Positive Topline Data from Phase 2 Older Adult Trial and Path Forward for RSV F Vaccine Programs

Investor Slide Deck
July 24, 2017
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<table>
<thead>
<tr>
<th>Agenda</th>
<th></th>
</tr>
</thead>
</table>
| **Introduction** | **Stanley C. Erck**  
President and CEO |
| **RSV F Vaccine for Older Adults**  
• Review of findings and clinical results  
• Path forward | **Gregory M. Glenn, M.D.**  
President, Research and Development  
**Louis Fries, III, M.D.**  
SVP, Chief Medical Officer |
| **RSV F Vaccine for Infants via Maternal Immunization**  
• Phase 3 trial status | **Gregory M. Glenn, M.D.**  
President, Research and Development |
| **Summary and Q&A** | **Stanley C. Erck**  
President and CEO |
We have learned:

• RSV F Vaccine demonstrated evidence of efficacy in several trials
  • OA Phase 2
    • Including in follow-up trial with repeat dosing over 2 seasons
  • IVM Program (2 seasons)
  • Primate Challenge Trials

• In Phase 3, the RSV F Vaccine, despite a lower attack rate year, had signs of efficacy in ARD and higher risk groups (i.e., COPD, >75 y)

• Immune response to RSV F Vaccine can be improved with adjuvant and second dose

• Vaccine antigen is a stable prefusogenic RSV F protein

• Vaccine antigen stimulates broadly neutralizing antibodies to multiple sites (pre-F and post-F), including some novel sites
RSV Vaccine Development Remains a Core Strength of Novavax

We remain the leader in RSV Vaccination

Older Adults

• Expect to conduct Phase 2 efficacy trial in higher risk groups, including COPD
• COPD represents a very large market opportunity
• Expand into all older adults

Infants via Maternal Immunization

• Continuing Phase 3 trial in pregnant women
• Now vaccinating women in 11 countries
• Expect to conduct an informational analysis by year-end
Significant Developments in Influenza Program Support Entry into First Clinical Trial This Quarter

• Important new data in a challenge study comparing our candidate with Sanofi’s High Dose flu vaccine

• Leading to a first clinical trial with our Matrix-M™ adjuvanted recombinant nanoparticle flu vaccine this quarter

We will announce data from the ferret challenge trial and the design of our coming Phase 1/2 influenza clinical trial during our quarterly earnings call on August 8th
RSV Vaccine Construct Update

Gregory M. Glenn, M.D.
**The Novavax RSV F Vaccine Development Path**

**Clinical Vaccinology Approach:** Following compelling clinical evidence to move to Phase 3

- **Clinical Signals:** Pali, Mota, PFP, Infectious Immunity
  - Full length purified F protein not stable
  - Modifications lead to **Stable F vaccine**

- **Stable RSV F Vaccine in Animal Model**
  - Cotton rats protected from RSV (POC)
  - F, PCA correlate with MN Abs
  - Efficacious Vaccine

- **RSV-101: 1st Clinical Trial**
  - PCA and MN broadly neutralizing Abs induced

**Structure-Based Approach**

- **Prefusion/postfusion Structures**
- **Novel, Potent Neutralizing mAbs**
- **Stable Prefusogenic RSV F Vaccine**
- **Processing of F during infection**

**IVM Vaccine Development**

- Protection in baboon model
- Dose optimization in WOCBA
  - Reduction in infection observed x 2
- Antibody Transfer, Pregnant Women

**OA Vaccine Development**

- E-102: PCA/MN Induced in OA
- E-201: OA efficacy
- **E-301 failed to meet endpoint**

**E-205**

- Evaluate adjuvants and two doses in Older Adults
- Enhancement of Abs more potent than palivizumab
- Boosting of prefusion antibodies

**Next Clinical Trial**

**M-301 in progress**
Review of RSV F Vaccine Clinical Development Program for Older Adults

2014/2015
E-201
Safety & Efficacy

2015/2016
E-202
Repeat Dosing

2016/2017
E-205
Adjuvant/Formulation

E-301 (Resolve)
Pivotal Efficacy
# Outline of Findings

## RSV F Vaccine Construct

- New insights into the vaccine responses confirm its potency
- Preclinical and clinical data confirm its potential for protection

## Dosing and Adjuvantation (E-205)

- Adjuvants and/or 2 dose regimens significantly improve multiple important measures of immunity
- Greater durability of vaccine-induced responses observed

## Clinical Trial Data (E-201 and E-301)

- Antibodies to RSV correlate with decreased infection risk
- Pre-existing RSV immunity decreased the attack rate and diminished the window to demonstrate efficacy
- Yet, in a high-risk population, efficacy observed in both trials
F Protein Structure Evolves During Infection

RSV Entry into Host Cells and the Fusion (F) Protein Processing Leads to an Activated F Protein, Membrane Fusion and Delivery of RSV RNA into the Cytoplasm

F Protein States Found in Nature: The Novavax RSV Vaccine is Similar to the Prefusogenic F

RSV F0

Pre-fusogenic

Prefusion & Postfusion

Novavax’ RSV Vaccine

= Furin Cleavage sites

All RSV F Vaccine Constructs are “Like” Constructs

Novavax Stable Prefusogenic Vaccine

Prefusion (NIH DS-Cav1)

Postfusion (NIH sF)
Our Vaccine Construct is a Stable Prefusogenic RSV F Nanoparticle

RSV F Vaccine Structure

- Prefusogenic F protein trimers
- 40nm protein/detergent nanoparticles
- Highly stable – resists denaturation and aggregation
- Phase 3 manufacturing process appropriate for commercialization

RSV F Vaccine Activity

- Induces **highly potent, broadly neutralizing antibodies**:
  - More potent than palivizumab and comparable to motavizumab
  - Epitopes displayed by both prefusion and postfusion forms of the F protein
Preclinical and Clinical Evidence of Vaccine Efficacy

• Cotton rat protection against virus challenge including mutants that are resistant to mAb-induced resistant strains\(^1,2\)

• Protection against challenge of infant baboons born to immunized mothers\(^3\)

• Prevention of infection in young women in two separate trials over two RSV seasons (M-201 and M-202) \(^4,5\)

• Decreased RSV acute respiratory disease in older adults after a single dose (E-201) \(^6\)

• Decreased RSV acute respiratory disease in older adults after a second annual dose (E-202) \(^6\)

• Reduction of hospitalization from COPD exacerbations in Phase 2 and 3 trials (E-201 and E-301; unpublished)
<table>
<thead>
<tr>
<th>No.</th>
<th>References</th>
<th>Links</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Fries F. Presentation at: RSV 16 10th International Respiratory Syncytial Virus Symposium; Sept. 29, 2016; Patagonia, AR.</td>
<td>N/A</td>
</tr>
</tbody>
</table>
## E-205
**Evaluation of Adjuvants and Dose Regimens with RSV F Vaccine**

<table>
<thead>
<tr>
<th>When</th>
<th>Trial initiated in Jan 2017 in Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Topline serology data through Day 119 now available for most parameters (Day 56 for RSV MN)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Design</th>
<th>300 healthy older adults</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomized, observer-blinded, placebo-controlled, evaluation of RSV F with and without aluminum phosphate or our proprietary Matrix-M™ adjuvant; in one or two-dose regimens</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Objectives</th>
<th>To ascertain whether adjuvantation or a two-dose primary regimen can alter the quantity and quality of the immune response to RSV F Vaccine in older adults</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>To identify one or a small number of regimens meriting further evaluation in additional safety and immunogenicity and eventual efficacy</td>
</tr>
<tr>
<td></td>
<td>To evaluate the safety of revised regimens and formulations of RSV F in older adults</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RSV-specific immune responses by MN, anti-F IgG, PCA with site II antibody avidity assessments, and B and T cell responses</td>
</tr>
</tbody>
</table>
Why Pursue a Quantitatively Better Immune Response?

Study participants without RSV disease had higher titers on average than participants with RSV disease.

No clear protective cut-off determined.

*Case-control analysis matching on age, site, and timing of illness.
## E-205 Treatment Groups

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Subjects Per Group</th>
<th>Study Day</th>
<th>Day 0</th>
<th>Day 21</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RSV F Dose</td>
<td>Aluminum Dose</td>
<td>Matrix-M1 Dose</td>
</tr>
<tr>
<td>A</td>
<td>25</td>
<td>135 µg</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>25</td>
<td>95 µg</td>
<td>0.3 mg</td>
<td>0</td>
</tr>
<tr>
<td>C</td>
<td>25</td>
<td>95 µg</td>
<td>0.3 mg</td>
<td>0</td>
</tr>
<tr>
<td>D</td>
<td>25</td>
<td>120 µg</td>
<td>0.4 mg</td>
<td>0</td>
</tr>
<tr>
<td>E</td>
<td>25</td>
<td>120 µg</td>
<td>0.4 mg</td>
<td>0</td>
</tr>
<tr>
<td>F</td>
<td>25</td>
<td>135 µg</td>
<td>0</td>
<td>50 µg</td>
</tr>
<tr>
<td>G</td>
<td>25</td>
<td>135 µg</td>
<td>0</td>
<td>50 µg</td>
</tr>
<tr>
<td>H</td>
<td>25</td>
<td>65 µg</td>
<td>0</td>
<td>50 µg</td>
</tr>
<tr>
<td>J</td>
<td>25</td>
<td>65 µg</td>
<td>0</td>
<td>50 µg</td>
</tr>
<tr>
<td>K</td>
<td>25</td>
<td>35 µg</td>
<td>0</td>
<td>50 µg</td>
</tr>
<tr>
<td>L</td>
<td>25</td>
<td>35 µg</td>
<td>0</td>
<td>50 µg</td>
</tr>
<tr>
<td>M (Placebo)</td>
<td>25</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Total 300 Subjects
Kinetics of Anti-F IgG in Representative Groups: Adjuvant Effect, 2\textsuperscript{nd} Dose Effect and Durability of Responses Enhanced

Fold Rises in Anti-F IgG

- Geometric Mean Rise from Day 0 (95%CI)
- Study Days from Dose 1

- 135µg F x 1
- 135µg F + M\texttimes M x 1
- 135µg F + M\texttimes M x 2

- p < 0.0001
- p = 0.0099
Kinetics of PCA in Representative Groups: Adjuvant Effect, 2nd Dose Effect and Durability of Responses Enhanced

Fold Rises in PCA

Geometric Mean Rise from Day 0 (95% CI)

Study Days from Dose 1

- 135µg F x 1
- 135µg F + MxM x 1
- 135µg F + MxM x 2

p < 0.0001
p = 0.004
p = 0.004
Enhancement of Neutralizing Antibody Responses
Induction of Antibodies to Prefusion Epitopes

E-205: Day 56 serum

n = 60 (10 per group) for ACE; all subjects for RSV MN
Enhancement of Antibody Avidity by Adjuvanted Regimens

Avidity Maturation of Site II Antibodies

Percentage of Subjects

Site II antibodies

K\text{off}

- <10^0 to -1
- <10^-1 to -2
- <10^-2 to -3
- <10^-3 to -4
- < 10^-4 to -5
- < 10^-5

day 0 | day 21 | day 56 | day 0 | day 21 | day 56 | day 0 | day 21 | day 56 | day 0 | day 21 | day 56
--- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | ---
Placebo | 135ug x 1 | 135ug + MxM x 1 | 135ug + MxM x 2

NOVAVAX
Creating tomorrow's Vaccines Today

24
F Protein-specific Memory B Cell ELISpot Responses are Strong with All Formulations

Counts of Memory B Cells Specific for RSV F per $10^6$ PBMC at Day 28

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Doses</th>
<th>Day 0</th>
<th>Day 28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>2</td>
<td>68</td>
<td>48</td>
</tr>
<tr>
<td>135µg F</td>
<td>1</td>
<td>52</td>
<td>630</td>
</tr>
<tr>
<td>120µg F + Al</td>
<td>1</td>
<td>76</td>
<td>991</td>
</tr>
<tr>
<td>120µg F + MxM</td>
<td>2</td>
<td>100</td>
<td>1075</td>
</tr>
<tr>
<td>135µg F + MxM</td>
<td>1</td>
<td>73</td>
<td>804</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>96</td>
<td>879</td>
</tr>
</tbody>
</table>

n = 54 (4 placebo, 10 per vaccine group)
Matrix-M Adjuvantation Enhances Triple Cytokine Positive RSV F-specific CD4+ Responses

CD4+ T Cell Responses by Intracellular Staining

CD4+ T cells Producing IFNγ, TNFα, and IL-2 After Stimulation with RSV F Peptide Pools

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Doses</th>
<th>Day 0</th>
<th>Day 28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>2</td>
<td>0.026</td>
<td>0.014</td>
</tr>
<tr>
<td>135µg F</td>
<td>1</td>
<td>0.028</td>
<td>0.124</td>
</tr>
<tr>
<td>120µg F + Al</td>
<td>1</td>
<td>0.016</td>
<td>0.093</td>
</tr>
<tr>
<td>135µg F + MxM</td>
<td>2</td>
<td>0.011</td>
<td>0.218</td>
</tr>
<tr>
<td>135µg F + MxM</td>
<td>1</td>
<td>0.023</td>
<td>0.223</td>
</tr>
</tbody>
</table>

n = 54 (4 placebo, 10 per vaccine group)
Adjuvant effects

- The adjuvants meaningfully increased immunity in measures shown to decrease infection and measures generally associated with effective immunity
  - Anti-F and PCA
  - MN titers
  - Avidity of antibodies to neutralizing epitopes
  - Memory B cell and CD4+ T cells specific for F protein
- Durability of the responses are important and are improved with 2 doses

The totality of the immune effects makes use of the adjuvants desirable, and likely to de-risk the next steps

- Both classic and new immune measures build our confidence that these are better formulations to use in the next steps

With respect to safety:

- All adjuvanted formulations were clinically tolerable
Evidence Base for RSV F Vaccine in Older Adults

Lou Fries III, M.D.
## Hypothesis for Outcomes

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RSV OA</strong></td>
<td>E-201</td>
<td>E-301</td>
</tr>
<tr>
<td>RSV ARD</td>
<td>4.9%</td>
<td>2.0%</td>
</tr>
<tr>
<td>RSV msLRTD</td>
<td>1.8%</td>
<td>0.4%</td>
</tr>
<tr>
<td><strong>RSV Circulation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>RSV Susceptibility</strong></td>
<td>E-201</td>
<td>E-301</td>
</tr>
<tr>
<td>MN-B (GMT) baseline</td>
<td>267</td>
<td>447</td>
</tr>
</tbody>
</table>

- Lower in 2015/16 on basis of trial data; confirmed by external data
- Lower in 2015/16 on basis of RSV/B MN data

Similar on basis of RSVAlert® data
Baseline RSV Immunity in E-201 and E-301

RSV MN Titer Distributions at Baseline

Proportion of Population

Log2 RSV MN Titers

E-201

E-301
### Hypothesis for Outcomes

#### 2014-2015

<table>
<thead>
<tr>
<th>RSV OA Attack Rates</th>
<th>E-201</th>
<th>E-301</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSV ARD</td>
<td>4.9%</td>
<td>2.0%</td>
</tr>
<tr>
<td>RSV msLRTD</td>
<td>1.8%</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

#### 2015-2016

- **Lower in 2015/16 on basis of trial data; confirmed by external data**

#### RSV Circulation

- **Similar on basis of RSVAlert® data**

#### RSV Susceptibility

<table>
<thead>
<tr>
<th>E-201</th>
<th>E-301</th>
</tr>
</thead>
<tbody>
<tr>
<td>MN-B (GMT) baseline</td>
<td>267</td>
</tr>
</tbody>
</table>

#### Vaccine Efficacy

- **Lower in 2015/16 on basis of trial data**

<table>
<thead>
<tr>
<th>E-201</th>
<th>E-301</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSV ARD</td>
<td>41%</td>
</tr>
<tr>
<td>RSV msLRTD</td>
<td>64%</td>
</tr>
</tbody>
</table>
## Flu Examples of Attack Rate Effects

<table>
<thead>
<tr>
<th>Series</th>
<th>Author</th>
<th>Year</th>
<th>Placebo Attack Rate</th>
<th>Circulating Strain(s) Match to Vaccine</th>
<th>Case Defined by:</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ohmit et al¹</td>
<td>2004-5</td>
<td>7.8%</td>
<td>Drifted</td>
<td>Culture or PCR</td>
<td>75% (42, 90)</td>
</tr>
<tr>
<td></td>
<td>Ohmit et al²</td>
<td>2005-6</td>
<td>1.8%</td>
<td>Good match</td>
<td></td>
<td>16% (-171,70)</td>
</tr>
<tr>
<td></td>
<td>Monto et al³</td>
<td>2007-8</td>
<td>10.8%</td>
<td>Low level drift</td>
<td></td>
<td>68% (46, 81)</td>
</tr>
<tr>
<td>2</td>
<td>Hoberman et al⁴</td>
<td>1999-2000</td>
<td>15.9%</td>
<td>Matched</td>
<td>Culture</td>
<td>66% (34, 82)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2000-1</td>
<td>3.3%</td>
<td>Matched</td>
<td></td>
<td>-7% (-247, 67)</td>
</tr>
<tr>
<td>3</td>
<td>Beran et al⁵</td>
<td>2005-6</td>
<td>0.2%</td>
<td>Matched A Viruses</td>
<td>Culture</td>
<td>25.1% (-261, 82)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.9% all</td>
<td>Largely mismatched</td>
<td></td>
<td>22.3% (-49, 59)</td>
</tr>
<tr>
<td></td>
<td>Beran et al⁶</td>
<td>2006-7</td>
<td>3.2%</td>
<td>Predominantly matched</td>
<td></td>
<td>61.6% (46, 73)</td>
</tr>
</tbody>
</table>

More Susceptible Populations MayProvide a Window to Show Efficacy

- Even in a season characterized by low population susceptibility/high population immunity, there are individuals or subsets of individuals who succumb to infection and/or complications of infection because of heightened susceptibility due to:
  - Immunosenescence
  - Frailty
  - Comorbidity

- Promising target population: COPD
# Impact of Vaccine on COPD Exacerbations

*Post-hoc* Analyses of Hospitalizations for **All Cause** COPD Exacerbations in E-201 and E-301

Data from the **Safety** Database

<table>
<thead>
<tr>
<th>E301 Day 0-182</th>
<th>Placebo</th>
<th>Vaccine</th>
<th>VE%</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD hospitalization rate in all subjects</td>
<td>23/5935 (0.39%)</td>
<td>9/5921 (0.15%)</td>
<td>60.8%</td>
<td>15.2—81.9</td>
<td>0.017</td>
</tr>
<tr>
<td>COPD hospitalization rate in subjects with baseline COPD</td>
<td>15/362 (4.1%)</td>
<td>9/403 (2.2%)</td>
<td>46.1%</td>
<td>-23—76.4</td>
<td>0.14</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>E201 Day 0-182</th>
<th>Placebo</th>
<th>Vaccine</th>
<th>VE%</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD hospitalization rate in all subjects</td>
<td>4/801 (0.50%)</td>
<td>0/798 (0%)</td>
<td>100%</td>
<td>NC</td>
<td>NC</td>
</tr>
<tr>
<td>COPD hospitalization rate in subjects with baseline COPD</td>
<td>2/62 (3.2%)</td>
<td>0/58 (0%)</td>
<td>100%</td>
<td>NC</td>
<td>NC</td>
</tr>
</tbody>
</table>

- After Day 182 (i.e., after the winter-spring RSV season) the effect on COPD exacerbation essentially disappears in E-301
- After Day 182, an effect appears to continue in E-201
COPD Hospitalizations in E-301

All-Cause COPD Exacerbation Hospitalization-Free Survival in E-301

Days From Treatment

Proportion of Population Free of COPD Exacerbation

Active
Placebo
Summary

Vaccine Construct

- Characterization has confirmed that our stable prefusogenic RSV-F protein is a highly potent immunogen that elicits broadly neutralizing antibodies to multiple epitopes

Adjuvant Formulation and Regimen

- The adjuvants and dose regimens significantly increased the magnitude, quality and durability of the immune responses

Phase 2 and Phase 3 Efficacy Results

- Antibodies that we measured were associated with reduced risk of RSV disease
- Unusually high background immunity led to a low attack rate and low vaccine efficacy in Phase 3
  - Influenza trials provide precedent for low efficacy in season with low attack rate
  - Profound vaccine effect seen in both E-201 and 301 against COPD populations

Next Steps

- Combination of potent immunogen, adjuvant and 2- dose regimen warrants a Phase 2 efficacy trial in older adults and evaluation of COPD exacerbations as a prospective endpoint
Phase 3 Study:
Infants via Maternal Immunization

Gregory M. Glenn, M.D.
RSV is the most common cause of lower respiratory tract infections among young children in the United States and worldwide\(^1\)

RSV is the leading cause of hospitalization among children <1 year old in the United States\(^2,3\)

Globally, RSV is second only to malaria as a cause of death in children <1 year old\(^4\)

The Bill and Melinda Gates Foundation has prioritized an RSV vaccine, as a reduction in RSV disease will decrease infant mortality and thus, the Foundation is supporting the Prepare trial through an $89M grant

RSV is largely a disease of healthy, full-term infants

The smaller airways and immature immune systems of infants make them more susceptible to severe disease

Natural immunity, derived from the mother, is relatively ineffective

---

**Policy Advances in Support of Maternal Immunization**

<table>
<thead>
<tr>
<th>Vaccine Injury Compensation Program (VICP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amendment in 21st Century Cures Act: As of December 13, 2016, program covers “both a woman who received a covered vaccine while pregnant and any child who was in utero” under government no-fault insurance program</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Support from Medical Community</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Growing acceptance of maternal vaccination for flu and pertussis among HCPs and mothers</td>
</tr>
<tr>
<td>• American College of Obstetrics and Gynecology conducts CME-accredited webinar: “Respiratory Syncytial Virus: The Need for a Maternal Immunization Strategy”</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ACIP RSV Working Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>• CDC Advisory Committee on Immunization Practices (ACIP) established RSV Working Group, May 2016</td>
</tr>
<tr>
<td>• First step towards ACIP consideration for recommendation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RESCEU (REspiratory Syncytial virus Consortium in EUrope)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• EU consortium of global leaders in RSV research (academia, public policy, industry)</td>
</tr>
<tr>
<td>• Epidemiology, surveillance and economic burden research</td>
</tr>
</tbody>
</table>
Novavax Has Conducted a Number of Phase 2 Trials with RSV F Vaccine

Non-pregnant women

- **Safety and immunogenicity confirmed** in dose selection trials
- Demonstration of **~50% reduction of RSV infections** in vaccine groups in two trials in two separate seasons

Pregnant women

- Vaccine was **well-tolerated**
- Response to RSV F vaccine in pregnant women **replicated immune response in non-pregnant women**
- **Anti-F, PCA, and neutralizing transplacental antibody transfer confirmed**
- Observed **half-life of ~40 days** for MN and PCA through first 60 days post delivery
- Suggests protection of infants for **up to 180 days**
## Phase 3 RSV F Vaccine for Infants via Maternal Trial: Goals and Design

<table>
<thead>
<tr>
<th>Primary Objective</th>
<th>Determine the efficacy of maternal immunization with the RSV F vaccine against symptomatic RSV lower respiratory tract infection (LRTI) with objective measures of medical significance of LRTI from 90-180 days of life in infants.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design</strong></td>
<td>Randomized, Observer-Blind, Placebo-Controlled, Group Sequential</td>
</tr>
<tr>
<td><strong>Number of participants</strong></td>
<td>• Minimum 4,600 women</td>
</tr>
<tr>
<td><strong>Global Sites</strong></td>
<td>• Year 3: US, Mexico, Chile, Argentina, UK, Spain, South Africa, Australia, New Zealand, Philippines, India</td>
</tr>
</tbody>
</table>
| **Length of Participation** | • Maternal Participants: 9 months  
• Infant Participants: 1 year                                                                                                                  |
|                   | 1 IM Injection (RSV F Vaccine or Placebo), 28-36 weeks EGA                                                                                                                                         |
The Phase 3 “Prepare Trial” has Entered its Third Year

Global Infrastructure has been established to drive enrollment and surveillance

Recruitment and surveillance are going well and indicate trial feasibility

- Global Season 1: 16 sites in 5 countries
- Global Season 2: 46 sites in 7 countries
- Global Season 3: 80 sites in 11 countries

Argentina
Australia
Chile
India
Mexico
New Zealand
Philippines
South Africa
Spain
United Kingdom
United States
Closing Remarks

Question/Answer

Stanley C. Erck
Vaccine Construct

- Characterization has confirmed that our stable prefusogenic RSV-F protein is a highly potent immunogen that elicits broadly neutralizing antibodies to multiple epitopes.

Adjuvant Formulation and Regimen

- The adjuvants and dose regimens significantly increased the magnitude, quality and durability of the immune responses.

Phase 2 and Phase 3 Efficacy Results

- Antibodies that we measured were associated with reduced risk of RSV disease.
- Unusually high background immunity led to a low attack rate and low vaccine efficacy in Phase 3:
  - Influenza trials provide precedent for low efficacy in season with low attack rate.
  - Profound vaccine effect seen in both E-201 and 301 against COPD populations.

Next Steps

- Combination of potent immunogen, adjuvant and 2-dose regimen warrants a Phase 2 efficacy trial in older adults and evaluation of COPD exacerbations as a prospective endpoint.
Summary of COPD Opportunity

- Efficacy of Novavax’ RSV F vaccine on COPD exacerbations observed in E-301, and retrospectively confirmed in E-201
- COPD represents an at-risk population for RSV disease
- A significant market opportunity exists with COPD, ~ $1.5 billion globally

Prevalence of COPD Diagnosis Among U.S. Adults (2013)¹

- 15.7M
- 9.3M ≥55 y

Actual prevalence may be >30M due to high proportion of undiagnosed COPD

COPD Mortality Among U.S. Adults

- Leading cause of death due to chronic lower respiratory diseases (>95%)¹
- The third leading cause of death overall in the United States¹

Acute Exacerbations of COPD Among U.S. Adults

- On average, 3 acute exacerbations annually per patient²
- Viral trigger is estimated in 43% of cases²
- RSV associated with 5-10% of exacerbations³

Prevention of acute exacerbations of COPD with the RSV F vaccine would have a significant impact on the clinical and economic burden of COPD in the United States

<table>
<thead>
<tr>
<th>Category</th>
<th>Estimate</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSV Infections</td>
<td>1,915,682</td>
<td>68.8/100 infant-years = 1,915,682 (in 2015)(^3)*</td>
</tr>
<tr>
<td>Pediatric Outpatient Visits</td>
<td>262,531</td>
<td>Outpatient pediatric practice, annual visits(^4)* Incidence: 132 (95% CI, 46-383) per 1000</td>
</tr>
<tr>
<td>ED Visits</td>
<td>109,388</td>
<td>Rate ≈ 55 (95% CI, 24-126)/1000(^4)*</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>33,612</td>
<td>Rate ≈ 16.9 (95% CI, 15-19)/1000(^4)*</td>
</tr>
<tr>
<td>Deaths</td>
<td>11-25</td>
<td>Annual estimate(^5,6)</td>
</tr>
</tbody>
</table>

\(^2\) Calculation 3,977,745 x 11/12.

* includes pre-term infants (<37 wks = .9.62% and <33wks = 2.75%)
NVAX RSV F Vaccine Franchise for Both Older Adults (OA) and Infants via Maternal (IVM) is On Track for Success

• NVAX to initiate Phase 2 efficacy trial in OA in 2018

• Pivotal efficacy trial for IVM on target
  • Informational analysis expected by year-end
  • Interim analysis expected to be triggered mid-2018
Questions?