

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

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# Today's Agenda

**GSK  
within the  
Vaccines  
Market**

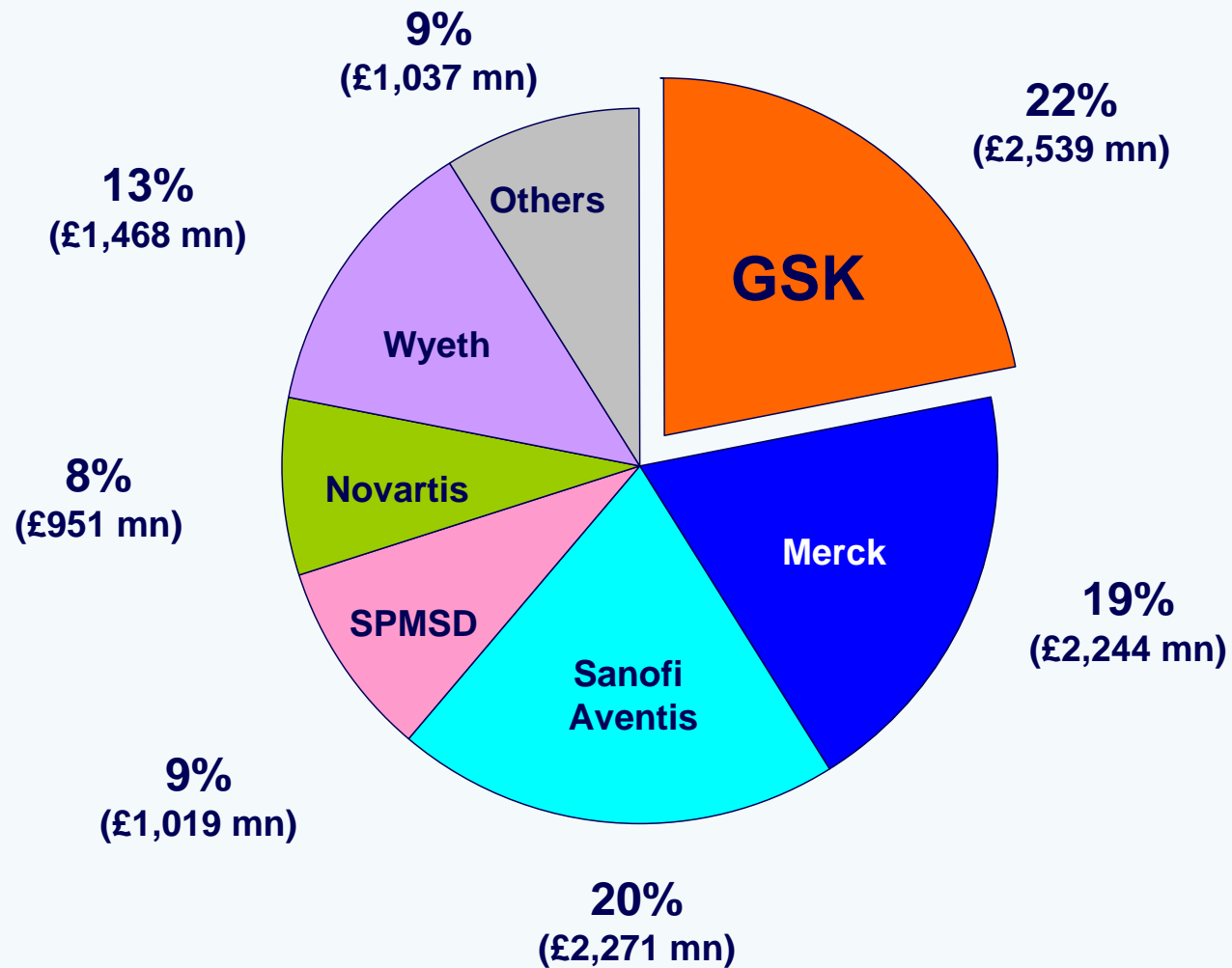
**GSK  
Vaccine  
Innovation**

**GSK  
Strategic  
Priorities**

# Vaccines Business Characteristics

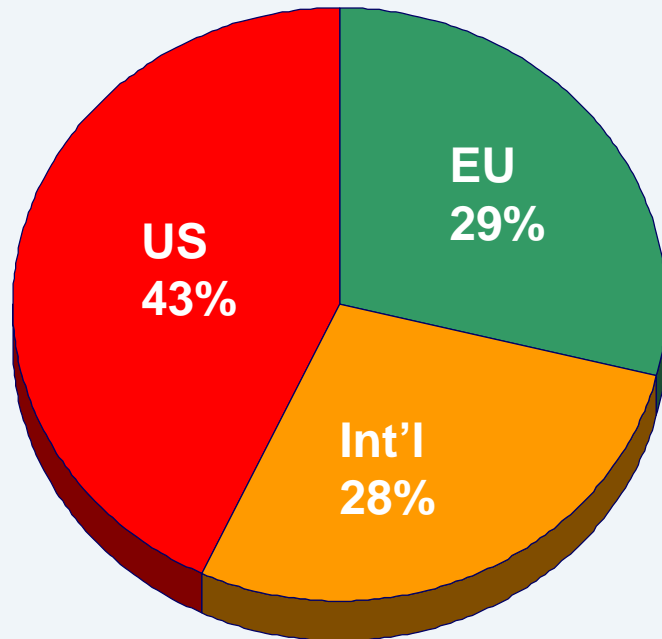
- Few Global Players and High Barriers to Entry
  - Complex Manufacturing
  - Large Scale Investment
- Long Product Life Cycles
  - Complex Intellectual Property
- High Probability of R&D Success
  - 70% post-POC
- New Technology/ Novel Products
- Better Pricing
- Operating Margin Comparable to Pharmaceutical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

# Global Vaccines Market 2008

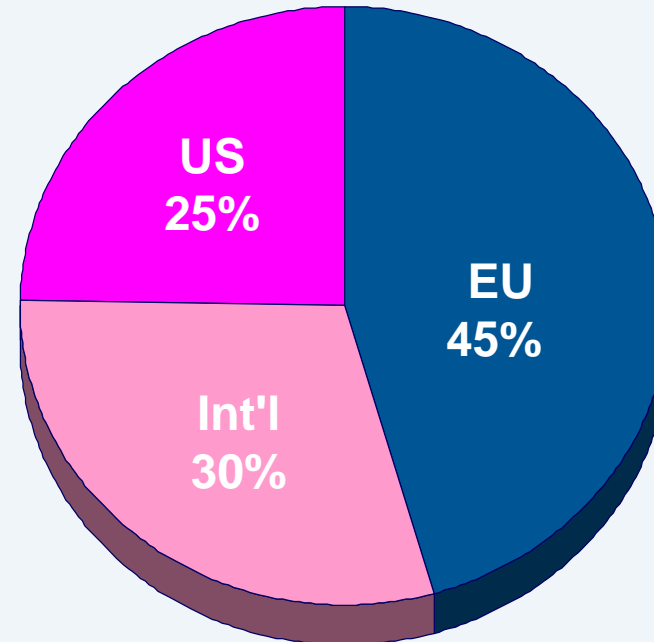


# GSK Vaccines: Broad Geographic Opportunity

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

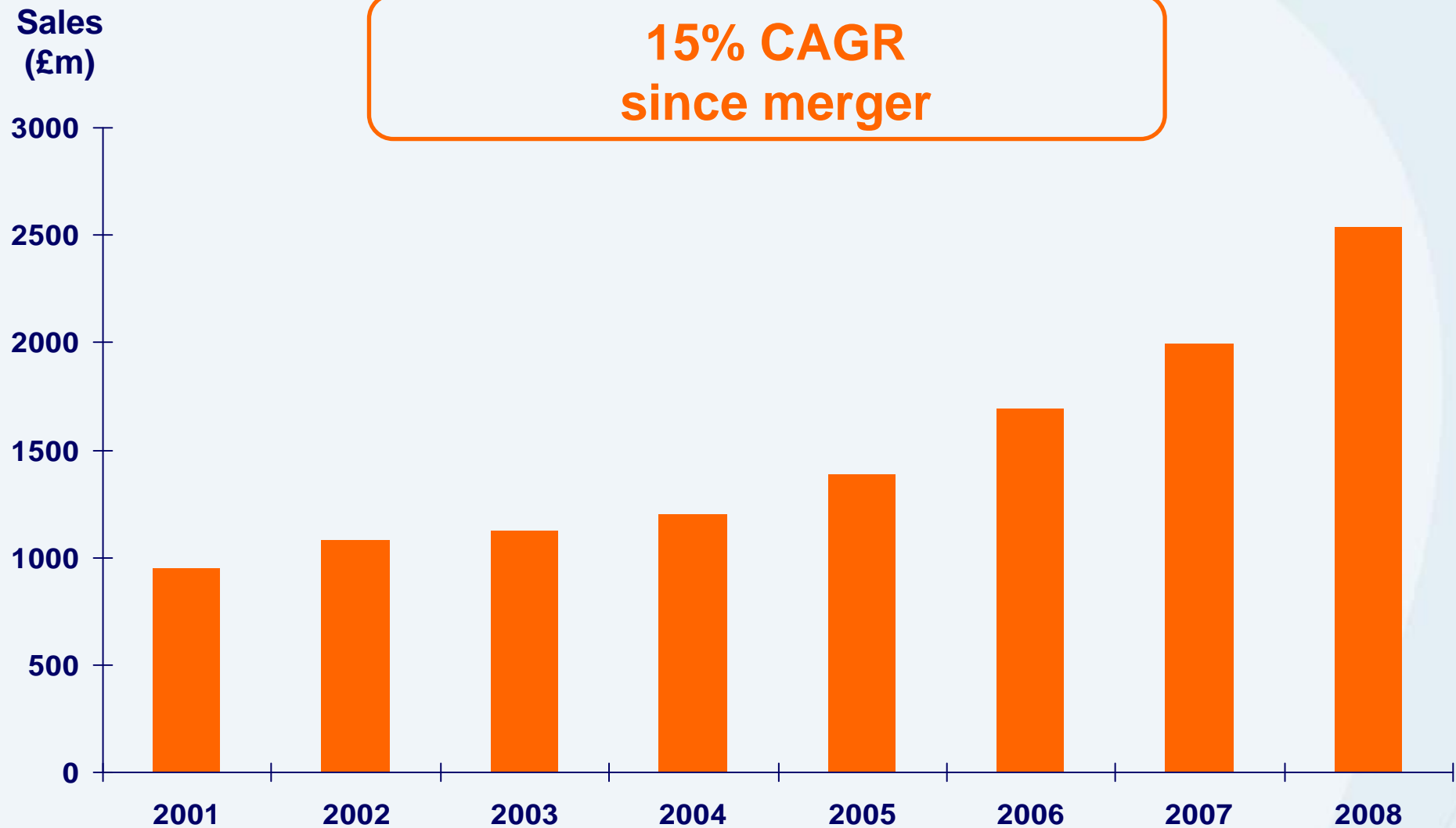


**GSK Vaccines 2008 sales**  
**£2.5bn**



\*GSK estimates from consolidated 2008 Annual Reports

# GSK Vaccines: Continuing Sales Growth



Reported Annual Sales. CAGR using CER is 17%

# 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**

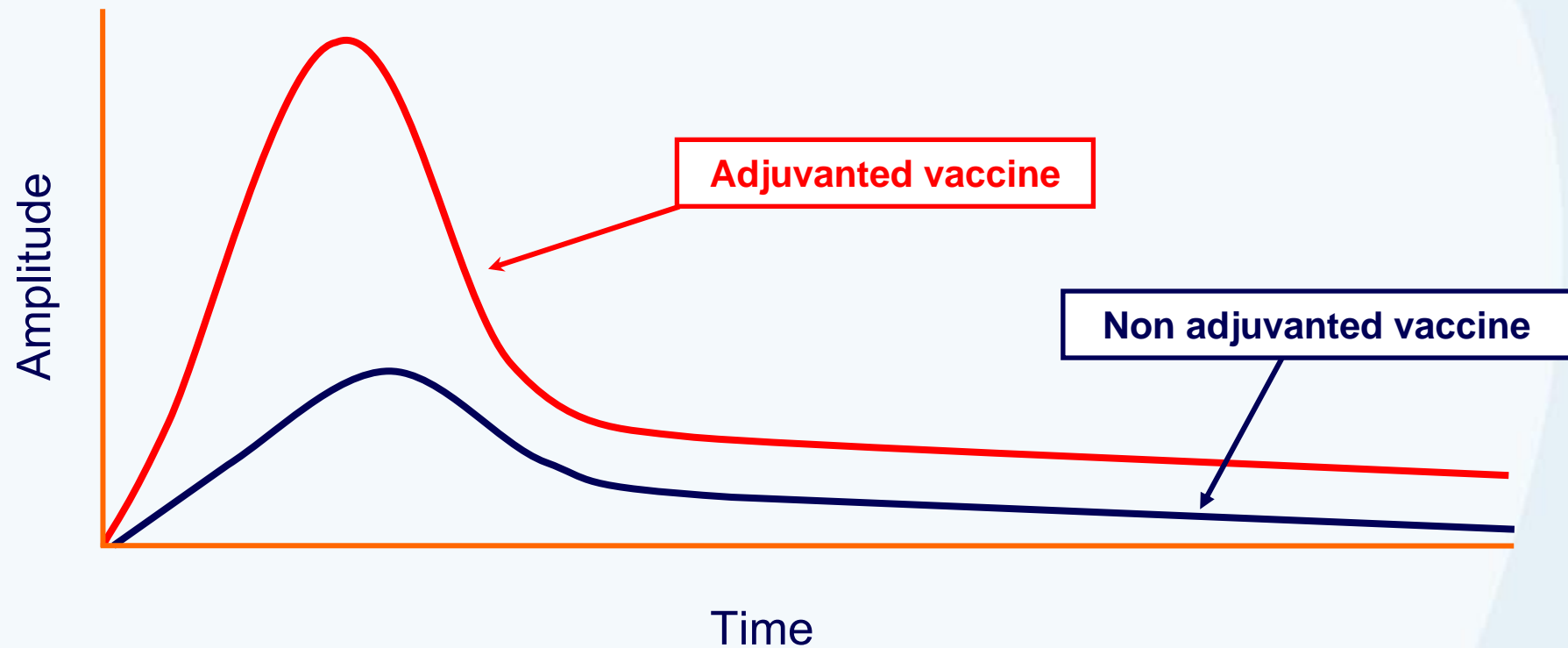
# Today's Agenda

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# 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™*
  - Flu vaccine for elderly (weakened immunity)
- To induce long-term protection
  - HPV vaccine, *Cervarix™*
- To induce broader immune response: Cross-protection
  - Pandemic Flu vaccines, *Prepandrix™*
  - HPV vaccine, *Cervarix™*
- To increase capacity by reducing antigen content/dose
  - Pandemic Flu vaccine, *Pandemrix™*

# Today's Agenda

**GSK  
within the  
Vaccines  
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Strategic  
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# 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**

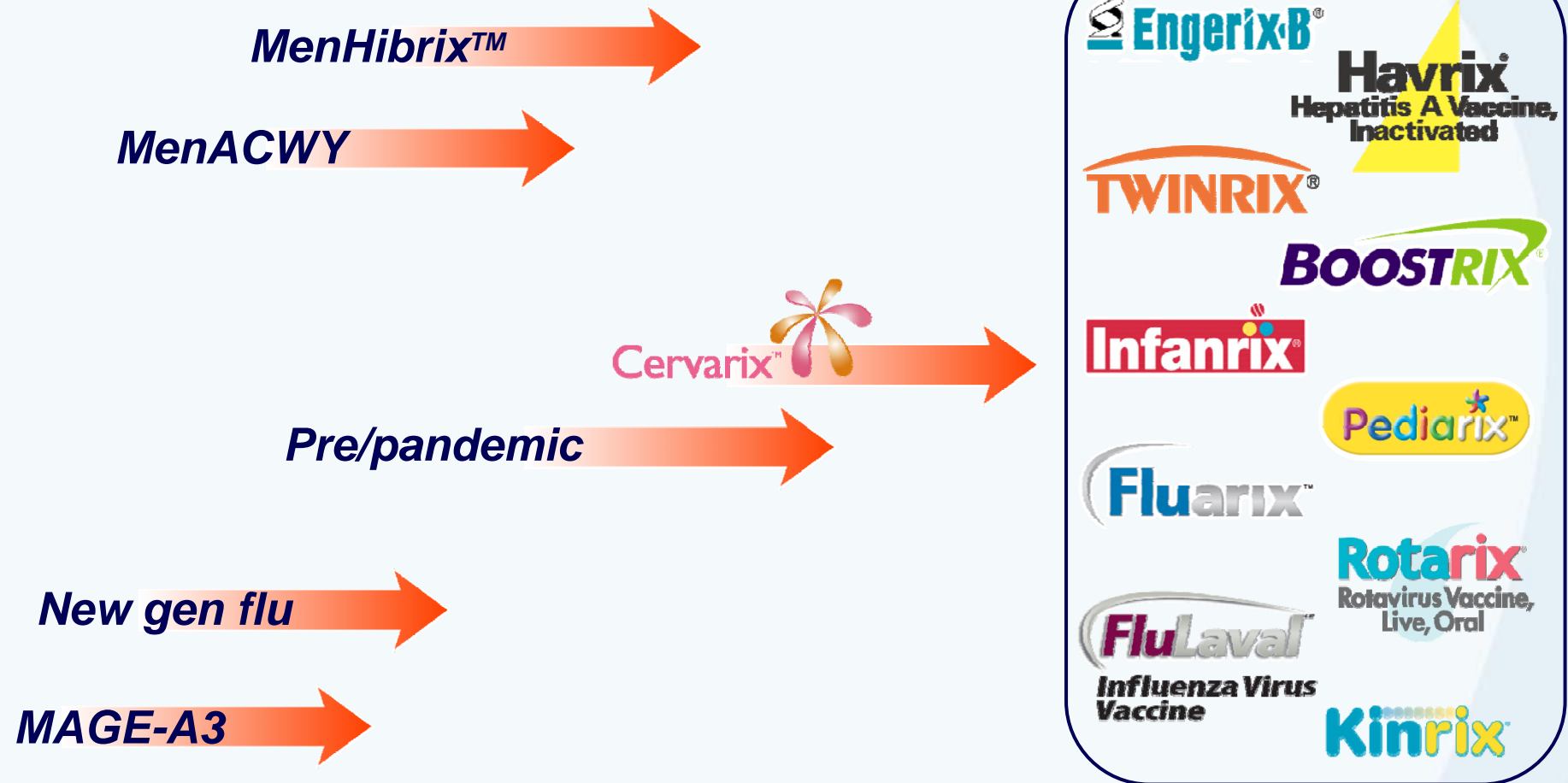
**Expanding Geographically**

# Grow a Diversified Global Business

Phase III

File

Marketed



United States

# 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

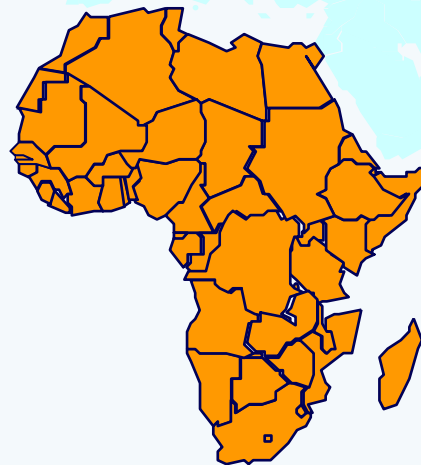
- Co-development of flu vaccines

# Grow a Diversified Global Business

- Over 25 year association 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

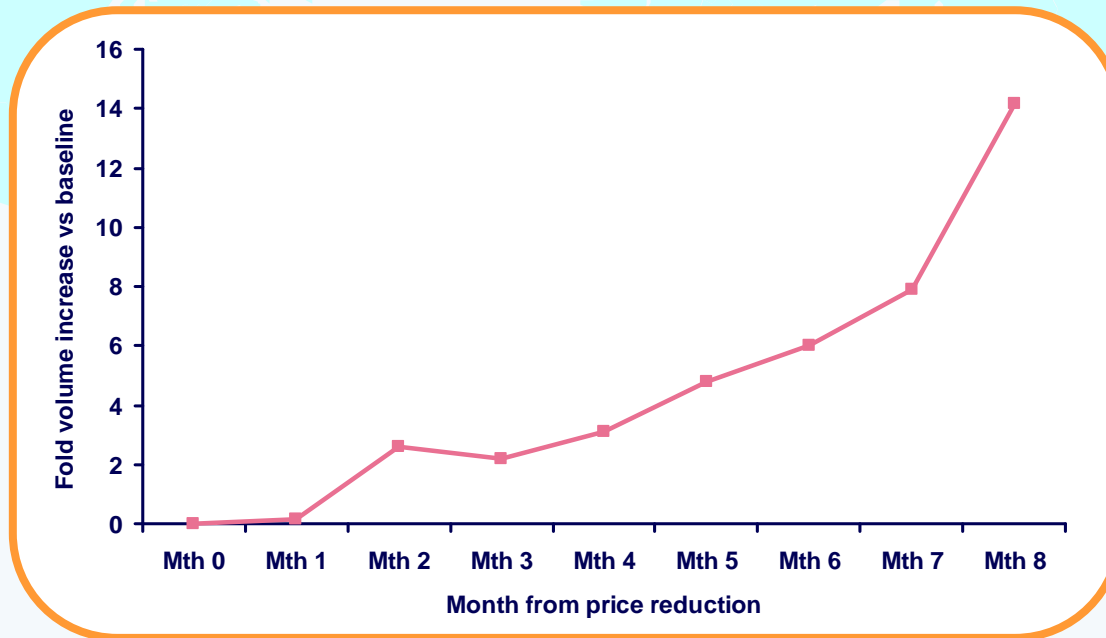
# Grow a Diversified Global Business

- 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

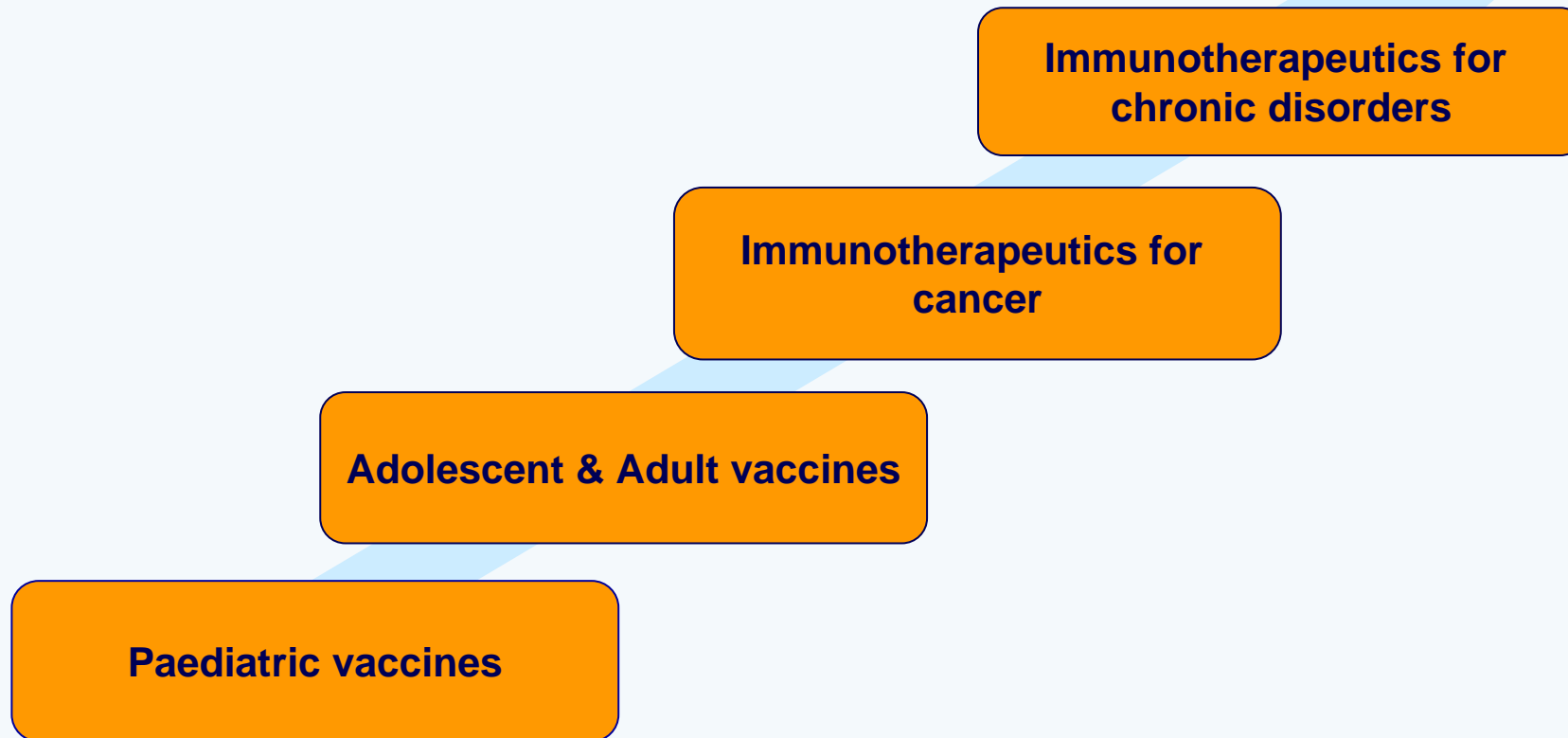


# Grow a Diversified Global Business

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

## Phase II

<b>Tuberculosis</b>
<b>Herpes zoster</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>Cervarix (BLA) *</b> Cervical cancer
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## Approved

<b>Flu Pre-pandemic *</b> Dresden (MAA)
<b>Flu Pandemic *</b> Dresden (MAA)
<b>Kinrix (BLA)</b> DTPa – IPV
<b>Rotarix (BLA) *</b> Rotavirus
<b>Boostrix (BLA)</b> DTPa
<b>Synflorix (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 96 countries
    - New launches
    - Increase market share in existing markets
- *Cervarix* in the US
  - Data submitted to FDA in March 2009
    - Final efficacy data from pivotal trial (HPV-008)
  - Anticipate 6 month FDA review process
- New data
  - Fulfilling the promise



# 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*, Jul 09  
*Human Vaccines*, May 09  
(and references above)

# 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)

\* ≥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.

# Head to Head: *Cervarix*<sup>®</sup> vs. *Gardasil*<sup>™</sup> (HPV-010)

- **Rationale**

- Immunogenicity data on the two vaccines cannot easily be compared because of differences in study design and assays used
- Gain insight into future potential differences in terms of long term protection

- 1,106 women (18 to 45 years)

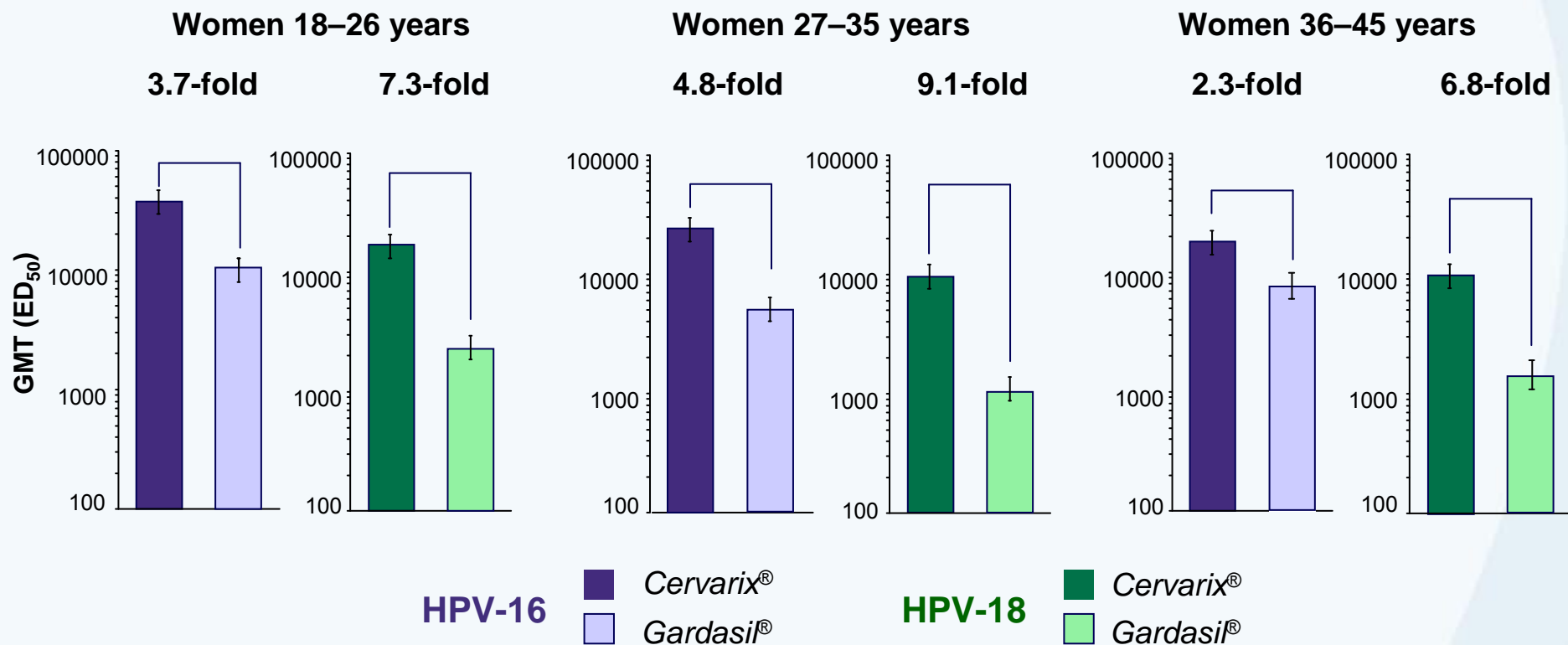
- **Primary endpoint**

- Compare the immune responses against HPV 16 and 18 measured by neutralization assay (women 18 - 26 years) for both *Cervarix* and *Gardasil*

# Head to Head: Cervarix<sup>®</sup> vs. Gardasil<sup>™</sup> (HPV-010)

## HPV 16 and 18 neutralizing antibody responses

### ATP Cohorts



Einstein MH on behalf of the HPV-010 study group. *25th International Papillomavirus Conference (Abstract)*, 2009; Einstein *et al Human Vaccines* (in press) 2009.

# *Cervarix*<sup>®</sup>: a growing body of data

## ■ What we know

- Major differences in measurable immune responses of *Cervarix* versus *Gardasil*
  - neutralizing antibodies (serum) for each antigen in all age groups
  - neutralizing antibodies at site of infection (cervix)
  - higher HPV-16/18-specific B- and T-cell responses
- Strong cross protection against oncogenic HPV types beyond HPV-16/18

## ■ If basic principles of vaccinology are applied

- Very high likelihood that *Cervarix* provides broad and long-lasting protection against ***cervical cancer***

# Synflorix™: Approval and launch

EU  
Approval  
March '09

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 57 countries  
Approved in 35 and launched in 10 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
  - *Pandemrix*
  - *Prepandrix*
- H1N1



# Pandemic Vaccines

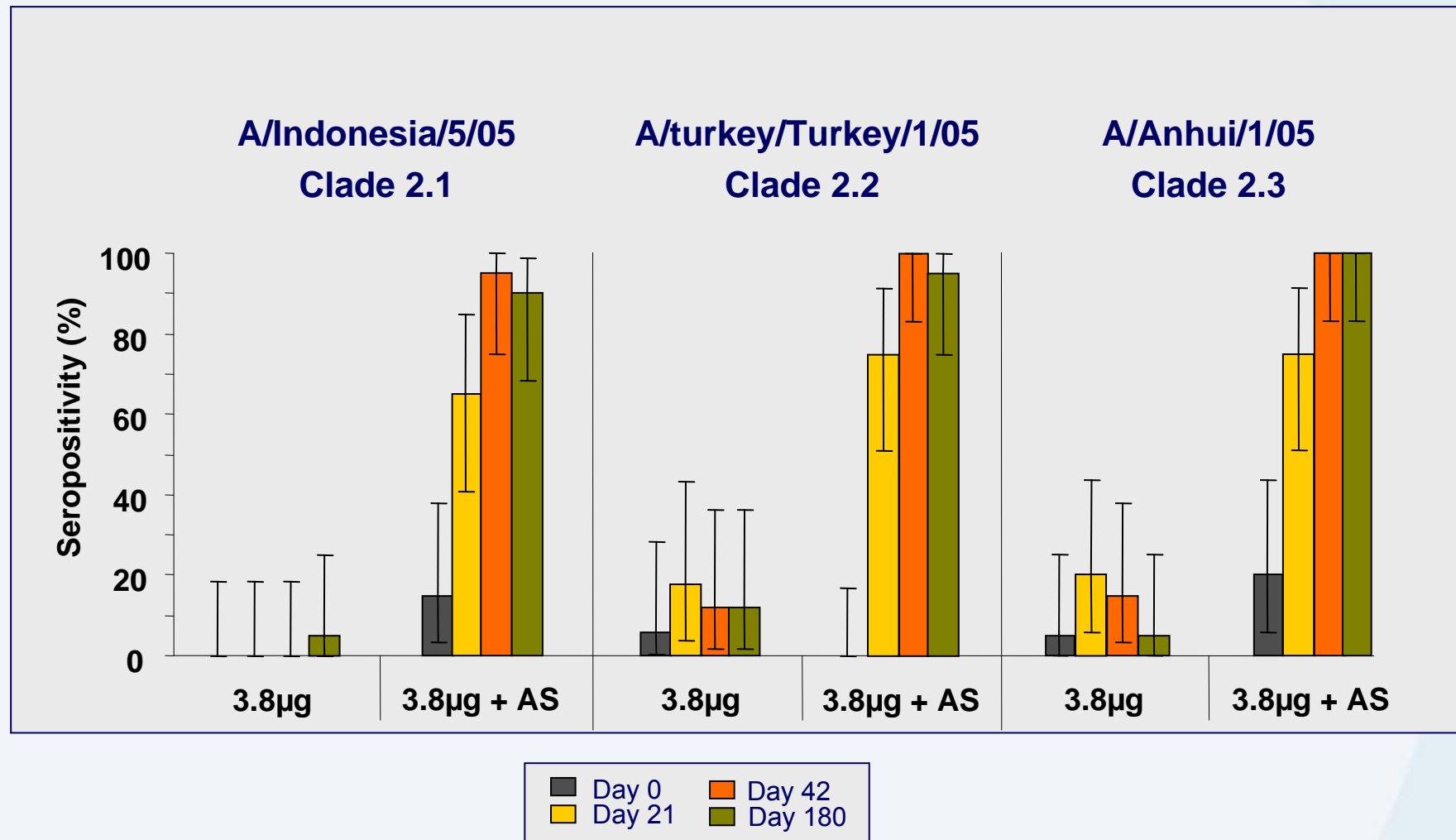
- **The Problem**

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

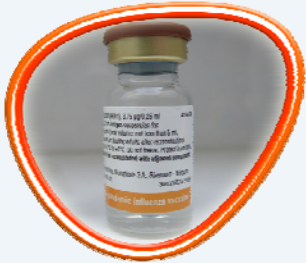
- **GSK Offering**

- H1N1 adjuvanted vaccine
  - Antigen sparing (higher supply)\*
  - Cross protection capability (cover drifting strains)\*

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



# Integrated GSK response to flu pandemic



- Adjuvanted vaccine offers potential for antigen sparing and increased immune response
- Production started June '09; first deliveries planned September onwards
- Contracts for 291m doses; in discussions with >50 governments



- 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%**

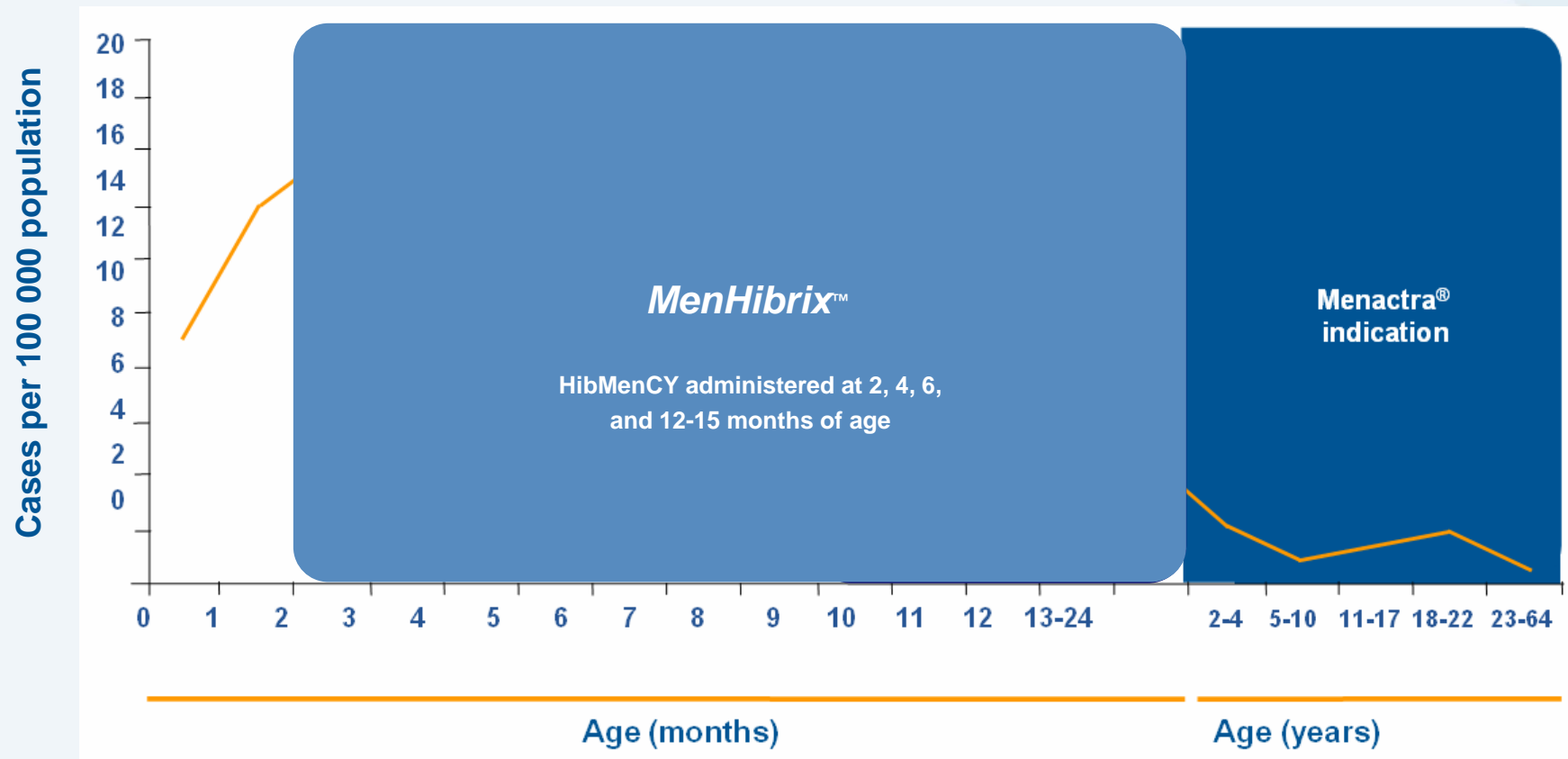
**Protection for infants, where the need is greatest**

**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  
Fast Track status granted**

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

## US Incidence of Culture Confirmed Meningococcal Disease



\*Infants defined as <12 months of age. Surveillance data from CDC sentinel sites (1997-2006). Cohn et al. Presented at the 48th annual ICAAC/46th annual IDSA. Washington, DC, October 25–28, 2008 - Presentation number: G1-413; Shepard et al. *Pediatr Infect Dis J* 2003; 22: 418-422; Lingappa et al. *Vaccine* 2001;19: 4566-4575;

# ...with no additional shots

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

**2 mos.**

*MenHibrix*



**4 mos.**

*MenHibrix*



**6 mos.**

*MenHibrix*



**12-15 mos.**

*MenHibrix*

**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
  - Most severe form of skin cancer
  - 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
  - Over 20 vaccines in clinical development
- 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**