Vaccines and Related Biological Products Advisory Committee
February 26, 2021 Meeting Presentation -

Emergency Use Authorization (EUA) Application for Ad26.COV2.S

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

Emergency Use Authorization (EUA) Application for Ad26.COV2.S

Janssen Pharmaceutical Companies of Johnson & Johnson

Vaccines and Related Biological Products Advisory Committee

February 26, 2021

Introduction

Johan Van Hoof, MD

Global Head of Vaccines R&D

Janssen Pharmaceutical Companies of Johnson & Johnson

Janssen's Vaccine Candidate (Ad26.COV2.S) Supports Global Effort to Fight COVID-19

- Phase 3 study enrolled > 44,000 participants and was conducted during height of pandemic
- Offers substantial protection, especially against severe COVID-19 including hospitalization and death, irrespective of variant
- Well-tolerated and safe
- Single-dose regimen with storage, transportation conditions compatible within existing distribution channels

Key Efficacy Findings From Ad26.COV2.S Phase 3, Single-Dose Study Support EUA

85% vaccine efficacy* against severe COVID-19 globally, including the United States

- Consistent vaccine efficacy against severe disease across all regions
- Equally high protection in South Africa (n > 6,500) where B.1.351 is highly prevalent (> 95%)
- Complete protection against COVID-19 related hospitalizations* and deaths

72% vaccine efficacy* against moderate to severe/critical COVID-19 in the United States

- Participants reflected diversity of US population (n > 19,000)

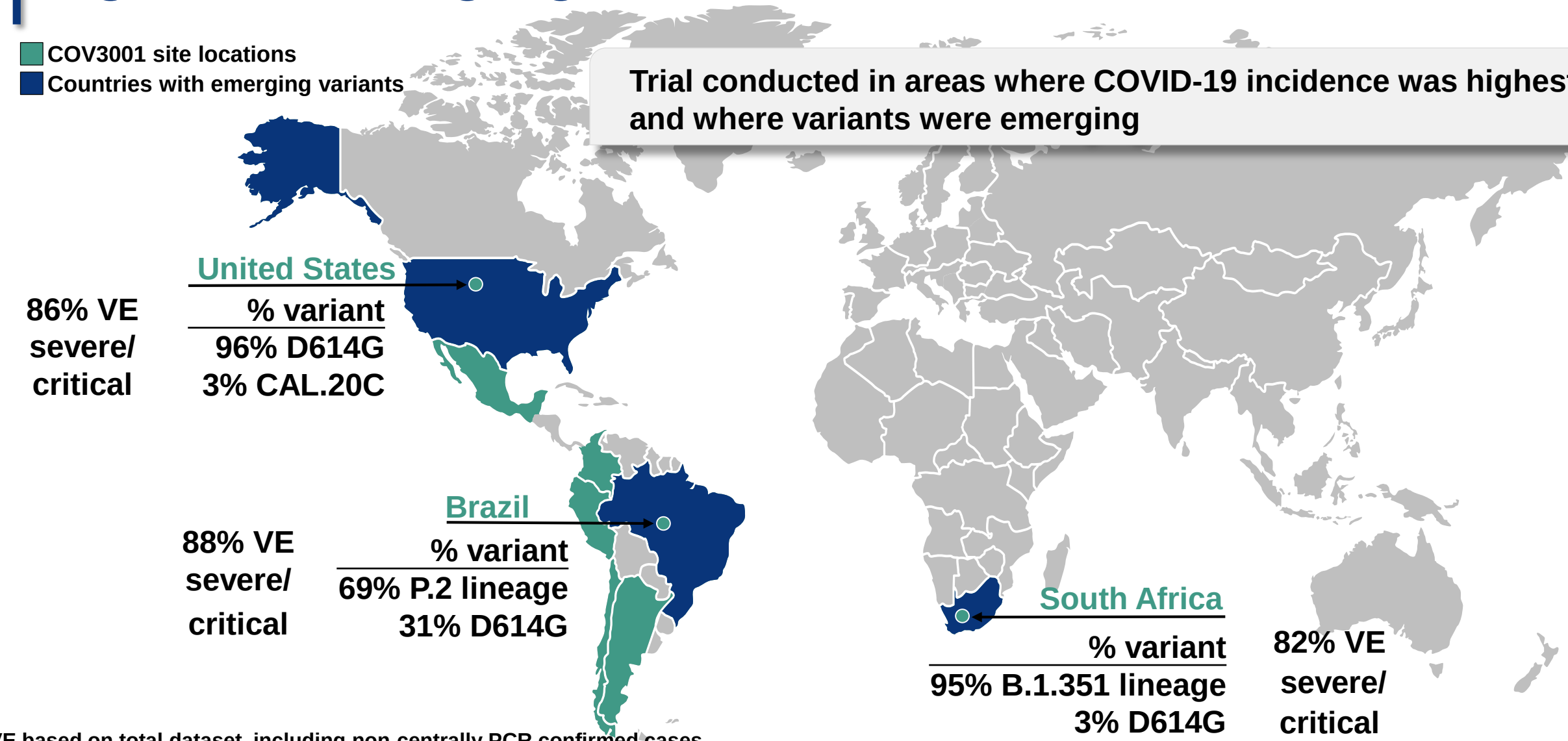
66% vaccine efficacy* against moderate to severe/critical COVID-19 across all countries

- Protection as of 2 weeks after vaccination

Similar vaccine efficacy demonstrated by age, comorbidities status, sex, race, and ethnicity

*> Day 28

Vaccine Efficacy (VE) Results Support Protection Against Emerging Variants



VE based on total dataset, including non-centrally PCR confirmed cases

Logistical, Practical Advantages to Help Simplify Distribution and Expand Vaccine Access of Single Dose Ad26.COV2.S

Single, 0.5ml dose offers ability to vaccinate population faster

5 doses per vial

No dilution required

Stored for 3 months at normal refrigerator temperatures, 2° to 8° C (36° to 46° F)

2-year shelf life when frozen, -25° to -15° C (-13° to 5° F)

Prepared for large-scale manufacturing

Expect to supply 100 million doses to US in first half of 2021

Shipping fits into existing supply chain infrastructure

Substantial Experience with Adenovirus 26-based Vaccines

Substantial clinical experience with Ad26-based vaccines (N > 193,000)

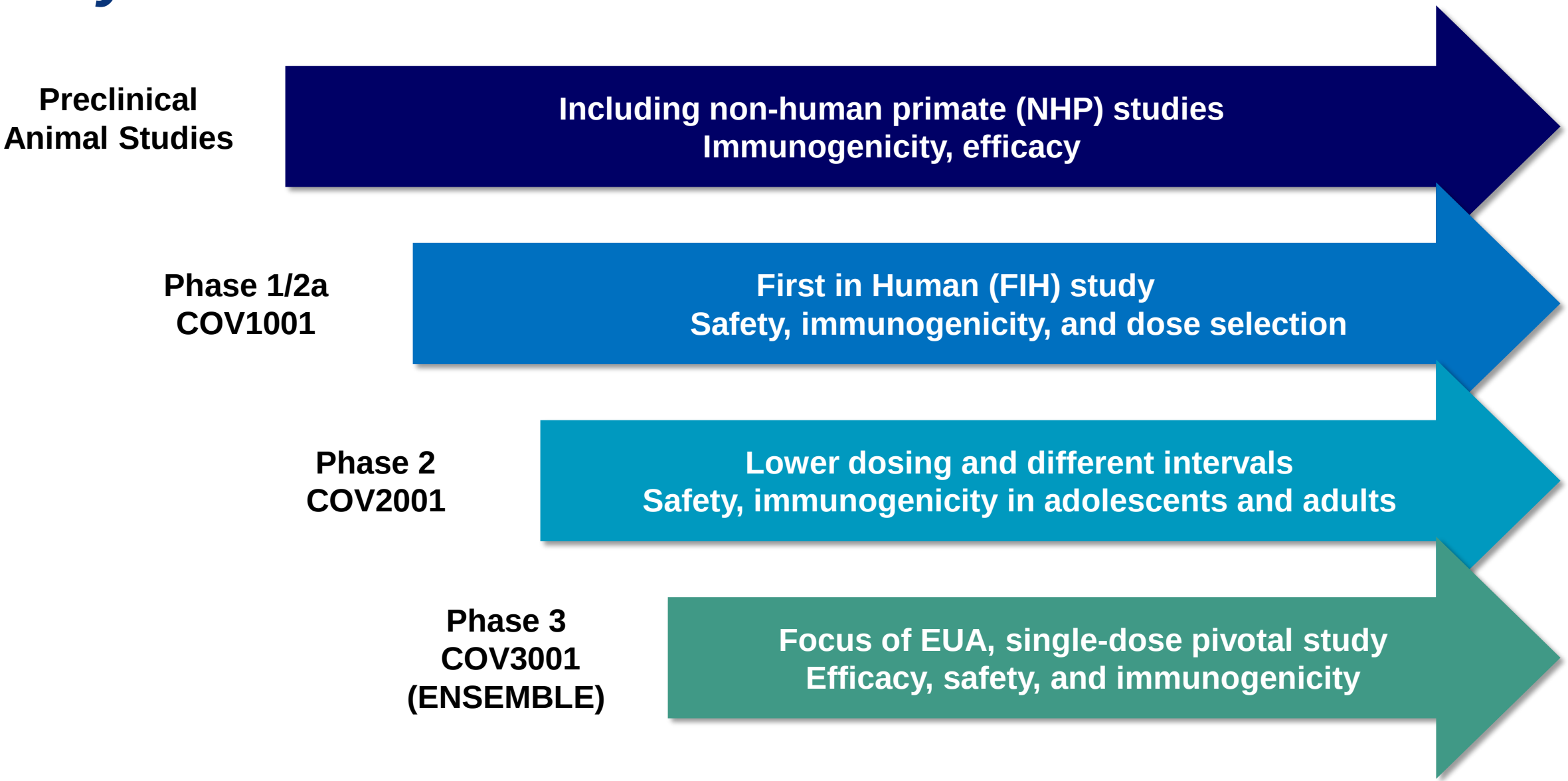
- Across continents
- Healthy adults
- Elderly > 65 years
- Various races, ethnicities
- Infants ≥ 4 months
- People with HIV
- Breastfeeding, pregnant women within Ebola program

Regular database reviews show good tolerability, safety

- Local, systemic reactogenicity in line with other licensed vaccines
- Database searches for AESIs revealed no safety signals

AESIs: Adverse Events of Special Interest

Comprehensive Development Program
Key Studies



Additional Key Studies

- COV3009: two-dose regimen Phase 3 efficacy study
- Immunogenicity and safety studies in children, 0 – 17 years
  - Adolescent study will open enrollment soon
- Pregnant women
  - Planned to begin late March/early April 2021
- Immunocompromised individuals
  - Planned to begin Q3 2021
- Post-authorization observational studies
  - Including pregnancy exposure registry

Agenda

Vaccine Design and Immunogenicity

Hanneke Schuitemaker, PhD
Global Head of Viral Vaccine Discovery and Translational Medicine
Janssen Pharmaceutical Companies of Johnson & Johnson

Efficacy and Safety

Macaya Douoguih, MD, MPH
Head of Clinical Development and Medical Affairs
Janssen Pharmaceutical Companies of Johnson & Johnson

Clinical Perspective and Benefit-Risk Assessment

Gregory A. Poland, MD, FIDSA, MACP, FRCP (London)
Mary Lowell Leary Emeritus Professor of Medicine
Distinguished Investigator of the Mayo Clinic
Director, Mayo Vaccine Research Group

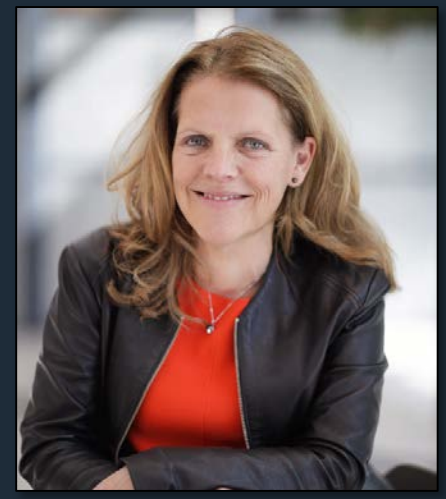
Vaccine Design and Immunogenicity

Hanneke Schuitemaker, PhD

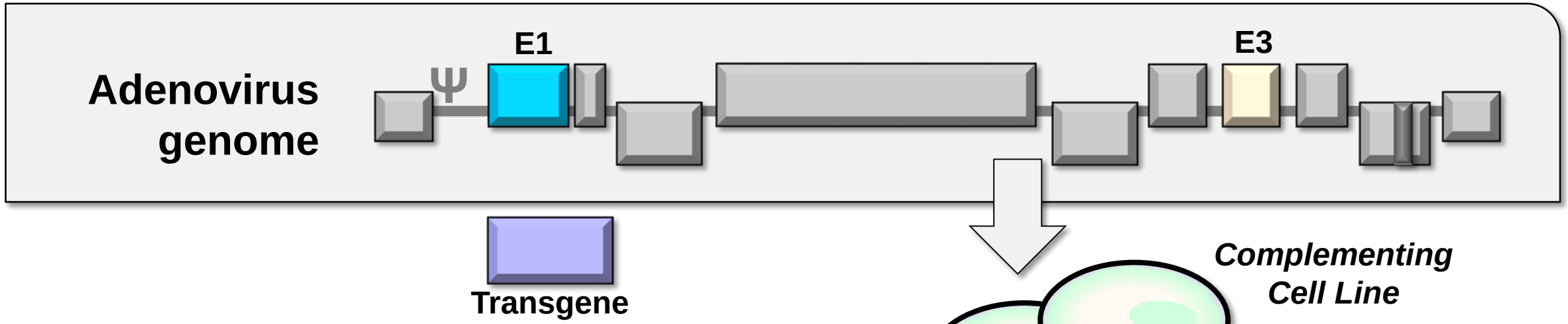
Global Head, Viral Vaccine Discovery and Translational Medicine

Janssen Pharmaceutical Companies of Johnson & Johnson

Professor in Virology, Amsterdam University Medical Center



Ad26 Vector is Replication Incompetent

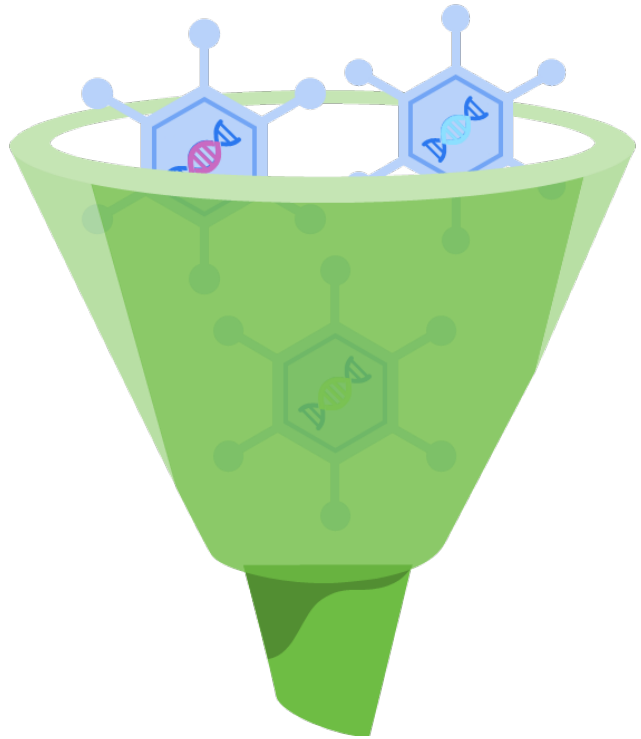


- Janssen Ad26 vector **can not replicate** in the human body
- Cell line grows in medium free of animal components
- Vial of Ad26-based vaccine contains buffer with commonly used ingredients in vaccines
  - No adjuvants, no antibiotics, no preservatives

Targeted Immune Response Against SARS-CoV-2 Spike (S) Protein Based on SARS-1 Experience

- Antibodies directed against S protein can neutralize the virus, T cells against epitopes in the S protein may contribute to protection against disease[1]
- Evaluated multiple transgenes encoding different S designs to select vaccine candidate with optimal:
  - Stabilization, expression, immunogenicity, nonclinical efficacy
- Selected S protein contains two proline mutations and a knocked out furin cleavage site for optimal stability in prefusion confirmation[2]
- Lead candidate Ad26.COV2.S selected based on above factors and optimal manufacturability

12 Candidates

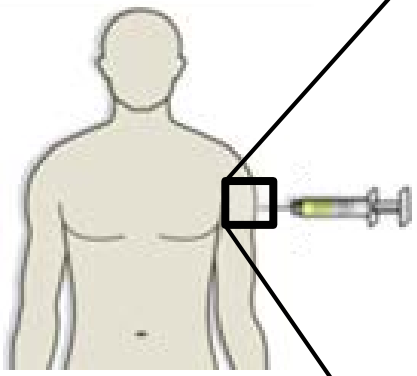


Selection of lead vaccine candidate Ad26.COV2.S

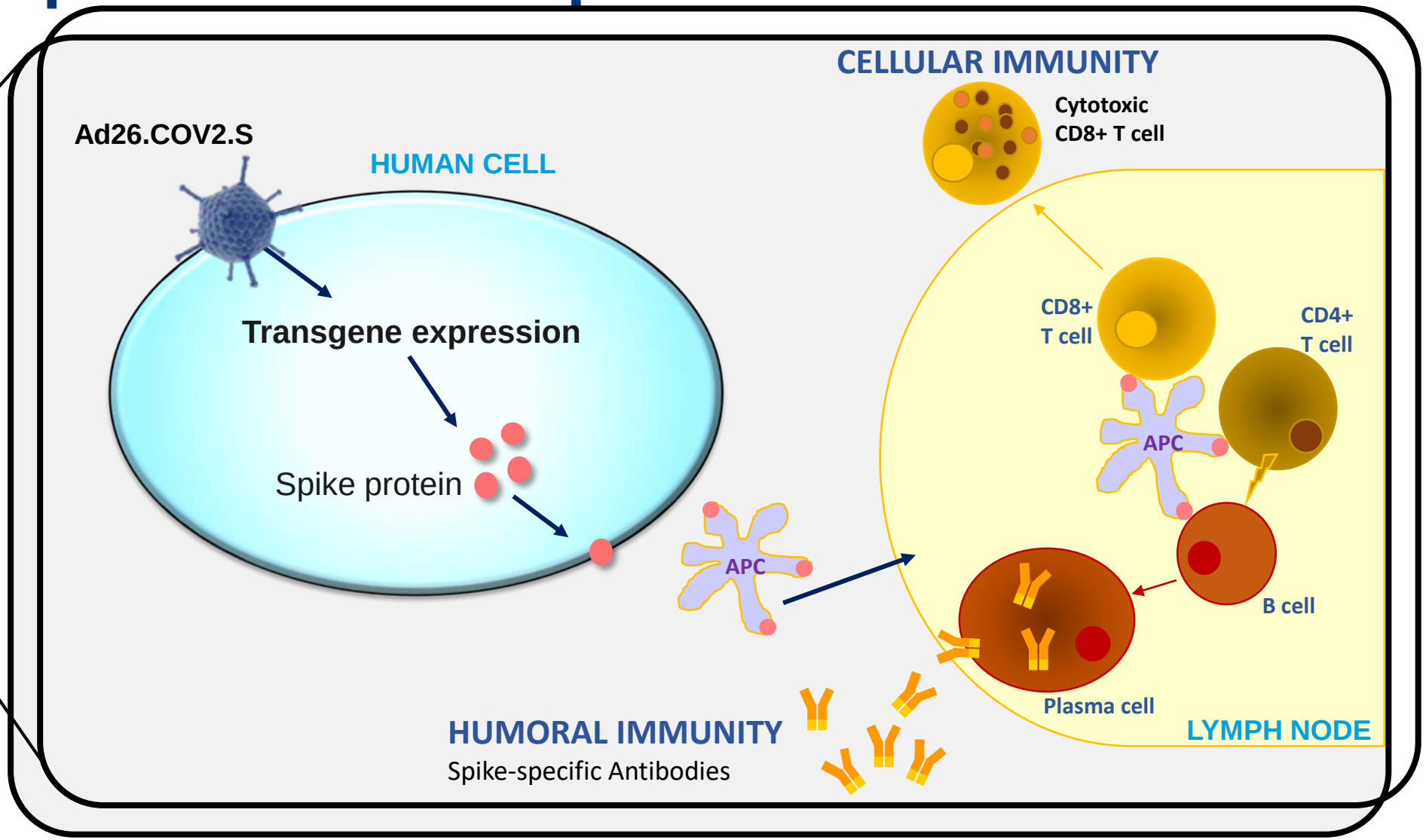
1. Martin, et al, 2008; Zhao, et al, 2010; Channappanavar, et al, 2014 2. Bos, Schuitemaker, et al, 2020; Wrapp et al, 2020

Ad26.COV2.S Expresses SARS-CoV-2 Spike Protein, Eliciting Multiple Immune Responses

I.M. injection of Ad26.COV2.S



Adenoviral vectors classified as non-integrating*



*FDA Guidance, 2020

Single-Dose Ad26.COV2.S Fully Protects Against SARS-CoV-2 Challenge in Non-Human Primates (NHP)

- Protection against viral replication
  - Near complete protection in nose
  - Full protection in lung
    - Durability > 6 months
    - Protection seen even with 4-fold lower vaccine dose
  - Nearly full protection in aged NHP
  - Protection in Syrian golden hamsters, no VAED
- Results met FDA criteria to progress to human clinical trials

VAED = Vaccine Associated Enhanced Disease

Phase 1/2a (COV1001): First in Human Study

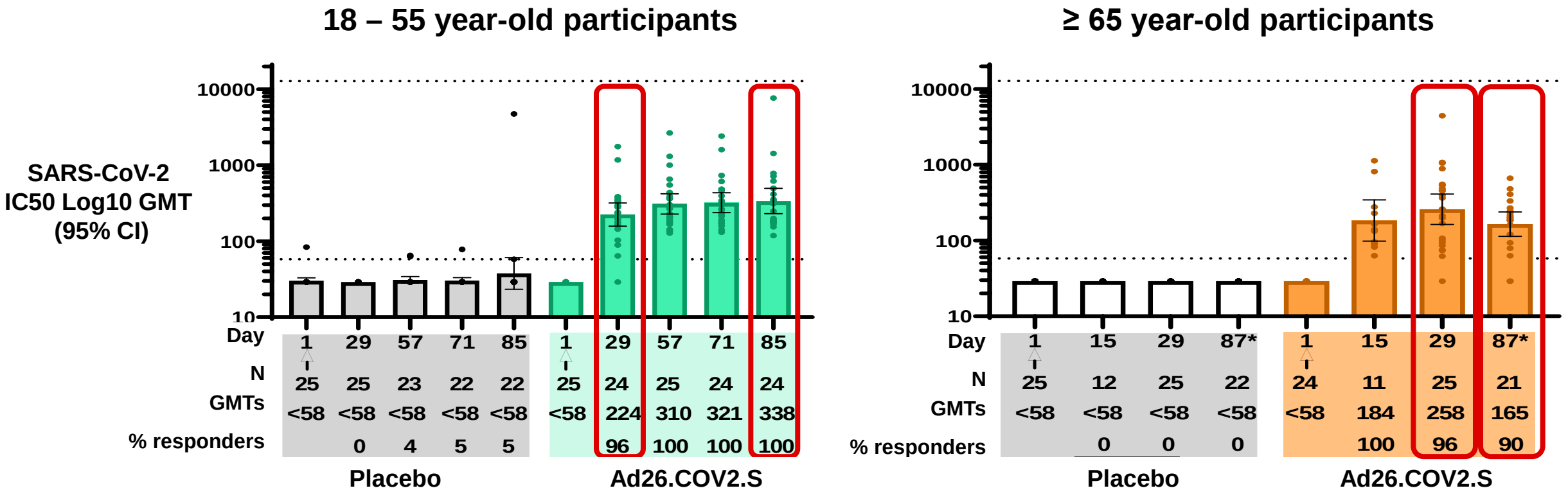
Focus: 2 groups of healthy adults 18 to 55 years and ≥ 65 years

COV1001 Evaluated 2 Dose Levels: $5x10^{10}$ vp and $1x10^{11}$ vp

- Administered in 1-dose or 2-dose regimen
  - Intramuscular injection
- Interim analysis conducted at Day 29
  - 28 days following 1st dose
  - Evaluated safety and immunogenicity

Similar and Durable Humoral Immune Responses After Single Dose $5x10^{10}$ vp Ad26.COV2.S in Adults 18-55 and ≥ 65 Years

- Observed neutralizing antibody response: 96% of Ad26.COV2.S group (Day 29)
  - Response lasted ≥ 85 days in both age groups

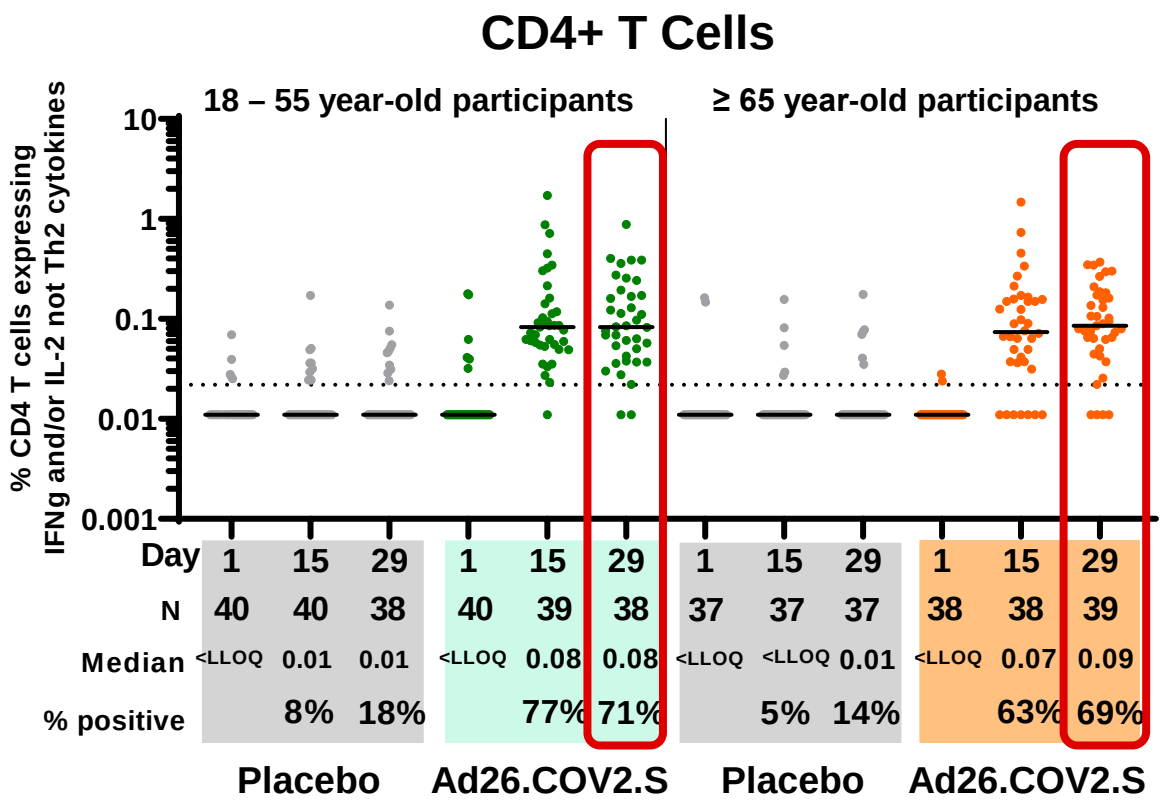


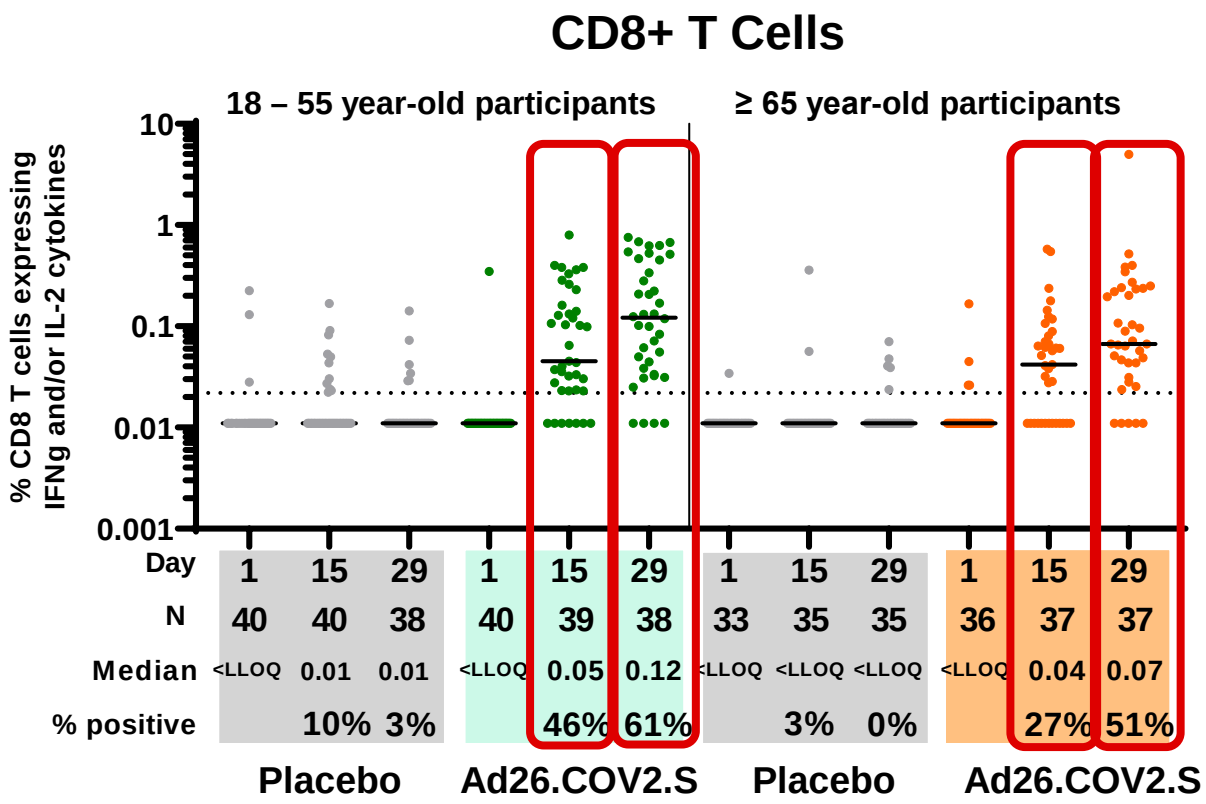
Adapted from Sadoff, Le Gars, NEJM, 2021

Additional Features of Ad26.COV2.S-Elicited Humoral Immunity

- Antibodies had non-neutralizing Fc tail mediated functionalities
  - Potentially important antiviral effector function, including against emerging variants
  - Not limited to epitopes in receptor binding site or N-terminal domain
- Phase 3: similar humoral immunogenicity observed in Brazil, South Africa, US despite baseline Ad26 seropositivity
  - Baseline Ad26 seropositivity: Brazil (33%), South Africa (69%), US (< 2%)
- Results in line with other experience across Ad26 based vaccines

Ad26.COV2.S Elicits CD4+ and CD8+ T Cell Responses





Th1/Th2 ratio well above 1

Responder defined by one-sided Fisher's exact test comparing non-stimulated versus S peptide stimulated wells

Adapted from Sadoff, Le Gars, NEJM, 2021

Summary of Phase 1/2 Immunogenicity Data Following Single Dose of Ad26.COV2.S

- Neutralizing antibody titers elicited in 96% of adults, independent of age
  - Titers detected as early as 14 days post vaccination
  - Increased in following weeks and maintained thereafter
- Strong CD8+ and Th1 dominated CD4+ T cell responses
  - Minimizes risk for vaccine associated enhanced disease (VAED)
- Both doses had favorable safety profile
  - Lower dose more favorable reactogenicity profile
- Ad26.COV2.S $5x10^{10}$ vp dose selected for COV3001

Phase 3 Study COV3001 (ENSEMBLE) Efficacy and Safety

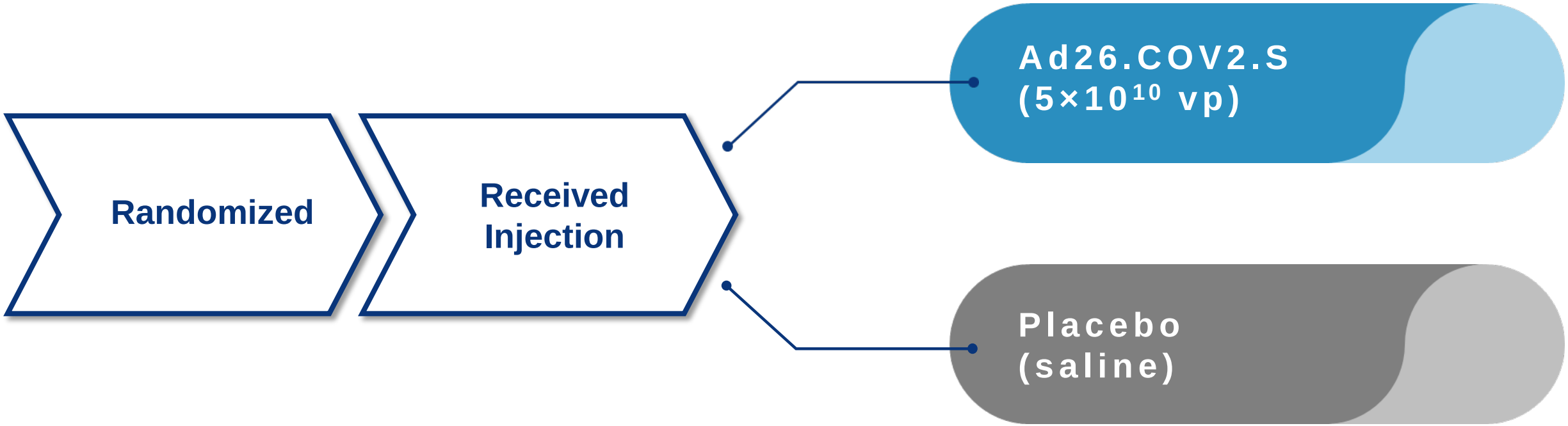
Macaya Douoguih, MD, MPH

Head of Clinical Development and Medical Affairs

Janssen Pharmaceuticals Companies of Johnson & Johnson

COV3001: Randomized, Double-Blind, Phase 3 Trial

- Evaluating efficacy, safety, immunogenicity of single dose of Ad26.COV2.S



- Randomization stratified by site, age group, and absence / presence of comorbidities

COV3001: Began Enrollment with Safety Run-in Phase

Stage 1a safety run in

- ~2,000 adults 18 – 59 years without comorbidities

→

Stage 1b initiated following DSMB review of 1a data

- Adults 18 – 59 years with and without comorbidities

Stage 2a safety run in

- ~2,000 adults ≥ 60 years without comorbidities

→

Stage 2b initiated following DSMB review of 2a data

- Adults ≥ 60 years with and without comorbidities

Study targeted at least 30% of total study population to be ≥ 60 years

COV3001: Co-Primary Endpoints

Vaccine efficacy to prevent moderate to severe/critical COVID-19

- **at least 14 days after vaccination**
- **at least 28 days after vaccination**

- **Primary Hypothesis: lower limit of 95% confidence interval > 30%**

Per Protocol Population

COV3001: Case Definition for Moderate COVID-19

RT-PCR or molecular test confirmation of SARS-CoV-2 infection

AND

At any time during observation period:

≥ 1 new or worsening sign or symptom

- **Respiratory rate ≥ 20 bpm**
- **Abnormal oxygen saturation (> 93% on room air)**
- **Evidence of pneumonia**
- **Deep vein thrombosis (DVT)**
- **Shortness of breath**

OR

≥ 2 new or worsening sign or symptoms

- **Fever**
- **Heart rate ≥ 90 bpm**
- **Shaking chills**
- **Muscle pain**
- **Malaise**
- **Headache**
- **Cough**
- **Sore throat**
- **Changes to olfaction or taste**
- **Gastrointestinal symptoms**
- **Red or bruised feet or toes**

COV3001:
Case Definition for Severe/Critical COVID-19

RT-PCR or molecular test confirmation of SARS-CoV-2 infection

AND

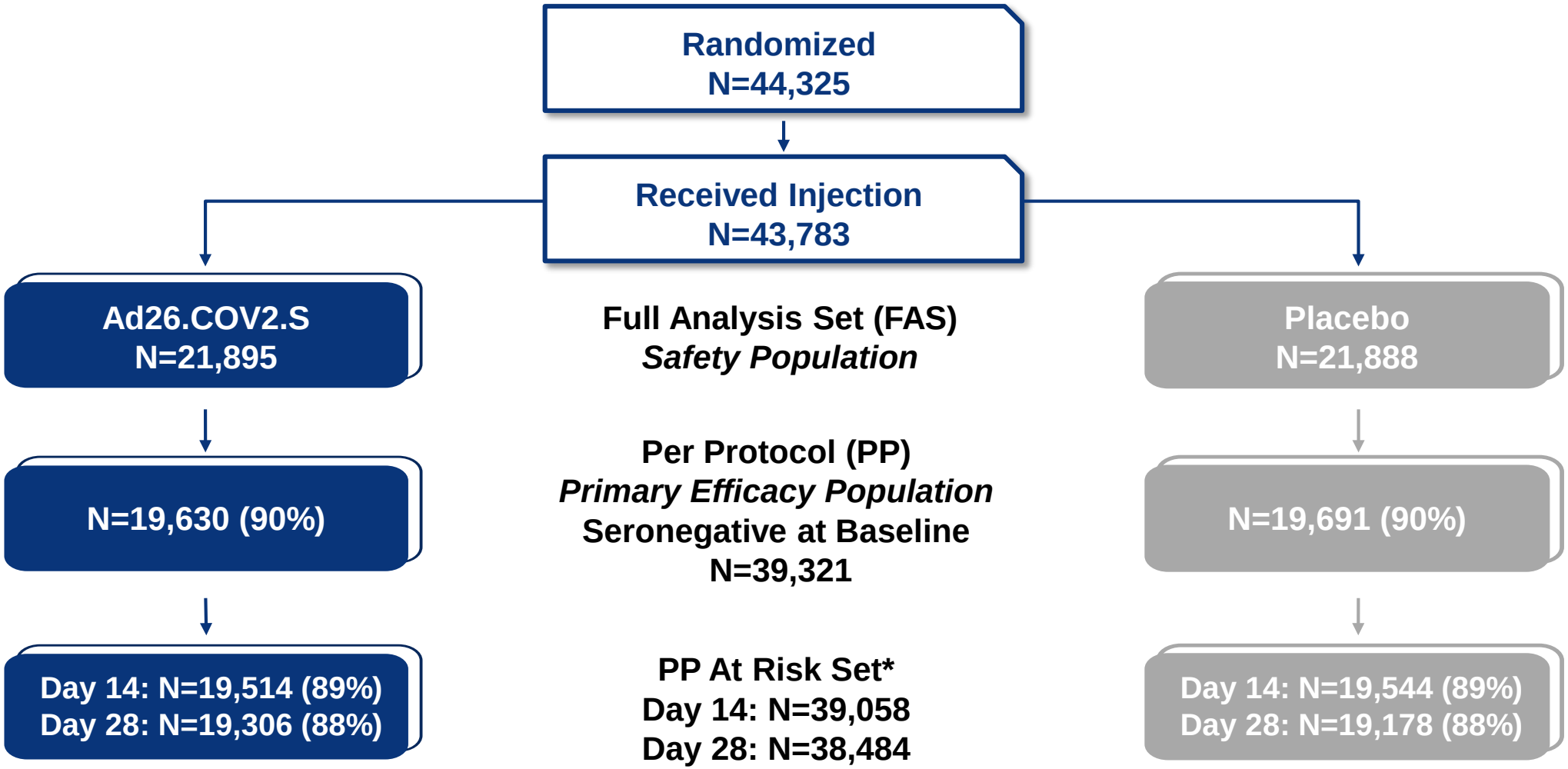
At any time during observation period:

≥ 1 of these signs or symptoms

- **Clinical signs indicative of severe systemic illness:** Respiratory rate ≥ 30 bpm, heart rate ≥ 125 bpm, SpO_2 ≤ 93% on room air at sea level or PaO_2/FiO_2 < 300 mmHg
- **Respiratory failure:** Needing high-flow oxygen, non-invasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation [ECMO]
- **Evidence of shock:** Systolic blood pressure < 90 mmHg, diastolic blood pressure < 60 mmHg, or requiring vasopressors
- **Significant acute renal, hepatic, or neurologic dysfunction**
- **Admission to ICU**
- **Death**

Study COV3001:
Disposition and Efficacy Results

COV3001 Disposition of Participants



*PP At Risk set: excluded participants with positive polymerase chain reaction (PCR) test for SARS-CoV-2 between vaccination and day of efficacy assessment

COV3001: No Relevant Differences at Baseline Between Vaccine and Placebo Groups Globally

Full Analysis Set	Ad26.COV2.S N = 21,895		Placebo N = 21,888	
	n	%	n	%
Sex, female	9,820	45%	9,902	45%
Mean Age (SD), years	50.7 (15.0)		50.7 (15.0)	
Age group				
18-59	14,564	67%	14,547	66%
≥ 60	7,331	33%	7,341	34%
≥ 65	4,259	19%	4,302	20%
≥ 75	809	4%	732	3%
Race				
American Indian or Alaska Native	2,083	10%	2,060	9%
Asian	743	3%	687	3%
Black or African American	4,251	19%	4,264	20%
Native Hawaiian or other Pacific Islander	58	0.3%	48	0.2%
White	12,858	59%	12,838	59%
Multiple, unknown, not reported	1,901	9%	1,989	9%
Ethnicity				
Hispanic or Latino	9,874	45%	9,963	46%

COV3001: Similar Baseline Demographics Between Vaccine and Placebo Groups in US

Full Analysis Set	Ad26.COV2.S N = 9,655		Placebo N = 9,647	
	n	%	n	%
Sex, female	4,292	45%	4,256	44%
Mean Age (SD), years	53.0 (14.7)		53.2 (14.7)	
Age group				
18-59	5,894	61%	5,870	61%
≥ 60	3,761	39%	3,777	39%
≥ 65	2,299	24%	2,369	25%
≥ 75	445	5%	416	4%
Race				
American Indian or Alaska Native	92	1%	95	1%
Asian	655	7%	597	6%
Black or African American	1,246	13%	1,264	13%
Native Hawaiian or other Pacific Islander	47	0.5%	41	0.4%
White	7,104	74%	7,090	74%
Multiple, unknown, not reported	510	5%	558	6%
Ethnicity				
Hispanic or Latino	1,381	14%	1,454	15%

COV3001: Global Participants with Comorbidities Similar Between Vaccine and Placebo Groups

Full Analysis Set Baseline Comorbidity* Category, ≥ 2%	Ad26.COV2.S N = 21,895		Placebo N = 21,888	
	n	%	n	%
≥ 1 risk factor	8,936	40.8%	8,922	40.8%
Obesity ≥ 30 kg/m^2	6,277	28.7%	6,215	28.4%
Hypertension	2,225	10.2%	2,296	10.5%
Type 2 Diabetes Mellitus	1,600	7.3%	1,594	7.3%
Serious heart conditions	497	2.3%	511	2.3%

*Pre-existing medical risk factor for developing severe COVID-19

COV3001: US Participants with Comorbidities Similar Between Vaccine and Placebo Groups

Full Analysis Set Baseline Comorbidity* Category, ≥ 2%	Ad26.COV2.S N = 9,655		Placebo N = 9,647	
	n	%	n	%
≥ 1 risk factor	4,227	43.8%	4,247	44.0%
Obesity ≥ 30 kg/m^2	3,085	32.0%	3,054	31.7%
Hypertension	1,139	11.8%	1,166	12.1%
Type 2 Diabetes Mellitus	743	7.7%	729	7.6%
Serious heart conditions	291	3.0%	304	3.2%
Asthma	160	1.7%	203	2.1%

*Pre-existing medical risk factor for developing severe COVID-19

COV3001 Met Co-Primary Endpoints: Ad26.COV2.S Protects Against Moderate to Severe/Critical COVID-19 Globally

PP At Risk Set	> Day 14		> Day 28	
	Ad26.COV2.S N = 19,514	**Placebo** N = 19,544	**Ad26.COV2.S** N = 19,306	**Placebo** N = 19,178
Number of confirmed cases, n	**116**	**348**	**66**	**193**
Person-years	**3,117**	**3,096**	**3,102**	**3,071**
Vaccine efficacy (adjusted 95% CI)	**66.9% (59.0, 73.4)**		**66.1% (55.0, 74.8)**	

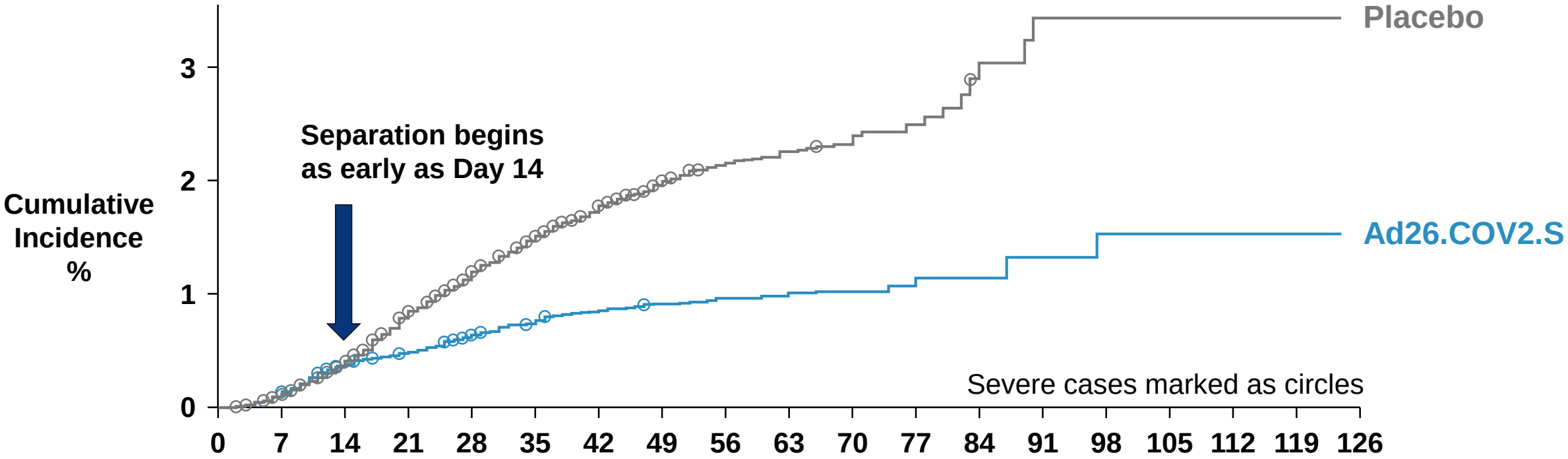
COV3001; confirmed: positive PCR centrally confirmed COVID-19 cases, global data

Ad26.COV2.S Protects Against Moderate to Severe/Critical COVID-19 in US Population

PP At Risk Set	> Day 14		> Day 28	
	Ad26.COV2.S N = 9,119	Placebo N = 9,086	Ad26.COV2.S N = 8,958	Placebo N = 8,835
Number of cases, n	**51**	**196**	**32**	**112**
Person-years	**1,414**	**1,391**	**1,403**	**1,376**
Vaccine efficacy (95% CI)	**74.4% (65.0, 81.6)**		**72.0% (58.2, 81.7)**	

COV3001; non-confirmed: all COVID-19 cases with a positive PCR from any source, regardless of central confirmation

Kaplan Meier Shows Early Onset of Protection Against Moderate to Severe/Critical COVID-19



Participants at risk

Ad26.COV2.S	19744	19725	19669	19642	19612	19578	18541	14909	10930	7831	3998	1468	713	484	483	482	142	31	0
Placebo	19822	19804	19745	19652	19579	19488	18411	14814	10823	7740	3876	1439	708	485	482	480	133	27	0

Cumulative number of cases

Ad26.COV2.S	0	27	76	96	126	151	168	178	184	188	189	191	191	192	193	193	193	193	193
Placebo	0	22	81	168	237	299	351	387	407	416	423	425	430	432	432	432	432	432	432

COV3001; Full Analysis Set; baseline seronegative; confirmed: positive PCR centrally confirmed COVID-19 cases

Use of Larger Dataset Justified

COVID-19 Case Data Set	Cases (N) > Day 14	Cases (N) > Day 28	Assessment
Molecularly (PCR) confirmed by central laboratory (confirmed)	**464**	**259**	Co-primary and secondary efficacy analyses
Global vaccine efficacy: moderate to severe/critical COVID-19	**66.9%**	**66.1%**	
PCR+ test from any source, regardless of central laboratory confirmation (non-confirmed)	**682**	**437**	Subgroup analyses, COVID-19 hospitalizations, COVID-19-related deaths
Global vaccine efficacy: moderate to severe/critical COVID-19	**66.3%**	**65.5%**	

- High concordance (90%) between COVID-19 case datasets
- Vaccine efficacy results differed between data sets by < 1% at both timepoints

Study COV3001:
Key Secondary and Other Endpoints

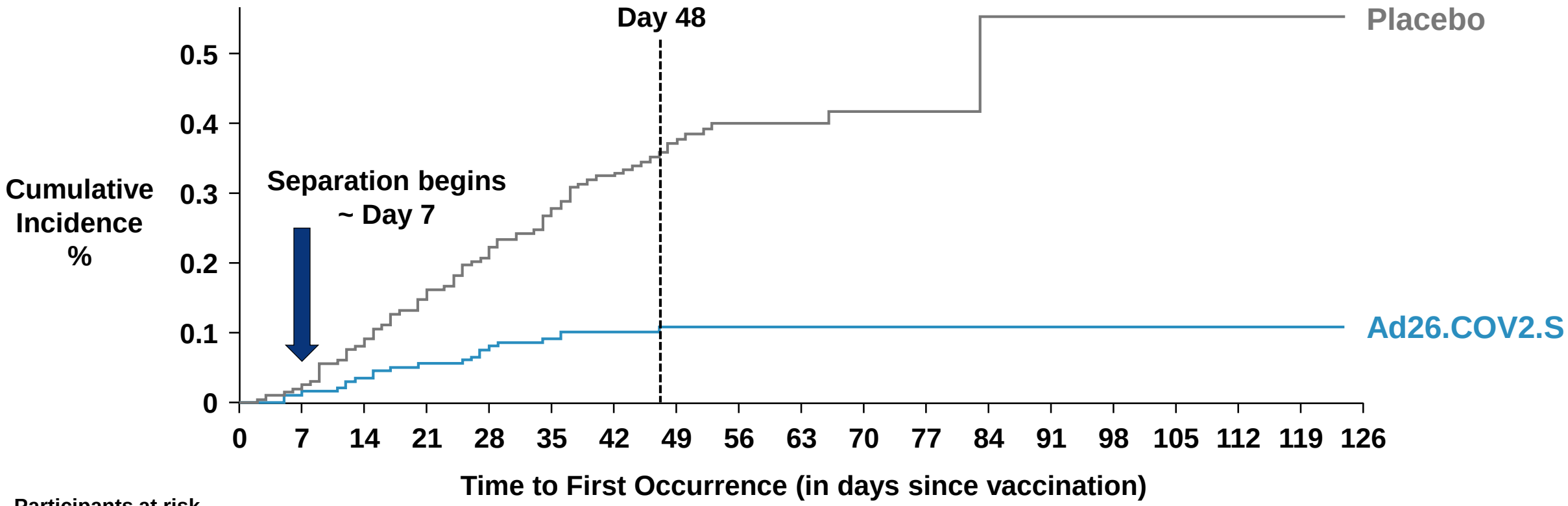
- Vaccine efficacy against severe/critical COVID-19
- Vaccine impact on hospitalization and prevention of death
- Vaccine impact on asymptomatic/undetected COVID-19

High Vaccine Efficacy Against Severe/Critical COVID-19

PP At Risk Set	> Day 14		> Day 28	
	Ad26.COV2.S N = 19,514	**Placebo** N = 19,544	**Ad26.COV2.S** N = 19,306	**Placebo** N = 19,178
Number of confirmed cases, n	**14**	**60**	**5**	**34**
Vaccine efficacy (adjusted 95% CI)	**76.7% (54.6, 89.1)**		**85.4% (54.2, 96.9)**	

COV3001; confirmed: positive PCR centrally confirmed COVID-19 cases

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



Participants at risk

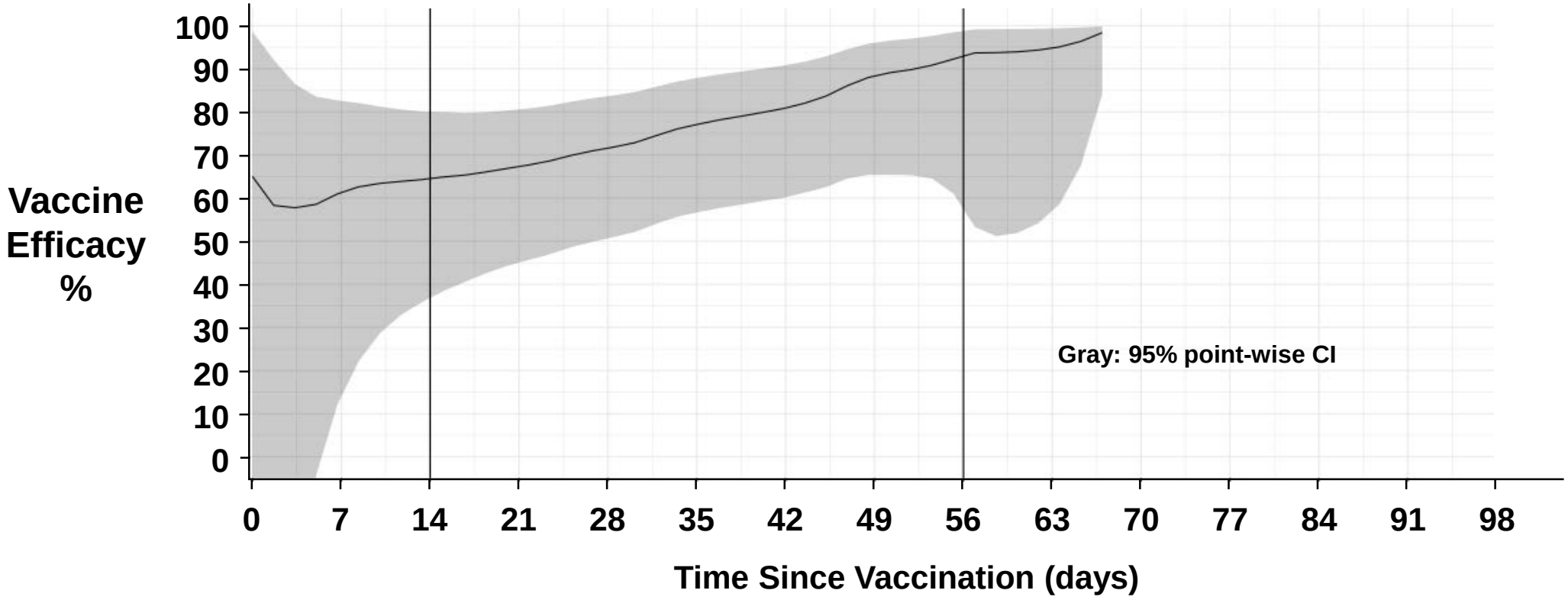
Ad26.COV2.S	19744	19741	19734	19725	19718	19705	18685	15043	11046	7919	4039	1481	720	490	490	489	146	31	0
Placebo	19822	19817	19799	19779	19760	19725	18682	15088	11069	7939	3995	1485	732	500	497	495	137	29	0

Number of cases

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

COV3001; Full Analysis Set; baseline seronegative; confirmed: positive PCR centrally confirmed COVID-19 cases

Vaccine Efficacy Against Severe/Critical COVID-19 Increased Over Time Through Day 56



Days of follow-up	7	14	28	42	56	70	84	98
% of participants with follow-up	~100%	~100%	99%	93%	55%	20%	4%	2%

COV3001; Full Analysis Set; baseline seronegative; confirmed: positive PCR centrally confirmed COVID-19 cases

Data Support Substantial Effect on Prevention of COVID-19 Related Hospitalizations

PP At Risk Set	**Ad26.COV2.S** Cases, n	**Placebo** Cases, n	**VE** (95% CI)
> Day 14			
PCR+ cases from any source, regardless of central confirmation	**2**	**29**	**93.1% (72.7, 99.2)**
> Day 28			
PCR+ cases from any source, regardless of central confirmation	**0**	**16**	**100.0% (74.3, 100.0)**

COV3001; Sources: MRU (Medical Resource Utilization), SAE, and MA-COV (medical attendance-COV)
Onset is earliest of either AE linked to COVID-19 or onset of COVID-19 episode following SAP algorithm

Ad26.COV2.S Data Support Complete Protection Against COVID-19-Related Deaths

Full Analysis Set *Through January 22, 2021*	**Ad26.COV2.S** N = 21,895	**Placebo** N = 21,888
All cause mortality	**3**	**16**
COVID-19 confirmed death > Day 1	**0**	**5***

***One PCR+ participant at baseline, not included**

Full Analysis Set *From January 22, 2021 to February 5, 2021*	**Ad26.COV2.S** N = 21,895	**Placebo** N = 21,888
Additional deaths reported	**2**	**4**
COVID-19 confirmed death > Day 1	**0**	**1**

- All COVID-19 associated deaths occurred in South Africa

COV3001; non-confirmed: all COVID-19 cases with a positive PCR from any source, regardless of central confirmation

Subset of Data Show Effect Against Asymptomatic/Undetected COVID-19

Per Protocol	> Day 29 Ad26.COV2.S N = 19,630	> Day 29 Placebo N = 19,691	VE (95%CI)
Serology Risk Set (Day 71 serology results)	**N = 1,346**	**N = 1,304**	
Seroconverted SARS-CoV-2 (Day > 29)[a]	**18**	**50**	**65.5% (39.9, 81.1)**
Seroconverted SARS-CoV-2 without previous symptoms (Day > 29)[a,b]	**10**	**37**	**74.2% (47.1, 88.6)**

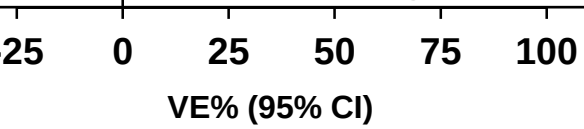
[a] Serologically converted: positive serology (Non-S protein) test without SARS-CoV-2 positive RT-PCR before positive serology test irrespective of previous symptoms
[b] Without previous symptoms: no COVID-19 symptoms occurred before positive serology test at any point during study

Study COV3001: Additional Analyses

- Vaccine efficacy by prespecified subgroups
- Vaccine efficacy by countries with emerging variants

Overall VE Against Moderate to Severe/Critical COVID-19 Consistent Across Prespecified Subgroups

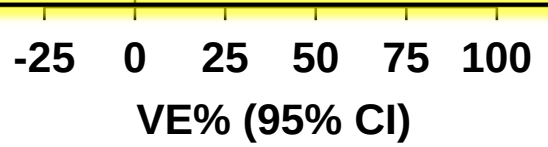
Per Protocol	# Events / N: Ad26.COV2.S N = 19,630	# Events / N: Placebo N = 19,691	Moderate to Severe/Critical COVID-19 > Day 28 Vaccine Efficacy (95% CI)
PP Risk Set	**113 / 19,306**	**324 / 19,178**	**65.5% (57.2, 72.4)**
Age			
18 – 59 years	**87 / 12,617**	**259 / 12,527**	**66.8% (57.5, 74.3)**
≥ 60 years	**26 / 6,689**	**65 / 6,651**	**60.4% (36.8, 75.9)**
Participants with comorbidities (all ages)			
Yes	**44 / 7,684**	**105 / 7,626**	**58.6% (40.6, 71.6)**
No	**69 / 11,622**	**219 / 11,552**	**68.8% (59.0, 76.6)**
Sex			
Male	**54 / 10,764**	**176 / 10,649**	**69.8% (58.9, 78.2)**
Female	**59 / 8,538**	**148 / 8,525**	**60.3% (46.0, 71.2)**
Race and ethnicity			
Non-Hispanic / Latino	**52 / 10,131**	**163 / 9,957**	**68.8% (57.2, 77.6)**
Hispanic / Latino	**59 / 8,688**	**153 / 8,741**	**61.3% (47.4, 71.8)**
White	**64 / 11,994**	**187 / 11,912**	**66.2% (54.8, 74.9)**
Black	**21 / 3,330**	**66 / 3,300**	**68.6% (48.0, 81.8)**



COV3001; global; non-confirmed: all COVID-19 cases with a positive PCR from any source, regardless of central confirmation

Vaccine Efficacy Consistently High Across Key Countries > Day 28

Country *% Variant*	Severity	# Events / N Ad26.COV2.S N = 19,306	# Events / N Placebo N = 19,178	> Day 28 Vaccine Efficacy (95%CI)
United States 96% D614G 3% CAL.20C	**Moderate-Severe/Critical**	**32 / 8,958**	**112 / 8,835**	**72.0% (58.2, 81.7)**
	Severe/Critical	**1 / 8,958**	**7 / 8,835**	**85.9% (-9.4, 99.7)**
Brazil 69% P.2 lineage 31% D614G	**Moderate-Severe/Critical**	**24 / 3,354**	**74 / 3,312**	**68.1% (48.8, 80.7)**
	Severe/Critical	**1 / 3,354**	**8 / 3,312**	**87.6% (7.8, 99.7)**
South Africa 95% B.1.351 lineage 3% D614G	**Moderate-Severe/Critical**	**23 / 2,449**	**64 / 2,463**	**64.0% (41.2, 78.7)**
	Severe/Critical	**4 / 2,449**	**22 / 2,463**	**81.7% (46.2, 95.4)**



South Africa *PP At Risk Set (N = 4,912)* **Hospitalizations > Day 28*: 0 vs 6 (Ad26.COV2.S vs placebo)**

Full Analysis Set (N = 6,576) **COVID-related deaths: 0 vs 5** (Ad26.COV2.S vs placebo)**

COV3001; non-confirmed: all COVID-19 cases with a positive PCR from any source, regardless of central confirmation
***Sources: MRU (Medical Resource Utilization), SAE, and MA-COV (medical attendance-COV); **6th case excluded due to PCR+ test at baseline**

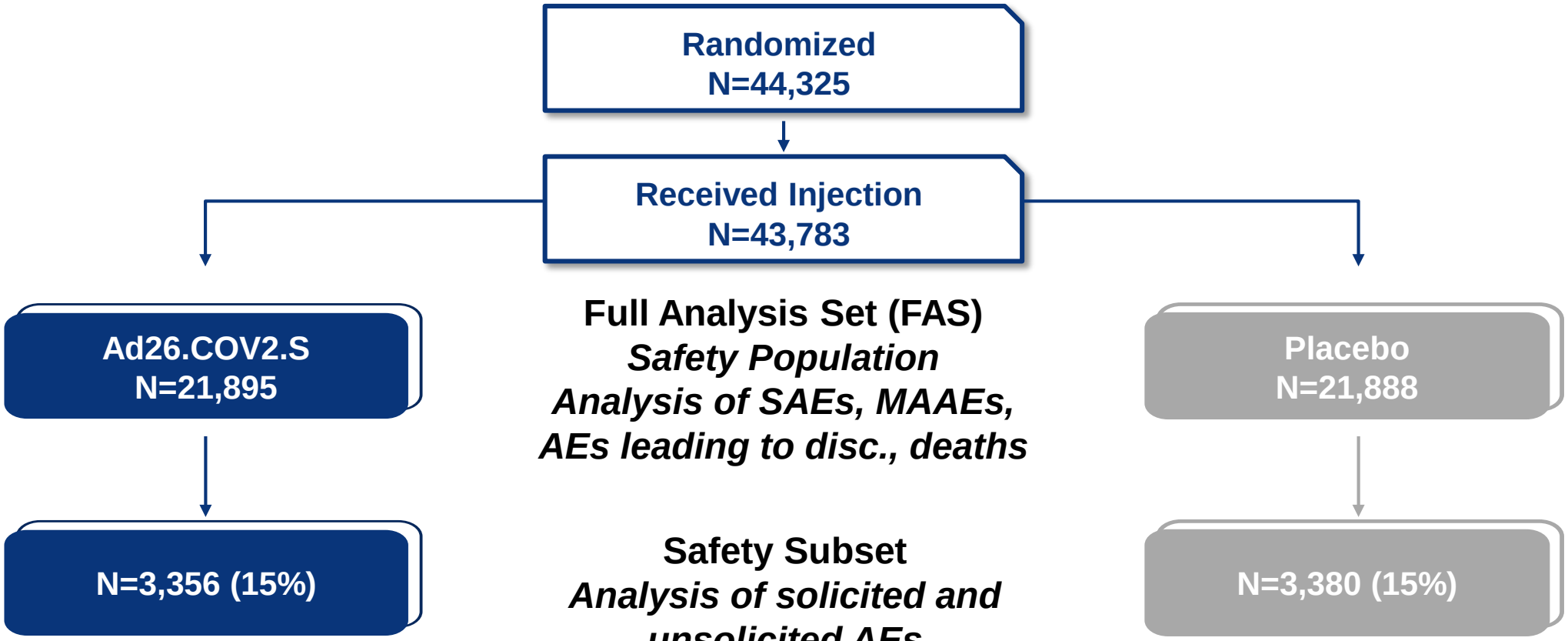
Single Dose of Ad26.COV2.S Offers Substantial Protection Against COVID-19

- 85% VE* against severe disease
  - Onset of protection as early as 7 days after vaccination
  - Complete protection against COVID-19 related hospitalizations* and deaths
- 66% VE* against moderate to severe disease across all countries
  - Onset evident as early as Day 14, and increased through Day 56
- 72% VE* against moderate to severe COVID-19 in US
  - Study participants reflected the diversity of the overall US population
- Protection against all symptomatic disease consistent with primary endpoint
- High-quality, robust data at a time when the incidence of SARS-CoV-2 was increasing, and new, highly transmissible variants were emerging
- High levels of protection consistent across subgroups, countries and regions*

*> Day 28

Study COV3001: Safety Results

COV3001 Safety Subset Includes Data on Solicited and Unsolicited Adverse Events



Safety analysis cut off date: January 22, 2021

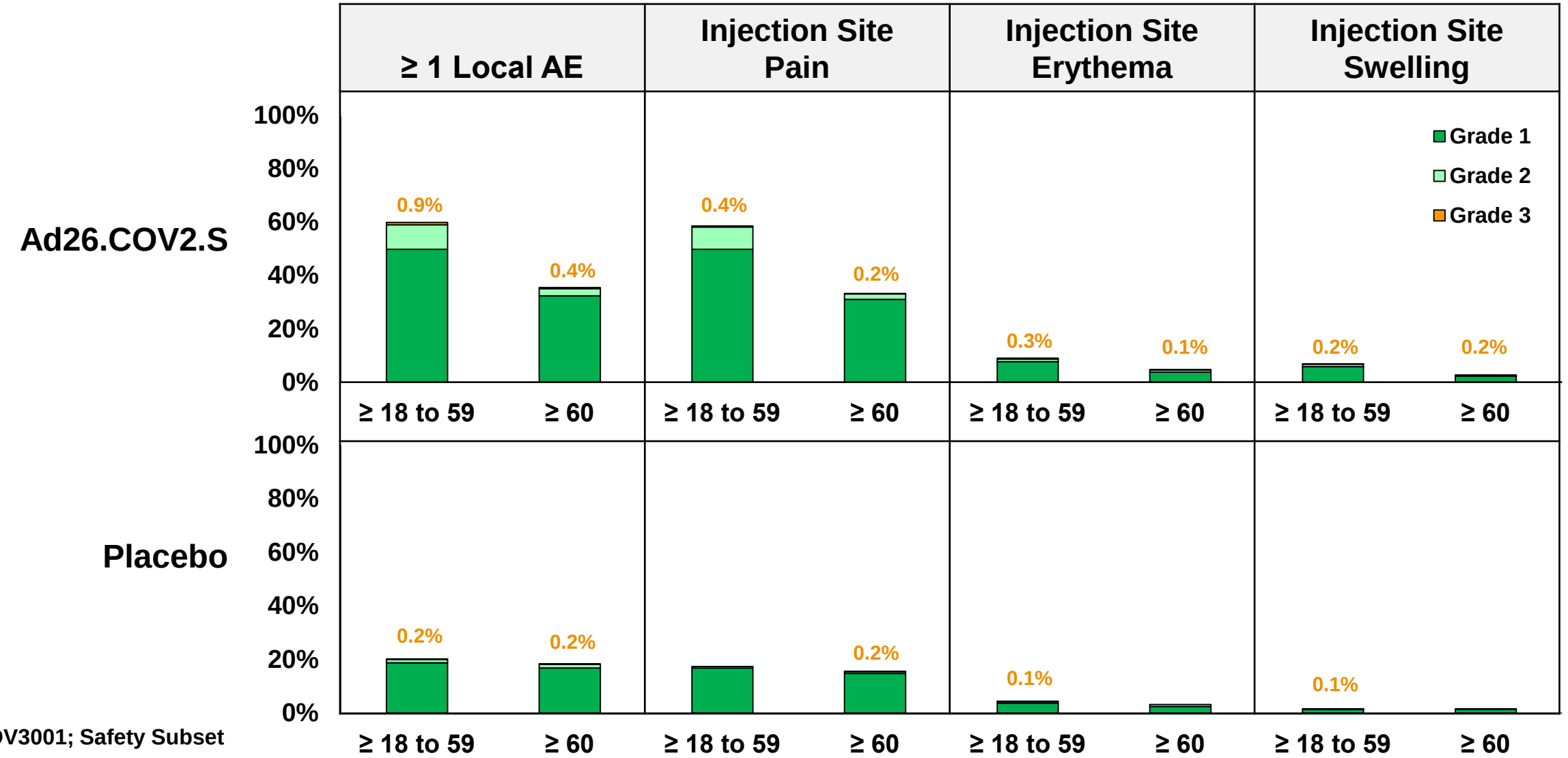
Safety Data Met FDA Guidelines for Median Follow-Up of At Least 2 Months

- Median follow up after vaccination was 58 days
- Full Analysis Set: 55% had ≥ 2 months of follow-up
- Safety Subset: nearly all (99.9%) completed post-vaccination period of Day 1-29

COV3001; safety analysis cut off date: January 22, 2021

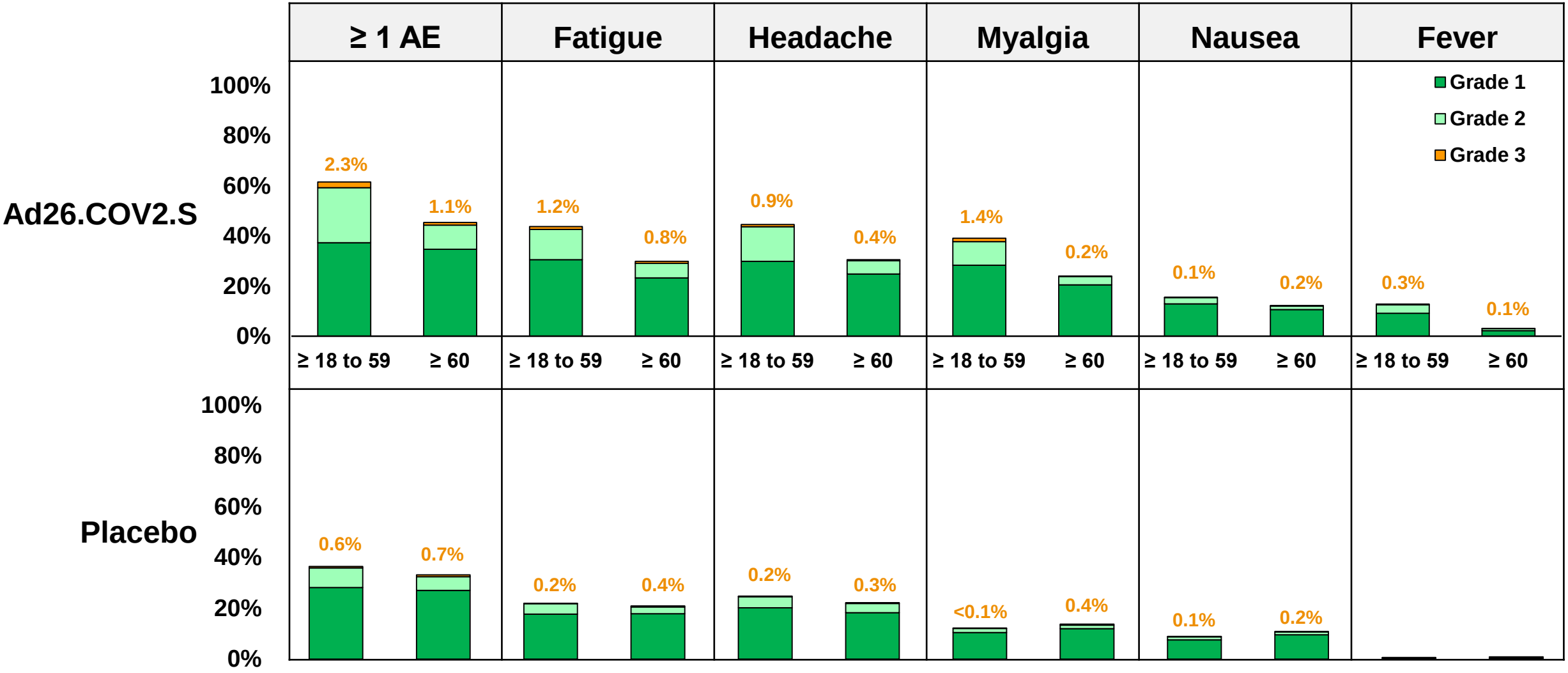
Study COV3001:
Solicited Adverse Events

Local Adverse Events, Nearly All Grade 1 and 2 in Severity, All Events Resolved 2-3 Days After Injection



COV3001; Safety Subset

Systemic Adverse Events Transient with Median Duration of 1-2 Days



COV3001; Safety Subset

Study COV3001:
Unsolicited Adverse Events

Similar Rates of Unsolicited AEs Between Groups

Unsolicited Adverse Events	Ad26.COV2.S		Placebo	
	n	%	n	%
Safety Subset	N = 3,356		N = 3,380	
Any Adverse Event (AE)	440	13%	407	12%
Full Analysis Set (FAS)	N = 21,895		N = 21,888	
Any Medically-Attended Adverse Event (MAAE)	304	1.4%	408	1.9%
Any Serious Adverse Event (SAE)	90	0.4%	137	0.6%
Not COVID-19-related SAE	83	0.4%	96	0.4%
Any death (reported through January 22, 2021)	3	<0.1%	16	0.1%
COVID-19 related deaths	0	-	5*	-

COV3001; *Excludes PCR+ participant at baseline

No Evidence of Vaccine-Associated Enhanced Respiratory Disease (VAERD) with Ad26.COV2.S

- Clinical data confirms nonclinical observations that theoretical risk for VAERD is low
  - Data demonstrated Th1 dominant immune responses
  - Breakthrough infections in Ad26.COV2.S group milder than those in placebo
- DSMB continuously monitored all cases of COVID-19 for patterns suggestive of VAERD, none found

Other Adverse Events of Interest

Full Analysis Set	Ad26.COV2.S N = 21,895 n	Placebo N = 21,888 n
Hypersensitivity*	77	65
Venous thromboembolic events**	14	10
Convulsions	4***	1
Tinnitus	6	0
Peripheral neuropathy	2	2
Guillain-Barre Syndrome	1	1
Bell's Palsy	3	2

COV3001

*No anaphylaxis

**Most participants had relevant predisposing medical conditions and/or other factors

***Three participants with history of epilepsy, one additional event followed transverse sinus thrombosis

Hypersensitivity Events

Full Analysis Set Preferred Term, n	Ad26.COV2.S N = 21,895	Placebo N = 21,888
Hypersensitivity Cases, n (%)	**77 (0.4%)**	**65 (0.3%)**
Rash	35	23
Urticaria	8	5
Hypersensitivity	9*	6
Dermatitis/eczema	10	16
Edema/swelling	7	3
Eye, nose, throat manifestation	10	16
Cardiovascular	0	1

* Includes 1 related SAE of Type IV (delayed) hypersensitivity

- Non-serious dermatologic conditions most common hypersensitivity AEs
- Mean time to onset after vaccination: 5.7 days
- Mean resolution time: 13 days
- Majority Grade 1 or 2

No cases met Brighton Collaboration criteria for anaphylaxis
Similar profile observed with other Ad26 vaccines

Thrombotic and Thromboembolic Events

Full Analysis Set	Ad26.COV2.S N = 21,895 n	Placebo N = 21,888 n
Total participants with any event	14	10
Venous thromboembolic events		
Deep vein thrombosis	6	2
Pulmonary embolism	4	1
Transverse sinus thrombosis	1	0
Thrombosed hemorrhoid	0	1
Total participants with venous events	11	4
Arterial thromboembolic events		
Cerebrovascular events	3*	3
Cardiovascular events	1	3
Total participants with arterial events	3	6

COV3001

* 2 events occurred in one participant

Benefits of Ad26.COV2.S Outweigh Known and Potential Risks

- Demonstrated acceptable safety and reactogenicity profile
- Overall, reactogenicity mild and transient
  - Grade 3 reactogenicity rare
- Most AEs mild or moderate
  - Generally resolved 1 to 2 days post vaccination
- Safety further supported by > 193,000 individuals exposed to Janssen Ad26-based vaccines

COV3001 Protocol Amendment to Facilitate Cross-Over of Placebo Participants

- Upon authorization by a regulatory authority, all placebo participants to receive 1 dose of Ad26.COV2.S
- All participants encouraged to remain in study up to 2 years to assess efficacy, safety, immunogenicity
- Amendment will allow assessment of
  - Duration of protection and immunogenicity of single dose by comparing 2 groups vaccinated ~4-6 months apart

Vaccine Safety and Effectiveness Monitoring During EUA Complements US, Other Systems

- Goal to quickly identify any potential safety signals
- Surveillance of Adverse Events Following Immunizations (AEFIs), prespecified AESIs, known vaccine concerns
- Signal detection through Janssen's global safety database and external databases, including VAERS
- Monitor long-term safety and effectiveness through observational and active surveillance studies
  - Health insurance claims databases, EHRs in US and Europe

VAERS: Vaccine Event Reporting System

Clinical Perspective and Benefit-Risk Assessment

Gregory A. Poland, MD, FIDSA, MACP, FRCP (London)

Mary Lowell Leary Emeritus Professor of Medicine

Distinguished Investigator of the Mayo Clinic

Director, Mayo Vaccine Research Group

Editor in Chief, *Vaccine*

COVID-19 Continues to Spread at Alarming Rates

Large proportion of US population still needs access to safe, effective vaccines

Reached exponential phase of viral spread

- No longer increasing on linear scale
- Periodically spiking at rapid rate

3 Ways Pandemics Can Be Controlled

- Hard lockdown, mandatory masking, distancing
  - *Largely unsuccessful in US*

- Virus mutates to be less transmissible
  - *More transmissible variants already emerging in US*

- Highly-efficacious, widely used vaccines
  - *Effective, well-tolerated, simple to deploy*

Role for Janssen's Vaccine Candidate, 1-Dose Regimen in Urgent Mass-Vaccination Campaign

Largest Trial To Date	• Multiple countries • More data to analyze, confidence in results
Replication Incompetent	• Engineered to express spike protein • Cannot propagate in cells of a vaccinated individual
Non-Adjuvanted	• Does not use additional ingredients • Fewer local, systemic reactions than adjuvanted vaccines
Traditional Shipping, Storage	• Stored at normal refrigerator temperatures • 2-year shelf life when frozen
1-Dose Vaccine	• Specifically studied as 1-dose regimen • WHO preference for 1-dose vaccine in Target Product Profile

Single Dose Regimen Offers Important Logistical, Practical Advantages for Mass Vaccination Campaign

- Can help reach individual and herd immunity more quickly
  - Simplifies the process
- Decreases burden on health care system, health care providers
- Could decrease health care utilization costs

Ad26.COV2.S Data Demonstrate Strong Vaccine Efficacy, Offers Protection Against COVID-19

- Pivotal study met *both* co-primary endpoints
  - Effective against symptomatic COVID-19
- Highly effective in preventing severe/critical COVID-19
  - Highly effective in preventing hospitalization and death
- Highly effective against newly emerging variants
- Milder breakthrough infections in vaccinated participants

Single Dose of Ad26.COV2.S Demonstrated to be Safe, Well Tolerated

- Comprehensive plan for ongoing safety monitoring
- Enrolled diverse population, including older adults and individuals with comorbidities
- No safety concerns raised for any assessed population
- Hypersensitivity reactions were rare, usually nonserious
  - No severe allergic reactions reported in COVID-19 studies
- Support sponsor's cross-over plan for placebo participants and post-authorization studies, including children and pregnant women

Attributes of Ideal COVID-19 Vaccine for Emergency Use Authorization

- ☐ Excellent safety profile
- ☐ Induces protective immunity, ideally with single dose
- ☐ Stimulates protective, balanced immune responses
- ☐ Does not elicit immunopathology after vaccination
- ☐ Quickly mass produced
- ☐ Stable at refrigerator temperatures
- ☐ Avoids ultra-cold chain transport
- ☐ Long-term storage
- ☐ Demonstrated long-term efficacy

Janssen Vaccine Candidates Fulfills Attributes of Ideal COVID-19 Vaccine for EUA

- ☑ Excellent safety profile
- ☑ Induces protective immunity, ideally with single dose
- ☑ Stimulates protective, balanced immune responses
- ☑ Does not elicit immunopathology after vaccination
- ☑ Quickly mass produced
- ☑ Stable at refrigerator temperatures
- ☑ Avoids ultra-cold chain transport
- ☑ Long-term storage
- ☐ Demonstrated long-term efficacy

Known Benefits Vastly Outweigh Known Risks for Janssen's COVID-19 Vaccine Candidate

- COVID-19 continues to be a deadly pandemic
- US urgently needs more vaccines under EUA to protect millions of Americans
- Clear and compelling evidence that Ad26.COV2.S is well tolerated and highly efficacious against COVID-19

Meets FDA criteria for Emergency Use Authorization

Emergency Use Authorization (EUA) Application for Ad26.COV2.S

Janssen Pharmaceutical Companies of Johnson & Johnson

Vaccines and Related Biological Products Advisory Committee

February 26, 2021