



# **STRATEGIC ALTERNATIVES IN THE PHARMACEUTICAL INDUSTRY**

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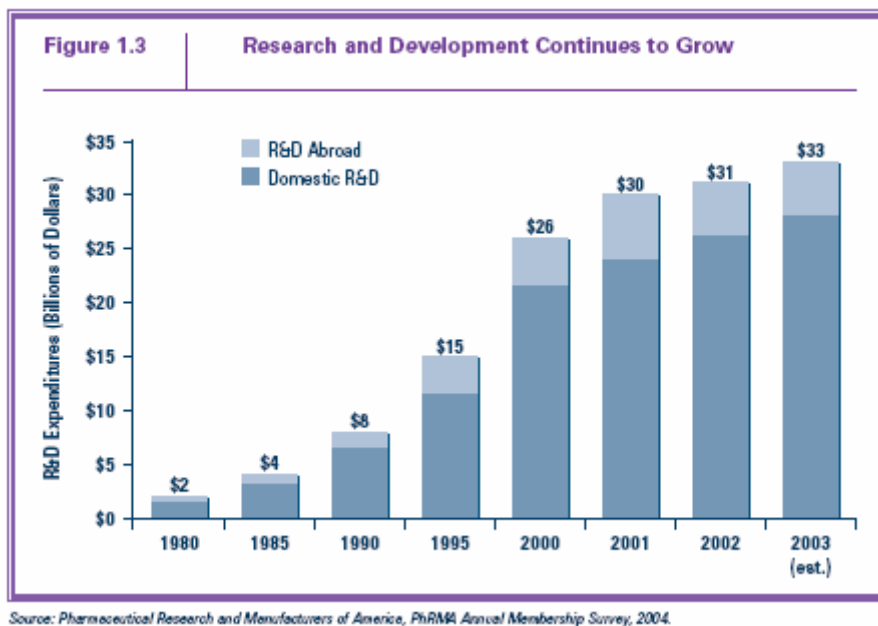
**HIMT-453  
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and Medical Device Industries  
Dr. Edward X. Hughes**

'Big Pharma' is facing a crisis. Not only are many blockbuster drugs for the world's largest pharmaceutical companies scheduled to go off-patent in the next few years, but the pipeline that would allow these firms to replace those lost earnings is distressingly empty. The small-molecule 'blockbuster' model for developing drugs – used by many Big Pharma companies over the last decade - is showing signs of weakness as companies find they have become increasingly dependant on blockbuster drugs to maintain the industry's historically-high growth rates. These blockbuster drugs have become 'double-edged swords', however, as liabilities have increased dramatically over the last decade for companies with drugs that target large patient populations. Many within the industry believe the time has come for Big Pharma to re-evaluate its growth strategies in order to ensure the industry's success over the next century. This paper will discuss not only the decrease in R&D productivity within Big Pharma as it relates to the industry's small-molecule, blockbuster drug discovery strategy, but also how the industry has reacted by trying to boost R&D productivity through mergers and acquisitions, in-licensing, and strategic alliances. The weaknesses of this historical approach will be analyzed and alternative strategies for the industry will be recommended to improve the future productivity of R&D and achieve its goal of producing innovative and profitable drugs.

## **Decline in R&D Productivity**

Over the past decade, the U.S. pharmaceutical industry R&D spending has more than doubled to \$33.2 billion in 2003 (see Figure 1).<sup>1</sup> This increase in spending is largely due to the increasing level of attrition which has helped to quadruple the cost of discovering and developing a New Molecular Entity (NME) since 1987. In 2001, the cost to discover and develop a New Molecular Entity (NME) ran to roughly \$800 million<sup>2</sup> and this figure has risen to \$900 in recent years.<sup>3</sup> Costs have been relatively stable in the preclinical phase, but have risen dramatically in the clinical phase both in terms of direct costs incurred and in time required to complete the trials.<sup>2</sup>

**Figure 1: R&D Expenditures, 1980-2003**



In his paper on the subject, DiMasi ventures several hypotheses to explain this phenomenon. First, the pharmaceutical industry has “increasingly focused on developing

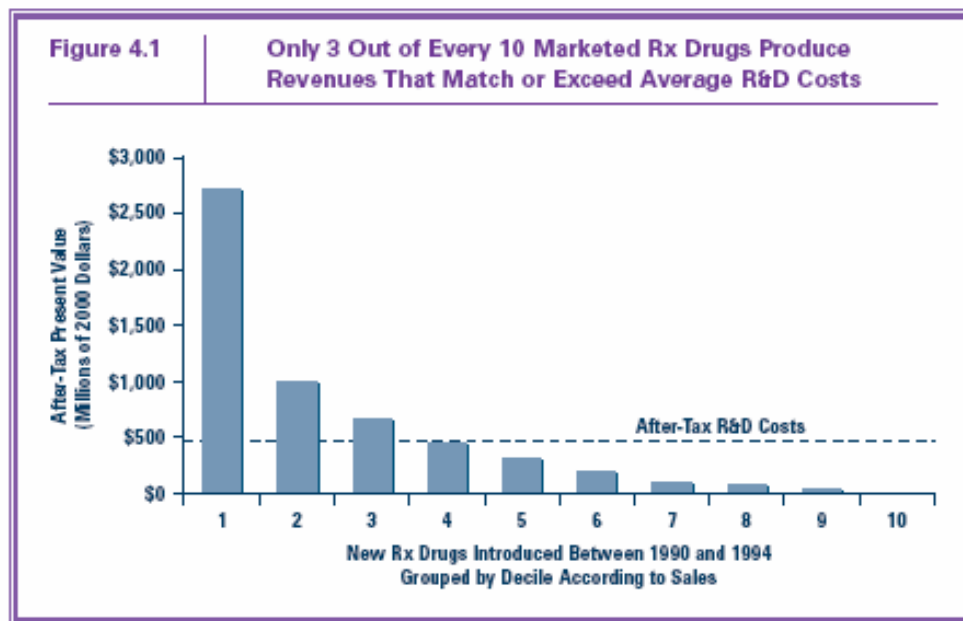
<sup>1</sup> PhRMA 2004 Pharmaceutical Industry Profile

<sup>2</sup> DiMasi, Joseph. *The Price of Innovation: New Estimates of Drug Development Costs*. *Journal of Health Economics*. Vol. 22. 2003. pp. 151-85.

<sup>3</sup> Kola, I. and Landis, J.; *Can the Pharmaceutical Industry Reduce Attrition Rates?* *Nature Reviews*. August 2004.

treatments for chronic and degenerative diseases or conditions associated with those diseases. Therapies for such conditions are generally more costly to test, as they typically require more complex patient care and monitoring, longer periods for effects to be observed, or larger trial sizes to establish their efficacy.” In other words, “the easy drugs have been done,” as one Harvard professor notes.<sup>4</sup> DiMasi also reasons that, as the number of drugs investigated increases, patient recruitment for clinical studies becomes more costly. Lastly, he suggests that the increased need to test drugs against competitor drugs have also led to more expensive clinical trials.<sup>2</sup>

**Figure 2: Unlikely Returns on Investment for R&D**



*Note: The drug development costs cited in this chart are out of pocket after tax in 2000 dollars for drugs introduced between 1990 and 1994. The same analysis found that the total cost of developing a new drug was \$802 million.*  
*Source: H. Grabowski, J. Vernon, and J. DiMasi, "Returns on Research and Development for 1990s New Drug Introductions," *Pharmacoeconomics* 20, suppl. 3 (2002): 11–29.*

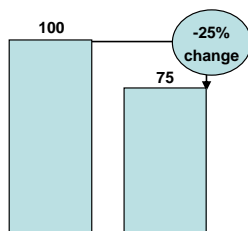
Post-marketing surveillance, increasingly stringent manufacturing quality controls, and more complex manufacturing processes are other costs which have also contributed to the

<sup>4</sup> Pollack, Andrew. *Despite Billions for Discoveries, Pipeline of Drugs is Far from Full.* The New York Times, April 19, 2002.

increased cost of clinical trials. This cloudy situation does not seem to have a silver lining as recent evidence suggests that most drugs are unlikely to produce revenues that match or exceed average R&D costs (see Figure 2).

To further compound the matter, the increase in R&D spending has not led to an increase in innovative new drugs. In fact, R&D productivity for the pharmaceutical industry has declined considerably with the number of New Molecular Entities (NMEs) submitted for approval dropping by nearly 50 percent, to about 40, and the number of New Chemical Entities (NCEs) produced per company declining by 41 percent (see Figure 3).<sup>5</sup>

**Figure 3: R&D Productivity, 1991-2000**



	1991-1995	1996-2000	% Change
<b>NCE Outputs (#/company)</b>	12.3	7.2	-41%
<b>R&amp;D Spend (\$USB/company)</b>	5.9	8.5	+44%
<b>NCE Sales (\$USM/drug)</b>	536.0	786.0	+46%
<b>New blockbuster launches</b>	15	12	-20%

- 1 R&D productivity metric, indexed to industry 1991-1995
  - 2 Total number of NCEs over 5 years for an average company in the industry
  - 3 Total R&D spend in US\$B over 5 years for an average company in the industry
  - 4 Sales for 4 years after launch for an average drug, all year 2000 dollars(millions)
  - 5 Change from 1991-95 period to 1996-2000 period
  - 6 Includes only drugs that were launched in that 5-year period which went on to peak sales of >\$1 billion
- Source: McKinsey analysis; PBJ Publications Pharmaprojects; FDA/CDER; Company reports; Analyst reports, IMS Health

At the other end of the drug development process, another worrisome trend is manifesting itself - the decline in FDA approval rates of new drugs. In 2002, FDA approvals of NCEs, at 17, were lower than at any other time in the past decade. In 2003, the FDA approved only 21 NCEs.

<sup>5</sup> Filmore, David et. al., *Pipeline Challenges*. Modern Drug Discovery. October 2004. pp. 28-34.

Furthermore, FDA priority reviews of NCEs (priority reviews are granted to drugs that show promise of addressing an unmet medical need), a good proxy for innovation, were lower in 2002 and 2003 than in any two-year rolling period in the preceding ten years.<sup>3</sup> According to another study, which defines innovative drugs slightly differently, the most innovative drugs, priority NMEs (as defined by the FDA's own classification system), accounted for just 13% of all drug approvals in the 1995-2000 period, down from 17 percent in the prior five-year period, 1989-1994.<sup>6</sup> Priority NMEs drive a disproportionate amount of the growth from consumption of new pharmaceutical products, so this decline in their rate of production is troubling news for pharmaceutical companies. In addition to implying a lower rate of innovation in the pharmaceutical industry, this trend also reflects the FDA's increasing aversion to risk.

This trend is the driving force behind Bain & Company's recent estimate of \$1.7 billion for the overall price tag of developing a new drug. They calculate that the odds of FDA approval for a given drug have dropped to 59 percent from 73 percent since 2000. Bain also estimates that only one in thirteen compounds put in preclinical trials reach the market today, compared to one in eight in the 1995-2000 period.<sup>7</sup> The fact that FDA approval rates have dropped significantly in the first few years of the new millennium lend some credence to their lofty cost estimates.

The problems contributing to the decline in approval rates affect all phases of the pipeline, but the most pressing issues relate to clinical testing. In the screening and preclinical phases, investments in new automation technology and new methods have not produced the expected increase in leads. Combinatorial chemistry, despite generating an enormous amount of

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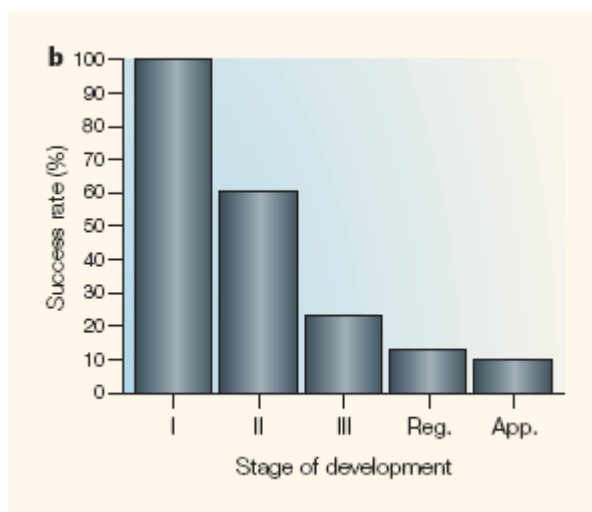
<sup>6</sup> *Changing Patterns of Pharmaceutical Innovation: A Research Report*. The National Institute for Health Care Management Research and Educational Foundation. Self-published. May 2002. pp. 15-6.

<sup>7</sup> Gilbert, J., et al.; *Rebuilding Big Pharma's Business Model*. In Vivo. November 2003.

data for researchers to comb through, has not produced successful drug candidates. Genomics also has left researchers awash in data but has not yet lived up to its promise as a cornucopia of new drug targets.<sup>4</sup> Evidence suggests, however, that new technologies, such as high-throughput screening, have at least kept down the rate of increase in discovery phase costs.<sup>2</sup>

Turning to the clinical phase, it is quite apparent that attrition rates of compounds are rising (see Figure 4). For the period 1991-2000, only one in nine compounds for which an Investigational New Drug (IND) was filed made it through development to approval by U.S. or European regulatory authorities.

**Figure 4: Success Rate by Phase of Development**



The graph above shows the percentage rate of success of compounds entering first-in-man that progress to subsequent development phase

Source: Kola, Ismail; Landis, John. Nature Reviews, Vol. 3. August 2004.

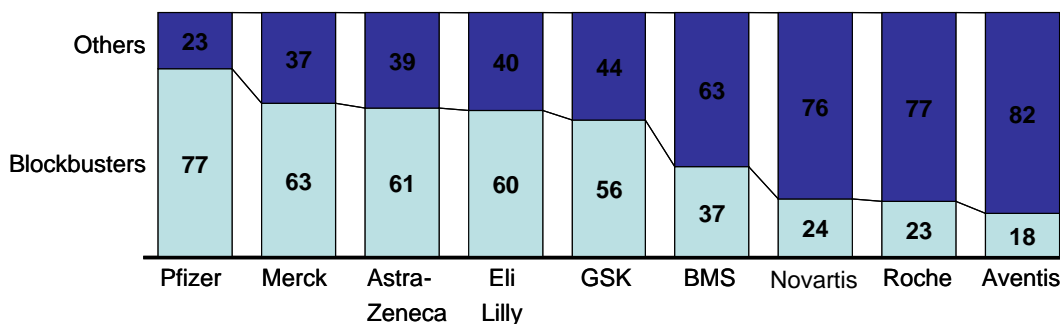
Current data suggests that 38 percent of compounds for which an IND is filed fail in Phase I. 63 percent of those that enter Phase II trials fail and 45 percent of those that make it to Phase III trials fail. Finally, 23 percent of compounds for which a New Drug Application (NDA) has been filed fail at the registration stage, after the NDA has been submitted. Thus for every

1,000 INDs filed, 620 compounds make it through Phase I, 229 emerge from Phase II, 126 pass Phase III trials and have NDAs filed and 97 make it through review to approval.<sup>3</sup> Failure in Phase III trials has become a particularly acute problem. The number of drugs failing the last stage of testing has also increased significantly. In fact, the number of drugs in Phase III trials has remained at 375-400 over the past decade, despite significant increases in the number of drugs in preclinical, Phase I and Phase II trials. This is a particularly troubling development for pharmaceutical companies, since Phase III is the most expensive point at which a drug can fail.

The major causes of drug attrition have changed significantly over time. “In 1991, adverse pharmacokinetic and bioavailability results were the most significant cause of attrition and accounted for 40 percent of all attrition.” By 2000, these factors contributed to less than 10 percent of attrition. In 2000, the major causes of attrition were lack of efficacy and safety issues, each accounting for about 30 percent of attrition.

The recent paucity of innovative new drugs has hit Big Pharma hard and has only been exacerbated by their dependency on large blockbuster drugs to drive growth (see Figure 5). Many analysts now believe that Merck’s withdrawal of Vioxx will make it much tougher for drug companies to win approval for products aimed at big patient populations as the FDA demand ever-greater proof that they are safe.

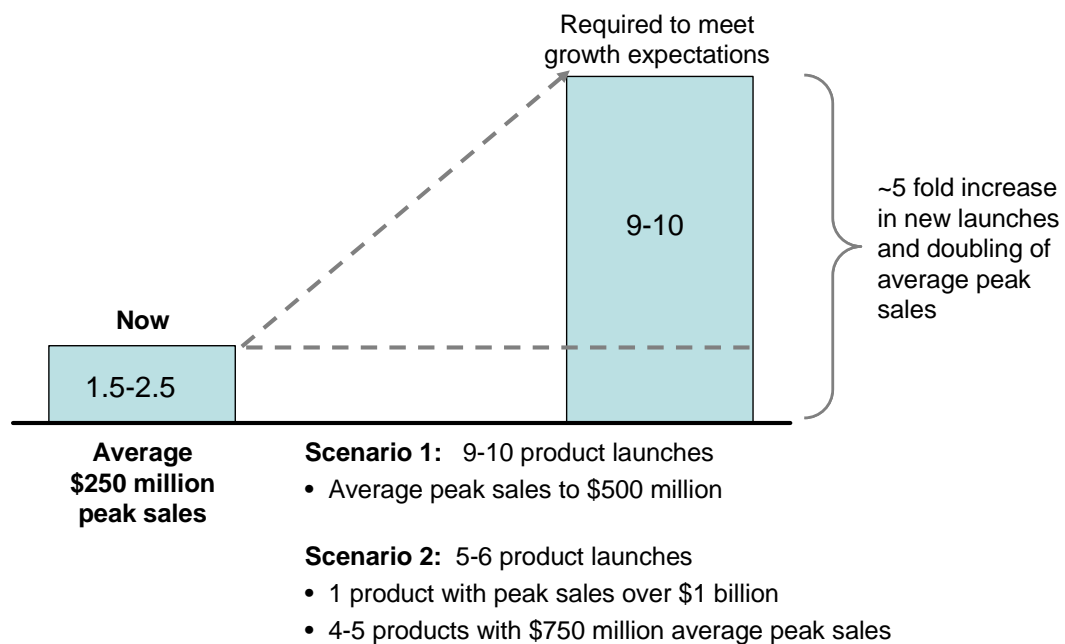
**Figure 5: Percent of Revenue on Large Blockbuster Drugs**



\* Total return to shareholders – growth in share price and dividends from 1994 to 1999  
 \*\* Blockbusters with sales >\$1 billion/year  
 Source: McKinsey Quarterly: Unlocking Value in Big Pharma, 2001 Vol. 2, McKinsey analysis

Compounding these problems is a business issue, namely that, through both organic growth and consolidation, large pharmaceuticals companies “have reached a scale at which they must generate several billion dollars in additional revenue each year in order to meet Wall Street growth targets.” (see Figure 6).<sup>6</sup>

**Figure 6: Number of product launches, per year, per company**



\*Assumes 18% earnings growth from 2000-15 and reversion to GDP growth rate (6.5%) beyond 2015  
 Source: Compustat; Lehman Brothers; McKinsey analysis

This pressure has led many large pharmaceutical firms to invest more R&D in incremental improvements to existing drugs, rather than in real innovations. As the authors of the NIHCM report note:

*[O]nly a handful of firms were able to bring 10 or more drugs with new active ingredients to market over the past decade, or at least one per year on average.*

*To address the shortfall, companies have grown their franchises by adding line extensions: new products using the same active ingredient, but differing from the original in some way, such as more convenient dosing forms.<sup>6</sup>*

### **Current Strategies for Addressing the Pipeline Woes**

In recent years, pharmaceutical companies looked outward to help fill their weak pipelines through: 1) mergers and acquisitions (M&A), 2) in-licensing new compounds, and 3) developing strategic alliances and partnerships with other pharmaceutical or biotechnology

companies. Although each strategy has varying costs and benefits, a study of past successes and failures may be useful as a guide for future decisions.

### Mergers & Acquisitions

The attempt to gain economies-of-scale in R&D through an unprecedented sequence of mergers has yet to yield conclusive proof that such economies exist. Some experts actually suggest that “such larger mergers might in fact give rise to diseconomies-of-scale, imposed by the costs attendant on managing an enormous and often geographically highly-decentralized research group.”<sup>8</sup>

To develop a successful strategy for the future it is helpful to briefly review past M&A strategies within the industry. Historically, Big Pharma has struggled when relying on a steady flow of profits and growth from new drugs. To address this issue in the late 1960’s and 70’s, many pharmaceutical companies (with the exception of Merck) were acquiring companies to horizontally diversify (e.g., Pfizer and Lilly acquired cosmetics companies, Abbott purchased nutritional products, American Home Products bought a house wares business]. Investing in less profitable businesses provided stability by balancing risk inherent in the drug discovery and development process.<sup>9</sup>

The diversification strategies quickly reversed in the 1980s because blockbuster drugs were providing the revenue to sustain corporate growth and advances in the life sciences convinced managements that pure-play pharmaceutical companies could succeed.<sup>8</sup> The newfound confidence in research and development spurred a new round of mergers, acquisitions,

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<sup>8</sup> Henderson, Rebecca. *Drug Industry Mergers Won’t Necessarily Benefit R&D*. Research Technology Management. Vol. 43. No. 4 (Jul/Aug 2000). pp. 10-11.

<sup>9</sup> Landau, Ralph. Achilladelis, Basil. Scriabine, Alexander. *Pharmaceutical Innovation: Revolutionizing Human Health*. Chemical Heritage Press, 1999. pg 100-105.

and joint ventures within the pharmaceutical industry. It was during this round of M&A activity that Big Pharma not only began to merge with equal-sized peers to build sales forces and fill their pipelines, but also began to invest in small biotechnology companies. Initially, through joint ventures, pharmaceutical companies provided funding for R&D projects and later for developing and marketing products. Eventually, as the pharmaceutical industry's in-house R&D productivity decreased, pharmaceutical companies began to focus on biologics and acquire some of the more successful biotech companies. Big Pharma companies have developed significant capabilities in biotechnology as they observed the commercial and scientific success of their biotech alliance partners. Despite this increase in internal science capability, "Big Pharma's track record for discovering and developing biotechnology-enabled drugs has been dwarfed by the biotech players and their internal R&D commitment remains highly skewed to the chemical synthesis approach to drug design."<sup>10</sup>

Although there have been a number of biotech acquisitions by Big Pharma companies, thus far, the results have been mixed. Merging cultures, retaining key researchers, and maintaining the innovative environment are just a few challenges faced by the acquiring company. Of the Big Pharma companies, Johnson & Johnson, appears to be the most successful at acquiring smaller biotech companies. Overall, due to the complexity of integrating an acquired company, the acquisition strategy is less appealing than licensing or alliance deals, however, Johnson and Johnson's unique decentralized organizational structure appears to be most capable of executing a successful acquisition strategy. Their ability to identify opportunities and its hands-off approach to operating the acquired companies has created a string

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<sup>10</sup> Wolpert, Jan. *The BUY vs. BUILD Challenge to Drug Makers' Performance*. Mergers and Acquisitions. Philadelphia. August 2004. Vol.39, Issue 8. pp. 22.

of successes. The strategy “proved to be successful with Centocor, and looks to be a key factor in the success of the Scios acquisition in 2003.”<sup>11</sup>

Pharmaceutical companies have often engaged in merger and acquisition activity to address the erratic nature of the drug discovery process. However, recent evidence suggests that this strategy serves mainly as a stop-gap measure to keep the revenue growth engines humming. As these companies grow larger and larger, they are finding it more difficult to grow organically and need to keep merging simply to meet growth expectations. Thus, consolidation turns out to be a mixed blessing, bringing the benefits of scale and diversification of risk, but also creating a monster of outsized growth expectations that must constantly be appeased. As Kathy Smith, head of Ernst and Young’s US pharmaceutical practice observes, “You end up with such a huge organization that the products it takes to sustain even high single-digit growth become quite substantial. Certainly in the short term, mergers do bolster pipelines, but I think the answers are still very mixed as to whether, at the end of the day, these present long-term results.”<sup>5</sup>

### Strategic Alliances & Partnerships

In an increasingly challenging marketplace, where M&A strategies are failing to deliver R&D productivity gains, the importance of alliances has increased significantly. In fact, research

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<sup>11</sup> Pavlou, A. *Biotechnology M&A insight: Deals and strategies*. Journal of Commercial Biotechnology. Vol 10. No I. September 2003. pp. 85-91.

suggests that products co-developed by a pharmaceutical and biotech company are more likely to be commercialized than those that are developed by a single entity.<sup>12</sup> Demonstrating the growing importance of strategic alliances, “the 20 biggest pharmaceutical firms formed nearly 1,500 alliances with biotech companies between 1997 and 2002.”<sup>13</sup> In the highly volatile drug industry, an effective alliance strategy provides an opportunity to proactively manage risk.

An interesting example of this focus on alliances may be Merck, which has recently undergone a business development transformation. Long-regarded as the industry’s best at internal R&D and admired for their ability to rely on this internal capability, Merck recently has changed course and now aggressively pursues external licensing and alliance opportunities to feed its pipeline. As CEO Ray Gilmartin states, “In 2001, we completely transformed our approach to external collaborations,” and in the last five years, Merck’s partnership transactions have risen by almost 80 percent. In addition, Merck is actively engaging in co-promotion. Three of its next four drug launches will most likely be co-promoted.<sup>14</sup>

The relationship between Roche and Genentech is often cited as the most successful strategic alliance to date in the industry. “In 1990, Roche bought 10 percent of Genentech for \$490 million, giving them a 60 percent stake and control.” Additionally, the agreement gave Roche “access to Genentech’s data after the completion of Phase II trials, with the option to decide whether they wanted a product or not.” If Roche took the product, they were “bound to pay 50 percent of all Genentech’s R&D cost to date, all the ongoing costs of getting registration statements outside of the United States, and royalties on all sales outside the U.S. Since

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<sup>12</sup> Shalo, Sibyl. *The Art of the Deal*. BioPartnerships - A Pharmaceutical Executive and Biopharm International Supplement. October 2004. pp. 8-16.

<sup>13</sup> Lam, Michael D. *Dangerous Liaisons*. Pharmaceutical Executive, May 2004. Vol. 24. Issue 5. pp.72.

<sup>14</sup> Bernard, Stan. *Back to the Pharma Future*. BioPartnerships - A Pharmaceutical Executive and Biopharm International Supplement. October 2004. pp. 6-7.

Genentech maintained its independence, Roche obtained ownership of a growing entrepreneurial company without fear of stifling innovation. Roche also gained access to a pipeline it could market outside of the U.S. The deal benefited Genentech by providing much needed funding and by freeing up management to focus on the core business rather than raising capital. In two separate deals, Roche's total investment in Genentech was about \$7.7 billion. Overall, Roche took out about "\$8 billion in cash after the IPO and they still own 54 percent of Genentech worth about \$28 billion."<sup>13</sup>

Unfortunately for pharmaceutical executives, the success of the Roche-Genentech deal is generally the exception to the rule. Numerous studies show that alliances in most industries have a failure rate exceeding 50 percent. Many pharmaceutical-biotech relationships have become mired in lengthy court battles over issues such as intellectual property disputes and royalty agreements. For example, the collaboration between Abbott Laboratories and Cambridge Antibody Technology (CAT) has deteriorated in a dispute over the size of royalty payments. The two companies should have a big success on their hands in Humira – a potential blockbuster treatment for rheumatoid arthritis. Peter Chambre, CAT's chief executive, says he would prefer to “delay licensing products to drugs companies until they are at a later stage to allow the company to generate more value from its technology.”<sup>15</sup> Culture incompatibility (whether differing company size, corporate culture, management personalities/egos, or nationalities) is most often claimed to cause alliance failures. Patricia Martin, executive director of alliance management at Eli Lilly, believes that alliances fail because, “1. The science doesn't work. 2.

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<sup>15</sup> Mills, Lauren. *Great science not all that matters developing treatments*. Financial Times. 11/10/2004, pp. 5.

The scientific decision isn't good because the communication isn't good. 3. There's no hope of a scientific decision, good or bad."<sup>16</sup>

### In-licensing

An alternative approach by Big Pharma to obtain new and innovative drugs is to in-license them from other companies. In 2003, licensed products accounted for more than \$70 billion in revenue for the top 20 global pharmaceutical companies. According to research by Wood Mackenzie, licensed products will account for \$100 billion by 2008 and will represent a third of the industry's total projected revenue. By all measures, licensing is and will continue to be big business for Big Pharma.<sup>17</sup> In fact, some companies have embraced it as its core business development strategy. Merck, for example, has accelerated its in-licensing activities in the past year to rebuild its pipeline and counter the failure of three high-profile Phase III clinical trials.

Pharmaprojects reports that, "24 percent of drugs in active R&D are available for licensing, while another 25 percent are already licensed out or in co-development." In addition, there is also a significant number of drugs that could be, but are not, being developed because companies have decided to drop them for strategic reasons, such as a shift of corporate focus or resources, rather than a lack of efficacy or adverse events."<sup>5</sup> The benefits of adopting an in-licensing approach is that it allows Big Pharma to spend less money to 'cherry-pick' the compounds that they desire instead of having to acquire the whole organization and dealing with the added complication of merging the two organizations. The only problem with this approach is that it is quickly becoming the 'pipeline solution du jour' where currently the typical licensing

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<sup>16</sup> Lam, Michael D. *Why Alliances Fail*. Pharmaceutical Executive. June 2004. Vol. 24. Issue 6. pp. 56.

<sup>17</sup> Hall, Jim. *A Decade (and 1/2) of Deals*. BioPartnerships - A Pharmaceutical Executive and Biopharm International Supplement. October 2004. pp. 18-24.

deal has at least five suitors vying for each compound versus less than three in 1988.<sup>14</sup> This increase in in-licensing activity is also having a measurable impact on prices. Competition for deals has driven up prices and has driven Big Pharma to invest in potential drugs at earlier stages of the development process. Jim Hall, president of life sciences advisory firm Wood Mackenzie says “the days of the small, testing-the-waters deal worth tens of millions of dollars is going away and will be replaced by very large equity investments.”<sup>16</sup> According to a McKinsey study, up-front payments in therapeutic alliances increased more than six-fold from 1988 to 2002, and average milestone payments soared, from \$6 million in 1988-1990 to \$85 million in 2000-2002. In order to avoid overpaying for a drug candidate, a well defined valuation methodology must be consistently applied to all potential in-licensing deals.

As we have shown above, research productivity in Big Pharma has been on the decline and is showing no sign of improving. According to Accenture,<sup>18</sup> “nine of the top ten pharmaceutical firms have in-licensed more than 40 percent of their marketed new molecular entities” and according to estimates from McKinsey & Co., “out of the top 25 drugs today, 12 were discovered or developed by a company other than the one that launched them.”<sup>19</sup> Given the current environment of public policy pressures and increasing regulatory scrutiny in the wake of recent high-profile cases, the costs and risks involved in bringing drugs to market are only going to increase. Given these factors, it is crucial that Big Pharma take the necessary steps today that will enable them to increase their research productivity and maintain their historical growth rates. Below we have analyzed several of the strategic alternatives that Big Pharma could pursue in order to confront these issues.

#### Strategic Alternative #1: Re-organize Research to Focus on Therapeutic Areas

One of the chief criticisms of Big Pharma is that as they get bigger - and arguably more bureaucratic - innovation becomes stifled. Could this be that these large companies ‘spread themselves too thin’ by trying to work in many disease areas? If so, one solution may be to focus only on a few disease areas with the goal of becoming *the* cardiovascular company or *the* oncology company. With this strategy, each company could offer drugs and related services for all the indications and disease levels within *each* therapeutic area rather than offering only one or two drugs for many therapeutic areas. For instance, Pfizer’s website boasts that, “Pfizer's search for new treatments spans hundreds of research projects across 18 therapeutic areas - more than any other company.” In our opinion, this is not something to boast about. In terms of revenue,

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<sup>18</sup> Accenture, *Commercial and R&D: Reinventing the relationship*. 2002.

<sup>19</sup> Myshko, Denise. *The Secret to Alliance Success*. PharmaVOICE. October 2004. Vol. 4, No. 10, pp. 14-24.

Pfizer certainly has many number one products, however, its claim brings to mind the old adage, ‘jack-of-all-trades, master-of-none.’ In this increasingly-educated world and intolerance for sub-standard medical care, patients want to know that the companies that provide the drug used to treat their specific condition are not only *experts* in using their own drug to treat the disease, but also are experts in treating the entire disease state. This includes having a stable of drugs to treat: 1) all stages of the disease, 2) all subtypes of the disease linked to the specific genetic profile of each patient, and 3) palliative drugs to treat the side effects that inevitably emerge from the drugs used to treat the patients. For a patient with metastatic lung cancer (or the physician that treats him/her), the knowledge that Company A has not just one, but several chemotherapy treatments for lung cancer, as well as drugs to treat the inevitable nausea and lethargy that typically result from chemotherapy, may lead the patient to trust this company more than Company B which only has one chemotherapy drug, and actually request Company A’s treatments.

How can a single company expect to do all of this for *every* therapeutic area? The simple answer is that it cannot. Companies may find that the increased brand name recognition and customer loyalty more than make up for the specialization in only a few therapeutic areas. Several concerns, however, emerge from adopting this strategy. The first concern is that this specialization will prevent the serendipitous cross-therapeutic area discoveries that sometimes emerge when two distinct group of scientists that are focused on different areas of research come together and realize that perhaps the drug they are using to treat one disease may also be used to treat a multiple diseases (e.g., Genentech’s cancer treatment, Rituxan, may also be used to treat rheumatoid arthritis). Although therapeutic area specialization may prevent the ‘cross-pollination’ of ideas that sometimes enable these serendipitous events, this strategy would allow

the company's scientists to focus more on understanding the disease itself which potentially could yield more productive and innovative research. In addition, therapeutic area specialization would play a crucial role in building the long-term patient trust that every pharmaceutical company desires. This trust could potentially translate into brand name recognition, future brand loyalty and increased revenues.

The second concern is government regulation. There is a strong risk that the Federal Trade Commission (FTC) would prevent any one company from owning all or most of the rights to treat a single disease due to anti-trust laws. However, since no drug effectively treats 100 percent of the afflicted patients due to each patient's distinct genetic profile, an unmet need exists to create tailored treatments to smaller patient populations all bearing similar genetic profiles. As scientists learn more about each disease state and the human genome, pharmacogenomics will play a key role in classifying diseases even further into subtypes – with each subtype affecting patients differently according to their genetic profile. This classification will then provide the opportunity for companies to develop individual therapies that will compete in treating these smaller patient populations.

#### Strategic Alternative #2: Re-organize Research to Focus on Targets (Treatment Platforms)

In contrast, an alternative reorganization strategy is for companies to shift their research focus to targets ('treatment-platforms') rather than therapeutic areas. After all, research shows that targets frequently overlap therapeutic areas. A company that develops therapeutics or therapeutic approaches that affect multiple medical conditions, possibly in different therapeutic areas, based on a shared mechanism-of-action, could become a powerhouse. An example of such a target is G-protein coupled receptors (GPCRs). GPCRs are proteins that are active in

almost every organ system and present a wide array of opportunities as therapeutic targets in disease areas such as cancer, cardiac dysfunction, diabetes, CNS disorders, obesity, inflammation, and pain. Drugs targeting GPCRs account for the majority of best-selling drugs and about 40 percent of all prescription pharmaceuticals on the market, including drugs such as Zyprexa, Clarinex, Zantac and Zelnorm.<sup>20</sup> By organizing research organizations by targets, the odds of a serendipitous cross-therapeutic area discovery increase due to the mix of researchers all housed together. One obvious problem with this approach, however, is that the company takes a lot of risk by focusing only on several targets. The odds are that most targets are not ‘druggable’ and therefore these companies may wish to diversify with many more targets to maximize their potential for success.

### Strategic Alternative #3: Spin-Off Research

While a seemingly draconian response to the slowdown in research productivity, a case could be made for Big Pharma divesting itself of early-stage research and focusing farther down the value chain. This would allow Big Pharma companies to concentrate on what they do best – development, sales and marketing. With marketing now commanding a larger budget than research in most pharmaceutical companies, it seems that perhaps Big Pharma is moving in this direction.<sup>21</sup> One of the most frequently cited reasons for smaller companies licensing products is the ability to leverage the sales and marketing capabilities of Big Pharma. Clearly the sales and marketing organizations of large pharmaceutical companies are a key strategic asset. But can that be a business on its own?

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<sup>20</sup> Filmore, David. *It's a GPCR World*. Modern Drug Discovery. November 2004, pp. 24-8.

<sup>21</sup> Koberstein, W. et al. *The Mergers: Miracles, Madness, or Mayhem?* Pharmaceutical Executive. March 2000.

Of the approximately \$35 billion spent on R&D in 2003, sources indicate that approximately 30 percent of this is spent on the research phase,<sup>22</sup> suggesting that firms could recognize substantial cost savings by divesting research. Obviously the cost savings are attractive. However, the key questions that arise are: What is lost by divesting research? And how will Big Pharma then fill the product pipeline? The first question is extremely difficult to answer and in some respects is a function of chance. Could the research organization be on track to develop the next blockbuster small molecule? Perhaps. But as we have shown above, the probability of that occurring is relatively low and decreasing every year. Research also provides a key scientific knowledge base from which the entire corporation derives its credibility in some sense. Evaluating licensing opportunities, designing appropriate clinical trials, and developing an effective and appropriate marketing plan require a fundamental understanding of the mechanisms-of-action and underlying science behind drug candidates. By divesting or even substantially reducing research capabilities, pharmaceutical companies risk losing this key capability. As we will discuss below, certain organizations have been able to achieve some success without having research as the backbone of the organization; however, it is unclear how sustainable this model is due to a lack of competitive differentiation, or if it could be expanded to the current scope of large pharmaceutical companies.

The second question – how to fill the pipeline – is easier to answer, yet raises additional questions. Big Pharma could simply use the biotechnology industry as their research organization. Licensing compounds from smaller companies, in particular biotechnology firms, is the likely avenue to pursue and is already a growing trend. The number of licensing and

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<sup>22</sup> Peter J. Johnson. Executive Director, Corporate Strategic Planning, Eli Lilly. Comments during HIMT 453, Kellogg School of Management, Northwestern University, November 16, 2004.

alliance deals reported in the biotech industry has grown from under 100 in 1993 to nearly 450 in 2001.<sup>23</sup> However, by utilizing the biotechnology industry as a feeder mechanism for new drugs, would drug discovery rates improve for Big Pharma or remain the same? In other words, is the biotech industry any better at drug discovery than Big Pharma (risk-adjusted)?

With increasing competition for late-stage compounds, large pharmaceutical companies must look to strike deals earlier in development. However, as this trend plays out, competition will increase for compounds of all stages and the natural outcome is for the licensing market to behave efficiently: the value of licensing deals at various stages of development will be bid up to their expected NPV. In the absence of specialized assets that would make a compound more valuable to one particular firm, Big Pharma will struggle to profitably fill its pipeline with in-licensed compounds.

An alternative model would be to increase academia's involvement in drug discovery. While politically controversial, this strategy is not as far-fetched as it sounds. Some may suggest this type of deal would represent a conflict-of-interest - that perhaps Big Pharma would influence the academic institution that historically has been best-suited for independent 'basic research' to now perform research benefiting the company and not the public good. Although certainly a valid concern, given the importance of academia for making quantum leaps in our understanding of diseases and the human body, this strategy could also potentially increase the flow of ideas and new approaches through collaboration. In fact, in November 2004, the Novartis Institutes for Biomedical Research (NIBR) and the Broad Institute of Massachusetts Institute of Technology and Harvard announced a unique joint project to unravel the genetic causes of type 2

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<sup>23</sup> Arnold, Katie et. al. *Value drivers in licensing deals*. Nature Biotechnology. November 2002.

diabetes.<sup>24</sup> This partnership, called the Broad-Novartis Diabetes Initiative is unique because it will make all of its findings immediately and freely available to the public. The Broad Institute brings genetics capabilities, large amounts of genomic information, and bioinformatics to the deal while Novartis will help elaborate the pathways and how they will be prioritized, perform the wet lab work to follow up on findings, and bring funding of \$4.5 million to the Initiative. David Altshuler, principal investigator at the Broad Institute states, “People seem most intrigued by the fact that an academic genetics group and a company are committing up front to putting all of the data out as soon as they themselves have it. We believe that the fundamental information about the genome and which pathways are altered in disease is precompetitive.” Altshuler further states, “I wouldn’t underestimate the knowledge of the disease that a company like Novartis has. There is a strong intellectual component of the knowledge one gets in a pharmaceutical company that is largely synergistic and non-overlapping with what an academic scientist thinks about.” Tom Hughes, Global Head of Diabetes and Metabolism Research at NIBR further states that the initial goal of the Initiative is to develop “information linking specific genes to the susceptibility of developing type 2 diabetes, as well as some information that may relate to the efficacy of certain drugs or the prognosis with regard to different courses of therapy.”<sup>24</sup> Achieving this goal would not only benefit Novartis, but also the public as a whole. While the use of academia would not be an end-all-be-all solution, it’s conceivable that similar types of partnership could be formed that would benefit both sides.

While there are clearly some concerns with spinning off research, we point out that a handful of firms have been able to develop such a business model with some degree of success.

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<sup>24</sup> Ratner, Mark. *Public-private Model Pursues Precompetitive R&D*. Nature Reviews Drug Discovery. November 2004. Vol. 3, pp. 987

One such example is Forest Laboratories which develops, manufactures and sells prescription and non-prescription products in collaboration with licensing partners. The company's R&D spending consists almost entirely of clinical development expense rather than early-stage research. Forest generated \$2.7 billion in sales in FY04, a 19 percent increase over FY03, while earnings increased 18 percent to \$736 million.<sup>25</sup> Clearly they have been able to make this model work. However, we note that the company's stock has declined over 50 percent from its high earlier this year due the early approval of generic Celexa and pending patent litigation against Lexapro, suggesting that even licensing the vast majority of the pipeline does not completely immunize a company against periodic gaps in the pipeline. Another example of a successful model that is not based on research is Quintiles Transnational, the largest provider of outsourced development and commercialization services to biotech and pharmaceutical companies. The company generated sales of just over \$2 billion in 2003 from clients like Eli Lilly and CV Therapeutics, demonstrating the breadth and depth of their expertise.<sup>26</sup> Thus far, the company has remained an outsourcing service provider, however, given their comprehensive capabilities, it is not difficult to imagine them expanding into in-licensing compounds for their own development and commercialization. There are clearly some strategic ramifications to doing so, but we highlight Quintiles as evidence of the increasing commoditization of the commercialization and, to a lesser extent, development functions.

Although the cost savings associated with divesting research are clearly attractive for any Big Pharma firm, the costs may outweigh the benefits. Not only does Big Pharma benefit from the potential for a new drug being developed through in-house research, but the research function

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<sup>25</sup> Forest Laboratories annual report, March 2004.

<sup>26</sup> Quintiles Transnational annual report, December 2003.

also augments several other critical elements of success. In particular, scientific expertise and credibility are essential to both success in evaluating licensing agreements and effectively selling in a highly competitive environment. Additionally, as demonstrated by Quintiles' ability to fairly rapidly integrate into the drug commercialization process, there is very little competitive differentiation in providing upstream services only. While it is true that Forest Labs has had some degree of success without investing in research, their approach is not without flaws. As discussed below, this type of success in licensing can be augmented by utilizing research organizations differently and more effectively.

#### Strategic Alternative #4: Form Consortium with Peer Companies

While several models of combining research capabilities among companies can be conceived (joint ventures, alliances, etc.) and are presented with a variety of justifications, philosophically it is difficult to distinguish these ventures from the financial reality of merging firms. Even if the venture is of smaller scope than the entire firm – for example, combining cardiovascular research to jointly-develop a product – these type of arrangements offer little or no value to the shareholders of the participating companies from a risk-sharing perspective. Going back to basic principles of finance, shareholders can diversify idiosyncratic risk on their own. Thus, the only justifiable rationale for any type of combination would be comparable to the justifications given for most M&A activity in the pharmaceutical industry: synergies, economies of scale, and science.<sup>21</sup> Synergies typically relate to administrative overhead or sales force consolidation; economies of scale and benefits of combining scientific prowess are cited as the benefits of combining R&D.

From a financial and theoretical perspective these justifications makes perfect sense. Increasing size should allow a company to place more bets on new technologies, and if blockbuster drug discovery is a somewhat random event, the chances of finding the next blockbuster should improve. Size should also provide an advantage in drug development and make companies more valuable as licensing partners.<sup>27</sup>

Theoretically, jointly-developing drugs should maximize the chances of discovery and make research more efficient through the sharing of otherwise proprietary information about drug targets, assay methods, toxicology studies, etc.<sup>28</sup> However, data does not support the theory that economies-of-scale exist in R&D. Despite increasing R&D spending by the industry as whole, the number of compounds approved by the FDA has decreased since 1996, suggesting that research productivity is decreasing.<sup>29</sup> Further, Datamonitor found that “there are no significant economies-of-scale in pharmaceutical research and development.”<sup>30</sup> This trend is reflected in the evidence that mergers within the pharmaceutical and biotech industries rarely succeed in achieving their desired outcomes. According to the publication In Vivo, “the size of a drug company hasn’t correlated with better returns to shareholders, at least in part because the companies doing the merging weren’t particularly strong”. A study by Patricia Danzon, et al similarly found that firms with lower earnings growth expectations were more likely to merge with another firm. Danzon also found that:

*Controlling for merger propensity, for large firms merger had no effect on the change in enterprise value, sales, employees, and R&D expense in the three years following a merger. Firms that merged experienced slower operating profit growth in the third year*

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<sup>27</sup> Garg, R et al, *The Value of Scale in Pharma’s Future*. In Vivo, September 2001.

<sup>28</sup> Kager, Patrick & Malek, Jan. *In the Eye of the Storm*. Pharmaceutical Executive. April 1, 2003. pp 44-50.

<sup>29</sup> Danzon, P. et al, *Mergers and Acquisitions in the Pharmaceutical and Biotech Industries*. National Bureau of Economic Research. June 2004.

<sup>30</sup> *Networked Pharma: Innovative Strategies to Overcome Industry Margin Deterioration*. Datamonitor, 2002.

*after merger. Thus, although merger is a response to being in trouble for large firms, there is no evidence that it is a solution.*<sup>29</sup>

While we cannot definitively conclude that there are no potential benefits of scale in R&D, the evidence suggests that to-date these benefits have not been recognized by merging organizations. Thus, firms facing lowered research productivity are unlikely to solve their problems by simply combining forces with industry peers.

#### Strategic Alternative #5: Shift Research Focus to Large Biological-based Drugs

For Big Pharma, the days of relying on huge-selling, small-molecule-based blockbuster drugs to sustain growth may be numbered as science drives toward the development of drugs directed at smaller, targeted groups of patients. “The application of science is becoming much more customized...you’re dealing with drugs that are efficacious for narrower populations,” says David Bellaire, a partner at Bain & Co.<sup>31</sup> For many pharmaceutical companies, the most important criterion in determining which drugs to develop is whether the drugs can generate \$1 billion a year in sales. Focusing on this type of strategy is very risky, however, because if the drugs fall through, there can be gaps in the companies’ pipeline - as recently witnessed at Merck this year with the high profile failures of three Phase III compounds. In addition, regulators are expected to take a much harder look at the safety profile of drugs aimed at millions of people following the withdrawal of Merck’s Vioxx earlier this year.

Typically, Big Pharma companies have sought to develop small-molecule drugs aimed at large patient populations, however, not all of those who take the drugs benefit. Small-molecule drugs generally do not bind as specifically to disease targets within the human body as do large, protein-based drugs. Because the small-molecule drugs do not bind as specifically to their

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<sup>31</sup> Clarke, Toni. *Reuters Summit – Is Big Pharma’s Golden Era Over?* [Reuters.com](http://Reuters.com). November 17, 2004.

protein targets, there is a greater probability that they will bind to a different target within the human body thus causing an unintended physiological response (i.e., ‘side-effect’).

Historically, this small-molecule drug strategy has been financially successful for Big Pharma, however, this business model may not work in the future as scientists develop drugs more closely aligned with the genetic makeup of specific groups of people. Donald Drakeman, CEO of Medarex Inc., supports this by stating, “Big pharmaceutical companies are looking for big products, but science is looking for small to medium.”<sup>31</sup> Furthermore, if the pharmacogenomics revolution reaches the lofty goals of identifying each how patient will respond to certain drug treatments, side effects may no longer be tolerated by patients. It is not too farfetched (especially with today’s low public-opinion of the pharmaceutical industry) to imagine a time in the not-too-distant future where large groups of people boycott products developed by Big Pharma companies that continue to stick with the blockbuster drug strategy. After all, this type of strategy is clearly designed to help companies recoup R&D costs and profit rather than offer the most efficacious and safest drugs to the patients.

Although many companies will continue to espouse their mission statements that claim their main goal is to develop life-saving treatments for patients, the financial conundrum for Big Pharma certainly does exist. The question of whether Big Pharma could maintain its historic growth rates with a personalized medicine model looms large. As David Bellaire from Bain & Company states, “How are you going to get to a billion-dollar drug for a small population?...You are going to have to charge very high prices.”<sup>31</sup> Although this type of pricing strategy has been adopted by several biotechnology companies (e.g., Genzyme), Big Pharma does not have to strictly follow this model in order for this shift in strategy to be successful. Not only can companies adapt in other ways, such as by reducing the costs of developing existing products or

reorganizing R&D groups to increase productivity, but also, they could embrace this strategy and by becoming an early adopter, reap the benefits.

The shift from a small-molecule-based blockbuster drug strategy to a large-molecule, biological-based ‘personalized medicine’ strategy has many benefits. As mentioned above, the large-molecule biological drugs are generally more specific and thereby have a reduced probability of causing side effects for patients. This fact alone creates many opportunities to improve revenue streams for companies marketing these types of drugs. With less chance of side effects, not only will patient compliance improve, resulting in more units of product sold, but also there will be a decrease in liabilities due to both less patients being harmed as well as smaller patient populations affected. In addition, with better safety profiles, companies can justify higher prices for these types of drugs since they reduce the costs of complications and hospital treatments that typically result from side effects. With biological-based drugs, companies do not have to be as concerned with patent expirations since there are no current FDA regulations that allow biological-based generics to be approved. With longer periods of exclusivity, companies making biological-based drugs have more time to recoup the costs of development and increase the lifetime revenue of the drugs. This shift in focus to smaller patient populations will also allow companies to decrease their selling, general and administrative costs. By focusing only on small patient populations, companies will require more knowledgeable, specialized sales representatives thus allowing Big Pharma companies to finally reduce the ‘armies’ of sales reps that they have been amassing over the last decade. Finally, by shifting to biological-based drugs that are more specific and have less side effects, companies can begin to earn patient loyalty – a goal that has thus far eluded pharmaceutical companies attempting to ‘brand’ their products.

As expected, this shift in strategy does not come without many costs and risks. By focusing on smaller patient populations, a decrease in volume sold is inevitable. As basic marketing dictates, unless a company makes up this drop in volume with higher prices, they will earn lower profits. To counter the potential drop in volume and decrease in profits, companies must adapt in other ways. First, the companies could reduce the costs of developing and manufacturing new and existing products. Although R&D costs have been increasing each year, it is quite likely that the new technologies invested in the late 1990's 'genomics era' will begin to bear fruit soon and reduce these costs. Second, manufacturing processes are considered by many within the industry to be wholly inefficient with many opportunities for productivity improvements. Third, although politically unpopular, an increasingly popular method to decrease costs is to outsource R&D to foreign countries. In China, pharmaceutical companies are finding highly educated scientists who work for a fraction of what their counterparts in the U.S. are paid and they are taking advantage of it since about 80 percent of their total R&D costs go toward scientists' salaries. "Doing research in a low-cost setting should allow drug companies to deploy the dollars" they spend in the U.S. and Europe more effectively, says Drew Senyei, a health-care venture capitalist at Enterprise Partners.<sup>32</sup> In addition, setting up facilities in China could also help companies establish strong ties with Chinese authorities, something that could prove valuable as the companies seek to expand operations in China, as well as explore new market opportunities there. Some companies have broadened their R&D operations to include clinical trials in China, where patient enrollment is easier and associated hospital fees much lower. Although intellectual property concerns still remain an issue, some of those concerns are abating with China now a member of the World Trade Organization.<sup>32</sup>

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<sup>32</sup> Santini, Laura. *Drug Companies Look to China for Cheap R&D*. The Wall Street Journal. November 22, 2004.

Shifting to the development and manufacture of biologically-based drugs is not only more costly and complex, but also it requires a reorganization within R&D, manufacturing, regulatory and sales and marketing groups. Typically, within Big Pharma's research and development divisions, more chemists than biologists are working within the labs. With this new strategy that focuses on biological drugs, a greater proportion of biologists and protein biochemists are required. In addition, new laboratory equipment and consumables must be purchased. Within manufacturing, not only will more biologists be required and new equipment purchases (e.g., fermentation tanks), but also there will be increased quality control demands. This will require 'clean rooms' for most steps in the manufacturing process – not just the last steps as currently required in the manufacture of small-molecule drugs. With this tougher quality control requirement comes the need for regulatory personnel that are knowledgeable in the development of biologics as well as in filing Biological License Applications (BLAs) vs. the New Drug Applications (NDAs) that are required for small-molecule drugs. Within sales and marketing, new sales reps will need to be hired or old ones re-trained to become more knowledgeable in order to deal with these small, specialized patient populations.

Potential risks also exist with shifting strategies from small-molecule drugs to biological-based drugs. First, there is the possibility that the FDA will require diagnostics to identify the patient population for which the drug would most benefit (see Strategic Alternative #6). Another risk to this strategy is that insurance and other 'payor' companies may balk at paying higher prices for these biological-based drugs unless pharmacoeconomic studies show that the benefits (i.e., decreased hospital stays) outweigh the costs of the new treatments. Although these types of pharmacoeconomic studies may soon be required by the FDA, they are very expensive and would significantly increase the development costs for Big Pharma.

### Strategic Alternative #6: Shift Research Focus to Diagnostic-Led Strategy

Even with well-established treatments for a condition, there are significant numbers of patients that are either not diagnosed in a timely manner or not diagnosed at all. Better diagnostics and physician education could significantly improve the number of people getting diagnosed and therefore increase the number of patients getting treated – thus resulting in increased revenues for drug companies. In order to adopt this approach, Big Pharma would have to: a) Shift marketing resources from promoting specific products to promoting diagnostic testing; b) Time the development of the diagnostic to coincide optimally with the development of the therapeutic; and c) Develop business models that motivate physicians and diagnostic providers to participate.

The development and marketing of Genentech's Herceptin is the perfect model for a true pharmacogenomic-diagnostic-led strategy. In what is perhaps the first example to demonstrate the benefits of a targeted medicine, the FDA required Genentech to develop a diagnostic method to identify women with metastatic breast cancer that had HER2 gene amplification, and who would most likely benefit from Herceptin therapy – before approving Genentech's breast cancer drug Herceptin. If this FDA requirement were to occur, most Big Pharma companies would be unprepared to meet this challenge. However, Roche Pharmaceuticals – in a direct departure from the rest of Big Pharma – has decided to place a bet in the future of medicine, rolling the dice that diagnostics and therapeutics will work 'hand-in-glove' as never before. Although this is a gamble on their part, Roche is well-positioned to succeed since their subsidiary, Roche Diagnostics is the world's leading provider of diagnostic systems. In fact, Roche (the majority-owner of Genentech) was the same company that developed the HER2 diagnostic test for Genentech's Herceptin.

### Strategic Alternative #7: Fine-Tune In-licensing Capabilities

As we outlined above, licensing products from smaller pharmaceutical firms and biotechs continues to be a key component of Big Pharma's strategy going forward. 34 percent of Big Pharma's sales will come from licensing deals by 2010 compared to 17 percent in 2001.<sup>33</sup> As competition for compounds increases, prices will increase as the market becomes more efficient. In order to generate returns under this scenario, bidding companies will need to bring specialized assets to the licensing process that will increase the value of compounds to them only. While the science and mechanics underlying this strategy are beyond the scope of this paper, we propose two high-level ways that pharma can achieve this end.

First, license earlier. Licensing deals generally have a relatively high failure rate – an average 37 percent are successful – but more than 60 percent of products licensed in Phase III or pre-regulatory stages reach market versus only 20 percent for Phase I and II compounds.<sup>17</sup> To date pharmaceutical companies have tended to favor licensing compounds in the later stages of the development cycle, after a significant portion of the risk has been eliminated. However, this strategy may be changing for many companies. For example, Amgen banks on early-stage deals – more than 80 percent of its agreements are for pre-clinical compounds and Merck's "back to the science" strategy includes more than 70 percent of its licensed portfolio in early-stage development.<sup>17</sup>

Although only about a third of all licensing deals occur in the pre-clinical phase,<sup>34</sup> research from Recombinant Capital shows the percentage of biotech-pharma licensing deals that are focused on early-stage products is increasing from 54 percent in 1991-1993 to 68 percent

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<sup>33</sup> Novartis presentation, "Trends in Partnering in Pharma: Biotech and Novartis", Victor Hartmann, Head of Global Business Development & Licensing, 2002.

<sup>34</sup> Kalmas, James et. al. *The new math for drug licensing*. The McKinsey Quarterly, 2002.

during 2000-2002, while alliances that focused on products in late-stage development dropped from 29 percent to 22 percent over the same time period.<sup>35</sup> According to a McKinsey study, pharmaceutical companies are losing out on a valuable opportunity by not licensing compounds earlier: “Pharma companies could dramatically increase the amounts they pay for compounds in early development and still come out ahead...The preference of biotech firms for late-stage deals is obviously rational, but with richer incentives to make deals earlier, that could change.” This study suggests that licensing earlier stage deals under current conditions is in the best economic interest of the pharmaceutical companies. In addition, as noted above, we believe competition for late-stage deals will force Big Pharma to look earlier in the development process. Those companies which develop a process to identify early-stage candidates are going to have the largest benefit, at least until pricing competition increases for early-stage deals.

This brings us to our second suggestion: license better. While this sounds patronizing, we believe there could be an opportunity to improve the effectiveness of the licensing process. By shifting some of the ineffective product research budget to discovering technologies to improve the compound evaluation process, companies can gain a competitive advantage in the licensing arena. Given the importance of licensing in the future of Big Pharma, this does not seem an unreasonable way to spend money. The licensing evaluation process should also be refined to maximize the use of a company’s specific (and specialized) assets, such as a niche sales force or deep knowledge-base in a certain therapeutic area.

Key to the effectiveness of this strategy is maintaining and augmenting research capabilities. As we concluded above, divesting research would be detrimental to the development

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<sup>35</sup> Howard, Ken. *Advice for Partnering with Pharma*. Nature Biotechnology. Vol. 22. No. 11. pp.1477-9

and commercialization functions. It may also prohibit a firm from establishing and maintaining a competitive advantage in licensing.

## **Conclusion**

Big Pharma's crisis in R&D productivity is not going to be solved soon. From declining rates of innovation to increased costs of development, the industry is getting hit from every side. If the industry were not in such a 'perfect storm' – with patent expirations, pricing pressures, low public opinion, challenges to intellectual property by increasingly aggressive generic companies, re-importation pressures, Medicare/Medicaid reform, and increasing regulatory hurdles – the R&D productivity issue may not be such a big deal. However, with the industry facing its greatest challenges in history, R&D productivity is a topic that few companies can ignore.

Although many of the strategic alternatives highlighted above could help improve R&D productivity, none of them alone will be the answer. It is likely that the next decade will see a hybrid model of pharmaceutical R&D that incorporates several of the strategic alternatives highlighted above. The possibility also exists for a 'disruptive innovation' to blindside the industry and change the way pharmaceutical companies operate.<sup>36</sup> For instance, a new online research firm called InnoCentive has claimed to provide a new R&D model that promises to revolutionize drug development and slash the costs of bringing a product to market.<sup>37</sup> The firm pairs individual pharmaceutical companies with thousands of scientists worldwide to enable these companies to find answers to vexing R&D problems at 1/10 the normal cost and time. Using the firm's website, a pharmaceutical company can anonymously post a research problem

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<sup>36</sup> Christensen, Clayton M., Raynor, Michael E. *The Innovator's Solution – Creating and Sustaining Successful Growth*. Harvard Business School Press. 2003.

<sup>37</sup> *Online Firm's Model for Drug R&D Promises Big Cost Savings*. Washington Drug Letter. Vol. 36, No. 46

along with a bounty and a deadline for responses. Then the 70,000 registered scientists from 150 countries can decide to take on the challenge. If a scientist can provide a solution that meets the firm's specified criteria, that person will collect the bounty. The benefit to the pharmaceutical company is that it only pays for success – not failure or effort, thereby reducing costs by orders of magnitude. It is estimated that this model could reduce the average costs of new drugs from \$1.7 billion to \$170 million within a fairly reasonable time frame, says Michael Raynor, author of "The Innovator's Solution." "The consequences of that are surely world-changing."<sup>37</sup>

At the end of the day, no matter what strategies Big Pharma adopts, the future of R&D will be unpredictable. As Dr. Daniel Vasella, Chairman and CEO of Novartis AG said in an interview with Business Today;

*"We can never read the future. You can put in place all the elements that you believe are essential: The people, the money, the technical resources, the skills, the continuous training, alliances with academia and with other partners...but there is no guarantee for success. You are constantly dealing with uncertainty. But having said that, you need to have people who are willing to bet their life that what they are doing is right. That's when you have programs that move forward and succeed, but then you also have more programs that move forward and don't succeed. It's a business with more failures than successes. It's just the fact and we have to accept it."<sup>38</sup>*

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<sup>38</sup> Carvalho, Brian. *The Population is Not Really the Attraction*. Business Today. December 19, 2004.