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9-707-509
REV: NOVEMBER 16, 2007

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Strategy in the Twenty-First Century Pharmaceutical Industry: Merck & Co. and Pfizer Inc.

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.

— George Merck, Founder of Merck & Co.

In May 2005, Richard Clark became CEO of Merck & Co. A little over a year later, Jeffrey Kindler was named CEO of Pfizer Inc. Clark had joined Merck in 1972 and came from a manufacturing background, while Kindler had joined Pfizer from McDonald's in 2002 as general legal counsel.[1] Like their CEOs, the two companies had historically followed very different paths; Merck was known for its research expertise, while Pfizer was considered a marketing powerhouse. Though different, the CEOs of the two companies faced similar challenges, including headline-grabbing litigation, imminent patent expirations, new technologies, rising drug development costs, generic-drug substitution, international competitors, and complex public-policy issues. How each tackled the difficult questions of scope, size, and vertical integration they faced would determine their future success.

Industry Size and Composition

In 2005, sales in the global pharmaceutical industry reached $602 billion, up from $298 billion in 1998 (**Exhibit 1**).[2] By 2010, the global pharmaceutical market was expected to exceed $767 billion.[3] Growth of the industry was attributed to increasing life expectancy; rising incomes, especially in poorer countries; and the discovery of new drugs for major diseases, such as coronary failure. One study found that the average life expectancy in 52 countries increased by almost two years between 1986 and 2000 and that 40% of this increase could be attributed to new chemical entities.[4]

The North American market accounted for nearly half the worldwide market at $266 billion, while Europe accounted for approximately $170 billion despite a population larger than that of the U.S.[5] Sales in China grew more than 20% in 2005 to reach $11.7 billion. Experts estimated that China would be the world's seventh-largest pharmaceutical market by 2009.[6]

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Grouped into about 30 major therapeutic categories according to targeted disease, the leading drugs in 2005 were cholesterol and triglyceride reducers—which included such blockbuster drugs as Lipitor (see **Exhibit 2** which shows U.S. drug sales in 2001). These were followed by cytostatics to treat cancer such as Lupron, anti-ulcerants such as Nexium, and antidepressants such as Zoloft.[7] Blockbuster drugs—those that sold over $1 billion per annum—numbered 94 (compared to 36 in 2000) and accounted for 33% of pharmaceutical sales in 2005, up from 6% of sales in 1991.[8]

In 2005, there were approximately 600 publicly traded pharmaceutical and biotechnology companies in the world with a total market capitalization of over $1.5 trillion (**Exhibit 3**).[9] Despite industry growth and a return on equity that averaged about 20%, a broad index of drug stocks had fallen 25% in five years, even while shares of biotechnology companies soared (**Exhibit 4**).[10]

Although most of the major pharmaceutical companies had existed for at least a century, there had been dramatic consolidation in recent years (**Exhibit 5**). Between 1985 and 2005, the value of pharmaceutical mergers and acquisitions exceeded $1 trillion. While no company held 5% of the market in 1987, Pfizer, GlaxoSmithKline, and Sanofi-Aventis all exceeded this mark by the end of 2005.[11] Some of the biggest companies in the industry merged several times between 1995 and 2005. Pfizer acquired Warner-Lambert in 2000 for $89 billion and then Pharmacia in 2003 for $60 billion to become the world's largest pharmaceutical company. In 2004, Sanofi-Synthelabo and Aventis merged, in another $60 billion deal, to form the industry number three.[12] Despite such significant mergers, the largest 10 companies still accounted for less than 50% of worldwide industry sales. Many believed consolidation would continue.[13]

Developing a Drug

Large U.S. pharmaceutical companies spent an average of 14% of sales, between $30 billion and $50 billion annually, on research and development (R&D). (The average U.S. manufacturing industry spent 4%.)[14] By the early years of the 21st century, it took 10 to 15 years and cost approximately $802 million (including the time value of money) to bring a new medicine to market. This amount had increased in constant dollars from $318 million in the late 1980s and $138 million in the late 1970s.[15]

One out of every 5,000 to 10,000 tested compounds became an approved drug, and half of all development dollars were spent on products that never reached the market.[16] Among drugs that were developed and marketed, about three in ten drugs produced revenues that exceeded their R&D costs.[17] As a result, most pharmaceutical companies were lucky to produce one blockbuster drug every few years (**Exhibit 6**). In 2005 there were over 2,300 products in clinical development, up 9% from the year before and 31% in the last three years.[18]

Pharmaceutical companies employed thousands of scientists and physicians, many specialists in certain fields. Motivated by curiosity and the desire to make a meaningful contribution, some scientists moved back and forth between industry and academia. However, relocating to a new laboratory could disrupt a research program, and many were reluctant to move. By 2005, Ph.D. researchers could expect compensation of $100,000 a year or more, while top research executives could earn upwards of $5 million. Although salaries at biotech firms were usually less than at pharmaceutical companies, employees enjoyed greater flexibility, responsibility, and stock options. [19]

Pharmaceutical research programs could either focus on specific therapeutic disease categories or seek to exploit the science behind any newly discovered disease pathway regardless of therapeutic area. Some in the industry believed that a focus on therapeutic categories increased efficiency, as scientists could leverage their expertise and ties with outside opinion leaders and other researchers.

One study found that the degree of therapeutic concentration by a company was correlated with economic returns.[20] Others felt it was always possible to hire scientists to explore a new disease mechanism, provided the firm committed to a long-term research program. Experts noted that "knowledge and capabilities accumulated in the pursuit of one therapeutic area [could] often be leveraged to others."[21] The scientific bases of diseases, although increasingly sophisticated, were widely and quickly disseminated among the research community.

Fast-growing therapeutic categories such as diabetes, Alzheimer's/memory, and anti-aging attracted the most research money.[22] In contrast, several diseases affected so few people that they had often been ignored by pharmaceutical companies.[23] In 1983, the Orphan Drug Act attempted to stimulate development of drugs for diseases that affected fewer than 200,000 people by providing seven years of market exclusivity, tax credits, and research grants.[24] By 2006, over 280 drugs had received marketing approval under the act.[25] Diseases such as malaria, which were concentrated in developing countries, also received relatively little attention in R&D budgets. Public health activists called this the 10/90 gap: only 10% of pharmaceutical R&D was aimed at diseases that affected 90% of the world population.[26]

Critics also belabored the industry for developing "lifestyle" drugs that made people look or feel better without necessarily resolving a health problem and "me-too" drugs similar to those already on the market, rather than new "life-saving" drugs. Even so, the pharmaceutical industry continued to market drugs such as Propecia for male pattern baldness and Viagra for erectile dysfunction, although some of these had originally been developed to treat diseases.

Many experts were predicting that an age of "personalized medicine" and "designer drugs" was on its way. Genomics (the study of an organism's genome and the expression of its 20,000 to 40,000 genes), proteomics (the study of the structures and functions of the roughly 400,000 proteins in the human body), and pharmacogenomics (the study of how genes affect an individual's response to a drug) were touted as the next great developments. No longer would a drug be sold indiscriminately to millions; rather, drugs would be developed based on an individual's genetic profile to "pinpoint the underlying cause of disease."[27]

The Process

Traditionally drugs were limited to compounds that could be isolated from natural sources or chemically synthesized; "drug compounds had been found, not designed."[28] As a result, pharmaceutical companies built vast libraries of chemical compounds that they tested against the 58,000 known diseases, and those firms that had tested the most were at an advantage. Over the previous two decades, however, drug development had become more molecular biology based. Via "rational drug design," scientists could design compounds for their effectiveness against a specific disease-causing mechanism or pathway. In addition, several new methods, such as combinatorial chemistry and high-throughput screening, had accelerated the search process. These advances allowed companies to screen up to 100,000 new compounds each year.[29] Computer modeling enabled scientists to manipulate compounds at the molecular level and run simulations before ever synthesizing the actual drug.[30]

Drug development involved discovery, preclinical trials, three phases of clinical trials (Phase I involving 50 to 100 healthy individuals, Phase II requiring 200 to 300 potential patients, and Phase III, which involved more than 3,000 individuals and accounted for the majority of development costs[31]), and government approval.[32] The total time to develop a drug from initial testing to regulatory approval had grown from an average of 8.8 years in the 1960s to 13.6 years in the 1990s but came back down to 10.9 years by the early 2000s.[33] Even a one-day delay in the development of a blockbuster

could result in millions of dollars in lost revenues. When a drug was approved, the FDA imposed severe restrictions on what could be claimed as the drug's benefits—the "label" that described chemical composition, dosage, side effects, and safety issues. The label defined a drug's potential market and relevant patient population since doctors were expected to follow its mandate.

Even after a drug was approved, trials often continued to investigate side effects or study broader outcomes. When cholesterol-lowering drugs were introduced, for example, their effects were evaluated in terms of reduced cholesterol levels. Once prescribed, studies demonstrated that the drugs actually reduced heart attacks and mortality (neither of which had been required for original FDA approval). These studies were part of the broader shift by pharmaceutical firms to "evidence-based medicine," which sought to demonstrate the cost effectiveness of drugs, not just their clinical performance. Nevertheless, critics claimed that the focus of clinical trials had shifted from proving safety and efficacy to generating a label that favorably positioned the drug against competitors.

The emergence of new technologies facilitated the outsourcing of aspects of R&D to specialist firms, and by 2002, some companies outsourced 30% of their R&D budgets, compared with an industry average of only 8% in 1990. New entities called contract research organizations (CROs) performed functions from initial product development and clinical trial implementation to preparation of applications for regulatory approval.[34] Several of these companies were in India and China where costs were up to 90% lower and access to patients for trials easier than in the U.S., Europe, or Japan.

The wide dissemination of scientific knowledge and the availability of new technologies facilitated the development of me-too drugs that could compete with a blockbuster without infringing its patent. Once a new disease pathway had been identified, multiple firms would research its mechanism and develop drugs that perhaps differed slightly in chemical composition or construction. This led to a decrease in the time a breakthrough drug could benefit from market exclusivity from a median of 10.2 years in the 1970s to 1.2 years in the late 1990s (**Exhibits 7a** and **b**).[35] According to critics, only about 14% of drugs approved by the FDA between 1998 and 2002 were considered by the agency to be "a significant improvement" over products already on the market.[36] However, the industry argued that follow-on drugs often provided therapeutic choices for patients.[37]

Burgeoning Biotech

Encompassing a variety of new biological techniques and processes, the biotech industry grew rapidly from its founding in 1976. By 2005 there were 1,444 biotech firms in the U.S., many founded by researchers from pharmaceutical companies and universities (**Exhibit 8**).[38] The biotechnology sector reached $52.7 billion in sales in 2005, having attracted more than $300 billion in capital over its history.[39] The two largest biotech companies in 2005, Amgen (with revenues over $12 billion[40]) and Genentech brought in 53% of the cash generated by all biotech firms, few firms had positive cash flow, and the entire sector had lost money since its creation. Despite high hopes, biotech companies spent about the same as pharmaceutical firms to develop and launch a new drug.[41]

Biotechnology firms had commercialized several new technologies, including gene therapy, recombinant DNA, and monoclonal antibodies that sped up and expanded the range of drug development. To capitalize on these technologies, pharmaceutical companies had invested in their own capabilities and increased the number of partnerships, deals, and joint ventures with biotechnology firms. These deals, which in the past had pharmaceutical companies paying large sums for the rights to market drugs already developed by biotech firms, began moving to earlier stages of the development process. Deals began to offer lower up-front payments with high payouts for attaining important "milestones," such as successful clinical trials, to allow pharmaceutical firms

more "shots on goal."[42] Merck, for example, agreed to pay Vertex $20 million up front, $14 million for research, and up to $350 million in milestone payments to develop cancer treatments.[43]

Growing Generics

The U.S. granted patent protection of 17 to 20 years to new chemical entities. However, clinical testing and FDA review processes shortened the effective life of a patent on a new drug to about 11 to 12 years.[44] Once off patent, drugs were vulnerable to competition from generic versions of the pharmaceutical. Traditionally, companies abandoned a top-selling drug or raised its price to extract revenue from the 5% to 10% of the market they could retain. Recently, however, some firms had begun selling "generic" versions of their most popular drugs after the patent expired.[45] In 2005 drugs with total sales of $17 billion lost patent protection, to be joined by an additional $21.3 billion in 2006. By 2010, more than 70 drugs would go off patent in the U.S., 19 of them blockbusters.[46]

In 1984, the U.S. Congress passed the Hatch-Waxman Act, which required generics manufacturers to show chemical and biological equivalence to the original drug rather than conduct their own clinical trials.[47] Specialist manufacturers of generics, such as Barr Pharmaceuticals, quickly emerged. Whereas it used to take 3–4 years for a generic to overtake its previously patented counterpart in sales, by 2005 the slide in sales occurred in months after patent expiration.[48] Typically, prices decreased 20% during the 180-day exclusivity period granted the first generic to market and then dropped by as much as 90% as other generics entered.[49] In 2005, the average brand-name prescription drug cost $101.71 compared with $29.82 for the average generic.[50]

While in 1984 generics manufacturers accounted for less than 20% of the volume of prescription drugs sold in the U.S., by 2005 this had reached 56%.[51] The value share of generics was much lower, reaching only 13%, in 2005.[52] Many generics came from overseas where they could be tested and manufactured for 20% to 40% of the cost in developed countries.[53] For example, Ranbaxy, the largest Indian pharmaceutical firm, had sales of $1 billion from generics and outsourced manufacturing.[54]

Increasing competition from generics led some pharmaceutical companies to obtain patents on component chemicals and manufacturing methods and to attempt product reformulations. Clinical trials for drug reformulations only cost from $10 million to $30 million. As a result, critics claimed only about one-third of drugs approved by the FDA between 1998 and 2002 were considered novel.[55] AstraZeneca, for example, created the drug Nexium from the same isomer as its drug Prilosec, which went off patent in 2001. Nexium proved to be slightly more effective, and sales reached $4.6 billion by 2005.[56] Some patent holders had also paid generics manufacturers to withhold their generic from the market until this practice was challenged under antitrust law and prohibited under new legislation.[57]

Manufacturing Drugs

Following the development of a drug in a laboratory, chemical engineers designed an economical process for mass production. The transition from pilot to full-scale production was often difficult and required expertise that many smaller firms and biotech companies did not have. While most chemicals used in the manufacture of drugs were commodities, manufacturers had to achieve a high degree of automation and operate consistently with precisely measured and often miniaturized particles. Under FDA regulation, quality control permeated every aspect of the manufacturing process from chemical procurement to destroying expired products.[58] While there were 2,500 sites in the U.S. in 2005, manufacturing only accounted for about 10% of the cost of a drug.

An increasing number of drug makers were outsourcing the manufacturing of commodity chemicals. China and India were already leaders in the basic manufacturing of pharmaceuticals, as India graduated more than 120,000 chemists and chemical engineers a year.[59] Drug companies were, however, concerned about intellectual property and counterfeiting, which were estimated to cost companies in developed countries nearly $35 billion a year.[60] The Chinese government also reported that many thousands had died from fake drugs that were toxic or lacked active ingredients.[61]

Pharmaceutical Consumption

Pharmaceuticals were usually marketed worldwide. Smaller firms with global aspirations had been aided by a 1994 EU decision to replace a complex country-by-country regulatory structure with pan-European product approval for prescription drugs.[62] Smaller countries typically allowed the sale of drugs that had regulatory approval elsewhere in the world or employed a simplified process that might cost $1 million–$2 million per country.[63]

Europe In Europe, the state provision of health care meant that, as the major reimburser of prescription drugs, governments had the power to affect prices and to limit prescriptions of newer, more expensive patented drugs. A 2005 study of 150 best-selling medicines concluded that average prices in Europe were 50% to 62% of those in America, and in Japan prices were 76% of U.S. prices.[64]

Many believed that Europe's cost-containment measures caused consumers to suffer. In the U.K., for example, a new drug had to be deemed cost effective by a committee of the National Health Service (NHS) before it could be prescribed. A number of drugs widely available in the U.S. failed this test and were not reimbursed by the NHS.[65] Others argued that lower drug prices had led European pharmaceutical companies to lose their competitiveness. From 1992 to 2002, R&D spending in the U.S. nearly tripled, to $26 billion, while in Europe it doubled, to $21 billion. From 1997 to 2002, the U.S. had twice the number of drug launches as Europe.[66]

Developing countries Pricing and access to drugs were of particular concern to the developing world. In 2001, the World Bank estimated that 2.7 billion people lived on less than $2 a day, putting most pharmaceuticals out of reach for over 40% of the world's population (**Exhibit 9**).[67] The price of antiretroviral drugs, for example, remained an important barrier for people suffering from HIV/AIDS; only 17% of the 4.7 million people in sub-Saharan Africa who needed such drugs were receiving them by 2005. Access to drugs in these countries was further limited by inadequate government health-care spending, a lack of medical staff, and poor medical infrastructure.[68] Some countries, such as Brazil, allowed local firms to produce patent-protected drugs in order to reduce prices, although this violated intellectual property rights.

Pharmaceutical firms responded to criticism by pointing to the many programs they sponsored in developing countries to provide reduced-cost or free medicines. Many companies, for example, sold antiretroviral drugs to countries in Africa and Asia at cost, and since 2000 drug manufacturers had invested more than $4.6 billion to provide health solutions for the developing world.[69]

Given differences across countries, pharmaceutical companies could position and market a drug the same way everywhere or position it according to the needs of each local market.[70] Many drugs prescribed for the prevention of a disease in wealthy countries were only prescribed after a patient was afflicted with the disease in less developed nations. Zocor, for example, was used in the U.S. to preventatively decrease cholesterol levels, while in lower-income countries governments would only reimburse for its use after the patient had a heart attack.

Pharmaceutical makers could also choose to charge a single price around the world for a drug or charge different prices in each country. Government intervention and income disparities between countries led most companies to pursue a differential pricing strategy. However, such pricing allowed for the development of "gray markets" where drugs could be bought inexpensively in one country and then resold for a premium in another.[71] Differential drug pricing with Canada, for example, resulted in an explosion of mail-order and Internet pharmacies selling to U.S. customers, with some claiming savings of up to 50%. It was estimated that in 2005 over $500 million was spent by U.S. consumers to purchase drugs from Canadian pharmacies.[72]

U.S. Market

The U.S. spent $1.7 trillion on health care in 2003, or about $5,700 per person. Between 1980 and 2003, the share of personal health-care expenditures attributed to hospital care decreased from 47% to 36%, while prescription-drug expenditure share doubled to 12% (**Exhibit 10**).[73] While part of this increase in share was the introduction of new and higher-priced drugs (new drugs accounted for 40% of the growth in value of pharmaceutical sales), part was due to the cost effectiveness of drugs.[74] One study found that an increase of 100 prescriptions resulted in 16.3 fewer hospital days and that a $1 increase in drug expenditure led to a decrease of $2.11 in other health-care spending.[75]

To obtain medicine in the U.S., a patient needed a prescription from a physician and access to a pharmacy. In 2005, 51.5% of U.S. prescriptions were dispensed through chains such as Walgreens, 21.7% through independent pharmacies, and the rest through food stores, long-term care facilities, and mail order.[76] When a patient had insurance coverage, the drug price was negotiated by the insurance company and the drug company—the retail pharmacy essentially received only a processing fee for filling the prescription. Pharmacies did, however, negotiate prices with drug wholesalers for prescriptions that were paid for directly by consumers. In 2006, Wal-Mart announced a $4 per month prescription price for most generic drugs paid for in this way.[77]

The rise of managed care Traditionally, patients had visited any doctor they chose and paid for services and drugs out of their own pockets or through an insurance plan, often offered by their employer. Rising health-care costs at the end of the twentieth century prompted a rise in managed care organizations (MCOs), which sought to curb those costs by contracting with employers to offer medical care to their employees. Between 1988 and 2002, traditional fee-for-service coverage declined from 73% to 5%, while managed care grew from 27% to 95%.[78] Insurance coverage for prescription drugs correspondingly grew sharply. By 2003, 70.4% of prescription spending was covered by government or private insurance, and only 29.7% was paid out of pocket.[79]

In order to reduce the costs of prescription drugs, MCOs often contracted with pharmacy benefits managers (PBMs). By aggregating purchases across MCOs—the largest PBM, Caremark, dispensed about 530 million patient prescriptions per year—PBMs received discounts of up to 40% from pharmaceutical companies. They also operated "formularies" to guide doctors to the least expensive drugs and encourage pharmacists to substitute generic drugs for brand-name ones wherever possible. [80] Many formularies were "closed," reimbursing different amounts depending on which "tier" a drug fell into. Generics on the lowest tier required the lowest copayment of $5 from patients, while new drugs on the highest tier were either not reimbursed or had a copay of up to $40. By 1997, 65% of formularies were closed, up from 35% in 1994.[81] Negotiations between pharmaceutical firms and PBMs covered volume discounts on individual drugs and overriding discounts that encouraged a formulary to substitute all that firm's drugs for their therapeutic equivalents whenever possible. Such deals were believed to be capable of moving market share.

During the 1990s, several drug companies integrated forward and purchased major PBMs.[82] In 1993, Merck acquired Medco Containment Services, then the largest PBM, for $6 billion. Within four years, most pharmaceutical companies had sold their PBMs; Merck spun off Medco in 2003, receiving $2 billion while shareholders received the stock of a company worth about $7.5 billion.[83] In 2006 CVS, the second-largest pharmacy chain, announced that it would acquire Caremark for $21 billion. [84]

MCOs and PBMs also developed "disease management programs" to help patients with chronic diseases treat their conditions in a consistent, coordinated, and low-cost way. Health-care experts estimated that 125 million people in the U.S. had chronic diseases, which accounted for 75% of health-care spending.[85] Poor compliance with long-term treatment regimens was very common, reaching up to 50%, and often led to expensive hospital admissions.[86] Increasing diagnosis was another objective of managed care. For example, health officials believed that 23 million Americans who could benefit from cholesterol-lowering drugs were not taking them.[87]

Access and pricing Access to prescription drugs was becoming a major U.S. public-policy issue by 2006 as the availability of health care came to the center of political debate. Approximately 14.2% of people in the U.S. had no health insurance, and the number of people under 65 years of age who received health insurance from government programs increased from 13.6% in 1997 to 16.8% in 2005.[88] The issue was particularly acute as "baby boomers" neared retirement since retirees accounted for 15% of the population and 40% of spending on prescription drugs.[89]

To address these concerns, Congress passed Medicare Part D in 2004, which provided prescription drug insurance to disabled and elderly Americans. By 2006, more than 39 million people had enrolled for the benefit, and Medicare was expected to pay for 28% of all prescription drugs in the U.S. This would make the government the nation's largest reimburser of prescription drugs with a total share of nearly 45% across all its programs.[90] Critics worried that the government had insufficient funds to cover these expenses. In their 2006 annual report, trustees revealed that the unfunded liability for Medicare Part D was $16.2 trillion compared with that of $13.4 trillion for Social Security. Many predicted the federal government would be forced to follow severe cost-reduction techniques such as quantity limits and strict drug formulary lists, as many states had done with their Medicaid programs.[91] Others saw this unfunded liability as likely to lead to pressure for the government to negotiate directly with pharmaceutical companies over prices—something that had been explicitly prohibited in the original Medicare Part D legislation.

As prescription drugs began to take up a greater share of the health-care budget, concern grew over their high price. Novel drugs were priced to capture part of the overall reduction in health-care costs they generated and were usually more expensive than existing treatments. On average drug prices had increased by about 3% per annum in real terms since the early 1980s.[92] Industry critics argued that drug development was often supported by government-funded research and called for price controls to make medicines more affordable.[93] Many in the industry noted that even the threat of price controls could decrease research spending. They also cited an independent report that found a "significant government investment in only four of 47 medicines with sales of $500 million or more."[94]

Selling and Marketing Drugs

Pharmaceutical companies had historically employed vast sales or "rep" forces to call on doctors and other influential health-care workers in order to promote the company's drugs in a practice called detailing (**Exhibits 11a** and **b**).[95] Companies generally had multiple sales forces, each organized around a particular therapeutic category or physician specialty.

As MCOs worked to have doctors see more patients per day, sales reps were left with less "face time" with physicians. Visits averaged three minutes, and reps could often do little more than drop off free samples and other promotional materials at the seven calls they made on average each day; the industry had tightened up on rep behaviors such as "dine and dash," whereby doctors were invited to dinners in return for little more than receiving literature on a new drug.[96] One study found doctors believed the information they received was biased (78%) and that detailing visits were inconvenient (50%). Many doctors put restrictions on rep visits, and some even prohibited them altogether. Some states, like Massachusetts, were threatening to require licenses for all reps. To confront these obstacles, reps began using the Internet to virtually visit doctors and cut costs from $200 for a rep visit to $110 for an online session.[97] By 2005, several firms had decided to market to large payors and PBMs as well as individual doctors, and the number of reps leveled off at 101,000.[98] However, providing free samples of drugs to doctors remained an effective way to market pharmaceuticals. One executive estimated that 50% of doctors required samples before prescribing a drug.[99] As a result, the retail value of free samples exceeded total promotional spending (**Exhibit 12**).[100]

Drug manufacturers also worked hard to maintain good relationships with "opinion leaders"—widely respected physicians who were instrumental in the adoption of a new drug by setting prescribing standards. Pharmaceutical companies often sponsored academic research in areas related to a drug or hired opinion leaders to conduct clinical trials of a promising compound. Academic papers frequently featured joint authorship between university researchers and top pharmaceutical company scientists. In 2006 it was found that pharmaceutical firms spent 14% of the marketing budgets for blockbuster drugs on "commercialization efforts involving key opinion leaders." Critics claimed that companies were simply buying endorsements in order to sell more drugs. In response, many firms were separating medical-liaison programs from commercial operations.[101]

In 1997 the FDA changed regulations to allow pharmaceutical companies to name a specific drug and the illness it treated in media advertisements. Direct-to-consumer (DTC) advertising by pharmaceutical companies then exploded, reaching $4.2 billion in 2005 (**Exhibit 12**).[102] Research demonstrated that 60% of patients who discussed a specific drug with their doctors received a prescription for it, and critics decried the increased spending on DTC advertising as "primarily a marketing machine to sell drugs of dubious benefit."[103] Pharmaceutical companies countered that DTC advertising helped to educate the public, caused patients to seek treatment for untreated conditions, and improved compliance with already prescribed drugs.[104] To address concerns about DTC advertising, an industry group established guiding principles for the medium in 2005.[105]

More broadly, in the wake of several highly visible drug recalls, pharmaceutical companies were suffering from a loss of credibility. A 2005 poll showed that "only 9% of Americans believed drug companies were generally honest, down from 14% in 2004." In contrast, 34% said they trusted banks, and 39% trusted supermarkets.[106]

Merck & Co.

Originally the subsidiary of a German company, Merck became an American firm in 1917. Through its Merck Research Labs, the company established a reputation for excellence in research and prided itself on being a "science-led" company. With a focus on breakthrough research, successes in areas such as antibiotics and hormones, and innovations such as streptomycin to treat tuberculosis, Merck became an industry leader. It was consistently among the most valuable and most admired companies in the U.S., with many doctors considering Merck the "gold standard" of pharmaceutical research.[107] During the 1990s the company sold its generics and specialty chemicals businesses to

focus more on R&D for novel drugs.[108] By 2001 it had one of the top two drugs in five therapeutic categories.[109]

Research Historically, Merck was good at assessing projects in the early stages of development; because it provided detailed biological and chemical profiles of its drugs, it was highly regarded by the FDA. Merck's drugs had an FDA approval rate of about 70% compared with an industry average of 50%. This success and a record of few drug withdrawals had been a source of pride at Merck and gave its labs prominence within the firm.[110] Merck's credo was to "hire brilliant scientists and let them follow their instincts." In 2001, the company persuaded Peter Kim, a top academic researcher in viruses, including HIV, to take over as head of R&D. Kim was interested in exploiting scientific breakthroughs, and executives assured him of Merck's unwavering commitment to research, promising to provide the necessary resources to be successful. By 2006, Merck had six major labs across North America and Japan, with smaller labs in the U.K., France, Spain, Italy, and Japan.[111]

The company had focused on developing blockbuster drugs, regardless of therapeutic area, ideally those that were taken once a day and that capitalized on newly discovered mechanisms or pathways. Its willingness to exploit science outside of its traditional expertise allowed Merck to enter new fields, such as diabetes in 1986, bone disease in 1991, and cancer in 2004.[112] As former CEO Ray Gilmartin had written in 1996, "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."[113] To achieve this, the firm had been dedicated to recruiting top scientific talent, decentralizing R&D to smaller facilities with perhaps 350 scientists, and leveraging in-house R&D with external collaborations. It viewed hiring scientists as one of its most important activities, seeking to find the best talent regardless of their specific area of expertise.

By 2005, Merck had $23 billion in annual sales, about 62,000 employees in 120 countries, and 31 factories worldwide (**Exhibits 13a** and **13b**). Fifty-eight percent of its revenues came from more than 200 countries outside the U.S. In the past, Merck had attempted to maintain uniform global prices but had backed away from this approach and moved toward differential pricing. A setback in 2003 strained Merck's late-stage development pipeline when two potential blockbuster drugs failed in clinical trials. Another blow came in late 2004 when the company voluntarily withdrew its arthritis drug, Vioxx, after the drug was linked to heart attacks. As a result, the company had seen its stock price fall by more than 60% from its high in 2000.[114]

Mergers Merck was one of few companies that had not merged with another drug firm. Gilmartin did not believe that huge R&D budgets led to more efficiency and once commented, "We don't see that large mergers add to long-term growth. Our approach, in addition to investing in our own internal research, is to continue to establish relationships with firms pursuing complementary research."[115] Clark agreed with his predecessor that "science not size wins" but left the option of a merger on the table: "It's evident to us that large-scale mergers haven't been very successful in the pharmaceutical industry, but we will still consider any situation that might make sense for us."[116]

Experts postulated that pharmaceutical firms merged to take advantage of economies of scale or to address a revenue shortfall that might follow patent expirations and gaps in drug development pipelines.[117] One study found that companies with strong financial performance were less likely to merge, that mergers were often not an effective growth strategy for pharmaceutical companies, and that many mergers absorbed and distracted more resources and managerial effort than had been anticipated premerger. In fact, merging firms were found to suffer from a 52.3% decrease in operating profit three years after the merger relative to similar companies that did not merge.[118]

While historically Merck had between 20% and 30% of its sales from externally licensed drugs (compared with an industry average of 47%), in 2000 Gilmartin stressed the need for external

partnerships to keep Merck competitive in cutting-edge science.[119] Dr. Kim agreed that the company was too insular, with an "inability to look at reality if it hadn't been thought up at Merck." In 1999, Merck entered into 10 outside alliances; after Kim's appointment, the company signed an average of 47 deals a year.[120] Merck believed strongly that its alliance activity should not be limited to purchasing the marketing rights to fully developed drugs. Rather, the company designed its partnerships to complement its internal R&D efforts and focused on collaborative basic research. The company argued that in forming an alliance it was important to have a parallel internal scientific capability to evaluate and build on its partner's expertise.[121]

Marketing Merck had historically maintained a functional organization structure that tended to undervalue sales and marketing. According to one marketing manager, Merck Research Labs "gave us the drug, it was best in class, and we sold it. Marketing was 'allowed' in much later in the process. It was a good strategy, it worked at the time." However, the growing importance of marketing was emphasized by a senior Merck executive in 2004 when he argued that "in the past, the molecule was the product, but now the label is the product." Merck had learned this lesson with its blockbuster drug Zocor. The drug had been introduced in 1991 to fight cholesterol and quickly became the best-selling drug in its class (statins). In 1996, Pfizer introduced a nearly identical but more concentrated drug, Lipitor, and focused its marketing efforts on showing that Lipitor reduced cholesterol by a higher percentage at the typical starting dose prescribed by doctors. In less than a year, Lipitor had a larger market share than Zocor, despite Merck's argument that at equivalent active-ingredient levels the reduction in cholesterol was equal.[122] By 2005, Lipitor sales reached $12.2 billion compared with Zocor's $4.4 billion.[123]

Under Gilmartin, Merck sought to create value for the patient through its marketing and sales efforts while increasing the power of those functions. Marketing shifted to "key franchise" management—the life-cycle management of a therapeutic category—and new data-driven approaches were adopted. Different sales forces were organized around top-selling drugs in specific categories, and each rep was focused on promoting one main drug and a "backup drug." The number of reps visiting doctors about the same drug—a strategy known as "mirroring"—was reduced. Meetings with physicians were designed to add value through information and to demonstrate the efficacy and cost effectiveness of the drugs discussed. Emphasis was placed on cross-functional coordination, such as the introduction of worldwide business strategy teams for each therapeutic category, and an increased role for marketing in the design of clinical trials. Operational excellence in all functions was stressed as a way to reduce costs and cut time to market.[124]

Current challenges and response One of the most significant issues facing Merck in 2006 was its litigation liability for the drug Vioxx. The company began selling Vioxx in 1999 and voluntarily withdrew it from the market in September 2004, when it had annual sales of $2.4 billion, following a Merck clinical trial that revealed increased risk of cardiovascular incidents in patients who used the drug for longer than 18 months. By 2006, the company faced 14,200 lawsuits covering almost 30,000 patients. Most analysts estimated the liability at $4 billion to $10 billion, although some put the total as high as $25 billion. Merck committed to fight each case individually rather than seek a broad settlement, arguing that it had withdrawn the drug as soon as it knew of the problem and that the cause of each heart attack could be different.[125]

Merck also faced the expiration of several of its most valuable patents. Some analysts called Merck's patent expirations the "even-year curse": the patent on Zocor, the largest-selling drug yet to face generic competition, expired in June of 2006; Fosamax, an osteoporosis treatment, faced generic competition in 2008; and two other major drugs would lose protection in 2010 and 2012.[126] While Merck gained regulatory approval in 2006 for Gardasil, the first vaccine to prevent cervical cancer,

and was set to release four additional novel drugs or vaccines, including the diabetes drug Januvia, analysts were concerned about the company's ability to replace its blockbusters.[127]

Merck announced a general restructuring program in late 2005. The company revealed that it would close five manufacturing plants, reconfigure operations to speed up production times, and lay off 7,000 employees. It was also slated to close three smaller research laboratories. The plan was to yield a pretax savings of $3.5 billion to $4 billion from 2006 to 2010. As Clark observed, the industry "was scientifically focused, at times like an academic institution," and it did not "spend a lot of time until now looking at its cost structure." Spending on R&D would be flat after almost doubling since 1999. Shares slid nearly 5% as investors remained skeptical of the company's efforts.[128]

In early 2006 Merck unveiled a new strategy to narrow its research focus to nine "priority disease areas."[129] According to the company, "the nine areas represented many of the world's most critically important health care challenges" and included Alzheimer's disease, atherosclerosis, cardiovascular disease, diabetes, novel vaccines, obesity, cancer, pain, and sleep disorders.[130]

Pfizer Inc.

In 2005, Pfizer was the largest pharmaceutical company in the world with sales of $51 billion, 106,000 employees, and a 10% share of the world's prescriptions. The industry's 14th-largest firm in 1990, Pfizer had grown quickly, mainly through mergers.[131] As a result, Pfizer was known as a "hunter, not a gatherer" of new drugs.[132] Among these, 15 were leaders in their therapeutic markets, and more than eight were blockbuster drugs including Lipitor, which reached sales of $12 billion in 2005, more than any other drug in history. Pfizer spent more than $7 billion on R&D, 47% higher than its closest competitor, and employed over 12,000 researchers.[133]

Research Industry pundits felt that Pfizer had "the worst pipeline relative to its size in the global industry."[134] Sales of recently launched drugs were disappointing, and the company was forced to delay the launch of anticipated drugs.[135] Pfizer also faced declining R&D productivity. In 2002 it spent $53 million for each of its products in development; by 2004, each product in its pipeline cost $70 million. Pfizer had not developed a blockbuster drug in its own lab since 1998 when it launched Viagra.[136] In 2006 Pfizer had nine major labs throughout the U.S., the U.K., and Japan as well as several satellite labs around the world.[137]

Marketing Pfizer was known for having effective marketing and had the largest sales force in the industry with nearly 9,000 reps. With a worldwide advertising budget across all media of $3.5 billion in 2005, Pfizer lagged behind only GM, Procter & Gamble, and Time Warner in advertising expenditure. It was estimated that each Pfizer rep cost $170,000 per year including car, computer, and benefits.[138] The company evaluated its reps on "reach and frequency," tracking the number of doctors and number of visits per doctor that each rep tallied. A doctor might be hit several times by different reps promoting the same Pfizer drugs. The "famously top-down Pfizer" sales force was recognized for excellence and was consistently ranked highly by physicians; it was "enormous, well-trained, and aggressive."[139] Intense training for reps included 40 simulated sales calls; reps would also rehearse 30-second briefs that could be presented in a hallway or parking lot.[140] The company believed that its sales force could sell a broad line of drugs; because they were with doctors more often, they could influence prescribing behavior, particularly for drugs with therapeutic equivalents available. Pfizer positioned itself as the "partner of choice" for biotech firms in marketing their new drugs. Scale also gave Pfizer the power to bundle drugs in negotiations with PBMs.

Mergers Because of its large sales force and marketing capabilities, Warner-Lambert had turned to Pfizer to market its blockbuster, Lipitor, in the 1990s. Pfizer then acquired the company in 2000 in a hostile $89 billion takeover in order to gain full control of the drug after a friendly merger of Warner-Lambert and American Home Products had already been arranged. The success of the post-merger integration, which cut $270 million in costs by "eliminating overlapping spending in research, sales and administration," encouraged Pfizer to try again.[141] A similar partnership had been established with Pharmacia to sell Cox-2 inhibitors to treat arthritis, and these deals culminated in the merger of the two companies in 2003. Already the biggest pharmaceutical company in the U.S., Pfizer was propelled by this merger to the top spot in Japan and in Europe, where it had been number four.[142] Analysts speculated that much of Pfizer's strong earnings growth during former CEO Henry A. "Hank" McKinnell Jr.'s term had come from cost cutting after acquisitions.[143] After the Pharmacia merger, Pfizer announced it would close three of its 25 major development centers and disperse many functions among the surviving facilities; early research would be conducted at four U.S. sites and in England and Japan, while clinical testing of drugs would happen at five U.S. sites and in England. Pfizer continued work on about 75% of the drugs that Pharmacia had in development, although it lost some scientists in the transition.[144] The Pharmacia merger brought in a generics-drug subsidiary which became the preferred vehicle for Pfizer to transition drugs going off patent.

Current challenges and response Pfizer's new CEO faced patent challenges on top-selling drugs such as Lipitor and Celebrex, as well as charges that Pfizer reps had improperly promoted drug uses that the FDA had not approved.[145] In the wake of the Vioxx withdrawal, the future of Pfizer's own Cox-2 inhibitors was uncertain. Celebrex, with 2004 sales of $3.3 billion, was under pressure, while Bextra, with $1.3 billion in revenue, was withdrawn from the market in 2005.[146]

Pfizer lost patent protection for one of its best-selling drugs, Zoloft, in 2006. It was expected that during 2007, two more drugs, with combined sales of $6.1 billion, would be opened to generic competition.[147] While Lipitor dominated the market with a 54.8% share of statin prescriptions and had a patent until 2011, experts expected the generic version of Zocor to claim 19% to 25% of prescriptions within six months.[148]

In 2005, Pfizer announced a cost-cutting initiative to save $4 billion over four years.[149] The plan included plant closings, administrative cutbacks, and streamlining of the sales force.[150] In 2006 the company announced the sale of its consumer health-care business, which had revenue of $3.9 billion, to Johnson & Johnson for $16.6 billion. This was primarily Pfizer's over-the-counter business, acquired as part of Warner-Lambert, and included products such as Listerine, Rolaids, and Rogaine. Analysts attributed the sale to the fact that the consumer health-care business was only growing at 3% to 4% per annum and involved a different set of consumer marketing skills than those Pfizer had built in pharmaceuticals.[151] With pressure to grow revenues, there was speculation that additional mergers might be in Pfizer's future. In 2006, the company announced that it would spend $17 billion of its excess cash on future acquisitions and another $17 billion to buy back stock.[152]

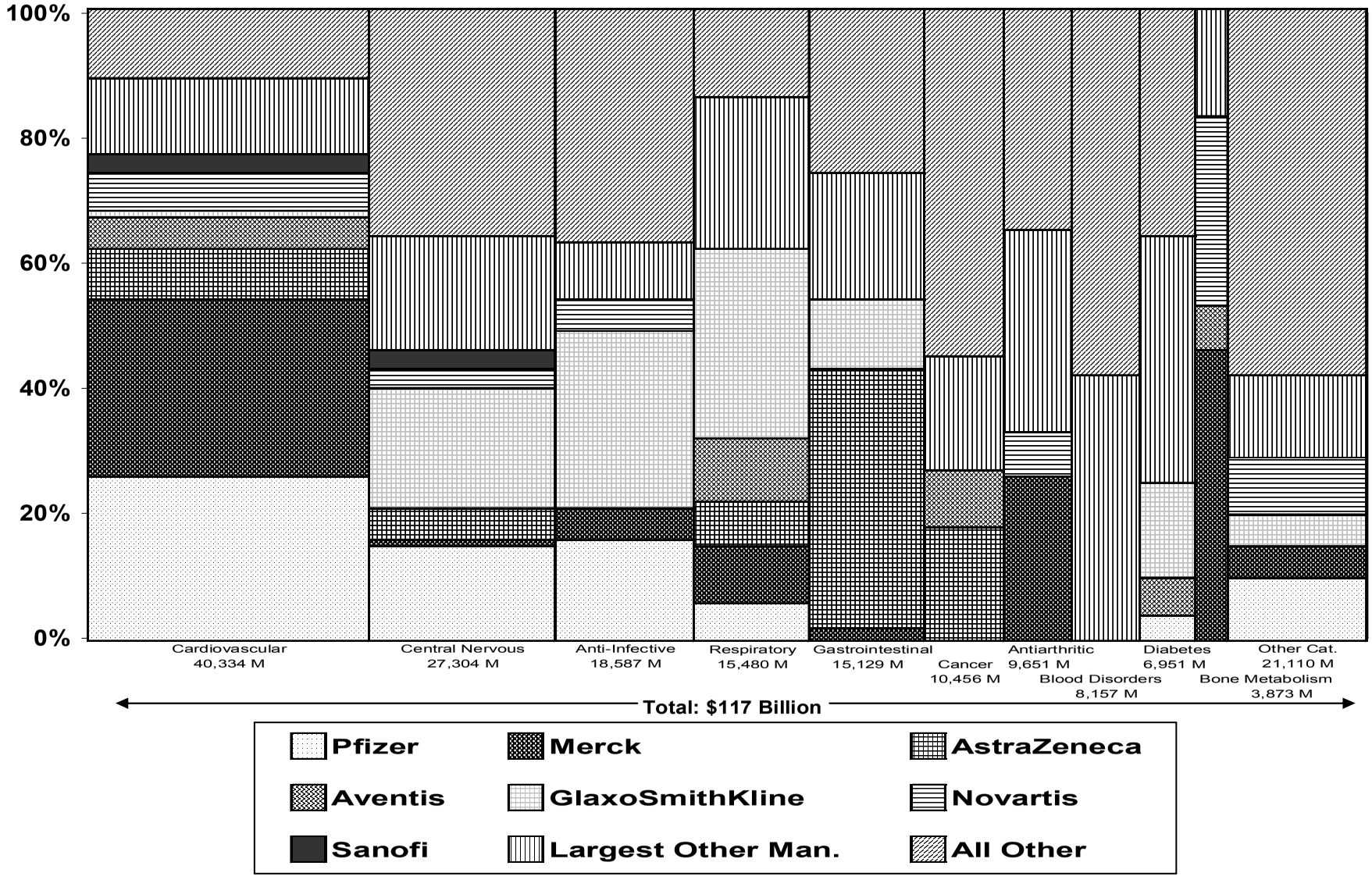
Exhibit 1 Global Prescription Drug Sales by Region

Revenues by Region ($ billions)	2000	2001	2002	2003	2004	2005	CAGR
North America	153	182	204	230	248	266	11.7%
Europe	75	88	102	130	153	170	17.6%
Japan	52	48	47	52	58	60	3.2%
Latin America	19	19	17	17	19	24	4.9%
Other	19	28	32	37	40	46	19.9%
Total	317	364	401	466	518	566	12.3%
% of Revenues							
North America	48.2%	49.9%	50.8%	49.2%	47.9%	47.0%	
Europe	23.7%	24.2%	25.4%	27.8%	29.5%	30.0%	
Japan	16.2%	13.1%	11.7%	11.2%	11.2%	10.7%	
Latin America	6.0%	5.2%	4.1%	3.7%	3.7%	4.2%	
Other	5.9%	7.7%	7.9%	8.0%	7.7%	8.2%	
Total	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

Source: Compiled from IMS Health, "Global Pharmaceutical Sales by Region" (2000–2005), www.imshealth.com, accessed August 2006.

Note: This total includes only audited markets and thus differs from the $602 billion quoted in the text.

Exhibit 2 Company Share of Prescription Drugs by Therapeutic Category in the U.S., 2001



Source: Compiled from "Top 200 prescription drugs by therapeutic category (*Med Ad News* 200) (statistical data included)," *Med Ad News*, Vol. 21, Issue 5, May 1, 2002, p. 52, via Factiva, accessed October 2006.

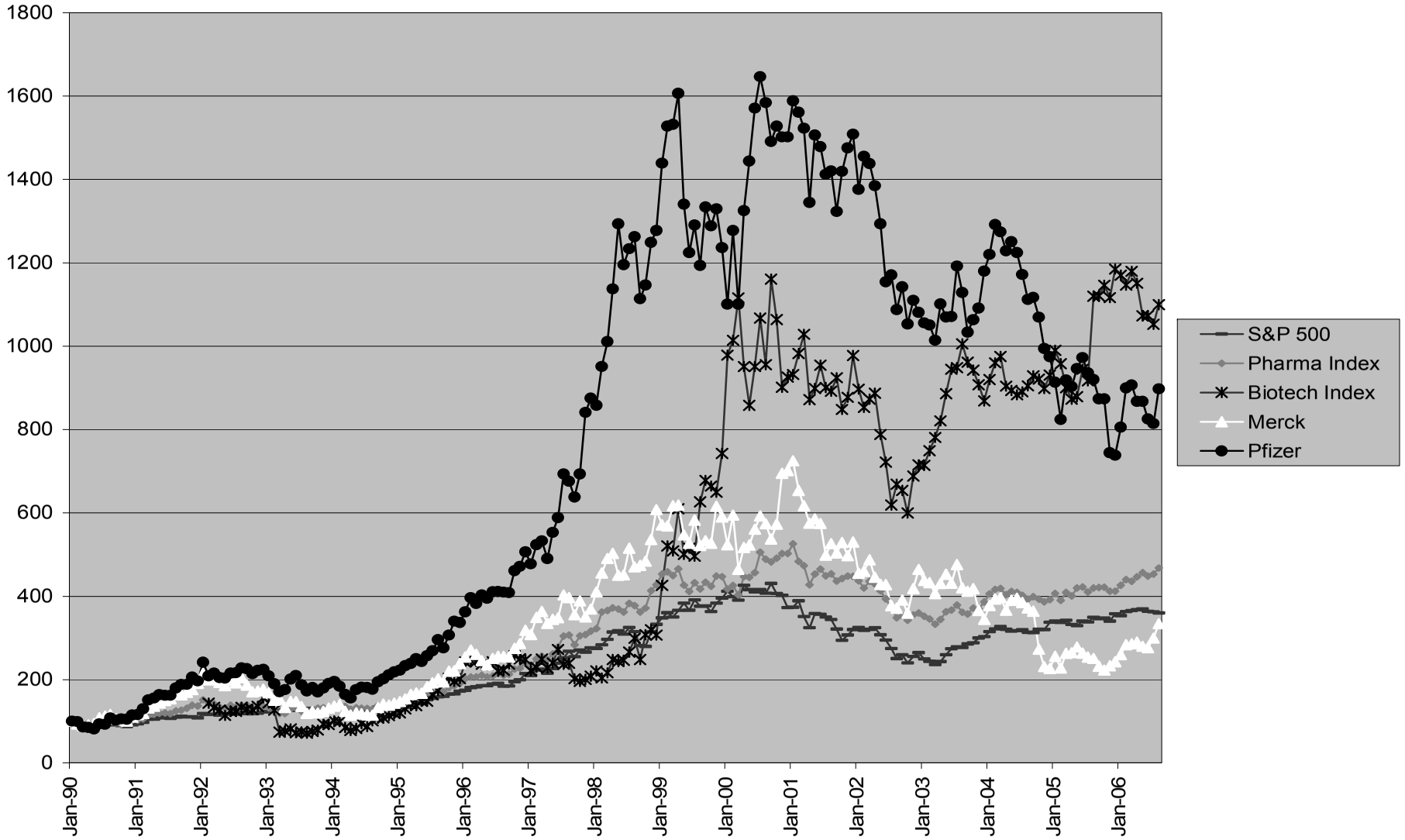
Exhibit 3 Financial Performance of Top 10 Pharmaceutical Companies, 2005

	Pfizer	GSK[a]	Sanofi-Aventis	Novartis	AstraZeneca	J&J[b]	Merck	Wyeth	BMS[c]	Eli Lilly	Average
Financial Results ($ billions)											
Revenue	51.3	39.4	35.5	32.2	24.1	50.5	23.8	19.3	20.1	15.1	31.1
Pharamceutical Revenue	44.3	34.0	32.3	25.0	24.0	22.3	22.0	15.3	15.3	14.7	24.9
% of total	86%	86%	91%	77%	99%	44%	92%	79%	76%	97%	80%
Cost of Goods Sold	8.5	8.7	9.4	8.9	5.4	14.0	5.1	5.4	5.9	3.5	7.5
Gross margin	42.8	30.7	26.1	23.3	18.7	36.6	18.7	13.9	14.2	11.6	23.7
R&D	7.4	5.7	5.0	4.8	3.4	6.3	3.8	2.7	2.7	3.0	4.5
Selling, Marketing, General Admin.	17.0	13.2	10.3	11.5	8.7	16.9	7.2	6.0	6.6	4.5	10.2
Operating Income	11.5	12.5	3.6	6.2	6.5	13.7	7.4	4.8	4.5	2.7	7.3
Net Income	8.1	8.5	2.8	6.1	4.7	10.4	4.6	3.7	3.0	2.0	5.4
Total Assets	117.6	50.0	108.3	57.7	24.8	58.0	44.8	35.8	28.1	24.6	55.0
Shareholder Equity	65.6	13.8	57.7	33.2	13.7	37.9	17.9	12.0	11.2	10.8	27.4
Financial Ratios (% of sales)											
Cost of Goods Sold	17%	22%	26%	28%	22%	28%	22%	28%	29%	23%	24%
Gross margin	83%	78%	74%	72%	78%	72%	78%	72%	71%	77%	76%
R&D	14%	14%	14%	15%	14%	12%	16%	14%	14%	20%	14%
Selling, General Admin.	33%	34%	29%	36%	36%	33%	30%	31%	33%	30%	33%
Operating Income	22%	32%	10%	19%	27%	27%	31%	25%	22%	18%	24%
Net Income	16%	22%	8%	19%	20%	21%	19%	19%	15%	13%	17%
Statistics											
Employees ('000)	106.0	103.2	97.2	90.9	64.9	116.2	61.5	49.7	43.0	42.6	77.5
Sales/Employee ($'000)	484	382	365	354	371	435	387	388	467	354	402
Return on Equity	12%	62%	5%	19%	34%	27%	26%	30%	27%	18%	20%
Return on Assets	7%	17%	3%	11%	19%	18%	10%	10%	11%	8%	10%

Sources: Compiled from company 2005 annual and financial reports; Nicole Gray, "Our 7th Annual Report on The World's Top 50 Pharmaceutical Companies," *Pharmaceutical Executive*, May 2006, http://www.pharmexec.com/pharmexec/data/articlestandard/pharmexec/182006/323799/article.pdf, accessed September 2006; and "Top 20 Pharma Companies Report," Contract Pharma, July/August 2006, www.contractpharma.com, accessed August 2006.

[a]GlaxoSmithKline. [b]Johnson & Johnson. [c]Bristol-Myers Squibb Company.

Exhibit 4 Stock Price Index, 1990–2006



Source: Thomson Datastream, accessed October 2006; "S&P 500 Biotechnology Index," Global Financial Data, Inc., accessed November 2006.

Note: Stock Price Index with January 1, 1990 set to 100. Biotechnology Index begins in February 1992.

Exhibit 5 Merger and Acquisition Activity over $2 Billion among Major Pharmaceutical Firms, 1985–2006

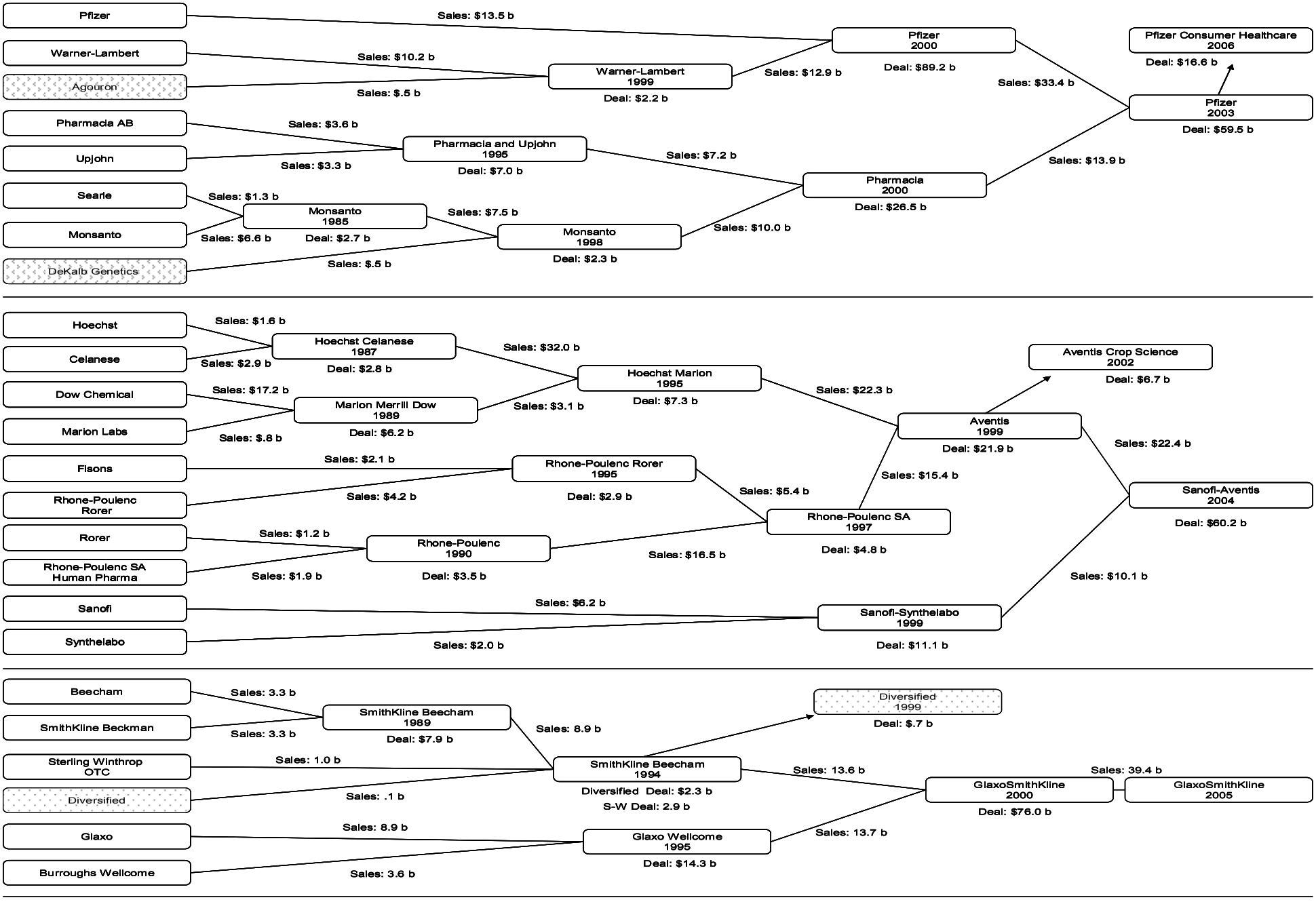
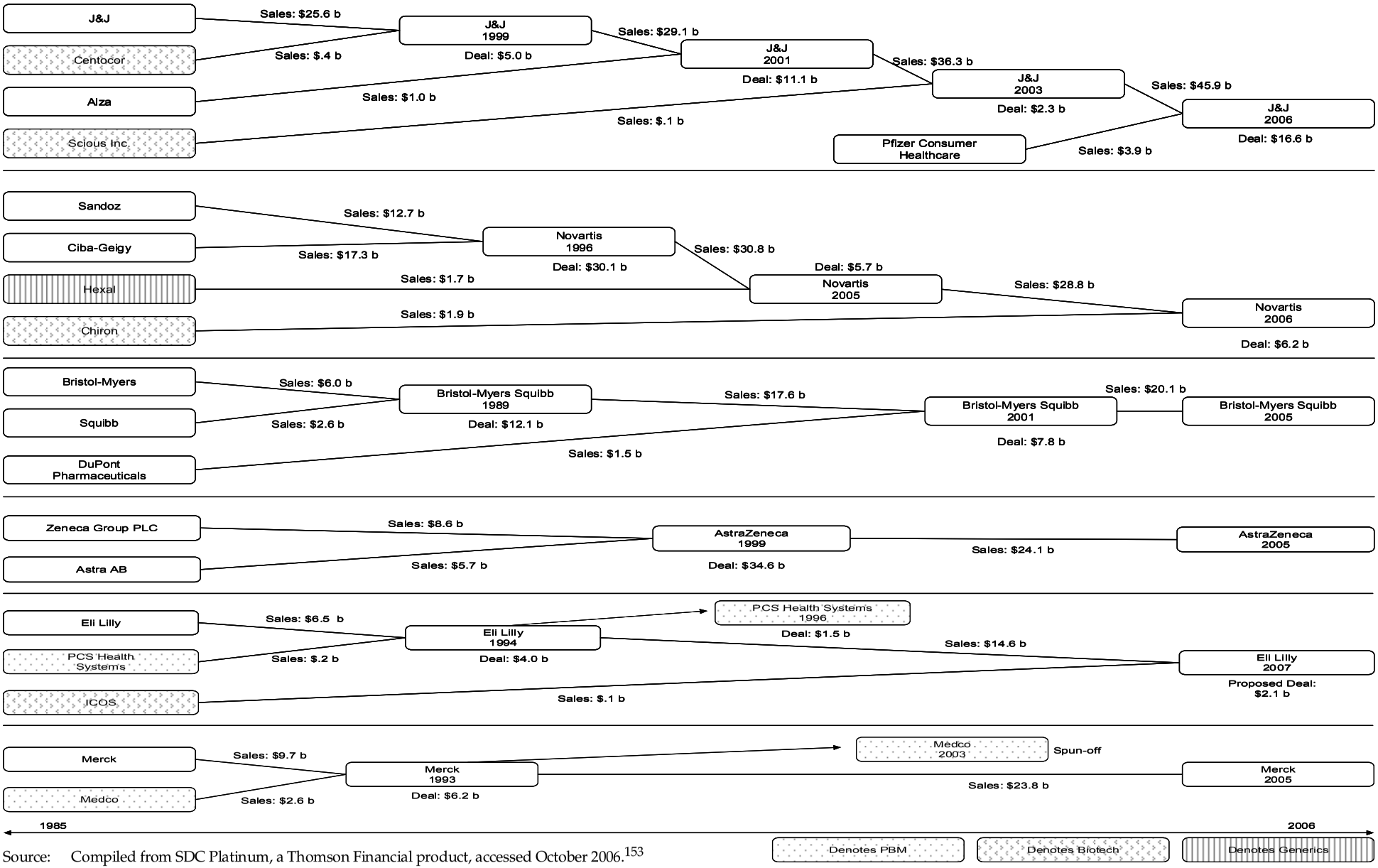
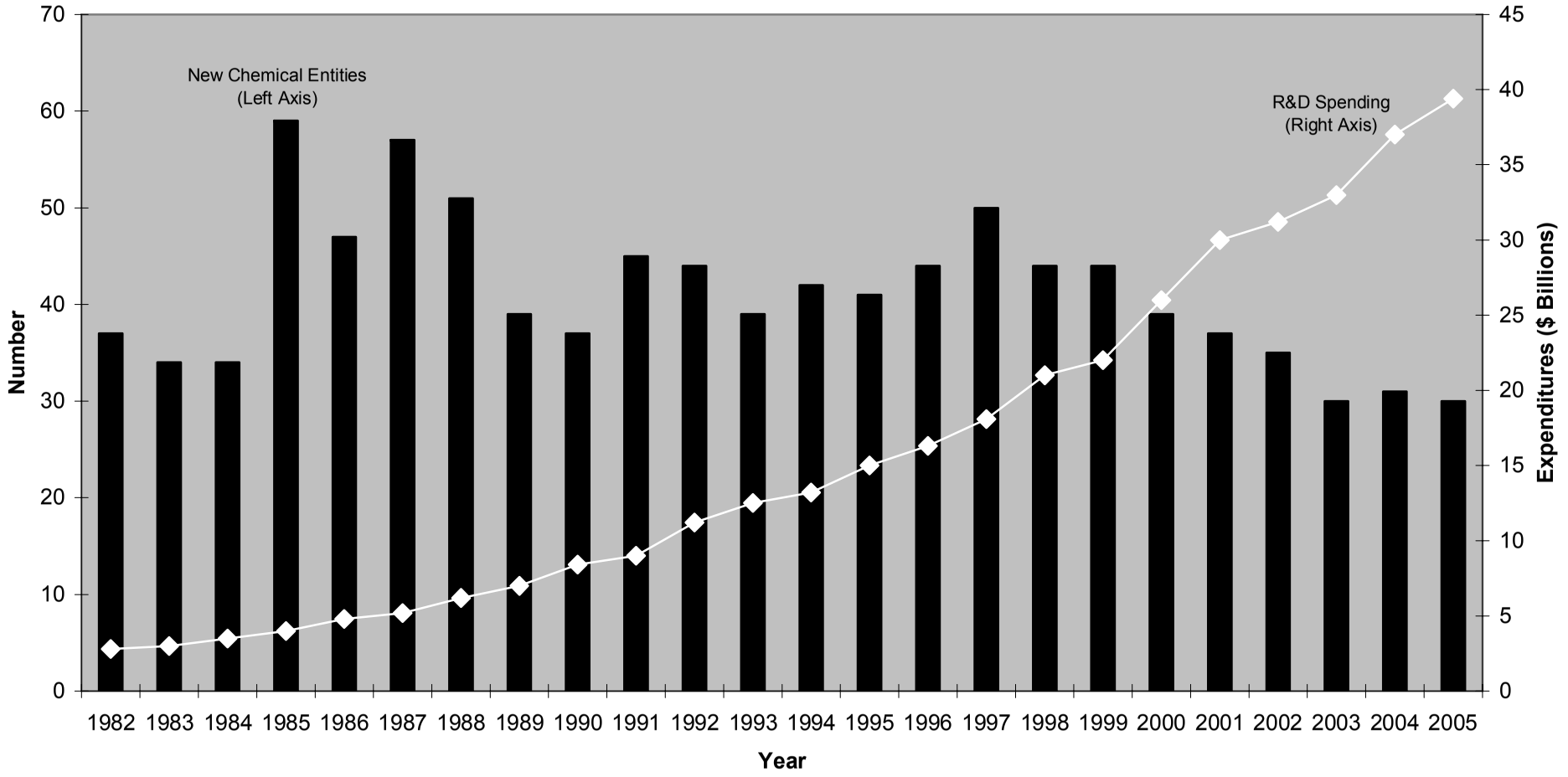


Exhibit 5 (continued)



Source: Compiled from SDC Platinum, a Thomson Financial product, accessed October 2006.[153]

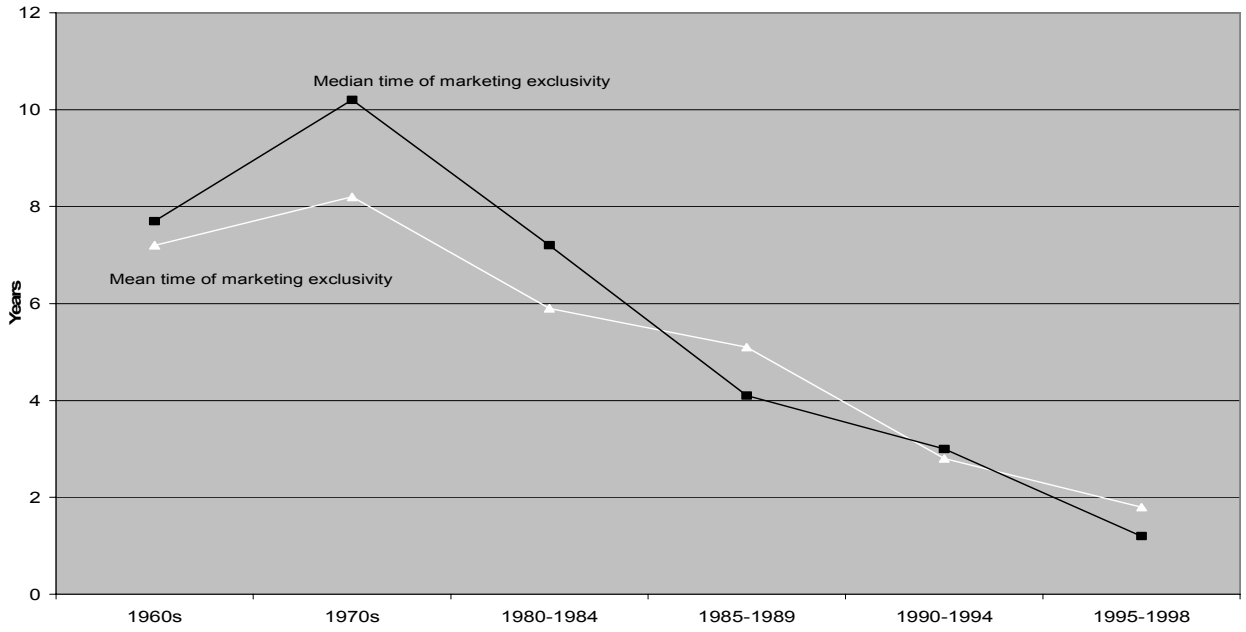
Exhibit 6 New Chemical Entities Introduced and R&D Spending by U.S. Pharmaceuticals, 1982–2005



Sources: Compiled from Frank R. Lichtenberg, "The Impact of New Drug Launches on Longevity: Evidence from Longitudinal, Disease-Level Data from 52 Countries, 1982–2001," National Bureau of Economic Research Working Paper No. 9754 (New York, NY, and Cambridge, MA: Columbia University and NBER), June 2003; "Looking to the East for New Active Substances," IMS Health, May 8, 2006, http://www.imshealth.com/web/content/0,3148,64576068_63872702_70261000_77974547,00.html, accessed November 2006; "06/07 Annual Report," Pharmaceutical Research and Manufacturers of America (PhRMA), August 2006, http://www.phrma.org/files/06_07_Annual%20Report.pdf, accessed September 2006.

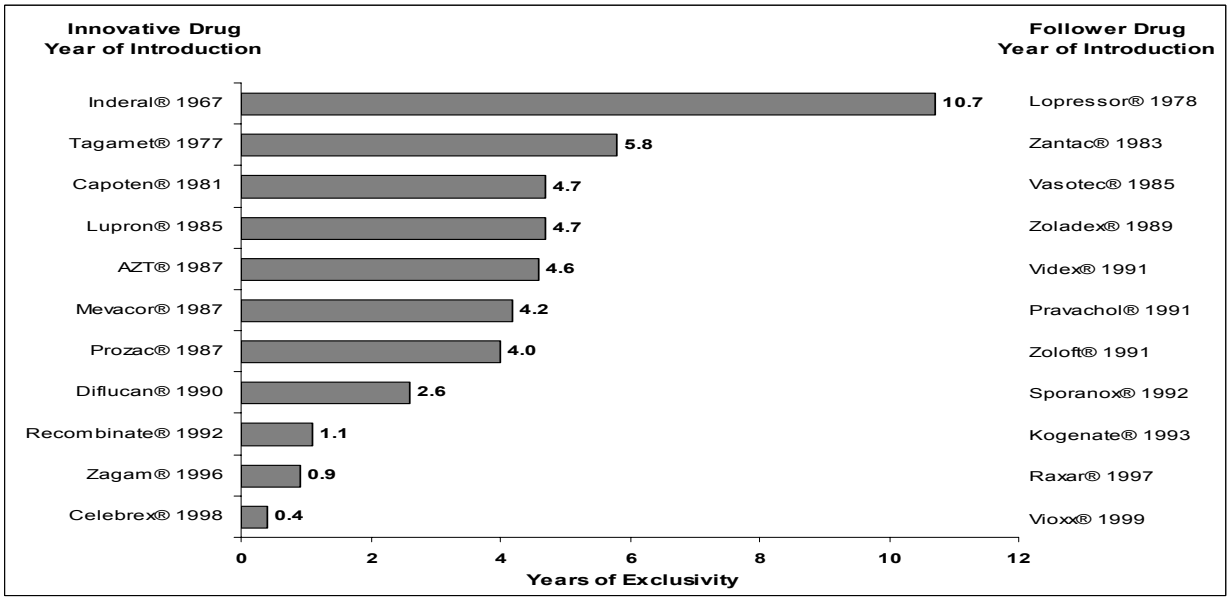
Note: R&D spending includes only money spent by members of the Pharmaceutical Research and Manufacturers of America (PhRMA).

Exhibit 7a Market Exclusivity Time for First-in-Class Pharmaceutical



Source: Compiled from Joseph A. DiMasi and Cherie Paquette, "The Economics of Follow-on Drug Research and Development," *PharmacoEconomics*, Vol. 22 (Supplement 2), 2004, pp. 1–14, via EBSCO, accessed September 2006.

Exhibit 7b Duration of Market Exclusivity for Selected Drugs



Sources: Compiled from Joseph A. DiMasi and Cherie Paquette, "The Economics of Follow-on Drug Research and Development," *PharmacoEconomics*, Vol. 22 (Supplement 2), 2004, pp. 1–14, via EBSCO, accessed September 2006; "Pharmacuetical Industry Profile 2003: Chapter 5 Incentive to Discover New Medicines: Pharmaceutical Patents," *PHRMA*, http://www.phrma-jp.org/publication/pdf/industry/2003/2003CHAPTER5.pdf, accessed September 2006.

Exhibit 8 Top 10 Biotech Companies Based on 2005 Revenues

Company	Headquarters	Headcount	Total Revenues ($ millions)	Revenues/ Head ($ '000)	Pharma Revenues ($ millions)	Net Income ($ millions)	R&D ($ millions)	R&D (% revenues)	Top-Selling Drug	Revenue of Top Seller ($ millions)
Amgen	California	18,000	12,430	691	12,022	3,670	2,314	*18.6%*	Aranesp	3,273
Genentech	California	9,563	6,633	694	5,488	1,279	1,262	*19.0%*	Rituxan	1,831
Serono	Geneva	4,750	2,586	544	2,339	-105	594	*23.0%*	Rebif	1,270
Biogen-Idec	Massachusetts	3,500	2,423	692	2,236	161	747	*30.8%*	Avonex	1,543
Gilead	California	1,900	2,026	1,066	1,809	814	278	*13.7%*	Viread	779
Genzyme	Massachusetts	8,000	2,734	342	1,773	441	503	*18.4%*	Cerezyme	932
MedImmune	Maryland	2,215	1,244	562	1,221	-17	385	*30.9%*	Synagis	1,063
Chiron	California	5,400	1,920	356	1,138	187	434	*22.6%*	TOBI	232
Millennium	Massachusetts	1,142	558	489	316	-198	342	*61.3%*	Velcade	194
ImClone	New York	991	384	387	221	86	99	*25.8%*	Erbitux	221
Total		55,461	32,938	594	28,563	6,318	6,958	*21.1%*		

Source: Compiled from "Top 10 Biopharma Companies Report," *Contract Pharma*, July/August 2006, www.contractpharma.com, accessed August 2006.

Exhibit 9 Country Comparison of Health-Care Spending, 2003

Country	GDP Spent on Health Care (%)	Per Capita Total Expenditure on Health ($)[a]	Pharmacists—Density per 1,000 Population[b]	Drug Expenditure per Capita ($)[c]
U.S.	15.2	5,711	0.88	728
France	10.1	2,902	1.06	606
Germany	11.1	3,001	0.58	436
Japan	7.9	2,244	1.21	393
Korea	5.6	1,074	1.08	309
Czech Republic	7.5	1,302	0.55	284
Mexico	6.2	582	0.03	125
Turkey	7.6	528	0.32	112
South Africa	8.4	669	0.28	82
China	5.6	278	0.28	70
India	4.8	82	0.56	11

Sources: Compiled from "The World Health Report 2006: Working Together for Health," World Health Organization, 2006, pp. 178–199, http://www.who.int/whr/2006/en/index.html, accessed November 2006; "Drug spending in OECD countries up by nearly a third since 1998, according to new OECD data," Organization for Economic Cooperation and Development, August 6, 2005, http://www.oecd.org/document/25/0,2340,en_2649_201185_34967193_1_1_1_1,00.html, accessed November 2006; Andrew Creese, Nadine Gasman, and Mamadou Mariko, "The World Medicines Situation," World Health Organization, 2004, pp. 122–129, http://www.searo.who.int/LinkFiles/Reports_World_Medicines_Situation.pdf, accessed November 2006; "The Market for Pharmaceuticals in Brazil, Russia, India, & China: Pharmaceutical Markets of the Future?" Espicom Business Intelligence, January 31, 2006, https://www.espicom.com/prodcat.nsf/Product_ID_Lookup/00000939?OpenDocument, accessed November 2006.

[a]At international dollar rate.

[b]Data from various years, 1997–2003.

[c]USD purchasing power parity. Amounts for South Africa, China, and India are based on casewriter estimates.

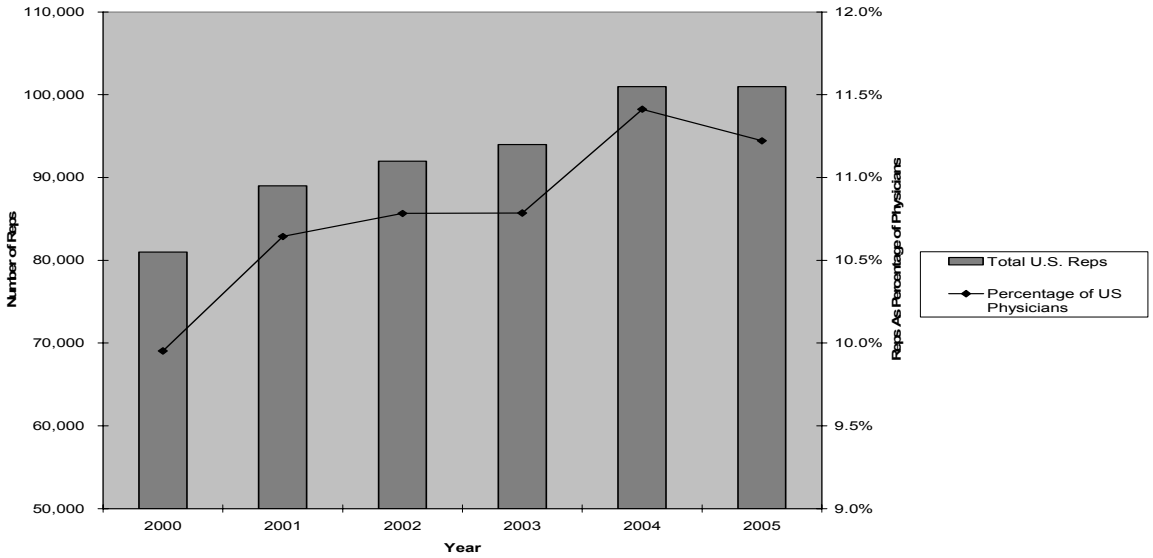
Exhibit 10 Breakdown of U.S. Health-Care Spending ($ millions)

	2000	2001	2002	2003	2004	2005 (E)	CAGR (% p.a.)
Hospital, Nursing Home, and Home Health	542,878	585,210	628,633	674,016	729,148	786,643	7.7%
Physicians, Dentists, Professional Care	426,749	465,359	503,190	543,333	587,407	631,325	8.1%
Prescription drugs	120,803	138,559	157,941	174,112	188,452	203,492	11.0%
Research and Structures/Equipment	93,980	98,663	108,785	116,090	124,609	133,796	7.3%
Medical Products	49,495	49,943	51,609	54,225	55,235	56,332	2.6%
Gov. Administration and Private Health Insurance	81,241	89,644	106,104	124,856	136,654	142,423	12.0%
Gov. Public Health Initiatives	43,364	46,791	51,681	53,966	56,117	62,035	7.5%
Total	1,358,510	1,474,169	1,607,943	1,740,598	1,877,622	2,016,046	8.2%
Hospital, Nursing Home, and Home Health	40.0%	39.7%	39.1%	38.7%	38.8%	39.0%	
Physicians, Dentists, Professional Care	31.4%	31.6%	31.3%	31.2%	31.3%	31.3%	
Prescription drugs	8.9%	9.4%	9.8%	10.0%	10.0%	10.1%	
Research and Structures/Equipment	6.9%	6.7%	6.8%	6.7%	6.6%	6.6%	
Medical Products	3.6%	3.4%	3.2%	3.1%	2.9%	2.8%	
Gov. Administration and Private Health Insurance	6.0%	6.1%	6.6%	7.2%	7.3%	7.1%	
Gov. Public Health Initiatives	3.2%	3.2%	3.2%	3.1%	3.0%	3.1%	
Total	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

Source: Adapted from Centers for Medicare & Medicaid Services, "National Health Expenditure (NHE) Amounts by Type of Expenditure and Source of Funds: Calendar Years 1965–2015 in PROJECTIONS format," nhe65-15.zip, http://www.cms.hhs.gov/NationalHealthExpendData/03_NationalHealthAccountsProjected.asp, accessed August 2006.

Note: Percentages based on total health-care expenditure, which consists of “personal health-care” expenditure and “health services and supplies” expenditure. While prescription drug spending in 2005 made up 12% of personal health-care expenditure (as cited in the text), it made up only 10% of total health-care expenditure.

Exhibit 11a Total Pharmaceutical Company Reps and as a Percentage of Number of Physicians



Sources: Compiled from Tara Hamm, "Verispan's 2005 Pharmaceutical Review: The Industry in Transition," May 4, 2006, http://www.amponline.org/AMP/amp_meeting_mayPres.html, accessed August 2006; "Physicians By Gender (Excludes Students)," American Medical Association, February 7, 2006, http://www.ama-assn.org/ama/pub/category/12912.html; U.S. Census Bureau, *Statistical Abstract of the United States: 2003* (123rd Edition), Washington, DC, 2003, p. 118.

Note: Total of physicians for 2005 is an estimate.

Exhibit 11b Top Companies' U.S. Sales Force Size, 2005

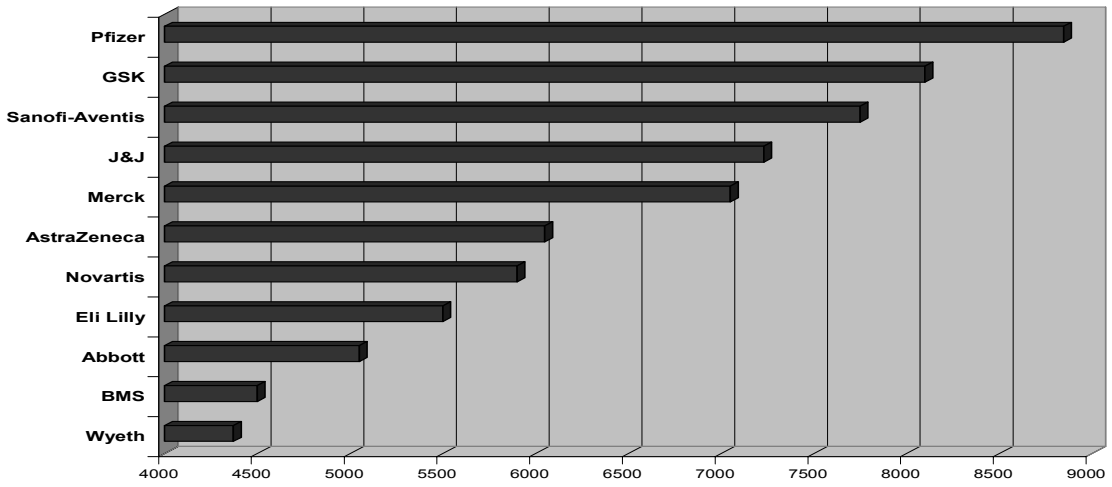


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Exhibit 12 Total U.S. Promotional Spending by Type (U.S. millions)

Promotional Spending Type	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Sales Rep Contacts	3,010	3,364	4,057	4,320	4,803	5,490	6,198	6,938	7,336	6,777
Journal Advertising	459	510	498	470	484	425	437	448	499	429
Direct-to-Consumer (DTC)	791	1,069	1,317	1,848	2,467	2,682	2,649	3,277	4,024	4,237
Total	4,260	4,943	5,872	6,638	7,754	8,597	9,284	10,663	11,859	11,443
Value of Free Samples	4,904	6,047	6,602	7,230	7,954	10,464	11,863	13,531	15,866	NA

Sources: Compiled from "Total U.S. Promotional Spend by Type, 2005," IMS Health, May 2006, http://www.imshealth.com/ims/portal/front/articleC/0,2777,6599_78084568_78152318,00.html, accessed November 2006; "Total U.S. Value of Free Product Samples, 2004," IMS Health, July 2005, http://www.imshealth.com/ims/portal/front/articleC/0,2777,6599_78152267_78152297,00.html, accessed November 2006; "Total U.S. Promotional Spend by Type, 2003," IMS Health, June 2004, http://www.imshealth.com/ims/portal/front/articleC/0,2777,6599_44304752_44889690,00.html, accessed November 2006.

Note: The "Value of Free Samples" is a retail measure of the approximate value of samples given to health-care professionals and not a direct cost to the drug company.

Exhibit 13a Financial Performance of Merck and Pfizer, 1990–2005

	Pfizer				Merck			
Year	**1990**	**1995**	**2000**	**2005**	**1990**	**1995[a]**	**2000**	**2005**
Financial Results ($ billions)								
Revenue	5.9	10.0	29.8	51.3	7.7	17.4	20.8	23.8
Cost of Goods Sold	1.8	2.2	4.9	8.5	1.8	7.5	3.3	5.1
Gross margin	4.1	7.9	24.9	42.8	5.9	9.9	17.5	18.7
R&D	0.6	1.4	4.4	7.4	0.9	1.3	2.3	3.8
Selling, Marketing, General Admin.	2.4	3.9	11.4	17.0	2.4	3.3	5.7	7.2
Operating Income	1.1	2.3	5.8	11.5	2.7	4.8	9.4	7.4
Net Income	0.8	1.6	3.7	8.1	1.8	3.3	6.8	4.6
Goodwill and Intangibles	0.5	1.2	1.8	51.6	NA	6.8	NA	1.6
Total Assets	9.1	12.7	33.5	117.6	8.0	23.8	40.2	44.8
Long-Term Debt	0.2	0.8	1.1	6.3	0.1	1.4	3.6	5.1
Shareholder Equity	5.1	5.5	16.1	65.6	3.8	11.7	14.8	17.9
Financial Ratios (% of revenue)								
Cost of Goods Sold	31%	22%	16%	17%	23%	43%	16%	22%
Gross margin	69%	78%	84%	83%	77%	57%	84%	78%
R&D	11%	14%	15%	14%	11%	8%	11%	16%
Selling, General Admin.	40%	38%	38%	33%	31%	19%	28%	30%
Operating Income	18%	23%	19%	22%	35%	28%	45%	31%
Net Income	14%	16%	12%	16%	23%	19%	33%	19%
Statistics								
Employees ('000)	41.5	43.8	90.0	106.0	36.9	45.2	69.3	61.5
Sales/Employee ($'000)	142.2	228.8	331.4	484.0	209.2	384.2	299.8	387.0
Return on Equity	15.7%	28.6%	23.2%	12.3%	46.5%	28.4%	46.0%	25.8%
Return on Assets	8.9%	12.4%	11.1%	6.9%	22.2%	14.0%	17.0%	10.3%

Exhibit 13b Pfizer and Merck Top Drugs, 2005

Top Drugs 2005	Therapeutic Category	Sales ($ billions)
Pfizer		
Lipitor	Cardiovascular	12.2
Norvasc	Cardiovascular	4.7
Zoloft	Central Nervous System	3.3
Zithromax	Anti-Infective	2.0
Celebrex	Antiarthritic	1.7
Viagra	Erectile Dysfunction	1.6
Xalatan	Ophthalmic	1.4
Zyrtec	Respiratory	1.4
Merck		
Zocor	Cardiovascular	4.4
Fosamax	Bone Metabolism	3.2
Cozaar/Hyzaar	Cardiovascular	3.0
Singulair	Respiratory	3.0
Proscar	Urinary Disorder	0.7
Primaxin	Anti-Infective	0.7
Vasotec	Cardiovascular	0.6
Trusopt	Ophthalmic	0.6

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[a]Includes the impact of the Medco acquisition on November 18, 1993, which had sales of over $5.5 billion in 1995.

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