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Drug companies in America

# The costly war on cancer

NEW YORK

New cancer drugs are technically impressive. But must they cost so much?

CANCER is not one disease. It is many. Yet oncologists have long used the same blunt weapons to fight different types of cancer: cut the tumour out, zap it with radiation or blast it with chemotherapy that kills good cells as well as bad ones.

New cancer drugs are changing this. Scientists are now attacking specific mutations that drive specific forms of cancer. A breakthrough came more than a decade ago when Genentech, a Californian biotech firm, launched a drug that attacks breast-cancer cells with too much of a certain protein, HER2. In 2001 Novartis, a Swiss drugmaker, won approval for Gleevec, which treats chronic myeloid leukaemia by attacking another abnormal protein. Other drugs take different tacks. Avastin, introduced in America in 2004 by Genentech, starves tumours by striking the blood vessels that feed them. (Roche, another Swiss drug giant, bought Genentech and its busy cancer pipeline in 2009.)

These new drugs sell well. Last year Gleevec grossed \$4.3 billion. Roche's Herceptin (the HER2 drug) and Avastin did even better: \$6 billion and \$7.4 billion respectively. Cancer drugs could rescue big drugmakers from a tricky situation: more than \$50 billion-worth of wares will lose patent protection in the next three years.

This month Pfizer, an American company, announced that America's Food and Drug Administration (FDA) would speed up its review of a cancer drug called crizotinib. Roche submitted an FDA application for a new medicine, vemurafenib. The industry is pouring money into clinical trials for cancer drugs (see chart).

This is part of a shift in how big drug firms do business. For years they have re-

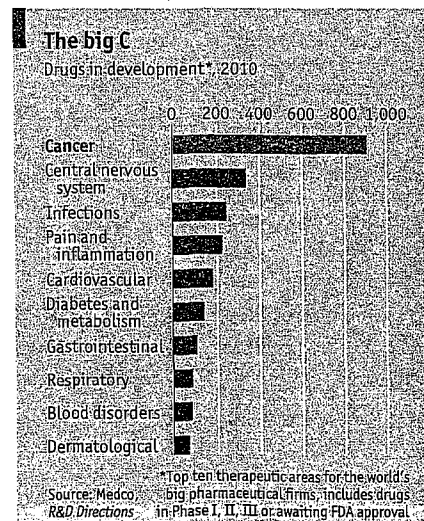
lied on blockbusters that treat many people. Now they are investing in more personalised medicine: biotech drugs that treat small groups of patients more effectively.

Last year the FDA approved Provenge, developed by Dendreon of Seattle to train the immune system to fight prostate cancer. In March the FDA approved Yervoy, Bristol-Myers Squibb's drug to treat melanoma. And there are promising drugs in the pipeline. Pfizer's crizotinib attacks a protein encoded by a gene found in fewer than 5% of patients with non-small-cell lung cancer. Roche's vemurafenib attacks advanced melanoma by blocking the mutated form of a gene, B-R.A.F. Both Pfizer and Roche are developing tests to help doctors identify suitable patients for their drugs.

The snag, from society's point of view, is that all these drugs are horribly expensive. Last year biotech drugs accounted for 70% of the increase in pharmaceutical costs in America, according to Medco, a drug-plan manager. This trend will continue as drug firms develop new ways to treat, for example, multiple sclerosis and rheumatoid arthritis.

Cancer plays a huge role in raising costs. America's National Institutes of Health predict that spending on all cancer treatment will rise from \$125 billion last year to at least \$158 billion in 2020. If drugs become pricier, as seems likely, that bill could rise to \$207 billion.

Not all these new drugs work. In December the FDA said that Avastin's side effects outweighed its meagre impact on breast cancer. (Genentech will argue otherwise in a hearing in June.) More generally, some people reckon that new cancer drugs offer small benefits at an exorbitant price. ▶▶



Provenge costs \$93,000 for a course of treatment and extends life by an average of four months. Yervoy costs \$120,000 for three-and-a-half months. Some patients live much longer, which fuels demand for the drugs. But others spend a lot and get little. Otis Brawley, chief medical officer for the American Cancer Society, calls the new treatments "the next frontier", but adds: "We are not buying a lot of life prolongation with these drugs."

Britain's National Institute for Health and Clinical Excellence, a public body that judges whether medicine is cost-effective (ie, what Sarah Palin would call a "death panel"), has rejected several new cancer drugs. That so upset patients and tabloid editors that the British government backtracked and created a separate fund to pay for expensive oncology drugs. The government now plans to introduce "value-based pricing" by 2014, with a system to price drugs not just for their efficacy but also for their "wider societal benefits".

America does things differently. The government health programme for the elderly is barred from considering price at all when it decides whether to cover injected drugs under something called Medicare Part B. Under Part B's loopy reimbursement system, the more a drug costs, the more the oncologist who prescribes it is paid. Patients have little reason to demand cheaper drugs. Part B usually covers 80% of a drug's price, and most patients have additional insurance to cover the remainder. Americans hate to be denied any kind of treatment: a delay in Provenge's approval prompted furious talk of rationing.

Private insurers have started to make patients pay a larger share of their drug bills. But drug companies often help to pay the patient's share, which stops the public from getting angry about soaring costs. Even when prices are high, demand for cancer drugs is largely inelastic, says Tomas Philipson of the University of Chicago. Dying patients understandably place a high value on life, so they are willing to pay more for treatment. All this means that firms can charge steep prices. "At some point it's just corporate chutzpah," says Peter Bach of the Memorial Sloan-Kettering Cancer Centre in New York. "There's no check in the system."

America's propensity to pay has one important benefit: it encourages investment in research. Drugmakers recoup their investments in America; other countries take a free ride. New research may yield better treatments. And today's cancer drugs may prove more effective when tested in combination with others, predicts Todd Golub, director of the cancer programme at the Broad Institute, a genetics research laboratory.

Who will reform this unsustainable system? Private insurers may haggle harder. Patients may grow restive—a recent

study found that 10% of cancer patients (not covered by Part B) fail to take prescribed drugs, largely because of the cost. Barack Obama's reforms are supposed to cajole all health-care providers into becoming more cost-effective, but that will require political bravery to enforce, and few politicians are brave enough to do anything that sounds like rationing grandma's cancer drugs. Congress recently authorised more than \$1 billion to compare the efficacy of drugs—while explicitly ignoring their cost. ■

#### Academic publishing

## Of goats and headaches

One of the best media businesses is also one of the most resented

**H**OW much would you pay for an annual subscription to *Small Ruminant Research*, *Queueing Systems* or *Headache*? University librarians pay rather a lot. In Britain, 65% of the money spent on content in academic libraries goes on journals, up from a little more than half ten years ago. With budgets tight, librarians are trying to resist price increases. But Derk Haank, the chief executive of Springer, a big publisher, is firm: "We have to make a living as well."

And what a living it is. Academic journals generally get their articles for nothing and may pay little to editors and peer reviewers. They sell to the very universities that provide that cheap labour. As other media falter, academic publishers have soared. Elsevier, the biggest publisher of journals with almost 2,000 titles, cruised through the recession. Last year it made

£724m (\$1.1 billion) on revenues of £2 billion—an operating-profit margin of 36%.

Academic publishers have jumped deftly from paper to the internet. For more than a decade the dominant model has been the "big deal". Publishers sell access to large bundles of electronic journals for a price based on what colleges used to pay for paper ones. Prices of big deals rise at about double the rate of inflation.

This model has provided an unprecedented wealth of material to researchers and fat profits to publishers. But fiscal crises, particularly in America, are straining big deals. State funding per university student in Arizona has fallen by roughly half since 2007-08. Libraries have taken a hit.

A library with a bundled subscription deal cannot make ends meet by dropping a few journals, as it could in the old days. Instead it must take the drastic step of leaving the all-you-can-eat buffet for the à la carte restaurant. Some universities have dropped big deals in favour of subscriptions to a few key journals, topped up by pay-per-view downloads of individual articles. Academics have not complained, they say. British universities are threatening to do the same en masse if subscription prices are not cut. Are they serious?

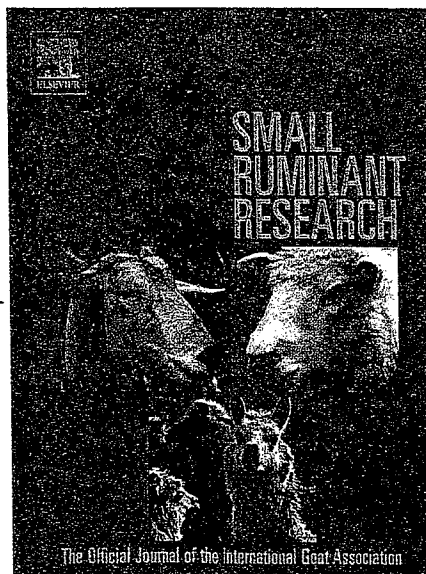
Certainly, some journals are more valuable than others. Ted Bergstrom, an economist at the University of California, Santa Barbara, has a nifty way of quantifying this. He divides the annual subscription price of a journal by the number of times its articles are cited in other journals. Results vary a lot. Influential journals such as the *Lancet* cost a few pennies per citation. Others cost hundreds of dollars.

If many universities drop big deals it will be calamitous for the publishers. They could raise the prices of individual journals to make à la carte buying less attractive. But that would stimulate a private trade in e-mailed articles. Claudio Aspesi of Bernstein Research points out that academic authors tend not to care much about copyright protection. Their main interest is in being read and cited.

Many customers resent high prices and have the means to bypass them. The music industry provides a salutary lesson in the dangers of building a business around charging too much for too-large bundles of content (in its case, CD albums).

Yet academic publishers do not have the rabbit-in-the-headlights look that music executives did a few years ago. They have moved quickly to cut or freeze subscription prices for the most troubled universities. They have minimised the threat from open-access journals, which seemed considerable a few years ago, in part by buying some of the best ones. And they are pushing into emerging markets, where universities and government research budgets are swelling.

So far, says Youngsuk Chi of Elsevier, ►



Something to chew on

publishers have behaved a bit like hunter-gatherers of research. They are trying to become information providers. That means investing in search and data-management tools to make sure relevant articles find their way to researchers. Earlier this year Elsevier opened some of its article databases to software developers, who have begun to build apps on top of their content. If publishers can hook academics on such innovations, and drive them to arti-

cles in relatively obscure journals, dropping big deals will seem a lot more painful. Academics are heroic complainers and not always well disposed to profit-maximising businesses. So the gripes are likely to continue. The best that the publishers can hope for is that they escape the fate of the music business and come to be viewed rather like pay-television companies. Customers complain about their cable bills, too. But they keep paying them. ■

new law, possibly requiring a complete shutdown within ten years (see chart). Mr Grossmann is not opposed to alternative energy. In 2008, five months into his job as chief executive, he set up a subsidiary called **rWE Innogy** that has built wind farms in Britain, the Netherlands, Spain and Germany. It also has partnerships developing carbon capture and storage, an unproven technology for making fossil fuels cleaner. Its latest piece of green-tech is a plant in the American state of Georgia that makes green wood pellets for burning in coal-fired power stations.

Still, renewables make up only 4% of **rWE's** energy mix. The rest comes from coal- and gas-fired plants, though the new ones are being adapted to take biomass too. It is less dependent on nuclear than **E.ON**, Germany's biggest power company, (which has six nuclear plants in Germany), and **ENBW** (which has four). "Only 10% of **rWE's** value is nuclear," says Mr Grossmann—though that figure is obviously deflated by politics.

The political winds favour small energy firms. The European Commission has forced big German firms to sell parts of the power grid that they own. **rWE** has spun its network into a subsidiary.

Mr Grossmann has the assurance of a self-made billionaire. In 1993 he took over a near-bankrupt steelworks in Lower Saxony for DM2 (\$1.21). He toiled at the furnaces himself to rally workers. Within a couple of years the firm was profitable. He still owns it. Mr Grossmann's pithiness ruffles feathers. In December he was named "dinosaur of the year" by a green group. "Man is a mayfly compared with the dinosaur," he retorted.

His mandate at **rWE** expires next year. Possible successors include Rolf Martin Schmitz, **rWE's** chief operating officer, and Leonhard Birnbaum, the firm's chief strategist. Mr Grossmann's nuclear legacy may endure longest outside Germany. On May 17th **rWE** announced that it was buying 30% of a nuclear reactor in the Netherlands. It is also part of a joint venture with **E.ON** to build two spanking new nuclear plants in Britain. ■



Nuclear power in Germany

## No one listens to Jürgen Grossmann

BERLIN

The lone stand of a power boss against his country's nuclear panic

**G**ERMAN tree-huggers have always hated nuclear power. The accident at an earthquake-stricken Japanese nuclear plant in March added to Germany's nuclear phobia. The government ordered a three-month moratorium for the nation's seven oldest nuclear plants while two commissions, one on safety, the other on "ethics", reviewed the nation's nuclear future.

One man dared to challenge the legal basis of the moratorium. He was Jürgen Grossmann, the boss of **rWE**, a big German power company that generates a quarter of its output from nuclear plants. He is a doughty warrior for a non-alarmist energy policy and, at 2.03m tall, a highly visible one. But his cause seems doomed.

He argues that until other forms of low-carbon energy improve, Germany will need nuclear power to meet its greenhouse-gas targets. The country aims to get 35% of its energy from renewable sources by 2020 and 80% by 2050. That could be hard. Germany has little sunshine for solar power. Wind power is intermittent. Greens

and nimbys detest both large power stations and power lines, which some imagine will give them cancer.

Last September four big energy producers in Germany—**E.ON**, **rWE**, **ENBW** and **Vattenfall**—negotiated a deal to prolong the lives of their 17 nuclear plants by an average of 14 years. There was still hope then that the nuclear industry could win over the German people, though the popular consensus since 2001 has been for an orderly abandonment of nuclear power.

Nuclear plants cost a fortune to build, but not much to run. So despite a steep tax on nuclear fuel, they are a cheap and reliable source of power that emits almost no greenhouse gases. But probably not for much longer. On May 17th Germany's Reactor Safety Commission delivered its verdict: generally positive, but it noted that none of Germany's 17 nuclear reactors could cope with al-Qaeda deliberately crashing a commercial jet into the roof. The ethics commission will report at the end of the month, and the government will pass a

### Nukes nuked

Germany's energy production, % of total

