NAIIIS – Developing COVID-19 Vaccines in Record Time

Nasdaq: NVAX | January 29, 2021
NVX-CoV2373 Vaccine Design
Vaccine Platform Technology: Nanoparticle vaccine formulated with Matrix-M1

Antigen expressed in baculovirus-\textit{S. frugiperda} system
- Codon-optimized
- Full-length protein, including transmembrane domain
- Furin cleavage site mutated and stabilized

Drug Substance
- Native conformation trimers
- Stable PS80 nanoparticle

Drug Product
- Co-formulated with adjuvant
- Dispensed in vial
- Stored 2-8\degree C

Matrix-M adjuvant
- Purified from \textit{Quillaja saponaria molina}

Matrix-M Adjuvant

\textit{NVX-CoV2373}

\begin{tabular}{|c|c|c|}
\hline
 & S1 & S2 \\
\hline
SS & NTD & RBD \\
\hline
1 & WT: NSPRRARSVAS & 3Q: NSPQAG5VAS \\
\hline
S1/S2 cleavage site & 682-QQAQ-685 & \textit{2P mutation} K586/FVBB7P \\
\hline
FP & WT: SRLDKEAEV & \textit{2P mutation} S682-QQAQ-685 mutation \\
\hline
S2' cleavage site & WT: SRLDKEAEV & \textit{2P mutation} K586/FVBB7P \\
\hline
CT & WT: NSPRRARSVAS & 3Q: NSPQAG5VAS \\
\hline
1273 & TM & HR1 \\
\hline
\end{tabular}
UK Phase 3 Study Design

Randomized, observer-blinded, placebo-controlled trial evaluating efficacy, immunogenicity and safety

15,000 Adults
>18 years
25% > age 65

R 1:1

5 µg + 50 µg Matrix-M™
(2 injections: Day 0 and Day 21)
n = ~7,500

Placebo
(2 injections: Day 0 and Day 21)
n = ~7,500

• Primary endpoint: PCR-positive symptomatic mild, moderate or severe COVID-19 illness diagnosed ≥ 7 days after second dose
• LBCI >30 success criteria
UK 501Y.V1 Mutant Strain Increased in Prevalence During Efficacy Collection Window

Efficacy Endpoint Accrual: November 11 – January 1

Figure Source: Nextstrain.org
Primary Endpoint Met

<table>
<thead>
<tr>
<th>Severity</th>
<th>NVX-CoV2373 (n=7,016)</th>
<th>Placebo (n=7,033)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>6</td>
<td>56</td>
</tr>
<tr>
<td>Mild</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>Moderate</td>
<td>5</td>
<td>40</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Vaccine Efficacy: 89.3% (95% CI: 75.2, 95.4)

- Preliminary PCR data show >50% of cases attributable to UK 501Y.V1 variant
- Final analysis to be conducted once at least 100 cases accrued

Primary Endpoint: PCR-confirmed mild, moderate, or severe COVID-19 illness occurring ≥7 days after second dose in baseline seronegative participants
### PCR-Confirmed Mild, Moderate or Severe COVID-19 by Strain (Original vs 501Y.V1 Variant)

<table>
<thead>
<tr>
<th></th>
<th>NVX-CoV2373 (n=7016)</th>
<th>Placebo (n=7033)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>501Y.V1</td>
<td>Original</td>
</tr>
<tr>
<td>PCR-Confirmed COVID-19 (Mild, Moderate, Severe)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Moderate</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Preliminary, post-hoc analysis based on PCR performed on strains from 56 of the 62 cases showed **96/94%** PP/Moderate-Severe efficacy in the original COVID-19 strain, **86/87%** efficacy in the 501Y.V1 variant strain.
South Africa Phase 2b Study Design

Randomized, observer-blinded, placebo-controlled trial evaluating efficacy, immunogenicity and safety

- Enrollment population includes cohort of 245 randomized participants who are HIV-positive
- Efficacy analysis at 23 - 50 events, LBCI success at 0.
- Primary endpoint: PCR-positive symptomatic mild, moderate or severe COVID-19 illness diagnosed ≥ 7 days after second dose
South Africa 501Y.V2 Escape Mutant Dominant During Efficacy Collection Window

Efficacy Endpoint Accrual: November 23 – December 30

Figure Source: Nextstrain.org
Attack Rate In Placebo Groups By Serostatus

No Evidence Of Resistance From Infection With Previous COVID Exposure

• Placebo Per-protocol population time frame (7 days post-dose 2)
  ▪ Seronegative: 29/1327  2.185% (1.468; 3.124)
  ▪ Seropositive: 13/514  2.529% (1.353; 4.286)

• Placebo ITT population (7 days post-dose 1)
  ▪ Seronegative: 58/1494  3.882% (2.961; 4.990)
  ▪ Seropositive: 26/674  3.858% (2.535; 5.601)
Cross-Protection Demonstrated Against South Africa Escape Variant

<table>
<thead>
<tr>
<th>Severity</th>
<th>NVX-CoV2373 (n=2,206)</th>
<th>Placebo (n=2,200)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>15</td>
<td>29</td>
</tr>
<tr>
<td>Vaccine Efficacy (HIV negative)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>60.1 % (95% CI: 19.9, 80.1)</td>
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</tr>
<tr>
<td>Vaccine Efficacy (overall)</td>
<td></td>
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<tr>
<td></td>
<td>49.4% (95% CI: 6.1, 72.8)</td>
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</tbody>
</table>

- Preliminary PCR data show 25/27 (93%) of cases attributable to SA 501Y.V2 escape variant

**Primary Endpoint:** PCR-confirmed mild, moderate, or severe COVID-19 illness occurring ≥7 days after second dose in baseline seronegative participants.
Two Independent Trials Demonstrate Statistically Significant Efficacy of NVX-CoV-2373

- Overall UK Phase 3 Vaccine Efficacy = 89.3%
  - Original/Strain matched VE = 96%
  - UK Variant 501Y.V1 VE = 86%
- ZA Phase 2b Vaccine Efficacy = 60%
  - Prior COVID-19 infection does not appear to protect against infection with 501Y.V2 variant
  - Conversely, NVX-CoV2373 achieved protection
- Developing 501Y.V2 variant, multiple candidates
  - 501Y.V2 rS vaccine candidate has been produced at lab-scale for testing
THANK YOU