Balancing Big Pharma's books

With patents running out on their big earning products and recent scandals undermining their image, drug companies are under pressure. **Andrew Jack** reports on their problems

When business chief executives joined politicians and public officials gathered at the World Economic Forum in Davos last month, one group of industry leaders was noticeably under-represented: those from the pharmaceutical sector. Some regulars in previous years, such as Hank McKinnell, the outspoken former head of Pfizer, the world's largest drug group, have lost their jobs. Others, like Richard Clark from Merck and Daniel Vasella from Novartis, pulled out at the last minute. The message was clear. At a time of investor dissatisfaction with their companies and employee disgruntlement at cutbacks, they would do better to stay in their headquarters and focus on internal problems rather than debate the broader issues of the world.

To many, it seems hard to believe that the drug industry—long spoilt by lavish revenues and little need for controls on spending—is in crisis. In fact, its current malaise is characterised by a series of problems.

Illusion of plenty

Judged by their accounts, "big pharma" companies look healthy. They spend heavily to market expensive medicines, generate large cash piles that shield them from the current credit crunch, and report high profits with margins envied by most other industries. Yet shareholders are sceptical. The cliché is that investors are focused on short term returns. But the share prices of quoted drug companies do not bear that out: they have low valuations precisely because the stock market is concerned at the bleaker longer term prospects.

Once seen as defensive growth stocks that offered investors a safe haven of steady future expansion, drug company shares have underperformed those in many other sectors in recent years. The reason is a belief that worse is to come, as pressure increases on pricing, sales of existing drugs come under threat, and replacements in the pipelines are scant.

The most pressing concern for drug companies is that the money is running out. Patents on existing medicines will expire over the next five years, reducing the industry's collective annual revenues by around \$100bn (£50bn; €70bn) (box). Furthermore, the increasingly powerful generic drug industry is sharply and swiftly undercutting the patented prices and attempting to win the advantage on their own competitors by launching legal challenges to patents even before they expire.

So far, biotechnology products have escaped generic competition. But the EU's biosimilars pathway, and discussions for a parallel process in the US, could start to expose Amgen and other large biological drug manufacturers in the coming years.

GlaxoSmithKline's shares dropped more than 7% earlier this month after it warned of a 3-7% decline in earnings for 2008, when it feels the effect of generic competition on six of its drugs (Coreg IR, Wellbutrin XL, Requip IR, Lamictal IR, Paxil CR, and Imitrex). A week before, AstraZeneca said it faced "increasingly challenging market conditions." Their peers are under similar pressures.

Companies are thrashing around trying to find responses, from cutting costs through thousands of job losses to new ways to unleash scientific talent from managerial bureaucracy and boosting research to swell their pipelines of drugs in development. None has delivered a long lasting remedy.

EXPIRING PATENTS

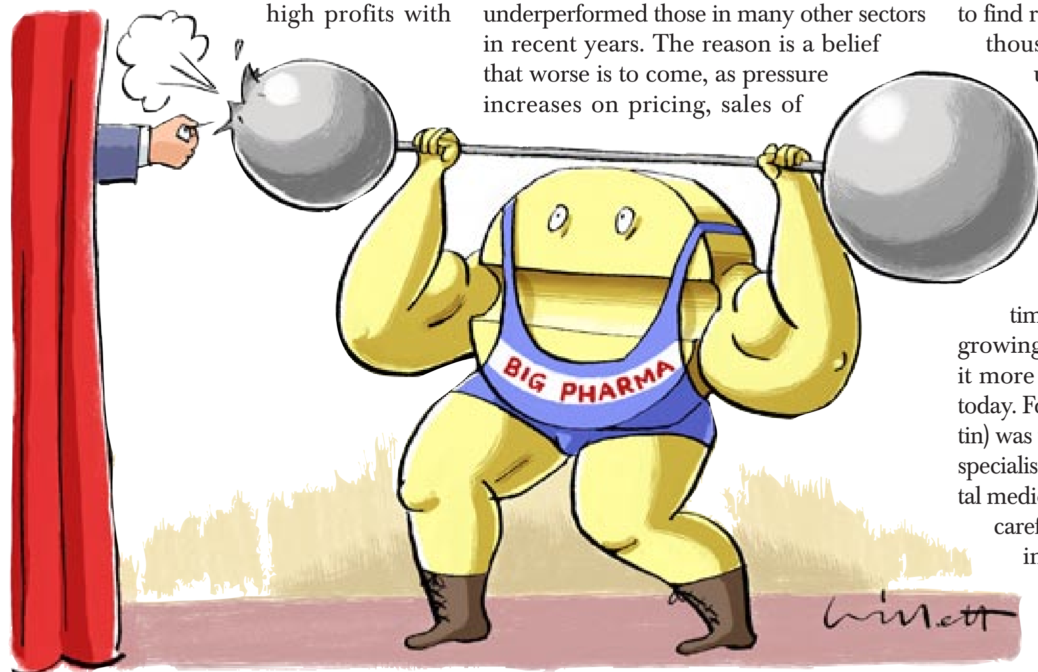
Pharmawire, a specialist agency owned by the FT Group, estimates that in 2008-12 \$114bn is at stake from blockbuster patented drugs alone. Few companies escape. The top selling drugs under pressure in the next few years include:

2008 Fosamax (Merck), Effexor (Wyeth), Keppra (UCB), and Topamax and Risperdal (Johnson & Johnson)

2009 Lamictal and Valtrex (GlaxoSmithKline), Lexapro (Forest), and Arimidex (AstraZeneca)

2010 Cozaar (Merck), Aricept (Eisai), Taxotere (Sanofi-Aventis), Protonix (Wyeth), and Levaquin (Johnson & Johnson)

2011 Lipitor (Pfizer), Plavix (Sanofi-Aventis/ Bristol-Myers Squibb), Seroquel (AstraZeneca), Advair (GlaxoSmithKline), and Zyprexa (Eli Lilly)



Burden of riches

The large drug companies are victims of their own success. Large and fast growing sales and profits in the past make it more difficult to sustain the momentum today. For example, Pfizer's Lipitor (atorvastatin) was the fifth statin in its class, which some specialists argue offers only modest incremental medical benefits over its predecessors.[1] Yet careful positioning and aggressive marketing turned it into the world's largest blockbuster drug, generating more than \$12bn a year in revenues.

That has helped sustain the

To many, it seems hard to believe that the drug industry—long spoilt by lavish revenues and little need for controls on spending—is in crisis

company in recent years but is presenting it with a curse as the expiry date of its patent approaches in 2011. Its attempt to extend exclusivity by combining Lipitor with the experimental drug torcetrapib was frustrated after additional patient deaths were reported, forcing it to abandon clinical trials in late 2006.[2]

Another effort to help shore up sales was the inhaled insulin Exubera, which Pfizer launched last year but then was embarrassingly forced to withdraw because sales were so low. Patients were frustrated by its cumbersome inhaler, doctors unconvinced of the benefits, and payers unimpressed by the price. The company had to write off nearly $3bn.[3]

Similar pressure has come from the mergers of the past decade that have helped build most of the big pharma companies. Some of their names still bear witness to the history (such as Sanofi-Aventis or Bristol-Myers Squibb) while others have since rebranded (such as Novartis, which was formerly Ciba-Geigy and Sandoz). Whether these groups merged to gain economies of scale or to strengthen their pipelines of experimental drugs, the result has been to create corporate monoliths with greater sales and profits. Maintaining significant growth on such large absolute numbers is ever tougher.

Science outstrips medicine

There is a chasm between science and medicine—the niche occupied by the drug companies and their best way to replace revenues as patents expire. Science has made extraordinary advances in recent years, including the cracking of the human genome. But the translation of this basic research into new medicines is proving slow, difficult, and costly. That partly relates to the continued technical challenges and limited understanding of this new knowledge and how to apply it effectively.

It reflects public opinion that is risk averse, sparked by fears such as the reported patient deaths caused by Merck's painkiller Vioxx (rofecoxib) or GSK's diabetes drug Avandia (rosiglitazone). Cautious regulators have responded by imposing ever tougher barriers that must be overcome to approve new medicines.

The slow progress of turning scientific discovery into new drugs also shows the limited ability of large companies—swollen into large bureaucracies by the mergers—to manage their researchers most effectively. They have turned increasingly beyond their own walls, buying smaller biotech companies or licensing in the rights to experimental drugs developed by others. In the process, they are competing in a commercial battle that has pushed up prices while not always delivering more successful new medicines.

However much dispute there is over the precise costs of successfully bringing a new drug to market, aggregating the total invested in research and development by the industry and dividing by the number of drugs approved by regulators in recent years suggests each one costs the staggering sum of more than $1bn.

Disappointing demand

On paper, an expanding global population, rising incomes and increasing life expectancy should offer the companies attractive commercial prospects for new drugs. Demand is increasing for sophisticated health care and for new drugs to cope with more commonly occurring and more frequently diagnosed diseases affecting the developed and developing worlds alike, including diabetes and cancer.

But even many rich societies are reluctant to pay. They are increasingly hostile to the high and rising costs of new drugs and suspicious of the true benefits of newer and more expensive drugs compared with cheaper generic alternatives.

They are introducing structures like the UK's National Institute for Health and Clinical Excellence, designed to recommend whether the National Health Service should reimburse new medicines based not only on clinical efficacy but also on cost effectiveness. Whoever wins the US presidential elections later this year, it is almost certain that spiralling healthcare costs and concerns about incomplete coverage will push in the direction of a tougher approach to value for money and pricing of medicines.

Healthcare payers also tend to take a "silo budgeting" approach, looking narrowly at the rising costs of medicines rather than the broader benefits they can offer. Proton pump inhibitors have all but eliminated far more costly ulcer surgery; and even modestly effective drugs for Alzheimer's disease can reduce the burden on social services and employees required to give up work to help care for ageing relatives. Such factors are rarely considered by payers. Whatever a drug's broader benefits, its price makes it a target.

Poor perception

Instead of being viewed as heroic providers of the latest life saving medicines, drug companies seem often to be viewed instead as 19th century snake oil salesmen. Popular films such as *The Constant Gardener* and Michael Moore's *Sicko*, let alone factual reports of research, regulatory and marketing abuses as well as safety scares, have not helped their reputation.

In the US, where patients until recently often paid the full price of their drugs and continue to be bombarded with advertising for prescription medicines, the companies have put themselves on the frontline. In Europe, where prescription charges are normally minimal and advertising to consumers is banned, there is still a sense of suspicion that companies are putting profits before people, whether using patients as guinea pigs or denying access to the poor.

Nellie Kroes, the European competition commissioner, left little doubt of her own mistrust of the industry when she launched an antitrust investigation into the drug industry in January. The public statement explaining the probe said she had no specific allegations but she had taken the unprecedented step of launching unannounced raids on the companies out of concern that sensitive documents might otherwise be destroyed.[4] With such sentiments further embittering their mood of frustration, drug companies may still be posting profits for now but they are likely to suffer much more pain ahead.

Andrew Jack is pharmaceuticals correspondent, *Financial Times*, London
Andrew.Jack@ft.com

Competing interests: None declared.

1 Institute for *the Qua*lity and Efficiency in Healthcare. *Evaluation of the effects of statins (with particular consideration of atorvastatin)*. Cologne, 2006. www.iqwig.de/download/06-01-30_Finaler__Evaluation_of_the_effects_of_statins_SIV-111_0_050815.pdf.
2 Food and Drug Administration. *Pfizer stops all torcetrapib clinical trials in interest of patient safety.* 2006. www.fda.gov/bbs/topics/NEWS/2006/NEW01514.html.
3 Pfizer. *Third quarter earnings teleconference, 18 October 2007*. www.pfizer.com/files/investors/q3earnings_october182007.pdf .
4 Kroes N. *European Commissioner for competition policy commission launches sector inquiry into pharmaceuticals*. Press release , 16 Jan 2008. http://europa.eu/rapid/pressReleasesAction.do?reference=SPEECH/08/18&format=HTML&aged=0&language=EN&guiLanguage=en.