

Biotechnology in India: Just What the Doctor Outsourced?

Always looking for a way to do things faster, cheaper, and with a lower potential for risk, biotech is turning its attention toward India, where opportunities are plentiful for research and development, manufacturing, and clinical trials.

By Sanuj K. Ravindran, MD, MBA

A “perfect storm,” some would say, is what has led the Indian biotechnology industry to gain worldwide visibility and embark upon a rapid evolutionary path. In recent years, it has become increasingly evident to both investors and biopharmaceutical executives that drug development in the Western world is becoming prohibitively expensive, more time consuming, and decreasingly productive (Fig. 1, p. 44). At the same time, it is becoming clear that drug development in India can be achieved at a fraction of the cost and in a significantly shorter time frame.

With a necessary interest in identifying alternative means for developing drugs faster, cheaper, and at a lower risk level, investors and biopharmaceutical executives are intrigued by India’s lower cost basis, strong English-speaking scientific talent, its burgeoning focus on research and development (R&D), and its large and diverse patient pool. Furthermore, on Jan. 1, 2005,

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India became compliant with the World Trade Organization’s Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement, which provides minimum standards for the international protection and enforcement of intellectual property (IP) rights in member countries. This agreement has largely assuaged investors’ and biopharmaceutical executives’ concerns about IP, thus contributing to what has become the Indian biotechnology “perfect storm.”

THE BEGINNINGS

Since the 1980s, India was among the first of developing countries to recognize the importance of biotechnology. In fact, biotech was formalized as a growth sector in India in 1982 when the National Biotechnology Board (NBTB) was established to identify priority areas and execute a long-term plan for the sector’s development. In 1983, the NBTB issued the “Long Term Plan in Biotechnology for India,” which spelled out biotech priorities, including self-sufficiency in

food, clothing, and housing; adequate health and hygiene; the provision of adequate energy and transportation; protection of the



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environment; gainful employment; industrial growth; and balance in international trade. In 1986, NBTB evolved into a full-fledged government department known as the Department of Biotechnology, under the Ministry of Science and Tech-

nology. In the past several years, the Indian biotech industry has experienced monumental growth in terms of revenue, new company formation, business model evolution, product pipelines, increased patent filings, and considerably higher amounts of venture capital and partnering activity.

CURRENT LANDSCAPE

The \$1.5 billion Indian biotech industry is centered on new drug discovery, bioinformatics, clinical research, synthetic chemistry, and manufacturing, with approximately 250 drugs in the market across 15 therapeutic segments. The industry accounts for 1.5 percent of the \$100

billion global biotechnology market, but is growing rapidly and is projected to achieve a 10 percent global share by 2020 (Biospectrum 2006). Exports comprise 42 percent of total biotech revenue, while the domestic market makes up 5 percent (Biospectrum 2006). Currently, India's greatest therapeutic strength is in vaccine production. One of every two children in the world is immunized by vaccines made in India, and the country is the world's largest producer of recombinant hepatitis B vaccine (Burrill 2006). In addition to vaccines, the country is emerging as a global player in recombinant human insulin, and is one of the main countries involved in stem cell research. While India's therapeutic strengths may one day be relied upon to fill the gaps in Western product pipelines, more immediate opportunities are found in the areas of R&D, manufacturing, and clinical trials.

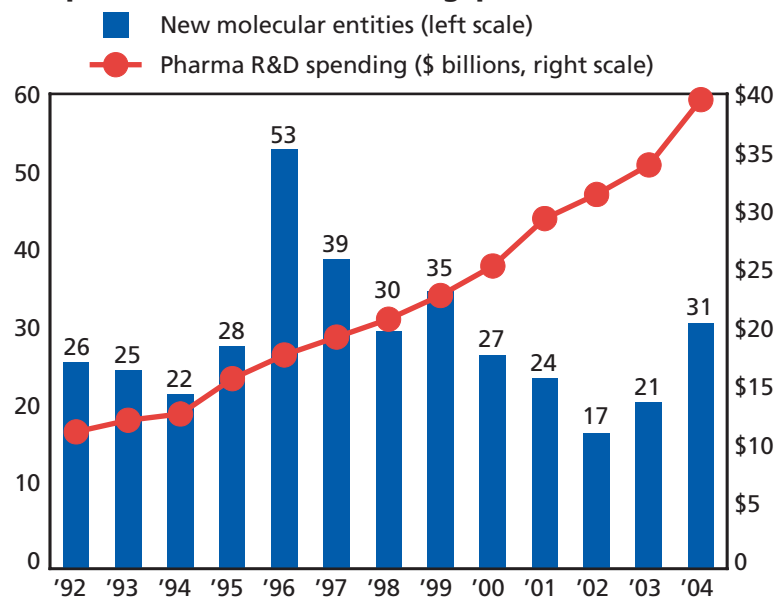
RESEARCH & DEVELOPMENT

Understanding India's R&D capabilities begins with understanding its rich history as a generics power. India's generic drug strength stems from its policies on IP. Because Indian IP policy has historically focused on process protection over product protection, its capabilities in chemistry and reverse engineering have been forced to become stronger to circumvent the process patents that served as the country's only means of product protection. As such, the Indian generics industry over time has created a scientific talent pool that complements many U.S. biotech companies, with capabilities that include medicinal chemistry, custom synthesis, process R&D, lead optimization, and pharmacokinetics and pharmacodynamics. In fact, the Indian biotech industry employs nearly 20,000 scientists and technicians, and the average full-

time equivalent cost for a scientist in India is one fifth of the cost in the United States (Burrill 2006).

The availability of such scientific talent is important in areas other than outsourcing. Since Indian IP law became TRIPS compliant, many companies that had thrived as generic and active pharmaceutical ingredients (API) manufacturers are redirecting their efforts to move up the value chain, and have begun focusing on innovation. In November 2006, an innovation-driven R&D firm, Advinus Therapeutics, entered into a \$150 million drug discovery and clinical development collaboration with Merck to develop drugs for such metabolic disorders as diabetes and obesity. The deal not only marks Merck's first research collaboration in India, but also serves to validate the country's emerging role in bringing innovative and life-saving drugs to market with speed and cost-effectiveness.

FIGURE
U.S. pharmaceutical innovation gap



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MANUFACTURING

India has emerged as an outsourcing destination of choice for the cost-effective production of API and formulations. In fact, India has more FDA-approved plants — currently more than 60 — than any country outside the United States, and is the world's largest filer of U.S. Abbreviated New Drug Applications (ANDAs) and the second largest supplier of API (Goldman Sachs 2005). Furthermore, with nearly 40 percent of the world's API produced in India, even major generic companies, such as Teva Pharmaceutical Industries, Mylan Laboratories, and Forest Laboratories source API from India.

From the biologic manufacturing standpoint, a number of Indian

companies are offering contract-manufacturing services to global biotech companies. Currently, however, there are only a few biologic manufacturers that are able to produce good manufacturing practice-grade biologics. Given the growing global demand for biologic manufacturing capacity, it is only a matter of time before conventional Indian pharmaceutical and chemical companies adapt to meet this need. Indian companies possess the talent and know-how to grow within this

area, and also hold an innate competitive advantage: it costs 40 percent and 20 percent less to set up a new manufacturing facility and to fund labor costs, respectively, in India than it does in the Western world (Goldman Sachs 2005).

CLINICAL TRIALS

India's value proposition in clinical trials is undeniable on many fronts. A large and diverse patient population, a sizeable group of English-speaking physicians and

healthcare providers, a growing number of high-quality medical facilities, and considerably lower costs for conducting clinical trials all contribute to its appeal. This infrastructure will enable clinical research to be conducted at a cost that is one third of that in the United States, and a patient enrollment rate that is three times faster, comparatively (Goldman Sachs 2005). Currently, there are more than 30 clinical research organizations working in India, and many major pharma-

TABLE
Global integration arbitrage opportunities generated by significant differences between India and the Western world in the biotechnology industry

Differences	United States	India	Opportunities
Technology	<ul style="list-style-type: none"> Advanced technology: more than 30 years of history Strong financing: a National Institutes of Health budget of \$30 billion 	<ul style="list-style-type: none"> Needs advanced technology: "late starter" Insufficient financing Historically poor intellectual property protection 	<ul style="list-style-type: none"> Technology transfer to capture value for products in the Indian market
Cost	<ul style="list-style-type: none"> High drug-development costs About \$1 billion for each successfully developed drug 	<ul style="list-style-type: none"> Low drug-development cost Preclinical drug development at approximately 20% of U.S. costs enables reduction of late-stage attrition 	<ul style="list-style-type: none"> Research and development and healthcare service outsourcing to India; leverage cost advantage to create risk and value arbitrage opportunities
Market	<ul style="list-style-type: none"> Largest market: 42% of worldwide market U.S. companies need top-line growth Many successful and proven business models 	<ul style="list-style-type: none"> Small market: less than 2% of worldwide sales High growth potential: India to become top 5 by 2010 Significant unmet market needs 	<ul style="list-style-type: none"> Cross-border expansions Technology transfer and infrastructure business model duplications in India
Drug Development	<ul style="list-style-type: none"> FDA compliant Less than 1% success rate from preclinical to new drug application More projects with the same level of financing 	<ul style="list-style-type: none"> Starting to be FDA compliant 	<ul style="list-style-type: none"> Transfer of FDA-compliant development experience and know-how to India

SOURCE: AUTHOR ANALYSIS

ceutical companies have their own clinical development groups conducting internationally regulated and approved clinical trials in more than 80 government and private hospitals (Burrill & Company 2006). The Indian CRO industry is currently valued at \$100 million, and is projected to be a \$1 billion sector within the next four years. Analysts project that by 2010, as much as one third of all global clinical trials will take place outside of the United States and Europe, and that India is well positioned to capture significant market share (Burrill 2006).

One highly debated limitation to the growth of India's CRO industry is its government's restrictive stance on phase 1 testing, which extends beyond safety protection of its population. The government believes that pharmaceutical companies will not pass the full benefit of reduced clinical trial costs onto the Indian consumer. However, a recent change to the rules governing clinical trial execution in India has contributed to the growth and expansion of its CRO industry. The modification was a result of pressure exerted by multinational companies that protested against the stringent Indian government rules designed to safeguard its citizens from being used as testing subjects for treatments of foreign origin that would be tested for safety elsewhere. Previously, only indigenous molecules developed in India were permitted to go through first-in-man studies. However, Schedule Y of India's Drugs and Cosmetic Act was amended to allow multicentric, early phase 1 trials in India on a case-by-case basis, as part of global multicountry trials sponsored by foreign biopharmaceutical compa-

nies. Clinical testing in India will likely duplicate or exceed Western standards, and will include principles of informed consent, oversight by institutional review boards, compensation for adverse reactions, and, for those patients enrolled in the trials who need it, drug availability between the end of phase 3 and NDA approval.

INVESTMENT OPPORTUNITY: GLOBAL INTEGRATION ARBITRAGE

India is rapidly becoming a leading global pharmaceutical development center. With clear competitive advantages in biotech areas ranging from R&D to manufacturing to clinical research, it is not surprising that the world is paying close attention. But just how will investors and biopharmaceutical executives leverage India's biotechnology oriented capabilities? From my perspective as a U.S.-based life science venture capitalist, both Indian companies and nonIndian companies with India-centric business models represent attractive opportunities. I believe that India is at a very early stage along its evolutionary path, and is limited by a paucity of sophisticated biopharmaceutical managers, inexperience in drug development for regulated markets, a dearth of early-stage funding, and lesser capabilities in innovative basic science research.

The challenges and opportunities facing India are twofold: first, to identify its comparative advantages and limitations, and second, to enable the bidirectional transfer of technology, capital, management talent, and other resources between India and the Western world. Approaching India from this perspec-

tive of global integration arbitrage will offer both investors and biopharmaceutical executives the greatest likelihood of a successful outcome (Table).

CONCLUSION

The traditional drug development process holds room for improvement, as it is prohibitively expensive and time consuming. Driven by investors and biopharmaceutical executives in the Western world, a new model is being created that would effectively integrate the most efficient drug development resources worldwide. This will enable India to upgrade its drug development infrastructure to meet international regulatory standards and thus increase external perception of its value. It also will permit India to leapfrog the development of its pharmaceutical industry by absorbing advanced biotechnology from the West. Through this platform, drugs developed in India in collaboration with Western companies would realize maximum value by addressing the needs of worldwide markets. The biotech industry in India may just evolve into "just what the doctor ordered!" **BH**

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DISCLOSURES

Sanuj K. Ravindran, MD, reports no financial arrangements or affiliations that might constitute a conflict of interest with respect to this article.