

# introduction

The investment climate in the world of drug discovery has certainly improved in the last six months or so although the jury is still out on the question of whether this improvement will be sustained. In any event, a number of initial public offerings (IPOs) are in progress in the biotechnology sector in the US. Although this trend has not yet spread to any extent to Europe, even there companies have raised significant sums using rights issues and other funding vehicles.

It is noteworthy, however, that the companies most likely to receive investor support are those presenting so-called 'near market opportunities' usually interpreted as having products either on the market or in Phase III of clinical development. Earlier stage companies, and particularly start-ups, are struggling to raise finance. This may be understandable but it is a matter for concern since it is from at least some of these companies that truly significant, novel and improved therapies are likely to emanate.

What can such companies do to improve their chances of attracting investment or indeed of doing appropriate deals? The first and most obvious thing to do is to ensure that the manner in which they present their case is professional and persuasive. We include an article in this edition of *DDW* on the 'pitch'. This gives advice on both the practical and psychological aspects of engaging the attention and interest of often cynical audiences who may well have the attitude that they have heard it all before or that it is all too novel and 'scientific' and therefore a long way from a product.

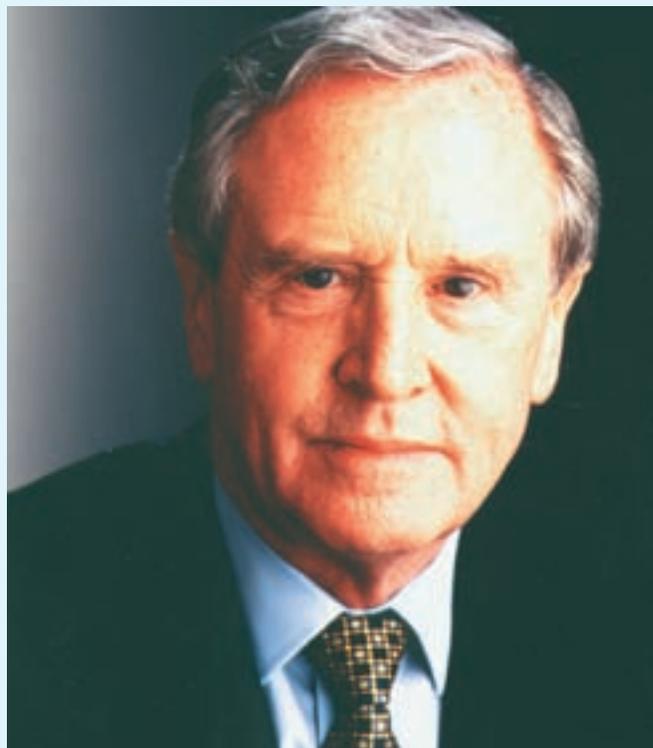
The cynicism referred to above has a number of origins. Rarely a week passes without another announcement concerning the withdrawal of a drug from development. And although those in the business recognise that failures are inevitable, nevertheless it behoves all concerned to do all that is possible to ensure that this attrition rate is reduced. This, of course, is easier said than done but we have in the pages of *DDW* over the past two years or so published a number of articles describing technologies and strategies which are aimed at selecting development candidates with maximum chance of success. It is still too early to have any clear view about which, if any, of these approaches have been successful, but it remains a fact that a lower failure rate in development would increase confidence and reduce cynicism.

A second cause of cynicism arises from the hype which accompanied the elucidation of the human genome, the subsequent mushrooming of genomics and proteomics and the unrealistic expectations, in some quarters at least, that these sciences would lead, as if by magic, to a flood of new therapeutic agents. This may still happen but it will take time and improvements in available technology. With proteomics the basic problem still lies in correlating expressed proteins with specific disease states. We include an article in which protein biomarker strategies are discussed. The authors conclude that parallel protein-based analyses have a potential 'to define a new era in diagnostics and drug development' although the optimal strategy to achieve this objective has not yet been defined and is unlikely to be so for a few years.

In another article the authors discuss advances which have been made in mass spectrometry technology and express the view that this technology is at the cornerstone of the new systems biology the goal of which is to integrate information from genomics, proteomics and metabonomics. The latter is a relatively new term to describe measuring the complete metabolic response of an organism to a drug.

Another technology which should lead to the discovery of novel therapeutic agents is patch-clamping, an electrophysiological technique for studying the actions of drugs on ion channels. Its value has, however, been limited by the absence of high-throughput techniques and although recent developments show promise there is still controversy concerning their usefulness in comparison to more traditional electrophysiological methods. This controversy is discussed in these pages.

We have, in earlier editions of *DDW*, carried a series of articles on recent



developments in therapeutic approaches in areas of unmet medical need. Some of these areas represent very large potential markets and it is surprising that so little attention is paid to some of them by big Pharma and biotech companies alike. Lower urinary tract dysfunction (LUTD) is one such area. With the changing demographics in populations this is an increasingly prevalent problem, but it is by no means confined to the elderly. It is quite common in women of childbearing age and represents a large and unsatisfied market. The annual sales of drugs for overactive bladder syndrome (OAB) alone have risen in the last 10 years or so from around \$50 million to about \$1.5 billion, although the available therapeutic agents are far from perfect. We include an article which reviews compounds in development. They include drugs aimed at either the 'plumbing' (musculature) or the 'wiring' (neurological control) of the lower urinary tract.

Another area which collectively represents a significant unmet medical need includes a large number of rare diseases. In our article on orphan drugs it is stated that 20-30 million patients suffer from such diseases in Europe alone. Attempts to incentivise research on such diseases by pharmaceutical and biotechnology companies have resulted in organ drug legislation around the world following the FDA's initiative in 1983. The details of the legislation and the definition of an orphan drug differs from country to country but it is concluded by our author that this legislation 'is having a significant impact'. Other companies may consider entering this arena.

Finally, we include an article on DNA repair inhibition as a method of treating cancer and other diseases. This approach has arisen from the counter intuitive realisation that temporary inhibition of the normally beneficial DNA repair pathways can have considerable therapeutic potential. This has led to an increasing interest in this area which should be watched with great interest during the next few years.

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