Business models and investment trends in the biotechnology industry in Europe

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Abstract This paper considers the continuing evolution of biotechnology company business models in relation to investment trends in the European public and private markets and in relation to the evolution of the industry as a whole. The origin, value generation potential, risk profile and revenue stream of the fully integrated pharmaceutical company (FIPCO) business model, the product business model, the platform or tool business model and the hybrid business model are reviewed and contrasted. Investment trends in the public markets are explored with reference to the 2001 performance of the European initial public offering (IPO) class of 2000, highlighting the fact that, in Europe, the individual public markets have had a more significant impact on biotechnology stock performance than have business models. Private equity and venture capital investment in European biotechnology companies over 2001 is examined, with trends demonstrating the continued attraction of the hybrid business model. Finally, the future evolution of biotechnology business models is considered in the context of their interrelatedness to the pharmaceutical industry and the rapid pace of technological advancement in the industry. While a small number of companies with access to a large supply of capital may be able to complete downstream integration and revert to the FIPCO model, the majority of biotechnology companies will instead need to further develop sophisticated relationship management skills in order to extract greater value from relationships with customers, collaborators and partners.

Keywords: business model, product, platform, hybrid, value generation, investment trend, Europe, relationship management

Introduction

While the dramatic rise and fall of the dotcom company has increased the profile of business models in general, in a bear market investors inevitably re-examine industry business models. Therefore, since the first quarter of 2000, biotechnology industry business models have come under close scrutiny from management and investors alike.

Generating value from innovation

Fundamentally, the business model outlines how a company generates revenues with
reference to the structure of its value chain and its interaction with the industry value system. A more explicit definition is offered by the consulting firm, KMLab, Inc.: a business model is a description of how your company intends to create value in the marketplace. It includes that unique combination of products, services, image and distribution that your company carries forward. It also includes the underlying organisation of people and the operational infrastructure that they use to accomplish their work.

For a biotechnology company, the business model serves to secure value from the company’s proprietary technology and know-how, and is currently often heavily reliant on large pharmaceutical or established biotechnology company customers, collaborators and partners. To be successful, such relationships must generate value for both parties and, therefore, there is a need to align the interests of biotechnology companies with those of their partners. A large pharmaceutical company may base its valuation of a technology on its ability to address a known problem in a more cost-efficient manner (for example high-throughput screening approaches to address bottlenecks in drug discovery) or its ability to generate novel and innovative solutions (for example novel drug target identification and validation).

It is important to recognise that the relationship between a company’s position in the biotechnology industry value system and its ability to generate value is not linear. This results from the dynamic nature of the industry value system (driven by rapid technological development) and the fact that the relationship between time spent in drug development and value generation is not linear. These interrelationships have impacted the evolution of biotechnology company business models over time.

The evolution of biotechnology business models

Institutional frameworks are recognised to strongly influence the development of business models. For the first biotechnology company, Genentech, Inc. (founded in 1976), this coupled with the founding management’s experience and industry perspectives resulted in the adoption of the fully integrated pharmaceutical company (FIPCO) business model, today epitomised by the success of Amgen, Inc. Among the first founded European biotechnology companies, British Biotech plc most notably pursued this goal, spurred on by the new availability of capital in the UK. The attraction of this vertically integrated model in terms of value generation was apparent: by managing and controlling the entire value chain, the companies hoped to maximise and sustain a superior financial return. However, in so doing the companies were also maximising the level of risk, with high levels of financing required to establish and maintain the FIPCO infrastructure and to fund drug development through to commercialisation. While the FIPCO model proved a successful path to profitability for Genentech, Inc. and Amgen, Inc., many companies had difficulty sustaining the levels of financing required to support this high-risk strategy, particularly when faced with late stage product setbacks.

The existing biotechnology business models have since evolved to meet market needs and deliver economic return. Whether a biotechnology company is a start-up or spin-off, the business models reviewed are broadly applicable. However, the relationship and licensing arrangements between spin-off and parent will ultimately impact the spin-off company’s business model.

The product business model

This business model has its origins in the FIPCO and aims to generate value in progressing products along the drug development process and either licensing them out to pharmaceutical and top tier biotechnology companies or, when the company has reached maturity and there is free cash flow available, taking them straight through to commercialisation. It generally takes 10–20 years to reach this
Business models and investment trends

level of maturity, although orphan drug legislation offers the opportunity to accelerate free cash flow generation. It is still a relatively high-risk model, although companies may partner initial products at an early stage of development to mitigate this risk. The majority of companies follow the classic product business model, having both drug discovery and development capabilities. European examples include Actelion Pharmaceuticals Ltd, Celltech Group plc, NeuroSearch A/S, NicOx SA, Novuspharma SpA and Shire Pharmaceuticals Group plc. However, these companies have all achieved the same end point via very different paths. For example, Actelion established drug discovery and development capabilities from the start and created a late stage pipeline through licensing in two drugs from Roche. By contrast, Shire Pharmaceuticals established development and marketing capabilities for in-licensed products and has only very recently established an in-house drug discovery capability through merger and acquisition activity. Relatively few companies today follow the virtual product business model as established by Shire Pharmaceuticals in 1986 and Vernalis Group plc (formerly known as Vanguard Medica Group plc) in 1990, relying on in-licensing in place of a discovery capability. This business model was formulated on the expectation that a management team with a successful clinical development track record would achieve greater success in compound selection and development and is not yet considered well proven.

As 19 of the top 22 biotechnology companies in the world with market capitalisations in excess of US$3bn are classed as product companies, the product business model is considered a proven model.

The platform or tool business model

This is considered a relatively new business model in the biotechnology industry, dating back to the late 1980s, although it has been around for some time in other high-technology industry sectors. It aims to generate value (predominantly from the front end of the industry value system) through licensing fees, subscriptions and service fees and can include the provision of new research tools (eg LION Bioscience AG), informatics (eg Compugen Ltd and Inpharmatica Ltd) and/or services and reagents (eg Qiagen NV). The evolution of the platform/tool model was driven by the need to reduce the risks in drug development through applying technological advances to drug discovery. The model rapidly became established in Europe, as there was a need for companies to generate near-term revenues to compensate for the lack of venture capital financing in comparison to their US counterparts. With what was perceived to be a lower-risk approach, the platform business model rapidly became popular with continental European investors. However, the attraction started to wear off in 2000 with concerns regarding the model’s ability to sustain value generation (ie market size and margins). In addition, many investors no longer perceive the platform model to offer a truly low-risk investment opportunity in the face of commoditisation and technology obsolescence. At the end of September 2001, Celera Genomics Group (Celera) and Qiagen NV remained the only platform biotechnology companies in the world with market capitalisations in excess of US$1bn, reflecting market sentiments. However, Celera’s parent company, Applera Corp., announced its downstream integration plans in July 2001 and Celera is now seen to be moving into drug discovery and transitioning to the ‘hybrid’ business model in an effort to maintain growth.

The hybrid business model

This business model is a hybrid of the product and platform business models and generally constitutes a platform technology capable of generating a pipeline of products. This model can be considered to be an evolution of the platform model, which aims to extract greater sustainable value from the industry value system through downstream integration. Several companies that
originally operated a platform business model, for example Millennium Pharmaceuticals, Inc. and Human Genome Sciences, Inc., have been able to move downstream to the hybrid business model in an attempt to capture greater value. In addition, over the past year, an increasing number of platform companies, including GENSET SA, have announced their own plans for downstream integration.\textsuperscript{6,11} The pipeline of products can be developed either organically through leveraging the company's own technology platform (e.g., Cambridge Antibody Technology Group plc, Crucell NV) or acquisitively through the in-licensing of product development opportunities (e.g., Oxford GlycoSciences plc, Medigene AG).

However, a transition from the platform to product business model is not without its difficulties. Timing is critical, to ensure the company maintains a healthy balance between the contributions of the platform and product components to the business, ideally maximising revenues from the platform to assist in financing the transition. Management skills to achieve this transition generally need to be specifically recruited and must include a strong track record in the planning and execution of clinical development programmes and the ability to raise the capital to meet the increasing cash burn requirements. As for the product business model, companies employing the hybrid business model often rely on partnering with pharma/top tier biotechnology companies to complete development and commercialisation.

The convergence of the product and platform business models to create the hybrid model affords investors the benefit of the reduced risk and downside protection associated with near-term revenue generation, without compromising the potential for greater value generation. As a result, it has become the dominant business model of the industry (Figure 1).

**Investment trends**

Investors have the power to drive the evolution of biotechnology company business models through their aim to maximise value generation and minimise investment risk.

**The public markets**

Kleinwort Benson, encouraged by British Biotech plc, assisted in rewriting the London Stock Exchange (LSE) listing rules and opened up the European public markets for

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![Fig. 1 The convergence of European biotechnology business models](image-url)
biotechnology companies in 1992, following the success generated by the US industry. Continental European markets followed with the introduction of high-technology oriented markets such as Easdaq and the Nouveau Marché in 1996, the Neuer Markt in 1997, the SWX New Market in 1999 and the rewrite of the Amsterdam Stock Exchange listing rules in 2000 to allow Crucell NV to float. In contrast to the UK, many of the new continental European companies followed the platform business model. This was particularly evident in Germany where a lack of venture capital necessitated the generation of near term revenues.

Several significant product setbacks in 1997 raised concerns in the UK public market that the level of risk outweighed the potential investment returns. Being a relatively immature market, the negative news had an impact on the entire UK biotechnology industry. The UK market remains cautious; however, similarly negative product development news from Scotia Holdings plc and Cantab Pharmaceuticals plc in 2000 did not affect the entire sector, suggesting that the UK market had achieved critical mass and a level of maturity similar to that seen in the USA, with investors able to differentiate companies. This contrasts with the less mature high-technology European markets and particularly the Neuer Markt, where biotechnology companies are suffering from the effects of an inflated initial public offering (IPO) market in 2000 and the collapse of the high-technology stock markets. To restore investor confidence, the Neuer Markt began its second tightening of listing requirements in July 2001, allowing penny stocks and insolvent companies to de-list. At the end of 2000, there were 10 European companies with market capitalisations above €1bn (six product companies, two platform companies and two hybrid companies). At the end of September 2001, only the top five companies remain above the €1bn mark (Elan Corporation plc, Serono SA, Shire Pharmaceuticals Group plc, Celltech Group plc and QIAGEN NV) and the youngest of these companies was established 15 years ago. The younger, less-established companies, which were above the €1bn mark at the end of 2000, have seen their market capitalisation driven down by the market correction following the run up on monoclonal antibody and genomic stocks and key product setbacks.

Classification of the 39 European IPOs of 2000 by business model, in Figure 2, highlights the predominance of the platform model (33 per cent of companies) and the growing importance of the hybrid business model (26 per cent of companies). The remaining 10 companies, not shown in Figure 2, were considered to warrant separate classification as either medical device, drug delivery or other service companies.

A review of the performance of the above companies’ stocks in 2001 (Table 1) indicates very little difference in the public markets’ perceptions of the three main business models, although companies following the hybrid business model did perform marginally better. This is in contrast to data published earlier this year by BioCentury Publications, Inc. (BioCentury), which indicated that, on a global basis, companies following a product business model significantly outperformed companies following a platform/tool business model, with product companies showing on average a 19 per cent reduction in market capitalisation since IPO and platform/tool companies showing on average a 40 per cent reduction in market capitalisation.

The classification of companies by business model is not black and white; the boundaries are blurred and there is, therefore, a degree of subjectivity involved: platform companies may be transitioning to the hybrid model and hybrid companies may be transitioning into product companies. Therefore, this may in part account for the differences observed. However, it is important to consider the fragmented nature of the European market. A review of the performance of the same 39 companies by market over 2001 (Table 2)
Fig. 2 Classification of the European IPOs of 2000 by business model. For classification purposes, platform companies generate revenues through the licensing of their technology platforms; product companies develop products exclusively and do not license out their technology for fees; and hybrid companies are a combination of both models.

Table 1 Performance of the European IPO class of 2000 over 2001, grouped by business model

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<tbody>
<tr>
<td>Platform companies</td>
<td>4,542</td>
<td>1,466</td>
<td>-68%</td>
</tr>
<tr>
<td>Hybrid companies</td>
<td>2,880</td>
<td>1,165</td>
<td>-60%</td>
</tr>
<tr>
<td>Product companies</td>
<td>3,344</td>
<td>1,270</td>
<td>-62%</td>
</tr>
</tbody>
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* Source: DataStream

Table 2 Performance of the European IPO class of 2000 over 2001, grouped by market

<table>
<thead>
<tr>
<th>Market</th>
<th>No. of companies</th>
<th>Combined market capitalisation at 1st Jan., 2001* (€m)</th>
<th>Combined market capitalisation at 28th Sept., 2001* (€m)</th>
<th>Change in market capitalisation from 1st Jan., 2001 to 28th Sept., 2001</th>
</tr>
</thead>
<tbody>
<tr>
<td>London Stock Exchange</td>
<td>6</td>
<td>1,722</td>
<td>1,079</td>
<td>-37%</td>
</tr>
<tr>
<td>Nasdaq</td>
<td>4</td>
<td>1,066</td>
<td>626</td>
<td>-41%</td>
</tr>
<tr>
<td>AIM London</td>
<td>5</td>
<td>403</td>
<td>236</td>
<td>-42%</td>
</tr>
<tr>
<td>Neuer Markt</td>
<td>11</td>
<td>3,958</td>
<td>820</td>
<td>-79%</td>
</tr>
</tbody>
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*Source: DataStream
Note: The Amsterdam, Copenhagen, Helsinki, Nuovo Mercato, Oslo, Stockholm, SWX New Market are not included in the above analysis. These markets listed only one or two life science companies in 2000 and as such, the data are considered to be company- rather than market-related.

highlights significant performance differences by market. As expected, the more mature markets such as the LSE and Nasdaq show significantly better performance than the Neuer Markt. Although the relative predominance of platform companies and dearth of product companies listed on the
Neuer Markt will have affected the performance of this market, it is still reasonable to conclude that in the fragmented European public biotechnology market, the specific market has had a greater impact on stock performance to date than company business models. When considering global rather than European IPOs of 2000, the vast majority of companies listed on Nasdaq. Therefore, it is likely that the global data published by BioCentury reflects the ability of investors in a more mature and established market, such as Nasdaq, to differentiate companies on the basis of their business model.

The private markets

60 European biotechnology companies received a total of US$859m in venture financing in the first three-quarters of 2001.14-15 A review of the business models of the companies which were successful in raising financing indicates that over 70 per cent of the financing was received by companies operating the hybrid business model (Table 3).

The average venture financing raised by a hybrid company was US$18.2m, which is over twice and a half times more than the US$6.8m average venture round raised by a platform company. Although this difference in part reflects the disparity in cash burn requirements of the two models, it may also reflect the fact that investors are willing to finance earlier stage platform companies, with the expectation that these companies will change to the hybrid model over time.

These trends confirm the dominance of the hybrid business model in the venture capital and private equity markets, the attraction being the downside protection conferred by near term revenues and the upside potential relating to successful product development.

Venture capitalists, through their close involvement with and support of investee companies, have the power to drive the evolution of biotechnology business models from the early stages of company development, in anticipation of future public market needs. While many stakeholders have the ability to influence the evolution of the biotechnology industry, it is arguably the venture capitalists, the pharmaceutical industry and the leading biotechnology companies that will steer the evolution of industry business models going forward.

Industry evolution

The biotechnology industry is characterised by rapid technological change and advancement, which gathered momentum in the 1990s, with notable breakthroughs such as the Human Genome Project. The platform/tool business model, characteristic of other high-technology industries, enabled companies to commercialise such breakthroughs and, where possible, establish first-mover advantage. However, the continuing rapid pace of technology development also made platform companies vulnerable to commoditisation of their tools and technology obsolescence or even irrelevance.

While the Boston Consulting Group expects genomics technology to offer companies cost savings in research and development (R&D) in the region of 35 per cent, research conducted jointly by McKinsey & Company and Lehman Brothers, Inc., projects that the accelerating technological advancements in drug discovery could double industry R&D costs between 2000 and 2005, with rising failure rates for drugs during the more costly later stages of development resulting from the application of relatively immature
technology in drug discovery. Such R&D budgetary increases would apply considerable pressure to the earnings of the large pharmaceutical companies. As the biotechnology industry is heavily reliant on the pharmaceutical industry, biotechnology business models will need to adapt to address technological improvement issues. With a moderate improvement in drug discovery technology, McKinsey & Company projects that R&D costs could return to near 2000 levels by 2010.

The future evolution of biotechnology business models will be heavily influenced by their interrelatedness to the pharmaceutical industry and its future development. In order to grow, biotechnology companies must retain control of their own value chains and optimise interactions within the pharmaceutical industry value system, rather than allowing themselves to become a small link in a more established pharmaceutical or biotechnology company’s value chain.

With continued downstream integration, the emerging hybrid business model could ultimately evolve into the FIPCO model. For this to be feasible, the hybrid model would need to become established as a path to profitability and even then, the FIPCO model would be viable only for the few companies with access to a large supply of capital. Therefore, an alternative open to the remaining companies would be to leverage their relationships within the industry value system. Relationships have evolved dramatically since the 1980s, with innovative deal structuring and true partnerships now emerging as the biotechnology companies’ bargaining position has been strengthened. Biotechnology and pharmaceutical companies now have an increasing need to manage multiple, multi-level, complex relationships with customers, partners and collaborators efficiently and effectively. Therefore, for hybrid companies to evolve to the next level, the management will require superior industry networks, a strong market orientation, creativity in deal structuring and well-developed relationship management skills in order to extract maximum value.

Conclusion

Evidence from the post-IPO stock performance of biotechnology companies that went public in 2000, indicates that investors in the more mature US public market do differentiate companies on the basis of their business model, with product companies outperforming their platform company peers. However, the fragmented nature of the European public market for biotechnology stocks makes it difficult to detect distinct trends in performance related to the business models of European companies. Notwithstanding the scarcity of deep product pipelines in Europe, the individual public markets had a more significant impact on biotechnology stock performance than business models, in 2001.

In the private markets, trends in private equity and venture capital investment in European biotechnology companies in 2001 have highlighted investors’ attraction to the hybrid business model and its potential to maximise value generation potential, while mitigating some of the associated risk. Driven by rapid technological advancement and innovation, biotechnology company business models will continue to evolve to meet market needs and deliver a sustainable economic return to investors. The majority of young hybrid biotechnology companies will not have the capital resources to complete downstream integration and come full-circle to form a FIPCO and, therefore, investors will increasingly be looking to management to deliver growth through the extraction of greater value from relationships with pharmaceutical and biotechnology companies.

Looking forward, there is potential for the key biotechnology industry stakeholders to establish a virtuous cycle, which drives forward the evolution of the business models to meet the productivity needs of pharmaceutical companies; the unmet medical needs of the general population and the financial needs of investors. However, to
achieve this in Europe there is a need for increased maturity in the public markets, a degree of integration of the markets and further development of the necessary relationship management skills within biotechnology companies.

References