


# New Vaccines and Monoclonals in the Pipeline

November 3, 2022

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## Pipeline analysis – Sources and Process

- BIO uses a public database called BioMedTracker – detailed global information on all bio-pharmaceuticals in development or submitted for regulatory approval
- Supplemented with analysis of company websites and ClinicalTrials.gov
- Look at:
  - Vaccines under FDA review or in Phase II or III in their clinical trails
  - Monoclonal antibody products being researched primarily for preventive use (may include post-exposure prophylaxis)



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# Vaccines



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## Vaccines in Late-Stage Development – BLA / Phase III

Disease	Number of Products	Phase III or FDA Review
SARS CoV-2	8	Updates to existing vaccines; Multiple vaccines using other platform technologies; partnership between US and Indian company
RSV	6	Maternal and older adult indications; various platforms deployed
HIV	1	Adeno virus approach
Seasonal Influenza	3	New mRNA and protein-based vaccines
Men ABCWY	2	Adding MenB to ACWY vaccines
Pneumococcal	1	21-valent pneumo conjugate for older adults
CMV	1	mRNA based vaccine for healthy young adult women
C Difficile	1	Targeting specific populations at risk
Chikungunya	2	One vaccine under FDA review; another in Phase III
Dengue	1	
Ebola / Marburg	1	BARDA / DoD bio-threat
Lyme	1	Partnership between two companies; multivalent, recombinant; potentially children and adults

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## Pfizer's RSVpreF Vaccine Candidate Program

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### Vaccine


**Bivalent stabilized prefusion F**

- Sequence based on contemporary **RSV A and RSV B strains**
- Elicited **high neutralizing titers** for both RSV A and RSV B in Phase 1/2 studies<sup>1,2,3</sup>




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### Targeted Indications




**Maternal**  
Immunize pregnant women to prevent RSV-associated lower respiratory tract illness (LRTI) in infants from birth through 6 months of age



**Older adult**  
Active immunization to prevent RSV-associated LRTI in adults ≥ 60 years of age

<sup>1</sup>Fairley A., et al. J. Infect Dis 2022;225(12):2056-2066. <sup>2</sup>Walsh E., et al. J. Infect Dis 2022;225(8):1357-1366. <sup>3</sup>Baber J., et al. J. Infect Dis 2022 May 11 jiaac189.



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<https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-10-19-20/03-RSV-Adults-Gurtma-508.pdf>

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### GSK's RSV older adult vaccine

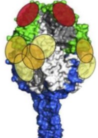
The combination of RSVPreF3 (120 µg) and AS01<sub>E</sub> is designed to induce a robust humoral and cellular immune response, to help protect older adults and those with underlying comorbidities

RSVPreF3 OA Vaccine

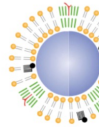
RSVPreF3 Antigen (120 µg)

+

AS01<sub>E</sub> Adjuvant System



Antigen engineered to preferentially maintain the pre-fusion conformation and display potent neutralizing epitopes to boost humoral immune response in older adults<sup>1,2</sup>



Boosts cellular immune response and restores the RSVPreF3 CD4+ T-cell level in older adults<sup>2</sup>

AS01<sub>E</sub>, Adjuvant System 01; (25 µg Quilja saponaria Molina, fraction 21, 25 µg 3-Oleacyl-4'-monophosphoryl lipid A); OA, older adults. Image of F protein reproduced from Graham BS, et al. *Curr Opin Immunol* 2015;35:30-38. Copyright 2015, with permission from Elsevier.

1. Graham BS, et al. *Curr Opin Immunol*. 2015;35:30-38. 2. Lemaire-Pardois L, et al. *J Infect Dis*. 2022;jae327.

Slides are confidential and provided to the ACIP voting members and are not for distribution.

<https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-10-19-20/02-RSV-Adults-Rizkalla-508.pdf>

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### Both clinical trials showed significant efficacy against lower respiratory tract disease/illness caused by RSV

- Efficacy point estimates against the primary outcomes in both trials exceeded 60%
- Based on a small number of total events (<50 in each trial)

GSK			Pfizer		
Outcome	n/N, vaccine	n/N, placebo	Outcome	n/N, vaccine	n/N, placebo
RSV LRTD <sup>a</sup>	7/12,466	40/12,494	RSV LRTI ≥2 symptoms <sup>b</sup>	11/16,306	33/16,308
			RSV LRTI ≥3 symptoms <sup>b</sup>	2/16,306	14/16,308

<sup>a</sup> Lower respiratory tract disease: ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours  
<sup>b</sup> Lower respiratory tract illness: ≥2 or ≥3 lower respiratory signs/symptoms lasting more than 1 day

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<https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-10-19-20/04-RSV-Adults-Melgar-508.pdf>



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### Both clinical trials showed significant efficacy against lower respiratory tract disease/illness caused by RSV

- Efficacy point estimates against the primary outcomes in both trials exceeded 60%

GSK		Pfizer	
Outcome	Efficacy (%), 96.95% CI	Outcome	Efficacy (%), 95% CI
RSV LRTD <sup>a</sup>	82.6 (57.9–94.1)	RSV LRTI ≥2 symptoms <sup>b</sup>	66.7 (32.5–84.8)
		RSV LRTI ≥3 symptoms <sup>b</sup>	85.7 (37.9–98.4)

<sup>a</sup> Lower respiratory tract disease: ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours  
<sup>b</sup> Lower respiratory tract illness: ≥2 or ≥3 lower respiratory signs/symptoms lasting more than 1 day

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**Expect efficacy against more severe outcomes to be at least as high as efficacy against lower respiratory tract disease/illness**

	GSK		Pfizer	
	Outcome	Efficacy	Outcome	Efficacy
Increasing severity ↓	RSV acute respiratory illness <sup>a</sup>	71.7%	RSV acute respiratory illness <sup>b</sup>	62.1%
	RSV lower respiratory tract disease <sup>c</sup>	82.6%	RSV lower respiratory tract illness ≥2 symptoms <sup>d</sup>	66.7%
			RSV lower respiratory tract illness ≥3 symptoms <sup>d</sup>	85.7%
	RSV lower respiratory tract disease with ≥2 lower respiratory <b>signs</b> or assessed as <b>'severe'</b> by investigator	94.1%		

<sup>a</sup> Acute respiratory illness: ≥2 respiratory symptoms/signs for ≥24 hours OR ≥1 respiratory symptom/sign +1 systemic sign for ≥24 hours  
<sup>b</sup> Acute respiratory illness: ≥1 respiratory symptom lasting more than 1 day  
<sup>c</sup> Lower respiratory tract disease: ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours  
<sup>d</sup> Lower respiratory tract illness: ARI with ≥2 or ≥3 lower respiratory signs/symptoms

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<https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-10-19-20/04-RSV-Adults-Melgar-508.pdf>


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## Vaccines in Phase II Development – Part 1

Disease	Number of Products	Phase III or FDA Review
SARS CoV-2	3	Updates to existing vaccines; Multiple vaccines using other platform technologies, including next generation mRNA and tablet form
RSV	2	Various platforms deployed targeting infant RSV vaccination
Seasonal Influenza	5	Includes mRNA flu vaccines, a live universal flu vaccine, a tablet platform and another universal flu approach
Pneumococcal	3	New mechanisms for developing higher valency pneumococcal vaccines
Pertussis	1	Live, attenuated nasal vaccine
Varicella	1	Updated strains
Zoster	1	New vaccine for older adults
Chikungunya	1	Recombinant vaccine
Norovirus	2	Bi-valent vaccine


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## Vaccines in Phase II Development – Part 2

Disease	Number of Products	Phase III or FDA Review
HIV	2	Includes vaccines based on adeno and modified vaccinia platforms
Malaria	3	New approaches leveraging mosquitos for malaria vaccines; adjuvanted version of existing vaccine
Dengue	1	
CMV	1	Vaccine focused on healthy young women

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## Trends is Earlier Stage R&D

- Over the next few years we will see new strategies for COVID-19 vaccines as well as possible seasonal respiratory combination vaccines – SARS CoV2 + Influenza + RSV.
- Several companies are working on vaccines for:
  - New vaccines for HPV, Herpes Simplex, pediatric combination vaccines
  - Hospital-acquired bacterial infections
  - Group B Strep
  - STI vaccines like Gonorrhea
  - New approaches to universal influenza vaccination

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# Monoclonal Antibodies



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## Monoclonal Antibodies in Late-Stage Development – BLA/NDA/Phase III

Disease	Number of Products	Phase III or FDA Review
SARS Cov-2	5	Updated versions of mAbs for prevention of severe disease; one is under review at the FDA
RSV	2	mAbs for population health use in infants for seasonal protection
Rabies	1	Post-exposure prophylaxis for those exposed to rabies
Staphylococcal	1	Long-acting mAb for prevention of ventilator-associated pneumonia in S. Aureus colonized patients



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## Nirsevimab for the prevention of RSV LRTI - an unmet public health need

- >550,000 infants receive medical attention for RSV LRTI annually in US
- Leading cause of infant hospitalization regardless of birth month

- Most medically attended cases, including severe cases, occur in healthy infants born at term<sup>5-9</sup>
- Infants on Medicaid at increased risk of serious disease

nirsevimab

RSV A2 F

- Highly potent recombinant human IgG1 kappa MAB
- Conserved epitope on pre-fusion RSV F protein
- Prolonged serum half-life (YTE technology)

- Once per RSV season fixed IM dosing
- Rapid protection
- Flexible administration relative to seasonality

IgG, immunoglobulin G; IM, intramuscular; LRT, lower respiratory tract; LRTI, lower respiratory tract infection; MAB, monoclonal antibody; RSV, respiratory syncytial virus.  
<sup>1</sup>Nair et al, *Lancet* 2010;375:1545-1555, <sup>2</sup>Shi et al, *Lancet* 2017;390:946-958, <sup>3</sup>Lambert et al, *Front Immunol* 2014;5:466, <sup>4</sup>Li et al, *BMC Medicine* 2020;18:82, <sup>5</sup>Sommer et al, *Open Microbiol J* 2011;5:144, <sup>6</sup>Murray et al, *PLoS ONE* 2014;9:e89186, <sup>7</sup>Bont et al, *Infect Dis Ther* 2016;5:217-298, <sup>8</sup>Hall et al, *Pediatrics* 2013;132:e341-348, <sup>9</sup>Rha et al, *Pediatrics* 2020;146:e20193611

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## Pooled MELODY All Subjects AND Phase 2b Recommended Dose

**MELODY subjects N=3012**  
**Ph 2b recommended dose subjects N=860**

**Efficacy through D151**

Definition	Placebo (N=1293)		Nirsevimab (N=2579)		Efficacy	
	n	%	n	%	Efficacy	95% CI
MA RSV LRTI	80	6.2	31	1.2	<b>79.0</b>	68.5-86.1
MA RSV LRTI with hospitalization	33	2.6	12	0.5	<b>80.6</b>	62.3-90.1
MA RSV LRTI (very severe)	28	2.2	7	0.3	<b>86.2</b>	68.1-94.0

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LRTI, lower respiratory tract infection; MA, medically attended; RSV, respiratory syncytial virus  
Very severe = hospitalization + requirement for supplemental oxygen and/or intravenous 16

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## Monoclonal Antibodies in Development – Trends

- Increasing research of this new preventive / treatment modality is leading to a deep pipeline of possible products
- Many may be indicated for both prevention of severe disease in specific populations as well as treatment of early stage disease
- The following therapeutic areas have mAbs on interest in development:
  - Influenza
  - HIV (Prep and prevention of severe disease)
  - Hospital-acquired infections for those at risk
  - Treatment and prevention of Sepsis

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Questions

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