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Janssen Pharmaceutical Companies of Johnson & Johnson

Vaccines and Related Biological Products Advisory Committee
October 15, 2021

Penny M. Heaton, MD
Global Therapeutic Area Head Vaccines
Janssen Pharmaceutical Companies of Johnson & Johnson
Ad26.COV2.S Development Strategy, Durable Efficacy and Breadth of Immune Response

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

Findings underscore promise of Ad26.COV2.S vaccine and opportunity to use booster dose to further increase protection against COVID-19
Clinical Program Supports Booster Dose is Safe, Increases Protection, Including Against Symptomatic COVID-19

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

Booster dose at 2 months provided 94% protection against symptomatic COVID-19 (US)
- Increase from 70% in single-dose study
- Complete protection against severe/critical COVID-19 globally

Booster dose at 6 months provided 12-fold increase in antibodies
- More potent than at 2 months

Booster dose increased antibodies against all variants tested, including Delta

Seeking Emergency Use Authorization for homologous booster dose
- For all individuals in US who received single-dose primary regimen
- May be given at least 2 months after primary regimen; data may suggest boosting at 6 months provides stronger immunologic response
Outline of Today’s Presentation

Single-dose Primary Regimen Provides Durable Protection
- Efficacy from COV3001: single-dose primary regimen study
- Real-World Evidence Study of Janssen vaccine
- Immunogenicity: up to 8-9 months

Boosting Substantially Increases Protection
- Efficacy from COV3009: booster 2 months after single-dose primary regimen
- Immunogenicity: booster 2-6 months after single-dose primary regimen

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

Conclusion
Efficacy and Immunogenicity of the Single-Dose Primary Regimen

Johan Van Hoof, MD

Managing Director Janssen Vaccines and Prevention, BV
Janssen Pharmaceutical Companies of Johnson & Johnson
COV3001 (Single-dose) Final Analysis of Double-Blind Period*

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

*Data cut off date of July 9, 2021
COV3001: Persistent VE Against Severe COVID-19

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

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

<table>
<thead>
<tr>
<th>Time Since Vaccination (days)</th>
<th>Numbers at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ad26.COV2.S</td>
</tr>
<tr>
<td>30</td>
<td>19562</td>
</tr>
<tr>
<td>60</td>
<td>19230</td>
</tr>
<tr>
<td>90</td>
<td>17764</td>
</tr>
<tr>
<td>120</td>
<td>15591</td>
</tr>
<tr>
<td>150</td>
<td>10284</td>
</tr>
<tr>
<td>180</td>
<td>5432</td>
</tr>
<tr>
<td>210</td>
<td>4045</td>
</tr>
</tbody>
</table>

Vaccine Efficacy %
COV3001: VE for Symptomatic COVID-19

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

Vaccine Efficacy

%  

Time Since Vaccination (days)

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

Numbers at risk

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ad26.COV2.S</td>
<td>19562</td>
<td>19111</td>
<td>17540</td>
<td>15290</td>
<td>10033</td>
<td>5256</td>
<td>3887</td>
<td>1193</td>
</tr>
<tr>
<td>Placebo</td>
<td>19589</td>
<td>18902</td>
<td>17052</td>
<td>14622</td>
<td>9328</td>
<td>4745</td>
<td>3531</td>
<td>1098</td>
</tr>
</tbody>
</table>

95% point-wise CI
COV3001: United States VE for Symptomatic COVID-19

- US: 70% VE against symptomatic COVID-19 >Day 28
- Gamma, lambda, mu and delta not prevalent in US during this period
Real-World Evidence (RWE) Study of Single-Dose Janssen Vaccine

Sebastian Schneeweiss, MD, ScD
Science Lead
Aetion, Inc
Professor of Medicine and Epidemiology
Harvard Medical School
Janssen-Aetion Real-World Evidence Cohort Study of Single-Dose Janssen Vaccine

CONTEXT

- **COV3001 RCT** demonstrated robust efficacy for single dose Ad26.COV2.S vaccine, **but no data on Delta in US**
- Published **RWE studies** (1-9) report range of vaccine effectiveness estimates for Ad26.COV2.S
  - **Hospitalizations/ER (60%-91%):** CDC (60%-84%, US), Janssen-Aetion study (81%, US), Sisonke (67%-84%, South Africa), Dutch Ministry of Health RWE (91%)
- Varying methodologies, sample sizes, follow-up times

OBJECTIVE of Janssen-Aetion RWE Study

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

- **Study Design:** Longitudinal cohort study of 422,034 Janssen-vaccinated subjects versus 1,645,397 unvaccinated subjects

- **Data Source:** HealthVerity data – validated, longitudinal, de-identified patient-level medical and pharmacy claims (including Medicaid participants) and laboratory data for ~160M lives

- **Cohort Balance:** Exact-matched by day, 3-digit ZIP, sex, age group, comorbidity index; further propensity score-matched on 17 predictors of COVID-19 severity**

- **Vaccine effectiveness estimates corrected for vaccination status misclassification in healthcare claims data***

*Polinski et al.  [https://www.medrxiv.org/content/10.1101/2021.09.10.21263385v1](https://www.medrxiv.org/content/10.1101/2021.09.10.21263385v1) - analysis till July 31, 2021; updated analysis till Aug 31st, 2021**

**COPD, CF, HIV, HTN, Liver Disease, Malignancies, Asthma, Cerebrovascular disease, CKD, Mod-Severe Asthma, PF, Obesity, Serious Heart conditions, Sickle-Cell Disease, Thalassemia, T1DM, T2DM; ***Assumed 40% under-recording of vaccinations (comparing CDC to HealthVerity vaccination percentages) and applied a correction factor to vaccine effectiveness estimates using standard methods for correcting exposure misclassification. This was confirmed in a linkage study between claims data and the Louisiana State vaccination registry
Month-Over-Month and Kaplan-Meier Plot Demonstrate Good and Durable Vaccine Effectiveness of Single-Dose Vaccine During July-August 2021, When Delta Dominant in US

**Graph: Stable month-over-month vaccine effectiveness including when Delta emerged to when it became dominant.**

**Probability of No COVID-19 Infection**

<table>
<thead>
<tr>
<th>Prevalence of Delta Variant in U.S.*</th>
<th>March</th>
<th>April</th>
<th>May</th>
<th>June</th>
<th>July</th>
<th>August</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>76</td>
<td>76</td>
<td>78</td>
<td>78</td>
<td>76</td>
<td>75</td>
</tr>
<tr>
<td>4%</td>
<td>82</td>
<td>78</td>
<td>83</td>
<td>78</td>
<td>82</td>
<td>80</td>
</tr>
<tr>
<td>15%</td>
<td>76</td>
<td>76</td>
<td>78</td>
<td>78</td>
<td>76</td>
<td>75</td>
</tr>
<tr>
<td>34%</td>
<td>82</td>
<td>78</td>
<td>83</td>
<td>78</td>
<td>82</td>
<td>80</td>
</tr>
<tr>
<td>87%</td>
<td>76</td>
<td>76</td>
<td>78</td>
<td>78</td>
<td>76</td>
<td>75</td>
</tr>
<tr>
<td>97%</td>
<td>80</td>
<td>80</td>
<td>83</td>
<td>80</td>
<td>80</td>
<td>80</td>
</tr>
</tbody>
</table>

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

**Table: Vaccine Effectiveness (%) (95% CI)**

<table>
<thead>
<tr>
<th>Vaccine Effectiveness (95% CI)</th>
<th>COVID-19 Infection</th>
<th>COVID-19 Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>66% (64%, 67%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>76% (75%, 77%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Graph: Time-to-event analyses show stable vaccine effectiveness during 183 days after vaccination.**

Median follow-up = 129 days; Schoenfeld residuals show proportional hazards throughout 183 days of follow-up (p=0.53); Uncorrected vaccine effectiveness was equally stable over 183 days
RWE demonstrates **single-dose Ad26.COV2.S** has good vaccine effectiveness in US clinical practice – consistent with COV3001 RCT data (US)

- Single dose vaccine offers good and durable protection over calendar time, in the pre-Delta and during Delta time periods

- Given vaccine effectiveness against hospitalization and infection, opportunity to improve the protection via booster dose especially against emerging variants
Kinetics and Durability of Ad26.COV2.S Induced Immune Responses

Dan Barouch, M.D., Ph.D.
Professor of Medicine
Harvard Medical School
Director, Center for Virology and Vaccine Research
Beth Israel Deaconess Medical Center
**Janssen COV1001**: Humoral Immune Responses Persist Over Time, Following a Single Dose (18-55 and ≥ 65 years)

<table>
<thead>
<tr>
<th>Days Post Primary Vaccination</th>
<th>Neutralizing Antibody GMT (95% CI)</th>
<th>Above LLOQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-55 Years, N=25</td>
<td>224 310 321 338 226</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>% Detectable antibodies</td>
<td>100 100 100 95</td>
<td></td>
</tr>
</tbody>
</table>

| ≥ 65 Years, N=24              | 184 258 165 168 164 114             |            |
| 24                           | 96                                  |
| % Detectable antibodies       | 90 86 81 68                         |

LLOQ = lower limit of quantification

N = Number of subjects

% Responders = Percentage of subjects with detectable antibodies
Ad26.COV2.S Induces Durable Antibody Responses

**Live Virus nAb**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>n</th>
<th>6mo</th>
<th>8mo</th>
<th>6mo</th>
<th>8mo</th>
<th>6mo</th>
<th>8mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNT162b2</td>
<td>27</td>
<td>543</td>
<td>53</td>
<td>5858</td>
<td>1524</td>
<td>133</td>
<td>146</td>
</tr>
<tr>
<td>mRNA-1273</td>
<td>29</td>
<td>1789</td>
<td>55</td>
<td>1524</td>
<td>133</td>
<td>146</td>
<td></td>
</tr>
<tr>
<td>Ad26.COV2.S</td>
<td>20</td>
<td>1789</td>
<td>55</td>
<td>1524</td>
<td>133</td>
<td>146</td>
<td></td>
</tr>
</tbody>
</table>

**Pseudovirus nAb**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>n</th>
<th>6mo</th>
<th>8mo</th>
<th>6mo</th>
<th>8mo</th>
<th>6mo</th>
<th>8mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNT162b2</td>
<td>29</td>
<td>700</td>
<td>262</td>
<td>160</td>
<td>1569</td>
<td>414</td>
<td>273</td>
</tr>
<tr>
<td>mRNA-1273</td>
<td>30</td>
<td>700</td>
<td>262</td>
<td>160</td>
<td>1569</td>
<td>414</td>
<td>273</td>
</tr>
<tr>
<td>Ad26.COV2.S</td>
<td>23</td>
<td>700</td>
<td>262</td>
<td>160</td>
<td>1569</td>
<td>414</td>
<td>273</td>
</tr>
</tbody>
</table>

**RBD IgG**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>n</th>
<th>6mo</th>
<th>8mo</th>
<th>6mo</th>
<th>8mo</th>
<th>6mo</th>
<th>8mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNT162b2</td>
<td>27</td>
<td>21564</td>
<td>2432</td>
<td>755</td>
<td>25677</td>
<td>4346</td>
<td>1361</td>
</tr>
<tr>
<td>mRNA-1273</td>
<td>30</td>
<td>21564</td>
<td>2432</td>
<td>755</td>
<td>25677</td>
<td>4346</td>
<td>1361</td>
</tr>
<tr>
<td>Ad26.COV2.S</td>
<td>23</td>
<td>21564</td>
<td>2432</td>
<td>755</td>
<td>25677</td>
<td>4346</td>
<td>1361</td>
</tr>
</tbody>
</table>

**Fold Change (Peak to 8 months)**

- **Live Virus nAb**
  - BNT162b2: -34
  - mRNA-1273: -44
  - Ad26.COV2.S: +4.3

- **Pseudovirus nAb**
  - BNT162b2: -4.5
  - mRNA-1273: -5.7
  - Ad26.COV2.S: -2.1

- **RBD IgG**
  - BNT162b2: -29
  - mRNA-1273: -17
  - Ad26.COV2.S: -1.6
Ad26.COV2.S Induces Durable Neutralizing Antibody Responses Against SARS-CoV-2 Variants

Collier et al. NEJM. October 15, 2021
Ad26.COV2.S Induces Durable CD8 T Cell Responses
Ad26.COV2.S Induces a Distinct and Complex Immunologic Profile with Robust Durability

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

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

Johan Van Hoof, MD

Managing Director Janssen Vaccines and Prevention, BV
Janssen Pharmaceutical Companies of Johnson & Johnson
COV3009: Evaluated Efficacy of Ad26 Following Administration of Booster 2 Months After First Shot

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

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

<table>
<thead>
<tr>
<th>Country</th>
<th>Post-dose</th>
<th>Study Day</th>
<th>Symptomatic COVID-19 VE% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>3001: Post-dose 1</td>
<td>Day &gt; 28</td>
<td>70% (61, 77)</td>
</tr>
<tr>
<td></td>
<td>3009: Post-booster</td>
<td>Day &gt; 71</td>
<td>94% (59, 100)</td>
</tr>
<tr>
<td>Global*</td>
<td>3001: Post-dose 1</td>
<td>Day &gt; 28</td>
<td>53% (47, 58)</td>
</tr>
<tr>
<td>(All)</td>
<td>3009: Post-booster</td>
<td>Day &gt; 71</td>
<td>75% (55, 87)</td>
</tr>
</tbody>
</table>

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

3001 Final analysis cutoff date: July 9, 2021 (all), June 16, 2021 (US)
3009 Final analysis cutoff date: June 24, 2021 (all), June 9, 2021 (US)
### COV3001 and COV3009: Booster Dose Increases VE Against Symptomatic COVID-19 Caused by Variants

<table>
<thead>
<tr>
<th>Variant</th>
<th>Post-dose</th>
<th>Study Day</th>
<th>Symptomatic COVID-19 Ad26.COV2.S vs Placebo</th>
<th>VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha (B.1.1.7)</td>
<td>3001: Post-dose 1</td>
<td>Day &gt; 28</td>
<td></td>
<td>70% (35, 88)</td>
</tr>
<tr>
<td></td>
<td>3009: Post booster</td>
<td>Day &gt; 71</td>
<td></td>
<td>94% (63, 100)</td>
</tr>
<tr>
<td>Mu (B.1.621)</td>
<td>3001: Post-dose 1</td>
<td>Day &gt; 28</td>
<td></td>
<td>36% (2, 59)</td>
</tr>
<tr>
<td></td>
<td>3009: Post booster</td>
<td>Day &gt; 71</td>
<td></td>
<td>63% (-28, 92)</td>
</tr>
</tbody>
</table>

3001 Final analysis cutoff date: July 2021; 3009 Final analysis cutoff date: June 2021
# COV3009: Protection Against Severe Outcomes

## PP At Risk Set

<table>
<thead>
<tr>
<th>Global</th>
<th>Ad26.COV2.S (N = 6,024)</th>
<th>Placebo (N = 5,615)</th>
<th>VE % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe COVID-19</td>
<td>0</td>
<td>8</td>
<td><strong>100%</strong> (33, 100)</td>
</tr>
<tr>
<td>COVID-19-related hospitalization</td>
<td>0</td>
<td>5</td>
<td><strong>N/A</strong></td>
</tr>
<tr>
<td>COVID-19-related death</td>
<td>0</td>
<td>1</td>
<td><strong>N/A</strong></td>
</tr>
</tbody>
</table>

> Day 71 (> 14 Days Post-Booster)

3009 Final analysis cutoff date: June 24, 2021
Immunogenicity Following Booster Dose of Ad26.COV2.S
# Clinical Immunogenicity Studies Supporting Ad26.COV2.S Booster Dose

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

*Variant wtVNA N=6 (Alpha, Beta); Data originates from studies COV1001, COV1002, COV2001; Sample size depicted are at baseline
Humoral Immune Responses as Measured by ELISA, wtVNA and psVNA Highly Correlated

wtVNA vs S ELISA Day 239 (18-55)

S ELISA vs psVNA Day 183 (18-55)

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

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

wtVNA IC50

S ELISA (EU)/mL

Spearman Correlation = 0.8391

Ad26 1e11, Placebo (n = 22) Ad26 1e11, Ad26 1e11 (n = 23)
Ad26 5e10, Placebo (n = 22) Ad26 5e10, Ad26 5e10 (n = 24)

S ELISA (EU)/mL

Spearman Correlation = 0.912

Ad26 5e10, Ad26 5e10 (n = 17)
COV2001: Boost at 2 Months Increases Antibody Titers by 3.5- to 6.2-fold

18-55 Years, N=52

≥ 65 Years, N=29

<table>
<thead>
<tr>
<th>N</th>
<th>52</th>
<th>52</th>
<th>54</th>
<th>54</th>
<th>53</th>
<th>52</th>
<th>50</th>
<th>N</th>
<th>29</th>
<th>28</th>
<th>29</th>
<th>29</th>
<th>29</th>
<th>28</th>
<th>27</th>
</tr>
</thead>
<tbody>
<tr>
<td>% responders</td>
<td>86</td>
<td>96</td>
<td>96</td>
<td>100</td>
<td>100</td>
<td></td>
<td></td>
<td>% responders</td>
<td>64</td>
<td>93</td>
<td>97</td>
<td>100</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% seropositive</td>
<td>89</td>
<td>98</td>
<td>98</td>
<td>100</td>
<td>100</td>
<td></td>
<td></td>
<td>% seropositive</td>
<td>64</td>
<td>93</td>
<td>97</td>
<td>100</td>
<td>100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LLOQ = lower limit of quantification
COV1001: Boost at 6 Months Increases Antibody Titers by 9- to 12-fold

Spike Binding Antibody GMC (95% CI)

Days

N 17 17 17

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

*GMI: geometric mean increase
**COV1001 and COV2001: Benefit of Booster Dose Higher When Given at 6 Months or Later**

*Data from COV2001 Group 1
**Data from COV2001 Group 9 / post-dose 1, data from parallel group
*** Data from COV1001 Cohort 2a

Fold-Increase in Spike Binding Antibody Titers 28 Days Post Boost vs 28 Days Post Dose 1

- Booster at 2 Months*: 4.6 (n=51)
- Booster at 3 Months**: 5.6 (n=27)
- Booster at 6 Months***: 12.0 (n=17)
COV1001: Booster 6 Months After Single-Dose Primary Regimen Proportionally Increases nAb Levels Against Variants of Concern

Estimated log10 GMT per visit per strain where titers at LOD of 20 used as values < 20, assuming Gaussian distribution for underlying log10 titers and calculated in Tobit model with subject, visit, strain and two-way interactions as factors.
Ad26.COV2.S Booster Dose Enhances Immune Response and Individual Protection

- Booster dose at 2 months provided robust anamnestic immune responses
  - More potent when booster administered at 6 months
- Booster dose increased nAbs against variant strains
- Enhanced immune response congruent with higher observed vaccine efficacy in COV3009
Safety Results of Ad26.COV2.S Booster

Macaya Douoguih, MD, MPH

Head of Clinical Development & Medical Affairs, Vaccines Janssen Pharmaceutical Companies of Johnson & Johnson
Outline for Safety Presentation

- Cumulative exposure to booster dose
- Reactogenicity of booster at 2 months (COV3009)
- Reactogenicity of booster at 6 months (COV1001 & COV2008)
- Safety profile of booster dose at 2 months (COV3009)
- Adverse events of interest / special interest
- Post-authorization safety
## Cumulative Exposure to Ad26.COV2.S Booster After Single-Dose Primary Regimen

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

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

**370 participants received booster in 3:3:1 ratio at dose level of 5 x 10^{10}, 2.5 x 10^{10}, or 1 x 10^{10}. Dose-level data remain blinded
COV3009: Safety Analysis Sets

Randomized and Received First Injection
N=31,293

Full Analysis Set

Ad26.COV2.S
N=15,705

Placebo
N=15,588

Received Second Injection at 2 Months

Safety Subset – Dose 1

Ad26.COV2.S
N=3,015

Placebo
N=3,052

Safety Subset – Dose 2

Ad26.COV2.S
N=8,646

Placebo
N=8,043

Ad26.COV2.S
N=1,559

Placebo
N=1,425
Reactogenicity of Booster Dose at 2 Months

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

18-59 Years
Primary N = 1,784; Booster N = 1,164

≥ 1 Systemic AE | Fatigue | Headache | Myalgia | Nausea | Fever
---|---|---|---|---|---
Primary | 2.5% | 1.8% | 1.2% | 0.9% | 1.0% | 0.7% | 1.1% | 0.6% | 0.4% | 0.1% | 0.1% |
Booster 2 mo | | | | | | | | | | | |

≥ 60 Years
Primary N = 1,231; Booster N = 395

≥ 1 Systemic AE | Fatigue | Headache | Myalgia | Nausea | Fever
---|---|---|---|---|---
Primary | 0.9% | 1.0% | 0.3% | 0.8% | 0.4% | 0.5% | 0.2% | 0.5% | 0.1% | 0.5% | 0%
Booster 2 mo | | | | | | | | | | | |

Reactogenicity of Booster Dose at 6 Months
Study COV1001 and Study COV2008
COV1001: Systemic Reactogenicity of Booster at 6 Months vs Primary Dose

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

- **Systemic AE**
  - ≥ 1 Systemic AE
  - Fatigue
  - Headache
  - Myalgia
  - Nausea
  - Fever

- **Grade 1**
  - Fatigue: 0%
  - Headache: 3.4%
  - Myalgia: 0%
  - Nausea: 0%
  - Fever: 0%

- **Grade 2**
  - Fatigue: 0%
  - Headache: 0%
  - Myalgia: 0%
  - Nausea: 0%
  - Fever: 0%

- **Grade 3**
  - Fatigue: 0%
  - Headache: 0%
  - Myalgia: 0%
  - Nausea: 0%
  - Fever: 0%

- **Primary**
  - Booster 6 mo
- **Booster**
  - 6 mo
COV2008: Preliminary Blinded Systemic Reactogenicity of Booster at ≥ 6 Months

- Ongoing randomized double-blind study of participants enrolled in Study 3001 where three Ad26.COV2.S booster dose levels are being evaluated ≥ 6 months following primary vaccination with Ad26.COV2.S
- 127 estimated to have received $5 \times 10^{10}$ vp
  - Blinded 7-day safety data available on 83 participants (N~32 ≥ 60 years)
- Dose-level data remain blinded; however, no Grade 3 systemic reactogenicity events have been reported
Unsolicited Adverse Events
Study COV3009
### COV3009: Similar Rates of Unsolicited AEs Between Groups

*Reported through June 25, 2021*

<table>
<thead>
<tr>
<th></th>
<th>Ad26.COV2.S</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Safety Subset – Dose 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any AE</td>
<td>454</td>
<td>332</td>
</tr>
<tr>
<td></td>
<td>15.1%</td>
<td>10.9%</td>
</tr>
<tr>
<td><strong>Safety Subset – Dose 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any AE</td>
<td>159</td>
<td>120</td>
</tr>
<tr>
<td></td>
<td>10.2%</td>
<td>8.4%</td>
</tr>
<tr>
<td><strong>Full Analysis Set (FAS)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any MAAE</td>
<td>1033</td>
<td>1003</td>
</tr>
<tr>
<td></td>
<td>6.6%</td>
<td>6.4%</td>
</tr>
<tr>
<td>Any SAE</td>
<td>104</td>
<td>136</td>
</tr>
<tr>
<td></td>
<td>0.7%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Non-COVID-19-related</td>
<td>98</td>
<td>104</td>
</tr>
<tr>
<td></td>
<td>0.6%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Any death*</td>
<td>4</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>&lt; 0.1%</td>
<td>0.1%</td>
</tr>
<tr>
<td>COVID-19-related</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>&lt; 0.1%</td>
</tr>
</tbody>
</table>
Adverse Events of Interest/Special Interest

Study COV3009
Two cases of thrombosis with thrombocytopenia during follow-up

- **Ad26.COV2.S**: DVT with thrombocytopenia on Day 100 post-vaccination
- **Placebo**: DVT (Day 27) and PE (Day 29) with thrombocytopenia

Neither case definitive TTS based on CDC criteria

- Tier 1: thrombosis in unusual location with thrombocytopenia; anti-PF4 supportive
- Tier 2: thrombosis with thrombocytopenia in more common site with positive anti-platelet 4 antibody
Potential TTS Events After Second Dose of Another Adenoviral COVID-19 Vaccine

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

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

<table>
<thead>
<tr>
<th>Adverse Event of Interest</th>
<th>Within 28 Days of Primary Dose</th>
<th>Within 28 Days of Booster Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embolic and thrombotic events (SMQ)</td>
<td>2 (&lt; 0.1%)</td>
<td>6 (0.1%)</td>
</tr>
<tr>
<td>Convulsions/seizures</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>4 (&lt; 0.1%)</td>
<td>2 (&lt; 0.1%)</td>
</tr>
<tr>
<td>Guillain-Barre Syndrome</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Facial paralysis</td>
<td>1 (&lt; 0.1%)</td>
<td>2 (&lt; 0.1%)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>24 (0.2%)</td>
<td>12 (0.1%)</td>
</tr>
</tbody>
</table>
Post-Authorization Safety
**Global Exposure of Ad26.COV2.S as of Aug 31, 2021**

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

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

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

- **Thrombosis with thrombocytopenia**
  - Warnings and Precautions and Adverse Reactions during post-authorization use sections

- **Guillain-Barre Syndrome**
  - Warnings and Precautions and Adverse Reactions during post-authorization use sections

- **Capillary Leak Syndrome**
  - Adverse Reactions during post-authorization use section
Reported Post-Authorization Cases of Thrombosis with Thrombocytopenia Globally

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

<table>
<thead>
<tr>
<th>CDC Criteria for TTS</th>
<th>Tier 1</th>
<th>Tier 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Female</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>23</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Tier 1</th>
<th>Tier 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean: 45.6</td>
<td>68</td>
<td>5</td>
</tr>
<tr>
<td>Median: 45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range: 18 to 87</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

*Demographic table above includes 2 cases from open-label studies and 1 case from a placebo-controlled study*
Reported Post-Authorization Cases of Guillain-Barre Syndrome Globally

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

<table>
<thead>
<tr>
<th>Sex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>90</td>
</tr>
<tr>
<td>Male</td>
<td>158</td>
</tr>
<tr>
<td>Not reported</td>
<td>7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age (years)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>18 to 35</td>
<td>24</td>
</tr>
<tr>
<td>36 to 50</td>
<td>68</td>
</tr>
<tr>
<td>51 to 64</td>
<td>106</td>
</tr>
<tr>
<td>≥ 65</td>
<td>39</td>
</tr>
<tr>
<td>Adult/Not reported</td>
<td>18</td>
</tr>
</tbody>
</table>

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

*Demographic table above includes 2 cases from placebo-controlled studies and 1 report from open-label study COV3012
7 post-authorization reports, all spontaneous (0.2 per million doses)
- US: 2  EEA: 5:  Rest of World: 0

### Sex

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Count</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

### Age (years)

<table>
<thead>
<tr>
<th></th>
<th>18 to 35</th>
<th>36 to 50</th>
<th>51 to 64</th>
<th>≥ 65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Count</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

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

- Events added as important potential risks in Pharmacovigilance Plan
  - Venous thromboembolism
  - Immune thrombocytopenia
- Events being evaluated by Sponsor as part of pharmacovigilance activities
  - Myocarditis / pericarditis, cardiomyopathy, acute hepatic failure, acute disseminated encephalomyelitis, transverse myelitis, autoimmune disorders, vasculitis
- Totality of post-authorization safety and efficacy data to date continue to support a positive benefit-risk
Conclusions on Safety of Homologous Boost of Ad26.COV2.S

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

Johan Van Hoof, MD

Managing Director Janssen Vaccines and Prevention, BV
Janssen Pharmaceutical Companies of Johnson & Johnson
Humoral responses persisted after a single-dose of Janssen vaccine
• Distinct immunologic profile
• Base of protection includes nAbs, functional antibodies, cell-mediated immune response

Administration of booster dose results in greater protection against COVID-19
• At 2 months, 2.5 fold titer increase after booster translates into 20-25% higher efficacy
• Efficacy against symptomatic infection boosted to 94% in US

Booster dose safe and well tolerated
• Large amount of randomized safety data, >9,000 exposures

Homologous booster dose with Ad26.COV.2.S preferred over heterologous boost
Homologous Boost with Ad26.COV2.S Helps Further Protect Individuals from COVID-19

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

Proposed dosing

- A booster dose is recommended at 6 months or later, based on the strength of the immune responses, although a booster dose may be administered as early as 2 months

- The need for a booster dose and/or its timing will depend on the local/epidemiological situation and the needs of individuals/specific populations

Janssen Pharmaceutical Companies of Johnson & Johnson

Vaccines and Related Biological Products Advisory Committee
October 15, 2021