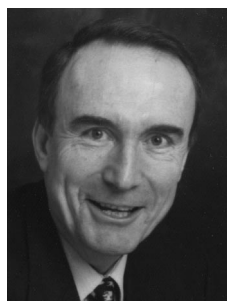


Investment status of biopharmaceuticals



'...many of these businesses will die. Why? Naivety.'

Stock Markets in the USA and Europe have given investors tremendous returns over the past ten years, and the price of companies' shares (stock) has increased out of proportion to the actual profits. The price/earnings (P/E) multiple has moved up, to a great extent driven by the perception that information technology (IT) is making companies more efficient, and technology, principally the IT sector itself, now represents a significant share of total stock market value.

The recent proposed merger of Glaxo Wellcome and SmithKline Beecham highlighted the value of the pharmaceutical and healthcare sector when it was apparent that the combined value, as determined by the world's stock markets, made a combined GW/SB the second largest company worldwide as valued by market capitalization. To be second largest in the world and yet have only a 7% share of this market segment means that pharmaceuticals/healthcare is now recognized, at least by the financial community, as one of the world's great industries.

Research is key

Companies with a strong R&D product pipeline focus on reducing the time to market, acquiring technologies, where necessary, from the so-called 'toolbox' companies, and investing heavily in sales and marketing (which, in the USA, includes direct consumer advertising) to drive up sales and market share. Those companies with poor product pipelines, as demanded by the financial community, are consolidating.

The consolidators in the top ten are gaining market share at the expense of their competitors for the first time ever. If this trend continues, and there is no reason why it should not, within a very few years, 80% of the market will be controlled by about five companies. Regulators will ensure that none

dominate the industry individually, but each may dominate a particular sector in terms of therapeutic area and/or geographical area. So what of the rest? It is important to remember two facts:

- This is one of the world's largest industries
- More than 40% of human disease is incurable today

So the market is still growing. And yet, by its own benchmarks, this industry is research driven and depends on new discoveries to continue this growth. Until very recently, company growth was reflected in expansion of the overall market, but the healthcare providers' ability to pay for the insatiable demand for healthcare is bringing pressures to bear on all suppliers to the industry, including pharmaceutical companies. This pressure is focused on R&D efficiency, not least because the pharmaceutical industry is the only one that has invested in R&D consistently and at a rate three-times greater than any national R&D programme (15% vs. 5%). Stock market analysts are now asking if the R&D investment by the pharmaceutical sector has room for improvement. To assess this, the analysts use the universal yardstick – cash.

Cash is king

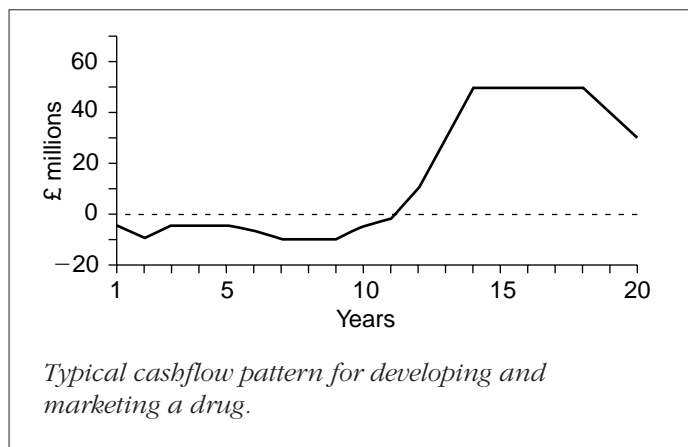
In a hypothetical example of the cash flow of a typical pharmaceutical product (see Figure), an investment approximating £50 million spread over ten years produces a drug with peak sales of £50 million per annum before patent expiry. R&D investment focuses on producing a continual stream of such products, and the most successful companies are those that are able to launch more products per annum.

However, analysis of the results for the market leaders Glaxo Wellcome and Merck indicates that, not only did these companies produce more products but, perhaps more importantly, they also produced these new chemical entities (NCEs) faster. Several years ago, both Merck and Glaxo were averaging 7.5 years from discovery to launch compared with an industry average of ten years or more. What does this mean in cash?

Effect of efficiency

Taking the example in the Figure, every year removed from the drug development time equates to an extra year of sales under patent protection. This means sales of £50 million per annum or say £1 million per week. As the current P/E ratio for the

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sector is about 40, if this £50 million of extra sales translates into £30 million profit after tax, the market capitalization of the business increases by $40 \times £30 \text{ million} = £1.2 \text{ billion}$.

Conversely, every week's delay loses £1 million per week or £200,000 for every working day, or £400 per min assuming an eight-hour day. This is why the focus is on increasing the efficiency of the R&D process, the result creates far more profit and a far more valuable business than just looking at the cost of R&D. In fact, the major drug companies are currently spending vast sums to acquire technologies that shorten the R&D timescale.

New technologies – new treatments

The new technologies, genomics, proteomics, combinatorial chemistry, pharmacogenomics and bioinformatics, are filling the product pipeline with new drug targets, drug candidates and more precise outcomes. Will the blockbuster drug become history as this vast array of new drugs focused on smaller patient populations emerge from R&D? Probably not. These new drugs are, in the main, focused on the 40% of human disease that has an unmet need. The 60% of treatable disease will be better treated, and the 'massive killers' and major chronic diseases will still require blockbuster drugs and blockbuster R&D budgets to produce them.

What is happening now is the emergence of numerous new companies spinning out from academia because universities worldwide are starved of cash and cannot (or will not) wait the ten years it takes to get the licence fee income from big pharma. The inventors and/or entrepreneurs are launching businesses at breakneck speed, and many of these businesses will die. Why? Naivety.

Entrepreneurs and the market

Academics are by nature not entrepreneurs. Even in the health-care sector in the USA (the most commercial market), most entrepreneurs started out wanting to do good first and make money second. Investors, by and large, are ignorant of the biological sciences and the rigorous demands of the regulators – they are naive. This naivety on both sides has created a potent mixture in which perceptions have been hyped and market sen-

timent is still driving the perceived value of these new technologies. Market sentiment blows hot and cold and ignores reality.

The reality is that in the USA there are some 1300 biotech companies and in the EU about 700. These companies believe that they will float on the public markets (at least their investors want them to), but most will fail to. At present, about 300 of the 1300 biotechnology companies in the USA are public, as are 50 of the 700 in the EU. What will start to happen in an accelerating fashion will be trade purchases as large- and medium-sized pharmaceutical businesses acquire these smaller companies for their technologies. The single technology companies will probably be unable to float because their future pipeline is limited or nonexistent; these businesses will have to merge with other complementary biotech businesses, be acquired by a pharma company or die.

The mid-size pharma companies will require a healthy product pipeline, which can be achieved by acquisition of smaller biotech businesses to enhance their limited R&D spend. Both biotechs and pharma will have to shorten product development times so that value added is translated into share price, enabling further acquisitions and more growth.

Stand and deliver

Finally, for those mid-size pharma companies that have a portfolio of products nearing patent expiry – in fact virtually all pharma companies – there has to be a serious investigation into the possibility of extending patent life by reformulation (i.e. drug delivery). The quickest win and lowest risk in investment is in drug delivery. This affects drugs at any stage in the process, but its greatest effect is when drug-delivery technology allows a drug nearing patent expiry to be repatented. Sales do not have to start from zero, but instead either increase, hold their position or slightly decrease from peak sales. The payback on this R&D is huge and fast – this is why companies like Alza and Elan are valued so highly. Also, drug delivery technologies will enable the fragile, large-molecule biopharmaceutical drugs to compete more even-handedly with the small-molecule drugs, designed for oral administration. In fact without these delivery technologies the new biopharmaceuticals will remain minor products as measured by sales.

Rewards and penalties

In conclusion, drug discovery, drug development and drug delivery technologies have to deliver in cash terms. The benefits of success are many multiples of the actual cost, with time being the major constraint. The demands of the financial markets on the whole industry is forcing R&D, both in companies and in academia, to produce results more quickly. The penalties of wasting time are lethal in this present climate of industrial change. The pharmaceutical industry is emerging as one of the world's greatest industries and biopharmaceutical technologies are the key to its future. Traditional R&D is under threat but the opportunities opened up by these changes are huge for those who respond positively.

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