Marketspace

Cancer remains the dominant disease target for biotech through to 2010

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Abstract

The two leading therapeutic areas for biological products, in terms of current sales and pipeline focus, are oncology and AIID (arthritis, immune and inflammatory disorders). Datamonitor's biotechnology strategic market analysis team recently analysed the AIID market, since this sector is currently powering biotechnology market growth, owing to high demand for biologicals to treat rheumatoid arthritis and psoriasis (Belsey, M. and Churchill, C. (2006) 'Autoimmune and inflammatory disorder biologicals will power biotech market growth through to 2010', *J. Comm. Biotechnol*., Vol. 12, No. 2, pp. 237–241). In the current paper, we have analysed the oncology market, since biologicals designed to treat cancer indications have underpinned the development of the biotechnology market since its inception in the 1980s. Biological products treat a wide variety of cancers, of which the most prevalent are the 'big four' tumour types – breast cancer, lung cancer, prostate cancer and colorectal cancer. In terms of technology focus, both monoclonal antibody therapeutics and recombinant proteins are set to drive cancer biological market growth. Key growth drivers include mainly Genentech and Roche products, such as Avastin (bevacizumab), Rituxan (rituximab) and Herceptin (trastuzumab), as well as Amgen products, including the second-generation recombinant proteins Neulasta (pegfilgrastim) and Aranesp (darbepoetin alfa). Across the major pharmaceutical markets, oncology biologicals generated US$10.7bn in 2004 (based on company-reported data), which Datamonitor forecasts to rise to US$29.0bn by 2010.

INTRODUCTION

Biotechnology drugs can broadly be grouped into four categories. There are two mature sectors that are set to generate more than 95 per cent of total biotech sales from 2004 to 2010: recombinant protein therapeutics (rDNA proteins) and monoclonal antibodies (mAbs). There are also two early-stage industries: nucleic acid therapeutics and therapeutic vaccines. However, neither of these is ready to launch products with significant revenue-generating potential over the short to mid-term.

Recent biotechnology strategic market analysis of leading rDNA proteins carried out by Datamonitor identified that sales of products targeting two therapeutic areas (oncology, and arthritis, immune and inflammatory diseases, AIID) are ready to account for approximately one-half of total top-20 rDNA protein sales through to 2010[1]. Historically, drugs in these therapy areas have driven biotechnology market evolution, and together they make up a significant proportion of total biotech market sales. In the current study, Datamonitor forecasts that the oncology franchise is set to retain its dominant position in the biologicals market, generating sales of US$29.0bn by 2010, up from US$10.7bn in 2004 (based on company-reported sales).

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There are a range of advantages for biotech companies in targeting cancer. Cancer tends to be life-threatening, and even marginal improvements in lifespan are likely to generate significant sales. Furthermore, improvements in quality of life are also a dominant concern, boosting sales potential further. Lastly, cancer drugs that are currently on the market – in particular small molecule cytotoxics – have a poor side-effect profile, and the recent success of biological drugs entering this market provides a good business plan template. Set against these factors, the aetiology of cancer is often multifactorial and with the development of multi-target small molecule kinase inhibitors, the development of expensive one-target biologicals is increasingly difficult to rationalise.

Given the importance of the oncology franchise in driving biotechnology market growth, Datamonitor has performed more detailed analysis to identify key cancer biological growth drivers across all sectors of the biotech market, together with characterising dynamics set to underlie market growth, to construct sales forecasts for leading oncology biotherapeutics.

LEADING ONCOLOGY PRODUCTS AND COMPANIES

Historically, cytotoxic therapies have been the mainstay of cancer treatment. However, the oncology arena has been highly receptive to biologicals, owing to the limited treatment benefit associated with traditional approaches. Cytotoxic agents used for chemotherapy are relatively non-selective in targeting rapidly dividing cells, and therefore have significantly detrimental side effects as a result of their effects on normal, healthy cell populations. This results in potentially significant toxicities, including myelosuppression, mucositis pain and neuropathy. Two factors have driven targeted therapy development. Primarily, it was the understanding of molecular pathways underlying the aetiology of cancer that allowed scientists to design targeted therapies. This was encouraged by the fact that virtually no cytotoxic is specific enough to destroy malignant cells without causing some systemic toxicity.

Amgen pioneered the commercialisation of rDNA therapeutics with the development of Epogen in the 1980s. The product initially received Food and Drug Administration (FDA) approval in 1989 for the treatment of anaemia associated with kidney dialysis. However, despite a lack of formal approval for oncology indications, there has been substantial off-label use of the drug in the treatment of cancer-related anaemia. Amgen continued to penetrate the oncology rDNA market following the launch of the human recombinant granulocyte colony-stimulating factors (G-CSF) Neupogen and second-generation pegylated version Neulasta, in 1991 and 2002, respectively, together with the second-generation epoetin product Aranesp in 2001.

Amgen's products revolutionised the oncology cytopenia-related supportive care market and the company remains more or less the sole player in this arena, having generated 82 per cent of the leading supportive care biological sales in 2004. Neulasta and Aranesp represent Amgen's greatest growth drivers, and together are forecast to increase in sales from US$3.5bn in 2004 to US$11.5bn in 2010 (Figure 1).

Within the mAb market, the Genentech and Roche partnership continues to spearhead the growth of the global bio-oncology market, as a result of its very strong portfolio. Rituxan was launched in 1997 and is approved for the treatment of relapsed, refractory low-grade and follicular non-Hodgkin's lymphoma (NHL), marking the arrival of the first mAb onto the cancer market. This was quickly followed by the launch of Herceptin in 1998 for the treatment of HER2-positive metastatic breast cancer, now a gold-standard mAb therapy within this market. Avastin, which is forecast to be a major growth driver for both Genentech and Roche, because of its

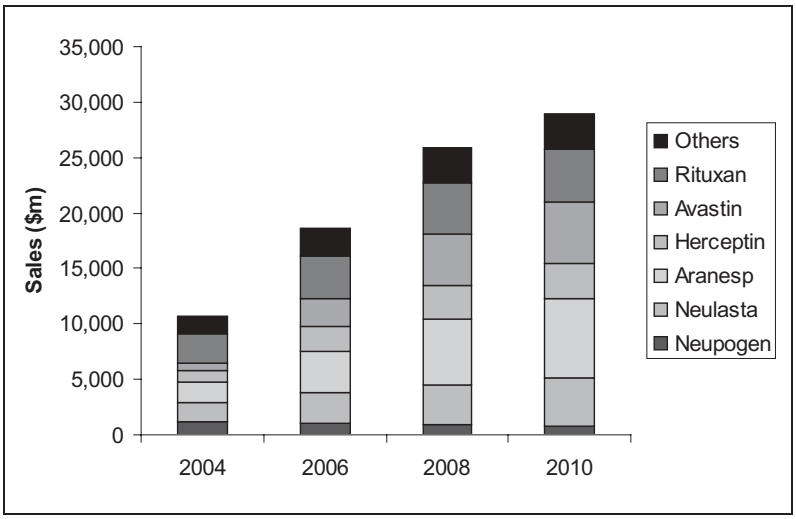

Figure 1: Total biologic oncology sales split by leading brands, 2004–2010. Note: Aranesp sales represent oncology indications only, renal failure anemia sales are excluded; True oncology sales may be higher due to the omission of Epogen sales, since the drug has no approved oncology indications.
Source: Datamonitor forecasts; company-reported information

applicability across a wide range of tumour types, was initially launched in 2004 for the first-line treatment of metastatic colorectal cancer. Total sales of Rituxan, Herceptin and Avastin were US$4.5bn in 2004, and are set to rise to US$13.6bn by 2010. Together, these products accounted for 90 per cent of the oncology mAb market in 2004.

Amgen, Genentech and Roche are ready to continue to dominate the oncology biologicals arena, via very strong growth of products that have already attained market leader status (Figure 2). While threats such as the establishment of a biosimilar approval pathway, better drugs in the pipeline and the development of small molecule tyrosine kinase inhibitors (TKis) exist, these are not expected to significantly dampen sales of the current leading products. Sandoz's growth hormone somatropin (Omnitrope) was approved in the European Union in April 2006 and the US in May 2006. This led to speculation that this would lead to a number of biosimilar approvals. However, the European approval process for biosimilars is relatively new, and there is no regulatory approval pathway for biosimilars of biologics that were approved as Biologic License Applications (BLAs) in the US (Belsey *et al.*, 2006)[2]. First-generation rDNA proteins are the likely target for biogenerics players, with second-generation rDNA proteins such as Aranesp and Neulasta, together with mAbs such as Avastin, unlikely to face generic substitution over the short to medium term. Furthermore, manufacturers of generic biologicals will face stringent

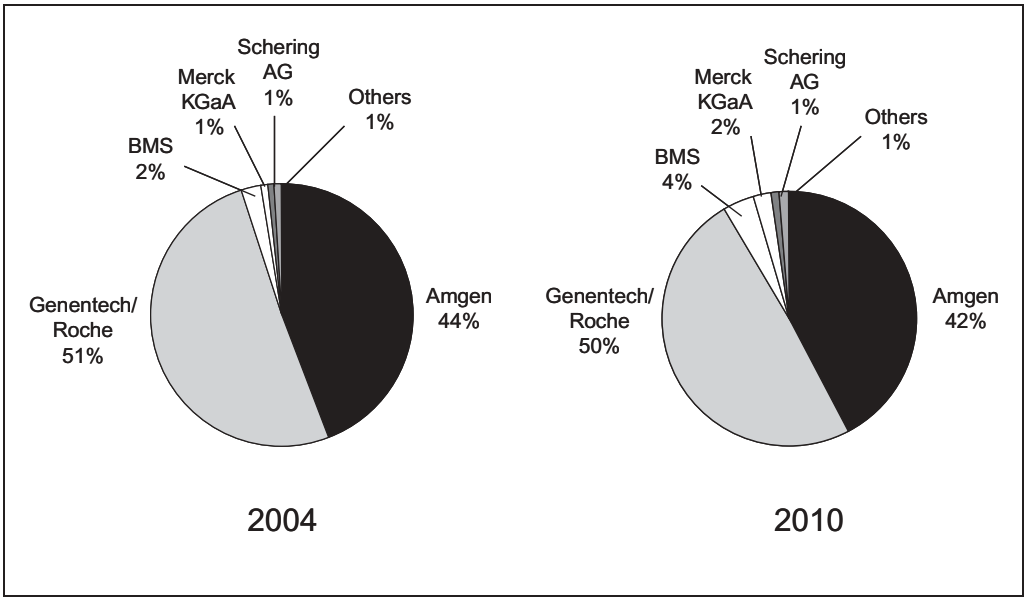

Figure 2: Leading bio-oncology product developers, 2004–2010.
Source: Datamonitor; company-reported information

testing procedures for their products in order to prove bioequivalence, and there are substantial disincentives for physicians to switch away from supportive oncology products such as Epogen, given the level of patient support provided by the branded drug maker, and brand loyalty. Therefore biosimilar manufacturers will face a tough time to maximise market penetration of the first-generation rDNA market.

The greatest risk to these biological blockbusters comes from small molecule therapeutics capable of targeting similar pathways to currently marketed mAbs. By their very nature, small molecule products are significantly cheaper and easier to manufacture, and therefore can command a lower price: an attractive prospect for cost-constrained healthcare systems. However, in addition to targeting a specific growth pathway, mAbs may also modulate the immune response, enhancing their effects. More importantly, the combination of mAbs and cytotoxics, which remain a cornerstone of cancer therapy, has been proven effective. This has not been as conclusively demonstrated for the combination of small molecule TKis and cytotoxics, which thus far have failed to demonstrate efficacy in clinical trials.

THERAPEUTIC FOCUS AND TARGET CHOICE

The oncology market covers a wide-reaching therapeutic area, encompassing a number of cancer indications. Bio-oncology drugs treat both specific tumour types, as well as more general areas, such as the treatment of adverse effects arising from chemotherapy. Cancer represents a significant health issue: more than 11 million diagnoses are made every year and 7 million cancer-related deaths occur annually.[3] By 2020, it is estimated that 16 million new cases of cancer will be diagnosed yearly.[3]

The most common cancers are the 'big four': breast cancer, lung cancer, prostate cancer and colorectal cancer, which account for nearly 55 per cent of all new diagnoses.[4] As a result of this high incidence, the 'big four' tumour types represent the key indications that drug developers have traditionally targeted, by virtue of their enormous commercial potential.

However, a shift has occurred recently, with drug developers increasingly targeting niche tumour types, which are characterised by a relatively lower incidence but with significant unmet need. A topical example is pancreatic cancer, which accounts for only 2 per cent of new diagnoses on an annual basis,[4] but is a highly resistant tumour type, showing little or no response to traditional therapies. As a result, any agent shown to confer even a minimal survival benefit will be greatly anticipated. In November 2005, Genentech/Roche's Tarceva (erlotinib) was granted FDA approval for the first-line treatment of locally advanced, unresectable or metastatic pancreatic cancer in combination with Eli Lilly's Gemzar (gemcitabine), based on a five-week survival benefit.[5]

Another attractive aspect of targeting niche indications is that drug developers are often able to gain an orphan drug designation for their product, which facilitates the road to commercialisation. Despite strong competition, drugs developers have found it very hard to improve on existing therapies in the 'big four' cancer markets. By seeking approval in niche indications, drug developers can stand a better chance of achieving stronger uptake for their product, particularly if few or no viable treatment options exist in that specific market. Once approval for one indication is gained, horizontal expansion can occur in order to increase the commercial potential of a product. A leading example is Genentech/Roche's Avastin, which is currently approved for colorectal cancer. However, the companies are currently awaiting FDA action for non-small cell lung cancer and breast cancer and they intend to file for marketing approval in breast cancer, ovarian cancer, renal cell carcinoma, prostate cancer and pancreatic

cancer, among others. It is likely that once late-stage clinical trial data are released showing that these products are efficacious in these cancers, significant off-label prescription will take place prior to formal marketing approval.

With the emergence of new diagnostic technologies and an increased understanding of the biological basis for cancer evolution, the molecular changes that distinguish malignant cells from normal cells are becoming increasingly apparent, offering a growing range of potential drug targets in the form of altered genes, proteins or corrupted pathways. The increased selectivity offered by these targets offers developers the opportunity to cultivate more efficacious and less toxic 'molecular-targeted treatment', such as the mAbs discussed above. Molecular targets may be tumour-site specific, such as CD20 targeted by Rituxan in B-cell non-Hodgkin's lymphoma, or exhibit commonality between tumour types, for example VEGF as targeted by Avastin. For those products targeting common tumour targets such as Avastin, there is significant potential for horizontal product expansion and enhanced product revenues.

CONCLUSION AND FUTURE PERSPECTIVES

Oncology biologicals are currently the leading therapeutic franchise in the biotech market and they are set to retain dominance through to 2010 and beyond. The leading oncology technology platform classes through to 2010 and beyond are mAbs and rDNA therapeutics, with nucleic acid therapeutics and therapeutic vaccines unlikely to make a significant impact on the market over the forecast period. Monoclonal antibodies generated 46 per cent of total oncology biological sales in 2004: a contribution that will increase through to 2010, where this class of biologicals is about to generate 55 per cent of total oncology biological sales. rDNA proteins will generate the remaining sales over this period.

Sales of mAbs are set to increase through to 2010 as horizontal expansion continues to take place and approval for additional indications is granted, thus representing new opportunities for drug developers. In contrast, the supportive care rDNA market is relatively mature, and oppurtunities for new growth in the rDNA sector are somewhat limited beyond the forecast increase in cancer incidence.

Amgen is set to retain its dominant position in the supportive care market, while Genentech/Roche will lead the mAb market, by virtue of their heavy investment and dedication to these areas. Although threat exists from potential biogenerics, better drugs in the pipeline and the development of small molecule targeted therapies, it is likely that the dominance of the leading products and their first-to-market status will be more than sufficient to counter this.

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