

# Pharmaceutical R&D: An Organizational Design Approach to Enhancing Productivity

By

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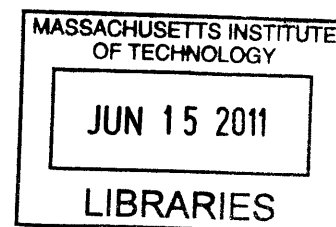
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## **Abstract**

The pharmaceutical industry is an \$837 billion a year industry that is being plagued by low R&D productivity. This decline in productivity has resulted in significant erosion of value. From December 2000 to February 2008, the top 15 pharmaceutical companies lost about \$850 billion in shareholder value and their stock price fell precipitously from 32 times earnings to an average of 13 (Garnier, 2008).

In an attempt to boost R&D productivity, pharmaceutical companies are jettisoning their old lumbering and bureaucratic R&D organizations for de-centralized and entrepreneurial models in a wave of organizational redesigns that is aimed at delivering innovation and creating value.

In this research, I have studied this new trend in organizational redesign by finding out what went wrong with the old model, what are the drivers for change, what is the new model and what strategic imperatives are they aimed at achieving. I have undertaken this by studying the top 5 research-based pharmaceutical companies. I have used interviews and extensive secondary research to gather facts and gain insight into issues and questions mentioned above. I then used the Three Organizational Lenses Framework by (Ancona et al, 2005) to analyze the new model at play in each of the 5 companies studied and proposed recommendations going forward.

I found that whilst organizational design provides strong tools, techniques and systems for enhancing R&D productivity, implementing a new organizational structure alone will not suffice. There has to be a comprehensive approach that involves structure, systems and incentives; as well as paradigm shifts in both leadership and culture.

## **Acknowledgment**

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I profoundly thank and appreciate my Wife Victoria for putting up with some level of discomfort in order for me to run with a dream and fulfill a long career vision of attending the Sloan Fellows Program. I am equally indebted to my Children, Christine and Jonathan for their support; and yes, they endured some level of discomfort also in order for me to be at MIT. I only believe that whatever the discomfort will be over-compensated by the value of new experience, new friends, new schooling and new opportunities that they have been exposed to and will continuously be exposed to going forward!

Finally, I express my thanks to God for His Many Mercies and Grace even as I look forward to the Future!

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# 1 Introduction

## 1.1 Overview

The Pharmaceutical industry is a research and development driven industry. The very essence of businesses in this industry is to seek out innovative and breakthrough medicines to help cure and manage some of the most chronic and challenging medical conditions faced by human beings and animals alike.

The importance, therefore, of pharmaceuticals, especially prescription drugs in healthcare systems and its overall impact on the global economy cannot be over-emphasized. An IMS health report in 2009, estimated the global market for pharmaceuticals to be \$837 billion. This is projected to grow by 5 to 8% annually reaching an estimated \$1.1 trillion by 2014<sup>1</sup>.

In the US, the largest market for pharmaceuticals, total spending on healthcare accounted for about 16.3% of GDP in 2009. This amount is project to rise faster than GDP growth in the coming years emphasizing the escalating cost of healthcare<sup>2</sup>.

According to a McKinsey Global Institute study in 2008, pharmaceuticals account for about 12% of total US healthcare spending. In Western Europe, healthcare spending as a share of GDP ranged from almost 8% in Ireland to over 11% in France in 2010.

Across the OECD countries, pharmaceutical spending as a share of total healthcare cost ranged from 10 – 20% in 2001<sup>3,4,5</sup>.

When these statistics are considered along with the challenges of an increasingly aging population, the role that pharmaceutical industry could play in ensuring full access to highly innovative, safe and efficacious medicines becomes critical across the world. The success of this is largely dependent on ongoing successes and high levels of productivity in R&D.

Unfortunately, R&D productivity has been on the decline in the last several years despite the usual huge capital investment outlays in R&D. In 2009, R&D spending amongst the top 20 research based pharmaceutical companies averaged 17.4% of revenues. This ranged from \$9.9 billion spent by Pfizer in 2009 alone to the \$1.5 billion spent at Otsuka pharmaceuticals of Japan in the same year<sup>6,7,8</sup>.

An incisive review of global R&D spending and productivity trends across the industry will be fully discussed in chapter 2.

## **1.2 Purpose of this research**

### **1.2.1 Overview of Industry Current Challenges**

Before delving into the research questions, it is useful to first contextualize the purpose of this work in the current challenges faced by the pharmaceutical industry. These manifold challenges, which pose a threat to the business model of research based pharmaceutical companies, include severe cost pressures, regulatory and compliance challenges, maturing markets and slowing growth for pharmaceuticals in western economies. Cost pressures come from the rising cost of R&D, fierce competitions and price pressures from generics as a result of patent expires and cost containment strategies of healthcare systems.

On the rising costs of R&D, depending on the literature you review, some researchers say it cost \$1.8 billion to bring a new drug to market (Paul, Mytelka et al; 2010) whilst others with more conservative models like Tuft University's Center for the Study of Drug Development (Tuft CSDD, 2008) estimate the cost at \$1.3 billion. These costs are expended over a period of 10 years or more, the time it takes to discover, develop and launch a new drug in the marketplace. (Paul, Mytelka et al; 2010) described these rising R&D costs as unsustainable<sup>9,10,11</sup>.

The second component of cost pressure has to do with the sudden loss of significant revenues to generic competition once a patent expires. Patent expiry and the virtual commoditization of branded drugs, otherwise known as patent cliff, are major and continuous threats to the drug blockbuster business model of pharmaceutical companies. A blockbuster drug is one that makes \$1 billion or more in annual sales. Once patent exclusivity is lost, generic competitors flood the market with the same drug at relatively cheap prices resulting in significant revenue loss to the original research based pharmaceutical company. An example of this loss was seen when Eli Lilly lost the patent exclusivity of Prozac, its blockbuster anti-depressant drug, in 2001. A report published by Analysis Group, an economic, financial and strategy consultancy, indicated that Eli Lilly lost 73% of its market share for new prescription of Prozac within two weeks of patent expiry. Commenting on the enormity of this loss, Sidney Taurel, the

then Chief Executive Officer of Eli Lilly said “ ...*With nearly two months of Prozac sales data available, the erosion in prescriptions is the most severe ever for a blockbuster product in our industry*”<sup>12,13</sup>.

Finally on cost pressures, as the cost of healthcare increases, especially in western markets, governments and payers are implementing cost cutting initiatives. This could impact profit margins of pharmaceutical companies. In the US, for example, insurance companies are increasingly trying to negotiate better deals on prescription drug prices. Also, the impact of the new US Healthcare Reform Law (The Patient Protection and Affordable Care Act of 2010) on pharmaceutical companies could be a bitter-sweet situation. Moran Lewis, an international law firm, reports that whilst demand for drugs could increase as a result of increased coverage, the law imposes an “*annual fee*” on “*covered entity engaged in the business of manufacturing or importing branded prescription drugs*”<sup>14</sup>. This, if implemented, will no doubt increase costs pressure on pharmaceutical companies.

On the regulatory front, key regulatory bodies around the world have approved 50% fewer numbers of new molecular entities (NME) in the past 5 years compared to the previous 5 years<sup>15</sup>. This trend might not be unconnected to regulatory bodies prioritizing drug safety over efficacy in recent years. In an interview conducted by Forbes Magazine in January 2011, Andrew Witty, the relatively new Chief Executive of GlaxoSmithKline said in his assessment of the industry that “*Drug companies became complacent in the 1990s. They were slow to react when insurers rebelled against me-too drugs and regulators became more worried about side effect.*”<sup>16</sup>.

With all these pressures, cost and regulatory alike, it is probably not an exaggeration to say that pharmaceutical companies are desperate for breakthroughs in increasing innovation and productivity of their R&D efforts.

### 1.2.2 Research Purpose

In reaction to a desperate need for change, pharmaceutical companies are embarking on restructuring R&D organizations and assets. The purpose of this work therefore is to

1. Critically review the rationale for this new wave of change



2. Evaluate the new organizational models and their relative abilities to help drive R&D productivity and innovation
3. Proffer recommendations based on analysis and evaluations conducted.

### **1.3 Scope of research and Limitations**

The scope of this research largely covers the qualitative assessment of R&D organizational forms in terms of how effective they will be in delivering on strategic aims as opposed to quantifying increases in productivity that the new model has delivered. This is because whilst bottom-line productivity accounts for the number of drugs brought to market before and after implementing new organizational model, the 10 years lead-time for bringing new medicines to market will not allow for such “before and after” comparisons.

Additionally, given the fact that this work was carried out within a limited but intense period of 2 months, the number of pharmaceutical companies interviewed was limited to the top 5 global corporations by annual revenues and market capitalization. Whilst the brevity of time limited scope and perhaps data collection, prospective areas for future research will be identified and discussed.

### **1.4 Methodology**

R&D organizational forms and restructuring efforts at the top 5 global research based pharmaceutical corporations were studied. These companies, Pfizer, Novartis, GlaxoSmithKline, Sanofi-Aventis and AstraZeneca have combined annual revenue of over \$243 billion, accounting for about 30% of the annual global market for pharmaceuticals<sup>17</sup>. The total market capitalization of all 5 corporations is over \$547 billion<sup>18</sup>. So whilst this is a small sample in terms of number of companies, their size, influence and combined market share is relatively significant given the highly fragmented nature of the industry and the numerous numbers of pharmaceutical companies around the world.

17 R&D senior executives at Senior Vice President, Vice President and Senior Director levels were interviewed in total. These interviews were captured both on tape recorder

and written notes. Primary data was analyzed and triangulated with findings from databases and extensive reviews of secondary data from scholarly publications in order to obtain unvarnished and holistic views.

(Ancona et al, 2005)'s Three Organizational Lenses framework was used to analyze the strategic, political and cultural dimensions of the new organizational models at play at the 5 companies studied.

In an attempt to link financial performance with R&D restructuring efforts, a review of investors' reactions on Wall Street to some restructuring announcements was done.

Assessment of each corporation's drug pipeline was done out to find out how many drug candidates are in early stage discovery vis-à-vis late stage development i.e. closer to being launched into the market. This gives a reasonably good indication of the rate of innovation and perhaps an indirect indication of productivity.

Finally, of the 5 companies studied, GSK is the company that has undertaken the most radical changes to its R&D Organization. As such, the study of GSK forms the most detailed case for analyzing R&D organizational redesign in the pharmaceutical industry. The study of the other 4 companies therefore provides complementary information, analysis and perspectives to those gotten from GSK.

The next section details a comprehensive and critical review of the pharmaceutical industry with highlights of

- Historical perspectives starting from the early years up to present time
- Key trends and developments
- Key drivers for industry change and
- Impact these changes have made industry dynamics

The aim of this review is to provide the background and insight into how the industry has evolved and the trends that have culminated in the current wave of R&D organizational redesign.

## 2 Critical Review of the Pharmaceutical Industry

### 2.1 Historical Review – The Early Years

The early years in pharmaceutical R&D were characterized by several serendipitous landmark discoveries; some illustrations follow. In 1872, the German scientist Paul Ehrlich discovered the selective lock and key mechanism through which drugs bind onto receptor sites in the body for therapeutic actions to take place. Then a medical student, Ehrlich discovered this concept while researching into the selective affinity of dyes for biological tissues (Pisano, 2006). This work was later complemented by J.N. Langley in 1905 when he asserted that the receptor sites in the body transmitted and or received biochemical signals during drug therapeutic process<sup>19</sup>.

In the same vein, motivated by the sheer desperation to help alleviate his father's pain from arthritis, German chemist Felix Hoffmann successfully extracted acetylsalicylic acid from willow tree in 1897. Hoffmann's employer Bayer, then a dye manufacturing company, went on to commercialize this discovery under the brand name of Aspirin<sup>20, 21</sup>.

Other early landmark accidental discoveries include insulin and penicillin. In the case of insulin, the initial understanding of diabetes occurred when two German doctors, researching the digestive system and pancreas of a dog, noticed that flies were attracted to the dog's urine because of high levels of sugar<sup>22</sup>. This along with progressive work on diabetes culminated in the discovery of insulin by Dr. Frederick Banting in 1921<sup>23</sup>. The discovery of penicillin happened in like manner. Alexander Fleming, in 1928, noticed that the mould that infested the dish in which he was growing experimental bacteria had restricted the spread of the bacteria. He went on to name the new anti-bacterial agent in the mould penicillin<sup>24</sup>.

Just as it did in the early years, serendipity has continued to play an important role in drug discovery. A case in mind is the chanced discovery of Viagra as a treatment for erectile dysfunction. Viagra, which is one of the fastest selling drugs of all times, was originally intended to treat angina prior to its launch in 1998 by Pfizer<sup>25</sup>. The role of serendipity can be encapsulated in Louis Pasteur's saying – "*In the fields of observation chance favors only the prepared mind*"<sup>26</sup>. As structures and systems are purposefully

designed and put in place to obtain desired outcomes, new ways and new paradigms of reviewing and solving old problems need to be built in. (Cunha, Clegg and Mendonca, 2010) writing on serendipity and organizing submit that “*seeing something in another thing*” and coming up with ...“*new ways of seeing may provide the necessary ingredients for creativity and exploratory learning*”. This, no doubt will be key in successfully prospecting for groundbreaking innovative drugs in the future.

### **2.1.2 The Structural Factor Conditions of Middle to Late 20<sup>th</sup> Century**

The mechanism through which prescription drugs got to patients in the early years was through physicians, who effectively decided what drug patients should buy, and independent pharmacists who sold the drugs. Patients did not have much influence over purchase decisions. In the US, which accounted for a third of global pharmaceutical sales in the early 1990s, patients had low motivation to seek out competitive prices because third parties (insurers and employers) increasingly extended drug benefit coverage over the years. In 1960, only 4% of prescription drug bills were paid by third parties. By 1993 this had increased to 50%. Additionally, whilst patients paid the residual out-of-pocket costs, they apparently did not see any alternative to the independent local pharmacies which represented 61% of pharmaceutical sales in the US in 1991<sup>27</sup>.

A highly fragmented prescription drug market along with high barriers to entry helped safeguard the high prices and significantly high profit margins that characterized the years up till the 1990s. This attractive scenario started to alter in the late 1980s and early 1990s as institutional and structural changes were fuelled by the emergence of Managed Care Organizations, Prescription Benefits Management and Health Maintenance Organizations as key industry stakeholders and pressure groups that relentlessly sought to reduce the rising cost of prescription drugs<sup>28</sup>.

Managed care refers to a tighter link between payment and decisions about provision of care. Whilst managed-care organizations provide the usual medical insurance and healthcare services, these are done by increasing volume and negotiating longer term competitive pricing and favorable discounts from healthcare providers. The growth of

managed-care organizations occurred in response to the increasing demand for lower costs of healthcare predominantly from private businesses that pay most of the insurance premiums<sup>29</sup>. By 1993, the amount of US insured population covered by managed-care organization had grown to 80% from a mere 5% in 1980<sup>30</sup>.

Managed-care organizations sought to exercise control over prescription drug usage and prices through the mechanism of drug formulary list. Health maintenance organizations (HMOs) operated by using approved formularies to compare therapeutic effects and prices. Doctors were encouraged to only prescribe drugs on the approved list. Formularies that are actively managed based on price would essentially favor generic drugs over the costly branded counterparts. A 1994 Smith Barney Shearson analyst report cited Medco estimates that organizations with actively managed formularies will reach 50% by 1999<sup>31</sup>. This suggests the increasing use of lower priced generic drugs and real price pressures that research-based pharmaceutical companies increasingly face.

Aside from active management of formularies, managed-care organizations also use drug utilization reviews to control cost. This is a process whereby administrators set-up systems to monitor type of drugs prescribed by doctors, prescription habits and pace at which patients use prescribed medicines. These audits provide tools and data for formulary administrators to further control deviations from the approved lists and thereby control drug price and cost of healthcare<sup>32</sup>.

Another crucial category of drug price influencers are the Prescription Benefits Management (PBM) organizations. In the US, PBMs started out in the 1960s. They verified and processed claims on prescription drug coverage on behalf of employers. They also acted as vital communication interface between retail pharmacists and physicians. Over the years, PBM grew in stature and influence in the US. This was achieved through acquisitions of mail order pharmacists who served patients who needed constant refill of medications without need to see either a physician or pharmacist to renew or alter their prescriptions. As the influence of PBMs grew through the 1990s and integration of several mail order pharmacists continued, managed-care organizations started contracting with PBMs to help administer formulary management

and drug utilization reviews; two powerful systems for controlling drug prices. Under PBMs, formulary management occurs when PBMs with mail order pharmacy operations instruct their pharmacists to actively call physicians and ask for drug substitutions in order to achieve cost savings. Physicians will normally oblige to such requests knowing that pharmacists are recommending drugs on a formulary that has been approved by managed-care organizations. As the power of PBMs grew, pharmaceutical companies, in response to this new threat of pricing cuts, started acquiring PBMs. This vertical integration was also motivated in part by the quest to acquire the huge repository of vital patient information and data on adverse drug interactions that PBMs possessed and which pharmaceutical companies hoped will assist in targeted marketing and R&D activities thereby giving the acquirer competitive advantage. An example of such attempt at vertical integration took place, in July 1993, when Merck bought Medco, then the largest PBM in the US with about 50% of the pharmacy mail order market share (McGahan, 1994).

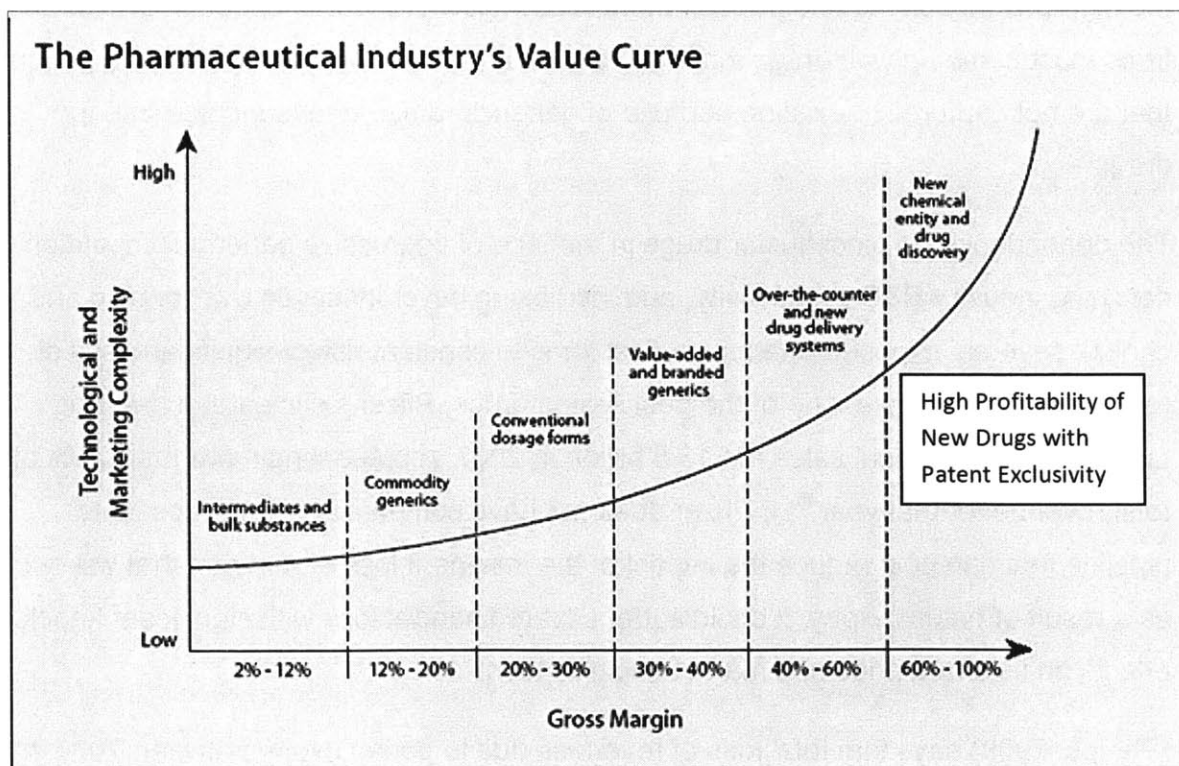
In summary, the pharmaceutical industry enjoyed tremendous profits in the years preceding the 1990s due to highly fragmented markets across therapeutic areas, high barriers to entry, poorly organized buyer organizations, and perhaps less informed patients. All started to change in the late 1980s and early 1990s as prescription drug buyer organizations integrated and morphed into formidable power players forcing pharmaceutical companies to give deep discounts for the first time thus impacting the hitherto huge profit margins as access to generics increased and structural changes came to the industry. One indication of the pressure and structural changes came in the years between 1991 and 1993 when pharmaceutical companies announced lay-offs of 23,000 jobs or 8% of total industry workforce. Jobs in sales and marketing were particularly affected as it became apparent that sales visits to physicians, a prevalent method for selling prescription drugs in the 1980s, might no longer be as effective as it used to be<sup>33</sup>.

The next subsection of this review will examine the traditional business model of the industry and how this is evolving in reaction to the structural challenges discussed above.

## 2.2 Pharmaceutical Industry Business Model

Despite huge capital outlays in R&D, pharmaceutical companies followed a business model that returned significantly high profit margins until, as noted, in the 1990s. For research based pharmaceutical companies, the underlying model is based upon the ability to successfully and continuously launch New Chemical Entities (NCEs) or New Molecular Entities (NMEs) into the marketplace. In an attempt to emphasize the high profitability of NCEs and NMEs with patent exclusivities relative to generics, (Bartlett & Ghoshal, 2000) mapped out the pharmaceutical industry's value curve depicting the various segments along with profitability levels in Exhibit 1 below. With profitability in mind, research-based pharmaceutical firms developed a business model that focused selectively on NCEs and NMEs that will maximize such returns and their entire R&D strategy was designed to support the so called blockbuster drug model.

**Exhibit 1: The Pharmaceutical Industry's Value Curve**



**Source:** Adapted from Harvard Business Review: Christopher A. Bartlett and Sumantra Ghoshal, March 2000.

### **2.2.1 The Blockbuster Drug Model**

By selectively focusing R&D capabilities only on new drugs that can achieve annual sales of \$1 billion and above across a wide spectrum of therapeutic areas, pharmaceutical companies racked in billions in revenues and profits. Supported by large armies of deployed sales and marketing staffers, this model worked well in the years prior to the 1980s; before the US Congress passed legislation that significantly increased access to generics and increased competition. At its height, the model emphasized that a firm only needs a few mega-selling drugs to be successful as a company.

But, over the years, it became increasingly harder to come up with blockbuster selling drugs. The R&D strategy of coming up with drugs that served therapeutic areas with large volumes of patients such as high blood pressure or high cholesterol began to wane as these areas became inundated with cheaper generics. Therefore to compete in the high patient volume and popular therapeutic space, research-based pharmaceutical firms must come up with drugs that have significantly high therapeutic value to patients that are not captured in existing portfolio of generics rather than launching “me too drugs”<sup>34</sup>.

The dependence on blockbuster drugs in the face of aggressive generic competition, declining industry R&D productivity, and increasing buyer influence over pricing and choice, severely exposed pharmaceutical firms to constant risk of significant loss of revenues. For example, one of the best selling drugs, Pfizer’s cholesterol lowering Lipitor achieved annual sales of \$13.5 billion in 2007, representing more than 25% of total revenue for that year<sup>35</sup>. If Pfizer does not have comparable new drugs in its pipeline that can help reduce the impact of the imminent loss of revenue that will occur as a result of patent expiry, it could suffer severe financial loss with significant knock on effects on its share price and market capitalization.

(Phelps, 2009) says that total loss of revenues due to patent expiry between 2007 and 2012 across the largest 50 pharmaceutical companies could reach \$115 billion<sup>36</sup>.



Exhibit 2 below shows 2007 sales figures of 6 selected drugs that will lose patent exclusivity between 2011 and 2014.

**Exhibit 2: 2007 Sales Figures for 6 Selected Drugs that will go off Patent in 2011 - 2014**

Drug	Company	2007 Sales (\$ Billions)	Year of Patent Expiry
Lipitor (Atorvastatin)	Pfizer	13.5	2011
Plavix (Clopidogrel)	Sanofi-Aventis	7.3	2011
Nexium (Esomeprazole)	AstraZeneca	7.2	2014
Zyprexa (Olanzapine)	Eli Lilly	5.0	2011
Seroquel (Quetiapine)	AstraZeneca	4.6	2011
Singulair (Montelukast Sodium)	Merck	4.5	2012

**Source:** Adapted from IMS Health & Parexel's R&D Statistical Sourcebook 2010/11.

A business model that generates such constant financial exposures is clearly not sustainable given the multi-faceted pressure from government cost containment policies as well as the aggressive competitive landscape discussed previously.

In response, the pharmaceutical industry has started transitioning to a more diversified risk model. This is a move away from solely focusing on blockbuster drugs that will sell to a large population. Firms are now focusing on smaller targeted populations. Instead of waiting for a drug that will deliver annual sales of \$1 billion, pharmaceutical companies are looking toward smaller R&D projects that will achieve \$200 million in annual sales or less<sup>37</sup>. Andrew Witty, the Chief Executive of GlaxoSmithKline (GSK) summarized this transition in 2008 by saying *"launching a handful of new products every year will be enough to replace lost revenue.....I would describe this as being a shift from blockbuster-dependent world to a blockbuster-capable world.....we're going to plan for what we know we can deliver, and we're going to make the most of the great surprise"* (Houlton, 2009). The pharmaceutical R&D strategy therefore is looking increasingly toward personalized medicine.

### 2.2.2 Personalized Medicine

Personalized medicine focuses on individual patients by developing personalized therapies that are based upon unique genetic and pathological make-up of individuals. These customized therapies would therefore involve genetic screening, tissue engineering and stem cell technologies; all of which necessitate deep understanding of the biology of diseases as opposed to just dealing with the chemical reactions that transpire during drug interactions alone. Personalized medicine depends on physicians who can determine the patients that possess the right genetic make-up that will respond most effectively to a specific therapy with minimum side effects<sup>38</sup>.

The move towards personalized medicine in the pharmaceutical industry can be said to be reflected in the shift from the one size fit all blockbuster drugs to smaller volumes of patients in the orphan and rare disease space. This shift will be increasingly characterized by the introduction of biomarker information on medications in order to maximize therapeutic benefits for patients. 80% of respondents to a February 2011 McKinsey and Co survey of 20 pharmaceutical companies confirmed that 30 to 50% of drugs being developed will have a biomarker program and they expect this number to rise<sup>39</sup>.

Deep expertise in these relatively new technologies with roots in biology and gene science will be needed to effectively serve the rare disease space; a segment that was singled out for R&D investment incentives through provisions in the Orphan Drug Act passed over 25 years ago in the US. There are between 6,000 to 7,000 rare medical diseases and medical conditions across the world. And 1 in every 10 Americans is diagnosed with a rare medical condition or disease according to the FDA<sup>40</sup>. It was therefore not a surprise when GSK announced a major shift in strategy towards rare diseases by launching a new specialist standalone R&D unit entirely focused on rare diseases in 2010<sup>41</sup>. It is envisaged that the trend towards unmet needs especially in the rare disease market will continue.

### 2.2.3 Industry Consolidation and Diversification Strategy

Until 1993, whilst the industry consisted hundreds of companies operating within several therapeutic areas, no one company had more than 5% market share<sup>42</sup>. As it became harder to discover blockbuster drugs and market pressures from generics and buyers increased, the industry reacted with a spate of large mergers and acquisitions to consolidate the highly fragmented market while embarking on the diversification of risks and product portfolios. Most of these M&A activities, and indeed the diversification of products, were spurred by the need to acquire assets that will help reduce loss of revenues from patent expiries and reduce costs through scale economies.

A particular example of a company that exemplified M&A described trend is Pfizer. During the years 1998 to 2004 Pfizer did not bring any new drug to the marketplace. This drought in new launches was masked by its successful acquisition of Warner Lambert for \$82.4 billion in 2000; essentially to secure full rights over Lipitor, the mega-blockbuster selling Cholesterol lowering drug<sup>43</sup>. In 2002, Pfizer made another big acquisition in Pharmacia for \$60 billion. This time, the acquisition was motivated in part by its quest to acquire Celebrex, a highly successful Arthritis drug. And 5 years later in 2009, Pfizer acquired Wyeth for \$68 billion. Pfizer hoped that this acquisition will help it diversify into biotech and vaccine products where Wyeth has a presence<sup>44</sup>.

A more recent example of continued diversification strategy through acquisition is the near hostile takeover of Genzyme, a US Biotech company with very strong presence in the rare disease market, by Sanofi-Aventis in February 2011. Sanofi-Aventis paid \$20.1 billion in a \$74 cash per share contingent value rights (CVR) transaction<sup>45</sup>. Speaking on CNBC about the acquisition on Wednesday 16 February 2011, Chris Viehbacher, Sanofi-Aventis' Chief Executive said *Biotech is really the medicine of the future.....have to have a strong presence in the US.....Cambridge is one of the hot-beds of research today.....look at MIT, Harvard and lots of biotechnology companies....this is an extremely important part of the world for the US to support*<sup>46</sup>.

The diversification by Sanofi-Aventis into biotech and the rare disease space is quite timely given the fact that its revenue is on the decline. It recorded negative growth of

minus 0.8% during in 2010 compared to 2009 figures. Commenting on the disappointing results in its Annual Report Chris Viehbacher said “2010 was the first year in which the patent cliff really became visible with generic competition for several of our products, notably Lovenox in the US”<sup>47</sup>.

In summary, the industry began with a business model focused on blockbuster drugs. But, as pressures mounted on several fronts, the industry has started a shift towards smaller targeted R&D projects enabled by relatively new technologies in biology and gene screening. The days of total dependence on blockbuster drugs with the prevalent focus on chemistry alone are seemingly over. The next stage of growth will most likely be driven by a deeper understanding of the biology of diseases and by focusing on unmet needs.

The next subsection deals with the impact of legislation and regulatory bodies on the industry.

### **2.3 Government Legislation and Regulatory Bodies**

One of the most critical government legislations that had significant impact on competition across the industry was the Waxman-Hatch Act of 1984. US Congress passed the Drug Price Competition and Patent Term Restoration Act in 1984 to simplify FDA approval process for generic drugs thereby increasing its accessibility. Prior to 1984, generics approval process was virtually the same as those for new branded drugs. Companies filling for generic drug approvals had to conduct expensive clinical trials. Also, these trials and other necessary activities required for marketing approvals could not be undertaken before the patent expiry of the drug they are trying to copy. Any early activities on the part of generic companies were regarded as patent infringement. The resultant effect was that there were not many companies willing to introduce generic drugs prior to the landmark legislation in 1984 (Vasanthakumar N. Bhat, 2005).

The Waxman-Hatch Act sought therefore to address this through protecting the rights of companies with new branded drugs whilst increasing access to generics. It did this by introducing a simple application for generic drug approval called Abbreviated New Drug Application (ANDA) for FDA filings. This expedited the process of generics approvals

as soon as patent on the original drug expires. On the other side, research-based pharmaceutical companies were incentivized to engage in R&D activities, under provisions of the Act, by compensating for time lost to undertaking clinical trials and FDA approval by granting patent extension by a fraction of the lost time. This extension could not go beyond 5 years<sup>48</sup>.

Whilst the Waxman-Hatch Act was intended to increase competition between research-based firms and generics, its effect was not immediate as it took some time to get physicians to change their prescription habits. Additionally, the 1989 scandal involving some generic companies falsifying scientific test results and bribing FDA officials undermined the integrity of generics and probably made it harder for doctors to readily substitute branded original drugs for generics (Anita M. McGahan, 1994).

However, as increased access to generics and increased competition kicked-in, research-based pharmaceutical firm started acquiring generic firms and or buying stakes in them during the 1990s in an attempt to retain market share and reduce loss of revenue by embarking on vertically integration.

Vertical integration continued over the years, and today one can see the biggest firms with a combination of diversified portfolio of businesses including pharmaceuticals, generics, medical device, consumer health and biotechnology. For example, Novartis owns Sandoz, a large Swiss generics manufacturer; along with its core pharmaceuticals as well as consumer health, diagnostics and vaccine businesses.

On the regulatory front, drug approvals from the FDA have generally being on the decline over the past several years. This is due to a more disciplined focus to uncover adverse effects new drugs gets to the marketplace. FDA is essentially prioritizing drug safety especially after the high profile withdrawal of Merck's Vioxx, its pain relieving drug in 2004. This event led to FDA Amendments Acts of 2007 giving it a whole host of new safety tools and authority to deploy even in post marketing stage of launch<sup>49</sup>. In 2007, the FDA only approved 19 new drugs; comprising 17 new molecular entities (NMEs) and 2 new biotech therapies. This is no way near the 53 new drugs approved in 1996 (Wechsler, 2008).

There have been pressures also from government legislation and regulatory systems making the pharmaceutical market ever more competitive whilst demands for duty of care and safety have significantly increased.

The last section of this chapter takes a look at the R&D landscape. I describe the various stages of drug research and development processes and identify trends and impacts of changes across the industry.

## **2.4 Research & Development**

(Gary P. Pisano, 2006) characterized drug R&D activities in the years prior to the 1930s as more or less a cottage industry with pharmaceutical companies undertaking small projects with limited technologies and opportunities for scale economies. The period up till the 1970s saw a focus on producing drugs from small chemical molecules with the prevalent underlying science based on studying the chemical interface and reactions between drug candidates and receptor sites in the body. This was based on the lock and key hypothesis of Paul Ehrlich in 1872 that chemoreceptor signals transpire between drugs – target sites.

As the years went by, the landscape of drug R&D became revolutionized by the introduction and practice of biology-based high technologies in monoclonal antibodies, genomics and proteomics. Monoclonal antibodies helped to advance the search for cancer treatment as its underlying mechanism works by selectively binding to specific proteins expressed by disease cells such as cancer cells. The specificity of this pathway allows small doses of highly potent drugs to be transmitted into specific cancer sites enough to destroy diseased cells. By 2002, about 25% of biotechnology products being developed were made up of monoclonal antibodies; and the FDA had approved 16 monoclonal antibody related drugs.

Other advances in technologies included the use of combinatorial chemistry to help create many chemical structures with potential therapeutic effects at a fast pace.

Perhaps underlying all these technologies is the concept of Rational Drug Design. This brings several different scientific disciplines together in a bid to effectively design

medicinal molecules (drug candidates) based upon the detailed knowledge of the specific disease sites, their structures and interactions as in the lock and key mechanism and opposes trying to locate naturally existing molecules. Rational drug design is also called structure-based drug design since the concept is based on the deliberate systematic design of molecular structures of drugs as opposed to trying to find such therapeutic molecules.

Thus, drug R&D evolved from small chemical molecules involving traditional scientific disciplines in organic chemistry and medicinal chemistry into large biological molecules involving multi-disciplinary functions such as computer science, chemistry, physics, math, molecular biology, protein engineering, statistics and bioinformatics, genomics and proteomics just to mention a few. Whilst the comprehensive engagement of all these disciplines in R&D is good for advancing innovation in drug discovery and development (Pisano, 2006) suggests that effectively integrating all facets of these diverse specialist disciplines poses a novel organizational challenge to the entire industry.

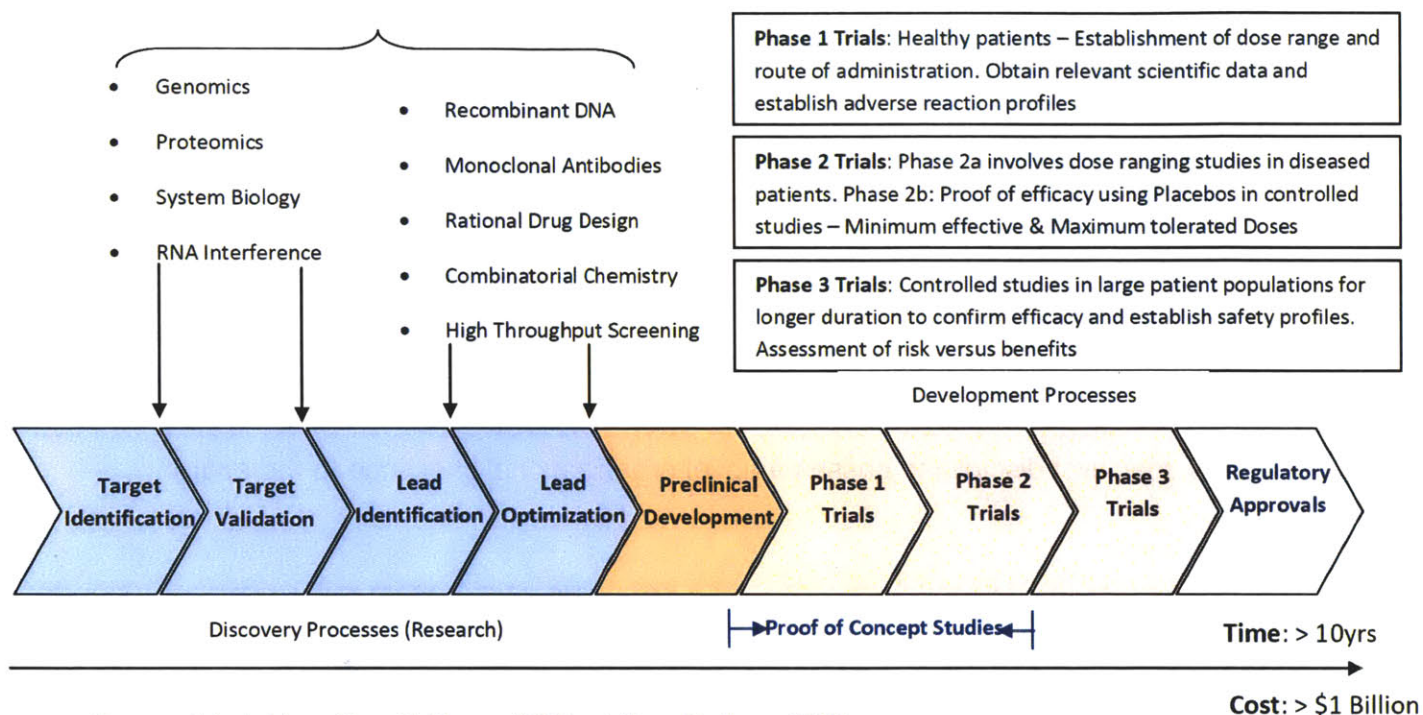
In order to build upon the overview of how R&D practices have evolved, it is pertinent to now discuss R&D processes and phases. This is done in the next section.

#### **2.4.1 Drug R&D Processes**

Drug R&D is a highly complex and expensive enterprise. Depending on the literature reviewed, it costs anywhere from \$800m to \$1.3b to produce a new drug and the process could take 10 to 12 years. Whilst the processes and phases are clearly defined as shown below in Exhibit 3, they are fraught with high levels of uncertainty and risk; and certainly not as linear in practice. For the sake of clarity, I adopt a simplified account based on (Pisano, 2006). As shown in Exhibit 3, drug R&D can be divided into 5 research (or discovery) stages and 4 development phases inclusive of the regulatory approval phase. Terminologies such as “early and late stage discovery” or “early and late stage development” are quite common in the industry and marks where a drug candidate is in the development process.

A hypothetical project based on producing a new drug for the treatment of rheumatoid arthritis (RA) is used as an example to explain the entire R&D process (Gary P. Pisano, 2006).

### Exhibit 3: Drug R&D Process



Source: Adapted from (Gary P. Pisano, 2006) and (Ross Tonkens, 2005)

**Proof of Concept Studies:** The probability of any potential medicinal compound making it to the marketplace is quite low. This is especially true in phase 3 clinical trials where failure rates are as high as 75%. Given the increasing costs of R&D, significant portions of which are incurred in phase 3 trials, it becomes critical therefore to implement systems and mechanisms that allow prudent decisions to be made on whether or not to proceed with a project. Proof-of-concept (PoC) fulfils this purpose. It is a set of limited and controlled tests carried out in humans to ascertain success in phase 3 and beyond. These studies are usually undertaken in phase 1 and early phase 2. Emphases are not only placed on PoC, but also the assumptions, metrics, meanings and strategies that underpin the definition of PoC; so that unnecessary costs associated with failure can be either minimized or avoided<sup>50</sup>.

### Target Identification and Validation

The first stage, target identification has to do with finding suitable receptors of the diseased cell as potential targets for drug action. The biochemical pathway through



which rheumatoid arthritis (RA) expresses itself as well as its interactions with potential receptor targets needs to be studied. Detailed studies are conducted into how RA expresses itself in specific and associated proteins and enzymes. One of the key questions at this stage is what is the most suitable receptor target protein or enzyme that a drug can latch onto in order to inhibit and or control the expressed RA condition at the molecular level? This is based on the hypothesis that when diseases or adverse medical conditions occur, there is either too much or too little production of certain enzymes or biochemical signals or protein. An example here will be diabetes. The physiological mechanism by which diabetes occurs involves the production of inadequate amount of insulin to metabolize sugar in the body. So, if an appropriate receptor (or target) molecule that is directly associated with the abnormal production of insulin could be identified in the body, then an attempt could be made to design a therapeutic molecule (drug) that could successfully bind onto this target in order to stimulate production of correct amount of insulin from the pancreas to stop the diabetic conditions. Whilst in reality, diabetic patients will normally get insulin injections, the general mechanism and concept described above for receptor molecules and targets are pertinent.

In the case of the hypothetical RA project, the aim of scientists, largely biologist, geneticists and biochemists, is to come up with the biochemical pathway by which inflammation occurs; inflammation being the key medical condition expressed in rheumatoid arthritis. The next task is to find how a drug molecule can interrupt or inhibit this pathway so that inflammation can be stopped. It is assumed that scientists are able to identify a number of targets in the pathway where drug candidates could bind to produce inhibition. This takes about 4 years to achieve.

The next stage is target validation. Since not all identified target molecules are compatible to drug intervention, detailed studies and experiments have to be done to narrow down the choice of the ones that will produce the best results. At this stage, protein chemists undertake the task of synthesizing the targets and statisticians determine the level of causality between inflammation and the target protein. Again it is assumed that a suitable target was successfully validated in this hypothetical project.

This takes an additional 2 years to accomplish. Thus, the first 6 years is spent identifying and validating a receptor target molecule or protein that drug candidates can bind onto in order to intervene in the inflammation pathway.

### **Lead Identification and Optimization**

The lead identification stage has to do with coming up with potential drug candidate compounds that can inhibit the target receptor protein. Based on the structure of this target protein, a team of chemists deploying a combination of high technology combinatorial chemistry and high throughput screening; as well as traditional chemistry techniques, produce suitable drug molecules that are synthesized and screened against specific drug characteristics. This process takes about a year.

After successfully synthesizing a potential drug candidate, several derivatives of this compound are produced in order to enhance its pharmacological and therapeutic properties. This iterative process of producing structural derivatives of the original compound is referred to as *lead optimization* process. Patent lawyers conduct due diligence on the compound at this stage to determine whether anyone else has patented it. Potential drug candidates generated as a result of this process have a 1 in 5,000 (or 0.02%) chance of proceeding into clinical trials and becoming a viable and marketable drug. Further experimentations are carried in vitro and in vivo to determine whether the drug candidate should progress to human clinical trial stages.

### **Preclinical Development**

The main objective in the preclinical stage is to determine safety and efficacy of the new drug candidate. This is done through several in vitro and in vivo animal tests. Key indicators such adsorption, distribution, metabolism and excretion rates; otherwise known as ADME, are measured. If results are not encouraging, other suitable analogues of the drug candidate are synthesized and put through the same tests to evaluate safety and toxicity; as well as initial effectiveness of therapeutic impact. Assuming positive results are achieved; comprehensive data and associated information are compiled and submitted to regulatory authorities for an Investigational

New Drug (IND) application in order to proceed to human clinical trials. The preclinical development stage could take a year to complete.

### **Phases 1 to 3 Human Clinical Trials**

Clinical trials are undertaken to determine drug safety and efficacy in humans and are required before any marketing approval can be granted by regulatory authorities such as FDA.

Phase 1 clinical trials are studies that involve a small but specified number of people. This could involve ten to one hundred health volunteers; although phase 1 studies in other more severe or life threatening medical conditions could involve the use of patients afflicted with the disease under study. Phase 1 could cost \$10m and take one year to complete.

In phase 2 clinical studies, safety and efficacy are determined at different drug doses such as at 10mg, 25mg, 50mg, 75mg and 100mg. The optimal balance between effectiveness of therapeutic impact and severity of side effects are determined in an iterative process which may involve phase 2b confirmatory stage on specific doses. Formulation scientists ensure the best tablet formulations, the pharmaceutical development scientists work with manufacturing professionals to ensure the drug can be produced in a cost effective manner. The marketing and commercial organizations get involved to ensure appropriate pricing vis-à-vis competitor product pricing. Phase 2 clinical trials could involve fifty to five hundred patients in controlled tests (i.e. administration of placebo and active ingredients). This phase could cost \$40m and take two years to complete.

Phase 3 involves confirmation of safety and efficacy in much larger patient populations. This could involve several hundreds to tens of thousands of patients in multi-site clinical trials operations. Since this phase involves observing patients over much longer timeframes, it could take four years to successfully undertake at costs in the range of \$50m to \$500m.

## **Regulatory Approval**

The final set of stages has to do with seeking marketing approvals from regulatory bodies such as the FDA in the US. A comprehensive history of all relevant data from the outset of studies is compiled for the marketing application for a new drug approval. The FDA takes about a year or more to review applications. During this time, the FDA could make several requests for data and or clarifications. At the end of this process, FDA may grant approval to market the new drug. The approval or license strictly specifies the dosage (e.g. 50mg as opposed to 75mg or 100mg etc), information about drug performance that the pharmaceutical company can claim the new drug can achieve and other marketing information.

## **Phase 4 - Post Marketing Studies**

Even after the FDA approves a new drug, clinical studies are continued in order to further determine any adverse safety issues, contrary interactions or side effects across a wider patient population. These are known as post-marketing clinical studies. The close monitoring of patients taking the new drug occurs for several years as part of FDA's strict approval requirements. These studies will normally form part of the product life cycle management strategy of pharmaceutical companies. New drugs are usually given specific labeling and signage on approved formularies for easy identification. In the UK, for example, there is a black triangle in the British National Formulary against the listing of newly licensed medicines. Underpinning all this is an adverse drug reporting mechanism that readily alerts appropriate regulatory authorities of incidents associated to the use of a new drug<sup>51</sup>.

These twists and turns associated with the entire process along with ongoing studies and surveillance even after a new drug is in the market underscores the huge clinical, operational and financial risks involved in drug R&D. The next section looks at what pharmaceutical companies are spending on R&D as well as spending trends across the industry.

## 2.4.2 Drug R&D Spending

A survey conducted by the Pharmaceutical Research and Manufacturers of America (PhRMA) in 2010 indicated that total R&D spending by research-based pharmaceutical member companies attained \$45.8b in 2009, accounting for 19% of revenues from US and exports. This represents a decline of 3.4% from the \$47.4b (or 19.4% of revenue) of 2008; a second consecutive year of such a fall in spending. A review of estimated spending from 1980 through to the 2009 estimate shows a year-on-year increase until 2007/08 when, for the first time in almost 28 years, R&D spending declined by about 1%.

Exhibit 4 below shows 5 out of the top 10 spenders recording declines in R&D spending in 2009. These five companies, Pfizer, Sanofi-Aventis, GlaxoSmithKline, Johnson & Johnson and AstraZeneca either suffered revenue fall or faced a significant threat from loss of patents in 2009.

**Exhibit 4: Top R&D Spenders in 2009**

<b>RANK</b>	<b>COMPANY</b>	<b>2008 (\$B)</b>	<b>2009 (\$)</b>	<b>ANNUAL GROWTH</b>
1	Pfizer	10.3	9.9	-4%
2	Merck & Co	8.2	8.6	+4%
3	Roche	7.3	8.2	+12%
4	Novartis	7.1	7.3	+4%
5	Sanofi-Aventis	6.7	6.4	-5%
6	GlaxoSmithKline	6.5	5.9	-9%
7	Johnson & Johnson	5.1	4.6	-10%
8	AstraZeneca	5.0	4.3	-12%
9	Eli Lilly	3.7	4.2	+13%
10	Takeda	2.9	3.3	+13%

Source: EvaluatePharma (30 April 2010)

For Pfizer, its best selling cholesterol lowering drug Lipitor accounted for 23% of its \$50b revenues in 2009<sup>52</sup>. The apparent over-reliance on one mega-selling drug is now under serious threat and Pfizer stands to lose \$13b annually as of November 2011 when Lipitor loses patent exclusivity. This imminent loss coincides with the 2009 reductions in R&D expenditure<sup>53, 54</sup>.

Several of Sanofi-Aventis' products came off patent protection around the same time in the US notably Lovenox, a blood thinner drug. This resulted in a 0.8 decline in Sanofi-Aventis' revenue in 2010. GlaxoSmithKline lost more than GBP1 billion in 2009 to generic competition in the US market<sup>55</sup>. Johnson & Johnson's Chairman and Chief Executive, William C Weldon, informed shareholders that 2009 was one of the most challenging years the company has faced since its founding in 1886. The company faced patent expires in 2009 that was estimated to cost \$3b<sup>56</sup>.

Commenting on R&D spending across the industry during a January 2010 interview by scrip 100, Mr. David Brennan, chief executive of AstraZeneca, said

*"I don't expect that you're going to continue to see R&D expense increase at the same level that it's increased over the last eight years. I think it will slow down because the revenue lines are slowing down and that's got to do with the patent cliff. If your overall growth rate is going to be 3 – 4%, then it's pretty difficult to justify spending more than that on R&D unless you've got the productivity....."<sup>57</sup>*

Mr. Brennan's comment reflects the industry's reluctance to continue to increase R&D spending, in the face of runaway costs or without commensurate increases in productivity. Projections made by EvaluatePharma, the pharmaceutical and biotech market intelligence firm, suggest that net growth in R&D spending from the top 20 pharmaceutical companies will only reach compound annual growth rate (CAGR) of +2% in 2016 from the 2009 figures.

The modest growth in projected spending underscores the importance of significantly increasing R&D productivity across the industry. The next subsection defines what productivity means and discusses its impact and trends.

### 2.4.3 Drug R&D Productivity

#### The Meaning of R&D Productivity

(Paul and Mytelka et al, 2010) defined Drug R&D productivity as the relationship between the commercial and medicinal *value* generated from producing a new drug (i.e. new molecular entity NME) and the *costs* associated with getting it to the marketplace. There are two components inherent in this definition. One has to do with the efficiency with the new drug is researched and developed; and the second highlights effectiveness of the drug to patients and other stakeholder customers such as the prescribing physicians and payer organizations.

R&D efficiency rest on the input and output elements of the process. The inputs are the science, efforts and capital outlay; whilst the outputs could be the attainment of key project milestones such as proof-of-concept, successful phase 3 trials and ultimately the number of drugs that get FDA approvals and get to the marketplace. Output can also be seen in the light of the number of drug candidates in the pipeline across these different stages or milestones.

R&D effectiveness, on the other hand, has to do with outcomes. Outcomes are associated with the ability of the R&D system to produce drugs that can deliver real therapeutic value and medical outcomes for patients.

(Paul and Mytelka et al, 2010) go on to abstract the elements of productivity into a mathematical formula that further decomposes productivity into quantifiable variables. The mathematical relationship below shows that productivity has five interconnected variables. These are work-in-progress R&D projects or drug candidates in the pipeline (WIP), probability of technical success  $p(TS)$ ; commercial value of the new drug ( $V$ ) measured in projected annual sales, cycle time from discovery through to product approval and registration ( $CT$ ) and the total cost of R&D ( $C$ ).

$$P \propto \frac{WIP \times p(TS) \times V}{CT \times C} \dots\dots\dots(1)$$

In order to increase productivity, costs and cycle times need to be reduced. The number of viable research projects and drug candidates at key phases, especially late stage development, need to be increased. Strategies that increase the probability of technical success such as choice of project and early proof-of-concept need to be deployed. And the potential for enhancing the commercial value of the drug have to increase. One way to achieve this is to reduce the cycle time for getting the drug to the market in order to maximize the residual time left for patent exclusivity. The shorter time it takes to discover, develop and get a new drug approved, the longer the exclusivity time before generic competition enters the market.

### **Industry Trends**

Drug R&D productivity has been on the downward spiral for several years. According to data from Parexel's Biopharmaceutical R&D Statistical Sourcebook 2010/2011, the various spending related metrics such as industry spending per New Drug Application (NDA) submission in the US and spending per New Molecular Entity (NME) approved in the US have been on the rise. In 1993, for example, the amount of R&D spending per NDA submission in the US was \$81.4m. This figure has increased to \$336.8m in 2009, equivalent to about 314% increase. This metric is defined as the total number of PhRMA member R&D spending divided by the number of NME submissions.

In the same vein, industry R&D spending per NME approved in the US in 1995 stood at \$543m. This number reached \$2.41 billion in 2009, an increase of 344%. This metric is calculated by dividing the total PhRMA member R&D spending by the number of NMEs approved by the FDA<sup>58</sup>.

One of the consequences of declining productivity is the corresponding fall in sales exclusivity. This is the residual time left on the patent before generic competitors enter the market. Since the clock starts ticking as soon as a patent is filed, sales exclusivity is therefore dependent on the time it takes to get the new drug to market; as mentioned earlier. The average exclusivity of drugs protected by patents, as weighted by sales generated, has declined since 1999 from 5.5 years to less than 4 years. This is the lowest ever experienced in the industry<sup>59</sup>.



In articulating reasons for the decline in R&D productivity across the industry, (Garnier, 2008) argued that whilst economic and market related factors such as increasing cost of R&D and pricing pressures, as well as scientific challenges in the form of increasing difficulty to discover new medicines are to blame; the huge, lumbering and complicated traditional R&D organization is also a culprit. (Garnier, 2008) went on to link increased organizational complexity and bureaucratization with the slowdown in innovation despite the advent of high technology R&D tools and techniques such as genome sequencing and combinatorial chemistry.

Whilst (Paul and Mytelka et al, 2010) created sophisticated quantitative models that seek to optimize the five variables in the formula discussed above, the human factor and organizational design issues raised by (Garnier, 2008) were not given consideration as major drivers for improving productivity. This research has thus focused on those human interactions and organizational issues with the objective of evaluating organizational models and forms along with the underpinning strategies for achieving productivity enhancement in the industry.

The next chapter makes connections between the ways people are organized to work and their performance and productivity. This will be done through a review of academic literature in the field of organizational design.

## 3 Organizational Structures, Innovation and Productivity

### 3.1 Organizational Structures and Strategic Design

(Fontaine, 2007) defines organizational structure as the ways and manner in which an organization arranges itself and utilizes its resources, especially human resources. These “ways and manners” are quite critical to both employees and companies as it provides the linkage between four essential management functions of *planning, organizing, leading and controlling*. Key questions such as who does what? How are jobs organized? Who reports to whom and how does information flow and knowledge flow across an organization and within the network of relationships and interdependencies? All these questions have underlying answers in how organizations are designed and what organizational structures are in place.

In the long run, organizational structure could make the difference between success and failure for individuals and firms. This is particularly true of situations when an organizational structure is not aligned to the strategic intent of a company. For example, a company might need to be very responsive to customer needs perhaps due the highly competitive market in which it operates. If this company however has a hierarchical structure where virtually every decision has to be approved by senior managers who are either removed from the day-to-day business operations or are not easily accessible, then there is the risk that the company might not be able to achieve the level of responsiveness it needs to attain due to the ways and manner of how people are arranged and the level of power and decision making authority vested in senior management. The substance behind this hypothetical example is brought to life by Mitch Thrower, the author of *The Attention Deficit Workplace*. Thrower asserts “*Too often ideas get rejected because they have travelled too far in the organization filled with fiefdoms and inevitable roadblocks*”. (Garnier, 2008) put this in the context of big pharmaceuticals when he suggests that as firms grow the size of bureaucracies, top scientists with little tolerance for high levels of bureaucracy leave. Those who stay aimlessly pursue interests that might not necessarily be aligned to the goals of the organization.

Companies therefore embark upon changes in organizational structures in reaction to challenges they face. These challenges could be external occurrences that impact company performance. In the case of the pharmaceutical industry, (Garnier, 2008) pin-points the challenges to big pharma as declining productivity and a frightening loss in financial value. From the fall of 2000 up to spring of 2008, the top 15 pharmaceutical companies lost close to \$850 billion in shareholder value; and their stock price fell from 32 times earnings to an average of 13. These challenges are wake-up calls and Garnier, suggests, they should propel pharmaceutical companies to undertake the redesign of their organizations. He argues they must shift from silo- based pyramids that stifle responsive decision making and result in management losing grip on the fast pace of science; to organizational models that empower and restore authority to scientists engaged in drug R&D.

### **Some Organizational Design Terminologies**

- a) Centralization and Decentralization: A Centralized organization is one in which decision making is directed by the top of the organization. Employees therefore may have to wait for directives from top management before acting upon or reacting to business issues. A decentralized organization is the opposite. Decision making authority is devolved down to people lower in the organization. This engenders speedily, and sometimes better, decision making as theoretically employees closer to day-to-day business and customers issues are able to make decisions with more detailed knowledge of what actually happens on the ground in a responsive manner. A disadvantage of decentralization could be the risk of potentially undermining the position of senior management.
- b) Hierarchy of Authority: Hierarchy of authority is a concept in organizational strategic design that says that there has to be clarity between the levels of authority. People must know who is in charge of various tasks and responsibilities. The implications for hierarchy of authority is that as tasks and roles are divided and spread across the organization, the degree of job specialization increases as the business environment becomes more sophisticated.

### **3.2 Types of Organizational Structures**

Before going into a discussion and analysis of the various types of organizational forms, it is pertinent at this stage to mention that the type of organizational model that best suits a firm is contingent upon several factors. As such, there are firms that do not adopt a single organizational structure for the entire company given the fact that firms might have a portfolio of different but complementary businesses operating in different geographies. Additionally, one might find, for example, that a matrix organizational model might be suitable for the R&D division of a firm; whilst the sales department of the same firm might benefit from a Divisional organizational structure (Fontaine, 2007).

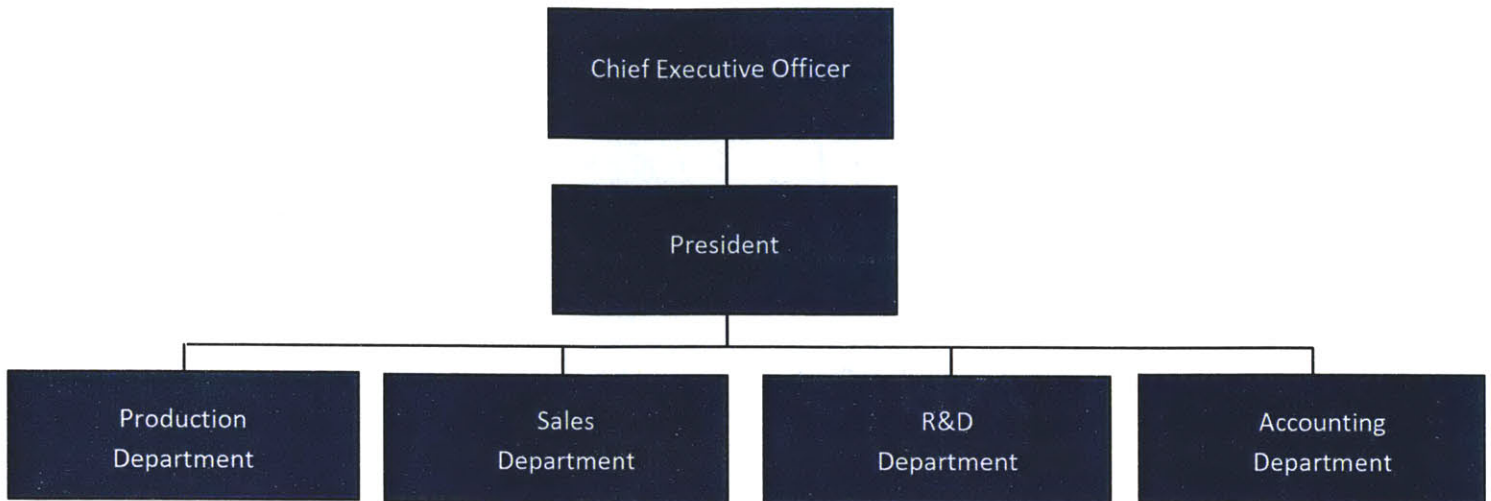
Fontaine broadly categorized the most common organizational structures into the following models

- The Functional Structure
- The Divisional Structure
- The Matrix Structure
- The Horizontally linked Structure

#### **The Functional Structure**

This structure separates the organizations into functional areas and departments such as production, sales R&D and Accounting. This organizational form is the most common model. It aggregates people of similar skill-set and roles into functional operating groups. Exhibit 5 below shows the functional silos and linear reporting lines. The head of each function would presumably be someone that has deep experience and expertise within respective functions.

**Exhibit 5: The Functional Organizational Structure**



Source: (Fontaine, 2007)

**Advantages and Disadvantages of Functional Organizational Model**

The functional structure engenders central decision making and strong management control. Additionally, this organizational form allows for upward career move within the respective functions from junior entry position through to management roles. By design it therefore gives some level of stability and perhaps efficiency within discrete functions.

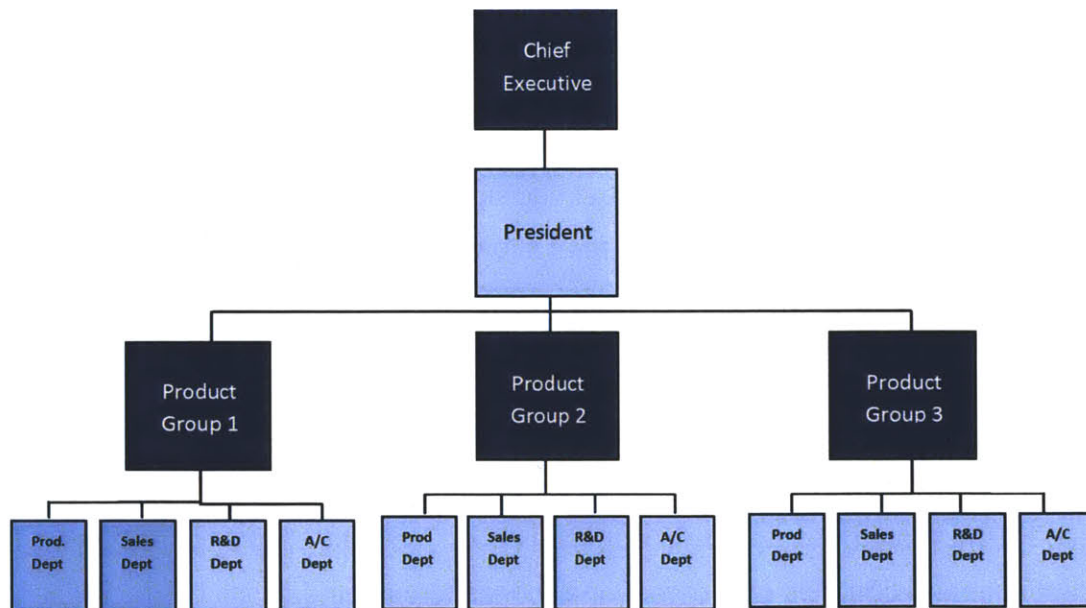
On the negative side, this model breeds silos or siloing. This is a situation whereby organizations individual operating departments work in isolation of other departments. This model therefore does not foster communication, collaboration and teamwork. The resultant scenario could be lack of responsiveness to customers which in worst cases could lead to loss of revenues as customers move over to competitors in search of better services.

An additional disadvantage could be that employees within discrete departments see themselves more as belonging to that department than as having a company-wide identity. This could further compound the siloing effect discoursed above and its associated negative impact (Fontaine, 2007).

## The Divisional Model

In the Divisional Organizational structure, people with different functional operating roles and skill-set are grouped under a product-line and or market segment to help run that part of the business. As shown in Exhibit 6 below, you will have Accountants, Sales, Manufacturing, and R&D personnel etc working within a business division. If the company has three divisions, then the functions mentioned would be found working across all three divisions i.e. there will be accountants across the three operating divisions as opposed to a central Accounting department.

**Exhibit 6: The Divisional Organizational Structure**



Source: (Fontaine, 2007)

## Advantages and Disadvantages of Divisional Organizational Model

Since professionals from various functions report to a single person in the division who coordinates and channels effort into fulfilling divisional objectives, there is inherent ability to respond quicker to customer requirements. Whether the division represents specific product-lines, market segments or geographic regions, the advantage of a single source of coordination of multi-functions discourages the level of siloing associated with the functional organizational structure.

Another advantage of divisional organizational model is that it fosters general management and executive skills and capabilities since employees are exposed to issues across multiple functions as they relate to particular business divisions.

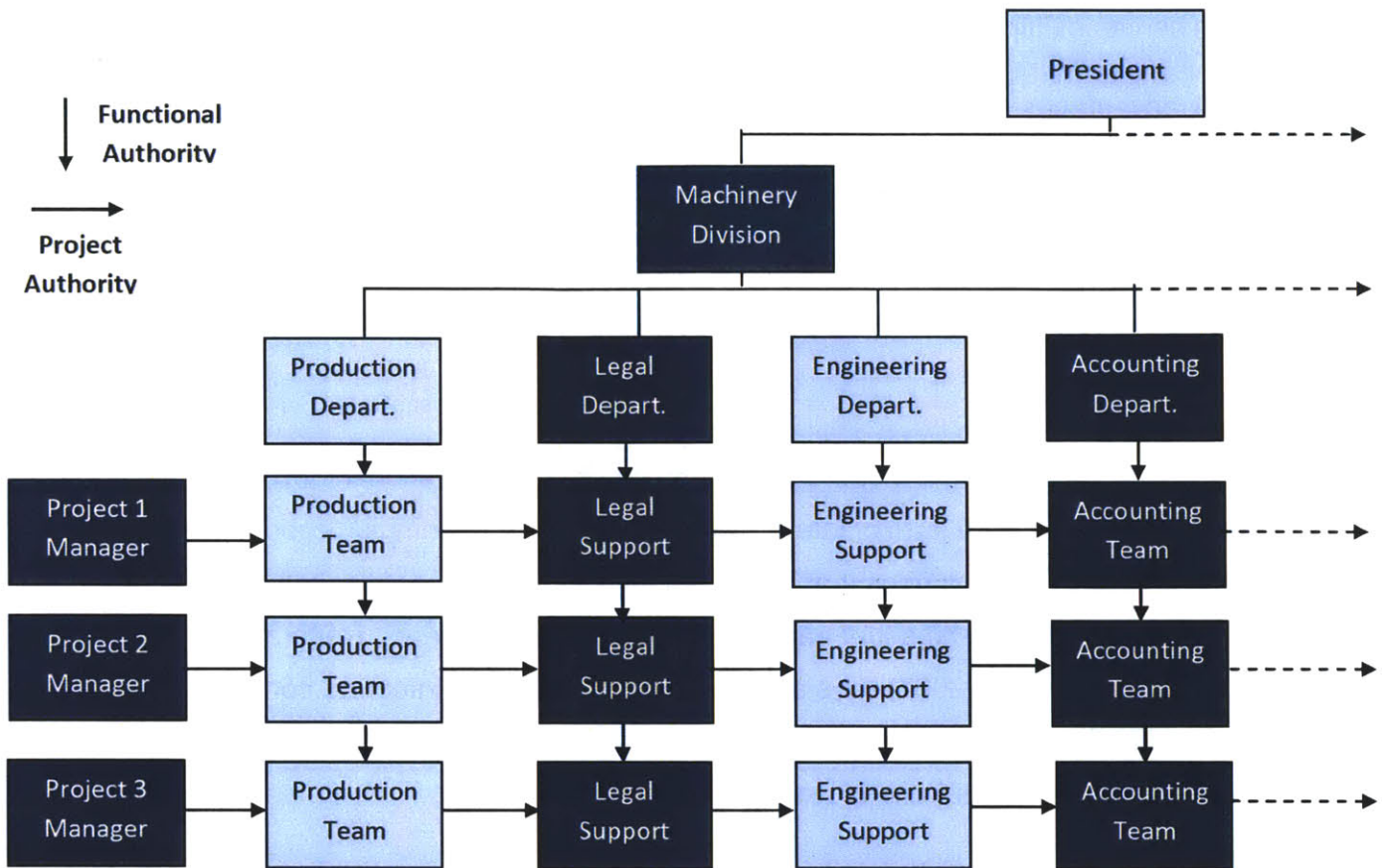
The disadvantages of this model are based on the fact that it creates redundancy of roles since functional roles are duplicated across divisions. This could result in in-company competition amongst divisions. Additionally, there tends to be reduction in the level of occupational specialization as high levels of functional specialism is traded-off with having more general management capabilities (Craig W. Fontaine, 2007).

### **Matrix Structure**

(Knight, 1976) described a matrix structure as a mixed organizational form that overlays vertical hierarchy with a form of lateral authority, influence or communication. This model therefore contains roles that have dual influences; and coordination is driven through lateral relationships that transcend functional departments. Reiterating this description, (Fontaine, 2007) says a matrix structure seeks to integrate components of functional and divisional organizational forms with the resulting model operating in a unique manner different from its individual constituents.

Exhibit 7 shows the underlying operating organizational components of matrixed a division in a large company. It shows the constituent functional areas such as production, legal, engineering and accounting departments; as well as cross-cutting project organizations that run horizontally through functional departments. So the dual lines of influence involve the head of functional departments and the project manager. The department heads have reporting line responsibilities for staffers in their respective departments; whilst project managers do not necessarily have line responsibilities for staff. Project managers assemble *borrowed* staffers and expertise from functional departments to execute projects. As resources are finite, project managers will have to persuade department heads to release resources. This could involve serious competition especially when several projects are running simultaneously.

**Exhibit 7: The Matrix Organizational Structure**



Source: (Craig W. Fontaine, 2007)

**Advantages and Disadvantages of Matrix Organizational Structure**

Matrix organizational structure allow for efficient use of expensive specialist resources as these resources are kept busy on projects. Due to the fact that resources can be pooled from across functional departments, this model facilitates quick start-up of projects. Additionally, this model fosters the development of cross-functional skills as employees are exposed to working with wide ranging specialists and functions in projects. This also increases employee involvement in advancing the company’s business through the participation of several *borrowed* specialist resources in project teams.

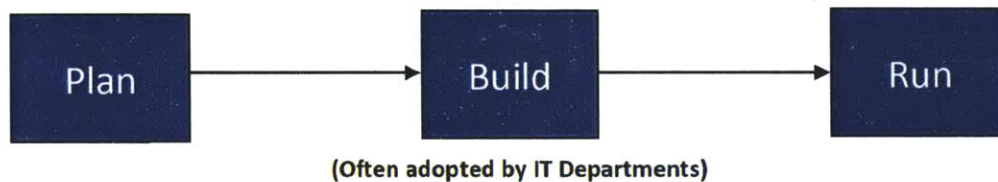


The key disadvantages of the matrix model have to do with the ambiguity of who is actually in control or who is the boss? Is it the departmental head or the project manager? This model therefore breeds serious conflicts across several points. There are conflict as to how to share and allocate scarce resources, there could be real conflict on business priorities between functional department and projects. There could also be conflicts between projects regarding priorities, deadlines and resource allocation. So the matrix organization is filled with conflict across many interjections and stakeholders.

### The Horizontally Linked Organizational Structure

A relatively new model is the horizontally linked structure which is gaining momentum amongst high-tech companies. In this structure, a company organizes its people according to discrete functions and activities along the value chain – these are processes that *produce, market and service* the company's products (Fontaine, 2007).

**Exhibit 8: The Horizontally Linked Model**



Source: (Fontaine, 2007)

In Exhibit 8 above, a simplified *Plan-Build-Run* shows how a company organizes horizontally. People in the *planning* department are charged with the responsibility for developing new projects; this could involve people from R&D and finance. *The building* department is involved in constructing and assembling the project. And the *Run* department involves sales, marketing, maintenance and other functions associated with the perpetuation of projects.

This model is said to foster a quick response to rapidly changing markets, customer needs and technological advances hence its adoption within the high tech sector. It might however not be suitable for firms that produce products with longer life span or service industries<sup>60</sup>.

### 3.3 The link between Organizational Form, Productivity & Innovation

(Wintrobe and Breton, 2001) in their study of the relationship between organizational structure and productivity asserted that firms that there is a positive correlation between vertical trust, that is the trust between employees and employers, and firms' productivity. This study which is backed by empirical data, suggests that an organizational structure which fosters such vertical trust could result in enhanced productivity.

Also making a case for the connection with between organizational structure, employee motivation and productivity, (Karlik, 2010) argued that a decentralized organization that gives people independence and resources to operate and unity of purpose in the form of longer term vision will increase employee motivation; and this will in turn translate into enhanced productivity.

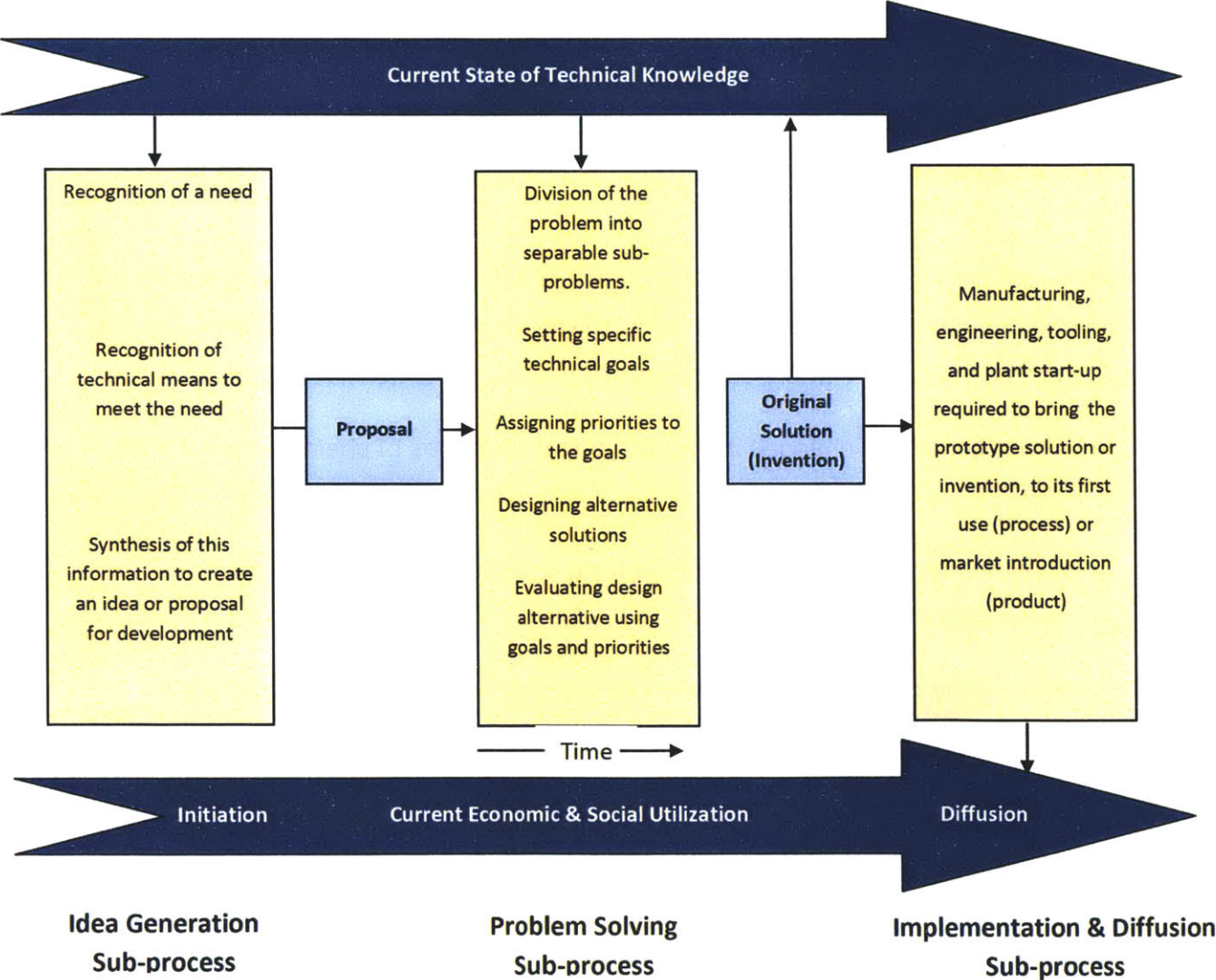
In a separate study of knowledge flow, organizational structure and organizational learning involving 163 high-tech company managers in Taiwan, (Wang and Lien, 2010) found out that of the many factors that facilitate the flow of learning, organizational structure is the most powerful. This, (Wang and Lien, 2010) purport, is because "*systematically formed organizational learning rules or routine cannot operate independently when separated from the organization structure*" Since knowledge flow and learning are important factors for innovation, it then follows that the way and manner in which people and resources are organized at work can impact innovation.

At this juncture it is pertinent to look at how innovation is both defined and viewed as a process. (Utterback, 1971), (Marquis, 1969) and (Schmookler, 1966) all agreed that innovation is not just invention. According to these scholars, invention can be said to be *the original solution to a need or want arising from the synthesis of information on the need or want; and the technical information of how the need or want can be met.*

Innovation, on the other hand, involves introducing invention to the market; in the case of a new product or in the case of process innovation, its first use. This implies that innovation means taking invention far enough such that it begins to have economic value and impact. It follows therefore that based upon (Utterback, 1971),

(Marquis, 1969) and (Schmookler, 1966) expositions, innovation can be viewed as a process. This is important in linking innovation with organizational structure. Exhibit 9 below clearly shows the innovation process as originated by (James M. Utterback, 1971). The current state of technical knowledge as well as all other components of the innovation process exist and operate within the cultural, political and social elements of an organization.

**Exhibit 9: The Process of Technical Innovation**



Source: (Utterback, 1971)

Additionally, and perhaps more importantly, for effective idea generation to take place, and indeed problem solving and implementation phases, there has to be good flow of knowledge and information in order to be able to synthesize relevant information about the need and how to meet the need. It then follows that since information flow is an important factor for innovation, organizational structure, which provides a mechanism for such flows, will be equally important. This underpins (Utterback, 1971)'s identification of the firm's internal characteristics as it influences the innovation process.

(Utterback, 1971)'s work is corroborated by (Tuan and Venkatesh, 2010)'s empirically grounded research in connecting organizational culture and structure with technological innovation. In their work (Tuan and Venkatesh, 2010) concluded that organizational structure, along with other factors, could either operate to support technological innovation or inhibit it.

In concluding this section, it is clear that the ways and manners people and resources are organized have a bearing on both productivity and innovation. With this in mind, I will progress to section 4 where I will discuss findings and qualitatively analyze the

- The rationale for changes in organizational structures of pharmaceutical R&D and
- Evaluate newly implemented or evolving organizational models in the pharmaceutical industry

This will be in the context of interviews conducted at five global pharmaceutical corporations; GlaxoSmithKline, Sanofi-Aventis, AstraZeneca, Pfizer and Novartis.

I will thereafter make recommendations and conclude in chapter 5 with areas where further work could be done.

## **4 Findings and Discussions**

This chapter details all findings from both interviews conducted at GlaxoSmithKline, Sanofi-Aventis, AstraZeneca, Pfizer and Novartis; as well as further secondary research undertaken into the specific situations facing these individual firms. I try here to present a cohesive picture of the R&D organizational structures of these companies, understand any changes either already executed or planned and the drivers for change and strategic intentions behind any reorganization in the five organizations.

Of the five companies, GlaxoSmithKline (GSK) is the only one that has undertaken the most fundamental redesign of its R&D organization. As such, I have used GSK as the primary case of study and the four others as complementary cases. I will therefore discuss and analyze GSK first. This will then be followed by Sanofi-Aventis, AstraZeneca, Pfizer and I will conclude with Novartis.

### **4.1 GlaxoSmithKline**

#### **4.1.1 Company Background**

Formed on 17 January 2000, through the \$75 billion mega merger between two British companies Glaxo Wellcome and SmithKline Beecham; GlaxoSmithKline (GSK) is one of the largest research-based pharmaceutical corporations in the world. The merger, orchestrated by Sir Richard Sykes, the former Chief Executive and Chairman of Glaxo Wellcome, was intended to achieve economies of scale particularly in research and development (R&D) and marketing as well as achieve market capitalization of \$190 billion at the time. Today, GSK is a diversified healthcare business engaged in research, development, manufacturing, sales and marketing of prescription medicines covering several therapeutic areas and wide ranging consumer health products. It has 5% market share of the global pharmaceutical market. With headquarters in London UK, GSK employs 96,500 people across 120 countries and sells its products in over 150 countries. In 2010 it recorded annual revenue of \$46.36 billion and has a market capitalization of \$97.93 billion. GSK generates its revenues from six business segments. Based on 2009 revenue analysis these segments can be quantified as; US pharmaceuticals accounting for 32.4% of total revenues, Europe pharmaceuticals

27.1%, Emerging Market 10.5%, Asia Pacific / Japan pharmaceuticals 9.5%, other trading pharmaceutical 4.2% and 16.4% for consumer healthcare<sup>62</sup>.

In 2010, GSK spent 14% of total annual revenues on R&D and has about 30 late stage drug candidates in its drug pipeline according to its 2010 annual report.

GSK is a global leader the in Infectious disease area and occupies a prominent position in the central nervous disease market. Some other disease areas in which it operates include cancer, heart and circulatory diseases, metabolic diseases and depression.

Additionally, GSK is the third largest player in the vaccine market with assets in Hepatitis A and B, Typhoid, Bacterial Meningitis and Polio to mention a few. In the consumer group category, it is operates in the dental, over-the-counter (OTC) and nutritional markets. Some of its product brands include Aquafresh (dental product), Agumentin (antibiotic drug), Avandia (anti-diabetic drug) and Zantac (used for the prevention and treatment of stomach ulcer) and Seretide / Advair (treatment of asthma and chronic obstructive pulmonary disease).

GSK's three-pronged corporate strategy, as articulated by new Chief Executive Andrew Witty in GSK's 2009 Annual Report, is to "*grow a diversified global business, deliver more products of value and simplifying the operating model*". Underpinning the strategy to deliver more valuable products is an R&D strategy focused on the best science, increasing externalization of projects when it's cost effective, re-personalization of R&D and increasing return on investment. These strategies are aimed at driving growth; particularly in emerging markets with a focus on rare disease areas and unmet needs.

#### **4.1.2 Methodology**

Four senior R&D executives based in Triangle Park North Carolina and the North American headquarters in Philadelphia were interviewed. The official positions of these executives are

- Vice President, Clinical Trial Optimization and Mobilization
- Senior Vice President, Center of Excellence in Drug Development (CEDD)

- Senior Vice President, Oncology Development
- Senior Vice President, Infectious disease

These interviews were done over the phone and lasted about an hour each. The interviews were both recorded on an audio device and on paper as written notes.

The areas covered during the interviews included

- An understanding of the past R&D organizational model
- Reasons and drivers for change
- An understanding of the new organizational model and the
- Strategic objectives that the new organization aims to achieve

In order to evaluate reactions of investors to the implementation of a decentralized R&D organizational model, historical stock price data were reviewed using the Bloomberg Database.

Finally, the Three Lenses Organizational Model by (Ancona et al, 2005) was used in providing qualitative analysis and critical reviews in the form of pros and cons of the new organizational structure. This organizational model provides a framework for reviewing organizations from the perspective of strategic design (tasks, information flow, job design etc), political lens (power and influence distribution) and cultural lens (how history and intangibles have shaped assumptions and behaviors).

#### **4.1.3 The Old R&D Organizational Model**

GSK's old R&D organization was very large and highly centralized. The efforts to transition from this model started very early on at the merger of Glaxo Wellcome and SmithKline Beecham in 2000. These efforts were led by former Chief Executive of SmithKline Beecham, Jean Pierre Garnier, who became the new Chief Executive of GSK; and his newly appointed Chairman of R&D Tachi Yamada.

The centralized organization was such that the responsibilities of research or discovery scientists ended once they came up with a drug candidate. These scientists would then literally hand-over drug candidates to development scientists to commence development work and take the drug candidates through clinical trials and approval processes with regulatory authorities. Such hand-offs were described as sending projects *over-the-wall*. This terminology emphasizes the organizational divide between Research and Development. Over 90% of such drug candidates handed over to development scientists never made it to the marketplace.

Decisions on whether to progress projects from discovery through to development was done through a single centralized committee. This committee, which reported directly to the global head of R&D, comprised functional heads of operating departments such as pharmacology, genetics research, clinical development, toxicology and regulatory affairs. Members met regularly to determine resource allocation, project funding and which projects to progress or abandon. These functional heads were chosen to be on the committee because of the knowledge of the company's R&D project portfolio rather than their disease area expertise. In fact, these committee members did not have particular specialism in any therapeutic area (Huckman and Strick, 2010).

The fact that such vital decisions were not led by therapeutic or disease area heads suggested that projects were not always aligned with disease area strategies. One of the senior R&D executives I interviewed who is a Vice President with 14.5 years experience in GSK described this situation "*...heads of pharmacology, biology and other operating functional departments heads were very important....but the heads of therapeutic areas were glorified figures heads*".

In addition to the misalignment in disease area strategy and centralized decision making, the traditional R&D organization fostered a culture of dependency on blockbuster drugs and large projects. Supporting all these were large amounts of R&D personnel literally scattered across multiple locations and geographical regions. As the cost of R&D rose astronomically, this became unsustainable.



#### 4.1.4 Reasons for Change

The cumulative effects of the traditional organizational model in the early years at GSK became the levers and reasons for change. These reasons include

- Dichotomy between discovery and development; as well as the disconnect between early and late stage development.
- The centralized organization and decision making process resulted in high levels of bureaucracy which in turn prolonged project lead-times
- Lack of accountability and full ownership of projects. Project leaders were not empowered. They were not given budgetary control for projects.
- Poor communication, information and knowledge flow across the R&D value chain. This was due to deeply entrenched siloing and its associated effects
- Need to reduce dependency on drug blockbusters and exposure to patent cliff
- Need to align project with disease area strategies and reduce therapeutic area footprint. The idea was to focus only on therapeutic areas where GSK has strong scientific capabilities to produce novel drugs that will add value to patients and stakeholders. Exiting areas where the science has moved on or where projects are best done externally.
- Need to increase externalization both in terms of project execution and licensing deals
- Need to realign incentives with R&D productivity. Bonuses were paid to R&D personnel based on company-wide performance in the traditional model.
- And lastly the need to significantly increase R&D productivity.

A GSK R&D Vice President interviewed summed up the impact all this had on R&D productivity by saying “...*the number of assets in late stage could be counted on your finger tips*”. This productivity problem persisted from GSK’s formation in 2000 to 2008

during which time its late stage R&D pipeline delivered relatively little sales growth of \$3.7 billion given the large amounts spent on R&D. The major growth drivers during this period were products that were not derived from its internal R&D operations; rather, these were products that were either gotten through acquisition or licensing and co-development deals with external parties. Such product included Lovaza; a cardiovascular drug which GSK got from its acquisition of Reliant Pharmaceuticals a privately held specialty pharmaceutical company based in the US in the fall of 2007. This \$1.65 billion cash transaction gave GSK access to the non-statin dyslipidemia segment of the US cardiovascular market where Lovaza had a 10% market share. Total sales in this segment were \$2.2 billion in 2006 and projected to grow by 20% a year<sup>63</sup>.

The drought in R&D productivity led GSK to over-depend on its select brand of blockbuster mega selling drugs thereby increasing its exposure and risks to patent cliff and commoditization from generic competitions.

Foreseeing the urgent need to change, the then Chief Executive Jean Pierre Garnier and Tachi Yamada, Chairman of Global R&D began the work to de-centralize GSK's R&D organization into Centers of Excellence in Drug Development (CEDDs) in 2000.

#### **4.1.5 The New Organizational Model**

The restructuring of GSK's R&D organization and creation of decentralized units can be said to have been implemented in two major phases. The first phase was done in 2001 with the implementation of Centers of Excellence in Drug Development (CEDD). As mentioned above, this was planned and implemented by Jean Pierre Garnier and Tachi Yamada. The second phase was the creation of Discovery Performance Units (DPUs) within the CEDD organization in 2008. This was implemented by the new Chief Executive Andrew Witty immediately upon assuming the top job.

#### **Phase 1 – Implementation of Centers of Excellence in Drug Development**

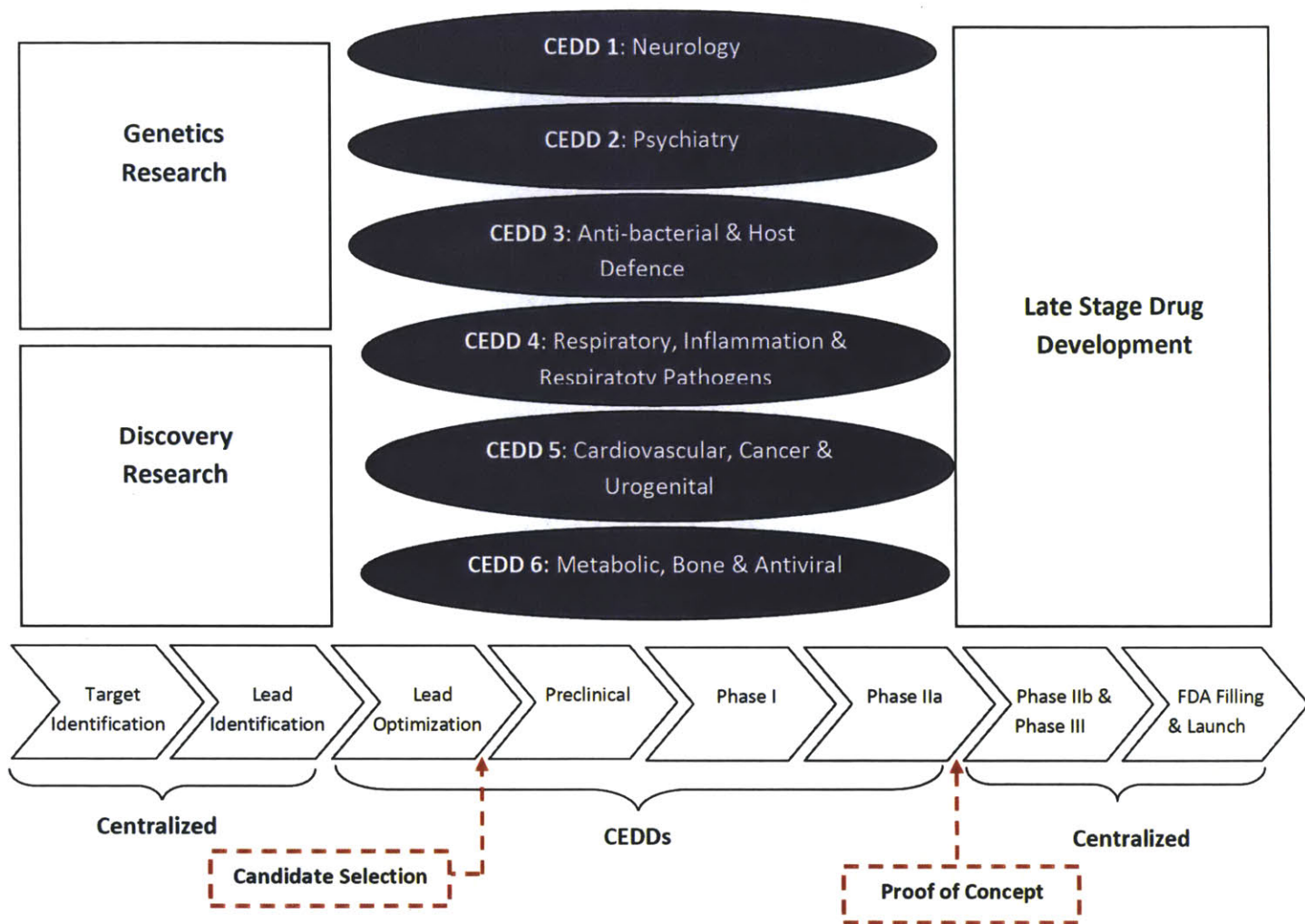
Six CEDDs were initially created in 2001(see exhibit 10 below). With more centers added over the years, GSK now has twelve CEDDs. Each CEDD is headed by a Senior Vice President who acts as its de-facto chief executive officer with full line

responsibilities for staff in the center and accountability for delivering objectives. Comprising a few hundred multi-functional scientists and clinicians, each CEDD is focused on a family of related diseases and charged with the mission to discover the most effective drug within respective therapeutic areas. Each center head (Senior Vice President) has the authority to initiate and abandon projects without seeking approval from an oversight committee. They develop and execute business plans based on set strategic objectives and have full budgetary control. Center heads have the freedom to choose the stage of R&D process required to deliver their objectives. They are at liberty to either commission GSK's internal R&D functional services such as chemistry, toxicology, drug metabolism and formulation or source these services from external parties based on how commercially competitive the internal services are compared with those of external parties.

The once powerful functional departments are not within the CEDD organization; rather they operate within their functional centralized organization as service provider units that are required to provide highly efficient and cost effective services to CEDD. These services are benchmarked against external providers. Functional groups are however allowed to license out any potential drug candidate they come up with that are not necessarily required by CEDDs.

As shown in Exhibit 10 below, the decentralized CEDD organizations' responsibilities along the R&D value chain is to take potential drug candidates supplied by centralized functional groups (genetics and discovery research) from *Lead Optimization* through to *Phase IIa* where they undertake *proof of concept* (POC). It is important to mention that potential drugs produced by the early discovery functional groups are shared with several CEDDs to determine whether the candidate can be used to treat other disease indications which other CEDDs might be working on.

**Exhibit 10: De-centralized Centers of Excellence in Drug Development**



Source: Huckman & Strick, 2010

Upon achieving POC, CEDDs present drug candidates to a central Development Investment Board (DIB) for funding approval to progress to the very expensive late stage development phases. Upon approval, CEDDs handover assets to a centralized late stage development team that takes such drug candidates through phases IIb, III, regulatory approvals and through product life-cycle management in post launch stages. DIB is comprised of senior corporate R&D executives from outside CEDDs and senior

commercial executives who ensure that drug candidates that are progressed to late stage development will be commercial viable drugs in the marketplace.

## **Phase 2 – Implementation of Discovery Performance Units**

Discovery Performance Units (DPUs) were created in 2008 by Andrew Witty, who succeeded Jean Pierre Garnier as Chief Executive on 21 May 2008. Commenting on the latest organizational changes to R&D on 23 July 2008 in a press release, Mr. Witty said *“The core of GSK has been and will remain pharmaceutical R&D.....we must be relentless in our efforts to improve R&D productivity and this is why we have started to implement a new vision for our R&D organization which is science-led and focused on value creation.....we believe that drug discovery is best optimized through research by small, focused teams. Building on the success of our CEDDs, we have now pushed our organizational design further to increase product flow and value”*<sup>64</sup>

A Discovery Performance Unit consists of a team of 5 to 70 scientists within the CEDD umbrella organization focused on research and development of potential drug candidates in a single disease area or pathway. For example, a DPU could focus on the biological pathway of Schizophrenia within the Neuroscience CEDD.

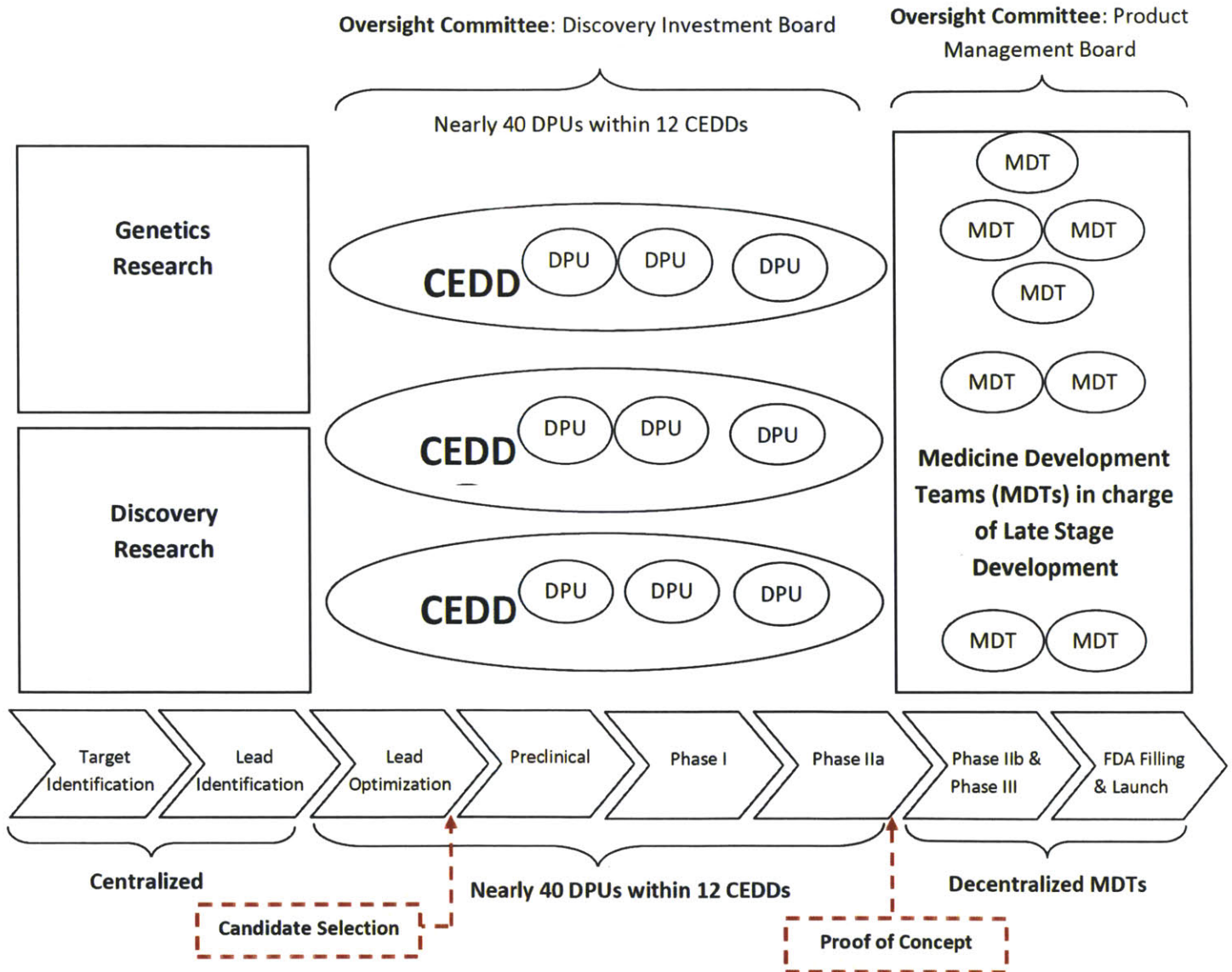
DPU heads develop and own 3 years business plans. They are fully accountable for budgets and decision making on projects. In executing their business plans, DPU heads have the latitude to outsource elements of the R&D process to external parties such as Contract Research Organizations (CROs). They could also collaborate with academia and other companies in joint development deals. Increasing externalization is in line with overall R&D strategy as articulated by GSK Chief Executive Andrew Witty in 2008 *“Externalizing R&D enables GSK capture scientific diversity and balance expenditure and risk in drug development. In the future, we believe that up to 50% of GSK’s drug discovery could be sourced from outside the company”*<sup>65</sup>

With a total of nearly 40 DPUs created within the existing 12 CEDDs, DPUs’ objectives and business plans are reviewed by the Discovery Investment Board (DIB). This board is chaired by Dr. Patrick Vallance Senior Vice President of Medicines Discovery and Development. Dr. Vallance is a member of GSK’s Corporate Executive Team.

## Medicines Development Teams

As shown in exhibit 11 below, the hitherto centralized last stage development part of the R&D value chain now comprise Medicines Development Teams (MDTs).

**Exhibit 11: Discovery Performance Units & Medicines Development Teams**



Source: Adapted from (Huckman & Strick, HBS 2010), GSK company information & interviews conducted

These teams consist of 6 to 10 multi-functional people with responsibilities to take a specific compound or drug candidate through late stage development and regulatory approvals. MDTs are comprised of both “employed staff”, that is permanent members of the project team; and “deployed staff”, resources that are deployed from centralized functional organization.

Each MDT is led by a Medicines Development Leader (MDL). MDLs are carefully selected for this crucial role. Characteristics and competencies required for an MDL include experience in drug development, ability to solve problems, strong leadership and project management skills. MDLs are usually medical doctors, although other people with differs background who possess good network of contacts and relationships across the organization could also be considered for the role. For example, someone with a background in the commercial strategy of the asset being developed could be an MDL.

The Product Management Board (PMB) is the oversight committee with responsibility for deciding progress of compounds through late stage development. This board jointly chaired by Global Chairman of R&D and the President of Pharmaceuticals in North America. At every decision points along the development process, the PMB evaluate the investment, commercial and technical case to commit resources and funding to progressing projects to the next level in the process.

On the whole, individual teams and units are usually co-located. And no single DPU or development project run by an MDT has a budget that exceeds 10% of the overall company-wide R&D expenditure.

### **Metrics and Incentives**

Underpinning all the changes to organizational structure are the various measurements of productivity metrics and the reward and incentives schemes. Productivity metrics for discovery includes (is not limited to)

- Number of drug candidates per number of people
- Drug attrition rates (i.e. drugs that fail to make it to the next development phase)

- Number of drug candidates successful at Proof of Concept

On the development side, metrics include number of drug approvals per resources employed

With respect to incentives, GSK changed its bonus scheme from one that compensates company-wide performance to compensating scientists' achievements. Once a drug candidate passes proof of concept, that is the drug's safety and efficacy in humans is proven, this triggers payment of significant bonus to the core team of discovery scientists that achieved this. Scientists are also rewarded for solving difficult problems such as finding a way to make a previously insoluble drug candidate soluble.

#### **4.1.6 Strategic Objectives of the New Organizational Model**

Whilst there are several strategic objectives that GSK aims to achieve with its new organizational model, perhaps the most important is a cultural one – that is the ability to wean themselves off the dependency on blockbuster drugs and the unsustainably high exposures to the impacts of patent cliff and erosion of revenues from generic competitions. A Vice President interviewed said “*GSK prefers producing several medium sized assets every 5 years that can generate \$500m a year in revenues as opposed to waiting 10 years for a blockbuster*”. Another senior R&D executive, a Senior Vice President articulated the objective as being the ability from 2015 to launch 5 – 7 new assets a year. This could be a combination of internally discovered drugs and assets from in-licensing deals with external parties.

Other objectives that GSK hopes to achieve include

- Fostering an entrepreneurial culture in R&D just like in biotech companies
- Enhanced communication and flow of knowledge from the co-location of DPUs and project teams; as well as the removal of the dichotomy between discovery and development
- Therapeutically aligned projects with common platforms to undertake discovery and development



- Focus on smaller projects in segmented disease areas and
- Empower teams; and build teams that are more project centric

The R&D executives interviewed hope that all this will more than double the productivity of R&D and that the significant cuts in bureaucracy and increased information flow will have real impact on lead-time to market. A Senior Vice President captures this impact by estimating that *“by vertically integrating discovery and development at least 1 year will be saved in R&D lead-time.....you also save time by having less formal meetings when you put people to work in multi-disciplinary teams”* .

In concluding findings in this section, it is pertinent to mention that significant amounts of people were laid off in 2008 as part of the restructuring exercise. Whilst a Vice President interviewed gave a positive outlook on any impact on morale, (Jean Pierre Garnier, 2008) gave a hint in to the extent and scope of the lay-offs in his Harvard Business School article. Garnier said *“...the roof of the old pyramid – the functional senior vice presidents – and any other vestiges of the silo organization should be eliminated. Their responsibilities should be distributed throughout the decentralized organization”*

#### **4.1.7 Investors’ and Stock Market Reactions to New R&D Organizational Model**

On the 22 February 2008, GSK made earnings announcements to investors. Along with this, news on further plans to boost R&D productivity were announced. GSK’s stock price and trading volume spiked in a positive reaction to the announcements. This is shown in Exhibit 12 below. The exact impact of the plans to boost R&D Productivity through creation of DPUs cannot be determined in isolation since the announcement was made along with earnings and financial performance.

A look, however, at GSK’s cumulative stock price performance since the merger in 2000 shows a downward trend. Exhibit 13 below shows a 31.74% decline in stock price from 2000 up till April 2011. This is not unconnected with both overall industry performance as well as GSK specific challenges discussed earlier. (Jean Pierre Garnier, 2008)

reiterates this by connecting industry challenges with significant loss of value from 2000 to 2008.

**Exhibit 12: GSK Stock Price & Trading Volumes on 22 Feb 2008 when Plans to Boost R&D Productivity were announced along with Earnings Performance.**



**Exhibit 13: GSK's Cumulative Stock Price Performance from Merger in 2000 to April 2011**



#### **4.1.8 The Three Lens Framework Applied to GSK**

##### **The Strategic Design Lens**

This section examines the pros and cons of GSK's new organizational model from the strategic design perspective.

On the positive side, GSK's new organizational model could enhance communication, flow of information and knowledge sharing as people now work in decentralized teams and interact cross-functionally. This in turn could enhance R&D innovation process since, according to (Utterback, 1971), easy flow of information, knowledge and good communication are important elements that drive innovation process.

Reductions in bureaucracy that are derived from eliminating silo organizations could drive down cost and shorten lead-time to market. Since a reduction of these two factors in (Paul and Mytelka et al, 2010)'s equation in chapter 3 results in an increase in productivity, it follows that the new organizational model could help facilitate productivity enhancement, all other things being equal.

The fact that each Senior Vice President in charge of a CEDD has full line responsibilities for cross-functional teams within their centers help remove the conflict of priorities and ambiguities sometimes associated with matrix organizations. This unique arrangement helps clarify purpose, priorities and direction of focus as opposed to being torn in different directions.

On the negative side, the fact that internal functional R&D departments such as toxicology, formulation science, drug metabolism, etc have to provide services that are continuously benchmarked against external profit maximizing providers could lead to unintended consequences. The morale of staffers in these internal departments could suffer especially if they are unable to achieve comparable cost with external competitors because of internal constraints such as staffing levels and volume of demand. In a worst case scenario, this might lead to a loss of good people as these professionals seek employment in other organizations where they feel more appreciated.

Another point closely linked to the above, is the fact that GSK intends to increasingly outsource R&D projects and sometime in the future achieve 50% externalization. Whilst this could increase speed of delivery of projects, potentially reduce cost and enhance innovation as GSK accesses external creativity and capabilities; on the other hand, this could lead to erosion of internal capability and ability to generate innovation within GSK itself. If a company embarks upon outsourcing 50% of its R&D, this could mean significant reductions in internal capacity and capability in what could be regarded as core activities. Proponents of such a significant level of outsourcing could argue that this will allow for a concentration and focus on what the company is really good at doing. However, the critical issue and risk here is that the significant depletion of internal capability in certain areas might affect its ability to be effective and innovative in the retained parts of the R&D value chain. In another hypothetical example, if a research based pharmaceutical company decides to outsource its entire discovery activities whilst retaining the development phases, will this alter its ability to successfully do development since discovery and development are linked?. Whilst this question and hypothesis are probably worth exploring further in another research project, suffice to say that there is a risk of impacting both the culture and effectiveness of successfully undertaking R&D if internal capabilities are significantly depleted in conjoined activities along the R&D value chain.

Another downside to outsourcing could be the risk of external party cutting corners in order to achieve milestone payments. Since external parties are highly motivated by profit maximization and would probably have other contracts with other clients, there is the risk of either intentionally or otherwise compromising certain parts of the process in order to create capacity to do other contracts or to collect monies attached to milestone achievements. In the pharmaceutical and medical setting such risks could result in death, product recalls and withdrawals, and significant loss of money in worst case scenarios. This concern was shared by one the senior R&D executives interviewed. Additionally, there are other challenges that could be encountered in making a partnership work. These include marketing, legal and intellectual property rights as well as revenue sharing issues; all of which could make outsourcing quite a complex enterprise to undertake.

## The Political Lens

This part of my discourse seeks to analyze the way power and influence are distributed and how different stakeholders are impacted by this.

The fact that CEDDs are aligned with therapeutic and disease areas, and CEDD heads are thought leaders and experts in their respective therapeutic areas, gives these leaders voice and significant influence in advocating and advancing the course of R&D in those areas. The knowledge and expertise of therapeutic area leaders as well as their colleagues stand a much better chance of been harnessed, promoted and deployed in the new organizational model since these leaders now have positional power and authority. If this is considered along with the fact that CEDD and DPU heads have full line responsibilities as well as budgetary controls to execute their respective business plans, it follows that GSK could be much stronger in its chosen therapeutic areas as power and influence are aligned in favor of therapeutic and disease area leaders.

Another political advantage with the new model is that its major oversight boards, the Discovery Investment Board and Product Management Board both have diverse members drawn from the R&D, commercial organization and selected members of the corporate executive management team of GSK. This diversity could enhance the rigor of the process of vetting and committing to progressing potential drug candidates along the R&D process. Additionally, the having two oversight boards, one for discovery and the over for development along with diverse membership, increases stakeholder participation in the company.

The apparent losers seem to be the former functional departments that have been relegated to being quasi-outsiders as their organization become service units with diminished power and influence especially given the new system that continuously compare them with profit making external parties. As previously discoursed, this might have a negative impact on the morale of this group of scientists and their continued motivation to work within GSK. That said, a select few of such *support scientists* who happen to be become permanent members of the *core teams* in CEDDs or DPUs, by

reason of their specialist experience, may gain recognition and motivation from being part of the influential team.

### **The Cultural Lens**

This section deals with how the new organizational model impact norms, belief systems, assumptions and behaviors; and any associated potential risks to GSK.

Whilst GSK's bonus system of compensating achievement of critical milestones such as proof of concept could foster entrepreneurial culture as obtains in biotech and venture capital firms, there could be a negative side to this. Unhealthy rivalry could ensue amongst CEDDs, and DPUs which if not curtailed could negate the good intentions of increasing communication and knowledge flow; and the original objectives of breaking down any silo effects and increasing overall productivity. Bonus payments achieved to team achievement, as laudable and motivating this might be, could create an atmosphere where teams do no longer openly share critical knowledge and information lest the other team gets the credit and bonus or at least partake in the sharing of such compensation.

Another closely associated risk, no matter the size of its probability, is that of cutting corners in order to achieve a metric or milestone because significant amounts of bonus will be paid out. This might occur more in situations where the metric is not definitive enough to demonstrate clear outcomes. So this is a metric issue as it is a perverse compensation issue. For example, compensating the number of drug candidates as opposed to those that are successful at proof of concept could create a situation where is just a number game as quality and efficacy is compromised. In GSK's case, it's the achievement of proof of concept that triggers payment of bonus. Proof of concept is an outcome based metric. Although key assumptions and underlying factors of what constitute successful proof of concept will also need to be clearly defined for individual assets.

Finally, GSK's new organizational model offers the opportunity to redefine the meaning of leadership within R&D since what used to be acceptable norms, practices and leadership behaviors will not suffice in the new model as organizational dynamics and

strategic imperatives have changed. This makes it tougher to cohesively execute and anchor these changes in the evolving culture of the new R&D organization.

I will like to conclude my analysis on GSK by mentioning that positive forecasts and reports have been made on the new organizational model and its ability to increase productivity. One of such forecasts is the Datamonitor April 2010 report that says *“GSK’s CEDD-driven R&D pipeline is forecast to contribute significant revenue growth over the period 2008 – 2014...aggregate 2014 global sales from new launch products are forecast at \$9.6 billion.....advancement of the late stage R&D pipeline will allow GSK pull itself further away from the barren spell of new drug launches that afflicted the company shortly after its creation in 2000”*<sup>66</sup>. In another analysis, UBS Analyst Gbola Amusa was reported by January 2011 edition of Fortune Magazine as saying that *“GSK has the best, the brightest, the most booming pipeline in the industry over the next three years”*<sup>67</sup>. Whilst these forecasts validate the potential effectiveness of GSK’s new R&D organizational model, realization of actual results will be contingent on continued rigorous execution across all dimensions.

## **4.2 Sanofi-Aventis**

### **4.2.1 Company Background**

Formed in 2004 from the merger of two French pharmaceutical giants Sanofi-Synthelabo and Aventis, Sanofi-Aventis Group is a Paris based multinational pharmaceutical and healthcare company. Its diversified portfolio of businesses includes prescription medicines, consumer over-the-counter (OTC) healthcare products, vaccines, generics and animal health products. In 2008 Sanofi-Aventis was rated the fourth largest pharmaceutical company in the world by prescription drug sales. With annual revenues of Euro 30,384m in 2010 and approximately 103,000 employees operating across 103 countries, Sanofi-Aventis engages in R&D, manufacturing, sales and marketing of its products. In 2010, its pharmaceutical business accounted for over 87% of total group revenues (Euro 26,576m), whilst human vaccines accounted for 12.5% (Euro 3,808m). As of year-end 2009, Europe was the largest geographical market of Sanofi-Aventis, accounting for 41.1% of total revenues in that year. This is



followed by the US which represented 32.2% of 2009 sales. And other countries together accounted for 26.7% of 2009 revenues<sup>68</sup>.

Sanofi-Aventis is one of the world's leading players in the antithrombotic drug market through its blockbuster drugs Lovenox and Plavix which had sales of \$3.8 billion and \$3.6 billion respectively in 2008. Some of its other branded products include cancer drugs Taxotere and Eloxatin, and Lantus an insulin analogue for treating diabetes.

Exhibit 14 below shows a summary of Sanofi-Aventis' R&D pipeline. There are 55 new molecular entities in its pipeline. Of this, only 13 drug candidates are in late stage development (Phase III and registration) as of 9 February 2011<sup>69</sup>.

**Exhibit 14: Sanofi-Aventis R&D Pipeline as of February 9, 2011**

Therapeutic Areas	Phase I	Phase II	Phase III	Registration	Total
Oncology	6	3	3	0	12
Metabolic Disorder	1	2	1	0	4
Cardiovascular	0	1	0	0	1
Thrombosis	1	0	2	0	3
Central Nervous System	4	2	1	0	7
Internal Medicine	7	2	0	0	9
Ophthalmology	1	3	0	0	4
Vaccines	4	5	4	2	15
<b>Total</b>	<b>24</b>	<b>18</b>	<b>11</b>	<b>2</b>	<b>55</b>

Source: Sanofi-Aventis 2010 Annual Results

**42 Drug Candidates  
in Phases I & II**

**13 Drug Candidates in  
Late Stage Development**

It could be said that having only 13 drug candidates in late stage development might be a bit risky given the usually high attrition rates at these stages. If this is coupled with its several patent expiries of oncology products, the risks of declining revenues becomes severe.

Faced with the real challenges of R&D productivity and major patent expiries, Sanofi-Aventis' CEO, Chris Viehbacher who joined from GSK in 2008, has refocused Sanofi-Aventis' growth strategy on driving sales in emerging markets and acquiring diversified assets in the US<sup>70</sup>. This has led to its acquisition of Genzyme; a Cambridge Massachusetts based Biotech Company, in a largely hostile takeover bid which eventually led to both parties agreeing to a price of \$20.1 billion in February 2011<sup>71</sup>.

**Exhibit 15: Investors Reactions to Sanofi-Aventis Acquisition of Genzyme**



Exhibit 15 above shows investors favorable reactions to the Genzyme acquisition at different periods during the prolonged process. These positive reactions support the fact that Sanofi-Aventis stands to benefit from sales in the US and in the rare disease areas

where Genzyme has a strong presence. All of which will help mitigate the potential erosion of revenues and perhaps allow more time for Sanofi-Aventis to restructure its R&D organization.

#### **4.2.2 Methodology**

Three R&D executives within the global oncology product-line were interviewed in person at Sanofi-Aventis sites in Cambridge, Massachusetts. The interviews lasted over an hour each. These executives fulfilled the following roles

- Head of Early Development Oncology Portfolio
- Head of Development Operations and Strategic Planning
- Lead Medical Operations Oncology – Clinical Science Operations (CSO)

Notes were taken at all the meetings and one of the interviews was recorded on audio tape. Topics covered during the GSK interviews were used as standardized subjects for all interviews i.e. an understanding of old organizational model, key drivers and reasons for change, the new organizational model and the strategic objectives Sanofi-Aventis aims to achieve with its implementation.

As with all cases, (Ancona et al, 2005)'s Three Lenses Organizational Model was used to analyze the new organizational model.

#### **4.2.3 Sanofi- Aventis' Old R&D Organizational Model**

As recently as early 2011, Sanofi-Aventis operated a largely centralized R&D organization that was typical of most industry players. This was characterized by people working in silos, dichotomies between discovery and development, hierarchical organizations with four to five layers of management, scientists moving from one project to another in functionally driven matrix organizations. Additionally, there did not seem to be full accountability for projects and budgetary controls.

Some of the challenges this model posed included high bureaucracy, low R&D productivity and long project leadtimes. Describing the level of bureaucracy, one of the

executives said “*at every step of the way, you require several approvals before decisions are made*”.

These issues were probably accentuated by the differences in cultures and management approaches from the merged legacy companies. Whilst Sanofi had a vibrant culture with a disposition to quick decision making, Aventis, which had a German and French heritage, was a little measured and old school.

#### **4.2.4 The New Organizational Model**

Whilst a gradual move towards a decentralized therapeutic business unit model started in 2008/ 09, full implementation of this and other changes did not come until recently when Dr. Elias Zerhouni was appointed as Sanofi-Aventis’ President of Global Research and Development on 1 January 2011. Dr. Zerhouni was tapped from John Hopkins University where he was a leading scholar and is still a Professor of Radiology and Biomedical Engineering. He served earlier as the 15<sup>th</sup> Director of the US National Institutes of Health (NIH) for 6 years.

In its 2010 annual report published in February 2011, Chris Viehbacher, Sanofi-Aventis’ Chief Executive highlighted that the first phase in working towards a new R&D approach to boost innovation includes Dr. Zerhouni’s appointment and

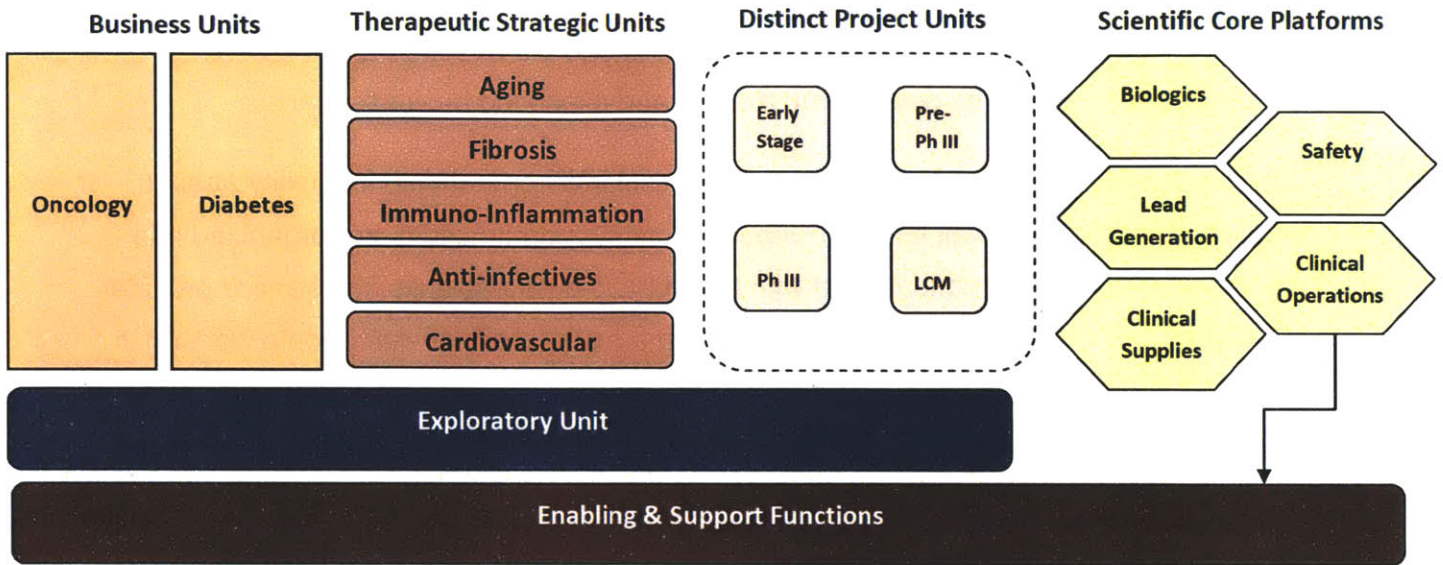
- Reducing the complexity of the R&D organization
- Deploying a new governance system
- Becoming more flexible and entrepreneurial and
- Becoming open to external sources of innovation and partnerships

In the same report, Dr. Zerhouni reported that one of the first set of achievements he has made is the streamlining of decision making within the new organization<sup>72</sup>.

Exhibit 16 below shows the relationships between various key elements of the decentralized and therapeutically aligned business unit organization.

**Exhibit 16: Sanofi-Aventis' New R&D Organizational Model**

Dr. Elias Zerhouni  
President Global R&D



**Key:** LCM = Lifecycle Management.  
Ph = Phase

Source: Adapted from Sanofi-Aventis 2010<sup>73</sup>

In this new model, business units are defined as the big therapeutic areas where Sanofi-Aventis has competitive market presence. Current business units include Oncology, Diabetes, Ophthalmology and Vaccines. Heads of business units are Senior Vice Presidents and global leaders of their respective therapeutic areas. These leaders have full accountability for discovery and development of new drugs, budgets and the people within their organizations.

Disease areas are further segmented into Therapeutic Strategic Unit (TSU). These are businesses that can be developed into growth engines and standalone business units in the future. TSUs include Aging, Fibrosis, Immuno-inflammation, Anti-infectives and Cardiovascular.

Projects that do not fall within the defined remit of business units and TSUs are undertaken within an organization known as Distinct Project Units (DPUs). DPUs execute development projects ranging from pre-phase III, phase III to post launch and product life-cycle management. The mission of all DPUs is not just to develop novel products but to expand the value of mature products by integrating several innovative solutions that ensures continued value to patients and other stakeholders. DPUs undertake this mission by developing, owning and executing business plans.

All clinical operations such as clinical data, clinical trials operations, feasibility studies, medical operations as well as other enabling and support functions are organized into centralized organization but aligned with therapeutic business units in a service provider – client relationship. This alignment happens in a matrix manner with people working in service provider organization such as Clinical Science Organization (CSO) having dual accountabilities; one to functional heads and the other to business units.

Underpinning the business units, TSUs and DPUs is the external facing Exploratory Unit that engages in collaborations with outside entities such as academia and other partnering organizations in order to harness and mobilize innovation in a patient centric manner.

On incentives and compensation, one of the executives interviewed said bonuses used to be based on 70% achievement of personal objectives and 30% on companywide performance. This is being changed to 50% personal objectives and 50% company performance under the new organizational model.

The implementation of this new model has not been without its challenges. Operating sites were rationalized and closed; and people have had to either leave the company through voluntary departures or transfer to other locations. For example, in order to co-locate global Oncology R&D which had half of its staff in France and the other half in the US; the staffers in France were asked to move to Cambridge, Massachusetts the new global headquarters for Oncology business unit.

As with GSK, Sanofi-Aventis' strategic objectives are to reduce dependencies on blockbuster drugs by focusing on several small to medium sized assets that can

generate revenues in shorter timeframes. And boost overall innovation and productivity across the R&D organization.

#### **4.2.5 The Three Lens Framework Applied to Sanofi-Aventis**

##### **The Strategic Design Lens**

The fact that business units and TSUs are therapeutically aligned will increase focus and strength in those disease areas as investments and expert resources are channeled into driving growth and market dominance. Additionally, the siloing effect that existed from the separation of research discovery and development will have been significantly reduced or eliminated through the integration both into operating business units.

The decentralized nature of the new model could facilitate communication, information flow and knowledge sharing; all of which could enhance the innovation process and productivity.

One downside in the new model has to do with potential tensions and conflicts that could arise from staffers in clinical science operations (CSO) working in a matrix manner with business units. Conflicts could ensue in matters relating to resource allocation and priorities. The net effect of this will be dependent on the strength or otherwise of the alignment of CSO with business units. If the alignment is strengthened with dedicated resources and shared goals and objectives, there might be less tension and conflict than would be the case in pure matrix organizations.

##### **The Political Lens**

Since heads of business units, TSUs and DPUs have full accountability for budgets and people; and can develop and execute business plans to achieve respective strategic objectives, this could lead to the development of an entrepreneurial culture and way of working. Additionally, with a more streamlined decision making process, the R&D organization becomes more flexible and responsive as leaders have the power and authority to execute faster with less bureaucracy.

As a French company, the relocation of global Oncology business unit out of France to Cambridge, Massachusetts could potentially lead to French stakeholders losing political power and influence in that business. One of the executives interviewed said this might not be received well as Sanofi-Aventis' breakthrough drugs such as Taxotere, a blockbuster cancer drug, was developed in France. This might impact morale and perhaps build up resistance to change if management does not find a way to motivate French key stakeholders and increase their participation in decision making in this or other business units in order to balance power and influence.

### **The Cultural Lens**

Increasing the weighting that company-wide performance has on bonus awards from 30% to 50% could increase collaboration across operating business units; even as stakeholders are incentivized for achieving interdependent goals and objectives.

One cultural challenge that Sanofi-Aventis might face is in embedding all these changes in its culture. As this new organizational model is only being implemented, leaders will have to ensure that actions are continuously aligned with key messages of the new model. One of the executives interviewed gave an example of where budgets are still being centrally controlled as opposed to full devolvement to operating unit; as some people struggle with moving to the new ways of working.

## **4.3 AstraZeneca**

### **4.3.1 Company Background**

Established in 1999 through the merger of Astra Pharmaceuticals, a Swedish firm and Zeneca Pharmaceuticals, a British company, AstraZeneca is today the second largest research based pharmaceutical in the UK and one of the top five in the world. With 2010 group annual revenues of \$33.3 billion, AstraZeneca has 61,000 employees operating in 100 countries. In 2010, the US market recorded total sales of \$13.727 billion representing 41.26% of total revenues. This makes the US AstraZeneca's largest market; although US sales declined by 7% in the same year. Western Europe achieved



\$9.168 billion or 27.56% of total revenues and Emerging Markets attained \$5.198 billion, accounting for 15.62% of total revenues in 2010<sup>74</sup>.

AstraZeneca is focused on competing and delivering patient value in the following disease areas: Cardiovascular / Gastrointestinal, Oncology, Respiratory and Inflammation, Neuroscience and Infections. Across these therapeutic areas, it had 10 blockbuster drugs with sales of over \$1 billion each in 2010. Some of this includes Crestor a cardiovascular medicine for treating cholesterol, Nexium a gastrointestinal drug for acid reflux and Seroquel IR neuroscience medicine for treating schizophrenia and bipolar disorder.

In 2010, AstraZeneca spent \$4.2 billion or 12.73% of total revenue on R&D. It has 15,700 staff employed in its R&D organization with 14 R&D centers in 8 countries. As of the end of year 2010, AstraZeneca had a total of 92 assets within its R&D pipeline. Of this, 34 drug candidates are in phase I, 32 are in phase II, there are 17 product-line extensions and only 9 assets are in late stage development (i.e. phase III).

With a less than encouraging pipeline and low overall productivity, David Brennan AstraZeneca Chief Executive said in his 2010 Annual Report address that “*The need to change is undiminished. Our R&D record over the past few years in disappointing and our results in 2010 were mixed*”<sup>75</sup>. This comment highlights the seriousness of AstraZeneca’s R&D productivity challenges. Key difficulties include recent product launch failures; notably Exanta a drug developed for the prevention of venous thromboembolic events (VTE) which was withdrawn from European markets in 2006 and never got FDA approval for US market. Other setbacks include Galida, a drug candidate for type II diabetes and NXY-059, a potential drug for stroke. Both of these were terminated in phase III in 2006. The inability to successfully launch new products has increased AstraZeneca dependency on its established blockbusters such as the Crestor franchise. This increases its exposure to revenue erosion when those blockbuster franchises lose patent exclusivity<sup>76</sup>.

With this in mind, Mr. David Brennan AstraZeneca's Chief Executive embarked upon a transformation of its R&D organization to resolve these issues and enhance productivity.

#### **4.3.2 Methodology**

Two R&D executives were interviewed. These executives who were based at the AstraZeneca R&D Center in Waltham, Massachusetts fulfilled the roles of

- Vice President Oncology Group and
- Vice President of Strategy infectious Disease

Both interviews were conducted over the phone and lasted an hour each. The interviews were recorded on audio-tape and written notes.

#### **4.3.3 AstraZeneca's Old R&D Organization**

AstraZeneca has run a traditional R&D organization, one typical of the old industry model. Research and development were independent organizations with centralized resources organized by functional departments. The impact of the disconnection between discovery and development was described by one of the executives interviewed "*A lot of drug candidates were PUSHED out of research that had no chance of being successfully developed and brought to market*".

Additional cultural and organizational issues arising from the post merger integration of the R&D infrastructure and capabilities of the legacy companies added to the level of bureaucracy and siloing effect.

Other reasons why the old organizational model was unsustainable included

- R&D activities were difficult to coordinate as a result of people working in silos
- Lack of communication between discovery and development as you have hand-offs once there is a potential drug candidate
- As mentioned before, productivity was low as was return on investment

#### **4.3.4 New R&D Organizational Model**

AstraZeneca's new R&D model is based on decentralizing key organizational components, empowering these operating units and integrating the entire model in a one firm single strategic umbrella organizational approach i.e. one integrated organization containing several fully empowered operating units.

In going about this reorganization, AstraZeneca as with other companies such as GSK, reduced their disease area foot-print by exiting several therapeutic areas they deemed either commercially unprofitable or did not have the scientific capabilities to deliver real value to patients. These changes which started with the appointment of Dr Martin Mackay as President Global R&D in the summer of 2010 culminated in the creation of an organizational operating model that comprises 9 Innovative Medicine Units (iMeds).

Eight of the iMeds are aligned with molecule types and operating therapeutic areas. For Small Molecules there are Oncology, Infection, Respiratory and Inflammation. For Small Molecule Biologics, disease areas covered are Cardiovascular and Gastrointestinal, and neuroscience. And for biologics, iMeds represented are Oncology, Infection and Respiratory and Inflammation. These iMeds take assets from discovery through to proof of concept in phase IIb development.

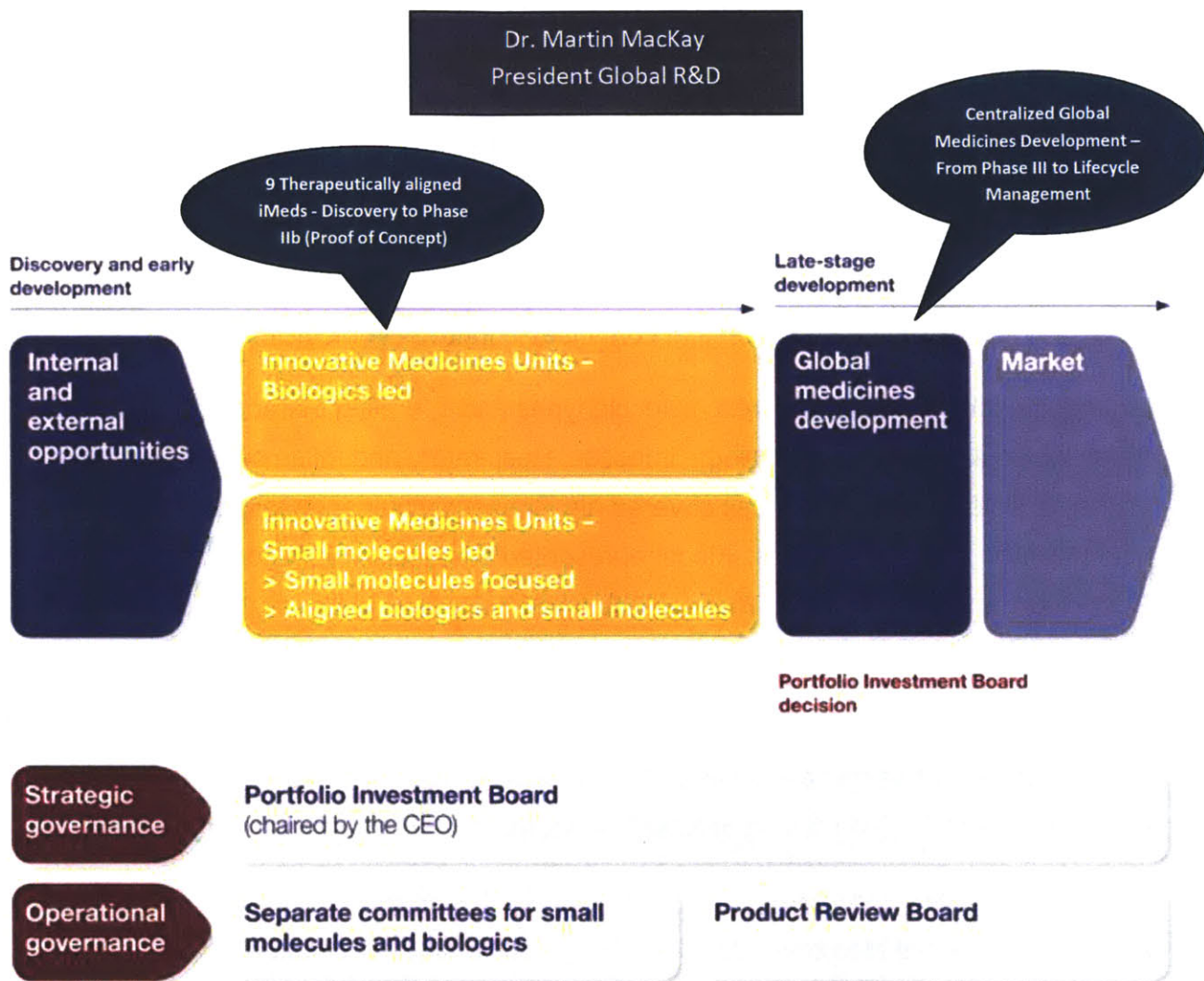
The ninth iMed is known as the New Opportunities iMed. This focuses on indentifying external opportunities that are either complementary to current research disease areas or are outside of it. The mission of New Opportunities iMed is to acquire commercial viable external assets in late stage development.

A centralized Global Medicines Development (GMD) organization takes assets that are successful at proof of concept to phase III clinical trials, product approval and launch through to lifecycle management.

The entire model is integrated through a number of both strategic and operating oversight boards. The Portfolio Investment Board (PIB) which is chaired by Mr. David Brennan Chief Executive approves funding of projects and asset acquisitions. Funding

system is similar to that of venture capital in that it is short term and based on milestone achievements<sup>77</sup>.

**Exhibit 17: AstraZeneca's New R&D Operating Model**



Source: Adapted from AstraZeneca R&D, 2010<sup>78</sup>.

Other key characteristics of the operating model include

- Unit leaders have to persuade oversight boards for funding and resources through developing and presenting business cases that demonstrate commercial viability and clinical value

- Marketing and commercial inputs are gotten very early during Early Discovery Stages with representatives from commercial organization embedded in project teams.
- Project leaders lead multi-disciplinary teams (MDT) but do not have direct reports. These leaders are expected to lead by influencing and persuading colleagues and stakeholders rather by giving instructions.

On metrics and performance measurement, one of the executives interviewed said *“Qualitative metrics should be emphasized more as its better to have an asset that can generate \$300m sales with high probability of successful launch than one with a potential to generate \$1 billion but only has a 10% chance of making it to the market”*

AstraZeneca’s strategy objectives for its new R&D organization are based on substantially increasing internal R&D productivity, increasing externalization of projects and sourcing 40% of pipeline from outside the company by 2014, and driving growth through personalized medicine and unmet medical needs.

#### **4.3.5 The Three Lens Framework Applied AstraZeneca**

##### **The Strategic Design Lens**

The alignment of Innovative Medicine Units with therapeutic areas and the fact that these units undertake discovery research and early stage development up to proof of concept, bridges the disconnection between research and development. Also, information and knowledge flow will be enhanced and bureaucracy reduced in the empowered and decentralized iMeds.

Whilst the no direct reports model for project leaders will increase communication and analytical rigor in decision making, it could have the unintended consequence of slowing down decision making process since the process of influencing and persuasion could take time. Additionally, conflict and tension might arise from issues appertaining resource allocation and priorities between projects and functional departments. The effects of this might be pronounced where certain staffers are not dedicated to a particular project. All these factors might place serious pressure on the project leader

who, of necessity, would require have superior leadership and influencing skills. These leaders would also be people that are respected by peers.

### **The Political Lens**

In addition to the power and authority dynamics of project leaders discussed above, the new operating model gives voice, power and authority to therapeutic leaders who are also Innovative Medicines Units Leaders. The balance of power, authority and influence favor therapeutic heads over functional heads such as head of Medicinal Chemistry, Pharmaceutical Sciences, Pharmacokinetics, Biostatistics etc. All of these functions now operate in support roles. As discussed in earlier sections, whilst this arrangement strengthens the capabilities of therapeutic areas, the operating support functions would need to increase participation in company R&D affairs in order to maintain motivation.

### **The Cultural Lens**

The adoption of venture capital based funding model where further project funding is attached to achievement of defined milestone could foster the culture of performance where leaders not only strive to achieve milestones, but also align and focus resources and employees on defined mission and objectives. On the negative side, if milestones are not clearly defined along with underlying assumptions, then there is a risk that people might be motivated to achieve a milestone at all costs. This could involve cutting corners or compromising on other factors in order to achieve a milestone to keep a project alive.

## **4.4 Pfizer**

### **4.4.1 Company Background**

Pfizer Incorporated is the world's largest research based biopharmaceutical company. With 2010 group annual revenues of \$67.8 billion, Pfizer's portfolio of diversified businesses include human and animal biologics, small molecule medicines, vaccines, nutritional and consumer products. Headquartered in New York, Pfizer employs 116,500 people and operates in over 150 countries<sup>79</sup>.

Pfizer generates its revenues from three main divisions. These are biopharmaceuticals, diversified business and other corporate business segment. In 2009, sales from biopharmaceuticals amounted to \$45.448 billion representing 90.9% of total group revenues; the diversified business segment recorded \$4.189 billion or 8.38% of total sales and other corporate businesses achieved \$372m equivalent to 0.74% of group sales<sup>80</sup>.

The US is Pfizer's largest market with sales of \$21.749 billion (43.50% of total sales) in 2009. This is followed by Europe with \$14.561 billion (29% of total sales). Revenues from Japan / Asia reached \$7.988 billion (16% of group sales); whilst Canada, Latin America, Africa and Middle East achieved \$5.711 billion (11.42% of group sales)<sup>81</sup>.

With 15 brands that exceeded \$1 billion each in sales in 2010, Pfizer operates in the following therapeutic areas

- Neuroscience
- Cardiovascular
- Metabolic and Endocrine disease
- Inflammatory and Immunology and
- Vaccines

Some of its best known branded biopharmaceutical products include Lipitor, the mega-blockbuster cholesterol lowering drug; Viagra, used for treating erectile dysfunction; Celebrex, anti-inflammatory drug; and Norvasc an anti-hypertensive drug<sup>82</sup>.

In 2010 Pfizer spent \$9.413 billion in R&D expenses representing 13.88% of total revenues in the same year. This figure is almost 20% less than the \$7.845 billion R&D spending in 2009. This cut in R&D spending is part of Pfizer's strategy to exit research in certain therapeutic areas such as allergy and respiratory disease; whilst at the same time embarking on major rationalization of R&D infrastructure and sites. The hardest hit by this restructuring are perhaps the R&D Sandwich site in Kent, United Kingdom where more than 2,400 jobs will be lost as the site closes in 18 to 24 months; and the R&D site

in Groton, Connecticut where about 1,100 jobs are earmarked for layoffs. All these are in line with Pfizer's goal of achieving \$4 billion to \$5 billion multi-year cost reductions by 2012 in an attempt perhaps to shore up profitability given the impending patent expiry of Lipitor in 2011<sup>83, 84</sup>.

As of 28 February 2011, Pfizer had 118 assets in its R&D pipeline. Of this 49 were in phase I, 35 in phase II, 25 in phase III and 9 were undergoing registration process with regulatory bodies<sup>85</sup>.

#### **4.4.2 Pfizer's Unique R&D Challenges**

From 1998 through to 2004, Pfizer failed to launch any new blockbuster drugs from its internal R&D pipeline. The effect of this drought was however masked by its \$110 billion megamerger with Warner Lambert in 2000 and its \$60 billion acquisition of Pharmacia in 2003. Lipitor, its best selling drug came from the Warner Lambert transaction; and Celebrex another blockbuster drug was gotten through the Pharmacia acquisition. The low R&D productivity therefore increased Pfizer's heavy dependence on Lipitor which recorded \$12.4 billion in sales in 2008 representing over 28% of its global prescription drugs revenue that year<sup>86,87,88</sup>.

In order to reduce the significant impact of the impending patent expiry of Lipitor, Pfizer embarked yet again on another mega acquisition. This time it was a \$68 billion acquisition of Wyeth in 2009. Whilst investors and the stock market responded favorably to this acquisition as shown in Exhibit 18 below, the question remains whether real and sustainable value will be created from these mega acquisitions on the longer term.

A 2009 Datamonitor report argues that whilst this acquisition will bring Pfizer the benefits of economies of scale, it will not deliver the sustainable growth in sales that Pfizer requires<sup>89</sup>. If this holds true, Pfizer will need to refocus on building its growth through ramping up its internal R&D productivity and pipeline rather relying on mega acquisitions.



**Exhibit 18: Stock Market Reaction to the 2009 Acquisition of Wyeth by Pfizer**



**4.4.3 Methodology**

Four senior R&D executives were interviewed. These executives held the roles of

- Senior Vice President, Biotherapeutic Development and Strategy Operations
- Global Head of Centers for Therapeutic Innovations
- Head of Portfolio Management and Analytics
- Senior Director, Biotherapeutic Innovation

These interviews were conducted over the phone. Written notes and audio tape device were used to record the interviews.

#### **4.4.4 Pfizer's Old R&D Organizational Model**

Pfizer's old R&D organizational model was characterized by a separation of discovery research from development along with the associated hand-off approach to progressing projects through the value chain, highly centralized departments operating in silos and bureaucratic decision making processes. All are hallmarks of the pharmaceutical industry's traditional R&D operating model.

But perhaps more important are the manifestations of the impact of Pfizer's unique challenges discussed above. The impact of these challenges can not only be seen in its operating model but also in the culture of its R&D organization. One of the executives interviewed said *"Pfizer has an extended problem in that most of its blockbuster drugs were largely derived from acquired companies. This has negatively impacted internal R&D by slowing down the pace of change; which in turn has resulted in poor productivity"*

Another executive summarized Pfizer's R&D culture as *"One that operated with a cost center mentality rather than a profit center and entrepreneurial culture"*. Yet another senior executive, who joined only a few years ago, observed that there is a culture of *"leave us alone, we know what we are doing"* even in the face of a less than stellar performance in R&D.

Pfizer has therefore been able to achieve the status of the largest biopharmaceutical firm in the world by virtue of acquiring companies rather than organic growth powered by internal innovation from R&D engine. As such, the traditional operating model it ran coupled with a culture that was not receptive to change led to a huge, lumbering bureaucracy with about 20,000 employees in R&D and low pipeline productivity; a situation that was not sustainable even for a \$67.8 billion company with 15 blockbuster drugs in 2010.

This is what has instigated a journey of change; one that is evolving and has had false starts.

#### **4.4.5 Pfizer's New R&D Organizational Model**

Before delving into a discussion of Pfizer's latest attempts at the organizational redesign of its R&D, it is pertinent to highlight several false starts that plagued its initial attempts at restructuring. These underscore the importance of the cultural dimension at play in Pfizer.

In the fall of 2007, Pfizer established research units known as Biotherapeutics and Bioinnovation Centers (BBC) in the Bay area of San Francisco California. These independently operated units were charged with the strategic objectives of researching biotherapeutic science and translating this into novel medicines. This was Pfizer's attempt at creating biotech-like entrepreneurial standalone units that would help fuel its much needed productivity and innovation especially in the high growth space of large molecular biologics. Commenting on the establishment of these units in November 2007, the then Chief Executive Jeffrey Kindler said *"We are also today launching a new Biotherapeutic and Bioinnovation center with a unique structure to discover, license and acquire more new product candidates that we can put into development.....we are leveraging Pfizer's excellence in drug R&D by complementing it with a distinct, California based enterprise led by world-class scientists charged with discovering and bringing in new compounds"*<sup>90</sup>.

Corey Goodman, leading scientist and successful entrepreneur was appointed as President of the Biotherapeutic and Bioinnovation Center in South San Francisco. After only 19 months in the job, Goodman resigned from Pfizer under circumstances that remain unclear. The departure came at about the same time Pfizer acquired Wyeth in 2009. It was reported that Pfizer no longer needed the Bioinnovation Center as it now has access to the big biotech assets that Wyeth possesses. Mr. Goodman was reported paid \$1.7m in severance compensation and sign a non-disclosure agreement<sup>91</sup>.

In the fall of 2010, Kindler abruptly retired from Pfizer as Chairman and Chief Executive after only 4.5 years at the helm citing a need to "recharge" (i.e. spend more time with his

family). Analysts said the departure was not unconnected with repeated failures to launch new blockbuster drugs and an overreliance on acquisitions and cost cutting as a strategy to deliver value<sup>92</sup>.

In November 2010, Pfizer announced it was establishing new Global Centers for Therapeutic Innovation<sup>93</sup>. These centers operate by forming close research alliances with top academic research institutions. In this model, Pfizer scientists and those of the partnering academic institutions are colocated on the site of the academic institution. Whilst this model will be analyzed later, suffice to mention that it is not de-similar in objective and form to the Biotherapeutic and Bioinnovation Center that was stopped in 2009. This back and forth suggest an uncoordinated approach to strategy and decision making as well as a cultural way of working influenced by the various political constituents from the acquired companies.

Pfizer's new R&D organizational model has evolved from when it was initially implemented in late 2008. These first attempts at change were aimed at bridging the divide between discovery and development; and integrate late stage development within three newly created commercial business units; namely:

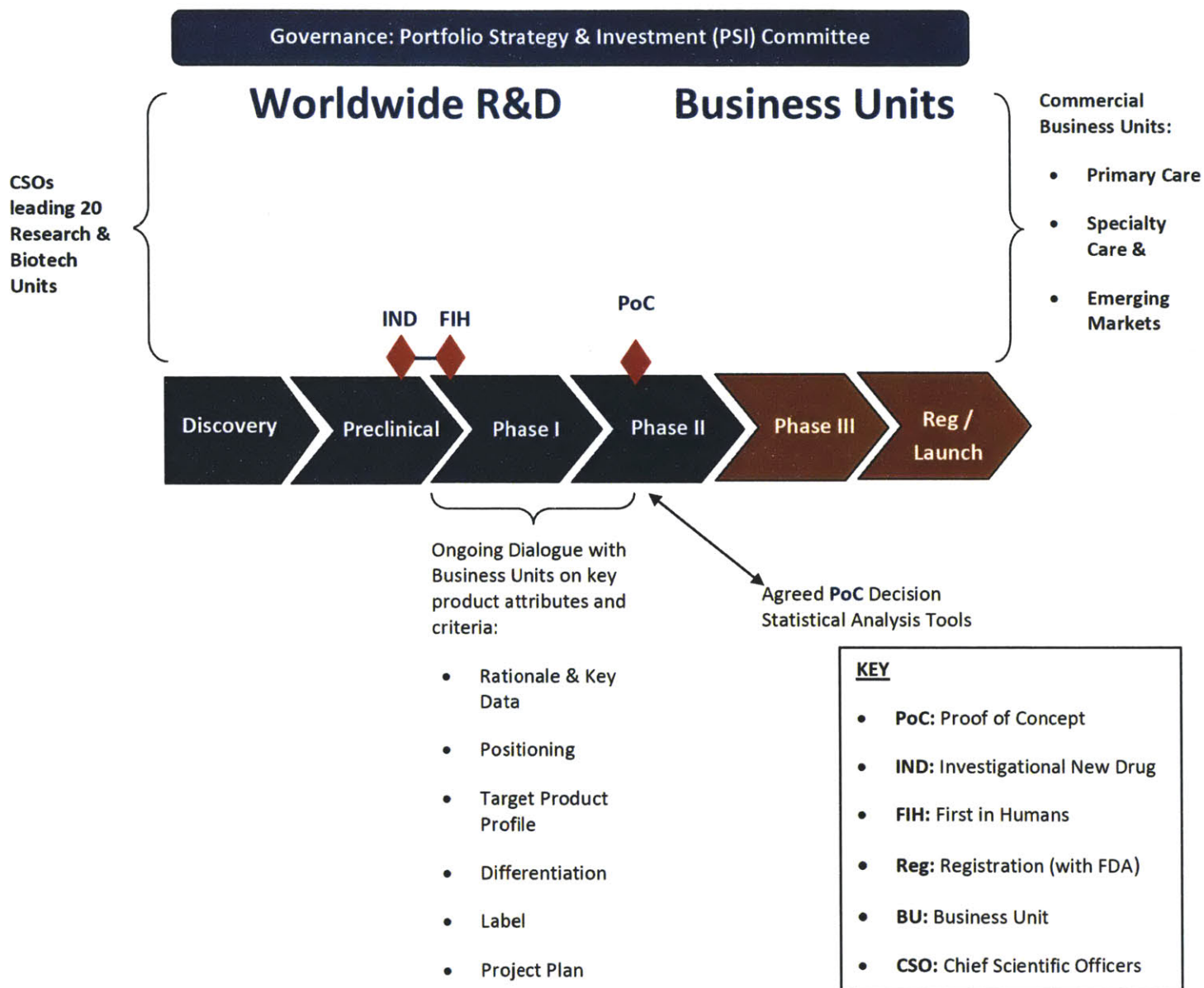
- Primary Care
- Specialty Care and
- Emerging Markets

As shown below in Exhibit 19 below, clinical development activities from proof of concept (PoC) through to product launch are embedded within each commercial business units. As business units are large commercial organizations, their leaders who run multi-billion dollar profit and loss (P&L) serve on the Corporate Executive Team and report to Pfizer Chief Executive.

Pfizer created the role of Chief Scientific Officers (CSOs) who lead 20 research and biotechnology units. CSOs have the responsibilities for identifying and progressing potential drug candidates from discovery research through to proof of concept in phase

Ila development. Embedded into this model are the Global Centers for Therapeutic Innovation described above which is lead by the equivalent of a CSO.

**Exhibit 19: Pfizer's New R&D Organizational Model**



**Note:** Exceptions are Vaccines unit which spans Discovery through Registration and NCE Oncology drugs, which transition to the BU at FIH

Source: Adapted from Pfizer, September 2010<sup>94</sup>.

The CSOs report to the President of Worldwide R&D whilst the senior leaders in charge of late stage development within each commercial business units report directly to business unit leaders.

On the progress of the new Global Centers for Therapeutic Innovation, its head who was one of the senior executives interviewed, said “*Whilst this is very new and we are experimenting; we have established partnerships with University of California and Sloan Kettering Cancer Center in New York*”. No externalization or performance targets have yet been set.

On governance, oversight is provided by a Portfolio and Strategic Investment Committee which is responsible for major investment funding and R&D priorities. This committee is co-chaired by the President of Worldwide R&D<sup>95</sup>.

The strategic objectives for this new organizational model as articulated by Dr. Mikael Dolsten, President of Worldwide R&D include

- Improving decision making process
- Improving clinical development of drug candidates
- Delivering smarter and more authentic integration of science and business
- Developing world-class scientific talent and
- Driving a culture of science and innovation

All of these Pfizer hopes will drive R&D productivity in its internal pipeline.

#### **4.4.6 The Three Lens Framework Applied to Pfizer**

##### **The Strategic Design Lens**

Embedding late stage development activities into individual commercial business units with the aim to integrate science and business will have the advantage of bringing the “voice of the customer” and patient needs closer to the scientific development process. This in turn could to lead to a more market led approach to developing medicine as well

as a customer centric culture that could deliver medicines with more value to patients. Rather than “me too” drugs being *pushed* into the market, this model could facilitate a *pulling* of specific customer requirements which will in turn help deliver value added drugs. So there could a shift from *push to pull* across the drug development value chain. Another advantage could be that as commercial professionals are fully integrated into the development value chain; faster assessment of the commercial viability of projects will result. Time and money could therefore be saved as unviable projects could be terminated earlier before further costs are incurred.

A disadvantage of this business unit model however could be the duplication of development infrastructure and resources across the various business units as well as potential dilution of the benefits associated with economies of scale. This net effect of this would probably depend on how individual business units interact operationally. The negative effects of duplication and waste could be minimized if management seeks out opportunities to optimize and leverage common platforms in the form of cross-cutting development projects as well as creation and utilization of shared services.

The creation of 20 research and biotechnology units to undertake discovery and development up to proof of concept could enhance innovation as units are liberated from the lethargy of highly centralized decision making process that slows down responsiveness. Organizationally, the effectiveness and perhaps success of these units might depend partly on the Chief Scientific Officers. If these CSOs are have full budgetary and line responsibilities for the people in their units, this could facilitate an entrepreneurial culture that will drive performance and innovation across the units. One of the executives interviewed specifically commented on this. This executive will like to see CSOs operate as de-facto Chief Executive Officers of their individual units just like the model at GSK. The advantages here will be based the freedom, ability and accountability to develop and execute business plans and respond swiftly to changing circumstances whilst taking measured risks without having to wait for approval from several bosses who are removed from day to day operations.

On the partnering with top research academic institutions, this could spark a wave of innovative discoveries as Pfizer taps the very best minds in these institutions to come

up with novel medicines. This Pfizer – academia decentralized model offers access to external innovation capabilities as well as the opportunity for Pfizer research personnel to learn and share knowledge and information critical for enhancing innovation process. This is accentuated by the fact that Pfizer scientists are co-located with academic scientists on the site of the partnering academic institutions.

As compelling the advantages of this partnership model is, its execution will not be without challenges. These challenges are those associated with the operation of any partnership. The cultural differences could be significant depending how it is handled. This will be discussed in the cultural lens section. There are also the issues associated with sharing intellectual property rights (IPR). For this to work, these issues will have to be carefully navigated and discussed upfront whilst channels of open communication and issue escalation are mapped out and agreed.

### **The Political Lens**

The balance of power and influence seem to be in favor of the business unit leaders. This is because they do not only run their multi-billion dollar commercial organization; they also have the important late stage development activities under their control. These leaders directly influence the type of drug that gets to the marketplace. Also, the fact that the senior vice presidents in charge of late stage developments in individual business units report directly to the business unit leaders in their respective business units and not to the President of Worldwide R&D.

The advantage of this arrangement politically is that it could facilitate clarity of priorities and purposes as leaders of late stage development get their priorities and objectives from their respective business unit leaders. This could avoid ambiguities and conflicts associated with having two bosses. This however seems to make the President of Worldwide R&D less powerful as this post holder is only responsible for CSOs as direct reports. This apparent diminished power seems to have been compensated for by the fact that the President of Worldwide R&D co-chairs the governance and oversight committee that makes strategic decisions covering the entire research and development value chain.



## **The Cultural Lens**

The fact that Pfizer's growth has been largely driven by acquisitions as opposed to growth from products produced within its own pipeline could have created an R&D organizational culture that is not used to creating big wins internally. This analysis is validated by the comments of a senior executive who joined Pfizer from the acquired Wyeth. This executive highlighted that none of the current CSOs have personally led successful product launches. Another executive suggested that perhaps Pfizer should totally outsource its discovery research activities and only undertake development since it has not seen much success in discovery in recent years. These comments suggest that Pfizer will need to revitalize its R&D culture by focusing efforts on driving internal R&D breakthroughs in innovations and productivity.

Since it takes time and effort to successfully integrate an acquisition operationally, and perhaps even longer to form a homogenous culture after an acquisition, it follows that Pfizer may not have had the time to properly integrate these entities into a One Firm culture. The consequences could be that different constituents will continue with its individual culture until full integration is achieved. Until this time however, there is a risk that the company could be pulled in different directions even with a single set of strategic vision and purpose in place. The execution of such a set of imperatives could be vulnerable to the existence and pull of different cultures. The net effect could be dependent on the strength, quality and effectiveness of the leadership in place.

On the Pfizer – academia partnership, the cultural challenges are perhaps rooted in the differences between a commercial enterprise that is motivated by profit maximization and one that is motivated by research and opportunity to publish in scholarly journals. Academicians want to change the world through novel discovery and publish papers like I mentioned earlier; whilst a commercial enterprise wants to get its products out into the marketplace fast in order to quickly grow its revenues from selling the groundbreaking product. As mentioned earlier these are not necessarily insurmountable challenges especially since both parties need each other. Pfizer has the capital to fund projects that academic institutions have the intellectual capabilities to undertake. Again, it would take good leadership on both sides for the mutual benefits to be maximized.

In conclusion, Pfizer's strategy of continuously acquiring companies and then slashing costs by consolidating operations and layoffs is not sustainable. Pfizer will need to refocus on organic growth fuelled by R&D productivity and innovation.

## **4.5 Novartis AG**

### **4.5.1 Company Background**

Formed in 1996 from the merger of Sandoz and Ciba-Geigy, two Swiss companies, Novartis is one of the largest biopharmaceutical companies in the world. With 2010 annual net sales of \$50.6 billion, a 14% increase on 2009, Novartis has a diversified portfolio of businesses comprising pharmaceuticals, vaccines and diagnostics, Sandoz a generics business, consumer health, and Alcon, a recently acquired eye care business.

In 2010, the pharmaceuticals division recorded \$30.6 billion in net sales a 6% increase on 2009 figures. In the same year, consumer health delivered \$6.2 billion in net sales a 6% increase on previous year; and the vaccines and diagnostics business achieved \$2.9 billion net sales representing a 25% increase to 2009 performance. The generics division Sandoz made \$8.5 billion in net sales in 2010, a 15% increase on previous year figures. Novartis realized \$2.4 billion from its consolidation of the newly acquired eye care business (Alcon) in 2010<sup>96</sup>.

With respect to geographical markets, Europe accounted for the largest sales in 2009 with 41.5% of total sales. This is followed by the Americas which accounted for 40.3%; and by Asia, Africa and Australasia which together accounted for 18.5% in the same year<sup>97</sup>.

Novartis' products range from branded prescriptions medicines, animal health products, generic prescription drugs to vaccines, ophthalmic and over the counter pharmaceuticals. Some of these products include Diovan its anti-hypertensive blockbuster drug, Glivec an anti-cancer medicine, also a blockbuster selling drug; and the CIBA Vision range of contact lens and lens care products.

In 2010, Novartis spent 16% of its group net sales on R&D. This figure is equivalent to 20% of all pharmaceutical sales in the same year. With 147 assets in clinical development of which 63 are new molecular entities (NMEs), Novartis has arguably the strongest R&D pipeline and productivity in the industry. During 2010, drugs launched since 2007 accounted for 21% (or \$6.6 billion) of total sales in the pharmaceutical division<sup>98</sup>.

Revenue forecasts from Novartis' R&D pipeline and launch portfolio is expected to be growth by \$6.2 billion up till 2014. This rather impressive growth driven by internal R&D productivity as well as revenues from current products is expected to over-compensate for any loss of revenues that might arise from patent expiries<sup>99</sup>.

#### **4.5.2 Methodology**

The rationale for studying Novartis R&D is to find out if there are any unique characteristics within its organizational model that seems to set it apart from the other large pharmaceutical companies explained above. Arguably, Novartis has the most productive R&D pipeline of all the top five global research-based pharmaceutical companies studied.

As such, rather than repeat organizational traits found to be common amongst all five companies, I have decided to focus on the unique characteristics of Novartis and analyze why these might be attributable to its current robust R&D performance.

Four senior R&D executives were interviewed. Three of these were conducted in person at the Cambridge Massachusetts headquarters of its Institute for Biomedical Research, its R&D organization. One of the interviews was done over the phone. The phone interview was recorded on audio tape device whilst the other three were recorded by written notes.

The executives interviewed held the following positions within Novartis Institute for Biomedical Research (NIBR):

- Global Head of NIBR Biologics Center
- Global Head of Developmental Molecular Pathways
- Senior Vice President & Global Head of Translational Sciences
- Global Head of Strategic Planning & Operations – Translational Sciences

#### 4.5.3 Novartis' R&D Organizational Model

Novartis' R&D organization is characterized by its de-centralized Institute for Biomedical Research, where it conducts all its discovery research and part of its development activities; and its pharmaceutical development units that are located globally across several sites.

NIBR was formed in 2002 with the aim of leveraging Novartis' various strengths across its discovery network to focus on high unmet medical needs by translating insights into the fundamental mechanisms and underlying biology of diseases into novel value added medicines. The organizational characteristics of NIBR include the following

- Matrix based organization at the project execution level with the usual core team members versus deployed members
- Co-location of project members
- Centralized governance and oversight as with all other firms studied
- Full integration and shared knowledge across all units with the ability to tap in to global repository of knowledge and expertise
- Unique culture
  - Self managed teams that are fully empowered to set their own goals and drive performance. One senior executive said "*he manages by trust....and create the atmosphere and culture needed for organized chaos to translate into serendipitous innovations...*"

- Flat organizational structure. One of the senior executives interviewed hypothesized that productivity could be inversely proportional to the gap between executive management and middle level managers. Whilst I do not have any data to back this up, it is the ethos and culture of devolved accountability and decision making at Novartis that is distinctive.
- On incentives and compensation, whilst these are tied to key performance indicators, scientists could be compensated at the same level as their bosses. One of the senior executives interviewed who is accountable for about 1,400 globally said he would rather compensate a scientist at the same level as himself rather than just promote scientists into management roles. This is a unique finding that seems fundamentally different from the norm.
- On metrics, a senior executive said whilst they do have metrics to drive performance, they do not set objectives where there are no guarantees that one can deliver. This refers to the very front end of the innovation funnel in discovery.

Discussion and analysis using the Three Lens framework will focus more on the uniqueness of this organizational model since common issues have been captured in the four earlier cases.

#### **4.5.4 The Three Lens Framework as It Applies to Novartis**

##### **The Strategic Design and Political Lenses**

The de-centralized organizational model of NIBR facilitates quick decision making and responsiveness as with other models studied. But Novartis' model is not just de-centralized; it is at the same time integrated. Disparate units are united by a set of common purpose and strategic objectives. It also claims to have a common platform for sharing knowledge and resources and one leader; Global Head of NIBR who serves on the corporate executive management team. This decentralized yet integrated model apparently fosters information and knowledge sharing across the organization at the

macro level as opposed to just within the site or project team level. As such, this model seems to lessen the impact of unwanted rivalry and internal competition.

The flat organizational structure and operating model will facilitate devolvement of accountability and increase participation in company activities. Particularly in the context of R&D, the most junior laboratory scientist could have the opportunity to contribute according thus maximizing the collective resources and talent within teams. The cumulative effective of highly motivated team members could go a long way in enhancing productivity as people take on stretch assignments and responsibility earlier in their careers than is the case in hierarchical and highly bureaucratic organizations.

On the negative side, the fact that there are matrix arrangements at project level with dual accountability could lead to tension and conflict. This, as discussed in earlier cases, could arise from differences in project priorities and resource allocation. The extent to which this affects performance is dependent on the leadership skills of project leaders as who must manage stakeholders through influence and persuasion.

Looking through the political lens, there does not seem to be an overtly conspicuous swing in power and influence in favor of a particular group to the detriment of others at Novartis. The model however accentuates the importance and value of research scientists who work on the laboratory floor. The bottom-up approach to management seems to reinforce this.

### **The Cultural Lens**

The fact that there are self-managing teams and senior research executives manage by trust will strengthen team member participation and accountability across the organization. Other advantages of self-managed teams include increased communication and knowledge flow, peer reviews that could drive performance and faster decision making all of which could enhance innovation process. This is supported by (Muthusamy, Wheeler and Simmons, 2005) who propose that the enhanced autonomy that comes from self-managed teams intensifies communication and commitment to both teams and the company at large behaviors which translate in to creativity and innovation. As beneficial self managing teams might be, there has to be

balance in the level of autonomy in order to ensure continuous direct alignment of team goals and objectives with those of the company<sup>100</sup>.

On incentives and compensation, the fact that scientists can receive substantial compensation for just being scientists without the need to assume a managerial role in order to get higher pay could make great scientists focus on doing what they know best. This in turn could lead to increased specialization and level of expertise as well as increased individual productivity. Additionally, since bonuses equally reflect company-wide performance, unnecessary inter-team rivalries that could stymie knowledge sharing are discouraged.

Finally on the cultural perspective, whilst it is not productive to force the delivery of a set of metrics if there are no guarantees, the absence of metrics could lead to the unintended consequences such as lack of alignment of resources and effort with the strategic imperatives. The negative issues associated with metrics, such as cutting corners to achieve them, could be avoided if the correct metrics are defined and used from the outset.

In conclusion, it seems apparent that Novartis has succeeded in building a culture of trust, team empowerment and strong leadership; all of which has supported and enhanced the effectiveness of the firm.

## **5 Recommendations and Conclusions**

In order to successfully use organizational design to enhance R&D productivity in the pharmaceutical industry, a comprehensive approach will be needed. As such, my recommendations in this chapter cover organizational structure, operating systems with particular reference to performance metrics, and incentives. These critical success factors need to be driven and coordinated by effective leadership in order to create a culture that helps deliver sustainable R&D performance and continuous improvement.

### **Organizational Structure**

Pharmaceutical R&D is a complex enterprise that brings together different functional expertise and professionals from both inside the company and external partners. These professionals have to be able to communicate freely and share information and knowledge in a manner devoid of constraints whilst being responsive to changes based on new information. I submit that the traditional departmental silo-based organizational structure is no longer suitable. This has to be replaced by an organizational form that allows for the interconnectedness of employees and stakeholders to facilitate responsiveness and quick decision making. Reducing hierarchy and bureaucracy will make R&D employees more accountable for their work will increase their commitment and motivation. I therefore recommend a form of de-centralized organization.

The de-centralized organization I recommend does not cover all activities in the R&D value chain. But, since one of the major problems with the traditional R&D model is that it creates a dichotomy between discovery and development. A de-centralized model, such as GSK's, provides a needed structural link between discovery and development up to proof of concept. The late stage development part of the value chain can remain centralized in order to harness the benefits of economies of scale.

Discovery research being at the front end of the innovation funnel lends itself to organized chaos whilst downstream activities in late stage development are process driven. Decentralization of discovery research makes sense in order to spark creativity, innovation and entrepreneurship whilst at the same time needed continuity and



necessary organizational linkage with development phases. In the companies studied in this thesis structural linkage operates up to proof of concept.

Whilst this model of de-centralization is good, and was found in different fashions in all companies studied, de-centralization alone will not be enough. There has to be a way to link all disparate units in the de-centralized organization. If this is not done, there is the risk that best practice, high valued knowledge and specialized capabilities might not be readily shared across all R&D units. And benefits for the company as a whole will be lost. Knowledge sharing is essential for pharmaceutical R&D organizations where the latest knowledge and best practice are critical to success or failure. To maximize the opportunity for the entire company to benefit from such knowledge sharing, I recommend an organizational form that integrates all de-centralized R&D units. This integration should be both tangible in terms of structure and common platforms as well as intangible in terms of common purpose, vision and culture.

In order for these de-centralized units to be effective, I recommend those who direct them be given the power and authority as de-facto chief executives to be fully accountable for all cross-functional staff, resources and budgets necessary to develop and execute business plans. This will foster an entrepreneurial culture and develop capabilities that will drive performance, productivity and innovation.

Another aspect of organizational structure that requires consideration is the one that drive projects. The consideration is between matrix relationships and fully employed resources in project teams. In a matrix relationship, project leaders either do not have direct reports at all or they only have partial reporting line of authority. In the companies studied, the argument in favor of matrix is that it is more beneficial for project leaders to operate through persuasion and influence. That way, better decisions will be made as stakeholders are engaged in decision making process. Whilst this can be good, I believe such benefits are over-shadowed by the disadvantages of ambiguity and lack of clear direction, especially in setting priorities and securing needed resources to implement projects. As such, I recommend a model where project leaders have a *core team* of cross-functional staff required for the entire duration of project reporting directly into them. Any extra specialist resource required over the life of the project could be

deployed to undertake specific assignments and then move on to other assignments. Such deployed specialist capabilities would retain reporting lines to their respective functional heads whilst being accountable to the project leader when on project assignment. This minimizes the scope of the matrix relationship and hence any associated negative effects.

### **Operating Systems - Metrics**

In order for the above organizational structure to be effective, it needs to be supported by operating systems that align resources and capabilities with company strategy and helps motivate people to deliver results that realize such a strategy. A key part of such systems are key performance indicators (KPIs) or metrics that measure performance. Whilst, I will not recommend specific metrics since metrics could be unique to specific organizational situations, I provide a framework for how R&D leaders might go about choosing and implementing suitable metrics.

Firstly, it is worth mentioning again that one of the issues that plagued the traditional R&D organizations was the fact that the wrong sets of metrics were being used. This then led behaviors and outcomes that were contrary to company objectives. In every company cases studied and mentioned by every senior executives interviewed, the volume of potential drug candidates produced from discovery research were being measured. Scientists and research professionals were compensated for the number of potential drugs produced. When this is coupled with the fact that discovery was separated from development; and that discovery scientists lost interest in their discovery once the handover to development team was made, the results were disappointing. Many drug candidates produced by discovery research teams did not make it to the market.

Whilst this issue has been resolved in the new model by now measuring the number of potential drugs that achieve proof of concept, a conceptual framework for selecting metrics still needed.

My recommended framework follows:

- First, clearly define the *outcomes* desired from a set of activities;
- Specify all the underlying assumptions that must be valid for the outcomes to be achieved;
- Then, choose specific metrics that *directly* measure the *desired outcomes*;
- Evaluate how effective the chosen metrics are at measuring the desired outcome;
- Iterate until a set of metrics that directly measure the desired outcome is found.

These seemingly simple steps are not new. They are widely used in manufacturing companies such as Toyota to drive performance and continuous improvement. However it is the case that even highly rated global corporations still have difficulty finding effective metrics to drive performance. I do not think these issues are peculiar to pharmaceutical companies alone. An example where wrong metrics were used to measure performance in another sector was at New Century Financial Corporation, a mortgage originator in the financial services sector. In early 2005, New Century Financial Corporation was one of the largest subprime loan originators in the US. But by spring of 2007, the company filed for Chapter 11 bankruptcy protection. Whilst several reasons led to New Century's demise, investigators found that the company focused on measuring the volume of originations alone as a key performance metric to the detriment of loan quality. Brokers and loan originators were incentivized with bonuses based on volume of originations made. Over time, loan quality fell precipitously and default rates rose. A culture that placed more emphasis on quantity of originations as opposed to loan quality was created by measuring and rewarding the wrong performance metric (Palepu et al, 2009).

As mentioned above, whilst proof of concept in phase IIa apparently resolves the issue of measuring quality in place of just volume, it is not enough. Proof of concept has to be defined. The underlying assumption and factors that constitute successful proof of

concept have to be defined in order for scientists and leaders to effectively measure and reward its achievement.

On implementation, I recommend that leaders seek consensus and buy-in amongst their staff on both the process of coming up with suitable metrics, the way it should be measured and what is expected of teams and individuals in order to achieve company objectives.

### **Incentives**

In the traditional pharmaceutical R&D model and perhaps even in the new one as well, scientists are compensated based on achievement of certain project milestones, meeting personal objectives, and contributing to company-wide performance. The weightings of these criteria can be altered to encourage certain behaviors and discourage others. For example, company-wide performance could be weighted higher than individual objectives where they are needed to increase collaboration across teams or in the company as whole. What is however unique is the idea of compensating R&D scientists in a way that removes the need for excellent and talented scientist to be promoted out of areas of technical expertise to a managerial position in order to get a raise in salary. The compensation and incentive system found in Novartis should be embraced. Not all talented scientists will be great managers or leaders. An incentive system that identifies highly talented scientists who just want to continue to do important and relevant research and then reward them at the same level as managers will create a culture where scientists are celebrated, valued and compensated well.

### **Conclusions**

In order for pharmaceutical companies to be able to continue producing breakthrough medicines that can be used to cure and treat some of mankind's most challenging diseases, they must focus on driving productivity and innovation within R&D.

Organizational design remains an important set of tools, systems and techniques that can be used to drive these changes.

Restructuring organizational forms alone however will not suffice. New organizational structures, systems and incentives must be implemented, not only designed. Implementation may require a shift in leadership and culture and such shifts are notoriously difficult to achieve.

In terms of needed future research, I would like to see more investigation of the impact of externalization on internal R&D capabilities. Most pharmaceutical companies seek to access innovation from outside their companies and there is an increasing wave of outsourcing or externalization of significant parts of the R&D pipeline assets. Some companies are setting targets as high as 50%, whilst some say they will like to externalize as high as 70% of their projects in the next few years. Pertinent research questions would include

- What impact, if any, does aggressive externalization have on a company's ability and capability to continue to execute remaining internal projects?
- Does the exodus of talent in pharmaceutical companies affect a firm's performance?
- How much externalization should a firm undertake?

Finally, it might be worthwhile to revisit how the companies studied in this short research fare in the next few years. Companies such as GSK that have undertaken the most radical and fundamental changes can be used as a benchmark to find out whether the changes were sustainable and how much productivity improvements have been achieved. Additionally, Pfizer, under the leadership of a new Chief Executive Mr. Ian Read, could be studied to find out whether the new leadership has changed course from pursuing mega acquisitions as growth strategy or not. An assessment of the success or failure of the new Global Centers for Therapeutic Innovation in partnering with top research institutions will also be useful.

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