Moncef Slaoui
Chairman of Vaccines
R&D programmes to deliver near-term growth with significant future opportunities and novel immunisation platforms

RSV=Respiratory Syncytial Virus; GBS=Group B Streptococcus; COPD=Chronic Obstructive Pulmonary Disease
Shingrix™ is not approved for use by the FDA or EMA
Existing zoster vaccine

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)

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*CDC: MMWR, February 2015; http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6404a6.htm; 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 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

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.
Shingrix - Efficacy against shingles

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 - Efficacy against shingles

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

Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Shingrix data based on clinical trials.
Existing vaccine - Immune response across age segments

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ZOE-50 and ZOE-70 pooled analysis – unpublished data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 ph III clinical trials.
Existing vaccine - Efficacy against PHN
PHN: post herpetic neuralgia, a severe complication of zoster

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

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

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

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

Changes in serogroup distribution in US over time

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

Sources: Santolaya et al. Hum Vac & Imm 2013 http://goo.gl/8oWB4P; * Strain 4 GSK data on file. Post hoc assays on a subset
Competing vaccine for MenB

- 1 antigen composition with 2 variants
- 3 dose regimen

ClinTrial.gov, study NCT01299480  https://goo.gl/Eqbmph
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MenAB CWY 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

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**MenACWY schedule**

- 11 years: MenACWY (~80% penetration)
- 17 years: MenACWY (~29% penetration)

**MenB additions**

- Bexsero or Other MenB

**MenABCWY combination planned**

- 2 injections: MenACWY
- 3-4 injections: MenACWY + MenB

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**Post dose 2 immune response rate**

- % of subjects with hSBA titer ≥threshold

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Saez-Llorens X et al. Hum Vacc Imm 2015 [http://goo.gl/PXXRs6]; GSK data on file. CDC MMWR: [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6429a3.htm#tab1](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6429a3.htm#tab1)
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

- MenABCWY Phase III start
- Bexsero US/UK paediatric data
- MenABCWY US filing
Respiratory Syncytial Virus (RSV)
Period of most severe RSV cases for young infants occurs from birth to 12 months

Paramore, Pharmacoeconomics 22:274-285, 2004
Period of most severe RSV cases for young infants occurs from birth to 12 months.

Paramore, Pharmacoeconomics 22:274-285, 2004
Candidate paediatric RSV vaccine, a novel approach

Genetically engineered recombinant CHAd155
Same vector used in ebola vaccine
Non-alum composition

Phase I
- Healthy men
- Sero+ infants 6-18 mos
- Sero-infants 6-11 mos
- Completed

Phase II
- Sero- infants 2-12 mos
- Proof of principle 2021

Phase III
- Sero-infants 2 mos
- Study start 2022

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

GSK Pre-F

Neutralising Ab Titer

Fold increase PCA

Day 0  Day 7  Day 30

>20 fold PCA increase after single dose without adjuvant

GSK internal data, unpublished
Stabilised Pre-F generated high titers by Day 7 and potent boost of PCA without adjuvant

GSK Pre-F

Neutralising Ab Titer

Fold increase PCA

Day 0

Day 7

Day 30

>20 fold PCA increase after single dose without adjuvant

Post-F

Neutralising Ab Titer

Fold increase PCA

Day 0

Day 7

Day 30

>10 fold PCA increase requires 120 ug + adjuvant


Presentation by Novavax at World Vaccine Congress April 2015 (data on 120 ug/alum dose PCA)
Novel candidate RSV maternal vaccine approach

Phase I: Healthy men
Phase IIa: Non-pregnant women
Phase IIb: Pregnant women
Phase III: VE in infants of vaccinated women

- Completed
- Ongoing
- Planned

Proof of principle 2018
Study start 2019
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 antibody concentration

- No GBS disease
- GBS disease

Gibbs, Obstet Gynecol, 104;1062-1075, 2004
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

Gibbs, Obstet Gynecol, 104;1062-1075, 2004
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

Le Doare, Vaccine 31(4) D7, 2013 ; GSK clinical data, unpublished
Maternal immunisation validated strategy to prevent diseases that afflict very young infants

Infants protected by maternal flu vaccination

![Graph showing proportion of confirmed influenza cases with vaccination and placebo over months.](image)

- **Proportion with confirmed influenza**
  - Placebo
  - Flu vaccine

**VE = 50.5%**

**p = 0.01**

GSK potential maternal immunisation vaccine portfolio

Pertussis

Winter K, MMWR 63:1122-1140, 2014

GBS

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

Influenza


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

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Data and planned filings support positive growth outlook

- **2016**
  - Q flu paediatric US filing
  - Shingrix US, EU, Japan filings

- **2017**
  - MMR US filing

- **2018**
  - Shingrix immuno-compromised efficacy filing

- **2019**
  - US/UK Bexsero paediatric data
  - MMR Japan filing

- **2020**
  - MenABCWY US filing
  - Rotarix liquid US filing

- **2021-2025**
  - RSV maternal filings
  - GBS maternal filings
  - RSV paediatric filings
  - COPD vaccine Phase III
R&D programmes to deliver near-term growth with significant future opportunities and novel immunisation platforms

1. Near/mid term key R&D focus:
   - Shingrix
   - Meningitis
   - Lifecycle management

2. Longer term R&D Focus
   - RSV
   - GBS

3. A new vaccine concept
   - COPD
Introducing the Vaccines panel

GSK’s leading scientists in vaccines

Alain Brecx
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