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FRANK T. ROTHAERMEL
MICHAEL MCKAY

Merck & Co., Inc.

Merck's chief executive officer (CEO) Kenneth Frazier reflects on his 22-year career at Merck as he leaves the corporate parking deck and heads into his office at the company's Whitehouse Station, New Jersey, headquarters in the wee hours of the morning. He has successfully helped shepherd the company through some of the most challenging times in its history and realizes that he faces yet another pivotal period ahead. The words of Dr. Roy Vagelos, former Merck CEO and chairman, echo foremost in his mind: "Organizations that don't change don't last unless they are in some very isolated, unchallenging environment. Organizations . . . need to be revitalized periodically if only because people tend to settle into routines and drop out of touch with their changing environments. One role of a leader is to convince people, before the fact, that they should change."[1] Indeed, Mr. Frazier has occupied a front-row seat to the company's biggest transition in recent years: the Schering-Plough (SP) merger in 2009. Shortly after they closed the deal, Mr. Frazier was promoted to CEO. Now he finds himself in the spotlight once again with full responsibility for leading Merck to a brighter future.

Merck faces multiple challenges. The pharmaceutical industry is in upheaval, due to ongoing consolidation and changing approaches to research and development (R&D). Scientists everywhere are scrambling to discover the next breakthrough therapy in order to stave off the disastrous effects of the patent cliff, with drugs combined over $100bn in annual sales losing patent protection.[2]. Such environmental uncertainty is further exacerbated by the implementation of the Affordable Care Act (ACA), as drug makers wait to see how many people enroll in the program, which kind of insurance plans they purchase, and how many qualify for governmental services like Medicare and Medicaid.[3] Internally, Merck is struggling to ensure that its recent merger with SP enhances Merck's reputation as an R&D powerhouse. The $41 billion deal represented a significant deviation from the closed R&D system on which Merck's historical identity has been based. The company's business model is deeply rooted in a strong competence in internal R&D that churns out blockbuster drug after blockbuster drug. The merger symbolized Merck's growing recognition that internal R&D would no longer suffice in a turbulent industry where thousands of innovative ideas are generated daily, both outside as well as inside the company.

Dr. Mervyn Turner, a 26-year Merck veteran, former chief strategy officer (CSO), and the man who had overseen the SP merger, had perhaps put it best as he advocated for change within Merck: "Merck accounts for about 1 percent of the biomedical research in the world. To tap into the remaining 99 percent, we must actively reach out to universities, research institutions, and companies worldwide to bring the best of technology and potential products into Merck. The cascade of knowledge flowing

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from biotechnology and the unraveling of the human genome—to name only two recent developments—is far too complex for any one company to handle alone."[4] Mr. Frazier had worked closely with Dr. Turner and had come to heavily rely on his insights during the SP integration. Unfortunately, Merck no longer has the luxury of a CSO: Turner's successor, Viet Cuong Do, retired quietly in April 2014 after just two-and-a-half years in office. His departure was the natural fallout from a megamerger and a radical change in business strategy that was proving more difficult to implement than anyone had expected.

Merck & Co., Inc. History

Merck is a global, research-driven company that discovers, develops, manufactures, and markets a broad range of innovative products to improve human and animal health. Merck was founded in 1668, when pharmacist Friedrich Merck acquired an apothecary in Darmstadt, Germany. Some 200 years later, Emanuel Merck discovered alkaloids in the company's laboratory and rapidly expanded the company's operations to include bulk manufacturing and sales of various chemical and pharmaceutical preparations. In 1891, Emanuel's grandson, George, assumed control of the firm's New York office and named the new subsidiary Merck & Co., firmly establishing its U.S. presence. After World War I, Merck severed ties with its German parent and incorporated as an independent U.S. company to become Merck & Co., Inc., although the Merck family continued to hold prominent leadership positions.[5]

Over the next few decades, Merck developed prominence as a research powerhouse, attracting the most highly respected scientists from around the world. By 1950, five Merck researchers had won Nobel prizes for their contributions to medicine. Head scientists were successful in the recruitment and retention of superior research personnel because Merck maintained an academic, university-like atmosphere in which scientists were given freedom to explore their personal research interests. The hallways in the research sites in Rahway, New Jersey, and Boston, Massachusetts, had academic disciplines written on them, such as "Biology" and "Chemistry." With a campus-like setting, world-renowned scientists, and cutting-edge research, Merck became known as "The Harvard of Pharma."

By 1989, Merck had expanded to six divisions, 70 business units, 13,000 products, 21,000 employees, and production facilities in 27 countries. Merck's internally focused, research-driven culture received accolades for excellence in the industry, landing Merck on *BusinessWeek*'s list of Top 10 Most Valuable Companies from 1987 to 1990.[6] *Fortune* magazine anointed Merck as the most-admired company in America from 1987 to 1993.[7] Even people who knew nothing about the pharmaceutical industry had heard of Merck.

The early 2000s proved, however, to be quite challenging. The company was unable to maintain its past rate of success as the landscape of pharmaceutical R&D changed to accommodate new methods of drug discovery and increasing pressure from generic drug manufacturers. Merck responded boldly, completing a reverse-merger with SP in 2009. The move bolstered sales and managed to stave off a revenue decline that was largely due to a variety of core Merck products losing market exclusivity. The cholesterol-lowering drug Zocor lost its patent protection for all formulations in the United States in 2006, followed by the osteoporosis-drug Fosamax in 2008. A third therapy, Cozaar/Hyzaar for the treatment of hypertension, went off patent shortly thereafter in 2010. Despite these significant financial hits, the addition of SP's pipeline and product portfolio to Merck's operations generated a net increase in sales in 2010 and 2011 (**Exhibit 1** contains Merck's 2013 income statement).

Merck & Co., Inc.

Unfortunately, with the subsequent loss of patent protection for two more key products in 2012 (Singulair to treat asthma and allergic rhinitis and Maxalt for migraine headaches), Merck's revenues began to decline. By 2013, the company's worldwide sales reached just $44.0 billion, a year-on-year decline of 7 percent. Worse still, Merck faces the prospect of even more patent expirations in the near future. Of greatest concern is the loss of market exclusivity for two products which contributed 8 percent of all sales in 2013: Nasonex (corticosteroid for the treatment of nasal allergy symptoms, in 2014) and Remicade (biologic capable of treating a broad range of inflammatory diseases, in 2015). At annual sales of $1.34 and $2.27 billion respectively, a decline in sales (resulting from both from the availability of generic alternatives and the need to lower prices in response to generic competition) of these two drugs will seriously affect Merck's revenue stream.

As if these issues are not enough, Merck faces two additional internal struggles with potentially significant ramifications. First, Merck continues to suffer fallout from drug recalls, which most famously include the arthritis and acute-pain medication, Vioxx. Merck invested almost $1 billion in the research and development of Vioxx, bringing the novel therapy to market in a record time of just six years. Upon the launch of Vioxx in May 1999, Merck's revenues increased by over 10 percent. However, increasing controversy in the medical community over the allegation that Vioxx caused heart attacks and strokes tarnished Merck's otherwise spotless reputation. On September 30, 2004, Merck announced the voluntary withdrawal of Vioxx from the market. The recall had a terrible impact on Merck's stock price and adversely affected the sales of Merck's other drugs. Shares fell 27 percent to $33, eradicating $27 billion in market value almost overnight. Merck has been burdened by lawsuits ever since and is still settling litigation claims throughout the United States and internationally. It is estimated that legal liabilities have cost Merck in excess of $30 billion thus far.[8] Merck also faces ongoing litigation related to Fosamax, a treatment for osteoporosis, which has been identified as a possible cause of femoral fractures and general bone necrosis/weakness.[9] Claims have not yet reached the magnitude of Vioxx, but the ongoing court battles are tarnishing Merck's reputation even further.

Second, Merck continues to face restructuring pressures following the SP merger. After the deal was brokered, restructuring of operations commenced in 2011 and was centered largely on eliminating sales, administrative and headquarter positions and the disposal or consolidation of manufacturing and R&D sites. The restructuring program was substantially completed by the end of 2013, culminating in the elimination of over 26,000 positions throughout the organization. In sum, the restructuring from the merger cost approximately $3.8 billion over a two-year period. This was over and above the global restructuring initiative the company undertook in 2013, which is projected to set the company back $2.5 to $3 billion by the time it is completed in 2015.[10]

Schering-Plough Merger

In 2008, Merck had 59,000 employees, sales revenues of $23.9 billion, and a market value of $44.4 billion. Schering-Plough (SP) had 51,000 employees, sales revenues of $18.5 billion, and a market value of $32.6 billion.[11] The joining of these two former rivals in March 2009 was seen as a necessary step toward diversification and increased economies of scale, propelled by imminent patent expirations and increasing pressure from shareholders, government, and customers to control costs. The newly formed Merck became the second largest pharmaceutical company by market share and the fifth largest by market cap. Currently, Merck is fifth by market share of worldwide prescription drug sales, and

fourth largest by market cap (See **Exhibits 2–4** for current comparative rankings and financial data for the global leaders in the pharmaceutical industry).

At the time, Merck Chairman and CEO Dick Clark justified the deal as follows: "The combined company will benefit from a formidable R&D pipeline, a significantly broader portfolio of medicines, and an expanded presence in key international markets, particularly in high-growth emerging markets."[12,13] As a result of acquiring SP, Merck gained a substantial new pipeline of compounds undergoing clinical investigation toward FDA approval (**Exhibit 5** shows Merck's current blockbuster drugs, with sales over $1 billion annually). Merck also gained an enhanced international presence, expanding its international footprint to over 140 countries. For the first time in its history, Merck expected that more than 50 percent of its revenues would come from outside of the United States.[14] In addition, Merck's yearly savings resulting from this merger were forecast to be as large as $3.5 billion after 2011.

The SP merger was the first major external venture Merck had participated in since 2006, when Dr. Turner led Merck's acquisitions of biotechnology firms GlycoFi and Abmaxis for a combined total of $480 million. In December of that same year, Dr. Turner also led the much larger acquisition of Sirna Therapeutics for $1.1 billion. Such strategic purchases helped to strengthen Merck's drug pipeline, and its stock price immediately rose more than 1 percent to a total of $34.84.[15] After Merck's announcement of the merger with SP, however, SP's stock rose by 14 percent to end the day at $20.13 a share, while Merck's stock price fell 7.7 percent to close at $20.99 a share.9 In the aftermath of the megamerger, the stock price of the combined entity traded between $30 and $40 for almost three years.

Indeed, throughout this period there were a number of questions about whether or not Merck had been wise to proceed with this transaction.[16] It is true that the company acquired a strong late-stage pipeline of drugs with tremendous promise to treat hepatitis C, osteoporosis, and heart disease, all markets that had the potential to generate blockbuster revenues. The new entity also experienced unprecedented geographical reach, particularly in emerging markets.[17] However, Merck ran into trouble in the clinical development of two drugs that were central to the $41 billion price tag associated with the merger. First, the blood thinner vorapraxar stumbled in development after being associated with an elevated risk of bleeding,[18] and shortly thereafter, sugammadex (indicated for reversal of the effects of anesthesia) was rejected by the FDA.[19] Both drugs originated from SP and their blockbuster potential was integral to the valuation of SP at the time of merger negotiations (vorapraxar was considered the crown jewel in SP's pipeline).[20] Their failure thus raised questions as to whether Merck had overpaid for SP and how much value Merck could generate from the SP pipeline it had acquired. The merger also added significant complexity to Merck's structure, businesses, and geography of operations, creating numerous implementation issues.

Consolidation of the Pharmaceutical Industry

The pharmaceutical industry is one of the largest and most profitable in the world, serving as a significant engine for innovation that supports an entire ecosystem of peripheral industries. In 2011, biotechnology and pharmaceutical companies combined created approximately 813,000 direct jobs and 3.4 million total indirect and induced jobs in the United States alone.[21] The industry sector accounted for almost $790 billion or 3 percent of total U.S. economic output. In 2011, the U.S. pharmaceutical market grew by about 4 percent to approximately $320 billion; however, 2013 showed a 1 percent contraction. Sales in 2014 are forecast to return to 2011 levels, as a result of a 2 percent growth rate (see **Exhibit**

6). Projecting forward, the industry is expected to continue to grow at a rate of 2 to 4 percent annually (CAGR). Globally, sales are anticipated to breach the $1 trillion mark in 2014.[22,23] Developing markets show particularly strong potential, with projected annual growth rates of 10 to 13 percent (CAGR).

The Merck-SP merger is just one example in a recent series of mega-deals in the pharmaceutical industry, which has been undergoing rapid consolidation. Drug companies across the board are experiencing acute declines in sales as multiple blockbuster products lose their patent protection and succumb to competition from generic drugs. The pharmaceutical industry in total is expected to lose as much as $94 billion through 2019 (see **Exhibit 7**). In response, many firms—like Merck—have recently acquired or merged with others to keep their pipelines stocked full of potential drug candidates (see **Exhibit 8**). [24] Smaller companies and biotech firms have eclipsed the R&D productivity of pharmaceutical giants like Merck. Acquiring these niche players therefore provides the larger companies access to a wealth of new therapies which can then be ushered through the FDA drug development process; something which big pharma is well equipped to do. Thus, Novartis bought Chiron for $5.4 billion in 2006, while AstraZeneca bought MedImmune for $15.6 billion in 2007. In the same year that Merck spent $41 billion to take on SP, Pfizer announced its takeover of Wyeth for $68 billion, and the Swiss firm Roche bought the remaining 44 percent of shares of biotech wunderkind Genentech for $47 billion. In March 2009, the CEO of Eli Lilly declared that the company, even after it had acquired ImClone for $6.5 billion, was still looking for additional acquisitions worth as much as $15 billion.[23] In 2011, Carl Icahn helped to orchestrate Sanofi's acquisition of Genzyme for $20 billion, the last significant tie-up between a pharmaceutical giant and a major biotech firm.

More recent years have seen fewer large-scale mergers and acquisitions (**Exhibit 9**), but instead have highlighted a related trend: more focused purchases of smaller companies and/or products aligned with a company's traditional therapeutic strengths and interests alongside the shedding of non-core businesses.[32] For example, Gilead, traditionally the leader in anti-HIV treatments, bought Pharmasset for $11 billion in 2011, giving the company an expanded anti-viral drug portfolio that included a promising hepatitis C drug.[27, 28] AstraZeneca bought Bristol-Myers Squibb's share of their preexisting partnership in diabetes in 2013 for $4.1 billion.[29, 30] 2014, Novartis bought GlaxoSmithKline's entire oncology unit for $14 billion at the same time that GlaxoSmithKline bought Novartis' vaccine unit for $5.4 billion.[31] Also in 2014, Merck sold its consumer health business to Bayer for $14 billion.[32, 33] Merck had acquired the consumer health business as part of the SP deal but was not traditionally active in this area of health care.

Another driver of recent M&A activity has been the tax inversion phenomenon. Tax inversions are tie-up deals where one of the primary motivations for the acquirer is to obtain a more efficient tax structure. In the pharmaceutical industry, this has typically involved a U.S.-based company seeking to acquire a competitor based in another country, affording the U.S.-based company the opportunity to move its corporate headquarters abroad to take advantage of more favorable corporate tax rates.[34, 35] This trend has played out in a number of scenarios, including Pfizer's (NY-based) contentious bid to takeover AstraZeneca (London-based) for $120 billion, which would have created the world's largest pharmaceutical company by sales.[36, 37] Similarly, U.S.-based AbbVie attempted to purchase Irish-based Shire Pharmaceuticals for $54 billion.[38] Both deals collapsed after the U.S. Treasury and Congress each issued new rules aimed at halting inversion-related transactions in late 2014, although the environment could turn more favorable again under the newly elected, Republican-controlled legislature.[39, 40, 41] Pfizer has since been rumored to be examining other potential European targets such as Actavis, a Dublin-based generic drug manufacturer.[42]

However, horizontal consolidation may not address the lack of innovation in the pharmaceutical industry as a whole. Many analysts fear that consolidation, while facilitating cost containment, will hinder breakthrough R&D needed to procure long-term, life-saving drugs. The concern is that "making R&D bigger does not make it more efficient,"[43] and that the large, bureaucratic organizations created through such M&A activity stifle the innovation needed to create new knowledge and products. A recent research study showed that as companies merge, the number of development projects declines by 34 percent as the combined companies trim their product pipelines.[44] Consequently, most mergers in the pharmaceutical industry neither achieve the anticipated synergies nor increase shareholder value. Partially in response to this criticism, big pharmaceutical outfits like GlaxoSmithKline have sought to break up their R&D operations into smaller, more nimble groups. The results of this decentralized approach on productivity and efficiency are still to be determined.[45, 46]

Drug Discovery, Development, and the FDA Approval Process

The science-driven process for drug development takes an average of 12 years and may exceed $1 billion (see **Exhibit 9**). It is estimated that out of every 5,000 to 10,000 compounds screened in the discovery phase, only 250 enter preclinical testing. Only five of those molecules enter the three phases of clinical testing, which is where most of the development costs are incurred. Companies must conduct large-scale clinical trials, in hundreds of patients, to demonstrate that a drug has adequate safety and efficacy before filing a new drug application (NDA) or biologics license application (BLA) with the Food and Drug Administration (FDA). An FDA advisory council then reviews the data provided by the company and holds a public hearing to determine if approval will be granted. Once approved, the drug is designated as a new molecular entity (NME) or new biologic and is cleared to be marketed exclusively for the approved indication(s).

Drug development has always been a costly and risky process. During the mid-2000s, spending accelerated rapidly, but it was tempered by the 2007–2009 global financial crisis. From 2006–2013, worldwide growth in R&D spending by pharmaceutical and biotech companies averaged 3.4 percent (CAGR, see **Exhibit 10**), with total spending reaching $137 billion in 2013. To put these numbers into perspective, the average cost to develop a NME (approved drug) is somewhere in the order of $3.7 billion (see **Exhibit 11**). Despite continued increases in R&D spending by pharmaceutical and biotech companies (see **Exhibit 12**) in recent years, there has been no corresponding increase in FDA approvals, suggesting that companies are actually becoming less efficient at getting new products to market. One study actually showed no correlation between the size of the R&D budget and productivity in 40 pharmaceutical firms from 1993 to 1998.[47] Moreover, only one of every five drugs that hits the market actually achieves enough financial success to recoup its investment.[48]

When a new drug provides a breakthrough for the health of a large patient population, it may reach sales levels of a "blockbuster." A blockbuster drug in the 1980s and 1990s was one whose annual sales topped $500 million. Since 2000, a drug must have annual sales of at least $1 billion to achieve blockbuster status. Despite predictions that the business model based on patent-protected blockbuster drugs is slowly dying, the number of blockbuster drugs has actually tripled in the last decade.[49] In 2006, 101 drugs each sold more than $1 billion worldwide.[50] Of these, 21 were biotechnology innovations (bioengineered vaccines and biologics). By 2013, 45 of the top 100 selling products worldwide were biotech innovations (see **Exhibit 13**), and it is estimated that this number will rise to 52 by 2020.[51]

Consequently, major pharmaceutical firms rushed to partner with or acquire biotech companies, hoping to discover the next great medical breakthrough and then apply their competencies in development, distribution, and marketing to maximize its profit potential. As of 2013, biotech product sales comprised up to 74 percent of worldwide sales by major pharmaceutical companies (see **Exhibit 14**). Yet biotechnology has hardly turned out to be the hoped-for panacea for the pharmaceutical companies' R&D problems.[52] Instead of providing more lucrative alternatives to traditional pharmaceuticals, the average R&D cost for a new biotech product is comparable to that of a new molecular entity, at a price tag of approximately $1.6 billion.[53] As a result, drug companies which anticipated accelerated FDA approvals at decreased costs through diversification via mergers with or acquisitions of biotechnology firms have been disappointed to find that profits have remained close to zero.

Affordable Care Act

Pharmaceutical companies face additional price pressures driven by changes in U.S. and worldwide regulatory restrictions on the industry. In March 2010, Congress approved and President Obama signed the Affordable Care Act (ACA) into law, creating significant uncertainties for health care companies. Under the new law, patients have increased access to health care, whether through Medicaid, subsidized employer plans, or state-run medical exchanges. Insurance companies are no longer able to impose lifetime limits, and coverage can no longer be denied for preexisting conditions. Nearly everyone is required to get insurance or pay a penalty, meaning that the law will likely expand the number of patients paying for prescription drugs.[54] Another change that is likely to benefit both pharmaceutical firms and patients is that insurers may no longer drop or limit coverage on individuals who participate in clinical trials for cancer or other life-threatening diseases.[55]

However, other aspects of the ACA law are likely to have a deleterious effect on pharmaceutical companies, at least in the short term. Namely, the ACA mandates pharmaceutical companies to increase the rebate given to Medicaid subscribers on prescription drugs. Pharmaceutical companies are also subject to the "donut hole": a phenomenon whereby Medicare (specifically, Part D) beneficiaries experience an insurance coverage gap. In this case, pharmaceutical companies are required by law to pay a 50 percent point of service discount to any beneficiaries seeking prescription drugs who lack insurance coverage. Merck incurred a revenue reduction of approximately $280 million in 2013 on account of these legal provisions. On top of this, pharmaceutical manufacturers are required to pay an annual health care reform fee, which cost Merck an additional $151 million in 2013.

Pharmaceutical firms rank second only to the tobacco industry in the corporations-hated-most department and have frequently been blamed by politicians for the nation's health care woes.[56] In an attempt to place its constituent firms in a more positive public relations light, the Pharmaceutical Research and Manufacturers of America (PhRMA), an industry advocacy group, made an unexpected $80 billion pledge over the next 10 years to help pay for health care reform. Its hope was to position pharmaceutical companies to take advantage of the enormous new customer base that would be created by expanding health care coverage. PhRMA's investment could potentially backfire, though, if the government uses its increased purchasing power to squeeze margins on prescription drugs and accelerate the shift to generics.

The Generic Challenge

The generic drug manufacturers also have a strong political lobby, the Generic Pharmaceutical Association (GphA). GphA is perceived as the voice of the American public, demanding ever-lower drug prices and pushing for importation of generics from foreign companies such as Israeli-based Teva Pharmaceuticals, the largest supplier of generic prescription medicines in the United States.[57] Generics as a percentage of all drug prescriptions grew from 68 percent in 2008 to 83 percent in 2013; the share of sales of generics increased from 14 percent to 22 percent over the same period.[58] Examination of the largest generic drug makers (**Exhibit 15**) shows that even those companies that have traditionally focused on branded, blockbuster drugs are becoming increasingly active in the generic industry. Because a loss of sales is inevitable after a new drug patent expires and generics reap the benefits, the major pharmaceutical companies are increasingly deciding to cannibalize themselves.

The legal basis for generic drugs dates back to the Hatch-Waxman Act of 1984, otherwise known as the Drug Price Competition and Patent Term Restoration Act of 1984. Under the Hatch-Waxman Act (which does not apply to biologics), the FDA may approve a generic drug in the form of an Abbreviated New Drug Application (ANDA) if the generic company can establish that its product is "pharmaceutically equivalent" to the drug it wishes to copy.[59] No clinical trials are required, which confers an important cost advantage on the generic manufacturers over the brand-name companies that developed the original compound. In essence, this law permits generic firms to copy the work of large pharmaceuticals without the up-front risk or cost, and then sell their copy-cat products at a discount. When a generic company files an ANDA, it also makes a patent certification claim, the most disruptive of which is Paragraph IV, alleging that the listed patent is invalid and will not be infringed upon. This provides generic companies with the right to copy an innovator's drug as soon as its exclusivity period elapses. The standard exclusivity period is five years for a new molecular entity, but there are additional provisions for special cases: seven years for "orphan drugs" (indications with a prevalence of less than 200,000 cases per year), three years for a new use or formulation, and six months for a pediatric drug.[60]

The generic industry continued to grow with the 2003 Medicare Act Amendments, which implemented several new rights for generics and limitations for the pharmaceutical industry. First, it increased regulation regarding agreements between generic companies and innovators. Next, it considered not one company, but all generic companies that file on the same day to be "first-filers," each with legal claims against the original patent. As a result, 2003 became the year that many more generic companies than ever before began to embrace Paragraph IV challenges as a viable strategy. By 2012, over 200 generic companies had active Paragraph IV filings, compared with fewer than 40 in 2001 (**Exhibit 16**).[61] A multitude of new players entered the generic industry, meaning that pharmaceutical companies like Merck now find virtually all of their commercially viable products under attack as soon as their patent protection expires.

Historically, biotechnology firms have not faced the same level of generic competition that makers of new molecular entities do when their patents expire. Prior to 2010, the FDA lacked authority to even approve generic biotechnology products. This changed with the passage of the Biologics Price Competition and Innovation Act, which finally cleared the pathway for the development of "biosimilars" through an abbreviated FDA approval pathway. However, the development of biosimilars is to take place under closer scrutiny than that of conventional generics given that, according to European

and U.S. regulators, biosimilarity does not imply interchangeability.[62, 63] Given the complexity of developing biologics that mimic the actions of branded counterparts, the safety of biosimilars remains an important question. Nevertheless, roughly $30 billion in U.S. sales of biologics will be lost due to patent expiration by 2020. With stakes this high, companies like Merck, Novartis, and Pfizer are themselves stepping up efforts to develop biosimilars that can tap into this significant market.[64]

Open Innovation[65]

With increasing pressures from the political sphere, regulatory environment, and generic competition, the strategic mantra for the pharmaceutical CEO is simple: innovate or die. The more challenging question is how to go about achieving this mission. According to the closed-innovation philosophy adopted by most pharmaceutical giants in the 20th century, successful innovation requires complete control. A company generates its own ideas and develops, manufactures, markets, and distributes the resulting products alone. This closed approach worked especially well for Merck in the past, forming a virtual circle in which fundamental scientific breakthroughs led to new drugs and increased sales, which were poured back into more R&D investment to create more new discoveries.[66] However, with the rise of the Internet and the increased mobility of knowledge workers (individuals, such as scientists, engineers, physicians, and consultants, valued for their ability to work with complex information and data), companies heavily dependent on human capital are increasingly unable to protect their intellectual property, causing the closed-innovation system to break down. This effect is further compounded by the ready availability of venture capital to fund risky startups. These changes were precisely what had prompted Mervin Turner, Merck's former CSO, to shift the company's R&D activities towards a more open-innovation paradigm.

Open (as opposed to closed) innovation involves companies opening up their business models by actively searching for and exploiting outside ideas, as well as allowing unused internal technologies to flow to the outside where other firms can unlock their latent economic potential (see **Exhibit 17**). Firms seek external R&D by bringing in new human capital, engaging in strategic alliances, or acquiring technology ventures, while continuing to innovate internally. At the same time, any internal inventions that the firm decides not to pursue are considered for commercialization through licenses, spin-offs, or joint ventures. Research indicates that fewer than half of companies actually use their patented technologies because the innovation either costs too much to develop, its potential value is uncertain, or it does not fit the company's business strategy. As a consequence, patented technology too often sits on the shelf.[67] Such inefficiencies in the innovation market are overcome when companies open up and share ideas, permitting technologies to flow freely to where they can be developed most efficiently. See **Exhibit 18** for a comparison of closed- and open-innovation principles.

Of course, open innovation comes with high risks that make many scientists, fiercely protective of their research and intellectual property, uncomfortable. It may be difficult for a company to capture the value that open innovation creates. While open innovation systematically increases the availability of knowledge by finding highly capable partners for scientific collaboration, it also inevitably leads to the loss of individual control over potentially invaluable technology. As a result, a company may end up giving away a billion-dollar patent to its direct competitor because it does not understand the value of a discovery. This loss of control coupled with uncertain monetary outcomes has led many scientists to wonder whether open innovation is worth all the hype. Is it really necessary to change?

Open Innovation at Merck

Merck found this new industry terrain especially challenging. The company had long relied on its ability to pump out blockbuster drug after blockbuster drug from its internal research pipeline. It would charge a premium under patent protection for the duration of the legally set exclusivity periods for existing drugs to help cushion the company's R&D costs for the next innovation. Former CEO Henry Gadsden once said, "We'd cut back in every part of the company. We'd cut back in sales and promotion. We'd tighten up our production. We'd do everything we could to hold down costs. But we'd try very hard not to cut back on research because that's our future."[68] This philosophy continues to play out in Merck's operations: in 2013, Merck spent approximately 17 percent of its (declining) revenues on R&D, despite the expenses associated with the SP acquisition. Merck leads the industry in terms of R&D spending because Merck believes that if it is the first to discover and develop a new drug, it will be the first to market. Merck's culture and organizational systems further perpetuate this logic. Because Merck hires the best people, the smartest people in the industry must work for Merck, and so the best discoveries must be invented at Merck.

Consequently, few people outside of the company truly appreciated the radical change that the SP merger represented for Merck. Changing from a closed-innovation system to operating within an open-innovation network required a fundamental shift in the company's mindset. Merck's researchers were simply not accustomed to listening to "outsiders"; they suffered from a severe case of "not invented here" syndrome, meaning that if a product was not created and developed at Merck, it could not be good enough.[69] In order to facilitate behavioral change among Merck's top scientists, Dr. Turner had even sent them to "charm school" where they could learn how to be courteous when corresponding with non-Merck people.

However, the jury is still out as to whether the deal will deliver the anticipated benefits. On the one hand, 55 percent of SP's new drugs originated from external sources, a significant infusion of new technology for Merck, where over 66 percent of R&D projects originate in-house. This represents a significant opening up of Merck's research ecosystem. A study by the Boston Consulting Group (BCG), which covers the top pharmaceutical industry alliances, shows how Merck has steadily climbed the rankings since 2006 to become best in class.[70,71] Critically, this was at a time where there was significant competition among smaller drug discovery and development outfits to partner with big pharmaceutical firms. On the other hand, Merck has not yet managed to convert potential blockbusters in the SP pipeline at the time of the merger into the string of pearls that the deal promised, with the two high profile development hiccups of vorapraxar and sugammadex as prominent examples. With such ambivalent results from its first major foray into an open-innovation environment, the likelihood that Merck will continue to expand its innovation boundaries through future cross-company transactions remains uncertain.

Still, Kenneth Frazier could see that several of Merck's competitors were well on their way to leveraging external research capabilities and feared that Merck would be left behind if it did not start to pursue outside opportunities more aggressively. For example, InnoCentive, a formerly wholly owned subsidiary of Eli Lilly, offers firms a mechanism to facilitate the development and commercialization of new technology. Using a global network of independent researchers, InnoCentive acts as a knowledge broker and facilitates the exchange of technological know-how, primarily associated with chemistry and biotechnology. Through this system of open innovation, InnoCentive has realized a success rate that is higher than the traditional internal R&D approach, at approximately one-sixth the cost.[72]

More specific to pharmaceutical companies, AstraZeneca has been active in reaching out to independent scientists via its Target Innovation Programme, soliciting proposals for new drug targets with the incentive of $100,000 grants and access to AstraZeneca facilities to further explore new ideas.[73] Similarly, Pfizer has established The Global Centers for Therapeutic Innovation that aim to fill the company's pipelines with drugs resulting from company-academic teams, who work side-by-side to speed drug discovery efforts.[74] Collectively, GlaxoSmithKline, Roche, and AstraZeneca are making previously prized and closely guarded raw data on drug development and clinical trials open to one other and to external scientists, with the aim of expediting the development of new therapeutics.[75, 76] Meanwhile, as a consequence of its historically closed R&D system, Merck has the lowest percentage of new approved drugs based on externally derived technology.[77] In 2014, Merck was ranked as the sixth most successful company by total number of active R&D projects, falling from third place in 2012 (see **Exhibit 19**).

Open Innovation: The Next Step

To help facilitate Merck's adaptation to the new industry norm, Kenneth Frazier hired Roger Perlmutter as president of research in March 2013.[78] Dr. Perlmutter had served as a prior Merck executive from 1997 to 2001, but then he left to become executive vice president and head of R&D at biotech giant Amgen from 2001 to 2012. While there, he ushered some of Amgen's most successful biotech products through the development process to market. With his return, Perlmutter brought some much-needed expertise in biologics back to Merck, which had inherited a portfolio of biotech treatments for the hepatitis C virus (HCV) as part of the SP acquisition. In fact, SP was in the process of developing its first HCV therapy, a protease inhibitor now called Vectrelis, at the time the megamerger was completed. Merck subsequently managed to gain FDA approval for the new biologic in May 2011 and has since become one of the most active players in HCV drug development. Analysts have conservatively estimated that the HCV market may balloon to $20 billion, making it a highly lucrative area for future research.[79]

However, the HCV market has changed tremendously since 2009 when Merck first acquired Vectrelis. Back then, treatment for HCV lasted 48 weeks and cured only 40 percent of cases. Patients also had to endure flu-like symptoms along with other side effects, which often prevented them from completing the treatment course successfully. Vectrelis pioneered a different approach to treating the disease, boosting the cure rate to 75 percent. However, patients were still required to take up to a dozen pills daily, and the flu-like side effects remained.

The landscape of the HCV market shifted yet again in December 2013, when the FDA approved a breakthrough product developed by antiviral specialist Gilead. SolvadiTM (sofosbuvir) is a once-a-day pill, with the potential to cure 80 to 90 percent of patients without any of the detrimental side effects. Gilead's advantage lies in the use of a nucleoside analog to prevent viral replication, an approach that has been used for decades to treat HIV. Despite its hefty $84,000 price tag, Solvadi rapidly gained traction among prescribing physicians, netting sales of nearly $9 billion in its first nine months on the market.[80] Gilead's second blow came in October 2014 with the FDA approval of Harvoni, a combination of sofosbuvir and another agent (ledipasvir) in a single pill taken just once a day. While the stand-alone price of $94,500 per 12-week regimen is more than Solvadi, the overall cost is less because it eliminates

the need for co-treatment with other HCV drugs (which either have troublesome side effects or come with their own high prices).[81] To make matters worse, AbbVie entered the fray with the December 2014 approval of its first HCV combination therapy, Viekira Pak, consisting of four different anti-viral pills to be taken daily. Both Harvoni and Viekira Pak boast cure rates of 95 percent to 100 percent, but the AbbVie medication is competitively priced at $83,319 per treatment.[82] Meanwhile, other major pharmaceutical companies like Bristol-Myers Squibb are working on bringing their own HCV combination regimens to market.

Merck does not have a traditional strength in the development of nucleoside-based therapies. There is no time for Dr. Perlmutter to put into place Merck's own nucleoside development program without losing ground to the likes of Gilead, AbbVie, and Bristol-Myers Squibb. Rather, if Merck is to remain a player in the increasingly competitive HCV market space, Dr. Perlmutter knows he has to consider the possibility of acquiring an existing nucleoside pipeline. He also knows this will be a hard sell to several members of Merck's executive team who recently pointed to Merck's lackluster financial performance after the SP merger (see **Exhibit 1**) as support for their belief that "Merck [sh]ould not consider large-scale mergers which might provide short-term benefits, but would not add to long-term growth prospects of the company."[83]

The company Perlmutter has been eyeing is Idenix, a specialist in nucleoside-based molecules with a pipeline that complements Merck's own HCV candidates nicely. Merck and Idenix were engaged in talks of collaboration when another company made a bid to buy Idenix, creating a competitive bidding situation.[84] Idenix was established in 1998 and had gained the attention of the big pharmaceutical companies early on. By 2003, Novartis had acquired a controlling stake in the company, attracted by Idenix's promising work in hepatitis.[85] The company subsequently went public in July 2004, raising $81 million on the open market.[86] By 2009, however, Novartis walked away from its option on Idenix's lead HCV drugs, which were struggling in clinical development.[87] Novartis' actions proved to be prophetic: by 2012, the FDA had placed a clinical hold on two of Idenix's lead drug candidates citing life-threatening side effects to patients enrolled in clinical trial investigations.[88, 89] By February 2013, the company ceased development work on both compounds.[90] Four months later, the FDA demanded more safety data on another of Idenix's lead HCV compounds.[91]

Shareholders were understandably rattled by the ongoing troubles that Idenix was experiencing in the clinic: in the space of 18 months, the stock price shed 74 percent dropping from $14 in January 2012 to $3.60 in July 2013. Still, Perlmutter believes the acquisition of Idenix and its remaining HCV candidates is potentially worth the risk, considering the billions in revenues that a successful HCV pill would bring. Analysts have speculated that the acquisition would make the hepatitis market a "two-horse race between Gilead and Merck."[92]

Ironically, Mr. Perlmutter finds himself facing a similar situation to what motivated him to leave Merck for Amgen back in 2001. He recalls how he and then-CEO Ray Gilmartin grew increasingly at odds over Merck's R&D strategy, and how he had told Mr. Gilmartin that Merck had become "really hidebound and risk averse and wasn't willing to take on new initiatives." [93] To Perlmutter, this not only included a move to newer (at the time) protein-based drugs made by biotech companies, but also to small molecule drugs.[94] Although Gilmartin could be excused for a risk averse approach after the Vioxx debacle that continued to tarnish Merck's reputation even today, Perlmutter still feels that Merck is not moving fast enough to adopt strategies that will ultimately keep it at the cutting edge of research.

Dr. Perlmutter saw firsthand at Amgen how a large biopharmaceutical company could successfully parlay its research discoveries to become a major player in the biotechnology industry through open innovation.[95] The question is whether he can convince Mr. Frazier and the other members of Merck's top management team to take a chance on yet another major acquisition while they are still dealing with the fallout from the SP merger.

Pulling the Trigger

As Mr. Frazier takes his seat in his office, he starts to page through the due diligence on Idenix's drug pipeline that Perlmutter and his team have put together. He is well aware of the market's impression of Idenix's pipeline of Hepatitis C (HCV) drug candidates. Worse yet, he also knows that the hiccups that the Idenix candidates have experienced in the clinic mean that the FDA will closely scrutinize any further clinical development involving these compounds. Idenix is indeed a risky acquisition target, but he has never shied away from a challenge, and he is not about to begin tempering his ambitions now.

Time is of the essence. Gilead is already generating substantial revenues from both Solvadi and Harvoni, and other companies are rapidly adding their own products to the mix of available HCV therapies. Delaying a decision whether to acquire Idenix would not only result in further lost ground, but it would invite potential disaster by having a competitor preemptively acquire the company first. But Frazier also knows that this is not a simple decision. The SP megamerger and its lackluster results are still fresh in the minds of his scientists and Merck's management team. Not only would this be the biggest acquisition Merck has undertaken since the SP deal, but the nature of Idenix and its product portfolio would significantly test the risk tolerance of Merck's conservative corporate culture.[96] Moreover, he is not so sure that Merck can successfully develop the lead nucleoside candidates from Idenix—aside from the extra scrutiny from the FDA, Merck is new to developing these kinds of compounds.

As he positions himself in front of his computer screen to begin drafting his recommendations to the board, Mr. Frazier cannot help but wonder whether the Idenix acquisition will be capable of delivering the benefits that the SP merger has not. More importantly, is it enough to compete with Gilead in the HCV market? And can Merck feasibly accelerate development of a drug class that the company is new to, without repeating a Vioxx-like catastrophe? With a deep breath, he sets to work . . .

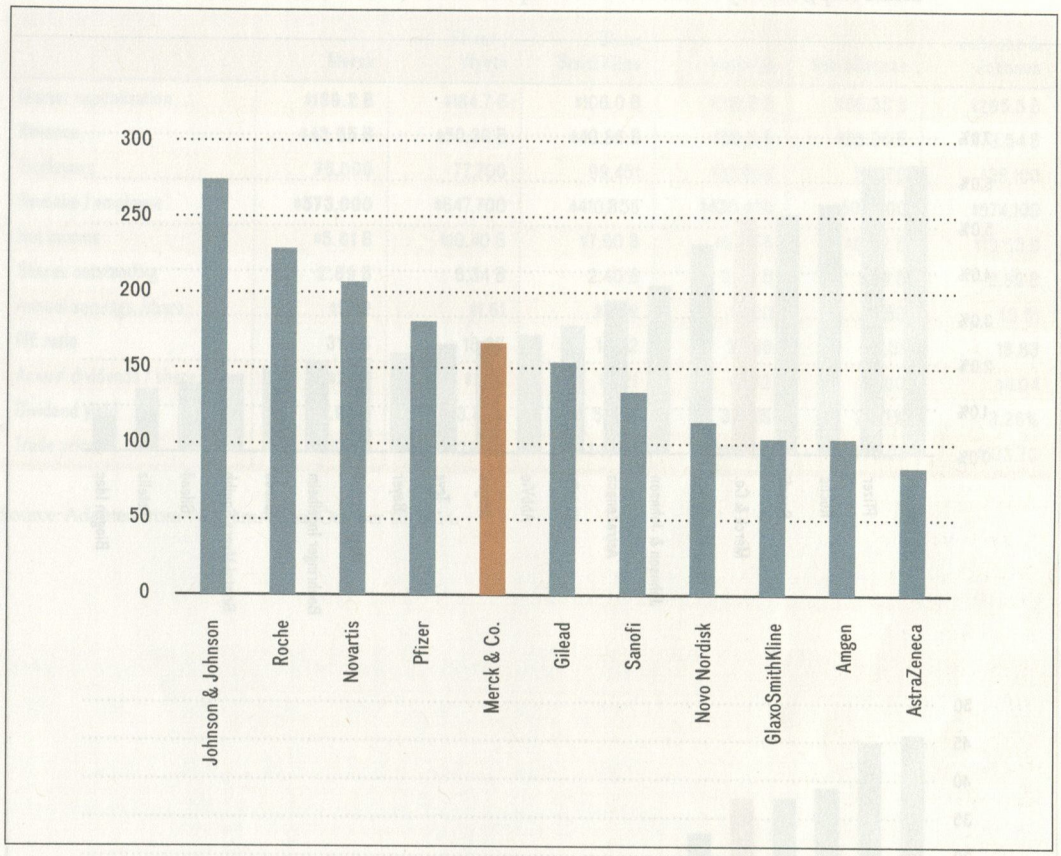
EXHIBIT 1 Selected Financial Data for Merck & Co., Inc. and Subsidiaries
($ millions, except EPS data)

	2013	2012	2011	2010	2009
Cash and Short-Term Investments	17,486	16,141	14,972	12,201	9,605
Receivables - Total	7,184	7,672	8,261	7,344	6,603
Inventories - Total	6,226	6,535	6,254	5,868	8,055
Property, Plant and Equipment - Total (Net)	14,973	16,030	16,297	17,082	18,274
Depreciation, Depletion, and Amortization (Accumulated)	18,121	17,385	16,176	13,481	12,595
Assets - Total	105,645	106,132	105,128	105,781	112,090
Accounts Payable - Trade	2,274	1,753	2,462	2,308	2,237
Long-Term Debt - Total	20,539	16,254	15,525	15,482	16,075
Liabilities - Total	53,319	50,669	48,185	48,976	50,597
Stockholders Equity - Parent	49,765	53,020	54,517	54,376	59,058
Sales/Turnover (Net)	44,033	47,267	48,047	45,987	27,428
Cost of Goods Sold	9,570	9,379	9,304	8,916	4,948
Selling, General and Administrative Expense	18,795	20,461	21,341	21,363	13,899
Income Taxes - Total	1,028	2,440	942	671	2,268
Income Before Extraordinary Items	4,404	6,168	6,272	861	12,901
Net Income (Loss)	4,404	6,168	6,272	861	12,901
Earnings Per Share (Basic) - Excluding Extraordinary Items	1.49	2.03	2.04	0.28	5.67
Earnings Per Share (Diluted) - Excluding Extraordinary Items	1.47	2.00	2.02	0.28	5.65

Source: S&P Capital IQ Compustat.

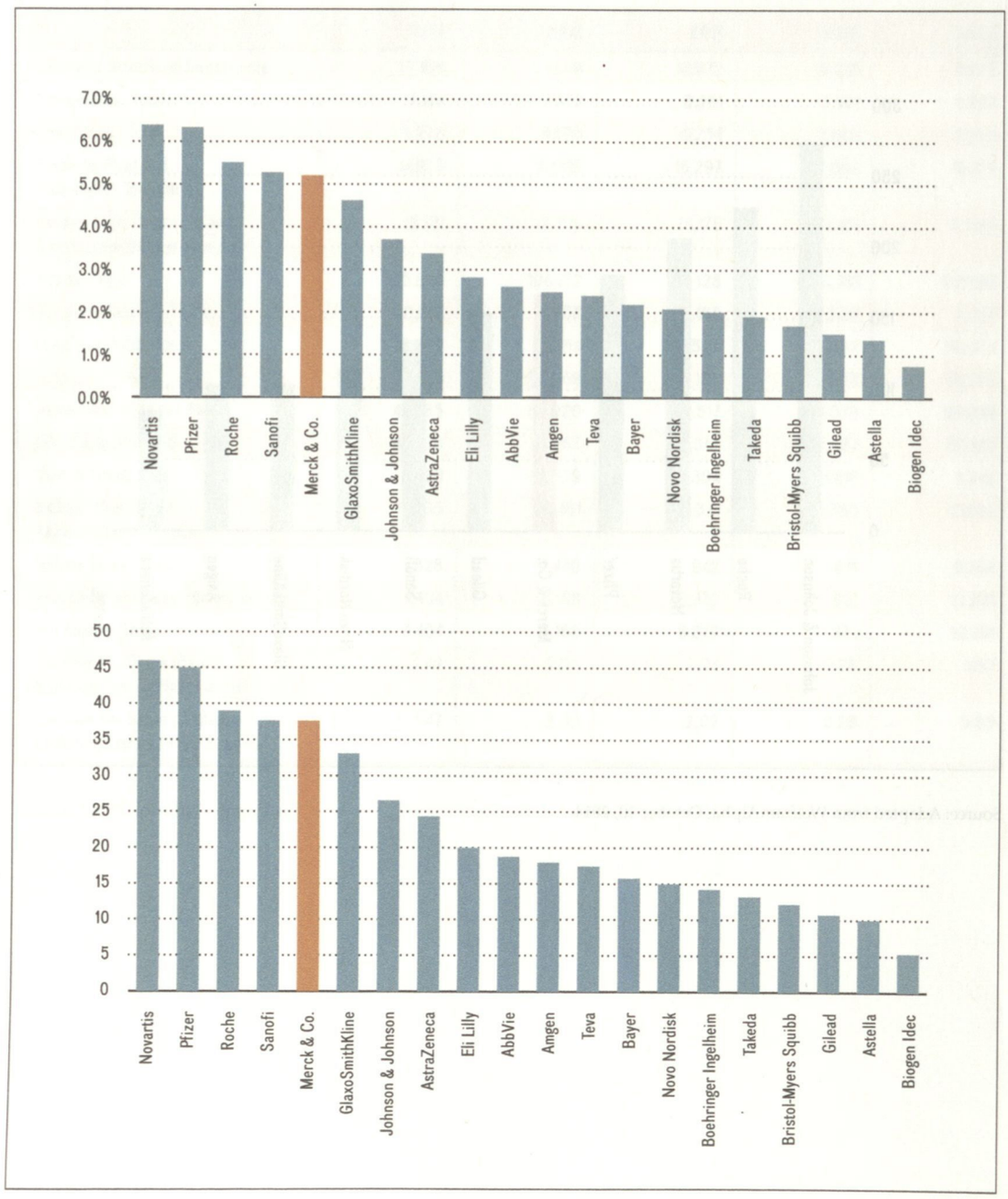
Merck & Co., Inc.

EXHIBIT 2 The Largest Pharmaceutical Players by Market Capitalization ($ billions)



Source: Adapted from WolframAlpha, October 10, 2014.

EXHIBIT 3 Global Rankings of Pharmaceutical Firms by Worldwide Prescription Drug Market Share (top), and by Worldwide Prescription Sales (bottom) ($ billions)



Source: Adapted from *EvaluatePharma® World Preview 2014, Outlook to 2020*, June 2014.

Merck & Co., Inc.

EXHIBIT 4 Financial Data for the Global Leaders in the Pharmaceutical Industry

	Merck	Pfizer / Wyeth	Glaxo SmithKline	Novartis	AstraZeneca	Johnson & Johnson
Market capitalization	**$169.2 B**	$184.7 B	$106.0 B	$212.8 B	$86.38 B	$285.5 B
Revenue	**$43.55 B**	$50.33 B	$40.86 B	$58.11 B	$25.96 B	$73.54 B
Employees	**76,000**	77,700	99,451	135,000	51,500	128,100
Revenue / employee	**$573,000**	$647,700	$410,856	$430,400	$504,200	$574,100
Net income	**$5.61 B**	$10.40 B	$7.90 B	$9.76 B	$2.02 B	$15.55 B
Shares outstanding	**2.89 B**	6.34 B	2.40 B	2.43 B	1.26 B	2.82 B
Annual earnings /share	**$1.92**	$1.61	$3.29	$4.00	$1.60	$5.51
P/E ratio	**31.36**	18.27	14.92	22.46	47.51	18.83
Annual dividends / share	**$2.19**	$1.50	$3.21	$2.72	$2.80	$4.04
Dividend yield	**2.93%**	3.47%	5.41%	3.03%	2.50%	3.26%
Trade price	**$60.11**	$29.39	$49.10	$89.84	$76.01	$103.73

Source: Adapted from WolframAlpha, October 10, 2014.

EXHIBIT 5 Merck's Blockbuster Drug Lineup ($ billions)

Drug	Indication	2011 Sales	2013 Sales
Singular	Asthma	$5.5	$1.2
Cozaar/Hyzaar	Hypertension	$1.7	$1.0
Gardasil	HPV vaccine	$1.2	$1.8
Januvia/Janumet	Diabetes	$4.7	$5.8
Remicade	Inflammatory diseases	$2.7	$2.3
Nasonex	Allergies	$1.2	$1.3
ProQuad/Varivax	MMR vaccine	$1.2	$1.3
Isentress	Infectious diseases	$1.4	$1.6
Zetia/Vytorin	Cholesterol	$4.3	$4.3

Source: Merck & Co. Annual Report (2013 10–K).

EXHIBIT 6 Global Pharmaceutical Sales, 2007–2014

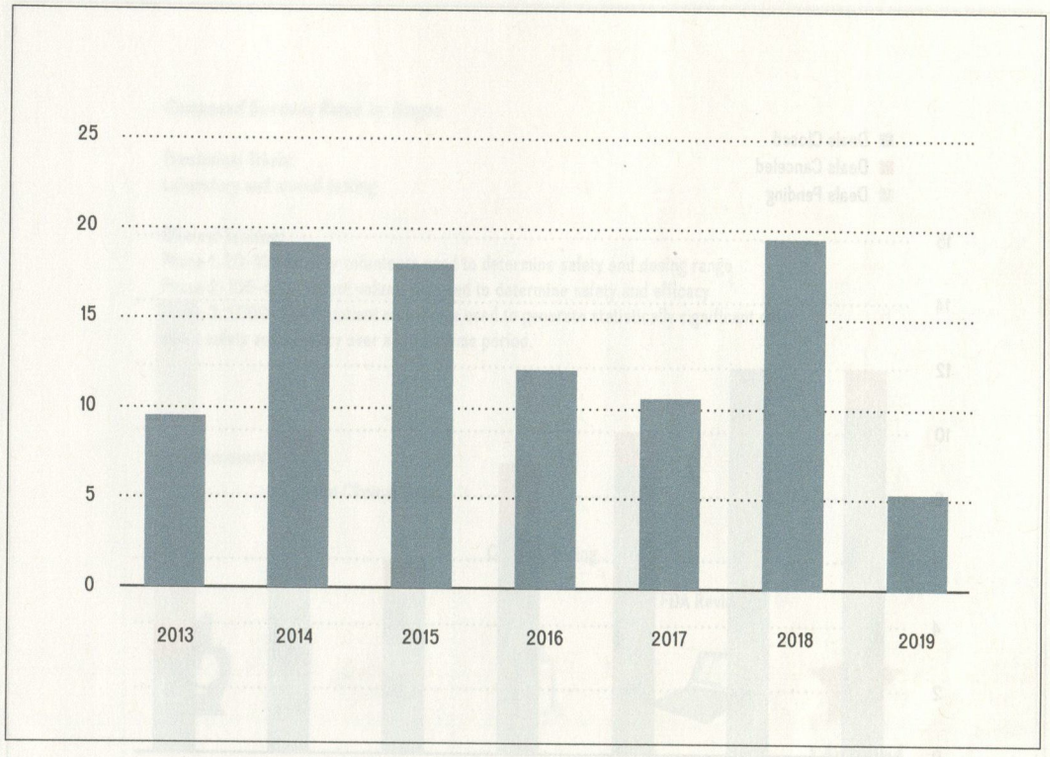
	2007	2008	2009	2010	2011	2012	2013	2014
Total world market (current $ billions)	739	786	842	889	936	959	980	1,000
Growth over previous year (growth rate in constant U.S. $)	7.0%	6.4%	7.1%	5.5%	5.3%	2.4%	2.2%	2.0%

Global Pharmaceutical Sales vs. Growth, 2007–2014. Figures for 2013 and 2014 are approximate, and forecast, respectively.

Source: Adapted from IMS Health Market Prognosis (includes IMS Audited and Unaudited markets) and 2014 Thompson Reuters Pharmaceutical R&D Factbook.

Merck & Co., Inc.

EXHIBIT 7 Loss of Exclusivity per year, Projected to 2019 (Exclusive of Biologics) ($ billions)



Source: Adapted from IMS Health, National Sales Perspectives November 2013.

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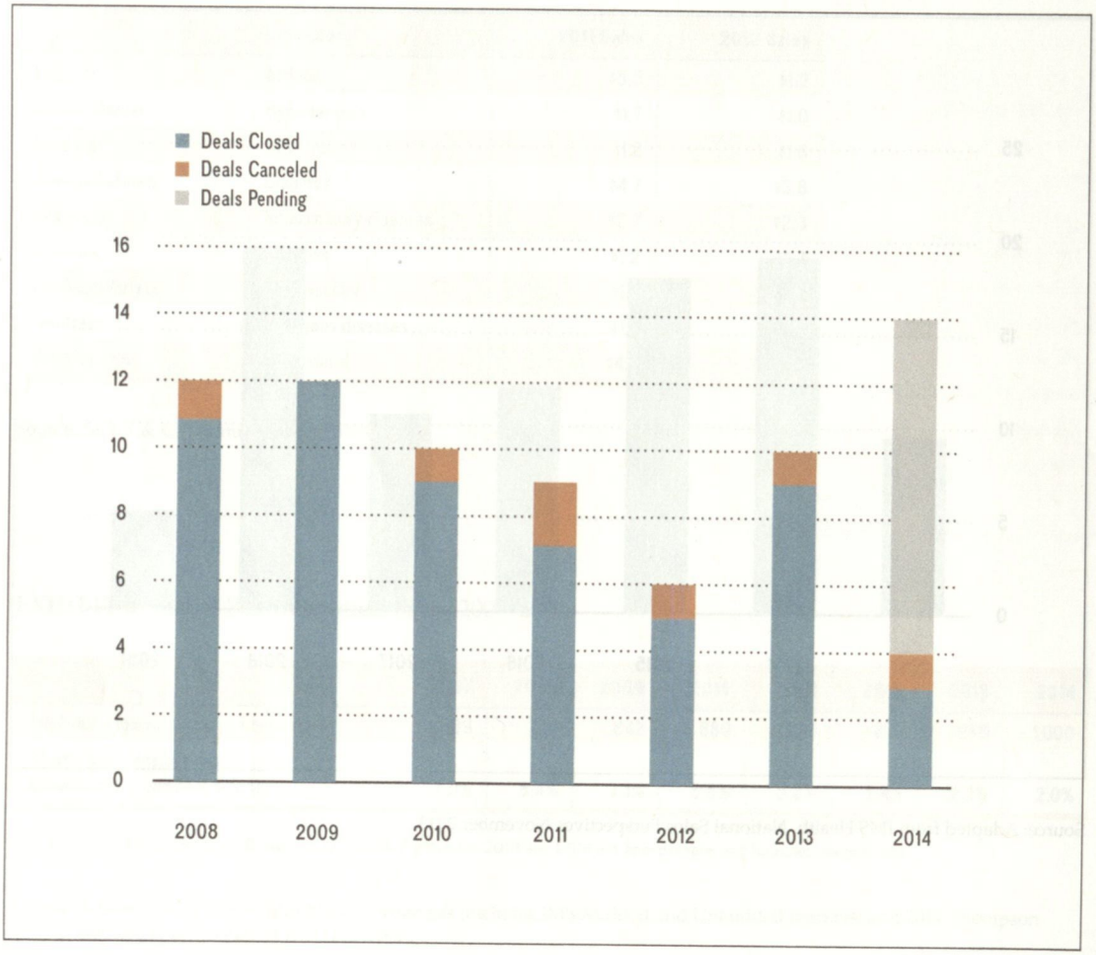
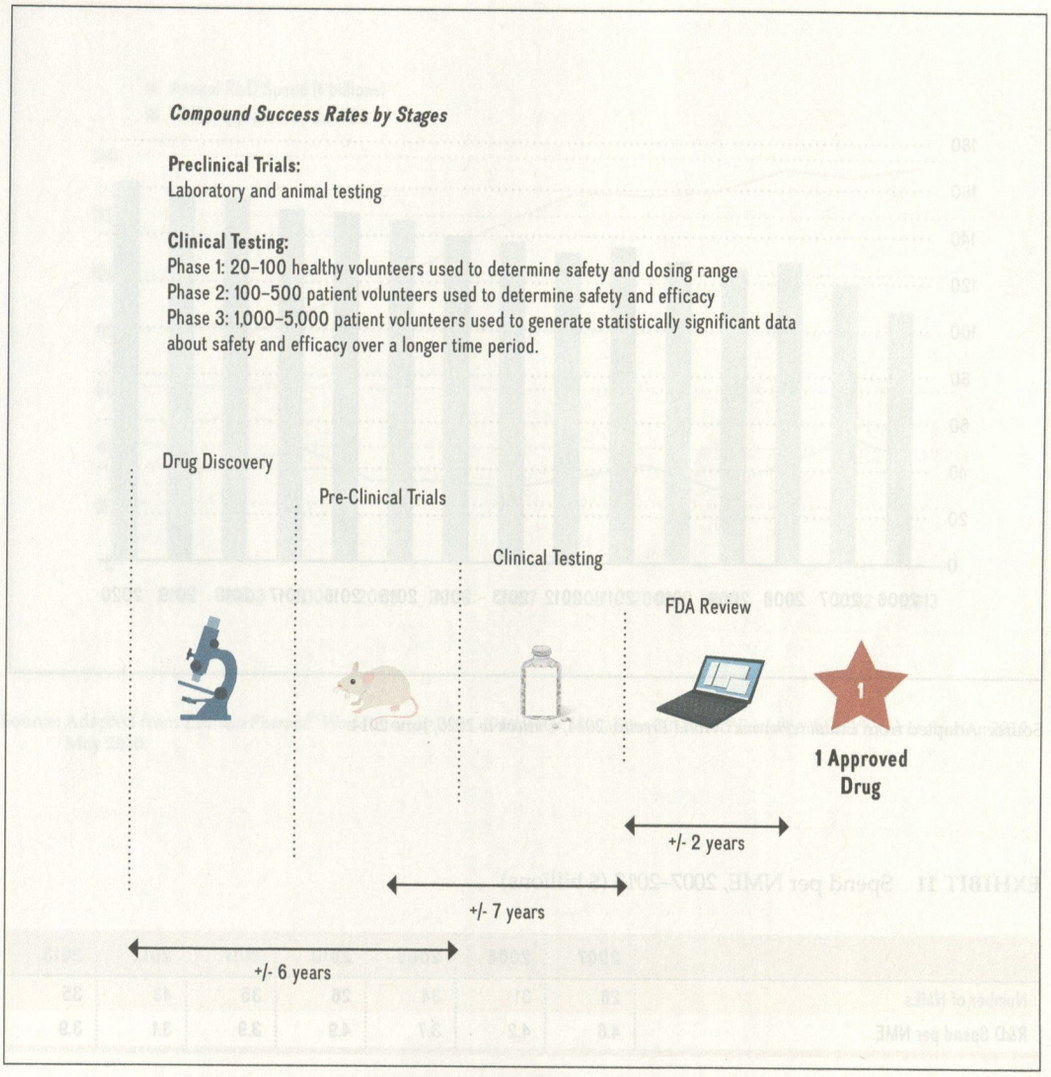
EXHIBIT 8 M&A Deals per year, 2008–2014



Source: Adapted from "Pharma Sector's M&A Pipeline Still Bubbling," *The Wall Street Journal*, May 20, 2014.

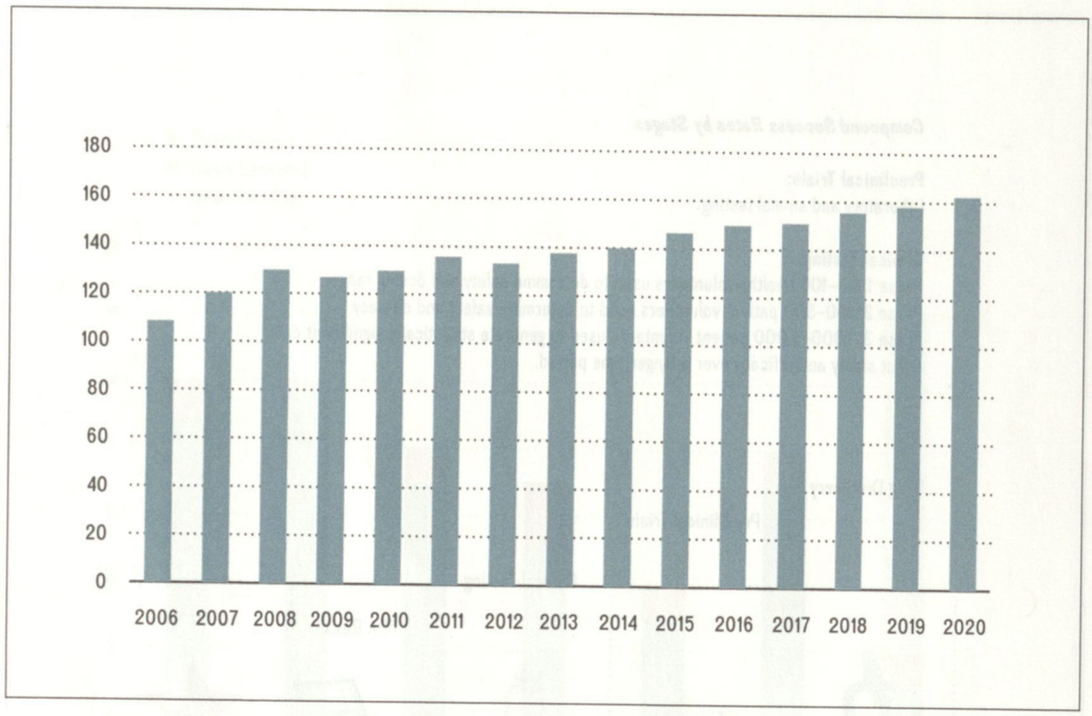
Merck & Co., Inc.

EXHIBIT 9 Stages in Drug-Discovery Process



Source: Adapted from Drug Discovery and Development: Understanding the R&D Process, www.innovation.org; CBO, Research and Development in the Pharmaceutical Industry, 2006.

EXHIBIT 10 Worldwide Total Pharmaceutical R&D Spend, 2006–2020 ($ billions)



Source: Adapted from *EvaluatePharma® World Preview 2014, Outlook to 2020*, June 2014.

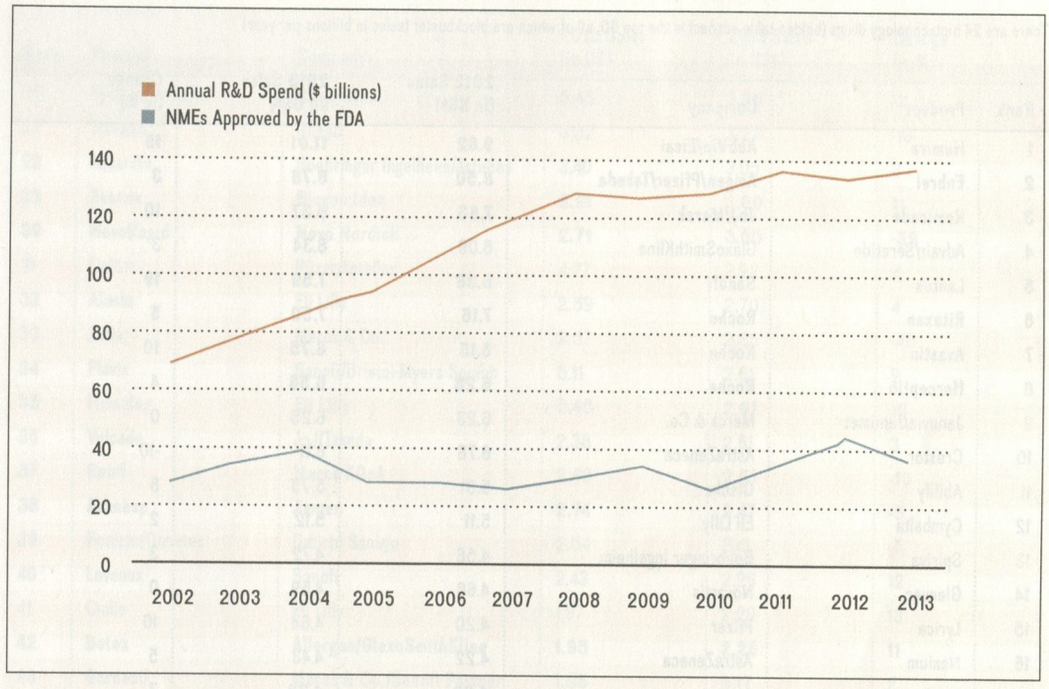
EXHIBIT 11 Spend per NME, 2007–2013 ($ billions)

	2007	2008	2009	2010	2011	2012	2013
Number of NMEs	26	31	34	26	35	43	35
R&D Spend per NME	4.6	4.2	3.7	4.9	3.9	3.1	3.9

Source: Adapted from *EvaluatePharma® World Preview 2014, Outlook to 2020*, June 2014.

Merck & Co., Inc.

EXHIBIT 12 Increase in Annual R&D Spend versus NMEs approved by the FDA, 2002–2013



Source: Adapted from *EvaluatePharma® World Preview 2014, Outlook to 2020*, June 2014, and *EvaluatePharma® World Preview 2010*, May 2010.

EXHIBIT 13 Top 50 Selling Products Worldwide

There are 24 biotechnology drugs (bolded table entries) in the top 50, all of which are blockbuster (sales in billions per year)

Rank	Product	Company	2012 Sales (in US$)	2013 Sales (in US$)	Change (in %)
1	**Humira**	**AbbVie/Eisai**	**9.62**	**11.01**	**15**
2	**Enbrel**	**Amgen/Pfizer/Takeda**	**8.50**	**8.78**	**3**
3	**Remicade**	**JnJ/Merck**	**7.63**	**8.37**	**10**
4	Advair/Seretide	GlaxoSmithKline	8.09	8.34	3
5	**Lantus**	**Sanofi**	**6.38**	**7.59**	**19**
6	**Rituxan**	**Roche**	**7.16**	**7.50**	**5**
7	**Avastin**	**Roche**	**6.15**	**6.75**	**10**
8	**Herceptin**	**Roche**	**6.28**	**6.56**	**4**
9	Januvia/Janumet	Merck & Co.	6.23	6.25	0
10	Crestor	AstraZeneca	6.78	6.11	-10
11	Abilify	Otsuka	5.31	5.75	8
12	Cymbalta	Eli Lilly	5.11	5.12	2
13	Spiriva	Boehringer Ingelheim	4.58	4.72	3
14	Gleevec	Novartis	4.68	4.69	0
15	Lyrica	Pfizer	4.20	4.64	10
16	Nexium	AstraZeneca	4.22	4.43	5
17	**Neulasta**	**Amgen**	**4.09**	**4.39**	**7**
18	Copaxone	Sanofi	4.03	4.33	7
19	Revlimid	Celgene	3.78	4.30	14
20	**Lucentis**	**Novartis/Roche**	**3.98**	**4.21**	**6**
21	**Prevnar 13**	**Pfizer**	**3.78**	**3.76**	**0**
22	Atripla	Gilead	3.57	3.65	2
23	Diovan	Novartis	4.44	3.54	-20
24	Symbicort	AstraZeneca	3.21	3.50	9
25	Celebrex	Pfizer/Astellas	3.17	3.36	-3

(continued)

Merck & Co., Inc.

EXHIBIT 13 (Continued)

Rank	Product	Company	2012 Sales (in US$)	2013 Sales (in US$)	Change (in %)
26	**Epogen/Procrit**	**Amgen/JnJ**	**3.45**	**3.35**	**-2**
27	Truvada	Gilead	3.32	3.27	-10
28	Micardis	Boehringer Ingelheim/Astellas	3.40	3.05	3
29	**Avonex**	**Biogen Idec**	**2.91**	**3.00**	**11**
30	**NovoRapid**	**Novo Nordisk**	**2.71**	**3.00**	**-39**
31	Lipitor	Pfizer/Astellas	4.77	2.92	4
32	Alimta	Eli Lilly	2.59	2.70	4
33	Zetia	Merck & Co.	2.57	2.66	-49
34	Plavix	Sanofi/Bristol-Myers Squibb	5.11	2.61	9
35	**Humalog**	**Eli Lilly**	**2.40**	**2.61**	**10**
36	Velcade	JnJ/Takeda	2.38	2.61	3
37	**Rebif**	**Merck KGaA**	**2.43**	**2.51**	**-10**
38	**Aranesp**	**Amgen**	**2.74**	**2.47**	**-5**
39	Benicar/Olmetec	Daiichi Sankyo	2.54	2.41	-7
40	Lovenox	Sanofi	2.43	2.26	12
41	Cialis	Eli Lilly	1.97	2.20	13
42	**Botox**	**Allergan/GlaxoSmithKline**	**1.95**	**2.20**	**11**
43	**Gardasil**	**Merck & Co./Sanofi Pasteur**	**1.95**	**2.17**	**2**
44	**Gammagard Liquid**	**Baxter International**	**2.07**	**2.12**	**1**
45	**Privigen**	**CSL**	**2.08**	**2.10**	**26**
46	**Victoza**	**Novo Nordisk**	**1.64**	**2.07**	**22**
47	**Levemir**	**Novo Nordisk**	**1.69**	**2.06**	**128**
48	**Eylea**	**Bayer**	**0.90**	**2.04**	**-19**
49	OxyContin	Purdue Pharma	2.47	2.00	4
50	**Advate**	**Baxter International**	**1.89**	**1.97**	**6**

Source: Adapted from *EvaluatePharma® World Preview 2014, Outlook to 2020*, June 2014.

EXHIBIT 14 Top Pharmaceutical Companies with Significant Portion of Sales Derived from Biotechnology Products (sales in U.S. $ billions)

Company	2013 Total Sales	2013 Biotech Sales	% Sales Derived from Biotech
Roche	39.1	29.0	74.2
Sanofi	37.7	14.5	38.5
Johnson & Johnson	26.5	9.5	35.8
Eli Lilly	20.1	5.7	28.4
Bristol-Myers Squibb	12.3	3.1	25.2
Pfizer	45.0	10.2	22.6
Merck & Co.	37.5	7.9	21.1

Source: Adapted from *EvaluatePharma® World Preview 2014, Outlook to 2020,* June 2014.

Merck & Co., Inc.

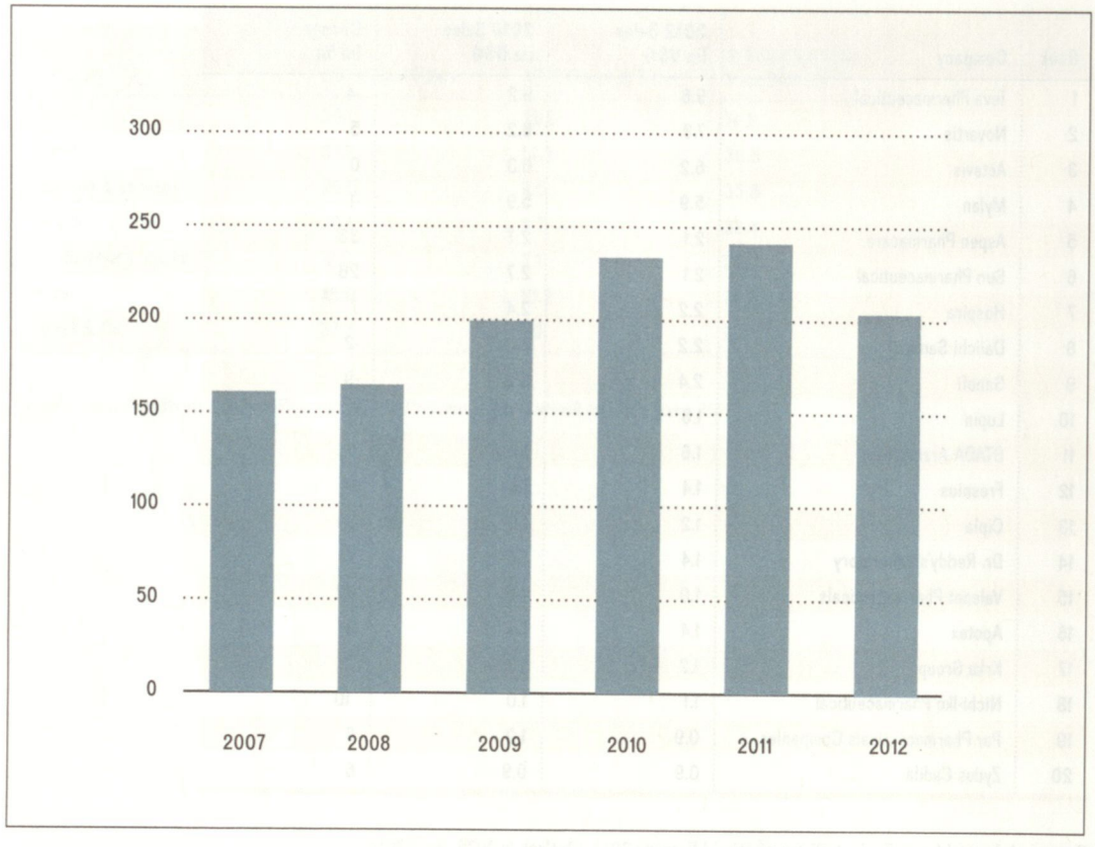
EXHIBIT 15 Top 20 Companies, Worldwide Generic Drug Sales, 2013 ($ billions)

Rank	Company	2012 Sales (in US$)	2013 Sales (in US$)	Change (in %)
1	Teva Pharmaceutical	9.6	9.2	-4
2	Novartis	7.8	8.2	5
3	Actavis	6.2	6.3	0
4	Mylan	5.9	5.9	-1
5	Aspen Pharmacare	2.1	2.7	33
6	Sun Pharmaceutical	2.1	2.7	26
7	Hospira	2.2	2.4	7
8	Daiichi Sankyo	2.2	2.2	-2
9	Sanofi	2.4	2.2	-9
10	Lupin	1.6	1.7	9
11	STADA Arzneimittel	1.6	1.6	5
12	Fresnius	1.4	1.6	14
13	Cipla	1.2	1.6	34
14	Dr. Reddy's Laboratory	1.4	1.6	12
15	Valeant Pharmaceuticals	1.0	1.5	42
16	Apotex	1.4	1.4	2
17	Krka Group	1.2	1.3	7
18	Nichi-Iko Pharmaceutical	1.1	1.0	-10
19	Par Pharmaceuticals Companies	0.9	1.0	6
20	Zydus Cadila	0.9	0.9	6

Source: Adapted from *EvaluatePharma® World Preview 2014, Outlook to 2020*, June 2014.

Merck & Co., Inc.

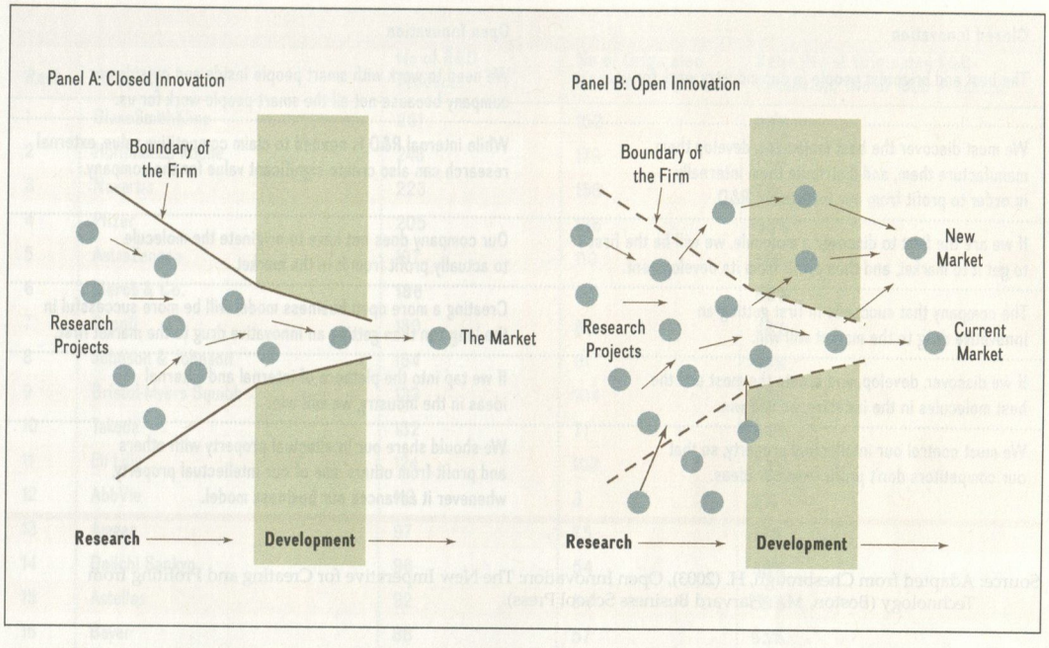
EXHIBIT 16 ANDAs with a Paragraph IV Challenge



Source: The Paragraph Four Report: Annual Trends, from Parry Ashford Inc., 2013.

Merck & Co., Inc.

EXHIBIT 17 The Closed-Innovation Model vs. the Open-Innovation Model



Source: Adapted from Chesbrough, H. (2003), "The era of open innovation," MIT Sloan Management Review, Spring: 35–41.

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EXHIBIT 18 Contrasting Principles of Closed and Open Innovation

Closed Innovation	Open Innovation
The best and brightest people in our industry work for us.	We need to work with smart people inside and outside our company because not all the smart people work for us.
We must discover the best molecules, develop them, manufacture them, and distribute them internally in order to profit from our investment R&D.	While internal R&D is needed to claim competitive value, external research can also create significant value for the company.
If we are the first to discover a molecule, we will be the first to get it to market, and thus profit from its development.	Our company does not have to originate the molecule to actually profit from it in the market.
The company that succeeds in first getting an innovative drug to the market will win.	Creating a more open business model will be more successful in the long run than getting an innovative drug to the market first.
If we discover, develop, and create the most and the best molecules in the industry, we will win.	If we tap into the plethora of internal and external ideas in the industry, we will win.
We must control our intellectual property, so that our competitors don't profit from our ideas.	We should share our intellectual property with others and profit from others' use of our intellectual property, whenever it advances our business model.

Source: Adapted from Chesbrough, H. (2003), Open Innovation: The New Imperative for Creating and Profiting from Technology (Boston, MA: Harvard Business School Press).

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EXHIBIT 19 Rankings of Most Successful Companies by Total Number of Active R&D Projects, 2014

Rank	Company	No of R&D Products	No of Originated R&D Products	Ratio (No of Originated R&D Products) / (No of R&D Products)*
1	GlaxoSmithKline	261	152	58%
2	Hoffman-La Roche	248	179	72%
3	Novartis	223	158	71%
4	Pfizer	205	136	66%
5	AstraZeneca	197	110	56%
6	**Merck & Co.**	**186**	**115**	**62%**
7	Sanofi	180	83	46%
8	Johnson & Johnson	164	81	49%
9	Bristol-Myers Squibb	133	104	78%
10	Takeda	132	71	54%
11	Eli Lilly	124	103	83%
12	AbbVie	113	3	3%
13	Amgen	97	75	77%
14	Daiichi Sankyo	96	54	56%
15	Astellas	92	54	59%
16	Bayer	88	57	65%
17	Teva	84	36	43%
18	Boehringer Ingelheim	81	57	70%
19	Eisai	79	45	57%
20	Dainippon Sumitomo Pharma	63	43	68%
21	Merck KGaA	61	24	39%
22	Otsuka	60	37	62%
23	Mitsubishi Tanebe Pharma	56	35	63%
24	Celgene	53	26	49%
25	Shionogi	52	25	48%

* Authors' own calculations based on data provided by Pharmaprojects.

Source: Citeline Pharma R&D Annual Review 2014, Pharmaprojects/Pipeline and Data Integration, http://www.citeline.com/.