Report:
The Relation of Biotech and Big Pharma: Feeding the Pipeline

“Blockbuster pharmaceuticals are on the verge of patent expirations while late-stage product pipelines are barren, thus shaking the foundations of an industry that was once the darling of Wall Street”

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1. Executive Summary

The new paradigm of industrial pharmaceutical drug discovery has yet to deliver on its promises. Despite molecular biologists having identified thousands of potential new disease targets, primarily through advances in genomics, cell signaling pathway research, bioinformatics, and major advances in IT for the biotechnology field, in addition to the advent of the new platform technologies of combinational chemistry and high throughput screening, there has not been the predicted increase in drug discoveries. The unpalatable truth for pharmaceutical R&D management is that its productivity is down while its costs have escalated dramatically. The cost of producing a marketable drug has skyrocketed in recent years due to greater regulatory oversight, increased competition, and globalization. More complex market issues of portfolio management, physician relationship management and consumer education have radically altered the pharmaceutical landscape.

To meet analyst expectations and satisfy shareholders, pharmaceutical industry giants must replenish their pipelines with potential blockbusters and hedge against droughts with a continuous, healthy flow of specialty and medium-sized drugs. Now more than ever, pharmaceutical companies must outsource R&D work to their biotech counterparts—and they are doing so in record numbers.

Nearly one third of new pharmaceutical products are now developed through alliances. Highlighting the increasing importance of these collaborations, five major pharmaceutical firms have no billion-dollar blockbusters in late-stage development.

The biotechnology industry has flourished on the back of fundamental technology advances, the hyperbole of the new paradigm of drug discovery, and the numbers of scientists on the market looking for new employment opportunities. It is now recognized that the "biotech sector" is going to be the driver for new drugs candidates and that "Big Pharma" will develop, market and distribute these new medicines. However, the economics of this new paradigm has yet to be tested, but it is likely that the industry will have to reinvent itself to accommodate to it.

2. Industry Overview

2.1. Overview of pharmaceutical industry

The last ten years have seen a spectacular rise and fall in the fortunes of pharmaceutical blockbusters. While the 'blockbuster model' was king in the 1990s, it looks increasingly unlikely that pharmaceutical companies will be able to rely on such products to drive growth in the latter half of this decade. Big Pharma companies need to rethink their strategies for the post-blockbuster era. The firms usually compete within therapeutic classes; for example an anti-cancer drug doesn’t compete with an arthritis treatment. Success had traditionally been based on two factors: R&D and Marketing.

While blockbuster revenues are set to experience year-on-year growth of 5.2 per cent, rising from $116bn in 2002 to $158bn in 2008, a slowdown in growth is expected to occur between 2005 and 2008. During this period, total blockbuster sales are forecast to
demonstrate a compound annual growth rate (CAGR) of 1.6 per cent, compared to a 9.0 per cent rate forecast between 2002 and 2005. This represents more than a five-fold slowdown in growth\(^1\).

In the short term, currently marketed products are anticipated to fuel growth, but after 2005 sales from current blockbusters will decline as products lose patent protection. This will leave company’s revenues exposed to erosion from generic competition; more than 30 of the current crop of 57 blockbusters are expected to lose patent protection between 2003 and 2008. Sales for these products exceeded $60bn in 2002. Indeed, for companies with blockbuster products, their contribution to ethical sales has increased from 40 per cent to 45.6 per cent over this period.

While there is little doubt that Big Pharma will continue to search for new blockbuster products, unless there is a significant productivity turnaround companies will be forced to shift their business strategies to reduce dependency on blockbusters. However, any alternative business model must be able to match the high returns offered by blockbusters. Understandably corporate pharmaceutical management have become somewhat disillusioned with this situation and inevitably the industry has gone through a prolonged period of consolidation and rationalization with the aim of maintaining profitability and returns to shareholders that they have come to expect.

**2.2. Overview of the biotechnology industry**

- History of the relationship; biotech’s origins

The development of the biotech industry can be characterized by three phases: seed, growth and a phase of consolidation.

### Developmental stages of the biotech industry

- **Phase I**
  - Seed
  - Growth

- **Phase II**
  - Number of companies

- **Phase III**
  - Maturation
  - Consolidation

The threat of consolidation in biotech industry has led to an increase in licensing activities and alliances between biotech companies.

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\(^1\) Datamonitor research
Pharmaceutical companies need to reduce their R&D costs, speed-up their R&D processes and fill in gaps in their R&D pipeline. This has resulted in an increase of alliances between pharmaceutical companies and biotechs.

3. Why Big Pharma needs biotech?

3.1. Big Pharma cannot easily change its “drug depend” strategy

The impending fall in revenue from current products is particularly concerning in light of weak blockbuster pipelines across the industry. Pharma industry pipelines usually contain many drugs with high-earning potential.

For instance the following four late-stage pipeline products have the potential to generate annual revenues of $1bn or more by 2008:
- Pfizer's Pregabalin, Inspra and Caduet
- AtheroGenic's AGI-1067.

Combined sales for these products are expected to reach $8,956m in 2008, representing a paltry 5.7 per cent of this year's total blockbuster revenue.

The ramifications of a blockbuster deficit to the pharmaceutical industry are compounded by the dependence many companies continue to place on blockbuster revenue. Aventis, GlaxoSmithKline, Johnson & Johnson, Pfizer, Novartis and Wyeth have all increased their reliance on blockbuster revenue by at least 10 per cent between 2000 and 2002.

**Meeting growth expectations requires many more, bigger products...**
If pharmaceutical companies are to continue to pursue a blockbuster-centric model they must identify licensing, acquisition and alliance strategies to source new products and bolster portfolios in the short term. Alongside such activities, there is a need to address R&D strategies and reinvent approaches of conducting drug discovery in order to ensure pipeline improvements in the long term.

Although many different strategies to reduce blockbuster dependence are likely to emerge over the coming years, time is unfortunately not on the industry's side. Given the long lead times required to implement major shifts in global business models, it seems unlikely that a sufficient reduction in blockbuster reliance can be achieved in time to counter the slowdown in growth forecast after 2005.

3.2. Big Pharma R&D productivity needs to be improved

3.2.1. Big Pharma is a R&D intensive Industry

**Pharmaceutical industry research in the U.S**

![Pie chart showing the percentage of research and development expenditure across different industries.](image)

**Source:** National Science Foundation, 1998

3.2.2. Big Pharma R&D has high failure rate

The R&D process is long and with only a few suitable outcomes. Researchers develop thousands of compounds which are then subject to a series of investigations via laboratory tests, animal trials, and three stages of human clinical trials in order to find one new drug. The drug’s profits have to be able to support the cost of the entire R&D process...
The development process and regulatory approval can consume more than half of the new drug’s patent life of 20 years before it even reached the market. Finding compounds that have the potential to become useful drugs takes the most time in the drug approval process.

The different phases (from compound to drug) are illustrated in the following figure:

The number of new products launches has sharply declined; in the US for example, dropping from about 45 per year in the 1960s to about 25 in the mid 1980s. Also, many of these new drugs didn’t provide significant therapeutic advances but were rather substitute of existing prescription drugs.

For 1200 compounds in Phase III only 10 are expected to become Blockbusters and this is not enough to allow Big Pharma to keep its preferred position…
Blockbuster Status Of Pipeline Products

The 2003 Phase III Development Pipeline

<table>
<thead>
<tr>
<th>Currently in Phase III</th>
<th>Expected to Succeed</th>
<th>Expected to be Blockbusters</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,200</td>
<td>600 (50%)</td>
<td>10 (1%)</td>
</tr>
</tbody>
</table>

“Not nearly enough to fill the void at Big Pharma”

Biotechnology is expected to improve R&D productivity to produce new blockbuster drugs and allow Big Pharma to maintain growth and earnings.

**3.2.3. Big Pharma has High Cost of development**

The average R&D expenditure of Big Pharma has doubled during the 1980s to more than 10% of sales. In spite of this increased investment, the new product pipelines of the leading firms have matured over the past decade.

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### Cost of Developing a New Drug

$\text{Millions}$

<table>
<thead>
<tr>
<th>Year</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td>$54</td>
</tr>
<tr>
<td>1987</td>
<td>$231</td>
</tr>
<tr>
<td>2000</td>
<td>$802</td>
</tr>
</tbody>
</table>

*Source: Tufts Center for the Study of Drug Development*
Clinical trials, especially Phase III, consume the greatest portion of R&D budgets....

![Allocation of money in the average R&D process](image)

**SRCE: Frost & Sullivan**

### 3.2.4. Big Pharma has a limited exclusivity on its drugs: Patents expiration

Along with high development costs, the major pharmaceutical firms face a wave of patent expiration on their leading drugs. In the US for instance, 120 of 1983’s best selling drugs were off patents by 1996 and 200 best selling drugs expired by 1990. Upon the expiration of the patent on drug a firm has several options:

- Maintain the product as a branded prescription
- Licence the product to generics producers
- Produce its own generic version
- Switch the product to an over the counter (purchasable in pharmacies) status.

Note that any change from the prescription status needs regulatory approval and none of the above options can maintain blockbuster revenue.
Also, once off patent most branded prescription drugs are subject to competition from generic producers, which copy the active ingredients of the branded drug. In most European countries generic firms can only begin the product development upon expiry of the branded drug’s patent. In the US, however, such development can begin before the product expiration, thus several competing equivalents could be launched the day the branded drug’s patent expire. More and more governments are looking for cost containment which favors lower priced drugs. The branded drug has to be effective enough to be preferred to its eventual generic alternative.

4. The advantages and disadvantages of the Big Pharma - Biotech relation

4.1. A Win-Win partnership?

The good news for pharmaceutical companies is that the market for pharma-biotech alliances can expand pipelines and help build the next great pharma company. A Wharton School of Business study shows that drugs produced by pharma-biotech alliances are 30% more likely to succeed in winning FDA approval than those developed by a single company.

Pharmaceutical companies are not the only ones that stand to gain from these partnerships. Opportunities abound for biotechs, as well. These companies often lack the marketing muscle and colossal sales forces required to prepare the market for a new drug. Biotechs need the strong arm of Big Pharma to achieve rapid sales uptake and boost peak annual sales.

So, naturally, pharma-biotech alliances are a perfect match, right? Not necessarily. While pharmas and biotechs work toward the same basic objectives—they are very different. Biotechs are smaller and more flexible than pharmaceutical companies and their most coveted
assets tend to be their scientific minds and proprietary technology. Pharmaceutical companies’ contributions to partnerships are more often based on regulatory, manufacturing, and sales and marketing expertise. However, companies’ lack of experience and expertise in managing pharma-biotech alliances creates uneven performance. Recent high-profile failures highlight the dangers of sloppy alliance execution.

Big Pharmaceutical companies may need small biotech companies to help fill their sparse new-drug pipelines, but the relationship remains one-sided. It is an asymmetry, since individual product deals are never going to matter as much to a large drug company as to a small biotech. Of course, Big Pharma needs products, but at the end of the day it still holds all the cards. If Big Pharma wants to stop a deal, then it will, and a biotech firm can be dependent on that product for its entire future. On the other side of the table, Pharma companies must know when to rein in their partnering impulses. The most lucrative deals turn disastrous if they do not fit with strategic objectives or if they depend upon non-existent expertise, resources or infrastructure.

4.2. Alliances that work

There is no single “best” method for getting the most out of pharma-biotech alliances. Many companies, unable to understand the critical challenges involved in these collaborations, have tried to simply apply pharma-pharma alliance models to their biotech relationships. Their reward is inconsistent results.

For example, Bristol-Myers Squibb’s Erbitux alliance with ImClone put the FDA approval process primarily in ImClone’s hands—and the FDA rejected the drug due to a shoddy filing (much to the dismay of Sam Waksal and Martha Stewart). One of the lessons learned from this and other high-profile FDA rejections is the importance of bringing the pharmaceutical partner’s regulatory expertise into the approval process.

More and more, biotechs perform early-stage drug target identification and leave the bulk of clinical trials, marketing, and later-stage development to the pharmaceutical companies. For instance, Vertex Pharmaceuticals Inc. has deals with GlaxoSmithKline and Novartis AG that it considers model relationships. The partnership is based on finding multiple drug candidates over several years; whereas, many of the relationships beforehand were aimed at finding candidates for single drugs.

As the pharmaceutical industry focuses on developing new blockbusters, the competition for innovative new technologies has increased to a fevered pitch. Spotting, evaluating and closing lucrative deals require companies to gain as much expertise at pharma-biotech alliances as they have at R&D.

Once a company has built its “partner of choice” strengths, it must build its reputation through traditional media channels, sales forces, corporate web sites and co-branding. The pharmaceutical and biotech industries judge alliance success both on financial merits and on intangibles such as goodwill and admiration. In discovering and pursuing future opportunities, companies that meet those criteria have a strong reputation card to play.

Several companies have employed innovative strategies and tactics to approach pharma-biotech alliances:
• Johnson & Johnson – J&J’s wide range of therapeutic areas provides the company opportunities to search for partners in both established and emerging technologies. Its partnership strategy allows the company to both innovate in new therapeutic areas and renovate existing products in lucrative niche markets. As a partner, J&J brings the experience of coordinating and communicating across its 150 divisions. Many smaller partners have come to see J&J as a giant with the attitude of an equal.

• Abgenix – Abgenix, a mid-sized biotechnology firm, has pursued and won several deals creatively structured to maximize benefits for both parties. This willingness to think outside the traditional pharma-biotech box earned the company a spot on many To-Be-Considered lists in top therapeutic areas, such as oncology.

• Bayer – CuraGen and Bayer’s $1.3 billion pact did more than just turn heads—it forced pharmaceutical executives to reconsider the strategic goals behind high-level resource allocations. Such deep pools of capital give front-line business development pros the green light to go after the most attractive—and highly valued—partnerships.

5. Conclusion

Some products brought to market from recent pharma-biotech alliances are generating significant value. The largest pharma-biotech deals have steadily increased in size in recent years, from SmithKline Beecham’s $125 million deal with Human Genome Sciences in 1993 to the $1.3 billion collaboration between Bayer and CuraGen in 2001. The pharmaceutical industry still views pharma-biotech alliances as a relatively untapped trove of new products. Approximately 30% of drugs now undergoing clinical trials come directly from biotechs, up from 7% a decade ago.

Pharma-biotech collaborations have yielded mixed results. While some substantial benefits have surfaced, no pharmaceutical company has emerged as the biotech industry’s “partner of choice.” Pharmaceutical and biotechnology companies should elaborate in depth their relationships to create mutually beneficial deals that will result in the development of new drugs.

The first biotechnology and pharmaceutical companies to build top-notch alliance reputations will gain a decided competitive advantage, and can apply that advantage to drive overall corporate success. To achieve partnership bliss, each party must understand the other’s business, the value proposition each brings to the table, and, importantly, the subtle nuances (such as corporate culture) that can ultimately make or break a deal.