Capital Allocation in R&D and DPU Deep Dive

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Delivering our strategy

Grow a diversified global business

Deliver more products of value

Simplify the operating model

- 38% sales generated outside US & EU
- £5.3bn of Group sales from strengthened EM business
- £3.5bn Vaccines sales (+22% vs 2008)
- £5.2bn Consumer Healthcare sales (+18% vs 2008)
- 22% of sales “White Pill Western Market” vs 40% in 2007
- Reduced sales force in US and EU by ~8,000; added ~7,500 in RoW since 2007
- Global support functions; 23% decrease in costs vs 2008
- Exited 19 manufacturing sites since 2006
R&D strategy

- Grow a diversified global business
- Deliver more products of value
- Simplify the operating model

Focus on return on investment
Focus on the best science
Re-personalise R&D
Diversify through externalisation

- Building late stage pipeline
- Re-engineering drug discovery organisation to ensure sustainability of the pipeline
- Enhancing returns on R&D investment

CULTURE
R&D competes for capital in GSK

Rigorous Capital Allocation Focus on RoI

- Capital investment
- R&D
- Dividends
- Share buybacks
- Bolt-ons
- Divestments

Focus on returns

EPS

Focus on returns

Free Cash Flow

Focus on returns

Sales growth
+ Operating leverage
+ Financial efficiency
+ Cash flow growth

Focus on returns

Returns to shareholders
Different approach to capital allocation in early and late stage pharma

Core R&D budget expected to be approximately £3.7bn in 2012
Rigorous capital allocation process within R&D

**Discovery Investment Board (Pharma R&D)**
- Allocates DPU funding on a fixed-term business cycle with committed deliverables and costs
- Earmarks funding but can revoke if DPU underperforms
- Clear financial incentives for successful DPUs

**Portfolio Investment Board***
- Asset investment decisions at Phase IIB, Phase III, file and launch, Phase III/IV
- Annual funding re-distribution across all R&D Units (incl. Rx and Vx)

*PIB governs Pharma R&D. An independent parallel body with equivalent inputs governs Vaccines (Vaccines Investment Board operates from Phase I)*
Absolute R&D spend is broadly flat but the shape has changed.

Overall spend has only increased ~£200m*

- **2007**
  - Discovery: 32%
  - Development: 31%
  - ViiV and Derms: 23%
  - Consumer: 11%
  - Rx central costs: 3%

- **2011**
  - Discovery: 22%
  - Development: 35%
  - ViiV and Derms: 4%
  - Consumer: 19%
  - Rx central costs: 15%

*Growth at CER

- Central costs include facilities, central support functions (i.e. HR, IT, Finance, Legal)
- Certain costs including those relating to EM and Japan R&D have moved from central costs to development since 2007.
  For consistency, they are shown in central costs in both years.
Some early impact of cost reduction is improving returns

- Doubled the Phase III pipeline
- Doubled the number of patients in GSK trials
- Fixed costs reduced by 16%
- FTEs reduced by 28%
- Facilities reduced by 46%

Data for Pharma R&D only
Shape of R&D pipeline is different

Exited
- Urology
- GI
- Hypertension
- Pain/ depression/ anxiety

Re-focussed
- Metabolic Pathways
- Infectious Disease
- Respiratory

Created
- Ophthalmology
- Dermatology
- Rare diseases

Grew
- Biopharmaceuticals
- Immuno-Inflammation
- Neurodegeneration
- Oncology
Execution is improving returns

**FDA approvals**
2008 - 2011

- Company A: 8
- Company B: 6
- Company C: 3
- Company D: 3

* FDA approvals include NCEs and NBEs
Source: FDA website

Highest number of approvals
Growing a sustainable late-stage pipeline
Pipeline delivery and visibility continues

- ~30 assets in phase III/registration
- 15 phase III assets with data in 2011-2012
- 5 products with sufficient data in-house to file in 2012
  - Promacta/Revolade, QIV Flu, Relovair, MEK, BRAF
- Phase III expected to complete for 4 additional drugs and vaccines by end 2012
  - albiglutide, dolutegravir, LABA/LAMA, Mosquirix

Since Q4 – BRAF and Relovair asthma have completed with sufficient data to file
Returns on R&D investment increased to 12%; on track to deliver 14% return rate

GSK assessment of R&D IRR

- Industry historical
- GSK Feb 2010 late-stage portfolio
- GSK Feb 2012 late-stage portfolio
- GSK target

- Increased risk adjusted sales following positive data
- Some early impact of cost reduction programmes
- Reduced late stage attrition

1. McKinsey, Nature Reviews, Drug Discovery (Aug 09) for small molecules. 13% for biopharms
2. Projected rate of return based on investment made to create late stage pipeline & expectations on future sales. Late-stage portfolio includes pharma assets and vaccines launched from 2007 onwards (2010 analysis) and 2009 onwards (2012 analysis) plus phase IIb & III pipeline
Patrick Vallance
President, Pharmaceuticals R&D
Drug discovery critical to sustain R&D pipeline delivery

- **2007**
  - Therapy Area Transformation

- **2008**
  - Business plans endorsed by DIB and DPU/BDUs created

- **2011**
  - End of first cycle – refresh and or confirm direction

- **2012**
  - Start new business cycle

**CULTURE**
- Focus on return on investment
- Focus on the best science
- Re-personalise R&D
- Diversify through externalisation
DPU approach to Drug Discovery is delivering

- TA rebalancing
- DPUs established
- Full review

- Extensive review completed Q4 2011
  - 4 DPUs created
  - 3 DPUs closed
  - 6 DPUs with >20% increased investment
  - 5 DPUs with >20% decreased investment
  - Overall Drug Discovery budget unchanged
Investment has been rebalanced according to scientific opportunity.
R&D pipeline promise: will it deliver?

Late stage visibility

~30 assets in phase III/registration
15 phase III assets with data in 2011-2012
5 products with sufficient data in-house to file in 2012
Phase III expected to complete for 4 additional drugs and vaccines by end 2012

Mid stage flow & decision gate

Up to 30 C2MDs expected in 2012-2014
Rigorous decision making to reduce attrition
Focus on medicines that will make a difference

Early stage sustainability

40 DPUs & >50 external discovery engines
Leadership/Talent/Culture
>20 publications in Nature and NEJM

Since Q4 – BRAF and Relovair asthma have completed with sufficient data to file
Pattern Recognition Receptor (PRR) DPU

John Bertin, Ph.D.

- Pioneer and expert in PRR Biology
- At GSK since 2008
- Biotech experience at Synta and Millennium Pharmaceuticals (Boston, USA)

Located in Philadelphia, USA
- Formed in 2008
- Team of 55 scientists
- Partnered with biotech & academics
- Renewed for additional 3 years

Focused on translating recent discoveries in PRR biology into novel therapeutics for the treatment of autoimmune diseases

Combining cutting-edge science and drug discovery provides platform that drives innovation and heightened sense of urgency

DPU has deep scientific expertise in PRR biology and uses innovative thinking to establish leadership positions in drug discovery and clinical utility
The time is right to invest in novel target discovery in COPD

- Great progress in COPD patient knowledge and stratification
- Will enable more efficient clinical development paths for future COPD medicines

We changed our target discovery strategy, starting our thinking in the patient

- Human *in vitro* systems resembling the patient
- Novel screening platforms to speed up target discovery
- End-to-end planning incorporating learnings from GSK late stage clinical expertise
Biopharm Discovery

Multidisciplinary team of 80 scientists located in Stevenage, UK

Created in 2012 from Biopharm Discovery Units formed in 2009

Working in partnership with DPUs across the therapeutic spectrum

DIB endorsed funding for 3 years

Steve Martin, Ph.D.
Protein engineering expert, pharma R&D leader
At GSK since 1994
Joined from the University of Oxford

Current focus on monoclonal antibody, recombinant protein and dAb medicines discovery

New platforms coming online over the next three years to maintain competitive edge

Previous biopharm discovery units succeeded in delivering clinical candidates and pioneering new technology platforms (2009-2011)

Evolved following DIB review to simplify and provide cleaner separation of pipeline delivery and technology innovation
Academic DPU

Cross-therapeutic unit with a diverse portfolio of GSK and academic-borne medicines

Small, agile team, with personal accountability
- Funding flexibility + devolved decision-making → opportunistic
- Testing different models of academic engagement and shared risk/reward

Focus is on individual academics and not institutions

Delivered 1 medicine to late stage development in 2011. Objective is to deliver 2 more in 2012-2014

Formed in 2009, with a team of 5
Grew in scope and size based on positive mid-term and final DIB reviews
Now an international team of 19
Remit extended globally and into earlier discovery

Pauline Williams, MD
Translational Medicine Physician
At GSK since 1992
Joined from hospital medicine

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Protein Dynamics DPU

Carolyn A. Buser, Ph.D.
Pharmaceutical Oncology
R&D & translational Science
At GSK since March 2011
Joined from Cancer Research, Merck & Co.

Co-localised with Cancer Research DPUs in Upper Providence, PA
Formed in 1Q2010; Team of 35 members
Partnered with biotech, precompetitive consortia and academia
Funded until interim review in 1H2013

DPU focus: Leverage emerging science to modulate expression and function of oncogenes and tumour suppressors
  • Defined patient populations for treatment

DPU differentiation: Focus on target class with depth and breadth to determine chemical and biological tractability of target class through internal efforts and partnerships

DIB implementation: Milestone-driven investment into novel target area with recognized therapeutic potential in cancer and other diseases
Heart Failure DPU

John Lepore, MD
Cardiologist, physician-scientist
At GSK since 2006
Joined GSK from faculty position at the University of Pennsylvania

An integrated, co-localised team located in Upper Merion, PA
Formed in 2008
Team of 60 scientists and clinicians
Funding extended for additional 3 years at last DIB review

Building on existing expertise from groundbreaking carvedilol (Coreg) programme
Leveraging emerging science to translate novel mechanisms into next generation therapies:
- inhibiting pulmonary edema formation (e.g. TRPV4 blockers)
- blocking hypertrophic signaling pathways
- improving cardiac metabolism

Pursuing novel CV indications for existing GSK molecules:
- losmapimod, p38 inhibitor for acute coronary syndrome
Reference Slide: Methodology to estimate the IRR of GSK R&D’s late-stage pipeline

Estimated Sales
- Late-stage pipeline includes pharma NCEs and vaccines launched from 2009 onwards plus current phase IIb & III pipeline. (Sales taken from 2009 in order to match the R&D costs from 2003 onwards).
- Actual sales 2009-11 for products launched since ’09.
- Estimated future sales for all products through 2032.
- Future sales estimates include risk-adjustment which is inline with current industry attrition rates.

R&D Costs
- R&D costs associated with the development of our current late-stage pipeline projects are included (including the costs of failed assets as well as infrastructure costs).
- For pharma, the following approach was used:
  - Total R&D costs split proportionately into early-stage (pre-CS), mid-stage (CS-C2MD) and late-stage (C2MD to launch).
  - In order to allocate all costs for this set of projects (e.g. late-stage pipeline) as accurately as possible, costs were included as follows:
    - 2003-05: All early-stage and 50% mid-stage costs.
    - 2006-09: All mid-stage and all late-stage costs excluding PLE and market support.
    - 2010 and beyond: All late-stage cost estimates for the assets which are included in the sales projections, and estimates for increasing regulatory support.
- Actual upfront and milestone payments for in-licensed assets, as well as estimates for future milestone payments, were also included.
- For vaccines, a similar approach was used.

Key Financial Assumptions
- Forecast operating profit margins after deduction of CoGS, selling and marketing and direct administration costs. Estimates are similar to current margin ratios.
- Includes estimates of capital investments and working capital requirements.
- Includes the Group estimated tax rates.

The methodology above was applied to estimate the annual net cash flows used to derive the estimated IRR%