Recombinant Nanoparticle COVID-19 Vaccine Platform Technology for EID

World Vaccine Congress Europe | October 20, 2020
Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine

Novavax Initiates Phase 3 Efficacy Trial of COVID-19 Vaccine in the United Kingdom

September 24, 2020

Clinical trial to enroll up to 10,000 volunteers across the UK to assess whether NVX-CoV2373 is effective in the prevention of COVID-19
Novavax COVID-19 vaccine

• NVX-CoV2373 vaccine: Prefusion spike protein in a nanoparticle with Matrix-M adjuvant
  • NHP challenge data
• Safety and immunogenicity update
• Clinical trial update
  • NVX-CoV2373 is in clinical efficacy evaluations
• Progress towards manufacturing
Novavax vaccine pipeline

<table>
<thead>
<tr>
<th>PROGRAM DESCRIPTION</th>
<th>PRECLINICAL</th>
<th>CLINICAL</th>
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<tbody>
<tr>
<td>NVX-CoV2373 – Coronavirus Vaccine Candidate</td>
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<td>PHASE 3</td>
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<tr>
<td>NanoFlu™ – Nanoparticle Seasonal Influenza Vaccine</td>
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<td>ResVax™ - RSV F Vaccine - Infants via Maternal Immunization</td>
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<td>RSV F Vaccine - Older Adults (60+ yrs)</td>
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<td>PHASE 2</td>
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<td>RSV F Vaccine - Pediatrics (6 mos – 5 yrs)</td>
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<tr>
<td>Combination Influenza/RSV F Vaccine - Older Adults (60+)</td>
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<td>PHASE 1</td>
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<td>Ebola GP Vaccine</td>
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- **Completed Phase 3** – March 2020 Successfully achieved all primary endpoints and achieved statistical significance in key secondary endpoints
- **Phase 3** – Initiated in the UK September 2020; U.S. Phase 2 ongoing; Initiating U.S. Phase 3 in Q4 2020
NVX-CoV2373 vaccine design

Antigen expressed in baculovirus-S. frugiperda system
• Codon-optimized
• Full-length protein, including transmembrane domain

Drug substance
• Native conformation trimers
• Stable PS80 nanoparticle

Drug product
• Co-formulated with adjuvant
• Dispensed in vial
• Stored 2-8°C

Matrix-M adjuvant
• Purified from Quillaja saponaria molina
NVX-CoV2373 in cynomolgus macaques
Induces neutralizing immune antibody in excess to convalescent human sera
Protects upper and lower airway from experimental wild-type challenge

100% wild-type neutralization
Lower airway protection
Upper airway protection

Doses administered on Day 0, 21 and challenged with 10log4 IT/IN on Day 37

bioRxiv. https://doi.org/10.1101/2020.08.18.256578
Rhesus macaques: upper and lower airway protection
Vaccinated Day 0 and Day 21; Challenged with SARS-CoV-2 wild-type $1.05 \times 10^6$ PFU IN/IT on Day 38
No viral replication detected in upper or lower airway following experimental wild-type challenge

Study conducted at Texas Biomedical Research Institute
Study 1 Part 1

- First-in-human safety and immunogenicity
- N=131; Adults 18-59 y/o in Australia

<table>
<thead>
<tr>
<th></th>
<th>N=131</th>
<th>Day 0</th>
<th>Day 21</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Antigen</td>
<td>Matrix-M</td>
</tr>
<tr>
<td>A</td>
<td>25</td>
<td>Placebo</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>25</td>
<td>25 µg</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>25 (+3)</td>
<td>5 µg + 50 µg</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>25 (+3)</td>
<td>25 µg + 50 µg</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>25</td>
<td>25 µg + 50 µg</td>
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Development Goal:

- FTiH safety
- Dose-selection and demonstration of adjuvant utility
High level safety summary

- No serious adverse events
- Adverse events of Special Interest
  - No PIMMC AESI
  - No confirmed COVID-19 AESIs
- Treatment emergent adverse events
  - All mild and moderate and balanced in active arms
- Solicited reactogenicity symptoms
  - Overall, reactogenicity was mild, and vaccinations were well-tolerated
    - Vast majority were Grade 0 or mild
    - Solicited symptoms increased with second dose in adjuvanted group
    - Mean duration <2 days
    - Resulted in no vaccination refusals or withdrawals
### Unsolicited treatment emergent adverse events

**No severe events reported**

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<tbody>
<tr>
<td></td>
<td>Dose 1</td>
<td>Dose 2</td>
<td>Dose 1</td>
<td>Dose 2</td>
<td>Dose 1</td>
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<tr>
<td>Mild</td>
<td>1</td>
<td>4</td>
<td>8</td>
<td>5</td>
<td>7</td>
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<tr>
<td></td>
<td>4%</td>
<td>17%</td>
<td>32%</td>
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<td>27%</td>
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<tr>
<td>Moderate</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
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<tr>
<td></td>
<td>9%</td>
<td>4%</td>
<td>4%</td>
<td>4%</td>
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<tr>
<td>Severe</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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1: Musculoskeletal Injury, Somnambulism (related)
2: Headache (related)
3: Headache
4: Hemoglobin decrease (related)
5: Biliary colic
6: Bronchitis
7: Scleritis/eye injury
Local reactogenicity symptoms collected 7 days after each dose

Majority of symptoms grade 0 or grade 1

- Local symptoms increased after dose 2
- Increased rate and severity in Matrix-M1 groups
- Pain and tenderness were reported most common
- Mean duration < 2 days
Systemic reactogenicity symptoms collected 7 days after each dose

Majority of symptoms grade 0 or grade 1

- Systemic symptoms increased after dose 2
- Increased rate and severity in Matrix-M1 groups
- Headache, fatigue and myalgia were most commonly reported
- Mean duration < 2 days
Anti-S IgG ELISA through Day 35
Reverse cumulative distribution of anti-S IgG ELISA Day 35
Matrix-M1 is dose-sparing: 5ug + Matrix-M1 and 25ug + Matrix-M1 is comparably immunogenic
100% IgG seroconversion response in 2 dose schedule with Matrix-M1

Keech et al. NEJM 02 September 2020
Anti-Spike IgG ELISA Kinetics

Vaccination on Day 0 and D21; Peak immune response on Day 35 in 2 dose schedule
Matrix-M1 required for optimal immune response; 2 doses schedule superior to 1 dose schedule

2 Doses: 5ug + Matrix-M1
2 Doses: 25ug + Matrix-M1
1 Dose: 25ug + Matrix-M1
2 Doses: 25ug (no adjuvant)
Placebo

Pre-publication data
Wild-type virus neutralization through Day 35

[Diagram showing neutralization values over time for rSARS-CoV-2 and rSARS-CoV-2 + Matrix M1, with data points for different groups such as Placebo, 25 µg, 5 µg, and Convalescent Sera.]

Human Convalescent Sera:
- Asymptomatic
- Outpatient Symptomatic
- Hospitalized

Note: The diagram includes specific neutralization values for each group and day point, indicating the effectiveness of the virus neutralization process over time.
Reverse cumulative distribution of 100% wild-type virus neutralization

5ug + Matrix-M1 and 25ug + Matrix-M1 induce high levels of functional antibody
100% neutralization seroconversion response in 2 dose schedule with Matrix-M1

* Dr Matthew Frieman Lab UMSOM

Partner: CEPI
Sponsor: Novavax

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Novavax.com

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100% wild-type neutralizing titer kinetics

- Placebo
- 25ug x 2 doses (no Matrix-M)
- 25ug + 50ug Matrix-M x 1 dose
- 25ug + 50ug Matrix-M x 2 dose
- 5ug + 50ug Matrix-M x 2 dose

IC50% Wild Type Virus Neutralization (Log 10)
Scatter plot of IgG vs wild-type neutralization
Adjuvanted vaccine induces IgG response that correlates tightly with neutralization response
Significant and consistent proportion of antibody is functional
Persistence of immunity with a nanoparticle vaccine in humans: Anti-Ebola GP IgG

Anti-GP IgG

Randomized, Blinded, Dose-Ranging Trial of an Ebola Virus Glycoprotein Nanoparticle Vaccine With Matrix-M Adjuvant in Healthy Adults

The Journal of Infectious Diseases

21 dose, MM
1 dose, MM
2 dose
Persistence of immunity with a nanoparticle vaccine in baboons: Anti-Ebola GP

Anti-GP IgG

Fries, et al. Ebolavirus glycoprotein subunit vaccine with saponin Matrix-M™ adjuvant is highly protective against virulent human ebolavirus Zaire in Macaca fascicularis: An alternative to virus vector-based vaccines; in preparation.

Boost
Intracellular cytokine staining Ag-specific CD4 T cells analysis

Matrix-M induced Th1-biased immune response as predicted by non-clinical data

Placebo

2 Doses: 5ug + Matrix-M

2 Doses: 25ug + Matrix-M

Pre-publication data
Intracellular cytokine staining Ag-specific CD4 T cells analysis (CD45+, CCR7-)
Double and triple Th1 cytokine response compared to double Th2 cytokine response

2 Doses: 5ug + Matrix-M

2 Doses: 25ug + Matrix-M

Pre-publication data
NVX-CoV2373 clinical development plan

1. **Dose confirmation based on Phase 1 data Aug 2020**
   - **Triggers:**
     - Phase 2 US/Australia (dose confirmation in >60 y)
     - Phase 2b South Africa efficacy study 18-65 y
     - Phase 2/3 UK efficacy study 18-84 y

2. **Dose confirmation in adults >60 y based on Phase 2: Oct 2020**
Novavax COVID-19 vaccine

• NVX-CoV2373 vaccine: Prefusion spike protein in a nanoparticle with Matrix-M adjuvant
  • The vaccine is stable and will utilize the standard cold chain
  • Appears safe in vaccines, with majority reporting no or mild reactions after immunization
  • Induces robust spike IgG, wild-type neutralizing antibodies at levels that exceed convalescent sera
  • Induces polyfunctional T cells

• NVX-CoV2373 is in clinical efficacy evaluations

• The vaccine is based on mature technologies
• The nanoparticle spike protein vaccine is highly immunogenic, which bodes well for efficacy
• Observed dose sparing (5ug) greatly expands the vaccine supply
• Global supply chain may produce up to 2 billion annualized doses when at full capacity in 2021
• NVX-CoV2373 has entered pivotal trial/efficacy evaluations
  • The UK trial is expected to support licensure
  • The US OWS-supported trial is expected to start soon
Questions?