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An acute talent for innovation

By Andrew Jack

Sir James Black places his walking stick on one side, eases himself into a plump yellow sofa at the Royal Society of Medicine's headquarters in London and begins to talk in a soft voice. But he is soon working himself up into a passion.

He becomes agitated when discussing a Harvard Business Review article from 2008 by Jean-Pierre Garnier, the former chief executive of GlaxoSmithKline, on the future of drug development. He agrees with the prognosis, but is fundamentally at odds over the prescription for change.

“In this time of gloom, the pharmaceutical companies ought to be doing extremely well,” he says in his Scottish lilt. “There is no market as unique as drugs; when people are distressed, their desire for relief pre-empts all others; and the industry has a reputation for being good at development. The trouble is that it keeps making promises.”



Distinguished scientist Sir James Black says the growing use of new technologies has proved a mixed blessing for drug discovery

Still working, debating and writing in his 83rd year, long after most of his peers have quietly retired, Sir James has plenty of recommendations for improvement in an industry that has suffered from a flagging product pipeline, and still more thoughts on what has gone wrong.

He has no time for classic industry clichés such as “blockbuster” medicines; no truck with the modern approach to peer review; and no patience with any re-writing of history to suggest a more complex contemporary era of drug discovery has replaced one of “low-hanging fruit” in the past.

This is no idle chatter from an armchair pontificator, nor an academic divorced from the pressures of business. He is a distinguished scientist, the recipient of the Nobel Prize for Medicine in 1988, not to mention a Royal Medal and an award from the Lasker Foundation. But his rare skill – reflected late last year in the lifetime achievement award

he received from Medical Futures, a British organisation established to commercialise doctors' medical ideas – is to have bridged the divide between university and business.

He was pivotal in the development of two of the most successful blockbuster medicines that the pharmaceutical industry has ever developed: propranolol, the first beta-blocker to treat hypertension; and cimetidine for stomach ulcers. Both transformed the lives of millions of patients and saved health systems enormous costs.

Raised in Fife, the fourth of five boys in a “staunch Baptist home”, Sir James says he was a daydreamer in school, and it was only in the “forbidding” atmosphere of St Andrew's University, where he studied medicine, that disciplined study took over.

He researched and taught in Singapore and then Glasgow, but was soon drawn into industry after a friend working in ICI's marketing division suggested that he contact the chemical company's pharmaceutical unit to co-operate in his research on beta blockers. To his astonishment, they invited the academic outsider on a site visit to their new laboratories in Alderley Edge. “They said it would be much easier if I did the work in their labs. They were just heaven compared with anything I'd worked in before.”

His approach highlighted one aspect that he believes is key to successful drug development: entrepreneurial teams of up to about 25 people, allowed to operate at arms' length from the rest of the company. “Lab researchers have an insatiable appetite for growth. But we were small. I had a chemist and a technician, and off we went. I had to fight, but I could chat up the head of R&D. We knew everyone by their first name.”

He raises his eyes skywards when he discusses last week's \$68bn (€53bn £48bn) takeover by Pfizer, the world's largest pharmaceutical group, of Wyeth, and says the restructuring to come will sap both teams. “Will they never learn? They will completely exhaust each others' energies for two years.”

Even in ICI in the 1960s – the pharmaceutical division of which is now part of AstraZeneca, the product of a mega-merger a decade ago – he began to feel too much bureaucracy and too much drift towards conformity for someone who considers himself “an inventor, not a discoverer”.

“They wanted me to concentrate on development,” he says, recalling with horror a senior colleague who was increasingly distracted from his research, forced instead to spend “two days a week meeting anaesthetists for talks and then eating and drinking their heads off”.

Keen to begin work on a different field – antihistamines – when a friend at SmithKline and French asked if he could recommend people to hire, he put forward himself.

The result was his second blockbuster, generating billions of pounds in revenues. But he winces

at the word, a symbol of what has gone wrong in drug development. “It’s a kind of obscenity. Very few of the drugs classified as blockbusters retrospectively were designed in that way. The people who know about markets can’t even predict what next year will do.”

He points out that the sales forecasts for propranolol were £250,000 a year, and those for cimetidine £5m. The reality in both cases was orders of magnitude greater. “All you can do is plan for something which will fulfil a need. Being first is most important.”

Sir James questions how far research can be successfully managed and quantified in advance. He is scathing of pharmaceutical executives’ focus on bonuses and incentives. “I remember vividly the managing director of ICI pharmaceuticals saying to me that he would pay to do his job, he enjoyed it so much. Now apparently we have to bribe people.”

He also recalls a senior researcher at the Wellcome Foundation – where he then moved but which subsequently merged with his former employer to become GlaxoSmithKline – who changed his research targets each year because he could not show results in the short term. “I said, ‘you pick one and we’ll stick with it’.” The result was a new type of anti-convulsant.

He rejects any suggestion that drug discovery was easier in the past. “I never found it easy. People say I was lucky twice but I resent that. We stuck with [cimetidine] for four years with no progress until we eventually succeeded. It was not luck, it was bloody hard work.”

On the contrary, he suggests that the growing use of new technologies and techniques, from molecular biology to genomics, has proved a mixed blessing. “The techniques have galloped ahead of the concepts. We have moved away from studying the complexity of the organism; from processes and organisation to composition.”

Sir James was not able to repeat his own blockbuster success a third time, either at Wellcome, at subsequent academic posts, in the James Black Foundation that he founded after retirement, or in his continuing research today. But, given the uncertainties of science, even a single success is more than most drug developers can ever hope for.

He believes that for true innovation, researchers’ projects should not be assessed prospectively by their peers but on their promise demonstrated in the past and over longer cycles. “I believe you should be judged by what you have done,” he says. On those grounds, no one can question his contribution to medicine over the past century.

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