Marketspace

Autoimmune and inflammatory disorder biologicals will power biotech market growth through to 2010

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Abstract

Biologicals designed to treat arthritis, immune and inflammatory disorders (AIID) are currently powering biotechnology market growth. Datamonitor's biotechnology strategic market analysis team has therefore analysed this market to identify key biological products, together with growth drivers and resistors shaping the growth of this market. The AIID market covers a wide range of indications; however, the most prevalent are rheumatoid arthritis and psoriasis, which together represent a significant healthcare burden. A range of monoclonal antibody therapeutics such as Abbott/CAT's Humira are set to drive AIID biological market growth, together with Amgen/Wyeth's fusion protein Enbrel. Owing to very strong sales of Enbrel as a result of continued label expansion, Amgen is set to record the greatest biological AIID sales from 2004 to 2010. Many of the highly efficacious AIID biologicals such as Enbrel target TNF, which is rapidly emerging as the leading cytokine target for many AIID indications. Overall, AIID biologicals generated US$5.4bn in 2004, and this is set to rise to US$14.3bn by 2010: a strong compound annual growth rate of 17.9 per cent.

Keywords: *inflammation, immune disorders, biologics, recombinant protein therapeutics, monoclonal antibodies, rheumatoid arthritis*

INTRODUCTION

Biotechnology drugs can broadly be grouped into four categories. There are two mature sectors which are predicted to generate >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. Neither of these is set 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) should 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 make up a significant proportion of all biotech market sales. In the recent study, Datamonitor identified that the AIID rDNA protein franchise has the strongest forecast growth rate from 2004 to 2010, with a compound annual growth rate (CAGR) of 16.8 per cent. This growth will be powered by Amgen's fusion protein Enbrel (etanercept), whose recent string of approvals and strong uptake

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across a range of immune disorder indications has transformed the AIID franchise into becoming the second-largest rDNA protein market after oncology by 2010.

There are a range of advantages for biotech companies in targeting AIID. AIID diseases tend to be long-term, chronic illnesses, with patients requiring treatment for life. Furthermore, quality of life issues are key, since a small benefit in disease treatment can dramatically affect quality of life. Lastly, AIID drugs that are currently on the market such as steroids and pain relief have a poor side-effect profile, and the recent success of biological drugs entering this market provides a good business plan example. Set against these factors, AIID is an increasingly crowded market, and since AIID diseases are not life-threatening, the risk–benefit ratio can be more difficult to justify.

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

LEADING AIID PRODUCTS AND COMPANIES

The launch of two anti-TNF (tumour necrosis factor) agents – J&J/Schering-Plough's Remicade (infliximab) and Amgen/Wyeth's Enbrel (etanercept) – in the late 1990s revolutionised the AIID market and reversed the previously stagnant growth of the small molecule-dominated market. The five biological AIID products that generated the greatest sales in 2004 were Enbrel, Abbott/CAT's Humira (adalimumab), Remicade, Genentech/Roche's Rituxan (rituximab) and Genentech's Raptiva (efalizumab), which together generated 91.5 per cent of the total US$5.4bn 2004 AIID biologicals sales (Figure 1). Remicade generated the greatest sales of all of these products in 2004, accounting for approximately one-third of sales in this year. However, with a 204.3 per cent increase in sales, Abbott's Humira generated the strongest growth from 2003 to 2004. Humira's very strong growth is predicted to continue over the forecast period, and the product is set to generate the second-greatest sales of AIID

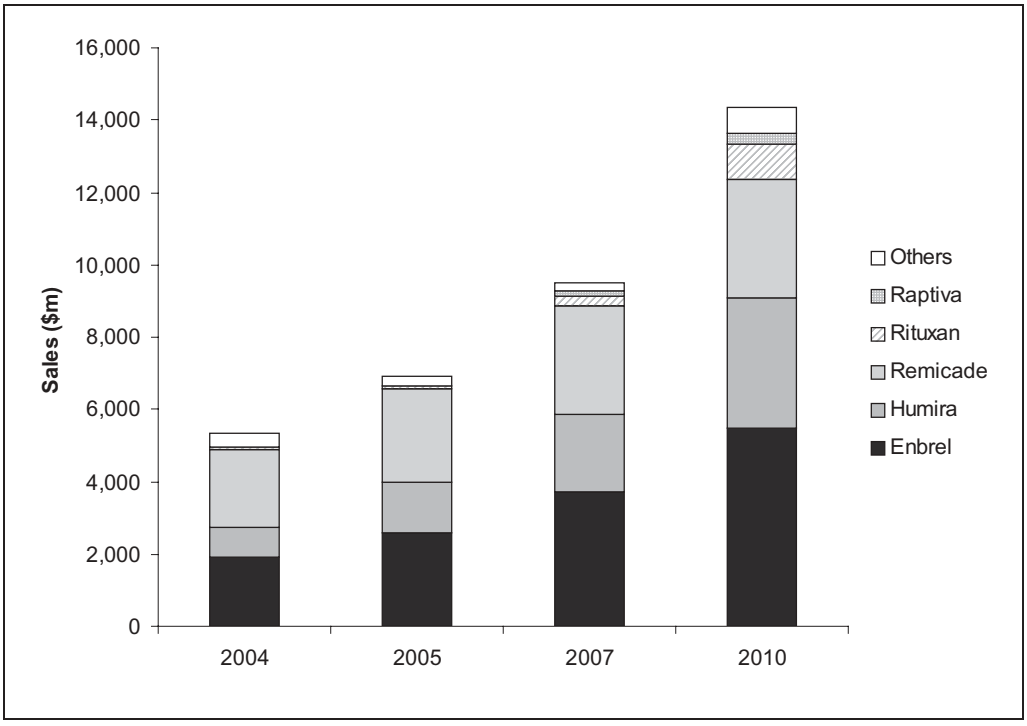

Figure 1: Total AIID sales split by leading brands, 2004–2010. Note: Enbrel sales represent the sales recorded by Amgen only; Remicade sales represent the sales recorded by J&J only Source: Datamonitor, company-reported information

products behind Amgen's Enbrel by 2010. From 2004 to 2010, the biological AIID market as a whole is set to record a strong CAGR of 17.9 per cent, powering market growth from US$5.4bn in 2004 to US$14.3bn by 2010 (Figure 1).

Humira, Enbrel and Remicade are predicted to generate between 86 and 95 per cent of total AIID sales from 2004 to 2010. All products target TNF; however, they are differentiated on factors such as the dosing regimes that they compete on. Biologicals have successfully penetrated the AIID market because of the way in which physician confidence in these treatments has been built up: a factor that is key to the long-term success of these products. In relative contrast to the COX-2 inhibitors targeting a similar market, Remicade and Enbrel where introduced for use in only the most severe patients to begin with, and built up a considerable amount of data in this population before use in all patients for both RA and other AIID indications.

It is interesting to note that all top-four companies (defined in terms of total AIID biological sales) detailed in Figure 2 achieved this status by acquiring or licensing leading biological products. Amgen obtained Enbrel via its acquisition of Immunex, which was announced in December 2001. Abbott gained access to Humira as a result of a licensing deal signed in 1993, while J&J obtained Remicade following its acquisition of Centocor in 1999. Lastly, Roche gained access to Rituxan following its acquisition of a majority stake in Genentech in 1999. These companies have followed different paths to attain the level of integration and capital necessary to be able to complete such transactions or collaborations. Companies such as Amgen have used the biotech business model to achieve fully integrated status (for example, in Amgen's case, this was based on rDNA proteins) to drive company growth, while others such as J&J and Abbott are primarily small molecule-dominated fully integrated pharmaceutical companies.

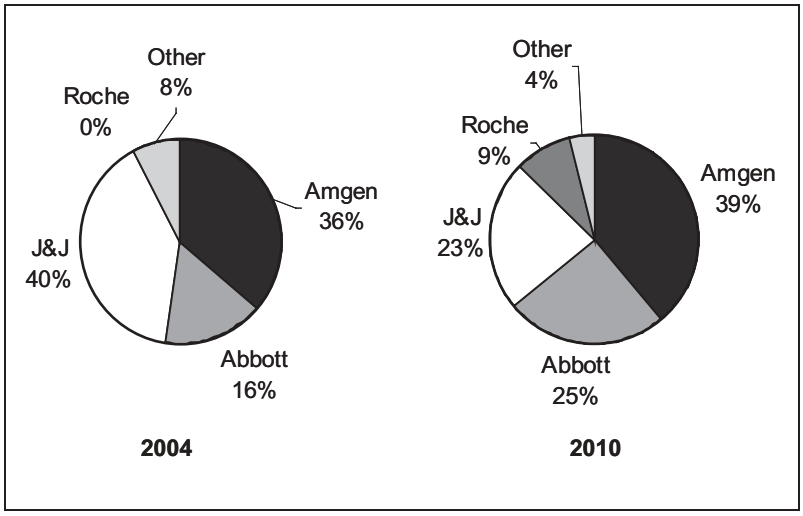

Figure 2: Leading AIID product developers, 2004–2010
Source: Datamonitor, company-reported information

THERAPEUTIC FOCUS AND TARGET CHOICE

The AIID market encompasses a wide-reaching therapeutic area in terms of the number of disease categories it covers. Indications include rheumatoid arthritis (RA), psoriasis, psoriatic arthritis, systemic lupus erythematosus, Crohn's disease, ulcerative colitis and ankylosing spondylitis. These diseases represent a significant health issue: in 2002, an estimated 43 million adults in the USA were thought to have some form of arthritis, RA, gout, lupus or fibromyalgia.[2]

The most common AIID diseases are RA, psoriasis and psoriatic arthritis. It is estimated that by 2030, almost 65 million US citizens over 18 years old will have arthritis,[2] although a significant proportion of these patients are likely to suffer from osteoarthritis, which is not currently treatable with biological therapies. Nevertheless, RA affects a significant proportion of the population: a summary of 18 population-based studies within Europe estimated the point prevalence of rheumatoid arthritis to be 1.7 per cent and the cumulative incidence to be 2.1 per cent.[3] As shown in Figure 3, RA is the dominant therapy area, in terms of total percentage sales for the key brands.

RA approvals are currently the most

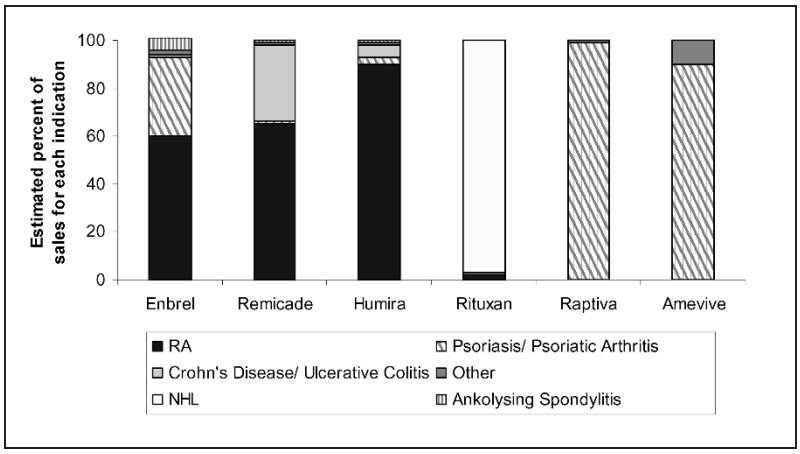

Figure 3: Estimated AIID indication spilt for leading brands
Source: Datamonitor

profitable of the AIID indications, and are therefore strongly targeted by biologicals developers. Currently, biological therapies dominate RA sales, with 84 per cent of 2004 sales believed to be generated by biologicals, even though these products accounted for only 2 per cent by market volume: a factor related to their high price point relative to small molecule AIID therapeutics. Biological therapy is set to remain the mainstay of market growth and, as use in combination with traditional therapies becomes the gold standard over the medium to longer term, both classes are set to show growth.

Psoriasis, which has historically been treated with topical steroids and less effective retinoids, is now increasingly the target of biotech companies. However, the sales of the first two biological products to be launched in this area have been disappointing. Biogen Idec's fusion protein Amevive (alefacept) and Genentech's anti-CD11a mAb Raptiva target cells involved in the inflammatory response but their efficacy in psoriasis was eclipsed by J&J/Schering-Plough's anti-TNF mAb Remicade when it was trialled in psoriasis.

Indications such as lupus and Crohn's disease are less prevalent than RA. For example, lupus is estimated to affect 0.51 per cent of the US population, which represents approximately 1.4 million people,[4] while the prevalence of Crohn's disease has been estimated at 0.13 per cent in the US population.[5] However, these indications still offer revenue-generating potential if they are targeting achieving orphan drug status, or if they are positioned on raising physician awareness and perception. Juvenile RA and the extremely debilitating diseases ankylosing spondylitis and lupus are systemic immune disorders that have a particularly high unmet need. However, the potentially less lucrative market potential that these indications offer have meant that biologicals developers have not focused primarily on these indications.

Given that there is significant cross-over in the pathophysiology of these conditions, the identification of a drug whose target plays a role in a number of conditions represents an attractive commercial target. Indeed, with the possible exception of oncology, AIID represents the greatest opportunity for the successful use of the same product across a range of patient populations. However, the immune response is a complex and as-yet not fully characterised system, and research has shown that a range of chemokines and cytokines are likely to be intricately involved with each other, suggesting that some mediators may not be as key to the process as others. For example, the disappointing results with treating psoriasis with biologicals targeting CD11a and CD2 highlights the unpredictable nature of this disease area and gives an indication of the level of work that is still needed to identify the mechanisms underlying the different AIID indications. In contrast, Enbrel's success across a range of AIID indications reinforces the strong rationale behind targeting TNF in AIID indications. However, the conclusion that it is unlikely that a product targeting a single cytokine will be universally effective seems obvious when the various physical manifestations of these immune disorders are considered.

CONCLUSION AND FUTURE PERSPECTIVES

AIID biologicals are one of the leading therapeutic franchises set to power

biotech market growth through to 2010. The leading AIID technology platform classes through to 2010 and beyond are mAbs and rDNA therapeutics, with AIID nucleic acid therapeutics and therapeutic vaccines unlikely to make a significant impact on the market over the forecast period. mAbs generated 58 per cent of total AIID biological sales in 2004: a contribution predicted to remain relatively constant through to 2010, where this class of biologicals is set to generate 60 per cent of total AIID biological sales. rDNA proteins (including fusion proteins and immunoglobulins) are predicted to generate the remaining sales over this period. Technologically, the mAb products appear more effective in psoriasis and inflammatory bowel disease (eg Crohn's disease), compared with RA. Remicade was in fact primarily launched in this indication, a strategy that has allowed it to build up a stronger perception among specialist physicians.

In the AIID market, indications range from musculoskeletal to gastrointestinal and skin disorders, so this appears a dauntingly wide area for any smaller innovative biotechnology company to address. However, the success of products such as Enbrel, which was originally produced by small biotech Immunex, offers hope to other start-up companies driving the growth and innovation in this area. However, to achieve the required production capacity, Immunex was bought by Amgen in 2001, highlighting that the expense and complexity of the fermentation production methods used can create a costly bottleneck in the road to success, and indicating that backing from fully integrated companies is necessary to gain significant market penetration. Indeed, acquisition or licensing deals have been used by fully integrated biotech and pharmaceutical companies to effect their transition into the leading AIID players.

In terms of volume, small molecules still dominate the treatment of AIID indications. However, the cost of biological products means that their sales far outweigh those of the heavily genericised small molecule classes. However, there is a concern that biologicals are set at too high a price point, particularly given that the cost–benefit analysis is getting more difficult to justify in the increasingly cost-conscious global healthcare markets (particularly in Europe). Therefore, small molecules targeting specific cytokines would be very well met in the AIID area, especially if they are available in oral form. The most promising cytokine target in AIID is increasingly emerging as TNF. The challenge of developing a small molecule anti-TNF inhibitor is being addressed by a number of companies but no candidates have yet made it past Phase II trials. This barrier is good news for the biological brands, given their rapid replacement if and when an oral anti-TNF small molecule inhibitor with good efficacy is produced.

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