



**ANALYSIS OF THE RISKS EMBEDDED IN ASYMMETRICAL ALLIANCES IN
THE PHARMACEUTICAL INDUSTRY**

By:

**John Hughes
Edna Lazar
Guilherme Maradei**

Report written for the course

Creating and Managing Strategic Alliances

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1. INTRODUCTION

Asymmetrical alliances are particularly interesting due to the imbalance of power between the two partners, sometimes leading to the acquisition of the smaller firm by its larger partner. In this paper, we analyze the specific dynamics of asymmetrical alliances in the pharmaceutical industry, where deals between large pharmaceutical companies and small biotechnology firms have been increasingly common.

The pharmaceutical sector attracted our attention primarily because of the natural tendency for deals between very large and very small companies. In this fast-paced, technology-driven industry, small biotechnology companies have proliferated rapidly in the last decade, leveraging the fact that research for new biotechnology-based drugs does not require large infrastructure. In recent years, biotechs have been responsible for a large portion of the research and development in the industry, attracting the interest of the large pharmaceutical firms. Through the so-called “pharma-biotech” alliances, pharmaceutical giants have found a way to supplement their drug development pipelines, whereas small biotech firms have been able to multiply the potential of their discoveries, leveraging the pharmaceutical companies’ regulatory experience and marketing strength.

Nevertheless, the differences between large pharmas and smaller biotechs pose significant threats to the success of deals. In this paper, we concentrate on analyzing the risks of those alliances. We start by weighing the opportunities and risks for both sides in a typical pharma-biotech alliance. Next, we analyze the key risks, in light of the concepts learned in class, during the course *Creating and Managing Strategic Alliances* (such as the Social Exchange Theory and the factors behind deciding when to own a function, find a partner or outsource it completely). In the third section, we analyze current partnerships in the pharmaceutical industry and speculate about the risks embedded in each of them.

2. ANALYSIS OF MOTIVATIONS BEHIND PHARMA-BIOTECH ALLIANCES

From a bird's eye view, an alliance between a pharmaceutical company and a biotech firm is a win-win situation, as both types of firms usually have complementary needs and competencies, while also sharing a mutual goal. However, there are also several risks inherent to this type of alliance, particularly due to the asymmetry that such types of deals naturally involve.

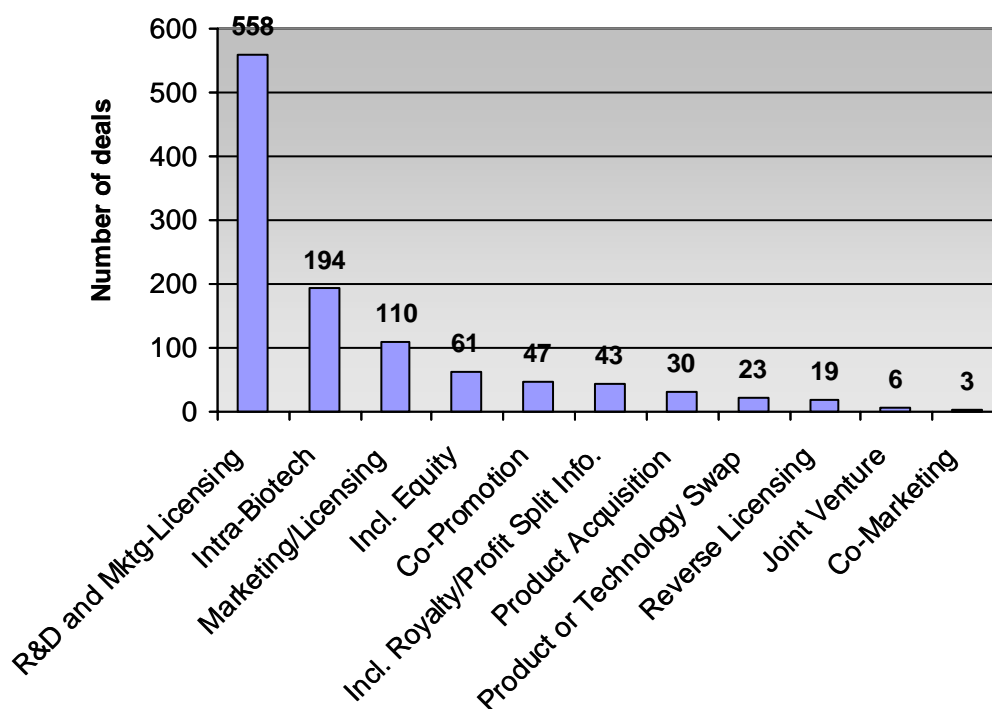
In this section, we describe the overall opportunities that an alliance represents for a large pharmaceutical company as well as for the small biotech firms. Next, we will describe the overall risks involved in pharma-biotech alliances.

2.1. Opportunities for large pharmaceutical companies

For a pharmaceutical company, creating a strategic alliance with a biotech firm for the development and commercialization of a drug means that not all the risk involved in the drug discovery process is borne solely by the pharmaceutical company, as is usually the case when a pharmaceutical company utilizes its own R&D. This risk is especially significant in the pharmaceutical world, where approximately only one out of 10,000 drug targets is effectively launched in the market, and the development of each drug can require investments close to one billion dollars. Alliances allow for a wise allocation of resources—partnering with as many drug discovery companies as possible increases the chances that a pharmaceutical company will have a sufficiently strong pipeline that allows for effectively launching new drugs periodically.

The wisdom of such alliances explains the high ratio of R&D and marketing-licensing deals in the pharmaceutical industry: out of 1,094 strategic alliances in the first six months of 2003, 558 were R&D and marketing-licensing deals (see Exhibit 1).

Exhibit 1 – Pharmaceutical Alliances by Deal Type (July 2002 – June 2003)



Source: Windhover’s Pharmaceutical Strategic Alliances, Vol. XIV - Statistics and Trends 2003

As a result of this attractive match, virtually all leading pharmaceutical companies have established a complex network of alliances – Pfizer boasts around 250 alliances, Bristol-Myers-Squibb 190 alliances, Johnson & Johnson 150 alliances, and Eli Lilly, 120 alliances¹. Between January and June, 2003, 355 pharmaceutical alliances were created, out of which 320 were between pharmaceutical and biotech firms².

Expanding to new therapeutic areas is also a key benefit best provided by alliances. Alliances offer the strategic flexibility that pharma companies need to help strengthen their drug pipelines. While

¹ According to information provided by companies in their websites.

² Windhover – pharmaceutical statistics and trends 2003

in-house R&D capabilities may focus on developing commercial drug candidates within key therapeutic areas, alliances with other companies allow for exploring new areas, in which the company's R&D may not have experience. For example, Pfizer partnered with Serono primarily because of its interest in that biotech's multiple sclerosis drug Rebif. While this drug was highly compatible with Pfizer's CNS portfolio, the company did not yet have a drug candidate to treat MS, so the pharmaceutical giant formed a development and commercialization alliance with Serono to gain access to its lucrative drug.

Similarly, creating a strategic alliance can also be a means of strengthening an existing therapeutic area, leveraging the experience in a market and improving the chances to remain competitive in that market. Aventis, for example, announced earlier this year its plans to seek in-licensing and alliance opportunities to supplement organic growth and enhance its in-house R&D efforts with high-value, late-stage products only within the therapeutic areas that are core for the company. Focusing on alliances at core TAs might also help a company diversify its R&D resources among other therapeutic areas, while still maintaining a strong pipeline in a core therapeutic area. Roche, for example, has a strong position in oncology and focuses its alliances on the diagnosis and treatment of cancer³.

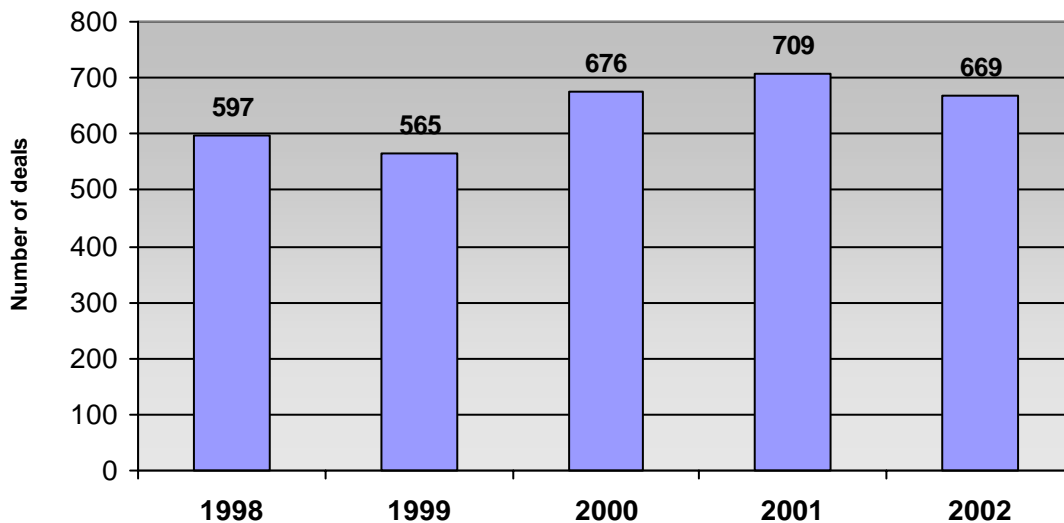
2.2. Opportunities for small biotech companies

On other side of the coin, biotech firms gain access to significant opportunities through alliances with big pharma. First, biotech firms need money to survive and continue their research and development efforts. When capital markets turn away from risky investments, biotech firms rely on pharmaceutical companies: in 2000, the amount of pharma-biotech alliances grew by almost 20% compared to 1999. In 2001 and 2002, the number of alliances only continued increasing. By the same

³ Out of 12 recent alliances that were noted in the media, 8 were directly linked to oncology.

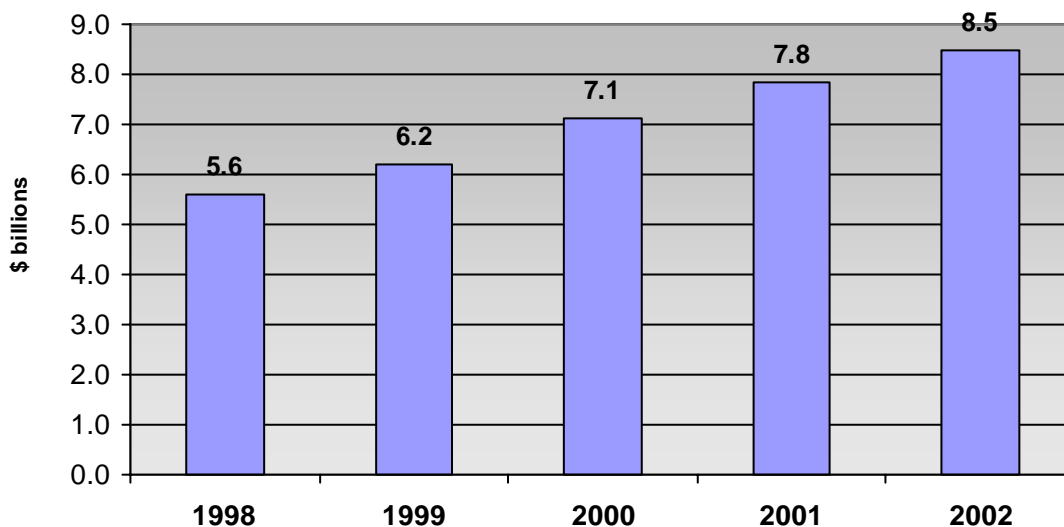
token, the total dollar volume invested in pharma-biotech alliances increased steadily from 1999 to 2002 by 14%, 10% and 8% respectively (Exhibits 2 and 3).

Exhibit 2 – Volume of Pharma-Biotech alliances (1998–2002)



Source: Windhover’s Pharmaceutical Strategic Alliances, Vol. XIV - Statistics and Trends 2003

Exhibit 3 – Total Dollar Volume in Pharma-Biotech Alliances (1998–2002)



Source: Windhover’s Pharmaceutical Strategic Alliances, Vol. XIV - Statistics and Trends 2003

Second, once a biotech company reaches the stage of developing and submitting clinical trials to the FDA, the presence of an experienced pharmaceutical company becomes a necessity. The

regulatory process of approving a drug is so complex and lengthy that it is easy for any company to make costly mistakes. The only factor that can help reduce mistakes in the approval process is previous experience. Since most biotech firms do not have previous experience, they often rely on pharmaceutical companies to help them through. In addition, late-stage clinical trials are extremely expensive—it would be very difficult for a biotech firm to manage through them without financing from a pharmaceutical partner. Moreover, in order for a drug to have the ability to compete successfully in the marketplace, a marketing force needs to back it up. As previously mentioned, biotech firms are only capable to develop R&D, but usually do not have resources to structure strong sales and marketing capabilities. Pharmaceutical companies thus complement their need for a marketing and sales arm, providing an efficient distribution channel to the new drug, once it is finally approved. This reason has been the backbone of various alliances, to the point that 12 out of the top 25 drugs today were discovered or developed by a company other than the one that launched them⁴.

Third, forging an alliance with a major pharma company may also improve a biotech firm's valuation in the market. According to a study by the National Bureau of Economic Research, biotech firms that signed deals received substantially higher valuations from venture capitalists and from the public equity market. As one can imagine, forming an alliance with a large and established pharmaceutical company sends a positive and validating signal to investors⁵.

Finally, biotech companies, which only a decade ago would have been happy to sell marketing rights, are now equally interested in acquiring new capabilities. Biotech companies are increasingly demanding participation in the design of clinical trials and the formulation of marketing campaigns, using alliances as a way to build capabilities in those areas. One example is the Indiplon deal signed by Neurocrine and Pfizer, in which Pfizer agreed to finance, create and train a 200 people sales force for

⁴ The McKinsey Quarterly, 2004 Number 1

⁵ Biotech-Pharmaceutical Alliances as a Signal of Asset and Firm Quality, Sean Nicholson, Patricia M. Danzon, Jeffrey McCullough, National Bureau of Economic Research, June 2002

Neurocrine and also gave Neurocrine the right to co-promote Zoloft together with Indiplon. A similar deal was made by Pfizer with Eyetech, in which Pfizer agreed to co-promote Eyetech's drug and help the company build its ophthalmology sales force, which will also sell Pfizer's Xalatan. Both of these alliances will be examined more closely later in this paper.

2.3. Overview of risks embedded in pharma-biotech alliances

The benefits of an alliance might be blindingly attractive at first, but a closer look reveals significant risks to both parties. The most apparent risk is the one inherent to the drug development, or, in other words, the risk that the drug which is the main subject of the alliance fails along the development process. This situation happens all too often and the risk is borne by both parties to the alliance. The pharmaceutical company loses time and potentially a significant amount of money, whereas the biotech firm loses most of its R&D investments, and usually a large portion of its total market value. The risk of an unsuccessful drug development process is usually higher for the biotech firm, for the simple fact that a pharmaceutical company has numerous alliances and parallel in-house R&D developments, all of which generally compensate for the loss in the long-term. The failure in a drug development process is much more detrimental to them, given their size and strong dependence on the success of that drug.

Secondly, there is the risk that the cultures of the two partners will clash and shake the stability of the alliance. This is particularly significant due to the highly different sizes, structures, management style and market position of pharmaceutical companies. This is an inherent risk to any type of strategic alliance but in the case of this asymmetrical type of alliance, this risk grows considerably. Biotech firms and pharma companies are two naturally different entities. While biotech firms are highly entrepreneurial and concentrated on innovative R&D, pharma companies are more established and have a much larger scale, thus being more conservative and slow. These two different worlds need to

work and make decisions together in an alliance. For that reason, it is evident that managing the differences in culture is a key component to any alliance. Thomas Honohan, Vice President of Alliance Management at Aventis, claimed that “the reason why most collaborations do not succeed is not the technical challenge, but the relationship challenge: it’s how the companies work together. Do they communicate clearly? Are they honest with each other? Is there trust between the partners?” The ability to successfully manage a strategic alliance is so crucial that most pharmaceutical companies have unfolded their alliance strategies on their websites, glorifying the importance they attribute to a strong alliance management team, recognizing the cultural obstacles for alliance. One of those examples is Eli Lilly, whose strategy relies on becoming the “partner of choice” for biotech companies, mainly through adjusting to the culture of smaller biotech firms. According to Sydney Taurel, Chairman and CEO of Lilly, the firm is not there yet: “if you look at the surveys, they usually place [Lilly] in the top three, but we want to become the best.”⁶

Specifically on the pharmaceutical companies’ side, many organizations may face the risk of weakening their own R&D departments after multiple alliance deals. As companies grow increasingly dependent on the fruits of alliances, such path may, at the end of the day, weaken their own R&D capabilities. In other words, alliances may supply growth to companies whose pipelines are weak, but an excessive focus on partnerships as opposed to developing in-house compounds may also represent a threat. The main reason behind that threat is the difficulty to retaining talented researchers by a company where R&D is left to a clear second priority (after marketing). Several analysts argue that this may be happening to Pfizer, as the company has relied excessively on alliances to launch new products in the last years.

Another issue associated to alliances is the fact that by creating an alliance (and not acquiring the partner), pharmaceutical companies forgo the ability to control the processes within that deal. Drug

⁶ “Lilly’s International Family” - Pharmaceutical Executive, March 2001, p.40

companies often times have to agree to let biotech companies lead the development of drugs, even though biotechs may be inexperienced in the clinical trial and regulatory processes. As a result, those processes may end up costing a lot more. Two well-known examples are the case of SmithKline (now GlaxoSmithKline), which in order to win rights for the cancer drug Bexxar agreed to let its owner Coulter Pharmaceuticals Inc. (later acquired by Corixa Corp.) take the lead in developing the product, only to see it stall for years at the FDA. A more recent example was the case of Bristol-Myers Squibb, that agreed to let ImClone Systems take the lead in filing Erbitux, after the small company had already done most of the development and regulatory work on it; the result was an FDA rejection and a severe damage to BMS's reputation in the oncology area.

On the biotech companies' side, the biggest risk is certainly the chance of being acquired by the company who was its ally. This was the case of Esperion, which had a co-marketing agreement with Pfizer and was then acquired by the pharmaceutical giant. Eli Lilly also started a development alliance with Applied Molecular Evolutions Inc., which was later acquired by Lilly. As partners, both companies share important information and are in privileged positions to evaluate the opportunities and threats associated with a drug under development. As the pharmaceutical company learns about the drug, the asymmetry between large and small companies is accentuated, making an acquisition likely—in case and at the time that the large company desires. For that reason, alliances can be perceived as a “trial period” in which pharma companies examine drug candidates; as soon as evidence for success concretizes, it may be cheaper for a pharma company to simply buy the biotech firm than continuing to deal with the management and profit sharing challenges of the alliance.

Another important risk involved in asymmetrical deals like these is the chance that a large pharmaceutical company only strikes a deal to lock in a biotechnology firm and prevent competitors from accessing that opportunity. An alliance also makes it more difficult for a competitor to acquire the biotechnology firm (many deals include a “right of first refusal” in case the company is liquidated).

This situation poses an enormous risk for the small biotech firm, given that the large partner may not be willing to invest in the rapid development of the drug, thus delaying the process significantly – to the detriment of the biotech firm. Already locked in the initial deal, the biotech company can't raise additional money and may gradually decline. A similar situation happened to Trimeris, a biotech which developed an AIDS drug, Fuzeon, and partnered with Roche for the development and marketing of the drug and additional drugs in Trimeris' pipeline. Fuzeon has since been approved by the FDA and achieved only sluggish sales. But in January, 2004, Trimeris and Roche put a hold on the clinical development of their second HIV drug. This leaves Trimeris without a single drug in clinical development and makes the company highly dependent upon Fuzeon to attain profitability. Since the sales profit from Fuzeon has not been so high and since most of the profit goes to Roche, Trimeris' future looks bleak.⁷

3. ANALYSIS OF REASONS BEHIND THE RISKS OF ASYMMETRICAL ALLIANCES

The previous section demonstrated that while it may be true that pharma-biotech alliances are win-win deals, one should not overlook the risks entwined in the benefits, and carefully check if there is potential for these risks to materialize. In this section, we will use some concepts learned in class to explain some reasons behind those risks.

3.1. From alliance to acquisition: when a product becomes core for the larger partner

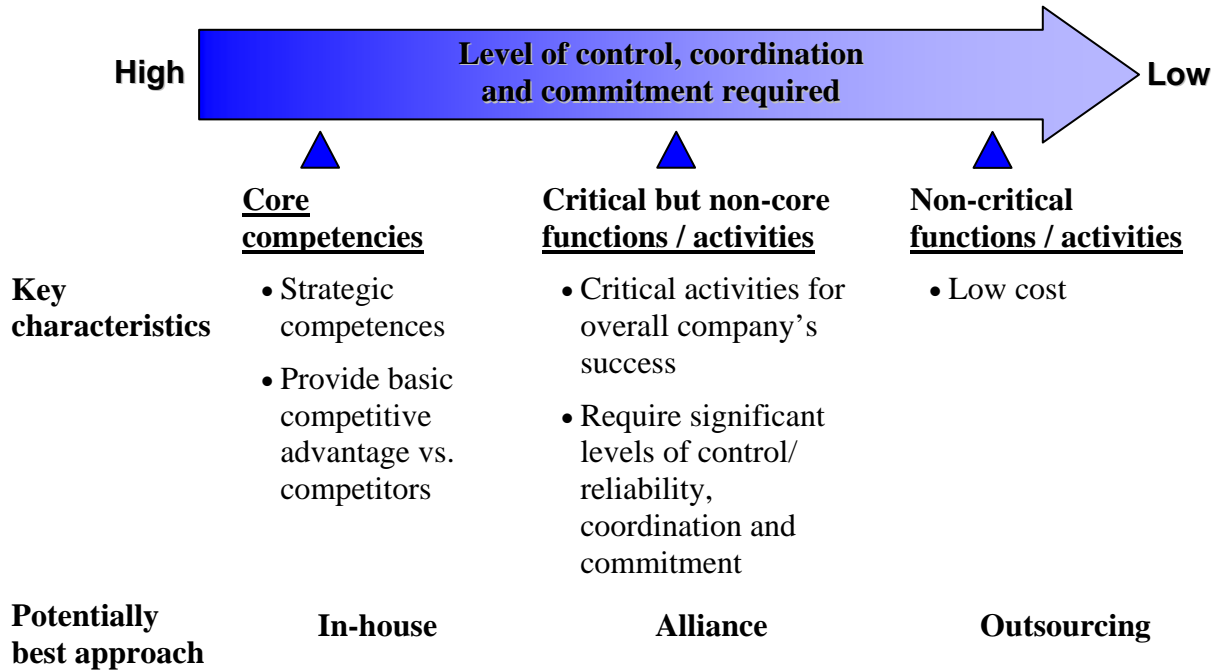
It has always been said that companies should know their core competencies, focus on doing what they are good at, and outsource the rest. With the addition of alliances to the reality of doing business, it is important to adjust that rationale accordingly, given that alliances are neither owning nor

⁷ In fact, mid-April 2004 Trimeris received a bill for \$7.5 million from Roche and it seems like this alliance is on its way to dispute.

outsourcing (they could in fact be interpreted as an “intermediate” level of commitment between owning and outsourcing).

Exhibit 4 presents a basic framework, seen in class, to guide the decision between doing an activity in-house, developing it with a partner or fully outsourcing it:

Exhibit 3 – Framework to decide between owning, partnering and outsourcing



Source: Adapted from MORS-454 class discussions

This framework helps explain why several asymmetrical alliances end up with the larger player acquiring the smaller one. In the pharmaceutical industry, Pfizer has been the protagonist of two large acquisitions of former allies: Warner-Lambert, acquired in 1999, and Pharmacia, acquired in 2002.

The first case originated in the alliance that Pfizer formed with Warner-Lambert, in 1995, to co-promote Lipitor, the cholesterol reduction drug developed by Warner-Lambert. After 4 years co-promoting the drug, Pfizer had seen Lipitor grow to become a blockbuster drug, in a therapeutic area that it dominated: cardiovascular drugs. Struggling to develop drugs in-house that could continue fueling its growth, the company had no choice other than the hostile takeover of Warner-Lambert, in

1999. The move called the attention of industry experts, as it exposed the challenges and potential threats embedded in alliances with a larger and dominant pharmaceutical company. An article of December 1999 reflected on Pfizer's radical move and emphasized that "licensors will become far more wary of entering into co-promotions—though the tactic will remain an important part of the industry. But the term length of deals, and thus their total dollar value to the licensor, will probably shrink." The move was seen as a change in the perceived dynamics of asymmetrical alliances, to the point that "few companies, apart from the very top-tier, will be invulnerable to takeovers"⁸

Indeed, the next large acquisition of similar nature did not take long to materialize. After years co-promoting Celebrex, a COX-2 inhibitor in partnership with Pharmacia, Pfizer bid on Pharmacia, in April 2002. The motivation behind the acquisition was remarkably similar to the one that led to the takeover of Warner-Lambert: Celebrex grew and became a multi-billion drug, while Pfizer remained unable to supplement its growth with its own drug pipeline. To make matters worse, the partners had just expanded their COX-2 franchise by launching Bextra, another COX-2 inhibitor. Again, Pfizer had no choice other than acquiring Pharmacia. This time, however, both companies were able to agree on a deal, crafting what was later often referred to as a "merger".

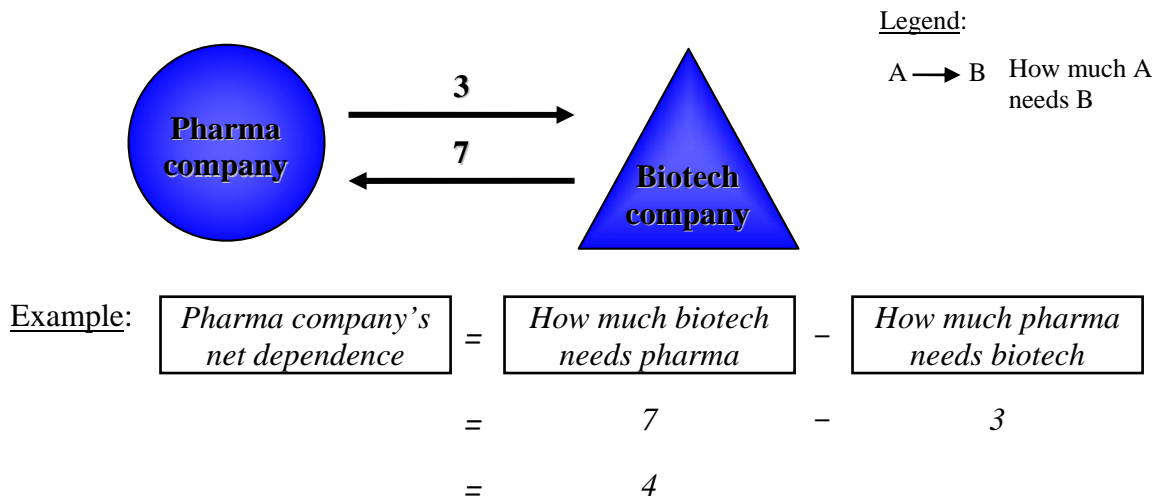
In both cases, Pfizer had allied with companies to co-promote products that later grew and became absolutely central for its own growth prospects. In the terms of the framework presented in Exhibit 4, Lipitor and the COX-2 inhibitors had moved from critical products to core products for Pfizer. As a result, Pfizer required a much higher degree of control, coordination and commitment than it could have through a partnership. That need led to the acquisition of its partners.

⁸ Longman, Roger - "Pfizer, Warner and the Drug Industry's Growth Crisis", InVIVO (December 1999)

3.2. “Net dependence” concept behind the dynamics of asymmetrical alliances

The Social Exchange Theory relies on the level of dependence between companies to evaluate the power that each company will have over the other in an alliance. The theory defines the concept of “net dependence” as the extent to which company A needs company B to survive, as explained in Exhibit 5, below:

Exhibit 5 – Social Exchange Theory as a predictor of power in alliances



Source: MORS-454 class material and discussions

According to the theory, the level of power of a company in an alliance is proportional to the *net dependence* of that company relative to its partner.

Analyzing the net dependence levels of pharmaceutical companies and biotech firms in typical alliances, we see that biotech companies usually need pharmaceutical partner more than the opposite. This happens particularly because of the large number of biotech companies, usually developing drugs that have uncertain potential in the future, but require financing in the short term. On the other hand, pharmaceutical companies are established firms, whose dependence on biotechnology firms comes from primarily their need for strengthening their pipeline and continue growing in their markets. They are not, therefore, directly dependent on any single biotechnology company with which they have an

alliance deal, whereas a biotechnology firm's survival usually depends on their alliance with the pharmaceutical company.

Given that dynamics, biotechnology firms are usually in a less powerful position, and should therefore not be surprised if their partners exert their power to their favor. Pharmaceutical companies certainly know of their power in this type of alliance and will naturally try to take advantage of that. One way for biotech firms to overcome that disadvantage could be emphasizing their alternative partner options (most large pharmaceutical companies are interested in partnerships with biotech firms developing promising drugs). However, biotech firms should also keep in mind that large pharmaceutical companies will hardly give up their advantageous position in an alliance; they will naturally expect to have more power than biotech firms. In that context, biotech firms that try to minimize the importance of that fact and act as an equal partner will often run the risk of getting negative responses from pharmaceutical companies, which in extreme cases could even lead to the termination of the alliance agreements.

In an industry like pharmaceuticals, however, virtually all large companies constantly need to make alliances deals to maintain a competitive position and continue growing. Consequently, large pharmaceutical companies have also been trying to carefully craft their image as good potential partners, in an effort to attract the best biotechnology firms and therefore put themselves in a privileged position versus other large competitors. This fact puts a natural limit to "abuses of power" by large pharmaceutical firms, as this might impact their long-term ability to continue attracting good partners.

From that perspective, Pfizer is described by experts as an aggressive company to partner with, particularly given their history of acquiring former partners. On the opposite side, Eli Lilly has

exploited that opportunity and developed an internal organization called “Office of Alliance Management”, with the objective of improving its image as “partner of choice” for biotech firms.⁹

4. FUTURE OUTLOOK: RISK ANALYSIS OF SELECTED ALLIANCES

Building upon many of the concepts and frameworks outlined previously, we will now examine several contemporary pharma-biotech alliances with an eye toward the potential strengths and risks of the deals. The first two examples involve pharmaceutical giant Pfizer in its co-promotion and licensing deals with Eyetech and Neurocrine. The third case will examine the joint venture between Eli Lilly and Icos.

4.1. Pfizer and Eyetech Pharmaceuticals

Pfizer’s near-unrivaled sales and marketing core competency makes it an attractive partner in resource and market-driven pharma and biotech alliances. In short, Pfizer offers unparalleled reach with its vast sales force, particularly in therapeutic areas often served by generalist physicians. Nevertheless, in the last few years Pfizer has undertaken several alliances that target specialized markets, such as their 2002 development, licensing, and co-promotion deal with then start-up Eyetech Pharmaceuticals (Eyetech [EYET] went public in 2/03).

Eyetech Pharmaceuticals is a small biopharmaceutical company focused on therapeutics to treat eye diseases. Eyetech has one principal product, Macugen, which will be submitted for fast-track FDA approval in 3Q 2004 for the treatment of age-related wet macular degeneration, one of leading causes of age-related blindness.

⁹ “Managing Alliances at Lilly”, InVIVO (June 2001), p.71-77

Key terms of the Pfizer – Eyetech Macugen deal are as follows:¹⁰

Upfront Financials:

- Pfizer paid an upfront licensing payment of \$75MM. Pfizer also made an upfront equity investment of \$25MM, which gave Pfizer a 9% stake in the start-up.
- Pfizer committed to a second equity investment of \$25MM; this payment was later agreed to take place at the Eyetech IPO at an agreed upon share price of \$19/sh.

Development and Commercialization:

- Pfizer agreed to “generally fund” the further clinical development of Macugen, both for age-related macular degeneration, and for an additional indication of diabetic macular degeneration. At the time of the deal, Macugen was in phase II/III for the first indication, phase II for the latter. Pfizer also agreed to fund other “ophthalmologic indications” for the drug, though no other specifics were given.
- Pfizer and Eyetech agreed to co-promote Macugen in the United States and to share the profits and losses from the US commercialization of Macugen. Eyetech retained the right to book all United States product sales. Further, Eyetech gained the right to detail Pfizer’s glaucoma drug, Xalatan, for a per detail fee and a percentage of sales generated.
- Pfizer gained license to commercialize Macugen outside of the US and pay net royalties on sales to Eyetech.

At-Risk Milestones:

- Pfizer is potentially obligated to pay up to \$195.5MM in milestone payments upon the completion of worldwide regulatory submissions and approvals for Macugen.
- Pfizer is potentially obligated to pay up to \$450MM in milestone payments upon the achievement of agreed upon sales levels for Macugen.

The Pfizer – Eyetech alliance exhibits many of the hallmarks of a trading alliance—both partners were able to gain access to dissimilar but highly complementary resources. What makes this alliance interesting, however, is the lengths to which Pfizer, the 900 pound gorilla in the industry, was willing to give power and resources to the fledgling start-up. For instance, Eyetech’s insistence to co-promote Macugen necessitates the creation of a commercial organization within Eyetech, a costly step

¹⁰ Eyetech Pharmaceuticals, S-1 Filing, www.sec.gov/edgar/

that seemingly duplicates the resource that Pfizer brings to the alliance. Further, Eyetech's detailing of Pfizer's Xalatan appears to be redundant with Pfizer's established sales force.

Eyetech's co-promotion moves make sense, however, when viewed through the lens of desired win-win of the alliance. Specifically, by having Pfizer subsidize and train its fledgling commercial organization, Eyetech accelerates its growth into a fully integrated pharmaceutical company (FIPCO), an evolutionary state rewarded with higher stock multiples than R&D-focused biotechs can often achieve. The development of a commercial organization decreases the likelihood that Eyetech will have to enter into marketing-focused trading alliances in the future, thereby ensuring that the profits from Eyetech's future products stay home. To help train its sales force, Eyetech will detail Pfizer's Xalatan as it awaits FDA approval for Macugen. A recent Eyetech announcement offered this perspective:

By participating in the detailing of Xalatan, we expect that our domestic sales force will be able to access and form relationships with retinal specialists and general ophthalmologists prior to commercial launch of Macugen. We view the Xalatan agreement as primarily a strategic arrangement and anticipate only a modest economic impact.¹¹

Though there is no indication that Eyetech has additional products of note in its pipeline, the creation of a tailored sales force under the tutelage of one of the world's most proficient sales organizations is a considerable win, particularly when coupled with the generous financial terms of the alliance.

From Pfizer's perspective, the creation of the Eyetech commercial organization does not necessarily represent redundant resources anathema to a trading alliance. Rather, under the terms of the deal, Eyetech's sales force will target Macugen to only the 1400 retinal specialists in the US who perform back of the eye procedures. Pfizer's sales force will thus be assigned to detail all general ophthalmologists, a target much larger and better suited to Pfizer's scale. By clearly delineating the

¹¹ Ibid.

targeted audience of both entities' sales forces, Eyetech and Pfizer avoid channel conflict which might both confuses customers and create tension in the alliance.

Ultimately, the success of Pfizer's "win" in its alliance with Eyetech will depend in large part on sales of Macugen. Currently, analysts estimate the drug, if approved, should reach the coveted \$1 billion in sales in its first year on the market.¹² Assuming this revenue will only grow as Macugen gains international approval and demographics of an aging population continue to increase, Pfizer is poised to earn back a great deal of revenue at a time when a number of its star products (Norvasc, Lipitor) are nearing patent expiration. Pfizer also gained considerably from their equity investments in Eyetech. At the current share price of \$36.75, Pfizer's two \$25MM equity investments are now worth almost \$150MM combined, a 200% gain in little over 18 months.¹³ Given Pfizer's penchant for purchasing past alliance partners, it will be interesting to see if Pfizer acts to acquire Eyetech, as well—particularly as they already hold over a 10% stake. Likewise, it will be interesting to learn if Eyetech might one day welcome being acquired by Pfizer, given that they have no certain products following Macugen and might be an unattractive candidate for alliances with other big pharmas given their close association with Pfizer.

4.2 Pfizer and Neurocrine Biosciences

In 2002, Pfizer embarked on another asymmetric alliance with a smaller biotech, this time Neurocrine Biosciences (NBIX). Neurocrine, based in San Diego, is focused on the development of new drugs to treat neurological and endocrine-related diseases. Pfizer's alliance with Neurocrine, as noted previously, focused on Indiplon, Neurocrine's treatment for insomnia. Indiplon is currently completing phase III trials with a NDA expected to be filed in 2004, and early reports indicate it to be an effective treatment with an attractive safety profile.

¹² Merrill Lynch estimate cited in "Pfizer's Visionary Partner", Fobes.com, April 14, 2004

¹³ $(\$25\text{MM}/\$9.10\text{sh}) + (\$25\text{MM}/\$19.00\text{sh}) = 4064042 \text{ shares}; 4064042 \text{ shares} * \$36.75 = \$149.3\text{MM}$

As with the Eyetech alliance, the Pfizer – Neurocrine alliance appears to be a trading alliance designed to couple Neurocrine’s key compound with Pfizer’s robust sales and marketing prowess.

Key terms of the deal include:¹⁴

Upfront Financing:

- Pfizer paid an upfront licensing fee of \$100MM.

Development and Commercialization:

- Pfizer agrees to pay all future third-party development, marketing and commercialization costs, save for pre-specified \$30MM in costs that Neurocrine will bear.
- Following NDA filing, Pfizer is obligated to pay for and support the creation of a 200-person Neurocrine sales force. This sales force will initially promote Pfizer’s anti-depressant, Zoloft, to US psychiatrists. Upon approval of Indiplon NDA, Neurocrine will co-promote the drug in the US.
- Pfizer has exclusive license to handle all international sales of Indiplon, with Neurocrine receiving a percentage of worldwide sales.

At-Risk Milestones:

- Neurocrine can receive up to \$300MM in milestone payments pending completion of pre-commercialization steps
- Following NDA approval, Pfizer will loan Neurocrine \$175MM “at commercial terms.”

On the surface, the Pfizer – Neurocrine alliance bears strong resemblance to the Eyetech alliance; both biotechs are gaining focused sales forces at the expense of Pfizer. Further, both new sales forces have gained rights to detail a Pfizer drug—in Neurocrine’s case Zoloft—to help forge relationships with pivotal physician constituencies prior to the approval of the biotech’s core drug. Lastly, both alliances contain financial terms that will handsomely reward each biotech pending completion of key development and commercialization goals.

¹⁴ Neurocrine Biosciences, 1Q 2004 10-K, www.sec.gov/edgar; Interestingly, Neurocrine licensed Indiplon in 1998 from DOV Pharmaceuticals, and DOV originally licensed Indiplon from what is now Wyeth. Neurocrine owes approximately 4% of Indiplon revenues to these licensors.

Despite these similarities in alliance structure, there are a number of key differences that suggest a different, and perhaps more risky, relationship between Pfizer and Neurocrine. First, this alliance is conspicuously absent of any equity stake. Though Neurocrine was a more “mature” biotech (NBIX IPO’d in 05/1996) than Eyetech at the time of deal, the absence of equity terms suggests that Neurocrine and Pfizer may have preferred to stay at greater arm’s length from one another than did Pfizer and Eyetech. Secondly, Neurocrine’s clinical development burden is significantly higher than for Eyetech, for whom Pfizer is covering all clinical development costs. For a deal potentially worth in excess of \$400MM in cash payments, it is curious that Neurocrine would be left on the hook to complete \$30MM worth of clinical development prior to NDA, particularly given that Pfizer agreed to cover all subsequent clinical costs for additional trials. Lastly, the at-risk milestone of \$175MM in loans “at commercial terms” is odd, again suggesting an arm length, perhaps more formal relationship between the two entities (how are “commercial terms” different than what Neurocrine might receive from a bank?).

One obvious answer to the differences in dollar amount and tone between the Pfizer - Eyetech and Pfizer - Neurocrine alliances might be that the two drugs—Macugen and Indiplon—have differing expected future revenues. As a result, Eyetech might be seen as having a lower net dependence on Pfizer than Neurocrine, and thus was able to extract better terms to its deal. To be sure, part of the differences between the two alliances may be explained by this straightforward supposition.

However, when contrasting the alliances, it is illuminating to consider additional reasons why Pfizer may have been less generous with Neurocrine. In contrast to Eyetech, Neurocrine has other key alliances with big pharma, specifically with GlaxoSmithKline for anxiety and depression, Wyeth for neurodegenerative and psychiatric diseases, and Eli Lilly for central nervous system disorders.¹⁵ In this light, Pfizer’s reluctance to impart Eyetech-equivalent terms to its alliance with Neurocrine may

¹⁵ Ibid. Neurocrine also has in-licensed a drug in mid-clinicals that would eventually compete with Pfizer’s Viagra in the erectile dysfunction category.

stem from the concern that a portion of every dollar extended to Neurocrine might go to fund development of drugs that might ultimately compete against Pfizer. If one were to visually map Neurocrine's alliances, Neurocrine's close involvement with multiple competing big pharmas might be contributing to a less stable alliance environment than for Eyetech. Given this threat of instability, the fact that Pfizer agreed to pay for and support the creation of Neurocrine's commercial organization is testament to the vast promise of Indiplon and the need of Pfizer to continually reload its blockbusters armamentarium.

4.3 Lilly Icos Joint Venture

Though Pfizer has been a leader in pursuing asymmetrical trading alliances, other large pharma organizations have been equally busy at alliances building, as well. One recent alliance that is now bearing fruit is the Eli Lilly and Icos Corporation joint venture supporting the commercialization and marketing of Cialis, an erectile dysfunction drug which competes against Pfizer's Viagra and Bayer AG's Levitra. Cialis was approved by the FDA in Q4 2003 and is Icos' only commercial product.

The key terms and structure of the Lilly Icos JV are as follows:¹⁶

Joint Venture Control:

- Lilly Icos JV is jointly controlled, 50/50, with equal representation on JV governing board
- Lilly Icos JV is co-located with Eli Lilly headquarters in Indianapolis (Icos is based in Seattle)

Upfront Financing

- Lilly agreed to pay \$75MM upfront licensing fee to Icos.
- Lilly agreed to create and fund a \$105MM pool to capitalize the joint venture

Development and Commercialization:

- Lilly Icos split all North American and European profits 50/50, and have equal rights to co-promotion in both geographies.

¹⁶ "Lilly Icos: A Complimentary Alliance," *In Vivo*, October, 2003, ps. 44-46.

- Lilly negotiated for rest-of-world (ROW) rights in exchange for 20% royalty to Lilly Icos JV, which then splits profits 50/50.
- Both Lilly and Icos can co-promote through each's sales force. Details are paid for by the JV at a predetermined price to whomever the sales entity is, in effect treating both Lilly and Icos sales forces as contract sales organizations to the Lilly Icos JV

At-Risk Milestones

- Lilly agreed to pay commercialization milestones of up to \$30MM

The Lilly Icos JV is notable for several reasons. First, the JV—much like the previous examples—is a trading alliance built upon the exchange of complimentary resources. In this light, Lilly Icos can be seen as a resource-driven JV. Second, Lilly Icos also handles potentially thorny co-promotion issues by explicitly delineating sales resources and contributions. Sales requirements are determined by a JV team staffed by both parent entities. Further, Icos has developed a specialized sales force of 165 people to focus principally on urologists; Lilly uses its vast scale to focus on the primary care physician market.

Where Lilly Icos has been truly pioneering, however, is in the evident desire shown by its two parents to put the interests of Cialis and the JV first. For instance, according to the original terms of the JV, Icos had the rights to develop a European sales force. Before proceeding, Icos recognized that European physicians often feel more comfortable interacting with well-established pharmaceutical organizations and not fledgling biotechs. As a result, Icos ceded the European sales market to Lilly reps. Lilly and Icos have shown admirable flexibility in other key decisions, too. For example, Lilly and Icos assigned JV functional responsibilities to employees from the parent that either had the expertise or greatest interest in taking on the new tasks. Consequently, Lilly now handles business-to-business marketing (HMOs and PBMs), direct to consumer marketing (seen as a strategic priority for

the parent), and marketing research. Icos, on the other hand, is developing a much desired skill in medical marketing to complement its nascent, specialized sales force.¹⁷

To date, the Lilly Icos JV has helped spearhead some very impressive gains by Cialis; six months post-launch, Cialis is already garnering 46% of all new scripts for ED. Ultimately, the strength of Lilly Icos JV does not lie solely with the business results it achieves. Lilly Icos has given each partner a supportive and dynamic environment to stretch and further refine the capabilities of its parent. For Icos, the JV has allowed for the development of highly trained specialty sales force and medical marketing competency. Further, Icos' equal footing in the JV has allowed it to achieve a visibility in the industry rarely obtained by small biotechs through vehicles such as co-branded consumer advertising and even Super Bowl ads.

For Eli Lilly, the JV represents an opportunity to aggressively enter and pursue a promising market opportunity. Also, the JV represents the significant opportunity for Lilly to stretch its functional capabilities and cultural norms to better prepare for a more competitive future. Through the JV, Lilly has gained valuable experience with mass-market direct to consumer advertising, widely believed to be a critical skill in the industry today. Lastly, time spent with a nimble and at times irreverent biotech has forced Lilly to confront its reserved culture and drawn-out decision-making norms. Lilly's JV experience has pumped fresh ideas and energy into the staid pharmaceutical manufacturer, a benefit, that while hard to monetize, is of profound value.

5. CONCLUSION

By examining the multiple interests that drive alliances, we have discovered that there is more to an alliance than the superficial complementary capabilities. While CEOs of biotechs and pharma companies frequently emphasize the obvious returns each company will generate from new alliances, it

¹⁷ "Small Companies Can Too Co-Promote," *In Vivo*, April 2004, ps. 43-46.

is those returns that are not so obvious that are the most interesting and usually can be better revealed (without inside information) by looking closely at the deal structure.

To a certain extent, coming into this project we believed that pharma-biotech alliances were, in general, clear win-win situations. Digging deeper into the rationales of the deals and by looking closer at concrete examples, we have discovered that in some cases the risks might outweigh the benefits and unless these risks are carefully handled in the alliance structure, their effect might be detrimental to the fate of the alliance or to one of the parties involved. A key lesson going forward is to carefully analyze the motives for the creation of the alliance, the goals each party has--both short term and long term—and to develop a deal structure that best mitigates the risks involved and provides the optimal chance for success.