The Bristol-Myers-Squibb - ImClone Deal

A Case Study

of

Changing Pharma-Biotech Dynamics

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Abstract

Bristol-Myers Squibb (BMY), an $80 billion pharmaceutical company, signed a landmark $2 billion dollar co-development and in-licensing deal with biotech firm ImClone Systems (IMCL) for a monoclonal antibody for cancer. The deal was the largest deal to date between a pharmaceutical company and a biotech firm. However, the FDA initially rejected the antibody, named C-225, citing invalid clinical trials.

This paper examines the motivations behind the deal from both BMY’s and IMCL’s perspective and seeks an understanding of the relative negotiating positions of the two parties. Two valuation frameworks are proposed and applied to determine the “fair” value of the deal. The agreement between BMY-IMCL is also examined from the perspective of the entire pharmaceutical industry. This paper seeks to employ the BMY-IMCL deal as a case study of an industry wide change in the dynamics between biotech firms and large pharmaceutical companies. This change has significant ramifications for the continued profitability of the industry at historic levels.
Introduction

The $400 billion a-year pharmaceutical industry is widely regarded as one of the strongest sectors of the economy. A decade of double digit growth, highflying stocks and some of the world’s loftiest profit margins have contributed to this impression\(^1\). However, it is becoming increasingly difficult for most of the larger pharmaceutical companies to meet the typical EPS (earnings per share) growth target of 10%\(^2\). Four years ago, the industry went through a wave of consolidation as it sought to boost the bottom line by driving cost savings from merger and acquisition synergies. This wave of activity created pharmaceutical behemoths with annual revenues in excess of ten billion dollars. For these companies, a 10% growth rate implied increasing EPS by at least a billion dollars each year. Over the last four years, realized synergies from the consolidation wave greatly reduced costs and brought about the required growth in earnings. Today, the potential for these cost savings has largely been realized. Bottom line growth must now come from top line expansion.

This poses a problem because it requires boosting the top line by 10% annually. This implies a significant rate of new product introduction – a difficult process due to the complexity of the underlying science and due to the regulatory intricacies in obtaining FDA approval before launching new drugs. The impending patent expiration of major blockbuster drugs compounds the problem. The drug development pipelines of most pharmaceutical companies are not robust enough to fill the anticipated revenue loss from blockbusters going off patent. Consequently, pharmaceutical companies have sought to preempt greatly decreased revenue streams by actively pursuing a strategy of in-licensing of potential block-buster drugs.

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This paper examines the motivations behind the deal from both BMY’s and IMCL’s perspective and seeks an understanding of the relative negotiating positions of the two parties. Two valuation frameworks are proposed and applied to determine the “fair” value of the deal. The agreement between BMY-IMCL is also examined from the perspective of the entire

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2 Yahoo Multex Investor – industry 5 yr growth average
3 Brand named Erbitux
4 The FDA has since agreed to accept a re-filing of the drug approval request, using data from European studies
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**The Big Pharma Perspective – BMY**

BMY is anticipating significant decreases in revenues from pharmaceutical sales. Pravachol, Glucophage IR, and Taxol - three of its top four blockbusters in 2001, will be off patent by 2005. These drugs represented combined revenues of $5.4 billion, or 35% of total BMY pharmaceutical revenues. Studies have shown that revenues from brand-name drugs decrease sharply once a drug goes off patent because the company cannot charge a premium for the drug and still expect to maintain the sales volume. With 35% of revenues currently generated by drugs with impending patent expirations, BMY has justifiable cause for concern. **Exhibit 1** shows the realized revenues for the period 1996-2001 for its top four blockbuster drugs in 2001. **Chart 1** shows BMY’s alarming dependency on the revenues generated by these drugs.

**Chart 1** uses the patent expiration dates as the basis of analysis because these dates are completely inflexible. Using alternative bases for analysis such as the date for the loss of marketing exclusivity is subject to greater variability; companies often litigate claiming patent infringement, and this tends to introduce significant variation in the impact on realized revenues. Note that for BMY the actual situation is worse – marketing exclusivity for these drugs expires before the patent expiration dates. For example, BMY is predicting “a $1.7 billion decline in sales due to loss of exclusivity for Glucophage IR”\(^5\) in 2002.

BMY’s pipeline is also not robust enough to cover the revenue losses associated with patent expiration. It has not had a brand-new drug approved since October 2000\(^6\). Further, a projected $3 billion-a-year blockbuster drug in its pipeline suffered a recent regulatory setback. BMY’s annual reports had been touting the promise of the antihypertensive Vanlev (omapatrilat) to achieve blockbuster sales. However, two large-scale clinical trials have cast doubt on the drug’s potential. In one study of more than 5,700 heart patients, Vanlev failed to beat Merck’s Vasotec in reducing death or hospital admissions due to worsening heart failure. In the second study, a potentially dangerous side-effect (angioedema) was observed with three times the frequency as observed with the Merck drug\(^7\). As a consequence, analysts are predicting maximum

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5 Press Release, BMY. December 13, 4:47pm EST. http://biz.yahoo.com/prnews/011213/nyth091_1.html
6 Forbes.com (03.20.02)
annual revenues of only $500 million for Vanlev, significantly less than the BMY projection of $3 billion.8

The Vanlev setback and a history of weak internal drug development casts a strong shadow over BMY’s internal pipeline. However, apart from specific instances where clinical studies come back unfavorable, or when drugs are rejected by the FDA, it is very difficult to get an accurate sense of the pipeline potential of a company. Most drugs under development are revolutionary and are heavily based on the complexities of the underlying science. These drugs are known to only a select group, and understood by even fewer people within that group. Consequently, new drugs under development tend to be disregarded in pipeline evaluations. This cannot be corrected for, however, it can be minimized by examining other factors in conjunction, such as the volume and size of in-licensing agreements. This analysis provides a sense of the company’s internal evaluation of its own pipeline vis-à-vis drugs under development by other firms. Large in-licensing deals, coupled with a limited history of new drug introduction, could potentially be indicative of weak internal resources. BMY fits this profile.

BMY has been forced to actively pursue in-licensing as a means of filling out its pipeline and of maintaining profitability. Not surprisingly, BMY’s current top four blockbusters are all in-licensed products. It has also engaged in the formation of numerous alliances to boost its access to new drugs. Exhibit 2 shows total alliance investment by BMY and Pfizer for the 1986-2000 period. Note that the BMY data excludes the investment in IMCL. Chart 2 shows the trend in total alliance investment for the two companies. Interestingly, Pfizer has been steadily increasing its alliance investment since 1996, while BMY has maintained approximately the same levels of investment year to year. For BMY, all this culminated in a massive investment in IMCL.

Pfizer’s own internal pipeline is much more robust than that of BMY. Further, its major drugs are not facing patent expiration. Pfizer’s alliance investments seem to be the result of a careful strategy of risk diversification. There are strategic implications to BMY’s alliance investment decisions; however, they are beyond the scope of this paper.

The BioTech Perspective - ImClone Systems

ImClone is an oncology focused biopharmaceutical company. It focuses on three strategies for treating cancer - growth factor inhibitors, therapeutic cancer vaccines and angiogenesis inhibitors.9 IMCL’s lead drug, C-225, is a growth factor inhibitor. It targets and

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8 ibid
9 Multex.com, ImClone Company Snapshot
inhibits the Epidermal Growth Factor receptor (EGFr) associated with tumor cell growth and repair.

On August 14 2000, the FDA agreed to evaluate C-225 based on data from only two test phases. Generally, the FDA requires three phases of drug testing before evaluating the effectiveness and marketability of drugs. This was followed closely by the FDA designating C-225 as “Fast Track”\textsuperscript{10} i.e. expediting the review process and potentially increasing the time that the drug could be marketed under patent protection. In fact, due to its “Fast Track” designation, C-225 became regarded as a potential blockbuster drug. This brought it to the attention of BMY.

From IMCL’s perspective, it lacked the marketing expertise to make C-225 a success. Its long list of collaborations included companies such as Merck, Abbott and DuPont\textsuperscript{11}, all of which could potentially provide the needed marketing expertise. (\textbf{Exhibit 3} shows list of collaborations). However, none of these companies had as well respected an oncology sales force as BMY, or were as committed to oncology. In fact, BMY described itself as “the number one provider, worldwide, of anti-cancer therapies”\textsuperscript{12}. Consequently, an alliance with BMY would enable IMCL to leverage BMY’s sales force to expedite C-225’s penetration to formularies and wholesalers. This would serve three purposes – accelerate sales of C-225, free IMCL resources for the development of other promising pipeline oncology products, and provide IMCL with the experience of developing a platform to market and sell its products.

Funding was not an issue for IMCL. The public markets had been friendly, and the rapid progress of C-225 through the regulatory channel had done much to strengthen IMCL’s access to adequate financing. IMCL concluded a secondary public offering in November 1999, and raised $80 million\textsuperscript{13}. \textbf{Chart 3} shows IMCL’s stock performance over the last five years. During the 2000-2001 period, the stock was above $40/share. Clearly, the secondary stock offering market remained a viable funding option for IMCL.

\textbf{Examining the Agreement}

On September 19 2001, IMCL entered into an agreement with BMY to co-develop and co-promote C-225. The terms of the agreement ran through at least 2018, and had three components. The first component was a $1.2 billion equity investment in IMCL by BMY (19.9% of outstanding equity); the second was a total of $0.9 billion in three cash payments for the achievement of the following milestones: signing of the agreement, completion of the Biologics

\begin{footnotes}
\item[10] February 1, 2001
\item[13] Source: www.ipo.com
\end{footnotes}
License Application submission with the FDA, and marketing approval of C-225. The final component gave IMCL a significant share of the product revenues (39%)\textsuperscript{14}.

This deal was the largest to date between a pharmaceutical company and a biotech firm. The huge amount of capital invested in this deal highlights its importance for BMY. Having spent $16.5 billion on R&D since 1990, without producing a single new “star” of its own\textsuperscript{15}, BMY’s internal drug development efforts were clearly not paying off. Its drug leadership position in oncology was under threat, and BMY was willing to pay heavily to defend its position.

**Exhibit 4** shows alliance investment by BMY since 1986. **Chart 4** shows total alliance investment by therapeutic category (note that both exclude the deal with IMCL). **Chart 4** highlights the importance of oncology for BMY. It spends a commensurate amount on oncology related alliances as it does on alliances for the general purpose broad-based screening technology. This commitment to oncology would to some extent justify the large capital investment.

However, the deal is better explained by examining the relative bargaining positions of the two firms. IMCL, adequately funded, with a large number of collaborators, and with a potential blockbuster oncology drug under its control, was clearly in the driving seat. BMY’s oncology leadership was under threat, both from expiring patents on its leading oncology products as well as from the possibility that a competitor could form an alliance with IMCL and acquire the rights to C-225. BMY risked losing its position with opinion leaders, which would affect all future drugs it introduced. Coupled with an appalling internal R&D track record and a weak development pipeline, this implied that BMY was clearly not dictating the terms of the alliance.

**Pricing the Agreement**

In light of the above analysis, it is interesting to ponder whether BMY overpaid IMCL. There are two ways of examining this.

One method involves projecting C-225’s cash flows and determining their present value. Multiplying these cash flows by a probability of realization would give some sense of the “fair value” of C-225 to BMY. Note that this method is conservative in that it does not explicitly take into account the fact that BMY’s equity stake provides it with a proportional share of other products in IMCL’s pipeline. However, the value of pipeline products is very speculative and estimates are subject to very high variation. Neither does this method explicitly price the competitive aspect of the deal i.e. BMY may have been willing to overpay to preclude a competitor from acquiring the product. However, these two issues notwithstanding, this method

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\textsuperscript{14} Source: Yahoo Multex Investor
\textsuperscript{15} The Wall Street Journal, Thursday, April 18 2002
serves as a good estimate of the value of the deal. It is a calculation likely to have been performed by BMY.

Revenues of Taxol for the period 1994-2001 were used as a proxy for the future revenues of C-225. Thus, C-225 revenues were projected until 2010. Sales were projected to start in 2004. A terminal value of $1 billion was used to estimate the value of all future sales. Note that this is a very conservative assumption. Taxol will very likely have sales close to that number in 2002 alone, implying a much higher terminal value equivalent for C-225. BMY’s equity stake in IMCL was taken into account in estimating the PV of C-225 cash flows. Present values conditional on various probabilities of success were computed to gain an insight into the milestone structure of the deal. Exhibit 5 provides the analysis methodology.

Some interesting conclusions emerge. The initial investment by BMY was approximately $1 billion, and this corresponds to a success probability of 0.45. Each milestone achieved increases the probability of success; with success probability 0.9, the conditional PV increases to approximately $2 billion. Note that the exact definition of what each probability number implies is open to some interpretation. A success probability of 1.0 is associated with realizing sales exactly equal to those of Taxol i.e. in some sense it requires C-225 to achieve blockbuster status. FDA approval is associated with success probability less than 1.0 - merely obtaining FDA approval does not ensure consumer acceptance. However, given C-225’s “Fast Track” classification and positive opinion leader reactions, FDA approval is likely to correspond to a success probability of approximately 1.0.

Consequently, this interpretation suggests that BMY did not overpay IMCL. However, the deal did not leave much value for BMY either i.e. it paid almost exactly what it would expect to receive. This is indicative of an increase in the bargaining power of well-funded biotech firms; they can extract maximum value from their alliances with big Pharma.

Alternatively, we can consider a staggered options framework to analyze the deal. BMY did not purchase IMCL outright, but only took a 19.9% equity stake. This gave it sufficient control as a major shareholder, but also minimized the capital at risk from C-225 not living up to expectations. The milestone payment structure enabled BMY to manage the risk associated with its investment in IMCL. We can view the investment as a series of staggered call options on IMCL with strike prices equal to each of the milestone payments, and with the underlying asset being the cash flows from C-225 to BMY. As calculated in Exhibit 6, the amount paid for these options is the difference between the value of 19.9% of IMCL equity and the price BMY paid in the first installment. Thus, the amount paid for the staggered options framework is $326.5 million.
We can price the options framework using the Black Scholes Formula. Let the underlying asset be the present value of the cash flows from Taxol, as projected in Exhibit 5. Let the strike price be the sum of the milestone payments, and the duration be the term of the contract i.e. 17 years. Assume that the variance in the underlying asset is 0.25. This is an assumption; however, the sensitivity analysis on the variance shows that small differences in the chosen value for the variance do not affect the call option value significantly. Further, note for comparison that the annualized variance of BMY’s daily stock returns between January 1999 and Dec 2001 was 0.17. The projected cash flows are likely to have a volatility of approximately the same value if we assume that Taxol and other drug cash flow volatilities are reflected in the stock return volatility of BMY. Exhibit 6 provides these calculations.

The options framework leads to a very interesting result – it suggests a value gain by BMY of approximately $1.4 billion as a result of this transaction. From an options perspective, the deal is positive NPV for BMY. This results from mainly three effects. First, the call option structure of the milestone payments is explicitly taken into account in this pricing calculation, as opposed to the projected cash flows valuation mechanism. Further, the term of the contract is explicitly taken into account. The long timeframe to maturity increases the value of the call option. Finally, by providing BMS with the option, but not the obligation, to make the milestone payments, the competitive aspect is priced to some extent as well. Note that taking into account the pipeline product ownership from BMY’s equity stake in IMCL would increase this value further. In fact, the interpretation that results from the staggered options framework is very similar to the data table of success probabilities and the associated conditional present values of C-225 cash flows suggested by the discounted cash flow valuation mechanism.

The conclusions from the two valuation methods are similar in that neither suggests that BMY overpaid; however, one suggests that the relatively stronger bargaining position of the biotech IMCL implied that less value was left on the table for BMY. Further, note that statistically speaking, in an expected sense BMY stood to, at worst, break even from the deal. However, even a small variance in the outcomes implies the possibility that BMY would lose money. Hence, the variance of the outcomes also becomes a relevant metric for evaluation. From this point of view, BMY’s position was less secure. Effectively, IMCL was dictating the terms of the agreement. This is a growing trend in the industry.
The Industry Context

Across the pharmaceutical industry, there is a trend of weak drug development pipelines and impending patent expirations. **Charts 5, 6, and 7** show the effect of patent expirations from different perspectives.

**Chart 5** shows the exposure of some of the major pharmaceutical companies to patent expiration on a yearly basis. Note that Pfizer alone seems to be in a relatively good position – its exposure is mainly limited to 2000. BMY, on the other hand, has an evenly spaced exposure until 2005. Vis-à-vis Pfizer, BMY is likely to feel the effects of patent expiration for a longer duration and hence to a greater extent. **Charts 6 and 7** examine the top ten blockbuster drugs in 2000 (**Exhibit 7**) and chart the ‘revenue at risk’ from patent expiration. ‘Revenue at risk’ is defined as revenues from the drugs in 2000, which patent expiration puts at risk. Assuming a constant gross margin, revenue at risk is an excellent proxy for the contribution of the blockbusters to the bottom line numbers of the respective companies. Patent expiration puts this contribution to the bottom line at risk as well.

Across the board, the large pharmaceutical companies are all facing decreased revenue streams from patent expiration. For the top four blockbusters as a whole, approximately $4 billion is at risk for each of the years between 2001 and 2010 (**Chart 7**). As **Chart 6** shows, there is very little variation in the exposure of the drug companies to patent expiration.

Determining the robustness of company pipelines is relatively more difficult. Apart from the difficulty in quantifying the potential revenue streams of an exploratory drug, companies are not forced to disclose full details about their pipeline. However, as indicated earlier, pharmaceutical companies have been pursuing a strategy of in-licensing to compensate for weak drug development pipelines. Examining some of these in-licensing deals can provide an insight into the pipeline potential of the larger pharmaceutical companies. It can also suggest implications for the relative bargaining positions of biotech and big Pharma.

An analysis of recent deals suggests an increasing ability of the biotech firms to drive favorable contracts, both in terms of initial monetary value and in terms of revenue sharing from potential product commercialization. For example, in September 1998, Millennium and Bayer signed a $465 million deal for the broad based discovery of genomics based drug targets. The primary goal of the alliance was for Millennium to supply 225 new drug targets in seven different indications relevant for cardiovascular diseases, cancer, pain, hematology and viral infections. The deal was hailed as a landmark deal at the time.\(^\text{16}\)

\(^{16}\) Class lecture by Ms. Ertel
Recent deals are typically akin to the BMY-IMCL deal or the Curagen-Bayer deal. The $1.3 billion Curagen-Bayer deal was for genomics derived targets for obesity and diabetes, with Curagen receiving 44% of the profits. Similarly, as mentioned, the BMY-IMCL deal gave 39% of net sales plus manufacturing fees to IMCL. In contrast to the Millennium deal, the deals of today involve higher monetary payments, in terms of both upfront investment and milestones, and allocate a much higher share of the profits to the biotech firm.

These, and other similar deals, signal a change in the dynamics between biotech and big Pharma. Increasingly, biotech firms are well funded and have better access to financing. They do not need to rely exclusively on the benevolence of big Pharma to support their research and development. This translates into biotech firms only forming alliances with big Pharma at later stages of drug development mainly to get access to sales forces and clout with the distribution channels. A lessening dependence on big Pharma implies higher payouts, and more favorable revenue sharing terms. Further, as more blockbusters go off patent, and pipelines fail to deliver, this dependence will lessen even further. Big Pharma will turn increasingly to biotech alliances to maintain profitability, and in so doing erode even the slight ascendancy that it now enjoys.

**Conclusion**

The BMY-IMCL deal is symptomatic of changing industry wide dynamics. Biotech is beginning to carry increasing competitive sway. For big Pharma, the outlook is grim. The complexities of the underlying science are such that merely investing or forming alliances with biotech firms is not enough to ensure profitability. Deals can, and do, fail to perform. BMY wrote off $735 million of its investment in IMCL after C-225 was rejected by the FDA. However, to refrain from making such alliances is also not a competitively viable strategy. Some alliances can be huge winners.

It is a game of chance. Other large pharmaceutical companies have made similar large investments in biotech firms, and are also playing the odds. While the BMY-IMCL fallout is the first such deal to go sour, given the vast number of large deals that have been made, it is not likely to be the last.
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