



The Pharma Giants: Ready for the 21st Century?

The primary challenge facing the pharmaceutical industry is accepting the fact that superior economic performance in the new millennium will require a new way of thinking. Relying on blockbuster drugs is no longer enough. In the future, companies must develop a mindset and culture of cost consciousness as well as an understanding of the critical role of marketing and sales, the need to use technology to improve every aspect of the organization, and the fact that every individual can make a difference.

—A.T. Kearney report¹

Over the past few years, the big-pharma companies have been playing . . . a giant game of pac-man—eat or be eaten. Firms have been swallowing one another in a search for economies of scale (and, all too frequently, a desire to purchase a pipeline with the profits of one or two blockbuster drugs, to compensate for internal research failures). . . . Meanwhile, the proliferation of small biotechnology firms suggests that those economies of scale count for less than they used to, and that barriers to entry are dropping.

—*The Economist*²

As the end of the twentieth century drew near, the giant companies in the \$222 billion³ global pharmaceutical industry faced a potent dual threat to their hegemony. While governments and large institutional buyers continued to exert strong downward pressure on drug prices and company earnings, a scientific and technological revolution promised to change the way in which drugs were discovered, developed, and tested, and in the process to expose the industry to a wave of new competitors. These might look nothing like the pharma giants of old, the huge, vertically integrated centenarians that historically had done everything from basic research through development, manufacturing, marketing, and distribution. Instead these competitors could be small, fleet of foot, highly specialized, and free from tradition.

¹ "Maximizing Pharmaceutical Health in the Next Millennium: A Prescription for Shareholder Value," A.T. Kearney, Inc., 1997, p. 27.

² Geoffrey Carr, "Survey of the Pharmaceutical Industry," *The Economist*, February 21, 1998, p. 16.

³ Source: IMS Pharmaceutical World Review.

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Turmoil in the Early 1990s

Traditionally, the global pharmaceutical industry was characterized by rapid growth, high profits, and competitive stability, even while showing dramatic innovation. The industry had been one of the most profitable in the world measured by standard accounting practice, although economic returns (i.e., returns adjusted to recognize R&D as an asset) were in line with the industry's cost of capital.⁴ The industry was highly fragmented, with hundreds of pharmaceutical companies competing in more than 20 different therapeutic categories, and no one company controlling as much as 5% of industry sales.⁵ (See **Exhibit 1** for worldwide market share data.) Nevertheless, a few giants, including Merck, Bristol-Myers Squibb, and Glaxo, had dominated their respective therapeutic categories for over half a century, and typically had not competed on price for leadership of individual categories. (See **Exhibit 2** for a comparison of pharma giant sales by therapeutic category.)

However, in the early 1990s, pharmaceutical company sales and earnings growth slowed dramatically. Company stock valuations fell precipitously: between 1991 and 1993 market capitalization for drug stocks plummeted by 35%. (See **Exhibit 3** for price movements of pharmaceutical stock indexes.) Downsizing followed. Merck, for example, announced it would reduce its workforce by 5% during the 1990s, while Pfizer announced plans to reduce its workforce by more than 10%.⁶

In the United States, which represented one-third of the world pharmaceutical market, pressure to reduce drug prices came from the growth of managed care organizations (MCOs), which sought to control prices through restricting the number of drugs offered to patients in a particular therapeutic category. In 1980 only 5% of the insured U.S. population was covered by managed care. By 1993 this figure had risen to 80%. Similarly, while in 1960 only 4% of prescription drug sales were funded by third-party payers, by 1995 MCOs alone accounted for 75% of drug purchases.⁷ Increased buying power enabled MCOs to extract large price concessions from drug manufacturers.

Indeed, cost containment was the "name of the game" among health care payers worldwide. In the United States, virtually all health maintenance organizations (HMOs) used formularies, or lists of approved medicines, to control costs. In 1997 an estimated 65% of HMOs used "closed" formularies, which limited payment to those drugs listed on the formulary. This figure had risen from 52% and 35% in 1995 and 1994, respectively.⁸

Pharmaceutical manufacturers were also under attack from generic substitutes for their flagship patented drugs, priced typically at a 30% to 90% discount to brand-name drugs. Generics' share of the U.S. prescription drug market rose from 19% in 1984 to over 40% in 1996.⁹ By 1996 an

⁴ One study estimated a rate of return on new drugs introduced between 1954 and 1978 of 21% (compared to a cost of capital of roughly 11%). See Meir Statman, *Competition in the Pharmaceutical Industry: The Declining Profitability of Drug Innovation*, Washington, D.C.: American Enterprise Institute, 1983, as quoted in Gary P. Pisano, *The Development Factory: Unlocking the Potential of Process Innovation*, Harvard Business School Press, 1997, p. 55. Several academic studies found that, once the industry's economic returns were adjusted to recognize R&D as an asset, returns were commensurate with the industry's cost of capital. See Grabowski and Vernon, "Returns to R&D on New Drug Introductions in the 1980s," *Journal of Health Economics*, Vol. 13, November 1994, pp. 383-406.

⁵ See Dale O. Cox, Greg Keller, Anita McGahan, and John F. McGuire, "The Pharmaceutical Industry in the 1990s," Harvard Business School Case No. 796-058.

⁶ See Pisano, *op cit.*, p. 57.

⁷ *Ibid.*, p. 60.

⁸ Source: PhRMA, *op. cit.*

⁹ Source: IMS America, 1997.

estimated 86% of HMOs routinely substituted generic products for patented drugs when possible.¹⁰ In a radical departure from normal pharmaceutical pricing, Eli Lilly became the first company to guarantee to match the Tariff price of a generic with a branded product.¹¹

The growth of generics had been fueled by the 1984 Waxman-Hatch Act, which reduced the barriers to generic entry by accelerating the approval process for the drugs. Instead of forcing generic drug makers to conduct their own lengthy and costly clinical trials, Waxman-Hatch mandated they show only that their drugs were chemically and biologically equivalent to the original patented versions. Whereas before Waxman-Hatch generic entry had taken years, after Waxman-Hatch generic substitutes began appearing in the market immediately after branded drugs lost patent protection, giving drug makers less time to recoup their research and development costs. The industry faced the expiration of patents on many blockbuster drugs: 42 major drugs by 2002, which would cost the industry \$32 billion in revenues.

Pharmaceutical companies also came under political attack following U.S. President Bill Clinton's election in 1992. The Clinton administration and many in Congress were highly critical of pharmaceutical companies for their high profit margins and their alleged contribution to runaway U.S. health care costs. Shortly after taking office, Clinton initiated a review of the entire U.S. health care system, which although not implemented, recommended a new system of federal controls on health care, including price controls on prescription drugs.

By the mid-1990s, price pressure had extended to Europe where governments had traditionally played a more direct role in the medical system. In 1994, the German government, having increased patient copayments the year before, imposed a 5% price reduction on many drugs. Drug sales subsequently declined 15% to 20% in the world's third-largest drug market. Price cutbacks initiated in Italy in January 1994 were expected to reduce annual state-reimbursed drug costs by one-third. Expectations for 1995 were that the combined pharmaceutical markets of the United Kingdom and Germany would grow by 3% to 4%, that of Spain would remain flat, and those of France and Italy decline by 1% and 9%, respectively. The Japanese government had also been reducing reimbursement amounts for prescription drugs, and this continued through 1997, when drug sales in Japan fell by 1% to \$41.7 billion.¹²

Rising Cost and Complexity

Downward pressures on prices coincided with growing complexity in drug development and approval cycles, which drove up R&D and capital expenditures. Industry R&D expenditures grew to \$18.9 billion in 1997. In the United States, R&D as a percentage of sales rose to 21.2% in 1997, up from 15.9% in 1990, and 11.7% in 1980.¹³ (In contrast, the average R&D to sales ratio for U.S. industries was less than 4%).¹⁴ (See **Exhibit 4** for R&D and capital expenditures of the large pharma companies.)

The high risk and research intensiveness of the pharmaceutical industry made drug development costly. According to one estimate, as much as 50% of all development dollars were expended on products that never reached the market.¹⁵ Only one in 5,000 compounds reached an end user. Of these, only 30% achieved the commercial success necessary to recover an average

¹⁰ *Ibid.*

¹¹ "GW's \$2bn Golden Egg Loses its Lustre," *Community Pharmacy*, November 1997, p. 27.

¹² Daniel Green, "Prescription drug sales rise 6% to 166bn," *The Financial Times*, March 5, 1998.

¹³ Source: PhRMA 1997 Annual Report.

¹⁴ Source: PhRMA, *op. cit.*

¹⁵ *Ibid.*

research investment. A study released in the early 1990s estimated that \$359 million and approximately 10 years were required to move a drug from test tube to end user, compared with approximately \$250 million in the mid-1980s. Total drug development time grew from an average of 8.1 years in the 1960s, to 11.6 years in the 1970s, to 14.2 years in the 1980s, to 15.3 years for drugs approved from 1990 through 1995.

Clinical trials—which in Phase I involved 50 to 100 healthy individuals, in Phase II 200 to 300 potential patients, and, in Phase III, more than 3,000 individuals in some cases—accounted for two-thirds of total product development costs. Firms applied to the authorities upon completion of testing and could begin marketing upon notification of approval.¹⁶ The cost of worldwide testing for an initial application of a new product was estimated to be \$20 to \$75 million. Approval by local governments added another \$1 to \$2 million per country or region (\$5 to \$6 million in Japan).

The drug development process was monitored carefully by the U.S. Federal Drug Administration (FDA) and comparable institutions around the world. Rejection of one of the applications required at each stage of the drug development process or other regulatory delays could jeopardize the scheduling of a series of interdependent activities and greatly delay time to market. For a “blockbuster” drug, one day’s delay could mean well over \$1 million in lost revenues. Although the United States led the world in drug discovery and development, 67% of drugs approved in the United States between 1990 and 1996 were marketed abroad first. The U.S. FDA had been criticized for the length of its review process and was working to speed up its review of new drug applications. Mean FDA approval times for new drugs fell to 17.8 months in 1996, down from 19.2 months and 30.3 months in 1995 and 1991, respectively.¹⁷

Marketing expenditures in the industry also seemed set to grow. It was still important to have large sales forces to detail doctors and explain product features and benefits. However, in fall 1997 the U.S. FDA changed the advertising rules for prescription drugs. Although firms had been allowed to take their messages directly to consumers in magazines for roughly a decade, there had been strict guidelines for ad content. For instance, warnings for drug side effects had to be prominent in print ads, while in TV ads there was usually no identifying information for a drug, only a description of symptoms followed by encouragement to see a doctor if those symptoms appeared.¹⁸ Under the new regulation, marketers of pharmaceuticals were allowed to name a prescription drug and the illness it treated in direct-to-consumer television advertisements. One of the first drug makers to take advantage of this change was Hoechst Marion Roussel, which launched a new TV ad campaign for its prescription antihistamine Allegra. Many observers believed that relaxed federal rules for consumer advertising would help firms increase pharmaceutical sales, and they expected advertising expenditures to increase significantly.

Pharmaceutical companies responded to these circumstances by challenging the success potential of products and compounds through centralized decision-making at the top management level, and by implementing control systems that would allow them to coordinate far-flung R&D activities. Ultimately, the major challenge for managers in the industry continued to be to mediate the legendary conflicts between R&D, production, and marketing.¹⁹

¹⁶ For a complete discussion of the drug discovery, development, and approval process, see Cox, Keller, McGahan, and McGuire, *op. cit.*, pp. 5-6.

¹⁷ *Ibid.*

¹⁸ “Advertising drugs: pill pushers,” *The Economist*, August 9, 1997, p. 56.

¹⁹ This section adapted from Jean-Pierre Jeannet, Carin-Isabel Knoop, and Michael Y. Yoshino, “Ares-Serono Abridged,” Harvard Business School case No. 9-396-104.

Increasing Scale and Scope

Intensified competition and price pressures in global pharmaceutical markets fueled merger and acquisition activity in what remained a highly fragmented industry. In 1995, even industry leaders Merck and Glaxo only claimed 3.5% and 4.4% of global market share each, respectively (1.3% earned a firm a place among the top 20). Through mergers and acquisitions firms sought global scale and scope advantages in research, manufacturing, marketing, and distribution. Merck, Eli Lilly, and SmithKline Beecham integrated *forward* by purchasing pharmaceutical benefits managers to gain greater control over drug distribution channels.²⁰

Firms like Glaxo and Wellcome, Sandoz and Ciba Geigy, and Pharmacia and Upjohn merged. The pooling of product portfolios, referred to as “one-stop shopping,” extended manufacturers’ coverage of therapeutic areas to afford greater clout with managed care customers. Acquirers instantly gained new products and customers and realized opportunities to reduce costs by rationalizing, for example, sales forces and manufacturing and R&D facilities. (See **Exhibit 5** for mergers and acquisitions in pharmaceuticals.)

Other firms like Merck and Pfizer decided not to merge and to instead rely on their own R&D programs to fuel growth. They divested themselves of unrelated businesses, ramped up their investment in R&D, and rededicated themselves to producing blockbuster drugs through “breakthrough” research.

Firms also attempted to leverage their marketing and distribution resources by acquiring technology from external sources through licensing agreements, R&D contracts, joint ventures, equity investments, and other forms of collaboration. From 1986-1993 the number of strategic alliances in the pharmaceutical industry increased from 121 to over 400.²¹

Finally, in an effort to further reduce costs in the health care system, HMOs, first in the United States and later in Europe, began seeking ways to manage disease comprehensively, rather than by component part. Supported by pharmaceutical companies, HMOs began offering “disease management programs,” which offered comprehensive disease treatment guidelines for health care providers and patients. An executive at Eli Lilly defined disease management as follows:

[Disease management was] an integrated system of customized interventions, measurements, and refinements to . . . processes of care designed to optimize clinical and economic outcomes within a specific disease state by facilitating proper diagnoses, maximizing clinical effectiveness, eliminating ineffective or unnecessary care, using only cost-effective diagnostics and therapeutics, maximizing the efficiency of care delivery and improving continuously.²²

Pharmaceutical companies used disease management programs to demonstrate the cost effectiveness of prescription drugs relative to hospital-based care, and to combat poor compliance

²⁰ Pharmaceutical benefits managers (PBMs) typically provided a range of services to large self-insured employers, insurance carriers, managed care organizations, and other private and governmental institutions that provide prescription drug coverage to their employees, retirees, or members. PBM services included assisting in the design of pharmacy benefit plans; processing prescription drug claims submitted for plan members from retail pharmacies; reviewing prescriptions to prevent drug interactions; implementing programs to encourage the use of lower-cost generic and brand name drugs; and dispensing drugs through mail service pharmacies. For a detailed discussion of PBMs, see Marie Bell and V. Kasturi Rangan, “Merck-Medco: Vertical Integration in the Pharmaceutical Industry,” Harvard Business School Case No. 598-091.

²¹ Source: Windhover’s Pharmaceutical Strategic Alliances, 1997.

²² William C. Castagnoli, “Disease Management—Background,” *Medical Marketing & Media*, January 1995.

rates for patients taking prescription drugs. Poor compliance was common across all chronic medical conditions, particularly when patients were asymptomatic, and encompassed a wide variety of behaviors: underuse (especially the failure to fill or renew prescriptions), overuse, the mistiming or skipping of doses, the sharing of drugs with family members, or the consumption of food or liquids that interacted with the prescribed drug. Poor compliance was believed to have large economic costs, as measured by the increased frequency of hospital admissions and readmissions, and costs associated with poor preventative health care (See **Exhibits 6 and 7** for patient noncompliance data; and **Exhibit 8** for types of disease management programs.) Disease management also went by other names—"population-based management of care," "disease state modeling," "outcomes management," and "care mapping."

Organizationally, pharmaceutical companies engaged in disease management in three basic ways. First, some companies used disease management programs as a "value-added" service to augment their traditional national accounts sales structures, which handled sales to hospitals, HMOs, and other group purchasers. Second, other firms like Merck, SmithKline Beecham, and Eli Lilly, developed and distributed disease management programs through their PBM subsidiaries. Third, firms set up separate subsidiaries to offer disease management programs, with the intent of making disease management a new, separate line of business unrelated to pharmaceuticals.

Some industry observers viewed disease management as an attempt by pharmaceutical companies to escape commodity status. According to a senior vice president at Merck-Medco Managed Care:

Pharmaceuticals appear[ed] headed for commodity status pushed by generics, formularies, and other cost pressures. Regardless of lowering prices there [wa]s an upside for drugs. They represent[ed] only seven percent of the health care bill and through disease management, they c[ould] draw funds from less efficient treatment methods [such as] hospitalization, surgery, etc. A pharmaceutical company c[ould] get itself out of the commodity/price box by seeing itself as a manager of health. It c[ould] draw off some of that 93% of non-drug spending to itself and at the same time save money for providers based on the cost efficiencies of pharmaceuticals and the contribution they make to the efficient management of the disease.²³

New Science and Technology

While pharmaceutical companies attempted to cope with major changes in the drug market, a revolution in science and technology was changing the way drugs were discovered, developed, and tested. Advances in genetics, molecular biology, and biochemistry created new competitive dynamics.

The revolution in molecular biology had two important effects on pharmaceutical research and development. First, it offered new techniques for working backward from known disease biochemistry to identify or design chemical "keys" to fit the biochemical "locks" of that disease. This method, known as "rational drug design," stood the traditional approach to drug discovery on its head. In the past, drug discovery occurred through the random screening of large numbers of organic chemical compounds (called libraries), the success of which was determined largely by chance. With the advent of rational drug design came the opportunity for firms to discover organic therapeutic compounds more quickly and efficiently than ever before.

²³ William C. Castagnoli, "Is Disease Management Good Therapy for an Ailing Industry?" *Medical Marketing & Media*, January 1995.

In competitive terms, however, the potential advantage was limited by the fact that all firms drew from the same publicly available knowledge base, which opened the door to fast follow-on products that were therapeutically similar, but different enough on a molecular level not to infringe on patents. New drugs once enjoyed, on average, a five-year monopoly before a competitor emerged. By 1998, the window had shrunk to a year or less. (See **Exhibit 9** for declining exclusivity periods for patented drugs.)

Second, the molecular revolution allowed the development of an entirely new class of drugs based on protein molecules synthesized through genetic engineering. Substances based on organic (or natural) raw materials were replaced by bio-genetically engineered products using a technique developed by Herbert Cohen and Stanley Boyer at the University of California in 1973. Within months of their invention they had formed Genentech, the first biotechnology company. Genentech's first commercial product, a growth hormone, was developed by the company in the mid-1980s and approved by the FDA in 1985. Within a few years, several hundred biotechnology firms had been formed to undertake commercial R&D.²⁴ Companies like Genentech, Amgen, Chiron, and Genzyme were among the first to demonstrate that competitive barriers in drug discovery could be breached. In addition, regulatory changes such as the 1994 European Community decision to grant pan-European product approval for prescription drugs were making it easier for these entrants to take their innovations to market. Shortly thereafter, biotechnology developer Biogen launched its beta-interferon drug on a pan-European level without the benefit of individual country organizations.

Traditional pharmaceutical companies became buyers of drug candidates—and the companies that discovered them. Large drug makers initiated a series of partnerships, alliances, and takeovers of biotechnology companies in the early to mid-1990s. In September 1990 Roche purchased a 60% stake in Genentech, one of the biotechnology pioneers, in a deal valued at \$2.1 billion. In January 1995 Ciba-Geigy acquired a 49% stake in biotechnology developer Chiron for \$2.1 billion. In exchange for marketing rights under licensing agreements, drug manufacturers provided biotech firms with development funds, production facilities, and access to large existing sales organizations. Research-based firms were being led increasingly beyond their traditional therapeutic strongholds.

By 1997 worldwide sales of the top seven biotech firms had climbed to \$6 billion, while worldwide sales of recombinant proteins were estimated at \$13 billion. (See **Exhibit 10** for the top seven biotech companies ranked by 1997 global sales.) Nevertheless, more than half of the approximately 1,200 biotechnology companies throughout the world in 1993 were located in the United States. Only 2% of these companies had sales of at least \$200 million, although the companies with the leading products ranged widely in size. The vast majority were in the process of developing a first product and hence reported no sales. Industry losses climbed from \$2.2 billion in 1990 to \$3.6 billion in 1993. R&D expenditures increased from \$2.8 billion to more than \$5.7 billion over the same period. It often took eight to ten years and more than \$100 million before a drug would be approved for marketing. Finally, because most biotech companies produced only one product at a time, plants often stood idle while active substances were under development. Nearly half of the biotech industry's capacity was believed to be idle in 1994.²⁵

Advances in science and technology promised breakthroughs beyond rational drug design and genetically-engineered drugs. Combinatorial chemistry allowed new organic molecules to be produced in vast quantities for the first time. Using traditional methods, an individual scientist would have been able to produce 50 to 100 new compounds per year. Using combinatorial chemistry that chemist could produce on the order of 2,000 new compounds per year. Because success in drug discovery had been correlated strongly with the size of a firm's chemical library of molecules, large libraries were prized assets. Moreover, only large companies could afford to develop large libraries. Combinatorial chemistry brought large libraries within many firms' reach. Another technique called

²⁴ See Pisano, *op. cit.*, pp. 64-65.

²⁵ Adapted from Jean-Pierre Jeannet, Carin-Isabel Knoop, and Michael Y. Yoshino, *op. cit.*, pp. 3-4.

“high-throughput screening” allowed for entire chemical libraries to be screened more quickly than ever before.

The preclinical stage of drug development, during which compounds were tested for toxicity, bioavailability, pharmacokinetics, and efficacy, was also being improved. “Cassette dosing” was a technique in which multiple drug candidates were tested simultaneously, instead of individually as had been industry practice.

Meanwhile, a new type of pharmaceutical company, the contract-research organization, employed advances in computer technology to manage phase-I through phase-IV clinical trials more effectively. Clinical trials were the most costly part of the drug development process. Drug makers hired contract research organizations to develop better and cheaper ways of conducting the trials, some of which occurred in multiple countries simultaneously and involved hundreds or even thousands of patients. Companies offering “virtual” clinical trials, in which trials were run by computer simulation using virtual patients, were also on the horizon. This method promised to make this stage of drug development ever faster and cheaper.

Finally the process of medical diagnosis itself was being revolutionized by “DNA chips” capable of identifying a piece of DNA from among a small number of known variants, thus allowing patients to be screened quickly and cheaply for genetic “defects,” or predisposition to disease.

As a result of these new technologies and approaches, by 1996 outsourcing as a percentage of R&D expenditure rose to over 16%, up from roughly 8% in 1990.²⁶ Some industry observers believed the rise of new research companies could be a two-edged sword for large drug makers. According to one analyst:

In the short term, at least, th[e] plethora of eager drug-discovery companies is a bonus for big pharma. Small concerns with only one or two promising compounds are frequently reluctant to take the risks, and bear the costs, of clinical trials by themselves. Big-pharma companies can often pick up joint-development rights to these substances fairly cheaply.

In the longer run, however, the big companies may inadvertently be nurturing powerful rivals. Many firms, following in the footsteps of Amgen, Genzyme and the other trail-blazers of the 1980s, have set their sights on becoming fully fledged pharmaceutical companies—if on a smaller scale than Merck, Novartis, Glaxo Wellcome, SmithKline Beecham and their kind—by not merely discovering, but also developing and marketing their own drugs.

In the past, this has been difficult . . . [but as] R&D becomes cheaper and quicker, small firms can more rapidly build up the cash flow they need to finance future products. Once a small company has a successful drug, it no longer needs to go cap-in-hand to the big boys. . . . This trend will be accentuated if pharmacogenomics and virtual clinical trials deliver their promises. As the knowledge they provide reduces the risk of a molecule dropping out of the pipeline late in the trials process, raising money to finance such trials will be easier. That will knock away one of the arguments for big pharma: its ability to survive costly failures.²⁷

Other analysts downplayed the threat to big pharma from upstart biotech companies, and argued instead that competitive mass and scale would be critical to success. According to one industry analyst:

²⁶ Source: PhRMA, *op. cit.*; Lehman Brothers.

²⁷ Geoffrey Carr, *op. cit.*

By the year 2000, we expect the minimum level of R&D investment required to stay competitive [in pharmaceuticals] will be in the range of \$1.5 to \$2.0 billion per year. This threshold will split the industry players into “haves and have nots,” differentiated by scale and the ability to invest in R&D.

Assuming that there is a relationship between R&D spending and the successful discovery of new products, it will become increasingly difficult for smaller companies to compete. In addition, some of the benefits of scale in R&D include being able to place multiple bets in a single therapeutic area (increasing the likelihood of owning the “right” discovery), being a more attractive development partner, and leveraging the infrastructure to undertake the costly development process. Consequently, all but top tier companies will have to consider strategic combinations, or risk being marginalized, since these statistics suggest that the necessary level of R&D investment is out of reach for smaller companies.²⁸

Big Pharma in 1998

In 1998, pharma firms continued to face increasing R&D costs, added research and development complexity, lengthy product development cycles, declining exclusivity periods for patented drugs, and pressures to reduce prices and to demonstrate the *value* of prescription drugs to powerful buyers.

The financial performance of pharmaceutical companies during the 1990s had been uneven. One survey found, however, that based on measures of economic returns,²⁹ the performance of many large pharma companies had been strong in 1996 (see **Exhibit 11**). But because drug development lead times were long, it was unclear whether the financial success of firms’ competitive strategy post-1992 could be gauged accurately in early 1998. Another study found that the degree of overall therapeutic concentration by drug companies was positively correlated with economic returns.³⁰ The finding raised an important strategic question for drug makers: Should they be opportunistic and allow themselves to be led into an increasing number of unfamiliar therapeutic categories by their heavily funded R&D programs, or should they concentrate on a limited number of categories where they had traditional strength?

Not surprisingly, the large firms continued their efforts to gain scale and scope advantages in the industry. In mid January 1998 drug giants SmithKline Beecham and American Home Products announced they would join forces. Drug share prices soared at the news amid Wall Street speculation that the attempted deal signaled a new wave of mergers and acquisitions in the industry. Two weeks later SmithKline announced it was forsaking its American suitor in favor of British counterpart Glaxo Wellcome, the largest drug company in the world. Their marriage, valued at \$70 billion, would have become the largest corporate merger in history. Even though the news had been welcomed on Wall Street, the plan later collapsed when the CEOs of the respective firms could not agree on a power sharing arrangement for the merged entity.

²⁸ Stephen Sands of Lazard Freres & Co., L.L.C., as quoted in A.T. Kearney, *op. cit.*, pp. 22-23.

²⁹ Market Value Added (MVA) and Economic Value Added (EVA). MVA was simply the difference between the market value and the book value of the debt and equity raised by the company. EVA was defined as after-tax net operating profit minus the cost of capital. Sources: *Fortune*, November 10, 1997; Credit Suisse First Boston report, January 10, 1997.

³⁰ A.T. Kearney, *op. cit.*, p. 24.

Some analysts believed that “big pharma” was ill prepared for the new competitive game in pharmaceuticals. Firms were regarded by many as “rigid,” “slow,” and “stuck in the glory days” of the past. According to one analyst: “Although some [pharma] executives are fighting the sleepy behavior of the past, they find it hard to win converts to a new way of thinking because of a cultural mindset that believes the next blockbuster drug is all that is needed for continued success.”³¹

Indeed, according to Andersen Consulting, between 1990 and 1994 the top 10 pharma companies launched an average of only 0.45 truly new drugs (i.e., novel molecules) a year each. To maintain their current annual revenue-growth rate of 10% without resorting to yet more mergers (whose principal benefits are often one-off cost cuts), these companies [would] have to increase their productivity tenfold, launching five new compounds a year, each with an annual sales potential of \$350 million. This is a tall order: half the newly introduced drugs in the industry rake in less than \$100 million a year.³²

As a result, firms looked to develop core capabilities beyond placing the right “bets” on new molecules. These included: clinical development and launch project management skills, operational excellence, marketing, sales, channel management, and organizational effectiveness. Most firms restructured in a quest to make their internal drug development processes faster, more efficient, and less costly.

In early 1998 there appeared to be almost as many strategies for achieving growth as there were big pharma companies. Each of the top five industry players by 1997 worldwide sales³³—Glaxo Wellcome, Merck, Novartis, Bristol-Myers Squibb, and Pfizer—seemed to be placing its own particular set of competitive bets. It remained to be seen which ones would pay off. (See **Exhibits 12** and **13** for a ranking of drug makers by global and U.S. pharmaceutical sales.)

Glaxo Wellcome PLC

*There is now a new paradigm for the pharma industry in the wake of the proposed combination of [Glaxo and SmithKline Beecham]: both companies have invested more in genomics, combinatorial chemistry, and high throughput screening [than their competitors]. These are the new technological platforms that could accelerate R&D productivity and produce a surge of new drug introductions in the next decade.*³⁴

Glaxo plc and Wellcome plc announced their merger in March 1995, and were effectively managed on a merged basis from July 1, 1995. By December 31, 1996, the merged company, Glaxo Wellcome plc, was the third largest company by market capitalization on the London Stock Exchange (valued at 33.6 billion British pounds) and the world’s largest pharmaceutical research firm with 54,000 employees. Glaxo booked revenues in 1997 of eight billion British pounds, with sales growth for the year of 5%, and earnings growth of 3% (at constant exchange rates). Sir Richard Sykes, Glaxo’s Chairman, summarized the company’s performance during 1997 as follows:

1997 has been a milestone year for Glaxo Wellcome. We have delivered on our promise by producing a creditable trading performance, achieving significant progress with filing, approval and launches of new medicines, and successfully implementing our strategy of regionalisation. At the same time, we have taken major

³¹ A.T. Kearney, *op. cit.*, p. 7.

³² Geoffrey Carr, *op. cit.*

³³ Excludes Johnson & Johnson.

³⁴ “Drug Industry Consolidation,” Salomon Smith Barney, February 3, 1998.

steps towards maintaining our leadership position at the cutting edge of medical science well into the next century. All this was achieved in a year in which we managed the expiry of the patent on the biggest selling pharmaceutical of all time in our largest market, the United States. In fact, we are taking that event in our stride. Sales by our American company actually increased in the year and, excluding Zantac, increased by 18%, a remarkable achievement.³⁵

The company expected to achieve sales growth “in the low single digits in 1998, despite the impact of generic competition.” In 1999, growth was expected to be in “double digits.”

Glaxo Wellcome described itself as an “integrated, research-based group of companies whose primary corporate purpose is to discover, develop, manufacture and market throughout the world safe, effective, high-quality medicines.”³⁶ To that end, in 1996 the company spent roughly \$1.8 billion on R&D, or 14% of sales. The company was particularly well known as a leader in HIV and gastrointestinal research and development, but its expertise in the respiratory diseases market had also been growing. Other significant areas of research included antiviral (e.g., herpes, hepatitis, as well as AIDS/HIV), anti-infective, central nervous system, cardiovascular, oncology, anesthesia, and metabolic (e.g., diabetes) diseases. According to an analyst report:

Glaxo was a late starter in the genetic research race, exploring the field through modest partnerships with biotech companies and academic groups. But the company made up for lost time [in 1997,] when it recruited star U.S. genetic researcher Allen Roses.

These days, the company is a true believer. Human genetics ‘will be the driving force not just in the pharmaceutical industry—but in the way medicine is practiced,’ Glaxo Research Director James Niedel predicted late [in 1997]. ‘When you understand that there are genetic predispositions to disease—and that you can understand what causes that and intervene before the disease occurs—you can prevent it.’

Glaxo’s biggest bet on the new technology revolutionizing [pharmaceutical] research was its purchase of Affymax [in 1995]. Affymax [wa]s a world leader in combinatorial, or automated, chemistry which promise[d] huge output gains compared with traditional methods of brewing new molecules. That ability, now widely deployed at the company’s research centers around the world, became the linchpin of a three-year drive by Dr. Niedel to introduce economies of scale to Glaxo’s labs for the first time.³⁷

Between 1996 and 2000 Glaxo planned to launch “no less than twenty new drugs.” This rate of new product introduction would average five products per annum, nearly tenfold higher than the average achieved by the industry 10 years before, and five times Glaxo’s own performance recently of one new drug a year.

In March 1997, company officials announced aggressive goals to begin human testing of 15 new prescription medicines annually.³⁸ The company had high hopes for new drugs to treat migraine, respiratory ailment (an area in which the company was already the world leader), and AIDS—Imigran, Serevent, and Eпивir, respectively.

³⁵ Source: Glaxo Wellcome worldwide web site.

³⁶ *Ibid.*

³⁷ “Glaxo, SmithKline Clout Stirs Great Expectations,” *Wall Street Journal Europe*, February 3, 1998.

³⁸ *Med Ad News*, March, 1997.

However, in December 1997, Glaxo was forced to suspend sales of its diabetes drug Rezulin in the United Kingdom due to severe side effects caused by the drug. The move sent shock waves through the U.S. medical community and Wall Street, which sent Glaxo's share price reeling: down 18%, or more than \$25 per share, immediately following the announcement. A Glaxo spokesperson stated:

Based on the severity of events coming in, the speed that they were coming in and their increasing volume, Glaxo Wellcome's medical team decided it could no longer quantify the risk-benefit of the drug, so our only choice was to move to suspend availability. It was a medical decision based on patient safety and our inability to get a good handle on the safety profile of the drug.³⁹

While mature markets such as North America, Europe, and Japan represented roughly 89% of the company's sales, Glaxo looked towards emerging markets for future growth. (See **Exhibit 14** for worldwide pharma sales by therapeutic category; and **Exhibit 15** for pharma company regional sales.) To achieve this the company "rejected the 'one size fits all' approach of treating the emerging markets as if they are simply extensions of our established markets."⁴⁰

In September 1996 Glaxo announced a new regional organization which was intended to capitalize on the diversity of new business opportunities across the globe. This was achieved by "devolving more decision making to regional and local management" and represented a "fundamental change in the way business was conducted." A significant challenge lay in finding a new role for the corporate center so that it could most effectively support business in emerging markets. The company was also aware of the need to develop more products and services tailored to particular countries or regions with the recognition that some of these areas might "offer lower operating margins than existing products."⁴¹

The company also took steps to facilitate the business effectiveness of its operations in its various markets. Glaxo increased its interest in foreign joint ventures: the company increased its equity ownership of joint ventures in Japan and India to 100% and 51%, respectively. In order to liberate cash for additional R&D investment, Glaxo sold some of its manufacturing plants. By mid-1997 sales of two plants had already brought in 200 million pounds, and some estimated that the company could still compete using only half of its remaining 40 plants worldwide.⁴² The company was also expecting to achieve radical cost reductions after the post-merger integration was complete, amounting to 700 million pounds by the end of 1998. In early 1998 the firm was confident that it was on its way towards meeting that goal.

Challenges

One of the most significant developments in Glaxo's recent history was the July 1997 expiration of the Zantac (antiulcer drug) patent—long the company's prime moneymaker and the biggest selling prescription drug of all time. With the appearance of similar generics in the U.S. market, sales of Zantac, the best selling prescription drug in the United States in 1996, plunged 37%, to \$1.097 billion in 1997. Zantac's share of Glaxo's sales was 17% in 1997, down from 23% in 1996, and down from a high of 43% in 1994.⁴³ The company forecast that Zantac's percentage of sales

³⁹ Elyse Tanouye, "Glaxo's Move on Diabetes Drug Perplexes U.S. Doctors," *The Wall Street Journal*, 12/03/97, p. B2.

⁴⁰ Sir Richard Sykes, from *Chief Executive's Statement*, Glaxo Wellcome 1996 Annual Report.

⁴¹ *Ibid.*

⁴² *Ibid.*

⁴³ *Ibid.*

would bottom out at 10%, but expected recent introductions of new products for other ailments (which accounted for 31% of sales and up 50% by July 1997) would compensate for Zantac's loss.⁴⁴

Another of the company's flagship drugs, Zovirax (acyclovir), was also expected to face strong competition and declining sales. Glaxo planned to combat the threat with heavy investment in R&D for new products across its portfolio. Sean Lance, ascending chief executive set to replace former CEO Sir Richard Sykes, remarked on Zantac's decline: "The organization got through the psychological shock of losing Zantac at least six months before we really went public on it. We said: 'That's it. Let's finish this. The caravan moves forward.'"⁴⁵

Merck & Co., Inc.

*Simply stated, our strategy is to discover new and better medicines through breakthrough research and then to demonstrate their value to physicians, payers and patients.*⁴⁶

*Merck plans to sail majestically on, forming a few alliances to bring outside compounds into its portfolio, but relying mainly on its own scientists to repeat successes such as [that of its AIDS drug] Crixivan.*⁴⁷

"We try never to forget that medicine is for the people. It is not for the profits. The profits follow, and if we have remembered that, they have never failed to appear."⁴⁸ In early 1998 Merck was considered by many to be the premier research-based ethical pharmaceutical company in the world. In 1997 the company had been among the top 100 of the *Fortune* 500 list of companies, with 1997 sales of \$23.6 billion, \$13 billion of which were in pharmaceuticals. Merck competed in 14 categories with 120 products worldwide. The company employed roughly 49,000 employees around the world.⁴⁹

By 1997 Merck was growing at roughly 20% a year in sales and earnings, making it a "high growth" company. Nine new products had been launched in the 1994-1996 period, more major products in an 18- to 24-month timeframe than had ever been launched in Merck's history. Merck had also returned to the top 10 of America's "most admired companies," as ranked by *Fortune* magazine, after having fallen off the list for two years. Merck had appeared on the 1997 "Business Week 50" list of top-performing companies, and had been ranked fifth on *Fortune's* 1997 list of "America's Greatest Wealth Creators." Furthermore, in January 1998 Merck had been named one of the 10 "Best Companies to Work for in America" by *Fortune* magazine.

Merck's espoused strategy was to grow through internal research and development, not by merger. According to Ray Gilmartin, Merck's chairman, president and CEO:

⁴⁴ *Ibid.*

⁴⁵ Sameena Ahmad, "Glaxo's heir apparent gets ready for his biggest test," *The Independent*, July 28, 1997.

⁴⁶ Merck Chairman, President and CEO Ray V. Gilmartin in his letter to investors in the 1996 Merck & Co., Inc. Annual Report, p. 3.

⁴⁷ Geoffrey Carr, *op. cit.*

⁴⁸ George W. Merck as quoted in "Merck Sharp & Dohme, A Brief History," Merck & Co., Inc., 1992, p. 18.

⁴⁹ Source: Merck press release, January 23, 1998; Merck 1996 Annual Report.

A merger [such as that between Glaxo and SmithKline Beecham] would not fit with our strategy for growth . . . it would be a distraction. Our Management Committee believes the Company has in-house the core capabilities to be highly competitive in both marketing and R&D.⁵⁰

The company increased R&D spending to \$1.7 billion for 1997 (16% more than the previous year and up from a CAGR since 1987 of 12%).⁵¹ To boost the introduction of new products, sales and marketing initiatives had been intensified in 1996 and were expected to continue through 1997.

When asked whether Merck's research capability would be outmatched by a merged Glaxo/SmithKline, Gilmartin responded:

Merck's research remains at the cutting edge of technology. No other pharmaceutical company's internal R&D program has been as successful as MRL's—over the long-term or over recent years. Over the last few years we have increased Merck's investment in basic research. The total productivity (internal + external) of Merck R&D over recent years is remarkable, when contrasted with the record of most major pharmaceutical companies that hope to introduce one or two new medicines a year. Since January 1995, Merck has introduced 10 new products, which now account for about 60% of the Company's growth in pharmaceutical sales—more than \$2.2 billion of revenue for 1997. Merck is awaiting marketing clearances on four additional new products: *Singulair* for asthma; *Cosopt* for glaucoma; *Maxalt* for migraine attacks; and *Aggrastat* for cardiovascular disorders.

Scale is certainly not the only factor determining the success of R&D, and the crucial issue is how to increase scale in ways that enhance productivity. One approach is to aggressively exploit new technologies and the spectrum of available product candidates. Merck pursues this approach not only through internal research but also through the many licensing arrangements we have, including the recently announced ones with Biogen and Aurora.⁵²

Glaxo and Burroughs Wellcome merged in March of 1995, becoming the world's largest pharmaceutical company. But Merck has been growing faster than Glaxo Wellcome—during 1997, Merck's sales and net income growth rates were about three times Glaxo's—and by the end of 1997 Merck had overtaken that merged company in terms of prescription drug revenues and market share to once again become the world's No. 1 pharmaceutical company...Some companies merge to acquire a pipeline to offset loss of revenue due to expirations of major product patents. On the other hand, Merck believes our new and pipeline products can generate enough growth to overcome our patent expirations in the critical period of 2000 and 2002.⁵³

Merck's second strategic goal was to demonstrate the value of its medicines to health care payers and patients. Medco Containment Services, the pharmaceutical benefits manager Merck had acquired in 1993, was central to this strategy. Medco was the company's first major acquisition since

⁵⁰ Source: *The Daily*, Merck & Co., Inc., February 4, 1998.

⁵¹ Merck annual reports, various years.

⁵² Early joint ventures included a 1980 partnership with Astra AB, which became a formal 50/50 joint venture in 1994 (developing and marketing Astra products), a 1989 venture with Johnson & Johnson (for OTC gastrointestinal products such as Pepcid AC and Mylanta), and a 1991 venture with DuPont (for cardiovascular, radiopharmaceutical, and central nervous system disorders).

⁵³ *Ibid.*

it had acquired drug maker Sharpe & Dohme in 1953. The Medco acquisition was an attempt by Merck to shape and influence the managed care environment for pharmaceuticals. Through Medco Merck was launching new services to help its customers improve the quality of patient care and manage costs, including new disease management programs.

In 1997 Merck's global market share in pharmaceuticals was estimated at 5.2%,⁵⁴ up from 4% in 1996. In 1996 54% of Merck's revenue was derived from sales in North and South America. Europe was the second largest market at 35%, followed by Asia Pacific at 11%.⁵⁵ Merck was growing in Western Europe, the world's largest pharmaceutical market, at more than double the rate of the overall marketplace. Demand for Merck products in other parts of the world were also increasing rapidly in 1996. While human health sales growth in Japan had more than doubled to between 8-9%, sales growth for the "intercontinental region" (the rest of the world excluding Western Europe and the United States) had topped 30% in 1996. Merck was also working to expand its presence in emerging markets, particularly Korea and Taiwan.

International joint ventures had been successful in many areas. JVs with Pasteur Mérieux Connaught in Europe and other companies in Japan, Australia and New Zealand focused on vaccine sales. In 1997 the company planned to enter into a joint venture with Rhône-Poulenc for the establishment of Merial, the world's largest R&D concern, for the animal health and poultry genetics industries. The two companies had previously been second (Merck) and fourth (Rhône-Poulenc) in the business and together the companies' market share in the animal health products market was almost 13%. Other foreign ventures in 1996 included the reestablishment of a subsidiary in South Africa, the rapid introduction of the HIV drug *Crixivan* to Latin America.

Challenges

In 1997 Merck had experienced a major setback for one of its blockbuster drugs, the cholesterol reducer Zocor, which had come under attack from Lipitor, a Warner-Lambert drug marketed by Pfizer. Wall Street was watching to see whether Merck could adequately defend its flagship drugs in the market, and whether the company could generate a sufficient number of new blockbuster drugs to meet its aggressive growth goals.

Novartis AG

*Our vision for the merger was to create the worldwide leader in life sciences, focused on innovation in healthcare, agribusiness and nutrition, [as well as] create a fast, focused, flexible company with a passion for competitiveness and implementation.*⁵⁶

On March 7, 1996 the chairmen of the boards of Ciba-Geigy and Sandoz announced their decision to merge the two companies. By December, Novartis (*new skills* in Latin) had cleared all regulatory approvals and became officially the world's second largest pharmaceutical company at the time. It ranked No. 11 in *Business Week's* ranking of the world's most valuable companies, second only to Merck & Co. in pharmaceuticals, and represented 20% of the Swiss stock market and over 10% of the market capitalization of the top 20 pharmaceutical companies worldwide. In 1996

⁵⁴ This share assumed a global industry market size of \$260 billion. Source: "GLX: Merger between GLX and SBH would create broad coverage," Schroder & Co. Inc., February 3, 1998.

⁵⁵ Excludes Medco sales.

⁵⁶ Srikant Datar and Carin-Isabel Knoop, "Novartis (A): Being a Global Leader," Harvard Business School case No. 198-041.

Novartis held 4.4% of the drug market and led the pack in research and development spending, with a budget of over \$2.9 billion. The company, headquartered in Basel, Switzerland, was represented by 87,000 employees in 100 countries and claimed operations in 142 countries worldwide through 275 affiliates.

Novartis was not a pure pharma play even though it was more focused on pharma than the combination of its predecessors.⁵⁷ In the first half of 1997, healthcare accounted for 59% of sales, nutrition for 10% and agribusiness 28%. Novartis was the largest health food producer in Europe and number two worldwide. In spring 1997, Novartis bought Merck's crop protection business for \$910 million. This was its biggest deal since the company's formation. The acquisition gave Novartis a significant U.S. presence in insecticides, fungicides, and herbicides to complement its existing strength in Europe, Asia, and Latin America.

In pharmaceuticals, Novartis held global leadership in several therapeutic areas, including immunology, inflammatory disease, central nervous system disorders, cardiovascular, endocrine and metabolic diseases, oncology, dermatology, and asthma. The company's top 10 products were anticipated to continue to grow strongly, partly because the company's seven key therapeutic areas were each delivering above industry growth. In 1997 six-month pretax profit surged 29%, to 4.1 billion francs from a pro forma 3.18 billion francs a year earlier. In 1997, sales increased 19% (in Swiss Francs) over 1996, and an average of 9% in local currencies. Some Novartis products had experienced very fast growth, including Lescol (cholesterol-lowering agent, +71%), Lamisil (fungal nail and skin infections, +68%), Miacalcic (osteoporosis, +26%), Cibacen/Lotensin (hypertension, +20%), Aredia (cancer, +64%), and Foradil (asthma, +77%).

To the year 2000, Novartis planned to launch nearly a dozen new drugs—including a potential blockbuster against Alzheimer's disease and a gene therapy against cancer—the first concrete result from multibillion-dollar gambles on advanced technologies. That, analysts said, should fuel annual revenue gains approaching 10%, comfortably above the 6%-7% growth projected for the drug industry overall. Novartis was also investing in its sales and marketing forces. Since the merger, Novartis nearly doubled its U.S. sales force, to 2,300 people—on a par with major American rivals Merck & Co. and Pfizer Inc.

In addition to having the drug industry's fattest research budget, Novartis also boasted the broadest web of alliances with fledgling biotechnology companies and big-name research institutes. "Going forward, we will do more alliances than acquisitions," Vasella told the press. "It's easier, faster, and much more flexible to do alliances."⁵⁸

However, Novartis President and Executive Committee head Daniel Vasella was unlike other pharmaceutical company executives when it came to banking on biotechnology for supporting his industry's drug development efforts. While research and development chiefs at Basel-based Roche Holding, Ltd. and London-based SmithKline Beecham plc had declared biotechnology, and genomics in particular, the drug discovery sciences of the future (accounting for most, if not all, products in their pipelines by the twenty-first century) Vasella believed that there was "still a place for traditional chemistry and combinatorial chemistry. I don't believe all drug inventions will come from biotech."⁵⁹ When asked how much of Novartis' drug development pipeline would be filled by products derived from biotechnology and genomics research, Vasella explained that he had "never looked at it. . . . If

⁵⁷ CIBA Specialty Chemicals, MBT and Gerber Childrenswear were divested in the merging process.

⁵⁸ Craig Charles, *op. cit.*

⁵⁹ Craig Charles, "Novartis chief isn't relying totally on biotech for drug development," *Bioworld Today*, February 7, 1997.

you have an investment in a special technology and you've made up your mind it's crucial . . . and I believe biotechnology is . . . it isn't necessary to make a quantitative judgment. It's academic."⁶⁰

In June 1997 Novartis announced a new regional management organization for the pharma sector. The United States, Japan, Europe, the Americas and the Asia/Pacific region would, together with the global marketing function, report directly to the head of Novartis' worldwide pharmaceuticals business, thereby eliminating two layers of management. The regions would participate in the Pharmaceuticals International Board, which provided overall sector leadership for the group's market activities. The regions would also include human resources and information technology functions.

More importantly, Novartis had concentrated on articulating and rolling out most of the elements of the so-called "high-performance company." Novartis defined its core values as "empowerment, simplicity, candor, and communication."

Challenges

Most analysts and the capital markets seemed to agree that Sandoz and Ciba had demonstrated that there was "real value in striking from a position of strength rather than one of need."⁶¹ By August 1997, 99% of pharmaceutical sales and marketing operations were fully integrated worldwide. However, the company's operating margins ran about 20% vs. 40% for Merck and 35% for Glaxo Wellcome. "Merck and Glaxo do it best," an analyst said. "Novartis is not even close."⁶²

Novartis sales were even down in some markets in which Ciba and Sandoz had been independently successful. "You clearly saw that the integration took a toll," Vasella told analysts in late August 1997. However, he believed that in a merger situation, "you have to push people so hard they don't have time to get into battles. . . . If you succeed at coping with a merger, it builds a lot of strength in an organization."⁶³ As an analyst summarized: "[Novartis was] off to a racing start . . . [but that] no one should underestimate the challenge of delivering the integration savings while at the same time keeping the ship moving along at high speed."⁶⁴ Analysts expected EBIT to increase 20% in 1997 and 18% in 1998.

Bristol-Myers Squibb

*Our goal is to achieve unit growth fueled internally by new products, geographic expansion and marketing innovation, and externally through acquisition, joint venture and licensing agreements; [and] to be recognized as the best in research and development across businesses and as the leader in scientific innovation and product performance.*⁶⁵

⁶⁰ *Ibid.*

⁶¹ "Pharma Strategies: M&A or technical excellence?" *Marketletter*, March 3, 1997.

⁶² An analyst quoted in Gail Edmondson, "At Novartis, a cure for culture clash?" *Business Week*, July 7, 1997, p. 50.

⁶³ Daniel Vasella quoted in Gail Edmondson, *op. cit.*, p. 50.

⁶⁴ Peter Laing, a London-based pharmaceutical analyst with Societe Generale Equities, quoted by Stephen D. Moore, "Novartis Considers How to Make a Giant Even Bigger," *Wall Street Journal*, August 29, 1997, B3.

⁶⁵ BMS worldwide web site.

BMS had been called the pharmaceutical industry's "quiet giant." Headquartered in New York City, Bristol-Myers Squibb Company (BMS) traced its roots to 1887. Its predecessor merged with the Squibb Corporation in 1989. BMS described itself as a diversified health and personal care company that was "a world leader in many of the categories in which it compete[d]."⁶⁶ The company was dedicated to "preeminence and market leadership" in its three core business groups: Worldwide Medicines, Nutritionals & Medical Devices and Worldwide Beauty Care. In 1996, 58% of its revenues came from pharmaceuticals, 18% from consumer products, and 12% each from medical devices and nutritionals.⁶⁷

The BMS Worldwide Pharmaceuticals group was a "leading maker" of innovative therapies for cardiovascular, metabolic and infectious diseases, central nervous systems and dermatologic disorders, and cancer. The company's 1997 global pharmaceutical market share was estimated at 3.8%.⁶⁸ It marketed products in nearly every country in the world and had operations in more than 50 countries. Worldwide Consumer Medicines was a collection of self-medication businesses focused on pain management and with important franchises in skin care, cough/cold remedies, vitamins and women's health care.

BMS employed 51,200 employees: 4,000 of whom worked at the BMS Pharmaceutical Research Institute, which was committed to using its \$1 billion budget to "translate frontier scientific knowledge into new, commercially viable pharmaceutical therapies."⁶⁹ In 1997 it had over 40 compounds in active development, eight major sites in the United States and Europe as well as links to smaller sites worldwide.

In 1994 BMS set out to double sales, earnings and earnings per share by the end of the year 2000. Many thought it was impossible for a company growing at 5% or less and facing the patent expiration of key products. Nevertheless, in 1997, Charles A. Heimbold, Jr., chairman and CEO, recommitted BMS to match industry growth rates in the short term and be at the top of the industry league in the long term.

In that year, the campaign "Making Growth Happen" seemed to be paying off. Annual sales increased 11% (14% excluding the effect of foreign exchange) to \$16.7 billion with pretax earnings up 12% and earnings per share up 13%. In pharmaceuticals, worldwide sales of Pravachol, the company's largest selling drug, increased 34% to \$1,437 million. The company's leaders believed that its direct-to-consumer advertising (including a 1-800-PREVENT information line) had significantly helped the drug's performance. The company's leading anticancer drug increased 16% to \$941 million. Sales of glucophage, the leading oral medication of the treatment of noninsulin-dependent diabetes, grew 74% to \$579 million. There, too, the company tried to reach the consumer directly by sponsoring public awareness programs. BMS also added 1,500 sales representatives in 1996-1997 and increased its marketing spending by more than \$300 million. Finally, in 1997, BMS managed over 30 collaborative and pharmaceutical licensing agreements concluded in the past few years.⁷⁰

Challenges

"When you look at the success of Pravachol, the take home message is that blockbuster drugs aren't always born—they're sometimes made," said Sol I. Rajfer, M.D., senior vice president,

⁶⁶ *Ibid.*

⁶⁷ *Ibid.*

⁶⁸ Schroder & Co. Inc., *op. cit.*

⁶⁹ *Ibid.*

⁷⁰ *Ibid.*

Worldwide Clinical Research and Development, BMS Pharmaceutical Research Institute.⁷¹ BMS managers believed that Pravachol had attained its superstar status through a “painstaking and carefully planned scientific campaign . . . and was just one of many examples of how the company [had] achieved sustained growth by maximizing the impact of key products and franchises in all of its businesses. . . . [All this] adds up to a company that knows how to manage growth, whether through innovation, development or performance in the market.”⁷²

Pfizer, Inc.

*Pfizer is forging alliances left, right and center, and is actively soliciting academics with bright ideas that would make good drugs.*⁷³

Pfizer’s goal was to become “the world’s premier research-based health care company.” To fulfill that mission, the company stated: “we abide by the enduring values that are the foundation of our business: Integrity, Innovation, Respect for People, Customer Focus, Teamwork, Leadership, Performance, and Community.”⁷⁴ In 1997 Pfizer was voted one of America’s “10 Most Admired Companies” and first in innovation by *Fortune* magazine.

Pfizer’s established products included cardiovascular Procardia XL, anti-inflammatory Feldene, and antifungal Diflucan. In addition, two major calcium channel blockers, the older Procardia XL and the more recent Norvasc accounted for roughly \$2.8 billion in sales in 1996. Pfizer launched six products in the United States between 1990 and 1996, among them Norvasc, antibiotic Zithromax (azithromycin), antidepressant Zoloft (sertraline), and antihistamine Zyrtec (cetirizine). In January 1997 the company launched Lipitor, a cholesterol-reducing drug developed by Warner-Lambert, and Aricept, Pfizer’s drug for Alzheimer’s disease. The company’s 1997 global pharmaceutical market share was estimated at 3.6%.⁷⁵

The company planned seven new product launches before 1999: the worldwide launch of Lipitor and Aircept, and the anticipated launches of a next-generation antibiotic, an antiarrhythmic, an antipsychotic, and treatments for male sexual dysfunction and migraine. The company also planned to develop further indications for existing products, and to pursue more than 100 discovery projects in more than 17 therapeutic areas while supporting more than 150 research partnerships.

Pfizer also offered disease management information packages to its managed care customers through its sales force. In late 1996 Pfizer launched the Pfizer Health Solutions Business to develop disease management packages as stand-alone products. According to company statements:

Henry A. McKinnell, Jr., president of Pfizer Pharmaceuticals Group, described the situation facing Pfizer in the early 1990s:

People really didn’t understand what we were doing. There were a lot of things we did—from financial reengineering, to increasing spending in research, to restructuring the culture of the company—that made us countercultural at the time. We were criticized for not having bought a pharmaceutical benefits manager, for not

⁷¹ For more details, see “Making Growth Happen,” special report, BMS worldwide web site.

⁷² *Ibid.*

⁷³ Geoffrey Carr, *op. cit.*

⁷⁴ Pfizer worldwide web site.

⁷⁵ Schroder & Co. Inc., *op. cit.*

having merged, for not having done all the “popular” things. But we were convinced that those weren’t right for us, given our capabilities and opportunities.

Today our strategy is well defined. With a focus on health care, we are committed to a strategy of innovation and internal growth together with productivity improvement as opposed to a strategy based on growth through merger and acquisition.⁷⁶

McKinnell described Pfizer’s approach to the consumer:

Our consumer strategy is linked to our pharmaceutical R&D strategy. To switch a prescription product to a consumer product, we need the appropriate product at the appropriate time and an OTC capability. We have that capability in the United States, Japan, Canada, and the United Kingdom. Recent acquisitions in Spain and Italy have added that capability in parts of Europe, and we have it in most of Asia. I want Pfizer to have the ability to take any prescription product appropriate for consumer use and direct it at the consumer ourselves, rather than have to rely on the marketing distribution capabilities of somebody else. Maximizing the opportunities that new pharmaceutical products provide can take many forms. Opportunities include continuing growth of the product once it is in the marketplace, growth through new indications and new dosage forms, and broad consumer usage once the product goes OTC.⁷⁷

Although Pfizer was not pursuing mergers and acquisitions, the company had developed more than 150 strategic relationships. In 1997 it had more than 20 alliances with research companies and other pharmaceutical companies. These relationships ranged from codevelopment and comarketing to joint ventures and research aimed at drug discovery. For instance, the firm had comarketing arrangements with Warner-Lambert for the cholesterol reducer Lipitor, and with Japanese pharmaceutical maker Eisai for Aricept. Pfizer had also launched a new venture, Anaderm, in conjunction with cancer researcher Oncogene Science and skin specialist New York University, to develop a new line of “cosmeceutical” products. Cosmeceuticals were treatments for skin problems such as baldness, wrinkles, and pigmentation disorders. Pfizer believed that through Anaderm it could do a better job of drug discovery and development than it could do alone, and it hoped the venture would lead to both new prescription and nonprescription products.

Although it conducted most of its own development and production scale-up, Pfizer also believed in outsourcing a portion of its drug production. In 1996 Pfizer purchased a 15% equity stake in Catalytica, a California-based fine chemical manufacturer, in order to strengthen its drug and process development capabilities, and to assist in commercial production. According to Pfizer’s manager of pharmaceutical research and development: “Having such a full [drug] pipeline. . . . Sometimes it is easier to outsource. . . . It allows us to conserve and focus our internal resources . . . and enables us to attack projects in parallel.”⁷⁸ The company expected its number of outside production partners to grow over time.

⁷⁶ Source: Wayne Koberstein, “A singular path to global power: Dr. Henry McKinnell of Pfizer,” *Pharmaceutical Executive*, 17(7):40-54, July 1997.

⁷⁷ *Ibid.*

⁷⁸ “Pfizer Outsources Production to Maximize Its Own Resources,” *Chemical Market Reporter*, February 3, 1997, p. 24.

Challenges

McKinnell summarized the major differences he saw between Pfizer and the other pharma giants as follows:

When I hear some of our competitors speak, they talk about the science. When you hear Pfizer people speak—from sales, marketing, or research—we talk about products derived from good science. That makes us more opportunistic than most others. Others may consider themselves primarily researchers, but we are more hunters than gatherers. We look for opportunity and aggressively pursue it. If the opportunity does not produce a lead candidate, we go on to something else. Unlike other companies, we have no therapeutic area restrictions.

We do development as well as anybody. We know how to run clinical trials, we know how to take time out of the process, and we know how to jointly develop research-based products with commercial appeal . . . [and] we hit the ground with a product fully developed, with most if not all of the comparative data we need.

Probably the biggest challenge we face now is to balance growth and investment. We are getting tremendous growth in sales and profit. For the first time in my experience, we have more opportunities than we can accommodate. . . . The simple fact is: We can't do all of them at once. So we have had to spend a great deal of time balancing technical risk against commercial opportunity and place the best bets.⁷⁹

⁷⁹ Wayne Koberstein, *op. cit.*

Exhibit 1 Market Shares of the Top 20 Pharmaceutical Companies, Worldwide^a

Company	1994	1995	1996
Novartis AG	4.5	4.4	4.4
Glaxo Wellcome	4.6	4.4	4.4
Merck	3.4	3.5	4.0
Hoechst Marion Roussel	3.8	3.5	3.3
Bristol-Myers Squibb	3.2	3.1	3.2
Johnson & Johnson	2.7	2.8	3.1
American Home Products	3.1	3.0	3.1
Pfizer Inc.	2.7	2.8	3.1
SmithKline Beecham	2.6	2.5	2.7
Roche Holdings	2.7	2.6	2.7
Bayer AG	2.2	2.2	2.1
Astra	1.7	1.9	2.1
Eli Lilly	2.1	2.0	2.1
Rhone-Poulenc Rorer	2.1	2.1	2.1
Abbot Laboratories	1.7	1.8	2.0
Schering-Plough	1.8	1.8	2.0
Pharmacia & Upjohn	2.0	1.8	1.8
Boehringer Ingelheim	1.4	1.5	1.5
Takeda	1.5	1.5	1.5
Warner-Lambert	<u>1.3</u>	<u>1.3</u>	<u>1.4</u>
Total	51.1	50.5	52.6

Source: IMS Pharmaceutical World Review.

^aBased on information from 57 countries; some nonretail sales excluded.

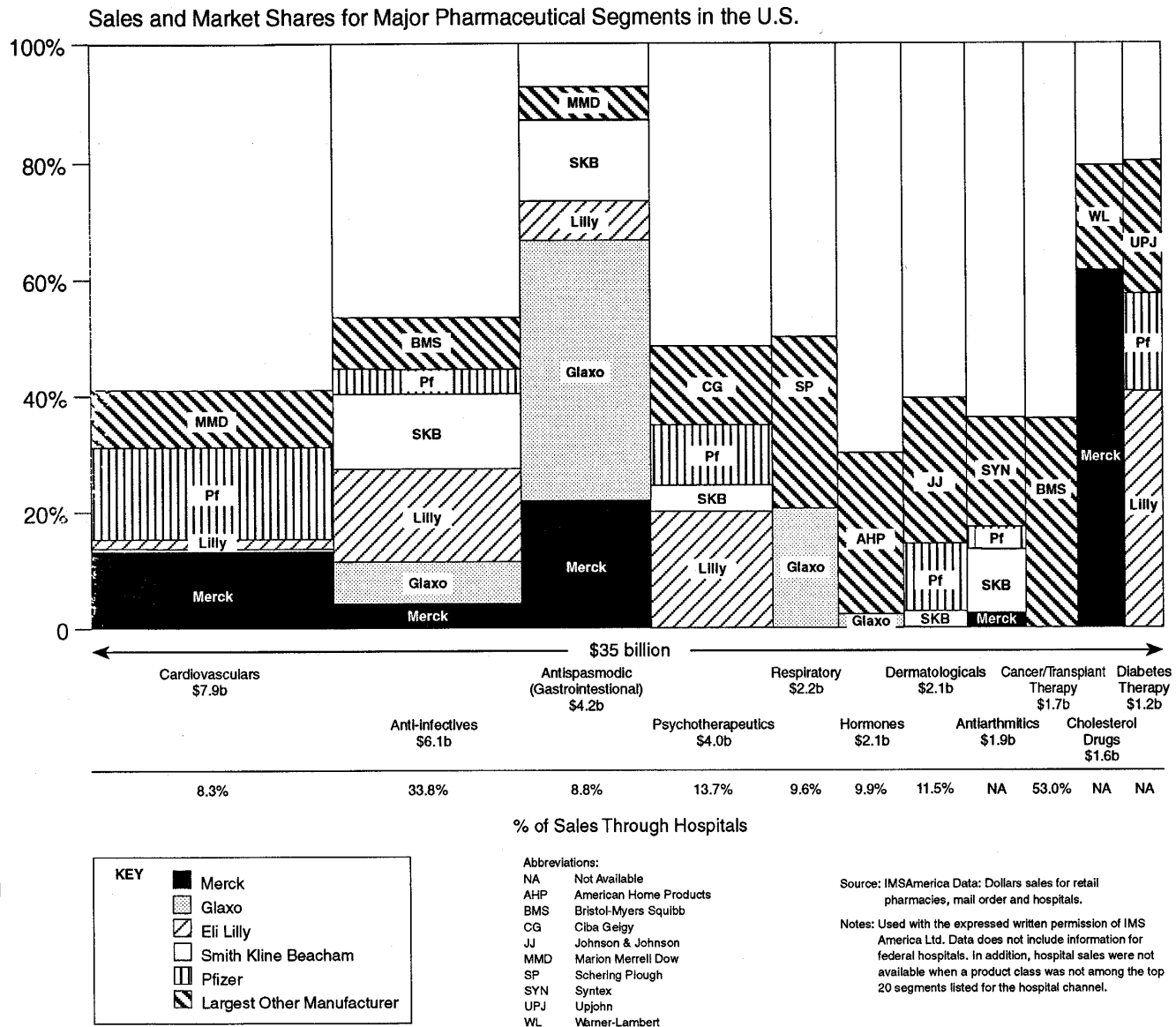


Exhibit 3 Pharmaceutical Stock Price Indexes, 1991-1998

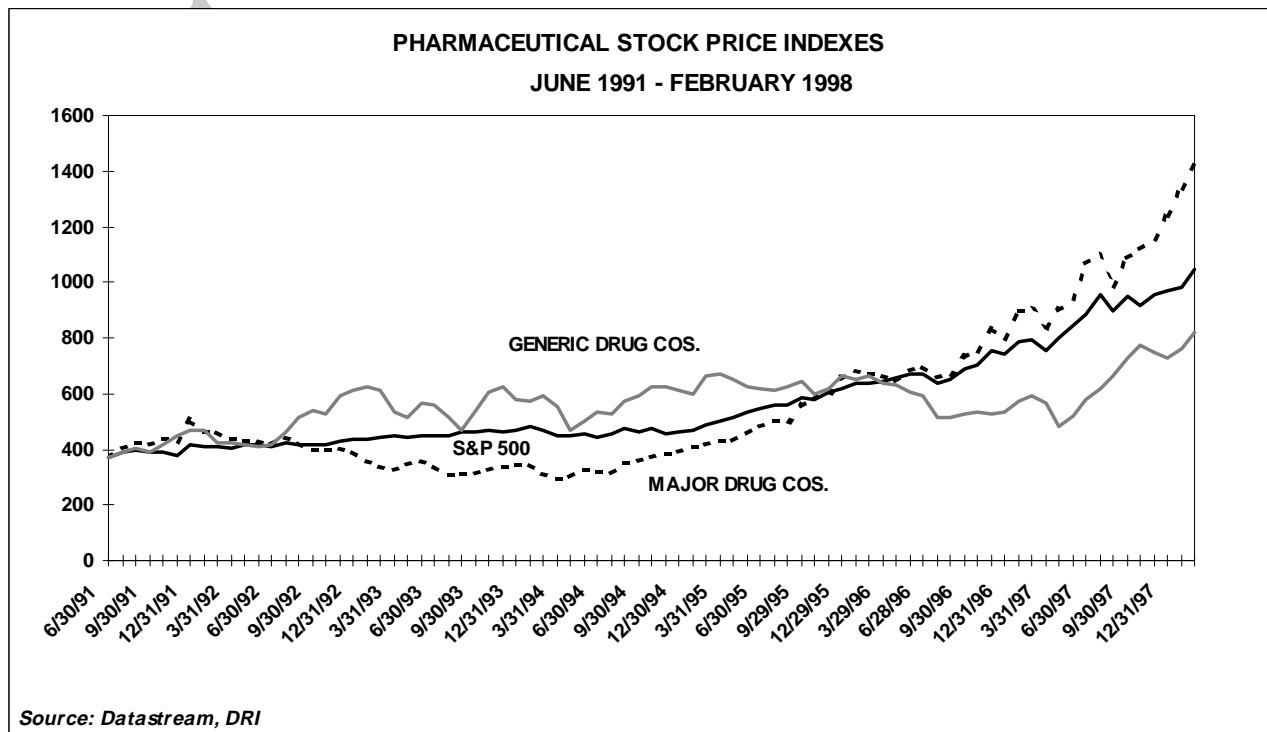


Exhibit 4 R&D and Capital Expenditures for Major Pharmaceutical Companies, 1996 (\$ millions)

Company Name	R&D Expense	Capital Expenditure
Novartis AG	2,961	2,453
Hoechst AG	2,580	4,021
Johnson & Johnson	1,905	1,373
Roche Holdings, Ltd.	1,827	1,213
Glaxo Wellcome PLC	1,811	626
Pfizer Inc.	1,684	774
Merck & Co., Inc.	1,487	1,197
American Home Products Corp.	1,429	652
Bristol-Myers Squibb	1,276	601
SmithKline Beecham PLC	1,172	903

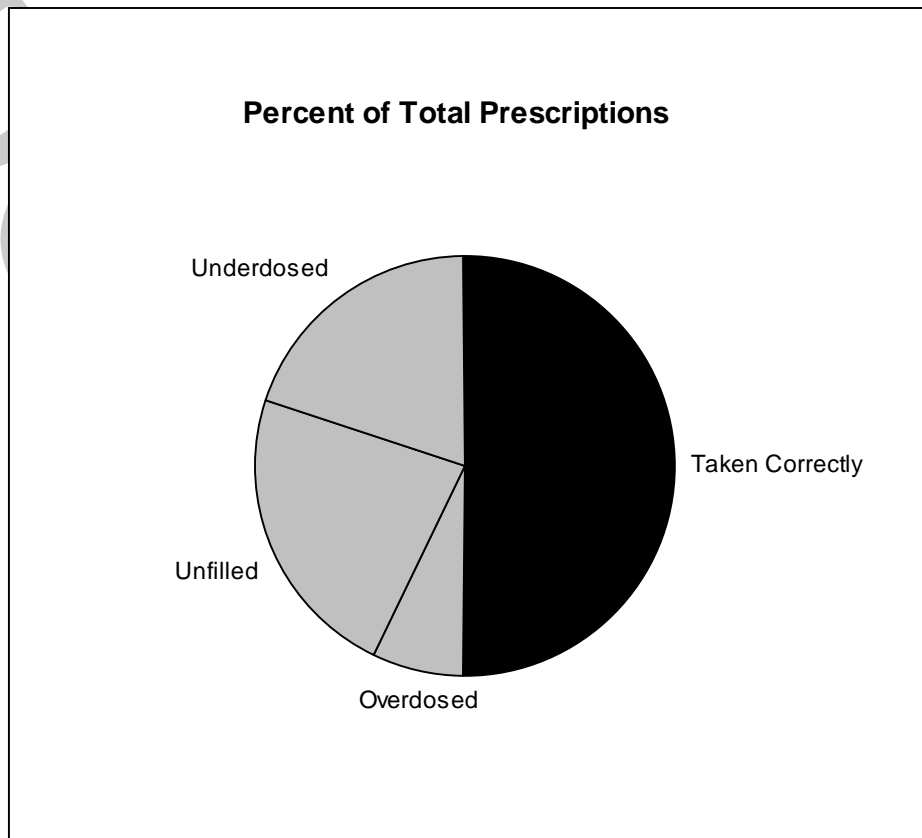
Source: Standard & Poor's, Compustat & Global Vantage, Bloomberg.

Exhibit 5 Mergers and Acquisitions in the Pharmaceutical Industry over \$500 million, 1985-1998

Date Effective	Target Name	Acquiror Name	Value of Transaction (\$ millions)
03/05/98	Corange Ltd	Roche Holding AG	10,200.0
02/11/97	Roussel-Uclaf SA (Hoechst AG)	Hoechst AG	3,393.7
12/17/96	Ciba-Geigy AG	Sandoz AG	30,090.2
07/01/96	Athena Neurosciences Inc.	Elan Corp. PLC	601.3
12/29/95	Fisons PLC	Rhone-Poulenc Rorer Inc.	2,888.4
11/02/95	Pharmacia AB	Upjohn Co.	6,989.1
07/18/95	Marion Merrell Dow Inc.	Hoechst AG	7,264.6
07/17/95	Circa Pharmaceuticals Inc.	Watson Pharmaceuticals Inc.	621.1
05/01/95	Wellcome PLC	Glaxo Holdings PLC	14,284.8
03/31/95	Boots Co. PLC-Pharmaceutical Op	BASF AG	1,583.6
03/01/95	Affymax NV	Glaxo Venture Limited (Glaxo)	592.7
01/05/95	Ciba-Corning Diag, Biocine	Chiron Corp.	616.5
12/30/94	Zenith Laboratories Inc.	IVAX Corp.	612.5
12/21/94	American Cyanamid Co.	American Home Products Corp.	9,560.9
11/03/94	Syntex Corp.	Roche Holding AG	5,307.2
11/02/94	Sterling Winthrop Inc.	SmithKline Beecham PLC	2,925.0
11/11/93	Copley Pharmaceutical Inc.	Hoechst Celanese Corp.(Hoechst)	546.0
06/03/93	Immunex Corp.	American Cyanamid Co.	736.3
05/06/93	Erbamont Inc., Farmitalia Carlo	Kabi Pharmacia AB (ProCordia)	1,126.2
01/16/92	Genetics Institute Inc.	American Home Products Corp.	667.0
08/30/91	Nicholas (Nicholas Kiwi AU)	Roche Holding AG	820.9
06/30/91	Sanofi-N Amer Ops, Latin America	Sterling Drug-N Amer Operation	2,400.0
01/03/91	El du Pont de Nemours-Pharm	Merck & Co.-European Prescript	1,250.0
07/31/90	Rorer Group Inc.	Rhone-Poulenc SA (France)	3,476.0
12/15/89	AH Robins Co., Inc.	American Home Products Corp.	3,194.0
12/02/89	Marion Laboratories Inc.	Dow Chemical Co.	6,209.0
11/18/89	Lyphomed Inc.	Fujisawa Pharmaceutical Co. Ltd	737.0
10/04/89	Squibb Corp.	Bristol-Myers Co.	12,094.0
07/26/89	SmithKline Beckman Corp.	Beecham Group PLC	7,922.0
02/29/88	Sterling Drug	Eastman Kodak Co., Inc.	5,100.0
09/30/87	Barnes-Hind, Coburn Optical Ind	Pilkington PLC	574.0
09/03/86	Baxter Travenol-Flint Prescrip	Boots Co. PLC	600.0
06/26/86	Key Pharmaceuticals Inc.	Schering-Plough Corp.	613.0
03/11/86	Mallinckrodt (Avon Products)	International Minerals & Chem	675.0
01/08/86	USV Pharmaceutical, Armour	Rorer Group Inc.	690.0
11/22/85	Richardson-Vicks Inc.	Procter & Gamble Co.	1,674.0
10/01/85	GD Searle & Co.	Monsanto Co.	2,700.0

Source: Securities Data Company, Inc.

Exhibit 6 Percentage Prescription Compliance in Chronic Care Setting



Source: The Wilkerson Group, 1995.

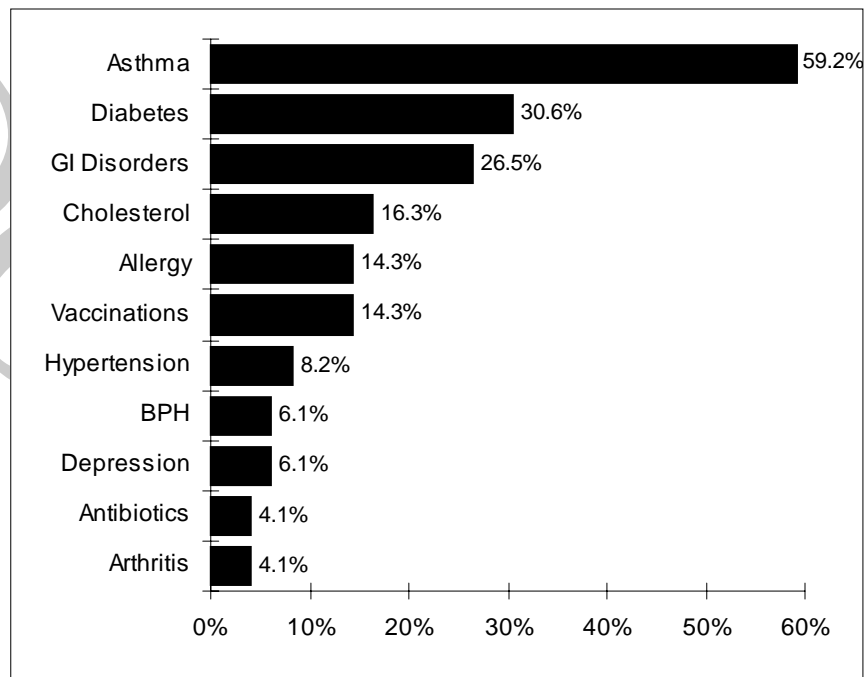
Exhibit 7 Percentage of Compliance with Various Medications

Treatment	Measure	Definition	Compliance Rate (%)
Penicillin prophylaxis for rheumatic fever	Urine assay	Medication in urine	33%
Anxiolytic in neurotics	Pill counts	Counts within 25% of prescribed amounts	54%
Antipsychotics in schizophrenics	Interview	Taking medications correctly	42%
Tuberculosis medications	Interview and urine testing	Taking medications throughout follow-up	55%
Tuberculosis medications	Record review	Continuing therapy	63%
Various medications used by elderly	Interview	Taking medications correctly	41%
Various medications for diabetes or congestive heart failure	Interview	Taking medications correctly	42%
Various medications used by patients in homes for the aged	Interview	Taking medications correctly	69%
Antihypertensives	Record reviews (same subjects)	Remaining in care and on therapy	1-year, 95% 2-year, 65% 3-year, 34%
Antihypertensives	Pill counts (same subjects)	Taking greater than 80% of medication	6-month, 53% 12-month, 53%

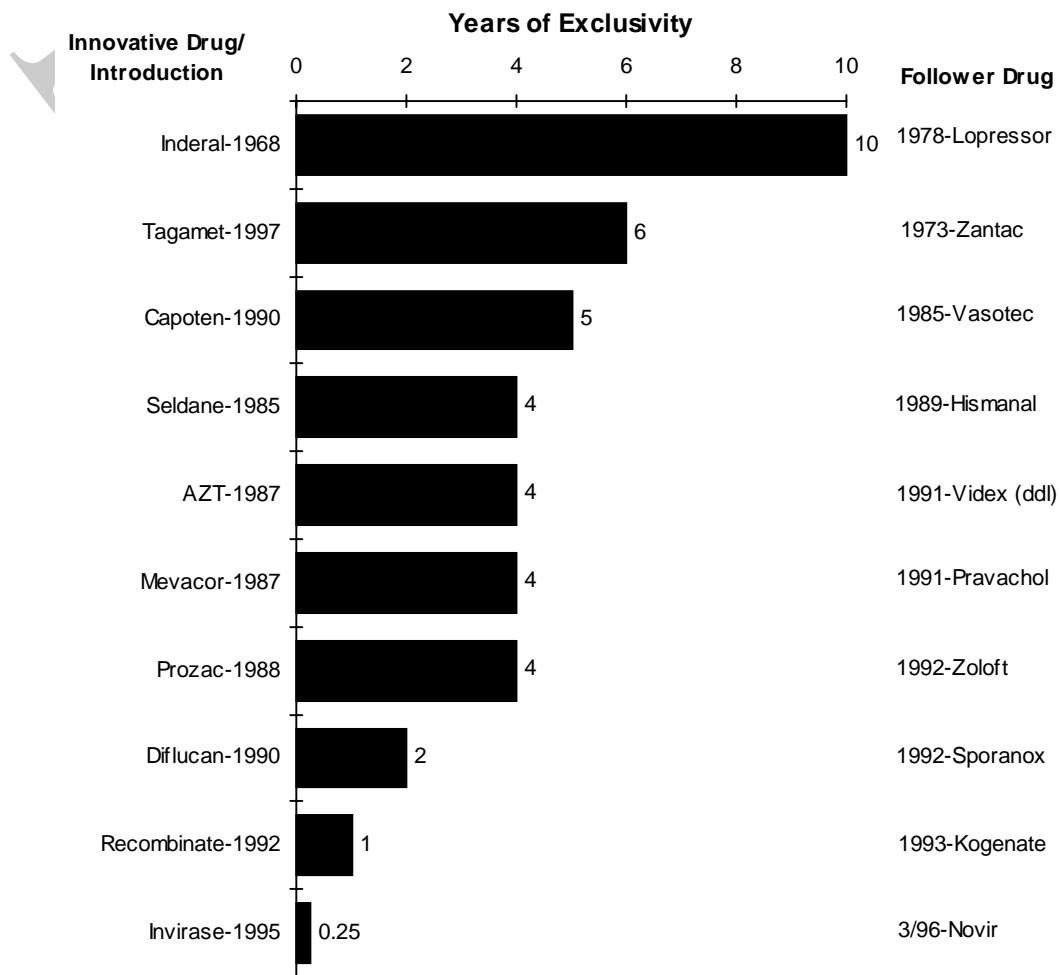
Source: L.S. Morris and R.M. Schulz, "Patient compliance—An overview," *Journal of Clinical Pharmacy and Therapeutics*, 17:283–295, as cited in *Drug Topics*, January 9, 1995.

Notes: This table represents articles that provided demographic descriptions of the subjects and employed statistically rigorous sampling techniques. Examples include the use of random population samples, three or more hospitals/clinics.

Exhibit 8 Types of DSM Programs Among HMOs



Source: CibaGeneva Pharmacy Benefits Reports, Trends and Forecasts Surveys, 1996.

Exhibit 9 Trend in Exclusivity Periods for Patented Pharmaceuticals


Source: The Wilkerson Group, 1995.

Exhibit 10 Top Seven Biotechnology Companies Ranked by 1997 Global Sales

Rank	Company	1997 Global Sales (billions)
1	Amgen	\$2.303
2	Chiron	1.313
3	Genentech	.967
4	Genzyme	.536
5	Alza	.466
6	Biogen	.277
7	Immunex	.153
Total Worldwide Sales		\$6.015

Source: Geoffrey Carr, "The Alchemists," *The Economist*, February 21, 1997.

Exhibit 11 Market Value Added and Economic Value Added of Selected Major Pharmaceutical Firms, 1996

Company	MVA ^a 1996 (\$ millions)	MVA Rank ^b	EVA ^c 1996 (\$ millions)
Merck	\$78,246	5	\$1,688
Johnson & Johnson	51,119	9	1,327
Bristol-Myers Squibb	42,910	10	1,515
Pfizer Inc.	42,391	11	1,139
Abbot Laboratories	32,077	15	1,187
Eli Lilly	31,057	18	181
American Home Products	28,219	21	797
Schering-Plough	20,031	32	790
Warner-Lambert	15,089	42	232
Pharmacia & Upjohn	10,665	58	2
Rhone-Poulenc Rorer	5,759	108	(168)

Source: *Fortune*, November 10, 1997.

^aMVA (Market Value Added) is simply the difference between the market value and the book value of the debt and equity raised by the company.

^bRank out of 1,000 firms surveyed by *Fortune* magazine.

^cEVA is aftertax net operating profit minus the cost of capital.

Exhibit 12 Pharma Giants Ranked by Global Pharmaceutical Sales

Rank	Company	1997 Global Sales ^a (billions)
1	Glaxo Wellcome	\$11.6
2	Merck & Co.	11.4
3	Novartis	11.0
4	Bristol-Myers Squibb	9.3
5	Johnson & Johnson	8.7
6	Pfizer	8.4
7	American Home Products	8.4
8	Roche	8.0
9	SmithKline Beecham	7.4
10	Hoechst Marion Roussel	<u>7.4</u>
Total Worldwide Sales of Top 10:		\$91.6

Source: Geoffrey Carr, "The Alchemists," *The Economist*, February 21, 1997.

^aTwelve months ending September 1997.

Exhibit 13 Pharma Giants Ranked by 1997 U.S. Pharmaceutical Sales

Rank	Company	1997 U.S. Sales (billions)
1	Bristol-Myers Squibb	\$5.7
2	Johnson & Johnson	5.7
3	Merck & Co.	5.6
4	Glaxo Wellcome	5.5
5	American Home Products	5.3
6	Pfizer	4.9
7	Eli Lilly	4.4
8	SmithKline Beecham	4.0
9	Novartis	4.0
10	Schering-Plough	<u>3.8</u>
Total U.S. Sales		\$48.9

Source: David J. Morrow, "New Ranking on Drug Sales in U.S. in '97," *The New York Times*, February 27, 1998, p. C3.

Exhibit 14 World Retail Pharmacy Drug Sales* by Therapeutic Category, 12 Months to November 1997 (\$ millions)

Category	United States	Japan	Germany	France	Italy	United Kingdom	Spain	Canada	Netherlands	Belgium	Total	(%) ^a
Cardiovascular	12,390	7,600	3,683	3,684	1,965	1,494	1,099	1,010	422	405	33,752	20
Alimentary/Metabolism	10,746	6,907	2,372	2,089	1,315	1,455	781	636	402	260	26,963	16
Central nervous system	13,153	2,572	1,751	1,865	954	1,270	713	696	244	309	23,527	14
Anti-infectives	6,687	4,939	1,249	1,544	1,175	463	532	298	127	227	17,241	10
Respiratory	6,756	2,702	1,448	1,277	690	1,124	512	392	254	198	15,353	9
Musculo-skeletal	2,453	2,897	672	653	482	442	245	175	64	89	8,172	5
Genito-urinary	4,270	852	889	781	433	430	187	221	108	85	8,256	5
Others	10,058	13,196	2,645	1,811	1,556	1,024	803	681	255	246	32,275	19
Total	66,513	41,665	14,709	13,704	8,570	7,702	4,872	4,109	1,876	1,819	165,539	
% Change ^b	10	-1	0	4	5	7	9	11	7	5		
% of Worldwide Sales ^a	40	25	9	8	5	5	3	2	1	1		

Source: IMS International.

*Sales for 10 largest markets.

^aDoes not add to 100 due to rounding error.

^bChange from prior 12 months. Changes exclude currency movements.

Exhibit 15 Pharma Giants' 1996 Sales by Region (%)

Company	Europe	Asia/Pacific	United States
Hoechst-Marion Roussel	55	17 ^d	28 ^a
Roche	37	16 ^c	47 ^b
Glaxo Wellcome	32	14	43
SmithKline Beecham	33	18 ^e	49
Johnson & Johnson	28	12 ^c	50
Pfizer Inc.	25	14	53
American Home Products	23 ^c	9	59
Bristol-Myers Squibb	25 ^f	10	56
Novartis	40	19 ^c	41 ^b
Merck & Co.	35	11	54 ^g

Source: Compustat; company annual reports.

^aNorth America

^bNorth America, South America, Mexico

^cIncludes Africa

^dIncludes Africa and South America

^eIncludes South America and misc. foreign

^fIncludes Africa and Middle East

^gIncludes Latin America; excludes Medco