

Executive Summary

Monoclonal antibodies, or mAbs, are highly specific antibodies produced in the laboratory by a variety of methods. In the nearly 35 years since the first process for creating mAbs was introduced, they have remained a centerpiece of the growing biotechnology industry. Thirty therapeutic mAbs have been approved around the world, including 24 in the United States, several of which have attained blockbuster status, with sales reaching the coveted billion-dollar mark and well beyond. Five drugs—Rituxan (rituximab), Remicade (infliximab), Avastin (bevacizumab), Herceptin (trastuzumab), and Humira (adalimumab)—generated sales of over \$4 billion each in 2008, and global sales for this entire sector surpassed \$30 billion in that year.

This report reviews the broad drug development effort that is focused on bringing improved mAb-based products to the market, concentrating on those used for therapeutic applications. It surveys the latest technologies being applied to the development of these compounds and profiles the major companies, drugs, and projects. It then draws conclusions about the future market potential for mAbs and discusses some of the major challenges faced by the industry.

The first-generation mAbs were murine (derived from mice), but these were soon discovered to have weaknesses. They were targeted for neutralization by the human immune system and also induced the formation of damaging immune complexes. The biotech industry devoted years to reducing the immunogenicity of mAbs, developing the technologies—detailed in this report—to progress from chimeric, to humanized, to fully human antibodies. These succeeding generations of mAbs have demonstrated incremental improvements in safety and activity, and the industry is currently in the middle of a major shift from murine toward humanized and human products. Much work has also been done on altering antibodies' outward form to boost their efficacy, enable them to more readily penetrate tumors, enhance their

ability to stimulate beneficial immune responses, or otherwise improve their characteristics. Into this realm fall such constructions as antibody fragments, diabodies, synthetic antibodies, bispecific antibodies, and antibody conjugates. This report looks at some of the engineered forms of antibodies and the companies that are leading the way in this research. Other complementary technologies, such as PEGylation and glycosylation, are also discussed.

The report goes on to evaluate the current state of mAb drug development. It identifies more than 250 therapeutic products now in clinical trials, which are largely concentrated in the areas of cancer, immunological and inflammatory diseases, and infectious diseases. Beyond these, hundreds more candidates are at the preclinical stage of development. Reviewed here are the products that are already available, those in clinical development, and those still at the preclinical stage that are likely to play an important role in the advancement of the field.