The R&D structure of GlaxoSmithKline and GSK’s activities in Hungary

Tim Morris
Hungarian Innovation Contest for Youth

The Association intends to promote the creation, spread, transfer, adoption and the practical utilization of intellectual products so that

- the performance and the income generating potential of the companies and the Hungarian economy should be increased,
- by making use of innovation the modernization and the development of economy as a result of it should be accelerated.
GlaxoSmithKline

- Second largest pharmaceutical company
- Over 100,000 employees in 117 countries
- £2.8 billion invested in R&D in 2004
- 191 countries supplied by 37 manufacturing sites in 6 continents
- Largest UK company charitable giver
- 6% of the world’s pharmaceutical market

Where Are We?

Our International region covers 80% of the world’s population
GlaxoSmithKline

- GSK's mission is to improve the quality of human life by enabling people to do more, feel better and live longer.

- One of the industry leaders, with an estimated six per cent of the world's pharmaceutical market. GSK has leadership in four major therapeutic areas
  - anti-infectives,
  - central nervous systems
  - respiratory
  - gastro-intestinal/metabolic.

- In addition, it is a leader in the important area of vaccines and has a growing portfolio of oncology products.
Pharmaceutical R&D investment is substantial

R&D Spending as a percentage of sales

Telecommunications 3.8%
Aerospace & Defense 3.8%
Automotive 3.8%
Electrical & Electronics 8.1%
Computer Software & Services 10.2%
Pharmaceutical R&D 17.7%
R&D is getting more and more expensive

Average R&D costs per NCE medicine launched

$M (in year 2000 dollars)

Year


R&D Heads @ IBC mtg 2003

Bain & Co Dec 03

Post-launch costs

54 231 95 802 1400 1700
Less Product, more cost: 
Need for innovation:

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**US New Chemical Entity (NCE) Approvals**

While the rate of new drug approvals in the US doubled over the past three decades, annual R&D spending has increased more than 12 times in inflation-adjusted dollars.

**R&D expenditure**

$ billions, 2001

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[Source: GlaxoSmithKline]
The Path to Modern Medicine
A Chronology of Medicines Innovation

- **1890**
  - Aspirin

- **1900**
  - Antibiotics

- **1910**
  - Beta-blockers

- **1920**
  - Cancer Therapies

- **1930**
  - Anti-arthritis
  - Tranquillisers

- **1940**
  - Antihypertensives

- **1950**
  - Focus on Tissue Biochemistry

- **1960**
  - Focus on Cell Biochemistry

- **1970**
  - Focus on Molecular Structure

- **1980**
  - Treatment for autoimmune disease

- **1990**
  - CNS drugs

- **2000**

- **2010**

**Accumulated Knowledge of Human, Cell and Molecular Biology**
The «old» way

Chemicals $\rightarrow$ Animals $\rightarrow$ People
Simple Guide to R&D

Research
"create it"

Technical
"make it"

Safety
"test it" (pre-clinical)

Medical
"test it" (man)

Regulatory
"register it"

Product Development

Commercial
"sell it"
Pharmaceutical R&D has been redesigned at every stage

Genetics, genomics & pharmacogenetics

Discovery Research automation

Experimental Medicine
Innovation in R&D
The central questions are now:

What do we target?

What do we make?
The new Discovery paradigm ...

- Until the 1990’s, all pharmaceutical R&D addressed only ~500 molecular targets
- The human genome provides the full menu of ~10,000 potential targets, of which ~2000 are currently tractable (well-understood receptor & enzyme classes)
- Advances in other technologies provide the tools required to exploit this potential wealth
- We still lack detailed understanding of the roles in disease of many genomic targets
<table>
<thead>
<tr>
<th>Genomics</th>
<th>Genetics</th>
<th>Pharmacogenetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identifying novel molecular targets amenable to pharmacological intervention</td>
<td>Identifying novel molecular targets associated with defined disease states</td>
<td>Identifying the patient sub-populations most likely to benefit and/or least likely to experience adverse events from a drug</td>
</tr>
</tbody>
</table>

1990's (therapeutic relevance still under investigation)  
On-going: 7-12 year pay-off?  
Viable now ...
PHARMACOGENETICS AND DRUG DEVELOPMENT

- In the lab and in the clinic
- Pharmacogenetics informs decision-making along the pharmaceutical pipeline.
- Growing literature of retrospective studies medicines describing efficacy or safety on the basis of patient genotypes
- Emphasises the potential prospective use of genome information to fine new medicines.

*Nature Reviews Genetics 5*, 645-656 (2004);
Capture the potential of the human genome: industrialisation of drug discovery

- Huge array of molecular targets
- Vast, diverse chemical libraries
- Rapid identification of leads
- Extensive survey of biological function

Genetics
Genomics
Proteomics
High-throughput chemistry
Ultra-high throughput screening
High-throughput biology

Novel technologies, including through partnerships
‘Biggest chemistry lab in the UK’

- “Built and equipped at a cost of over £45 million, the new three-storey, 9000m2 facility will house GSK’s chemistry capability with a particular emphasis on automated high-throughput chemistry (HTC). Harlow will also become a global storage centre for GSK’s compound collection, home to vast automated compound stores with capacity for 1 million solid samples and 4 million frozen liquid samples.”
21st Century Drug Discovery

Drug candidates optimised for selectivity, potency, efficacy & safety

High-throughput chemistry

High-throughput screening

Human genome - unprecedented opportunities
Innovation in R&D
Centres of Excellence for Drug Discovery

• Within the middle stages of the process, small, nimble therapeutically aligned units, called Centres of Excellence for Drug Discovery (CEDDs), enable scientists to direct the course of their research, studying how diseases develop and progress and identifying compounds which show the most promise to become safe and effective medicines.

• quick, alert, clever conception, comprehension, or resourcefulness <a nimble mind>
Discovering new drugs

Characterising possible medicines

Studies in humans

Lead optimization

Safety and efficacy

Drugs

Databases
Genes
Drug targets
Chemical Diversity
Hit identification
Lead compounds
Candidates

Studies in humans

Discovering new drugs

Characterising possible medicines

Safety and efficacy

Drugs

Databases
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Genes
Drug targets
Chemical Diversity
Hit identification
Lead optimization

Studies in humans

Discovering new drugs

Characterising possible medicines

Safety and efficacy

Drugs
Capturing external innovation

ADI partnerships to help capture the value of GSK’s discovery engine

ADI partners prepared to share some of the risk of drug discovery & to move quickly with GSK assets

Research Development Commercialisation

Genetics Research Development

Preclinical Development

Discover Research Worldwide Development
Innovation in R&D
THE LIFE OF A MEDICINE

**RESEARCH**
- Preclinical
  - 250 animals Phase 1
  - 1750 animals Phase 2-3
- Animal Toxicology studies
- Data: 1,000,000 compounds
- 10-15 years, average 12 years
- Research for drug targets and chemical entities
- Licence required
- Patent

**DEVELOPMENT**
- Phase 1
  - 20-100 healthy people
- Phase 2
  - 100-500 patients
- Phase 3
  - 1000-5000 patients

**APPROVAL**
- Medicine licensed
- Registration Process
- Medicines
- Safety
- Dosage
- Efficacy
- Government Pricing & Reimbursement negotiations
- Continuous monitoring

**LIFE**
- 20 years
- 10 years
- (8 years data + 2 years market)
- 5 years maximum
- + 1 year

**GENERIC**
- Application for abridged approval of generic
- Note: Graphic depicts Data Exclusivity arrangements in the EU as of Autumn 2005
- Supplementary Protection Certificate
- Note: Graphic depicts Data Exclusivity arrangements in the EU as of Autumn 2005
Will the drug be safe: Toxicity testing

Nature Reviews Drug Discovery 3; 226-236 (2004);
Experimental Medicine:

- clinical imaging
- pharmacogenetics
- *in silico* clinical research
- advanced human experimentation
Experimental Medicine

- the early introduction of the human as the model experimental species, to validate preclinical knowledge in order to:
  - eliminate waste & delay in clinical trials
  - provide patients with better medicines, sooner
  - protect patients against predictable adverse events
21st Century Drug Discovery

New disease understanding & better treatment

Massive scale
High speed
Reduced cost
Expanded insight
Informatics

Human genome - unprecedented opportunities
Has innovation, in science and organisation, increased productivity?

A «wall» of new products
Demonstrate the healthcare benefits of new medicines

- Health outcomes research (and directed studies)
- Pharmaco-economics
- Epidemiology
- Disease & risk management programmes
- Outreach to patient groups
- Experimental medicine
- Predictive toxicology
Wider responsibilities?

Old product, new indication

over 1 billion people currently at risk
GSK aims to eliminate Lymphatic Filariasis
by 2020 - $1 billion commitment

GSK shipped 94 million free treatments for LF in 2003
New ways of working

“The biggest story of all is the story of vaccination. There are 30 million children being vaccinated each year. It is invisible because it is happening one at a time, largely out of view. And new vaccines are being developed that can save another 3 million children. When you think about it, it is pretty stunning.”

Bill Gates

Vaccines save lives

Bill & Melinda Gates Foundation website
www.gatesfoundation.org
World Distribution of Falciparum Malaria

Anopheles gambiae

Prevalence >50%
Prevalence 11-50%
Prevalence <10%

> 100 countries affected

Snow RW et al., Nature 434:214, 2005
Vaccines for All

Development of new vaccines, combinations of vaccines and technological advances will extend vaccination, to build a lifelong immunity

- Paediatric Vaccines
- Adolescent Vaccines
- Adult Vaccines
- Travellers Vaccines
- Elderly Vaccines
- Vaccines for Diseases of the Developing World
- Therapeutic Vaccines
- Monoclonal Antibodies
Vaccine Innovation: Adjuvants

GSK adjuvant systems offer stronger and broader immune responses
# A Rich Pipeline of Vaccines

## Pre-clinical
- Respiratory *
- Syncitial Virus
- Cytomegalo Virus *
- Men B (paed)
- Chlamydia *
- Staph.aureus *
- SARS *
- Other Cancer *
- Allergy *
- Flu TC

**Total = 9**

## Phase I
- HIV *
- S.Pneumoniae * (elderly)
- TB *
- Zoster *
- Prostate Cancer *(1)
- Breast Cancer *(1)

**Total = 6**

## Phase II
- Hib-MenCY
- MenACWY
- Flu improved *
- Epstein Barr Virus *
- Mosquirix * (4)
- Hepatitis E
- Dengue (4)
- Lung Cancer *(1)
- Melanoma *(1)

**Total = 9**

## Phase III / Filed
- Menitorix (HibMenC)
- DTPw-HepB
- Hib-MenAC
- Rotarix (2)
- Streptorix
- Cervarix * (3)
- Priorix tetra
- Simplirix *
- Boostrix Polio (DTP IPV)
- Fendrix *

**Total = 9**

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**A Well Balanced Pipeline from Preclinical to Phase III**

- Vaccine containing GSK adjuvant proprietary systems
- (1) Therapeutic Vaccines; (2) Avant collaboration; (3) MedImmune collaboration; (4) WRAIR collaboration

*June 30 2005-GSK Biologicals*
GSK and Vaccines

- Integrated Organisation
- Vaccines for Developed and Developing Countries
- The Largest Supplier to UNICEF
- Technologies
Ongoing high tech investment in Hungary
GSK Hungary: High Tech production

- EUR 15 million project launched in July 2002
- Plant upgraded and GSK Bio’s production capacity for core ingredients in diphtheria toxoid, tetanus toxoid, and whole-cell pertussis vaccines was expanded.
- 2003: GlaxoSmithKline Biologicals investment in a EUR 60 million project in Hungary. Current staff of over 100 persons will be doubled within 3 years
- Gödöllő/Hungary will be one of the world’s major producers of DTP vaccine core ingredients.
- Worldwide source for compulsory diphtheria - tetanus - pertussis vaccination administered to children from the age of 3 months.
GSK Kft

- Sales, marketing and distribution
  - Prescription medicines
  - Over the counter medicines
  - Healthcare products
- 24 billion HUF sales, 4.5% market share
- Major expansion of clinical trials
  - Doubled capacity by 2007
The economic benefit of knowledge

- Graduate recruitment
  - “Economic development in highly competitive world markets requires a direct engagement in the generation of knowledge.”

- Sir David King, Chief Scientific Advisor to the UK Government

Figure 2 Comparing economic and scientific wealth. National science citation intensity, measured as the ratio of the citations to all papers to the national GDP, shown as a function of the national wealth intensity, or GDP per person, Nature 430, 311 - 316 (15 July 2004);
International competitive environment

Singapore sweetens the pills
Formula that lures British scientists: no animal rights protests, minimal red tape and ample cash incentives
Heather Tomlinson
Thursday August 26, 2004
The Guardian

Geographic Income Inequality Map


Hourly costs


U.S. Europe Japan

28 Foreign Economies (trade-weighted average)

Asian NIEs Canada

Mexico
The environment for innovation:

- An environment that promotes R&D and innovation
  - Strong intellectual property rights
  - Realistic pricing for the long term
  - Fair distinction and balance between branded and generic drugs
- A common European regulatory system
- Appropriate use of health technology assessments (HTAs) to guide expenditure
Europe must turn political objectives into policy reality

Lisbon Objectives March 2000

The most competitive and dynamic knowledge based economy in the world by 2010

3% GDP investment in R&D
(1/3 public; 2/3 private)

Innovation Policy Initiatives

Proposed x2 budget for Framework 7

European Technology Platforms
(Research agenda for public-private partnerships defined by stakeholders with industry leadership)
The Strategic Research Agenda is a proposed partnership of industry and the EU focuses on bottlenecks in biomedical R&D.
Innovation

- Innovation depends not on structure or size
- People, their motivation, the environment and infrastructure can lead to innovation
- Environment and Infrastructure comes from both business and the government
- Innovation can benefit all