

GSK VACCINES IN 2010

Thomas Breuer, MD, MSc

Senior Vice President
Head of Global Vaccines Development
GSK Biologicals



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 for newer vaccines
 - HPV vaccines (*Cervarix*, *Gardasil*)
 - Pneumococcal vaccines (*Synflorix*, *Prevnar-13*)
- Operating margin comparable to pharmaceutical products
- Heightened awareness
- New markets

Research & development timelines



Research (inc. Immunology)

Pre-Clinical Development (inc. Formulation Science)

Clinical Development
(inc. Post Marketing Surveillance)

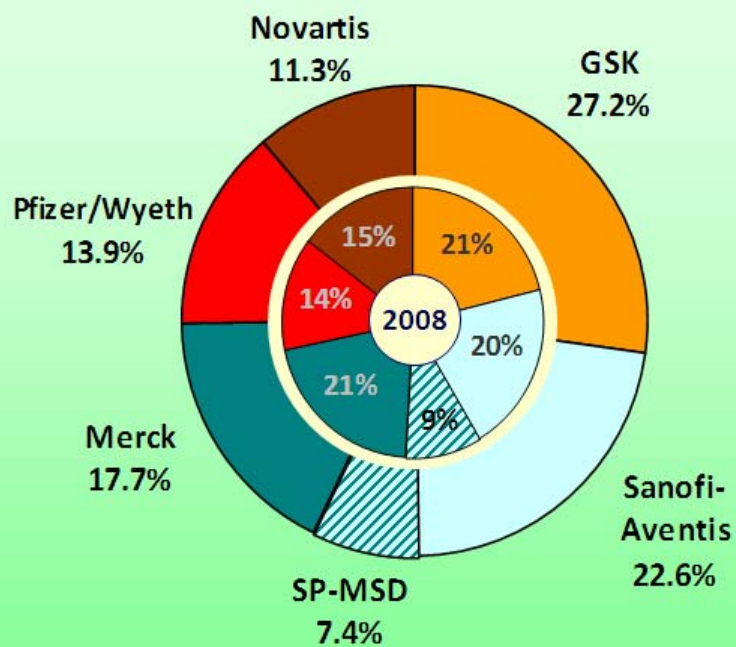
Transfer Process to Manufacturing

Build Facility



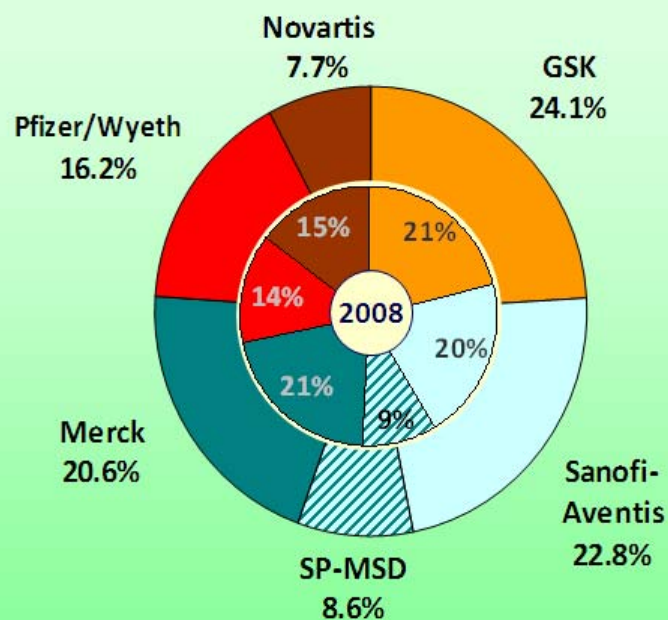
Global vaccines market 2009

2009 total sales



Total 2009 = \$21,493m

2009 excluding H1N1



Total 2009 excl. H1N1 = \$18,432m

GSK vaccines business

2009 sales £3.7 billion (+30%)

Vaccines represent 13%
of total GSK sales

Recent approvals:

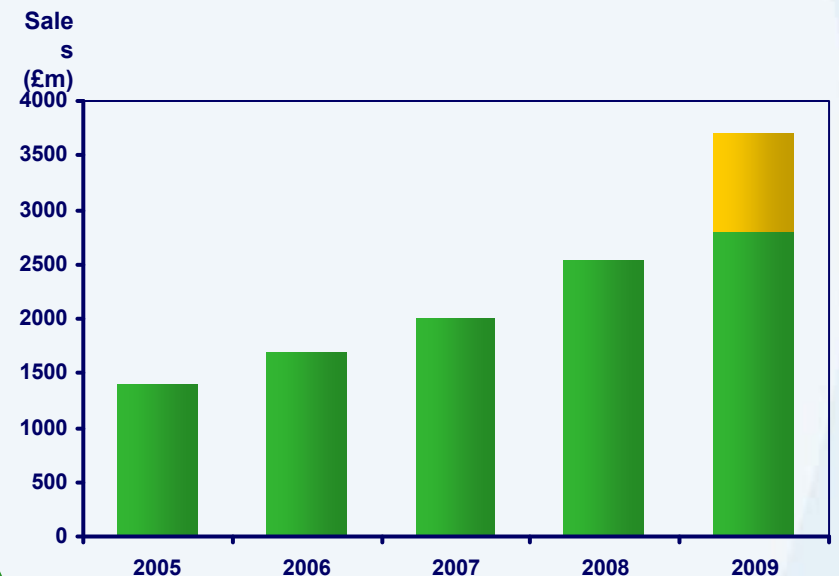
US: *Cervarix*

EU: *Synflorix*

Pandemic: *Pandemrix*; *Arepanrix*

Increased Emerging Market presence

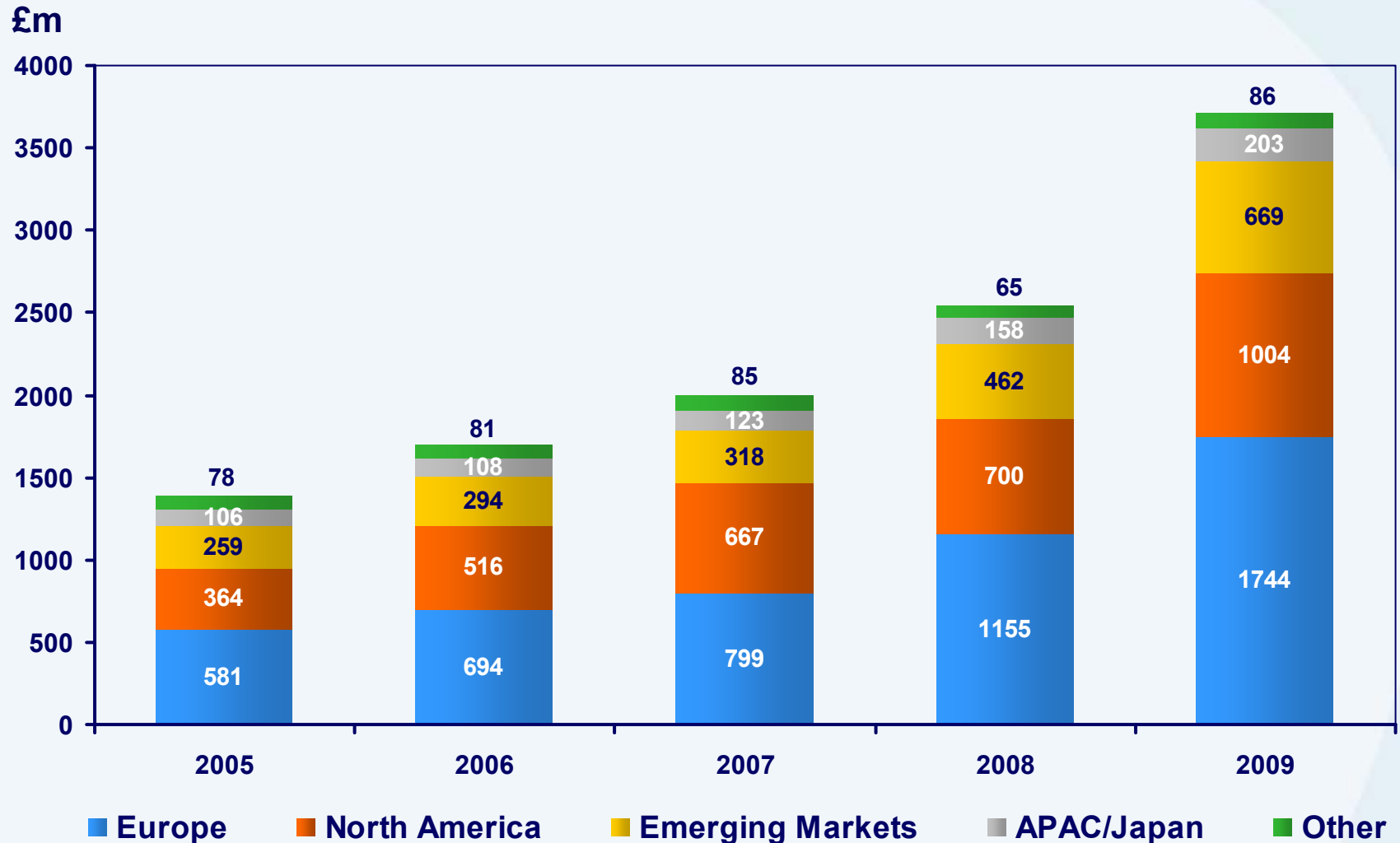
+19% CAGR excl. H1N1
since 2005



GSK vaccines: fastest growing part of GSK in 2009

	2009 Sales	Share	Growth (CER)
Respiratory	£ 6,977m	25%	+5%
Consumer	£ 4,654m	16%	+7%
Anti-virals	£ 4,150m	15%	+12%
Vaccines	£ 3,706m	13%	+30%
CV & Urogenital	£ 2,298m	8%	+8%
CNS	£ 1,870m	7%	-44%
Anti-bacterials	£ 1,592m	6%	+2%
Metabolic	£ 1,181m	4%	-14%
Oncology & Emesis	£ 629m	2%	10%
Stiefel	£ 248m	1%	n/a
Other	£ 1,063m	4%	+1%
Total	£ 28,368m		+3%

GSK vaccines: a history of growth



Note: All figures expressed at actual rates
Includes H1N1 pandemic sales

GSK vaccines business

**Over 30 approved vaccines and 20
in development**

**Distributed 1.4 billion vaccine doses
to 182 countries in 2009**

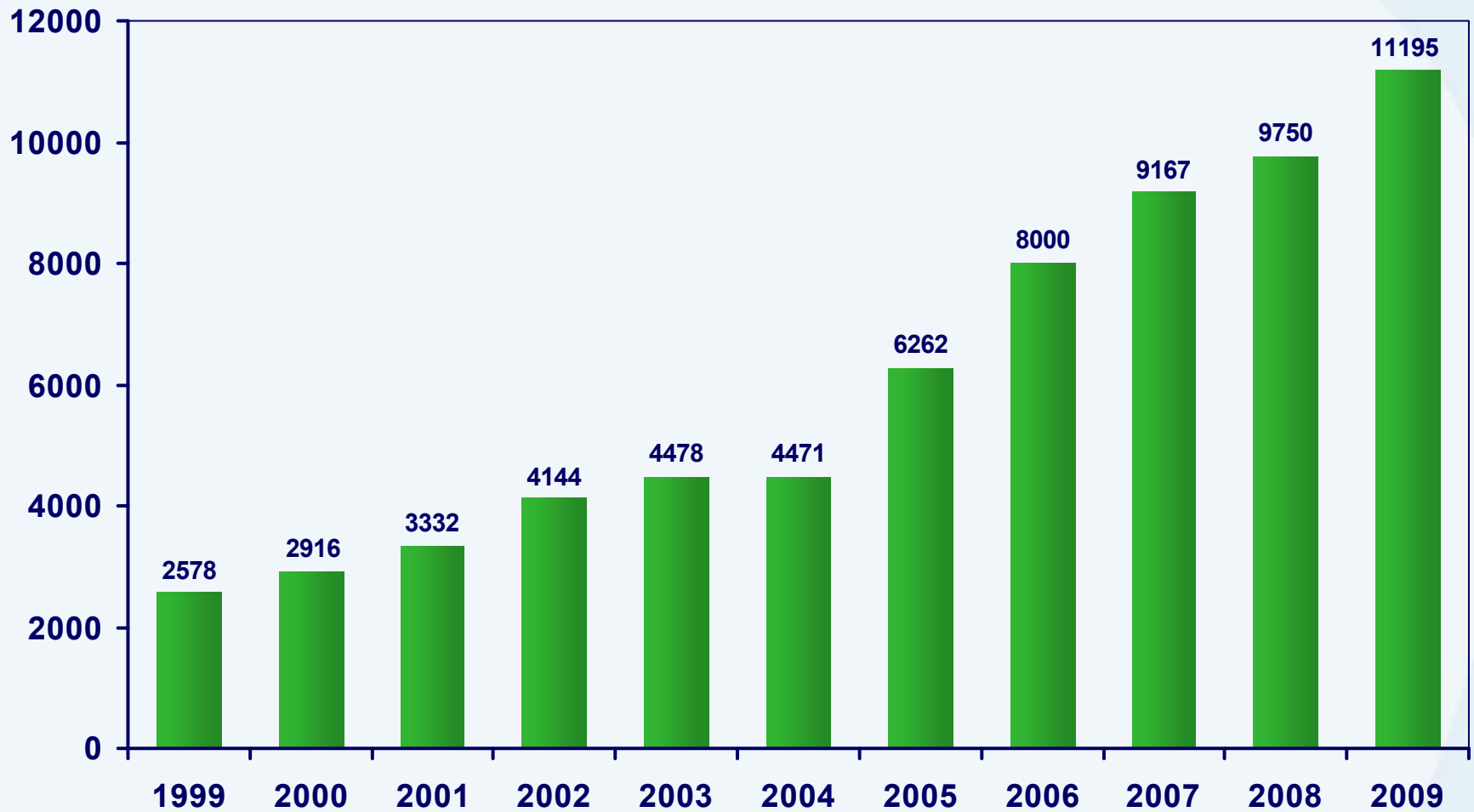
**Over 11,000 employees worldwide,
including over 1650 scientists**

**Global manufacturing network:
15 sites around the globe**

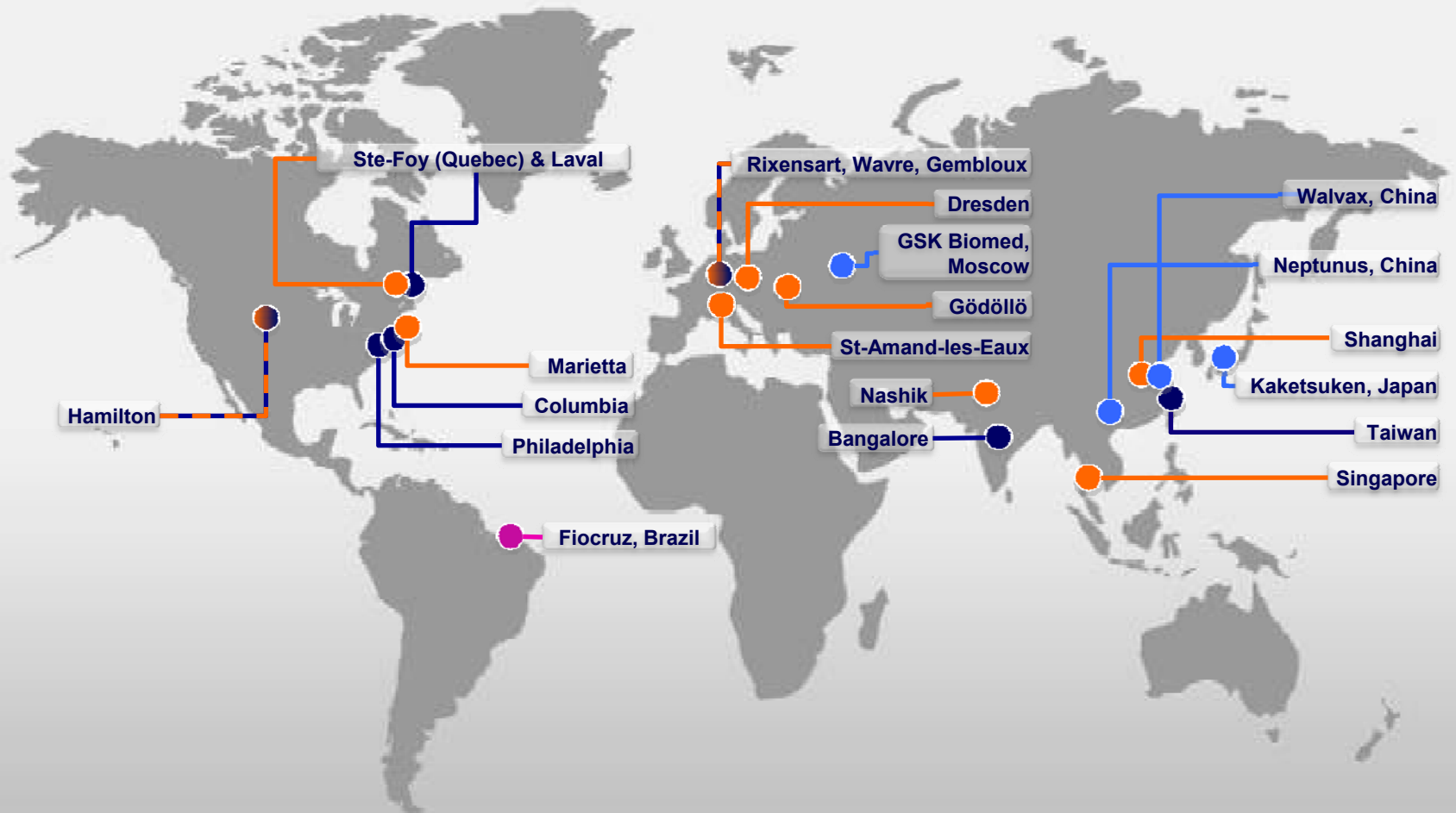
**Succession plan for management
of vaccines business**



GSK vaccines worldwide personnel



Global manufacturing footprint



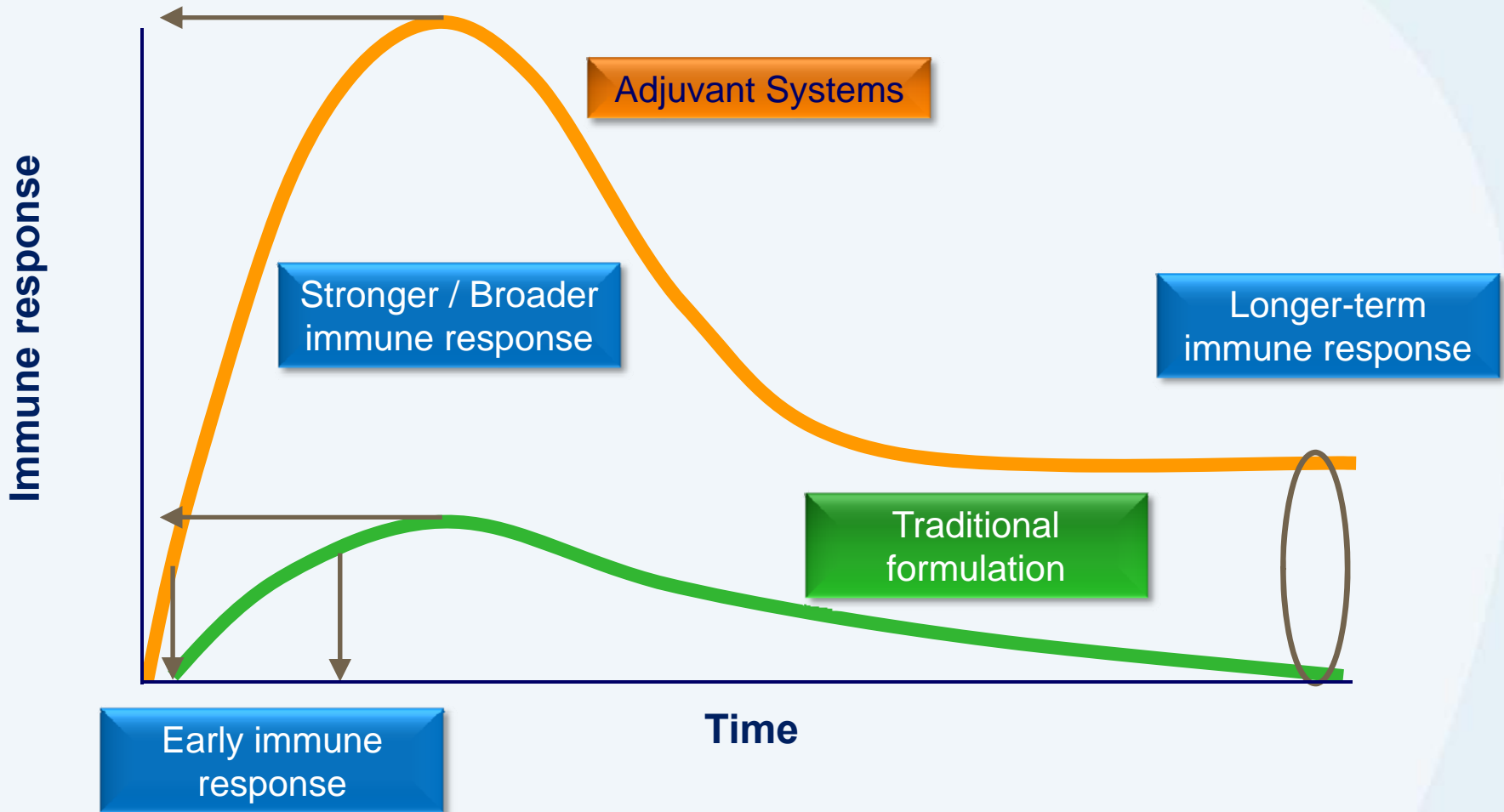
Industrial Operations

Joint Ventures

Alliances

R&D / Clinical / Regulatory

Adjuvants: advantages of adjuvant systems



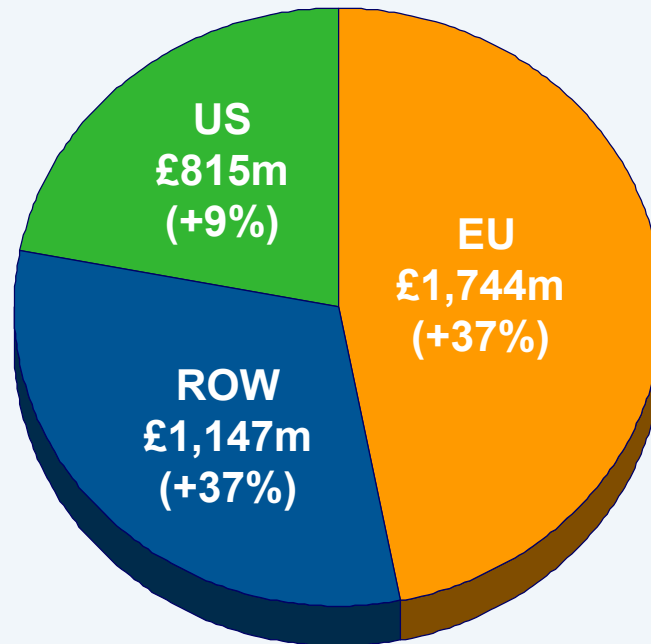
Adjuvants: why do we need better adjuvants?

- To induce strong immune responses
 - Malaria, RTS,S (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; Arepanrix*
 - HPV vaccine, *Cervarix*
- To increase capacity by reducing antigen content/dose
 - Pandemic Flu vaccines, *Pandemrix; Arepanrix*

‘One size does not fit all’

GSK vaccines: broad geographic opportunity

GSK vaccines 2009 sales
£3.7bn (+30%)



Geographical opportunity

US

 **Engerix-B®**

Havrix®
Hepatitis A Vaccine,
Inactivated

TWINRIX®

BOOSTRIX®

Infanrix®

Pediarix™

Fluarix™

Rotarix®
Rotavirus Vaccine,
Live, Oral

FluLaval™
Influenza Virus
Vaccine

Kinrix®

Cervarix™

Hiberix®

Emerging Markets

Cervarix™

Infanrix

Rotarix®
Rotavirus Vaccine,
Live, Oral

Fluarix™

Synflorix

BOOSTRIX®

Havrix®
Hepatitis A Vaccine,
Inactivated

Arepanrix

Japan

Cervarix™

Arepanrix

GSK has the broadest vaccine portfolio in EM

	GSK	Merck	Sanofi	Pfizer	Novartis
DTPw combos	✓		✓		✓
DTPa combos	✓		✓		
MMR / <i>Varicella</i>	✓	✓	✓		
Hepatitis A	✓	✓	✓		
Rotavirus	✓	✓			
Meningococcal	✓		✓		d
Pneumococcal	✓			✓	
Influenza	✓		✓		✓
HPV	✓	✓			
Malaria	d				
Dengue	d		d		

✓ = available in EM; d = in development

Emerging markets opportunity: China



China

£116m
+36%
(2009)

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

- Co-development of seasonal and pre-pandemic/pandemic influenza vaccines



Joint venture with Walvax

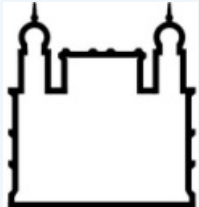
- Develop and manufacture paediatric vaccines for use in China
 - *Priorix* and other paediatric vaccines

Emerging markets opportunity: Brazil



Brazil

**£117m
+10%
(2009)**



FIOCRUZ

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)
 - Included in National Immunization Programme

Opportunity in Japan

Japanese vaccine market
underdeveloped: £500m in 2009

Cervarix first HPV vaccine
approved in Japan

Rotarix first rotavirus vaccine
filed in Japan

GSK key supplier of H1N1 pandemic
vaccine to Japanese government

Partnership with Kaketsuken in flu
and flu cell-culture

Japan fully integrated into key global
phase III clinical trial programmes



GSK vaccines: a rich pipeline

Phase I	Phase II	Phase III	Submitted
HIV	Tuberculosis	<i>Mosquirix</i> TM Malaria	<i>MenHibrix</i> TM (HibMenCY-TT)
Cytomegalovirus	Dengue	New generation seasonal flu	
NTHi-Pneumo	WT1 Acute myelogenous leukaemia ¹	MAGE-A3 ASCI Non-Small Cell Lung Cancer ¹	Approved
Alzheimer's disease	Heptavalent combination vaccine	MAGE-A3 ASCI Melanoma ¹	<i>Cervarix</i> TM Cervical cancer
	Hexavalent combination vaccine	<i>Nimenrix</i> TM (MenACWY-TT)	<i>Synflorix</i> TM <i>Streptococcus pneumoniae</i> & <i>non-typeable Haemophilus influenzae</i>
	<i>S. pneumo</i> paediatric new generation	<i>Simplirix</i> TM <i>Herpes simplex virus</i>	<i>Arepanrix</i> TM H1N1 Pandemic Flu
		Flu Pre-pandemic (Quebec)	<i>Hiberix</i> TM <i>Hib</i> paediatric booster
		Herpes Zoster	

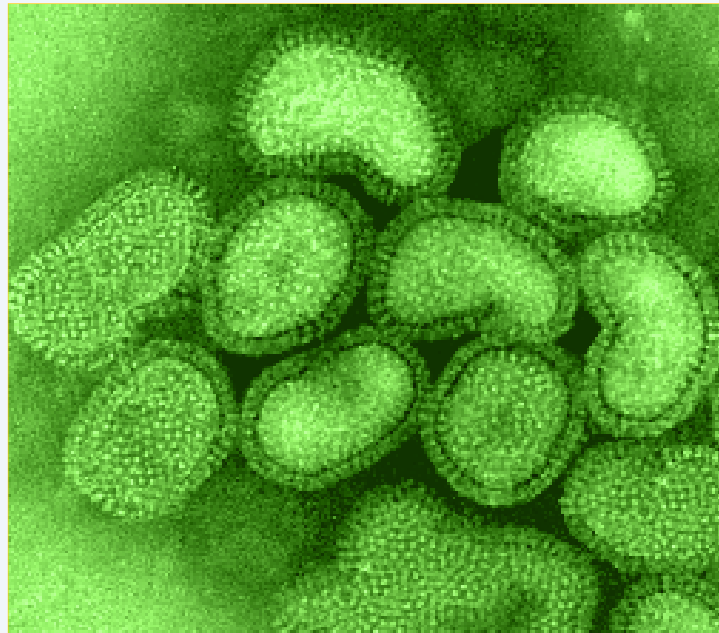
Late-stage assets: meningitis

- **Meningococcal disease causes permanent disability or death**
 - Fatality rate 9-12%
- **Five serogroups (A, B, C, W135, Y) cause the majority of invasive meningococcal disease**
- **GSK developing tailored meningitis vaccines to fulfil regional and age-related needs:**
 - ***MenHibrix (HibMenCY)***
 - Protection for infants, where the need is greatest (2-24 months)
 - Filed in US (August 2009)
 - Complete Response Letter received (June 2010)
 - ***Nimenrix (MenACWY)***
 - Protection against 4 major serotypes (A, C, W, Y) in 1-55 years of age
 - Planned EU filing H1 2011

Late-stage assets: influenza

- **Improved seasonal flu vaccines**
 - Inclusion of additional B strain (quadrivalent)
 - Need for improved efficacy in both paediatric and elderly populations

- **Ongoing commitment to pandemic flu**
- **Continuous innovation**
 - Cell-culture
 - New delivery systems



GSK response to H1N1 pandemic



- **Integrated GSK response to pandemic**
 - *Pandemrix, Arepanrix, Relenza, Actiprotect*
- **Largest global supplier of H1N1 vaccine**
 - Doses supplied to over 60 countries; approximately £1.9 billion sales
 - £883 million (Q4 2009)
 - £973 million (H1 2010)
 - 60 million dose donation to WHO
- **In Europe over 30 million doses of *Pandemrix* administered¹**
 - *Pandemrix*: approximately 80% of European doses administered
- **Excellent vaccine efficacy demonstrated^{2,3}**
- **Extensive safety experience with adjuvanted H1N1 vaccine gathered**
 - Positive benefit:risk profile confirmed

¹22nd pandemic pharmacovigilance weekly update (EMA/527985/2010) 19 August 2010; ²Wichmann et al *Euro Surveill.* 2010;15(18):pii=1956

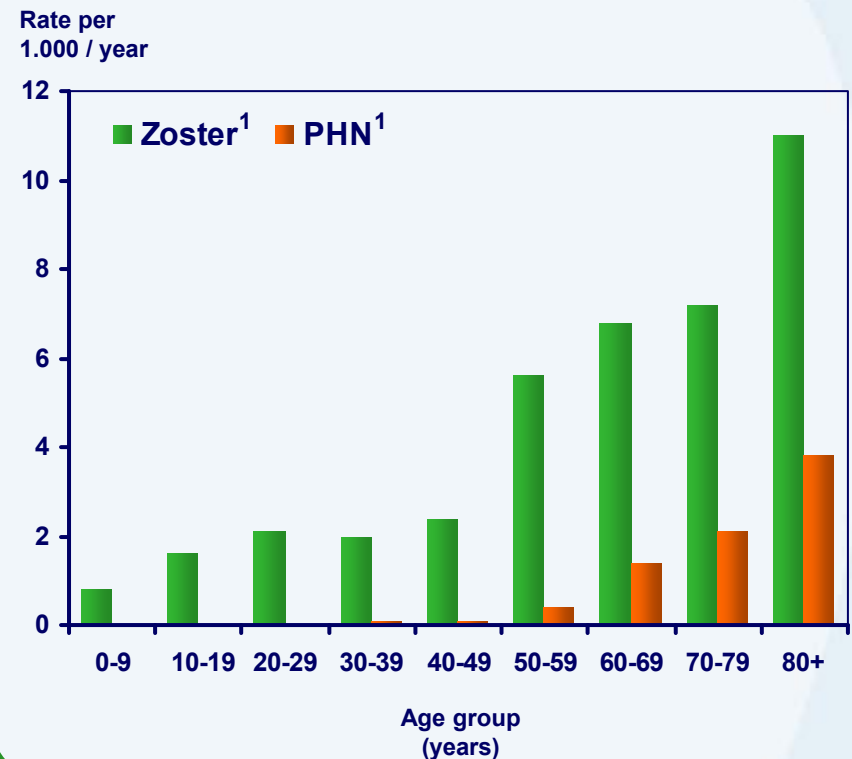
³Waddington et al *BMJ* 2010;340:c2649

Late-stage assets: *Herpes zoster vaccine*

- *Herpes zoster (HZ) & Post-herpetic neuralgia (PHN)*
 - After initial varicella zoster infection (chickenpox), VZV DNA remains latent in nerve cells
 - May reactivate later in life to cause HZ (shingles)
 - 1 in 4 will suffer from shingles (lifetime)²
 - 1 in 5 shingles patients develop chronic pain (PHN)³
- Risk factors
 - Age \geq 50 years
 - Impaired cellular immunity

GSK Herpes zoster vaccine candidate

- Adjuvanted sub-unit vaccine
- Phase III commenced August 2010



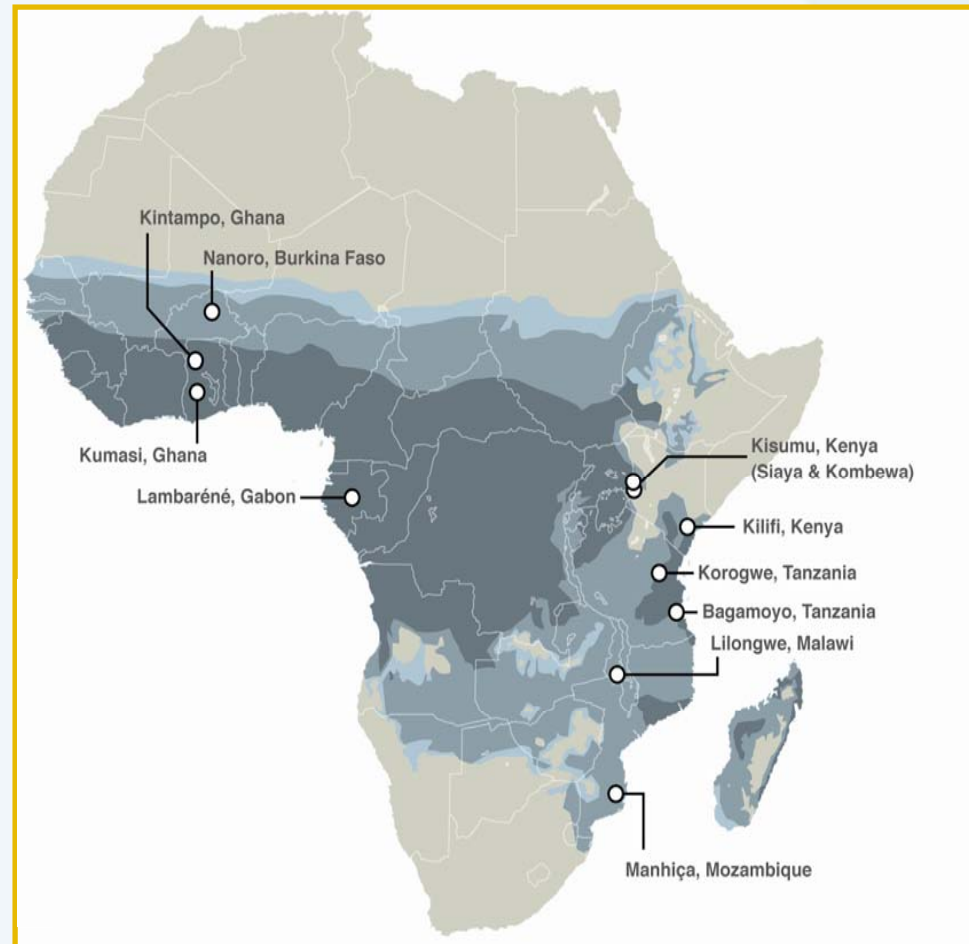
Late-stage assets: malaria (RTS,S)

- **Significant burden of disease**

- Malaria kills almost 900,000 people every year¹
 - Many in sub-Saharan Africa
 - Majority are children under the age of five

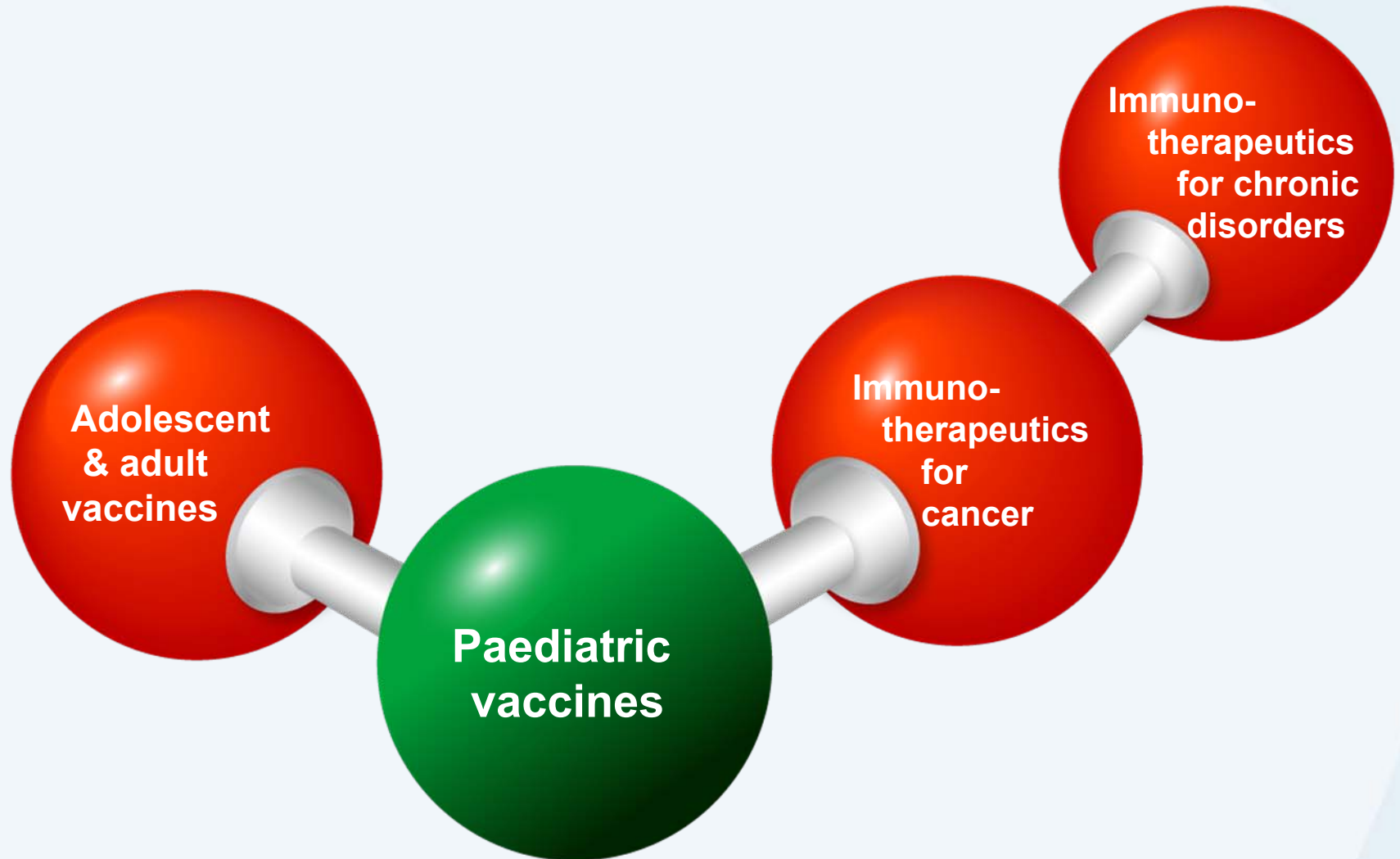
- **Phase III trials underway**

- 11 trial sites across 7 African countries
- Current enrolment
 - **8,923** children
 - **3,246** infants

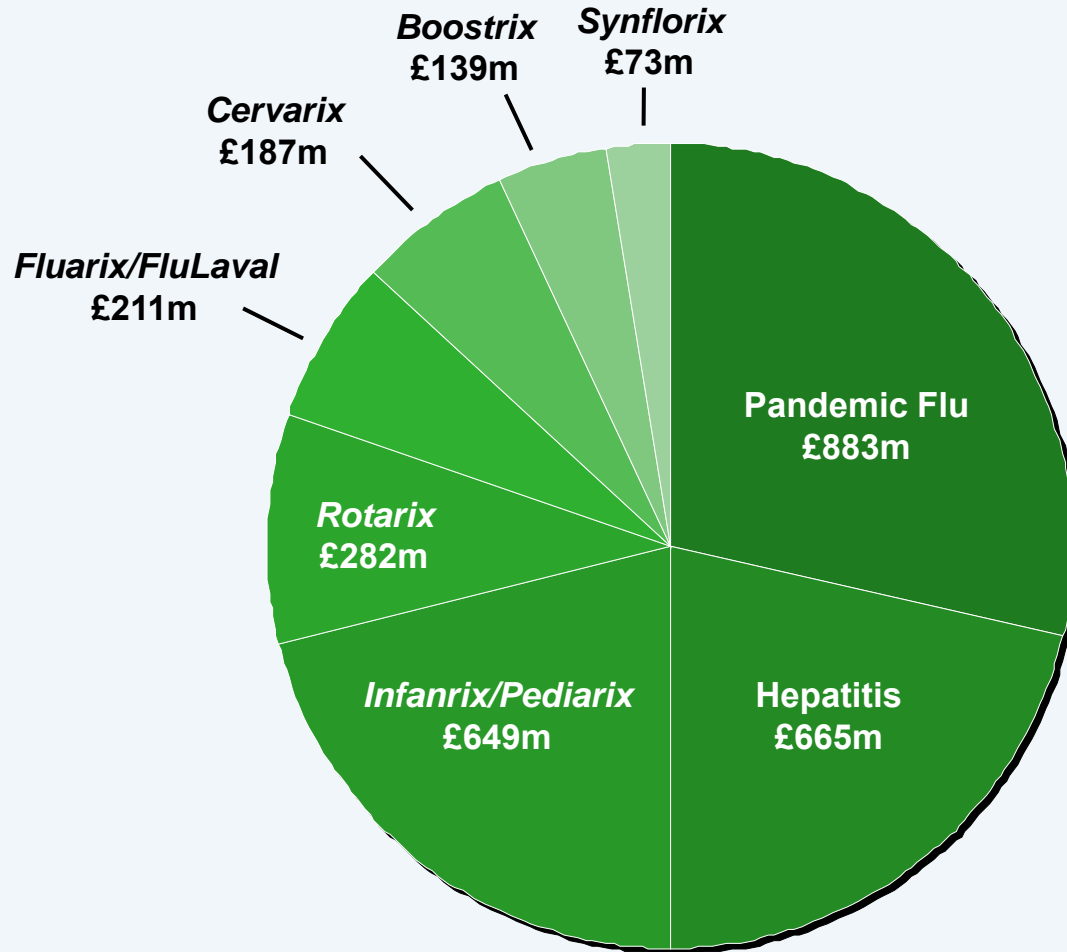


¹World Health Organization (WHO) World Malaria Report, 2009

Evolution of a diversified business



GSK key vaccines: 2009 sales



2009 sales: £3.7 billion (+30%)

Rotarix in 2010: returning to growth



Approved in 116 countries
Filed in Japan (November 2009)

2009 sales £282 million
H1 2010 sales £104 million

Rotarix global market share increased significantly in 2009 to 44%

Geographic expansion into EM & Japan
US currently accounts for 60% of global market

WHO prequalification (June 2009)

Development of PCV-1-free Rotarix ongoing

Cervarix in 2010: future opportunities



Approved in 111 countries
Including US and Japan (October 2009)

2009 sales £187 million (+38%)
H1 2010 sales £127 million (+4%)

Over half of competitive tenders won
Over two-thirds by volume

WHO Prequalification (July 2009)
Global access to *Cervarix* via UNICEF & GAVI

Synflorix: successful launch



Approved in 71 countries
Filed in additional 31 countries

Significant tender wins and market share gains
H1 2010 sales £83 million

Long-term contract signed with Brazilian government
€1.5 billion over 10 years

Advance Market Commitment (AMC) for pneumococcal vaccines launched (March 2010)
300 million doses of *Synflorix* over 10 years



WHO prequalification (October 2009)
Enables UN agency purchase

Antigen-Specific Cancer Immunotherapeutics (ASCI): an overview

- **ASCI represent a novel class of compounds based on tumour antigens**
- **MAGE-A3 in Non-Small Cell Lung Cancer (NSCLC)**
 - 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)
- **MAGE-A3 in Melanoma**
 - Phase III study ongoing (DERMA)
- **Collaboration with Abbott on molecular diagnostic tests**
 - MAGE-A3 in NSCLC and melanoma
- **WT1 in Acute Myelogenous Leukaemia (AML)**
 - Phase II study commenced

Therapeutic vaccines

ASCI

MAGE-A3 in Phase III

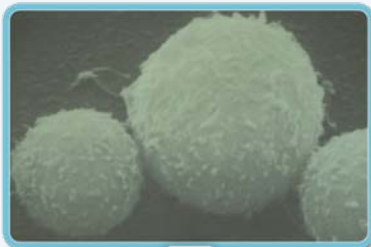
- NSCLC and melanoma

WT1 in Phase II

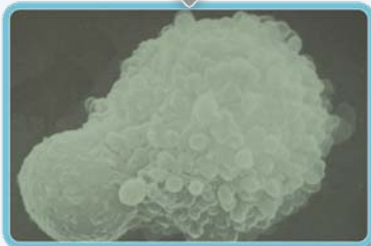
- AML

Novel mechanism of action

- Tumour-specific
- Patient-selective



± 20 min
(in vitro)

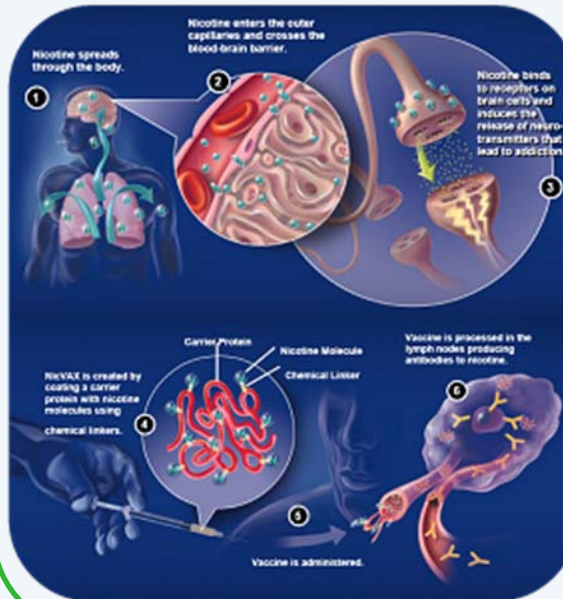


Nicotine Addiction

Nicotine conjugate vaccine (*NicVAX*)¹

Aid to smoking cessation and
long-term abstinence

Two Phase III studies ongoing

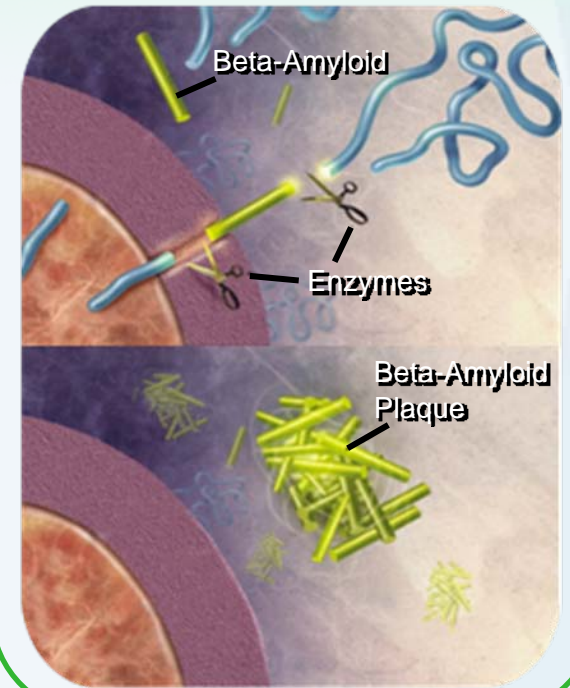


Alzheimer's

Two candidate vaccines
in development²

Targets beta-amyloid

- Pivotal role in plaque formation



¹ Licensed from Nabi Biopharmaceuticals

² Licensed from AFFIRIS

GSK vaccines in 2010

- A world leader in vaccines
- One of the broadest portfolios and fastest growing vaccines businesses in the world
- Unique expertise in adjuvant technology
- Strong pipeline including innovative therapeutic vaccine approaches
- Global footprint: ideally positioned to capture a significant market share in all territories



GlaxoSmithKline