

A History of RSV Vaccine Development: 60 Years. One Goal.



1950s/60s/70s



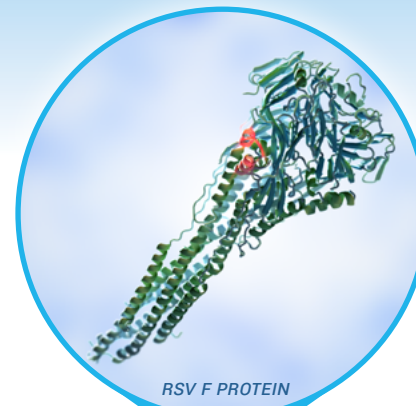
1980s/EARLY 1990s



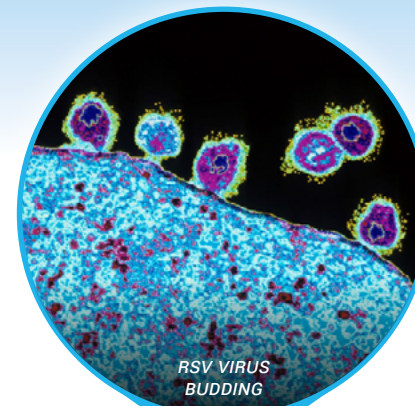
1990s/EARLY 2000s



2000s/2010s



2014



ONGOING

2015

ANNUALLY IN THE US, IN ADULTS 65 AND OLDER
RSV INFECTIONS:
2,400,000
MEDICAL INTERVENTIONS:
900,000
DEATHS: **14,000**

1956

RSV is first isolated from a group of chimpanzees

1957

Virus identified in humans¹

1963

Robert Chanock isolates and characterizes the virus

1966-69

Formalin-inactivated RSV was tested in infants and young children²

- The vaccine stimulated moderately high levels of serum antibodies but failed to induce resistance to infection
- Some vaccinated infants developed a more serious disease when later infected with the disease
- 2 infants died following infection with RSV

1970s

Sf insect cells first isolated from the ovaries of the fall armyworm (*Spodoptera frugiperda*)

Early 1980s

Novavax senior scientist and VP of Vaccine Development, Gale Smith, Ph. D., discovered the "Sf9" insect cell line could grow in apparent perpetuity in a special culture medium and can produce recombinant proteins upon infection with a baculovirus, a virus that infects only insects

1980s

Ribavirin, which decreases replication *in vitro*, shown to have no clinical utility in trials

1985-86

MedImmune develops monoclonal antibody; Palivizumab

Early 1990s

Wyeth tests a purified fusion (F) protein vaccine in children with cystic fibrosis³

- While protection against RSV infection was not observed, there was a significant reduction in lower respiratory tract illnesses, antibiotic courses and days ill

1994-97

MedImmune takes Palivizumab into clinical trials

1998

Palivizumab (Synagis; **MedImmune**) approved to treat lung disease and respiratory infections that result from RSV infection in premature infants

Early 2000s

Wyeth tests a subunit RSV vaccine with purified F protein via maternal immunization⁴

Wyeth tests a third-generation purified fusion protein vaccine in children with cystic fibrosis⁵

2007

Sanofi tests a subunit vaccine containing the RSV fusion (F), attachment (G) and matrix (M) proteins in the elderly⁶

2009

Initial **Novavax** preclinical data

2010-2013

Novavax Phase 1 clinical trials with Recombinant RSV F Vaccine⁷

- Vaccine induced anti-F IgG and palivizumab-competing antibody titers at levels associated with decreased risk of hospitalization

2013

Novavax announces positive data from Phase 2 trial of RSV F Vaccine in women of childbearing age

- Significant anti-F IgG antibody response across all vaccine doses

Novavax initiates Phase 2 dose-confirmatory trial of RSV F Vaccine in women of childbearing age

2013-2014

GSK Phase 1 clinical trial of recombinant RSV vaccine in healthy men⁸

Novavax announces positive data from Phase 2 dose-confirmatory trial of RSV F Vaccine in women of childbearing age

- Highest immune responses observed with a single dose of vaccine combined with aluminum phosphate adjuvant
- High levels of antibodies developed within 14 days after immunization and persisted over the 91-day observation period

MedImmune in Phase 1 with RSV sF antigen vaccine in older adults⁹

Novavax initiates Phase 2 clinical trial of RSV F Vaccine for protection of infants via maternal immunization

Novavax initiates Phase 2 clinical trial of RSV Vaccine in older adults (ages 60+)

Novavax granted Fast Track Designation by U.S. FDA for RSV F Vaccine for protection of infants via maternal immunization

2011-Ongoing

MedImmune/NIH/NIAID Phase 1 with recombinant live-attenuated vaccine in adults, children and infants¹⁰

2013-Ongoing

NIH/NIAID testing recombinant live-attenuated vaccines in Phase 1 with infants and children¹¹

ReiThera Srl in Phase 1 with vaccine based on the RSV viral proteins F, N and M2-1 encoded by Simian Adenovirus (PanAd3-RSV) and Modified Vaccinia Virus Ankara (MVA-RSV) in healthy and older adults¹²

2014-Ongoing

Novartis in Phase 1 with RSV F subunit vaccine in healthy adults¹³

GSK begins Phase 2 trial of recombinant RSV vaccine in healthy women¹⁴

Bavarian Nordic developing recombinant MVA-BN vaccine encoding two RSV surface proteins¹⁵

- Vaccine candidate induced protective immune response in a preclinical model, without inducing inflammation in the lungs as measured by induction of eosinophils

ImmunoVaccine in Phase 1 with SHe Antigen vaccine for older adults¹⁶

Crucell Holland BV in Phase 1 with human adenovirus-vectored vaccine in healthy adults¹⁷

Novavax announces first ever RSV vaccine to demonstrate efficacy in a prospective controlled clinical trial in any population

REFERENCES:

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⁴ Munoz, et al. 2003
⁵ Piedra, et al. 2003
⁶ Falsey, et al. 2008

⁷ Glenn, et al. 2013
⁸ <https://clinicaltrials.gov/ct2/show/NCT01905215>

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¹² <https://clinicaltrials.gov/ct2/show/NCT01805921?term=ReiThera+Srl&rank=1>
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