

September 2, 2009

FORTY YEARS' WAR

For Profit, Industry Seeks Cancer Drugs

By [ANDREW POLLACK](#)

SAN DIEGO — [Pfizer's](#) fortunes in the past were built on cardiovascular drugs, like the [cholesterol](#) buster [Lipitor](#) and the [blood pressure](#) pill Norvasc.

But the future of Pfizer, the world's largest pharmaceutical company, may rest in a cluster of buildings on a bluff not far from the Pacific Ocean. It is here that Pfizer has amassed about 1,000 researchers for an all-out effort to develop drugs for [cancer](#), a disease the company once largely ignored.

Virtually every large pharmaceutical company seems to have discovered cancer, and a substantial portion of the smaller biotechnology companies are focused on it as well. Together, the companies are pouring billions of dollars into developing cancer drugs.

Two industry trends are driving the push. Recent scientific discoveries have suggested new targets for cancer drug researchers to attack. And as drug companies see profits beginning to wane from mainstays like Lipitor, the high prices that cancer drugs can command have become an irresistible lure.

About 860 cancer drugs are being tested in clinical trials, according to the pharmaceutical industry's main trade group. That is more than twice the number of experimental drugs for heart disease and stroke combined, nearly twice as many as for [AIDS](#) and all other [infectious diseases](#) combined, and nearly twice as many as for [Alzheimer's](#) and all other neurological diseases combined.

But for all the industry's spending and effort, only a trickle of new cancer drugs make it to market. Last year there were two, and this year there has been only one.

And even some of those drugs offer only a few months at most of extra life or [tumor](#) stabilization despite prices that often reach thousands of dollars a month. The drug [Tarceva](#), which costs about \$3,500 a month, was approved as a treatment for [pancreatic cancer](#) because it improved survival by 12 days.

The battle to treat cancer has become, as a commentary in a leading journal put it, a "grinding war of the trenches."

Why? Experts say the same factors that attract drug companies to the cancer business help explain the slow progress.

One reason is scientific. Studies are rapidly revealing the genetic changes in cells that cause cancer and spur its growth. That is providing drug companies with dozens of molecules, or "targets," that drugs could block.

But those same studies have shown that cancer is devilishly complicated. There are so many aberrant molecules in a tumor that blocking just one or two is like trying to stop all traffic in Manhattan with a roadblock at a single intersection.

Tumor cells, like bacteria, can develop resistance to drugs. Some experts believe that drugs that kill most tumor cells do not affect cancer [stem cells](#), which can regenerate the tumor.

And even two people with [breast cancer](#), or two people with lung cancer, might have two very different diseases on the molecular level, so a drug that works for one might not work for the other.

“Cancer is not a single disease,” said Robert A. Weinberg, a cancer biologist at the Whitehead Institute and the [Massachusetts Institute of Technology](#). “It’s really dozens, arguably hundreds of diseases.”

The other reason for the drug makers’ interest is financial. Patients are often desperate, and insurers risk outrage by denying payments for a cancer drug, even if the odds say it will have little benefit. That has allowed pharmaceutical companies to charge thousands of dollars a month for cancer medicines. Such prices can make drugs for even rare cancers, or drugs that do not work very well, into big moneymakers.

Take [Erbix](#), developed by ImClone Systems, which costs \$10,000 a month. A study in Canada showed that as a last-ditch treatment for [colorectal cancer](#), Erbix lengthened lives by an average of about one and a half months compared with not treating the cancer at all. Using the price of the drug in the United States and the average length of treatment, the extra cost per patient was about \$50,000.

Erbix, which is also approved to treat head and neck cancers, recorded global sales of \$1.6 billion last year, higher than all but about 70 other drugs. Last year, as part of the industry scramble into cancer drugs, [Eli Lilly & Company](#) outbid [Bristol-Myers Squibb](#) to acquire ImClone for \$6.5 billion.

In 1998, there were only 12 cancer drugs on the list of the world’s 200 medicines with the highest sales, compiled by the trade magazine Med Ad News. Taxol, No. 21, was the only cancer drug among the 30 drugs with sales of at least \$1 billion.

The same list for last year contained 23 cancer drugs among the top 200 — and three in the top 10. Of the 126 drugs with \$1 billion in sales, 20 were for cancer.

Cancer drugs have been the biggest category of drugs in terms of sales worldwide since 2006 and in the United States since 2008, according to the market researcher [IMS Health](#).

Such money attracts companies. “Cancer is such an emotional issue that the free market doesn’t work like it does for bicycle wheels and umbrellas,” said Robert L. Erwin, a biotechnology industry executive who heads the Marti Nelson Cancer Foundation, a patient advocacy group. “As long as the health care system will pay the price, the money will flow in that direction.”

But Mr. Erwin and some other experts say that is not always a good thing for patients because it can set the bar too low for drug companies.

“As long as the marketplace does not distinguish between modestly effective drugs and dramatically effective drugs, there won’t be an incentive to shift resources to a greater emphasis on a larger benefit,” said Dr. Neal J. Meropol, an oncologist at the Fox Chase Cancer Center in Philadelphia who has been studying drug prices.

Many executives dispute this, saying they would produce drugs offering bigger gains if they knew how. But they must balance their portfolio of experimental drugs between long shots and some drugs that have a better chance of making it to market and sustaining the enterprise.

“If you always swing for home runs, you strike out a lot,” said George A. Scangos, chief executive of [Exelixis](#), a biotechnology company with 11 cancer drugs in clinical trials. “It’s not the companies’ profit motives,” he said. “It’s largely the difficulty of hitting home runs.”

With health care costs rising, there is new pressure on companies to be more selective in drugs they develop. Some experts now talk about “financial toxicity” as a side effect of cancer drug treatment, along with nausea and [hair loss](#).

“A question is how the system can tolerate 400 new drugs on the market, all at the same price” of \$50,000 a year, said Dr. Lee Newcomer, senior vice president for oncology at United Healthcare, a big insurer.

Such cost pressures, and the fact that only a handful of cancer drugs get to market each year, mean the big investments now being made into cancer drugs are likely to turn sour for many companies.

"It's the biggest bubble you've ever seen," said Dr. Mark Ratain, an oncologist at the [University of Chicago](#).

But Pfizer is counting on cancer to help save the company. It hopes to reach \$11 billion in sales of cancer drugs by 2018. That would be more than four times the category's sales last year of \$2.5 billion, which represented only 5 percent of Pfizer's revenue.

Cancer was once unattractive for big pharmaceutical companies like Pfizer. There were relatively few patients with any one type of cancer, and they died fairly quickly. By contrast, there were millions of patients with chronic diseases like [hypertension](#) who would take drugs for life.

Indeed, the three main cancer drugs Pfizer now sells came to it with its 2003 acquisition of a rival, Pharmacia, a deal done mainly to acquire the [arthritis](#) drug [Celebrex](#).

But there are now many good cardiovascular drugs. Lipitor, the world's best-selling drug, will lose patent protection in 2011, and Pfizer failed to develop a successor.

So Pfizer is scaling back cardiovascular research and has made cancer drugs one of its six focus areas. About 20 percent of Pfizer's more than \$7 billion in research and development spending is on cancer, and 22 of the roughly 100 drugs in clinical trials are cancer drugs.

"I've taken a lot of personal interest in this business unit," said [Jeffrey B. Kindler](#), Pfizer's chief executive. "We think we are positioned to be a top leader in oncology."

Cancer research is concentrated here in San Diego, in a cluster of buildings once owned by one of the many biotechnology companies in the region. Pfizer has tried to retain some of the looser culture of entrepreneurial start-ups, like Friday afternoon beer parties. The head of the site, Catherine Mackey, a transplant from Pfizer's laboratories in Connecticut, has become an avid early-morning surfer.

The clinical trials for cancer are being overseen by Dr. Mace L. Rothenberg, an oncologist recruited this year from [Vanderbilt University](#). He hopes Pfizer can develop those home-run drugs. "Having treated patients for 20 years," Dr. Rothenberg said, "I know their needs are not for singles."

The big thrust in cancer drug development for the last few years has been so-called targeted therapies. These drugs aim, so far with modest success, to block aberrant molecules in tumor cells while leaving normal cells unscathed.

But even most targeted therapies have limited impact. One reason is that most [tumors](#) are fueled by numerous, often redundant, genetic anomalies. That means that drugs with different targets need to be used in combination. But combinations increase both the costs and side effects of therapy. And it is difficult to test two experimental drugs in combination because the regulatory system is geared to assessing a single drug at a time.

Another reason is that tumors differ among people. Dr. Bert Vogelstein, a cancer geneticist at Johns Hopkins, said a typical tumor might have 50 to 100 genetic mutations. But two patients with the same type of cancer might have only five mutations in common.

So even though a drug might work well for patients whose tumors have a particular mutation, when the drug is used for a broader population, it shows only a small effect.

One solution is to try to determine which patients should get which drug based on the genetic profile of the tumor.

Pfizer is moving in that direction. It plans soon to start a late-stage clinical trial of a drug for lung cancer. But the only patients in the trial will be from the 5 percent or so of lung cancer patients with a mutation in a gene called

A.L.K.

“What we’re looking for,” said Dr. Rothenberg of Pfizer, “is not a small benefit in a large group, but a larger benefit in a smaller group.”

For now at least, making the ballpark smaller may be the industry’s best chance to hit home runs.

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