Creating Tomorrow’s Vaccines Today

Efficacy Data Updates from Novavax’ Protein-based Vaccine Candidate

New York Academy of Sciences

Nasdaq: NVAX | February 2, 2021
Certain information, particularly information relating to future performance and other business matters, including expectations regarding clinical development, market opportunities and anticipated milestones constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act.

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Additional information on Risk Factors are contained in Novavax’ filings with the U.S. Securities and Exchange Commission, including our Annual Report on Form 10-K for the year ended December 31, 2019, our Quarterly Reports on Form 10-Q, and our Current Reports on Form 8-K, which are all available at http://www.sec.gov.

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Matrix-M and NanoFlu are trademarks of Novavax, Inc.
Agenda

• Review of NVX-CoV2373 program
• Clinical development updates
  ▪ Preclinical
  ▪ Phase 1-2 studies
  ▪ Phase 2b & 3 efficacy studies
• Next steps: Bivalent approach
• Manufacturing
NVX-CoV2373 Progress Built Upon Years of Vaccine Research
NVX-CoV2373 Vaccine Design

Vaccine Platform Technology: Nanoparticle vaccine formulated with Matrix-M™

**Antigen**
- Expressed in baculovirus (*S. frugiperda*) system
- 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 10-dose vial
- Stored 2-8°C, ready-to-use

**Matrix-M adjuvant**
- Purified from *Quillaja saponaria molina*

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Bangaru et al. bioRxiv 06 August 2020 and Tian et al. bioRxiv 30 June 2020
Saponin Adjuvant/Nanoparticle, Influenza Antigen Drift
More RBD & HA1/HA2 Epitopes Recognized

More – and thicker – bars represent increased distribution and frequencies of antibodies to unique epitopes on the antigen.

Saponin adjuvant results in epitope spreading. In three serial trials, vaccine induced H3N2 HAI showed good responses to drifted strains.

SARS-CoV-2 will clearly undergo antigenic drift

Chung, K.Y., et al., 2015. DOI: 10.1016/j.vaccine.2015.06.047
Portnoff, A.D., et al., 2020. DOI: 10.3390/vaccines8010099
Shinde, V., et al., 2020. DOI: 10.1093/cid/ciaa1673
NVX-CoV2373 Protected Lower & Upper Airways in Rhesus Macaques

No viral replication observed following Day 38 challenge with WT SARS-CoV-2

Lower Airway

Upper Airway

Placebo

NVX-CoV2373

Placebo

NVX-CoV2373

5 µg vaccine + 50 mg Matrix-M

25 µg vaccine + 50 mg Matrix-M
NVX-CoV2373 Clinical Development Plan

1. **Dose confirmation based on Phase 1 data:** Aug 2020
   - **Phase 1 AU** N=131; 18-59 years

2. **Dose confirmation in adults >60 y based on Phase 2:** Oct 2020
   - **Phase 2 AU/US** N=1,288; 18-84 years (n=583 >60 years)
   - **Phase 2b South Africa** N=4,422; 18-84 years (n=240 HIV+)

**Safety and Immunogenicity**
- Includes Efficacy Assessment

**Ongoing study**

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**Study 1**
- Part 1 (2019nCoV-101)

**Study 2**
- (2019nCoV-501)

**Study 3**
- (2019nCoV-302)

**Study 4**
- Sponsor = SIIPL

**Study 5**
- (2019nCoV-502)

**Study 6**
- Sponsor = Takeda

**Study 7**
- (2019nCoV-301)
NVX-CoV2373 Phase 1-2 Study (US & Australia)
US and Australia Phase 1 Study Design

131 Adults 18-59 years

- 5 µg + 50 µg Matrix-M™
  (2 injections: Day 0 and Day 21)

- 25 µg + 50 µg Matrix-M
  (2 injections: Day 0 and Day 21)

- 25 µg
  (2 injections: Day 0 and Day 21)

- 25 µg + 50 µg Matrix-M
  (Day 0) Placebo (Day 21)

- Placebo
  (2 injections: Day 0 and Day 21)
Phase 1: Spike IgG and Neutralization Response at Day 35

Keech, C. et al. DOI: 10.1056/NEJMo2026920
Phase 1: Spike IgG Response Through Six Months

Matrix-M™ required for optimal immune response; 2 adjuvanted doses superior to 1 dose
Matrix-M is dose-sparing

Phase 1: n = 131; 18-59 years of age; Vaccination on Day 0 and D21 (pre-publication)
Adjuvanted Vaccine Induces IgG Response that Correlates Tightly with Neutralization Response
Significant and consistent proportion of antibody is functional

Convalescent Serum (Baylor)  2 Dose: 25µg (no adjuvant)  2 Dose 5µg + Matrix-M™ combined with 2 Dose 25µg + Matrix-M™

Keech, C. et al. DOI: 10.1056/NEJMoa2026920
US and Australia Phase 2 Study Design
Includes ~50% of adults age 60-84 years

- 1,288 Adults >18 years
  - 5 µg + 50 µg Matrix-M™ (2 injections: Day 0 and Day 21)
  - 25 µg + 50 µg Matrix-M (2 injections: Day 0 and Day 21)
  - 5 µg + 50 µg Matrix-M (Day 0) Placebo (Day 21)
  - 25 µg + 50 µg Matrix-M (Day 0) Placebo (Day 21)
  - Placebo (2 injections: Day 0 and Day 21)
Phase 2: Reproduced Phase 1 Lessons

2 Matrix-M™-adjuvanted doses of 5 µg and 25 µg induced comparable, robust immune responses Consistent with Phase 1 data

Phase 2:  
- 2 Doses: 25 µg + Matrix-M
- 2 Doses: 5 µg + Matrix-M
- 1 Dose: 25 µg + Matrix-M
- 1 Dose: 5 µg + Matrix-M
- Placebo

Phase 2: n =1288; ≥ 18 years of age (n = 583 >60 years of age) *(pre-publication)*
Phase 2 Local Reactogenicity: Well-tolerated

Many participants experienced no reactions, and when they did occur, all were mild-to-moderate in severity with a mean duration ~2 Days.

- Pain and Tenderness reported most frequently
- Rates after Dose 2 were higher in adjuvanted groups
- Reactogenicity attenuated in adults >60 years of age

Worst grade reported for 7 days after each dose. Raw blinded data Oct 5 cut-off (pre-publication data)
Phase 2 Systemic Reactogenicity: Well-tolerated

Many participants experienced no reactions, and when they did occur, all were mild-to-moderate in severity with a mean duration ~2 Days

- Fatigue, Headache and Myalgia reported most frequently
- Increased rates seen in adjuvanted groups especially after Dose 2
- Reactogenicity attenuated in adults >60 years of age

Worst grade reported for 7 days after each dose. Raw blinded data Oct 5 cut-off (pre-publication data)
5µg Dose is Well-tolerated, with Strong and Consistent Responses
Phase 1-2 Summary

- **Consistent** results from Phase 1 and Phase 2
- **Immunogenicity**
  - High levels of antibody maintained through six months (Phase 1)
  - Antibody responses compare favorably to convalescent response
- **Safety**
  - No SAEs, no AESIs, AEs balanced and mostly mild/moderate
  - Vaccine **well-tolerated** with symptoms of ~2-day duration
- **Confirmed 5µg dose** for late-stage development
NVX-CoV2373
UK
Phase 3 Study
UK Phase 3 Study Design

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

- **Primary endpoint**: PCR-positive symptomatic mild, moderate or severe COVID-19 illness diagnosed ≥ 7 days after second dose
- LBCI >30 success criteria; with success Interim analysis, became final analysis

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
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 in Interim Analysis

<table>
<thead>
<tr>
<th>Severity</th>
<th>NVX-CoV2373 (n=7,016)</th>
<th>Placebo (n=7,033)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total (n=62)</strong></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>
<tr>
<td><strong>Vaccine Efficacy</strong></td>
<td><strong>89.3%</strong> (95% CI: 75.2, 95.4)</td>
<td></td>
</tr>
</tbody>
</table>

- Preliminary PCR data show >50% of cases attributable to **UK 501Y.V1** escape 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 (Ancestral 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>Ancestral</td>
</tr>
<tr>
<td>PCR-Confirmed COVID-19 (Mild, Moderate, Severe)</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Mild</td>
<td>1</td>
<td>0</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>

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

Post-hoc analysis based on PCR from 56 of 62 cases: 96/94% Primary/Moderate-Severe efficacy in the **ancestral COVID-19 strain**; 86/87% efficacy in the **501Y.V1 variant strain**.
## Favorable Preliminary Safety Profile

<table>
<thead>
<tr>
<th>Event</th>
<th>NVX-CoV2373 (n=7,016)</th>
<th>Placebo (n=7,033)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Severe TEAE</td>
<td>81 (1.1 %)</td>
<td>53 (0.7%)</td>
</tr>
<tr>
<td>Treatment Emergent Adverse Event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any Serious TEAE</td>
<td>31 (0.4%)</td>
<td>30 (0.4%)</td>
</tr>
<tr>
<td>Treatment Emergent Adverse Event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any MAAE</td>
<td>202 (2.7%)</td>
<td>201 (2.8%)</td>
</tr>
<tr>
<td>Medically Attended Adverse Event</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Due to topline data, limited safety available
NVX-CoV2373
South Africa
Phase 2b Study
South Africa Phase 2b Study Design

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

4,400 Adults
18-65 years
(n=245 HIV+)

5 µg + 50 µg Matrix-M™
(2 injections: Day 0 and Day 21)
\( n = \sim 2,200 \)

Placebo
(2 injections: Day 0 and Day 21)
\( n = \sim 2,200 \)

Partner: BMGF
Sponsor: Novavax

• Enrollment population includes cohort of 245 randomized participants who are HIV-positive
• Efficacy analysis at 23 - 50 events, LBCI success ≥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
Previous Infection Did Not Protect Against COVID Due To Variant

- Volunteer sera tested for SARS-CoV-2 spike IgG at Day 0
- ~30% had evidence of previous infection
  - Likely non-501Y.V2 due to enrollment timing
- No difference in rates of infection/reinfection

- Placebo ITT population (7 days post-dose 1), symptomatic COVID
  - Seronegative: 3.9% (58/1494; 2.961; 4.990): 2.3% Mod/Severe (35/1494)
  - Seropositive: 3.9% (26/674; 2.535; 5.601); 2.4% Mod /Severe (16/674)
# Cross-Protection Demonstrated Against South Africa Escape Variant

<table>
<thead>
<tr>
<th>Primary Endpoint</th>
<th>NVX-CoV2373 (n=1,357)</th>
<th>Placebo (n=1,327)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cases</strong></td>
<td>15</td>
<td>29</td>
</tr>
<tr>
<td><strong>Vaccine Efficacy</strong></td>
<td>49.4% (95% CI: 6.1*, 72.8)</td>
<td></td>
</tr>
<tr>
<td><strong>HIV–</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cases</strong></td>
<td>11</td>
<td>27</td>
</tr>
<tr>
<td><strong>Vaccine Efficacy</strong></td>
<td>60.1% (95% CI: 19.9, 80.1)</td>
<td></td>
</tr>
</tbody>
</table>

- Preliminary sequencing data (n=27) show 25/27 (93%) attributable to **SA 501Y.V2** escape variant
- 1 severe case in placebo
- Success criteria: LBCI ≥0

**Primary Endpoint:** PCR-confirmed mild, moderate, or severe COVID-19 illness occurring ≥7 days after second dose in baseline seronegative participants
# Comparison of PP Efficacy: Seropositive vs Seronegative

<table>
<thead>
<tr>
<th>Serostatus</th>
<th>NVX-CoV2373 % (n/N)</th>
<th>Placebo % (n/N)</th>
<th>Efficacy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>1.1% (15/1357)</td>
<td>2.2% (29/1327)</td>
<td>49.4% (6.1, 72.8)</td>
</tr>
<tr>
<td>+</td>
<td>1.2% (6/500)</td>
<td>2.5% (13/514)</td>
<td>52.6% (-23.8, 81.8)</td>
</tr>
<tr>
<td>+/-</td>
<td>1.1% (21/1857)</td>
<td>2.3% (42/1841)</td>
<td>50.4% (16.6, 70.5)</td>
</tr>
</tbody>
</table>

Primary – mild/moderate/severe (HIV- & HIV+)
NVX-CoV2373 PREVENT-19 US & Mexico Phase 3 Study
PREVENT-19 Phase 3 Trial Currently Enrolling

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

Enrollment goals:
25% > age 65 years
15% Black/African American
10-20% LatinX
1-2% American Indian

30,000 Adults 
≥18 years

R 2:1

5 µg + 50 µg Matrix-M™
(2 injections: Day 0 and Day 21)
n = ~20,000

Placebo
(2 injections: Day 0 and Day 21)
n = ~10,000

- Primary endpoint: PCR-positive symptomatic mild, moderate or severe COVID-19 illness diagnosed ≥ 7 days after second dose
- Interim analysis at 72 events, final analysis at 144 events*

*Protocol version 3.0 to be updated on website
### PREVENT-19 Phase 3 Enrollment Update

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Current Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Randomized as of February 1, 2021</td>
<td>19,438</td>
</tr>
<tr>
<td>≥ 65 Years</td>
<td>16%</td>
</tr>
<tr>
<td>Black/African American</td>
<td>13%</td>
</tr>
<tr>
<td>LatinX</td>
<td>16%</td>
</tr>
</tbody>
</table>

- Enrollment expected to complete first half of February
- Unblinding rate: **1.5%** overall, 55% of which are ≥ 65 years
- **January 25**: Protocol amended to incorporate **blinded crossover**
Higher attack rates mean:

- Increased vaccine demand & trial participation
- Faster endpoint accrual

A quicker path to determining vaccine efficacy

Source: New York Times

As of January 13, 2020
Variant Strains On The Rise in the US

First Person Dosed: December 27
Last Person Dosed: Late February

https://www.washingtonpost.com/nation/2021/01/30/covid-coronavirus-updates/

Figure Source: nextstrain.org
Booster / Bivalent Vaccine Development
Variant Strains Already Under Development Against Emerging COVID-19 Mutations

• To address an evolving pandemic, the optimal vaccine for all regions may need to contain multiple strains

• Lab-scale manufacturing underway for multiple strains

• Will be able to rapidly scale up production of additional recombinant protein vaccine candidates as new molecular entity (rS) is biochemically very similar to NVX-CoV2373
UK and SA Variants: Production in Sf9 Cells

<table>
<thead>
<tr>
<th>Lane</th>
<th>Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mwt</td>
</tr>
<tr>
<td>2</td>
<td>UK Variant BV2425.1.1, 2.1 a</td>
</tr>
<tr>
<td>3</td>
<td>UK Variant BV2425.1.1, 2.1 b</td>
</tr>
<tr>
<td>4</td>
<td>Mwt</td>
</tr>
<tr>
<td>5</td>
<td>SA Variant BV2426.1.1, 2.1 a</td>
</tr>
<tr>
<td>6</td>
<td>SA Variant BV2426.1.1, 2.1 b</td>
</tr>
</tbody>
</table>

Western blot anti-rS polyclonal antibody
NVX-CoV2373
Manufacturing & Distribution
Global Supply Chain Established
Annual capacity of over 2 billion* doses starting in 2021

* When all planned capacity is online by mid-2021
Two Independent Trials Demonstrate Statistically Significant Efficacy of NVX-CoV2373

- Overall UK Phase 3 Vaccine Efficacy = 89.3%
  - Ancestral/Strain matched VE = 95.6%
  - UK Variant 501Y.V1 VE = 85.6%

- ZA Phase 2b Vaccine Efficacy = 60.1%
  - Prior infection does not protect against COVID due to 501Y.V2 variant
  - Conversely, NVX-CoV2373 achieved protection against 501Y.V2

- Data indicate Matrix-M™-adjuvanted nanoparticle highly efficacious

- Technology can rapidly adapt to make 501Y.V2 variant -rS
  - Candidate has been produced at lab-scale
Acknowledgements

• UK-Paul Heath, St Georges, London
  ▪ Seth Toback, Novavax

• Shabir Mahdi-University of Witswatersrand, Johannesburg
  ▪ Vivek Shinde, Novavax

• Filip Dubovsky, CMO, Novavax

The Great team at Novavax, UK and South Africa

Sincere thanks to the many volunteers
THANK YOU