Marketspace

Trends in biotherapeutics

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Abstract

Analysis of the leading and emerging biotechnology companies identifies current and future trends in biotherapeutics. The ten leading biotechnology companies are forecast to generate cumulative revenues of US$31.7bn in 2007, with niche therapeutic areas and oncology forecast to account of 31 per cent and 27 per cent of these revenues, respectively. Small molecules are forecast to play a central role in the emerging sector's quest for revenue generation. Indeed small molecules carry the potential to become the dominant technological trajectory in terms of pipeline development, eclipsing antibody-based and rDNA technologies. Critical to the industry's future performance will be the ability of emerging companies to generate sustained businesses, and to validate their newly developed pipelines with the leading biotechnology or pharmaceutical players.

INTRODUCTION

Since its birth in the early 1970s, the biotechnology industry has achieved three major research milestones: the discovery of recombinant DNA technology, the development of monoclonal antibody technologies and the sequencing of the human genome. These innovations have been complemented by other discoveries in the areas of gene therapy, stem cells, xenotransplantation and, most recently, RNAi gene silencing. Such developments have driven the formation of more than 4,000 public and private biotechnology companies in 25, mainly western, countries. Currently, there are at least 1,457 biotechnology companies in the USA, of which 342 are publicly held with a combined market capitalisation of approximately US$250bn in early 2003.

More than 300 million people worldwide have been helped by more than 130 biotechnology drugs and vaccines that have been approved by the Food and Drug Administration (FDA). Between 1992 and 2001, the US biotechnology industry saw its revenues increasing from US$8bn to US$27.6bn and employment numbers growing from 79,000 to 191,000.[1] There are now more than 300 biotechnology drug products and vaccines in development targeting more than 200 therapeutic indications, including oncology, inflammation, chronic degenerative central nervous system (CNS) diseases, cardiovascular disorders and infections.

Over the next decade the industry will face significant challenges related to increasing productivity, maintaining profitability and strengthening shareholder value. The industry needs to prove that it can drive down drug discovery and approval times, and demonstrate the commercial potential carried in genomics discoveries. Critical to the industry's future performance will be the ability of emerging companies to generate sustained businesses, and to validate their newly developed pipelines with the leading biotechnology or pharmaceutical players.

BUSINESS EVOLUTION

Datamonitor has recognised the following business models in the biotechnology industry. The *vertical model* is representative of the business followed by

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the leading biotechnology players. It consists of a fully integrated organisational structure with access to independent development, manufacturing and marketing capabilities. Although the model operates in a high-risk environment, it can target high returns on research investment and strong profit margins, similar to the pharmaceutical sector. The *horizontal model* includes the discovery and development of a technological platform to aid the drug discovery process. This model is followed by hundreds of companies that are developing bioinformatics solutions (functional or population genomics, for example Incyte Genomics and deCode Genetics) and bio-analytical systems (DNA and protein chip manufacturers). Compared with the vertical model, the horizontal model operates in a low-risk environment with weaker profit margins, as it is heavily dependent on licensing income. Notably an emerging group of biotechnology players are evolving a hybrid business model – developing or licensing technological platforms, and growing in-house vertical capabilities – that is marrying previously established biotechnology knowledge with new discoveries in molecular medicine and genetics. Similar to any other technological sector, the success of this model will be primarily dictated by the level of pipeline risk and financial return.

Over the next four years, the 12 emerging players (Millennium, Human Genome Sciences, Vertex, Celera, Scios, XOMA, Isis, CAT, British Biotech, Antisoma, Oxford GlycoSciences and MorphoSys) are destined to spend more on drug discovery and development than they will earn from product marketing or licensing deals. Horizontal (technology provision) or vertical (drug discovery and development) out-licensing deals will continue to be the main source of income. Datamonitor estimates that the ten leading companies (Amgen, Genentech, Serono, Genzyme, Biogen, Chiron, MedImmune, Gilead, IDEC and Celltech) will generate cumulative revenues of US$31.7bn in 2007, with Amgen increasing its share of this revenue from 36 per cent in 2002 to 42 per cent in 2007, with sales of US$13.2bn. In 2007, the 12 emerging players are forecast to generate product revenues of US$1.6bn, with Millennium expected to lead the race with forecast revenue of US$710m in 2007, or 43.5 per cent of total product revenue generated by the group. Despite the large revenue gap between the emerging players and the industry leaders, the former are expected to record higher annual growth rates, thus showing their potential for long-term business expansion.

The level of business diversification and the success of intrabiotechnology acquisitions or alliances, will decide the degree of evolution for the emerging business model. When looking at the emerging biotechnology sector, different success models are evident. For example, Millennium, covering predictive medicine and chemogenomics, has used vast genetic databases to identify disease-related genes aiming to link its in-house research with small molecule or protein-based product development. In contrast, Scios is a pure vertical player with a relatively low level of diversification. Its business expansion has been based on the development and marketing of Natrecor, showing that, when focused enough, an emerging player is able to select a target, develop the drug in-house, and market it using its own sales team. The success of Natrecor's development and marketing potential are the main reasons behind Johnson & Johnson's decision to acquire Scios.[2]

Consolidation activity is expected to move the emerging companies closer to full integration and potentially to sustainable profitability. In the past two years Millennium acquired Cor Therapeutics, Vertex acquired Aurora, Celera acquired Axys Pharmaceuticals and HGS acquired Principia Pharmaceuticals. The US$2bn acquisition of Cor Therapeutics by Millennium brought one marketed product, Integrilin (with

revenue potential of over US$300m in 2007), and increased the size of the company's pipeline to 19 programmes. In addition, the acquisition of Axys provided Celera with a genuine small molecule pipeline and a strong intellectual property portfolio with potential in the areas of inflammation and cancer.

Biotechnology firms have traditionally been subordinate partners in their deals with leading pharmaceutical players, supplying a service in return for fees. However, in recent years, deals executed by companies such as HGS, Millennium, Vertex and CuraGen have resulted in a partnership premium and a greater degree of commercial freedom. Although there is a growing trend towards mutually beneficial alliances between pharmaceutical and biotechnology partners, the increase in partnerships that involve exclusively biotechnology companies is interesting. This new type of partnering can either involve biotechnology companies with fee-for-service offerings collaborating with each other, or smaller biotechnology companies seeking drug development partnering opportunities exclusively with other biotechnology players.

However, manufacturing the molecules that form the basis of the biotechnology industry is a technically demanding and often expensive process. The returns for players with the skills and the capital to produce the compounds could be considerable and the market is growing faster than the supply capacity. While the global biotechnology industry produced a strong biologics pipeline of hundreds of programmes in 2002, there is a danger that the industry might fall victim to its own success if efforts are not made to avoid the approaching manufacturing crisis.

The options available to emerging biotechnology companies are limited, but Datamonitor believes that forming strategic relationships with contract manufacturing organisations will be key to ensuring access to sufficient capacity. In addition to potential manufacturing hurdles, the emerging sector is likely to face significant challenges linked to the complexities found in drug–drug or drug–protein interactions.

Datamonitor believes that new technologies such as antisense or gene therapy, although successful in preclinical tests or small-scale clinical trials, may find it hard to show efficacy in later stages of development. The key to success will be the selection of commercially attractive therapeutic indications, efficient drug delivery methods and the choice of partners to co-develop these new products in the later stages of development.

LEADING PRODUCTS AND THERAPIES

Datamonitor estimates that nine biotechnology blockbusters from the ten leading companies will generate combined revenues of US$17,809m in 2007, representing 56 per cent of the total product revenue generated by such companies. Three of Amgen's products – Enbrel, Epogen and Aranesp – are forecast to lead the group, with forecast combined revenues in 2007 of US$8.9bn. Scios's Natrecor, Millennium's Integrilin and Velcade, and Isis's Alicaforsen will lead the emerging biotechnology sector in 2007 with combined forecast revenues of US$1,330m. Natrecor, approved in August 2001, will be the leading product with forecast revenues of US$243m in 2004 and $542m in 2007 (Figure 1).

In the leading biotechnology sector, niche areas – including anaemia, dominated by Amgen, growth/metabolism diseases, dominated by Serono, and genetically inherited disorders, led by Genzyme – are forecast to post revenues of US$9.7bn in 2007, accounting for 31 per cent of the combined revenues of the leading ten biotechnology players (Figure 2). Oncology is likely to be the second most important area, with forecast revenues of US$8.7bn in 2007 accounting for 27 per cent of the leading players' revenues. Overall, these two key areas are expected

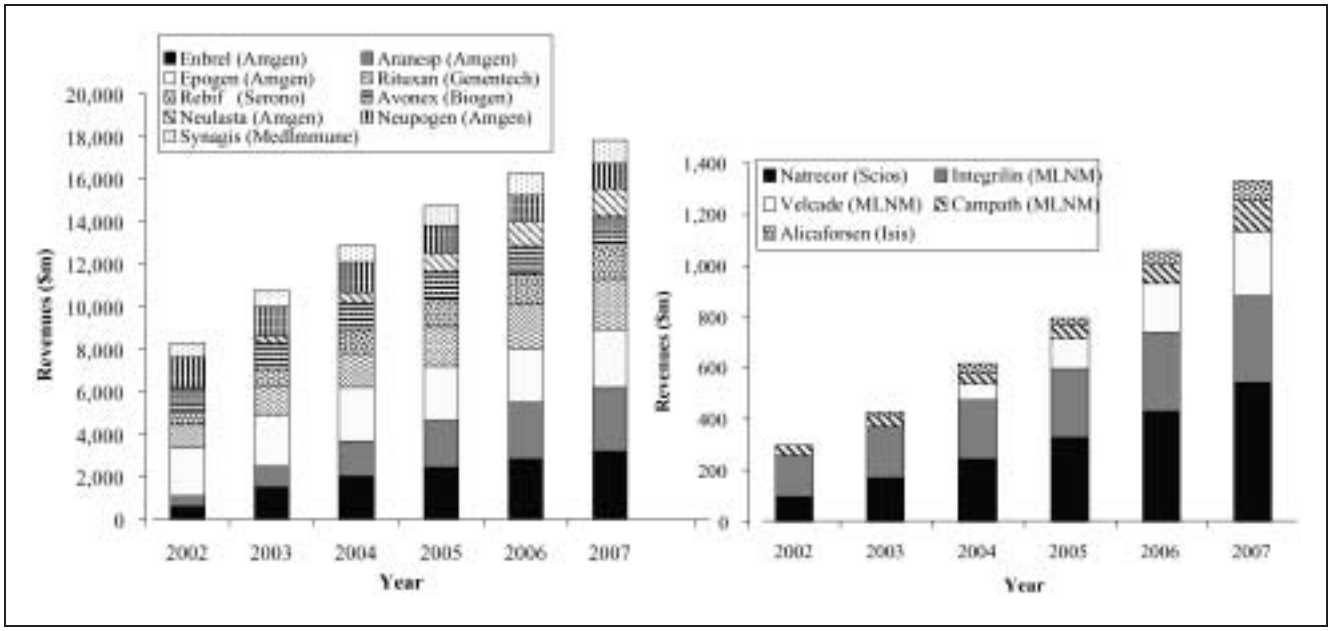

Figure 1: Revenue by leading products, 2002–2007

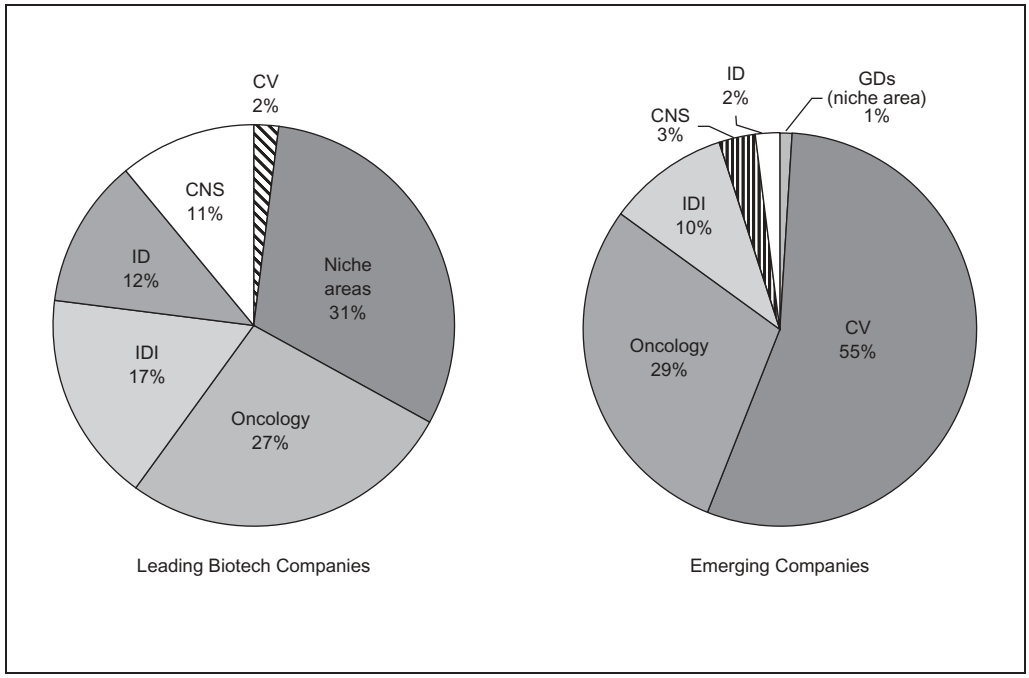

Figure 2: Revenue contribution by therapy area, 2007 (CV, cardiovascular; GDs, genetic disorders; ID, infectious diseases; IDI, immune disorders and inflammation)

to generate revenues of US$18.4bn in 2007, representing 58 per cent of the total revenues generated by the ten biotechnology leaders. For the emerging players cardiovascular will be the leading therapy area in terms of revenue generation with sales forecast to reach US$882m in 2007, representing 55 per cent of total product revenues for the group. This will be followed by oncology, with forecast 2007 revenues of US$474m contributing 29 per cent of total product revenues (Figure 3).

LEADING TECHNOLOGIES

Therapeutic proteins will be the main growth drivers for the ten leading companies, with forecast revenues of US$19,053m, followed by antibodies, which are forecast to reach sales of

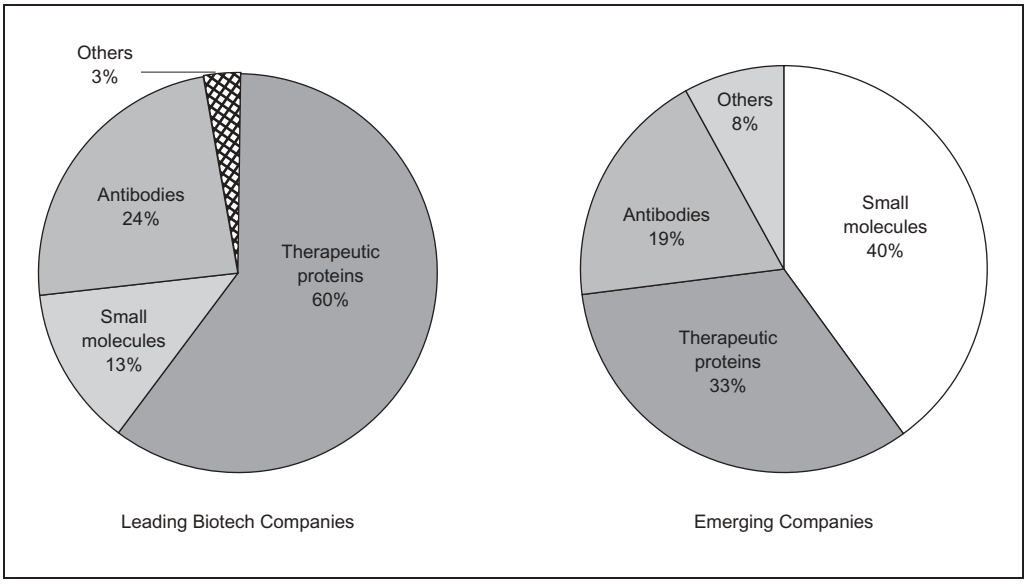

Figure 3: Revenue contribution by technology, 2007

US$7,635m, and small molecules, with 2007 forecast revenues of $3,997m (Figure 3). Genzyme's kidney disease drug, Renagel, will be the leading small molecule, with forecast sales of US$756m, followed by Gilead's antiviral compound, Viread, and Genentech's cancer drug, Tarceva. Together these three compounds will account for 40.8 per cent of small molecule revenue.

Small molecules will play a central role in the emerging sector's quest for revenue generation. When looking at technological evolution of the portfolios of the 12 emerging players, Datamonitor found that small molecule-based drugs were leading the race, with 57 pipeline programmes accounting for 37 per cent of a total of 157 programmes, followed by monoclonal antibodies with 46 programmes (29 per cent) and therapeutic proteins with 35 programmes (22 per cent), thus showing a significant switch to new market opportunities.

In terms of pipeline productivity and revenue generation, Millennium's and Vertex's small molecule-based drugs will drive the emerging sector over the next five years. Two new technology platforms – antisense and gene therapy – are forecast to generate income in 2007 of US$116.9m and US$11.7m, respectively. Datamonitor believes that small molecules carry the potential to become the dominant technological trajectory in terms of pipeline development over the next ten years, eclipsing antibody-based and rDNA technologies.

Indeed, rDNA technologies and the field of big protein development are ageing and their return is expected to show signs of decline. Recombinant DNA and antibody development technologies will not be able to meet increasing demand in areas of high unmet need such as oncology and CNS. This can be explained by an increasing wave of scientific research that is aimed at understanding the complexity of gene–protein and protein–protein interactions at the molecular level using highly advanced bio-analytical techniques and materials. In chronic degenerative disease areas (CNS, cancer, cardiovascular), research into the molecular changes during the onset of complex disease mechanisms is revealing a new world of potential small-sized drug candidates that could interfere with these complex processes and prevent or inhibit disease progress.

CONCLUSION

Therapeutic proteins are expected to dominate the technological and product landscape of the leading biotechnology sector. Leading players such as Amgen, Genentech and Biogen will continue to

invest heavily in niche disorders and oncology, leveraging on their world-leading expertise and manufacturing capabilities in protein and antibody engineering. Emerging players are investing more in new market opportunities using antisense, gene therapy and genomics-based small molecule platforms, with the latter destined to play a central role in their development.

Datamonitor believes that emerging players demonstrating the following attributes are most likely to succeed:

- a multi-product, multi-franchise, diversified model;
- global focus with geographical expansion and partnering;
- innovation and access to novel drug discovery and development techniques using advances in genomics and proteomics;
- financial stability to support the increasing costs of drug development;
- autonomy in manufacturing.

The evolution of the emerging biotechnology business will not be without pipeline disappointments or partnering failures. In order to gain competitive advantage, emerging biotechnology companies need to fully understand and exploit the metabolic function and genetic regulation of the human proteome (metabolome). To date the industry has somewhat suffered through failed projects, misleading visions and at times poorly managed businesses. What it now needs are players who can skilfully blend innovation and business acumen. Intrabiotechnology or bio-to-pharma partnering and astute technology acquisition will be critical to supporting the race for innovation and sustainable growth.

Clearly, this is the survival of the fittest, both in the present and the future.

References and notes

1. Biotechnology Industry Organization.
2. On 29 April 2003, Johnson & Johnson announced the completion of Scios's acquisition. Scios shareholders will receive $45 for each outstanding Scios share. The transaction is valued at approximately $2.4 billion, net of cash.