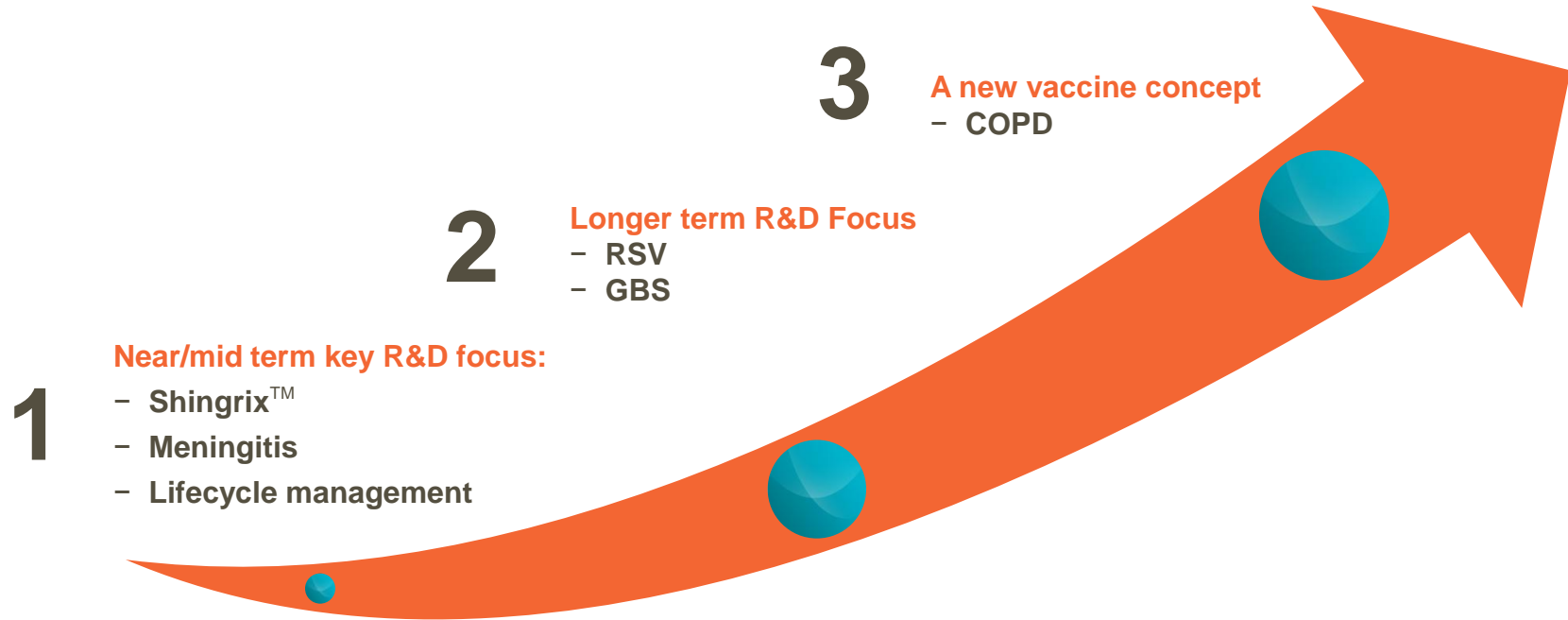




Moncef Slaoui

Chairman of Vaccines

R&D programmes to deliver near-term growth with significant future opportunities and novel immunisation platforms





Shingrix™

Shingrix™ is not approved for use by the FDA or EMA

One dose, live attenuated vaccine

Efficacy: 51% against shingles in ages 60+

- Inverse correlation between age at vaccination and protection
- Limited persistence of protection

Indication for ages 50+

US ACIP recommendation for ages 60+

Contraindicated in immunocompromised individuals

Estimated to have <25% coverage in US*

2014 reported sales of \$868m (>\$600m in US)

Shingrix candidate vaccine developed to differentiate



Two doses, sub-unit (non-live) vaccine, novel adjuvant

Efficacy: 91% - 97% against shingles

- High efficacy across identified age groups
- Persistence over time

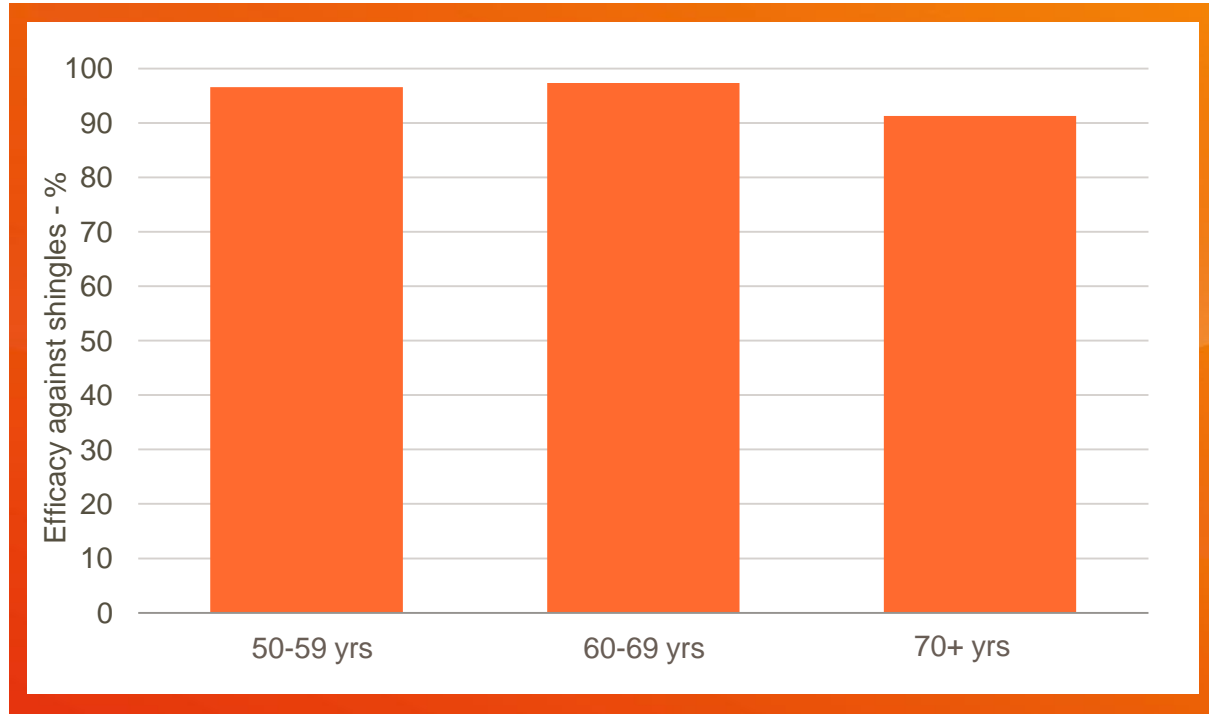
Targeting indication and recommendation in ages 50+

Data on immunocompromised individuals in 2017

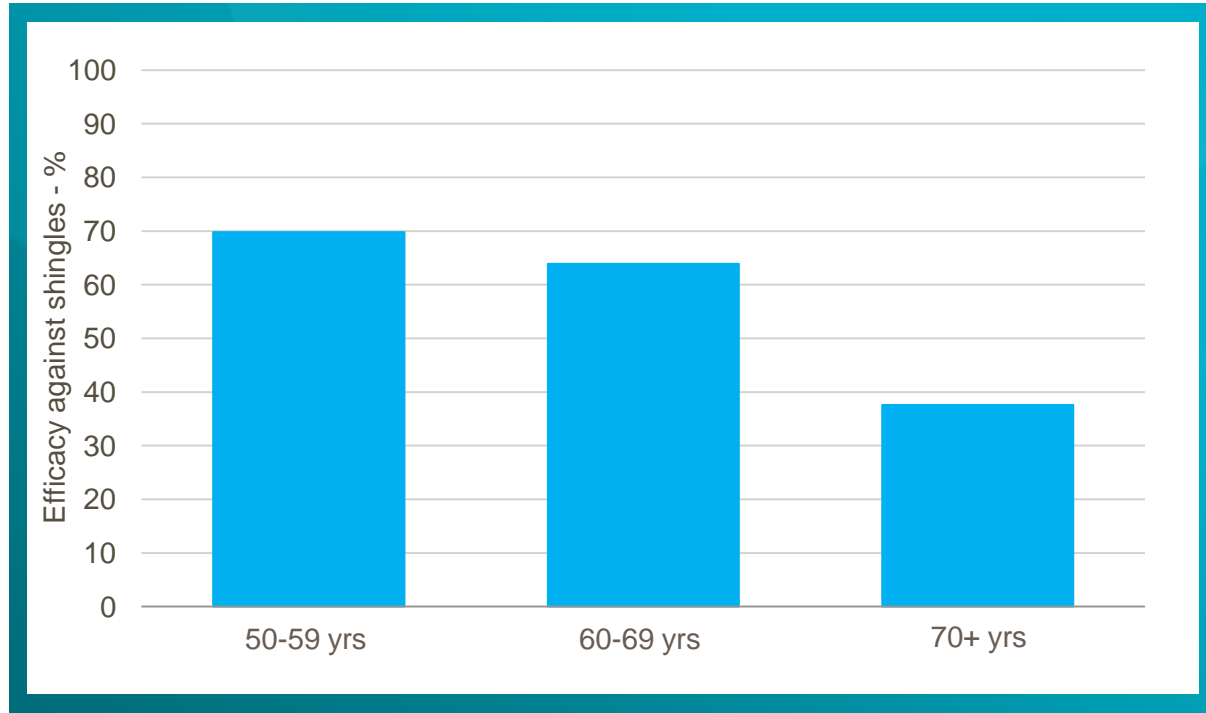
Expect US, EU, Japan filings in 2H 2016

Expected to contribute ~1/3 of 2020 sales growth targets for GSK vaccines

Shingrix - Efficacy against shingles



Existing vaccine - Efficacy against shingles



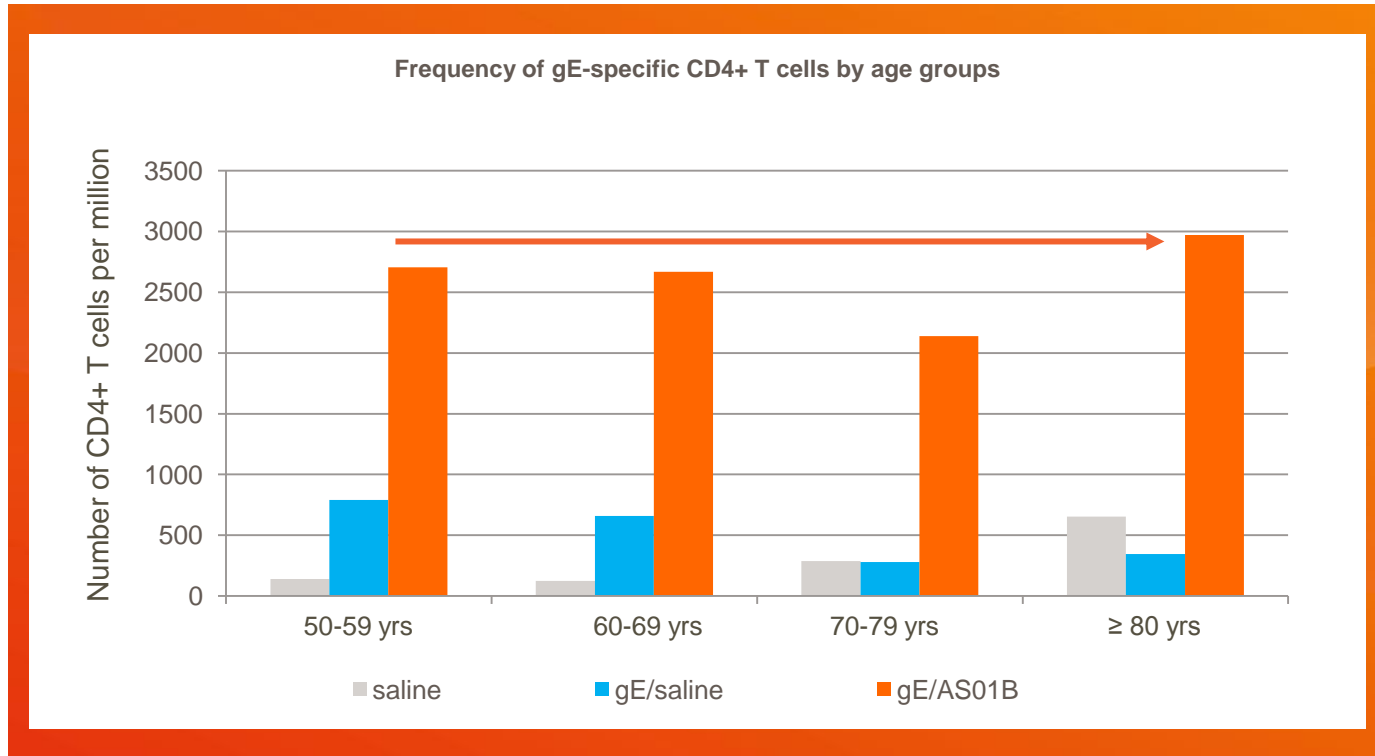
Oxman *et al.* N Engl J Med 2005; 352: 2271–84;

Schmader *et al.* Clinical Infectious Diseases 2012;54(7):922–8;

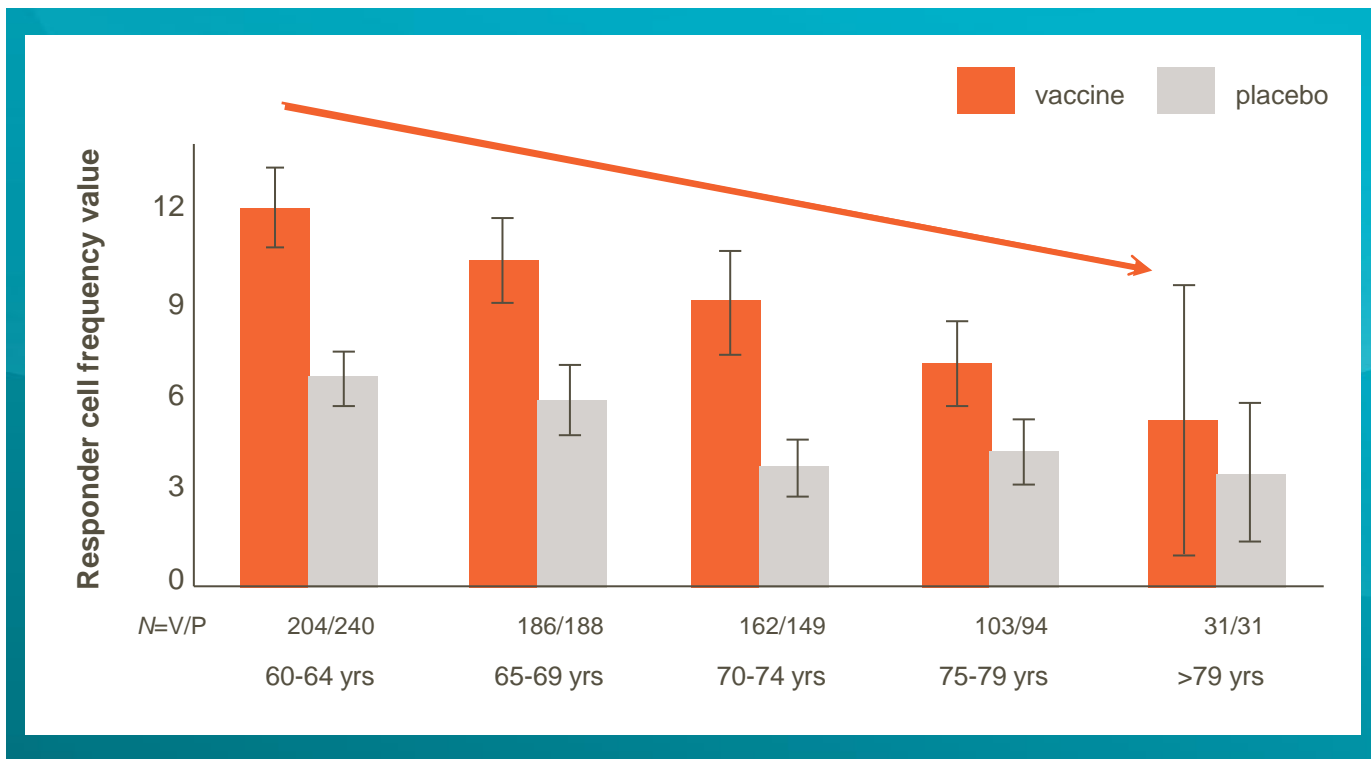
Zostavax™ US PI

Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Zostavax data based on US PI.

Shingrix - Immune response across age segments



Existing vaccine - Immune response across age segments

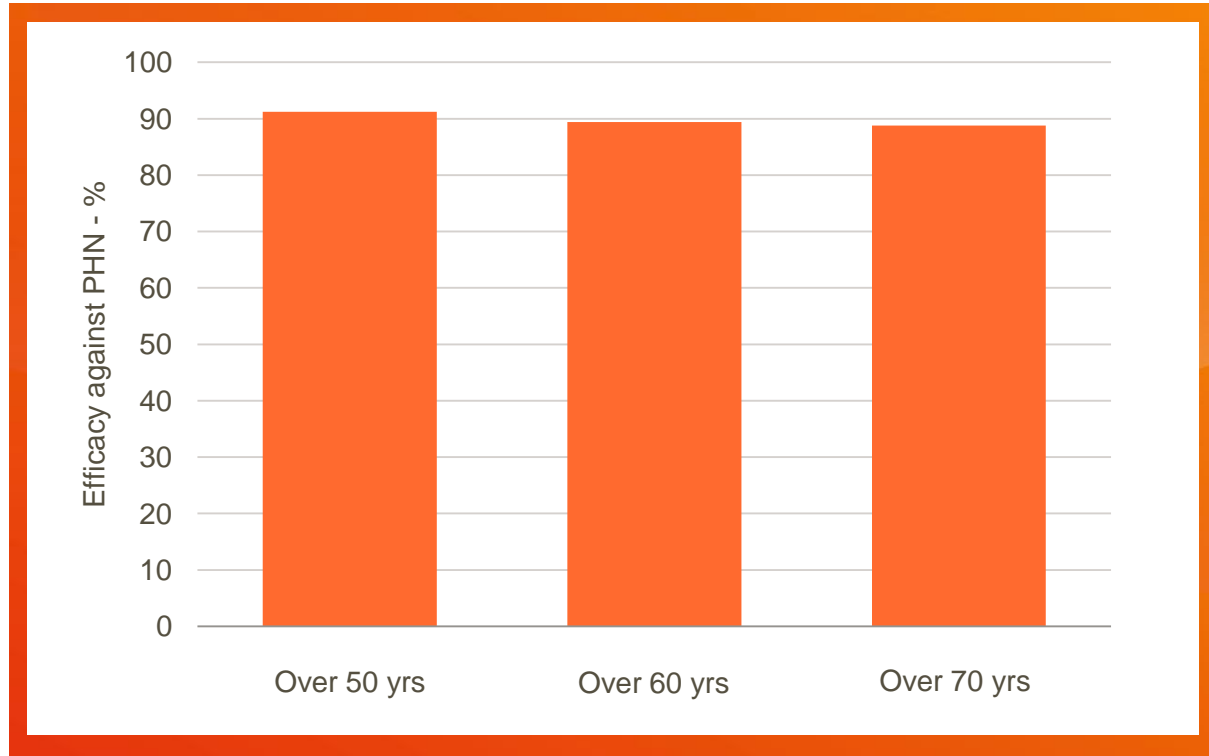


Levin *et al.* J Infect Dis 2008; 197:825–35

Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Zostavax data based on published data.

Shingrix - Efficacy against PHN

PHN: post herpetic neuralgia, a severe complication of zoster

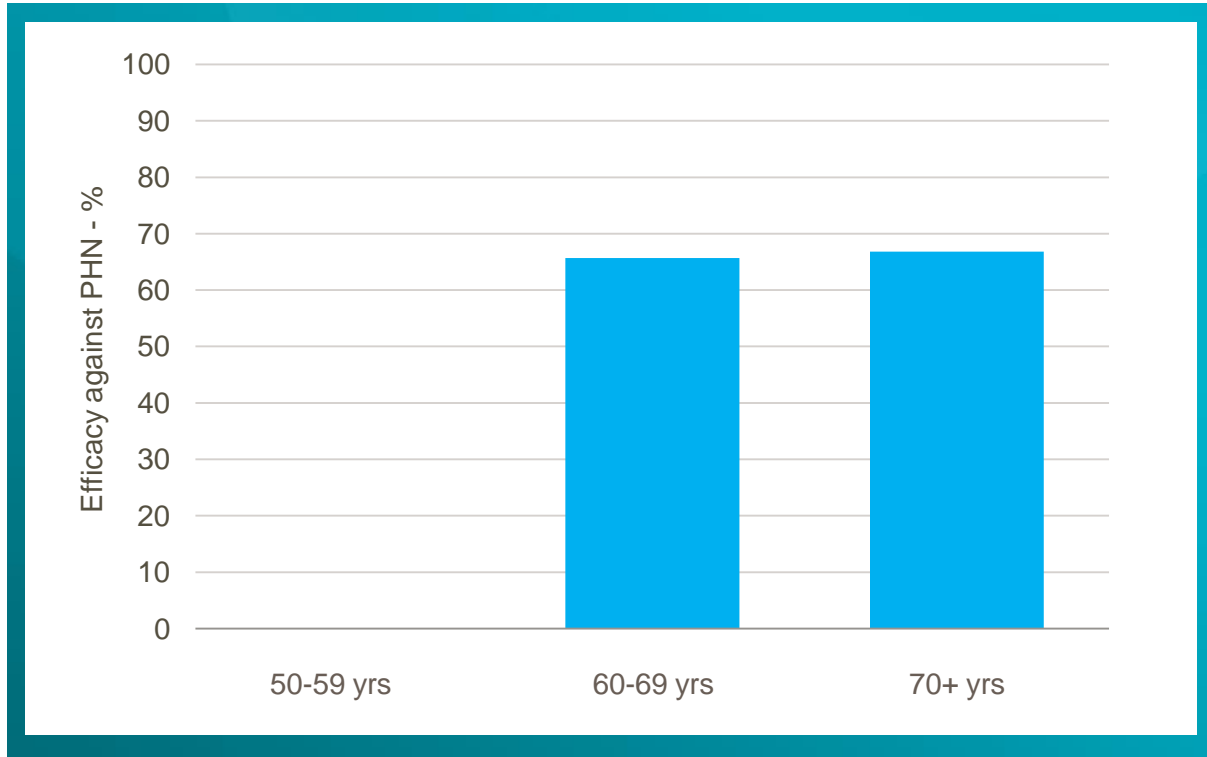


ZOE-50 and ZOE-70 pooled analysis – unpublished data

Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Shingrix data based on phase III clinical trials.

Existing vaccine - Efficacy against PHN

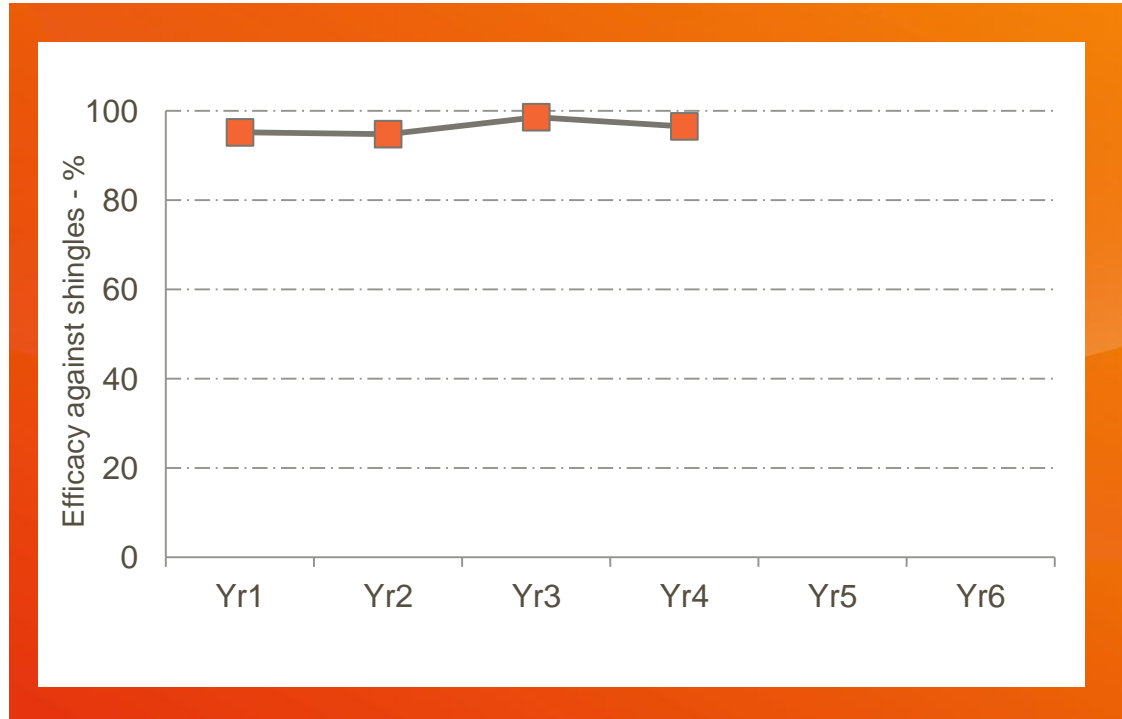
PHN: post herpetic neuralgia, a severe complication of zoster



Zostavax US PI; Oxman *et al.* N Engl J Med 2005

Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Zostavax data based on published data.

Shingrix - Duration of protection against shingles



ZOE-50 statistical report – unpublished data

Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Shingrix data based on ph III clinical trials.

Existing vaccine - Duration of protection against shingles



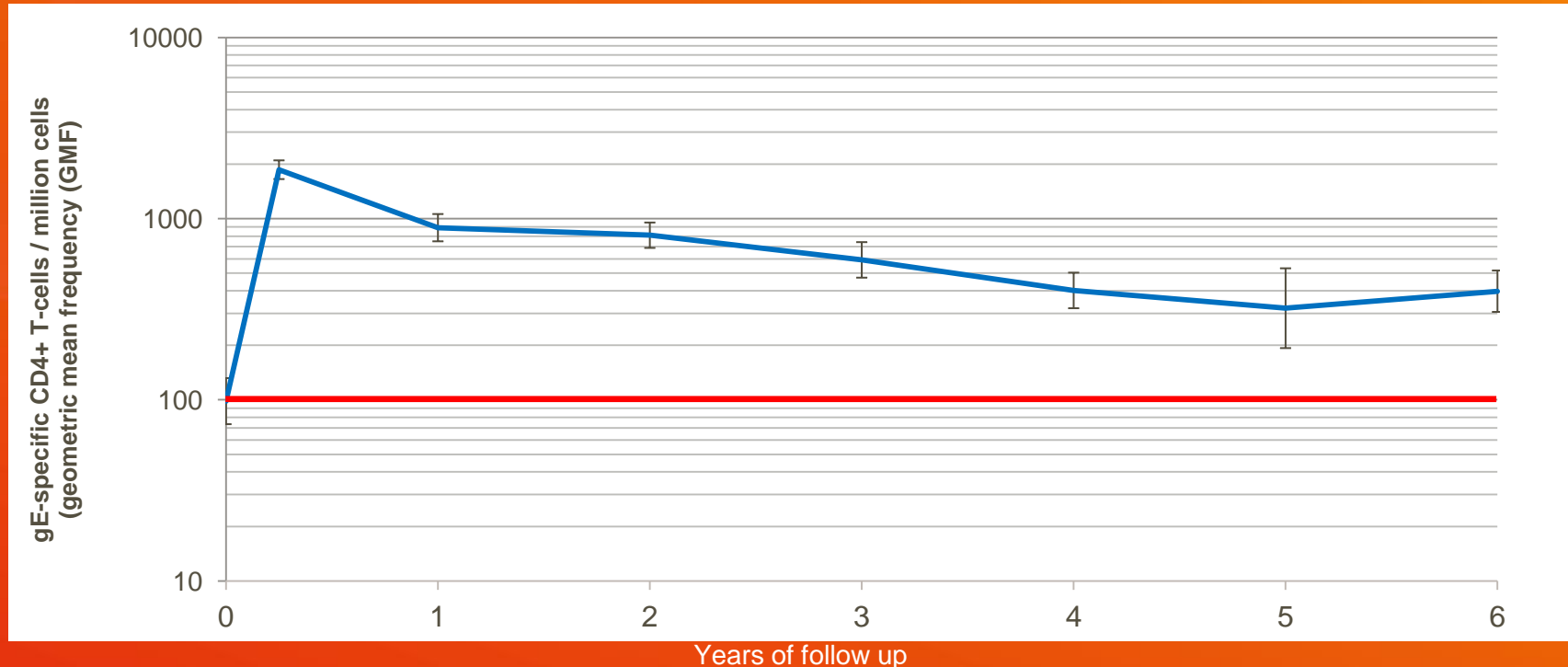
Morrison *et al.* Clin Infect Dis 2015; 60: 900-909

Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Zostavax data based on published data.

Immune response persistency is a good predictor of duration of efficacy



Shingrix immune response



Shingrix: a potentially significant advance in vaccination to prevent shingles



High overall vaccine efficacy across identified age groups, including oldest persons

Persistence of vaccine efficacy up to 4 years across all ages

Six-year persistence of immune response, modeled to persist above baseline for at least 15 years (based on 6 year data)

Clinically acceptable reactogenicity

AS01 adjuvant = new platform for elderly vaccines

Annual capacity of ~25-30m doses by 2020



●
H2: US, EU, Japan
Filings

Planned/ongoing studies:

- Vaccine co-administration
- Revaccination of Zostavax* population
- Comparative tolerability

●
Phase III efficacy study
in immuno-compromised

*Zostavax is a trademark of Merck & Co

Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Shingrix data based on clinical trials.



Meningococcal Meningitis

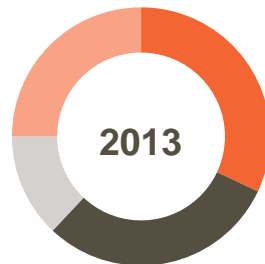
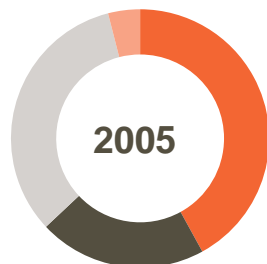
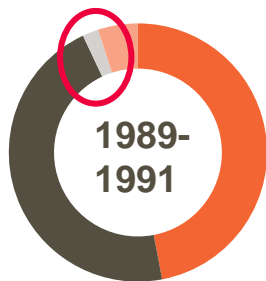
Meningococcal disease: evolving and unpredictable epidemiology – requires combination vaccine



~139 million annual global birth cohort ¹

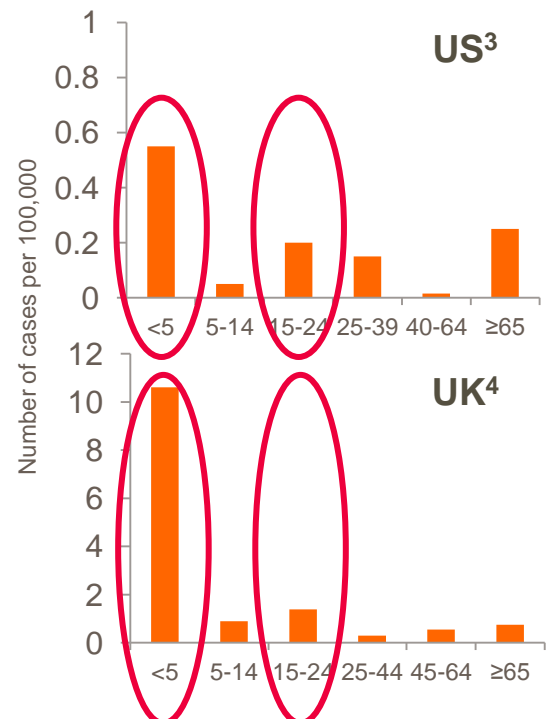
~4m US, ~5m EU, ~130m ROW

Changes in serogroup distribution in US over time²



■ B ■ C ■ Y ■ W, A & Other

Disease incidence by age (2012)



Most advanced meningitis vaccines portfolio, including candidate pentavalent



Menveo™

- MenACWY tetravalent vaccine
- Approved in US and EU (2010)
- ACIP recommendation for adolescents
- Approved in 64 countries
- 2015 sales (Mar – Sept): £135m

Bexsero™

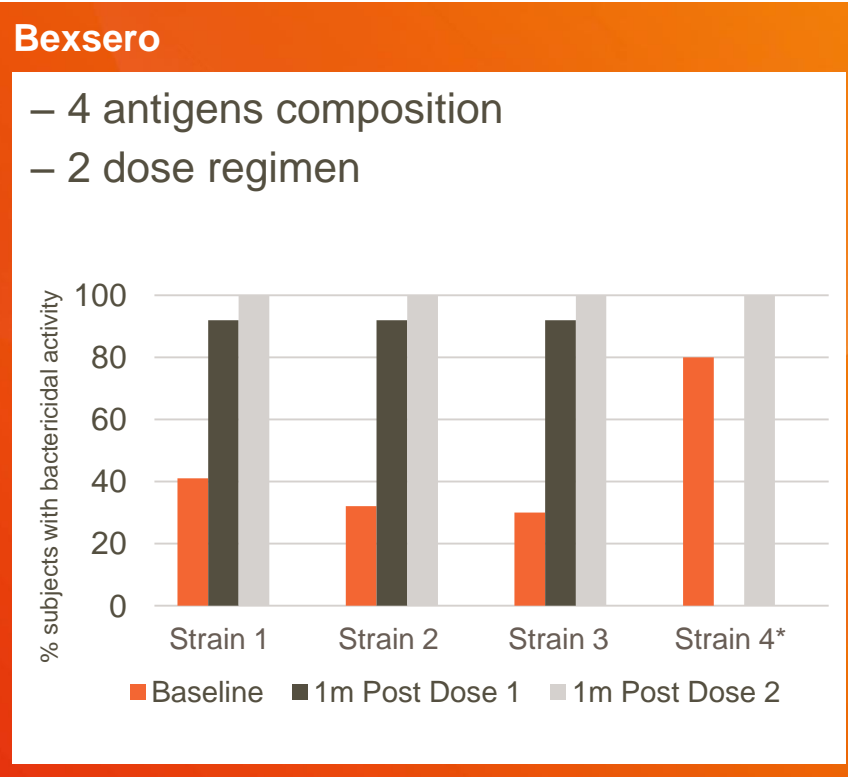
- MenB vaccine
- Approved in US in 2015 (adolescents) and EU (2 months old and above)
- ACIP category B (permissive) recommendation
- Approved in 38 countries
- 2015 sales (Mar – Sept): £78m

MenABCWY

- Candidate pentavalent combination vaccine for adolescent in US
- Most advanced in development
- Phase III start in 2017
- US filing expected in 2020

Meningitis portfolio expected to contribute ~1/3 of 2020 sales growth targets for GSK vaccines

Bexsero: multi-component antigen composition adds value, differentiation

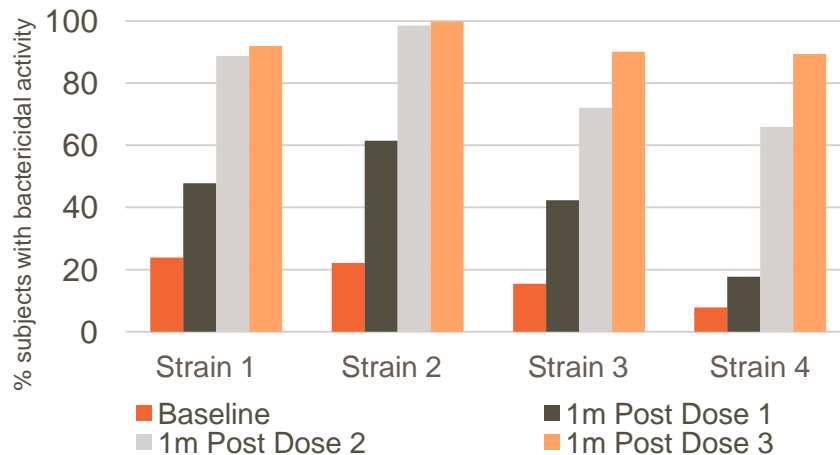


Competing vaccine for MenB



Competing vaccine

- 1 antigen composition with 2 variants
- 3 dose regimen



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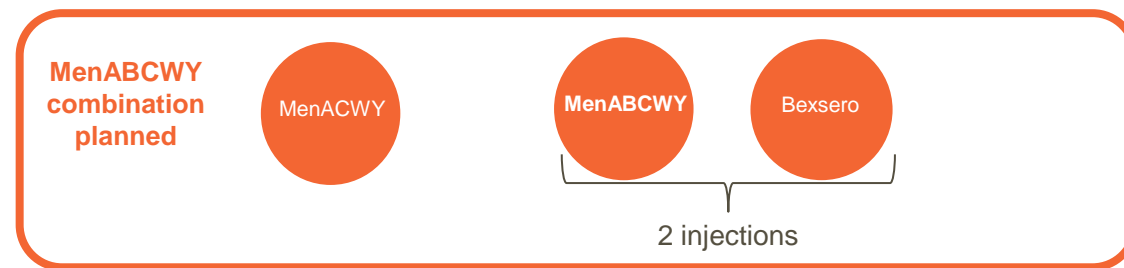
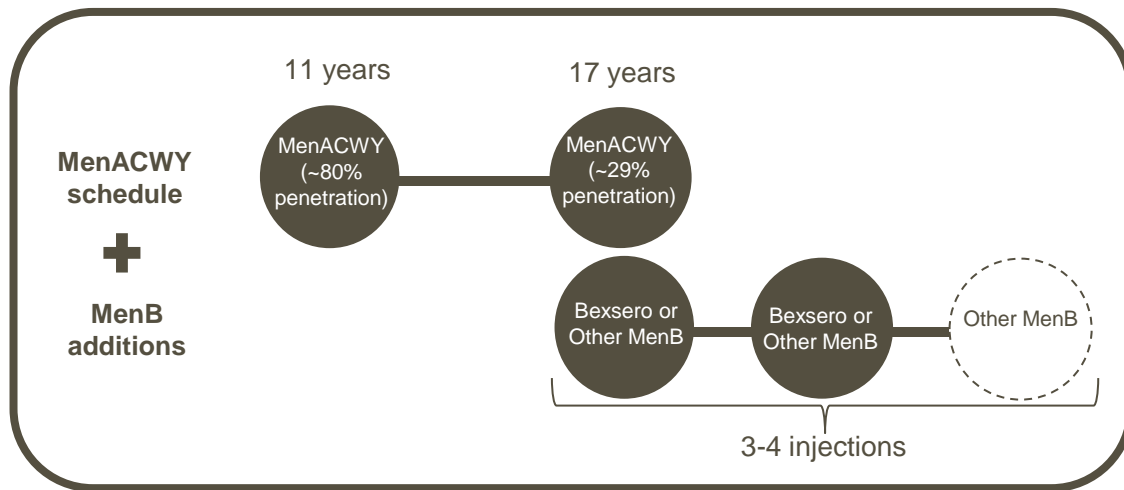
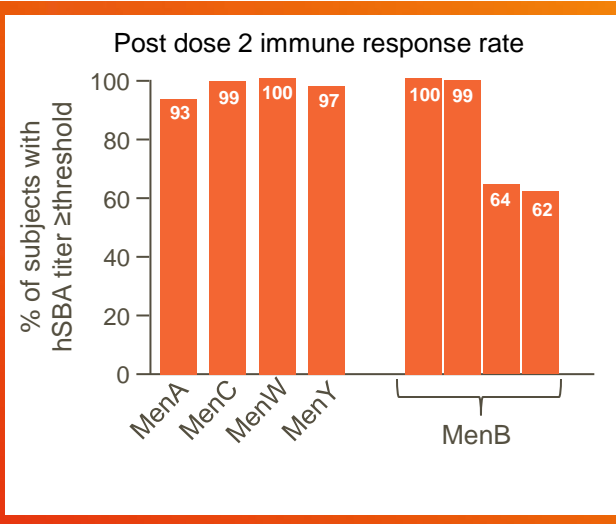
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MenABCWY Phase III starts in 2017



- US focused development
- 1 dose adolescent booster
- Phase III programme start in 2017
- Filing expected 2020 for adolescents previously immunised for MenACWY



Meningitis portfolio presents significant opportunity

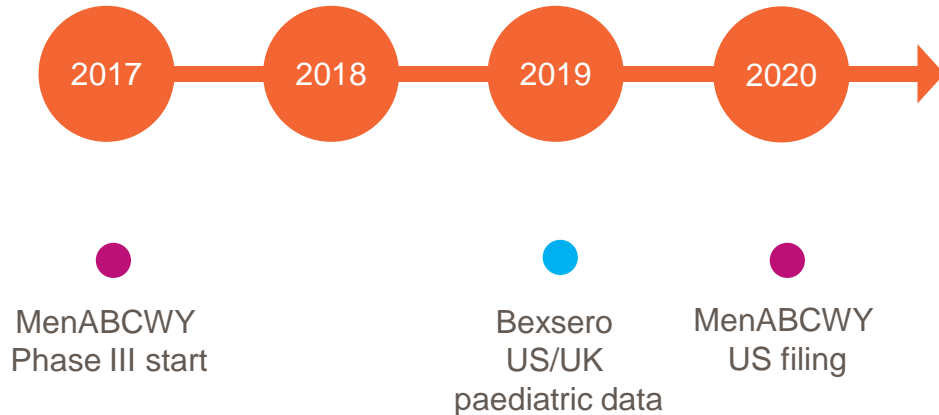


GSK has most advanced and comprehensive portfolio for meningitis vaccines

Bexsero demonstrated significant public health benefit, could drive further UMV recommendations

Combination approach is optimal option for prevention

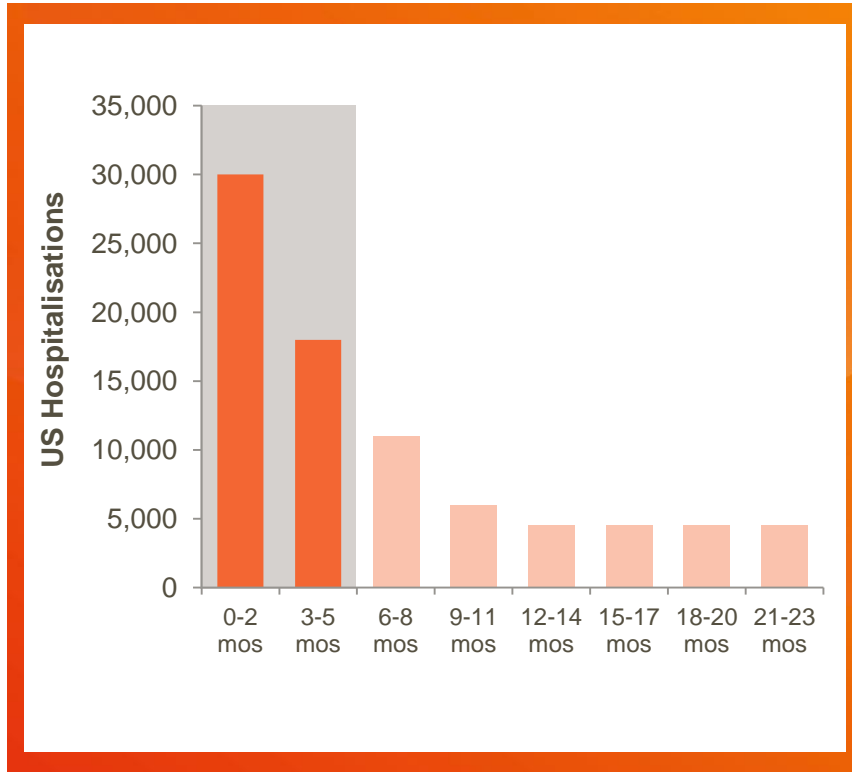
Bexsero capacity ~25m doses in 2018



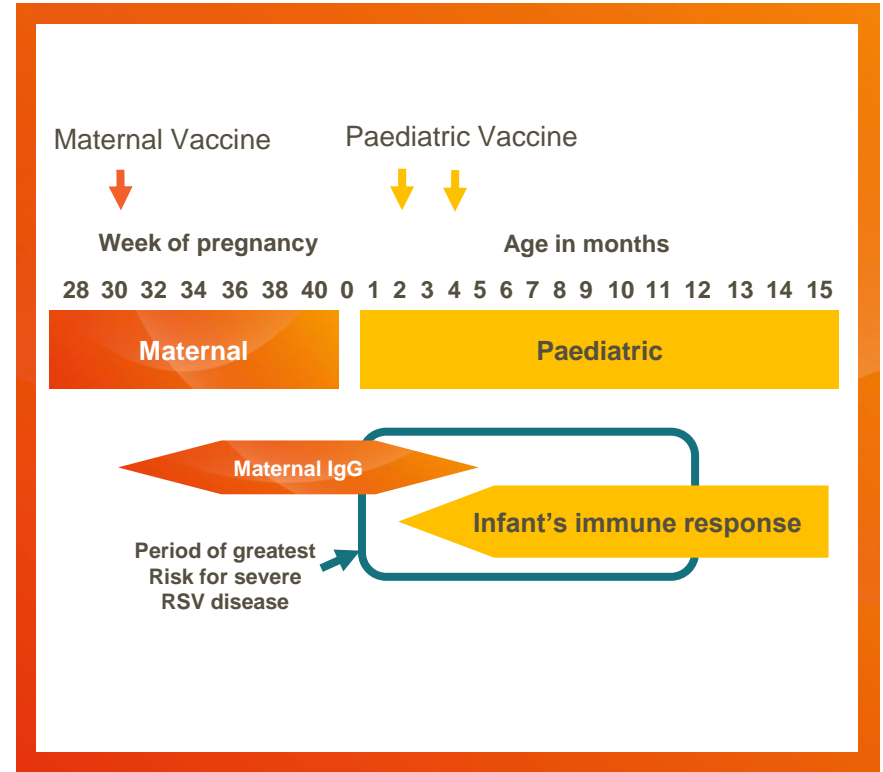
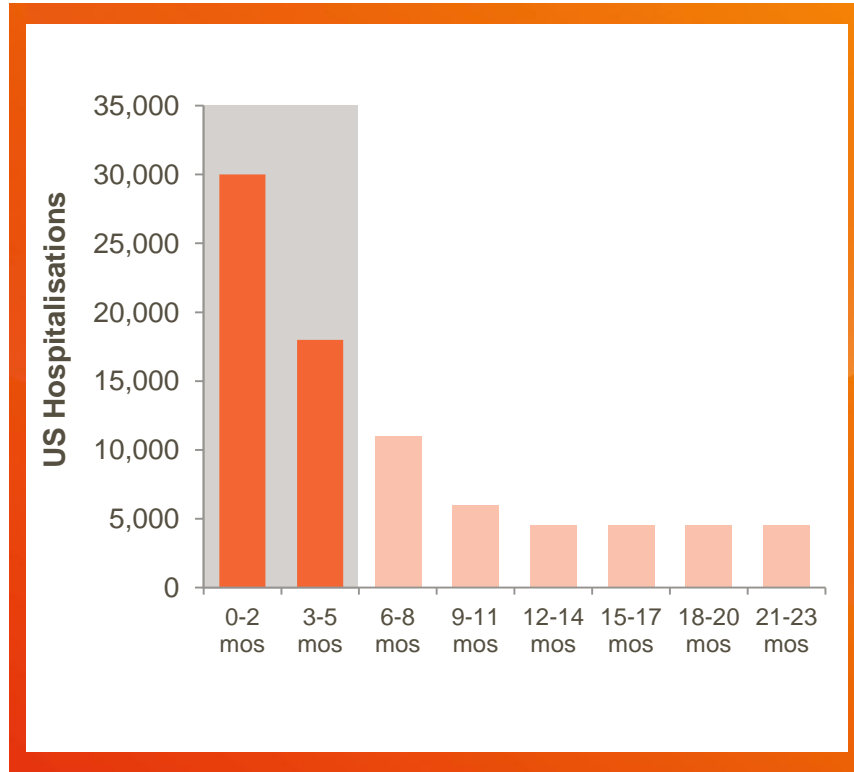


Respiratory Syncytial Virus (RSV)

Period of most severe RSV cases for young infants occurs from birth to 12 months



Period of most severe RSV cases for young infants occurs from birth to 12 months



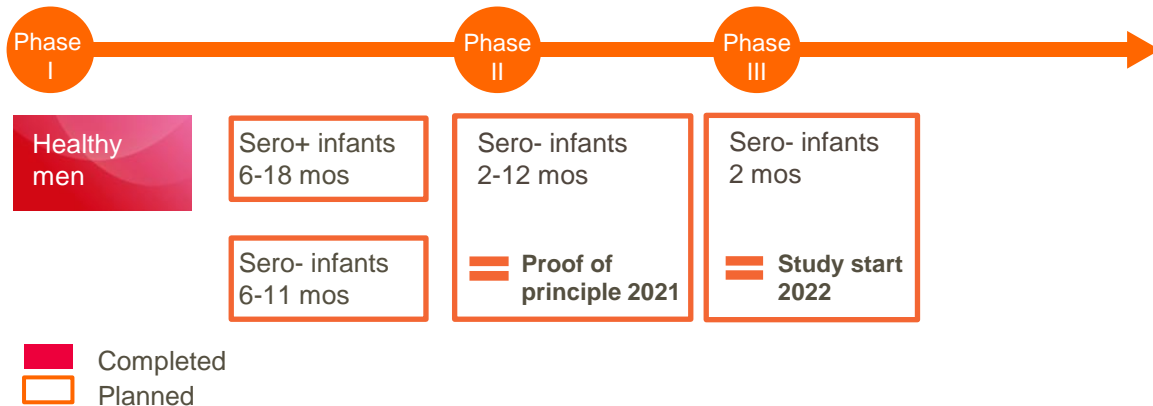
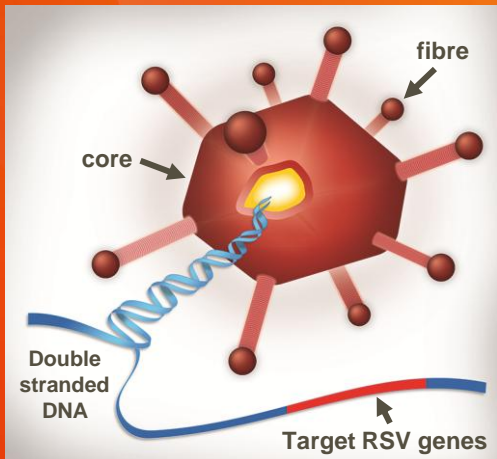
Candidate paediatric RSV vaccine, a novel approach



Genetically engineered recombinant CHAd155

Same vector used in ebola vaccine

Non-alum composition

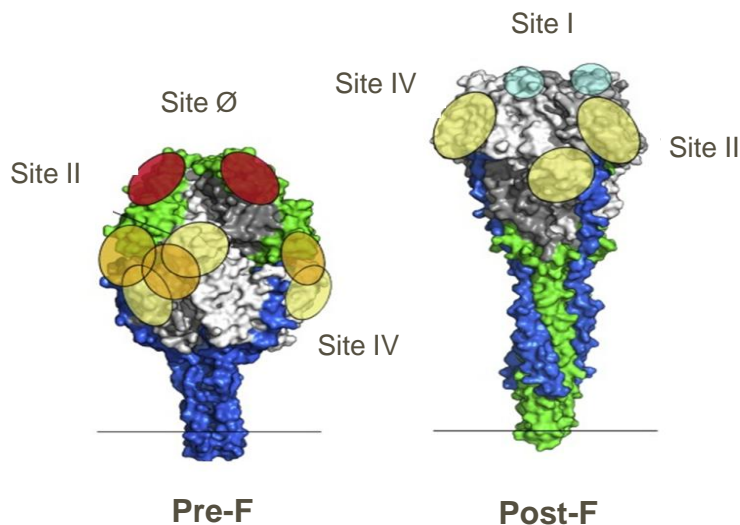


Novel candidate RSV maternal vaccine approach



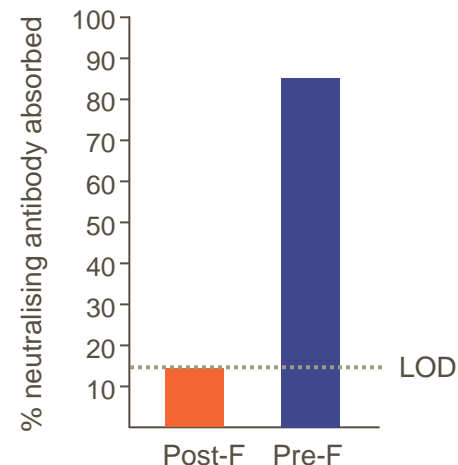
For RSV F protein, the correct antigen structure is critical

Pre-F absorbs out neutralising RSV antibodies more than 10x better than Post-F and induces potent antibody responses in humans



Graham B et al., Current Opinion in Immunology 35; 30-38, 2015

Absorption with Pre-F but not Post-F depletes neutralising IgG from convalescent serum

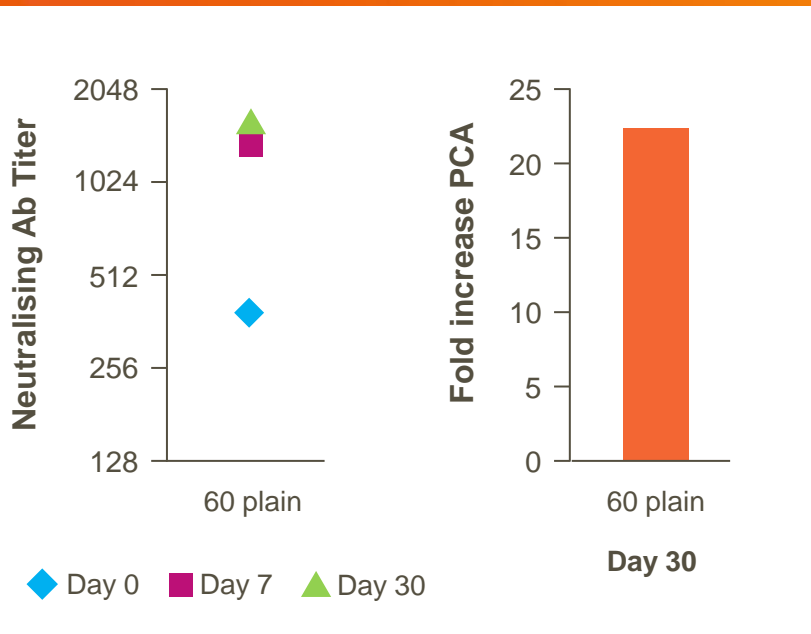


GSK preclinical data, unpublished

Stabilised Pre-F generated high titers by Day 7 and potent boost of PCA without adjuvant



GSK Pre-F

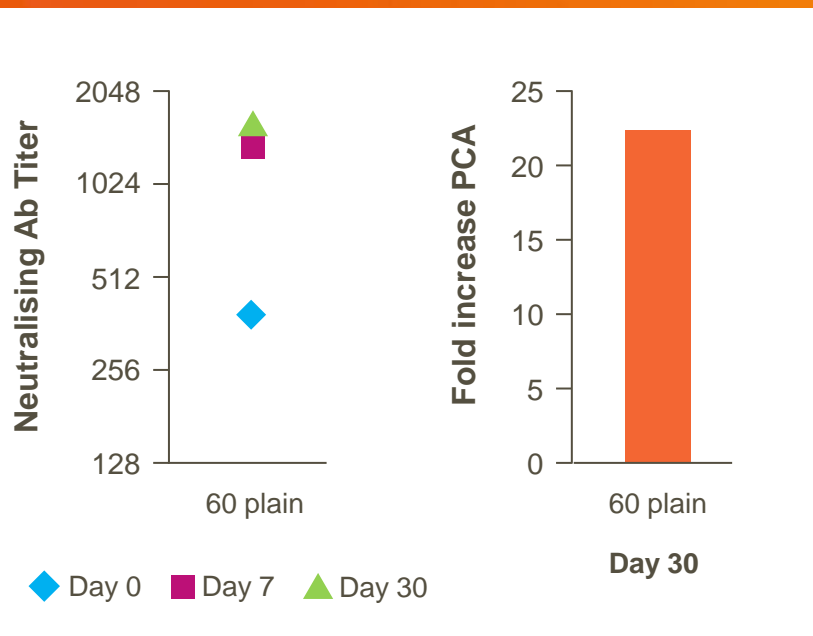


>20 fold PCA increase after single dose without adjuvant

Stabilised Pre-F generated high titers by Day 7 and potent boost of PCA without adjuvant

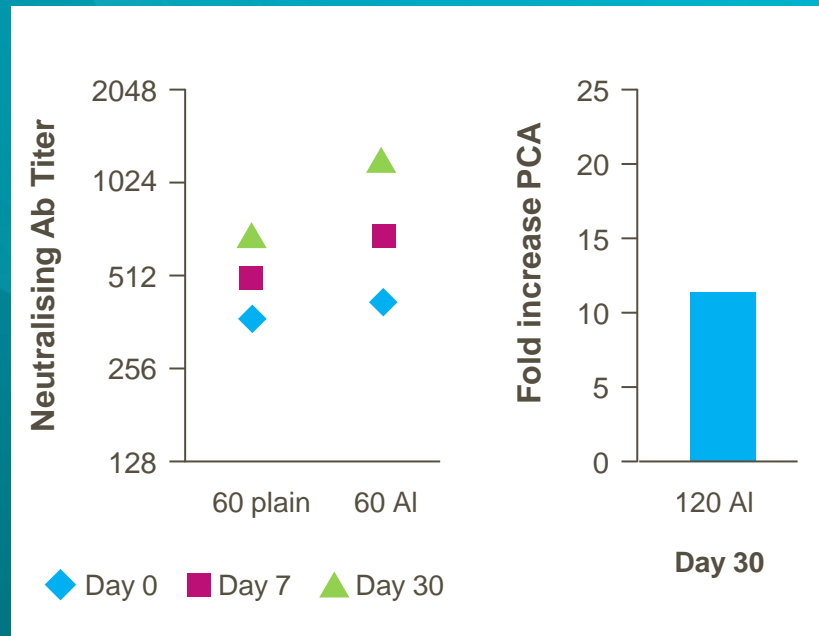


GSK Pre-F



>20 fold PCA increase after single dose without adjuvant

Post-F



>10 fold PCA increase requires 120 ug + adjuvant

Novel candidate RSV maternal vaccine approach



Healthy men

Non-pregnant women

Pregnant women
Dose selection

==

**Proof of principle
2018**

VE in infants of vaccinated women

==

**Study start
2019**

-  Completed
-  Ongoing
-  Planned



Group B Streptococcus (GBS)

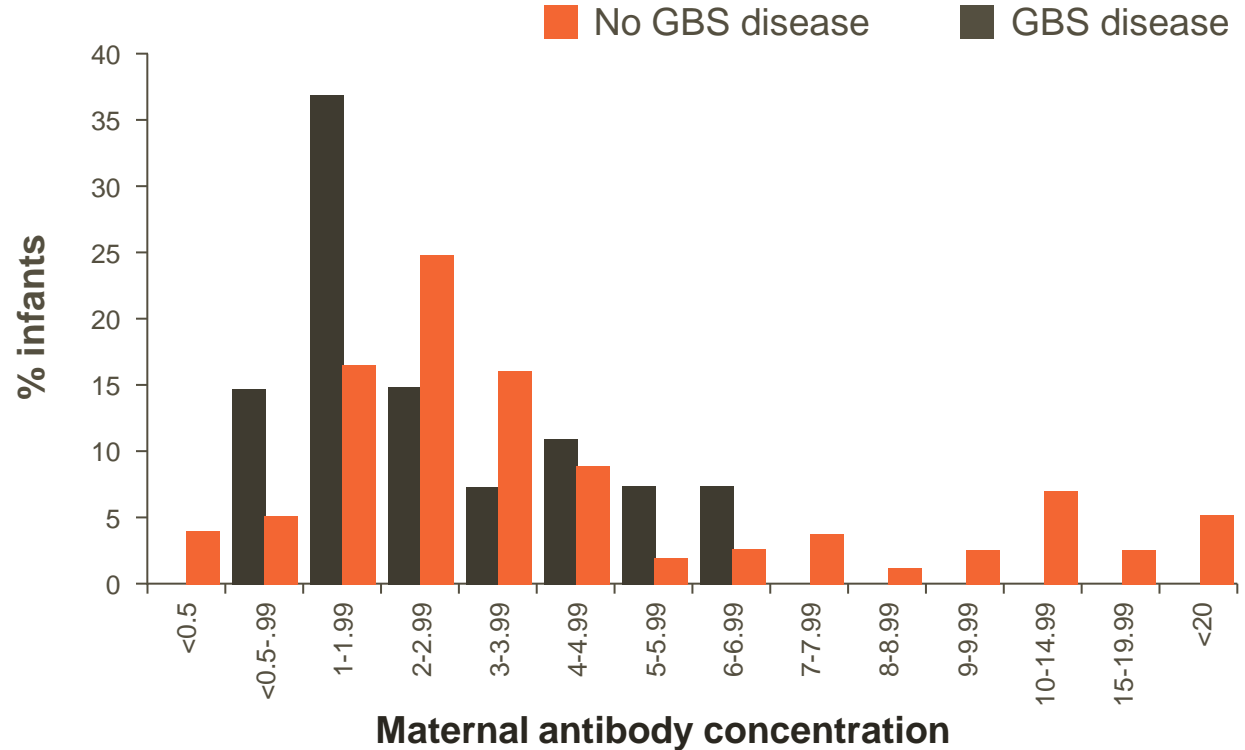
Maternal immunisation for GBS



The leading cause of pneumonia, meningitis and sepsis in neonates

1 in 2500 of babies develop GBS disease despite antibiotic prophylaxis of colonised mothers

No vaccine is available



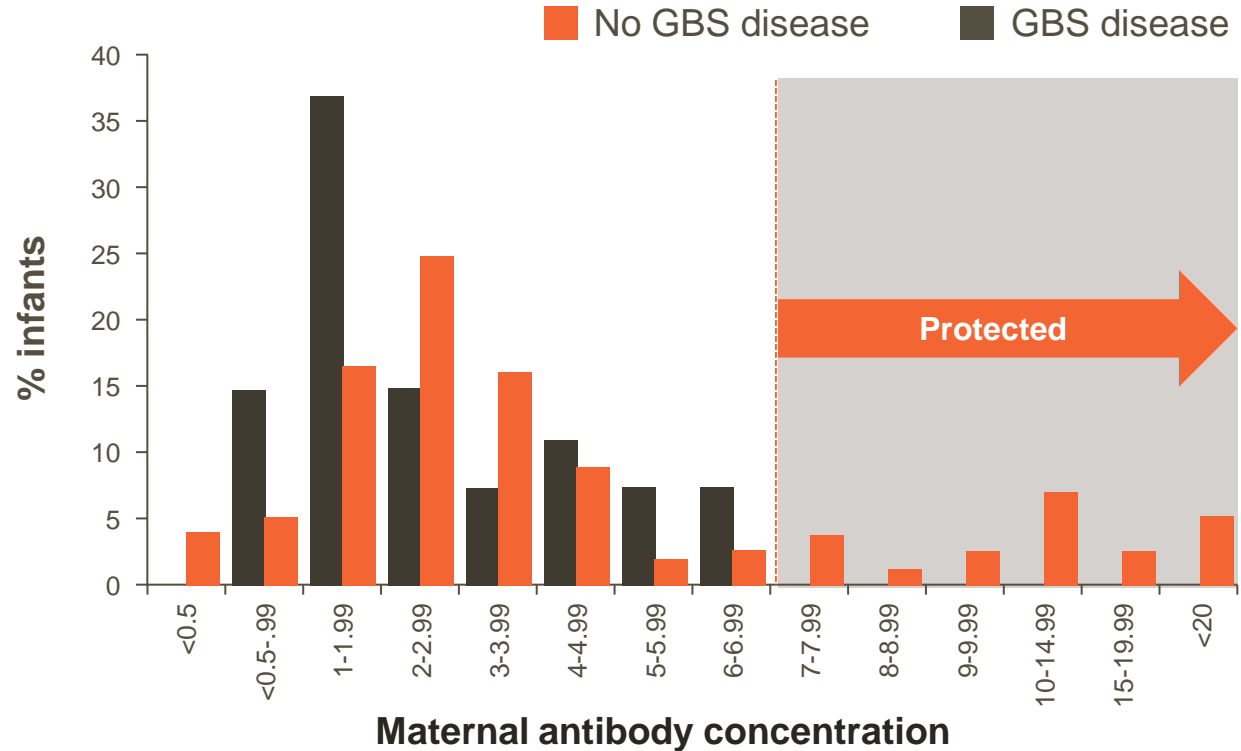
Maternal immunisation for GBS



The leading cause of pneumonia, meningitis and sepsis in neonates

1 in 2500 of babies develop GBS disease despite antibiotic prophylaxis of colonised mothers

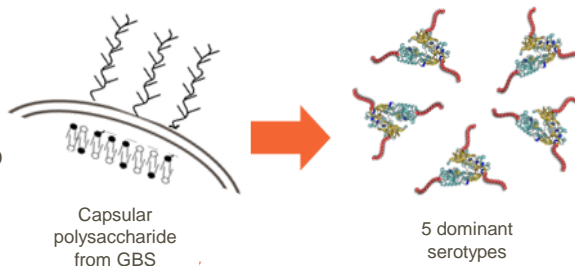
No vaccine is available



GBS maternal immunisation expanded programme

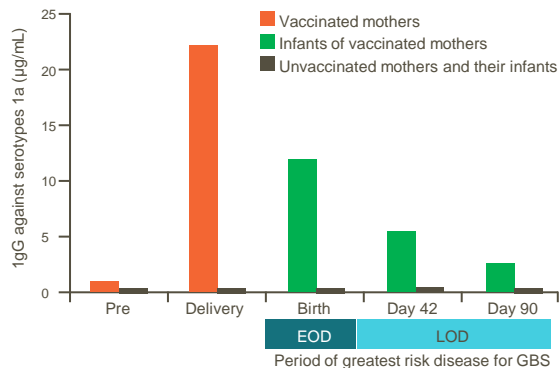


Based on Capsular polysaccharide (CPS) from 5 dominant GBS serotypes conjugated to a protein carrier



Designed to help protect against >95% of globally prevalent serotypes

Phase II trivalent vaccine antibody data shows response at period of greatest risk

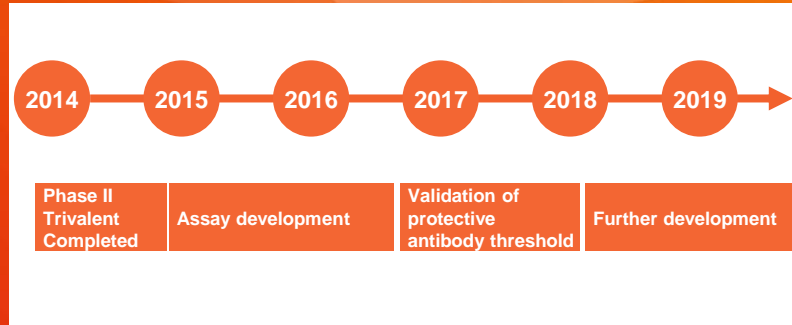


Large Phase II trivalent completed

Decision to expand composition to pentavalent

Validate correlate of protection with FDA

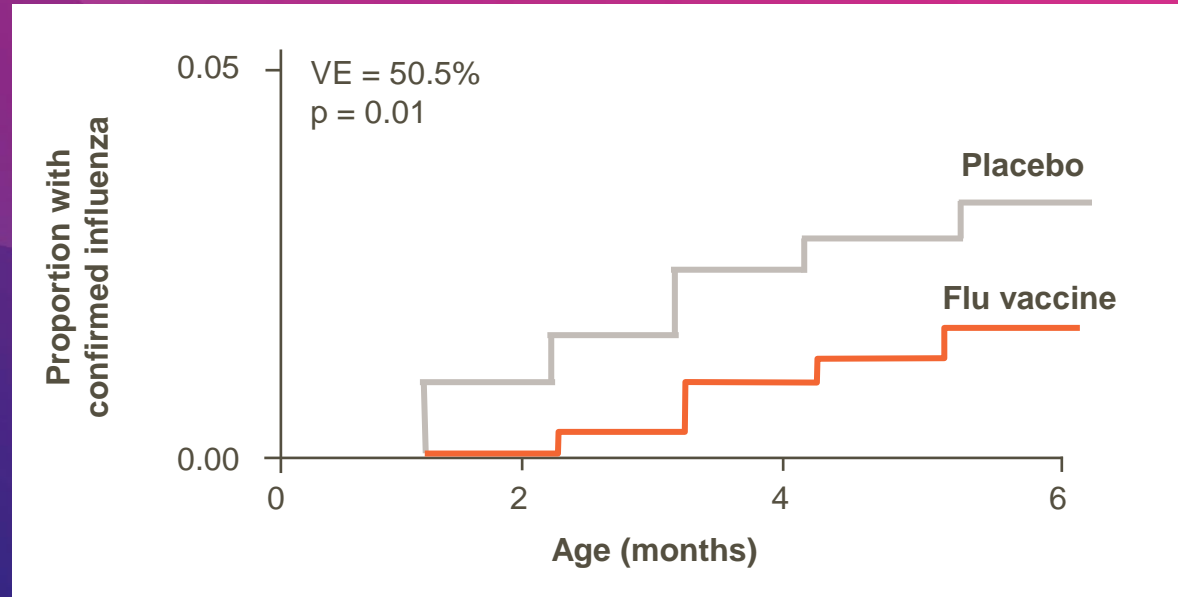
Clinical development plan to be agreed with FDA



Maternal immunisation validated strategy to prevent diseases that afflict very young infants



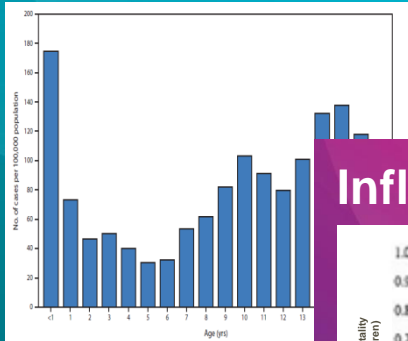
Infants protected by maternal flu vaccination



GSK potential maternal immunisation vaccine portfolio

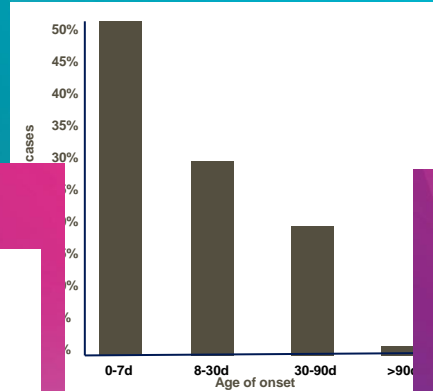


Pertussis



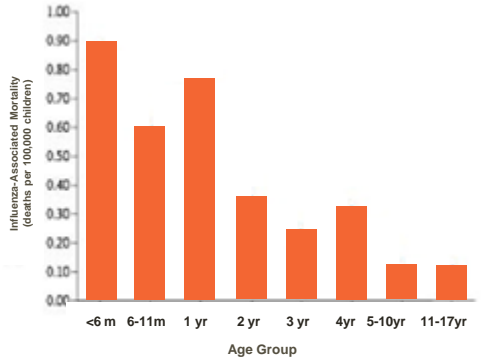
Winter K, MMWR 63:1122-1140,2014

GBS



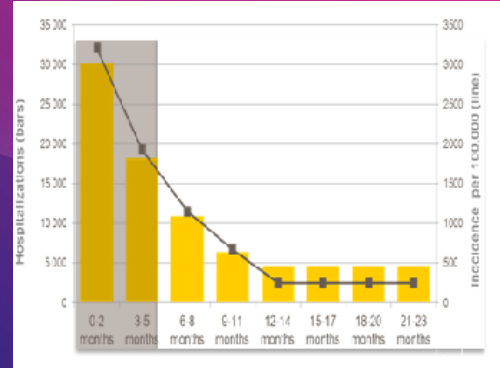
Melin, Clin Microbiol Inf, 17:1294-1303, 2011

Influenza



Bhat N Engl J Med.353:2559-67, 2005

RSV



Paramore, Pharmacoeconomics 22:274-285, 2004



A new vaccine concept

Testing hypothesis for a COPD vaccine



Epi studies show association between lung infections & COPD exacerbations^{1,2}

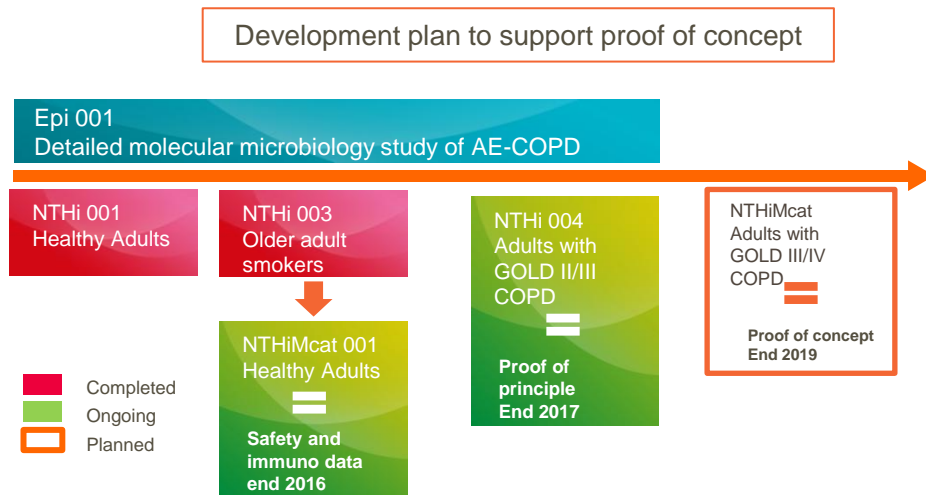
NTHi and Mcat: 2 lung pathogens potentially associated with 30-50% of COPD exacerbations^{1,2}

75% effective vaccine could eliminate 20-35% of exacerbations

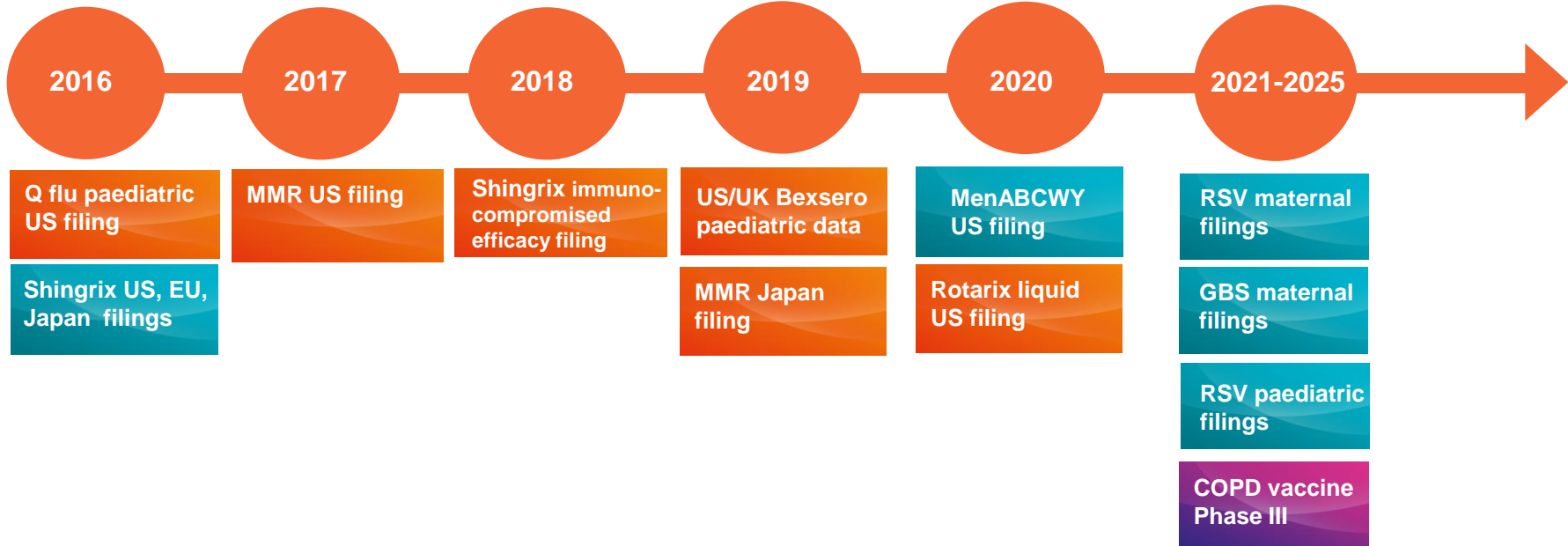
3 antigen vaccine covering NTHi using AS01 adjuvant in Phase II POC trial

Key POC data in COPD patients = 2017

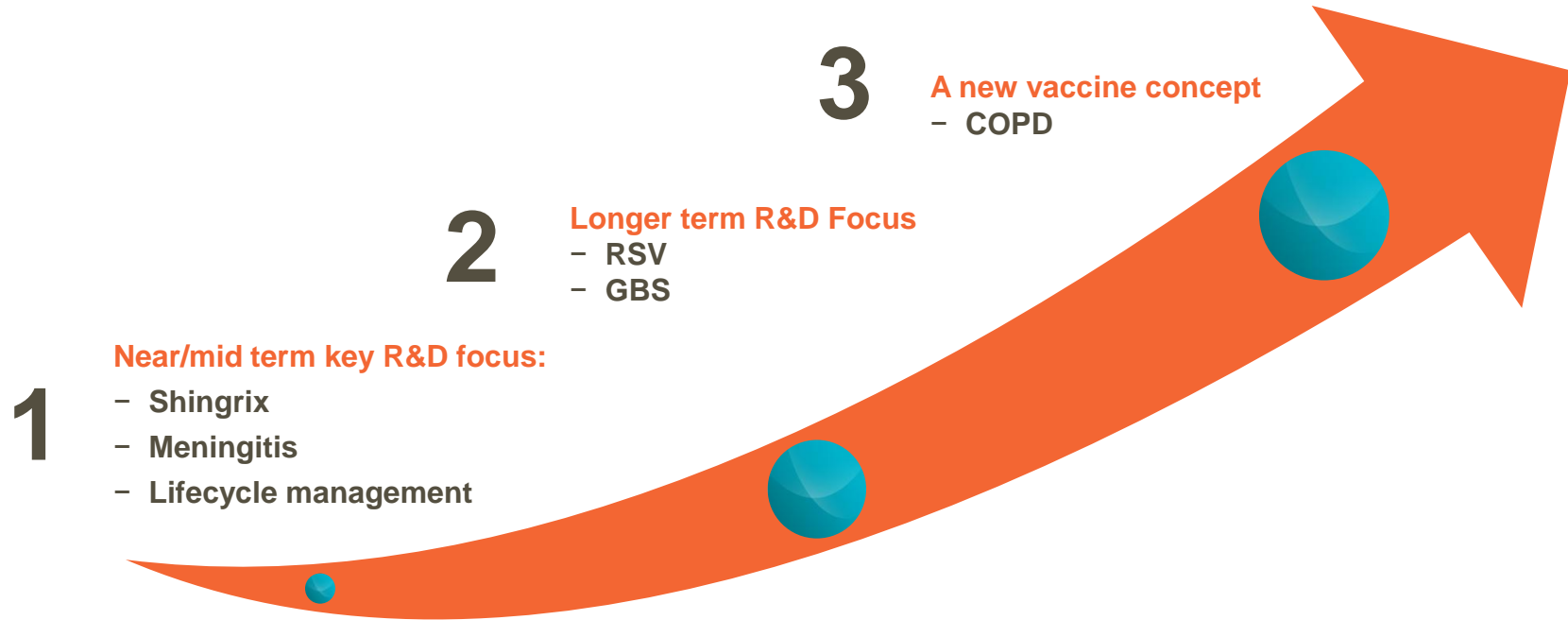
Phase III to be defined based on POC data



Data and planned filings support positive growth outlook



R&D programmes to deliver near-term growth with significant future opportunities and novel immunisation platforms



Introducing the Vaccines panel

GSK's leading scientists in vaccines



Alain Brecc

Vice President
Vaccine Development Lead - Zoster



Emmanuel Hanon

Senior Vice President,
Head of Vaccines R&D



Giovanni Della Cioppa

Vice President,
Head of Siena R&D Centre



Rip Ballou

Vice President
Head of Rockville R&D Centre



Q&A