Marketspace

Increased uptake of biologics in historically small molecule blockbuster-dominated therapeutic areas

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Abstract

The two leading therapeutic areas for biologic products, in terms of current sales and pipeline focus, are oncology and AIID (arthritis, immune and inflammatory disorders). Datamonitor has recently analysed these markets.[1,2] Biologics designed to treat cancer indications have underpinned the development of the biotechnology market since its inception in the 1980s, while AIID biologics are currently driving biotechnology market growth, due to the high demand for biologics to treat diseases such as rheumatoid arthritis and psoriasis. In this paper, we have looked outside these markets to identify whether biologic drugs are having an impact in other therapeutic markets. Many of these therapeutic markets (eg cardiovascular, central nervous system, respiratory, gastrointestinal) are dominated by small molecule blockbusters prescribed by primary care physicians. Here, we examine the cardiovascular therapeutic franchise as a case study for a market that has relied heavily on small molecule blockbusters to drive growth, and in which there is relatively low exposure to biologics. Marketed and pipeline cardiovascular biologics can largely be split into two categories: (i) early-evolution versions of drugs from mature biologic sectors (eg first-generation recombinant proteins and chimeric monoclonal antibodies), which are in the mature low-growth stages of their sales growth trajectories; and (ii) early-stage therapies based on innovative biologic technology platforms (eg gene therapies and oligonucleotides), which have the potential to help power cardiovascular franchise growth in the future. With the identification of more protein targets that play a role in specific disease aetiology, targeted therapies are set to power overall market growth. While companies operating in the oncology and AIID franchises are best equipped to use a targeted therapy strategy, franchises such as cardiovascular are beginning to awaken to the potential of a targeted therapy approach.
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INTRODUCTION

Biotechnology drugs can broadly be grouped into four categories. There are two mature sectors that are set to generate >95 per cent of total biotech sales from 2004 to 2010 (based on Datamonitor forecasts): recombinant protein therapeutics (rDNA proteins) and monoclonal antibodies (mAbs). There are also two early-stage industries: nucleic acid therapeutics and therapeutic vaccines, which are unlikely to launch many products with significant revenue-generating potential over the short- to mid-term.

Recent analysis of leading rDNA proteins carried out by Datamonitor shows that sales of products targeting two therapeutic areas (oncology, and arthritis, immune and inflammatory diseases (AIID)) are set to account for approximately one-half of total top-20 rDNA protein sales through to 2010.[3] Historically, drugs in these therapy areas have driven biotechnology market evolution, and together they make up a significant proportion of total biotech market sales.[1,2]

Outside these key therapeutic areas, four other franchises dominate the remaining sales: haematology, diabetes and endocrinology, central nervous system diseases (CNS) and infectious diseases. With the exception of haematology, in which a range of recombinant blood factors contributes to sales, there is limited technology platform and disease target diversity in these therapy areas, in contrast to AIID and oncology. Indeed, one rDNA protein class generates the majority of sales in these therapy areas: insulin for diabetes and endocrinology, interferon beta for CNS and interferon alfa for infectious diseases. Although some indications do not lend themselves to treatment with biologic therapy, it does indicate that these franchises have been slow to harness biologic innovation.

Outside these therapeutic franchises, the evolution of other franchises has instead been driven by small molecule blockbusters prescribed by primary care physicians (PCPs). Such franchises include cardiovascular, gastrointestinal and respiratory. Going forward, diseases such as cancer and AIID that are currently the focus of a targeted therapy approach are forecast to be the strongest growth drivers through to 2010, while indications dominated by broad-spectrum non-targeted small molecules are set to be the slowest-growing franchises, highlighting the importance of adopting a targeted therapy approach.

To effectively harness stronger growth and provide access to lower-prevalence indications, many small molecule-dominated franchises are turning to biologic products. Successful examples of this strategy include the development of Roche/Genentech/Tanox's Xolair (omalizumab), a humanised anti-IgE mAb for the treatment of moderate to severe, atopic asthma, and Genentech/Novartis's Lucentis (ranibizumab), a humanised anti-vascular endothelial growth factor Fab fragment for the treatment of wet age-related macular degeneration. Together, these drugs are set to generate approximately $1.7bn by 2010, and are leading growth drivers in the respiratory and ophthalmology franchises.

In the current study, Datamonitor uses the cardiovascular franchise as a case study to examine the success of biologic penetration of a historically small molecule blockbuster-dominated franchise.

MARKETED AND PIPELINE CARDIOVASCULAR BIOLOGICS

Cardiovascular is one of the leading therapeutic franchises by sales and has historically been a significant growth driver of the overall healthcare market. Out of the top-10 leading drug classes according to 2005 IMS sales data,[4] three classes fall under the cardiovascular umbrella – cholesterol and triglyceride reducers (lipid altering drugs), angiotensin-II inhibitors and calcium antagonists (antihypertensives). Based on these data, these classes account for approximately one-third of total top-10 sales.

Lipid-altering drugs and antihypertensives both fit the typical small molecule blockbuster profile: both are prescribed primarily in the PCP setting and both have had significant direct-to-consumer advertising spending to drive sales. Overall, these two sectors contributed to 68 per cent of total 2004 cardiovascular sales. Their dominance of the

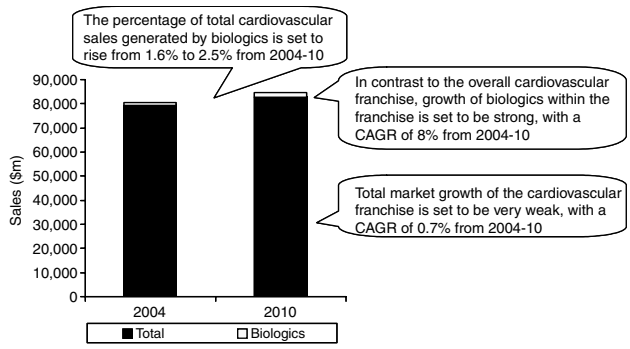

Figure 1: Cardiovascular biologics are set to record strong growth from 2004 to 2010, in contrast to the total franchise.
Note: this analysis was performed using company-reported data and Datamonitor estimates constructed in April 2005

cardiovascular franchise, however, is set to fall to 63 per cent following forecast sluggish growth over the 2004–2010 period, due to the fact that many drugs in these sectors are in the mature stage of their growth trajectories and a significant number are facing patent expiry.

In contrast to weak forecast overall growth of the cardiovascular franchise, and the forecast decline in sales of antihypertensives and lipid-altering drugs, cardiovascular biologics are set to show strong growth over the 2004–2010 period, demonstrating a compound annual growth rate (CAGR) of 8 per cent as shown in Figure 1.

The relatively strong overall growth of cardiovascular biologics is based on the launch of a number of new biologics between 2004 and 2010 (eg Bristol-Myers Squibb/ Corgentech's graft failure oligonucleotide edifoligide). The launches of these drugs are set to support currently marketed well-established cardiovascular biologics that are in the mature stage of their lifecycle (eg Roche/ Genentech's recombinant alteplase, Activase).

EARLIER-STAGE BIOLOGIC TECHNOLOGY PLATFORMS DOMINATE PIPELINE DEVELOPMENT

The shift towards targeting lower-prevalence indications using targeted therapies is part of an overall drive spearheaded by the biotech industry. The increasing adoption of this strategy is the result of increased pressure on blockbusters, as both regulators and payers are shifting away from me-too drugs, which in the past have generated the greatest blockbuster sales. Furthermore, blockbusters attract significant generic competition and may also stifle R&D innovation. Therefore, in the future, franchises such as cardiovascular, which have been heavily dominated by blockbusters, are transitioning more towards utilising innovative technology platforms to access niche markets.

A small number of cardiovascular biologics are set to generate sales of ⩾$100m by 2010. These include biologics that are in the mature stage of their lifecycle, together with drugs based on earlier-stage technology platforms. In contrast to small molecule blockbuster classes, cardiovascular biologics target lower-prevalence indications, which are treated by specialist physicians. Such indications include vessel remodelling (eg angioplasty, angiogenesis therapy and vascular regeneration, peripheral arterial occlusions, and prevention of vein graft failure following coronary artery bypass graft (CABG)), heart failure and thrombosis.

The rDNA market as a whole has evolved over the last 20 years from first-generation proteins to more complex pegylated versions. Cardiovascular rDNA proteins set to generate ⩾$100m sales by 2010 are primarily first-generation proteins (eg Activase), which are already recording sales of ⩾$100m. Similarly, mAb market evolution has followed a trajectory beginning with murine and chimeric mAbs and evolving through to humanised and fully human mAbs.[5] Cardiovascular mAbs set to generate ⩾$100m

sales by 2010 are early-evolution mAbs, such as Johnson & Johnson/Lilly's chimeric mAb ReoPro (abciximab), which again are already generating this level of sales. The successful adoption of early-evolution versions of mature biologics suggests that companies operating in the cardiovascular therapeutic franchise have not had a great degree of success in capitalising on the biologic technology platform evolution in the mature biologic sectors.

In contrast with the mature biologic sectors, pipeline cardiovascular biologics utilise earlier-stage innovative biologic technology platforms to target specific proteins involved in the aetiology of lower-prevalence diseases, with the aim of reshaping disease progression. An example of this is edifoligide, an oligonucleotide in Phase III trials for the treatment of vein graft failure following CABG. Another example where drug developers are harnessing early-stage biologic technology platforms to develop a targeted therapy is Daiichi/AnGes's hepatocyte growth factor gene therapy DS-992, currently in Phase III trials for the treatment of peripheral arterial disease. Therefore, there are signs that the cardiovascular market is turning to early-stage biologic sectors to harness innovation and power stronger future sales growth.

CONCLUSION AND FUTURE PERSPECTIVES

Companies operating in the cardiovascular therapeutic franchise have historically been highly successful in developing and marketing small molecule blockbusters that have driven not only strong franchise growth but have also helped to power overall market growth. Pfizer's cardiovascular antidyslipidemic drug Lipitor (atorvastatin) is currently the biggest-selling prescription drug, and it generated sales of more than $12bn in 2005. Additionally, a wide range of other cardiovascular small molecule drugs has achieved blockbuster status. Drugs companies, however, are becoming increasingly disincentivised in relying exclusively on a blockbuster-driven growth strategy, and instead are turning to the biotech sector as part of the focus to develop targeted therapies. Companies operating in the oncology and AIID franchises are best equipped to utilise a targeted therapy strategy; however, franchises such as cardiovascular are beginning to awaken to a the potential of a targeted therapy approach, and there are a number of targeted cardiovascular therapies using innovative technology platforms. Although the overall number of these therapies is currently small relative to the total pipeline, any success of such therapies will drive greater future investment in the innovative early-stage biotech sectors.

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