

**NOVAVAX**  
Creating Tomorrow's Vaccines Today

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

November 2018

# Safe harbor statement

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.

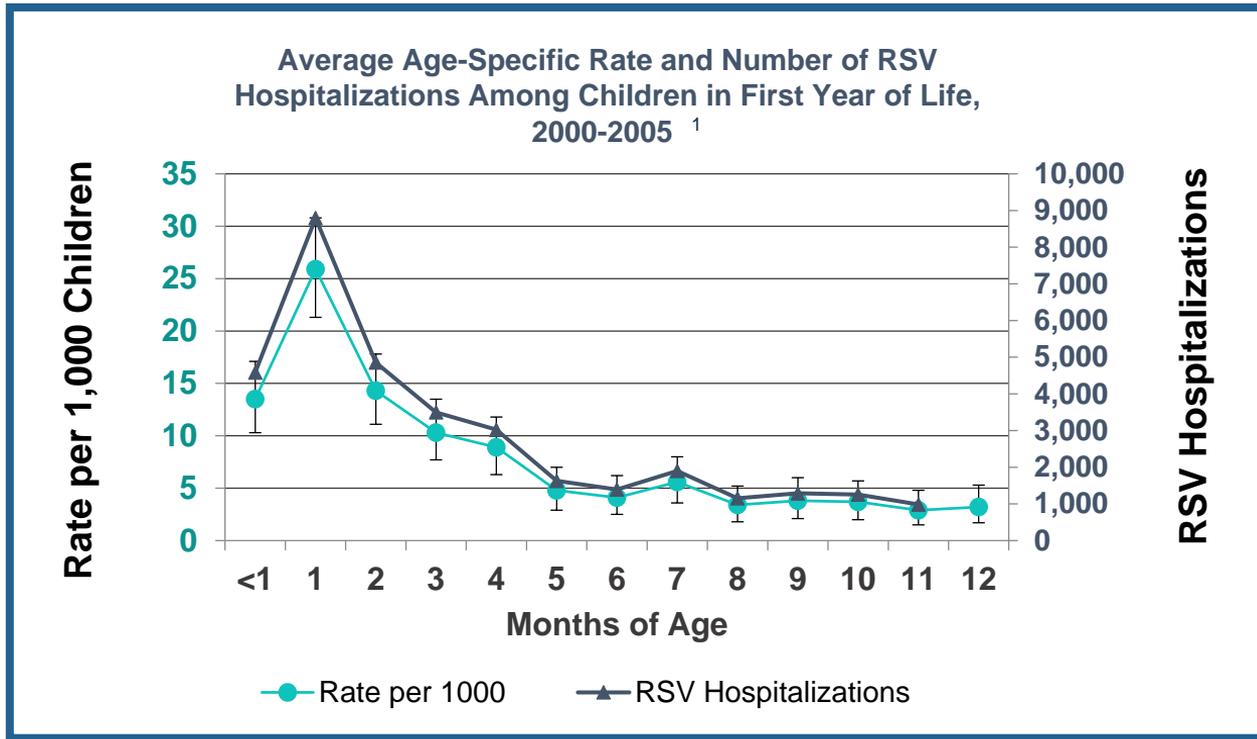
You should not place undue reliance on forward-looking statements which speak only as of the date hereof.

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.

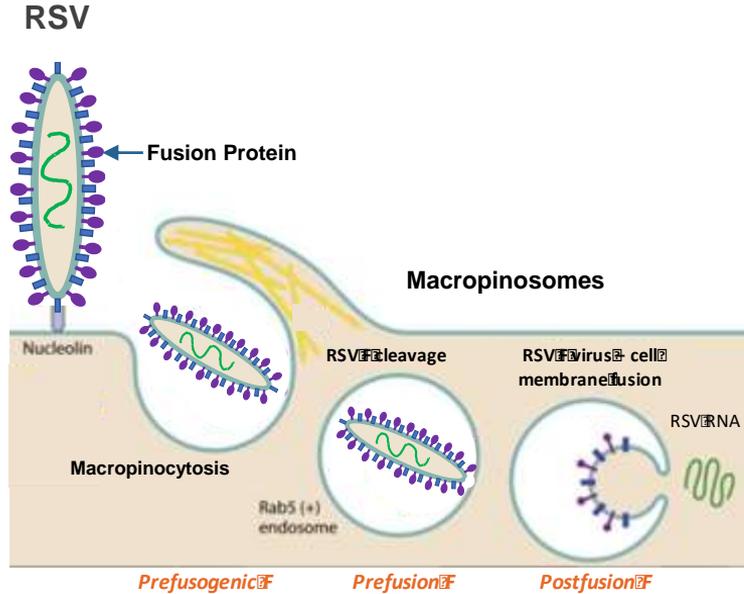
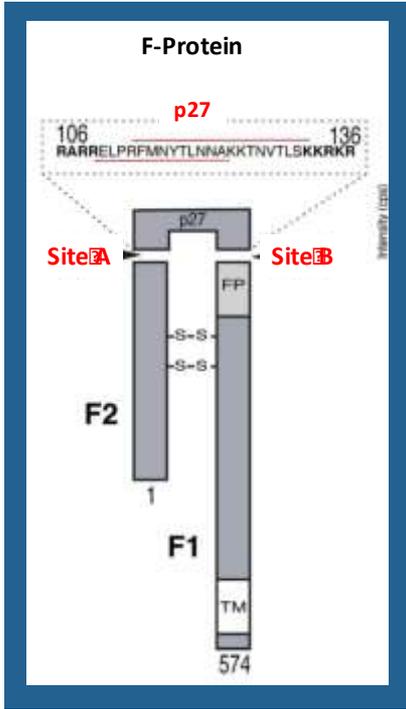
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# Problem statement:

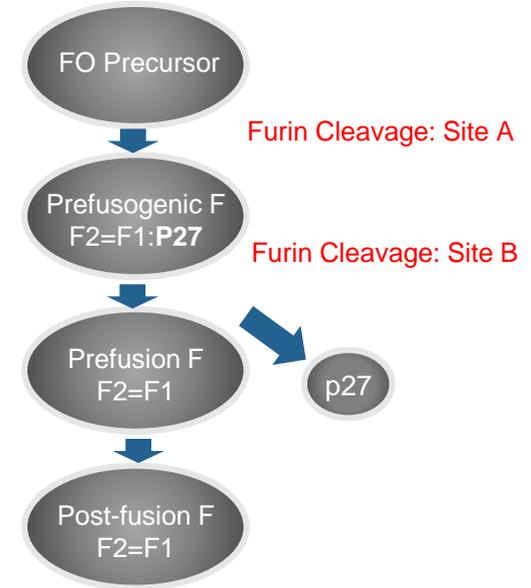
Severe RSV disease occurs in the first 3-4 months of life



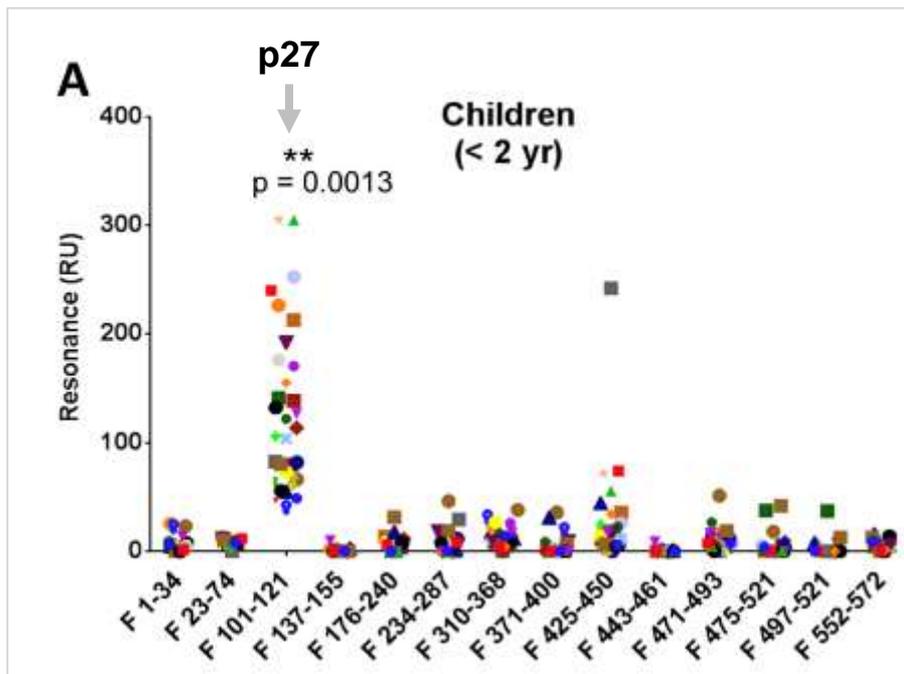
# Fusion (F) protein key to infectivity, structure evolves during infection



## F-Protein Form



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



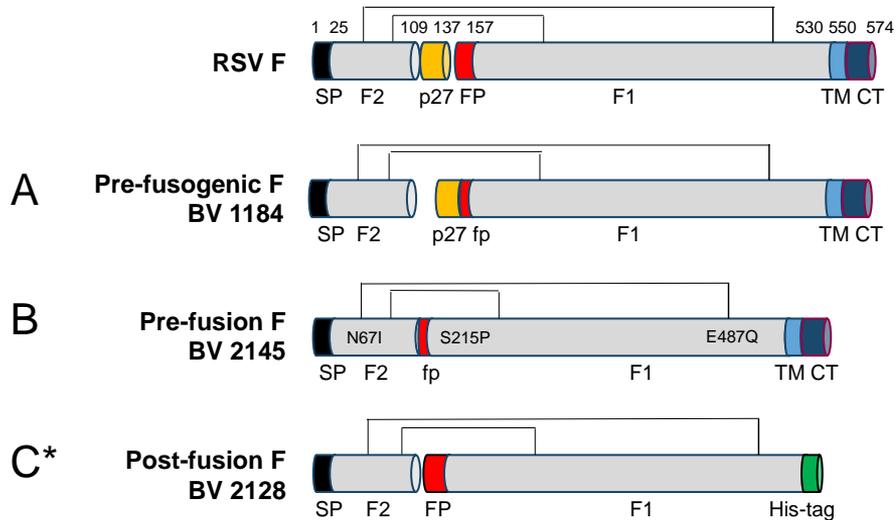
Whole genome fragment phage display libraries

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

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# RSV F constructs: ResVax is based on a prefusogenic F protein

## Highly characterized F protein constructs



ResVax is a near full length nanoparticle with mutation of the second Furin cleavage site and retention of p27

\*Post-fusion F: Swanson, et al. 2011. PNAS. 108(23):9619-9624  
TMCT: transmembrane C-terminus  
FP: fusion peptide; fp: truncated fusion peptide  
SP: signal peptide

# RSV F vaccine development through the Phase 3 trial



# Key data leading to Phase 3

## 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 $<8 \log_2$ achieve 5-6-fold rises:

- Optimal fold-rises attained with aluminum adjuvant
- Strong and rapid rises are achieved with 120 $\mu$ g 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

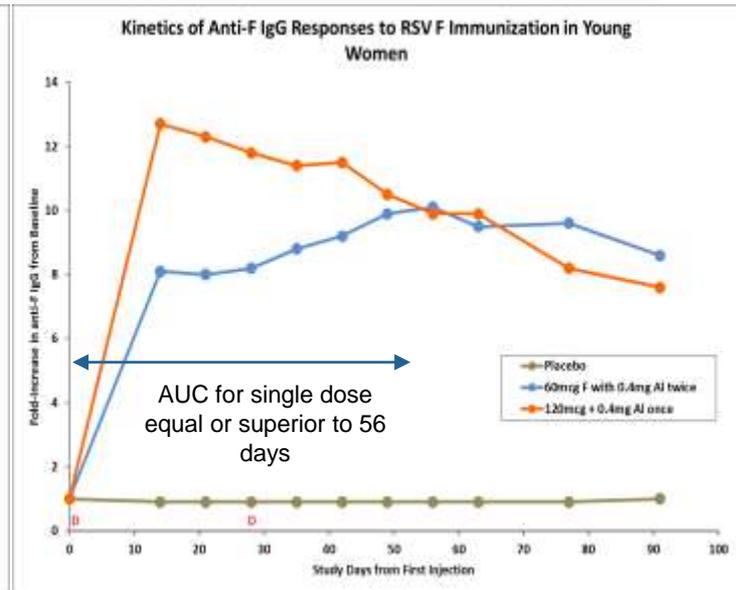
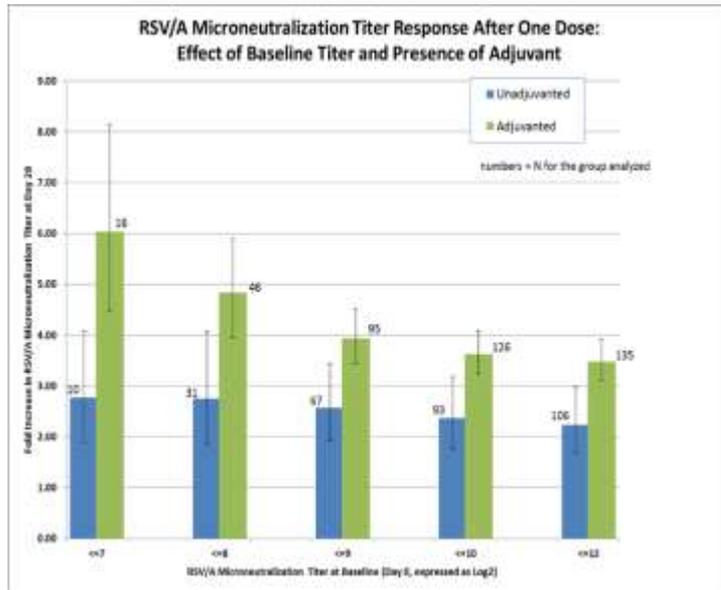
### In third trimester pregnant subjects and their infants:

- Overall RSV antibody transfer to cord blood is 90-100%, but
- Approximately 120% when interval between dosing and delivery is  $\geq 30$  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:

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



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

<b>Primary objective</b>	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	
<b>Design</b>	Randomized, observer-blind, placebo-controlled	
	Number of participants	<ul style="list-style-type: none"><li>• Minimum of 4,600 third trimester pregnant women and their infants</li></ul>
	Global study	<ul style="list-style-type: none"><li>• 87 sites in 11 countries</li></ul>
	Length of study participation	<ul style="list-style-type: none"><li>• Maternal participants: up to 9 months</li><li>• Infant participants: 1 year after delivery</li></ul>
	1 intramuscular (IM) Injection of RSV F Vaccine or Placebo at 28-36 weeks Estimated Gestational Age (EGA)	
	Safety assessment	<ul style="list-style-type: none"><li>• Through 6 months post-partum in mothers</li><li>• Through 1 year in infants</li></ul>
	Efficacy assessment	<ul style="list-style-type: none"><li>• Active/passive surveillance in mothers and infants<ul style="list-style-type: none"><li>• Confirmation of RSV infection by RT-PCR</li><li>• Medically significant tachypnea or pulse oximetry (infants only)</li><li>• Confirmation of LRTI</li></ul></li></ul>

# Trial participant visit schedule

## MATERNAL SUBJECTS (9 months)

(9 months)



### Legend



Mothers



Blood draw for RSV serology and/or safety labs



Maternal + cord blood to be drawn at delivery



Infant Serology Cohorts

Cohort 1: D+14, D+90

Cohort 2: D+35, D+120

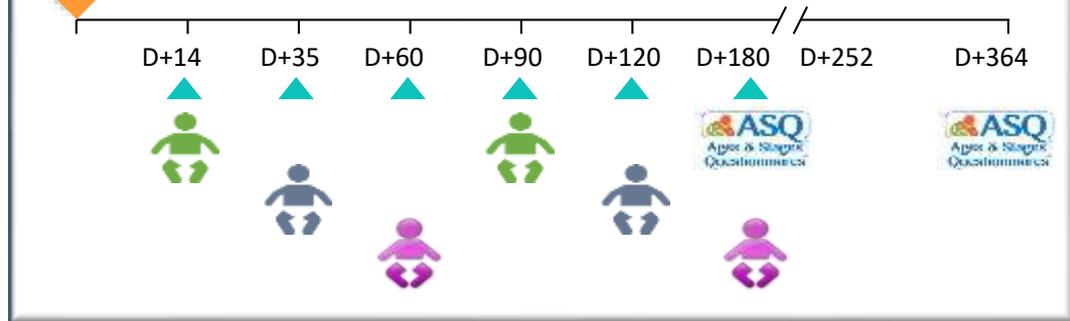
Cohort 3: D+60, D+180



ASQ Development Assessment at 6 and 12 months on all infants

## INFANT SUBJECTS (1 year)

(1 year)



# Global enrollment in the Prepare trial since 2015

THE  Prepare™ TRIAL

Single protocol  
approved by 13  
Regulatory  
Authorities

Enrollment at 87  
sites in 11 countries



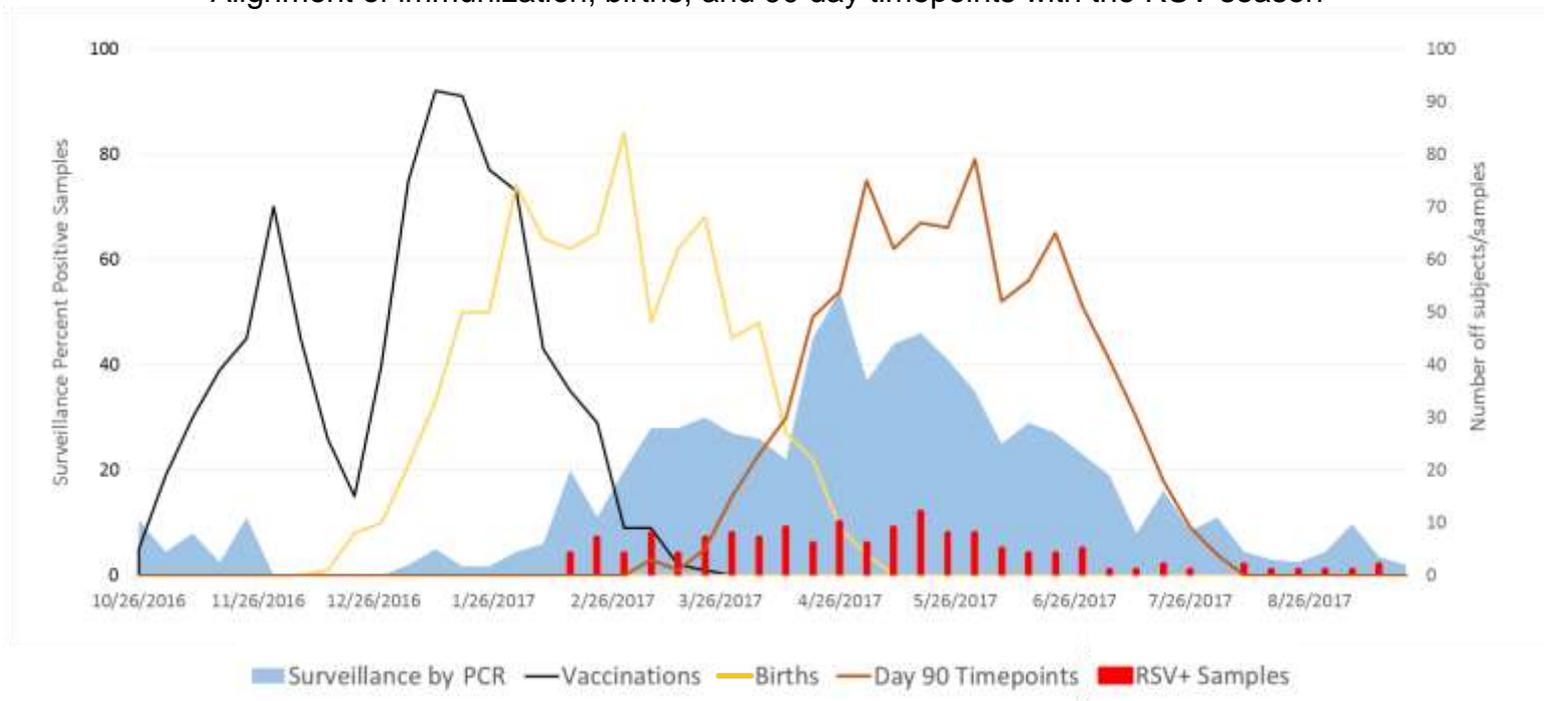
Seasonal enrollment  
(Northern & Southern  
Hemisphere)  
completed over 31  
months

Total of 4,636  
maternal subjects  
enrolled

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# Period of intense RSV transmission bracketed in the first 90 days of life for most infants

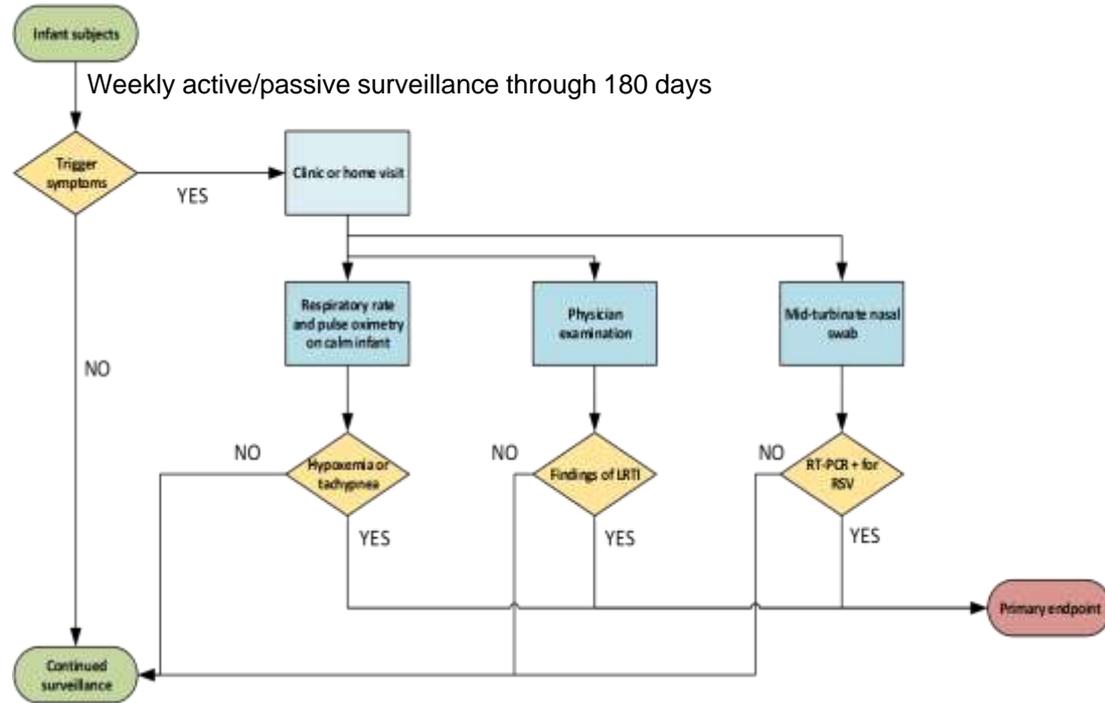
Season 2, South Africa  
Alignment of immunization, births, and 90 day timepoints with the RSV season



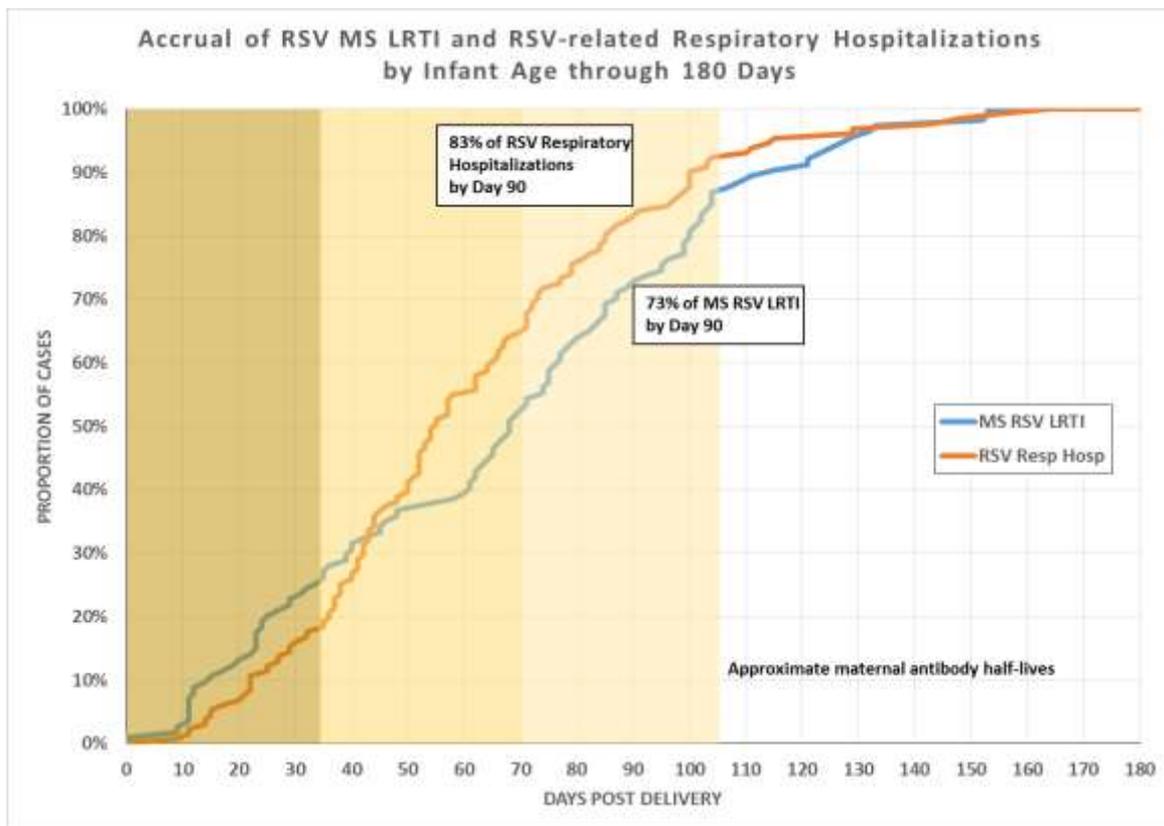
# Surveillance has been successful

## 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



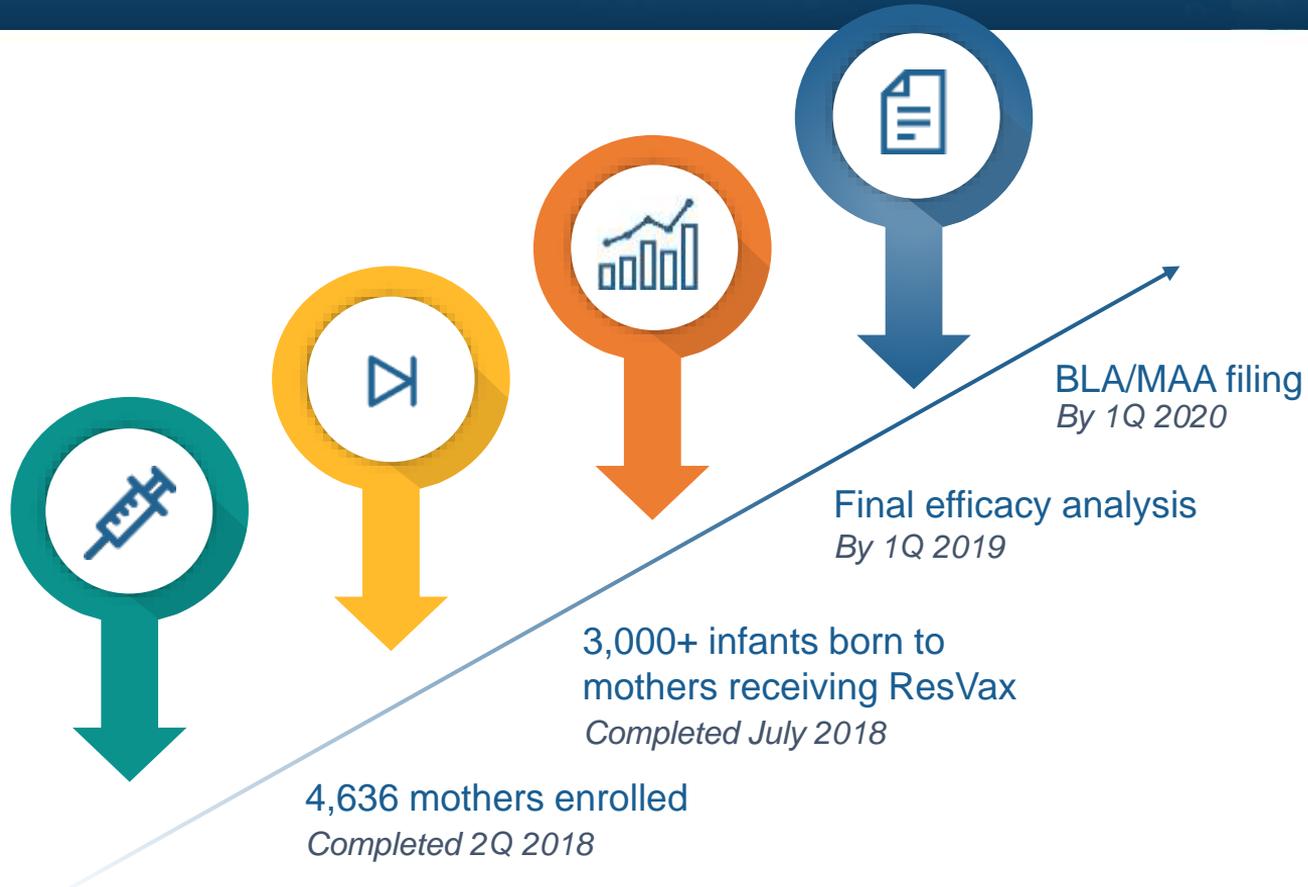
- ~90% of MS RSV LRTI cases (with hypoxemia or tachypnea), and
- ~95% of RSV-related hospitalization occur within the first 120 days of life, or about 3 antibody half-lives.
- ~ 44% of all cases with RSV, LRTI findings, and hypoxemia or tachypnea are hospitalized.

- 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.

# “Informational analysis” of RSV M-301 - 2017

- 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  $\geq 90\%$  that the vaccine efficacy was  $\geq 0\%$  at the time of the analysis.
  - Approximated an efficacy point estimate  $\geq 40\%$  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



## 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

**BILL & MELINDA**  
**GATES** *foundation*

**\$89 Million** in grants



**\$7 Million** in grants

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