Next-generation monoclonals less profitable than trailblazers?

A new study has suggested that therapeutics based on monoclonal antibodies (mAbs) are far more likely to be commercially successful than their small-molecule predecessors. For the next generation of mAb-involved biotech companies, it may not be as easy as before to sustain that trend. Although mAbs have been successful so far, the competition among the new crop of mAbs and from other types of biological products is likely to intensify, especially in fields like oncology.

According to a study completed in June 2005 by London-based consultancy Propagate Pharma, about half the mAbs launched so far appear to be profitable. That means mAbs are recouping more in revenues than their estimated $1 billion to $1.8 billion cost of development and marketing. By comparison, the study estimates that only 30% of conventional small-molecule drug launches ever recover their costs.

The data are admittedly preliminary, since calculating the exact profitability of a drug would entail counting its revenues all the way to the end of its life cycle. No mAb has yet been through this process. To get around this, Propagate used peak annual sales as a proxy measurement for total profit. It concluded that a drug is likely to be profitable if peak revenues pass the $300 million mark. So far, of the 17 mAbs launched in the US, eight have achieved this benchmark. And of these, four have become blockbusters earning over a billion dollars a year (see **Box 1**). The other nine are mostly 'question marks,' whose ultimate profitability is not yet resolved.

Recombinant proteins exhibit a similar though not quite as spectacularly fast-growing trend. Of 57 launched so far, 16 have become blockbusters, 14 have at least recouped their costs, and the other 27 are either question marks or failures. The high success rate of biotherapeutics is due to low levels of competition in the markets they address, says Jo Collett, author of the Propagate study. Sales and marketing costs for mAbs are also less than for traditional small-molecule drugs, because they tend to be injectables focused on specialist disease areas, rather than being aimed at the intensive primary care market (*Nat. Biotechnol.* **23**, 269–269, 2005).

Moreover, there are signs that the tail end of a biotherapeutic product's life cycle might be more profitable than that of a small-molecule drug. In particular, according to the Washington, DC-based Biotechnology Industry Organization, it will be difficult for would-be competitors to demonstrate the bioequivalence of their own antibodies, making it much harder for them to launch rival generic equivalents.

Generics makers naturally disagree, and opposing feelings are running high (*Nat. Biotechnol.* **23**, 765, 2005). As a result, delays in the introduction of biogenerics on the US market are expected until an approval methodology is agreed on; a US Food and Drug Administration white paper is due out this August. Meanwhile, the European market has a regulatory framework in place but still no biogenerics approved. "These delays buy existing branded products more time on the market, and bring branded companies closer to launching their second-generation biologics," says analyst Mike Mitchell of London-based broker Evolution Securities.

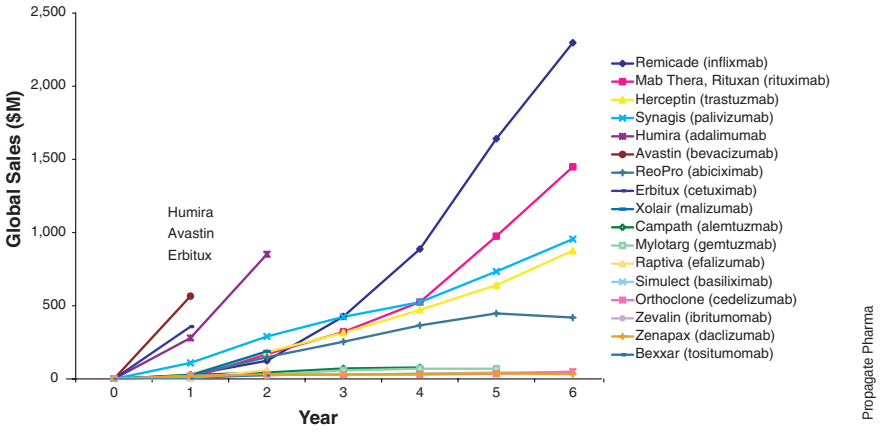
However, this high level of success may be difficult to sustain as competition increases, especially in the cancer market, says Propagate's Collett. "It's not going to be quite as easy as it was for the pioneers," she prophesies. "There is a danger that firms may be tempted to rest on their laurels and think that every mAb is going to be like Avastin [bevacizumab]."

There are now more than 150 mAbs in development worldwide, over 100 of which are in phase 2 or phase 3 trials. Nearly 40% of these are in the oncology field; 18 are in development for breast cancer alone. Collett predicts that companies launching the next generation of mAb therapeutics will have to be more commercially acute with a better understanding of their products' positioning than the pioneers of the field were.

Moreover, the success of the first wave of mAbs may be atypical, says independent consultant David Glover, formerly CSO at UK immunotherapeutics firm Cambridge Antibody Technology. "It's easy to get sidetracked by the success of Rituxan [rituximab] and Avastin, but these are the low-hanging fruit," he notes. "People go for the easiest opportunities first."

Although there is respectable data showing that obtaining regulatory approval tends to be easier for antibodies than for other drug classes, he warns it is too early to make firm predictions. "The mid and longer term future may look quite different in terms of competitive threats, so past performance is not necessarily a guide."

Peter Mitchell, London



The most recent monoclonal antibodies to reach the market have sold much faster than the first.

Box 1 mAbs success

mAbs currently represent about half of all new drug launches, so their success is changing the economics of the industry, says Jo Collett of London-based consultancy Propagate. Remicade (infliximab; by Johnson & Johnson), Rituxin (rituximab; by Roche and Genentech), Synagis (palivizumab; by Medimmune and Abbott), Herceptin (trastuzumab; by Roche and Genentech) and ReoPro (abciximab; by Eli Lilly) have already brought in revenues of over $3 billion apiece.

And some of the most recently launched mAbs—including Humira (adalimumab; by Abbott and Cambridge Antibody Technology), Avastin (bevacizumab; by Roche and Genentech) and Erbitux (cetuximab; by ImClone, Bristol-Myers Squibb and Merck)—have shown runaway early growth that bodes well for their total lifetime sales. According to analyst Tim Race of UK merchant bank ING, Roche's Avastin is becoming the gold standard for solid tumors with peak sales forecast at $8.4 billion and real competition still "years away." *PM*