

# **GSK: DELIVERING A UNIQUE VACCINES PIPELINE**

**Thomas Breuer, MD, MSc**

**Senior Vice President Global Clinical R&D  
& Chief Medical Officer, GSK Biologicals**



# Today's Agenda

**GSK  
within the  
Vaccines  
Market**

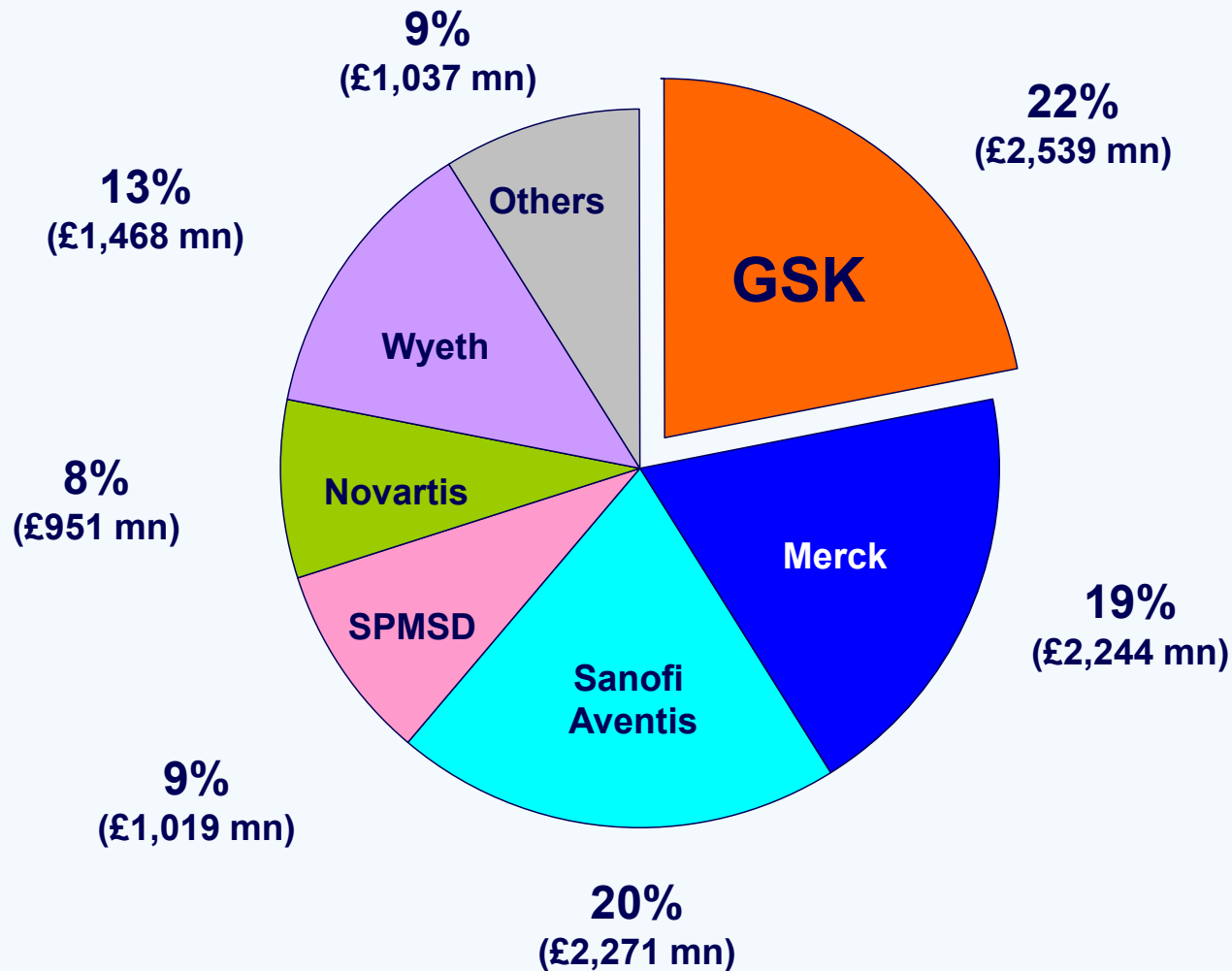
**GSK  
Vaccine  
Innovation**

**GSK  
Strategic  
Priorities**

# Vaccines Business Characteristics

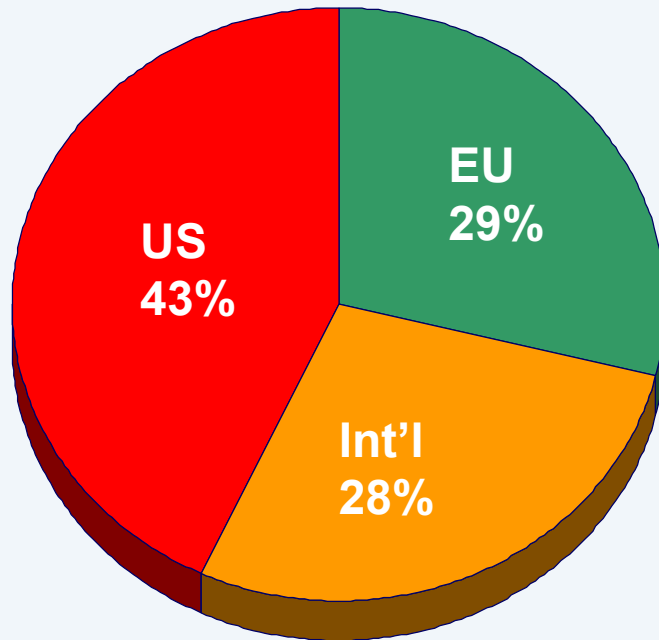
- Few Global Players and High Barriers to Entry
  - Complex Manufacturing
  - Large Scale Investment
- Long Product Life Cycles
  - Complex Intellectual Property
- High Probability of R&D Success
  - 70% post-POC
- New Technology/ Novel Products
- Better Pricing
- Operating Margin Comparable to Pharmaceutical Products
- Heightened Awareness
- New Markets

# Global Vaccines Market 2008

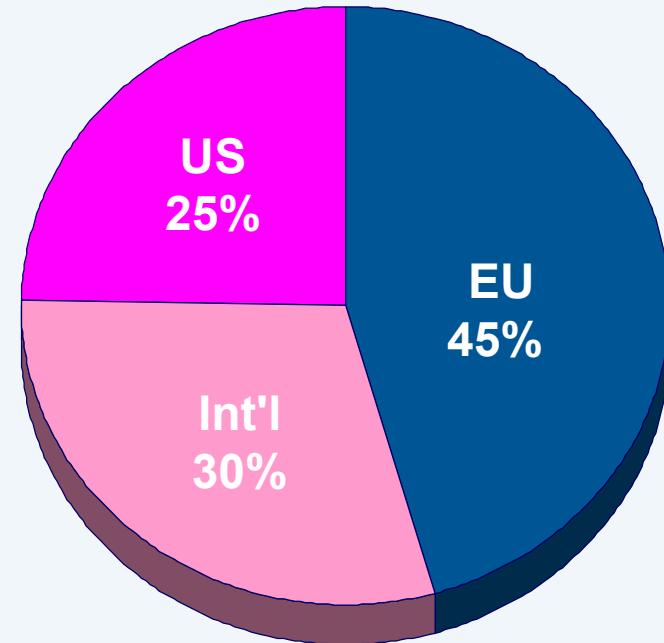


# GSK Vaccines: Broad Geographic Opportunity

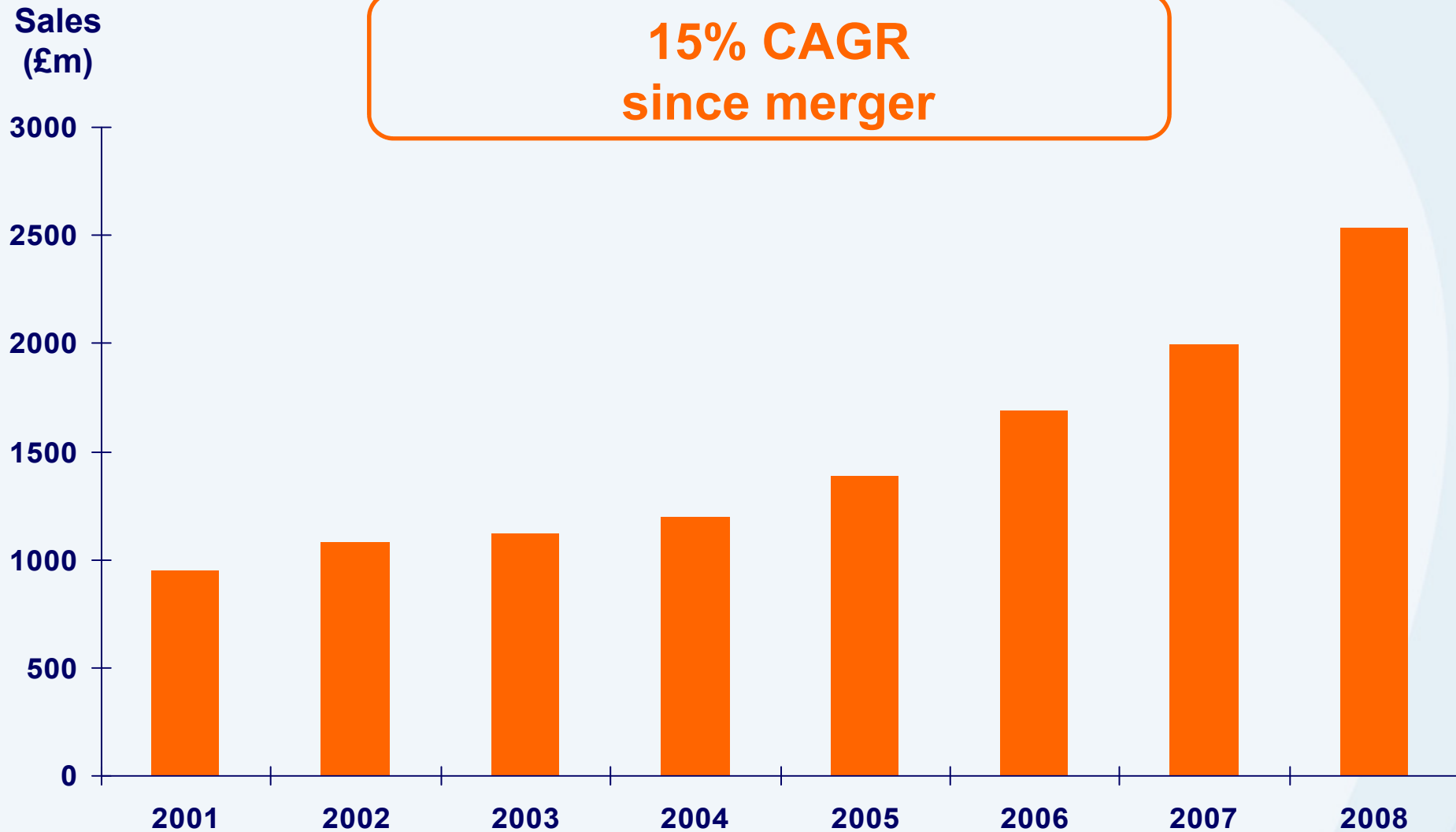
**Total Vaccines Market 2008\***  
**£11.5bn**



**GSK Vaccines 2008 sales**  
**£2.5bn**



# GSK Vaccines: Continuing Sales Growth



# GSK Vaccines in 2008

**Vaccines sales £2.5 billion (+15%)**

**Vaccines represent 10.4%  
of GSK sales (2008)**

**Approvals:**  
**US: *Rotarix, Kinrix, Boostrix (adult)***  
**EU: *Prepandrix, Pandemrix***

**Increased Emerging Market  
presence**

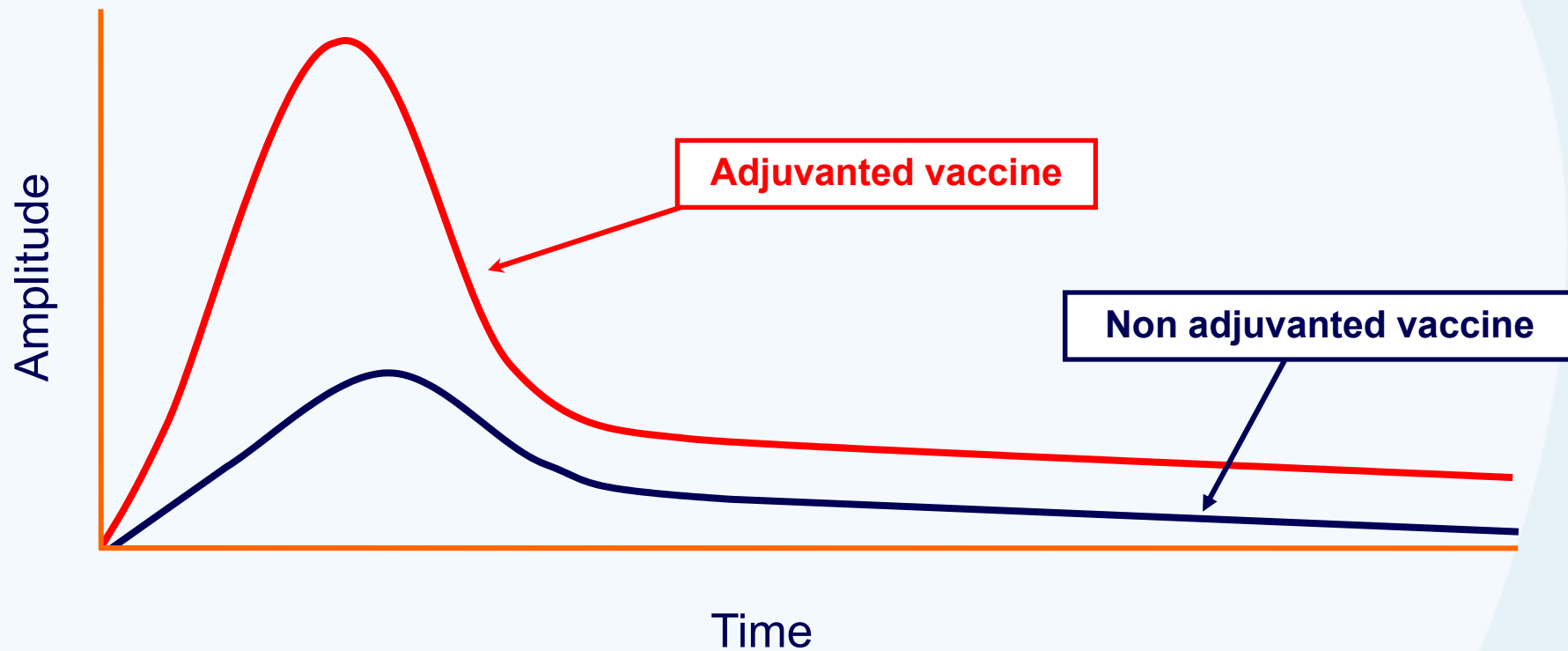
# Today's Agenda

**GSK  
within the  
Vaccines  
Market**

**GSK  
Vaccine  
Innovation**

**GSK  
Strategic  
Priorities**

# Adjuvanted Vaccines – Immune Response



# Why Do We Need Better Adjuvants?

- To induce strong immune responses
  - Malaria (complex disease)
  - Hepatitis B vaccine for haemodialysed (immunosuppression), *Fendrix*<sup>TM</sup>
  - Flu vaccine for elderly (weakened immunity)
  
- To induce long-term protection
  - HPV vaccine, *Cervarix*<sup>TM</sup>
  
- To induce broader immune response: Cross-protection
  - Pandemic Flu vaccines, *Prepandrix*<sup>TM</sup>
  - HPV vaccine, *Cervarix*<sup>TM</sup>
  
- To increase capacity by reducing antigen content/dose
  - Pandemic Flu vaccine, *Pandemrix*<sup>TM</sup>

# Today's Agenda

**GSK  
within the  
Vaccines  
Market**

**GSK  
Vaccine  
Innovation**

**GSK  
Strategic  
Priorities**

# GSK Strategic Priorities

**Grow a diversified global business**

**Deliver more products of value**

**Simplify the operating model**



# Grow a Diversified Global Business



## United States Emerging Markets

**Diversification through  
growth of existing business & launch of new products**

# Grow a Diversified Global Business

Phase III

File

Marketed

*MenHibrix™*

*MenACWY*

*Cervarix™*

*Pre/pandemic*

*New gen flu*

*MAGE-A3*

**Engerix-B®**

**Havrix®**  
Hepatitis A Vaccine,  
Inactivated

**TWINRIX®**

**BOOSTRIX™**

**Infanrix®**

**Pediarix™**

**Fluarix™**

**Rotarix™**  
Rotavirus Vaccine,  
Live, Oral

**FluLaval™**  
Influenza Virus  
Vaccine

**Kinrix™**

# Grow a Diversified Global Business

## ■ Licensed vaccines

- *Infanrix, Infanrix-Hib, Boostrix, Fluarix, Engerix-B, Hiberix, Havrix, Twinrix, Priorix, Varilrix*

## ■ Vaccines in development

- *Cervarix* (phase III trials ongoing in China)
- *Infanrix-IPV/Hib* (IND)

## ■ Joint venture with Neptunus (NIBT) in China

- Co-development of flu vaccines

# Grow a Diversified Global Business

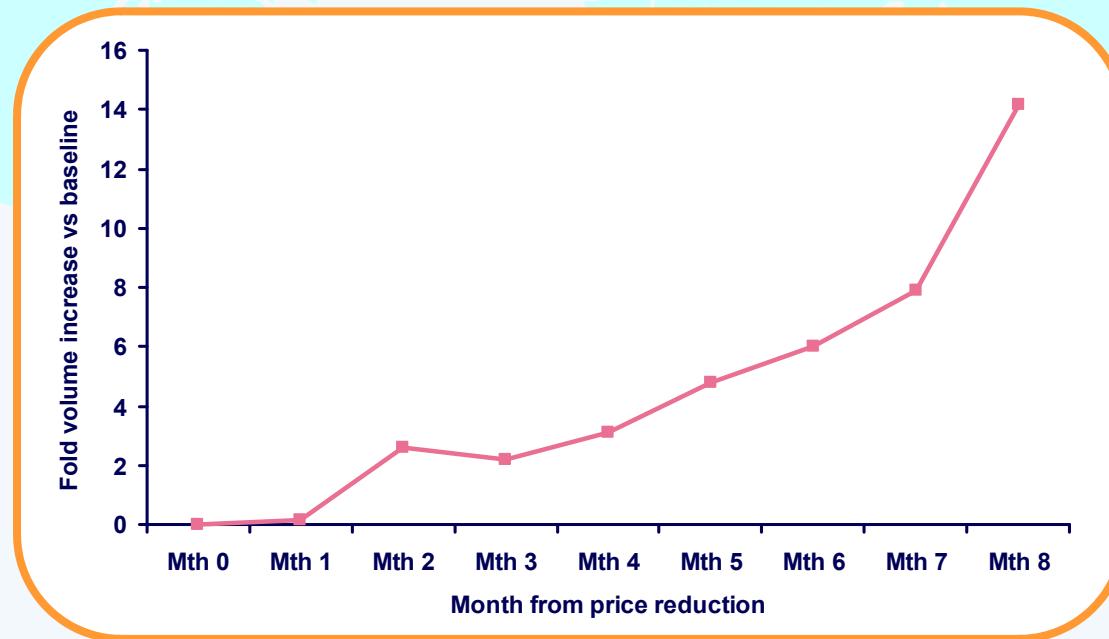
- Over 25 year collaboration with Brazilian Ministry of Health (Fiocruz)
- Long term governmental contracts
  - Technology transfer agreements
    - Oral polio vaccine (1980's)
    - *Hiberix* (1998)
    - *Priorix* (2003)
    - *Rotarix* (2008)
      - Included in National Immunization Programme
    - *Synflorix* (2009)
      - Inclusion in National Immunization Programme

# Grow a Diversified Global Business

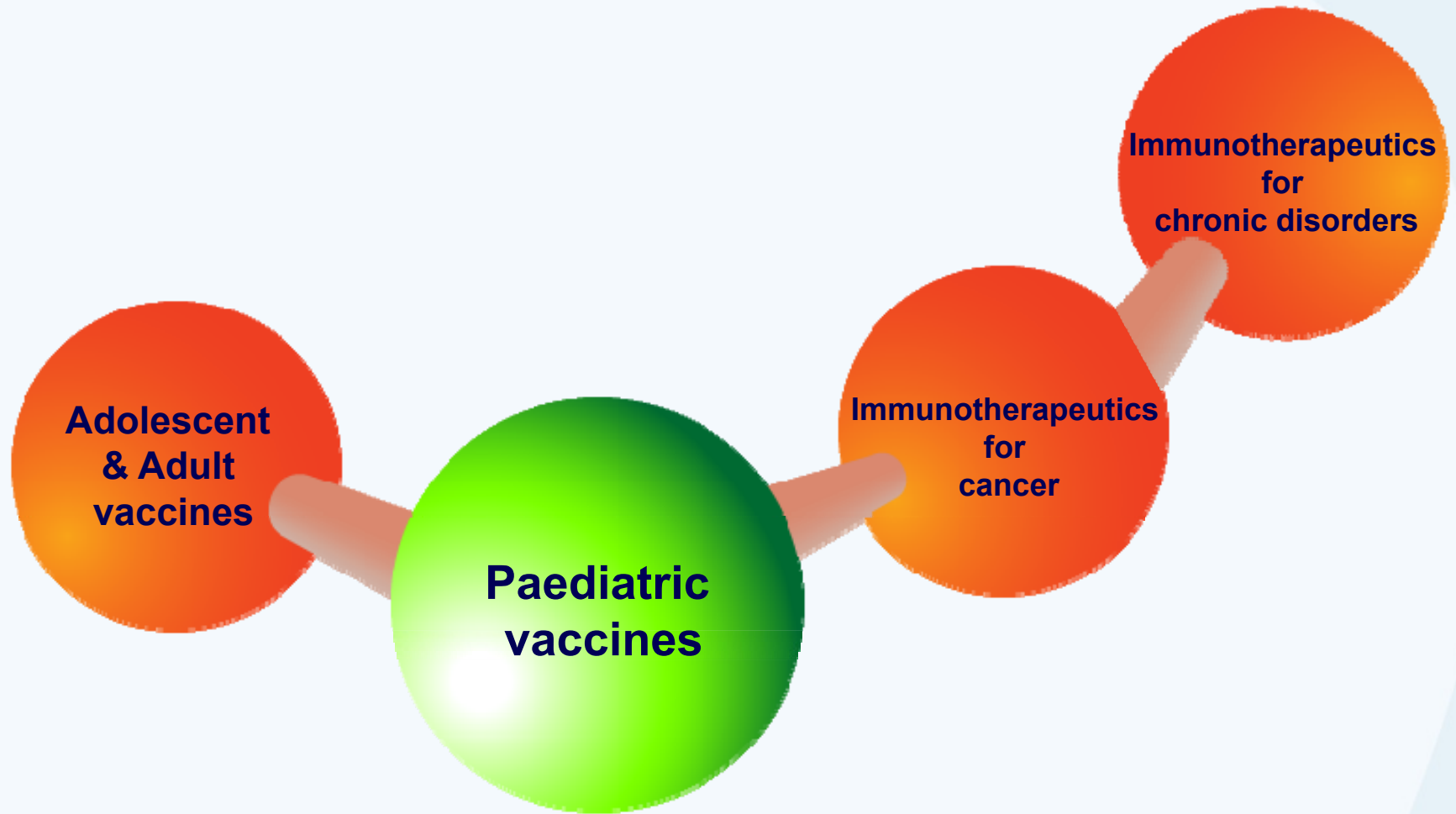
- Supranational high volume tenders
  - GSK Bio pioneered tiered pricing over 20 years ago
    - Pricing varies with
      - Countries' ability to pay
      - volumes purchased
      - duration of commitment
- 
- This approach will also be used to increase the availability of new vaccines, including *Rotarix*, *Synflorix* and *Cervarix* in the future

# Grow a Diversified Global Business

- Unlocking price elasticity
- Cervarix* in The Philippines
  - 60% price cut
  - 14-fold volume increase in 8 months



# Grow a Diversified Business



# GSK Strategic Priorities

**Grow a diversified global business**

**Deliver more products of value**

**Simplify the operating model**

# A Rich Pipeline

## Phase I

<b>HIV</b>
<b><i>S. pneumo</i> adult</b>
<b>Cytomegalovirus</b>
<b>NTHi-Pneumo</b>
<b>WT1 ASCI</b> Acute Myelogenous Leukaemia

## Phase II

<b>Tuberculosis</b>
<b><i>Herpes zoster</i></b>
<b>Dengue</b>

## Phase III

<b>New generation flu</b>
<b>MAGE-A3 ASCI</b> Non Small Cell Lung Cancer
<b>Flu Pre-pandemic *</b> Quebec
<b>Flu Pandemic *</b> Quebec
<b>MAGE-A3 ASCI</b> Melanoma
<b>Hib-MenCY-TT</b>
<b>MenACWY-TT</b>
<b>Mosquirix</b> Malaria
<b>Simplirix</b> Herpes simplex virus

## Submitted

<b><i>Cervarix</i> (BLA)</b> *
Cervical cancer

## Approved

<b>Flu Pre-pandemic *</b> Dresden (MAA)
<b>Flu Pandemic *</b> Dresden (MAA)
<b><i>Kinrix</i> (BLA)</b> DTPa – IPV
<b><i>Rotarix</i> (BLA)</b> *
Rotavirus
<b><i>Boostrix</i> (BLA)</b> DTPa
<b><i>Synflorix</i> (MAA)</b> ( <i>Streptococcus pneumoniae</i> & non-typeable <i>Haemophilus influenzae</i> )

\* In-license or other third-party alliance

# Cervarix<sup>®</sup> in 2009

- Continue to increase *Cervarix* coverage
  - Now approved in 99 countries
    - New launches
    - Increase market share in existing markets
- *Cervarix* in the US
  - Final data submitted to FDA in March 2009
    - Anticipate 6 month FDA review process
  - FDA Advisory Committee favourable recommendation
    - VRBPAC vote in support of efficacy and safety
  - FDA Action Date 29 September
- WHO Prequalification
  - Global access to *Cervarix* via UNICEF & GAVI
- New data
  - Fulfilling the promise



# Final Efficacy Analysis (HPV-008)

## ● TVC naïve\* (n=11,641) CIN2+

- Approximates the primary target population for organized vaccination programs i.e. young women before sexual debut

## ● Vaccine type specific efficacy (CIN2+)

● HPV 16/18	(1/63)	<b>VE 98.4</b> (90.4-100)
● HPV 16	(1/56)	<b>VE 98.2</b> (89.1-100)
● HPV 18	(0/12)	<b>VE 100</b> (61.3-100)

\*  $\geq 1$  dose, case counting start on Day 1, At Month 0: Normal cytology, HPV DNA negative for 14 oncogenic types, seronegative for HPV-16 and -18. Paavonen et al. *The Lancet* 2009; 374: 301-314.

# Final Efficacy Analysis (HPV-008)

- **TVC naïve (n=11,641), CIN2+**

- Vaccine efficacy against **5 most frequent** oncogenic non-vaccine types (*combined analysis*)

- HPV 31/33/45/52/58 (15/47) **VE 68.2** (40.5-84.1)

- **Vaccine efficacy against 3 most frequent oncogenic non-vaccine types (*individual analysis*)\***

- HPV 31 (0/20) **VE 100.0** (78.3-100)

- HPV 33 (5/18) **VE 72.3** (19.1-92.5)

- HPV 45 (0/5) **VE 100.0** (-19.5-100)

# HPV-008: Efficacy against HPV-16/18 and beyond

CIN 2+ protection regardless of HPV type

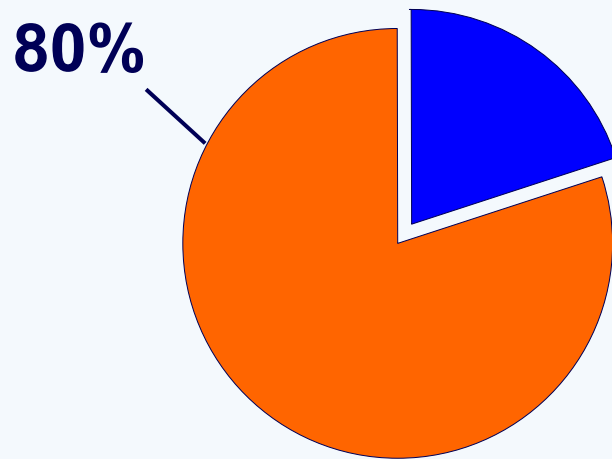
**70.2%**  
in TVC naïve

**This cohort approximated young girls  
prior to sexual debut**

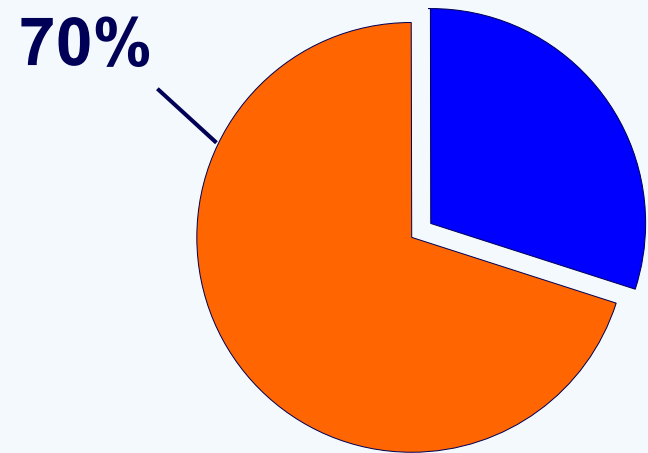
The total vaccinated naïve cohort (TVC-naïve) included women who received at least one vaccine dose, were evaluable for efficacy i.e. had a baseline PCR or cytology sample and one further sample available), and at baseline had normal cytology, were DNA negative for all 14 oncogenic HPV types evaluated, and were seronegative for HPV-16 and -18. This cohort approximated young girls prior to sexual debut.

Paavonen et al. *The Lancet* 2009; 374: 301-314.

# HPV-008: HPV naïve at baseline



**15 – 17 years old**



**18 – 25 years old**

# Cervarix<sup>®</sup>: Fulfilling the Promise

Significant  
new data  
presented and  
published

**Study-008**

**High efficacy against HPV-16/18 confirmed  
& significant protection beyond HPV-16/18**

IPvC, May 09  
*The Lancet*, July 09

**Study-010**

**Superior immune profile**

IPvC, May 09  
*Human Vaccines*, Oct 09

**Study-007**

**Continued efficacy: 6.4 yrs so far**

EUROGIN, Nov 08

**Study-023**

**Sustained immune response: 7.3 yrs so far**

IPvC, May 09

**All studies**

**Long-term safety**

*The Lancet*, July 09  
*Human Vaccines*, May 09  
(and references above)

# Synflorix™: Approval and launch



**3 additional serotypes (1, 5 & 7F) are associated with severe disease and high potential to cause infectious epidemics**

**Potential to prevent up to 90 % of paediatric invasive pneumococcal disease in Europe**

**Uniquely designed to target two major pathogens with huge healthcare burden<sup>1</sup>**

**Filed in 74 countries  
Approved in 44 and launched in 14 countries  
Seeking WHO prequalification**

**Large-scale phase III studies ongoing to confirm efficacy against NTHi**

<sup>1</sup> *Streptococcus pneumoniae* and non-typeable *Haemophilus influenzae* (NTHi)

# Flu Vaccine Portfolio: Product Differentiation

- **Seasonal flu vaccines**

- Life-cycle management

- *FluaRix*

- *FluLaval*



- **Flu next generation (>65 years)**

- Phase III ongoing



- **Pandemic vaccines**

- H5N1

- *Prepandrix*

- H1N1

- *Pandemrix*



# Pandemic Vaccines

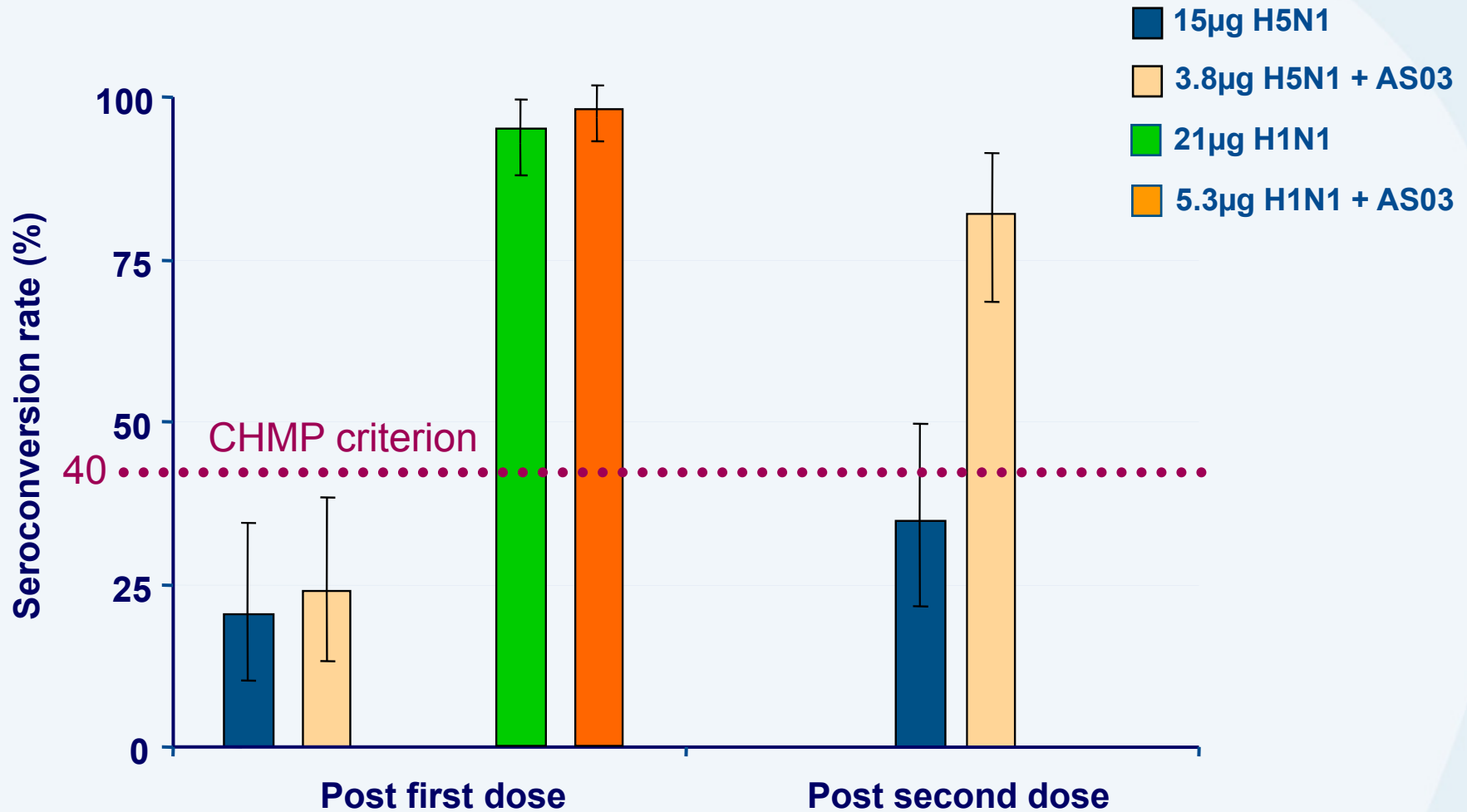
## ● The Problem

- Newly emerged strain (“shifted strain”)
  - Expected strain variation over coming seasons (“drifting”)
- Global pandemic vaccine demand far greater than supply

## ● GSK Offering

- H1N1 adjuvanted vaccine
  - Low antigen content (higher supply)\*
  - Cross protection capability (cover drifting strains)\*

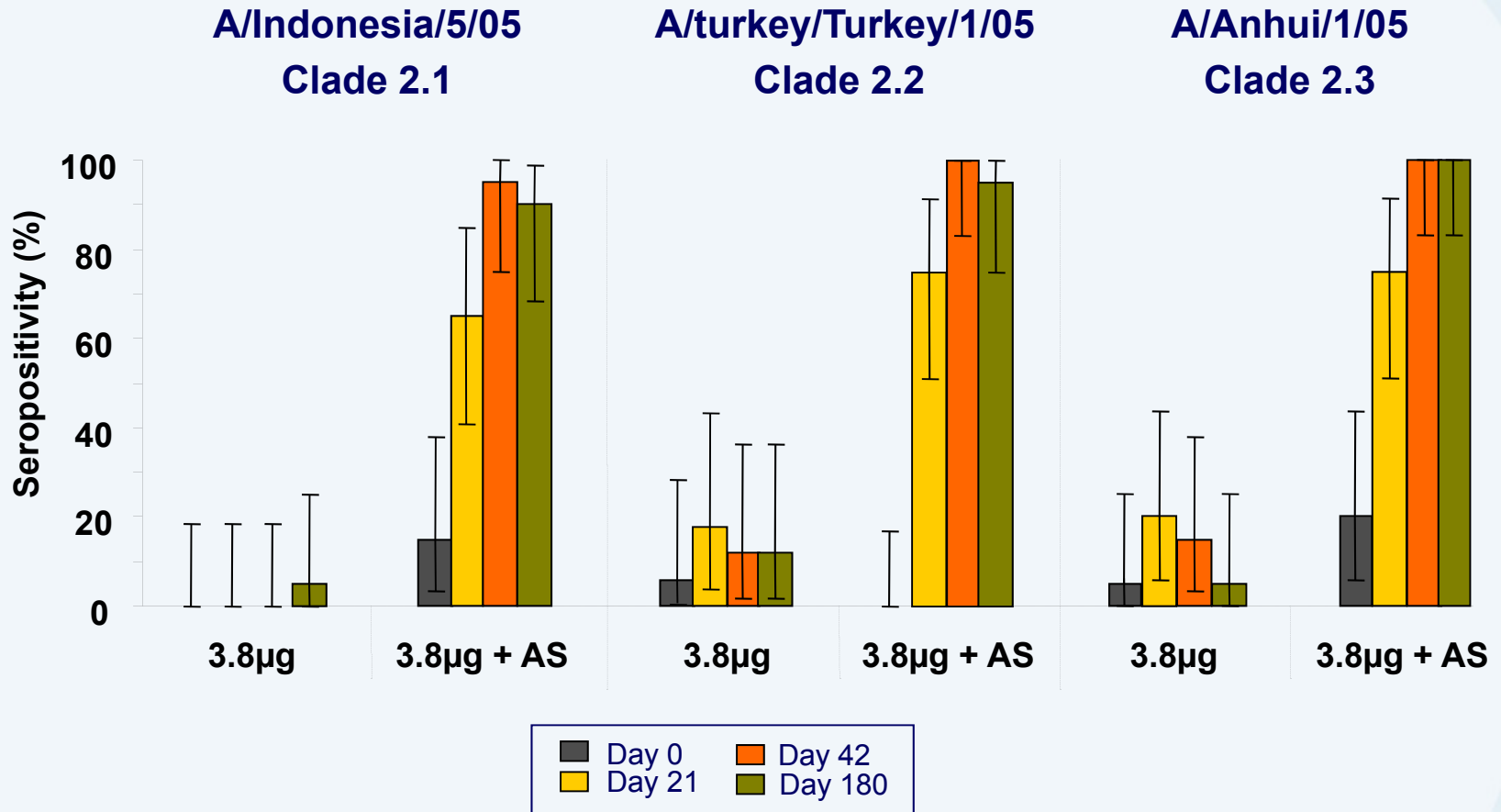
# Comparing H5N1 with H1N1 influenza vaccine: adjuvanted & unadjuvanted



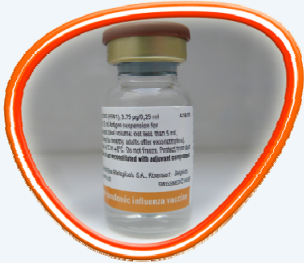
Leroux-Roels et al. Antigen sparing and cross-reactive immunity with an adjuvanted rH5N1 prototype pandemic influenza vaccine: a randomised controlled trial. *Lancet* 2007; 370: 580–589.

Presented at 3 Deutscher Influenza-Kongress, Erfurt, Germany, 24-26 September 2009.

# Persistence Of Cross-Reactive Neutralizing Antibodies: Seropositivity (%)



# Integrated GSK response to flu pandemic



- Production started June '09; first deliveries planned October onwards
- 291 million doses of H1N1 adjuvanted vaccine ordered
- Negotiations with additional governments ongoing
- Donation of 50 million doses of H1N1 adjuvanted vaccine to WHO



- Contracts to supply *Relenza* to >60 governments
- Annual production capacity of 190m treatment courses by end '09
- Increasing production of Diskhaler; building new capacity for Rotacaps



- *Actiprotect* – new disposable respirator mask with an antiviral coating
- Inactivates all influenza virus strains tested, including previous strains of H1N1 and H5N1
- Approved in EU / some int'l markets and for occupational use in the US
- Working to increase manufacturing capacity



- Agreement with Enigma Diagnostics to develop and supply the first point-of-care diagnostic influenza tests
- Pilot study planned 2009; potential launch 2011

# **MenHibrix™ (HibMenCY)**

**Positive  
pivotal Ph III  
results**

An investigational combination vaccine for early protection against *Haemophilus influenzae* type b (Hib) and meningococcal C&Y diseases

**Meningococcal disease causes permanent disability or death –  
Fatality rate 9-12%**

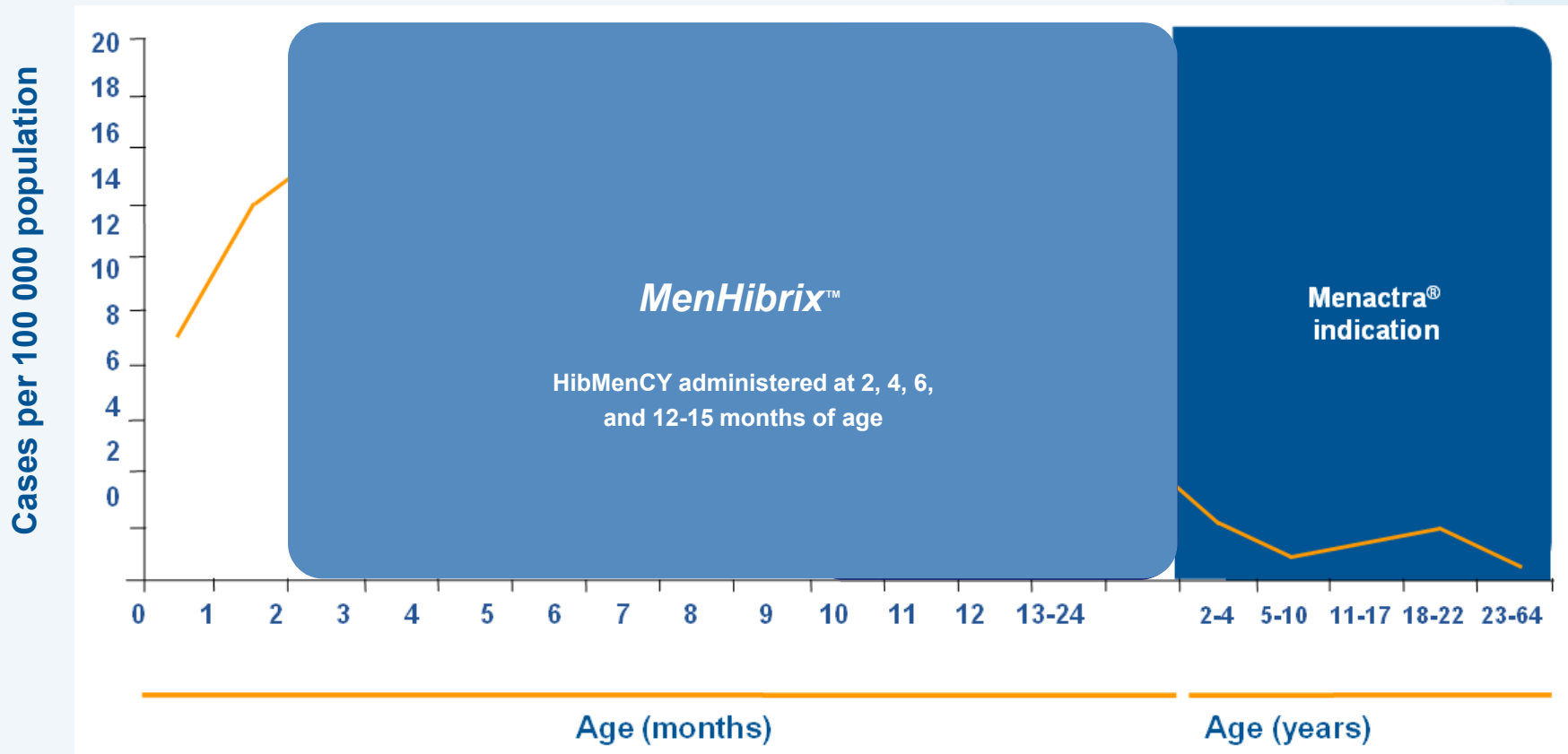
**Protection for infants, where the need is greatest**

**New pivotal Phase 3 data shows positive results to support filing  
Data to be presented at a scientific congress H2 09**

**FDA filing in H2 09**

# We can uniquely address where the risk is greatest...in infants

## US Incidence of Culture Confirmed Meningococcal Disease



# ...with no additional shots

**MenCY combined with monovalent Hib means no additional shots**



**and complements *Pediarix* and *Rotarix* to create a full GSK infant portfolio**

# Antigen-Specific Cancer Immunotherapeutics (ASCI)

- Novel class of compounds based on tumour antigens
- MAGE-A3 in Non-Small Cell Lung Cancer (NSCLC)
  - NSCLC is the most common form of lung cancer (80-85%)
  - Positive phase II data
    - 25 % reduction in the relative cancer recurrence following surgery at 44 months
    - Well-tolerated with excellent compliance
  - Ongoing phase III study (MAGRIT)
    - Planned recruitment of 2,270 patients
- MAGE-A3 in Melanoma
  - Phase III study commenced December 2008
- WT1 in Acute Myelogenous Leukaemia (AML)
  - Phase I trial started October 2008

# GSK Strategic Priorities

**Grow a diversified global business**

**Deliver more products of value**

**Simplify the operating model**

# Simplify the Operating Model

## Simplification Agenda

- Manufacturing and Supply
  - Increase productivity
  - Reduce lead-time (then inventory)
  - Reduce variability
- Clinical R&D
  - Clinical Development Plan design
  - Lean organization
  - Process excellence
  - Resourcing strategy & planning
- Support functions
  - HR, Global Ops
  - Payables management

# GSK Vaccines in 2009

- GSK is a world leader in vaccines
  - We develop vaccines that meet public health needs in both developed and developing countries (“emerging markets”)
- GSK has one of the strongest vaccine pipelines in the industry
- We expect GSK’s unique expertise in adjuvant technology to make the difference
- As a global company, GSK is ideally positioned to capture a significant market share in all territories



**GlaxoSmithKline**