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Reprinted from December 1, 2003

Cover Story

Battling Big Pharma

| By William T. Quinn

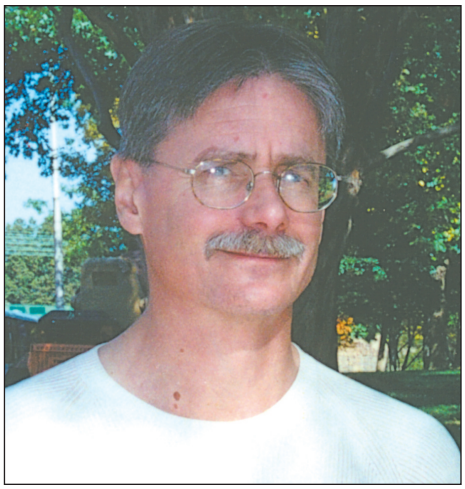
Generic drugmakers from India gain a foothold in the U.S. by launching bold attacks on patents held by brand-name companies

Photo | Dave Hollander

Ranbaxy's Chattaraj produces drugs for the prescription and over-the-counter markets.

It's tough moving from a supporting role to a place in the front ranks of the world's pharmaceutical business. But it's a passage that India's biggest drug companies are determined to make. Having conquered their Darwinian home market, where some 20,000 companies scrap to supply generic drugs at the lowest possible cost, they want to play on a bigger stage.

Two Indian companies, Ranbaxy Laboratories and Dr. Reddy's Laboratories, have secured a firm foothold in the U.S. market and are mounting widely watched challenges to the patents on some of the biggest-selling prescription drugs owned by U.S. drug companies.



Reid says Dr. Reddy's hopes to become a full-fledged drug-discovery company.

These challenges pose a major threat to brand-name companies. "If Pfizer were to lose a Lipitor challenge or Eli Lilly was to lose Zyprexa, their largest drug, it would be a severe, severe blow," says Ruairi O'Neill, an analyst who follows the generic industry for PNC Advisors in Philadelphia.

Like most Indian drug companies, Ranbaxy and Dr. Reddy's have built their businesses by making reverse-engineered copies of products developed in other countries and producing chemical ingredients for other drugmakers.

Now they want to grow into full-fledged research companies. "We are trying to move toward being a discovery-led global pharmaceutical company," says Cameron Reid, president of the U.S. unit of Dr. Reddy's. To get there, Dr. Reddy's and Ranbaxy are drawing on their proven manufacturing skills and access to low-priced scientific talent back home.

In the U.S., meanwhile, the companies have the legal tools offered to generic drugmakers by the Hatch-Waxman Act. That 1984 law created incentives for generic manufacturers to challenge patents held by brand-name drugmakers. It awards 180 days of market exclusivity to the first company that files to make a generic drug with the Food and Drug Administration and wins a patent challenge in court.

The Medicare reform bill Congress passed last week gives the generic companies some added leverage, including the right to bring patent issues to court without having to wait to be sued by a brand-name company. In addition, the law limits brand-name companies to one use of the automatic 30-month stay they can invoke to delay the FDA's approval of a generic drug.

The Indian companies face obstacles of their own. These include entrenched generic competitors in the U.S. and brand-name companies willing to pay any

price to defend their patent rights in court.

At the same time, the Indian companies are driven by their own legal imperatives. After more than 30 years of ignoring drug patents awarded in Western countries, India plans to start recognizing and enforcing such patents in 2005. That leaves India's domestic drugmakers with a choice of staying in the low-price end of the market or working their way up the pharmaceutical food chain.

Ranbaxy, which is India's largest pharmaceutical company, and Dr. Reddy's have both opted for upward mobility. "We, as a company, have been welcoming patents for a long time," says Dipak Chattaraj, head of Ranbaxy's U.S. operations.

Both companies have made New Jersey their base of operations in the U.S.—Ranbaxy's headquarters are in Princeton and Dr. Reddy's are in Upper Saddle River—and both are expanding here. Dr. Reddy's is moving early next year from its present offices to bigger space in Bridgewater. Ranbaxy is spending more than $11 million to refit a former Hershey Foods plant in New Brunswick that it recently bought and to upgrade its Ohm Laboratories plant in North Brunswick.

Dr. Reddy's has drawn attention with its patent challenge to Norvasc, one of Pfizer's top-selling drugs. But Ranbaxy has the distinction of being the first generic company to throw down a patent challenge to Pfizer's Lipitor, the world's biggest prescription drug.

Norvasc, which treats hypertension, generated worldwide sales of $3.8 billion for Pfizer last year and its main patent doesn't expire until 2007. Lipitor generated sales of $8 billion and its patent is valid through 2010.

Dr. Reddy's won a major ruling last year when U.S. District Judge Katherine Hayden in Newark held that its method of making an analogous compound called amlodipine maleate doesn't infringe on Pfizer's patent rights. Pfizer appealed the ruling to the federal circuit court in Washington, D.C., which has jurisdiction over patent cases. The case was argued in July and a decision is expected soon.

Reid says a victory would open up opportunities to make analogues—also called salts—of a limited number of other patented drugs. He says Dr. Reddy's has one new drug application pending at the FDA for a compound it hasn't yet disclosed.

Meanwhile, Dr. Reddy's executives in India plan to bring the company's Norvasc knockoff to market under the name AmVaz. Reid says the company will be free to launch it in Europe in March when Pfizer's period of market exclusivity expires there.

The Norvasc campaign is just one of a series of patent attacks Dr. Reddy's has underway. Another is a challenge to Zyprexa, the anti-psychotic medication which is Eli Lilly's top-selling drug. "It's a simple business philosophy," Reid says. "If you play enough of these, you will win some."

In fact, generic companies have won most of the patent challenges they have brought against brand-name companies under Hatch-Waxman. A 2002 study by the Federal Trade Commission found generic companies had won 73% of the time in patent challenge cases.

The study also found that the volume of patent litigation has risen sharply in the years since Hatch-Waxman was adopted. In the 1980s, only 2% of applications to the FDA for the right to make a generic version of a drug included a patent challenge. By 1998, the rate was running at more than 20%.

With more patent claims being made and more aggressive legal theories being advanced, the win rate for generic companies may start to slip. But incentives remain strong for taking a chance.

When generic companies wait for a brand-name drug to go off-patent before starting to sell their version, they are likely to face heavy competition and rapid price erosion. "In the generic business, as more and more players come in, the price only goes south," says Chattaraj of Ranbaxy.

But if they win a patent challenge, they

RANBAXY LABORATORIES

World headquarters New Delhi, India
U.S. headquarters Princeton

Chairman Tejendra Khanna
President U.S. operations Dipak Chattaraj

Employees
Worldwide 8,000
U.S. 360, including 320 in Princeton and at its Ohm Laboratories manufacturing plant in North Brunswick.

2002 Sales* $764 million
Net Income $129 million
U.S. Sales $296 million

Top-selling generic drugs in U.S.
Cefuroxime Axetil antibiotic, formerly sold as **Ceftin** by Glaxo
Amoxicillin, clindamycin and **amoxicillin plus clavulinic acid,** formerly sold as **Augmentin** by Glaxo

Major Patent Challenges Pending
Ranbaxy has filed 27 claims with the FDA challenging patents on brand-name drugs. Target drugs include:
Atorvastatin anti-cholesterol, sold as **Lipitor** by Pfizer
Gabapentin anti-seizure, sold as **Neurontin** by Pfizer
Modafinil anti-narcolepsy, sold as **Provigil** by Cephalon
Fenofibrate anti-triglyceride, sold as **Tricor** by Abbott Labs
Pravastatin anti-cholesterol, sold as **Pravachol** by Bristol-Myers Squibb

*Sales and profit figures are for Ranbaxy Laboratories Ltd. of India
Source: company reports

GENERICS VS. BRAND-NAME DRUGS IN THE U.S.

Period January 2002, through November 2002

Generic drug sales $19.4 billion
Brand-name sales $98.6 billion

Prescriptions written for generics
51% in 2002, up from 47% in 2001

Average cost per prescription
Generics $19
Brand-name $65

Sources: IMS Health, Generic Pharmaceutical Association

can usually charge about 90% of the brand-name price for a drug during a six-month period of market exclusivity. In 2001, Dr. Reddy's scored its first breakthrough when it won market exclusivity for one dosage form of fluoxetine, better-known as Prozac, the blockbuster anti-depressant developed by Eli Lilly. Fluoxetine has generated sales of more than $100 million for Dr. Reddy's.

Ranbaxy won exclusivity last year for cefuroxime axetil, a generic form of an antibiotic previously marketed as Ceftin by GlaxoSmithKline. Last June it won exclusivity for ganciclovir, a drug that treats lesions caused by herpes that Roche previously sold as Cytovene.

Ranbaxy has focused on anti-infective drugs for its entry into the U.S. market. Along with cefuroxime axetil, its top sellers here are the antibiotics amoxicillin, clindamycin and a generic form of GlaxoSmithKline's Augmentin. Chuck Caprariello, Ranbaxy's vice president of business development, says the four drugs should generate sales of $200 million this year.

Even with the sales and profit boost that market exclusivity has given Ranbaxy and Dr. Reddy's, they are still far from overtaking generic giants like Israel's Teva Pharmaceuticals, which posted sales of $2.5 billion last year. Industry analysts says Teva and four other companies—Mylan, Watson, Geneva (a unit of East Hanover-based Novartis) and Ivax—claim more than half of all generic drug sales in the U.S., which totaled about $15 billion in 2002.

Ranbaxy and Dr. Reddy's hope to win more market share through a barrage of legal filings. Ranbaxy has brought patent claims with the FDA against 27 brand-name drugs. Dr. Reddy's has filed 21 claims.

Caprariello says his company isn't opposed to patents in principle and is working on new drug-delivery systems that it hopes will qualify for patent protection. But he says brand-name companies must get used to the idea that the pharmaceutical business has changed.

"The R&D companies need to look at products not as having an indefinite life, but as having a limited life of 17 to 18 years," he says.

Patent lawyers say brand-name companies aren't ready to give up the fight. They say a full-fledged legal battle over the validity of a patent on a prescription drug can easily cost each side $5 million at the trial level, and double that with a full round of appeals. Reid puts Dr. Reddy's annual budget for legal expenses at $12 million.

Bill Mentlik of Lerner, David in Westfield, who represents generic companies in patent battles, says the money is no deterrent to brand-name drugmakers. "A biopharmaceutical [company] has no incentive not to do whatever it can to keep the generic off the market," Mentlik says. "Each one of these drugs is [worth] one, two, three million [dollars] a day. They're making back their legal fees by lunchtime."

DR. REDDY'S LABORATORIES

World headquarters Hyderabad, India
U.S. headquarters Upper Saddle River

Chairman Anji Reddy
President U.S. subsidiary Cameron Reid

Employees
Worldwide 6,000
U.S. 75

2002 Sales* $380 million
Net Income $74 million
U.S. Sales $123 million

Top-selling generic drugs in U.S.**
Fluoxetine anti-depressant, originally sold as **Prozac** by Eli Lilly
Ranitidine anti-ulcer & acid reflux, originally sold as **Zantac** by Glaxo
Tizanidine muscle relaxant, originally sold as **Zanaflex** by Elan

Major Patent Challenges Pending
Dr. Reddy's has filed 21 claims with the FDA seeking to overturn unexpired patents on brand-name drugs or to win rulings that its formulations do not infringe on existing patents. Target drugs include:
Amlodipine Besylate hypertension, sold as **Norvasc** by Pfizer
Olanzapine anti-psychotic, sold as **Zyprexa** by Eli Lilly
Ondansetron anti-nausea, sold as **Zofran** by Glaxo
Terbinafine anti-fungal, sold as **Lamisil** by Novartis
Clopidogrel anti-clotting, sold as **Plavix** by Sanofi/Synthelabo
Fexofenadine anti-allergy, sold as **Allegra** by Aventis

*Fiscal year ended March 31, 2003 **Marketed by Par Pharmaceutical
Source: company reports

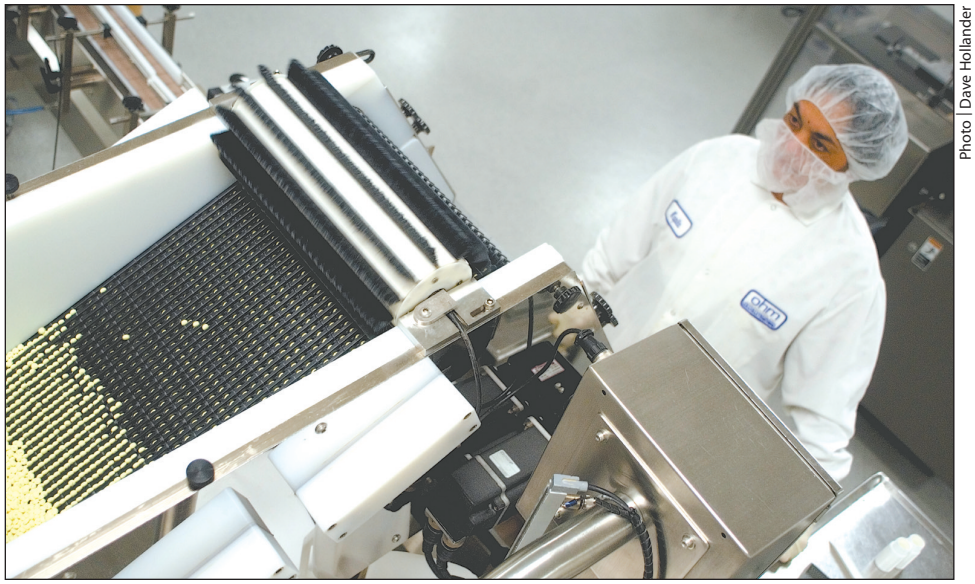


Photo | Dave Hollander

Products of Ranbaxy's North Brunswick plant include the pain reliever ibuprofen. The facility, acquired in 1995, is the company's main North American manufacturing operation.

Photo | Dave Hollander

Ranbaxy is investing more than $11 million to upgrade its present plant and acquire and refit a former Hershey Foods facility that stands vacant in New Brunswick.

Photo | © 2003 davidlubarsky.com

Attorney De Lorenzi often represents the brand-name side of patent disputes.

As the generic companies bring more products to market "they're building war chests" as well, says David De Lorenzi, who chairs the intellectual property department at Gibbons, Del Deo in Newark. "It's a whole new world," he says. The 37 lawyers in his department are busy defending brand-name drug companies like Pfizer from patent challenges in what De Lorenzi admits is a sensitive area of the law.

"You've got the need to compensate the brand-name companies for their research and development weighed against the need to provide, at a reasonable cost, prescription pharmaceuticals to the buying public," he says. "It's a delicate balance. Our legislators are trying to get us to that balance. In the meantime, it's a real chess game between the generics and the branded-pharmaceutical companies."

Dr. Reddy's has turned over much of its patent litigation to the law firm Budd Larner in Short Hills. That has helped fuel a growth spurt in the firm's patent department. Reid says it now has 30 people assigned to his cases.

As a series of blockbuster drugs come off-patent over the next few years, Reid says brand-name companies can expect the legal waters to stay choppy. Prior to the 1984 adoption of Hatch-Waxman, Reid says, big drugmakers were more relaxed about their patenting. "They didn't have to do as much protection," he says. There was little prospect that generics would make it to market because they were required to undergo the same range of clinical tests for safety and efficacy as branded drugs.

But Hatch-Waxman lifted that burden and made generic competition a reality. That forced the brand-name companies to scramble to close the potential loopholes in their patent portfolios. "They did a lot of post-patenting," Reid says.

The result was a rash of patents to protect not just the active ingredients of a drug, but its method of use, its formulation and the manufacturing process. "Many [such patents] can be challenged," Reid says.

Of course, not every challenge to a pharmaceutical patent is successful. Merck recently beat back an assault by Teva on its patents on Fosamax, a treatment for osteoporosis. But these days, nearly every big-selling prescription drug is fighting a patent challenge, says O'Neill of PNC Advisors.

Ranbaxy's Chattaraj is aware of the fury that patent-busting suits generate in the halls of Big Pharma. But before World War II, he says, "every company was more or less a generic company."

Meanwhile, the patent wars are generating some new alliances. In October, after Ranbaxy won its battle to make a generic version of Glaxo's antibiotic Ceftin, the two companies agreed to establish a joint research venture to pursue new drug leads. Sometimes, the best therapy can be cooperation. ■

| email *wquinn@njbiz.com*