

# THE MOLECULE MILLIONAIRES

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*By focusing on drug research, a clutch of avant-garde drug companies is trying to create a new global niche for itself.*

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From outside, there is nothing remarkable about Dr Reddy's Research Foundations' (DRF) campus, west of Hyderabad. But step into the state-of-the-art facility, and you can't help but feel the quiet excitement that comes with the knowledge that what's being worked on here at this pioneering outfit is something profound, pathbreaking and, yes, profitable. There's an additional reason why DRF's 250 odd scientists have a spring in their step these days. Barely three weeks ago, DRF's licensed its third molecule—DRF 4158, a novel insulin sensitiser—to Novartis Pharma AG, for a cool \$55 million. If the molecule hits the market in the form of a drug, DRF could dream of getting even a billion dollars, while its cost of discovering the molecule is relatively low at around Rs 12.41 crore.

It is this compelling equation that is prompting other Indian pharma companies to dust cobwebs off their R&D labs, and focus on discovering new molecules that can be licensed to global drug majors. Ranbaxy, the largest Indian drug maker, signed a \$65-million deal with Bayer in August, 1999, for a ciprofloxacin molecule. And there are at least seven other companies—Torrent, Wockhardt, Sun Pharma, Zydus-Cadila, Orchid, Lupin and Cipla—who haven't licensed any molecule yet, but either have some in their bags or are working on creating one. Says Kallam Anji Reddy, Chairman, Dr Reddy's Labs: "Research is a viable proposition for middle-order company, because the investment is small (Rs 5 crore), and the success depends on a small band of researchers, and what you pick for the R&D effort."

Some others, not so modest as Reddy, believe that what's being created in the staid labs of such Indian drug companies is the next blockbuster industry (after software). And they may not be totally off the mark. Here's why: typically, discovering a new molecule from scratch takes an average of \$500 million and 10 years. The strike rate is low, too. Only one in 10,000 molecules makes it to the chemist's shop. Indian pharma companies, who do not have the financial means to launch new drugs on their own, are doing the next best thing: picking up a molecule developed by some other lab, and adding a carbon here, or a nitrogen there to create a legitimate new chemical entity. The result? The cost involved in developing a new drug through basic research is slashed from 80 percent to 20 percent. The appetite of the \$350-billion global drug industry for such low-cost molecules is, to say the least, ravenous.

A new stream of revenue will become especially critical when the new patents regime of 2005 bars companies from copying drugs launched internationally—a process that built the Indian drug industry. Building capabilities in drug research will, then, allow Indian companies to become either global laboratories or new drug manufacturers, even if in association with a foreign player. There are six alchemists who, BT thinks, will put India—and themselves—on the global pharma map.

## THE DRL FACTFILE

NO. OF SCIENTISTS: 250

INVESTMENT ON RESEARCH: Rs 111.75 crore in eight years

PATENTS: Filed 55 US patents, 19 have been granted

HEAD OF RESEARCH: Dr. R. Rajagopalan; joined in 1994 from Hoechst

CONTRACT RESEARCH: No plans as of now

On a hot day in 1992, when Dr Kallam Anji Reddy asked a farmhand to hold steady a ladder as he climbed up the water tank atop his farmhouse, it was not the view he was after. Rather, the scientist-turned-promoter of Dr Reddy's Lab (DRL) wanted to prospect a site for his new research foundation.

Sacrificing his farmhouse for laboratory has paid Reddy rich dividends. Today, not only is Dr Reddy's Foundation (DRF) a leader in molecule discovery, it is also the most profitable of them all. In March 1997, DRF licensed its first molecule (DRF 2593)—and in August 1998, DRF 2725—to Novo Nordisk. Its booty: \$8 million so far. If the molecules pass the third stage of clinical trials, then the company could get a total of \$17.3 million in fee.

That's not all. In May this year, DRL licensed its novel insulin sensitiser compound, DRF 4158, to Swiss multinational, Novartis Pharma, for a staggering \$55 million (that's Rs 258 crore) in upfront and milestone payments. If any of the three molecules becomes a blockbuster drug at the hands of Novo Nordisk or Novartis, DRL could rake in an amount that will make the milestone payments look like loose change. And there are six other molecules (see table) that DRF is working on.

<b>LIST OF MOLECULE</b>	<b>THERAPEUTIC SEGMENT</b>	<b>STAGE OF DEVELOPMENT</b>
DRF 2593	Diabetes	Licensed to Novo Nordisk, is in late Phase II of clinical trials
DRF 2725	Diabetes/Dyslipidemia	Licensed to Novo Nordisk, is in late Phase II of clinical trials
DRF1042	Cancer	Phase I of clinical trials under way in India
DRF 4158	Metabolic disorder	Licensed to Novartis, is in initial stages of clinical trial
DRF NPPC	Diabetes	Pre-clinical trials over, being hawked for licensing
DRF 1644	Cancer	Pre-clinical trials over
DRF 3188	Cancer	Is into late pre-clinical trials
DRF 4832	HDL Elevator	Contracted to Simbec, late pre-clinical trials underway
DRF 4848	Pain Management	Is into late pre-clinical trials, being hawked for licensing

The credit for DRL's early start and success must go to Reddy, who brings a rare combination of business acumen and scientific spirit to the table. As he says, "I began looking at molecular structures and realised to my surprise that many players, including some of the global majors, were just tinkering around with the molecular structure. Seeing this, I realised that if this is what it takes to discover drugs, then we could also be in the race."

In fact, DRF 2593 was based on a molecule (thiazolidinedione) developed by a lab in Japan. The new insulin sensitiser was developed by

picking up an opportunity let go by Pfizer. Says Reddy: "Pfizer was already working on something similar, but gave up as somebody there felt it was not worth pursuing. I felt exactly the opposite."

The most important part of this high-risk research game is deciding which areas to play in. At DRL, the ground rule is that the new chemical entity (NCE) should be in development, and not in the market. As for the areas, the focus has been on diabetes, cancer, bacterial infections, and inflammation. The reason for picking these areas: market demand and, as G. V. Prasad, Reddy's son-in-law and Vice-Chairman & CEO of DRL says, "Existing regulations, particularly in US, make it possible to take these drugs faster to the clinical trial stage."

Like in the case of other pharma companies, DRL will need a strong grounding in research to compete under a new patent regime that begins 2005. No more will companies like DRL be able to copy drugs developed elsewhere and launch them locally for a fraction of the cost. Says an analyst with a foreign brokerage firm: "Companies will have to wait for drugs to go off patent, by which time the drug would have become a commodity."

Since the cost of developing a drug is prohibitively high, DRL prefers to stop at the pre-clinical stage, and license the molecule to a foreign drug company to take it through the three stages of clinical trial. But as the money generated from research increases, DRL plans to go further up the research value chain. Explains Reddy: "Licensing the compound will continue for sometime, but not forever. It took 15 months for me to negotiate a deal (for DRF 4158). I can save a lot of time by doing initial phases of clinical trials. That will also increase the value of the deal."

In 2000-01, DRL invested 7 percent of its Rs 899 crore turnover in R&D. The budget is to go up significantly post its \$132.8-million ADS (American Depository Shares) issue (including a greenshoe option worth \$17.3 million). For instance, \$30 million has been earmarked for drug discovery and development, and \$75 million for acquisitions and beefing up of marketing. Notes Anji Reddy's son Satish Reddy, MD & COO, DRL: "Research involves a lot of risk, and does not have a quick payback. Therefore, it is important that the company undertaking research is in a phase of growth, is willing to take bold steps, and has the ability to raise resources."

In the case of DRL, its recent merger with Cheminor Drugs has strengthened its balance sheet, and once the proposed merger with American Remedies is completed, DRL will become the eighth largest pharma company in India. Also, so far, it has been able to leverage India's low-cost, high quality scientific talent to plug gaps/opportunities left open by global research firms. But, DRL's detractors point out that the game will only get more difficult from here on.

For one, global companies will start plugging the gaps themselves, and then move towards biological research—a move that could erode the talent advantage, since biological research is not India's strong point.. It is to counter these hurdles that DRL in 2000 established Reddy US Therapeutics Inc. in Atlanta, US, to expand the drug discovery work to the new area of biology, where biomedical knowledge is used.

But even DRL's worst critics admit that it is ideally placed to exploit the coming boom in molecule outsourcing (or inlicensing). According to Subrojeet Syam, Manager, Arthur Andersen Business Consulting, 14 of the 55 global blockbuster drugs are inlicensed. And the global trend is to move more of the R&D budget to licensing. In the next few years, more than 20 percent of the global research spend could be on inlicensing. When that happens, Reddy would probably want to climb the water tank of his new farmhouse.