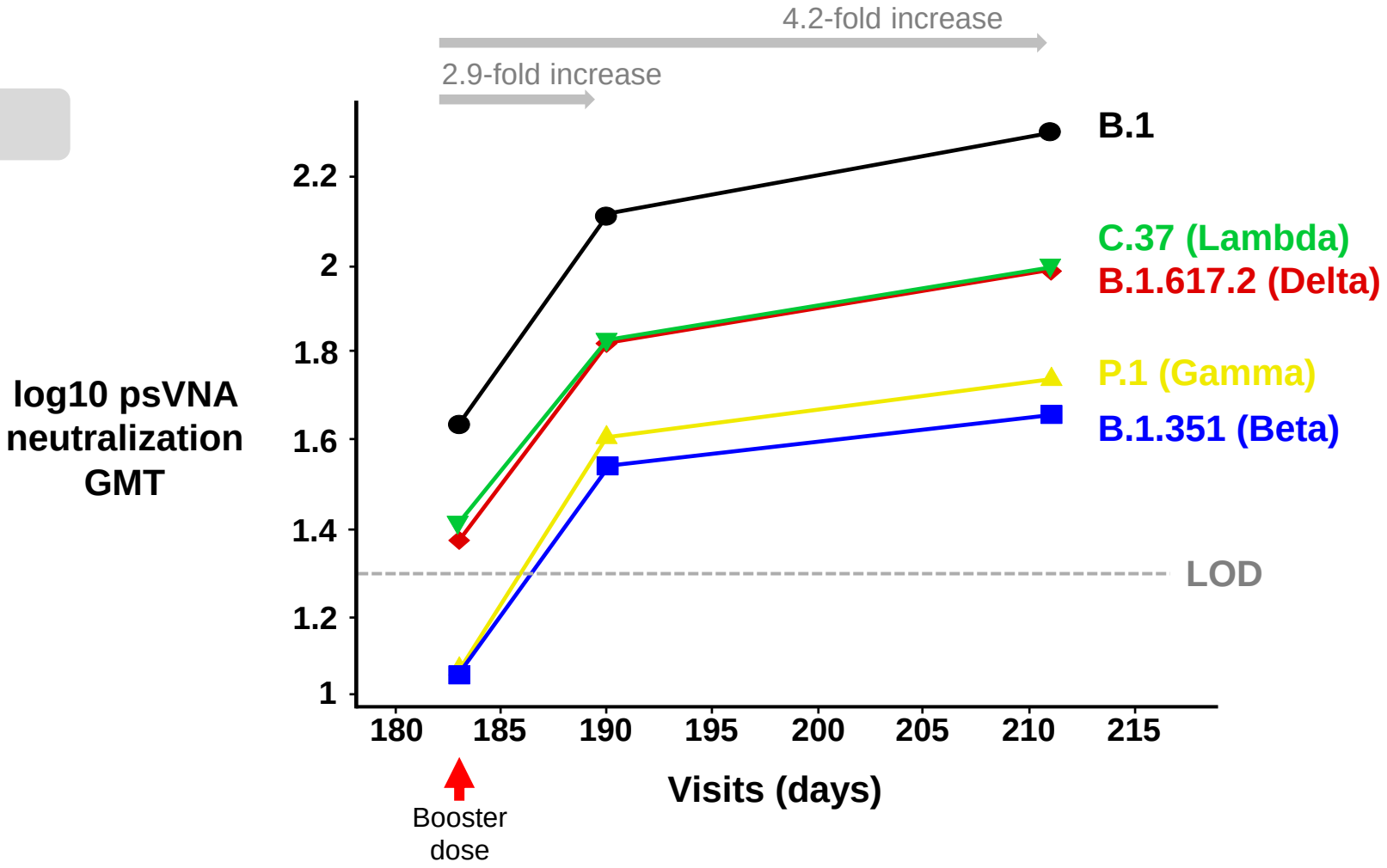
COV1001 and COV2001: Benefit of Booster Dose Higher When Given at 6 Months or Later



*Data from COV2001 Group 1
**Data from CVO2001 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 log10 GMT per visit per strain where titers at LOD of 20 used as values < 20, assuming Gaussian distribution for underlying log10 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.COV2.S Booster

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Janssen Pharmaceutical Companies of Johnson & Johnson

Outline for Safety Presentation

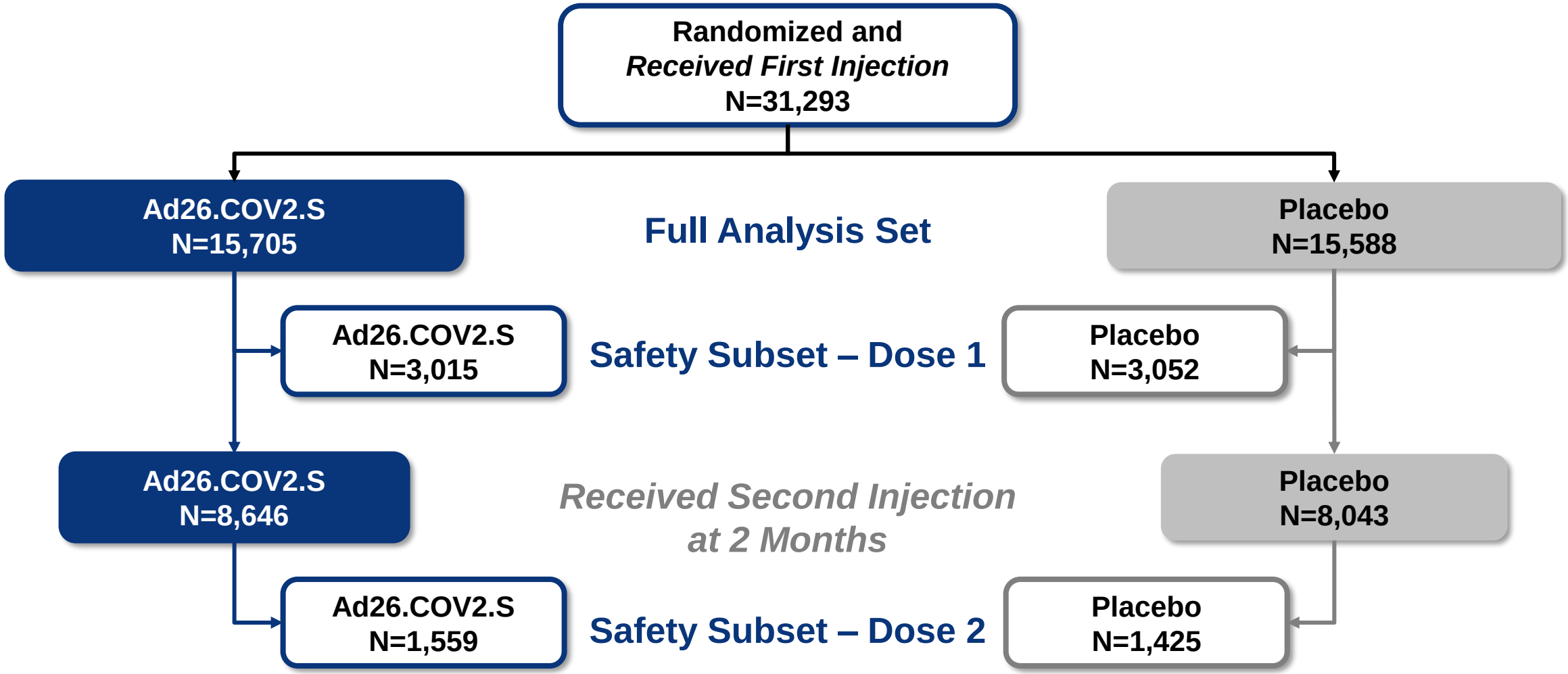
- Cumulative exposure to booster dose
- Reactogenicity of booster at 2 months (COV3009)
- Reactogenicity of booster at 6 months (COV1001 & COV2008)
- Safety profile of booster dose at 2 months (COV3009)
- Adverse events of interest / special interest
- Post-authorization safety

Cumulative Exposure to Ad26.COV2.S 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^{10})	**190**	**77***	**19**
COV1002 (5 x 10^{10})	**91**	**0**	**0**
COV2001 (5 x 10^{10})	**137**	**51**	**0**
COV2008 (5 x 10^{10})	**0**	**0**	**127**** (blinded)
COV3009 (5 x 10^{10})	**8,655**	**0**	**0**
Total by Interval	**9,073**	**128**	**19**
Overall Total		**9,220**	

***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^{10}, 2.5 x 10^{10}, or 1 x 10^{10}. Dose-level data remain blinded**

COV3009: Safety Analysis Sets



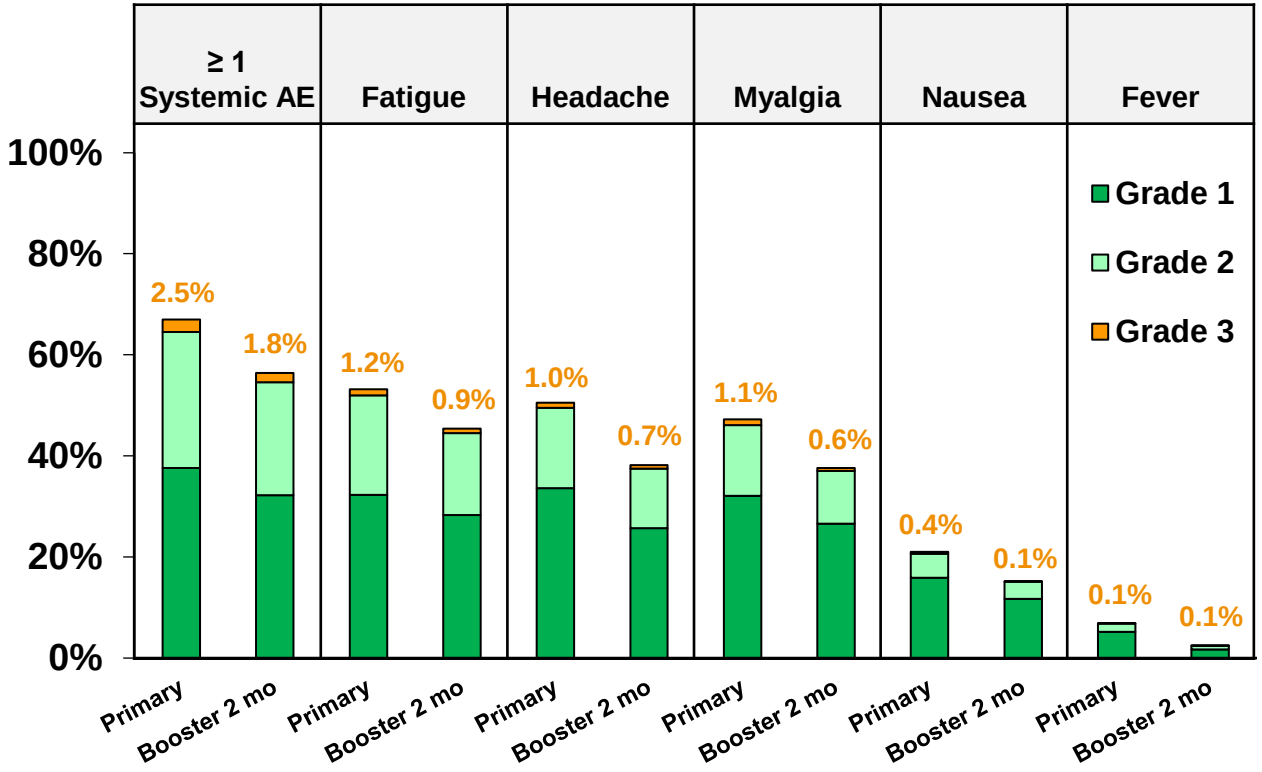
Reactogenicity of Booster Dose at 2 Months

Study COV3009

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

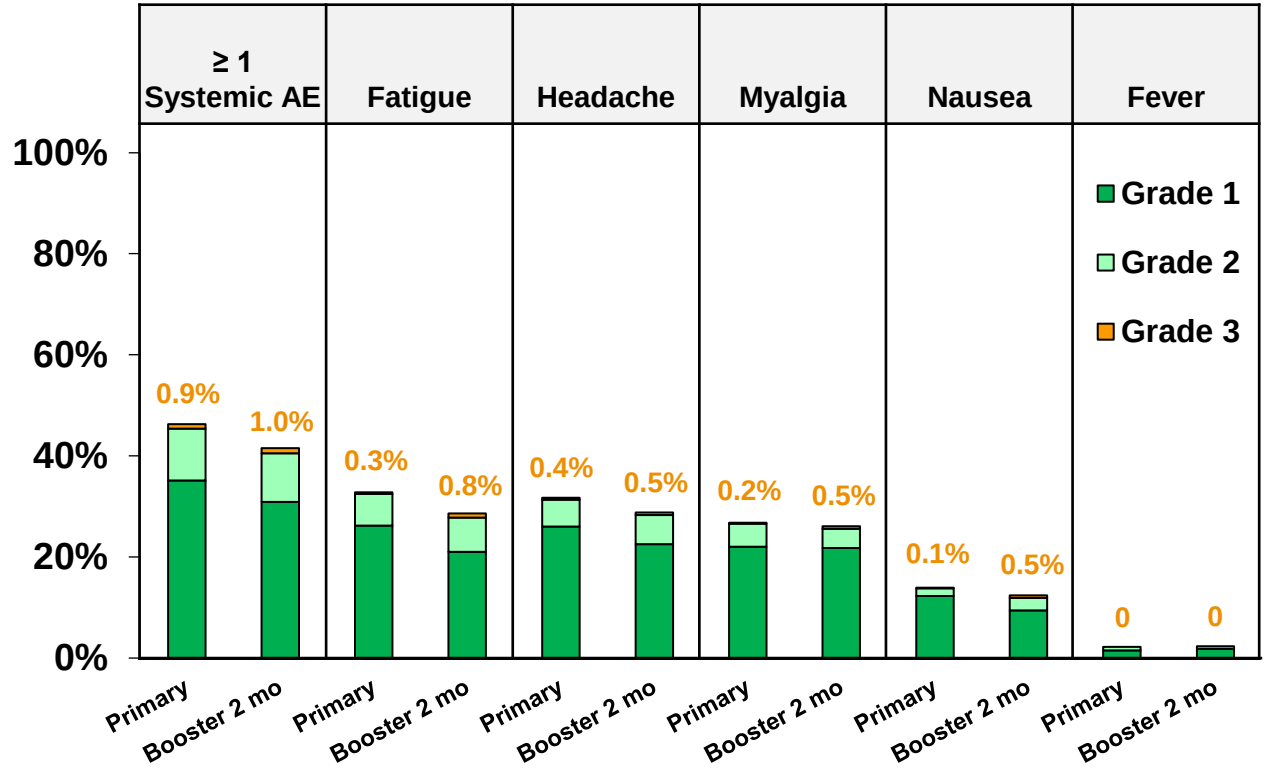
18-59 Years

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



≥ 60 Years

Primary N = 1,231; Booster N = 395

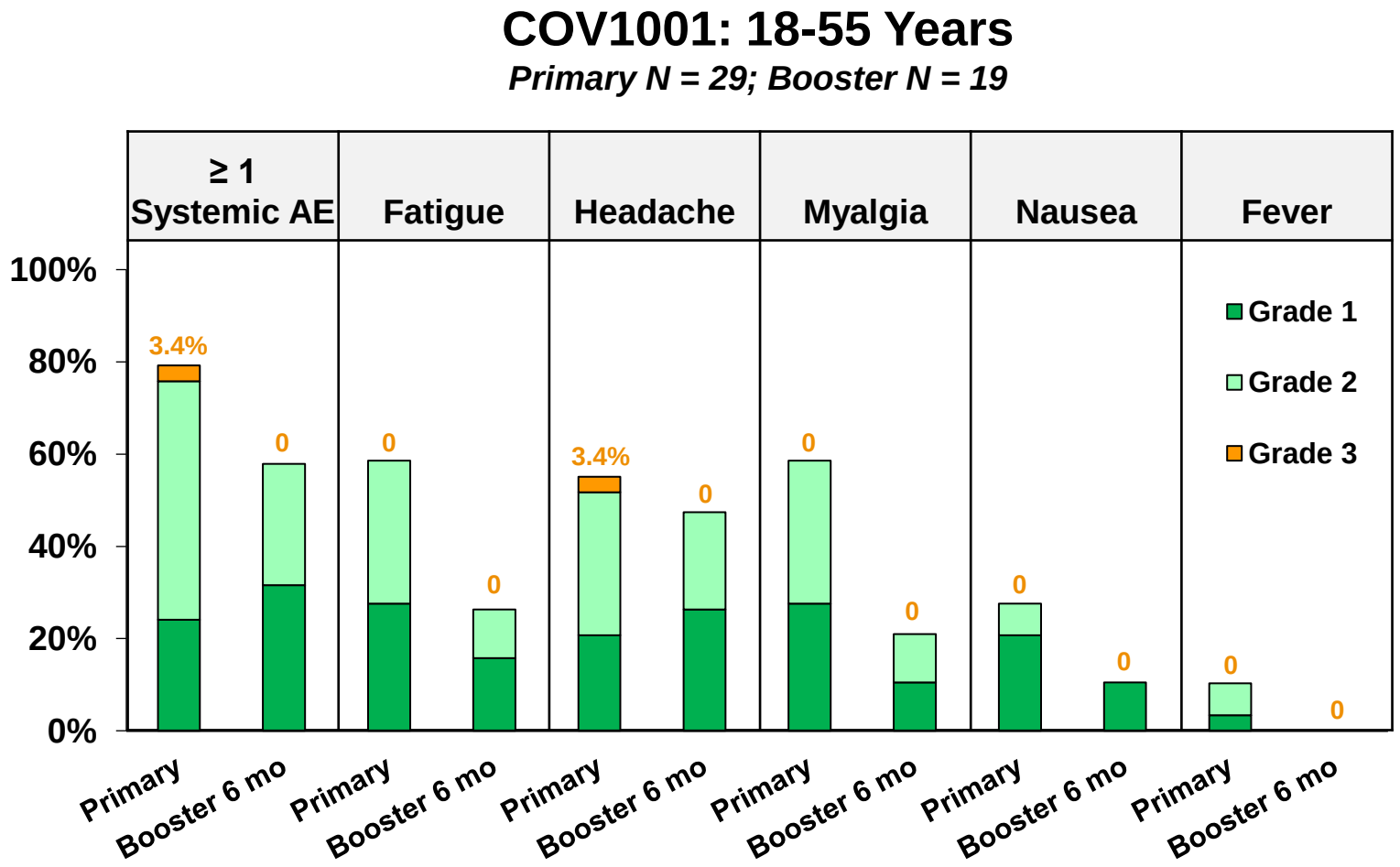


COV3009; Safety Subset

Reactogenicity of Booster Dose at 6 Months

Study COV1001 and Study COV2008

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



COV2008: Preliminary Blinded Systemic Reactogenicity of Booster at ≥ 6 Months

- Ongoing randomized double-blind study of participants enrolled in Study 3001 where three Ad26.COV2.S booster dose levels are being evaluated ≥ 6 months following primary vaccination with Ad26.COV2.S
- 127 estimated to have received 5 x 10^{10} vp
  - Blinded 7-day safety data available on 83 participants (N~32 ≥ 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	
Safety Subset – Dose 1	**N = 3,015**		**N = 3,052**	
Any AE	454	**15.1%**	332	**10.9%**
Safety Subset – Dose 2	**N = 1,559**		**N = 1,425**	
Any AE	159	**10.2%**	120	**8.4%**
Full Analysis Set (FAS)	**N = 15,705**		**N = 15,588**	
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"*

https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting

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)
Embolic and thrombotic events (SMQ)	2 (< 0.1%)	6 (0.1%)	3 (< 0.1%)	3 (< 0.1%)
Convulsions/seizures	0	0	0	0
Tinnitus	4 (< 0.1%)	2 (< 0.1%)	2 (< 0.1%)	2 (< 0.1%)
Guillain-Barre Syndrome	0	0	0	0
Facial paralysis	1 (< 0.1%)	2 (< 0.1%)	1 (< 0.1%)	0
Arthritis	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

Data cut-off date for case numbers: Aug 24, 2021

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)**

CDC Criteria for TTS	Tier 1	68
	Tier 2	5
Sex	Female	50
	Male	23
Age (years) 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

***Demographic table above includes 2 cases from open-label studies and 1 case from a placebo-controlled study**

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

Sex	Female	90
	Male	158
	Not reported	7
Age (years) 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[1-4]

***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

Sex	Female	4
	Male	3
Age (years) 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

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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.COV2.S

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

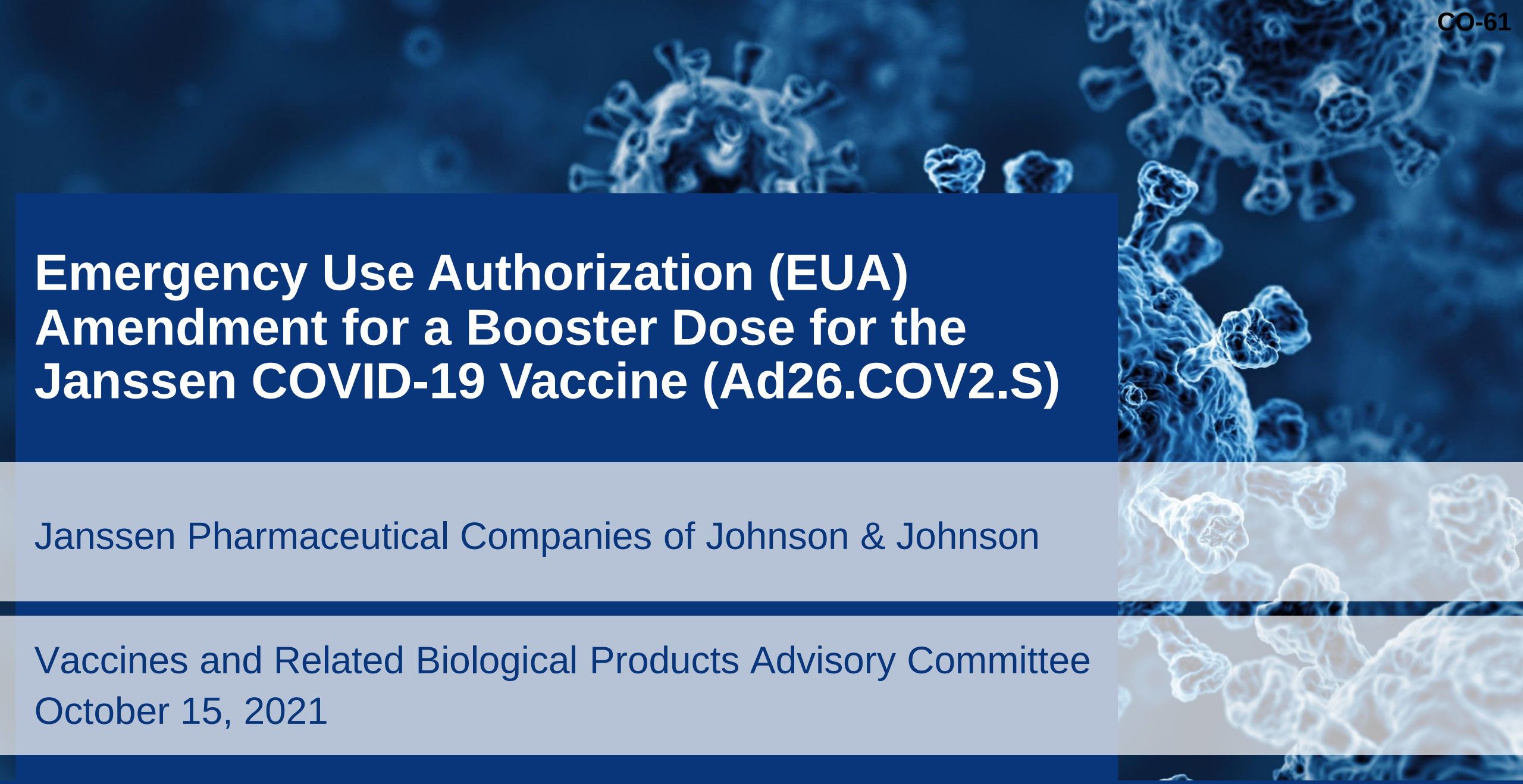
Homologous booster dose with Ad26.COV.2.S preferred over heterologous boost

Homologous Boost with Ad26.COV2.S 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

janssen
PHARMACEUTICAL COMPANIES OF
Johnson & Johnson