Vaccines and Related Biological Products Advisory Committee Meeting

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U.S. FOOD & DRUG ADMINISTRATION

Vaccines and Related Biological Products Advisory Committee Meeting

FDA Review of Efficacy and Safety of the Janssen COVID-19 Vaccine Emergency Use Authorization Request

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Outline

- Introduction
- Clinical development program
- Efficacy data
- Safety data
- Pharmacovigilance plan/future studies
- Benefit/risk assessment in context of proposed use under EUA

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- **Introduction**
- Clinical development program
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Janssen COVID-19 Vaccine Ad26.COV2.S

Vaccine composition	• Recombinant, replication-incompetent adenovirus type 26 (Ad26) vectored • Encodes SARS-CoV-2 spike (S) protein • Produced in PER.C6 cells
Dosing regimen	Intramuscular, single-dose regimen $5x10^{10}$ vp
Proposed indication and usage under EUA	For active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older

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Clinical Development to Date

Ongoing, randomized, double-blinded, placebo-controlled studies

Study Number	Phase	Vaccination Schedule	No. of Dose Levels	Description
1001	1/2a	1-dose and 2-dose	2	Regimen selection
1002*	1	2-dose	2	Safety and immunogenicity study in Japan
2001	2a	1-dose and 2-dose	4	Dose-ranging; includes adolescents
3001	3	1-dose	1	Efficacy, safety, immunogenicity
3009	3	2-dose	1	Efficacy, safety, immunogenicity

*Non-US IND study

Study 3001 data used to support EUA application

Study 1001

Phase 1/2a safety and immunogenicity study (N=1,045)

- Age cohorts: 18 to 55 yrs (n=670) and ≥65 yrs (n=375)
- Dose levels: $5x10^{10}$ vp and $1x10^{11}$ vp
- Schedule: 1-dose and 2-dose

Immunogenicity:

- Single dose ($5x10^{10}$ vp) induced SARS-CoV-2 binding and neutralizing antibodies in both age cohorts
- Th1-skewed CD4+ T-cell response elicited

Safety:

- Safety profile supported further clinical development

Study 2001

Phase 2 safety and immunogenicity study in healthy adults and adolescents (N=1,285)

- Age cohorts: 18-55 years, ≥65 years (n=625), 12-17 years (n=660)
- Dose levels: $1.25x10^{10}$ vp, $2.5x10^{10}$ vp, and $5x10^{10}$ vp, $1x10^{11}$ vp
- Schedule: 1-dose and 2-dose

Immunogenicity: Elicited SARS-CoV-2 neutralizing antibody responses

Safety: No safety concerns identified to date

Study 3009

Phase 3 efficacy, safety, and immunogenicity study of 2-dose regimen (N=30,000)

- Multicenter study in US, South Africa, Brazil, Colombia, Philippines, and 5 European countries
- Age cohorts: 18-59 years, ≥60 years
- Randomized 1:1 to 2 doses of vaccine ($5x10^{10}$ vp) or placebo, 56-day interval

- Initiated November 16, 2020
- Enrollment ongoing
- No safety concerns identified based on review of blinded SAE reports to date

Study 3001

Phase 3 efficacy, safety, immunogenicity of 1-dose regimen (N=44,325)

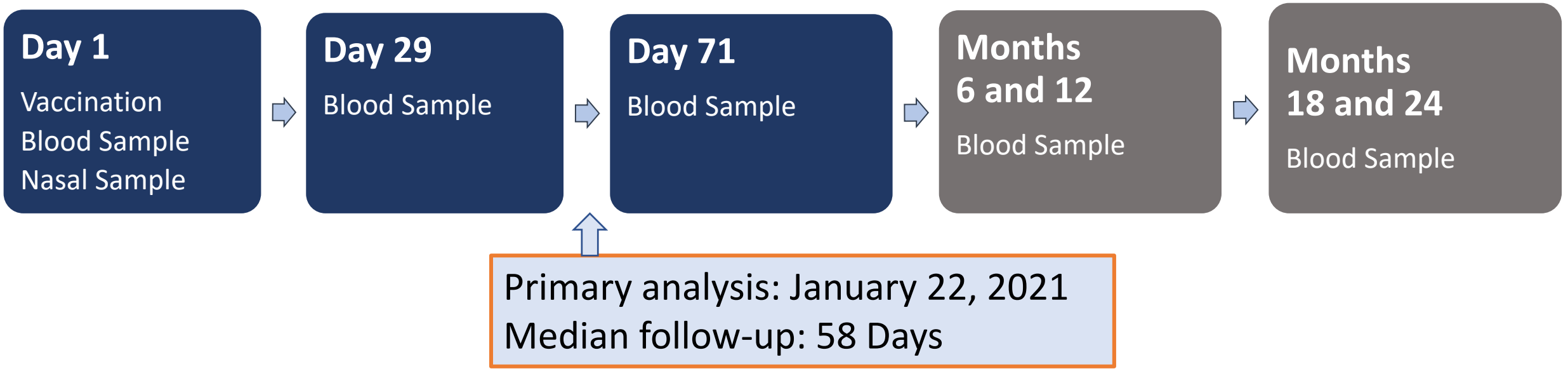
- Multicenter study across US, South Africa, and 6 countries in Latin America
- Age cohorts: 18-59 years, ≥60 years
- Randomized 1:1 to a single dose of vaccine ($5x10^{10}$ vp) or saline placebo

- Initiated September 21, 2020
- Staged enrollment:
  - 18 to <60 years without comorbidities
  - 18 to <60 years with and without comorbidities
  - ≥60 years without comorbidities
  - ≥60 years with and without comorbidities

  } Goal of 30% of total study population

- Planned study duration: 2 years

Study 3001 Scheduled Visits and Assessments



- Active COVID-19 surveillance by eDiary: prompts 2x weekly for first year, 1x every 2 weeks thereafter
- Safety Subset (N=6,736): solicited adverse reactions for 7 days post vaccination; unsolicited AEs through 28 days post vaccination
- All participants: medically-attended AEs captured for first 6 months; SAEs, MAAEs leading to study discontinuation for study duration
- Blood samples collected at scheduled visits for immunogenicity assessments

Moderate COVID-19 Case Definition

Positive SARS-CoV-2 PCR* plus:

Any 1 of the following new or worsening signs or symptoms: • Respiratory rate ≥20 breaths/minute • Abnormal saturation of oxygen (SpO_2) but still >93% on room air at sea level • Clinical or radiologic evidence of pneumonia • Radiologic evidence of deep vein thrombosis • Shortness of breath or difficulty breathing	**OR**	Any 2 of the following new or worsening signs or symptoms: • Fever (≥38.0°C or ≥100.4°F) • Heart rate ≥90 beats/minute • Shaking chills or rigors • Sore throat • Cough • Malaise as evidenced by loss of appetite, fatigue, physical weakness, and/or feeling unwell • Headache • Muscle pain (myalgia) • Gastrointestinal symptoms (diarrhea, vomiting, nausea, abdominal pain) • New or changing olfactory or taste disorders • Red or bruised looking feet or toes

*PCR or molecular test result from any respiratory tract sample (e.g., nasal, throat, sputum, saliva) or other sample. Nasal swab specified by protocol for the testing during suspected COVID-19.

Severe/Critical COVID-19 Case Definition

Positive SARS-CoV-2 PCR plus:

Any 1 of the following new or worsening signs or symptoms:

- Clinical signs at rest indicative of severe systemic illness
- Respiratory failure
- Evidence of shock
- Significant acute renal, hepatic, or neurologic dysfunction
- Admission to the ICU
- Death

All cases meeting the severe/critical definition and all cases meeting the moderate case definition and that included >3 signs and/or symptoms were evaluated by an independent, blinded adjudication committee.

Primary Efficacy Endpoint and Analysis

Co-primary endpoints

Vaccine efficacy to prevent moderate to severe/critical COVID-19, confirmed by central laboratory, occurring:

- at least 14 days after vaccination
- at least 28 days after vaccination (added as co-primary while study ongoing)

The primary efficacy success criterion is met if the null hypothesis of VE ≤30% is rejected **and** the VE point estimate is ≥50% for **both** co-primary endpoints.

Prespecified criteria to trigger primary efficacy analysis included accrual of at least 42 centrally confirmed moderate to severe/critical cases of COVID-19 with onset ≥28 days post vaccination

Key Secondary Efficacy Endpoints

Vaccine efficacy to prevent or vaccine impact on:

- Any symptomatic COVID-19 (mild, moderate, severe)
- COVID-19 per the FDA harmonized COVID-19 case definition
- Severe/critical COVID-19
- COVID-19 requiring medical intervention
- COVID-19-related death
- Asymptomatic COVID-19 as inferred through seroconversion using serology against nucleocapsid protein

Additional Considerations

Protocol specified that primary analysis be based on centrally confirmed cases at the time of data cutoff

By January 22, 2021:

- 70% of the accrued cases had undergone central confirmation process
- 18% in shipping process, 12% pending at central laboratory
- Based on samples already tested, 90.3% concordance between local and central laboratory results

Primary efficacy analysis: centrally confirmed cases only

Subgroup efficacy analyses: positive PCR results from any source

Study 3001 Analysis Populations

Population (N)	Description
Full Analysis Set (FAS) (N=43,783: 21,895 vaccine; 21,888 placebo)	All randomized participants with a documented study vaccine administration
Per-Protocol Set (N=39,321: 19,630 vaccine; 19,691 placebo)	All participants in the FAS who had no immunologic or virologic evidence of prior SARS-CoV-2 infection at the time of vaccination.
Safety Subset (N=6,736: 3,356 vaccine; 3,380 placebo)	Subset of the FAS for the analysis of solicited and unsolicited AEs

Median Follow-Up Duration

Participant Group Follow-up	Ad26.COV2.S N=21895	Placebo N=21888	All Participants N=43783
18-59 overall	14564	14547	29111
Participants with ≥8 weeks follow-up	62.8%	63.1%	63.0%
Median follow-up after vaccination (days)	61.0	61.0	61.0
18-59, no comorbidities	9332	9371	18703
Participants with ≥8 weeks follow-up	70.0%	69.9%	70.0%
Median follow-up after vaccination (days)	64.0	64.0	64.0
18-59, with comorbidities	5232	5176	10408
Participants with ≥8 weeks follow-up	49.9%	50.8%	50.4%
Median follow-up after vaccination (days)	56.0	57.0	57.0
≥60 years overall	7331	7341	14672
Participants with ≥8 weeks follow-up	38.2%	37.8%	38.0%
Median follow-up after vaccination (days)	52.0	52.0	52.0
≥60 years, no comorbidities	3627	3595	7222
Participants with ≥8 weeks follow-up	47.6%	49.0%	48.3%
Median follow-up after vaccination (days)	54.0	55.0	54.0
≥60 years, with comorbidities	3704	3746	7450
Participants with ≥8 weeks follow-up	29.0%	27.1%	28.0%
Median follow-up after vaccination (days)	50.0	50.0	50.0

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Demographics, Efficacy Population, Study 3001

Subgroup	Ad26.COV2.S	Placebo	All Participants
Per-protocol set	**19630**	**19691**	**39321**
Age (years)			
Mean (SD)	51.1 (15.0)	51.2 (15.0)	51.1 (15.0)
Median	52.0	53.0	53.0
Range	(18, 100)	(18, 94)	(18, 100)
Age group (years)			
18-59	12830 (65.4%)	12881 (65.4%)	25711 (65.4%)
≥60	6800 (34.6%)	6810 (34.6%)	13610 (34.6%)
≥65	3984 (20.3%)	4018 (20.4%)	8002 (20.4%)
≥75	755 (3.8%)	693 (3.5%)	1448 (3.7%)
Sex			
Female	8702 (44.3%)	8777 (44.6%)	17479 (44.5%)
Male	10924 (55.6%)	10910 (55.4%)	21834 (55.5%)
Undifferentiated	2 (<0.1%)	4 (<0.1%)	6 (<0.1%)
Unknown	2 (<0.1%)	0	2 (<0.1%)
Race			
American Indian or Alaska Native	1643 (8.4%)	1628 (8.3%)	3271 (8.3%)
Asian	720 (3.7%)	663 (3.4%)	1383 (3.5%)
Black or African American	3374 (17.2%)	3390 (17.2%)	6764 (17.2%)
Native Hawaiian or other Pacific Islander	54 (0.3%)	45 (0.2%)	99 (0.3%)
White	12200 (62.1%)	12216 (62.0%)	24416 (62.1%)
Multiple	1036 (5.3%)	1087 (5.5%)	2123 (5.4%)
Unknown	603 (3.1%)	662 (3.4%)	1265 (3.2%)

Demographics, Efficacy Population, Study 3001

Subgroup	Ad26.COV2.S	Placebo	All Subjects
Ethnicity			
Hispanic or Latino	8793 (44.8%)	8936 (45.4%)	17729 (45.1%)
Not Hispanic or Latino	10344 (52.7%)	10259 (52.1%)	20603 (52.4%)
Unknown	493 (2.5%)	496 (2.5%)	989 (2.5%)
Country			
Brazil	3399 (17.3%)	3390 (17.2%)	6789 (17.3%)
Chile	531 (2.7%)	540 (2.7%)	1071 (2.7%)
Argentina	1402 (7.1%)	1414 (7.2%)	2816 (7.2%)
Colombia	1858 (9.5%)	1869 (9.5%)	3727 (9.5%)
Peru	571 (2.9%)	581 (3.0%)	1152 (2.9%)
Mexico	206 (1.0%)	220 (1.1%)	426 (1.1%)
United States	9185 (46.8%)	9171 (46.6%)	18356 (46.7%)
South Africa	2478 (12.6%)	2506 (12.7%)	4984 (12.7%)
Presence of baseline comorbidity			
One or more	7830 (39.9%)	7867 (40.0%)	15697 (39.9%)
None	11800 (60.1%)	11824 (60.0%)	23624 (60.1%)

Subject Disposition, Efficacy Population, Study 3001

Disposition	Ad26.COV2.S n (%)	Placebo n (%)	Total n (%)
Randomized	22174	22151	44325
Vaccinated[a]	21895	21888	43783
Full analysis set	21895 (100.0)	21888 (100.0)	43783 (100.0)
Participants excluded from per-protocol set	2265 (10.3)	2197 (10.0)	4462 (10.2)
Positive SARS-CoV-2 status at time of vaccination	2233 (10.2)	2166 (9.9)	4399 (10.0)
Major protocol deviation evaluated to possibly impact efficacy	33 (0.2)	36 (0.2)	69 (0.2)
In/exclusion criteria	18 (0.1)	23 (0.1)	41 (0.1)
Received wrong treatment or incorrect dose	9 (<0.1)	11 (0.1)	20 (<0.1)
Received a disallowed concomitant medication	2 (<0.1)	2 (<0.1)	4 (<0.1)
Other	4 (<0.1)	1 (<0.1)	5 (<0.1)
Per-protocol set	19630 (89.7)	19691 (90.0)	39321 (89.8)
Participants with at ≥2 months follow-up	10715 (54.6)	10776 (54.7)	21491 (54.7)
Discontinued from study	41 (0.2)	89 (0.5)	130 (0.3)
Withdrawal by participant	30 (0.2)	62 (0.3)	92 (0.2)
Death	1 (<0.1)	11 (0.1)	12 (<0.1)
Lost to follow-up	6 (<0.1)	4 (<0.1)	10 (<0.1)
Physician decision	2 (<0.1)	1 (<0.1)	3 (<0.1)
Protocol deviation	0	1 (<0.1)	1 (<0.1)
Other	2 (<0.1)	10 (0.1)	12 (<0.1)
Participants included in per-protocol set until treatment unblinding	1046 (5.3)	1138 (5.8)	2184 (5.6)

[a] Denominators for percentage calculations

Primary Efficacy Endpoint

	Onset at Least 14 Days			Onset at Least 28 Days		
Co-primary Endpoint Subgroup	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**
All participants	116 (19514) 3116.6	348 (19544) 3096.1	**66.9%** (59.0, 73.4)	66 (19306) 3102.0	193 (19178) 3070.7	**66.1%** (55.0, 74.8)
Age 18-59 years	95 (12750) 2106.8	260 (12782) 2095.0	**63.7%** (53.9, 71.6)	52 (12617) 2097.6	152 (12527) 2077.0	**66.1%** (53.3, 75.8)
Age ≥60 years	21 (6764) 1009.8	88 (6762) 1001.2	**76.3%** (61.6, 86.0)	14 (6689) 1004.4	41(6651) 993.6	**66.2%** (36.7, 83.0)

Subgroup Analyses of Primary Efficacy Endpoint

	Onset at Least 14 Days			Onset at Least 28 Days		
Subgroup	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**
Sex						
Male	85 (10861)	269 (10832)	**68.8%**	54 (10764)	176 (10649)	**69.8%**
	1739.0	1715.9	(60.1, 75.9)	1732.4	1704.2	(58.9, 78.2)
Female	88 (8649)	240 (8708)	**63.4%**	59 (8538)	148 (8525)	**60.3%**
	1374.2	1372.6	(53.1, 71.7)	1367.1	1361.1	(46.0, 71.2)
Region						
Northern	51 (9119)	196 (9086)	**74.4%**	32 (8958)	112 (8835)	**72.0%**
America (U.S.)	1414.0	1391.3	65.0, 81.6)	1403.4	1375.6	(58.2, 81.7)
Southern Africa	43 (2473)	90 (2496)	**52.0%**	23 (2449)	64 (2463)	**64.0%**
(South Africa)	377.6	379.2	(30.3, 67.4)	376.1	376.9	(41.2, 78.7)
Latin America	79 (7922)	223 (7962)	**64.7%**	58 (7899)	148 (7880)	**61.0%**
	1322.2	1318.5	(54.1, 73.0)	1320.8	1313.3	(46.9, 71.8)
Age group (yrs)						
18-64	157 (15544)	441 (15552)	**64.7%**	101 (15378)	286 (15253)	**65.1%**
	2527.8	2504.8	(57.6, 70.8)	2517.1	2485.9	(56.1, 72.5)
≥65	16 (3970)	68 (3992)	**76.5%**	12 (3928)	38 (3925)	**68.6%**
	586.1	584.3	(59.1, 87.3)	583.1	580.0	(38.6, 85.1)

Subgroup Analyses of Primary Efficacy Endpoint

	Onset at Least 14 Days			Onset at Least 28 Days		
Subgroup	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE%[a] (95% CI)**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE%[a] (95% CI)**
Race						
Amer. Indian/Alaska	21 (1634)	41 (1621)	**49.4%**	18 (1628)	26 (1604)	**31.7%**
	279.0	275.4	(12.4, 71.6)	278.4	274.4	(-29.4, 64.8)
Asian	6 (714)	12 (649)	**54.4%**	2 (689)	7 (626)	**74.0%**
	99.5	90.6	(-31.1, 86.0)	97.9	89.1	(-36.5, 97.3)
Black/African Amer.	37 (3362)	101 (3361)	**63.7%**	21 (3330)	66 (3300)	**68.6%**
	495.7	491.4	(46.6, 75.8)	493.7	487.3	(48.0, 81.8)
Native HI/ other Pac. Isl.	1 (54)	0 (44)		1 (54)	0 (43)	
	8.0	6.6		8.0	6.6	
White	94 (12123)	288 (12133)	**67.6%**	64 (11994)	187 (11912)	**66.2%**
	1975.4	1958.3	(59.0, 74.6)	1967.0	1944.4	(54.8, 74.9)
Multiple	10 (1028)	48 (1080)	**78.6%**	4 (1018)	28 (1055)	**85.4%**
	166.6	170.8	(57.3, 90.4)	166.0	169.2	(58.4, 96.3)
Ethnicity						
Hispanic/	81 (8733)	237 (8869)	**65.6%**	59 (8688)	153 (8741)	**61.3%**
Latino	1418.6	1429.3	(55.5, 73.6)	1415.7	1421.4	(47.4, 71.8)
Not Hispanic/	88 (10289)	257 (10184)	**66.4%**	52 (10131)	163 (9957)	**68.8%**
Latino	1620.3	1587.7	(57.1, 74.0)	1610.1	1573.1	(57.2, 77.6)

[a] VE not shown if less than 6 cases are observed for an endpoint

Subgroup Analyses of Primary Efficacy Endpoint

	Onset at Least 14 Days			Onset at Least 28 Days		
Co-primary Endpoint Subgroup	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**
Age and comorbidity presence						
18-59, no	89 (8346) 1433.5	258 (8411) 1428.2	**65.6%** (56.1, 73.3)	58 (8267) 1428.2	180 (8254) 1418.3	**68.0%** (56.8, 76.6)
18-59, yes	48 (4404) 671.5	131 (4371) 661.0	**63.9%** (49.4, 74.7)	29 (4350) 668.1	79 (4273) 654.8	**64.0%** (44.3, 77.3)
≥60, no	14 (3391) 541.6	57 (3335) 530.0	**76.0%** (56.3, 87.6)	11 (3355) 539.0	39 (3298) 527.6	**72.4%** (45.0, 87.3)
≥60, yes	22 (3373) 467.4	63 (3427) 469.9	**64.9%** (42.2, 79.4)	15 (3334) 464.9	26 (3353) 465.2	**42.3%** (-13.1, 71.6)

Subgroup Analyses of Primary Efficacy Endpoint, by Comorbidity

	Onset at Least 14 Days			Onset at Least 28 Days		
Subgroup	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE%[a] (95% CI)**
Comorbidity, presence						
Yes	70 (7777) 1138.8	194 (7798) 1130.9	**64.2%** (52.7, 73.1)	44 (7684) 1133.0	105 (7626) 1120.0	**58.6%** (40.6, 71.6)
No	103 (11737) 1975.1	315 (11746) 1958.2	**67.6%** (59.4, 74.3)	69 (11622) 1967.3	219 (11552) 1945.9	**68.8%** (59.0, 76.6)
Comorbidity, type						
Asthma	1 (238) 34.3	9 (278) 39.5	**87.2%** (7.6, 99.7)	0 (235) 34.1	4 (270) 38.9	
COPD	1 (213) 30.2	5 (195) 28.0	**81.5%** (-65.2, 99.6)	1 (211) 30.1	3 (192) 27.8	
Serious heart conditions	3 (460) 65.3	13 (487) 67.7	**76.1%** (12.9, 95.6)	1 (455) 64.9	5 (472) 66.8	**79.4%** (-83.7, 99.6)
HIV infection	5 (467) 69.1	5 (498) 72.4	**-4.8%** (-355.2, 75.9)	2 (461) 68.7	4 (493) 72.2	**47.5%** (-266.0, 95.3)
Hypertension	14 (1999) 283.3	38 (2019) 282.8	**63.2%** (30.6, 81.6)	11 (1978) 281.9	17 (1977) 280.2	**35.7%** (-45.6, 72.8)
Obesity	51 (5383) 794.1	151 (5352) 780.3	**66.8%** (54.1, 76.3)	30 (5318) 790.0	86 (5223) 772.0	**65.9%** (47.8, 78.3)
Type 2 diabetes mellitus	15 (1399) 198.7	32 (1410) 199.5	**52.9%** (10.5, 76.3)	10 (1380) 197.5	13 (1378) 197.7	**23.0%** (-90.1, 69.8)

Note: Only comorbidities with ≥6 cases at either of the 2 time points are shown

[a] VE not shown if less than 6 cases are observed for an endpoint

Subgroup Analyses of Primary Efficacy Endpoint, by SARS-CoV-2 Status at Baseline

	Onset at Least 14 Days			Onset at Least 28 Days		
Baseline SARS-CoV-2 Serostatus	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE%[a] (95% CI)**
Any baseline SARS-CoV-2 status	176 (21636) 3450.2	513 (21574) 3409.8	**66.1%** (59.7, 71.6)	114 (21424) 3436.3	326 (21199) 3385.9	**65.5%** (57.2, 72.4)
Positive	3 (2122) 336.3	4 (2030) 320.8	**28.5%** (-322.8, 89.5)	1 (2118) 336.1	2 (2021) 320.0	
Negative	173 (19514) 3113.9	509 (19544) 3089.1	**66.3%** (59.9, 71.8)	113 (19306) 3100.3	324 (19178) 3065.9	**65.5%** (57.2, 72.4**)**

[a] VE not shown if less than 6 cases are observed for an endpoint

Secondary Efficacy Analysis: All Symptomatic/ FDA Harmonized

	Onset at Least 14 Days			Onset at Least 28 Days		
	Ad26.COV2.S No. of Cases (Person-yrs)	**Placebo No. of Cases (Person-yrs)**	**VE% (95% CI)**	**Ad26.COV2.S No. of Cases (Person-yrs)**	**Placebo No. of Cases (Person-yrs)**	**VE% (95% CI)**
Symptomatic COVID-19, any severity*	117 (3116.5)	351 (3095.9)	**66.9%** (59.1, 73.4)	66 (3102.0)	195 (3070.53)	**66.5%** (55.5, 75.1)
FDA harmonized COVID-19 cases	114 (3116.6)	345 (3096.3)	**67.2%** (59.3, 73.7)	65 (3102.0)	193 (3070.6)	**66.7%** (55.6, 75.2)

* Includes mild, moderate, and severe/critical cases

Secondary Efficacy Analysis: Severe COVID-19

	Onset at Least 14 Days			Onset at Least 28 Days		
	Ad26.COV2.S Cases (N) Person-yrs	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**
Centrally confirmed cases						
Overall	14 (19514) 3125.1	60 (19544) 3122.0	**76.7%** (54.6, 89.1)	5 (19306) 3106.2	34 (19178) 3082.6	**85.4%** (54.2, 96.9)
18-59 years	8 (12750) 2114.3	41 (12782) 2115.1	**80.5%** (57.8, 92.1)	2 (12617) 2101.0	24 (12527) 2086.7	**91.7%** (66.7, 99.1)
≥60	6 (6764) 1010.7	19 (6762) 1006.9	**68.5%** (18.1, 89.7)	3 (6689) 1005.1	10 (6651) 995.9	**70.3%** (-15.5, 94.7)
Including non-centrally confirmed cases						
Overall	19 (19514) 3124.7	80 (19544) 3121.0	**76.3%** (57.9, 87.5)	8 (19306) 3106.0	48 (19178) 3082.0	**83.5%** (54.2, 96.9)
18-59 years	12 (12750) 2114.0	52 (12782) 2114.5	**76.9%** (56.2, 88.8)	5 (12617) 2100.9	33 (12527) 2086.3	**85.0%** (61.2, 95.4**)**
≥60 years	7 (6764) 1010.7	28 (6762) 1006.4	**75.1%** (41.7, 90.8)	3 (6689) 1005.1	15 (6651) 995.7	**80.2%** (30.0, 96.3**)**

COVID-19 Requiring Medical Intervention

Definition: Requiring hospitalization, ICU admission, mechanical ventilation, and/or ECMO

Post hoc analysis of all COVID-19 related hospitalizations in the study using:

- Medical Resource Utilization (MRU) questionnaires
- SAEs
- Clinical event listings (e.g., during a severe/critical COVID-19 episode)
- In setting of a positive SARS-CoV-2 PCR at onset of COVID-19 episode or onset of AE

Onset After Vaccination	Ad26.COV2.S No. of Cases Person-yrs	Placebo No. of Cases Person-yrs	VE% (95% CI)
At least 1 day (FAS, seronegative at baseline)			
Centrally confirmed	6 (3202.75)	18 (3213.07)	**66.6%** (12.06, 89.13)
Any positive PCR	6 (3202.75)	42 (3211.60)	**85.7%** (66.13, 95.02)
At least 14 days			
Centrally confirmed	2 (3125.82)	11 (3125.93)	**81.8%** (16.69, 98.04)
Any positive PCR	2 (3125.82)	29 (3125.09)	**93.1%** (72.74, 99.20)
At least 28 days			
Centrally confirmed	0 (3106.31)	6 (3084.38)	**100%** (15.67, 100.00)
Any positive PCR	0 (3106.31)	16 (3083.94)	**100%** (74.26, 100.00)

COVID-19 Related Deaths as of February 5, 2021

	Ad26.COV2.S N=21895	Placebo N=21888
All cause mortality	5	20
COVID-19 related deaths	0	7*

Group	Study Day	Age/Sex	Comorbidity
Placebo	15	63F	Obesity, Hypertension
Placebo	18*	52F	Obesity, Diabetes
Placebo	31	54M	Obesity, Hypertension, Diabetes, Heart failure
Placebo	38	49M	Obesity, Hypertension
Placebo	39	68F	Obesity
Placebo	49**	60F	Obesity
Placebo	55	60M	Asthma

*Participant was SARS-CoV-2 PCR positive at baseline

**Reported after data cutoff date for primary analysis

All COVID-19 related deaths are from study sites in South Africa

Asymptomatic Infection

Defined as:

- Participant does not fulfill criteria for suspected COVID-19 based on signs and symptoms

  AND

- Positive SARS-CoV-2 PCR

  OR

- Positive serology by SARS-CoV-2 nucleocapsid (N) specific immunoglobulin assay

Two time points

1. Onset Day 1 to 29
   - Modest, non-statistically significant vaccine efficacy
2. Onset after Day 29
   - Limited N-serology data available from Day 71 visit (N=2,892)
   - Available serology results not evenly distributed across subgroups

Efficacy in US, South Africa, Brazil

	Onset at Least 14 Days			Onset at Least 28 Days		
Country Subgroup	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% 95% CI**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**
United States						
Moderate to severe/critical	51 (9119) 1414.0	196 (9086) 1391.3	**74.4% (65.0, 81.6)**	32 (8958) 1403.4	112 (8835) 1375.6	**72.0% (58.2, 81.7)**
Severe/critical	4 (9119) 1417.2	18 (9086) 1404.8	**78.0% (33.1, 94.6)**	1 (8958) 1405.2	7 (8835) 1382.2	**85.9% (-9.4, 99.7)**
South Africa						
Moderate to severe/critical	43 (2473) 377.6	90 (2496) 379.2	**52.0% (30.3, 67.4)**	23 (2449) 376.1	64 (2463) 376.9	**64.0% (41.2, 78.7)**
Severe/critical	8 (2473) 380.2	30 (2496) 382.9	**73.1% (40.0, 89.4)**	4 (2449) 377.0	22 (2463) 379.0	**81.7% (46.2, 95.4)**
Brazil						
Moderate to severe/critical	39 (3370) 555.7	114 (3355) 548.8	**66.2% (51.0, 77.1)**	24 (3354) 554.8	74 (3312) 546.1	**68.1% (48.8, 80.7)**
Severe/critical	2 (3370) 558.9	11 (3355) 556.8	**81.9% (17.0, 98.1)**	1 (3354) 556.2	8 (3312) 549.8	**87.6% (7.8, 99.7)**

Sequencing

- 71.7% of centrally confirmed cases with sufficient viral load have been sequenced
- Prioritization given to moderate to severe/critical cases and cases occurring ≥14 days after vaccination
- No case identified to date from B.1.1.7 or P.1 lineages

Country	Molecularly Confirmed Cases	Molecularly Confirmed Cases With Sequence Data (%)	Variant SARS-CoV-2 Distribution Over Sequence Cases
US	268	197 (73.5%)	96.4% with D614G 2.5% with CAL.20C 1.0% with variant of P.2 lineage
South Africa	136	91 (66.9%)	94.5% with 20H/501Y.V2 (B.1.351) 3.3% with D614G 2.2% with variant of P.2 lineage
Brazil	179	124 (69.3%)	69.4% with variant of P.2 lineage 30.6% with D614G

Summary - Efficacy

Efficacy against moderate to severe/critical COVID-19 met prespecified success criteria:

- Onset ≥14 days after vaccination: 66.9%, (95% CI 59.0, 73.4)
- Onset ≥28 days after vaccination: 66.1% (95% CI 55.0, 74.8)

Efficacy against severe/critical COVID-19 (key secondary efficacy endpoint):

- Onset ≥14 days after vaccination: 76.7% (54.6, 89.1)
- Onset ≥28 days after vaccination: 85.4% (54.2, 96.9)

Reduction in COVID-19 requiring medical intervention:

- Onset ≥14 days after vaccination: 2 in vaccine group vs. 29 in placebo group
- Onset ≥28 days after vaccination: 0 in vaccine group vs. 16 in placebo group

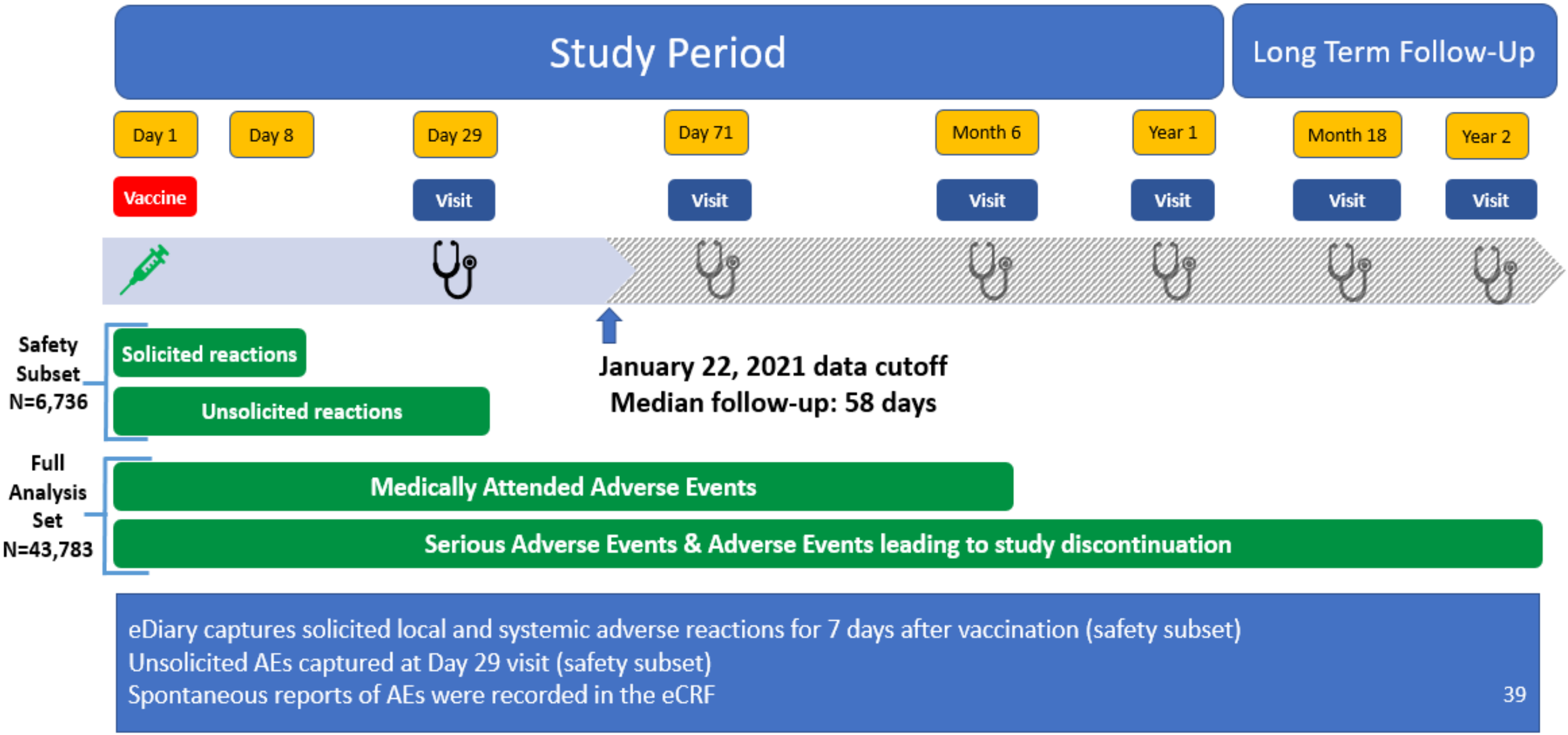
Summary - Efficacy

- Efficacy outcomes were generally consistent across demographic subgroups
- Lower efficacy estimate observed among participants ≥60 years of age with comorbidities
  - VE increased and CI narrowed with inclusion of more cases, indicating the observed result potentially reflects imprecision associated with smaller numbers of cases in this subgroup
  - Vaccine reduced COVID-19-related hospitalizations in this subgroup
- Country to country variation in VE, but confidence intervals were overlapping

Outline

- Introduction
- Clinical development program
- Efficacy data
- **Safety data**
- Pharmacovigilance plan/future studies
- Benefit/risk assessment in context of proposed use under EUA

Study 3001 Safety Monitoring



eDiary captures solicited local and systemic adverse reactions for 7 days after vaccination (safety subset)
Unsolicited AEs captured at Day 29 visit (safety subset)
Spontaneous reports of AEs were recorded in the eCRF

Disposition, Safety Population, Study 3001

Disposition	Ad26.COV2.S n (%)	Placebo n (%)	Total n (%)
Randomized	22174	22151	44325
Vaccinated	21895	21888	43783
Vaccinated with incorrect vaccine	6	5	11
Full analysis set	21895 (100.0)	21888 (100.0)	43783 (100.0)
Participants with ≥2 months follow-up	11948 (54.6)	11955 (54.6)	23903 (54.6)
Participants unblinded to treatment	1080 (4.9)	1177 (5.4)	2257 (5.2)
Discontinued from study	49 (0.2%)	96 (0.4%)	145 (0.3)
Reason for discontinuation			
Withdrawal by participant	35 (0.2)	66 (0.3)	101 (0.2)
Death	2 (<0.1)	12 (0.1)	14 (<0.1)
Lost to follow-up	6 (<0.1)	5 (<0.1)	11 (<0.1)
Physician decision	2 (<0.1)	1 (<0.1)	3 (<0.1)
Protocol deviation	0	1 (<0.1)	1 (<0.1)
Other	4 (<0.1)	11 (0.1)	15 (<0.1)
Safety subset	3356 (15.3)	3380 (15.4)	6736 (15.4)
Completed post vaccination (Day 1-29)	3354 (99.9)	3376 (99.9)	6730 (99.9)

Demographics, Safety Subset (N=6736), Study 3001

Subgroup Safety Subset	Ad26.COV2.S N=3356	Placebo N=3380	Total N=6736
Age group (years)			
18-59	2036 (60.7%)	2049 (60.6%)	4085 (60.6%)
≥60	1320 (39.3%)	1331 (39.4%)	2651 (39.4%)
Sex			
Female	1637 (48.8%)	1615 (47.8%)	3252 (48.3%)
Male	1719 (51.2%)	1765 (52.2%)	3484 (51.7%)
Race			
Amer Indian/Alaska Native	9 (0.3%)	9 (0.3%)	18 (0.3%)
Asian	114 (3.4%)	105 (3.1%)	219 (3.3%)
Black or African American	267 (8.0%)	260 (7.7%)	527 (7.8%)
Native Hawaiian/Pacific Is	9 (0.3%)	10 (0.3%)	19 (0.3%)
White	2798 (83.4%)	2823 (83.5%)	5621 (83.4%)
Multiple	97 (2.9%)	112 (3.3%)	209 (3.1%)
Unknown	20 (0.6%)	17 (0.5%)	37 (0.5%)
Country			
Brazil	1291 (38.5%)	1299 (38.4%)	2590 (38.5%)
United States	1727 (51.5%)	1735 (51.3%)	3462 (51.4%)
South Africa	338 (10.1%)	346 (10.2%)	684 (10.2%)
Baseline SARS-CoV-2 serostatus			
Positive	154 (4.6%)	147 (4.3%)	301 (4.5%)
Negative	3117 (92.9%)	3129 (92.6%)	6246 (92.7%)
Missing	85 (2.5%)	104 (3.1%)	189 (2.8%)
Comorbidity at baseline			
One or more	1135 (33.8%)	1164 (34.4%)	2299 (34.1%)
None	2221 (66.2%)	2216 (65.6%)	4437 (65.9%)

Solicited Local Reactions Within 7 Days After Vaccination

Adverse Reaction	18-59 Years Ad26.COV2.S N=2036 n (%)	18-59 Years Placebo N=2049 n (%)	≥60 Years Ad26.COV2.S N=1320 n (%)	≥60 Years Placebo N=1331 n (%)
Any Local	1218 (59.8%)	413 (20.2%)	467 (35.4%)	244 (18.3%)
Grade 3	18 (0.9%)	4 (0.2%)	5 (0.4%)	2 (0.2%)
Pain	1193 (58.6%)	357 (17.4%)	439 (33.3%)	207 (15.6%)
Grade 3	8 (0.4%)	0	3 (0.2%)	2 (0.2%)
Erythema (≥25mm)	184 (9.0%)	89 (4.3%)	61 (4.6%)	42 (3.2%)
Grade 3 (≥100mm)	6 (0.3%)	2 (0.1%)	1 (0.1%)	0
Swelling (≥25mm)	142 (7.0%)	32 (1.6%)	36 (2.7%)	21 (1.6%)
Grade 3 (≥100mm)	5 (0.2%)	2 (0.1%)	2 (0.2%)	0

The rate of local ARs among vaccine recipients who were seronegative for SARS-CoV-2 at baseline (n=3,202) was similar to that of those seropositive at baseline (n=154): 50.0% vs. 53.9%.

Solicited Systemic Reactions Within 7 Days After Vaccination

Adverse Reaction	18-59 Years Ad26.COV2.S N=2036 n/N (%)	18-59 Years Placebo N=2049 n/N (%)	≥60 Years Ad26.COV2.S N=1320 n/N (%)	≥60 Years Placebo N=1331 n/N (%)
Any Systemic	1252 (61.5%)	745 (36.4%)	598 (45.3%)	440 (33.1%)
Grade 3	47 (2.3%)	12 (0.6%)	14 (1.1%)	9 (0.7%)
Fatigue	891 (43.8%)	451 (22.0%)	392 (29.7%)	277 (20.8%)
Grade 3	25 (1.2%)	4 (0.2%)	10 (0.8%)	5 (0.4%)
Headache	905 (44.4%)	508 (24.8%)	401 (30.4%)	294 (22.1%)
Grade 3	18 (0.9%)	5 (0.2%)	5 (0.4%)	4 (0.3%)
Myalgia	796 (39.1%)	248 (12.1%)	317 (24.0%)	182 (13.7%)
Grade 3	29 (1.4%)	1 (<0.1%)	3 (0.2%)	5 (0.4%)
Nausea	315 (15.5%)	183 (8.9%)	162 (12.3%)	144 (10.8%)
Grade 3	3 (0.1%)	3 (0.1%)	3 (0.2%)	3 (0.2%)
Fever (≥38.0℃)	261 (12.8%)	14 (0.7%)	41 (3.1%)	6 (0.5%)
Grade 3 (39.0-40℃)	7 (0.3%)	0	1 (0.1%)	0
Antipyretic/Analgesic Use	538 (26.4%)	123 (6.0%)	130 (9.8%)	68 (5.1%)

Among vaccine recipients, rates of systemic ARs by baseline SARS-CoV-2 serostatus were similar: 55.4% vs. 50.0%, for seronegative (n=3,202) and seropositive (n=154) vaccine recipients, respectively.

Unsolicited Adverse Events

Adverse Event Type	Ad26.COV2.S n (%)	Placebo n (%)
Full analysis set	**N=21895**	**N=21888**
Medically attended AE	304 (1.4)	408 (1.9)
Related medically attended AE*	22 (0.1)	22 (0.1)
SAE	83 (0.4)	96 (0.4)
Related SAE*	7 (<0.1)	2 (<0.1)
Deaths	3 (<0.1)	16 (0.1)
Related deaths*	0	0
AE leading to study discontinuation	0	0
Safety subset	**N=3356**	**N=3380**
Unsolicited AE up to 28 days after vaccination	440/3356 (13.1)	407/3380 (12.0)
18-59 years of age	285/2036 (14.0)	275/2049 (13.4)
≥60 years of age	155/1320 (11.7)	132/1331 (9.9)
Grade 3 unsolicited AE	16/3356 (0.5)	16/3380 (0.5)
Grade 4 unsolicited AE	3/3356 (0.1)	2/3380 (0.1)

* Relatedness per investigator

Unsolicited Adverse Events Occurring in ≥1% of Vaccine Group Participants Within 28 Days Following Vaccination, Safety Subset

System Organ Class Preferred Term	Ad26.COV2.S N=3356 Any Grade n (%)	Ad26.COV2.S N=3356 ≥Grade 3 n (%)	Placebo N=3380 Any Grade n (%)	Placebo N=3380 ≥Grade 3 n (%)
General disorders, administration site	211 (6.3%)	5 (0.1%)	134 (4.0%)	2 (0.1%)
Chills	67 (2.0%)	1 (<0.1%)	19 (0.6%)	0
Fatigue	64 (1.9%)	1 (<0.1%)	77 (2.3%)	1 (<0.1%)
Vaccination site pain	42 (1.3%)	1 (<0.1%)	22 (0.7%)	0
Musculoskeletal and connective tissue	103 (3.1%)	3 (0.1%)	89 (2.6%)	4 (0.1%)
Myalgia	49 (1.5%)	0	58 (1.7%)	2 (0.1%)
Arthralgia	35 (1.0%)	1 (<0.1%)	24 (0.7%)	2 (0.1%)
Nervous system disorders	98 (2.9%)	3 (0.1%)	108 (3.2%)	5 (0.1%)
Headache	72 (2.1%)	1 (<0.1%)	82 (2.4%)	1 (<0.1%)
Respiratory, thoracic and mediastinal	93 (2.8%)	3 (0.1%)	88 (2.6%)	4 (0.1%)
Nasal congestion	40 (1.2%)	1 (<0.1%)	38 (1.1%)	2 (0.1%)
Cough	33 (1.0%)	1 (<0.1%)	33 (1.0%)	0
Gastrointestinal disorders	87 (2.6%)	2 (0.1%)	90 (2.7%)	2 (0.1%)
Diarrhea	33 (1.0%)	2 (0.1%)	35 (1.0%)	0
Infections and infestations	57 (1.7%)	3 (0.1%)	87 (2.6%)	6 (0.2%)

FDA Review of AEs of Clinical Interest

Imbalance between vaccine group vs. placebo

Embolic and thrombotic events (SMQ)

Vaccine: 0.06% (n=14), placebo: 0.05% (n=10)

- Deep vein thrombosis: vaccine n=6, placebo n=2
- Pulmonary embolism: vaccine n=4, placebo n=1
- Sinus venous thrombosis: vaccine n=1, placebo n=0
- Vaccine cannot be excluded as a contributing factor
- Assessment confounded by risk factors in participants

Tinnitus (PT) Vaccine n=6, placebo n=0

- 3 events occurred within 2 days of vaccination; 3 events within 12-22 days
- Vaccine cannot be excluded as a contributing factor
- Assessment confounded by risk factors in participants

Urticaria (PT) Vaccine n=8, placebo n=3

- Within 7 days of vaccination, 5 vaccine vs. 1 placebo
- Plausible relationship to vaccination

Serious Adverse Events

Likely Related (FDA Assessment)	• 42 yo male: hypersensitivity event, with diffuse urticaria on Day 3 and angioedema of the lips (no respiratory distress) on Day 5. • 30 yo male: vaccine site pain on Day 1 that progressed to greater portion of arm. Non-responsive to analgesics. Symptoms ongoing. • 35 yo male: extreme generalized weakness, fever, headache on Day 2. Admitted to hospital. CPK elevation consistent with mild myositis. Resolved on Day 4.
Indeterminate Relationship (FDA Assessment)	Facial paralysis (Bell's palsy): • 2 SAEs (Days 3 and 16) in vaccine group vs. 2 non-serious AEs in placebo group (Days 2 and 29) Guillain-Barré syndrome: • 1 SAE (Day 16) in vaccine group vs. 1 SAE (Day 10) in placebo group Pericarditis: • 68 yo male experienced sudden, sharp chest pain on Day 17; subsequently diagnosed with pericarditis. No etiology determined.

Deaths

Deaths: 19 total
(3 vaccine, 16 placebo)

Post data cutoff: 6 additional
(2 vaccine, 4 placebo)

Vaccine group deaths:

- 61 yo: pneumonia Day 13; died Day 24
- 42 yo with HIV: lung abscess Day 33; died Day 59
- 66 yo: unknown cause, Day 45

Post data cutoff:

- 77 yo: unknown cause, Day 52
- 68 yo: decompensated cardiac disease, Day 50

Pregnancies

Participants of childbearing potential were screened and excluded if pregnant or planning a pregnancy within 3 months of vaccination

8 pregnancies (as of January 22, 2021)

- 4 vaccine, 4 placebo
- Vaccination prior to last menstrual period (LMP): 1 vaccine, 0 placebo
- Vaccination within 30 days after LMP: 3 vaccine, 4 placebo
- Pregnancy outcomes in vaccine group:
  - 1 spontaneous abortion
  - 1 ectopic pregnancy
  - 2 ongoing

Summary - Safety

- The totality of the clinical data submitted with the EUA request meets the expectations for duration of follow-up
- Evaluation of the safety population provides data from >43,000 participants
- Reactogenicity events among vaccine recipients were frequent, mostly mild to moderate, and occurred less frequently in adults ≥60 years old compared to those 18-50 years old.
- A single SAE of hypersensitivity and more cases of urticaria were reported in vaccine group.
- Numerical imbalance in reported thromboembolic events and tinnitus. Vaccine as contributing factor could not be excluded.

Outline

- Introduction
- Clinical development program
- Efficacy data
- Safety data
- **Pharmacovigilance plan/future studies**
- Benefit/risk assessment in context of proposed use under EUA

Pharmacovigilance Plan

Safety specifications of Sponsor's pharmacovigilance plan for Ad26.COV2.S

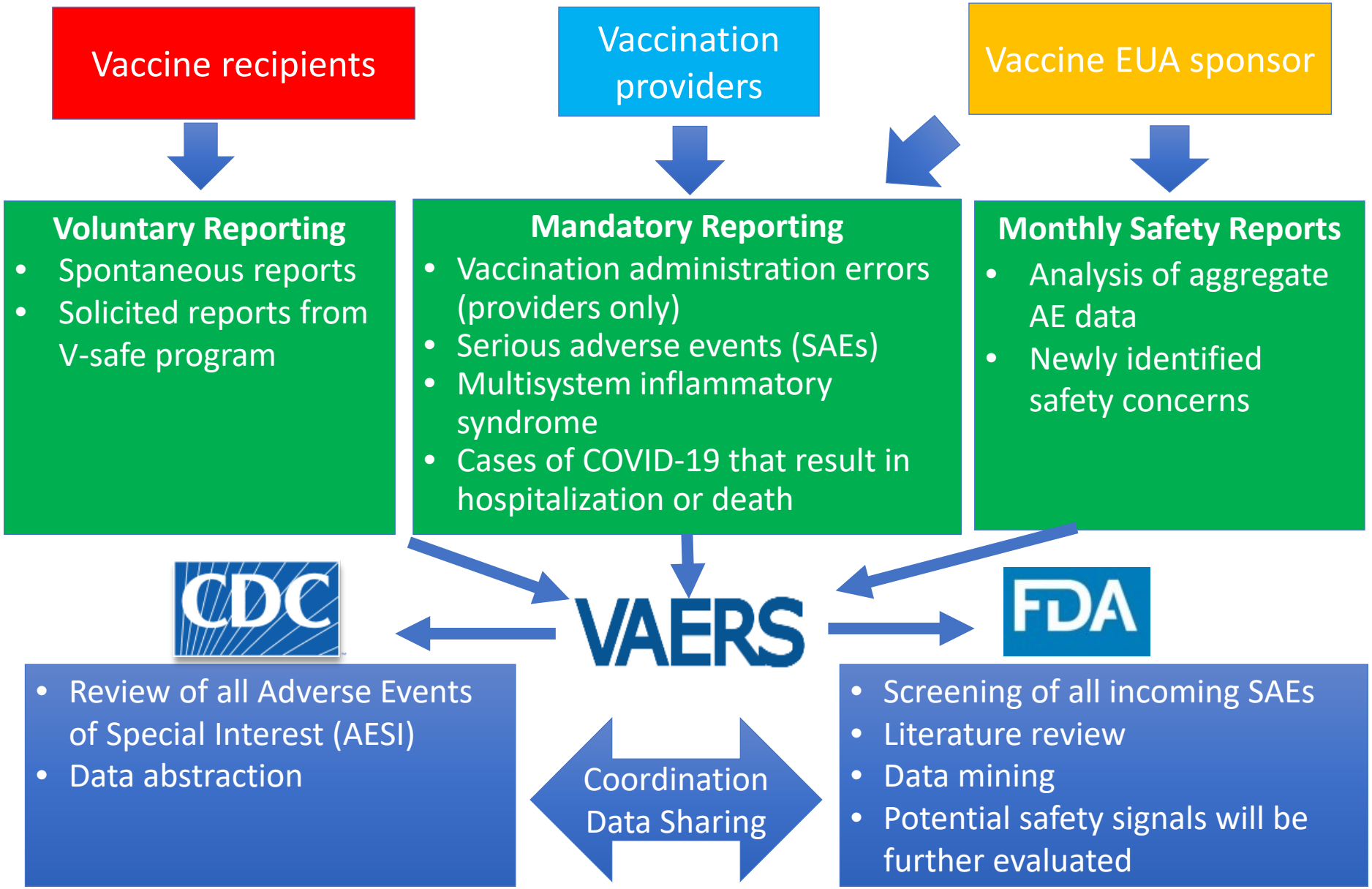
Important potential risks

- Vaccine-associated enhanced disease, including vaccine-associated enhanced respiratory disease
- Anaphylaxis
- Thromboembolic events

Important missing information

- Use in pregnant and breastfeeding women
- Use in immunocompromised patients
- Use in patients with autoimmune or inflammatory disorders
- Immunogenicity in subjects with immunosuppression
- Use in frail patients with comorbidities
- Interaction with other vaccines
- Long-term safety
- Use in the pediatric population

Adverse Event Reporting Under EUA



Surveillance Studies Planned by the Sponsor

Pregnancy study: multi-country, observational, prospective cohort study of pregnant women vaccinated with Ad26.COV2.S to assess obstetric, neonatal, and infant outcomes

Active surveillance study of safety: retrospective, observational, propensity-scored matched cohort study using health insurance claims and electronic health records to assess the risk of prespecified adverse events of special interest following vaccination with Ad26.COV2.S

Active surveillance study of effectiveness: retrospective, observational propensity-scored matched cohort study using health insurance claims and electronic health records to estimate the effectiveness of Ad26.COV2.S to prevent medically attended COVID-19 in individuals vaccinated according to national immunization recommendations

Outline

- Introduction
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- **Benefit/risk assessment in context of proposed use under EUA**

Benefit/Risk Assessment in Context of Proposed EUA

Benefits

- Reduced risk of symptomatic COVID-19 at least 14 days after vaccination
- Reduced risk of severe/critical COVID-19 at least 14 days after vaccination
  - Reduced risk of COVID-19 related hospitalizations and deaths
  - Efficacy against severe/critical COVID-19 was similar across geographic regions
- Efficacy appears generally consistent across demographic groups
- Administered as a single-dose regimen

Benefit/Risk Assessment in Context of Proposed EUA

Risks

- Reactogenicity: Local and systemic adverse reactions
  - Injection site pain (48.6%), headache (38.9%), fatigue (38.2%) and myalgia (33.2%)
- Adverse events likely related to vaccination: hypersensitivity reactions
- Adverse events for which vaccine could not be excluded as contributing factor: thromboembolic events, tinnitus

Benefit/Risk Assessment in Context of Proposed EUA

Data Gaps/Unknown Risks

- Duration of immune protection
- Efficacy against asymptomatic infection or transmission
- Efficacy against new variant strains
- Safety in subpopulations: pregnant and lactating, pediatric, immunocompromised, individuals previously infected with SARS-CoV-2
- Adverse events that are uncommon and/or require longer follow-up to be detected
- Vaccine-enhanced disease: evidence suggests low risk; longer follow-up needed to fully evaluate risk

Question for VRBPAC Vote (yes/no)

Based on the totality of scientific evidence available, do the benefits of the Janssen COVID-19 vaccine outweigh its risks for use in individuals 18 years of age and older?

Extra Slides

Subgroup Analyses of Primary Efficacy Endpoint

	Onset at Least 14 Days			Onset at Least 28 Days		
Co-primary Endpoint Subgroup	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**
Age group, comorbidity (centrally confirmed)						
18-59, no	61 (8346)	178 (8411)	**65.8%**	33 (8267)	112 (8254)	**70.7%**
	1434.5	1431.9	(54.0, 74.9)	1429.0	1421.0	(56.5, 80.8)
18-59, yes	34 (4404)	82 (4371)	**59.1%**	19 (4350)	40 (4273)	**53.4%**
	672.3	663.0	(38.3, 73.4)	668.6	656.0	(17.6, 74.5)
≥60, no	8 (3391)	44 (3335)	**82.2%**	6 (3355)	29 (3298)	**79.7%**
	542.1	530.5	(61.8, 92.8)	539.4	528.0	(50.4, 93.1)
≥60, yes	13 (3373)	44 (3427)	**70.3%**	8 (3334)	12 (3353)	**33.2%**
	467.7	470.6	(43.8, 85.3)	465.0	465.7	(-77.6, 76.3)
Age group, comorbidity (all PCR+ including nonconfirmed)						
18-59, no	89 (8346)	258 (8411)	**65.6%**	58 (8267)	180 (8254)	**68.0%**
	1433.5	1428.2	(56.1, 73.3)	1428.2	1418.3	(56.8, 76.6)
18-59, yes	48 (4404)	131 (4371)	**63.9%**	29 (4350)	79 (4273)	**64.0%**
	671.5	661.0	(49.4, 74.7)	668.1	654.8	(44.3, 77.3)
≥60, no	14 (3391)	57 (3335)	**76.0%**	11 (3355)	39 (3298)	**72.4%**
	541.6	530.0	(56.3, 87.6)	539.0	527.6	(45.0, 87.3)
≥60, yes	22 (3373)	63 (3427)	**64.9%**	15 (3334)	26 (3353)	**42.3%**
	467.4	469.9	(42.2, 79.4)	464.9	465.2	(-13.1, 71.6)

Severe/critical COVID-19, by age and presence of comorbidity

	Onset at Least 14 Days			Onset at Least 28 Days		
Co-primary Endpoint Subgroup	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**
Age group, comorbidity (molecularly confirmed)						
18-59, no	6 (8346)	22 (8411)	**72.6%**	1 (8267)	16 (8254)	**93.8%**
	1439.4	1446.5	(30.3, 90.9)	1431.3	1428.4	(59.9, 99.9)
18-59, yes	2 (4404)	19 (4371)	**89.6%**	1 (4350)	8 (4273)	**87.7%**
	674.9	668.7	(56.8, 98.8)	669.7	658.2	(8.4, 99.7)
≥60, no	0 (3391)	9 (3335)	**100.0%**	0 (3355)	6 (3298)	**100.0%**
	542.7	533.8	(50.2, 100.0)	539.8	529.9	(16.6, 100.0)
≥60, yes	6 (3373)	10 (3427)	**39.4%**	3 (3334)	4 (3353)	**24.9%**
	468.1	473.1	(-84.2, 81.9)	465.3	466.0	(-344.0, 89.0)
Age group, comorbidity (all PCR+)						
18-59, no	9 (8346)	27 (8411)	**66.5%**	3 (8267)	20 (8254)	**85.0%**
	1439.2	1446.2	(26.6, 86.1)	1431.2	1428.3	(49.5, 97.2)
18-59, yes	3 (4404)	25 (4371)	**88.1%**	2 (4350)	13 (4273)	**84.9%**
	674.8	668.4	(61.1, 97.7)	669.7	658.0	(33.2, 98.3)
≥60, no	0 (3391)	12 (3335)	**100.0%**	0 (3355)	8 (3298)	**100.0%**
	542.7	533.7	(64.6, 100.0)	539.8	529.8	(42.5, 100.0)
≥60, yes	7 (3373)	16 (3427)	**55.8%**	3 (3334)	7 (3353)	**57.1%**
	468.0	472.7	(-13.5, 84.6)	465.3	465.9	(-88.0, 92.8)

Alternate Age Groups, Moderate to Severe/Critical

	Onset at Least 14 Days			Onset at Least 28 Days		
Co-primary Endpoint Subgroup	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**
Age group, comorbidity (centrally confirmed)						
18-64, no	67 (9871)	198 (9903)	**66.3%**	38 (9776)	127 (9731)	**70.3%**
	1681.0	1671.9	(55.4, 74.9)	1674.3	1659.8	(57.1, 79.9)
18-64, yes	40 (5673)	99 (5649)	**60.1%**	22 (5602)	43 (5522)	**49.7%**
	849.3	839.3	(41.8, 73.1)	844.4	830.3	(14.0, 71.3)
≥65, no	2 (1866)	24 (1843)	**91.8%**	1 (1846)	14 (1821)	**93.0%**
	295.7	290.6	(67.0, 99.1)	294.1	289.2	(53.8, 99.8)
≥65, yes	7 (2104)	27 (2149)	**73.7%**	5 (2082)	9 (2104)	**44.0%**
	290.6	294.3	(38.2, 90.4)	289.2	291.4	(-86.0, 85.3)
Age group, comorbidity (all PCR+)						
18-64, no	100 (9871)	285 (9903)	**65.2%**	67 (9776)	199 (9731)	**66.7%**
	1679.4	1667.9	(56.1, 72.5)	1673.2	1657.0	(55.8, 75.1)
18-64, yes	57 (5673)	156 (5649)	**64.0%**	34 (5602)	87 (5522)	**61.6%**
	848.4	836.9	(50.9, 73.9)	843.9	828.9	(42.3, 75.0)
≥65, no	3 (1866)	30 (1843)	**90.2%**	2 (1846)	20 (1821)	**90.2%**
	295.7	290.3	(68.4, 98.1)	294.1	288.9	(59.6, 98.9)
≥65, yes	13 (2104)	38 (2149)	**65.4%**	10 (2082)	18 (2104)	**44.1 %**
	290.4	294.0	(33.6, 83.1)	289.1	291.1	(-27.8, 76.9)

Alternate Age Groups, Severe/Critical Only

	Onset at Least 14 Days			Onset at Least 28 Days		
Co-primary Endpoint Subgroup	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE%[a] (95% CI)**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE%[a] (95% CI)**
Age group and comorbidity, molecularly confirmed						
18-64, no	6 (9871)	27 (9903)	**77.8%**	1 (9776)	19 (9731)	**94.8%**
	1686.3	1687.9	(45.0, 92.5)	1677.0	1668.3	(67.1, 99.8)
18-64, yes	5 (5673)	23 (5649)	**78.4%**	1 (5602)	9 (5522)	**89.1%**
	852.1	845.9	(42.0, 93.6)	845.8	832.6	(21.1, 99.8)
≥65, no	0 (1866)	4 (1843)		0 (1846)	3 (1821)	
	295.8	292.4		294.1	290.0	
≥65, yes	3 (2104)	6 (2149)	**49.1%**	3 (2082)	3 (2104)	**-0.8%**
	290.8	295.9	(-138.2, 91.8)	289.3	291.7	(-652.8, 86.5)
Age group, comorbidities (all PCR+)						
18-64, no	9 (9871)	33 (9903)	**72.7%**	3 (9776)	23 (9731)	**87.0%**
	1686.1	1687.6	(41.7, 88.5)	1676.9	1668.2	(57.1, 97.5)
18-64, yes	6 (5673)	33 (5649)	**82.0%**	2 (5602)	15 (5522)	**86.9%**
	852.1	845.3	(56.4, 93.8)	845.7	832.4	(43.6, 98.5)
≥65, no	0 (1866)	6 (1843)	**100.0%**	0 (1846)	5 (1821)	
	295.8	292.3	(16.1, 100.0)	294.1	289.9	
≥65, yes	4 (2104)	8 (2149)	**49.1%**	3 (2082)	5 (2104)	**39.5%**
	290.8	295.8	(-89.9, 88.8)	289.3	291.6	(-210.8, 90.6)

[a] VE not shown if less than 6 cases are observed for an endpoint

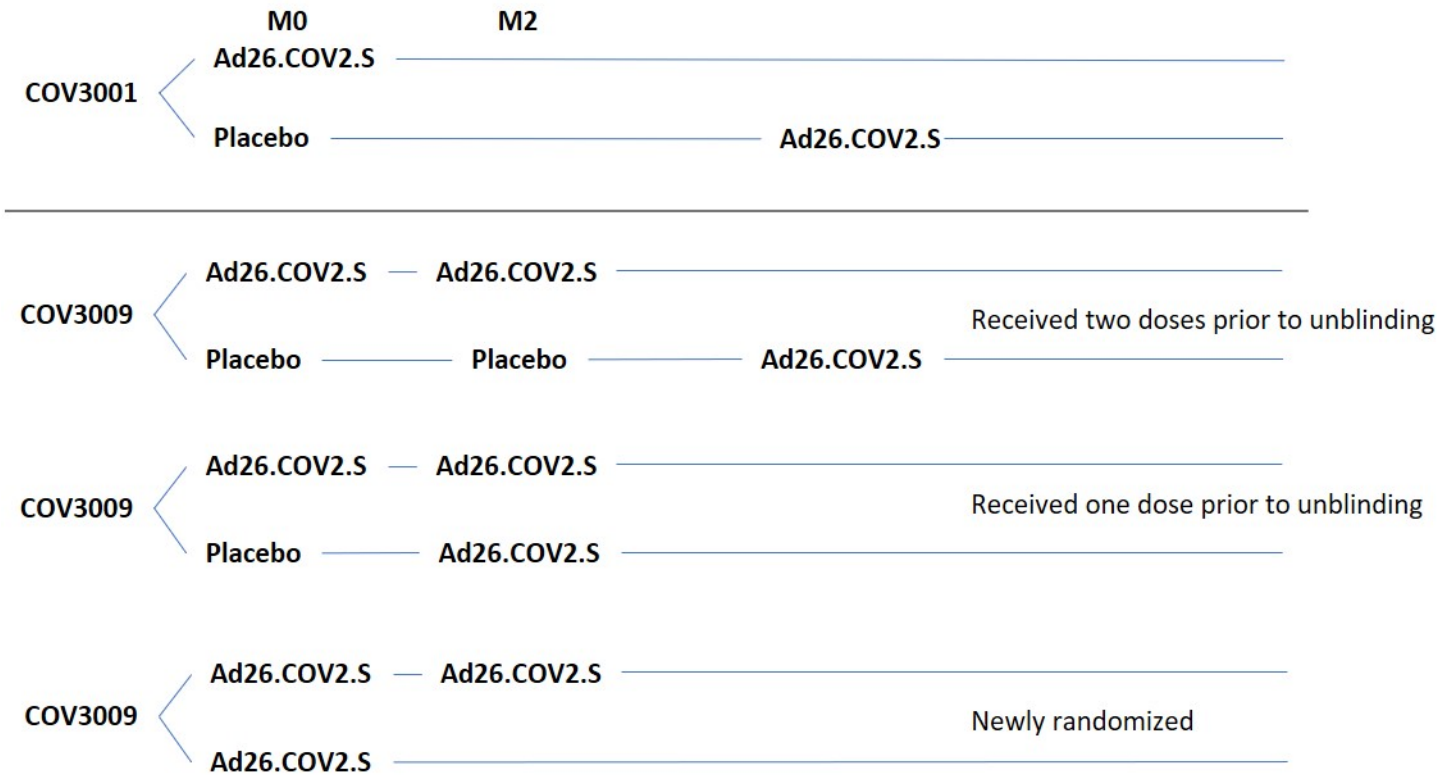
Participants with Obesity, Moderate to Severe/Critical

	Onset at Least 14 Days			Onset at Least 28 Days		
Co-primary Endpoint Subgroup	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**
By age group and comorbidity						
18-59, Obesity	40 (3417)	113 (3350)	**65.7%**	24 (3374)	68 (3269)	**66.0%**
	522.1	506.0	(50.4, 76.7)	519.5	500.8	(45.1, 79.6)
≥60, Obesity	11 (1966)	38 (2002)	**70.8%**	6 (1944)	18 (1954)	**66.6%**
	272.0	274.3	(41.7, 86.5)	270.6	271.2	(12.1, 89.1)
18-64, Obesity	45 (4235)	129 (4169)	**66.1%**	26 (4181)	73 (4069)	**65.5%**
	635.9	618.5	(52.0, 76.4)	632.5	612.0	(45.4, 78.9)
≥65, Obesity	6 (1148)	22 (1183)	**72.1%**	4 (1137)	13 (1154)	**68.7%**
	158.2	161.9	(29.0, 90.7)	157.5	160.0	(-1.2, 92.6)

Participants with Obesity, Severe/Critical Only

	Onset at Least 14 Days			Onset at Least 28 Days		
Co-primary Endpoint Subgroup	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**	**Ad26.COV2.S Cases (N) Person-yrs**	**Placebo Cases (N) Person-yrs**	**VE% (95% CI)**
By age group and comorbidity						
18-59, Obesity	2 (3417)	22 (3350)	**91.1%**	1 (3374)	11 (3269)	**91.2%**
	524.9	512.5	(63.9, 99.0)	520.7	503.8	(39.5, 99.8)
≥60, Obesity	6 (1966)	13 (2002)	**53.2%**	2 (1944)	6 (1954)	**66.5%**
	272.2	275.8	(-31.9, 85.4)	270.7	271.7	(-87.1, 96.7)
18-64, Obesity	5 (4235)	28 (4169)	**82.5%**	1 (4181)	12 (4069)	**91.9%**
	638.8	625.6	(54.1, 94.7)	633.9	615.2	(45.3, 99.8)
≥65, Obesity	3 (1148)	7 (1183)	**56.0%**	2 (1137)	5 (1154)	**59.3%**
	158.3	162.7	(-92.9, 92.7)	157.6	160.3	(-148.6, 96.1)

Proposed Amendment to Study Design After EUA



ITT Analysis: Vaccine Efficacy With Onset at Least 1 Day After Vaccination

Table 15: Summary of Vaccine Efficacy Against COVID-19 With Onset at Least 1 Day After Vaccination; Full Analysis Set (Study VAC31518COV3001)

	Ad26 5e10 vp		Placebo			
	#Cases	(N)/Person-Years	#Cases	(N)/Person-Years	VE	95% CI
Analysis set: Full analysis set		(21895)		(21888)		
FAS Seronegative at baseline[a]		(19744)		(19822)		
Primary endpoint						
Moderate and severe/critical COVID-19	193	3183.02	432	3172.77	55.5%	(47.11; 62.62)
Age 18-59 years	151	2150.57	316	2146.75	52.3%	(41.91; 60.97)
Age >=60 years	42	1032.45	116	1026.02	64.0%	(48.38; 75.34)
Secondary endpoints						
All SARS-CoV-2 infections	325	3171.12	609	3159.41	46.8%	(39.07; 53.67)
Any symptomatic COVID-19 severity	195	3182.80	435	3172.56	55.3%	(46.97; 62.46)
Mild	2	3182.80	3	3172.56		
Moderate	172	3183.02	354	3172.77	51.6%	(41.73; 59.87)
Severe/critical	21	3201.49	78	3207.89	73.0%	(55.86; 84.18)
Asymptomatic/Undetected SARS-CoV-2 infections[c]	130	3171.12	174	3159.41	25.6%	(6.03; 41.16)
All symptomatic COVID-19 (BOD)[b]	195	3182.80	435	3172.56	57.9%	(49.71; 64.64)
Age 18-59 years	152	2150.46	316	2146.75	54.9%	(44.77; 63.04)
Age >=60 years	43	1032.34	119	1025.81	65.3%	(49.57; 75.84)
Req. Medical intervention[d]	5	3202.82	14	3213.38	64.2%	(-5.28; 89.90)
Supplementary Endpoints						
Primary endpoint including non-confirmed cases	263	3178.80	617	3163.20	57.6%	(50.92; 63.42)
US FDA Harmonized COVID-19 cases	192	3182.93	429	3172.95	55.4%	(46.99; 62.57)

Vaccine Efficacy by Virus Variant

Strain	Onset After Vaccination	Ad26.COV2.S No. of cases (N) Person-years	Placebo No. of cases (N) Person-years	VE%[a] (95% CI)
Reference Strain: D614G mutation (B1.1 lineage)	At least 14 days	40 (19514) 3116.57	182 (19544) 3096.12	**78.2** (69.11, 84.9)
	At least 28 days	28 (19306) 3102	95 (19178) 3070.65	**70.8** (55.12, 81.58)
20H/501Y.V2	At least 14 days	25 (19514) 3116.57	45 (19544) 3096.12	**44.8** (8.05, 67.57)
	At least 28 days	13 (19306) 3102	37 (19178) 3070.65	**65.2** (33.05, 83.04)
P.2 lineage	At least 14 days	14 (19514) 3116.57	48 (19544) 3096.12	**71.0** (46.57, 85.25)
	At least 28 days	6 (19306) 3102	27 (19178) 3070.65	**78.0** (45.61, 92.57)
CAL.20C	At least 14 days	3 (19514) 3116.57	2 (19544) 3096.12	
	At least 28 days	1 (19306) 3102	2 (19178) 3070.65	
Non D614 variants combined (20H/501Y.V2, P.2, CAL.20C)	At least 14 days	42 (19514) 3116.57	95 (19544) 3096.12	**56.1** (36.21, 70.21)
	At least 28 days	20 (19306) 3102	66 (19178) 3070.65	**70.0** (49.89, 82.78)

N: Risk Set

[a] VE not shown if less than 6 cases are observed for an endpoint

Variant Strains of Any PCR-positive Case, by Country (U.S. or not), Study 3001

	Inside U.S.		Outside U.S.		All countries	
Population Strain	**Ad26.COV2.S n (%)**	**Placebo n (%)**	**Ad26.COV2.S n (%)**	**Placebo n (%)**	**Ad26.COV2.S n (%)**	**Placebo n (%)**
All PCR positive cases	161	317	252	467	413	784
All PCR positive cases with sequencing data	51 (31.7%)	146 (46.1%)	102 (40.5%)	213 (45.6%)	153 (37.0%)	359 (45.8%)
Reference strain: D614G mutation	48 (94.1%)	142 (97.3%)	43 (42.2%)	93 (43.7%)	91 (59.5%)	235 (65.5%)
Non D614 variants combined	3 (5.9%)	4 (2.7%)	59 (57.8%)	120 (56.3%)	62 (40.5%)	124 (34.5%)
20H/501Y.V2	_	_	31 (30.4%)	55 (25.8%)	31 (20.3%)	55 (15.3%)
P.2 lineage		2 (1.4%)	28 (27.5%)	65 (30.5%)	28 (18.3%)	67 (18.7%)
CAL.20C	3 (5.9%)	2 (1.4%)	_	_	3 (2.0%)	2 (0.6%)

Variant Strains of Any PCR-positive Case, by Country (U.S. or not), Age Group, and Presence of Comorbidity at Baseline, Study 3001

		Inside U.S.		Outside U.S.		All countries	
Strain	**Subgroup**	**Ad26.COV2.S n (%)**	**Placebo n (%)**	**Ad26.COV2.S n (%)**	**Placebo n (%)**	**Ad26.COV2.S n (%)**	**Placebo n (%)**
Reference strain: D614G mutation (B1.1 lineage)	Overall	**48 (94.1%)**	**142 (97.3%)**	**43 (42.2%)**	**93 (43.7%)**	**91 (59.5%)**	**235 (65.5%)**
	18-59 years	34 (91.9%)	98 (97.0%)	39 (44.3%)	75 (46.6%)	73 (58.4%)	173 (66.0%)
	18-59 without comorbidities	16 (84.2%)	64 (97.0%)	26 (46.4%)	56 (52.8%)	42 (56.0%)	120 (69.8%)
	18-59 with comorbidities	18 (100.0%)	34 (97.1%)	13 (40.6%)	19 (34.5%)	31 (62.0%)	53 (58.9%)
	≥60 years	14 (100.0%)	44 (97.8%)	4 (28.6%)	18 (34.6%)	18 (64.3%)	62 (63.9%)
	≥60 without comorbidities	22 (88.0%)	86 (96.6%)	28 (45.2%)	66 (49.6%)	50 (57.5%)	152 (68.5%)
	≥60 with comorbidities	26 (100.0%)	56 (98.2%)	15 (37.5%)	27 (33.8%)	41 (62.1%)	83 (60.6%)
20H/501Y.V2	Overall	_	_	31 (30.4%)	55 (25.8%)	31 (20.3%)	55 (15.3%)
	18-59 years	_	_	26 (29.5%)	38 (23.6%)	26 (20.8%)	38 (14.5%)
	18-59 without comorbidities	_	_	12 (21.4%)	17 (16.0%)	12 (16.0%)	17 (9.9%)
	18-59 with comorbidities	_	_	14 (43.8%)	21 (38.2%)	14 (28.0%)	21 (23.3%)
	≥60 years	_	_	5 (35.7%)	17 (32.7%)	5 (17.9%)	17 (17.5%)
	≥60 without comorbidities	_	_	13 (21.0%)	24 (18.0%)	13 (14.9%)	24 (10.8%)
	≥60 with comorbidities	_	_	18 (45.0%)	31 (38.8%)	18 (27.3%)	31 (22.6%)
P.2 lineage	Overall		2 (1.4%)	28 (27.5%)	65 (30.5%)	28 (18.3%)	67 (18.7%)
	18-59 years		2 (2.0%)	23 (26.1%)	48 (29.8%)	23 (18.4%)	50 (19.1%)
	18-59 without comorbidities		2 (3.0%)	18 (32.1%)	33 (31.1%)	18 (24.0%)	35 (20.3%)
	18-59 with comorbidities	_	_	5 (15.6%)	15 (27.3%)	5 (10.0%)	15 (16.7%)
	≥60 years	_	_	5 (35.7%)	17 (32.7%)	5 (17.9%)	17 (17.5%)
	≥60 without comorbidities		2 (2.2%)	21 (33.9%)	43 (32.3%)	21 (24.1%)	45 (20.3%)
	≥60 with comorbidities	_	_	7 (17.5%)	22 (27.5%)	7 (10.6%)	22 (16.1%)
CAL.20C	Overall	3 (5.9%)	2 (1.4%)	_	_	3 (2.0%)	2 (0.6%)
	18-59 years	3 (8.1%)	1 (1.0%)	_	_	3 (2.4%)	1 (0.4%)
	18-59 without comorbidities	3 (15.8%)		_	_	3 (15.8%)	
	18-59 with comorbidities		1 (2.9%)	_	_		1 (1.1%)
	≥60 years		1 (2.2%)	_	_		1 (1.0%)
	≥60 without comorbidities	3 (12.0%)	1 (1.1%)	_	_	3 (3.4%)	1 (0.5%)
	≥60 with comorbidities		1 (1.8%)	_	_		1 (0.7%)
Non D614 variants combined (20H/501Y.V2, P.2, CAL.20C)	Overall	3 (5.9%)	4 (2.7%)	59 (57.8%)	120 (56.3%)	62 (40.5%)	124 (34.5%)
	18-59 years	3 (8.1%)	3 (3.0%)	49 (55.7%)	86 (53.4%)	52 (41.6%)	89 (34.0%)
	18-59 without comorbidities	3 (15.8%)	2 (3.0%)	30 (53.6%)	50 (47.2%)	33 (44.0%)	2 (3.0%)
	18-59 with comorbidities		1 (2.9%)	19 (59.4%)	36 (65.5%)	19 (38.0%)	37 (41.1%)
	≥60 years		1 (2.2%)	10 (71.4%)	34 (65.4%)	10 (35.7%)	35 (36.1%)
	≥60 without comorbidities	3 (12.0%)	3 (3.4%)	34 (54.8%)	67 (50.4%)	37 (42.5%)	70 (31.5%)
	≥60 with comorbidities		1 (1.8%)	25 (62.5%)	53 (66.3%)	25 (37.9%)	54 (39.4%)

Variants reported in the US*

Variant	Reported Cases in US	Number of States with ≥1 Case Reported
B.1.1.7	1,523	42
B.1.351	21	10
P.1	5	4

*February 19, 2021; https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html

Subgroup Analyses of Primary Efficacy Endpoint, by Comorbidity

	Onset at Least 14 Days			Onset at Least 28 Days		
	Ad26.COV2.S Cases (N)	Placebo Cases (N)		Ad26.COV2.S Cases (N)	Placebo Cases (N)	
Subgroup	**Person-yrs**	**Person-yrs**	**VE%[a] (95% CI)**	**Person-yrs**	**Person-yrs**	**VE%[a] (95% CI)**
Comorbidity, type						
Asthma	1 (238)	9 (278)	**87.2%**	0 (235)	4 (270)	
	34.3	39.5	**(7.6, 99.7)**	34.1	38.9	
Cancer	0 (104)	2 (108)		0 (102)	0 (105)	
	14.2	15.0		14.1	14.8	
Chronic kidney disease	0 (106)	1 (109)		0 (102)	0 (106)	
	15.1	15.3		14.8	15.1	
COPD	1 (213)	5 (195)	**81.5%**	1 (211)	3 (192)	
	30.2	28.0	**(-65.2, 99.6)**	30.1	27.8	
Serious heart	3 (460)	13 (487)	**76.1%**	1 (455)	5 (472)	**79.4%**
conditions	65.3	67.7	**(12.9, 95.6)**	64.9	66.8	**(-83.7, 99.6)**
HIV infection	5 (467)	5 (498)	**-4.8%**	2 (461)	4 (493)	**47.5%**
	69.1	72.4	**(-355.2, 75.9)**	68.7	72.2	**(-266.0, 95.3)**
Hypertension	14 (1999)	38 (2019)	**63.2%**	11 (1978)	17 (1977)	**35.7%**
	283.3	282.8	**(30.6, 81.6)**	281.9	280.2	**(-45.6, 72.8)**
Immuno-compromised	2 (38)	0 (33)		1 (35)	0 (32)	
from blood transplant	4.9	4.6		4.7	4.5	
Liver disease	1 (97)	2 (100)		1 (96)	0 (98)	
	14.5	14.7		14.4	14.6	
Neurologic conditions	0 (77)	1 (115)		0 (77)	1 (114)	
	11.1	16.5		11.1	16.5	
Obesity	51 (5383)	151 (5352)	**66.8%**	30 (5318)	86 (5223)	**65.9%**
	794.1	780.3	**(54.1, 76.3)**	790.0	772.0	**(47.8, 78.3)**
Type 2 diabetes	15 (1399)	32 (1410)	**52.9%**	10 (1380)	13 (1378)	**23.0%**
mellitus	198.7	199.5	**(10.5, 76.3)**	197.5	197.7	**(-90.1, 69.8)**

[a] VE not shown if less than 6 cases are observed for an endpoint

Study 1002 (non-US IND)

Phase 1 safety and immunogenicity study in Japan (N=250)

- Age cohorts: 20-55 years (n=125), ≥65 years (n=125)
- Dose levels: $5x10^{10}$ vp and $1x10^{11}$ vp
- Schedule: 2-dose, 56-day interval

Immunogenicity:

- Two-dose regimen ($5x10^{10}$ vp) elicited SARS-CoV-2 neutralizing antibody response

Safety:

- No safety concerns based on submitted data to date