A pharmaceutical *Braveheart* – battle lines are drawn

Two of the world's major pharmaceutical companies, Pfizer and GlaxoWellcome, are squaring up for a fight. For those who have seen the film *Braveheart*, Pfizer can be regarded as the Scots, a smaller army but eager to engage the enemy, while numerically superior GlaxoWellcome are confident of victory.

At the beginning of November last year, 200 financial analysts assembled at the new GlaxoWellcome Research Centre at Stevenage for a briefing on the final stages of the integration of the two UK giants that has made the new organization the largest drug company in the world. The summer of 1995 was a very difficult period for the company; every R&D project was under close scrutiny and employees felt insecure. Although the total number of R&D staff has been reduced from 11,500 to 9,700 worldwide, the remaining researchers are assured of a bright future.

In all, 93 projects are to be continued (Table 1), spread across most major therapeutic areas, and although most of the senior management consists of former Glaxo staff, many Wellcome projects are to receive continued funding. In addition, R&D spending is set to remain steady at about £1.2 billion a year for the immediate future. The company plans to invest heavily in robotics and extend its existing automated procedures. According to UK Research Director, Dr Alan Baxter, the present automated system for screening new molecules for biological activity handles 50,000 samples per week and this is set to rise to 50,000 per day during 1996. The company also plans to allocate less money to internal R&D and increase external collaboration with university departments and small biotechnology companies, especially in the USA. Its ultimate goal is an ambitious one, even for such a major company; the company aims to bring three important new drugs to the market each year, starting in 2000.

Table 1. GlaxoWellcome research projects

Therapeutic area	No. projects
Respiratory	22
Antiviral	12
CNS	18
Oncology	11
Cardiovascular	10
Gastrointestinal/metabolic	13
Anti-infective/immunologic	7

Less than two weeks before this announcement, Pfizer's Vice President for R&D, Dr John Niblack, addressed analysts in New York to inform them that Pfizer was going to attempt "something that no other pharmaceutical company has ever really brought off before". This would be the launch of multiple waves of new products. Within the next 2 years, the company will seek approval for five new chemical entities in the USA and elsewhere. These new compounds are: the acetylcholinesterase inhibitor, E-2020, for Alzheimer's disease; the quinolone antibiotic, trovafloxacin; the class III antiarrhythmic, dofetilide; ziprasidone for schizophrenia and sildenafil for erectile dysfunction. Another ten new chemical entities are also at an advanced stage of development and include agents for the treatment of diabetic complications, congestive heart failure, depression, breast cancer, migraine, fungal infections and sepsis.

It is never wise to take historical analogies too far, and although Sir Richard Sykes of GlaxoWellcome makes a convincing Edward Longshanks, Dr John Niblack will not be very keen to play William Wallace, even if his side did win in the end.

David B. Jack

Combinatorial biology

Marine organisms have proven to be an extremely rich repository of bioactive compounds and a source of continuing headaches when it comes down to the practical aspects of drug discovery. Frequently, bioactive compounds are too complex for laboratory synthesis, the marine organism cannot be collected in large quantities, or the organism refuses to grow under laboratory conditions, thereby blocking the acquisition of sufficient material for study.

Now a small company in San Diego, ChromaXome, Inc., has accomplished the transfer of the entire biosynthetic pathway of various secondary metabolites from marine microorganisms into commercial microbes, such as *Escherichia coli*. This will enable the production of large quantities of bioactive chemicals that would otherwise be prohibitively scarce. In addition, the company's scientists have succeeded in mixing and matching synthetic pathways from different microbes to produce totally novel 'natural products'. They call the new technology 'combinatorial biology'.

Just as combinatorial chemistry overturned old paradigms for the synthesis of chemicals for drug discovery, combinatorial biology may revolutionize the pharmacognosy field. In initial studies, ChromaXome focused on the transfer of anti-infective compounds and succeeded in transferring the biosynthetic pathway for the production of various polyketides, a chemical class that has provided a rich source of bioactive compounds in the past. Currently, ChromaXome is involved in a major collaboration to use combinatorial biology to generate novel compounds from the well-characterized

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