The SWOT Analysis of Antibody Therapeutics in China

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The total global sales of therapeutic monoclonal antibodies in 2008 reached $31.9 B, an impressive 21% growth from the previous year. It is estimated that the revenue for antibody therapeutics will reach $60 B by 2014. Monoclonal antibodies have become a major drug class of high commercial importance and account for more than 30% of the worldwide sales of biologic drugs. The majority (90%) of antibody drug revenue comes from the treatment of cancers and autoimmune diseases. Research and development activity related to monoclonal antibodies has intensified and the number of candidate drugs gaining regulatory approval is likely to rise exponentially. Rising cancer prevalence, as well as the current low market penetration of monoclonal antibody therapies for patients with autoimmune disorders, further drives the demand for antibody therapies. Despite the inevitably increased competition for antibody targets, pricing pressure and patent expiration on high-revenue monoclonal antibodies, monoclonal antibody therapies are undoubtedly on the rise and look set to play a greater role in the global healthcare in the future, especially in cancer therapy and autoimmune disorders. There will be significant opportunities in the therapeutic monoclonal antibody market in China over the next 20 years. Currently only 0.3% of total pharmaceutical revenues in China is generated by antibody drugs compared with 4% in the international markets. Both the Chinese pharmaceutical industry and the Chinese government are fully aware of the economic impact and healthcare benefits of monoclonal antibody therapies. While most of the candidate drugs in the industry pipelines are biosimilars, novel antibodies that can demonstrate clinical superiority over existing treatments fill an unmet medical need for certain diseases or offer improved administration methods and are likely to become the monoclonal antibody blockbusters of the future. These drugs should gain commercial success in a dynamic market that is increasingly oriented towards proven cost-effectiveness and superiority over existing therapies.

Strengths

Monoclonal antibodies are target-specific

The specific nature of monoclonal antibodies to their targets and the availability of the wide variety of disease targets are the key to the recent commercial success of monoclonal antibodies. Oncology and rheumatoid arthritis indications have generated a vast majority of the revenues. Monoclonal antibodies have also been marketed in the ophthalmology, antiviral and cardiovascular therapeutic areas. The high specificity and broad applications are important drivers of the monoclonal antibody market. Many

more potential targets are being identified, which will allow these therapies to expand into new areas of the pharmaceutical market making entering the monoclonal antibody market even more attractive.

Chronic diseases and diseases of aging populations generate high revenues

Therapeutic monoclonal antibodies target mostly chronic diseases and diseases of aging. Niche indications (such as age-related macular degeneration, paroxysmal nocturnal haemoglobinuria, and rarer cancers) that are difficult to manage by other therapies are also well-suited to monoclonal antibody therapies. By 2050, China will have more than 438 million people over the age of 60, with more than 100 million of them aged 80 and above. All these factors have combined to allow the possibility of generating high revenues for monoclonal antibody therapies and further growth in the market.

Manufacturing improvements

Other major drivers in the monoclonal antibody industry are the technological improvements and new innovations in antibody manufacturing technology. Improved antibody yields from cell culture supernatants, which reduce the volume of product, and new production methods, such as disposable bioreactors and improved purification techniques, reduce costs. New formats of antibodies, such as antibody fragments, can be produced less expensively by bacterial fermentations. Investigation of yeast and plants as alternatives to mammalian cell cultures for producing monoclonal antibodies continues. These potential improvements in antibody manufacturing technology may lead to further reduced production costs and consequently improved patient access to monoclonal antibody therapeutics worldwide. It is expected that with the return of many Western trained scientists to China, the biopharmaceutical industry in China will gain the necessary expertise in the manufacturing of antibodies.

Deep pipeline

Monoclonal antibody developers and manufacturers possess a rich pipeline of promising new therapies for many human diseases. Clearly, this rich pipeline will allow the launch of many new antibodies in years to come and will be a driving force for overall market growth. This pipeline includes the development of existing monoclonal antibodies for expanded indications and for use in combination with other drugs. Most of the antibodies in clinical development are novel full-sized naked antibodies for oncology, autoimmune disorders and other indications. Development of various antibody fragments and conjugated monoclonal antibodies for oncology are also promising. Although most antibodies under development in China are biosimilars, novel therapeutic antibodies are emerging. It is expected that more and more novel antibodies will be entering clinical trials in China.

Monoclonal antibodies for oncology have lower risk

Side effects are one of the major reasons why drugs fail in clinical trials. The side effects associated with monoclonal antibody therapies are generally less serious than those of other drugs, particularly in the oncology field. Cancer therapy has traditionally been known to cause debilitating side effects including nausea, vomiting and hair loss. Most side effects from monoclonal antibody treatments are related to the mode-of-administration. Allergic reactions such as localized swelling and rashes, flu-like reactions, and gastrointestinal upsets are also common. For potentially-terminal oncology indications, however, these side effects are out weighed by the benefits of prolonged life and improved quality of life.

Weaknesses

High development and manufacture costs limit growth

Compared with other drugs, monoclonal antibodies are larger and more-complicated protein molecules, and therefore it is more challenging to develop and manufacture them. From large-scale bioreaction to downstream purification, procedures for manufacturing monoclonal antibodies are technically more difficult. Expertise in mammalian cell culture and bioprocess is required, both of which are costly and challenging processes to perform on a commercial scale. Monoclonal antibody therapies typically require relatively high doses, thus production requires high-volume bioreactors, which further increase cost. The complexity and expense of the monoclonal antibody development process slows down the process of bringing the drug to the market. Emphasis on the development of cost-effective processes will be important to allow the monoclonal antibody market to grow.

Market competition for biosimilar monoclonal antibodies

Patents for current high-revenue monoclonal antibody therapeutics will start to expire in the major markets of

the US and Europe in 2011. Generic versions of these monoclonal antibodies will enter the market to compete with the brand name antibodies. Unlike small-molecule drugs, monoclonal antibodies are large and complex biologic drugs which are difficult to manufacture and characterize. It is not possible to manufacture exact copies of originator monoclonal antibodies. "Biogeneric" monoclonal antibodies therefore are "biosimilars". Dr. Reddy launched the first biosimilar monoclonal antibody, Reditux (rituximab), in India in 2007. A number of companies, largely based in India and China, are developing other biosimilar monoclonal antibodies. These biosimilar antibodies will remain restricted to Asia and will not constitute a major impact to the global monoclonal antibody market. However after patents on top-selling monoclonal antibodies expire, there will be a demand for cheaper antibody therapies. Unfortunately, biosimilar monoclonal antibodies may not achieve the cost savings and high market penetration currently enjoyed by generic small-molecule drugs. The complexity of monoclonal antibodies and their potential for immunogenicity mean that the development of these biosimilars will be considerably more expensive and time-consuming than traditional generics until new innovations bring the cost down. Currently there are no established regulatory approval processes for biosimilar versions of monoclonal antibodies in the major markets in North America or Europe so one must be developed.

Mode of administration

Antibody drugs on the market today are administrated by injection. Therapeutic proteins tend to be large and relatively unstable making them difficult to administer orally. Injectable formulations may not be a major restriction for oncology treatments since chemotherapy treatments that are commonly used in conjunction with antibody drugs are also injected. However, for the treatment of rheumatoid arthritis there is an increased risk of infection following the administration of injection. Additionally, issue associated with patient compliance could limit the use of antibody drugs. Oral, transdermal, or pulmonary treatments with equivalent efficacies to the injected monoclonal antibody drugs could provide an advantage to capture some of the market share held by currently-marketed products.

Immunogenicity is a concern

In general monoclonal antibodies have low toxicity and are well tolerated. However, they are still recognized as foreign proteins in the human body and can elicit some levels of immune response which will vary from patient to patient. It is therefore difficult to predict how immunogenic an antibody will be in humans. Neutralizing antibodies produced by the patient can also reduce the effectiveness of the treatments. To mitigate immunogenicity, humanized antibodies are generated by changing murine protein residues to human protein residues. Alternatively, therapeutic antibodies are identified directly from human antibody libraries. However, a product's degree of "humanization" (closeness to human) does not necessarily correlate with its immunogenicity. Even full human proteins can be immunogenic in some cases. Although there has been considerable progress in this area, the issue of immunogenicity is still very relevant to the monoclonal antibody market. Unfortunately the only reliable test to date is still human clinical trials.

Strong competition for many targets

An important factor that negatively affects the amount of revenues from a specific monoclonal antibody is the increasing competition. Many lucrative antibody targets are in the pipeline of multiple companies. Since significant differences in clinical efficacy may be difficult to establish, a deciding factor for healthcare providers may be the price. Ideally, manufacturers want their products to be used in as large a patient population as possible and want to be reimbursed at prices that reflect the high research and development costs. However, developers of future biosimilar monoclonal antibody drugs may find that their therapies are used only in a relatively small number of patients or generate lower than expected revenues. This may restrict the commercial success of individual drugs and may negatively affect the monoclonal antibody market as a whole. Therefore the number of future monoclonal blockbusters may be smaller than what the current pipeline might suggest.

Monotherapy for oncology

One weakness of oncology monoclonal antibodies is their often insufficient efficacy as a single agent. As a result, the cost of the cancer treatment is elevated by the need for multiple agents, usually including chemotherapy. Therefore these monoclonal antibodies are vulnerable to governments and healthcare providers who focus on limiting the costs of healthcare, and thus give cheaper treatments higher priority and often assign monoclonal antibody therapies as second- or even third-line treatments.

Opportunities

Increasing cancer prevalence

Cancer is a leading cause of death worldwide, causing approximately 15% of all deaths. In China there are 1.6 million deaths due to cancer each year and 25% of all deaths are caused by cancers. There are an estimated 15 million new cases diagnosed each year. The 5- year survival rate in China is only 50% compared to 70% in the US. Cancer is a major priority for healthcare providers. Lung cancer leads cancer deaths each year, followed by stomach cancer, colorectal cancer, liver cancer and breast cancer. The incidence of cancer increases with age. Reports suggest that cancer incidence and mortality will increase by around 50% by 2024, driven primarily by the continuing industrial growth and the increasing of aging population.

Autoimmune disorders are under-treated

Monoclonal antibodies for the treatment of autoimmune disorders are the second major class of antibody drugs and they generated 39% of total antibody revenues. Currently there are around 50 million patients worldwide with rheumatoid arthritis but only a small proportion of these patients is treated with antibody drugs. The rate of increase in prevalence of autoimmune diseases is lower than that of cancer due to the fact that increasing age is not the primary risk factor for these diseases. Nevertheless, most autoimmune disorders are increasing in prevalence, with a consequent increase in the burden of disability and associated economic costs to society. Penetration of monoclonal antibody therapies in autoimmune disorder patients remains low. Increasing this penetration will be the major opportunity for this sector of the market.

Threats

Lack of reimbursement for monoclonal antibodies

The high cost of monoclonal antibodies has restrained the growth of the market. A proportion of patients have not been able to afford expensive monoclonal antibody therapies. High prices have also led to healthcare providers deeming these therapies not cost-effective, and therefore not eligible for reimbursement. Controversy over the costs of new medicines and budgetary provisions has affected the development of new drugs, and monoclonal antibody drugs are most seriously affected.

Reimbursement prospects for monoclonal antibodies are unlikely to improve during the present global economic downturn in 2009, as governments and private healthcare services are under pressure to limit their expenditures. In the longer term, however, the prospects for reimbursement of monoclonal antibody therapies could improve, particularly for new treatments with proven clinical superiority over existing treatments. Treatments for niche indications with no alternative treatments are also likely to be reimbursed relatively generously.

Increased regulatory concerns

Safety concerns are a major threat to monoclonal antibodies. The risks can be target-related or antibody-related. The regulatory agencies place increasingly heavy emphasis on safety. New monoclonal antibody treatments will have to establish a strong body of evidence showing that treatments are safe, especially if they use novel modes of action. Nevertheless, a good safety profile remains one of the main strengths of the monoclonal antibody market.

Current financial limitations

Developing monoclonal antibodies is costly. Production of antibodies requires considerable capital investment, time and expertise in mammalian cell biology and bioprocess. Smaller biotechnology companies are often forced to collaborate with larger partners. These companies require substantial returns on their investments to continue research and development. In the current financial climate, the barrier of entry for companies wishing to develop and market monoclonal antibodies is increasing. Limited research and development may pose a threat to the future high revenues of the monoclonal antibody therapeutics sector. In addition, downward cost pressure by healthcare payers is increasing during the current economic downturn in 2009 and may further discourage R&D activities in this area.