Progress toward a vaccine for maternal immunization to prevent Respiratory Syncytial Virus Lower Respiratory Tract Illness (RSV LRTI) in infants

November 2018
Certain information, particularly information relating to future performance and other business matters, including expectations regarding clinical development, our planned use of the proceeds from the offering, market opportunities and anticipated milestones constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act.

Forward-looking statements may generally contain words such as “believe,” “may,” “could,” “will,” “possible,” “can,” “estimate,” “continue,” “ongoing,” “consider,” “intend,” “indicate,” “plan,” “project,” “expect,” “should,” “would,” or “assume” or variations of such words or other words with similar meanings. Novavax cautions that these forward-looking statements are subject to numerous assumptions, risks and uncertainties that change over time and may cause actual results to differ materially from the results discussed in the forward-looking statements.

Uncertainties include but are not limited to clinical trial results, dependence on third party contractors, competition for clinical resources and patient enrollment and risks that we may lack the financial resources to fund ongoing operations.

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, 2017, our Quarterly Reports on Form 10-Q, and our Current Reports on Form 8-K, which are all available at http://www.sec.gov.

Forward-looking statements are based on current expectations and assumptions and currently available data and are neither predictions nor guarantees of future events or performance.

Current results may not be predictive of future results.

You should not place undue reliance on forward-looking statements which speak only as of the date hereof.

The Company does not undertake to update or revise any forward-looking statements after they are made, whether as a result of new information, future events, or otherwise, except as required by applicable law.

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Problem statement:
Severe RSV disease occurs in the first 3-4 months of life

Average Age-Specific Rate and Number of RSV Hospitalizations Among Children in First Year of Life, 2000-2005

Fusion (F) protein key to infectivity, structure evolves during infection

Immune responses in recently-infected infants recognize p27, indicating pre-fusogenic F forms are present during infection.

Fuentes, et al. Antigenic fingerprinting following primary RSV infection in young children identifies novel antigenic sites and reveals unlinked evolution of human antibody repertoires to fusion and attachment glycoproteins. CBER, FDA, Silver Spring, MD. PLOS Pathogens 10.1371, 2016

Whole genome fragment phage display libraries
RSV F constructs: ResVax is based on a prefusogenic F protein

Highly characterized F protein constructs

RSV F

Pre-fusogenic F 

Pre-fusion F 

Post-fusion F 


TMCT: transmembrane C-terminus

FP: fusion peptide; fp: truncated fusion peptide

SP: signal peptide

ResVax is a near full length nanoparticle with mutation of the second Furin cleavage site and retention of p27
RSV F vaccine development through the Phase 3 trial

Animal Studies
- NZW Rabbit Repeat Dose Tox Study
- Baboon Maternal Antibody Transfer & Infant Protection (4-Part study)
- Guinea Pig Maternal Antibody Transfer Study
- Multiple Cotton Rat Challenge Studies (Active & Passive)
- NZW Rabbit and Rat Repro Tox Studies

Clinical Studies
- Phase 1 Healthy Adult Clinical Trial (n=120): initial safety and immunogenicity
- Phase 2 WOCBA Clinical Trial (n=330): selected AlPO₄ adsorbed formulation
- Phase 2 WOCBA Clinical Trial (n=720): selected single dose
- Phase 2 Maternal Immunization Clinical Trial (n=50)
- Phase 3 Maternal Immunization Clinical Trial (n=4636)

- Enrollment Completed
- Efficacy Data
- BLA/MAA
RSV F nanoparticle vaccine induces anti-F IgG, palivizumab competitive antibodies, and RSV/A and B neutralizing antibodies in adults

**Immunized women with baseline RSV/A MN titers <8 log2 achieve 5-6-fold rises:**
- Optimal fold-rises attained with aluminum adjuvant
- Strong and rapid rises are achieved with 120µg F and 0.4mg Al with a single dose
- ~50% reduction in acquisition of “recent infection” Western blot patterns across a transmission season vs. placebo

**In third trimester pregnant subjects and their infants:**
- Overall RSV antibody transfer to cord blood is 90-100%, but
- Approximately 120% when interval between dosing and delivery is ≥30 days
- Half-life of anti-F IgG, PCA, and RSV MN antibodies is 30-40 days
Choice of single-dose, aluminum adjuvanted vaccine

To be practical and useful, we reasoned our vaccine had to:

a) Have a strong impact on mothers with the lowest background RSV MN titers at baseline – the highest risk group,
b) Provide a rapid response, and
c) Preferably, do these things with one dose for compliance

AUC for single dose equal or superior to 56 days

Phase 3 trial goals and design (RSV M-301)

<table>
<thead>
<tr>
<th>Primary objective</th>
<th>Determine the efficacy of maternal immunization with the RSV F vaccine against medically significant symptomatic RSV lower respiratory tract infection (LRTI) through 90, 120, 150 and 180 days of life in infants</th>
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</thead>
<tbody>
<tr>
<td>Design</td>
<td>Randomized, observer-blind, placebo-controlled</td>
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<tr>
<td>Number of participants</td>
<td>• Minimum of 4,600 third trimester pregnant women and their infants</td>
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<tr>
<td>Global study</td>
<td>• 87 sites in 11 countries</td>
</tr>
</tbody>
</table>
| Length of study participation | • Maternal participants: up to 9 months  
• Infant participants: 1 year after delivery                                                                                                                                                    |
| 1 intramuscular (IM) Injection of RSV F Vaccine or Placebo at 28-36 weeks Estimated Gestational Age (EGA)                                                                                      |
| Safety assessment | • Through 6 months post-partum in mothers  
• Through 1 year in infants                                                                                                                                                                |
| Efficacy assessment | • Active/passive surveillance in mothers and infants  
• Confirmation of RSV infection by RT-PCR  
• Medically significant tachypnea or pulse oximetry (infants only)  
• Confirmation of LRTI                                                                                                                 |
Trial participant visit schedule

**MATERNAL SUBJECTS**
(9 months)

- Screening
- Day 0
- Day 7
- Day 14
- Day 28
- D+35
- D+180

**Legend**
- Mothers
- ▲ Blood draw for RSV serology and/or safety labs
- ▲ Maternal + cord blood to be drawn at delivery

**INFANT SUBJECTS**
(1 year)

- D+14
- D+35
- D+60
- D+90
- D+120
- D+180
- D+252
- D+364

- ASQ Development Assessment at 6 and 12 months on all infants

- Cohort 1: D+14, D+90
- Cohort 2: D+35, D+120
- Cohort 3: D+60, D+180
Global enrollment in the Prepare trial since 2015

- Single protocol approved by 13 Regulatory Authorities
- Enrollment at 87 sites in 11 countries
- Seasonal enrollment (Northern & Southern Hemisphere) completed over 31 months
- Total of 4,636 maternal subjects enrolled
Period of intense RSV transmission bracketed in the first 90 days of life for most infants

Season 2, South Africa
Alignment of immunization, births, and 90 day timepoints with the RSV season
Surveillance has been successful

To date:

- >99% of live born infants have been the subject of active or passive surveillance contacts at least once.
- Parents report a trigger symptom in the first 180 days of life in approximately 79% of all infants.
- ~96% of infants with trigger symptoms have been fully evaluated at least once; ~91% of all episodes.
- RSV has been detected in ~19% of infants swabbed, and in ~11% of all episodes.
- RSV has also been detected in approximately 5% of symptomatic mothers between enrollment and day 180 post-partum.
Accrual of medically-significant RSV LRTI by age

- ~90% of MS RSV LRTI cases (with hypoxemia or tachypnea), and
- ~95% of RSV-related hospitalization occur within the first 120 days of life, or about 3 antibody half-lives.
- ~44% of all cases with RSV, LRTI findings, and hypoxemia or tachypnea are hospitalized.
RSV M-301 Safety

- Oversight of safety via DSMB:
  - Serial pre-planned futility analyses.
  - Iterative completely unblinded review of safety and efficacy outcomes by an international DSMB of obstetricians and pediatricians, supported by an independent statistician.

- 15 consecutive DSMB reviews: no advice to slow, pause, or alter protocol

- 2015 Brighton Collaboration list of pregnancy and peri-partum safety endpoints adopted as adverse events of special interest (AESI) and treated as serious adverse events (SAE).
  - Overall blinded AESI rates are below global backgrounds, and
  - AESI rates are similar to, or less than, published country-specific rates in the U.S. and South Africa, which together are responsible for ~76% of the data.
  - South African rates also compare favorably w/influenza vaccine trials.
In order to justify continuing the trial, Novavax performed an informational analysis in Q4 2017 targeting a minimum point estimate of efficacy against the MS RSV LRTI endpoint at day 90 of ~ 40%.

Bayesian analysis, reflecting the underlying analysis plan, using a success criterion of a posterior probability ≥ 90% that the vaccine efficacy was ≥ 0% at the time of the analysis.

- Approximated an efficacy point estimate ≥40% based on the sample size and event count at the time.

The DSMB statistician performed the analysis, the company remains blinded

- The DSMB communicated that the analysis was positive Q4 2017
- Assuming perfect randomization of 1,307 per-protocol infant subjects in the analysis and the known N of endpoints, the efficacy point estimate at the time of the analysis was between 45 and 100%.

Based on this, we plan to unblind for the final analysis of efficacy through 180 days in Q1 2019.
ResVax: pathway to licensure

- 4,636 mothers enrolled
  - Completed 2Q 2018
- 3,000+ infants born to mothers receiving ResVax
  - Completed July 2018
- Final efficacy analysis
  - By 1Q 2019
- BLA/MAA filing
  - By 1Q 2020
Thanks to:

- Our conscientious advisors and investigators and clinical site staff around the world; and of course the subjects themselves
- The Novavax manufacturing, QA, regulatory, clinical operations, biostatistics, pharmacovigilance and clinical immunology teams
- The DSMB members
- Baylor College of Medicine Molecular Virology and Microbiology lab
- The Marshfield Clinical Research Foundation
- The Bill and Melinda Gates Foundation and PATH

- $89 Million in grants
- $7 Million in grants