

PHARMACEUTICALS

THE WANING OF THE BLOCKBUSTER

What's promising now are drugs that target niche diseases. That means painful restructuring ahead for Big Pharma

FOR A LOOK AT HOW THE drug industry is changing, compare the latest news on Big Pharma powerhouse Merck & Co., with \$22.5 billion in sales last year, and tiny biotech Medarex Inc., which racked up revenues of just \$11.2 million. Merck took a body blow when it pulled its popular arthritis drug Vioxx off the market on Sept. 30 because it increases the risk of heart attack and stroke in some patients; the move will instantly slice more than 11% from revenues. Nor does Merck have a new blockbuster waiting in the wings to replace it. Four of its most promising new drugs were dropped last year when they failed clinical testing. Medarex, meanwhile, learned in early October that the Food & Drug Administra-

tion will speed up the approval process for the company's vaccine to fight advanced melanoma, now in late-stage trials. Two weeks earlier, Medarex announced a collaboration with Pfizer Inc., the world's largest pharmaceutical company, to develop up to 50 drug candidates over 10 years, on top of the 13 Medarex already has in clinical trials. And while Merck's stock fell from \$45 in early September to \$31.67 in the wake of the Vioxx news, Medarex shares almost doubled over the same period, from \$4.37 to about \$8.

RECALL RESISTANT

THERE'S A LESSON HERE. Pharmaceutical giants such as Merck have built one of the world's richest industries on blockbusters such as Vioxx that treat millions for the most common diseases. But the

most promising drugs in the pipeline now are designed for a much smaller slice of patients. Blockbusters they are not.

This change is a nightmare in the making for Big Pharma. Drugs that bring in billions of dollars, such as Lipitor for high cholesterol, Nexium for hyperacidity, and Zoloft for depression, turned pharmaceuticals into one of the globe's most profitable industries, enabling drugmakers to spend \$32 billion on research and development last year and put 40,000 sales reps on the street. A shift toward less lucrative medicines means the world's massive drugmakers face wrenching restructuring that few are eager to embrace.

The exceptions are those that have already fallen out of the top tier. Bristol-Myers Squibb, Abbott Laboratories, and Wyeth have all switched their efforts away

from blockbusters. Abbott has been the most drastic, downsizing from a focus on 13 areas in 2002 to just 5 today: immunology, oncology, neuroscience, diabetes, and antivirals.

NIMBLER LABS
R&D will have to get by on smaller profits

By developing drugs for less common medical problems, these companies hope to protect themselves from recalls. Patients on Vioxx could easily turn to another pain drug rather than risk a heart attack or stroke, no matter how small the risk. But Dr. James B.D. Palmer, Bristol-Myer Squibb's chief scientific officer, says a drug such as the one Bristol is developing to prevent organ-transplant rejections would have a captive patient group. They would likely be willing to accept more risk rather than go off an effective drug.

Vioxx highlights the dangers of staying the present course. It was designed to treat millions of people, but it turned out to also cause deadly side effects in some, just as Baycol, Bayer Group's cholesterol-lowering drug, and the diet drug Redux did before it. Merck now faces the prospect of the same massive lawsuits that hobbled Bayer and Wyeth, maker of Redux. Vioxx rivals such as Pfizer's Celebrex may also be in danger: European regulators plan to probe their safety.

MEDICARE HIT

BESIDES BEING RISKY, blockbusters may also lose their status as cash cows in the next few years. Once Medicare drug benefits start in 2006, pharma execs worry that the program will end up paying a set price for just one or two drugs for a given disease. Given that 50% of blockbusters are heavily marketed me-too drugs, offering little benefit over others in their class, the



industry is sure to take a financial hit. "Clearly," says Bain & Co. consultant Preston Henske, "the blockbuster business model is irreparably broken."

It's getting harder to come up with new blockbusters anyway. Pfizer will spend \$7.6 billion on R&D this year, but hasn't launched a blockbuster from its own labs since 1998. AstraZeneca PLC, still reeling from an FDA rejection in September of its Exanta anti-blood-clotting drug, said on Oct. 6 that a new diabetes drug will be delayed until 2007.

Scientists and industry consultants believe that the pharmaceutical industry will ultimately shift from blockbusters to targeted drugs, often referred to as personalized medicine. Getting to that future, though, will be a hard slog for the traditional kings of the drug industry. They are trapped in their own business model: the fully integrated company that tries to come up with widely used drugs for as many diseases as possible.

That model will become tougher to sustain. Though some drugs will still be relatively widely used, even they could see sales diminish through more careful targeting. Still, an arthritis drug like Vioxx with a diagnostic test that would screen out patients at risk of stroke could achieve huge sales, even if 20% of potential customers were eliminated. Companies might be able to make up for the loss of volume with a higher price. "We believe drugs will really have to show—in

order to get a premium price—a much better benefit-to-risk ratio," says Dr. Nancy Simonian, senior vice-president of clinical development at the biotech firm Millennium Pharmaceuticals Inc. "The way to do that is to identify the patients who get the greatest benefit."

In place of one or two blockbusters, pharma companies will have to churn out three or four \$300 million to \$500 million drugs. To survive, drugmakers will have no choice but to streamline R&D and sales, focusing on just a few diseases. They will also have to be more aggressive about forming development partnerships, such as the Pfizer-Medarex pact.

OFF-PATENT DESERT

MOST OF BIG Pharma remains understandably hooked on blockbusters. Boston Consulting Group estimates that 80% of growth for the 10 biggest drug-

makers during the last decade came from the eight or so blockbusters a year launched during the 1990s. That pace has slowed to almost nil since then, however, and many of the best-selling drugs from the '90s will go off patent soon. The major drugmakers' lack of new drugs stands in sharp contrast to the biotech industry. Boston Consulting reports that the hundreds of tiny biotechs, while responsible for only 3% of the drug industry's total R&D spending, can lay claim to 67% of the drugs in clinical trials. Almost all are personalized drugs.

Big drugmakers insist that they see the rise of targeted drugs. But most also argue that blockbusters are far from dead. "Personalized medicine" is a laudable aim, but we are not anywhere near there yet," says Dr. Declan P. Doogan, Pfizer's head of medical and development science. "I think biotech has investigated some niche disease areas with targeted approaches. But it is in the early days."

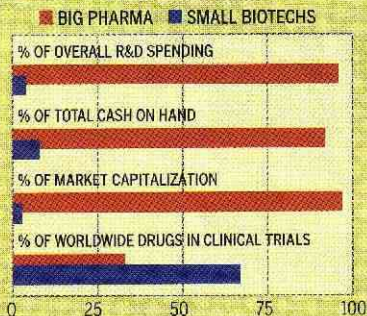
Not that early. Already, targeted therapies are on the market for cancer, allergies, and rheumatoid arthritis, and many others are in development. The sooner Big Pharma gets behind personalized medicine, the sooner the industry will regain its ability to innovate. And that would be the best news for patients. ■

—By Catherine Arnst in New York, with Amy Barrett in Philadelphia, Michael Arndt in Chicago, and John Carey in Washington

SHAWN G. HENRY; CHART BY RAY VELLA/BW

LOSING THE EDGE

Big Pharma* has big bucks but lags smaller biotechs in promising new drug development.



*INCLUDES TRADITIONAL PHARMACEUTICAL COMPANIES AND THE TEN LARGEST BIOTECHNOLOGY OUTRITS

Data: Boston Consulting Group