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

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Vaccines and Related Biological Products Advisory Committee Meeting

FDA Review of Effectiveness and Safety of Janssen COVID-19 Vaccine (Ad26.COV2.S) Booster Dose *Emergency Use Authorization Amendment*

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October 15, 2021

Outline

- Background/Study overview
- Efficacy Data
  - COV3001
  - COV3009
- Immunogenicity Data
  - 2-3 month interval
  - 6 month interval
- Safety Data
  - 2-3 month interval
  - 6 month interval
- Summary

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Janssen COVID-19 Vaccine (Ad26.COV2.S)

Vaccine composition	Dosing Regimen
Recombinant, replication-incompetent human adenovirus type 26 (Ad26) vector, constructed to encode a stabilized form of the Spike protein (from the isolate Wuhan-Hu-1)	Intramuscular single dose of 5×10^{10} viral particles (vp) in a liquid volume of 0.5 mL

- Janssen COVID-19 Vaccine (Ad26.COV2.S) has been available under EUA since February 27, 2021 for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older.
- On October 4, 2021, Janssen (the Sponsor) submitted a request to amend their EUA to include use of a booster dose (5×10^{10} vp) in individuals 18 years of age and older. Janssen's proposed interval between the primary vaccination and booster dose is: "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."

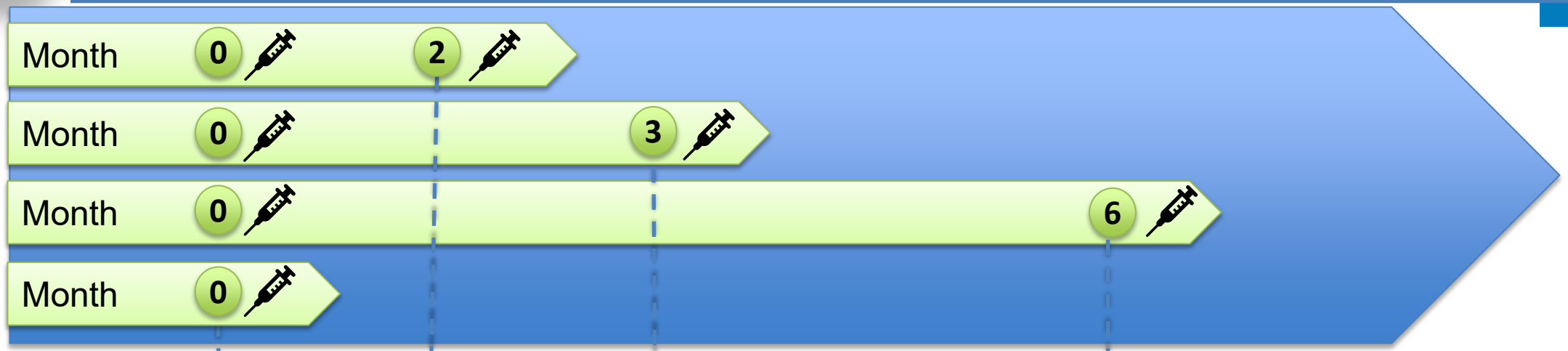
Overview of Relevant Studies (2 doses: 5 x 10^{10} vp dose)

Study Number #	Study Description	Interval(s) Between Doses	Sponsor Analyses Reviewed
COV1001	Phase 1 safety, immunogenicity randomized, double-blind, placebo-controlled	2 months 3 months 6 months	Immunogenicity Safety
COV1002 (non-IND study in Japan)	Phase 1 safety, reactogenicity randomized, double-blind, placebo-controlled	2 months 3 months	Immunogenicity
COV2001	Phase 2a safety, immunogenicity randomized, double-blind, placebo-controlled	2 months 3 months	Immunogenicity
COV3009	Phase 3 efficacy, immunogenicity, and safety randomized, double-blind, placebo-controlled	2 months	Efficacy Safety

Other dosing regimens evaluated in the studies but not considered relevant to the booster dose EUA request are not listed

For comparative purposes, data from COV3001, a Phase 3 efficacy, immunogenicity, and safety randomized, double-blind **single dose** study, was included (n= ~40,000)

Overview of Relevant Data Sources



COV3001 (E, I, S)

COV1001 (I, S)
COV1002 (I, S)
COV2001 (I,S)
COV3009 (E,S)

COV1001 (I, S)
COV1002 (I, S)
COV2001 (I,S)

COV1001 (I, S)

I= Immunogenicity data
S= Safety data
E= Efficacy data
= 5 x 10^{10} vp

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Efficacy Studies: COV3001 Study Design

COV3001: Phase 3 efficacy, safety, immunogenicity of **1-dose regimen**

Multicenter study across US, South Africa, and 6 countries in Latin America

Age cohorts: 18-59 years, ≥60 years with and without comorbidities

N=44,325
Randomized 1:1

$5x10^{10}$ vp Ad26.COV2.S 

OR

Placebo 

The co-primary endpoints were efficacy of a single dose of vaccine to prevent centrally confirmed, moderate and severe/critical COVID-19 occurring (1) at least 14 days after vaccination and (2) at least 28 days after vaccination in study participants without evidence of prior SARS-CoV-2 infection at baseline.

Efficacy Studies: COV3001 Study Data

Vaccine efficacy against centrally confirmed moderate and severe/critical COVID-19 with onset at least 14 days after vaccination, primary analysis and final efficacy analysis

	Primary Analysis (cutoff date January 22, 2021; median follow up 2 months) VE% (95% CI)	Final Analysis (cutoff date July 9, 2021; median follow up 4 months) VE% (95% CI)
Moderate and severe/critical COVID-19	66.9% (59.0, 73.0)	56.3% (51.3, 60.8)
Age 18-59 years	63.7% (53.9, 71.6)	56.6% (51.0, 61.7)
Age ≥60 years	76.3% (61.6, 86.0)	55.0% (42.9, 64.7)
Severe/critical COVID-19	76.7% (54.6, 89.1)	73.3% (63.9, 80.5)
COVID-19 requiring medical intervention	75.0% (-25.3, 97.4)	76.1% (56.9, 87.7)
COVID-19 related deaths	Not calculated	84.5% (47.3, 97.1)

Janssen analyses of July 9, 2021 data cutoff not verified by FDA

Efficacy Studies: COV3001 Study Data

Exploratory Analysis of vaccine efficacy against centrally confirmed COVID-19 with onset at least 14 days after vaccination **by time since vaccination**
(Final Efficacy Analysis)

	Moderate and severe/critical COVID-19 VE% (95% CI)	Severe/critical COVID-19 VE% (95% CI)
Day 15-28	72.3% (62.1, 80.1)	65.5% (27.3, 85.0)
Day 29-56	61.7% (52.5, 69.2)	85.7% (71.0, 93.7)
Day 57-112	50.8% (40.2, 59.7)	67.8% (44.2, 82.2)
Day 113 to end DB Phase	45.2% (33.0, 55.3)	71.7% (51.4, 84.3)

Janssen analyses not verified by FDA

Efficacy Studies: COV3001 Study Data (US Cases Only)

Exploratory analysis of the primary efficacy endpoint (moderate and severe/critical COVID-19) including only **US cases**.

The majority of cases from the U.S. were sequenced to be D614G, with some cases due to B.1.1.7 (Alpha) between February and April.

	Primary Analysis (cutoff date January 22, 2021) VE% (95% CI)	Final Analysis (cutoff date July 9, 2021) VE% (95% CI)
Moderate and severe/critical COVID-19	76.6% (65.5, 84.6)	72.9% (65.7, 78.7)
Severe/critical COVID-19	71.7% (9.8, 93.2)	69.0% (37.3, 85.8)

Janssen analyses of July 9, 2021 data cutoff not verified by FDA

Efficacy Studies: COV3001 Study Data

Post-hoc analyses of vaccine efficacy against centrally confirmed moderate and severe/critical COVID-19 with onset at least 14 days after vaccination by virus variant (final efficacy analysis)

	Ad26.COV2.S N=19400 Cases	Placebo N=19398 Cases	VE% (95% CI)
Reference strain	32	108	71.5% (57.3, 81.4)
B.1.1.7 (Alpha)	9	29	70.1% (35.1, 87.6)
B.1.351 (Beta)	36	56	38.1% (4.2, 60.4)
B.1.617.2/AY.1/AY.2 (Delta)	11	10	-6.0% (-178.3, 59.2)
B.1.427/429 (Epsilon)	8	17	54.7% (-10.8, 83.1)
P.1 (Gamma)	74	112	36.4% (13.9, 53.2)
C.37 (Lambda)	43	46	10.0% (-39.5, 42.0)
P.2 (Zeta)	34	93	64.9% (47.3, 77.0)
B.1.621 (Mu)	38	57	35.8% (1.5, 58.6)

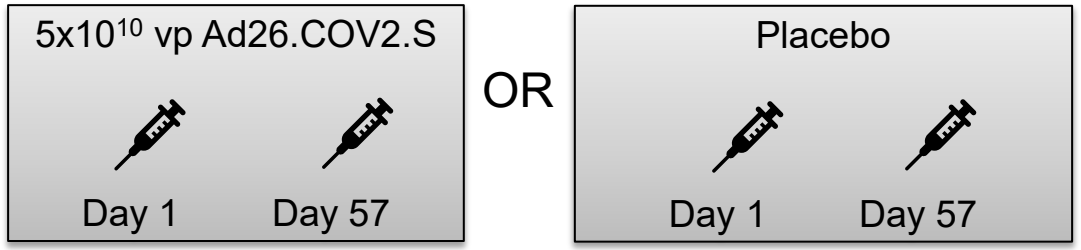
Janssen analysis not verified by FDA

Efficacy Studies: COV3009 Study Design

COV 3009: Phase 3 efficacy, safety, immunogenicity of **2-dose regimen**

- Multicenter study across North and South America, Africa, Europe, Asia
- Age cohorts: 18-59 years, ≥60 years with and without comorbidities

N=31,300
Randomized 1:1



Due to EUA of vaccine, all placebo recipients unblinded and offered 1 dose of vaccine, all new enrollments randomized to 1 or 2 doses (open-label)

The primary endpoint was the first occurrence of molecularly confirmed, moderate and severe/critical COVID-19, with onset at least 14 days after the second vaccination (Day 71) in study participants without evidence of prior SARS-CoV-2 infection at baseline or at Day 71.

Efficacy Studies: COV3009 Study Data

Vaccine efficacy against centrally confirmed moderate and severe/critical COVID-19 with onset at least 14 days after second vaccination (Day ≥71), primary analysis

	Ad26.COV2.S Cases (N) Person-years	Placebo Cases (N) Person-years	Primary Analysis (cutoff date June 25, 2021; median follow up 36 days) VE% (95% CI)
Moderate and severe/critical COVID-19	14 (6024) 1730.0	52 (5615) 1595.0	75.2% (54.6, 87.3)
Age 18-59 years	10 (4692) 1386.9	41 (4359) 1276.3	77.6% (54.4; 90.0)
Age ≥60 years	4 (1332) 343.1	11 (1256) 318.6	66.2% (-14.0; 92.2)
US cases only	1 (2232) 632.4	14 (1999) 559.7	93.7% (58.5; 99.9)
Severe/critical COVID-19	0 (6024) 1730.2	8 (5615) 1598.9	100% (32.6, 100.0)
COVID-19 requiring medical intervention	0 (6024) 1730.2	5 (5615) 1599.1	Not calculated
COVID-19 related deaths	0 (6024) 1730.2	1 (5615) 1599.4	Not calculated

Janssen analyses not verified by FDA

Efficacy Studies: COV3009 Study Data

Post-hoc analyses of vaccine efficacy against centrally confirmed moderate and severe/critical COVID-19 with onset at least 14 days after second vaccination by virus variant

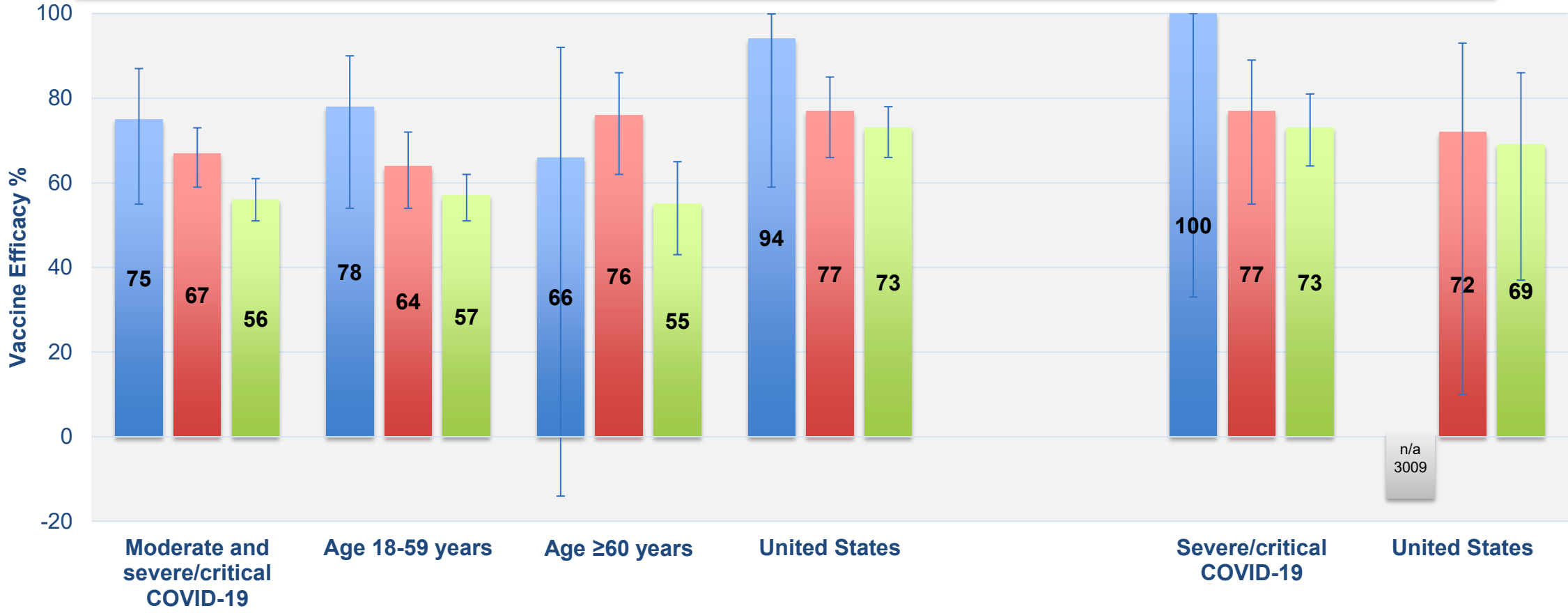
Sequencing data available from 68% of COVID-19 cases

	Ad26.COV2.S N=6024 Cases	Placebo N=5616 Cases	VE% (95% CI)
B.1.1.7 (Alpha)	1	16	75.2% (54.6, 87.3)
B.1.617.2 (Delta)	2	1	Not calculated
B.1.621 (Mu)	4	10	64.1% (-27.9, 91.6)

Janssen analyses not verified by FDA

Efficacy Studies: COV3001 and COV3009

Vaccine efficacy against centrally confirmed moderate and severe/critical COVID-19 with onset at least 14 days after single dose (3001) or second dose (3009)



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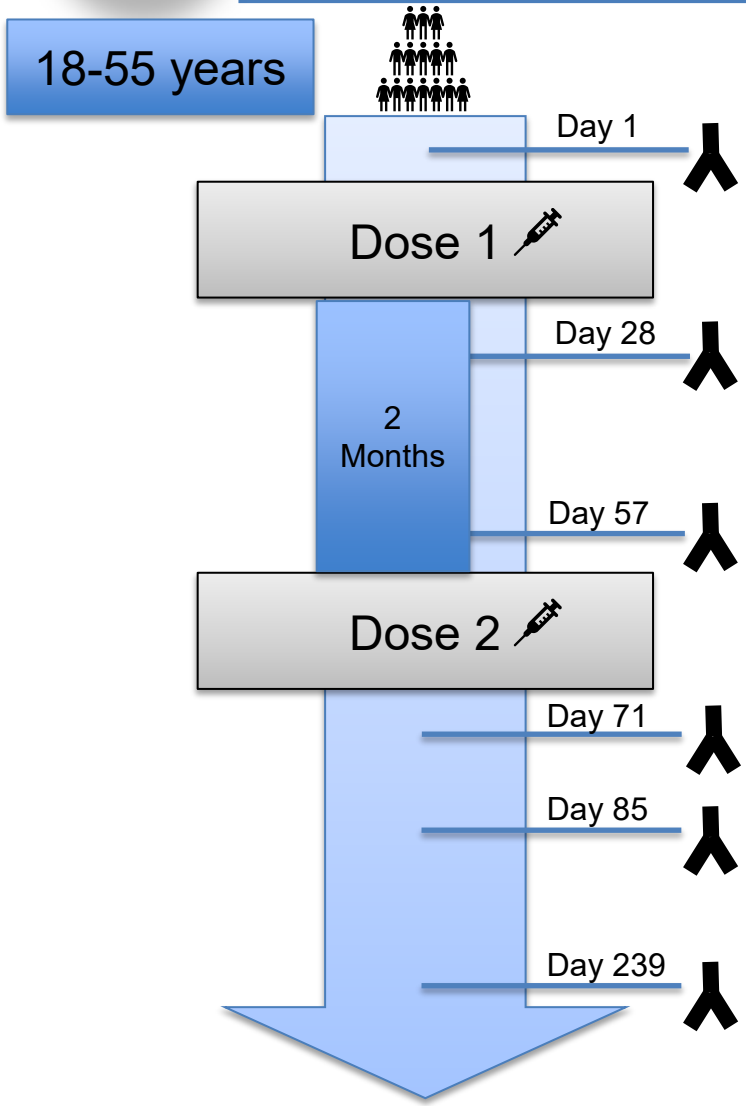
Immunogenicity Data: 2-month Interval COV1001 Cohort 1a Group 1



COV1001 Cohort 1a Group 1, Per Protocol Immunogenicity Set

	Baseline (D1)	28 Days Post Dose 1 (D29)	Pre-Dose 2 (D57)	14 Days Post Dose 2 (D71)	28 Days Post Dose 2 (D85)	Day 239
N	25	25	25	24	24	24
Geometric mean (95% CI)	<LLOQ (<LLOQ, <LLOQ)	224 (168, 298)	228 (221, 376)	827 (651, 1052)	849 (664, 1086)	465 (348, 620)
Geometric mean increase (95% CI) from baseline	n/a	3.8 (2.8, 5.0)	4.9 (3.7, 6.3)	13.9 (10.9, 17.7)	14.3 (11.2, 18.3)	7.8 (5.9, 10.4)
Geometric mean increase (95% CI) from pre-Dose 2 (D57)	n/a	n/a	n/a	2.9 (2.3, 3.8)	**2.9 (2.1, 3.8)**	1.6 (1.2, 2.0)

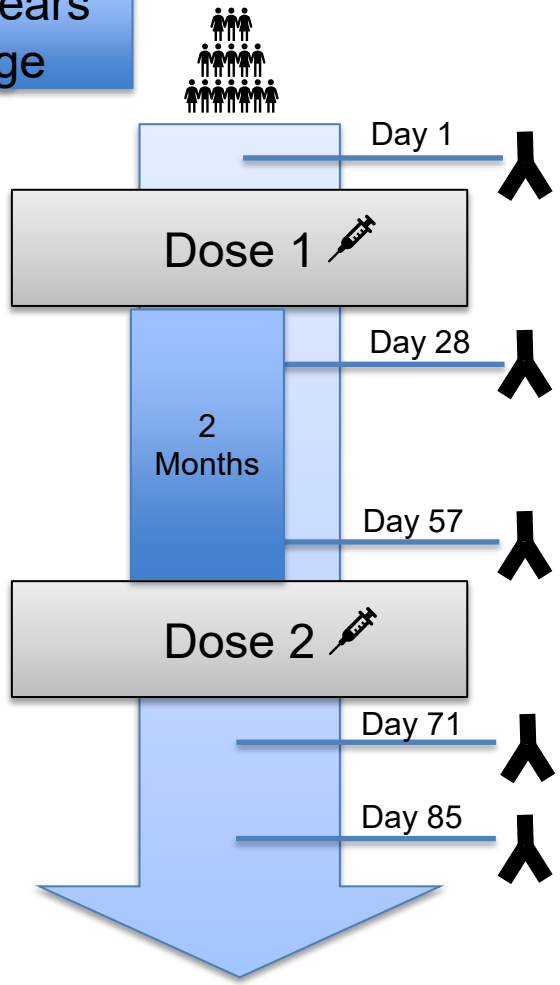
LLOQ: lower limit of quantification

Janssen analyses not verified by FDA

Responses (IC50) were measured using a qualified Wild-Type Virus Neutralization Assay VICTORIA/1/2020

Immunogenicity Data: 2-month Interval COV1002 Cohort 2 Group 1

≥ 65 years of age



COV1002 Cohort 2 Group 1, Per Protocol Immunogenicity Set

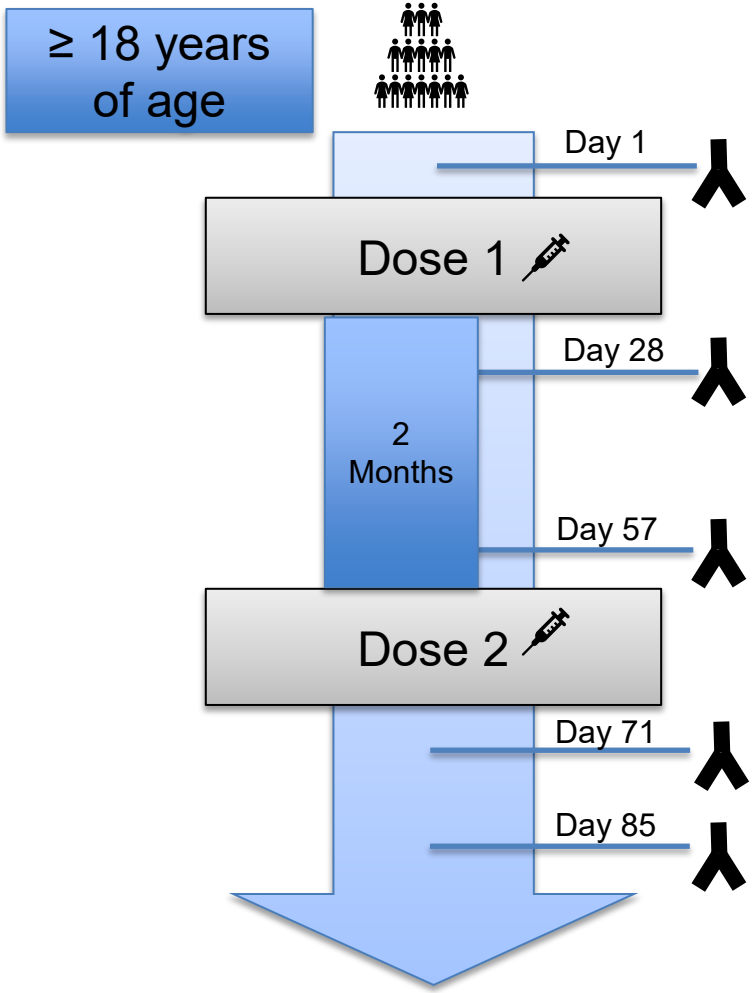
	Baseline (D1)	28 Days Post Dose 1 (D29)	Pre-Dose 2 (D57)	14 Days Post Dose 2 (D71)	28 Days Post Dose 2 (D85)
N	50	50	49	48	48
Geometric mean (95% CI)	<LLOQ (NE, NE)	311 (259, 374)	281 (204, 386)	504 (404, 627)	429 (335, 550)
Geometric mean increase (95% CI) from baseline	n/a	5.4 (4.6, 6.5)	4.9 (3.6, 6.7)	8.7 (7.0, 10.8)	7.4 (5.8, 9.5)
Geometric mean increase (95% CI) from pre-Dose 2 (D57)	n/a	n/a	n/a	1.7 (1.3, 2.4)	**1.5 (1.1, 2.0)**

LLOQ: lower limit of quantification

Responses (IC50) were measured using a qualified Wild-Type Virus Neutralization Assay VICTORIA/1/2020

Janssen analyses not verified by FDA

Immunogenicity Data: 2-month Interval COV2001 Group 1



COV2001 Group 1, Per Protocol Immunogenicity Set

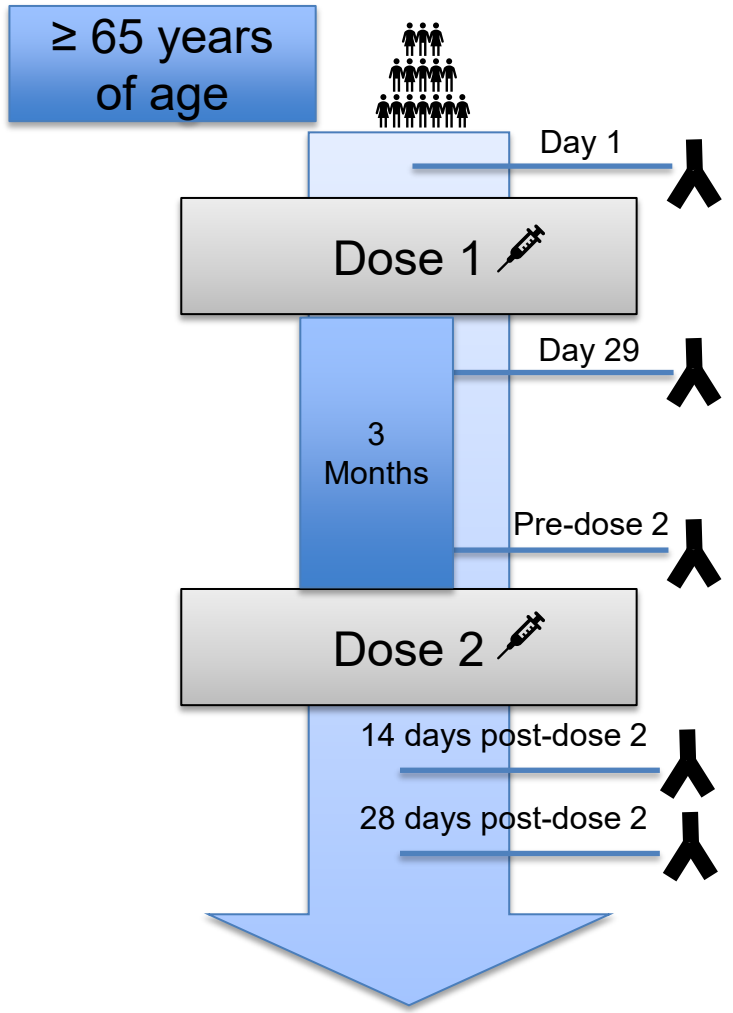
	Baseline (D1)	28 Days Post Dose 1 (D29)	Pre-Dose 2 (D57)	14 Days Post Dose 2 (D71)	28 Days Post Dose 2 (D85)
N	38	39	39	39	38
Geometric mean (95% CI)	<LLOQ (<LLOQ, <LLOQ)	260 (196, 346)	212 (142, 314)	518 (354, 758)	424 (301, 597)
Geometric mean increase (95% CI) from baseline	n/a	4.4 (3.3, 5.7)	3.7 (2.6, 5.2)	8.8 (6.1, 12.8)	7.4 (5.4, 10.2)
Geometric mean increase (95% CI) from pre-Dose 2 (D57)	n/a	n/a	n/a	2.3 (1.7, 3.1)	**1.8 (1.4, 2.4)**

LLOQ: lower limit of quantification

Janssen analyses not verified by FDA

Responses (IC50) were measured using a qualified Wild-Type Virus Neutralization Assay VICTORIA/1/2020

Immunogenicity Data: 3-month Interval * COV1001 Cohort 3 Group 1



*Protocol specified 2 doses, 56 days apart. Due to study pause, actual timing of Dose 2 ranged from 86-107 days (median: Day 87)

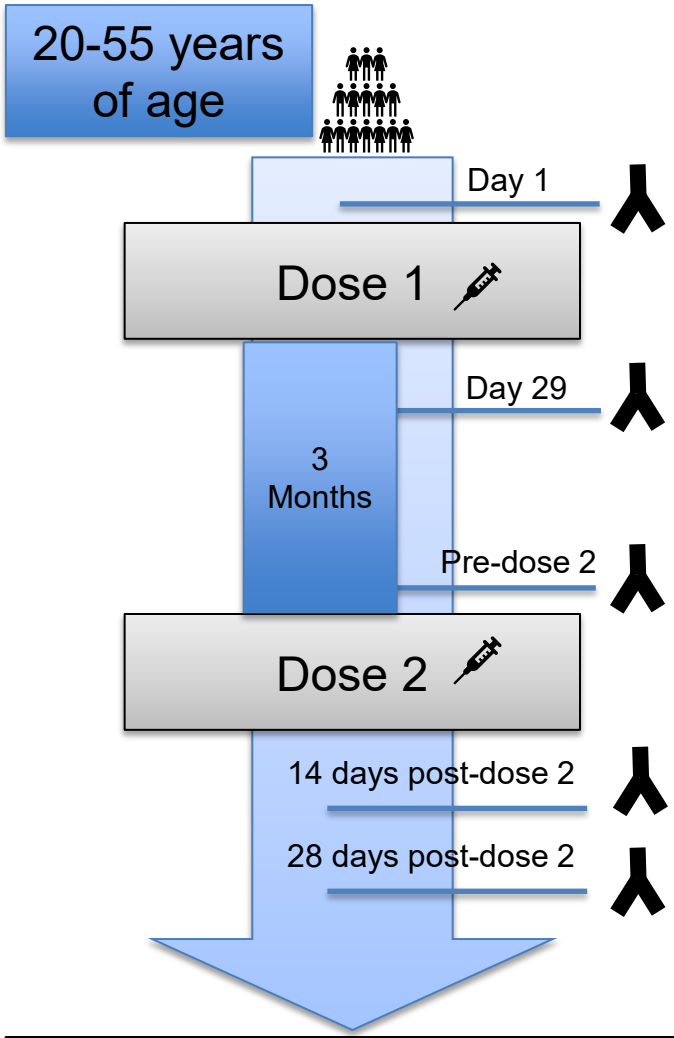
COV1001 Cohort 3 Group 1, Per Protocol Immunogenicity Set

	Baseline (D1)	28 Days Post Dose 1 (D29)	Pre-Dose 2 (D87)	14 Days Post Dose 2 (D100)	28 Days Post Dose 2 (D114)
N	25	25	21	21	21
Geometric mean (95% CI)	<LLOQ (<LLOQ,<LLOQ)	298 (200, 444)	242 (147, 399)	945 (578, 1546)	1067 (630, 1807)
Geometric mean increase (95% CI) from baseline	n/a	4.8 (3.3, 6.9)	4.0 (2.6, 6.1)	15.0 (9.5, 23.8)	17.0 (10.4, 27.6)
Geometric mean increase (95% CI) from pre-Dose 2 (D87)	n/a	n/a	n/a	3.8 (2.5, 5.6)	**4.3 (3.1, 5.8)**

Responses (IC50) were measured using a qualified Wild-Type Virus Neutralization Assay VICTORIA/1/2020

Janssen analyses not verified by FDA

Immunogenicity Data: 3-month Interval*
COV1002 Cohort 1 Group 1



*Protocol specified 2 doses, 56 days apart. Due to study pause, actual timing of Dose 2 ranged from 73-88 days (median: Day 78)

COV1002 Cohort 1 Group 1, Per Protocol Immunogenicity Set

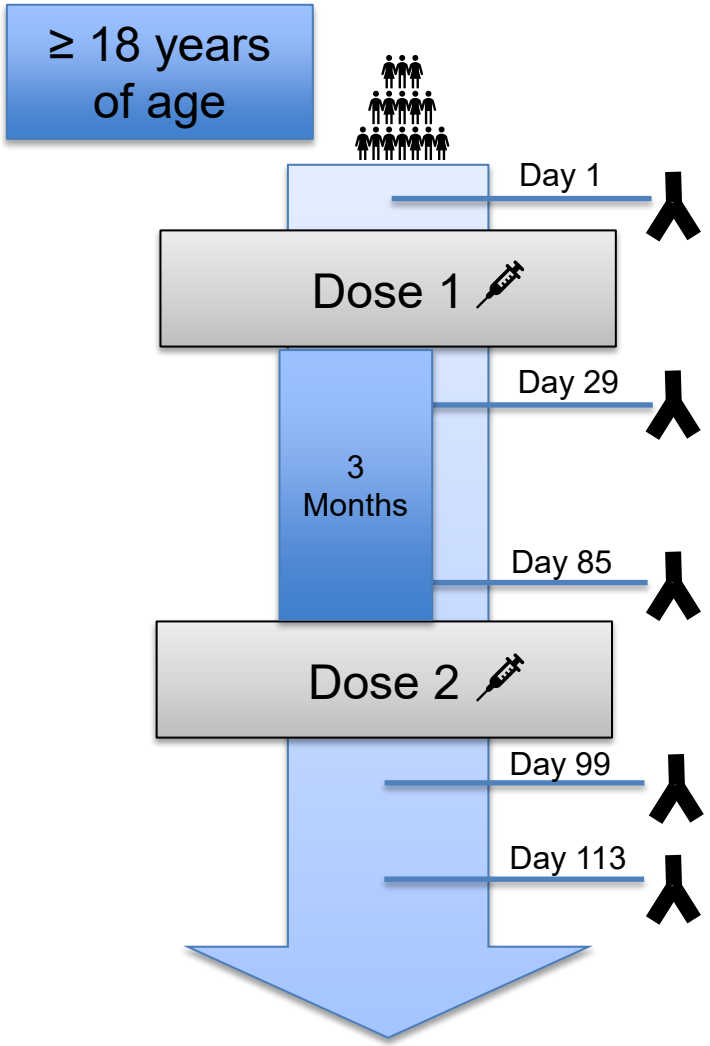
	Baseline (D1)	28 Days Post Dose 1 (D29)	Pre-Dose 2 (D78)	14 Days Post Dose 2 (D92)	28 Days Post Dose 2 (D106)
N	51	50	43	43	43
Geometric mean (95% CI)	<LLOQ (<LLOQ, <LLOQ)	269 (228, 318)	469 (382, 576)	1049 (828, 1329)	1088 (817, 1449)
Geometric mean increase (95% CI) from baseline	n/a	4.6 (3.9, 5.4)	8.0 (6.5, 9.8)	17.9 (14.2, 22.7)	18.6 (14.0, 24.7)
Geometric mean increase (95% CI) from pre-Dose 2 (D78)	n/a	n/a	n/a	2.2 (1.8, 2.8)	**2.3 (1.8, 3.0)**

LLOQ: lower limit of quantification

Responses (IC50) were measured using a qualified Wild-Type Virus Neutralization Assay VICTORIA/1/2020

Janssen analyses not verified by FDA

Immunogenicity Data: 3-month Interval COV2001 Group 9



COV2001 Group 9, Per Protocol Immunogenicity Set

	Baseline (D1)	Pre-Dose 2 (D85)	14 Days Post Dose 2 (D99)	28 Days Post Dose 2 (D113)
N	37	35	34	37
Geometric mean (95% CI)	<LLOQ	236 (169, 328)	904 (691, 1184)	694 (473, 1018)
Geometric mean increase (95% CI) from baseline	n/a	4.1 (3.0, 5.7)	15.6 (11.9, 20.4)	12.2 (8.4, 17.6)
Geometric mean increase (95% CI) from pre-Dose 2 (D85)	n/a	n/a	3.7 (2.6, 5.3)	**2.9 (2.0, 4.3)**

LLOQ: lower limit of quantification

Responses (IC50) were measured using a qualified Wild-Type Virus Neutralization Assay VICTORIA/1/2020

Janssen analyses not verified by FDA

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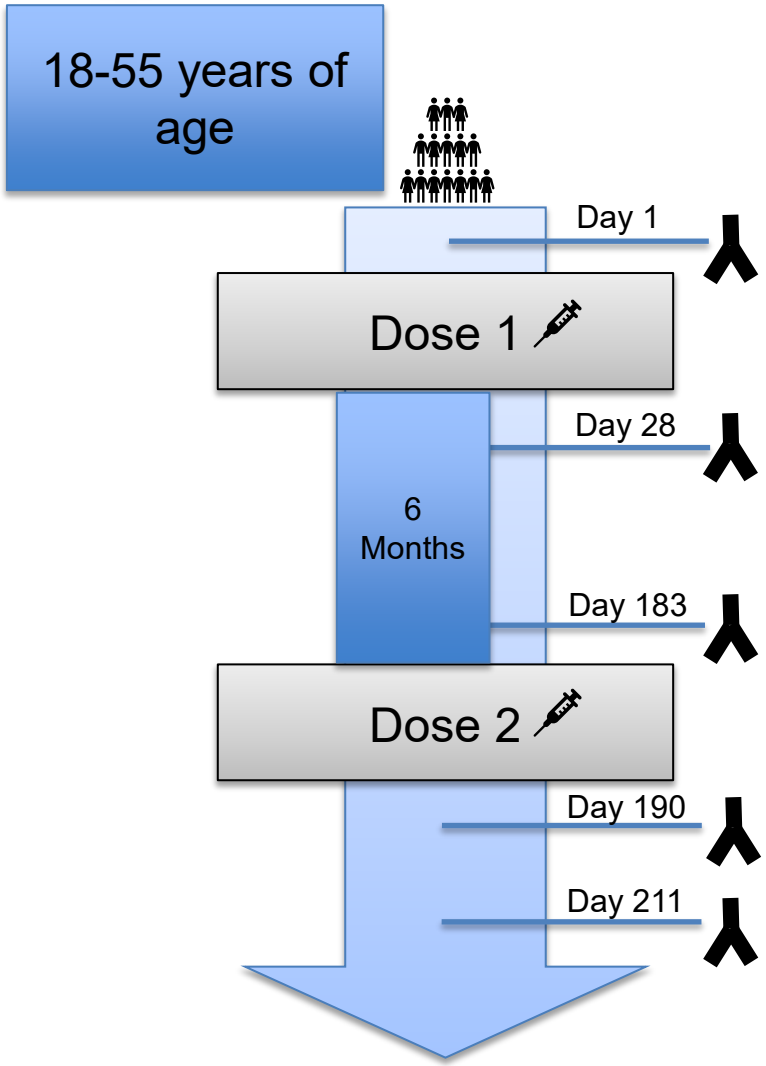
Immunogenicity Data: 6-month Interval COV1001 Cohort 2a Group 2



COV1001 Cohort 2a Group 2, Per Protocol Immunogenicity Set

	Baseline (D1) N= 17	28 Days Post Primary (D29) N= 17	Pre-Booster (D183) N= 17	7 Days Post Booster (D190) N= 17	28 Days Post Booster (D211) N= 15
Geometric mean (95% CI)	<LOD (NE, NE)	<LOD (<LOD, <LOD)	32 (<LOD, 67)	136 (89, 209)	209 (144, 303)
Geometric mean increase (95% CI) from baseline	n/a	1.1 (0.9, 1.2)	2.1 (1.2, 3.9)	6.8 (4.4, 10.5)	10.5 (7.2, 15.1)
Geometric mean increase (95% CI) from pre-booster (D183)	n/a	n/a	n/a	3.2 (2.3, 4.3)	**4.5 (2.8, 7.3)**

LOD: limit of detection
NE: non-evaluable

psVNA

Responses (IC50) were measured using pseudotyped particles harboring the spike protein from the original WA1/2020 strain (with D614G mutation). Assay is not yet qualified or validated.

Immunogenicity Data: 6-month Interval COV1001 Cohort 2a Group 2

Post-hoc Analyses: GMTs of psVNA against WA1/2020 strain with D614G mutation at 7 days and 28 days post-booster compared to 28 days post primary vaccination in participants in Cohort 2a/Group 2

	Post-Booster N GMT (95% CI)	Post- Primary Vaccination (Day 29) N GMT (95% CI)	GMT Ratio (Post-Booster/Post-Primary Vaccination)
7 Days Post Boost	N=17 136 (89, 209)	N=17 <LOD (<LOD, <LOD)	**6.3 (4.4, 9.0)**
28 Days Post Boost	N=15 209 (144, 303)	N=17 <LOD (<LOD, <LOD)	**9.6 (7.0, 13.1)**

LOD: limit of detection
Values below the LOD at 29 days post-Dose 1 were imputed with the LOD

Limitations:

- Post-hoc analysis that included data from only 17 participants.
- Interpretation of GMT ratios may be confounded by low sensitivity of the assay
- No analysis of difference in seroresponse rates (post-booster - post-primary dose) was provided.

Immunogenicity Data: 6-month Interval Delta Variant COV1001 Cohort 2a Group 2

Descriptive analyses: Neutralizing antibody response against the SARS-CoV-2 Delta variant (B.1.617.2) in participants in Cohort 2a/Group 2

	D614G Pre-Booster (D183) N= 17	B.1.617.2 Pre-Booster (D183) N= 17	D614G 7 Days Post Booster (D190) N= 17	B.1.617.2 7 Days Post Booster (D190) N= 17	D614G 28 Days Post Booster (D211) N= 15	B.1.617.2 28 Days Post Booster (D211) N= 15
Geometric mean (95% CI)	32 (<LOD, 67)	<LOD (<LOD, 35)	136 (89, 209)	68 (43, 109)	209 (144, 303)	98 (64, 148)
Geometric mean increase (95% CI) from pre-booster (D183)	n/a	n/a	3.2 (2.3, 4.3)	2.2 (1.8, 2.8)	**4.5 (2.8, 7.3)**	**3.0 (2.1, 4.2)**

LOD: limit of detection

Limitations:

- The psVNA assay is non-validated and non-qualified assay (assay status: developed) and different from the wtVNA used in the immunogenicity analyses for the other cohorts, precluding comparisons to other studies.
- The psVNA does not appear to be a fit for purpose assay for use in immunobridging analysis comparing GMT post-boost to GMT post-primary dose as the post-primary response was <LOD and did not allow for a meaningful comparison.

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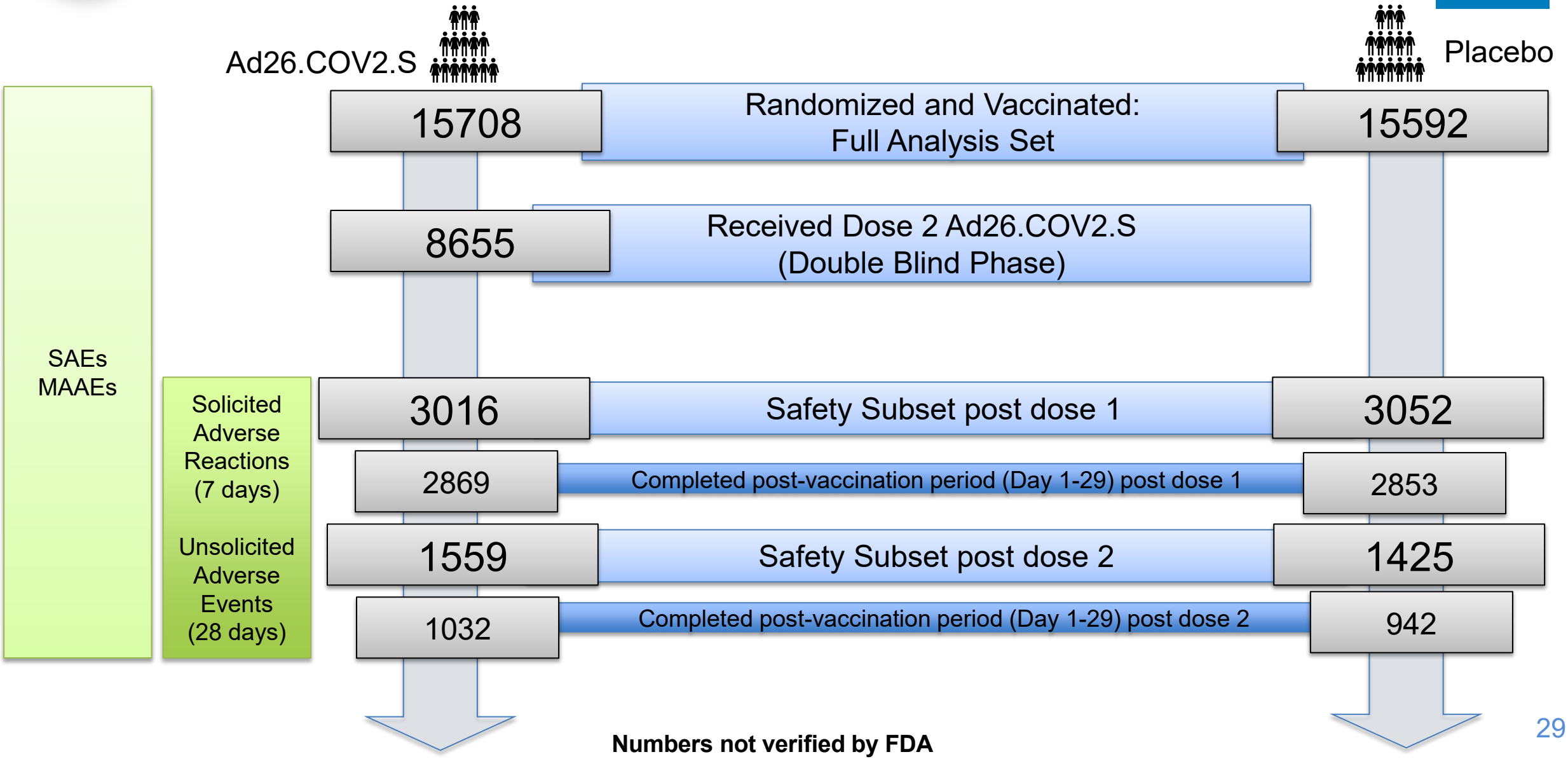
Safety Analyses: COV3009 Analysis Population



Numbers not verified by FDA

Safety Analyses: COV3009
Solicited Adverse Reaction Overview

Adverse Event Type	Post-Dose 1 Ad26.COV2.S n (%)	Post-Dose 1 Placebo n (%)	Post-Dose 2 Ad26.COV2.S n (%)	Post-Dose 2 Placebo n (%)
Safety subset	**N=3016**	**N=3052**	**N= 1559**	**N= 1425**
18-59 years of age	**N=1784**	**N=1822**	**N=1164**	**N=1077**
≥60 years of age	**N=1231**	**N=1230**	**N=395**	**N=348**
Solicited local adverse reaction				
18-59 years of age	1170 (65.6%)	445 (24.4%)	726 (62.4%)	209 (19.4%)
≥60 years of age	506 (41.1%)	208 (16.9%)	170 (43.0%)	43 (12.4%)
Grade 3 solicited local adverse reaction				
18-59 years of age	7 (0.4%)	4 (0.2%)	7 (0.6%)	2 (0.2%)
≥60 years of age	2 (0.2%)	2 (0.2%)	3 (0.8%)	1 (0.3%)
Solicited systemic adverse reaction				
18-59 years of age	1194 (66.9%)	767 (42.1%)	657 (56.4%)	353 (32.8%)
≥60 years of age	570 (46.3%)	371 (30.2%)	164 (41.5%)	89 (25.6%)
Grade 3 solicited systemic adverse reaction				
18-59 years of age	44 (2.5%)	8 (0.4%)	21 (1.8%)	3 (0.3%)
≥60 years of age	11 (0.9%)	6 (0.5%)	4 (1.0%)	2 (0.6%)

Analyses Not Verified by FDA

Safety Analyses: COV3009
Solicited Local Adverse Reactions within 7 days (Safety Subset)

Adverse Reaction	Dose 1 18-59 Years Ad26.COV2.S N=1784 n (%)	Dose 2 18-59 years Ad26.COV2.S N=1164 n (%)	Dose 1 ≥60 Years Ad26.COV2.S N=1231 n (%)	Dose 2 ≥60 Years Ad26.COV2.S N=395 n (%)
Any Local	1170 (65.6%)	726 (62.4%)	506 (41.1%)	170 (43.0%)
Grade 3	7 (0.4%)	7 (0.6%).	2 (0.2%)	3 (0.8%)
Pain	1141 (64.0%)	715 (61.4%)	493 (40.0%)	162 (41.0%)
Grade 3	3 (0.2%)	2 (0.2%)	0	1 (0.3%)
Erythema	204 (11.4%)	113 (9.7%)	59 (4.8%)	15 (3.8%)
Grade 3	2 (0.1%)	5 (0.4%)	0	2 (0.5%)
Swelling	130 (7.3%)	81 (7.0%)	37 (3.0%)	7 (1.8%)
Grade 3	2 (0.1%)	2 (0.2%)	2 (0.2%)	2 (0.5%)

Local Pain Grade 1: Does not interfere with activity/Discomfort to touch. Grade 2: Requires modification in activity or use of medications/Discomfort with movement. Grade 3: Incapacitating symptoms, any use of Rx pain reliever/prevents daily activity.
Local Erythema or Swelling: Grade 1: 25-50mm, Grade 2: 51-100mm, Grade 3: >100mm.

Analyses Not Verified by FDA

Safety Analyses: COV3009
Solicited Systemic Adverse Reactions within 7 days (Safety Subset)

Adverse Reaction	Dose 1 18-59 Years Ad26.COV2.S N=1784 n (%)	Dose 2 18-59 years Ad26.COV2.S N=1164 n (%)	Dose 1 ≥60 Years Ad26.COV2.S N=1231 n (%)	Dose 2 ≥60 Years Ad26.COV2.S N=395 n (%)
Any Systemic	1194 (66.9%)	657 (56.4%)	570 (46.3%)	164 (41.5%)
Grade 3	44 (2.5%)	21 (1.8%)	11 (0.9%)	4 (1.0%)
Fatigue	951 (53.3%)	528 (45.4%)	404 (32.8%)	113 (28.6%)
Grade 3	22 (1.2%)	11 (0.9%)	4 (0.3%)	3 (0.8%)
Headache	901 (50.5%)	444 (38.1%)	390 (31.7%)	114 (28.9%)
Grade 3	18 (1.0%)	8 (0.7%)	5 (0.4%)	2 (0.5%)
Myalgia	841 (47.1%)	438 (37.6%)	331 (26.9%)	103 (26.1%)
Grade 3	20 (1.1%)	7 (0.6%)	3 (0.2%)	2 (0.5%)
Nausea	375 (21.0%)	176 (15.1%)	171 (13.9%)	49 (12.4%)
Grade 3	8 (0.4%)	1 (0.1%)	1 (0.1%)	2 (0.5%)
Fever	122 (6.8%)	29 (2.5%)	28 (2.3%)	9 (2.3%)
Grade 3	2 (0.1%)	1 (0.1%)	0	0
Antipyretic/Analgesic Use*	384 (21.5%)	207 (17.8%)	118 (9.6%)	36 (9.1%)

Grade 1: Minimal symptoms; no interference with activity; Grade 2: Notable symptoms; interference with activity, Grade 3: Incapacitating symptoms; prevents daily activity, Grade 4: Hospitalization; interference with basic self care

Analyses Not Verified by FDA

Safety Analyses: COV3009
Unsolicited Events Overview by Age

Adverse Event Type	Post-Dose 1 Ad26.COV2.S n (%)	Post-Dose 1 Placebo n (%)	Post-Dose 2 Ad26.COV2.S n (%)	Post-Dose 2 Placebo n (%)
Safety subset	**N=3016**	**N=3052**	**N= 1559**	**N= 1425**
18-59 years of age	**N=1784**	**N=1822**	**N=1164**	**N=1077**
≥60 years of age	**N=1231**	**N=1230**	**N=395**	**N=348**
Unsolicited adverse event up to 28 days after vaccination				
18-59 years of age	272 (15.2%)	226 (12.4%)	124 (10.7%)	93 (8.6%)
≥60 years of age	182 (14.8%)	106 (8.6%)	35 (8.9%)	27 (7.8%)
Grade 3 unsolicited adverse event				
18-59 years of age	10 (0.6%)	9 (0.5%)	7 (0.6%)	6 (0.6%)
≥60 years of age	8 (0.6%)	5 (0.4%)	5 (1.3%)	1 (0.3%)
Grade 4 unsolicited adverse event				
18-59 years of age	2 (0.1%)	0	0	0
≥60 years of age	1 (0.1%)	2 (0.2%)	0	0
Related unsolicited adverse events				
18-59 years of age	175 (9.8%)	130 (7.1%)	62 (5.3%)	39 (3.6%)
≥60 years of age	108 (8.8%)	49 (4.0%)	17 (4.3%)	10 (2.9%)

Analyses Not Verified by FDA

Safety Analyses: COV3009 Unsolicited Events

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

System Organ Class Preferred Term	Dose 1 Ad26.COV2.S N=3015 n (%)	Dose 1 Placebo N=3052 n (%)	Dose 2 Ad26.COV2.S N=1559 n (%)	Dose 2 Placebo N=1425 n (%)
General disorders and administration site conditions				
Fatigue	105 (3.5%)	94 (3.1%)	29 (1.9%)	28 (2.0%)
Grade 3 fatigue	2 (0.1%)	2 (0.1%)	1 (0.1%)	1 (0.1%)
Vaccination site pain	66 (2.2%)	19 (0.6%)	-	-
Nervous system disorders				
Headache	107 (3.5%)	98 (3.2%)	34 (2.2%)	25 (1.8%)
Grade 3 headache	8 (0.3%)	3 (0.1%)	1 (0.1%)	0
Musculoskeletal and connective tissue disorders				
Myalgia	82 (2.7%)	66 (2.2%)	22 (1.4%)	22 (1.5%)
Grade 3 myalgia	2 (0.1%)	1 (<0.1%)	1 (0.1%)	0
Gastrointestinal disorders				
Nausea	33 (1.1%)	29 (1.0%)	-	-
Grade 3 nausea	2 (0.1%	2 (0.1%)		

Grade 1: Minimal symptoms; no interference with activity; Grade 2: Notable symptoms; interference with activity, Grade 3: Incapacitating symptoms; prevents daily activity, Grade 4: Hospitalization; interference with basic self care

Analyses Not Verified by FDA

Safety Analyses: COV3009
Related[1] Serious Adverse Events after Ad26.COV2.S

Related SAEs after Ad26.COV2.S (as determined by PI)

Preferred Term	Age Group/Sex	Most recent dose	Day of Onset*	Outcome	Study Phase
Pyrexia	≥60 M	Dose 1	1	Recovered/resolved	Blinded
Allergy to vaccine	18-59 F	Dose 1	2	Recovered/resolved	Blinded
Myocardial necrosis marker increased; **Vertigo;** **Injection site swelling**	18-59 M	Dose 1 Dose 1 Dose 1	10 10 2	All 3 SAEs Recovered/resolved	Blinded
Pericarditis	≥60 F	Dose 1	11	Recovering	Blinded
Hemoptysis	≥60 F	Dose 1	67	Recovered/resolved	Blinded
Thrombocytopenia; **Leukopenia;** **Deep vein thrombosis**	≥60 F	Dose 1 Dose 1 Dose 1	87 87 100	All 3 SAEs Recovered/resolved	Open label
Pulmonary embolism	≥60 M	Dose 2	10	Not recovered/resolved	Blinded
Facial paresis	18-59 F	Dose 2	11	Recovered/resolved	Blinded
Thrombosis	≥60 M	Dose 2	21	Recovered/resolved	Open Label
Cerebrovascular accident	18-59 F	Dose 2	31	Recovered/resolved	Open Label
Venous thrombosis limb	18-59 M	Dose 2	58	Recovering	Open Label
Cerebrovascular accident	18-59 F	Dose 2	79	Recovered/resolved	Blinded

*Relative to Last Dose
[1]Considered related by investigator

Analyses Not Verified by FDA
Narratives of SAEs were not submitted by the Sponsor (which limits FDA's assessment of causal relationship)

Safety Analyses: COV3009
Deaths after Ad26.COV2.S

Preferred Term	Age Group/Sex	Most recent dose	Day of Onset*	Study Phase
Death from unknown cause	18-59 M	Dose 1	25	Blinded
Heroin overdose	≥60 F	Dose 1	51	Open Label
Cerebral hemorrhage	≥60 F	Dose 1	55	Blinded
Lung adenocarcinoma	≥60 M	Dose 1	57	Blinded
Death from unknown cause	18-59 M	Dose 1	96	Open Label
Chronic obstructive pulmonary disease	18-59 F	Dose 2	5	Open Label
Myocardial infarction	18-59 F	Dose 2	33	Blinded
COVID-19 pneumonia	≥60 M	Dose 2	64	Open Label

*Relative to Last Dose
All considered unrelated to vaccine by Janssen

Analyses Not Verified by FDA
Narratives of SAEs were not submitted by the Sponsor (which limits FDA's assessment of causal relationship)

Additional Safety Data: COV1002 and COV2001

(2- to 3-month interval) Adverse Events of Special Interest

- Study COV1002 (Cohort 1, Group 1):
  - Sudden hearing loss 34 days after dose 1
- Study COV2001:
  - Two thrombotic events were reported in this study:
    - Thrombophlebitis one day after dose 1 ($5x10^{10}$ vp)
    - Grade 3 ischemic stroke 8 days after the $1.25x10^{10}$ vp dose at Month 6

Outline

- Background/Study overview
- Efficacy Data
  - COV3001
  - COV3009
- Immunogenicity Data
  - 2-3 month interval
  - 6 month interval
- **Safety Data**
  - 2-3 month interval
  - 6 month interval
- Summary

Safety Analyses: COV1001 Cohort 2a Group 2 (6-month interval) Solicited Adverse Reactions

Frequency of Solicited Local Adverse Reactions Within 7 Days After Primary Vaccination Compared to After Booster Dose (18-55 years of age)

	Post-Primary Vaccination N=29 n (%)	Post-Booster Dose N=19 n (%)
Any solicited local AR	**24 (82.8)**	**15 (78.9)**
Grade 3 or higher solicited local AR	**0**	**0**
Any Pain	23 (79.3)	15 (78.9)
Any Erythema	1 (3.4)	0
Any Swelling	1 (3.4)	0

Injection site pain- Grade 1: does not interfere with activity; Grade 2: requires modification in activity or use of medication; Grade 3:incapacitating, requires Rx pain reliever
Erythema and Swelling- Grade 1: 25-50mm; Grade 2: 51-100mm; Grade 3: >100 mm

Analyses Not Verified by FDA

Frequency of Solicited Systemic Adverse Reactions Within 7 Days After Primary Vaccination Compared to After Booster Dose (18-55 years of age)

	Post-Primary Vaccination N=29 n (%)	Post-Booster Dose N=19 n (%)
Any solicited systemic AR	**23 (79.3)**	**11 (57.9)**
Grade 3 or higher solicited systemic AR	**1 (3.4)**	**0**
Any Fatigue	17 (58.6)	5 (26.3)
Any Headache	16 (55.2)	9 (47.4)
Grade 3	1 (3.4)	0
Any Myalgia	17 (58.6)	4 (21.1)
Any Nausea	8 (27.6)	2 (10.5)
Any Fever	3 (10.3)	0
Antipyretic or pain medication use	12 (41.4)	6 (31.6)

Fatigue, Headache, Myalgia, Nausea– Grade 1: no interference with activities; Grade 2: requires modification in activity or use of medications; Grade 3: incapacitating; prevents daily activity; use of Rx pain reliever.
Fever– Grade 1: 38-38.4 C, Grade 2: 38.5-38.9 C; Grade 3: 39.0-40.0

Analyses Not Verified by FDA

Safety Analyses: COV1001 Cohort 2a Group 2 (6-month interval) Unsolicited Adverse Events

Overview of Unsolicited Adverse Events Within 28 Days After Primary and Booster Dose in Studies COV1001 Cohort 2a, Full Analysis Set (18- 55 years of age)

	Regimen: Ad26.COV2.S + Ad26.COV2.S Post-Primary Vaccination N=29 n (%)	Regimen: Ad26.COV2.S + Placebo Post-Primary Vaccination N=90 n (%)	Regimen: Ad26.COV2.S + Ad26.COV2.S Post -Booster Dose N=19 n (%)	Regimen: Ad26.COV2.S + Placebo Post-Booster Dose N=62 n (%)
Unsolicited AE	5 (17.2)	22 (24.4)	2 (10.5)	2 (3.2)
Unsolicited AE of grade 3 or higher	0	0	0	0
Unsolicited AE considered related to study vaccine	2 (6.9)	10 (11.1)	1 (5.3)	0
Unsolicited grade 3 AE considered related to study vaccine	0	0	0	0
Serious Adverse Events	0	0	0	0
Deaths	0	0	0	0
AE leading to study discontinuation	0	0	0	0

Analyses Not Verified by FDA

Outline

- Background/Study overview
- Efficacy Data
  - COV3001
  - COV3009
- Immunogenicity Data
  - 2-3 month interval
  - 6 month interval
- Safety Data
  - 2-3 month interval
  - 6 month interval
- Summary

Summary: Effectiveness

FDA summary of Janssen analyses (not verified by FDA)

COV3001

- Final placebo-controlled vaccine efficacy analyses for a single dose suggest:
  - Stable efficacy over time against severe/critical COVID-19
  - Decreasing efficacy over time when including moderate cases (may be due at least in part to vaccine-resistant strains in study regions outside the U.S.)

COV3009

- Placebo-controlled efficacy analyses for two doses administered 2 months apart suggest higher efficacy estimates than those for a single dose studied in COV3001.
- Conclusions regarding improved efficacy from a second dose are limited by:
  - Small numbers of COVID-19 cases and wide confidence intervals around efficacy estimates that overlap with those for efficacy estimates from study COV3001
  - Median follow-up of only 36 days after the second dose

Summary: Immunogenicity and Safety

FDA summary of Janssen analyses (not verified by FDA)

- A second/booster dose of Janssen COVID-19 Vaccine administered at 2-6 months after the first dose elicits geometric mean increases in neutralizing antibody titers of approximately 1.5-fold to 4.5-fold above pre-booster baseline. Interpretation of the data is limited by:
  - Small sample sizes (including data from only 17 participants for 6-month interval)
  - Exploratory (non-validated) pseudovirus neutralization assay used in assessment of immune responses to the booster dose given at 6-month interval, and pre-boost titers suggest low sensitivity of assay

- No new safety signals identified following a second/booster dose. Interpretation of the data is limited by:
  - Small sample size for 6-month interval (data from 17 participants)
  - Limited duration of safety follow up after a second/booster dose, including in study COV3009 (main source of safety data for study participants exposed to two doses)

END