Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine


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# Novavax vaccine pipeline

<table>
<thead>
<tr>
<th>PROGRAM DESCRIPTION</th>
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<td><strong>PHASE 2</strong></td>
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<td><strong>PHASE 3</strong></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>Combination Influenza/RSV F Vaccine - Older Adults (60+)</td>
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<td>Ebola GP Vaccine</td>
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**Matrix-M**

- NVX-CoV2373 – Coronavirus Vaccine Candidate
- NanoFlu™ – Nanoparticle Seasonal Influenza Vaccine - Older Adults (65+ yrs)
- ResVax™ - RSV F Vaccine - Infants via Maternal Immunization
- RSV F Vaccine - Older Adults (60+ yrs)
- RSV F Vaccine - Pediatrics (6 mos – 5 yrs)
- Combination Influenza/RSV F Vaccine - Older Adults (60+)
- Ebola GP Vaccine

**Completed Phase 3 – March 2020 Successfully achieved all primary endpoints and achieved statistical significance in key secondary endpoints**
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*
Study 1 Part 1

- First-in-human safety and immunogenicity
- N=131; Adults 18-59 yo in Australia

<table>
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<tr>
<th></th>
<th>N=131</th>
<th>Day 0</th>
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<tr>
<td></td>
<td>Antigen</td>
<td>Matrix-M</td>
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</tr>
<tr>
<td>A</td>
<td>25</td>
<td>Placebo</td>
<td>Placebo</td>
</tr>
<tr>
<td>B</td>
<td>25</td>
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<tr>
<td>C</td>
<td>25 (+3)</td>
<td>5 µg + 50 µg</td>
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<tr>
<td>D</td>
<td>25 (+3)</td>
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<tr>
<td>E</td>
<td>25</td>
<td>25 µg + 50 µg</td>
<td>Placebo</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 mild-moderate
    • Solicited symptoms increased with second dose in adjuvanted group
    • Mean duration <2 days
    • Resulted in no vaccination refusals or withdrawals
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 adjuvanted groups
- Pain and Tenderness were reported most common
- Mean duration < 2 days

<table>
<thead>
<tr>
<th>Localized Symptoms</th>
<th>Vaccine Group</th>
<th>Dose 1 NVX/M1 (µg)</th>
<th>Dose 2 NVX/M1 (µg)</th>
<th>Vaccination 1</th>
<th>Vaccination 2</th>
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<td>5 µg + Matrix-M1</td>
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<td>5 µg + Matrix-M1</td>
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<td>Plc</td>
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<td>Swelling</td>
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<td>Plc</td>
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Majority of Symptoms Grade 0 or Grade 1

- Systemic Symptoms increased after Dose 2
- Increased rate and severity in adjuvanted groups
- Headache, Fatigue and Myalgia were most commonly reported
- Mean duration < 2 days
Anti-S IgG ELISA through Day 35

Human Convalescent Sera
- Asymptomatic
- Outpatient Symptomatic
- Hospitalized
Wild Type Virus Neutralization through Day 35
Adjuvant and Two Dose Effects: MN at Day 35

Neutralizing Antibodies: Reverse Cumulative Distribution indicates >90% of subjects have MN>1,000
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
rSARS-CoV-2 CD4+ T-cell Responses with or without Matrix-M1 Adjuvant

Frequencies of antigen-specific CD4+ T cells producing T helper 1 (Th1) cytokines interferon-gamma (IFN-γ), tumor necrosis factor-alpha (TNF-α), and interleukin-2 and for T helper 2 (Th2) cytokines interleukin-5 and interleukin-13 indicated cytokines from four participants each in the placebo (group A), 25-µg unadjuvanted (group B), 5-µg adjuvanted (group C), and 25-µg adjuvanted (group D) groups at baseline (day 0) and 1 week after the second vaccination (day 28) after stimulation with the recombinant spike protein. “Any 2Th1” indicates CD4+ T cells that can produce two types of Th1 cytokines at the same time. “All 3 Th1” indicates CD4+ T cells that produce IFN-γ, TNF-α, and interleukin-2 simultaneously. “Both Th2” indicates CD4+ T cells that can produce Th2 cytokines interleukin-5 and interleukin-13 at the same time.
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 vaccinees, 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
NVX-CoV2373 Clinical Development Plan

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

1. Study 1 Part 1 (2019nCoV-101)
   - Phase 1 AU Adults N=131, 18-59 years

2. Study 1 Part 2 (2019nCoV-101)
   - Phase 2 AU/US Adults N=1,500 (n=750 >60 years)

3. Study 2 (2019nCoV-501)
   - Phase 2b South Africa N=2,904 18-65 years (n=240 HIV+)

4. Study 3 2019nCoV-601
   - Phase 3 UK N=~9,000 18-84 years (n=400 IIV co-admin)

5. Study 7 2019nCoV-301
   - Phase 3 US N=30,000 Adults ≥18- years

1. Dose confirmation in adults >60 y based on Phase 2: Oct 2020
Looking Ahead

- The nanoparticle spike protein vaccine is stable and highly immunogenic
- Matrix M adjuvant drives high quality antibody and T cell responses
- Observed dose sparing (5ug) greatly expands the vaccine supply
- Global supply chain will produce capacity of over 2 billion annualized doses when at full capacity in 2021
- NVX-CoV2373 has entered the efficacy evaluations
Questions?