When products fail

Biotechnology companies have several options when it comes to alleviating the "sting" of failing to get a lead product to market, says Max Herrmann.

Regardless of the turmoil currently being experienced by high-technology and biotechnology shares on stock markets around the world, the most significant risk to any individual biotechnology company remains the failure of a lead product in clinical development.

This was highlighted in December 2000 when news emerged that an advisory panel to the US Food and Drug Administration declined to approve Maxim Pharmaceuticals' (San Diego, CA) lead compound Maxamine for the treatment of patients with advanced metastatic melanoma and liver metastases, questioning the drug's effectiveness; Maxim's shares plummeted 44% in one day. Many other biotechnology companies with product failures have suffered a similar devastating loss of investor confidence.

Many companies have been criticized for their overdependence on one key product. However, unfortunately, this is rarely intentional. The high attrition rates seen in both drug discovery and clinical development mean that even initially broad-based businesses find themselves reliant on one successful development candidate. Furthermore, with only around 10% of drugs that enter human clinical trials ever reaching the market, the list is growing of companies in the sorry position of having to deal with product failure.

However, companies that have suffered product failures have several options. These include renaming the company, closing it down, merging, changing the management, or refocusing drug discovery efforts. The strategy adopted depends on the company's cash position, the financial community's regard for its management, and the company's remaining development opportunities.

A.K.A.

Changing the name of the company is probably the most commonly used rescue strategy, and its obvious purpose is to distance the renamed company from its past experiences. In the United Kingdom, for example, Cortecs (Cambridge, UK) changed its name to Provalis in November 1999 after its oral calcitonin drug, Macritonin, was not approved for the treatment of osteoporosis. Peptide Therapeutics changed its name to Acambis (Cambridge, UK) after its lead allergy peptide vaccine failed in clinical development and the group shifted its focus from peptide-based drugs to vaccine development.

In the United States, Magainin Pharmaceuticals (Philadelphia, PA) changed its name to Genaera in March 2001 after repeated development setbacks of Magainin-based drugs.

Disposing assets

Disposal of what remains of a company's assets, and returning them to shareholders, is often the only strategy left open to biotechnology companies that are frequently short of financial resources.

Scotia Holdings (Stirling), one of the UK's early biotechnology stars, saw its share price collapse after the FDA failed to approve its photodynamic cancer therapy Foscan in October 2000. Foscan's rejection by European regulators in January 2001 proved to be the final nail in Scotia's coffin, forcing the company into administration (*Nat. Biotechnol.* 19, 191, 2001). Although the company could have refocused its business on other drugs in its pipeline, a rescue fund-raising was futile: a £50 million convertible bond meant that any equity raised would have gone to the bondholders, not the shareholders.

Perhaps one of the highest profile drug failures in biotechnology's short history was that of Synergen's sepsis drug Antril, an interleukin-1 receptor antagonist. Despite a cash pile of $111 million, Synergen agreed to a proposed acquisition by Amgen for $251 million in December 1994. Synergen had decided

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that its future, and that of its employees, was best served as part of a larger group. Indeed, although the company is no more, this strategy has been successful and its drug pipeline lives on: The FDA is currently reviewing Kineret, a drug based on Antril, for the treatment of rheumatoid arthritis. If sales of Kineret achieve analyst expectations of $500 million a year, Amgen's investment will have paid off handsomely.

Musical chairs

Failure of key products can also prompt investors to demand management changes. The recent high-profile failure of British Biotech's (Oxford, UK) anticancer drug Marimastat, a matrix metalloproteinase inhibitor, is a good example.

Following press and investor accusations that the prospects for Marimastat had been misrepresented, the company's shareholders decided that management needed to be changed. The company was well funded, having raised £143 million in a follow-on offering in July 1996. However, several rounds of redundancies were required to preserve the cash. Since then, Marimastat has failed to show benefit in a broad clinical program.

Perseverance pays

Even the most successful biotechnology companies have suffered major product failures during their history. But some have managed to cope by targeting the drug at another indication.

For instance, Celltech (Slough, UK) developed an antibody CDP571 to treat septic shock—a well-known graveyard for drug development—and had licensed it to Bayer. When Bayer dropped development of the drug in May 1997, Celltech's shares fell 46% in one day. However, Celltech has since developed CDP571 for the treatment of Crohn's disease and could launch the drug next year.

Take out insurance

Perhaps the best strategy of all is to reduce the potential impact a product failure could have in the first place. During the development of any biotechnology company, investor enthusiasm for its technology and products will naturally wax and wane. A company should take advantage of investor enthusiasm to raise funds for merger and acquisition activity and in-licensing, and to explore new product opportunities to diversify risk away from its lead product. The key objective is to broaden a company's pipeline without burdening the business with unacceptably high costs of clinical development.

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Unfortunately, there will always be disappointments in drug development, and biotechnology companies and their investors need to be prepared for a bumpy ride.