Vaccines and Related Biological Products Advisory Committee Meeting

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Novavax, Inc.

Gregory M. Glenn, MD
President, Research and Development

Vaccines and Related Biological Products Advisory Committee
June 28, 2022
Agenda

- Structural features of our **recombinant trimeric spike** protein vaccine leads to broadly cross neutralizing antibodies
  - Displays conserved epitopes across prototype and emerging variants
  - Adjuvant causes epitope spreading and enhanced recognition of conserved epitopes on spike protein
- Previously infected individuals and those vaccinated with NVX-CoV2373 demonstrate broad recognition of variants following booster doses
- Antigenic cartography shows boosting minimizes effect of variant escape
- Status of ongoing clinical boosting study and vaccine supply
Novavax Vaccine Platform
Recombinant Protein Plus Matrix-M™

Recombinant protein

Matrix-M adjuvant

NVX-CoV2373
# High Levels of Protection Achieved in Two Phase 3 Trials with NVX-CoV2373

<table>
<thead>
<tr>
<th>Study</th>
<th>Overall Efficacy (Mild, Moderate, Severe)</th>
<th>Severe Disease</th>
<th>Against Variants of Interest and Variants of Concern*</th>
<th>Symptomatic &amp; Asymptomatic Illness Through 6 Months (Any Infection)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 302 UK(^1)</td>
<td>90%</td>
<td>100%</td>
<td>86%</td>
<td>83%</td>
</tr>
<tr>
<td>Study 301 US/MX(^2)</td>
<td>90%</td>
<td>100%</td>
<td>93%</td>
<td>71%</td>
</tr>
</tbody>
</table>

*Variants of Interest and Variants of Concern in circulation at time studies were conducted

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Novavax NVX-CoV2373 and Omicron Variant Vaccines: Full Length Spike Protein Trimers

NVX-35.13 Conserved Epitope

Prototype NVX-CoV2373
Omicron BA.1
Omicron BA.2
Omicron BA.4
Omicron BA.5
Omicron BA.2.12.1

Nanoparticles
NVX-CoV Prototype and Omicron Vaccines Share Conserved Neutralizing Epitopes

Prototype NVX-CoV2373

Omicron BA.1

Omicron BA.2

Omicron BA.4

Omicron BA.2.12.1
Clinical Evidence of Enhanced Breadth of Antibody Responses

Previously infected individuals and those vaccinated with NVX-CoV2373 demonstrate broad recognition of variants following booster doses
Study 301 (US/MX): IgG, Associated with COP Reaches High Levels After Boosting, Variant Responses Comparable to Phase 3 Levels

Youyi Fong, Peter B. Gilbert et al., Immune Correlates Analysis of the PREVENT-19 COVID-19 Vaccine Efficacy Clinical Trial
Fred Hutchinson Cancer Center, Vaccine Infectious Disease Division, University of Washington, Department of Biostatistics
Study 301 (US/MX): ACE-2 Receptor Binding Inhibition Antibodies Reach High Levels After Prime and Boosting, Variant Responses Comparable to Phase 3 Levels

Receptor Inhibition Assay, Mechanistic, Functional and Correlates with Microneutralization

<table>
<thead>
<tr>
<th>Receptor Inhibition (Log_{10}) (95% CI)</th>
<th>Prototype</th>
<th>BA.1</th>
<th>BA.2</th>
<th>BA.5</th>
<th>Prototype</th>
<th>BA.1</th>
<th>BA.2</th>
<th>BA.5</th>
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</thead>
<tbody>
<tr>
<td>Day 0, 21</td>
<td>151</td>
<td>18</td>
<td>18</td>
<td>16</td>
<td>380</td>
<td>194</td>
<td>167</td>
<td>117</td>
</tr>
<tr>
<td>8-month Boost</td>
<td>18</td>
<td>18</td>
<td>16</td>
<td>117</td>
<td>167</td>
<td>117</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Approximates Phase 3
Study 301 (US/MX): ACE-2 Receptor Binding Inhibition Antibodies in Individuals Who Were Previously Infected, Given a Priming (D0, 21) Series

Seropositive Adults, Before and After Priming Series with NVX-CoV2373

<table>
<thead>
<tr>
<th>History of SARs-CoV 2 Infection</th>
<th>After NVX-CoV2373 (Prototype) Vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receptor Inhibition (Log_{10}) (95% CI)</td>
<td>Approximates Phase 3</td>
</tr>
<tr>
<td>Prototype</td>
<td>BA.1</td>
</tr>
<tr>
<td>Day 0</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>11</td>
</tr>
</tbody>
</table>
Phase 2: Boosting Reduces Antigenic Distance, for Broader Recognition of New Variants, “Universal-like” Response

Fold Difference:
- Wuhan → BA.5 = 9.9
- Wuhan → BA.5 = 4.2
- Wuhan → BA.5 = 2.1
Rhesus Macaque: Boosting with Either Prototype or Omicron Drives Antibody Responses to More “Universal-like” Profile

Receptor Inhibition Antibodies 6 months after Primary Series
Study Evaluating Prototype, Omicron Monovalent, and Bivalent Boosting

- Adults 18 to 64 previously vaccinated with mRNA
- Three arms:
  - NVX-CoV2373
  - Monovalent Omicron BA.1
  - Bivalent prototype + Omicron BA.1
- Comparison of antibody responses between arms
- Study start May 2022
Summary

- High levels of efficacy in two Phase 3 trials demonstrated against variants
- Novavax technology induces cross-reactive immunity
  - Driven by recognition of conserved epitopes on Novavax recombinant spike protein
  - Adjuvant enhances breadth and duration of immune response
- Broadly cross-reactive immunity increases with boosting
  - Individuals may prefer prototype specific vaccine based on known efficacy, extensive safety data
- Boosting with Omicron in NHPs appears to better cover forward drift
  - No advantage with Bivalent
- Boosting study ongoing and Omicron-specific vaccine available Q4