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# Analyzing the Efficacy of the Pharmaceutical Patent System

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## **Abstract**

The purpose of this thesis is to provide insight into the complexities of the pharmaceutical industry and the subsequent role that patent protection influences both consumer markets and business operations. The methods used are a combination of detailed market research, case studies and a comprehensive analysis of fifteen industry leaders. The sector is heavily reliant on exceedingly high research and development expenditures which exemplifies the incessant need for an adequate patent system. The market is dominated by few, large multinational corporations and their patented brand name drugs. The results show that the current environment has led to several imbalances in the global pharmaceutical market. The predominant issues in the industry are limited access to affordable drugs, monopolistic market power created by extensive exclusivity periods, and skewed incentives that impact firm decision-making. The current system does not address traditional market forces that are inherent to private firms and subsequently influence research investments focused on Western markets. This has important implications on both developing nations and overall global health standards.

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## List of Abbreviations

AIDS – Acquired Immune Deficiency Syndrome  
BLA – Biologics License Application  
CAGR – Compound Annual Growth Rate  
CETA – Comprehensive Economic Trade Agreement  
CNIPA – Chinese National Intellectual Property Administration  
CPTPP – Comprehensive and Progressive Agreement for Trans-Pacific Partnership  
CRISPR – Clustered Regularly Interspaced Short Palindromic Repeats  
DNA – Deoxyribonucleic Acid  
EPO – European Patent Office  
EMA – European Medicines Agency  
FDA – Federal Drug Administration  
FDI – Foreign Direct Investment  
GDP – Gross Domestic Product  
HIV – Human Immunodeficiency Virus  
IMF – International Monetary Fund  
IP – Intellectual Property  
IPR – Intellectual Property Rights  
LDC – Least Developed Countries  
M&A – Mergers and Acquisitions  
MNE – Multinational Enterprise  
NAFTA – North American Free Trade Agreement  
NGO – Non-governmental Organization  
NIH – National Institutes of Health  
NME – New Molecular Entity  
R&D – Research and Development  
SIPO – State Intellectual Property Office  
TCM – Traditional Chinese Medicine  
TRIPS – Trade-Related Aspects of Intellectual Property Rights  
TTP – Trans-Pacific Partnership  
TTIP – Transatlantic Trade and Investment Partnership  
OECD – Organization for Economic Co-operation and Development  
UNCTAD – United Nations Conference on Trade and Development  
USMCA – United States Mexico Canada Agreement  
USPTO – United States Patent and Trademark Office  
WTO – World Trade Organization  
WHO – World Health Organization  
WIPO – World Intellectual Property Organization

## List of Definitions

**Active ingredient** – The biologically active, primary component in a pharmaceutical

**Biosimilars** – equivalent of generics for biologic pharmaceuticals. Unlike generics, biosimilars are not identical to the original biologic but possesses similar properties.

**Brand names** – Innovator pharmaceuticals patented by multinational corporations

**Exclusivity rights** – Exclusive rights to market a pharmaceutical that are granted by the local government regulatory body. Can run concurrently or independently from a patent

**Generics** – Pharmaceuticals with the exact same dosage, active ingredient, side effects, safety, strength and intended use as the brand name pharmaceutical they are copies of

**Novel pharmaceuticals** – innovator drugs that fill a previously unmet need. Their chemical composition has not been approved before

**Top 3** – Pharmaceuticals that generate the first, second or third largest revenue for their respective companies





## 1. Introduction

The motivation for this topic emanates from a particular interest in the pharmaceutical sector and the reasoning behind the difficulties in providing access to affordable medication around the world. This industry encapsulates the modern globalized business environment which closely aligns with the International Business profile. Understanding the perspectives of governments, multinational corporations and the general public provides an insight into the operational complexities associated with divergent interests. Healthcare is an essential human right that remains a pillar of governmental policy across all nations, yet products are provided by private firms operating in a highly competitive marketplace. Both the commercial and consumer markets are dominated by industrialized nations, further adding to the contentious discourse. The incentives of varying stakeholders create a difficult environment to enable mutually propitious results. Incorporating intellectual property rights only adds to the intricacies related to this sector. The evolving nature of intellectual property protection enables extensive research to be conducted in order to identify both the beneficial components and potential inefficiencies of the current system.

The pharmaceutical sector represents one of the most important global industries for its economic and societal implications. Various aspects of this industry have been researched thoroughly but mainly focuses on pricing, research and development and regulatory processes. Intellectual property protection is a subject undergoing intense study due to the increasing prevalence in the modern business climate. The key areas of interest reside in the effects on innovation, competitive markets and economic development. Intellectual property encompasses a broad range of protection that includes trademarks, copyrights, industrial designs, geographical indications, trade secrets, unfair competition and patents (WIPO, 2004). Because of these varying applications, research on intellectual property rights comprises of an expansive set of industries and many contributing factors. Few papers further specify the effects of patent protection on particular components in the pharmaceutical industry such as generic competition, legal ramifications and access to drugs. This research aims to provide a detailed analysis on the current state of affairs surrounding increasingly prevalent patent protection and pharmaceutical industry development. The general research question that this thesis focuses on is the following:

*How do inefficiencies in the current patent system affect the pharmaceutical sector?*

To address this question, the following structure will be utilized. An in-depth analysis from both the organizational and public standpoint will enable an impartial perspective on these issues. The thesis will be divided into three components. Firstly, the research will be addressing the importance and complications that arise from intellectual property protection for advanced and developing economies. This section elucidates the role of intellectual property in economic development, international trade and foreign direct investment. Secondly, the research will then focus on the impact that the current system has on the pharmaceutical sector around the world. This section illustrates the effects on innovation, pricing, allocating resources and accessing drugs. Thirdly, an analysis of market leaders over the past twenty years will be utilized to identify recent developments. The initial research focuses on the inherent trade-offs associated with implementing intellectual property protection for developing nations and the increasing prevalence in geopolitical affairs. This general overview is followed by the pervasive impact the current system has on firm decision-making and the subsequent effects on global health standards. Finally, the company analysis provides substantiated context on the practical implications in the competitive marketplace. Due to the convoluted nature of relevant research, intellectual property rights and patent protection are both used extensively across all industries however, patent protection in the pharmaceutical sector becomes the predominant focus as the analysis progresses.

The unique circumstances that befall the pharmaceutical sector compared to other industries curtails the argument from whether patent protection is needed, but rather the optimal level required. This industry is capital intensive and heavily reliant on research and development. Due to the simplistic nature of products consisting of chemical compounds, imitation is easily accessible from competitors. Initially, discovery research is needed that entails significant costs and excessive risk. Thereafter, an extensive regulatory process begins in order to ensure safety and efficacy before gaining market approval. This lengthy procedure is referred to as commercialization, ranging from eight to twelve years on average from application to approval (NASEM, 2018). The expenditure needed for the entire commercialization process varies but leading researchers in this field provided recent estimates of \$2.87 billion (DiMasi, Grabowski, & Hansen, 2016). The exact figure is disputed due to the incorporation of opportunity costs but the general consensus ranges from \$1.5-2 billion (OECD, 2017). These estimates exclude public funding, with the clinical trial phases accounting for 48.5% of total expenditure (EFPIA, 2018). The extensive process and exuberant costs are debilitating yet even more profound when

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considering that nearly nine out of every ten drugs entering clinical trials fail (NASEM, 2018). Even though manufacturing and distribution is inexpensive, the overall costs must be recuperated to enable a viable marketplace. Firms are incentivized to continually allocate capital through granted monopoly power permitted in the patent system.

The patent system is complex and varies around the world. The fundamental premise of implementing patent protection is to stimulate innovation and publicly disclose inventions in order to encourage the diffusion of knowledge. The conditions for approval require patentable subject matter, industrial applicability, novelty and an inventive step, or ‘non-obviousness’. The vague terminology surrounding the question of whether the invention “would have been obvious to a person having ordinary skill in the art” is considered the most difficult standard to determine. Once granted, the inventor is rewarded with monopoly access to the market for a finite time frame, generally twenty years. After expiration, competitors may commercially exploit the invention, allowing for both society and the inventor to mutually benefit. The patent system is widely used, with 3,168,900 applications being filed in 2017. The sheer number of patents is not necessarily applicable given the array of industries but the pertinent components that need to be understood are as follows: First, there are various types of patents granted that differ in terms of value and application. Focus will be placed on the discrepancy between utility patents and design or process patents. The latter patents refer to manufacturing and industrial processes while utility patents are commonly referred to as patents for invention. These distinctions are particularly relevant in the pharmaceutical sector and will be alluded to frequently throughout the analysis. Second, International standards attempt to create a unified system, but patents are granted at the regional level and legal autonomy is given to individual countries. (WIPO, 2018; WIPO, 2004)

Globalized standards have been gaining precedence since the adoption of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) by all members of the World Trade Organization on January 1<sup>st</sup>, 1995. The TRIPS Agreement fundamentally changed the pharmaceutical industry by enforcing the adoption of pharmaceutical protection which was not present in many developing nations such as India (WTO, 1995). The pharmaceutical industry is dominated by multinational corporations residing in the United States and Europe, hence, supplementary protection is continually advocated from these governments. The perceived benefits of additional protection disproportionately affect multinational firms, leaving developing

nations in a difficult predicament. As the research progresses, emphasis on China, India, Europe and the United States will be used to illustrate the far-reaching effects from a global perspective. Increasing standards, or adding protection, may come in many forms but most notably, data exclusivity. Data exclusivity allows the owner to protect vital clinical trial information that was obtained through expensive studies (CPTPP, 2018). Without adequate efficacy and safety precautions, generic competitors are unable to gain approval and access the commercial market. Furthermore, an important industry development that is frequently referenced is biologics, which describe “a product that is produced using biotechnology processes and that is, or, alternatively, contains, a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product, for use in human beings for the prevention, treatment, or cure of a disease or condition” (USMCA, 2018).

It is imperative to understand the practical implications that certain aspects of the current system have on firm decision making and public health. Several case studies will be referenced including Pfizer operations in the Chinese market, the North American opioid crisis and the global HIV/AIDS epidemic. This research will discuss the positive and necessary attributes associated with the current patent regime but also highlight the inherent consequences of implementing such a system. Ideally, if the patent system worked sufficiently, multinational corporations would be incentivized to adamantly invest in research and development and given the opportunity to recuperate their costs based on traditional market forces. In turn, firms would perpetuate the cycle of innovation by reinvesting these profits and further advancing pharmaceutical capabilities. For those developing and least developed countries (LDCs) that cannot afford initial drug prices, would subsequently be able to access these medicines after the eight to twelve year time period when generic manufacturing vastly reduces the costs. Adequate standards should also increase multinational prevalence in terms of both operational functions and commercial viability. These investments, as a result, could reduce costs, increase profits and improve access to affordable drugs. This analysis will aim to explore the accuracy of this scenario and provide detailed insight into the complexities that this unequivocally important industry bestows upon societies around the world.

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## 2. Importance of Intellectual Property

Intellectual Property protection has been debated across all disciplines for its role in industrial and economic development. As technological progress continues to grow exponentially, leaders attempt to protect businesses and stimulate innovation while subsequently promoting competitive markets and international trade. The liberalization of trade and globalized supply chains offer opportunities for multinational corporations to utilize the principles of comparative advantage and division of labour while emerging nations are able to participate in a global marketplace and develop their economies. The divergent interests between industrialized and developing nations occurs due to the disparity in technological capacity. Innovative and technologically advanced economies are significantly more likely to benefit from stronger IP protection and in turn, develop and administer a more effective IPR system (Maskus, 2000). Conversely, countries with low levels of development, education and market freedom exhibit little to no perceived benefit from adopting intellectual property protection (Qian, 2007). This is due to the progression of economic and technological development which provides an insight into the corporate and governmental perspectives surrounding the divisive nature of IPR protection between advanced, developing and least developing economies.

IPR protection requires an expensive and complex system to stipulate compliance, enforcement and thus, beneficial results. Technological advancement generally exhibits similar patterns as nations transition from low to high income. Initially, little to no resources are devoted to innovation with economic output reliant on non-IP related industries. As development occurs, technological capabilities generally rely on transfers or imitation from more advanced economies. Over time, domestic firms and competitive markets emerge, creating overall growth and poverty alleviation. Demand gradually shifts toward higher quality products, with domestic companies encouraging IPR enforcement to protect their emerging technological capacity. Historically, this stage of economic development has been the most beneficial to ratify intellectual property protection as domestic innovation becomes globally competitive and alters the resulting dynamics of trade. Qian (2007) argues that even developed economies of Germany and Switzerland opposed national patent legislation while they were still technology importers. Post-war Japan implemented a utility model system, or second-class patent, aimed at promoting incremental innovation and the diffusion of knowledge, which was widely criticized as it encouraged numerous filings of narrow

claims that built on existing technology. In an analysis of patent activity from 1960-1993, the results strongly suggest that the utility system had a stronger effect on Total Factor Productivity growth than patent applications with the authors concluding “diffusion and imitation were more important than pure invention” (McDaniel & Maskus, 1999). The decades of rapid economic expansion have allowed Japan to become a global leader in technology creation and a member of the trilateral patent offices alongside the USPTO and EPO.

It is important to distinguish intellectual property protection as not just legislation, which many countries have adopted, but compliance from businesses and enforcement from government institutions. Ginarte and Park (1997) developed a patent index for 110 countries from 1960-1990 considering five criteria: duration, extent of coverage, membership in international agreements, loss of protection and enforcement measures. The results indicated the increase in average protection from middle income to high income countries was considerably higher than low to middle income countries while the variability amongst developed nations was significantly lower (Ginarte & Park, 1997). A follow-up study found that patent strength correlated positively to GDP per capita, share of R&D in GDP, human capital, freedom of markets and openness to international trade (Park & Ginarte, 1997). These findings suggest that overall patent protection is more of a reactive development to domestic demands. Furthermore, freedom of markets and openness to international trade are meaningful as it correlates the liberalization of trade with economic development and patent protection. A particularly noteworthy study determined there is a significant range of incomes before protection becomes stronger than the poorest nations, indicating an inverted-U relationship between patent strength and real per capita income (Maskus, 2000). This advocates that as economies develop, an initial *negative* period of IPR protection occurs. These findings are dated, but provide a viewpoint into ongoing discussions between developed and developing nations regarding intellectual property protection. Theories of economic development are consistent with regards to these analyses, although uniformly following these principles moving forward would be ill-informed in our increasingly interconnected and technological societies. In conclusion, it can be acknowledged that as economies become highly advanced, sufficient intellectual property protection is necessitated but ambiguity occurs for the optimal protection less developed nations require to stimulate technological and economic progression.

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The notion of transfers of technology is oft cited by the Organization for Economic Co-operation and Development (OECD) as a beneficial component of protection enhancement. The mode and type of technology transfer from foreign companies is influenced by the host country's patent system, opting for older technology and wholly-owned subsidiaries in order to circumvent imitation in weak environments (Fosfuri, 2000). This concept was surveyed by Edwin Mansfield (1994) and how it affects foreign investment decisions from American multinational firms. There were six industries investigated, with chemicals and pharmaceuticals being integrated, which found a stronger concern about IPR protection as the type of investment facility grew more complex (Mansfield, 1994). All sectors displayed similar results but unsurprisingly, chemicals and pharmaceuticals were the most influenced by IP protection. Decisions were strongly affected 46% of the time for rudimentary production, 71% for components manufacturing, 87% for complete products and 100% for research and development facilities, with India being cited as being the least likely country to permit joint ventures and licensing for their newest or most effective technology (Mansfield, 1994). Although this survey is dated, it indicates the effects IP rights have on decision-making strategies from foreign entities and governments determined to progress past basic manufacturing processes. There are significant benefits attributed to the development of a local industry which can utilize a reduction in transportation costs and dependence on foreign suppliers while increasing expertise and local employment.

Access to affordable medicines is a pillar of governmental policy across all nations but one that becomes much more manageable with economic stability. Investing in policies related to education and healthcare have dramatic effects on the standard of living and economic development of a country. Societal benefits are multi-faceted as access to affordable medicines and economic development occur simultaneously. Research and development investments are difficult in low income countries but proven to enhance innovation and technological capacity. It is important to distinguish between private and government investments as two interconnected but entirely separate factors. In 2014, the United States government expenditure on health-related R&D was 0.2% of GDP (\$33 billion), 0.05% (\$11 billion) in Europe and 0.03% (\$1.6 billion) in Japan (OECD, 2017). China has begun to increase public investment, rising from \$0.6 to \$2 billion from 2007-2012, while India has remained stagnant at \$400 million (Chakma, et al., 2014). These substantial investments contribute to the distinct separation between developed and developing nations in this research-intensive industry. In 2004, only 4% of the entire global public expenditure

on health research was done by low and middle-income countries (GFHR, 2004). Private enterprises still make up the majority of research investments exemplifying the need to continually scale domestic firms.

Several studies reinforce the difficult quandary government officials face to correctly balance domestic industry, innovation and affordable medicines while simultaneously encouraging foreign investment. Qian (2007) analyzed pharmaceutical patent coverage from 1978-2002 and found no statistically significant relationship between pharmaceutical patent protection and domestic R&D investments in developing nations. These findings align with the progression of economic development but do not examine the effects in an international context. Lerner (2002) analyzed 177 changes in patent policy across sixty countries over 150 years and their subsequent effects on patent applications from both domestic and foreign entities. A ten-year period spanning before and after a significant policy change was used, showing a dramatic increase in foreign entity applications in combination with a considerable domestic decline in developing nations (Lerner, 2002)(See Appendix Figure 1a). This comprehensive study controls for confounding factors and references a nation with relatively constant IP protection, Great Britain, to highlight the disparity from foreign and domestic firms. Many papers analyze the effects of intellectual property on innovation from a domestic perspective but the importance of foreign entities cannot be understated. For countries in the initial stages of economic development, incorporating all of these factors is needed to determine an adequate level of IP protection to satisfy foreign and domestic industry. From a macro perspective, China has maintained an unprecedented economic growth period but replicating the governmental policies may not generate similar results. The policies developing nations like India or Brazil utilize will have significant implications on their capacity to emerge as economic powers. The subsequent impact on trade relations should be addressed when considering the optimal level of IP protection, and most importantly, enforcement.

## 2.1 US-China Relations

While intellectual property has always been prevalent regarding companies expanding to new markets, recent instances of IP theft have leapt to the forefront of discussions. The economic success of China has captured the world's attention and created a frenzy of businesses attempting



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to gain exposure to this rising power. The economic growth of China has been unparalleled in recent decades, resulting in the world's second largest economy with a GDP in 2017 of \$12.24 trillion (IMF, 2018). While many factors are involved in this success, ascending into the World Trade Organization in December 2001 was a significant component in allowing China to attain its current trading power. This can be seen in comparison with the United States' economy, with a notable exponential growth occurring since the 2000s (Trading Economics, 2019)(See Appendix Figure 2a). As China transitions from an industrial to a more complex services-based economy, ensuring IPR protection will be a critical component to achieving success.

International trade dynamics shift in relation to other developed nations as technology advances and services become the dominant output. Patent intensive industries have become a substantial component of trade for the EU with the United States, representing 69% of imports and 71% of exports (EPRS, 2014). In the United States, IP-intensive industries account for 38.2% of annual GDP, supporting 45.5 million jobs, or 30% of all employment (USPTO, 2016). These significant figures detail the impact that intellectual property has on employment, international trade and the overall economy. The United States holds the world's largest trade surplus in services at \$250.6 billion in 2016, followed by the United Kingdom at \$129.1 billion (USITC, 2018). These figures are substantial considering the growing trade deficit between the United States and China which has become a contentious political discussion (US Census Bureau, 2019)(See Appendix Figure 2b). As China rapidly develops its innovative and technological capacity, there will be an inevitable shift in the balance of trade. China's intellectual property office, CNIPA, has been exponentially increasing its global share of patent applications, contributing 43.6% of total submissions in 2017 while the USPTO and EPO only filed 19.2% and 5.3%, respectively (WIPO, 2018). Reducing the technology gap will affect international trade relations with both advanced and developing nations which will dramatically impact China's economy.

Advanced economies provide additional benefits that exceed traditional trade dynamics, with services supplied by U.S. owned foreign affiliates totaling \$1.4 trillion dollars in 2015, having the United Kingdom, Canada and Ireland representing roughly one third (USITC, 2018). The wage disparity between IP-intensive and non-IP intensive industries is also worth noting to provide context on the extent of economic multipliers. The wage premium in the U.S. has grown from 22% in 1990 to 46% in 2014, with patent intensive industries amongst the highest at a 74% premium

(USPTO, 2016). With wages increasing rapidly in China, consumer demand and employee expectations should only enhance the desire for higher quality products and job opportunities. Due to their remarkable economic development, China has pulled millions of people out of poverty in a finite time frame. As urbanization, improved working conditions and demand for adequate healthcare occurs, China must address intellectual property concerns in order to achieve sustainable growth. The next steps will be critical; a dramatic technological transition must transpire so levels of economic output equal to the United States, EU and other developed nations are attainable. Although these are broad economic indicators that incorporate a variety of industries, intent is to provide an insight into the stages of economic development that can be referenced in a similar country like India.

## 2.12 Dispute Resolution

The World Trade Organization (WTO) is an important entity as it's principled on being an impartial party encouraging fair trade and developing market economies around the world. The fundamentals of open market economies have enabled the development of integrated supply chains and a global marketplace. Important information pertaining to intellectual property is found in the Agreement on Trade-Related Aspects of Intellectual Property Rights, or TRIPS, which came into effect on January 1<sup>st</sup>, 1995 and incorporates all members of the World Trade Organization. The TRIPS Agreement introduced global standards of IPR protection, including a minimum patent requirement of 20 years and forbids the exclusion of pharmaceuticals (WTO, 1995). This comprehensive agreement is considered to have the greatest impact on the pharmaceutical industry, with over forty countries in the world not granting patent protection for pharmaceutical products prior to this agreement (WHO, 2019). Specific requirements of product patents enable absolute protection, whereas prior process patents enabled different forms of manufacturing that led to generic versions of patented medicines (WHO, 2019). Countries were given different transitional periods, depending on their economic status, in order to fulfill these requirements with developing nations receiving an additional five years and least developed nations given ten years (WHO, 2019). China is still considered a developing nation under the WTO, enabling more leniency through certain provisions than other members. The Doha Declaration, enacted in 2001,

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allowed for least developed nations to not enforce market exclusivity or data protection for pharmaceutical products until 2016 (Abbott, 2002).

In this Agreement, there is a specific emphasis on dispute prevention and settlement, with resolution occurring through the engagement of *multilateral* procedures (WTO, 1995). This is an important principle because as more countries are participating in global trade, following this precedent is critical to reduce conflicts and minimize negative geopolitical factors. The notion of integrating economies to encourage cooperation was the underlying theory of the Marshall Plan, established in Europe after the Second World War. The creation of the European Union in 1993 has created fully interconnected economies of the 28 Member States, with limited conflicts arising from a continent that had constantly changing borders throughout history. Moreover, fair and unbiased dispute resolution measures have allowed successful free trade agreements, such as the North American Free Trade Agreement, to occur between the significantly smaller and less developed nation of Canada and Mexico with the economy of the United States. According to Chapter 11, a private investor can enter a lawsuit towards a host government by immediately bypassing domestic courts and is given the right to an impartial tribunal which consists of three members, one chosen by each party and a mutually agreed third party representative (NAFTA, 1994). There has been a total of eighty-five claims put forth, eight involving pharmaceutical companies, with a total of \$386 million in damages being paid out since the bill was enacted (CCPA, 2018).

Since China's accession into the World Trade Organization in 2001, contentious disagreements have occurred surrounding IP protection. The United States has continually used WTO regulations as a mechanism for combatting infractions from China however, futile efforts have caused a recent change in administrative policy that promises new unilateral tools outside of the WTO (Donnan, 2018). The US wants to end what is has labelled as decades of state-coordinated Chinese theft of American intellectual property. The annual cost to the US economy is estimated between \$225 and \$600 billion, with 87% of seized counterfeit goods originating from just China and Hong Kong (NBAR, 2017). These figures are predominantly based off of copyright and trademark infringement, but display the economic importance and specific focus on Chinese practices. Strategic usage of mandatory joint ventures, local content requirements and forced technology transfers have developed China's technological capacity while frustrating

multinational organizations. Two examples will be cited to illustrate the consequential effects. In the early 2000s, foreign companies from France, Germany and Japan controlled roughly two thirds of the Chinese market for high-speed railway systems where they subcontracted manufacturing of simple components to state owned enterprises. In 2009, every new contract required a joint venture where 49% was the maximum equity stake, 70% of each system had to be made locally and companies had to foreclose their latest designs. The subsequent impact was a reduction of market share below 20% and global competitors who outbid on contracts in Australia and New Zealand shortly thereafter. Similarly, from 1996-2005, foreign companies held a 75% share in wind energy projects when the government introduced corresponding measures. By 2009, foreign market share fell below 33% while failing to win a single government-funded wind energy project after 2005 (Hout & Ghemawat, 2010).

Although extremely multifaceted, these factors have certainly contributed to the current US-China trade war which has enveloped tariffs on \$250 billion worth of goods and put stress on the global economy. The OECD, World Bank and International Monetary Fund (IMF) have pared back expectations on global growth, with the WTO citing the worst-case scenario of a continuing trade conflict would result in a reduction of 17% for global trade by 2022, higher than the 12% decrease following the 2008 financial crisis (WTO, 2019). While concessions have been made by both parties, intellectual property rights continue to impede negotiations. Out of 369 cases since China has been a member of the WTO, China and the United States have utilized this process against one another 38 times, with an extensive 18 member complaint towards China on March 23<sup>rd</sup>, 2018 regarding “certain measures concerning the protection of intellectual property rights” (WTO, 2019). The recent unilateral actions that have recently taken place have caused the WTO to launch an investigation into the validity of the United States’ China tariffs under the violation of the ‘most favored nation’ rule to not discriminate against trading partners. The impartial dispute settlement process has been one of the fundamental principles since the establishment of the World Trade Organization in 1995. WTO Director-General Roberto Azevedo recently stated, “If we forget the fundamental importance of the rules-based trading system we would risk weakening it, which would be an historic mistake with repercussions for jobs, growth and stability around the world” (WTO, 2019). The global economy awaits the resulting effects of the current trade war with implications to continue for years to come. The World Trade Organization was established to

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encourage global trade under beneficial rules for all parties but faces an existential threat that could have a wide-ranging impact.

### 2.13 Pfizer in China

The case of Viagra in China provides a brief insight into the complexities of operating within the Chinese market. Throughout its history, China has implemented unique restrictions on providing market access to foreign businesses. Companies must adhere to specific rules that require a partnership with a local Chinese company. This may be in the form of an equity joint venture, cooperative joint venture, a wholly foreign owned enterprise or a representative office. Certain sectors are restricted and navigating through the business climate provides its own set of difficulties that have proved fatal for highly established companies like eBay. Pfizer began Chinese operations in the 1980's that included a joint venture in 1986, a \$60 million-dollar plant in 1989 and a representative office for its animal health line in 1995 (Abrami & Manty, 2010). Pfizer is currently the leading foreign pharmaceutical company with over 11,000 employees and an accumulated investment of \$1.5 billion (Pfizer, 2019). It is safe to assume that Pfizer had been a beneficial foreign entity and was viewed positively by Chinese officials.

The circumstances surrounding Viagra as it became accessible around the world was complex due to a number of high-profile lawsuits involving competitors such as Eli Lilly, Bayer, Merck, Sanofi and Bristol Myers Squibb (Liu, 2013). Pfizer won their lawsuit in the United States, however, lost several cases around the world, mainly due to obscurities in the patent application process. The Supreme Court of Canada unanimously invalidated Pfizer's patent for the sole reason of insufficient disclosure, by stating:

Why did the disclosure not simply state that the compound in Claim 7 was sildenafil? The patent plays "hide and seek" with the reader. The reader is expected to look for the "needle in the haystack", or "the tree in the forest". Remember, Claim 1 is for a range of compounds which includes *260 quintillion compounds*. (SCC, 2012, p. 135).

While each case entails its own investigation into the patent applications and relevant evidence, China provides a unique set of circumstances. China has a four-tier judicial system with the Supreme People's Court being the highest level in the land. Formerly known as the State

Intellectual Property Office (SIPO), the Chinese National Intellectual Property Administration (CNIPA), is the primary entity responsible intellectual property rights protection in China. Patent applications undergo either a preliminary examination for utility model or design patents which are granted ten-year terms, while a substantive examination occurs for inventive applications with subsequent protection being granted for twenty years. Contrary to the cascading claims present in other applications, the Pfizer patent in China included only one compound, *sildenafil*. In addition, trademarks were registered on the shape, colour and names of Viagra in English and Chinese. Pfizer applied in 1994 and was granted a patent in September 2001 for its single claim:

The use of 5-[2-ethoxy-5-(4-methyl-1-piperazinylsulphonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d] pyrimidin-7-one or of a pharmaceutically acceptable salt thereof, or of a pharmaceutical composition containing any of the same, for manufacture of a medicament for curative or prophylactic treatment of erectile dysfunction in a male animal, including man. (Chen, 2010, p. 31).

The same day Pfizer was granted its patent in 2001, a consortium of Chinese companies, whose legal representative was a former employee of the Patent Re-examination Board, requested an invalidation. Shortly after Viagra was launched, it quickly became known as “Wei Ge” across China, while its trademarked brand name was “Wan Ai Ke.” In 2003, a Chinese company, Welman, launched an erectile dysfunction drug named “Wei Ge” with a similarly blue colour and rhombus shape. Pfizer filed a lawsuit in 2005 citing Article 6bis of the Paris Convention which states, “cancel the registration, and to prohibit the use...of any such well-known mark or an imitation liable to create confusion therewith” (WIPO, 1979). In July 2004, the Patent Re-examination Board invalidated Pfizer’s patent after three years of investigation which was quickly followed by a group of Chinese companies forming a joint-stock company to produce a similar drug at half the price. Pfizer filed an appeal and sued the Re-examination Board for wrongful invalidation. The Beijing Intermediate Court ruled in favour of Pfizer in 2006, which was, unsurprisingly, further appealed by the Chinese consortium, bringing the case to the Beijing High People’s Court. The issue became very politicized with international news coverage and threats of sanctions from the United States if the Beijing High Court did not rule in favour of Pfizer. (Abrami & Manty, 2010)

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There was major backlash following the initial 2004 ruling from SIPO. It was deemed the Viagra Heist by U.S. media, citing “China decided to ignore market principles, its own World Trade Organization commitments and the long-term interests of its people by overturning the drug’s patent” (WSJ, 2004). The Deputy U.S. Trade Representative claimed there may be retaliation with tariffs aimed at China’s domestic pharmaceutical industry if Pfizer ended up losing its patent (Kyne, Hensley, & King, 2004). Furthermore, American officials stated that “it’s difficult not to view this case within a pattern of intellectual property infringement,” and asserted it was a test of their commitment to international trade rules (Gardiner, 2004). The American Chamber of Commerce in China stated that the decision caused great concern in not only pharmaceutical industry but the entire business community (Andrews, 2006). The far-reaching consequences of this initial decision are revealing to the extent of political influence that the pharmaceutical industry possesses. Since the beginning of the lawsuit in 2001, almost every high-ranking US official discussed this matter with their Chinese counterpart (Sun, 2006).

The Beijing High Court ended up ruling in favour of Pfizer, which was monumental as less than 20% of SIPO decisions were reversed during that time (Flicker & Dunne, 2005). There are several underlying aspects of this case that incorporate both the importance and complexity of the global patent system. The patent system is subject to national interpretation, adding to a convoluted series of processes that an international organization must adhere to in order to gain global protection. This is a costly, time-consuming endeavour that has a significant effect on corporate decision making. Three major pharmaceutical companies including Eli Lilly & Co., operate in China but have been unwilling to establish R&D facilities, nor bring its most current pharmaceutical advancements due to protection concerns (Andrews, 2006). Disclosure is an important component that international companies must incorporate into their strategic decisions. Sufficient information must be submitted to government agencies which presents a risky but necessary step in order to be granted legal protection. While it is entirely reasonable that corporate leaders may express their concerns, government officials rarely engage in such widespread criticism, as demonstrated through the Pfizer case. The potential adverse effects that were threatened by foreign governments upon an entirely independent judicial process signifies the growing importance and highly politicized nature that intellectual property entails. There was no negative feedback from government officials on the invalidation verdicts from the United Kingdom or Canada.

While China has been justifiably criticized for its violations, significant progress has been made to the relatively new litigation system since its adoption in 1985. The fact that a consortium of Chinese companies chose the legal route instead of illegally mass-producing generics pays homage to the legitimacy and recognition of pharmaceutical patent protection. This recognition has led China to surpass the United States as the most litigious patent country in the world (Bloomberg, 2014). Furthermore, China has agreed to virtually every international IP agreement (See Appendix Figure 3a). The adoption of these standards is important, however, enforcement becomes the critical factor to truly achieve a successful worldwide system. In an updated patent strength index that encompasses enforcement dimensions over book-law conditions, China experienced volatility but showed no overall improvement from 1998-2011 (Papageorgiadis, Cross, & Alexiou, 2014). In 2017, the U.S Administration initiated a probe into allegations of IP theft but only six companies were willing to come forward even though thousands of government complaints were registered (Sherman, 2017). This is a clear indication of the immense bargaining power the Chinese market possesses and the inherent risks associated with any public criticism. The balance of power is typically heavily one sided in favour multinational corporations but the unique characteristics of economic growth and the world's largest marketplace have caused the inherent predicament that businesses face around the world. This example represents a microcosm into business operations in China, with similar difficulties occurring with technology companies such as Google and Facebook. The intricacies of each specific allegation can be examined further to determine an unbiased outcome. The noteworthy facet of this case is the immense backlash that China received, which demonstrates the importance and geopolitical influence that intellectual property protection garners. There have been several high-profile lawsuits in recent years in China and the burgeoning pharmaceutical markets of India and Brazil. As developing countries transition their economies, IP protection will remain at the forefront of political discussions and trade talks. While trademark and copyright infringement are important issues, the consequences are less severe and predominantly economical. The specific intricacies of the pharmaceutical industry have significant consequences that need to be addressed as a pertinent global issue.



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## 2.2 Ethical Issues

Economic development is prioritized by every nation with difficult trade-offs becoming inevitable. As the global economy becomes increasingly interconnected, ensuring adequate intellectual property protection is a necessity in order to maintain a fair, open trading system and reduce the threat of nationalistic policies. While copyright and trademark infringement are important issues that have notable economic consequences, a unique importance befalls protection in the pharmaceutical industry. Governments face an undesirable predicament enumerating from combatting public health crises, providing access to affordable, innovative medicines while subsequently encouraging foreign direct investment and maintaining positive geopolitical relations. On the other hand, this highly competitive, research intensive industry compels companies to recuperate their astronomical R&D and commercialization costs in a finite time frame. Extensive societal scrutiny arises given that companies have a marginal cost of virtually zero for new medicines, exacerbating public discourse. These inimitable circumstances have substantiated the rise of one the most socially, economically, and politically influential global industries.

The Pfizer case incorporates the underlying objectives that encompass the pharmaceutical sector, providing global access to drugs while minimizing the potential adverse health effects. Viagra is deemed a lifestyle drug which is an important distinction from life-saving medicines that affect public health. Viagra quickly became the most counterfeited drug in the world, with 90% of Viagra sold in Shanghai being faked (Abrami & Manty, 2010). The majority of counterfeit drugs contain inefficacious compounds, making Viagra an easy target with limited risk as opposed to oncology, HIV or malaria drugs. The World Health Organization (2017) analyzed 100 studies from 2007-2016, covering 48,000 drug samples, and concluded that 10.5% of worldwide drugs were fake or substandard. The difficulty in measuring is ostensible but it is estimated that the global counterfeit medicine trade generates \$30 billion dollars annually (WHO, 2006). The stark divide across nations is perpetuated with a prevalence of less than 1% in developed countries while Nigerian health officials estimate at least 70% of drugs in circulation are counterfeited from China, India, Pakistan and Indonesia (WHO, 2006). These significant concerns encapsulate innocent citizens and cause hundreds of thousands of unwarranted deaths every year. One of the key motives for this illicit business is an inadequate legal framework where counterfeiting is only

treated as a trademark violation, creating a low risk environment (World Bank, 2005). Out of 193 World Health Organization member states, only 20% have sufficient regulation and enforcement for medicines (WHO, 2006). There is an incessant need to provide access to affordable medicines and developing pharmaceutical industries outside of OECD countries is a beneficial means, but the complex oversight of pharmaceutical products and ease of global distribution invokes a detrimental burden of responsibility that goes far beyond the consequences of copyright or trademark theft.

The patent system plays an important role in society but occasionally encounters ethical and moral disputes. In the 1980s, Harvard University produced a genetically modified mouse, deemed the oncomouse, specifically designed to be highly susceptible to cancer by introducing a gene that can trigger the growth of tumours (WIPO, 2006). Patent authorities faced a moral dilemma and were required to set a highly controversial precedent. The United States granted the patent, Canada ruled that higher life forms were not patentable while the EPO applied a utilitarian test; granting the patent on the likelihood of substantial medical benefits outweighing the potential animal harm (WIPO, 2006). This was an interesting approach because a similar application for the Upjohn mouse was denied due to the fact that treatment for hair loss did not outweigh the moral concerns (Mayer & Alexander, 1991). Similar genetic engineering cases have gained media attention and public scrutiny including Monsanto seeds, a company recently acquired by Bayer for \$63 billion. In 1980, the U.S. Supreme Court allowed seed patents in a 5-4 decision, paving the way for Monsanto to become the world leader in genetically modified seeds and winning 674 biotechnology patents (Mercola, 2014). Agricultural practices subsequently changed, with farmers not being able to re-plant or sell naturally growing seeds without a license fee. Patents will undoubtedly continue to play a significant role in ethical discussions with new technologies coming to fruition such as the gene-editing tool CRISPR. The potential benefits and ramifications from modifying DNA are incomprehensible. In 2014, the USPTO granted the Broad Institute of the Massachusetts Institute of Technology a patent for “CRISPR-Cas systems and methods for altering expression of gene products” (US Patent No. 8,697,359, 2014). Patents establish a legal precedent that have long term consequences on not only domestic industries, but international policies as well.

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## 2.3 Multi-lateral Trade Agreements

While it is difficult to quantify the role of intellectual property on the decisions of government officials, it becomes apparent that there is an increasing importance on pharmaceutical protection due to the prevalence in recent trade deals. Many skeptics argue that recent trade deals are inherently formed in large part for corporations to enhance the protection of global assets while expanding to new markets. Osgood and Feng (2018) found that in twelve recent U.S. trade agreements, patent focused firms were more likely to join ad hoc coalitions and pursue political behaviours both publicly and directly to lawmakers through lobbying. According to the U.S. Special 301 Report, pharmaceutical reform is currently being pressured by the United States towards South Korea, Japan, China, India, Indonesia, Argentina, Saudi Arabia, United Arab Emirates, Canada and Mexico (USTR, 2018). While Free Trade Agreements are generally supported, the pharmaceutical industry receives the most scrutiny by opposition parties for the potential negative consequences in accessing affordable drugs. Because the industry is dominated by industrialized countries, it can be construed that the interests of multinational firms are prioritized over the needs of developing nations. From the company's perspective, protecting their fundamental invention is necessary in order to adequately compensate for extensive research and development, further enabling the innovation process that will contribute to the improvement of global health standards. Encouraging global trade through the usage of free trade agreements is critical to reduce barriers and enable the allocation of financing around the world. The inclusion of detailed pharmaceutical protection in recent trade deals incorporates the growing sentiment on the political and economic importance of this industry.

### *CPTPP – Comprehensive and Progressive Agreement for Trans-Pacific Partnership*

This agreement has been recently implemented as of December 2018 and includes the nations of Australia, Brunei, Canada, Chile, Japan, Malaysia, Mexico, New Zealand, Peru, Singapore and Vietnam. Formerly known as the twelve country Trans-Pacific Partnership (TPP), the United States have withdrawn their support resulting in the ratified eleven nation CPTPP agreement. Before their departure, U.S. Trade Representative Michael Froman stated that data protection on biologics is “one of the most difficult outstanding issues in the negotiation” (Hernandez, 2015). While there were several quarrelsome issues, discussions surrounding patent

exclusivity for biologics was a persistent topic. This is an interesting trade agreement as the Party that would benefit the most from additional protection withdrew, enabling the remaining parties to amend certain aspects. Enhanced patent protection is found in certain provisions relating to patent linkage and grace periods. Patent Linkage refers to notifying original patentees when generic suppliers are hoping to gain marketing approval through the brand name drug's clinical trial information. Critics argue this enables drug companies to further extend patent protection while advocates claim this procedure provides a safeguard because it provides a legal mechanism for early resolution and ensures regulatory entities do not inadvertently infringe on the rights of a foreign entity by granting marketing approval (Son, Lopert, Gleeson, & Lee, 2018).

Article 18.38 refers to the grace period, which provides the inventor up to one year of protection after they publicly disclose an invention. This is a common provision in patent law and particularly important for public research institutes, universities, individual inventors or small sized companies. The provision encourages researchers to quickly publish works, enabling amelioration, additional funding and advancing access to knowledge. Grace periods are commonplace, however several countries, including China and the EPO, opt for a six-month term. While there were very few changes from the original agreement, almost the entirety of Article 18 Section F Subsection C: Measures Relating to Pharmaceutical Products – is suspended. Article 18.37 suspends obligations dealing with new uses, methods and processes of a known product as well as inventions derived from plants. Article 18.46 removes patent term adjustments for unreasonable granting authority delays, unreasonable curtailment from the marketing approval process and patent applicant requests to expedite the examination process. The major distinction incorporates data exclusivity, where pharmaceutical products lost their five-year exclusivity but agricultural chemical products maintained a 10-year exemption. Biologics were completely suspended, removing the eight-year exclusivity set forth in the TPP agreement. It is certainly noteworthy that the majority of pharmaceutical patent protection was suspended when the United States withdrew from the agreement. (CPTPP, 2018)

#### *TTIP – Transatlantic Trade and Investment Partnership*

Negotiations began in 2013 between the United States and European Union. This would become the world's largest trade agreement but talks have been suspended since 2017. While

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Japan, the United States and European Union have the most advanced IPR standards, there are still conflicts that arise in negotiation processes surrounding these issues. An important distinction is that US businesses are starkly divided on “reconciling across the board differences,” with the pharmaceutical industry viewing this as a necessity moving forward while internet and software companies are advocating to not even have an IPR chapter included (EPRS, 2014). Many business leaders in internet and technology have supported reform and limiting patent protection however, further research would be needed to determine other industry perspectives. The world’s two largest economies with a dominant market share in the pharmaceutical sector would have a dramatic impact on access to drugs and global protection standards. According to the European Parliament and the European Commission’ Joint Transparency Register, GlaxoSmithKline had fifteen meetings with the EU Commission, Novartis had eight, while Johnson and Johnson and Sanofi each had six in a five month span during TTIP negotiations (Tansey, 2015). The pharmaceutical lobbying industry is always influential but even more so during trade negotiations; having quadrupled its budget and the percentage of total corporate lobby meetings from 2012-2014 increased from 2.4% to 16.5% (Cann & Silva, 2015). Even though negotiations have been suspended, it should be emphasized the significance of this potential deal and the subsequent effect it could have on nations around the world. (European Commission, 2015)

#### *CETA – The Comprehensive and Economic Trade Agreement*

This recent trade agreement is between the European Union and Canada. Pharmaceuticals were of particular concern for European parties, as they are Europe’s most valuable category of exports to Canada (Webster, 2014). Some of the notable provisions include extending patent protection, “*sui generis*,” for an additional two years, totalling twenty-two from the time of filing. Although aligning with Canada’s current IP regime, guaranteeing data protection for eight years restricts future governments from ever shortening the term length. Article 20.28 details “if a Party relies on patent linkage mechanisms...it shall ensure all litigants are afforded equivalent and effective rights of appeal.” Canada introduced Notice of Allegation linkage regulations in 1993 where the patent holder has 45 days to initiate a lawsuit when a generic manufacturer is attempting to gain market approval (Lexchin & Gagnon, 2014). The one-sided nature of the patent linkage system is perplexing, given the European Union gains access to Canada’s system but is not required to enforce one themselves, and considering they formally requested that Italy remove

theirs and adhere to EU rules when they attempted implementation (European Commission, 2012). It is estimated that this Right to Appeal provision could further delay generic entry in Canada by 6-18 months (Grootendorst & Hollis, 2011). This comprehensive agreement contains extensive details on the pharmaceutical industry with a focus on strengthening Canada's current IP regime. (CETA, 2016)

#### *USMCA – United States Mexico Canada Agreement*

The updated version of the North American Free Trade Agreement was recently signed by all three leaders but still needs to be ratified by the governments of Mexico, Canada and the United States. There were only a few notable changes from the original North American Free Trade Agreement which include the dairy industry, automobile manufacturing, labour regulations and intellectual property. Article 20.F.14 refers specifically to biologics, citing all parties must “provide effective market protection...*mutatis mutandis*, for a period of at least ten years from the date of first marketing approval of that product in that Party.” This refers to data exclusivity which is an increase from Canada's eight-year and Mexico's five-year term but still lower than the United State's twelve-year protection that was enacted in the Affordable Care Act. A noteworthy addition to this agreement is included in Article 32.10, which obliges all parties to be informed three months prior to negotiations with any non-market economy, with the ability to “terminate this Agreement on six-months notice.” This is widely assumed to provide veto power to the United States for any country involved in negotiations with China. (USMCA, 2018)

These examples of Free Trade Agreements exemplify the importance that is placed on the pharmaceutical industry. The consistent discussions and common occurrence validate the disputable nature of the ultimate beneficiaries from strengthening protection. The withdrawal of the United States from the TPP and subsequent suspension of several provisions validated the notion that they were the Party responsible for such extensive protection. While the CPTPP and USMCA involve highly dissimilar IP economies, CETA incorporates numerous provisions even though intellectual property standards are closely aligned. The EU has a distinctive advantage in the pharmaceutical industry, leading to apparent concessions from their Canadian counterparts. Deriving data from the U.S. Chamber of Commerce's International IP Index, Canada is shown to have considerably lower patent indicators, notably pharmaceutical-related enforcement, than their

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U.S., EU and Japanese counterparts (GIPC, 2017)(See Appendix Figure 4a). The reasoning for Canada's ranking is cited as the Federal Court decisions to invalidate patents on the basis of lack of utility for 28 biopharmaceutical cases including a Supreme Court verdict against AstraZeneca versus a generic manufacturer. By incorporating all patent related indicators, India obtains a score of 1.25, China 4.35 and Canada 5.05 while the U.S., EU and Japan all received scores above 7 out of a possible 8. This has contributed to an overall IP ranking of 43<sup>rd</sup> from India, 27<sup>th</sup> from China, 17<sup>th</sup> from Canada while the U.S., UK, Germany, Japan, France and Switzerland are ranked within the top 7. China was scrutinized for not having a patent linkage system, something Canada possesses but EU members do not.

While IPR protection must continually adapt to new technologies and sharing of information in our increasingly knowledge-based economies, trade agreements are able to provide minimum requirements and set a global precedent. The TRIPS agreement covers roughly half of intellectual property regulations while the original TPP agreement covers approximately 70% when compared with the benchmark index of the top forty-five global economies (GIPC, 2017)(See Appendix Figure 5a). As economies become increasingly more diverse, IP protection will be needed to ensure effective beneficial results through trade negotiations. The inclusion of less developed nations into the world economy through the WTO and multi-lateral trade agreements is critical in providing adequate opportunities to realize economic potential. The accession into NAFTA, European Union and WTO have resulted in monumental economic growth for the nations of Mexico, Poland and China. Reducing trade barriers is a necessary component to achieve comparative advantages but ensuring proper IP protection is vital to facilitate fair market practices. The TRIPS agreement provided an adequate global standard for intellectual property protection that remains a sufficient benchmark. With many newly established comprehensive trade agreements in negotiations or recently finalized, it becomes evident that increasing intellectual property protection is prioritized with a notable emphasis on the pharmaceutical industry.

## 2.4 Foreign Direct Investment

Countries are shifting towards liberalization and free market economies, as exemplified in 84% of policies from 2003-2017 promoting international investment while only 16% were restricting (UNCTAD, 2017)(See Appendix Figure 6a). Foreign Direct Investment (FDI)

accounted for 39% of total incoming finance for developing economies and accounted for 47% of the \$1.43 trillion invested in 2017 (UNCTAD, 2017). These FDI flows are mainly from MNEs in developed nations, accounting for roughly one trillion dollars. This is the leading source of external financing and the most resilient to economic shocks. These numbers are staggering and provide a perspective on the importance of the allocation of money around the world. FDI is an important indicator and can provide adequate resources to transition a country economically and increase the standard of living for its citizens. China is an excellent example of this transition, with record inflows of \$136 billion in 2017 and hundreds of millions of people being lifted out of poverty over the course of a generation (UNCTAD, 2017). While there are many contributing factors to economic development, FDI is an instrumental component and indicates a level of stability since MNEs are able to offset the potential risks to achieve positive returns on investment.

Globalization has allowed multinational organizations to reap the economic benefits of comparative advantages, divisions of labour and advancements in technology. The evolving operations of multinational organizations have enabled FDI in developing countries to increase from less than \$10 billion in 1980 to \$670 billion in 2017 (UNCTAD, 2019). Extensive research has been conducted on the drivers of FDI in developing nations that include market size, openness, country risk levels, geographic location and traditional endowments. Due to the relatively new acquisition of IP standards for many countries since the inception of the TRIPS agreement, an inflection point occurs to accurately assess the effect on FDI for these nations. TRIPS was enacted on January 1<sup>st</sup>, 1995, in the middle of a remarkable upsurge of FDI growth in developing countries from 39\$ billion in 1991 to 231\$ billion in 2000 (UNCTAD, 2019)(See Appendix Figure 7a). The fundamental premise of the TRIPS agreement was to “engender positive impacts in developing countries, including more local innovation and additional inward foreign direct investment and technology transfer” (UNCTAD, 1996). Focusing specifically on the relationship between IPR protection and FDI in developing nations, ambiguous results have occurred. Glass and Saggi (2002) concluded IPR protection had a negative impact on FDI and innovation due to a resource wasting and imitation disincentive effect, while Li and Qiu (2014) found strengthening IPR protection increased FDI and innovation. Distinguishing between general IPR and FDI complexities and patent protection surrounding technology intensive FDI enables a more detailed analysis into the specific issues concerning China and India’s pharmaceutical industries.



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Adversaries of the TRIPS Agreement argue there is an inherent disadvantage that technology importing nations face while the main beneficiaries will be top producing technology countries like the United States. Proponents of the Agreement emphasize that any losses occurred will be more than offset by the gains in market access, efficiency and innovation. McCalman (2001) concluded patent protection generates large transfers of rent appropriation for inventions, with the United States receiving 40% of the gains associated with trade liberalization. Overlooking the potential benefits arising from role of trade and multinationals, developing countries paid 64% of net transfers, alongside Canada contributing over \$1 billion dollars in net losses (McCalman, 2001). The harmonization of patent standards inadvertently effects smaller developed nations, as the United States is able to unilaterally benefit from seeking international patent protection while inventors already sought protection in the United States beforehand. This can be used to explain the net losses attributed to twenty-two nations, while only six countries, including Germany, US and France, benefitted (McCalman, 2001). Zhang and Yang (2016) analyzed FDI data from 1985-2012 for twenty-three developing economies, specifically focusing on seven drivers of FDI which include GDP, trade, R&D, openness, country risk, investment safety and TRIPS adoption. Utilizing the System Generalized Method of Moments econometric technique, the results show TRIPS enforcement has a positive relationship with inward FDI, at the 1% significance level (Zhang & Yang, 2016). In addition, R&D levels were positively correlated with inward FDI. These results further validate the notion that while it is in the best interest of technologically innovative countries like the United States, developing nations are able to extract value through foreign direct investment.

China has benefited immensely from FDI inflow since becoming a more market-based economy in 1978, with the World Bank citing FDI as a key factor in their economic growth after this period (World Bank, 1997). China's recent IP reform provides a desirable timeline to analyze the effects of these modifications on FDI decisions. Awokuse and Yin (2009) investigated the impact of China's IP laws on FDI from 1992-2005. The analysis uses two measures as a proxy to determine IPR strength; annual foreign patent applications and the previously alluded to Ginarte and Park (1997) index, which was further updated by Park (2008). China had an average patent strength score of 1.33 from 1960-1990, before exponentially increasing to 2.12 in 1995, 3.09 in 2000 and 4.08 in 2005 (Park W. G., 2008). From 1992-2005, foreign patents exponentially increased at an annual growth rate of 19%, the majority coming from United States, Japan and EU

members, with the results demonstrating a 1% increase in foreign patent applications led to an FDI increase of 0.6% (Awokuse & Yin, 2010). Panel data was used for 38 countries, signifying the strengthening of IP protection had a positive effect on FDI inflows and supported a market expansion effect (Awokuse & Yin, 2010). These findings suggest that IPR protection was able to stimulate horizontal FDI in a country with a discernable threat of imitation. Although many issues are still prevalent, the swift introduction of a patent system positively influenced China's attractiveness to foreign investors.

There are many factors involved in the strategic decision making of multinational firms for the location of FDI which is even further exasperated when comparing across nations due to the various country specific factors involved. Du, Lu and Tao (2008) analyzed the role of intellectual property rights and contract enforcement, referred to as economic institutions, on the FDI location choices of US multinationals, focusing on locations within China. The data set includes 6288 US multinationals that have invested in various regions across China from 1993-2001. A discrete choice model was used, analyzing four key factors which include IP protection, government intervention, government corruption and contract enforcement. Controlling for agglomeration, wages, infrastructure, education, US embassy or consulates and government promotion policies, the results show a positive correlation between all four factors. Intellectual Property Rights protection, at the 1% significance level, is a critical component in determining the location of US multinational FDI decisions. This study is particularly insightful as it avoids important variables such as culture, language, political systems, corporate tax, national trade and investment policies that vary across countries. (Du, Lu, & Tao, 2008)

Multinational corporations have several options when accessing a foreign market: exports, FDI, joint ventures and licensing. Host countries want to incentivize investments and spur economic activity in order to develop domestic industries and enable technological progression. Licensing, however, increases costs for domestic firms while reducing overall investment. Aligning with several related studies, Smith (2001) found strong foreign patent rights, or FPRs, reduce affiliate output and sales, while increasing licensing agreements. Deterring licensing agreements and persuading optimal investment decisions allows for high quality FDI, enabling pervasive technological advancement and economic capabilities. Utilizing a unique firm level data set, Javorcik (2004) examined FDI inflows for Eastern European countries following the collapse

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of the Soviet Union. Lack of adequate IP protection was found to be a deterrent for all investors, especially IP intensive industries, as well as a dissuading factor for undertaking local production (Javorcik, 2004). As a result, foreign entities instead focused on distribution networks, which was present across all sectors. This aligns with the previously alluded to analysis from Mansfield (1994) relating to firm decision making and technology transfers. Additionally, Nunnenkamp & Spatz (2004) analyzed FDI on a disaggregate level, finding R&D expenditure by US affiliates rises with stronger IP protection. IP effects are significant only when the host country has a local imitative capacity, while particularly strong IP protection induces a substitution of licensing for FDI (Nunnenkamp & Spatz, 2004). While FDI inflows and IP protection vary significantly across industries, the pharmaceutical sector has a distinctive global supply chain in which developing nations and domestic industry can benefit from foreign investment. Strengthening intellectual property protection suffers from diminishing returns, exemplifying the need to strike the correct balance in order to encourage the optimal foreign investment, R&D expenditure.

Government officials face difficult decisions due to the flexibilities offered under the TRIPS agreement. Members are able use the subject matter of a patent without authorization in the case of a “national emergency or other circumstances of extreme urgency or in cases of public non-commercial use” (WTO, 1995). Public non-commercial use refers to member states being able to issue compulsory licenses as long as the product is not intended for monetary compensation. Contentious discussions have surrounded the ambiguous phrasing of these provisions. Several countries have utilized these provisions for epidemics such as HIV/AIDS but it imposes particularly convoluted boundaries. Between 2006-2008, Thailand issued compulsory licenses under this provision for two HIV drugs, a heart disease drug and four anti-cancer drugs (Ho, 2009). Plavix, a popular heart disease drug manufactured by Sanofi, became the first “lifestyle drug” or non-infectious disease to be targeted for compulsory licenses. The arguments can be justified from both parties involved. Heart disease and cancer are leading causes of death so providing access to all citizens is a public health priority. 25% of Thai citizens lived on less than two dollars per day while Plavix was listed at roughly two dollars per dose (Ho, 2009). With Thailand being classified as a middle-income country, the pharmaceutical industry proposed valid concerns with this precedent. Low income countries will be more inclined to follow suit and it is not a sudden national emergency such as AIDS or the recent Ebola outbreak. In addition, it provides a disincentive for

private R&D investment while disproportionately affecting publicly funded R&D from developed countries and risking the viability of TRIPS if it contains significant loopholes (DeRoo, 2011).

The WTO has not defined public non-commercial use which has allowed for not-for-profit government healthcare to fall under this definition and thus, provides limited legal justification for pharmaceutical companies. Moreover, government health care programs make up the majority of purchasing power for pharmaceuticals which imposes an innate quandary. Difficult circumstances are inevitable as finding the correct balance between reducing public healthcare costs and appeasing foreign entities must occur. Thailand experienced immense political pressure and global backlash as a consequence of these decisions. The United States elevated Thailand to the Priority Watch List in 2007, citing the specific use of compulsory licenses even while acknowledging the ability to issue such licenses under WTO rules (USTR, 2007). The potential consequences of governmental decisions are not limited to middle-income countries. AstraZeneca simply removed their drug from the New Zealand market amid pressure to lower prices while Novartis announced it would redirect hundreds of millions of R&D investments as a result of Indian's patent office not granting its Gleevec patent (Friedman, 2009). While oncology and life-saving drugs provide a reasonable justification for government action, Viagra does not fall under that classification. Egypt, the largest and most established pharmaceutical market in the Middle East, authorized twelve local companies to produce a generic version of Viagra just two months after being on the market, citing the "interests of the poor people" (Allam, 2002). This was allowed under the phase in clause that permitted a grace period for enforcement from LDCs and developing nations. Political pressure ensued, and American direct investment fell to \$390 million that fiscal year, down from \$1.6 billion two years prior (Allam, 2002). While there are several contributing factors that affect the decision making and risk assessment involved in foreign direct investment, intellectual property protection is indicative when it comes to the pharmaceutical industry.

It is a difficult predicament that government officials must face with multiple power levers at play. While providing affordable, generic access may win public support in the short-term, potential adverse effects may occur in the long term. The research surrounding IP protection and economic growth is unclear, but generating foreign direct investment is a critical component for emerging economies. An extensive study analyzed panel data of 103 countries between 1970-2009 and found that a 10% increase in a country's ratio of FDI to GDP leads to a 3% increase in

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economic growth (Kashcheeva, 2013). While introducing the optimal patent laws are widely discussed, enforcement was shown to provide “clear evidence that all countries can potentially benefit from strengthened levels of patent enforcement, this being the case especially if they also receive high levels of FDI” (Alexiou, Nellis, & Papageorgiadis, 2016). FDI flows have a mediating effect on patent enforcement and economic growth, particularly for developed countries but nonetheless, still positively correlated across all economies. The central distinction is the differentiating factors of enforcement and patent law; exemplified by increased patent law protection having a negative effect on developing countries while being insignificant for developed nations (Alexiou, Nellis, & Papageorgiadis, 2016). This suggests that developing nations can improve both domestic industry and FDI through patent enforcement. These results can be explained by the essential need for compliance from companies while agreeing to a complex system without the adequate resources may render it ineffective. With many countries around the world focusing on developing their pharmaceutical industries, it is important to consider the strategic implications of governmental policies.

Mergers and Acquisitions are an important tool for multinational corporations to generate value, improve cost efficiency and access new markets. With many companies becoming conglomerates possessing subsidiaries around the world, smaller firms are able to benefit by accessing this lucrative market. Cross-border M&A transactions totalled \$98 billion in 1990, while that figure reached \$887 billion in 2016 (UNCTAD, 2017). Although these business transactions can achieve positive growth for the target company and host country, a focus on greenfield investments provides more predictable outcomes. Greenfield investments simply refer to foreign direct investment that establishes a new project or firm in the host country, while M&A transfers ownership of an existing firm. Shesha (2018) analyzed the effects of these two foreign investment options and the subsequent impact on economic growth across 51 countries from 2003-2017. Greenfield investments had a positive growth effect that was robust across various estimation methods and subsamples, whereas M&A had no significant effect on growth (Shesha, 2018). Focusing on the beneficial interests of both developing nations and multinational corporations, mergers and acquisitions provides ambiguous results that differ each transaction based on the interests of the acquiring firm. Undoubtedly, M&A represents a considerable component of growth strategies in the pharmaceutical sector, epitomized by several multi-billion dollars blockbuster deals in recent years including Bristol-Myers Squibb acquiring Celgene for \$74 billion dollars

(BMS, 2019). However, due to the unpredictability and variance across firm's motives, mergers and acquisitions will not be considered when addressing the effects of IP protection on multinational decision making.

The growth and development of the Indian pharmaceutical industry has been directly impacted from global standards relating to patent protection. In the 1970s, the national sector was extremely small, accounting for less than 25% of the domestic market and only two of the top firms in retail sales were Indian (Redwood, 1994). India implemented the Patents Act in 1972, greatly weakening intellectual property protection by making pharmaceutical product innovations unpatentable, shortening the statutory term on medicines to 5-7 years, and endorsing Licenses of Right after three years "on the ground that the reasonable requirements of the public with respect to the patented invention have not been satisfied or that the patented invention is not available to the public at a reasonable price" (IPIndia, 1970). The impending results show a steep decline in patents granted; from 3,923 (3,294 foreign) in 1970-1971 to 1,019 (670 foreign) in 1980-1981 (OPPI, 1996). It is evident that foreigners, in particular, did not perceive utility from obtaining Indian patent protection after the implementation of these measures. By the 1990s, Indian firms accounted for six of the top ten firms by pharmaceutical sales, 70% of bulk drugs and 80% of formulations (Hamied, 1993). India became a dominate player in the pharmaceutical sector, containing the largest number of US FDA approved drug manufacturing facilities outside the United States (Sampath, 2005). Predominantly focusing on generic manufacturing, India was the most active country in adamantly opposing the requirement of product patents for pharmaceutical innovations in the TRIPs Agreement (Lanjouw J. O., 1998).

The Indian marketplace offers multinational corporations a great opportunity to access a large, growing consumer market and incorporate distinct cost advantages into business operations. The generic drug manufacturing industry incorporates a unique business model that aligns with India's comparative advantages. Strong reverse engineering and chemistry skills in conjunction with a low-cost structure has enabled India to test, develop, manufacture and market a generic medicine at a cost of 20-40% of an identical drug in the West (Lanjouw J. O., 1998). There are several stages in the commercialization of a new drug, from discovery research to lengthy clinic trials before approval is granted. At the time, most projects from Indian companies had to be licensed out to multinationals for later stage development, mainly clinical trials, due to limited

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capital, inadequate facilities and lack of expertise (Jha, 2007). Indian had capitalized on their comparative advantages by developing a successful pharmaceutical industry based on generic manufacturing, but enhanced expertise and technology would be needed for further development and innovative capabilities. An increase in R&D expenditure would be needed, which averaged 1.9% of total sales from 2000-2005, far below their American and European counterparts (Sampath, 2005). The TRIPs Agreement provided both difficulties and opportunities for the Indian market to exploit, as multinationals could reduce costs while Indian companies could obtain capital and gain expertise. For perspective, starting salaries for research scientists were 20% of those in the United States (Lanjouw J. O., 1998). India quickly became a favoured destination for large scale clinical trial research in Stage 2 and 3 of development (Jha, 2007). While the TRIPs Agreement had negative implications, India was forced to adapt their existing patent regime which had dramatic impact on their pharmaceutical sector. India had an average patent score of 1.03 from 1960-1990, out of a possible 5, before dramatically increasing to 2.27 in 2000 and 3.76 in 2005 (Park W. G., 2008). Subsequently, the share of FDI in the pharmaceutical sector increased from 2.5% from 1998-2002 to 4.6% between 2002-2006 (Jha, 2007).

The similarities of the Chinese and Indian markets allow for an in-depth perspective on the role that patent protection has played in the development of their pharmaceutical sectors. A comparative analysis by Rai (2009) provides insight into India's pharmaceutical industry *vis-à-vis* China from 1990-2007. India and China often get compared from an economic perspective due to the unique market size, regional proximity and similar development stages. China has far surpassed India economically in recent years, providing a reasonable path for India to follow. From a multinational perspective, however, China and India offer dissimilar comparative advantages in the pharmaceutical industry. India has an expertise in chemistry processes and a larger base of low cost, IT-skilled and an English proficient population. China has a scientific workforce alongside a large number of R&D centers, better port facilities and less regulation paired with a well-defined incentive structure. Ratio transformation was used on the Inward FDI Potential Index and inward FDI Performance Index of both countries to account for these negatively related factors. These indexes are broad indicators of the attractiveness and absorptive capacity of FDI worldwide by the UNCTAD. While both countries provide distinctive differences, the results found China's business environment has a direct impact on FDI decisions in India. Strong patent law in combination with administration and enforcement were found to strongly influence foreign decision making.

Furthermore, incentive policies and riskiness in terms of economic and political stability were negligible factors. These results further validate that IP protection is a substantial factor in FDI decisions in this industry, while China and India are vying for the same global market share despite inherent differences. Limitations occur because full compliance of the TRIPS Agreement was not mandated until 2005, and economic disparity has further increased so additional research would be needed for a present-day perspective. (Rai, 2009)

There are certainly trade-offs that governments, companies and the public must address when administering global pharmaceutical protection standards. There are immanent opportunities for developing nations to extract from these additional measures. Pliva, a small Croatian company, discovered a new antibiotic but did not have the resources necessary to mass produce and market. After developing a patent globally, they entered into a licensing agreement with Pfizer and the drug subsequently became the market leader for antibiotics with total sales peaking at \$2 billion in 2005 (Jelic & Antolovic, 2016). In addition, 23 correlating benefits are recognized for economies with IP protection above the median average which include fifteen times more clinical trial activity in biomedical FDI and overall being 53% more attractive for FDI (GIPC, 2018). The globalized supply chain of the pharmaceutical sector has enabled developing nations to benefit from multinational investments and contribute towards economic development. To summarize, governments hoping to entice foreign investors need to understand the implications on both domestic industries and multinational decision making. Stronger IP protection reduces the threat of imitation and may encourage higher quality FDI, moving past basic production and distribution networks. On the other hand, enhanced IP protection creates a monopolistic effect that may reduce affiliate output and encourage licensing, resulting in lower FDI and higher costs for domestic firms. This innate conundrum requires government officials to espouse the precise level of IP protection and enforcement.

While debate can endure on the righteousness of the increasingly globalized standards enforced upon nations, the importance of intellectual property cannot be ignored and is only becoming more prevalent in today's modern business environment. Similarities are found across several global indicators. In the Ease of Doing Business Index, the US ranks 6<sup>th</sup>, UK 7<sup>th</sup>, Canada 18<sup>th</sup> and China 78<sup>th</sup> (World Bank, 2018). In the Global Innovation Index, the US ranks 4<sup>th</sup>, UK 5<sup>th</sup>, Canada 18<sup>th</sup> and China 22<sup>nd</sup> (WIPO, 2017). In the Global IP Index, US ranks 1<sup>st</sup>, UK 2<sup>nd</sup>, Canada



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18<sup>th</sup> and China 25<sup>th</sup> (GIPC, 2018). There are various contributing factors related to these indexes but IP protection has become an indicative component on the hierarchy of economic powers. As developing economies around the world discuss essential policies in their growth strategies, enabling adequate IP protection should become a priority in order to fully embrace their economic potential. There is not a consensus on the direct relation between intellectual property protection and foreign direct investment but it is indicative that IP intensive industries are more affected and strategic decision making on technology transfers is strongly correlated. While it is difficult to quantify the effects of IP protection on bilateral relations, the persistent political engagement and detailed requirements in several new trade agreements suggests a significant importance on international trade.

### 3. Impact of IP Protection

The underlying assumption is that creating adequate IP protection permeates the incentive to innovate. By granting exclusivity and preventing competitors for a fixed time period, the patent system allows for sufficient access to a highly profitable market. The subsequent economic incentives would be to heavily invest these profits into research and development, enabling constant innovation. The ensuing benefits would be the democratization of knowledge, inventive medicines and an overall improvement of public health. Once the protection has expired, the world will obtain affordable, potentially life-saving medicines through an ensuing competitive market. While the theoretical justification is rightly principled, the current business climate offers a much more ambiguous contemplation. Innovation is a complex topic in and of itself, becoming difficult to quantify the effects of the underlying factors. There has been sufficient research into this domain, providing tangible results and subsequent discussions but ultimately unable to enumerate the optimal level of protection needed to maximize innovation.

Munos (2009) analyzed 1,222 new drugs, classified as new molecular entities (NMEs) or new biologics (BLAs), approved by the US FDA from 1950-2008. The new drug output from pharmaceutical companies has essentially remained constant over this time period despite a significant increase in expenditure. This analysis highlights the difficulties many companies face, the extremely low success rate as exemplified by only 261 organizations registering a new

innovation while 4300 companies were engaged. Substantial turnover has occurred, with 229 of those organizations having been acquired, merged or failed while only 32 have remained in existence throughout the entirety of this period. This study primarily focuses on new drug innovations which does not provide the full innovative perspective, but elaborates on the difficulties of discovery and limited advancements despite exponential investments. In 2008, only 27% of companies had costs under \$1 billion per NME, while the cost has grown at an annual compound rate of 13.35% since the 1950s (Munos, 2009). Deriving data from the Federal Drug Administration Approval Reports, an updated perspective on new drug approvals can be determined. Incorporating a time period from 2009-2018, results vary significantly from year to year (See Appendix Figure 8a). In 2018, NMEs and BLAs both totaled highs of 41 and 17, respectively, while 2016 saw lows of 15 and 7 (FDA, 2019). The skewed nature of innovation incorporates many different factors, making a conclusive argument on the effects of certain aspects of IP protection unattainable.

Adversaries argue the simple invention of new drugs is not an adequate indicator of innovation, but rather focusing on therapeutic benefits. From 1975-1994, only 11% of internationally marketed new drugs were considered pharmacologically innovative and therapeutically beneficial (Barral, 1996). Furthermore, more recent studies have concluded similar results, indicating approximately 85-90% of all new drugs provide few or no clinical advantages to patients (Light & Lexchin, 2012; Luijn, Gribnau, & Leufkens, 2010). This has occurred despite the fact that there has been a 50% increase in real terms of R&D expenditure by OECD countries from 2004-2014, leading to a steady decline in approvals per inflation-adjusted R&D expenditure (OECD, 2017). This contradictory pattern has been coined “Eroom’s Law,” attributing the effect of constant output with rising costs despite technological advancements as a combination of regulatory costs, a focus on complex conditions and rising drug prices (OECD, 2017). The research process is exceedingly complex, but innovation in the pharmaceutical industry is imperative for advancing society. The advent of innovative medicines has widely contributed to the overall health improvements of nearly every indicator over the past century. As we continue to push the limits of science, inventive medicines and newly discovered research will play a predominant role in the progression of global health standards.

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Biologics were marked to become a revolutionary industry that could alter the research and innovation process. This potential disruptive industry led to all OECD members to include biotechnology as part of their strategic development plans and science & technology policies (OECD, 2004). Investments were strategically prioritized towards biotechnology, attaining tens of billions of private investments annually (Ernst and Young, 2004). Despite governmental initiatives that allow R&D tax credits, easier clinical trials and lower regulatory hurdles, the biologic revolution remained at a relatively constant initial growth rate (Hopkins, Martin, Nightingale, Kraft, & Mahdi, 2007). Due to a variety of factors including a complex research process and longer development time, biologics require a much higher level of R&D investment and overall price point (OHE, 2012). While the prevalence of biopharmaceuticals has increased substantially in recent years, it is difficult to determine the role of IP protection. Williams and Sampat (2015) explored a new field of research, human genomes, to test the effect of patenting on subsequent scientific research and commercial investments. Due to the specificity of gene sequences, comparisons can be made when examining successful and unsuccessful patent applications on how it impacts follow-on innovation. The results find no difference between ensuing research and investment between the invalidated and patented genomes (Sampat & Williams, 2015). Furthermore, Williams (2013) examined the impact on genetic sequencing firm Celera, finding evidence that patented genes saw a reduction in subsequent research and investment by 20-30% compared to genes that were available in the public domain. This suggests a short-term negative effect on innovation and contradicts the perception that insufficient patent protection would inhibit commercial investments.

While innovative new medicines have certainly contributed to the consistent increase in public health indicators, it is difficult to quantify the role of intellectual property rights empowering this innovation. The constant increases in pharmaceutical protection appear to have a limited effect, but several contributing factors distort an overall conclusion to this topic. Eliminating protection standards would assume to disincentivize the excessive R&D spending but evidence of subsequent innovations resulting from an increase in IP standards cannot be determined. Similar to investigating the role of intellectual property rights on industry development, the pharmaceutical sector deviates from other industries. After finding patent invalidation leads to a 50% increase in subsequent citations to the focal patent, Galasso and Schankerman (2014) conclude that patent rights block downstream innovation, but is not found to

be the case in drugs or chemicals. The unique characteristics of the pharmaceutical industry require specific attention in order to address the potential impact of policy initiatives. From an economic development and competitive advantage standpoint, it is certainly desirable to develop innovative capabilities. Countries and companies who lead economically are consistently at the forefront of innovation however, the complexities associated with the pharmaceutical industry make it difficult to enumerate the role of additional protection standards on incentivizing innovation.

### 3.1 Healthcare Costs

One of the fundamental principles that spans across political spectrums is the intent on providing citizens with access to affordable healthcare. The cost of healthcare is complex, incorporating many different factors as societies contain varying levels of government involvement. The cost comparisons between the United States and other developed nations is staggering, with the U.S. expenditure as a percentage of GDP approximately twice as high on average (Papanicolas, Woskie, & Jha, 2018). In fact, the United State's spends more money annually than the entire gross domestic product of all but four nations worldwide. These costs encompass an array of factors however, pharmaceutical spending per capita was \$1443 in the U.S. compared to a range from \$466 to \$939 for other nations (Papanicolas, Woskie, & Jha, 2018). This information is particularly important given that intellectual property protection is closely aligned, indicating that other governmental policies are a much more significant factor in healthcare pricing than pharmaceutical protection. An oft cited argument is that the excessive costs in the United States offset the lower healthcare costs for the rest of the world. If the revenues were on par with other nations, the level of investment and research would greatly diminish, curtailing a subsidizing effect that the U.S. provides to the world. While no politician or citizen would be against a reduction in healthcare expenditure, the United States is by far the most influential market in terms of both revenue and multinational firms. The reliance on the United States market predates its role as the influential global leader in relegating access to affordable medicines around the world. A primary focus on the U.S. market in relation to developing nations enables more valuable insight as opposed to a comparison with Japanese or European markets.

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By granting a monopolization effect, pricing power is given to owners with few restrictions. There is a lack of basic economic principles incorporated in the healthcare industry due to the price inelasticity of consumers regarding medical treatment. To illustrate the vulnerable position consumers are placed in, it is estimated that two-thirds of personal bankruptcies in the United States can be partly or entirely attributed to medical expenses (NASEM, 2018). The unwillingness of consumers to forego medicines contradicts the basic supply and demand notion, leaving the marketplace susceptible to unfair pricing practices. As a result, the cost of medicines continually increases at one of the highest rates of any industry comparative to the consumer price index, increasing 127% compared to 11% from 2008-2014 (Rockoff & Silverman, 2015). Moreover, between 2009-2015, brand name drugs rose by 12.9% annually, eight times the rate of inflation (Patel, 2017). The effect is particularly prevalent in life-saving drugs, illustrated by the average annual price of cancer therapy in 1999 between \$5000-\$10,000 to over \$100,000 by 2012 (Kantarijan & Rajkumar, 2015). The exuberant prices do not necessarily correlate with safety or efficacy, but rather the ability to circumvent traditional market forces through monopolistic tendencies.

Unfair pricing practices are pervasive throughout the industry, resulting in constant media and public scrutiny. Known as price fixing, several recent examples have gained national attention. Valeant Pharmaceuticals has developed a business model on acquisitions and price gauging, having raised the list price 122 times by at least 20% from 2011-2015 (Rockoff & Silverman, 2015). Onerous markups of 500% or more are commonplace, leaving the burden on government, insurance plans and ultimately costing private citizens. In 2013, Valeant acquired the intellectual property rights on a lead poisoning treatment, raising the price from \$950 to \$26,927, a 2700% increase in one year (Patel, 2017). 500 miles away, 8000 children in Flint Michigan suffered one of the worst lead poisoning crises in history. Other notable examples include the price of Daraprim increasing from 13.50-750\$ overnight, alongside a 50-\$600 dollar hike for a two-pack EpiPen (Patel, 2017). These anticompetitive practices have overwhelming societal implications that affect the lives of millions of citizens. Many of these issues are a result of the fragmented United State's healthcare system, but intellectual property protection and generic entry have a profound effect on drug pricing. On average, the cost of a generic drug in the United States is between 80-85% less than its brand-name counterpart (FDA, 2018). Ideally, generic products should gain market access the day after patent expiration and provide affordable drugs to the public, however this is not

always the case. Several of the largest generic manufacturers are divisions of major pharmaceutical firms which are currently involved in an illegal price fixing collusion that is “pervasive and industrywide” and alleges price inflations up to 1,000% (Murphy, 2019). This further exemplifies the importance of a sufficient generic pharmaceutical industry to provide an adequate competitive market and limit oligopolist tendencies after patent expiration. Analyzing Medicare expenditure data from 1991-2008, Kelton et al. (2014) concluded that for every additional generic introduced, the relative reimbursement price would decrease by 13%. Diminishing returns occur after five entrants, indicating an increasingly competitive generic market would inhibit some of these undesirable practices, especially regarding orphan drugs.

Orphan drugs refer to drugs specifically designed for small patient groups, affecting less than 200,000 people. The Orphan Drug Act was enacted in 1983 and included several incentives like research grants, tax credits, quicker approval processes and a 7-year market exclusivity provision. This 7-year exclusivity is the longest lasting protection granted by the FDA, with new chemical entities only gaining five years and pediatrics receiving six months. This additional protection allows for the delay of generic entry into the market, enabling extended pricing power. The median annual cost for an orphan drug is almost \$100,000, compared to \$5000 for non-orphan drugs. Although aligned with good intentions, these protections have enabled the ‘everyone is an orphan’ notion where orphan drugs currently account for more than 40% of FDA approval. There are several manoeuvres that are exploited to garner the benefits of additional market protection. ‘Spillover pricing’ is accomplished through off-label use, where the drug is distributed for a use other than the one described in the initial application. ‘Salami slicing’ refers to separating the patient population into different stages of the disease, reducing the intended population to the 200,000 target. Cancer related drugs have been the main recipient of these designations. Overall, the cost impact has not been justified, with one third of orphan drugs since 1983 being either repurposed mass market drugs or drugs that have received multiple orphan designations. This dramatic increase in designations has inflated the price and created perverse incentives that organizations continue to exploit. (Feldman, 2018)

Patent protection is not the most important but just one of many relevant factors involved, with European nations experiencing far fewer issues with similar standards. Notably, the United States does not regulate excessive drug prices with only a violation of antitrust law providing legal

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justification (OECD, 2018). The obscene prices incurred in the United States compared to the rest of the world are significant however, the advent of generic manufacturers should induce competitive markets and affordable drugs once protection has expired. It is difficult to properly incentivize private firms on essential public concerns such as rare diseases, but curtailing exploitive behaviour is in the best interest of the public. The substantial burden of responsibility is placed on the FDA, given the responsibility of the approval process on the length of protection. While discussions surrounding the role of patent protection on innovation or research decisions can be disputed, pharmaceutical prices indubitably increase as rights are enhanced. The multifaceted issue of incentivizing innovation while providing access to affordable drugs requires sufficient regulatory oversight. The occurrence of price manipulation appears to have become more commonplace in recent years, indicating the significant importance on adequate regulations. Due to the highly profitable U.S. marketplace, market forces will inevitable exploit any deficiencies in the governing process. Policies and regulatory procedures can induce a consequent impact on not only pharmaceutical pricing, but public health as well.

### 3.12 Regulatory Influence

One of the unique characteristics that has been trending upwards is the increasing priority status given by the FDA. After deriving data, it was found that Priority Status of New Drug Approvals has increased at a CAGR of 20% while Biologics License Application have increased at a CAGR of 33% from 2009-2018 (FDA, 2019). The FDA has granted priority review status to 44% of all new drugs from 2000-2010 (FDA, 2019). This trend is significant as the FDA began to receive funding from companies for the approval process in 1992, strongly correlating with the rise in accelerated reviews (Lexchin & Gagnon, 2014). Regulatory agencies outside of the United States have indicated noticeably lower results of both accelerated reviews and assigning significant therapeutic advancement classifications (Lexchin J. R., 2012). Known as “Pay To Play,” companies are able to influence FDA policies and processes. This review process garners the majority of expenditure from companies and provides vital information to ensure public safety. Regulatory institutions in the pharmaceutical process have a significantly larger responsibility over controlled substances than other industries due to the widespread potential impact on public health.

An example of regulatory negligence occurred over the past two decades, with the consequences still being felt across North America today.

OxyContin was approved in 1995 after just 11 months and 14 days, representing the quickest approval of any analgesic product by the FDA. There are specific reasons as to why this pain killer became the leading drug of abuse in the United States by 2004. The FDA regulates the advertising and promotion of prescription drugs however, OxyContin was aggressively marketed as a miracle drug with no side effects. In 2001, the company spent \$200 million dollars alone and ignored doctor's perception that OxyContin was weaker than morphine and could be prescribed for minor back pain. While proclaimed as a long-lasting alternative, the simplistic capabilities to circumvent the long-lasting effects of the drug by grinding the pills for inhalation or injection has been widely considered as the leading cause for the increase in opioid addictions. Reports began to immediately surface of widespread abuse and addiction. The most fascinating aspect of this case is the fact that OxyContin was not an innovative new product that was underestimated. OxyContin had a unique time-release design but was just oxycodone in pure form, a drug which has been used for many years in common medications such as Percocet. Clinical trial testing in 1995 even revealed that 68% of the oxycodone could be extracted from an OxyContin tablet when crushed. It becomes abundantly clear that the commercial success of OxyContin was not because of its innovative capabilities, but rather regulatory neglect. (Zee, 2009)

As a result of illegal marketing strategies, Purdue was forced to pay \$600 million in 2007, even though they had amassed revenues of \$2.8 billion by 2001 (Griffin & Miller, 2010). Other than a label change in 2001 and a warning letter to the manufacturer in 2003, the FDA did not begin addressing the situation until 2009 (FDA, 2017). Purdue Pharma, the manufacturer of OxyContin, designed a new formulation in 2010 called OxyNeo that was unable to be crushed and therefore, abuse deterrent. In Canada, authorities simply removed OxyContin from the market with only OxyNeo being available to patients, and subsequent dispensing rates fell by 46.4% (Gomes, et al., 2017). This is due to the addictive nature of OxyContin which, alongside heroin and other prescription painkillers, are widely considered the most difficult drugs to quit. As health officials began reducing the number of available prescriptions, the millions of addicted patients turned to stronger drugs such as fentanyl and heroin. The FDA originally approved the use of fentanyl in 1998, and further granted off-label, transmucosal immediate-release fentanyl in 2011 (FDA, 2017).



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Fentanyl has become the predominant drug of choice with illicit variations contaminating drug supplies such as cocaine, causing a spike in accidental overdoses. China is the main source of supply for illicit fentanyl that flows into Canada, the United States, and Mexico while China itself does not to have a fentanyl consumption issue (DEA, 2018). China only recently agreed to ban all variants of synthetic fentanyl, as part of trade negotiations. Chinese regulators previously assessed each classification of a controlled substance on a case by case basis, which has been widely criticized as ineffective and profiting from deaths (Myers & Goodnough, 2019). As a result, there has been a total of 399,230 drug overdoses involving opioids in the United States from 1999-2017 (CDC, 2018). The overwhelming societal ramifications of this issue have led the United State's government to declare a state of emergency under federal law in October 2017. Authorities, undoubtedly, bear a significant responsibility to ensure public safety and in this instance, the unintended consequences have been detrimental to society.

These unfortunate events have occurred even though OxyContin "had not been shown to have a significant advantage over conventional, immediate-release oxycodone" (Zee, 2009). By increasing patent protection, the power being authorized to companies is justified on the basis of recovering exuberant research costs in a finite timeframe for the overall improvement of public health. Feldman (2018) did a comprehensive study on all market drugs between 2005-2015 and concluded that "rather than creating new medicines, pharmaceutical companies are largely recycling and repurposing old ones." Analyzing 60,000 data points in which every instance a company added a new patent or exclusivity was documented, the results found that 78% of new patents were from existing drugs. There was also a strong correlation of extending patent protection amongst blockbuster drugs, with 80% of the 100 best selling drugs having extended at least once while 50% extended multiple times (Feldman, 2018). This has become a common occurrence with many companies creating patent thickets around their top selling products. Aside from the product patent claim, or active ingredient patent, companies can obtain a process, formulation or method of use patent to inhibit competition and extend protection past the initial expiry date. The world's top selling drug Humira and OxyContin have both been granted over 100 patents during their life cycle (USPTO, 2019). This unfortunate case incorporates another important component of the pharmaceutical industry; as OxyContin continues to remain the most litigated trade name in pharmaceutical patent cases (Lex Machina, 2015).

### 3.2 Litigation Costs

In the United States, patent litigation is becoming more prevalent, with the number of cases growing at a compound annual growth rate of 6% from 1991-2016. There were over 5000 cases filed in 2016 with a steadily increasing \$8.9 million dollars as the median damage awarded. This is a critical component of business operations that becomes a costly endeavour that companies must adhere to. Importantly, patent lawsuits are a frequent occurrence in the pharmaceutical industry, accounting for 14% of all identified cases, exceeding both the computer electronics and software industries and second only to consumer products. Nevertheless, medical devices, biotechnology and pharmaceuticals far exceed any other industry in terms of median damages awarded from 1997-2016. An interesting caveat that befalls owners is the 33% success rate by patentees. This surprisingly low rate is worrisome for patent holders, and further intensified by the fact that from 2006-2014, 75% of decisions were appealed and more than half resulted in a modified outcome. These figures indicate the both the pervasiveness of patent litigation and onerous costs associated with extensive court cases that engulf the pharmaceutical industry. (PwC, 2017)

From an international perspective, China has become a dominate market, surpassing the United States as the most patent litigated country with over 30,000 cases between 2006-2012 (Bloomberg, 2014). The Chinese patent and legal systems are still maturing and impose distinct differences from operating in the American market. The international influence is ubiquitous, with companies in the US, France, Japan and Germany representing 50% of all plaintiffs but less than 5% of all defendants (Cox & Sepetys, 2009). These figures indicate the risk associated with the Chinese market and the predictable costs related to numerous litigation disputes. The distinct difference in patent infringement is representative by an average median damage award of \$3.8 million from 2001-2007 while the median award across all IPR cases was only \$15,000 (Cox & Sepetys, 2009). The prevalence of global patent litigation is dominated by the United States and China for economic and market factors as well as unique legal characteristics. China is considered to have the fastest time to trial, while the United States has the highest damage awards and lowest chance of going to trial (Bloomberg, 2014). The commonness of settlements and higher potential rewards entices frequent litigation in the United States while a quick process and imitative business environment has escalated Chinese disputes over Asian and European counterparts. From 2008-

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2013, patent infringement filings in China, the United States and Germany have grown at a CAGR of 19%, 25%, and -1%, respectively (Bloomberg, 2014).

As emerging markets, especially China, begin to develop sufficient intellectual property standards and dominate economies, multinational firms need to incorporate expected costs and risks associated with obtaining patent protection and potential legal disputes. Legal costs vary significantly across jurisdictions due to a multitude of factors. Even within a similar European market, estimates for each party range from \$60,000 to \$250,000 for France and Germany while the U.K. exceeds one million (WIPO, 2018). These differences represent a microcosm into the complexities of global operations for an industry that is dependent on IP protection as a company's predominant comparative advantage. These circumstances should change within Europe however, as a unitary patent and unified patent court system will provide a more simplified process. There are several reasons as to why patent litigation has become so rampant. IMAK (2018) analyzed the top-selling drugs on the market and found an average of 71 granted patents and 38 years of attempted protection per drug. The sheer number of patents granted nullifies the intended purpose of the patent system and becomes a strategic ploy for major firms. The vast majority of patents are obtained from large firms and unsurprisingly, more than twice as many patents from large firms are unused compared to small firms, at 40% and 18%, respectively (Giuri, et al., 2007). Considering almost half of patents obtained are unused signifies the strategic importance placed on either seeking potential infringement lawsuits, or patent trolling, and preventing competition from entering the market. These added costs negatively impact all parties involved but disproportionately hinder smaller firms and create additional barriers to entry.

It is easy to construe patent litigation as a specific form of intellectual property that has similar litigation tendencies across all forms and industries. As alluded to previously, the pharmaceutical industry represents a distinctive set of characteristics from other sectors. The disparate differences are demonstrated by the litigation costs significantly outweighing the profits gained from patents in all other industries while the inverse occurs for the pharmaceutical/chemical sector (See Appendix Figure 9a, 9b). This can be explained by the ambiguous boundaries of certain patents; most notably software patents which have the highest rate of appeals over the meaning of patent claims (Bessen & Meurer, 2008). Furthermore, litigation costs are particularly low for compounds with higher patent values while electronics and software have higher litigation rates

and lower values (Bessen & Meurer, 2008). The lower frequency of lawsuits for compounds can be explained by the specific nature of the patent leading to less ambiguity and interpretation. Interestingly, invention patents in China only account for 11% of total cases while design patents represent 46% (Bloomberg, 2014). These findings further exemplify the unique characteristics associated with patent protection in the pharmaceutical industry. The value and strategic importance organizations allocate to patents is significantly higher than any other sector by a substantial margin. Although excessive patenting is a frequent occurrence, the distinct characteristics associated with patenting a specific compound provide an optimistic component compared to other sectors.

From a multinational firm's perspective operating in a hyper competitive global market, the legal implications cause an inevitable burden that embodies non-negligible opportunity costs. The exponential increases of both patents granted and infringement lawsuits around the world influence strategic and operational decision making. The difficulties of obtaining national patents and subsequent lawsuits entails barriers that negatively impact resulting pricing and accessibility. The magnitude of this issue can be epitomised by a recent case involving Idenix Pharmaceuticals, a wholly owned subsidiary of Merck and Co., who won the largest patent infringement verdict in U.S. history against Gilead Sciences, valued at \$2.54 billion (Merck & Co., 2018). Roche (2018), Pfizer (2018), and Novartis (2018) have all spent in excess of \$700 million dollars from 2016-2018 on litigation costs, notwithstanding ongoing investigations. It becomes very convoluted if all lawsuits and legal proceedings are included due to the additional product liability lawsuits inherent in this business. To put this in perspective, Merck (2018) has approximately 4,085 cases for Fosamax, 775 for Proscar, 1235 for Januvia, that are filed or pending as of December 31<sup>st</sup>, 2017. Novartis (2018) claims to have over 1000 individual cases currently pending, with an aggregate total of \$1.5 billion, in which a provision is not even stated due to a payment being "either not probable or cannot be reliably estimated." The complexities and considerable number of ongoing lawsuits have a dramatic impact on strategic operations and generic competition entering the market.

The cycle of patenting and exclusivity creates a dilemma for generic drug companies. Before gaining market approval, there are two paths a company can take. In order to compete for market access of an off-patent molecule with still-patented cousins, they must prove the derivative

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patents are either invalid or that they are not infringing upon those patents (Collier, 2013). Even if a generic company is found to not be infringing upon existing patents, brand-name companies are still able to sue for infringement after the product is already on the market. Furthermore, patent linkage systems that are being encouraged around the globe force generic companies to send a notice to the patent holder, allowing for subsequent lawsuits to delay clinical data to be accessed. The notion of extending patents and preventing competition is known as evergreening, and it becomes evident there is a strong correlation between blockbuster drugs, the number of patents, and imminent litigious action. The exuberant number of patents granted and impending lawsuits represents a burden on legal systems and company's operations. The compounding effects of consistently incorporating significant sums of expenditure on patent costs and ongoing legal disputes defers from adequate investment in research, innovation and providing affordable medicines around the globe. The sheer number of cases is overwhelming and inhibits further growth opportunities for multinational firms. The fact that a small minority of all infringement cases involve inventive patents and the pervasive nature of patent fortresses amongst the best-selling drugs indicates an inefficient system that represents a significant barrier to generic entry. The compounding effects of costly lawsuits and delayed competition must be overcome to ensure the world is able to access affordable drugs.

### 3.3 Access to Drugs

These unique circumstances apparent in the pharmaceutical industry play an intricate role in the fundamental objective; providing the world with access to drugs. The provoking nature of this industry can be summarized by a canonical statement: "The first pill can cost more than \$1 billion while the second costs only a dime" (NASEM, 2018). The realistic illustration of this development process incorporates the innate predicament that all stakeholders must confront. Business operations are reliant on research and development and the recurrent revenues associated with blockbuster drugs. The underlying quandary is the marginal cost of additional medicines is completely negligible and could help the lives of millions of people. On a case by case basis, the solution seems obvious from a moral standpoint but accounting for world population and business operations, the resolutions become much more ambiguous. Providing access to life-saving drugs

is a highly contentious issues that encompasses fundamental human rights and morality in a complex business environment. The complexities of successfully operating a multinational corporation heavily involved in risk and capital expenditure do not align with public health objectives. Many diseases only occur in impoverished nations, creating a public issue that has not been solved by private industry. Several initiatives have been brought forth, but this remains one the most pressing global issues with an estimated two billion people unable to access essential medicines (WHO, 2017).

In 2005, North America, Japan and Europe accounted for 90% of the world's pharmaceutical purchases (IMS Health, 2006). In contrast, Sub-Saharan Africa represented only 1-2% of the global market share (CIPHI, 2006). The disparate figures create perverse market incentives for multinational firms to maximize shareholder value. Public health issues are present in all nations, but certain diseases are more prevalent in developing nations. The private marketplace does not provide the adequate incentives for firms to heavily invest in these life-saving drugs, even if it is the most beneficial for society. Due to the inherent market failures that exist, research and investment is predominantly focused on the lucrative Western markets. This is known as the 10/90 gap, where only 10% of R&D spending is directed at 90% of the global disease burden (GFHR, 2004). After analyzing 1393 new chemical entities discovered from 1975-1999, Trouiller et al. (2002) determine that only 16 were directed at tropical diseases and tuberculosis. This represents 1% of marketed drugs, 13 times lower than central-nervous-system or cancer related discoveries (Trouiller, et al., 2002). The asymmetric interests between advanced and developing nations only intensifies the difficulties surrounding this issue. The burden of cost is overwhelmingly placed on the United States, resulting in a justified desire for other countries to adopt stronger protection policies and reduce imitative capabilities. Trade negotiations certainly pigeon hole countries to agree to disproportionately strict pharmaceutical protection. The results of this are difficult to quantify and striking the right balance of enforcement remains a unique question that developing nations need to address.

The ongoing discussion culminates around how to create global access to drugs while protecting the interests of pharmaceutical companies. Lanjouw and Cockburn (2001) studied the initial effects of the TRIPS agreement on the forty less-developed signatories that implemented pharmaceutical protection for the first time and found R&D remained level or slightly decreased

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on products specifically intended for those markets. Similarly, Kyle and McGahan (2009) examined clinical trial data and concluded the increase in patent protection did not alter R&D investments. These results are in stark contrast to one of the principle arguments for introducing patent protection, which was the inevitable increase in investment and research for previously neglected diseases. Unsurprisingly, even though additional protection may bring higher prices and stronger revenues, developing nations still represent a fraction of total sales for multinational firms. An imperative determinant is the difference in healthcare expenditure; in which the cost is almost entirely received from third parties in developed nations while consumers pay directly more often in LDCs and developing countries. Even with a monopoly, companies are limited with their pricing power due to the elastic nature of the demand side. During the 1990's, 70% of Indians did not have national health insurance (Lanjouw J. O., 1998). This additional revenue, in turn, would be negligible for companies to differ research focus or enhance innovative capabilities. The resistance to TRIPs from developing nations was rational, given the power bestowed upon member states. The obligation of minimum standards prevents countries from changing their laws to suit national interests if they are at variance with the Agreement and furthermore, cross-sectoral retaliation through the dispute settlement process can occur in the event of noncompliance (WHO, 2008). By introducing pharmaceutical standards, countries were conceding pricing power that would dramatically impact pharmaceutical access.

Drug prices subsequently increased for patented medicines but research activities remained largely focused on Western markets. Added protection enables many beneficial effects, however, it innately causes higher pricing. When China introduced exclusive marketing rights in 1991 and amended its patent law in 1992, uncontrolled prices of protected drugs had risen by a factor of three to four on average (Maskus, 2000). The importance of domestic industries is fundamental in the goal of providing worldwide access to drugs. Many countries, especially LDCs, lack the technological capacity or manufacturing capabilities to satisfy the demands of their citizens. The incessant need for generic alternatives and increased competition enables a cost reduction and easier access to medicines. In addition, Bate (2008) confirms that research decisions are altered by regional implication, demonstrated by increased investment in local diseases by Indian firms compared to international companies. The TRIPs Agreement was an audacious attempt to globalize standards but incorporated several provisions that allowed sufficient flexibility

developing nations. The discourse between advanced and developing nations reached its culmination over a particularly crisis, the HIV/AIDS epidemic.

The TRIPs Agreement came to fruition during an influx in HIV infections, with 4.7 million new diagnoses occurring in southeast Asia and sub-Saharan Africa in 1995 alone (Mann & Taratola, 2000). Although initial outbreaks occurred in California during the 1980's, the disease quickly spread to impoverished nations, resulting in fourteen million fatalities and becoming the number one cause of death in Africa by 1999 (WHO, 1999). By the 21<sup>st</sup> century, AIDS had the highest percentage imbalance amongst any indicator related to death on the poorest 25% of the world (GFHR, 2005). The global crisis mobilized extensive research and complex treatment options to combat the spread and devastation of this disease. However, at a cost in excess of \$10,000 per patient per year, only 1000 people living in Africa had access to treatment during the first International AIDS Conference held in South Africa (Berger, Hoen, Calmy, & Moon, 2011). Although flexibilities were enabled through the TRIPs Agreement via compulsory licensing, the United States successfully deterred implementation through trade legislation in the form of benefits under the Generalized System of Preferences, or GSP, and Special 301 Watch Lists (DeRoo, 2011). Africa was dealing with a crisis of unprecedented proportions, leading Nelson Mandela to issue compulsory licenses and sign amendments to South Africa's Medicines and Related Substances Control Act in order to buy cheaper drugs via parallel importation. Remarkably, the following occurred in the subsequent year: thirty-nine pharmaceutical companies filed a lawsuit against the South African government, the USTR placed South Africa on the Special 301 Watch List, GSP benefits were suspended and the U.S. Congress cut off all aid into the country (DeRoo, 2011). This overt reaction to a justifiable resolution from an impoverished nation in crisis received global scrutiny for both government and industry actions.

The United States government and pharmaceutical companies eventually conceded amidst immense pressure from the public, NGOs and world organizations. Following this international crisis, members agreed upon the Doha Declaration in November 2001, affirming that "each Member has the right to grant compulsory licenses and the freedom to determine the grounds upon which such licenses are granted" (DeRoo, 2011). Furthermore, LDCs were given an extended time period until 2016 to implement pharmaceutical protection alongside a set deadline in which a solution was to be found for countries unable to produce generic alternatives themselves (UNDP,



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2006). This provision enabled India to export low cost, generic versions with one Indian manufacturer introducing the same ARV therapy for \$350 dollars per year (WHO, 2008). Due to the predominantly lower income population affected, five million people were able to gain access to ARVs as a result (Berger, Hoen, Calmy, & Moon, 2011). Prior to the its adoption period in 2005, the Indian pharmaceutical industry was critically important in providing access to cheap drugs, with an estimated 30% of all generic drugs in developing nations being supplied by India (WHO, 2008). Overall, the DOHA Declaration was monumental in the fight against HIV/AIDS and has since provided more than 60 lower income countries large scale generic versions of patented medicines (Berger, Hoen, Calmy, & Moon, 2011). The success of combatting this spiralling epidemic is a testament to the capabilities of global cooperation and effective use of the pharmaceutical industry. This case is a representation of both the immense implications and political influence associated with the pharmaceutical sector.

Progress was made during this time period but as previously alluded to, significant protection is being implemented in recent trade negotiations. Compulsory licensing has been internationally accepted for HIV/AIDS, as stated in Article 18.6, "...it being understood that public health crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency" (CPTPP, 2018). Although HIV/AIDS had a positive impact on TRIPs flexibilities, the United States and other developed nations are frequently enforcing TRIPs-Plus provisions as part of negotiations. These provisions may seem minor, but could have a profound effect on nations in years to come. For example, Canada granted 613 compulsory licenses for generic medicines from 1969-1992, leading to the lowest medicine prices in the industrialized world (Berger, Hoen, Calmy, & Moon, 2011). After agreeing to NAFTA, the median price difference for medicines was found to be 56% higher in Canada compared to the United States by 2001 (WHO, 2002). Although placing a substantial burden industrialized healthcare budgets, the significance of additional protection disproportionately affects access to drugs in lower income countries. The HIV/AIDS still remains prevalent but has been contained due to successful research efforts and billions of dollars of investment from governments, non-profit organizations and multinational corporations.

### 3.31 Research funding

The justification for exceedingly high drug prices is the massive amount of R&D investments and inventive capabilities of pharmaceutical companies. In theory, the system grants substantial revenues for inventors and as a result, all stakeholders benefit from innovative medical discoveries. In reality, unbeknownst to the majority of the public, discovery research is heavily funded by public resources. A recent study examined all 210 NMEs approved from the FDA between 2010-2016 and found the National Institute of Health, or NIH, contributed to every single process (Ekaterina Cleary, Khanuja, McNamee, & Ledley, 2018). In total, over \$100 billion, or 20% of the total budget, was spent on these discoveries from 2000-2016. During this same time period, the budget of the NIH has ballooned at a CAGR of 24%, increasing from \$973,146,000 in 2000 to \$32,311,349,000 in 2016 (NIH, 2019). The funds are generally allocated to exceedingly risky basic research, which complements industry investments that are primarily focused on applied research. Public resources play an intricate role in the success of pharmaceutical research however, transparency is imperative for the public to understand the sizeable role that taxpayer funds contribute to this sector.

Deriving data from clinical trial information provided by NIH's U.S. National Library of Medicine, insights can be determined on the extent of public and charitable funds for certain classes of medicines. For HIV/AIDS, there are currently 3735 ongoing or recently completed clinical studies with funding from industry contributing to 1429, or 38% of the studies. For diabetes, 46% or 2481 out of 5440 clinical trials received funding from the pharmaceutical industry. Malaria only received funding for 29% of the 103 studies conducted while cancer is the most predominant source of clinical trial studies with 34,023 trials being conducted and only 40% funded by the private industry investment (NIH, 2019). These results enable an understanding on the significant contributions provided by government entities, charitable organizations and academic institutions. Incorporating cancer-related patent data from the USPTO Cancer Moonshot Database, Stanford University contains the largest number of patents applications at 241, while Novartis sits atop private industry with 85 (USPTO, 2019). Furthermore, a comprehensive study was conducted by Robert Kneller (2010) who identified 252 new drugs approved by the FDA from 1998-2007 in which 215 were classified as New Molecular Entities and 37 were under Biologics Licence Applications. By identifying the inventors and their places of employment, stark contrasts

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were found. 61% of new drugs discovered in the United States came from academia or small biotech companies while it was less than 25% across European and Japanese markets (Kneller, 2010). To put this in perspective, universities and small biotech companies in the United States accounted for more drug discoveries than Japan, Germany, Switzerland, Canada, Australia and the rest of the world excluding Europe combined (See Appendix Figure 10a).

While it is noteworthy to determine the sources of inventive discoveries, attention should be focused on results and societal implications. Budish, Roin and Williams (2015) investigated the source of research investments on the decision making strategies of firms. The empirical study uses cancer research data using critical trials, determining whether late-stage treatment is prioritized due to shorter project durations and approvals. Separating the stages based on five-year survival rates, the results visibly show a significant inclination for late-stage cancer research with terminal patients receiving the majority of research (See Appendix Figure 11a). These results are insightful and indicate time to market is a critical component of research decisions. Secondly, the study contrasts the decision making based on public or private investment sources. Although commercialization lags reduce both public and private investments, the correlation is significantly more negative for privately funded research. Additionally, it was determined that all cancer prevention and chemoprevention drugs have been publicly funded with no private investment. One of Roche's top selling drugs, Avastin, was initially approved to extend to the life of late-stage lung cancer patients by two months. The findings suggest that market forces and corporate short-termism impact the research decisions of private organizations and the patent system does not incorporate these incentive effects. (Budish, Roin, & Williams, 2015)

To help fill this funding gap, non-profit foundations have increased their investments in discovery and development for new drugs specific to their diseases of interest. The Bill and Melinda Gates Foundation continues to impact global health with several initiatives aimed at combatting malaria, pneumonia, diarrheal diseases and Ebola. To illustrate the significance of the Gates Foundation, the 2007 expenditure of \$1.65 billion on global health programs equaled the World Health Organization's annual budget. The crowning achievement thus far has been the impact on malaria research, as evidenced by \$2.9 billion spent on grants and \$2 billion towards the Global Fund to Fight AIDS, Tuberculosis and Malaria. The Gates Foundation is the largest private grant-making foundation in the world which has aided the exponential increase in malaria

research from \$84 million annually in the late 1990s. The magnitude of this disease can still be felt as 90% of deaths were in African nations, with 60% being children under the age of five and an estimated 219 million people suffering in 2017. These neglected diseases provide a limited market for private firms, but signify a dramatic social and economic impact for entire regions. The \$4.9 billion dollars in expenditure have enabled hopeful results, reducing the number of deaths by half since 2000. From 1998-2007, \$8.95 billion was allocated to various organizations, with 40% expended to multinational firms and \$3.27 billion specifically towards basic science research. The significant figures and important influence that non-profit organizations possess can dramatically impact research focus and considerably effect global health initiatives. (McCoy, Kembhavi, Patel, & Luintel, 2009) (Gates Foundation, 2019)

While it is easy to criticize multinational firms for exceedingly high prices and selective research decisions, one must examine the countless clinic trials and failures along the commercialization process to gather an unbiased perspective. The attrition rate of Alzheimer's disease was found to be 99.6% between 2002-2012, representing substantial expenditure for virtually no return (Cummings, Morstorf, & Zhong, 2014). The excessive long-term costs of bringing drugs to market requires substantial capital with a distressingly high risk tolerance. Even with government and non-profit funding for discovery research, it is estimated that 90% of drugs do not complete the clinical trial requirements (NASEM, 2018). The pharmaceutical industry is also the most charitable, donating considerably more than any other sector in proportion to revenue. Pharmaceutical companies represented 5% of all companies, but contributed 40% of total donations from 2009-2015 (CAF, 2016). The constant public scrutiny and misaligned expectations from private firms operating in a globally competitive market creates an inexorable environment. However, the perception is understandable from the average citizen. The innate conundrum that predisposes American taxpayers is that although 85% basic cancer research is publicly funded, they pay a 50-100% price increase compared to other nations (Kantarijan & Rajkumar, 2015). Due to the vital importance and global impact of this industry, the public should be rightly concerned about regulatory processes, research funding, and access to affordable medicines.

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### 3.4 Current Industries

As countries continue to develop economically, healthcare becomes a primary focus of both governmental policy and societal demands. The current state of affairs for China and India vary from an operational and consumer expenditure standpoint. Both countries have burgeoning pharmaceutical sectors that will enable a more dispersed marketplace for revenues and an increasingly competitive environment in terms of innovative capabilities and generic manufacturing. The international business environment is becoming globalized and the pharmaceutical industry will continue to dominate political discussions, trade negotiations and public interest. Integrating an adequate level of intellectual property protection is a complex and multifaceted issue that encompasses a wide range of benefits and challenges that many industries must address. The pharmaceutical sector incorporates a distinct set of characteristics that necessitates sufficient protection to recover excessive R&D costs but also dramatically impacts public access and global health standards. The complexities involved with enforcing universal standards and continual pressure of adopting advanced economy's IP rights has affected both emerging and industrialized nations. The Chinese and Indian economies are at different stages in development but provide an insightful perspective on the challenges and opportunities these pharmaceutical markets present for the near future.

The sheer size of the Chinese middle class represents significant commercial opportunities that are difficult to ignore. It is estimated that two thirds of the world's middle class will come from greater Asia by 2030, with China accounting for upwards of 780 million. China is, undoubtedly, a significant economic superpower but still lags behind OECD countries on a per capita basis and almost all health-related indicators. Priorities have shifted in concurrence with economic development, exemplified by the Chinese pharmaceutical market expanding from the 9<sup>th</sup> largest segment in 2007 to currently the second largest. China contains an aging population and boasts the world's largest medical insurance system which enabled pharmaceutical sales to increase at a CAGR of 15.5% between 2010-2015. Housing and healthcare are projected to become the fastest growing categories in consumer spending so in its current state, demand far exceeds supply and a historic reluctance to trust domestic manufacturers remains high. Quality and safety will need to be addressed but a shift in innovative capabilities has the potential to alter this global industry. The domestic industry is still dominated by generics at a market share of 75% with an

additional 11% towards Traditional Chinese Medicines, or TCMs. As previously alluded to, the United States and Europe dominate new discoveries, with China only representing 4% of the total market over the previous decade. R&D reinvestment currently accounts for approximately 5% of sales, which is far below Western counterparts but expected to increase alongside considerable government spending. Many new initiatives, including Healthy China 2030, have been implemented with a notable emphasis on research funding, biopharma development and regulatory overhaul. The anticipated expansion of the National Reimbursement Drug List reveals an equivalent prioritization towards Western medicines and herbal/TCMs. This sizeable revenue stream should induce further research to an already exponentially growing herbal medicines industry, expected to eclipse over \$200 billion globally in the next five years. As domestic industries and the prospering population evolves, innovation will become more prevalent and alternative herbal or TCM medicines could seriously impact the pharmaceutical sector going forward. (GBR, 2018)

Similar to China, the Indian market represents a vast population with rising incomes and increasing public demand for adequate health standards. The Indian government recently launched the world's largest publicly funded medical insurance scheme, labelled 'Modicare,' which drastically increases expenditure aimed at covering an additional 500 million people. Government disbursement has increased 13.1% and medicine spending is projected to grow at a CAGR between 9-12% over the next five years, leading India to ascend into the top ten consumer markets. Comprising of a vast population in the earlier stages of economic development, generic access is imperative for improving health standards. The domestic pharmaceutical industry in India is the largest provider of generic drugs globally, accounting for 50% of global vaccines and 40% of the U.S. generic market. Notably, exports represented \$17.3 billion in sales while domestic revenue amounted to \$18.1 billion in 2018. FDI has contributed immensely in the development process, accumulating \$15.9 billion between 2000-2015 with a predominant focus on greenfield investments. The Indian pharmaceutical sector is a representation of the positive spillover effects associated with a maturing domestic industry. India's globally competitive generic sector contains the most FDA approved manufacturing facilities outside of the United States and received the largest number of Abbreviated New Drug Application approvals with 304 in 2017. This can be attributed to technological advancement and reinvestment in R&D which continues to steadily rise, increasing from 1.9% between 2000-2005, 5.3% in 2012, to 8.5% in 2018. Collaboration with

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Western companies through licensing or private equity deals is pervasive and new government initiatives included in Pharma Vision 2020 are aimed at becoming a global leader in end-to-end manufacturing through incentive schemes. The market share of generic manufacturing is 71% and continues to decline as companies further develop technological and innovative capabilities. The pharmaceutical sector is poised for growth and represents one of India's most important industries in terms of global competitiveness, employment and societal impact. (IBEF, 2019)

The vital importance of this industry cannot be overstated for both the Indian marketplace and global partners. In 1999, industrialized nations accounted for 93% of global pharmaceutical exports with domestic industries predominantly focusing on the local market (WHO, 2012). From research processes to distribution networks, business operations have become globalized with significant opportunities for India and China to capitalize. China's economic expansion has created a highly competitive technological capacity that could influence research and inventive capabilities in years to come. Domestic demand for intellectual property rights and increasing enforcement should stimulate innovation and a dominate consumer market will garner substantial growth. For India, adequate standards and advanced manufacturing capabilities have enabled a burgeoning industry that should present further opportunities for innovative proficiency and technological advancement. Extensive and trustworthy regulatory processes have given India a significant comparative advantage over its Chinese counterparts for growing market share in global drug supply. Focusing on a macro perspective, Africa faces the biggest challenges regarding access to essential medicines. Limited infrastructure and domestic industries necessitate the vast majority of drugs to be imported, which has resulted in widespread counterfeit medicines. The India-Africa partnership for access to medicines is fundamental for safe, affordable pharmaceuticals and substantial investments in distribution and development show positive signs for a growing industry. Indian firms account for the majority of vaccines and currently supply over 80% of the antiretroviral drugs used globally to combat HIV/AIDS come from Indian companies (IBEF, 2019). The Meningitis Vaccine Project was a successful partnership between the Gates Foundation and an Indian vaccine company which saw a key conjugation technology transferred by the FDA to organize clinical trials across Africa, resulting in a \$0.50 cent vaccine that was successfully launched in six countries (Wilson & Rao, 2012). Collaboration needs be utilized in order to address global concerns over access to affordable medicines and align both public and private interests in this worldwide industry.

The pharmaceutical sector continues to be dominated by industrialized economies but the advent of the Chinese and Indian markets will play a predominant role in the years to come. The importance of mature industries outside of OECD nations is critical for distribution networks, regional focus, and providing sufficient competitive markets. The United States may be the largest beneficiaries as they represented over 40% of the \$1.14 trillion dollar pharmaceutical market in 2017 (EFPIA, 2018). A globally competitive market can facilitate cost reductions and comparative advantages to enable a more efficient and accessible pharmaceutical sector. Health standards are prioritized in governmental policies and growing consumer demand provides ample opportunities for sufficient revenue streams. Multinational firms are able to mutually benefit from population growth, untapped markets and globalized supply chains. Collaboration is necessary between government, non-profit organizations and multinational firms from around the world to mutually benefit and support paramount objectives. The success of improving health standards and access to affordable medicines is predicated on the evolving intellectual property rights system. The unique characteristics of the pharmaceutical sector represent distinct challenges for multinational firms to overcome and necessitates adequate protection to recuperate a capital intensive commercialization process. Elements of the current patent system enable exploitative tendencies and inhibit a fully competitive marketplace. An insight into the market leaders can provide a thorough perspective on the impact that the patent system has in this vitally important industry.

## 4. Company Analysis

Fifteen of the biggest pharmaceutical companies are analyzed in order to provide a detailed insight into the day-to-day operations and present a unique perspective into the current business climate that the patent system has created. The fifteen companies were chosen based on annual revenues in 2017, with a focus on brand name pharmaceuticals. For instance, Celgene was chosen over Abbott Laboratories even though revenues were less than half in 2017, because Abbott's main sources of income focus on medical devices, diagnostics and generic pharmaceuticals while Celgene produces the second-best selling drug, Revlimid. The analysis also includes AbbVie, previously Abbott Laboratories' branded pharmaceutical business that spun off from Abbott Laboratories in 2013. We use the same fifteen companies throughout 20 years, from 1997 to 2017,



in order to analyse the historical development for these companies. The companies we define as the biggest in 2017 may not have been amongst the fifteen biggest historically, but they have all been major players in the global pharmaceuticals market since 1997 and therefore provide a solid foundation to build the analysis on. The fifteen multinational enterprises included in the analysis are composed of many different subsidiaries and have a diverse range of corporate structures. The headquarters are based in the United States and Europe, with nine corporations residing in the U.S., two in Switzerland, two in the United Kingdom, one in France and one in Germany. Japan is the third largest market, outside of the US and EU, with several pharmaceutical companies exceeding \$1 billion in annual revenue. The majority of drug patents held by these companies are valid across the US, EU and Japan with only minor variations on application and expiry dates. The fifteen companies by highest aggregated pharmaceutical revenue in 2017 are presented below. Revenue is in USD billion.

<b>Roche</b>	54,123
<b>Pfizer</b>	52,546
<b>Novartis AG</b>	43,085
<b>Johnson &amp; Johnson</b>	36,256
<b>Merck &amp; Co.</b>	35,390
<b>GlaxoSmithKline</b>	28,917
<b>Sanofi</b>	28,387
<b>AbbVie</b>	28,216
<b>Gilead Sciences</b>	26,107
<b>Eli Lilly</b>	22,871
<b>Amgen</b>	22,849
<b>AstraZeneca</b>	22,465
<b>Bristol-Myers Squibb</b>	20,776
<b>Bayer</b>	19,037
<b>Celgene</b>	13,003

The largest pharmaceutical market is the United States alongside the majority of headquarters so US dollars are utilized to create a comparable analysis. Four organizations used different currencies in their reporting, consisting of Euros, British Pounds and Swiss Francs. The annual average conversion rates were used aligned with the company's intended method, in order to provide all information in reference to US dollars. All data in the following section is based on the companies' annual reports, the FDA drug approval database, the European Medicines Agency and the national medicines registers for select European Union and European Economic Area member states unless otherwise specified. Due to an incomplete repertoire of 2018 annual reports, the data presented is for the previous 20 years starting in fiscal year 2017.

The term *Top 3* will be referenced frequently to highlight the pharmaceuticals that generate the first, second or third largest revenues for their respective companies. In other instances, the *Top 3* pharmaceuticals are grouped into nine main categories. This enables a more detailed perspective on the variances in the pharmaceutical market. The following categories will be utilized throughout the analysis:

*Cancer* – pharmaceuticals that are primarily used to treat different types of cancer or health-related issues related to cancer.

*Blood Medication* – pharmaceutical used to treat issues related to the patient's blood stream. Includes hypertension, i.e. high blood pressure medications, hypotension, i.e. low blood pressure, anticoagulants to prevent blood clots, anemia medication and blood thinners.

*Immunosuppressants* – pharmaceuticals used to reduce or suppress the strength of the body's immune system. Often related after organ transplants, rheumatoid arthritis, psoriasis and Crohn's Disease.

*Antivirals* – pharmaceuticals used to kill or inhibit a virus. *Antivirals* include both antiviral and antiretroviral pharmaceuticals. Drugs included in the category are used to treat a multitude of viral infections but most antivirals are used to treat Hepatitis C while most antiretrovirals are used to control the HIV and AIDS virus.

*Antibiotics* – pharmaceuticals used to treat infections bacterial infections. Also includes anti-inflammatories that reduce inflammation and often relieves pain.

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*Diabetes* – pharmaceuticals used to treat symptoms of Type 1 and Type 2 diabetes. Regulates the body's insulin.

*Statins* – lipid-lowering pharmaceuticals used to treat high or low cholesterol. Often related to cardiovascular disease.

*Other* – all *Top 3* pharmaceuticals that do not treat any symptoms included in the main categories.

## 4.1 Research and development

The pharmaceutical industry is the most research and development intensive industry in the world and spends the most on R&D relative to revenue annually. The development of any pharmaceutical is both time-consuming and costly. There are multiple stages of research and development required to ensure the pharmaceutical is both safe and effective. After basic research and drug discovery, each pharmaceutical goes through multiple stages of clinical trials before going through approval processes from government regulatory bodies. The average time from basic discovery to market is ten to fifteen years, which is higher than in any other industry. The analysis does not consider R&D expenditures in relation to specific pharmaceuticals but focuses on total company and industry expenditures. Funding of R&D in pharmaceuticals often comes from a complex mix of both private and public sources. Whether a pharmaceutical is funded by public, private or a combination of sources is not included in the analysis as the aim is to get a clearer picture the total amounts spent on research and development in the industry. The analysis shows how research and development expenses have developed for the fifteen major companies and the industry as a whole. All research and development expenses for the firms are only related to pharmaceuticals and not other industries the respective firm might operate in. All amounts are in USD billions. Because of limited data, only the R&D analysis excludes 1997 and 1998.

Data on total global R&D expenditures from 1999 to 2017 was collected from Raghavendra et.al. (Raghavendra, Raj, & Seetharaman, 2012), total industry R&D expenditures for the U.S. collected from Statista (Statista, 2019) and expenditures for the fifteen companies are collected from their annual statements.

#### 4.1.1 Main findings

The accumulated research and development expenditures for the fifteen companies in the analysis show an average annual increase of 8 percent. Only three years contain a decrease in accumulated R&D spending; 1999 to 2000, 2009 to 2010 and 2011 to 2012. The decreases in 2010 and 2012 are most likely reactions to the ‘Great Recession’ that occurred in the U.S. between 2007 and 2009 that lead to a global economic downturn. Total R&D expenditures in the pharmaceutical industry in the U.S and globally follow a similar pattern in fluctuation. The U.S., on average, accounts for 42.77 percent of the annual total global R&D expenditures. At an all time high in 2016, the U.S. accounted for 58 percent of total global pharmaceutical R&D expenditures. For comparison, the same year Japan held the second highest share at 13 percent. For a full overview of shares of R&D expenditures of leading pharmaceutical R&D countries (APBI, n.d.), see Figure 12 in the Appendix. The fifteen major companies included in the analysis account for 46 to 70 percent of total global pharmaceutical R&D each year, with an average of 56 percent.

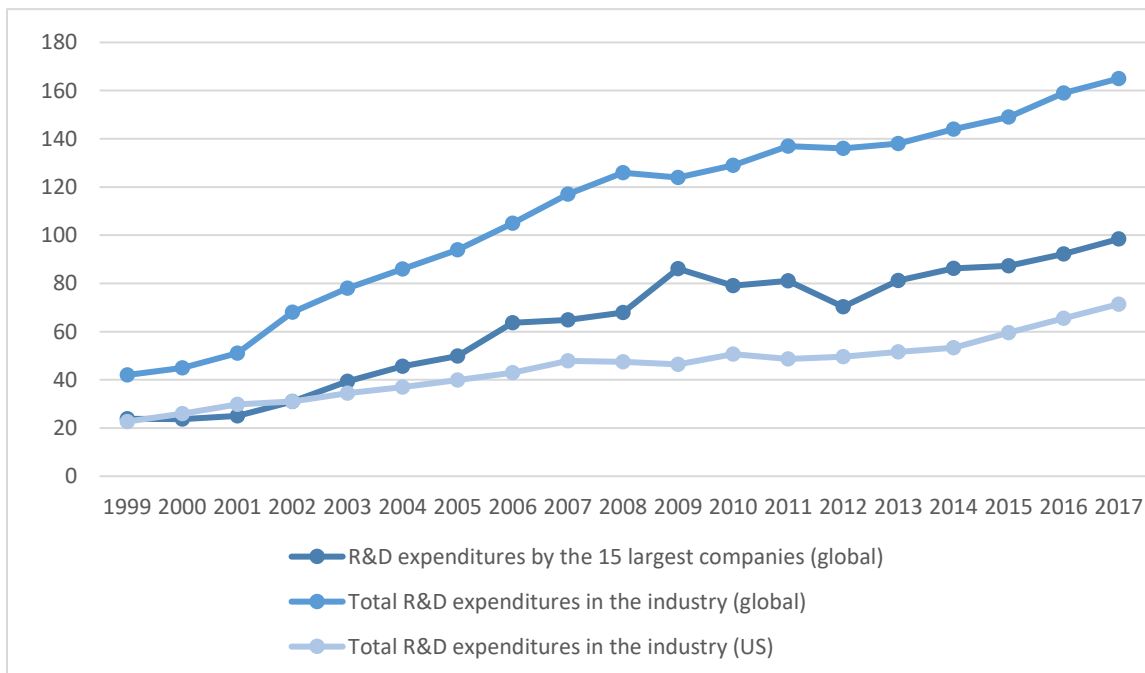


Figure 1: Overview of Pharmaceutical R&D expenditures

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There are no clear cycles of increased R&D expenditures among the top fifteen companies and investment has remained stable for all companies between 1999 and 2017. Dollar amounts each company spends on research and development varies based on company size and generated revenue. However, all companies have similar R&D expenditure to revenue ratios. On average, the fifteen companies included in the analysis invests 26.15 percent of their annual revenue on research and development between 1999 and 2017. Comparable technology companies, which had the highest R&D to revenue ratio between 2014 and 2016, spend less than half that of pharmaceutical companies with an average of ten percent of their revenue being spent on research and development investments (Kim, 2017). This continuous and constant investment in development within the pharmaceutical industry is mainly because of the significant resources it takes to bring a product to market. With ten to fifteen years from initial discovery to market launch, the companies cannot begin development in ‘bulks’ as patent expiration of current top selling pharmaceuticals are expiring to cover lost revenue from generic competition. Instead, new products must always be in the pipeline. This becomes even more critical as companies face constant risk of their pharmaceuticals becoming discontinued or patents being invalidated in court, thereby losing both revenue and exclusivity rights connected to the product. Discontinuation often happens in cases where long-term negative side effects that were not discovered in initial clinical trials come to light after the product is brought to market. Patent invalidation can include the full patent or certain claims related to a patent, narrowing its scope and rights.

R&D in relation to revenue does not vary significantly across companies or years and there is no clear correlation between research and development investments and new FDA drug approvals, market launches or patent expirations. Accumulated annual averages for R&D spending as a percentage of revenues for all companies are illustrated in Figure 2.

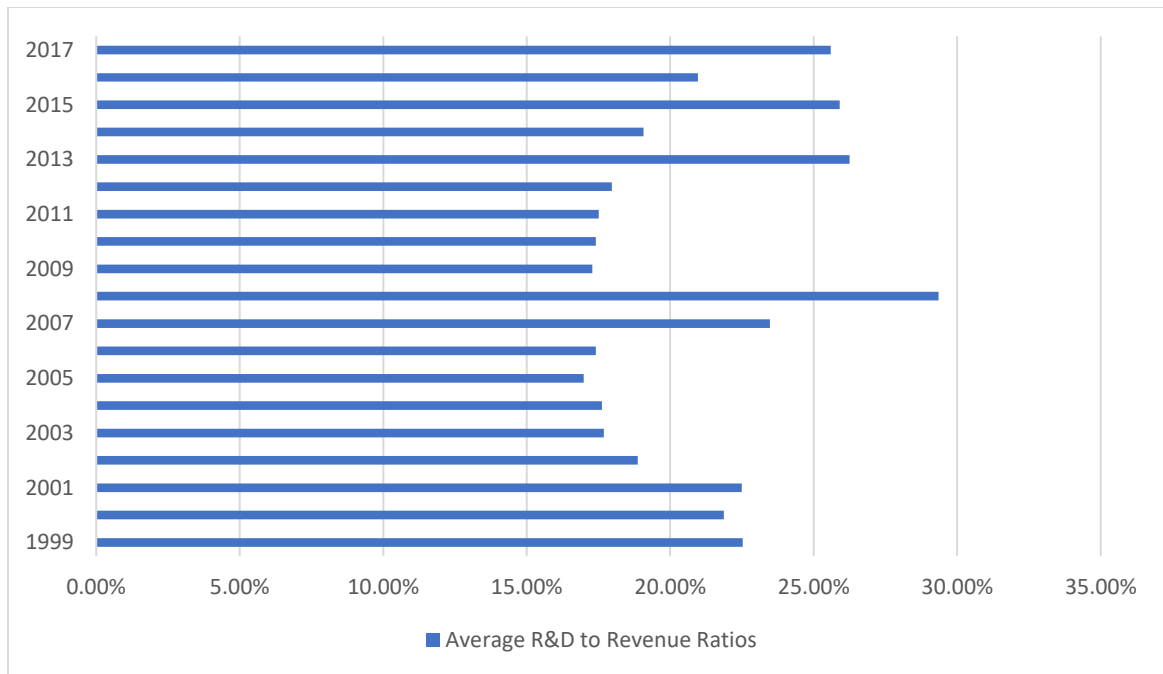


Figure 2: Accumulated average R&D to Revenue Ratios

## 4.2 FDA and EMA approvals

The U.S. Food and Drug Administration (FDA) protects public health by regulating a wide range of products including human and animal drugs, medical devices, biologics, food, cosmetics, tobacco products and electronic products that give out radiation. Pharmaceuticals cannot legally be sold in the US without FDA approval that is granted if the agency can prove the drug is safe and effective for its intended use (FDA U. F., 2018). Dates for FDA approval are included in the analysis to highlight that, with few exceptions, FDA approval is the deciding factor for when a pharmaceutical product enters the U.S market. Data was collected from the FDA's drug products approval database (FDA, Drugs@FDA: FDA Approved Drug Products, n.d.). In Europe, the European Medicines Agency grants and consolidates pharmaceutical approvals for market authorization in Europe. All data on EMA approvals is collected from the EMA drug approval database (EMA, n.d.). EMA approval is predominantly used in European Union (EU) Member States. Some pharmaceuticals are granted approval in one or more European countries through national procedures prior to receiving EMA approval or going through consolidation processes to assure consistent guidelines throughout the EU. Approvals through local regulatory bodies are not

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included in the analysis. All data on European approval is based on EMA approval because this date reflects the most accurate date of when the given pharmaceutical was granted approval in most European countries.

The pharmaceutical approval system helps highlight the complexities associated with this industry. Most pharmaceuticals go through a multitude of FDA and EMA approval processes for different variances of the same drug. This includes new or supplemental indications for already approved drugs. We illustrate this by using the examples of Gilead Sciences' blockbuster drug, Harvoni, and Eli Lilly's Humulin. The Harvoni case highlights how additional approvals can expand a pharmaceuticals patient population, while Harvoni shows how approval can be given to extend the products uses in treatment for varying symptoms of a disease. By extending uses and patient population, in addition to performing new clinical trials for the same product but in treatment of other symptoms, the company can extend its total exclusivity period in the market further.

Harvoni was granted initial FDA approval for treatment of Hepatitis C virus in adults in 2014. In 2015, the drug received an additional approval for a new dosing regimen. In 2016, approval for new patient population was given, expanding its use to patients with other genotypes. In 2017, the drug once again received approval for a new patient population; this time to include treatment of adolescents aged 12 to 17.

Humulin was granted its initial FDA approval under the name Humulin R and Humulin N, both in 1982. It went on to receive additional approvals in 1985, 1986, 1987, 1989 and 1992 for Humulin, Humulin BT, Humulin U, Humulin 70/30 and Humulin 50/50, respectively. Each of these consist of the same active ingredient but with minor variations within the insulin molecules that affect how fast acting the medication is and the amount of time effects of the drug lasts (Humulin, n.d.). All variations also hold its own set of patents. In the analysis, data for Humulin is based on information pertaining to Humulin as it accounts for the largest global revenue share.

To ensure consistency throughout the analysis, the initial FDA approval dates for each drug are used. With few exceptions, the brand name drugs included in the analysis enter the U.S market the same year it is granted FDA approval and the European market the same year approval is granted by the EMA. Most pharmaceuticals are approved and launched in the U.S. one year prior to Europe.

#### 4.2.1 Main findings

The most significant pattern related to approvals and market entry is the tendency for pharmaceuticals in the same category to receive FDA approval and subsequently enter the market in clusters. Two classes of pharmaceuticals are highlighted to illustrate the patterns found. In *Antidepressants and antipsychotics*, consisting of ten separate pharmaceuticals marketed by six different companies, all but one product is launched around the same time as another, similar brand name pharmaceuticals. In 1996 alone, three antidepressants from three separate pharmaceutical companies were launched on the U.S. market – Zyprexa by Eli Lilly, Seroquel by AstraZeneca, Risperdal by Johnson&Johnson. All three of these pharmaceuticals also leave their status as *Top 3* within 2011. For an overview of all pharmaceuticals in the category of antidepressants & antipsychotics and the year they enter the U.S market, see Table 1.

Company name	Pharmaceutical	Revenue as in years as Top 3	Status last year as a Top 3 drug	Years as a Top 3 drug	Market entry U.S.	Loses status as Top 3 drug
GlaxoSmithKline	Welbutrin XL	1,558	3	1	1985	2003
Eli Lilly	Prozac	12,548	2	5	1987	2001
Pfizer	Zoloft	24,432	3	10	1991	2006
GlaxoSmithKline	Seroxat(EU)/Paxil(US)	13,127	3	5	1992	2004
Eli Lilly	Zyprexa	54,467	1	15	1996	2011
AstraZeneca	Seroquel	35,311	3	10	1996	2011
Johnson & Johnson	Risperdal	28,686	3	7	1996	2011
Bristol-Myers Squibb	Abilify	20,146	1	9	2002	2014
Eli Lilly	Cymbalta	26,890	1	8	2004	2013
Johnson & Johnson	Trevicta/Invega Trinza	2,569	3	1	2015	Still Top 3

Table 1: Antidepressants and antipsychotics

The same pattern is found in the category *Blood pressure*. Except for Zestril (AstraZeneca) and Adalat (Bayer) that are launched in 1988 and 1985 respectively, all pharmaceuticals in this category enter the market within the same five years from 1992 to 1997 (see Table 2).



Company name	Pharmaceutical	Revenue as in years as Top 3	Status last year as a Top 3 drug	Years as a Top 3 drug	Market entry U.S.	Loses status as Top 3 drug
Bayer	Adalat	8,074	2	9	1985	2006
AstraZeneca	Zestril	3,506	2	3	1988	2001
Novartis	Cibacen/Lotensin	0,475	3	1	1991	2001
Pfizer	Norvasc	39,944	2	11	1992	2007
AstraZeneca	Seloken/Toprol-XL	2,590	3	9	1992	2005
Novartis	Lotrel	1,352	3	1	1995	2006
Merck & Co.	Cozaar/Hyzaar	19,379	2	6	1995	2009
Novartis	Diovan	54,579	2	13	1996	2013
Sanofi	Aprovel	1,502	3	4	1997	2002
Bristol-Myers Squibb	Avapro	2,186	3	2	1997	2007

Table 2: Blood Pressure

### 4.3 From approval to *Top 3* pharmaceuticals

#### 4.3.1. Clarifications

For the twenty year time period, three pharmaceuticals with the highest revenue are collected for each of the fifteen companies. These products are called *Top 3 drugs* throughout the analysis. All data on pharmaceutical specifics and total revenue was collected from each company's annual statements for the given year. Where data is not available for all twenty years, the nearest possible date to 1997 was used.

When analyzing the time period when FDA or EMA approval is granted until a pharmaceutical becomes *Top 3*, the products ranked as *top 3* in 1997 are excluded. This is because of the of lack information on revenue and sales volume prior to 1997 and thus, cannot accurately portray the accumulated years they have been a *Top 3* drug. Furthermore, certain pharmaceuticals that still hold their *Top 3* position in 2017 are excluded from averages of how many years each pharmaceutical retains its status.

FDA approval records in certain cases far outdate available data on pharmaceutical revenue and sales volume. In addition, some pharmaceuticals included were launched before the modern-day FDA was founded in 1938 and there is no data available for approvals granted prior to 1939. For example, Bayer's Aspirin was first marketed globally in 1899. The date of FDA and EMA approval used for these pharmaceuticals is set to 1939.

Certain pharmaceuticals, through licensing agreements, are distributed by more than one major company. For these cases, data is collected from both firms to show total revenues generated by the pharmaceutical and market variances. For example, both Merck & Co. and Johnson&Johnson market Remicade, one of the highest grossing pharmaceuticals in the world. It received FDA approval in 1998 and became one of Johnson&Johnson's *Top 3* pharmaceuticals in 2002 and for Merck&Co. in 2010. Until 2011, Merck&Co marketed Remicade in Canada, Central and South America, the Middle East, Africa and Asia Pacific, while Johnson&Johnson held exclusive marketing rights in Europe and the U.S. In 2011, when the global patents protecting Remicade neared their expirations, Merck&Co. relinquished its exclusive marketing rights back to Johnson&Johnson, only retaining rights to market the drug in Europe, Russia and Turkey (Merck, 2011).

In the following discussion, only FDA approval is used because pharmaceuticals tend to be launched either the same year in the U.S. and Europe or one year prior in the U.S. There are no significant differences between the effects of FDA and EMA approvals on the chosen pharmaceuticals and FDA approval is used to illustrate the trends in the market. For data regarding time from EMA approval until market launch in Europe, see Supplementary Material.

#### 4.3.2 Main findings – Time to *Top 3*

The analysis reveals a clear pattern on how long it takes from when a pharmaceutical receives its initial FDA approval to becoming a *Top 3* pharmaceutical across all categories. Most pharmaceuticals do not become *Top 3* before new approvals that extend the drugs scope in both patient populations and uses are granted. For example, Pfizer's Celebrex was granted its initial FDA approval for treating adults suffering from osteoarthritis, but it does not become a *Top 3* drug until 2007, one year after FDA granted an extension to include treating signs of Juvenile Rheumatoid Arthritis in patients from the age of two or older (FDA, FDA Centennial, 2006). The average time it takes a pharmaceutical to achieve status as *Top 3*, i.e. each company's top three drugs by revenue after receiving its initial FDA approval is between six and seven years. Only the *Cancer* and *Antiviral* pharmaceuticals become *Top 3* within four and three years, respectively.

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In 2018, cancer was the second leading cause of death globally, indicating an incessant need for pharmaceuticals to treat the disease. In addition, the cost of cancer drugs are exorbitantly high. Despite prices of patented cancer drugs being far greater in the US than any other country, they are generally less affordable in low and middle-income countries than high-income countries. Surprisingly, cancer drugs are the least affordable in India (Clark, et al., 2017). Both high sales volumes and prices contribute to make the period between FDA approval and becoming a top-selling drug shorter than the market average.

*Antivirals*, which also includes antiretrovirals, consists of pharmaceuticals used to treat symptoms of viruses like Hepatitis C (Hep C), HIV and AIDS. Most pharmaceuticals in the *Antiviral* class were launched within a short timespan after the increase in global awareness previously alluded to. The first antiretroviral was approved by the FDA in 1987, only two years after clinical trials were initiated. However, treatments did not show long-term effects until 1995, when antiretrovirals started being prescribed in various combinations and pharmaceuticals of this classification began receiving its status as *Top 3* drugs. This category has the shortest time from approval to becoming *Top 3* because they were the first treatments for HIV to be brought to market and there was little competition. Many of the antivirals only remain a *Top 3* for a short amount of time, the average being 3.87 years. On the other hand, pharmaceuticals in the cancer category, once achieving *Top 3* status, keep this position for an average of 6.59 years. Most of the antivirals have faced little competition from similar treatments but almost all patented pharmaceuticals in this category will have lost their market exclusivity rights after 2017. Therefore, it is likely time from FDA approval to *Top 3* for future antivirals will approach the market average.

#### 4.3.3 Accumulated Time as *Top 3*

Time as *Top 3* is the range and average of how many years each pharmaceutical spends as the highest grossing product for its distributing company over the past twenty years across the pharmaceutical categories. *Cancer*, *Blood Medication*, *Statins* and *Diabetes* hold the highest averages for years spent as *Top 3*. With an average of 8.6 years, *Blood Medication* is the category with the highest average of remaining *Top 3*. By excluding the pharmaceuticals that remain *Top 3* in 2017, the average is lower at 5.18 years. The pharmaceuticals among each company's *Top 3* in 2017 have held their position for an average of 7.54 years, about a year longer than the average for

all pharmaceuticals between 1997 and 2017. Because many of these still hold exclusivity rights, it is likely they will remain *Top 3* for several years to come as they will not face significant competition from generics. Nearly 40% of the *Top 3* pharmaceuticals in 2017 have held their position ten years or more. For complete information, see Table 3.

Categories	Years as Top 3 for all pharmaceuticals	Exclusion of 2017 Figures
<b>Blood Medication</b>	8.60	8.31
<b>Asthma</b>	7.20	4.67
<b>Antidepressants</b>	7.10	7.78
<b>Statins</b>	7.00	6.17
<b>Diabetes</b>	7.00	3.25
<b>Cancer</b>	6.59	4.79
<b>Immunosuppressants</b>	5.71	4.80
<b>Others</b>	4.73	4.10
<b>Antivirals</b>	3.85	4.47
<b>Antibiotics</b>	3.43	2.43

Table 3: Average years spent as *Top 3* pharmaceuticals

The *Cancer* category currently has the highest number of pharmaceuticals in *Top 3* for 2017 and nearly 26 percent of all pharmaceuticals in this category have remained *Top 3* for 10 or more years since first entering the list. For individual pharmaceuticals, cancer drug Neulasta, anemia drug Aranesp and insulin drug Lantus have topped the list of highest revenues for the longest period. Neulasta remains Amgen's second highest grossing pharmaceutical after twenty-one years on the *Top 3* list, while Aranesp from Eli Lilly and Sanofi's Lantus remain *Top 3* for their respective companies after 17 years as *Top 3* pharmaceuticals. *Asthma* is the only category that does not include one or more pharmaceuticals to only remain as *Top 3* for one year. All five *Asthma* pharmaceuticals spent three or more years as *Top 3*, with an average of 7.2 years.

#### 4.3.4 Differences Across Categories

Most of the *Top 3* antiviral pharmaceuticals over the past 20 years are, or have been, marketed by Gilead Sciences. Eight out of nine *Top 3* pharmaceuticals for Gilead Sciences have

been antivirals and antiretrovirals, accounting for 98.91 percent of their total pharmaceutical revenue since 1997. Only half of the fifteen other companies have had antivirals on their top-selling pharmaceutical list, a stark contrast to the category *Cancer* where twelve out of fifteen companies have had one or more pharmaceuticals on the *Top 3* list. Celgene has eight different pharmaceuticals in which six are in the *Cancer* category. The consistent pattern of having several top-selling pharmaceuticals in the same category continues across all the fifteen companies included in the analysis. However, most typically have a more diversified portfolio than Celgene and Gilead Sciences. Pfizer and Merck & Co. contain the most diversification – each have eleven different *Top 3* pharmaceuticals in nine different categories. Figure 3 shows the number of main categories and total categories all fifteen major companies operate in.

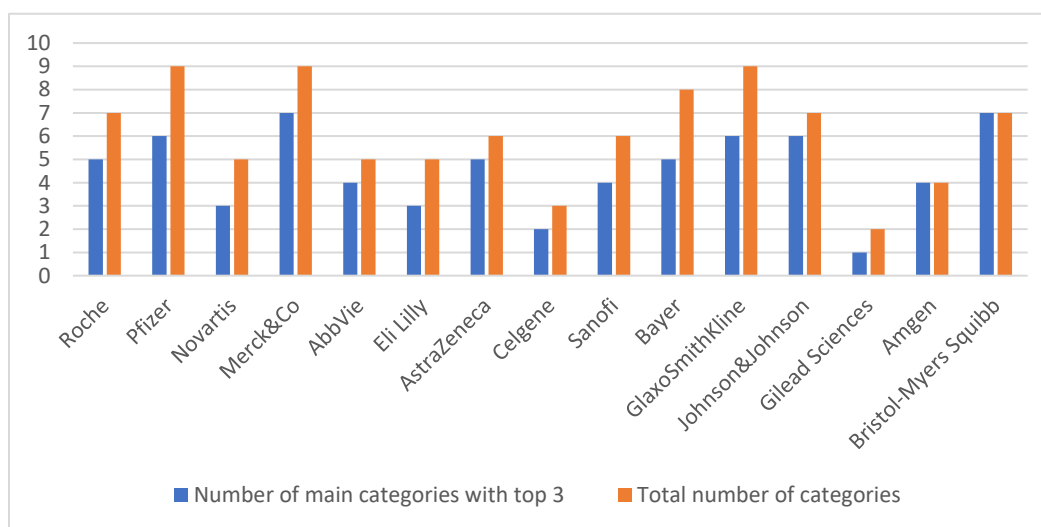


Figure 3: Top 3 pharmaceuticals category distribution by company

All categories except *Asthma* have one or more pharmaceuticals that only remain a *Top 3* pharmaceutical for just one year. The pharmaceuticals that are only a *Top 3* for a year often generate higher revenues for a short period because of extraordinary circumstances like pandemics, exemplified by the case of GlaxoSmithKline’s Relenza during the flu pandemic in 2009 and 2010. Because Relenza’s status as a *Top 3* pharmaceutical was a result of extraordinary circumstances, it does not reflect general market trends and is excluded from the analysis. Certain pharmaceuticals also enter the *Top 3* list only to lose their position after national emergencies are declared, allowing generics to enter the market prior to the brand name patent expiration. The implementation of

compulsory licenses has predominantly affected the *Antivirals* category. Eight out of nine *Antivirals* became *Top 3* within a year of initial FDA approval, yet they remain as one of the shortest *Top 3* categories. Antivirals remain *Top 3* for an average of two years, with Amgen's Infergen holding its position the longest at four years. This is a huge contrast to categories like *Blood Medication* where pharmaceuticals remain *Top 3* for over eight years on average. For further information, see Supplementary Material.

#### 4.4 Revenues

This section examines pharmaceutical revenues from 1997 to 2017 for the industry's major corporations and their subsequent *Top 3* drugs. Because of limited data available, the analysis does not include information pertaining to revenue prior to 1997. For certain firms, the dataset begins later than 1997 because of a lack of publicly available data or newly established companies. For these cases, data from the nearest possible year is used.

In the following calculations, all revenue relates solely to pharmaceutical revenue, unless specified otherwise. For companies that operate in medical devices, veterinary pharmaceuticals and/or other business not directly connected to human pharmaceuticals, e.g. Johnson&Johnson, only pharmaceutical revenue is extracted from the annual statements. Other revenue is removed to enable comparable data for those firms that operate primarily in pharmaceuticals, e.g. AbbVie.

##### 4.41 Total company and market revenues

Figure 2 illustrates the historical development of global revenues for the *Top 3* pharmaceuticals, accumulated revenue of the fifteen major companies and the pharmaceutical industry as a whole. Notably, the percentage increase of annual revenue is highly correlated amongst all three variables. Both *Top 3* revenue and accumulated company revenue have faced occasional decreases. These have been incremental, only occurring in four and three years for *Top 3* and company revenue, respectively. On the other hand, the global pharmaceutical industry remained extremely constant with a CAGR of 6.5 percent. From 1999-2017, the pharmaceutical industry as a whole generated revenues exceeding \$14,444.5 billion, in which 43 percent was

generated by the top fifteen companies. Figure 4 shows the market revenue distributions across these three segments.

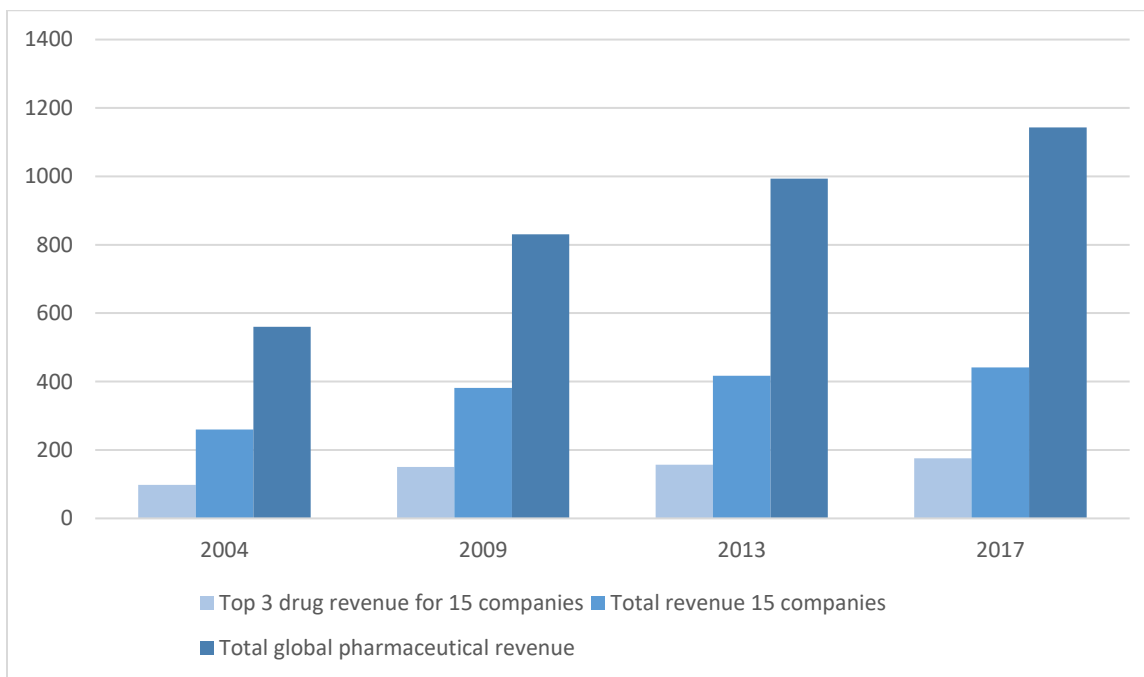


Figure 4: Market revenue distributions

On average, the accumulated revenue for the *Top 3* pharmaceuticals account for 36.34 percent of the fifteen companies' revenue and nearly 16 percent of total revenue for the global pharmaceutical industry. In 2013, 2009 and 2004 these drugs accounted for 15.83, 18.10 and 17.47 percent, respectively. For many companies, a major proportion of total revenue is generated by one or few blockbuster drugs. For example, 84 percent of AbbVie's revenue generated between 1997 and 2017 comes from a single *Immunosuppressant* pharmaceutical – Humira.

Minor variations occur for companies facing patent expiration dates, or patent cliffs, which occurs with the loss of several main patents protecting top pharmaceuticals. However, the variations are minor because the companies tend to have new pharmaceuticals in their pipeline. Through constant development and launches of new products, all companies are able to maintain high revenues even after major pharmaceuticals lose their status as *Top 3*.

In general, the *Top 3* pharmaceuticals generate higher revenues nearing their main patent expirations, however, exceptions to this trend occur for certain pharmaceuticals. For example, *Blood Medications* Aranesp and Procrit saw decreases in revenue after 2007, despite their exclusivity periods being valid. This was a result of new studies linking these pharmaceuticals with a higher risk of death among certain cancer patients. Due to the nature of the pharmaceutical industry, discoveries of long-term side effects often lead to market reactions such as new labelling guidelines by the FDA and hesitation to prescribe the medication from doctors. Nevertheless, these occurrences are relatively rare and generally have minor consequences for long-term revenue.

#### 4.42 Revenue across categories

Revenues are shown to vary significantly across categories. Out of the ten categories identified, *Cancer* is the largest in terms of both revenue and number of pharmaceuticals that have been among the *Top 3* between 1997 and 2017. The second category in terms of revenue is *Blood Medication*, which includes pharmaceuticals to treat symptoms of anemia, high and low blood pressure and blood clots. There are twenty different pharmaceuticals in the *Blood Medication* category that generate 16 percent of the total revenues from all *Top 3* pharmaceuticals, exceeding \$387 billion. The *antiviral* category also consists of twenty separate pharmaceuticals, but each generate lower revenues and only accounts for approximately 6.5 percent of total *Top 3* revenue during the timespan. Total revenues generated by *antivirals* have been \$156.18 billion, an average of \$7.81 billion per drug, while the cancer category generated total revenues of \$487.7 billion, an average of \$18.06 billion for each of the 27 pharmaceuticals. Differences in revenue can be attributed to only one third of name cancer pharmaceuticals having faced generic competition in the US market as of 2017. Figure 5 shows a breakdown of revenue as a percentage of company revenue across all ten categories.



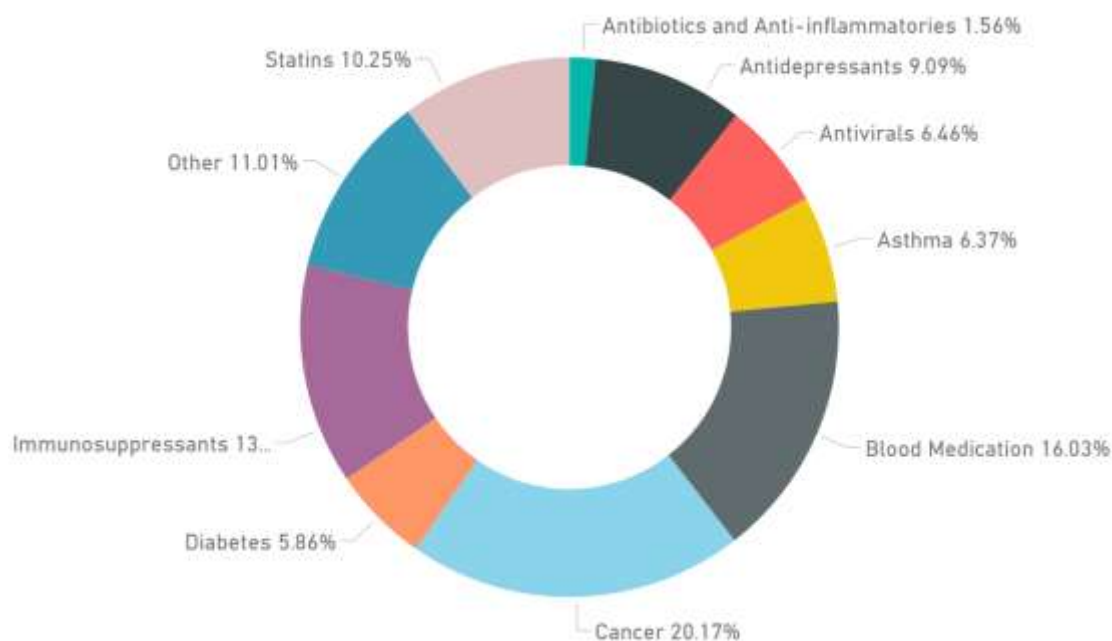


Figure 5: Revenue from each pharmaceutical category as percentage of accumulated revenue from all 15 companies 1997-2017

From the distribution of pharmaceuticals in each category, it becomes clear that all major companies mainly invest and develop pharmaceuticals that treat symptoms pertaining to the most common diseases in developed countries. Pharmaceuticals with the highest aggregated revenues are the ones that treat widespread diseases on a global scale. For example, both blood-related issues and viral infections are equally prevalent in advanced, developing and least developed nations. Intuitively, pharmaceuticals with a larger global market will generate higher revenues. However, due to the huge variations in sales prices for pharmaceuticals sold in different countries, investment decisions are mainly driven by demand in developed countries, most notably in the U.S, because this is where the majority of revenue for global pharmaceutical companies is generated. *Cancer* is the category generating the highest revenue per pharmaceutical, in addition to holding the highest number of pharmaceuticals brought to market. *Cancer* is not considered a leading cause of death in developing countries and has a limited market outside developed countries, yet 95 percent of revenue generated by Roche between 1997 and 2017 comes from its three main *Cancer* pharmaceuticals.

## 4.5 Patent Expiration and Generic Entry

Data on patent information is obtained through each company's annual statements. Data on generic approval in the U.S. and Europe is based on the FDA and EMA drug approval databases. In circumstances where generic approval is granted prior to the expiration of the brand name pharmaceuticals, the year of generic market entry is set to the same year as patent expiration due to the fact that generic manufacturers will have produced their products to be ready for commercial launch as soon as exclusivity rights expire. Dates of generic market entry are then compared to both the generic and brand name companies' press releases on generic launches. The largest generic pharmaceutical companies globally are the U.S based company Mylan Pharmaceuticals, Israeli based Teva Pharmaceuticals and Indian based Sun Pharma, Cipla, Ranbaxy Laboratories and Dr. Reddy's Laboratories. Most generics launched in the U.S., Europe and India are pharmaceuticals developed by these five companies.

Generics are copies of a small-molecule reference brand name pharmaceutical that is made from synthesized chemicals. Generics are identical in use, dosage, side effects, strength and active ingredient, i.e. it is chemically identical, to the original drug. Biologic pharmaceuticals are more complex, larger molecules derived from living cells. Because of their complex nature, most regulatory bodies have laid out stricter guidelines for producing 'generic' biologics, or so-called biosimilars. Unlike generics, biosimilars must go through several trials to prove they have similar effects and safety as the reference biologic. These processes significantly increase the cost of developing a biosimilar compared to synthesizing generics, though they are still significantly lower than developing novel pharmaceuticals (Biogen, n.d.). In the analysis, both biosimilars and generics are referred to as generics where specification is not decisive for the results.

There is limited public data on generic entry into the European market. Nevertheless, similar to brand name pharmaceuticals, it appears generics are launched within one year from U.S. launch. If they receive tentative approval prior to the brand name pharmaceuticals patent expiration, the launch date simultaneously occurs with the loss of exclusivity rights. Because of data limitation and correlation to the U.S. market, only data from India and the U.S. is utilized in the following section. A full overview of patents granted, expiration dates, generic market entry and number of years for brand name drugs to lose their *Top 3* position after generic competition is introduced in the European, U.S. and Indian markets can be found in Supplementary Material.

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Total exclusivity periods vary across the pharmaceuticals and markets included in the analysis however, when exclusivity periods are longer than 20 years, this is often a result of patent extensions through evergreening. On the contrary, certain pharmaceuticals also show shorter exclusivity periods. Some pharmaceuticals have been discontinued voluntarily by the companies or had their active ingredients banned by government regulatory bodies. In these cases, the year of market ban has been used for patent expiration date because the active ingredient will not be approved by generic or other brand name manufacturers. Average exclusivity time includes estimated future expiration dates that may be subject to change through extensions or invalidations. A separate calculation includes only the patents that had already expired as of 2017. The results do not show a significant difference between both calculations. The average exclusivity time discussed in the following section therefore includes all *Top 3* products.

Data on patent grant and expiration dates in India prior to 2005 are not available, nor is data on the initial launch for brand name drugs. Therefore, this is not included in the analysis. Launch of generics on the Indian market is included to examine how generic competition affects brand name revenues.

#### 4.51 Main findings

Brand name pharmaceuticals predating India's new intellectual property protection laws of 2005 face the highest generic competition in India. Numerous low-income countries rely on India for access to safe, affordable pharmaceuticals and the Indian government has faced resounding pressure from advocates to ensure the availability of generic pharmaceuticals to control major price increases after the new IP law was implemented. This is evident when looking at patent grant activity in India which grant far fewer patents than their counterparts. To achieve a successful grant, patents are required to have a more detailed scope, making evergreening and patent extensions less prevalent. The 2005 amendment states "the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy" is not patentable (WHO, 2008). There have been many cases of patents being revoked, invalidated or narrowing of patent claims in Indian courts over the past ten years. Fewer brand name pharmaceuticals have been granted patents in India than in the U.S. and Europe, while many have had their patents revoked after generic manufacturers have challenged them in court. Pegasys was the first brand

name drug to be granted a patent under India's new laws, which was upheld by the Indian government in a 2009 litigation process. However, the patent was revoked on the grounds of uninventiveness in 2013. AbbVie's Kaletra, which holds over 75 patents worldwide, was not granted a patent by the Indian government because they deemed it non-inventive. This is not an unusual occurrence, mainly due to the lack of novelty if a generic is already in circulation. India allowed generics that were already being produced and sold prior to 2005 to continue operations even after brand name pharmaceuticals have been granted patents according to the amended IP laws. These factors have led to multiple generics being available on the Indian market for several years before the brand name pharmaceutical has lost its exclusivity rights. The societal implications of continued production have resulted in increased accessibility domestically and in developing nations abroad.

In addition, several brand name companies license to Indian generic companies to sell the brand name or generic versions in India and other developing countries while their pharmaceuticals still hold patents in the U.S. and Europe. For example, Gilead Sciences introduced generic versions of its brand names Epclusa, Harvoni and Sovaldi over ten years prior to its patent expirations. Gilead marketed the generics in the U.S. and Europe itself but licensed the drugs to Indian companies for marketing in other territories. Harvoni became a *Top 3* pharmaceutical one year after it was introduced in 2015 and despite facing generic competition, still generates the highest revenue of Gilead's pharmaceuticals in 2017. However, from 2015 to 2016 both Harvoni and Sovaldi experienced a decrease in revenue of 32 and 24 percent, respectively. In three years, Harvoni has generated a revenue of \$27.32 billion worldwide. Sovaldi only remained a *Top 3* pharmaceutical for three years but within those years, had accumulated revenues of \$19.56 billion and remains a high grossing drug for the company. The case of these three pharmaceuticals show that facing generic competition does not necessarily mean they cannot maintain high revenues. It is important to note that in this case, it was Gilead itself that produced and licensed its own generics and despite being lower than brand names, prices were likely kept higher than independent generic competitors.

When looking at total global revenues and the introduction of generic competition, the results shows that most brand name pharmaceuticals and their position as a *Top 3* are not affected by generics being launched in India. Furthermore, the results indicate that generic competition has

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little effect on generated revenue before entry into the U.S. market. On average, generics are marketed in India 4.7 years prior to the brand name pharmaceuticals losing their U.S. and European patent protection. Most pharmaceuticals also generate the highest revenues in the years leading up to a pending patent expiration, several years after generics have been introduced in countries outside the U.S. Both Novartis' Gleevec and Eli Lilly's Alimta had generic versions launched in India within two years of market launch in the U.S. in the early 2000's, yet both brand name drugs still currently reside in the *Top 3*. Additionally, generics for GlaxoSmithKline's Valtrex were first marketed in India in 2007, the same year it became GSM's third highest earning drug. It spent its last year as a *Top 3* two years later, in 2009, which was the same year Valtrex' patents expired and generics entered the U.S. market. The results suggest this is the most common occurrence.

The majority of the *Top 3* pharmaceuticals lose their status as soon as generics enter the market in the U.S. Tentative FDA approval is often granted to generic pharmaceuticals prior to the brand names patents expire and are therefore ready to be launched immediately after patent expiration. Additionally, the first generic manufacturer to launch its product receives a 180-day exclusivity period, allowing the generic to take over a large portion of market share soon after its launch. When brand name pharmaceuticals lose their patent protection late in the year, they tend to hold their position as *Top 3* most of the following year even if a generic becomes available right after patent expiration. This can be explained by limited competition during the six-month exclusivity period. The largest revenue loss for brand name pharmaceuticals happens once this exclusivity expires and the market becomes open for all approved generics. For example, Teva secured an exclusivity period for its generic version of Pfizer's Zoloft after it lost patent protection. During those 180 days, the price of Zoloft decreased by approximately 40 percent. After the initial exclusivity, the market was flooded with other generics, including one from Pfizer itself, and Zoloft's price dropped an additional 40 percent. The excessive loss of revenue causes many companies to attempt further protection through additional patent applications.

Two of Celgene's blockbuster drugs, Revlimid and Thalomid, have dominated the *Top 3* pharmaceuticals for 12 and 13 years, respectively. Revlimid was launched in the U.S. in 2006 and generated the second highest revenue for Celgene its first year on the market and subsequently spent eleven consecutive years as the company's number one pharmaceutical. As of 2017, Revlimid had spent a total of sixteen years under patent protection in the U.S. Through

evergreening, Celgene has extended Revlimid's total exclusivity period to twenty-six years with an estimated patent expiration date in 2027. Generics of the products were launched in India in 2015, with no significant effect on revenue. The main European patent is expected to expire in 2024. One of Celgene's strategies to protect Revlimid from generic competition has been to build an impermeable fortress of patents in addition to preventing other companies from obtaining large enough quantities of the pharmaceutical to develop feasible alternatives (Williams S. , 2019). The lack of competition has allowed Celgene to charge exorbitant prices for Revlimid and the drug earned an aggregated revenue of \$43.791 billion from 2006-2017. Extending monopolistic market power is not uncommon and proves the exploitative capabilities inherent in the current system. \

#### 4.6 Limitations and Further Research

The research conducted has provided useful analyses but has limitations. The sample size pertaining to the top 3 drugs does not enable a complete perspective on the product line for each company. Furthermore, the analysis does not focus on the effects of specific policies but rather on recent developments in the industry as a whole. Local differences may not be reflected in the findings. Limited access to data on patent grants and expiration, generic market entry in Europe and India as well as estimations for future loss of exclusivity may contort the results. In addition, relative to the market size, the data sample is small. However, the fifteen major companies and data from the U.S. market, which dominates the industry, undoubtedly gives a good indication on general industry trends. Generic pharmaceutical companies are not analyzed, and it would be beneficial to conduct further studies into their effect on the global market. More in-depth analysis should be performed to uncover more specific effects of regional differences and other categories of pharmaceuticals. The thesis provides recommendations to counteract the imbalances and inefficiencies in the market, but further research must be done to determine feasibility and the potential impact of these changes. Because the patent system influences numerous stakeholders, successful execution will be challenging and time-consuming. Other options should be evaluated to discover the best course of action going forward.

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## 5. Conclusion

The most significant finding in the company analysis is how revenue and pharmaceuticals are distributed amongst the nine main categories. Out of the 117 pharmaceuticals that have held *Top 3* positions between 1997 and 2017, only twenty-six were found outside of the main categories. When examining the categories, it becomes apparent that the predominate focus is on the Western markets. The subsequent profitability of drugs used to treat diseases prominent in industrialized countries incentivizes companies to focus their research and development efforts into these areas. As a result, it is indicative that medication for less developed countries was not prioritized, aligning with previous literature on the negligent impact of additional protection on research decisions. From an economic perspective, it is expected that pharmaceutical companies emphasize profit maximization over social welfare. This innate conundrum that is beholden on the pharmaceutical industry involves a major ethical component, namely providing global access to life-saving medication. Expecting private firms to solve a public issue is futile and unrealistic. For the pharmaceutical industry to consolidate the needs of both corporations and patients, the system regulating it must facilitate a mutually beneficial arrangement.

The analysis uncovered that introducing generic products in markets outside the U.S. had little effect on the companies aggregated revenue. In addition, the pervasive nature of counterfeit drugs in developing nations indicates an incessant need to adequately regulate manufacturing processes, mainly in India and China. Enforcing sufficient intellectual property standards can encourage licensing agreements, leading to high quality generics for developing nations. Furthermore, collaboration through partnerships and alliances between governments, non-profit organizations, regulatory authorities, multinational firms and generic manufacturers can be utilized to ensure objectives are unified and technology is protected. Enabling globalized standards allows for the allocation of resources to be optimized, creating efficiency and development opportunities for emerging nations. For this solution to be viable, several changes must be made to the current system. The obscure definitions of ‘obviousness’ create a convoluted process that has enabled the excessive granting of patents and subsequent increase in court cases. The initial grant of patents should have a narrower scope, focusing on the active ingredient or biologic of a pharmaceutical and not design, process or other frivolous claims. Companies should be able to inquire with local

patent authorities whether infringement has occurred, potentially limiting the extensive litigious process that greatly inhibits business operations.

Steps should also be made to limit patent extensions however, one imbalance is created by the patent system itself. A fixed patent term incentivizes companies to focus research efforts on pharmaceuticals that require shorter clinical trials and a quick commercialization process. Therefore, investment decisions are not based on pharmaceutical need but rather on which products will provide the longest exclusivity protection. One possible solution to rectify this issue is to implement a more flexible patent term based on the length of clinical trial processes required to develop different types of drugs. The pharmaceutical sector is unique compared to any other industry given the reliance on patent protection in business operations. Specific provisions for pharmaceutical protection are continuously incorporated into international agreements, leading to an optimistic outlook to address potential concerns.



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## Appendix

Figure 1a

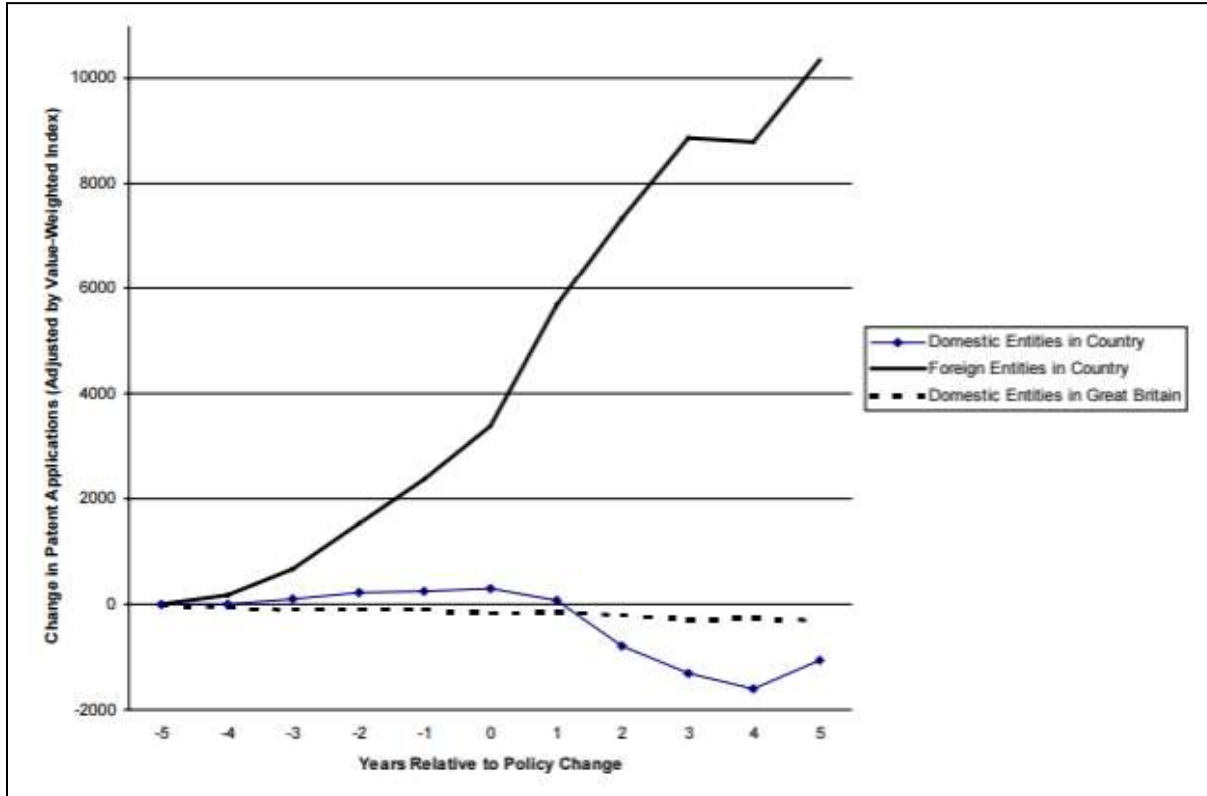


Figure 2a

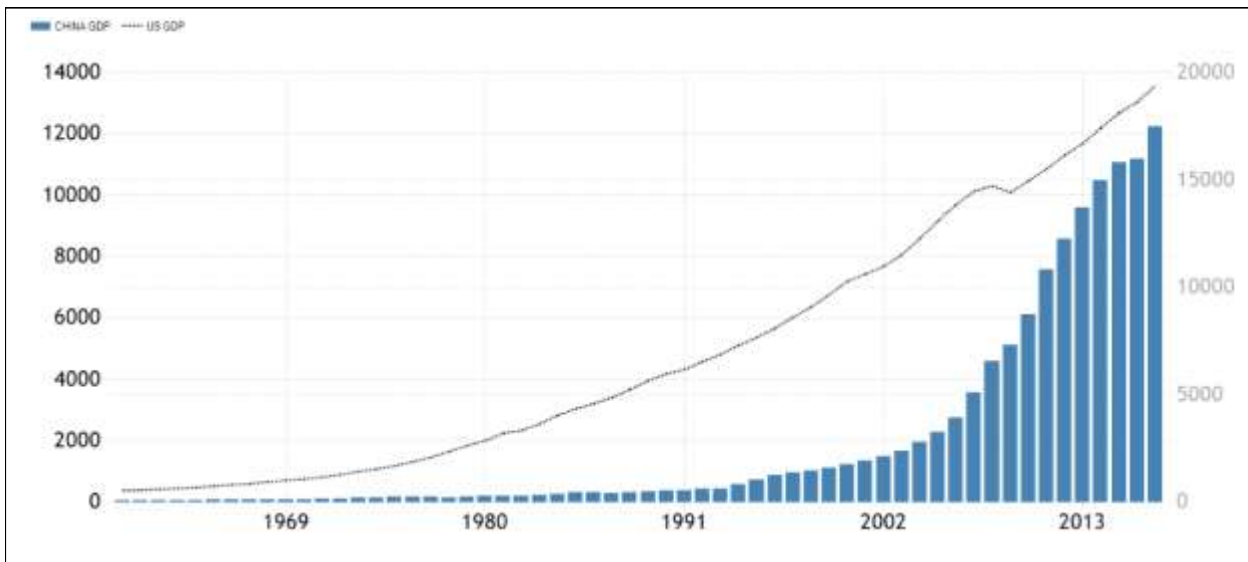


Figure 2b

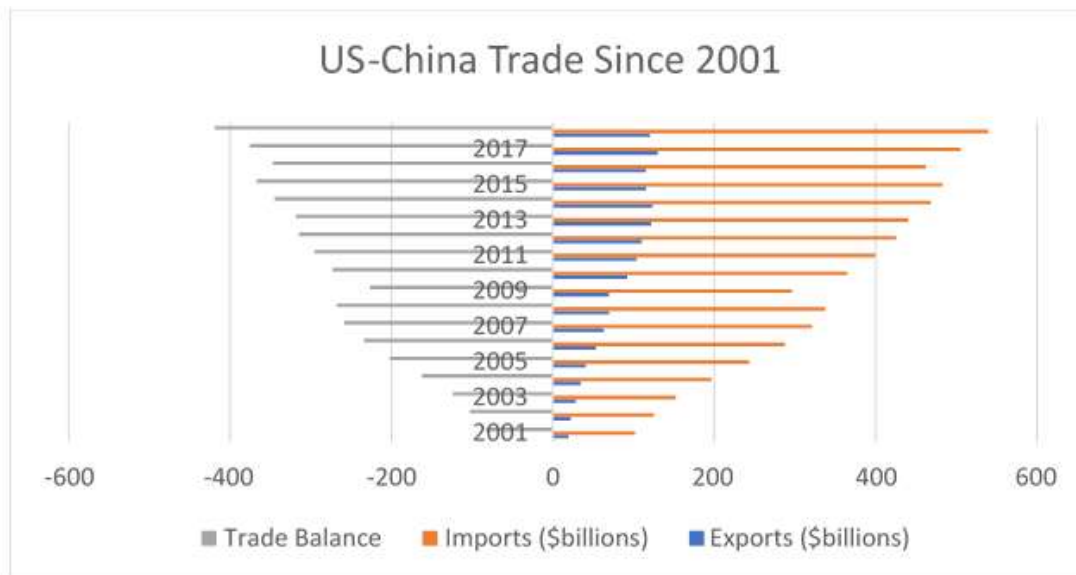


Figure 3a

Time of Accession	Name of Convention or Treaty
June 3, 1980	Convention Establishing the World Intellectual Property Organization (WIPO)
December 19, 1984	Paris Convention
March 19, 1985	Paris Convention for the Protection of Industrial Property
June 27, 1989	Madrid Protocol
February 1989	Washington Convention
October 9, 1992	Berne Convention Universal copyright Convention
May 1, 1993	Geneva Phonograms Convention
January 1, 1994	Patent Cooperation Treaty
July 1, 1995	Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure
September 19, 1996	Locarno Agreement Establishing an International Classification for Industrial Designs
June 19, 1997	Strasbourg Agreement Concerning the International Patent Classification
December 10, 2001	Agreement on Trade-Related Aspects of Intellectual Property Rights

Figure 4a

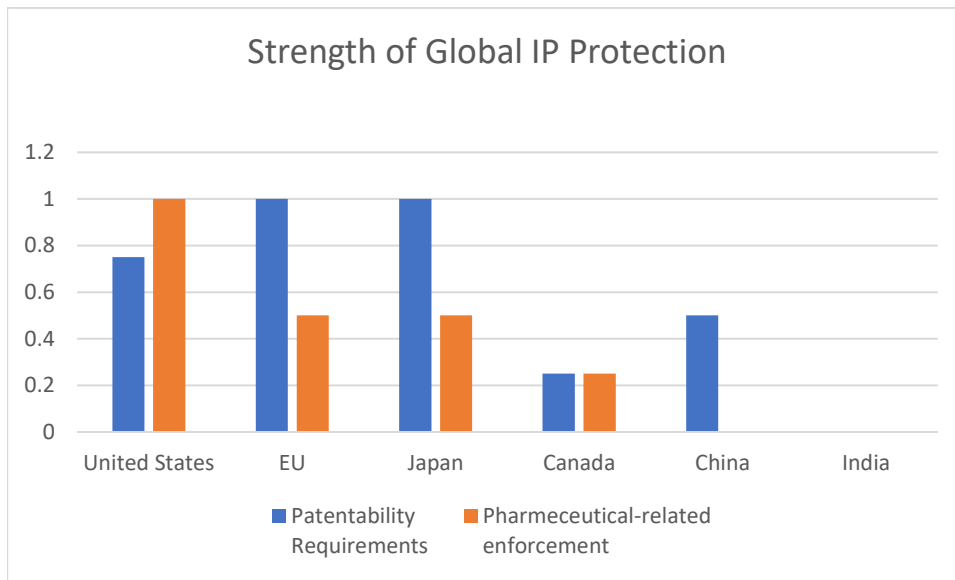


Figure 5a

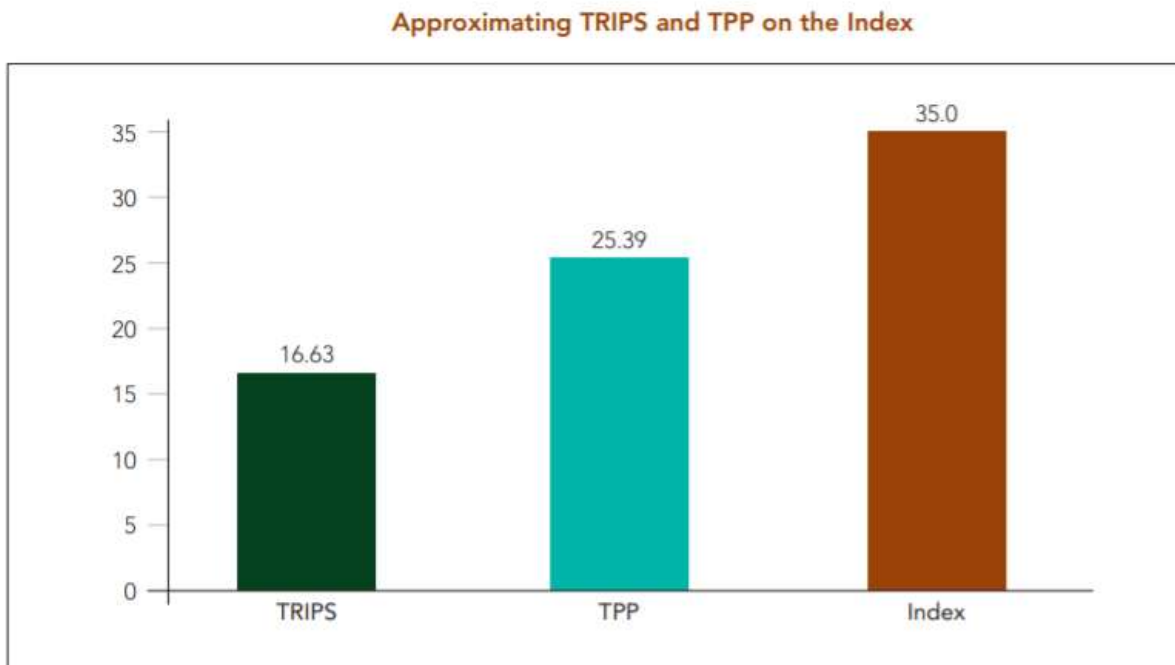


Figure 6a

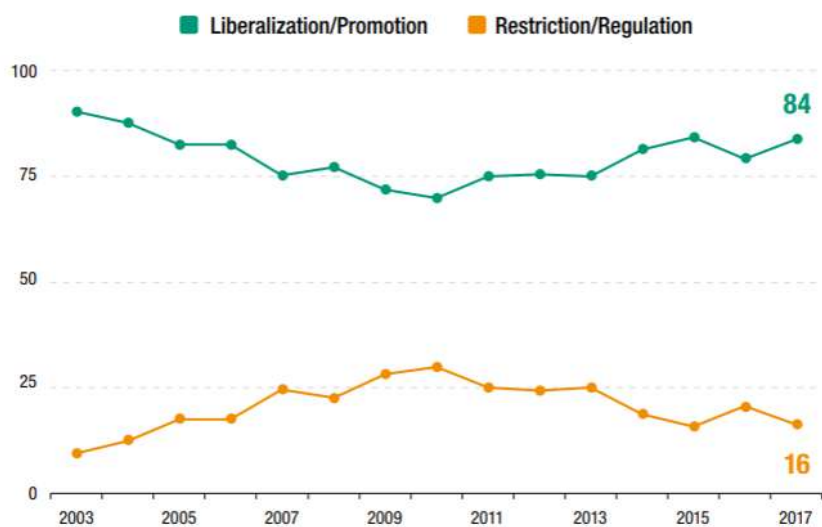
**Figure 6.** Changes in national investment policies, 2003–2017 (Per cent)

Figure 7a

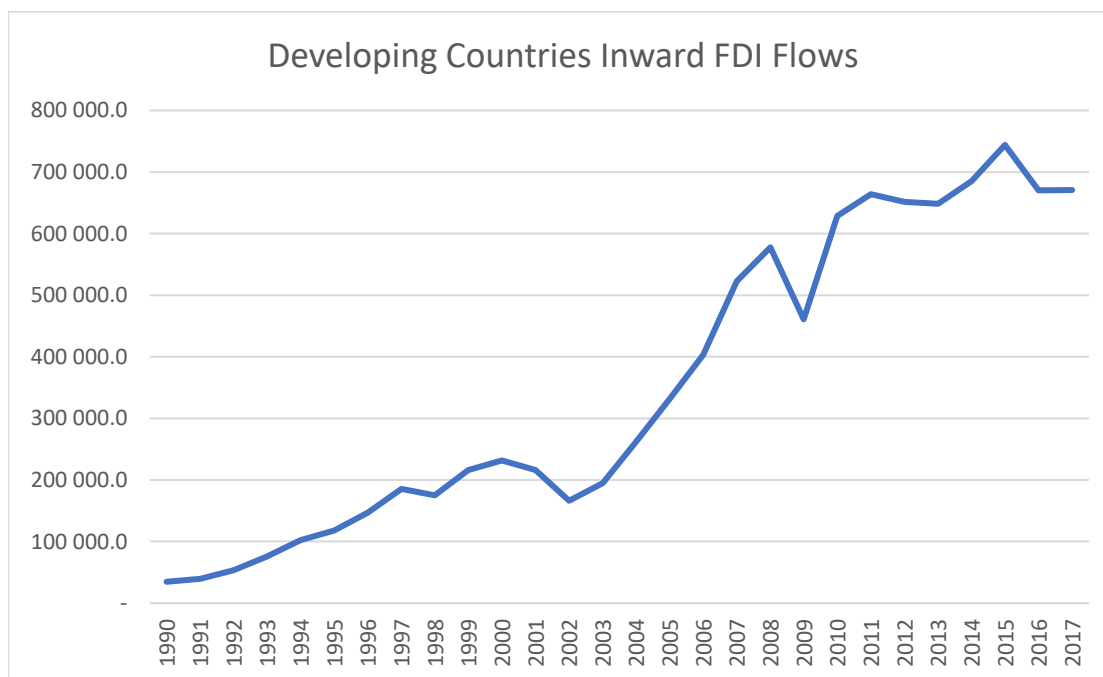


Figure 8a

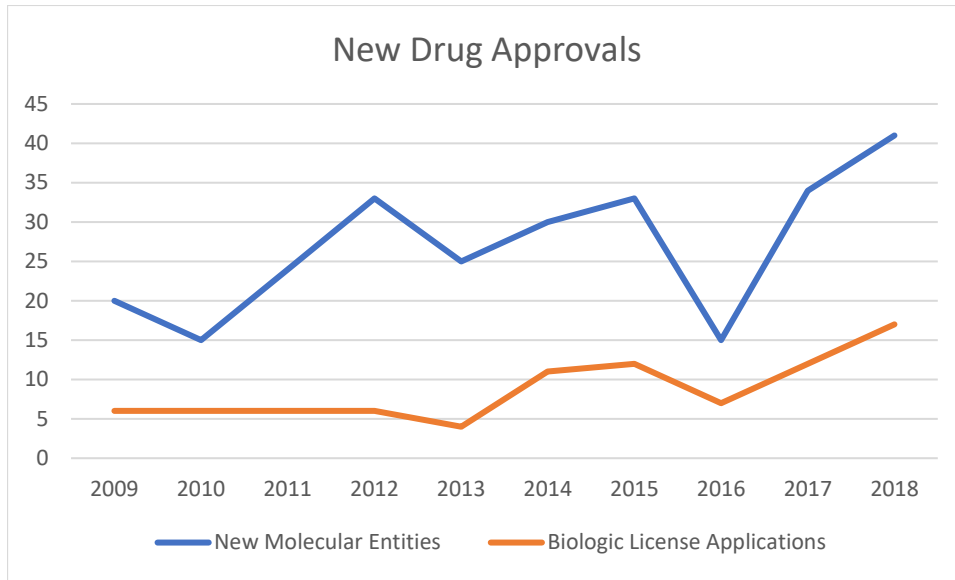


Figure 9a

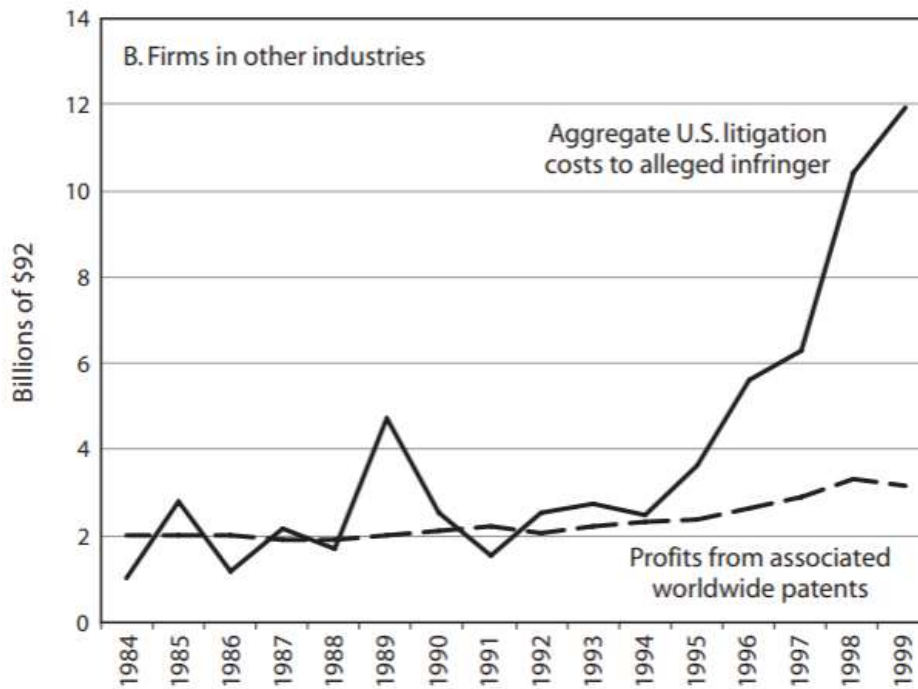




Figure 9b

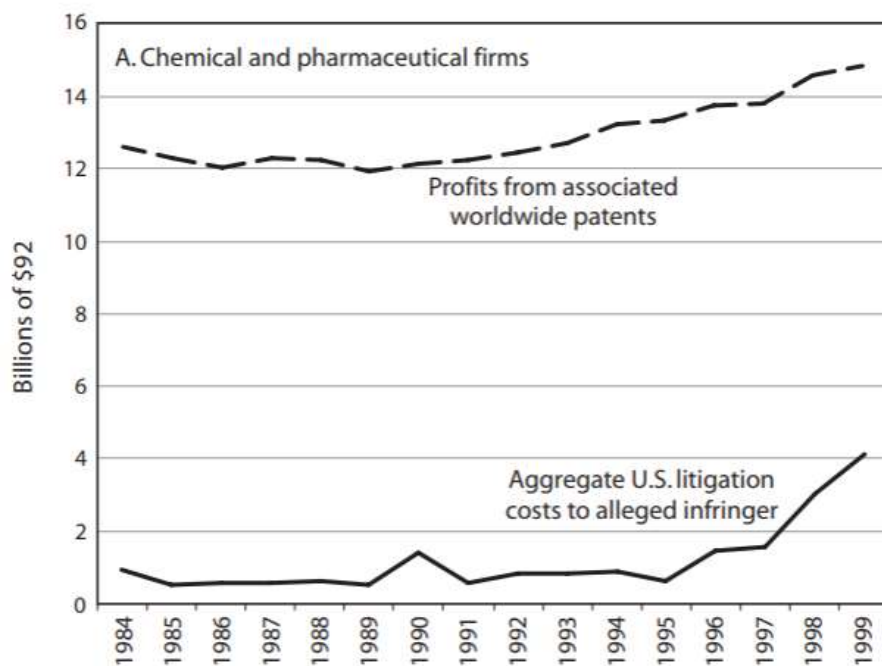


Figure 10a

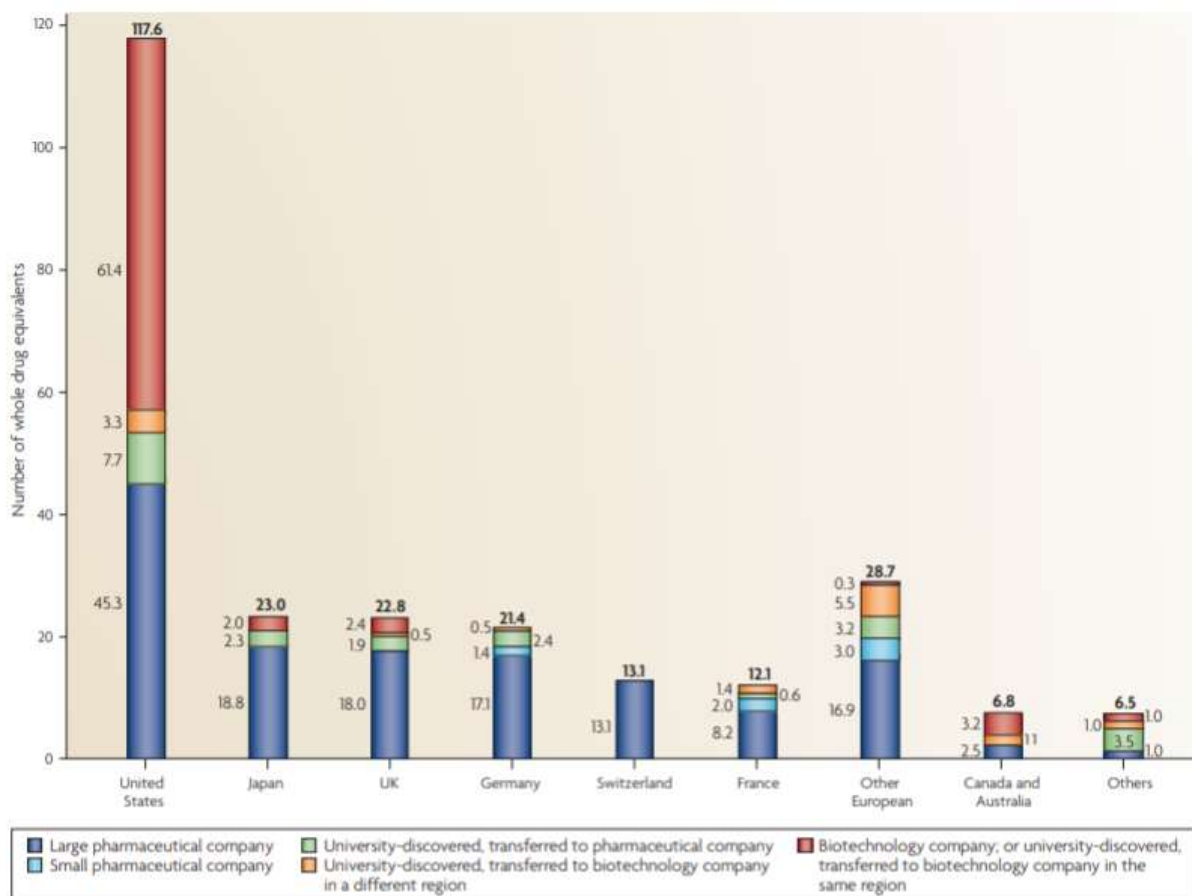


Figure 11a

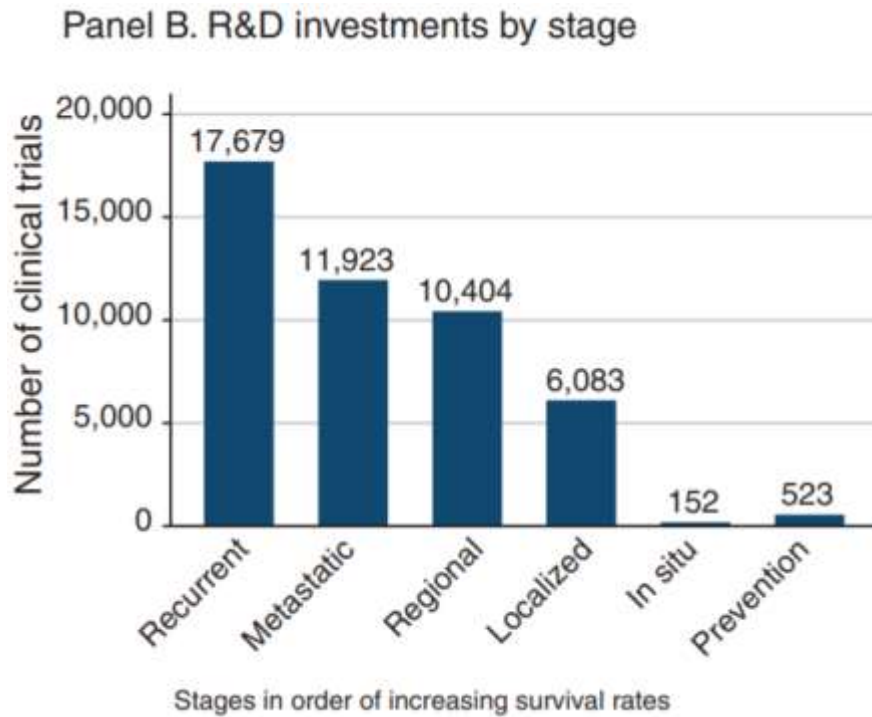
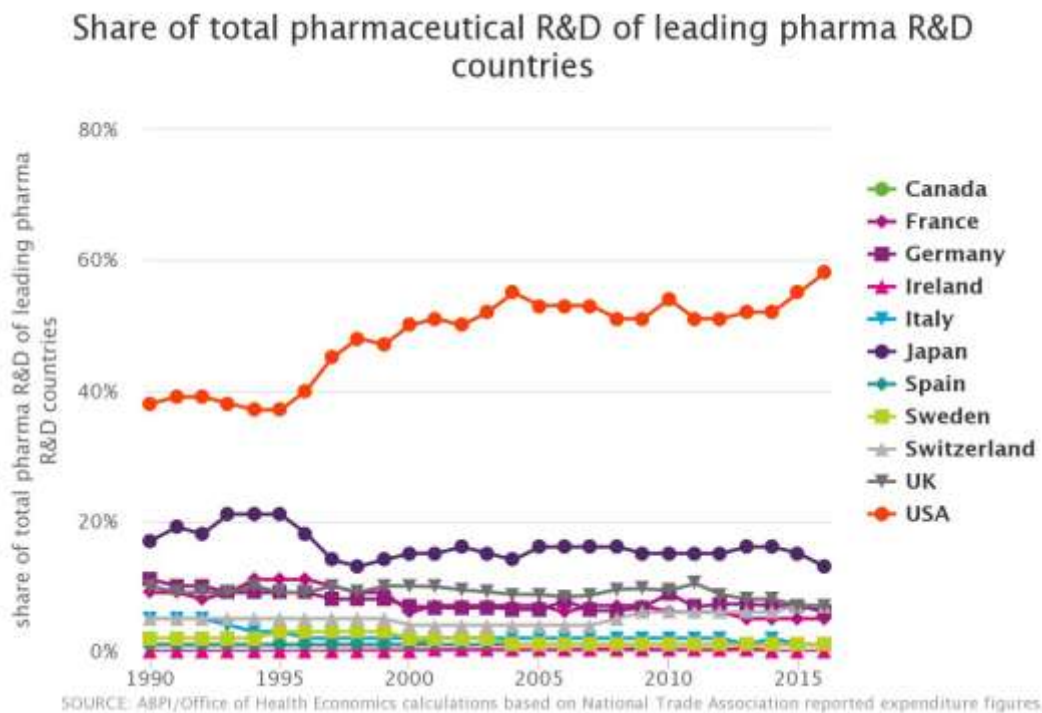


Figure 12a



## Supplementary Material

## Company overviews

Exchange rate averages CPF-USD	Year	Roche										Revenue (\$ billions)		
		Annual Revenue (\$ billions)	Annual Revenue (\$ billions) Pharmaceutical Division	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending (\$ billions)	R&D to Revenue	% of total Revenue from top 3 drugs	% of pharmaceutical Revenue from top 3 drugs	Name of 2		Name of 3	
1,015454	2017	54,123	41,837	Rituxan	7,502	13,86%	10,553	19,50%	39,57%	51,19%	Herceptin	7,122	Avastin	6,791
1,014806	2016	51,349	39,679	Rituxan	7,408	14,43%	10,047	19,57%	41,24%	53,36%	Avastin	6,883	Herceptin	6,882
1,036876	2015	49,874	38,675	Rituxan	7,305	14,65%	9,643	19,33%	42,14%	54,34%	Avastin	6,930	Herceptin	6,779
1,084623	2014	51,520	39,801	Rituxan	7,484	14,53%	9,667	18,76%	41,25%	53,39%	Avastin	6,960	Herceptin	6,806
1,073566	2013	50,221	38,974	Rituxan	7,462	14,86%	9,340	18,60%	41,22%	53,12%	Avastin	6,714	Herceptin	6,526
1,062474	2012	48,342	37,433	Rituxan	7,126	14,74%	9,004	18,63%	40,35%	52,11%	Herceptin	6,257	Avastin	6,124
1,113761	2011	47,369	36,525	Rituxan	6,888	14,12%	8,991	18,98%	38,91%	50,47%	Avastin	5,894	Herceptin	5,851
0,957983	2010	45,478	35,501	Avastin	6,190	13,61%	8,670	19,06%	38,43%	49,24%	Rituxan	6,083	Herceptin	5,201
0,974275	2009	47,789	37,993	Avastin	6,062	12,68%	9,620	20,13%	35,83%	45,07%	Rituxan	5,930	Herceptin	5,131
0,918114	2008	41,882	33,016	Rituxan	5,875	14,03%	8,121	19,39%	38,25%	48,52%	Avastin	5,155	Herceptin	4,989
0,800338	2007	36,922	29,439	Rituxan	4,415	11,96%	6,711	18,18%	31,37%	39,35%	Herceptin	3,883	Avastin	3,286
0,747482	2006	31,425	24,887	Rituxan	3,617	11,51%	4,925	15,67%	27,90%	35,23%	Herceptin	2,935	Avastin	2,214
0,753915	2005	26,772	20,598	Rituxan	3,132	11,70%	4,301	16,07%	24,08%	31,36%	NeoRecormon/Epogii	1,698	Herceptin	1,618
0,757836	2004	23,700	16,441	Rituxan	2,560	10,80%	3,860	16,29%	24,58%	35,43%	NeoRecormon/Epogii	2,082	Pegasys+Copegus	1,184
0,655957	2003	19,997	14,137	Rituxan	1,820	9,58%	3,044	16,03%	21,41%	28,77%	NeoRecormon/Epogii	1,345	Rocephin	0,902
0,445564	2002	11,827	8,602	Rituxan	1,039	8,79%	1,735	14,67%	19,11%	26,27%	Rocephin	0,690	NeoRecormon/Epogii	0,531
0,313068	2001	9,130	5,905	Rocephin	0,532	5,82%	1,219	13,35%	15,63%	24,17%	Rituxan	0,531	Accutane	0,365
0,310856	2000	8,562	5,498	Accutane	0,398	4,65%	1,218	14,23%	9,88%	15,38%	CellCept	0,248	NeoRecormon/Epogii	0,202
0,496159	1999	13,678	8,180	Rocephin	0,873	6,38%	1,876	13,72%	13,57%	22,68%	Accutane	0,516	Xenical	0,466
0,551142	1998	13,592	7,923				1,878	13,82%						
0,549802	1997	10,318	6,636				1,596	15,47%						
Average														
Max														
Min														

MB Some of the changes are bc of changes in local cu

Pfizer												
Year	Annual Revenue (\$ billions)	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending (\$ billions)	R&D to Revenue	% of Revenue from top 3 drugs	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)	Pfizer world's largest pure pharma revenue (therefore pharma division not included)
2017	52,546	Prevnar 13	5,601	10,66 %	7,657	14,57 %	26,25 %	Lyrica	5,065	Ibrance	3,126	
2016	52,824	Prevnar 13	5,718	10,82 %	7,872	14,90 %	25,73 %	Lyrica	4,966	Enbrel	2,909	
2015	48,851	Prevnar 13	6,145	12,58 %	7,690	15,74 %	29,31 %	Lyrica	4,839	Enbrel	3,333	
2014	49,605	Lyrica	5,168	10,42 %	8,393	16,92 %	27,18 %	Prevnar 13	4,464	Enbrel	3,850	
2013	51,584	Lyrica	4,595	8,91 %	6,678	12,95 %	23,93 %	Prevnar 13	3,974	Enbrel	3,774	
2012	58,986	Lyrica	4,158	7,05 %	7,870	13,34 %	20,08 %	Lipitor	3,948	Enbrel	3,737	
2011	67,425	Lipitor	9,577	14,20 %	9,112	13,51 %	25,12 %	Lyrica	3,693	Enbrel	3,666	
2010	67,809	Lipitor	10,733	15,83 %	9,413	13,88 %	25,17 %	Enbrel	3,274	Lyrica	3,063	
2009	50,009	Lipitor	11,434	22,86 %	7,845	15,69 %	33,31 %	Lyrica	2,840	Celebrex	2,383	
2008	48,296	Lipitor	12,401	25,68 %	7,945	16,45 %	36,16 %	Lyrica	2,573	Celebrex	2,489	
2007	48,418	Lipitor	12,675	26,18 %	8,089	16,71 %	37,11 %	Norvasc	3,001	Celebrex	2,290	
2006	48,371	Lipitor	12,886	26,64 %	7,599	15,71 %	41,06 %	Norvasc	4,866	Zoloft	2,110	
2005	47,405	Lipitor	12,187	25,71 %	7,442	15,70 %	42,50 %	Norvasc	4,706	Zoloft	3,256	
2004	48,988	Lipitor	10,862	22,17 %	7,684	15,69 %	38,14 %	Norvasc	4,463	Zoloft	3,361	
2003	44,736	Lipitor	9,231	20,63 %	7,487	16,74 %	37,30 %	Norvasc	4,336	Zoloft	3,118	
2002	32,373	Lipitor	7,972	24,63 %	5,176	15,99 %	44,98 %	Norvasc	3,846	Zoloft	2,742	
2001	29,024	Lipitor	6,448	22,22 %	4,776	16,46 %	42,70 %	Norvasc	3,581	Zoloft	2,365	
2000	29,574	Lipitor	5,031	17,01 %	4,435	15,00 %	35,62 %	Norvasc	3,362	Zoloft	2,140	
1999	27,376	Lipitor	3,795	13,86 %	4,036	14,74 %	32,08 %	Norvasc	2,991	Zoloft	1,997	
1998	13,544	Novartis	2,575	19,01 %	3,305	24,40 %	40,25 %	Zoloft	1,836	Zithromax	1,041	
1997	11,055	Novartis	2,217	20,05 %	1,805	16,33 %	41,66 %	Zoloft	1,507	Diflucan	0,881	
			161,409	17,96 %		15,78 %	33,60 %					
				26,64 %		24,40 %	44,98 %					
				7,05 %		12,95 %	20,08 %					

Exchange rate averages CPF-USD	Year	Novartis												
		Annual Revenue (\$ billions)	Annual Revenue Pharmaceutical Division (\$ billions)	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending (\$ billions)	R&D to Revenue	% of total Revenue from top 3 drugs	% of pharmaceutical Revenue from top 3 drugs	Revenue (\$ billions)	Name of 2	Name of 3	Revenue (\$ billions)
	2017	49,109	43,085	Gilenya	3,185	6.49%	9,000	18.33%	14.66%	16.71%	Cosentyx	Gleevec	2,071	1,943
	2016	48,518	42,706	Gleevec	3,323	6.85%	9,024	18.60%	17.04%	19.36%	Gilenya	Lucentis	3,109	1,836
	2015	49,414	39,602	Gleevec	4,658	9.43%	8,900	18.01%	19.21%	23.97%	Gilenya	Lucentis	2,776	2,060
	2014	57,996	47,169	Gleevec	4,746	8.18%	9,917	17.10%	16.66%	20.49%	Gilenya	Lucentis	2,477	2,441
	2013	57,920	47,424	Gleevec	4,693	8.10%	9,846	17.00%	18.30%	22.35%	Diovan	Lucentis	3,524	2,383
	2012	56,873	46,448	Gleevec	4,675	8.25%	9,116	16.09%	20.27%	24.74%	Diovan	Lucentis	4,417	2,398
	2011	58,566	48,608	Diovan	5,665	9.67%	9,239	15.78%	21.13%	25.46%	Gleevec	Lucentis	4,659	2,050
	2010	50,624	48,198	Diovan	6,053	11.96%	8,080	15.96%	23.41%	24.59%	Gleevec	Lucentis	4,265	1,533
	2009	44,267	44,200	Diovan	6,013	13.58%	7,469	16.87%	25.81%	25.85%	Gleevec	Zometa	3,944	1,469
	2008	41,459	41,459	Diovan	5,740	13.85%	7,217	17.41%	26.03%	26.03%	Gleevec	Zometa	3,670	1,382
Both Sand	2007	39,800	39,800	Diovan	5,012	12.59%	6,430	16.16%	23.52%	23.52%	Gleevec	Zometa	3,050	1,297
Before 200	2006	37,020	37,020	Diovan	4,223	11.41%	5,349	14.45%	21.96%	21.96%	Gleevec	Lotrel	2,554	1,352
	2005	31,212	31,212	Diovan	3,676	11.78%	4,846	15.53%	22.65%	22.65%	Gleevec	Zometa	2,170	1,224
	2004	28,247	28,247	Diovan	3,093	10.95%	4,207	14.89%	20.85%	20.85%	Gleevec	Lamisil	1,634	1,162
	2003	24,864	24,864	Diovan	2,425	9.75%	3,628	14.59%	18.39%	18.39%	Gleevec	Neoral/Sandimmun	1,128	1,020
0.445564	2002	14,442	14,442	Diovan	1,150	7.96%	1,933	13.39%	17.10%	17.10%	Neoral/Sandimmun	Lamisil	0,716	0,604
0.313068	2001	10,030	9,471	Diovan	0,589	5.87%	1,311	13.08%	16.32%	17.28%	Neoral/Sandimmun	Cibacem/Lotensin (inc	0,573	0,475
0.496159	2000	9,050	8,617		N/A	N/A	1,247	13.78%	N/A					
0.551142	1999	12,607	11,797		N/A	N/A	1,744	13.83%	N/A					
0.549802	1998				N/A	N/A								
	1997				N/A	N/A								
Average			654,368			9.80%		15.83%	20.19%	21.84%				
Max						13.85%		18.60%	26.03%	26.03%				
Min						5.87%		13.08%	14.66%	16.71%				

Merek and Co.													
Year	Annual Revenue (\$ billions)	Annual Revenue (\$ billions) at Division	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending (\$ billions)	R&D to Revenue	% of total Revenue from top 3 drugs	% of pharmaceutical Revenue from top 3 drugs	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)
2017	40,122	35,390	Januvia	5,896	14,70 %	10,208	25,44 %	29,94 %	33,94 %	Keytruda	3,809	Gardasil	3,809
2016	39,807	35,151	Januvia	6,109	15,35 %	10,124	25,43 %	30,10 %	34,09 %	Zetia/Vigroin	3,701	Gardasil	2,173
2015	39,498	34,782	Januvia	3,863	9,78 %	6,705	16,98 %	21,62 %	24,55 %	Zetia	2,526	Janumet	2,151
2014	42,237	36,042	Januvia	3,931	9,31 %	7,180	17,00 %	21,20 %	24,94 %	Zetia	2,650	Remicade	2,372
2013	44,033	37,437	Januvia	4,004	9,09 %	7,503	17,04 %	20,29 %	23,86 %	Zetia	2,658	Remicade	2,271
2012	47,267	40,601	Januvia	4,086	8,64 %	8,168	17,28 %	16,73 %	19,48 %	Remicade	2,076	Zetia	1,747
2011	48,047	41,289	Singulair	5,479	11,40 %	8,467	17,62 %	23,87 %	27,78 %	Januvia	3,324	Remicade	2,667
2010	45,987	39,811	Singulair	4,987	10,84 %	10,991	23,90 %	21,93 %	25,33 %	Remicade	2,714	Januvia	2,385
2009	27,428	25,237	Singulair	4,669	17,02 %	5,845	21,31 %	37,01 %	40,23 %	Cozaar/Higzaar	3,561	Januvia	1,922
2008	23,850	23,620	Singulair	4,337	18,18 %	4,805	20,15 %	39,61 %	40,00 %	Cozaar/Higzaar	3,558	Fosamax	1,553
2007	24,198	23,939	Singulair	4,266	17,63 %	4,883	20,18 %	44,55 %	45,03 %	Cozaar/Higzaar	3,350	Fosamax	3,163
2006	22,363	22,080	Singulair	4,358	19,49 %	4,783	21,39 %	47,14 %	47,74 %	Cozaar/Higzaar	3,049	Fosamax	3,134
2005	22,012	21,825	Zocor	4,382	19,91 %	3,848	17,48 %	48,20 %	48,61 %	Fosamax	3,191	Cozaar/Higzaar	3,037
2004	22,937	22,715	Zocor	5,197	22,66 %	4,010	17,48 %	48,75 %	49,22 %	Fosamax	3,160	Cozaar/Higzaar	2,824
2003	22,486	22,257	Zocor	5,011	22,28 %	3,280	14,59 %	45,53 %	45,99 %	Fosamax	2,677	Vioxx	2,549
2002	51,790	18,867	Zocor	5,600	10,81 %	2,700	5,21 %	19,89 %	54,59 %	Vioxx	2,500	Fosamax	2,200
2001	47,716	17,792	Zocor	5,264	11,03 %	2,500	5,24 %	19,31 %	51,80 %	Vioxx	2,358	Fosamax	1,594
2000	40,363	16,058	Zocor	2,207	5,47 %	2,300	5,70 %	10,97 %	27,58 %	Vioxx	1,518	Fosamax	0,704
1999	32,714	15,661				2,068	6,32 %						
1998	26,898	13,985				1,812	6,74 %						
1997	23,637	14,197				1,684	7,12 %						
Average		558,736			14,09 %		15,70 %	30,37 %	36,93 %				
Max					22,66 %		25,44 %	48,75 %	54,59 %				
Min					5,47 %		5,21 %	10,97 %	19,48 %				

AbbVie												
Year	Annual Revenue (\$ billions)	Annual Revenue (\$ billions) Pharmaceutical Division	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending (\$ billions)	R&D to Revenue	% of Revenue from top 3 drugs	Name of 2	Name of 3	Revenue (\$ billions)	Revenue (\$ billions)
2017	28,216	18,427	Humira	18,427	65.31%	4,982	17.66%	77.36%	Imbruvica	Lupron	2,573	0,829
2016	25,638	16,078	Humira	16,078	62.71%	4,366	17.03%	75.79%	Imbruvica	Viekira	1,832	1,522
2015	22,859	14,012	Humira	14,012	61.30%	4,285	18.75%	72.08%	Viekira	Lupron	1,639	0,826
2014	19,960	12,543	Humira	12,543	62.84%	3,297	16.52%	71.88%	AndroGel	Kaletra	0,934	0,870
2013	18,790	10,659	Humira	10,659	56.73%	2,855	15.19%	67.35%	AndroGel	Kaletra	1,035	0,962
2012	18,012	9,265	Humira	9,265	51.44%	2,778	15.42%	63.93%	AndroGel	TriCorrTriil	1,152	1,098
2011	17,022	7,932	Humira	7,932	46.60%	2,618	15.38%	61.53%	TriCorrTriilpiix	Kaletra	1,372	1,170
2010	19,894	6,508	Humira	6,508	32.71%	2,495	12.54%	45.67%	TriCorrTriilpiix	Kaletra	1,355	1,223
2009	16,486	5,500	Humira	5,500	33.36%	1,707	10.35%	33.36%				
2008	16,708	4,500	Humira	4,500	26.93%			26.93%				
2007	14,630	3,000	Humira	3,000	20.51%							
	Information prior to 2007 not possible to obtain for pharmaceuticals											
Average	218,215				47.31%		15.43%	59.59%				
Max					65.31%		18.75%	77.36%				
Min					20.51%		10.35%	26.93%				

Eli Lilly & Co.											
Year	Annual Revenue (\$ billions)	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending (\$ billions)	R&D to Revenue	% of Revenue from top 3 drugs	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)
2017	22,871	Humalog	2,865	12.53 %	5,282	23.09 %	32.67 %	Cialis	2,323	Alimta	2,283
2016	21,222	Humalog	2,842	13.39 %	5,244	24.71 %	36.03 %	Alimta	2,493	Cialis	2,311
2015	19,959	Humalog	2,842	14.24 %	4,796	24.03 %	38.31 %	Alimta	2,493	Cialis	2,311
2014	19,616	Alimta	2,792	14.23 %	4,734	24.13 %	40.11 %	Humalog	2,785	Cialis	2,291
2013	23,113	Cymbalta	5,084	22.00 %	5,531	23.93 %	44.99 %	Alimta	2,703	Humalog	2,611
2012	22,603	Cymbalta	4,994	22.09 %	5,278	23.35 %	43.77 %	Alimta	2,594	Humalog	2,306
2011	24,287	Ziprexa	4,622	19.03 %	5,021	20.67 %	46.30 %	Cymbalta	4,162	Alimta	2,461
2010	23,076	Ziprexa	5,026	21.78 %	4,884	21.17 %	46.34 %	Cymbalta	3,459	Alimta	2,209
2009	21,836	Ziprexa	4,916	22.51 %	4,327	19.81 %	45.56 %	Cymbalta	3,075	Humalog	1,959
2008	20,378	Ziprexa	4,696	23.04 %	3,841	18.85 %	44.80 %	Cymbalta	2,697	Humalog	1,736
2007	18,634	Ziprexa	4,761	25.55 %	3,487	18.71 %	45.38 %	Cymbalta	2,103	Gemzar	1,592
2006	15,691	Ziprexa	4,364	27.81 %	3,129	19.94 %	45.17 %	Gemzar	1,408	Cymbalta	1,316
2005	14,645	Ziprexa	4,202	28.69 %	3,026	20.66 %	45.98 %	Gemzar	1,335	Humalog	1,198
2004	13,858	Ziprexa	4,420	31.89 %	2,691	19.42 %	48.61 %	Gemzar	1,214	Humalog	1,102
2003	12,583	Ziprexa	4,277	33.99 %	2,305	18.32 %	50.54 %	Humulin	1,060	Gemzar	1,022
2002	11,078	Ziprexa	3,689	33.30 %	2,149	19.40 %	50.26 %	Humulin	1,004	Gemzar	0,875
2001	11,543	Ziprexa	3,087	26.74 %	2,235	19.36 %	53.18 %	Prozac	1,990	Humulin	1,061
2000	10,862	Prozac	2,574	23.69 %	2,019	18.58 %	55.59 %	Ziprexa	2,350	Humulin	1,115
1999	10,003	Prozac	2,613	26.13 %	1,784	17.83 %	49.53 %	Ziprexa	1,885	Gemzar	0,456
1998	9,237	Prozac	2,812	30.44 %	1,739	18.83 %	50.58 %	Ziprexa	1,443	Axid	0,418
1997	8,158	Prozac	2,559	31.37 %	1,382	16.94 %	46.77 %	Ziprexa	0,730	Axid	0,527
Average	355,250			24.02 %		20.56 %	45.74 %				
Max				33.99 %		24,71 %	55.59 %				
Min				12.53 %		16,94 %	32.67 %				



Astra Zeneca												
Exchange rate averages SEK-USD	Year	Annual Revenue (\$ billions)	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending (\$ billions)	R&D to Revenue %	% of Revenue from top 3 drugs	Revenue (\$ billions)	Name of 2	Name of 3	Revenue (\$ billions)
	2017	22,465	Symbicort	2,803	12.48 %	5,757	25.63 %	31.69 %	2,365	Crestor	Nexium	1,952
	2016	23,002	Crestor	3,401	14.79 %	5,890	25.61 %	36.61 %	2,989	Symbicort	Nexium	2,032
	2015	24,708	Crestor	5,017	20.31 %	5,997	24.27 %	44.14 %	3,394	Symbicort	Nexium	2,496
	2014	26,095	Crestor	5,512	21.12 %	5,579	21.38 %	49.70 %	3,801	Symbicort	Nexium	3,855
	2013	25,711	Crestor	5,622	21.87 %	4,821	18.75 %	50.47 %	3,872	Symbicort	Nexium	3,483
	2012	27,973	Crestor	6,253	22.36 %	5,243	18.74 %	47.87 %	3,944	Nexium	Symbicort	3,194
	2011	33,591	Crestor	6,622	19.71 %	5,523	16.44 %	50.25 %	5,828	Seroquel	Nexium	4,429
	2010	33,269	Crestor	5,691	17.11 %	5,318	15.98 %	47.98 %	5,302	Seroquel	Nexium	4,969
	2009	32,804	Nexium	4,959	15.12 %	4,409	13.44 %	43.67 %	4,866	Seroquel	Crestor	4,502
	2008	31,601	Nexium	5,200	16.46 %	5,179	16.39 %	41.93 %	4,452	Seroquel	Crestor	3,697
	2007	29,559	Nexium	5,216	17.65 %	5,162	17.46 %	40.73 %	4,027	Seroquel	Crestor	2,796
	2006	26,475	Nexium	5,182	19.57 %	3,902	14.74 %	40.14 %	3,416	Seroquel	Crestor	2,028
	2005	23,950	Nexium	4,633	19.34 %	3,379	14.11 %	38.12 %	2,761	Seroquel	Seloken/Toprol-XL	1,735
	2004	21,426	Nexium	3,883	18.12 %	3,803	17.75 %	36.67 %	2,027	Seroquel	Losec/Prilosec	1,947
	2003	18,849	Nexium	3,302	17.52 %	3,451	18.31 %	39.02 %	2,565	Losec/Prilosec	Seroquel	1,487
	2002	17,841	Losec/Prilosec	4,623	25.91 %	3,069	17.20 %	43.42 %	1,978	Nexium	Seroquel	1,145
	2001	16,480	Losec/Prilosec	5,684	34.49 %	2,687	16.30 %	45.85 %	1,097	Zestril	Pulmicort	0,775
	2000	15,804	Losec/Prilosec	6,260	39.61 %	2,616	16.55 %	51.77 %	1,188	Zoladex	Nexium	0,734
	1999	18,445	Losec/Prilosec	5,309	32.04 %	2,454	13.30 %	42.61 %	1,221	Zestril	Pulmicort	0,730
0.12698	1998	7,262	Losec/Prilosec	4,015	55.29 %	1,346	18.54 %	71.12 %	0,697	Pulmicort	Seloken/Toprol-XL	0,453
	1997	5,702	Losec/Prilosec	2,733	47.94 %	1,112	19.51 %	65.94 %	0,625	Pulmicort	Seloken/Toprol-XL	0,402
	Average	483,012			24.23 %		18.11 %	45.70 %				
	Max				55.29 %		25.63 %	71.12 %				
	Min				12.48 %		13.30 %	31.69 %				

Celgene											
Year	Annual Revenue (\$ billions)	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending (\$ billions)	R&D to Revenue	% of Revenue from top 3	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)
2017	13,003	Revlimid	8,187	62.96 %	5,915	45.49 %	85.21 %	Pomalyst	1,614	Otezla	1,279
2016	11,229	Revlimid	6,974	62.10 %	4,470	39.81 %	82.83 %	Pomalyst	1,311	Otezla	1,017
2015	9,256	Revlimid	5,801	62.67 %	3,697	39.94 %	83.75 %	Pomalyst	0,983	Abraxane	0,968
2014	7,670	Revlimid	4,980	64.92 %	2,431	31.69 %	84.84 %	Abraxane	0,848	Pomalyst	0,680
2013	6,494	Revlimid	4,280	65.91 %	2,226	34.28 %	88.27 %	Vidaza	0,803	Abraxane	0,649
2012	5,507	Revlimid	3,767	68.40 %	1,724	31.31 %	91.10 %	Vidaza	0,823	Abraxane	0,427
2011	4,942	Revlimid	3,208	66.25 %	1,600	33.05 %	88.79 %	Vidaza	0,705	Abraxane	0,386
2010	3,626	Revlimid	2,469	68.10 %	1,128	31.12 %	93.57 %	Vidaza	0,534	Thalomid	0,390
2009	2,690	Revlimid	1,706	63.44 %	0,795	29.55 %	94.08 %	Thalomid	0,437	Vidaza	0,387
2008	2,255	Revlimid	1,325	58.75 %	0,931	41.30 %	90.30 %	Thalomid	0,505	Vidaza	0,207
2007	1,406	Revlimid	0,774	55.05 %	0,399	28.35 %	92.08 %	Thalomid	0,447	Alkeran	0,074
2006	0,899	Thalomid	0,433	48.17 %	0,259	28.77 %	89.43 %	Revlimid	0,321	Alkeran	0,050
2005	0,537	Thalomid	0,388	72.22 %	0,191	35.53 %	82.28 %	Alkeran	0,050	Focalin	0,004
2004	0,378	Thalomid	0,309	81.75 %	0,161	42.61 %	97.30 %	Alkeran	0,017	Focalin	0,042
2003	0,271	Thalomid	0,224	82.40 %	0,123	45.20 %	97.75 %	Alkeran	0,018	Focalin	0,024
2002	0,136	Thalomid	0,012	8.77 %	0,085	62.54 %	37.20 %	Focalin	0,039	N/A	0,000
2001	0,114	Thalomid	0,082	71.78 %	0,068	59.26 %	73.70 %	Focalin	0,002	N/A	0,000
2000	0,084	Thalomid	0,062	73.59 %	0,053	62.57 %	73.59 %	N/A	0,000	N/A	0,000
1999	0,026	Thalomid	0,024	91.98 %	0,020	74.81 %	91.98 %	N/A	0,000	N/A	0,000
1998	0,004	Thalomid	0,003	78.95 %	0,020	521.05 %	78.95 %	N/A	0,000	N/A	0,000
1997	0,001	N/A	N/A	N/A	0,017	1553.6 %	N/A	N/A	0,000	N/A	0,000
Average	70,427			65.41 %		136.75 %	84.85 %				
Max				91.98 %		1553.6 %	97.75 %				
Min				8.77 %		28.35 %	37.20 %				
					Average R&D	41.86 %					
					Max R&D to	74.81 %					

Sanofi												
Year	Annual Revenue (\$ billions)	Annual Revenue (\$ billions) Pharmaceutical Division	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending (\$ billions)	R&D to Revenue	% of total Revenue from top 3 drugs	% of pharmaceutical Revenue from top 3 drugs	Revenue (\$ billions)	Name of 3	Exchange rate average as of 12/31/13
2017	39,611	28,387	Lantus	5,223	13.18%	6,183	15.61%	22.15%	30.91%	1,780	Aubagio	1,771
2016	37,437	32,371	Lantus	6,325	16.89%	5,725	15.29%	26.30%	30.41%	1,811	Plavix	1,709
2015	41,019	33,064	Lantus	7,090	17.29%	5,639	13.75%	27.15%	33.69%	2,140	Lovenox	1,907
2014	44,856	36,820	Lantus	8,427	18.79%	6,408	14.28%	29.33%	35.73%	2,473	Lovenox	2,257
2013	43,777	36,203	Lantus	7,593	17.34%	6,337	14.48%	28.15%	34.04%	2,467	Lovenox	2,263
2012	44,936	37,123	Lantus	6,378	14.19%	6,329	14.08%	25.52%	30.89%	2,657	Lovenox	2,434
2011	46,495	38,837	Lantus	5,453	11.73%	6,699	14.41%	24.16%	28.92%	2,940	Plavix	2,841
2010	42,923	35,244	Lantus	4,655	10.84%	6,030	14.05%	26.07%	31.75%	3,721	Taxotere	2,814
2009	40,876	36,018	Lantus	4,296	10.51%	6,392	15.64%	29.81%	33.83%	4,232	Plavix	3,659
2008	40,557	36,348	Lovenox	4,028	9.93%	6,731	16.60%	28.28%	31.56%	3,838	Lantus	3,604
2007	39,466	34,656	Lovenox	3,582	9.31%	6,221	16.17%	25.19%	27.96%	3,324	Lantus	2,785
2006	35,658	32,475	Lovenox	3,060	8.58%	5,567	15.61%	23.58%	25.89%	2,801	Stilnox/Ambien	2,546
2005	33,979	31,413	Lovenox	2,666	7.85%	5,031	14.81%	21.16%	22.88%	2,521	Taxotere	2,002
2004	18,496	17,647	Lovenox	2,368	12.80%	2,971	16.06%	34.29%	35.95%	2,107	Allegra	1,868
2003	9,113	8,800	Stilnox/Ambien	1,523	16.71%	1,490	16.35%	43.41%	44.96%	1,500	Eloxatin	0,933
2002	7,048	6,760	Stilnox/Ambien	1,348	19.12%	1,153	16.35%	39.92%	41.62%	0,934	Approvel	0,532
2001	5,812	5,679	Stilnox/Ambien	0,704	12.11%	0,924	15.89%	29.50%	30.19%	0,632	Approvel	0,379
2000	5,505	5,114	Stilnox/Ambien	0,537	9.76%	0,872	15.85%	22.12%	23.81%	0,403	Approvel	0,277
1999	5,700	5,027	Stilnox/Ambien	0,421	7.38%	0,971	17.03%	16.62%	18.84%	0,314	Plavix	0,212
1998												
1997												
Average		497,987			12.86%		15.39%	27.51%	31.25%			
Max					19.12%		17.03%	43.41%	44.96%			
Min					7.38%		13.75%	16.62%	18.84%			

R&amp;D includes both pharma and diagnostic

Bayer														
Year	Annual Revenue (\$ billions)	Annual Revenue (\$ billions) Pharmaceutical Division	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending (\$ billions)	R&D to Revenue	% of total Revenue from top 3 drugs	% of total Pharmaceutical Revenue from top 3 drugs	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)	Exchange rate average EUR-USD
2017	39,566	19,037	Xarelto	3,727	9.42%	5,089	12.86%	18.00%	37.42%	Ejlea	2,124	Mirena	1,272	1.13
2016	51,769	18,176	Xarelto	3,241	6.26%	5,165	9.98%	12.23%	34.83%	Ejlea	1,799	Kogenate	1,291	1.1069
2015	51,400	15,251	Xarelto	2,499	4.86%	4,742	9.23%	10.01%	33.72%	Ejlea	1,363	Kogenate	1,282	1.1096
2014	56,105	16,008	Xarelto	2,230	3.97%	4,747	8.46%	8.54%	29.93%	Kogenate	1,473	Mirena	1,088	1.3283
2013	53,351	14,864	Kogenate	1,597	2.99%	4,238	7.94%	7.94%	28.50%	Betaseron	1,379	Xarelto	1,261	1.3285
2012	51,125	12,901	Betaseron	1,564	3.06%	3,874	7.59%	8.66%	34.32%	Kogenate	1,520	YAZ/Yasmin	1,344	1.2868
2011	50,866	13,854	Betaseron	1,555	3.06%	4,083	8.03%	8.93%	32.79%	Kogenate	1,497	YAZ/Yasmin	1,490	1.3925
2010	46,532	14,466	Betaseron	1,599	3.44%	4,049	8.70%	9.46%	30.45%	YAZ/Yasmin	1,473	Kogenate	1,331	1.3262
2009	43,473	14,599	YAZ/Yasmin	1,783	4.10%	3,830	8.81%	10.84%	32.29%	Betaseron	1,693	Kogenate	1,239	1.3948
2008	48,428	15,747	YAZ/Yasmin	1,798	3.71%	3,903	8.06%	9.76%	30.03%	Betaseron	1,683	Kogenate	1,248	1.4712
2007	44,407	14,078	YAZ/Yasmin	1,429	3.22%	3,535	7.96%	8.92%	28.13%	Betaseron	1,410	Kogenate	1,122	1.3712
2006	36,391	9,398	Kogenate	999	2.72%	2,887	7.93%	6.83%	26.46%	Adalat	826	Betaseron	672	1.2568
2005	34,068	5,060	Ascensia	883	2.59%	2,346	6.89%	7.42%	49.96%	Kogenate	825	Adalat	820	1.2441
2004	37,012	5,458	Ciprobay	1,041	2.81%	2,621	7.09%	7.17%	48.63%	Adalat	833	Ascensia	780	1.2438
2003	32,349	5,373	Ciprobay	1,598	4.94%	2,734	8.45%	9.38%	56.48%	Adalat	765	Ascensia	672	1.1324
2002	28,034	4,511	Ciprobay	1,335	4.76%	2,439	8.70%	9.45%	58.74%	Adalat	757	Aspirin	557	0.9463
2001	27,122	4,286	Ciprobay	1,759	6.49%	2,293	8.45%	12.10%	76.55%	Adalat	873	Aspirin	648	0.8959
2000	28,592	5,668	Ciprobay	1,648	5.76%	2,209	7.73%	11.55%	58.24%	Adalat	1,066	Lipobay/Bajcol	587	0.9232
1999	29,108	5,327	Ciprobay	1,618	5.56%	2,399	8.24%	11.42%	62.40%	Adalat	1,088	Aspirin	618	1.0654
1998	31,213	4,828	Ciprobay	1,404	4.50%	2,229	7.14%	9.73%	62.92%	Adalat	1,045	Aspirin	589	1.0502
1997	31,282	4,774				2,205	7.05%	N/A					1,2594	
Average		223,665			4.41%		8.35%	9.92%	42.64%					
Max					9.42%		12.86%	18.00%	76.55%					
Min					2.59%		6.89%	6.83%	26.46%					

R&amp;D includes pharma and crop. Revenue lower % of revenue than others. Big Crop sciences segment

GlaxoSmithKline														
Year	Annual Revenue (\$ billions)	Annual Revenue (\$ billions) Pharmaceutical Division	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending (\$ billions)	R&D to Revenue	% of total Revenue from top 3 drugs	% of pharmaceutical Revenue from top 3 drugs	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)	Exchange rate average EUR-US\$
2017	38,906	28,917	Advair/Seretide	4,034	10.37 %	5,769	14.83 %	23.17 %	31.8 %	Triumeq	3,172	Triumeq	1,810	1.2889
2016	37,650	27,939	Advair/Seretide	4,705	12.50 %	4,898	13.01 %	22.13 %	29.83 %	Triumeq	2,342	Triumeq	1,287	1.35
2015	36,559	27,237	Advair/Seretide	5,625	15.39 %	5,440	14.88 %	21.50 %	28.86 %	Infanrix/Pediaris	1,120	Triumeq	1,116	1.5282
2014	37,319	30,773	Advair/Seretide	6,970	18.38 %	5,131	13.53 %	25.48 %	31.40 %	Infanrix/Pediaris	1,365	Avodart	1,327	1.6482
2013	41,464	33,349	Advair/Seretide	8,251	19.90 %	5,319	12.83 %	26.38 %	32.80 %	Infanrix/Pediaris	1,348	Avodart	1,341	1.5644
2012	41,899	33,798	Advair/Seretide	7,999	19.09 %	5,507	13.14 %	25.01 %	31.01 %	Avodart	1,252	Infanrix/Pediaris	1,229	1.5852
2011	43,915	35,585	Advair/Seretide	8,115	18.48 %	6,273	14.28 %	23.97 %	29.58 %	Flixotide	1,304	Infanrix/Pediaris	1,106	1.60351
2010	43,871	36,130	Advair/Seretide	7,941	18.10 %	6,125	13.96 %	25.13 %	30.51 %	Relenza	1,842	Flixotide	1,242	1.5452
2009	44,449	37,157	Advair/Seretide	7,798	17.54 %	6,434	14.47 %	25.22 %	30.17 %	Valtrex	2,028	Relenza	1,384	1.56686
2008	45,144	37,783	Advair/Seretide	7,669	16.99 %	6,824	15.12 %	25.70 %	30.71 %	Valtrex	2,215	Lamictal	1,717	1.85383
2007	45,480	38,507	Advair/Seretide	7,005	15.40 %	6,661	14.85 %	24.34 %	28.75 %	Lamictal	2,196	Valtrex	1,870	2.00211
2006	42,789	36,991	Advair/Seretide	6,104	14.26 %	6,969	14.88 %	24.58 %	28.43 %	Avandia	2,578	Lamictal	1,835	1.84239
2005	39,403	33,948	Advair/Seretide	5,463	13.86 %	5,705	14.48 %	23.11 %	26.83 %	Avandia	2,099	Lamictal	1,544	1.81917
2004	37,311	31,423	Advair/Seretide	4,510	12.09 %	5,203	13.94 %	22.79 %	27.06 %	Avandia	2,045	Seroquel/Paill	1,948	1.83265
2003	35,041	29,714	Advair/Seretide	3,618	10.33 %	4,561	13.02 %	23.53 %	27.74 %	Seroquel/Paill	3,068	Velbutrin	1,558	1.53432
2002	31,879	27,044	Seroquel/Paill	3,088	9.69 %	4,358	13.67 %	22.99 %	27.10 %	Advair/Seretide	2,451	Augmentin	1,790	1.50286
2001	29,504	24,775	Seroquel/Paill	2,674	9.06 %	3,679	12.47 %	20.46 %	24.37 %	Augmentin	2,046	Flixotide/Flovent	1,318	1.44001
2000	28,906	23,376	Seroquel/Paill	2,348	8.12 %	3,789	13.11 %	19.13 %	23.85 %	Augmentin	1,847	Flixotide/Flovent	1,333	1.51606
1999	26,151	22,032					14.14 %							1.61788
1998	24,754	20,819					13.87 %							1.65714
1997														
Average	752,997	617,297			14.42 %		13.91 %	23.59 %	28.89 %					
Max					19.90 %		15.12 %	26.38 %	32.80 %					
Min					8.12 %		12.47 %	19.13 %	23.85 %					

Johnson & Johnson													
Year	Annual Revenue (\$ billions)	Annual Revenue (\$ billions) Pharmaceutical Division	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending on pharmaceuticals (\$ billions)	R&D to Revenue	% of Revenue from top 3 drugs	% of pharmaceutical Revenue from top 3 drugs	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)
2017	75,450	36,256	Remicade	6,315	8.37%	8,360	23.06%	17.09%	35.57%	Stelara	4,011	Trevicta	2,569
2016	71,890	33,464	Remicade	6,966	9.69%	6,967	20.82%	17.33%	37.23%	Stelara	3,232	Zytiga	2,260
2015	70,074	31,430	Remicade	6,561	9.36%	6,821	21.70%	16.08%	35.84%	Stelara	2,474	Zytiga	2,231
2014	74,331	32,313	Remicade	6,868	9.24%	6,213	19.23%	15.35%	35.30%	Dlystio/Sovriad	2,302	Zytiga	2,237
2013	71,312	28,125	Remicade	6,673	9.36%	5,810	20.65%	14.06%	35.71%	Zytiga	1,698	Prezista	1,673
2012	67,224	25,351	Remicade	6,139	9.13%	5,362	21.15%	13.54%	35.90%	Velcade	1,500	Procrit/Eprex	1,462
2011	65,030	24,368	Remicade	5,492	8.45%	5,138	21.09%	13.36%	35.89%	Procrit/Eprex	1,623	Risperdal/Consta	1,583
2010	61,587	22,396	Remicade	4,610	7.49%	4,432	19.79%	13.06%	35.92%	Procrit/Eprex	1,934	Risperdal/Consta	1,500
2009	61,897	22,520	Remicade	4,304	6.95%	4,591	20.39%	13.08%	35.96%	Procrit/Eprex	2,245	Levaquin/Floxin	1,550
2008	63,747	24,567	Remicade	3,748	5.88%	5,095	20.74%	14.02%	36.39%	Topamax	2,731	Procrit/Eprex	2,453
2007	61,095	24,886	Remicade	3,327	5.45%	5,276	21.20%	14.18%	34.82%	Procrit/Eprex	2,885	Topamax	2,453
2006	53,324	23,267	Risperdal/Consta	4,183	7.84%	4,956	21.30%	19.46%	44.60%	Procrit/Eprex	3,180	Remicade	3,013
2005	50,514	22,322	Risperdal/Consta	3,552	7.03%	4,442	19.90%	18.63%	42.16%	Procrit/Eprex	3,324	Remicade	2,535
2004	47,348	22,128	Procrit/Eprex	3,589	7.58%	3,629	16.40%	18.55%	39.70%	Risperdal	3,050	Remicade	2,145
2003	41,862	19,517	Procrit/Eprex	3,984	9.52%	3,201	16.40%	19.65%	42.14%	Risperdal	2,512	Remicade	1,729
2002	36,298	17,151	Procrit/Eprex	4,269	11.76%	2,693	15.70%	21.25%	44.97%	Risperdal	2,146	Remicade	1,297
2001	32,317	14,849	Procrit/Eprex	3,426	10.60%								
2000	29,172	12,659											
1999	27,357	11,232											
1998	23,811												
1997	22,522												
Average		448,801			8.45%		19.97%	16.17%	37.99%				
Max					11.76%		23.06%	21.25%	44.97%				
Min					5.45%		15.70%	13.06%	34.82%				



Amgen											
Year	Annual Revenue (\$ billions)	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending (\$ billions)	R&D to Revenue	% of Revenue from top 3 drugs	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)
2017	22,849	Enbrel	5,433	23.78 %	3,562	15.59 %	52.61 %	Neulasta/Neupoc	4,534	Aranesp	2,053
2016	22,991	Enbrel	5,965	25.94 %	3,840	16.70 %	55.27 %	Neulasta/Neupoc	4,648	Aranesp	2,093
2015	21,662	Enbrel	5,364	24.76 %	4,070	18.79 %	55.54 %	Neulasta/Neupoc	4,715	Aranesp	1,951
2014	20,063	Neulasta/Neupogen	5,755	28.68 %	4,297	21.42 %	58.14 %	Enbrel	4,688	Xgeva	1,221
2013	18,676	Neulasta/Neupogen	5,790	31.00 %	4,063	21.86 %	65.60 %	Enbrel	4,551	Aranesp	1,911
2012	17,265	Neulasta/Neupogen	5,352	31.00 %	3,380	19.58 %	67.35 %	Enbrel	4,236	Aranesp	2,040
2011	15,295	Neulasta/Neupogen	5,212	34.08 %	3,167	20.71 %	73.33 %	Enbrel	3,701	Aranesp	2,303
2010	15,053	Neulasta/Neupogen	4,844	32.18 %	2,894	19.23 %	72.42 %	Enbrel	3,534	Epogen	2,524
2009	14,351	Neulasta/Neupogen	4,643	32.35 %	2,864	19.96 %	75.17 %	Enbrel	3,493	Aranesp	2,652
2008	15,003	Neulasta/Neupogen	4,659	31.05 %	3,030	20.20 %	75.94 %	Enbrel	3,598	Aranesp	3,137
2007	14,771	Neulasta/Neupogen	4,277	28.96 %	3,266	22.11 %	75.29 %	Aranesp	3,614	Enbrel	3,230
2006	14,268	Aranesp	4,121	28.88 %	3,366	23.59 %	73.98 %	Neulasta/Neupoc	3,923	Epogen	2,511
2005	12,430	Neulasta/Neupogen	3,504	28.19 %	2,314	18.62 %	75.22 %	Aranesp	3,273	Enbrel	2,573
2004	10,550	Epogen	2,601	24.65 %	2,028	19.22 %	66.10 %	Aranesp	2,473	Enbrel	1,900
2003	8,356	Neulasta/Neupogen	2,522	30.18 %	1,655	19.81 %	77.79 %	Epogen	2,435	Aranesp	1,544
2002	5,523	Epogen	2,261	40.93 %	1,117	20.22 %	81.83 %	Neulasta/Neupoc	1,843	Aranesp	0,416
2001	4,016	Epogen	2,005	49.93 %	0,865	21.54 %	93.77 %	Neupogen	1,346	Aranesp	0,416
2000	3,629	Epogen	1,963	54.09 %	0,845	23.28 %	91.81 %	Neupogen	1,224	Infergen	0,145
1999	3,340	Epogen	1,759	52.66 %	0,823	24.64 %	98.13 %	Neupogen	1,257	Infergen	0,262
1998	2,718	Epogen	1,382	50.85 %	0,663	24.39 %	99.37 %	Neupogen	1,161	Infergen	0,168
1997	2,401	Epogen	1,161	48.34 %	0,631	26.28 %	93.73 %	Neupogen	1,056	Infergen	0,034
Average	265,210			34.98 %		20.84 %	75.16 %				
Max				54.09 %		26.28 %	99.37 %				
Min				23.78 %		15.59 %	52.61 %				



## Bristol-Myers Squibb

Year	Annual Revenue (\$ billions)	Top-selling drug	Annual Revenue (\$ billions)	% of Revenue from top-selling drug	R&D Spending (\$ billions)	R&D to Revenue	% of Revenue from top 3 drugs	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)
2017	20,776	Opdivo	4,948	23.82 %	6,411	30.86 %	59.20 %	Eliquis	4,872	Orencia	2,479
2016	19,427	Opdivo	3,774	19.43 %	4,940	25.43 %	48.29 %	Eliquis	3,343	Orencia	2,285
2015	16,560	Orencia	1,885	11.38 %	5,920	35.75 %	32.40 %	Eliquis	1,860	Sprycel	1,620
2014	15,879	Abilify	2,020	12.72 %	5,434	34.22 %	32.53 %	Orencia	1,652	Sprycel	1,493
2013	15,879	Abilify	2,289	14.42 %	4,535	28.56 %	34.35 %	Sustiva	1,614	Regataz	1,551
2012	17,621	Abilify	2,827	16.04 %	3,904	22.16 %	39.16 %	Plavix	2,547	Sustiva	1,527
2011	21,244	Plavix	7,087	33.36 %	3,839	18.07 %	53.73 %	Abilify	2,758	Regataz	1,569
2010	19,484	Plavix	6,666	34.21 %	3,566	18.30 %	54.97 %	Abilify	2,565	Regataz	1,479
2009	18,808	Plavix	6,146	32.68 %	3,647	19.39 %	53.91 %	Abilify	2,592	Regataz	1,401
2008	20,597	Plavix	5,603	27.20 %	3,585	17.41 %	43.93 %	Abilify	2,153	Regataz	1,292
2007	19,348	Plavix	4,755	24.58 %	3,282	16.96 %	39.38 %	Abilify	1,660	Avapro/Avalide	1,204
2006	17,915	Plavix	3,257	18.18 %	3,067	17.12 %	32.02 %	Abilify	1,282	Pravachol	1,197
2005	19,207	Plavix	3,823	19.90 %	2,746	14.30 %	36.76 %	Pravachol	2,256	Avapro/Avalide	0,982
2004	19,380	Plavix	3,327	17.17 %	2,500	12.90 %	35.88 %	Pravachol	2,635	Taxol	0,991
2003	20,894	Pravachol	2,827	13.53 %	2,279	10.91 %	29.81 %	Plavix	2,467	Taxol	0,934
2002	18,119	Pravachol	2,266	12.51 %	2,218	12.24 %	27.72 %	Plavix	1,900	Taxol	0,857
2001	19,423	Pravachol	2,173	11.19 %	2,259	11.63 %	28.69 %	Glucophage	2,049	Plavix	1,350
2000	18,216	Pravachol	1,817	9.97 %	1,939	10.64 %	28.22 %	Glucophage	1,732	Taxol	1,532
1999	20,222	Pravachol	1,704	8.43 %	1,843	9.11 %	22.26 %	Taxol	1,481	Glucophage	1,317
1998	18,284	Pravachol	1,643	8.99 %	1,577	8.63 %	21.80 %	Taxol	1,481	Glucophage	0,862
1997	16,701	Pravachol	1,437	8.60 %	1,385	8.29 %	17.71 %	Taxol	0,941	Glucophage	0,579
Average	393,984			18.01 %		18.23 %	36.80 %				
Max				34.21 %		35.75 %	59.20 %				
Min				8.43 %		8.29 %	17.71 %				

Average R&D to revenue		
2017	25,59 %	22,53 %
2016	20,97 %	21,87 %
2015	25,90 %	22,49 %
2014	19,07 %	18,87 %
2013	26,25 %	17,69 %
2012	17,97 %	17,62 %
2011	17,51 %	16,98 %
2010	17,41 %	17,41 %
2009	17,28 %	23,47 %
2008	29,35 %	29,35 %
2007	23,47 %	17,28 %
2006	17,41 %	17,41 %
2005	16,98 %	17,51 %
2004	17,62 %	17,97 %
2003	17,69 %	26,25 %
2002	18,87 %	19,07 %
2001	22,49 %	25,90 %
2000	21,87 %	20,97 %
1999	22,53 %	25,59 %
max	29,35 %	
min	16,98 %	
Average R&D to revenue all years		26,15 %

## Revenue and R&amp;D 1999-2017

Year	Company	Total company rev.	R&D Expend	Top 3 drugs revenue	Company	Total company reven	R&D Expend	Top 3 drugs revenue
2017	Roche	41,837	10,553	21,146	Roche	39,679	10,047	21,174
	Pfizer	52,546	7,657	13,792	Pfizer	52,824	7,872	13,593
	Sanofi	28,387	6,138	8,773	Sanofi	32,371	5,725	9,645
	Bayer	19,037	5,089	7,123	Bayer	18,176	5,165	6,330
	GlaxoSmithKline	28,917	5,769	9,016	GlaxoSmithKline	27,939	8,898	8,333
	Johnson&Johnson	36,256	8,36	12,895	Johnson&Johnson	33,460	6,967	12,458
	Merck & Co.	35,39	10,208	12,013	Merck & Co.	35,151	10,124	11,983
	Novartis	43,085	9	7,199	Novartis	42,706	9,024	8,267
	AbbVie	28,216	4,982	21,829	AbbVie	25,638	4,366	19,432
	Eli Lilly	22,871	5,282	7,472	Eli Lilly	21,222	5,244	7,646
	Amgen	22,849	3,562	12,02	Amgen	22,991	3,840	12,706
	Gilead Sciences	26,107	3,734	11,554	Gilead Sciences	30,390	5,098	16,646
	Bristol Meyers Squibb	20,776	6,411	12,299	Bristol Meyers Squibb	19,427	4,940	9,382
Celgene	13,003	5,915	11,08	Celgene	11,229	4,470	9,302	
Astra Zeneca	22,485	5,757	7,12	Astra Zeneca	23,002	8,422	5,890	
		441,742	98,417	175,601		436,205	92,202	147,039
2018	Roche	38,074	9,340	20,702	Roche	37,433	9,004	19,507
	Pfizer	51,584	6,678	12,343	Pfizer	58,986	7,870	11,843
	Sanofi	36,203	6,337	12,322	Sanofi	37,123	6,329	14,668
	Bayer	14,884	4,238	4,237	Bayer	12,901	3,874	4,427
	GlaxoSmithKline	33,349	5,319	10,94	GlaxoSmithKline	33,798	5,507	10,480
	Johnson&Johnson	28,125	5,81	10,044	Johnson&Johnson	25,351	5,362	9,101
	Merck & Co.	37,437	7,503	8,933	Merck & Co.	40,601	8,168	7,909
	Novartis	57,92	9,846	10,6	Novartis	46,448	9,116	14,930
	AbbVie	18,79	2,855	12,656	AbbVie	18,012	2,778	11,515
	Eli Lilly	23,113	5,531	10,398	Eli Lilly	22,603	5,278	9,894
	Amgen	18,676	4,083	12,252	Amgen	17,265	3,380	11,628
	Gilead Sciences	11,202	2,12	7,743	Gilead Sciences	9,703	1,760	7,600
	Bristol Meyers Squibb	15,879	4,535	5,454	Bristol Meyers Squibb	17,621	3,904	6,901
Celgene	6,494	2,226	5,732	Celgene	5,507	1,724	5,017	
Astra Zeneca	25,711	4,821	12,977	Astra Zeneca	27,973	5,243	13,391	
		417,421	81,242	167,333		411,925	70,293	152,171
2019	Roche	37,993	9,620	17,123	Roche	33,016	8,121	16,019
	Pfizer	50,009	7,845	16,657	Pfizer	48,296	7,945	17,463
	Sanofi	36,018	6,392	12,186	Sanofi	36,348	6,731	11,471
	Bayer	14,599	3,830	4,714	Bayer	15,747	3,903	4,728
	GlaxoSmithKline	37,157	6,434	11,209	GlaxoSmithKline	37,783	6,824	11,601
	Johnson&Johnson	22,52	4,591	8,099	Johnson&Johnson	24,567	5,095	8,939
	Merck & Co.	25,237	5,845	10,152	Merck & Co.	23,260	4,805	9,448
	Novartis	44,2	7,469	11,426	Novartis	41,459	7,217	10,792
	AbbVie	16,496	17,07	5,5	AbbVie	16,708		4,500
	Eli Lilly	21,836	4,327	9,949	Eli Lilly	20,378	3,841	9,129
	Amgen	14,351	2,864	10,788	Amgen	15,003	3,030	11,394
	Gilead Sciences	7,011	0,94	5,539	Gilead Sciences	5,336	0,722	3,000
	Bristol Meyers Squibb	18,808	3,647	10,139	Bristol Meyers Squibb	20,597	3,565	9,048
Celgene	2,69	0,795	2,531	Celgene	2,255	0,931	2,036	
Astra Zeneca	32,804	4,409	14,327	Astra Zeneca	31,601	5,179	13,249	
		381,719	86,078	150,339		372,354	67,929	140,117

2015	2014	2010	2006	2007
Company	Company	Company	Company	Company
Roche	Roche	Roche	Roche	Roche
Pfizer	Pfizer	Pfizer	Pfizer	Pfizer
Sanofi	Sanofi	Sanofi	Sanofi	Sanofi
Bayer	Bayer	Bayer	Bayer	Bayer
GlaxoSmithKline	GlaxoSmithKline	GlaxoSmithKline	GlaxoSmithKline	GlaxoSmithKline
Johnson&Johnson	Johnson&Johnson	Johnson&Johnson	Johnson&Johnson	Johnson&Johnson
Merck & Co.	Merck & Co.	Merck & Co.	Merck & Co.	Merck & Co.
Novartis	Novartis	Novartis	Novartis	Novartis
AbbVie	AbbVie	AbbVie	AbbVie	AbbVie
Eli Lilly	Eli Lilly	Eli Lilly	Eli Lilly	Eli Lilly
Amgen	Amgen	Amgen	Amgen	Amgen
Gilead Sciences	Gilead Sciences	Gilead Sciences	Gilead Sciences	Gilead Sciences
Bristol Meyers Squibb	Bristol Meyers Squibb	Bristol Meyers Squibb	Bristol Meyers Squibb	Bristol Meyers Squibb
Celgene	Celgene	Celgene	Celgene	Celgene
Astra Zeneca	Astra Zeneca	Astra Zeneca	Astra Zeneca	Astra Zeneca
Total company re- R&D Expe Top 3 drugs revenue	Total company re- R&D Expe Top 3 drugs revenue	Total company re- R&D Expe Top 3 drugs revenue	Total company re- R&D Expe Top 3 drugs revenue	Total company re- R&D Expe Top 3 drugs revenue
36,675 21,014	36,675 21,014	36,525 18,433	29,439 11,584	38,675 21,014
9,643 7,630	9,643 7,630	8,991 16,963	6,711 17,966	8,393 13,482
5,639 1,138	5,639 1,138	6,639 1,233	6,221 9,69	6,408 13,157
4,742 7,861	4,742 7,861	4,083 10,525	3,535 11,072	4,747 9,662
5,143 11,266	5,143 11,266	5,138 8,698	6,661 8,665	5,131 11,070
6,821 8,540	6,821 8,540	8,467 11,470	5,276 10,779	6,213 11,070
8,900 9,494	8,900 9,494	9,239 12,374	4,883 10,779	7,180 8,953
4,285 16,477	4,285 16,477	2,618 10,474	6,430 3,000	3,237 14,347
4,796 7,646	4,796 7,646	5,021 11,245	4,877 8,456	4,730 7,868
12,030 22,589	12,030 22,589	3,167 6,838	1,229 8,638	4,237 11,664
3,014 5,365	3,014 5,365	2,818 10,474	3,839 4,299	2,854 17,093
5,320 7,752	5,320 7,752	1,245 16,879	1,600 12,939	5,434 11,070
3,697 10,907	3,697 10,907	5,523 16,879	5,523 16,879	2,431 6,508
416,535 171,543	416,535 171,543	87,399 171,543	80,999 166,603	26,095 12,968
Company	Company	Company	Company	Company
Roche	Roche	Roche	Roche	Roche
Pfizer	Pfizer	Pfizer	Pfizer	Pfizer
Sanofi	Sanofi	Sanofi	Sanofi	Sanofi
Bayer	Bayer	Bayer	Bayer	Bayer
GlaxoSmithKline	GlaxoSmithKline	GlaxoSmithKline	GlaxoSmithKline	GlaxoSmithKline
Johnson&Johnson	Johnson&Johnson	Johnson&Johnson	Johnson&Johnson	Johnson&Johnson
Merck & Co.	Merck & Co.	Merck & Co.	Merck & Co.	Merck & Co.
Novartis	Novartis	Novartis	Novartis	Novartis
AbbVie	AbbVie	AbbVie	AbbVie	AbbVie
Eli Lilly	Eli Lilly	Eli Lilly	Eli Lilly	Eli Lilly
Amgen	Amgen	Amgen	Amgen	Amgen
Gilead Sciences	Gilead Sciences	Gilead Sciences	Gilead Sciences	Gilead Sciences
Bristol Meyers Squibb	Bristol Meyers Squibb	Bristol Meyers Squibb	Bristol Meyers Squibb	Bristol Meyers Squibb
Celgene	Celgene	Celgene	Celgene	Celgene
Astra Zeneca	Astra Zeneca	Astra Zeneca	Astra Zeneca	Astra Zeneca
Total company re- R&D Expe Top 3 drugs revenue	Total company re- R&D Expe Top 3 drugs revenue	Total company re- R&D Expe Top 3 drugs revenue	Total company re- R&D Expe Top 3 drugs revenue	Total company re- R&D Expe Top 3 drugs revenue
36,501 17,479	36,501 17,479	67,809 8,413	24,887 4,325	39,801 9,667
8,413 17,070	8,413 17,070	6,03 11,9	7,559 18,862	8,393 13,482
6,03 11,9	6,03 11,9	6,03 11,9	5,967 8,408	6,408 13,157
4,404 11,025	4,404 11,025	4,404 11,025	2,887 2,487	4,747 9,662
4,320 8,044	4,320 8,044	4,320 8,044	6,369 10,516	5,131 11,070
10,981 10,086	10,981 10,086	10,981 10,086	4,956 10,376	6,213 11,070
8,080 11,851	8,080 11,851	8,080 11,851	4,783 10,541	7,180 8,953
2,495 9,066	2,495 9,066	2,495 9,066	5,349 8,129	3,237 14,347
4,884 10,694	4,884 10,694	4,884 10,694	3,129 7,088	4,730 7,868
2,894 10,902	2,894 10,902	2,894 10,902	10,555 3,366	4,237 11,664
3,566 6,309	3,566 6,309	3,566 6,309	3,026 2,089	4,237 11,664
1,128 3,393	1,128 3,393	1,128 3,393	3,067 5,736	2,854 17,093
5,318 15,962	5,318 15,962	5,318 15,962	1,406 1,295	2,431 6,508
410,906 147,18	410,906 147,18	79,036 147,18	5,162 12,039	26,095 12,968
Company	Company	Company	Company	Company
Roche	Roche	Roche	Roche	Roche
Pfizer	Pfizer	Pfizer	Pfizer	Pfizer
Sanofi	Sanofi	Sanofi	Sanofi	Sanofi
Bayer	Bayer	Bayer	Bayer	Bayer
GlaxoSmithKline	GlaxoSmithKline	GlaxoSmithKline	GlaxoSmithKline	GlaxoSmithKline
Johnson&Johnson	Johnson&Johnson	Johnson&Johnson	Johnson&Johnson	Johnson&Johnson
Merck & Co.	Merck & Co.	Merck & Co.	Merck & Co.	Merck & Co.
Novartis	Novartis	Novartis	Novartis	Novartis
AbbVie	AbbVie	AbbVie	AbbVie	AbbVie
Eli Lilly	Eli Lilly	Eli Lilly	Eli Lilly	Eli Lilly
Amgen	Amgen	Amgen	Amgen	Amgen
Gilead Sciences	Gilead Sciences	Gilead Sciences	Gilead Sciences	Gilead Sciences
Bristol Meyers Squibb	Bristol Meyers Squibb	Bristol Meyers Squibb	Bristol Meyers Squibb	Bristol Meyers Squibb
Celgene	Celgene	Celgene	Celgene	Celgene
Astra Zeneca	Astra Zeneca	Astra Zeneca	Astra Zeneca	Astra Zeneca
Total company re- R&D Expe Top 3 drugs revenue	Total company re- R&D Expe Top 3 drugs revenue	Total company re- R&D Expe Top 3 drugs revenue	Total company re- R&D Expe Top 3 drugs revenue	Total company re- R&D Expe Top 3 drugs revenue
29,439 11,584	29,439 11,584	29,439 11,584	29,439 11,584	39,801 9,667
8,089 17,966	8,089 17,966	8,089 17,966	8,089 17,966	8,393 13,482
6,221 9,69	6,221 9,69	6,221 9,69	6,221 9,69	6,408 13,157
3,535 11,072	3,535 11,072	3,535 11,072	3,535 11,072	4,747 9,662
6,661 8,665	6,661 8,665	6,661 8,665	6,661 8,665	5,131 11,070
4,883 10,779	4,883 10,779	4,883 10,779	4,883 10,779	6,213 11,070
6,430 3,000	6,430 3,000	6,430 3,000	6,430 3,000	7,180 8,953
4,877 8,456	4,877 8,456	4,877 8,456	4,877 8,456	3,237 14,347
3,266 11,121	3,266 11,121	3,266 11,121	3,266 11,121	4,730 7,868
0,591 3,105	0,591 3,105	0,591 3,105	0,591 3,105	4,237 11,664
7,619 3,282	7,619 3,282	7,619 3,282	7,619 3,282	2,854 17,093
0,399 1,295	0,399 1,295	0,399 1,295	0,399 1,295	2,431 6,508
5,162 12,039	5,162 12,039	5,162 12,039	5,162 12,039	26,095 12,968
356,301 113,789	356,301 113,789	64,843 113,789	64,843 113,789	416,535 171,543

2005	2004	2000
<b>Company</b>	<b>Company</b>	<b>Company</b>
<b>Total company rev</b>	<b>Total company rev</b>	<b>Total company rev</b>
<b>R&amp;D Expend</b>	<b>R&amp;D Expend</b>	<b>R&amp;D Expend</b>
<b>Top 3 drugs revenue</b>	<b>Top 3 drugs revenue</b>	<b>Top 3 drugs revenue</b>
<b>Roche</b>	<b>Roche</b>	<b>Roche</b>
<b>Pfizer</b>	<b>Pfizer</b>	<b>Pfizer</b>
<b>Sanofi</b>	<b>Sanofi</b>	<b>Sanofi</b>
<b>Bayer</b>	<b>Bayer</b>	<b>Bayer</b>
<b>GlaxoSmithKline</b>	<b>GlaxoSmithKline</b>	<b>GlaxoSmithKline</b>
<b>Johnson&amp;Johnson</b>	<b>Johnson&amp;Johnson</b>	<b>Johnson&amp;Johnson</b>
<b>Merck &amp; Co.</b>	<b>Merck &amp; Co.</b>	<b>Merck &amp; Co.</b>
<b>Novartis</b>	<b>Novartis</b>	<b>Novartis</b>
<b>Eli Lilly</b>	<b>Eli Lilly</b>	<b>Eli Lilly</b>
<b>Amgen</b>	<b>Amgen</b>	<b>Amgen</b>
<b>Gilead Sciences</b>	<b>Gilead Sciences</b>	<b>Gilead Sciences</b>
<b>Bristol Meyers Squibb</b>	<b>Bristol Meyers Squibb</b>	<b>Bristol Meyers Squibb</b>
<b>Celgene</b>	<b>Celgene</b>	<b>Celgene</b>
<b>Astra Zeneca</b>	<b>Astra Zeneca</b>	<b>Astra Zeneca</b>
<b>20,558</b>	<b>16,441</b>	<b>259,964</b>
<b>4,301</b>	<b>3,86</b>	<b>45,582</b>
<b>6,447</b>	<b>5,826</b>	<b>97,816</b>
<b>29,159</b>	<b>18,686</b>	
<b>7,189</b>	<b>6,343</b>	
<b>2,528</b>	<b>2,654</b>	
<b>9,107</b>	<b>8,504</b>	
<b>9,411</b>	<b>8,784</b>	
<b>10,610</b>	<b>11,181</b>	
<b>7,070</b>	<b>5,889</b>	
<b>6,734</b>	<b>6,736</b>	
<b>9,350</b>	<b>6,974</b>	
<b>1,567</b>	<b>1,062</b>	
<b>0,442</b>	<b>0,367</b>	
<b>9,129</b>	<b>7,857</b>	
<b>49,899</b>	<b>45,582</b>	
<b>115,804</b>	<b>97,816</b>	
<b>5,305</b>	<b>5,498</b>	
<b>1,219</b>	<b>1,218</b>	
<b>1,427</b>	<b>0,846</b>	
<b>12,394</b>	<b>10,533</b>	
<b>1,715</b>	<b>1,218</b>	
<b>3,281</b>	<b>3,301</b>	
<b>6,038</b>	<b>5,528</b>	
<b>14,849</b>	<b>12,659</b>	
<b>9,216</b>	<b>4,429</b>	
<b>1,636</b>	<b>1,247</b>	
<b>6,138</b>	<b>6,038</b>	
<b>3,766</b>	<b>3,332</b>	
<b>0,180</b>	<b>0,141</b>	
<b>5,572</b>	<b>5,141</b>	
<b>0,080</b>	<b>0,053</b>	
<b>7,556</b>	<b>8,182</b>	
<b>25,002</b>	<b>23,683</b>	
<b>58,999</b>	<b>48,742</b>	



	Top 3 drug revenue for 15 companies	Change from previous year	% of total for 15 companies	% of total in 15 companies	Total revenue 15 companies	Change from previous year	% of total industry revenue	Total global pharmaceutical revenue	Change from previous year	top 3	companies	market
1999	35,372		19.94 %	9.68 %	180,46		48.56 %	371.6				
2000	48,742	36.48 %	31.39 %	12.63 %	155,259	-13.96 %	40.22 %	386	3.88 %			
2001	58,999	21.04 %	35.99 %	15.12 %	163,911	5.67 %	42.01 %	390.2	1.09 %	2009	806 %	8.24 %
2002	73,411	24.43 %	40.24 %	17.17 %	182,447	11.31 %	42.67 %	427.6	9.58 %	2010	2.39 %	4.64 %
2003	86,494	17.82 %	37.95 %	17.37 %	230,351	26.26 %	46.26 %	498	16.46 %	2011	1.45 %	3.59 %
2004	97,816	13.09 %	37.63 %	17.47 %	259,964	12.86 %	46.43 %	569.9	12.43 %			
2005	115,804	18.39 %	40.41 %	19.26 %	286,54	10.22 %	47.66 %	601.2	7.38 %			
2006	108,794	-6.05 %	34.78 %	16.77 %	312,763	9.15 %	48.21 %	648.7	7.90 %			
2007	113,789	4.59 %	31.94 %	15.66 %	356,301	13.92 %	49.05 %	726.4	11.98 %			
2008	140,117	23.14 %	37.64 %	17.54 %	372,254	4.48 %	48.59 %	799	9.99 %			
2009	150,339	7.30 %	39.38 %	18.10 %	391,719	2.64 %	48.36 %	830.6	3.85 %			
2010	147.18	-2.10 %	35.05 %	16.57 %	413,906	10.00 %	47.28 %	888.2	6.93 %			
2011	166,603	13.20 %	38.64 %	17.30 %	431,157	4.47 %	48.44 %	963.2	8.44 %			
2012	162,171	-6.66 %	37.00 %	15.78 %	411,325	-4.60 %	42.65 %	964.4	0.12 %			
2013	157,333	3.39 %	37.69 %	15.83 %	417,421	1.48 %	42.00 %	993.8	3.05 %			
2014	167,642	6.55 %	40.62 %	15.76 %	412,704	-1.13 %	38.80 %	1063.6	7.02 %			
2015	171,549	2.33 %	41.18 %	15.99 %	416,535	0.93 %	38.82 %	1073.1	0.89 %			
2016	147,039	-14.29 %	33.71 %	13.18 %	436,205	4.72 %	39.10 %	1115.7	3.97 %			
2017	175,601	19.42 %	39.75 %	15.36 %	441,742	1.27 %	38.64 %	1143.3	2.47 %			
AVG		9.95 %				5.43 %			6.53 %			
Max		35.48 %				26.26 %			16.46 %			
Min		-14.29 %				-13.96 %			0.12 %			
	Total R&D spend 15 companies	% of total global R&D in pharma	Total global pharma R&D spend	Total US pharma R&D	% of total global spend all industries	Total R&D spend 15 companies	Change from previous year	Total global pharma R&D spend	Change from previous year	Total US pharma R&D spend	% of total global spend all industries	
1999	23,825	56.73 %	42	22.7	64.05 %	1999		23,825		42	22.7	
2000	23,683	52.63 %	45	26	67.78 %	2000		23,683	-0.60 %	45	26	
2001	25,002	49.02 %	51	29.8	68.43 %	2001		25,002	5.67 %	51	29.8	
2002	30,960	45.93 %	68	31	45.69 %	2002		30,960	23.89 %	68	31	
2003	39,403	50.52 %	78	34.5	44.23 %	2003		39,403	27.27 %	78	34.5	
2004	45,692	53.01 %	86	37	43.02 %	2004		45,692	15.71 %	86	37	
2005	49,899	52.08 %	94	39.9	42.45 %	2005		49,899	9.45 %	94	39.9	
2006	63,691	60.66 %	105	43	40.95 %	2006		63,691	27.64 %	105	43	
2007	64,843	56.42 %	117	47.9	40.94 %	2007		64,843	1.81 %	117	47.9	
2008	67,939	53.91 %	126	47.4	37.62 %	2008		67,939	4.76 %	126	47.4	
2009	86,078	69.42 %	124	46.4	37.42 %	2009		86,078	26.72 %	124	46.4	
2010	79,036	61.27 %	129	50.7	39.30 %	2010		79,036	-8.18 %	129	50.7	
2011	80,999	59.12 %	137	48.6	35.47 %	2011		80,999	2.48 %	137	48.6	
2012	70,293	51.69 %	136	49.6	36.47 %	2012		70,293	-13.22 %	136	49.6	
2013	81,242	58.87 %	138	51.6	37.39 %	2013		81,242	15.58 %	138	51.6	
2014	86,278	59.92 %	144	53.3	37.01 %	2014		86,278	6.20 %	144	53.3	
2015	87,359	59.63 %	149	59.6	40.00 %	2015		87,359	1.25 %	149	59.6	
2016	92,202	57.99 %	159	65.5	41.19 %	2016		92,202	5.54 %	159	65.5	
2017	98,417	59.65 %	165	71.4	43.27 %	2017		98,417	6.74 %	165	71.4	
AVG		56.16 %				AVG			8.81 %			
Max		69.42 %				Max			27.64 %			
Min		45.53 %				Min			-13.22 %			

Category overviews

Cancer				
Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling
1 Roche	Rituxan	85,983	Still no 1	17
2 Roche	Avastin	69,204	Still no 3	12
3 Roche	Herceptin	69,381	Still no 2	13
4 Pfizer	Ibrance	3,126	Still no 3	1
5 Novartis	Gleevec	51,112	Still no 3	15
6 Novartis	Zometa	5,372	3	5
7 Merck & Co.	Keytruda	3,809	Still no 2	1
8 AbbVie	Imbruvica	4,405	Still no 3	3
9 AbbVie	Lupron	1,655	Still no 3	2
10 Eli Lilly	Alimta	20,028	Still no 3	8
11 Eli Lilly	Gemzar	7,902	3	9
12 AstraZeneca	Zoladex	0,734	3	1
13 Celgene	Revlimid	43,731	Still no 1	12
14 Celgene	Pomalyst	4,587	Still no 2	4
15 Celgene	Vidaza	3,453	2	6
16 Celgene	Thalomid	3,314	3	13
17 Celgene	Abirakan	3,277	2	5
18 Celgene	Alkeran	0,208	2	5
19 Sanofi	Taxotere	4,816	3	6
20 Sanofi	Eloxatin	0,933	3	1
21 Johnson & Johnson	Zytiga	8,426	3	4
22 Johnson & Johnson	Velcade	1,500	2	1
23 Amgen	Neulasta	67,987	Still no 2	21
24 Amgen	Xgeva	1,221	3	1
25 Bristol-Myers Squibb	Opdivo	8,722	Still no 1	2
26 Bristol-Myers Squibb	Taxol	8,277	3	8
27 Bristol-Myers Squibb	Sprycel	3,113	3	2
Total revenue		486,942	For all	
Average		18,035		6,59
Max		85,983		21
Min		0,208		1

Antidepressants and antipsychotics				
Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling
1 Eli Lilly	Zyprexa	54,467	1	15
2 AstraZeneca	Seroquel	35,311	3	10
3 Johnson & Johnson	Risperdal	28,686	3	7
4 Johnson & Johnson	Trevicta/Invega	2,569	3	1
5 Bristol-Myers Squibb	Abilify	20,146	1	9
6 Eli Lilly	Cymbalta	26,890	1	8
7 Eli Lilly	Prozac	12,548	2	5
8 Pfizer	Zoloft	24,432	3	10
9 GlaxoSmithKline	Seroquel(EU)/P	13,127	3	5
10 GlaxoSmithKline	Welbutrin XL	1,558	3	1
Total revenue		219,734	For all	For no longer top
Average		21,973		7,10
Max		54,467		15,00
Min		1,558		1,00

Asthma				
Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling
1 Merck & Co.	Singulair	28,096	1	6
2 AstraZeneca	Symbicort	19,664	Still no 1	6
3 AstraZeneca	Pulmicort	2,827	3	5
4 GlaxoSmithKline	Advair(US)/Ser	98,260	Still no 1	16
5 GlaxoSmithKline	Flixotide/Flovent	5,197	2	3
Total revenue		154,044	For all	For no longer top
Average		30,809		7,20
Max		98,260		16,00
Min		2,827		3,00

Antivirals (including Antiretrovirals)				
Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling
Roche	Pegasys+Copegus	1,184	3	1
AbbVie	Viekira	3,161	3	2
GlaxoSmithKline	Relenza	3,225	2	2
Johnson & Johnson	Olysio/Sovriad	2,302	2	1
Gilead Sciences	Harvoni	27,315	Still no 1	3
Gilead Sciences	Sovaldi	19,560	2	3
Gilead Sciences	Eplusla	3,510	Still no 3	1
Gilead Sciences	Vistide	0,018	1	2
Amgen	Infergen	0,599	3	4
AbbVie	Kaletra	4,225	3	5
GlaxoSmithKline	Truimeq	6,63	Still no 2	3
GlaxoSmithKline	Valtrex	6,113	2	3
GlaxoSmithKline	Tivicay	3,096	Still no 3	2
Johnson & Johnson	Prezista	1,673	3	1
Gilead Sciences	Truvada	30,223	3	13
Gilead Sciences	Atripla	21,004	2	9
Gilead Sciences	Viread	8,237	3	13
Gilead Sciences	Genvoya	3,674	Still no 2	1
Bristol-Myers Squibb	Reyataz	7,292	3	6
Bristol-Myers Squibb	Sustiva	3,141	2	2
Total revenue		156,182	For all	
Average		7,8091		3,85
Max		30,223		13
Min		0,018		1

Blood medication (including medication for blood pressure, blo				
Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling
1 Roche	NeoRecormon	5,858	2	6
2 Johnson & Johnson	Procrit/Eprex	30,955	3	11
3 Amgen	Aranesp	33,995	Still no 3	17
4 Amgen	Epogen	20,601	3	16
5 Sanofi	Plavix	36,218	3	17
6 Bristol-Myers Squibb	Plavix	48,928	2	12
7 Bristol-Myers Squibb	Eliquis	10,075	Still no 2	3
8 Bayer	Kogenate	15,412	3	12
9 Bayer	Xarelto	12,957	Still no 1	5
10 Pfizer	Norvasc	39,944	2	11
11 Novartis	Diovan	54,579	2	13
12 Novartis	Lotrel	1,352	3	1
13 Novartis	Cibaocel/Loter	0,475	3	1
14 Merck & Co.	Cozaar/Hyzaar	19,379	2	6
15 AstraZeneca	Zestril	3,506	2	3
16 AstraZeneca	Seloken/Toprol	2,590	3	9
17 Sanofi	Aprovel	1,502	3	4
18 Bayer	Adalat	8,074	2	9
19 Bristol-Myers Squibb	Avapro	2,186	3	2
20 Sanofi	Lovenox	39,048	Still no 2	14
Total revenue		387,634	For all	
Average		19,382		8,60
Max		54,579		17,00
Min		0,475		1,00



Antibiotics and anti-inflammatories						Diabetes					
Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling		Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling	
Roche	Rocephin	2,937	3	5		AbbVie	AndroGel	3,121	2	3	
Pfizer	Zithromax	1,041	3	2		Eli Lilly	Dialis	9,236	Still no 2	4	
21,675	Bayer	10,404	1	7		Eli Lilly	Avid	0,945	3	2	
GlaxoSmithKline	Augmentin	5,683	3	3		Celgene	Focalin	0,111	3	5	
Johnson & Johnson	Levaquin/Floxin	1,55	3	1		Sanofi	Stillnow/Ambler	7,079	3	6	
Pfizer	Celebrex	7,162	3	3		Sanofi	Allegra	1,868	3	1	
Merck & Co.	Vioxx	8,925	3	3		Bayer	Aspirin	2,412	3	5	
Total revenue		37,762		For all		GlaxoSmithKline	Avodart	3,920	3	3	
Average		5,395				Roche	Accutane	1,279	3	3	
Max		10,404				Roche	Xenical	0,466	3	1	
Min		1,041				Total revenue		267,080		For all	
						Average		10,272		4,731	
						Max		61,702		16,000	
						Min		0,111		1,000	

Others					
Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling	
Pfizer	Lytica	40,960	Still no 2	10	
GlaxoSmithKline	Lamictal	7,292	3	4	
Johnson & Johnson	Topamax	5,184	2	2	
Pfizer	Plevinar 13	20,184	Still no 1	5	
Merck & Co.	Gardasil	4,481	Still no 3	2	
GlaxoSmithKline	Infanrix/Pediar	6,168	2	5	
Pfizer	Diflucan	0,881	3	1	
Novartis	Lamictil	1,766	3	3	
Galilead Sciences	AmBisome	1,251	3	7	
Bayer	Yaz/Yasmin	9,316	3	6	
Bayer	Mirena	2,960	Still no 3	2	
AstraZeneca	Mexium	61,702	Still no 3	16	
AstraZeneca	Losecr/Prilosec	33,736	3	8	
Novartis	Lucentis	14,700	3	7	
Bayer	Eylea	5,286	Still no 2	3	
Merck & Co.	Fosamax	21,376	3	9	

Immunosuppressants						Statins (cholesterol medication)					
Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling		Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling	
Roche	CellCept	0,246	2	1		Pfizer	Lipitor	129,180	2	14	
Pfizer	Enbrel	24,543	3	7		Merck & Co.	Zocor	27,661	1	6	
Amgen	Enbrel	52,266	Still no 1	14		Merck & Co.	Zetia	13,282	2	5	
Novartis	Gilenya	11,547	Still no 1	4		AbbVie	TriCor/Tripik	3,825	3	1	
Novartis	Neoral/Sandimmun	2,309	3	3		AstraZeneca	Crestor	53,406	Still no 2	12	
Novartis	Cosentyx	2,071	Still no 2	1		Bristol-Myers Squibb	Pravachol	19,955	3	10	
Merck & Co.	Remicade	12,100	3	5		Bayer	Lipobay/Baycol	0,587	3	1	
Johnson & Johnson	Remicade	71,722	Still no 1	16		Total revenue		247,896		For all	
Johnson & Johnson	Stelara	9,717	Still no 2	3		Average		35,414		7,000	
AbbVie	Humira	108,424	Still no 1	11		Max		129,180		14,000	
Celgene	Dorzol	2,296	Still no 3	2		Min		0,587		1,000	
Sanofi	Aubagio	1,771	Still no 3	1							
Bayer	Betaferon	11,556	2	8							
Bristol-Myers Squibb	Orencia	8,281	Still no 3	4							
Total revenue		318,849				Average revenue all pharmaceuticals				19,176	
Average		22,775		5,714							
Max		108,424		16,000							
Min		0,246		1,000							

Roche		Annual Revenue			Annual Revenue			Annual Revenue			Annual Revenue			Annual Revenue			Annual Revenue			
Year	Top-selling drug	Revenue (\$ billions)	Classification	Name of 2	Revenue (\$ billions)	Classification	Name of 3	Revenue (\$ billions)	Classification	Name of 3	Revenue (\$ billions)	Classification	Top 3 drugs through 20 years	Revenue (\$ billions)	Classification	Name of 3	Revenue (\$ billions)	Classification	Top 3 drugs through 20 years	
1,0155	2017	Rituxan	7,502	Cancer and Autoimmune disease	Herceptin	7,122	Cancer	Avastin	6,791	Cancer	Rituxan	Cancer (Blood, lymph nodes)	6,791	Cancer	Avastin	6,882	Cancer	Rituxan	Cancer (lung, kidney, ovarian, cervical cancer, glioblastoma/brain)	
1,0148	2016	Rituxan	7,408	Cancer and Autoimmune disease	Avastin	6,893	Cancer	Herceptin	6,882	Cancer	Avastin	Cancer (lung, kidney, ovarian, cervical cancer, glioblastoma/brain)	6,882	Cancer	Herceptin	6,779	Cancer	Herceptin	Cancer (breast)	
1,0369	2015	Rituxan	7,305	Cancer and Autoimmune disease	Avastin	6,930	Cancer	Herceptin	6,930	Cancer	Avastin	Cancer (breast)	6,930	Cancer	Herceptin	6,806	Cancer	Rituxan	Antibiotic	
1,0846	2014	Rituxan	7,484	Cancer and Autoimmune disease	Avastin	6,960	Cancer	Herceptin	6,960	Cancer	Avastin	Cancer (breast)	6,960	Cancer	Herceptin	6,526	Cancer	NeoRecormon/Epogri	Anemia	
1,0736	2013	Rituxan	7,462	Cancer and Autoimmune disease	Avastin	6,714	Cancer	Herceptin	6,714	Cancer	Avastin	Cancer (breast)	6,714	Cancer	Herceptin	6,124	Cancer	CellCept	Immunosuppressant (Lupus)	
1,0625	2012	Rituxan	7,126	Cancer and Autoimmune disease	Avastin	6,257	Cancer	Herceptin	6,257	Cancer	Avastin	Cancer (breast)	6,257	Cancer	Herceptin	5,851	Cancer	Pegasisy+Copegus	Antiviral (Hep C)	
1,1158	2011	Rituxan	6,698	Cancer and Autoimmune disease	Avastin	5,894	Cancer	Herceptin	5,894	Cancer	Avastin	Cancer (breast)	5,894	Cancer	Herceptin	5,201	Cancer	Accutane	Severe acne	
0,9743	2010	Avastin	6,190	Cancer	Rituxan	6,089	Cancer and Autoimmune disease	Herceptin	6,089	Cancer and Autoimmune disease	Herceptin	Cancer and Autoimmune disease	6,089	Cancer and Autoimmune disease	Herceptin	5,131	Cancer	Accutane	Severe acne	
0,9181	2009	Avastin	6,062	Cancer	Rituxan	5,930	Cancer and Autoimmune disease	Herceptin	5,930	Cancer and Autoimmune disease	Herceptin	Cancer and Autoimmune disease	5,930	Cancer and Autoimmune disease	Herceptin	4,989	Cancer	Accutane	Dietary	
0,8003	2007	Rituxan	5,875	Cancer and Autoimmune disease	Avastin	5,155	Cancer	Herceptin	5,155	Cancer	Avastin	Cancer	5,155	Cancer	Herceptin	3,286	Cancer	Herceptin		
0,7475	2006	Rituxan	4,415	Cancer and Autoimmune disease	Herceptin	3,883	Cancer	Avastin	3,883	Cancer	Avastin	Cancer	3,883	Cancer	Avastin	2,214	Cancer	Herceptin		
0,7539	2005	Rituxan	3,617	Cancer and Autoimmune disease	Herceptin	2,935	Cancer	Avastin	2,935	Cancer	Avastin	Cancer	2,935	Cancer	Avastin	1,618	Cancer	Herceptin		
0,7578	2004	Rituxan	3,132	Cancer and Autoimmune disease	NeoRecormon/Epogri	1,638	Anaemia	Herceptin	1,638	Anaemia	Herceptin	Cancer	1,638	Anaemia	Herceptin	1,184	Antiviral	Herceptin		
0,6556	2003	Rituxan	2,560	Cancer and Autoimmune disease	NeoRecormon/Epogri	2,082	Anaemia	Pegasisy+Copegus	2,082	Anaemia	Pegasisy+Copegus	Cancer	2,082	Anaemia	Pegasisy+Copegus	1,902	Antibiotic	Rituxan		
0,4456	2002	Rituxan	1,820	Cancer and Autoimmune disease	NeoRecormon/Epogri	1,345	Anaemia	Rituxan	1,345	Anaemia	Rituxan	Cancer	1,345	Anaemia	Rituxan	0,531	Anaemia	NeoRecormon/Epogri		
0,3131	2001	Rituxan	1,039	Cancer and Autoimmune disease	Rituxan	0,690	Antibiotic	NeoRecormon/Epogri	0,690	Antibiotic	NeoRecormon/Epogri	Cancer	0,690	Antibiotic	NeoRecormon/Epogri	0,365	Severe acne	Rituxan		
0,3103	2000	Accutane	0,398	Severe acne	Rituxan	0,531	Cancer and Autoimmune disease	Accutane	0,531	Cancer and Autoimmune disease	Accutane	Severe acne	0,531	Cancer and Autoimmune disease	Accutane	0,202	Anaemia	CellCept		
0,4962	1999	Rituxan	0,873	Antibiotic	CellCept	0,246	Immunosuppressant	NeoRecormon/Epogri	0,246	Immunosuppressant	NeoRecormon/Epogri	Anaemia	0,246	Anaemia	NeoRecormon/Epogri	0,486	Dietary	Accutane		

Pfizer																			
Year	Top-selling drug	Annual Revenue (\$ billions)	Classification	Name of 2	Revenue (\$ billions)	Classification	Name of 3	Revenue (\$ billions)	Classification	Name of 3	Revenue (\$ billions)	Classification	Top 3 drugs through 20 years	Revenue (\$ billions)	Classification	Name of 3	Revenue (\$ billions)	Classification	Top 3 drugs through 20 years
2017	Pevnar 13	5,601	Vaccine	Lyrica	5,085	Anticoagulant	Ibrance	3,126	Cancer	Ibrance	3,126	Cancer	Pevnar 13	3,126	Cancer	Ibrance	2,909	Autoimmune disease	Vaccine (pneumococcal bacteria)
2016	Pevnar 13	5,718	Vaccine	Lyrica	4,966	Anticoagulant	Enbrel	2,909	Autoimmune disease	Enbrel	2,909	Autoimmune disease	Lipitor	2,909	Autoimmune disease	Enbrel	2,909	Autoimmune disease	Statin (cholesterol)
2015	Pevnar 13	6,145	Vaccine	Lyrica	4,839	Anticoagulant	Enbrel	3,333	Autoimmune disease	Enbrel	3,333	Autoimmune disease	Norvasc	3,333	Autoimmune disease	Enbrel	3,333	Autoimmune disease	Blood pressure
2014	Lyrica	5,168	Anticoagulant	Pevnar 13	4,484	Vaccine	Enbrel	3,850	Autoimmune disease	Enbrel	3,850	Autoimmune disease	Enbrel	3,850	Autoimmune disease	Enbrel	3,850	Autoimmune disease	Immunosuppressant (e.g. rheumatoid arthritis)
2013	Lyrica	4,595	Anticoagulant	Pevnar 13	3,974	Vaccine	Enbrel	3,774	Autoimmune disease	Enbrel	3,774	Autoimmune disease	Ibrance	3,774	Autoimmune disease	Enbrel	3,774	Autoimmune disease	Cancer (breast)
2012	Lyrica	4,158	Anticoagulant	Lipitor	3,948	Statin	Enbrel	3,737	Autoimmune disease	Enbrel	3,737	Autoimmune disease	Celebrex	3,737	Autoimmune disease	Enbrel	3,737	Autoimmune disease	Anti-inflammatory
2011	Lipitor	9,577	Statin	Lyrica	3,693	Anticoagulant	Enbrel	3,666	Autoimmune disease	Enbrel	3,666	Autoimmune disease	Zolof	3,666	Autoimmune disease	Enbrel	3,666	Autoimmune disease	Antidepressant
2010	Lipitor	10,733	Statin	Enbrel	3,274	Autoimmune disease	Lyrica	3,063	Anticoagulant	Lyrica	3,063	Anticoagulant	Lyrica	3,063	Anticoagulant	Lyrica	3,063	Anticoagulant	Anticoagulant (seizures)
2009	Lipitor	11,434	Statin	Lyrica	2,840	Anticoagulant	Celebrex	2,383	Anti-inflammatory	Celebrex	2,383	Anti-inflammatory	Zithromax	2,383	Anti-inflammatory	Celebrex	2,383	Anti-inflammatory	Antibiotic
2008	Lipitor	12,401	Statin	Lyrica	2,573	Anticoagulant	Celebrex	2,489	Anti-inflammatory	Celebrex	2,489	Anti-inflammatory	Diflucan	2,489	Anti-inflammatory	Celebrex	2,489	Anti-inflammatory	Antifungal
2007	Lipitor	12,675	Statin	Norvasc	3,001	Blood pressure	Celebrex	2,290	Anti-inflammatory	Celebrex	2,290	Anti-inflammatory		2,290	Anti-inflammatory	Celebrex	2,290	Anti-inflammatory	
2006	Lipitor	12,886	Statin	Norvasc	4,866	Blood pressure	Zoloft	2,110	Antidepressant	Zoloft	2,110	Antidepressant		2,110	Antidepressant	Zoloft	2,110	Antidepressant	
2005	Lipitor	12,187	Statin	Norvasc	4,706	Blood pressure	Zoloft	3,256	Antidepressant	Zoloft	3,256	Antidepressant		3,256	Antidepressant	Zoloft	3,256	Antidepressant	
2004	Lipitor	10,862	Statin	Norvasc	4,403	Blood pressure	Zoloft	3,361	Antidepressant	Zoloft	3,361	Antidepressant		3,361	Antidepressant	Zoloft	3,361	Antidepressant	
2003	Lipitor	9,231	Statin	Norvasc	4,336	Blood pressure	Zoloft	3,118	Antidepressant	Zoloft	3,118	Antidepressant		3,118	Antidepressant	Zoloft	3,118	Antidepressant	
2002	Lipitor	7,972	Statin	Norvasc	3,846	Blood pressure	Zoloft	2,742	Antidepressant	Zoloft	2,742	Antidepressant		2,742	Antidepressant	Zoloft	2,742	Antidepressant	
2001	Lipitor	6,448	Statin	Norvasc	3,581	Blood pressure	Zoloft	2,365	Antidepressant	Zoloft	2,365	Antidepressant		2,365	Antidepressant	Zoloft	2,365	Antidepressant	
1999	Lipitor	5,031	Statin	Norvasc	3,362	Blood pressure	Zoloft	2,140	Antidepressant	Zoloft	2,140	Antidepressant		2,140	Antidepressant	Zoloft	2,140	Antidepressant	
1998	Norvasc	2,575	Blood pressure	Norvasc	2,991	Blood pressure	Zoloft	1,937	Antidepressant	Zoloft	1,937	Antidepressant		1,937	Antidepressant	Zoloft	1,937	Antidepressant	
1997	Norvasc	2,217	Blood pressure	Zoloft	1,836	Antidepressant	Zithromax	1,041	Antibiotic	Zithromax	1,041	Antibiotic		1,041	Antibiotic	Zithromax	1,041	Antibiotic	
				Zoloft	1,507	Antidepressant	Diflucan	0,881	Antifungal	Diflucan	0,881	Antifungal		0,881	Antifungal	Diflucan	0,881	Antifungal	

Novartis																																																		
Year	Top-selling drug	Annual Revenue e(\$ billions)	Classification	Name of 2	Revenue e(\$ billions)	Classification																																												
2017	Gilenya	3,185	Immunosuppressant	Cosentyx	2,071	Immunosuppressant																																												
2016	Gleevec	3,323	Cancer	Gilenya	3,103	Immunosuppressant																																												
2015	Gleevec	4,658	Cancer	Gilenya	2,776	Immunosuppressant																																												
2014	Gleevec	4,746	Cancer	Gilenya	2,477	Immunosuppressant																																												
2013	Gleevec	4,633	Cancer	Diovan	3,524	Blood pressure																																												
2012	Gleevec	4,675	Cancer	Diovan	4,417	Blood pressure																																												
2011	Diovan	5,665	Blood pressure	Gleevec	4,659	Cancer																																												
2010	Diovan	6,053	Blood pressure	Gleevec	4,265	Cancer																																												
2009	Diovan	6,013	Blood pressure	Gleevec	3,944	Cancer																																												
2008	Diovan	5,740	Blood pressure	Gleevec	3,670	Cancer																																												
2007	Diovan	5,012	Blood pressure	Gleevec	3,050	Cancer																																												
2006	Diovan	4,223	Blood pressure	Gleevec	2,554	Cancer																																												
2005	Diovan	3,676	Blood pressure	Gleevec	2,170	Cancer																																												
2004	Diovan	3,033	Blood pressure	Gleevec	1,634	Cancer																																												
2003	Diovan	2,425	Blood pressure	Gleevec	1,128	Cancer																																												
2002	Diovan	1,150	Blood pressure	Neoral/Sandimmun	0,716	Immunosuppressant																																												
2001	Diovan	0,589	Blood pressure	Neoral/Sandimmun	0,573	Immunosuppressant																																												
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Merck and Co.																																																						
Year	Top-selling drug	Annual Revenue e(\$ billions)	Classification	Name of 2	Revenue e(\$ billions)	Classification																																																
2017	Januvia	5,896	Diabetes	Keytruda	3,809	Cancer																																																
2016	Januvia	6,108	Diabetes	Zetia/Vytorin	3,701	Statin																																																
2015	Januvia	3,663	Diabetes	Zetia	2,526	Statin																																																
2014	Januvia	3,931	Diabetes	Janumet	2,850	Statin																																																
2013	Januvia	4,004	Diabetes	Remicade	2,658	Statin																																																
2012	Januvia	4,066	Diabetes	Zetia	2,076	Autoimmune disease																																																
2011	Singulair	5,479	Asthma and allergies	Remicade	3,324	Diabetes																																																
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2008	Singulair	4,337	Asthma and allergies	Cozaar/Hyzaar	3,558	Blood pressure																																																
2007	Singulair	4,266	Asthma and allergies	Cozaar/Hyzaar	3,350	Blood pressure																																																
2006	Singulair	4,358	Asthma and allergies	Cozaar/Hyzaar	3,049	Blood pressure																																																
2005	Zocor	4,362	Statin	Fosamax	3,191	Osteoporosis																																																
2004	Zocor	5,197	Statin	Cozaar/Hyzaar	3,160	Osteoporosis																																																
2003	Zocor	5,011	Statin	Fosamax	2,677	Osteoporosis																																																
2002	Zocor	5,600	Statin	Vioxx	2,500	Anti-inflammatory																																																
2001	Zocor	5,264	Statin	Vioxx	2,358	Anti-inflammatory																																																
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AbbVie						
Year	Top-selling drug	Annual Revenue (\$ billions)	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)
2017	Humira	18,427	Autoimmune disease	2,573	Cancer	0,823
2016	Humira	16,078	Autoimmune disease	1,832	Cancer	1,522
2015	Humira	14,012	Autoimmune disease	1,639	Antiviral	0,826
2014	Humira	12,543	Autoimmune disease	0,934	Androgen	0,870
2013	Humira	10,659	Autoimmune disease	1,035	Androgen	0,962
2012	Humira	9,265	Autoimmune disease	1,152	Androgen	1,098
2011	Humira	7,332	Autoimmune disease	1,372	Statin	1,170
2010	Humira	6,508	Autoimmune disease	1,355	Statin	1,223
2009	Humira	5,500	Autoimmune disease			
2008	Humira	4,500	Autoimmune disease			
2007	Humira	3,000	Autoimmune disease			

Top 3 drugs through 20 years	
Humira	Immunosuppressant (e.g. rheumatoid arthritis)
Imbruvica	Cancer (blood)
Viekira	Antiviral (Hep C)
Kaletra	Antiretroviral (HIV)
AndroGel	Androgen (testosterone)
TriCor/Tripix	Statin (cholesterol)
Lupron	Cancer (prostate)

Eli Lilly & Co.						
Year	Top-selling drug	Annual Revenue (\$ billions)	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)
2017	Humalog	2,865	Diabetes	2,323	Erectile dysfunction	2,283
2016	Humalog	2,842	Diabetes	2,493	Cancer	2,311
2015	Humalog	2,842	Diabetes	2,493	Cancer	2,311
2014	Almita	2,792	Cancer	2,785	Diabetes	2,291
2013	Cymbalta	5,084	Anti-depressant	2,703	Cancer	2,611
2012	Cymbalta	4,994	Anti-depressant	2,594	Cancer	2,306
2011	Zyprexa	4,622	Atypical antipsychotic	4,162	Anti-depressant	2,461
2010	Zyprexa	5,026	Atypical antipsychotic	3,459	Anti-depressant	2,209
2009	Zyprexa	4,916	Atypical antipsychotic	3,075	Anti-depressant	1,959
2008	Zyprexa	4,696	Atypical antipsychotic	2,697	Anti-depressant	1,736
2007	Zyprexa	4,761	Atypical antipsychotic	2,103	Anti-depressant	1,592
2006	Zyprexa	4,364	Atypical antipsychotic	1,408	Cancer	1,316
2005	Zyprexa	4,202	Atypical antipsychotic	1,335	Cancer	1,198
2004	Zyprexa	4,420	Atypical antipsychotic	1,214	Cancer	1,102
2003	Zyprexa	4,277	Atypical antipsychotic	1,060	Diabetes	1,022
2002	Zyprexa	3,689	Atypical antipsychotic	1,004	Diabetes	0,875
2001	Zyprexa	3,687	Atypical antipsychotic	1,990	Anti-depressant	1,061
2000	Prozac	2,574	Anti-depressant	2,350	Atypical antipsychotic	1,115
1999	Prozac	2,613	Anti-depressant	1,865	Atypical antipsychotic	0,456
1998	Prozac	2,812	Anti-depressant	1,443	Atypical antipsychotic	0,418
1997	Prozac	2,559	Anti-depressant	0,730	Atypical antipsychotic	0,527

Top 3 drugs through 20 years	
Gemzar	Cancer (breast, lung, ovarian, pancreatic)
Almita	Cancer (lung)
Cymbalta	Anti-depressant
Zyprexa	Atypical antipsychotic (schizophrenia, bipolar disorder)
Prozac	Anti-depressant
Cialis	Erectile dysfunction
Humalog	Diabetes
Humulin	Diabetes
Axid	H2 blocker (ulcers)

Astra Zeneca									
Year	Top-selling drug	Annual Revenue e (\$ billions)	Name of 1	Revenue e (\$ billions)	Name of 2	Revenue e (\$ billions)	Name of 3	Revenue e (\$ billions)	Top 3 drugs through 20 years
2017	Symbicort	2,803	Asthma (Corticosteroid)	2,365	Statin	2,969	Nexium	1,952	Symbicort Pulmicort Nexium
2016	Crestor	3,401	Statin	2,589	Asthma	3,394	Nexium	2,032	Asthma (Corticosteroid) Asthma (Corticosteroid)
2015	Crestor	5,017	Statin	3,801	Asthma	3,801	Nexium	2,496	Proton pump inhibitors (lansacid) Proton pump inhibitors (lansacid)
2014	Crestor	5,512	Statin	3,872	Proton pump inhibitors	3,944	Symbicort	3,655	Proton pump inhibitors (lansacid) Statin (cholesterol)
2013	Crestor	5,622	Statin	5,828	Atypical antipsychotic	5,302	Nexium	3,184	Seroquel Zestril
2012	Crestor	6,253	Statin	5,828	Atypical antipsychotic	4,866	Nexium	4,423	Atypical antipsychotic (schizophrenia, bipolar disorder) Blood pressure
2011	Crestor	6,622	Statin	5,302	Atypical antipsychotic	4,452	Nexium	4,303	Seroquel/Toprol-XL Blood pressure
2010	Crestor	5,891	Statin	4,027	Atypical antipsychotic	4,502	Nexium	4,502	Seroquel/Toprol-XL Blood pressure
2009	Nexium	4,959	Proton pump inhibitors	3,416	Atypical antipsychotic	4,027	Crestor	3,597	Cancer (Breast and prostate)
2008	Nexium	5,200	Proton pump inhibitors	2,761	Atypical antipsychotic	3,416	Crestor	2,766	
2007	Nexium	5,216	Proton pump inhibitors	2,761	Atypical antipsychotic	3,416	Crestor	2,028	
2006	Nexium	5,182	Proton pump inhibitors	2,761	Atypical antipsychotic	3,416	Crestor	2,028	
2005	Nexium	4,633	Proton pump inhibitors	2,761	Atypical antipsychotic	3,416	Crestor	2,028	
2004	Nexium	3,683	Proton pump inhibitors	2,761	Atypical antipsychotic	3,416	Crestor	2,028	
2003	Nexium	3,302	Proton pump inhibitors	2,761	Atypical antipsychotic	3,416	Crestor	2,028	
2002	Losec/Prilosec	4,623	Proton pump inhibitors	2,585	Proton pump inhibitors	1,947	Proton pump inhibitors	1,397	
2001	Losec/Prilosec	5,684	Proton pump inhibitors	1,978	Proton pump inhibitors	1,487	Atypical antipsychotic	1,487	
2000	Losec/Prilosec	6,260	Proton pump inhibitors	1,037	Blood pressure	0,775	Asthma	0,775	
1999	Losec/Prilosec	5,303	Proton pump inhibitors	1,188	Blood pressure	0,734	Cancer	0,734	
1998	Losec/Prilosec	4,015	Proton pump inhibitors	1,221	Blood pressure	0,730	Asthma	0,730	
1997	Losec/Prilosec	2,733	Proton pump inhibitors	0,637	Asthma	0,453	Blood pressure	0,453	
				0,625	Asthma	0,402	Blood pressure	0,402	

Celgene									
Year	Top-selling drug	Annual Revenue e (\$ billions)	Name of 1	Revenue e (\$ billions)	Name of 2	Revenue e (\$ billions)	Name of 3	Revenue e (\$ billions)	Top 3 drugs through 20 years
2017	Revlimid	8,167	Cancer	1,614	Cancer	1,279	Immunosuppressant	1,279	Revlimid Thalomid Pomalyst
2016	Revlimid	6,374	Cancer	1,311	Cancer	1,017	Immunosuppressant	1,017	Cancer (bone marrow, mantle cell lymphoma-MCL) Cancer (bone marrow)
2015	Revlimid	5,801	Cancer	0,983	Cancer	0,968	Cancer	0,968	Cancer (bone marrow, who has already received 2 other drugs) Cancer (bone marrow)
2014	Revlimid	4,980	Cancer	0,848	Cancer	0,680	Cancer	0,680	Cancer (blood, bone marrow) Cancer (Breast, pancreas, lungs)
2013	Revlimid	4,280	Cancer	0,803	Cancer	0,649	Cancer	0,649	Cancer (Bone marrow, breast, ovarian, neurosarcoma) ADHD
2012	Revlimid	3,767	Cancer	0,823	Cancer	0,427	Cancer	0,427	ADHD Immunosuppressant (psoriasis, psoriatic arthritis)
2011	Revlimid	3,208	Cancer	0,705	Cancer	0,390	Cancer	0,390	
2010	Revlimid	2,469	Cancer	0,534	Cancer	0,367	Cancer	0,367	
2009	Revlimid	1,706	Cancer	0,437	Cancer	0,207	Cancer	0,207	
2008	Revlimid	1,325	Cancer	0,505	Cancer	0,074	Cancer	0,074	
2007	Revlimid	0,774	Cancer	0,447	Cancer	0,050	Cancer	0,050	
2006	Thalomid	0,433	Cancer	0,321	Cancer	0,004	ADHD	0,004	
2005	Thalomid	0,368	Cancer	0,050	Cancer	0,042	ADHD	0,042	
2004	Thalomid	0,303	Cancer	0,017	Cancer	0,018	Cancer	0,018	
2003	Thalomid	0,224	Cancer	0,039	ADHD	0,039	ADHD	0,039	
2002	Thalomid	0,012	Cancer	0,002	ADHD	0,002	ADHD	0,002	
2001	Thalomid	0,062	Cancer						
2000	Thalomid	0,062	Cancer						
1999	Thalomid	0,024	Cancer						
1998	Thalomid	0,003	Cancer						

Sanofi									
Year	Top-selling drug	Annual Revenue (\$ billions)	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)	Top 3 drugs through 20 years	Indications	
2017	Lantus	5,223	Diabetes	1,760	Blood thinner	1,771	Immunosuppressant	Diabetes	
2016	Lantus	6,325	Diabetes	1,811	Blood thinner	1,703	Anticoagulant	Blood thinner	
2015	Lantus	7,090	Diabetes	2,140	Anticoagulant	1,907	Blood thinner	Blood pressure	
2014	Lantus	8,427	Diabetes	2,473	Anticoagulant	2,257	Blood thinner	Anticoagulant (prevents clotting, increased blood flow)	
2013	Lantus	7,593	Diabetes	2,467	Anticoagulant	2,263	Blood thinner	Insomnia	
2012	Lantus	6,378	Diabetes	2,657	Anticoagulant	2,434	Blood thinner	Immunosuppressant (Multiple sclerosis)	
2011	Lantus	5,453	Diabetes	2,940	Blood thinner	2,841	Anticoagulant	Cancer (breast, lung, prostate, stomach, head/neck)	
2010	Lantus	4,655	Diabetes	3,721	Blood thinner	2,814	Cancer	Cancer (colon, rectum)	
2009	Lantus	4,296	Diabetes	4,232	Blood thinner	3,659	Anticoagulant	Antihistamine (allergies)	
2008	Lovenox	4,028	Blood thinner	3,838	Anticoagulant	3,604	Diabetes		
2007	Lovenox	3,562	Blood thinner	3,324	Anticoagulant	2,765	Diabetes		
2006	Lovenox	3,060	Blood thinner	2,801	Anticoagulant	2,546	Insomnia		
2005	Lovenox	2,666	Blood thinner	2,521	Anticoagulant	2,002	Cancer		
2004	Lovenox	2,368	Blood thinner	2,107	Anticoagulant	1,868	Antihistamine		
2003	Silnox/Ambien	1,523	Insomnia	1,500	Anticoagulant	0,933	Cancer		
2002	Silnox/Ambien	1,348	Insomnia	0,934	Anticoagulant	0,532	Blood pressure		
2001	Silnox/Ambien	0,704	Insomnia	0,632	Anticoagulant	0,379	Blood pressure		
2000	Silnox/Ambien	0,537	Insomnia	0,403	Anticoagulant	0,277	Blood pressure		
1999	Silnox/Ambien	0,421	Insomnia	0,314	Blood pressure	0,212	Anticoagulant		

Bayer									
Year	Top-selling drug	Annual Revenue (\$ billions)	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)	Top 3 drugs through 20 years	Indications	
2017	Xarelto	3,727	Anticoagulant	2,124	Eye disease	1,272	Contraceptive	Anticoagulant (prevents clotting)	
2016	Xarelto	3,241	Anticoagulant	1,739	Eye disease	1,291	Blood clots	Blood clots (aid blood clots, stop bleedings)	
2015	Xarelto	2,499	Anticoagulant	1,363	Eye disease	1,282	Blood clots	Blood pressure	
2014	Xarelto	2,230	Anticoagulant	1,473	Blood clots	1,068	Contraceptive	Immunosuppressant (Multiple sclerosis)	
2013	Kogenate	1,597	Blood clots	1,379	Immunosuppressant	1,261	Anticoagulant	Antibiotic	
2012	Betaferon	1,564	Immunosuppressant	1,520	Blood clots	1,344	Contraceptive	Contraceptive	
2011	Betaferon	1,555	Immunosuppressant	1,497	Blood clots	1,490	Contraceptive	Diabetes	
2010	Betaferon	1,599	Immunosuppressant	1,473	Contraceptive	1,331	Blood clots	Eye disease	
2009	YAZ/Yasmin	1,763	Contraceptive	1,633	Immunosuppressant	1,239	Blood clots	Pain relief	
2008	YAZ/Yasmin	1,798	Contraceptive	1,663	Immunosuppressant	1,248	Blood clots	Statin (cholesterol)	
2007	YAZ/Yasmin	1,429	Contraceptive	1,410	Immunosuppressant	1,122	Blood clots		
2006	Kogenate	0,989	Blood clots	0,826	Blood pressure	0,672	Immunosuppressant		
2005	Ascensia	0,863	Diabetes	0,625	Blood clots	0,620	Blood pressure		
2004	Ciprobay	1,041	Antibiotic	0,833	Blood pressure	0,760	Diabetes		
2003	Ciprobay	1,598	Antibiotic	0,765	Blood pressure	0,672	Diabetes		
2002	Ciprobay	1,335	Antibiotic	0,757	Blood pressure	0,557	Pain relief		
2001	Ciprobay	1,759	Antibiotic	0,873	Blood pressure	0,648	Pain relief		
2000	Ciprobay	1,648	Antibiotic	1,066	Blood pressure	0,587	Statin		
1999	Ciprobay	1,618	Antibiotic	1,068	Blood pressure	0,618	Pain relief		
1998	Ciprobay	1,404	Antibiotic	1,045	Blood pressure	0,569	Pain relief		

GlaxoSmithKline						
Year	Top-selling drug	Annual Revenue e (\$ billions)	Name of 2	Revenue (\$ billions)	Name of 3	Revenue e (\$ billions)
2017	Advair/Serotide	4,034 Asthma	Triumeq	3,172 Antiretroviral	Twicay	1,810 Antiretroviral
2016	Advair/Serotide	4,705 Asthma	Triumeq	2,342 Antiretroviral	Twicay	1,237 Antiretroviral
2015	Advair/Serotide	5,625 Asthma	Infanxyl/Pedialix	1,120 Vaccine	Triumeq	1,116 Antiretroviral
2014	Advair/Serotide	6,370 Asthma	Infanxyl/Pedialix	1,365 Vaccine	Avodart	1,327 Benign prostatic hyperplasia
2013	Advair/Serotide	8,251 Asthma	Infanxyl/Pedialix	1,348 Vaccine	Avodart	1,341 Benign prostatic hyperplasia
2012	Advair/Serotide	7,999 Asthma	Avodart	1,252 Benign prostatic hyperplasia	Infanxyl/Pedialix	1,229 Vaccine
2011	Advair/Serotide	8,115 Asthma	Flixotide	1,304 Asthma	Infanxyl/Pedialix	1,106 Vaccine
2010	Advair/Serotide	7,341 Asthma	Relenza	1,842 Antiviral	Flixotide	1,242 Asthma
2009	Advair/Serotide	7,798 Asthma	Valtrex	2,028 Antiretroviral	Relenza	1,384 Antiviral
2008	Advair/Serotide	7,669 Asthma	Valtrex	2,275 Antiretroviral	Lamictal	1,717 Anticonvulsant
2007	Advair/Serotide	7,005 Asthma	Lamictal	2,196 Anticonvulsant	Valtrex	1,870 Antiretroviral
2006	Advair/Serotide	6,104 Asthma	Avandia	2,578 Diabetes	Lamictal	1,835 Anticonvulsant
2005	Advair/Serotide	5,463 Asthma	Avandia	2,099 Diabetes	Lamictal	1,544 Anticonvulsant
2004	Advair/Serotide	4,510 Asthma	Avandia	2,045 Diabetes	Seroxat/Paxil	1,948 Antidepressant
2003	Advair/Serotide	3,618 Asthma	Seroxat/Paxil	3,068 Antidepressant	Valbutrin	1,558 Antidepressant
2002	Seroxat/Paxil	3,068 Antidepressant	Advair/Serotide	2,451 Asthma	Augmentin	1,730 Antibiotic
2001	Seroxat/Paxil	2,674 Antidepressant	Augmentin	2,046 Antibiotic	Flixotide/Flovent	1,318 Asthma
2000	Seroxat/Paxil	2,348 Antidepressant	Augmentin	1,847 Antibiotic	Flixotide/Flovent	1,333 Asthma

Johnson & Johnson						
Year	Top-selling drug	Annual Revenue e (\$ billions)	Name of 2	Revenue (\$ billions)	Name of 3	Revenue e (\$ billions)
2017	Remicade	6,316 Autoimmune disease	Stelara	4,011 Immunosuppressant	Trevicta	2,569 Atypical antipsychotic
2016	Remicade	6,966 Autoimmune disease	Stelara	3,232 Immunosuppressant	Zyloga	2,260 Cancer
2015	Remicade	6,561 Autoimmune disease	Stelara	2,474 Immunosuppressant	Zyloga	2,231 Cancer
2014	Remicade	6,868 Autoimmune disease	Dlysto/Soviad	2,302 Antiviral	Zyloga	2,237 Cancer
2013	Remicade	6,673 Autoimmune disease	Zyloga	1,698 Cancer	Prestiza	1,673 Antiretroviral
2012	Remicade	6,139 Autoimmune disease	Velcade	1,500 Cancer	Procrit/Eprex	1,462 Anemia
2011	Remicade	5,932 Autoimmune disease	Procrit/Eprex	1,623 Anemia	Risperdal/Consta	1,583 Atypical antipsychotic
2010	Remicade	4,610 Autoimmune disease	Procrit/Eprex	1,934 Anemia	Risperdal/Consta	1,500 Atypical antipsychotic
2009	Remicade	4,304 Autoimmune disease	Procrit/Eprex	2,245 Anemia	Levaquin/Floxin	1,550 Antibiotic
2008	Remicade	3,748 Autoimmune disease	Topamax	2,731 Anticonvulsant	Procrit/Eprex	2,460 Anemia
2007	Remicade	3,327 Autoimmune disease	Procrit/Eprex	2,885 Anemia	Topamax	2,453 Anticonvulsant
2006	Risperdal/Consta	4,163 Atypical antipsychotic	Procrit/Eprex	3,180 Anemia	Remicade	3,013 Autoimmune disease
2005	Risperdal/Consta	3,552 Atypical antipsychotic	Procrit/Eprex	3,324 Anemia	Remicade	2,535 Autoimmune disease
2004	Procrit/Eprex	3,569 Anemia	Risperdal	3,050 Atypical antipsychotic	Remicade	2,145 Autoimmune disease
2003	Procrit/Eprex	3,984 Anemia	Risperdal	2,512 Atypical antipsychotic	Remicade	1,729 Autoimmune disease
2002	Procrit/Eprex	4,269 Anemia	Risperdal	2,146 Atypical antipsychotic	Remicade	1,237 Autoimmune disease
2001	Procrit/Eprex					

Top 3 drugs through 20 years

Advair/Serotide  
Flixotide  
Augmentin  
Relenza  
Triumeq  
Twicay  
Valtrex  
Seroxat/Paxil  
Valbutrin  
Lamictal  
Avandia  
Infanxyl/Pedialix  
Avodart

Top 3 drugs through 20 years

Remicade  
Risperdal  
Trevicta  
Procrit/Eprex  
Stelara  
Dlysto/Soviad  
Prestiza  
Levaquin/Floxin  
Zyloga  
Velcade  
Topamax  
Anticonvulsant (seizure)

Asthma (corticosteroid)  
Asthma (corticosteroid)  
Antibiotic (penicillin)  
Antiviral (flu pandemic)  
Antiretroviral (HIV)  
Antiretroviral (HIV)  
Antiretroviral (genital herpes, cold sores, shingles)  
Antidepressant  
Antidepressant  
Lamictal  
Diabetes  
Vaccine (combination toddlers)  
Benign prostatic hyperplasia

Autoimmune disease (e.g. rheumatoid arthritis)  
Atypical antipsychotics (Schizophrenia, bipolar disease etc)  
Atypical antipsychotic (schizophrenia)  
Anemia  
Immunosuppressant (Psoriasis)  
Antiviral (Hep C)  
Antiretroviral (HIV)  
Antibiotic  
Cancer (Prostate)  
Cancer (bone marrow, lymphnodes)  
Anticonvulsant (seizure)



Gilead Sciences						
Year	Top-selling drug	Annual Revenue e (\$ billions)	Name of 2	Revenue (\$ billions)	Name of 3	Revenue e (\$ billions)
2017	Harvoni	4,370	Antiretroviral	3,674	Antiretroviral	3,510
2016	Harvoni	9,081	Antiviral	4,001	Antiviral	3,566
2015	Harvoni	13,864	Antiviral	5,276	Antiviral	3,459
2014	Sovaldi	10,263	Antiviral	3,470	Antiretroviral	3,340
2013	Atripla	3,648	Antiretroviral	3,196	Antiretroviral	3,053
2012	Atripla	3,574	Antiretroviral	3,181	Antiretroviral	2,849
2011	Atripla	3,225	Antiretroviral	2,875	Antiretroviral	2,738
2010	Atripla	2,927	Antiretroviral	2,650	Antiretroviral	2,732
2009	Truvada	2,490	Antiretroviral	2,382	Antiretroviral	2,068
2008	Truvada	2,107	Antiretroviral	1,572	Antiretroviral	1,621
2007	Truvada	1,583	Antiretroviral	0,903	Antiretroviral	0,612
2006	Truvada	1,194	Antiretroviral	0,689	Antiretroviral	0,206
2005	Viread	0,779	Antiretroviral	0,568	Antiretroviral	0,221
2004	Viread	0,783	Antiretroviral	0,212	Antifungal	0,068
2003	Viread	0,566	Antiretroviral	0,199	Antifungal	
2002	Viread	0,226	Antiretroviral	0,186	Antifungal	
2001	AmBisome	0,165	Antifungal	0,016	Antiretroviral	
2000	AmBisome	0,141	Antifungal			
1999	AmBisome	0,123	Antifungal			
1998	Vistide	0,006	Antiviral			
1997	Vistide	0,012	Antiviral			

Top 3 drugs through 20 years  
 Harvoni  
 Sovaldi  
 Eplusa  
 Vistide  
 Atripla  
 Truvada  
 Viread  
 Genyoza  
 AmBisome  
 Antiviral (Hep C)  
 Antiviral (Hep C)  
 Antiviral (Hep C)  
 Antiviral (treats eye disease in AIDS patients)  
 Antiretroviral (HIV)  
 Antiretroviral (HIV)  
 Antiretroviral (HIV)  
 Antiretroviral (HIV)  
 Antifungal

Amgen						
Year	Top-selling drug	Annual Revenue e (\$ billions)	Name of 2	Revenue (\$ billions)	Name of 3	Revenue e (\$ billions)
2017	Enbrel	5,433	Autoimmune disease	4,534	Cancer	2,053
2016	Enbrel	5,365	Autoimmune disease	4,648	Cancer	2,093
2015	Enbrel	5,364	Autoimmune disease	4,715	Cancer	1,951
2014	Neulasta/Neupogen	5,755	Cancer	4,688	Autoimmune disease	1,221
2013	Neulasta/Neupogen	5,730	Cancer	4,551	Autoimmune disease	1,311
2012	Neulasta/Neupogen	5,352	Cancer	4,236	Autoimmune disease	2,040
2011	Neulasta/Neupogen	5,212	Cancer	3,701	Autoimmune disease	2,303
2010	Neulasta/Neupogen	4,844	Cancer	3,534	Autoimmune disease	2,524
2009	Neulasta/Neupogen	4,643	Cancer	3,493	Autoimmune disease	2,652
2008	Neulasta/Neupogen	4,659	Cancer	3,598	Autoimmune disease	3,137
2007	Neulasta/Neupogen	4,277	Cancer	3,614	Anemia	3,230
2006	Aranesp	4,121	Anemia	3,923	Cancer	2,511
2005	Neulasta/Neupogen	3,504	Cancer	3,273	Anemia	2,573
2004	Epogen	2,601	Anemia	2,473	Anemia	1,900
2003	Neulasta/Neupogen	2,522	Cancer	2,435	Anemia	1,544
2002	Epogen	2,261	Anemia	1,843	Cancer	0,416
2001	Epogen	2,005	Anemia	1,346	Cancer	0,415
2000	Epogen	1,963	Anemia	1,224	Cancer	0,145
1999	Epogen	1,759	Anemia	1,257	Cancer	0,262
1998	Epogen	1,362	Anemia	1,161	Cancer	0,158
1997	Epogen	1,161	Anemia	1,056	Cancer	0,034

Top 3 drugs through 20 years  
 Enbrel  
 Neulasta/Neupogen  
 Aranesp  
 Xgeva  
 Intergen  
 Autoimmune disease (e.g. rheumatoid arthritis)  
 Cancer (stimulate white blood cells in bone marrow after Chemo)  
 Anemia  
 Cancer (bone marrow, bone)  
 Antiviral (Hep C)

Enbrel, most revenue to Amgen but partner with Pfizer who sells it outside US (and Pfizer partner with Takeda in Japan)

Bristol-Myers Squibb									
Year	Top-selling drug	Annual Revenue (\$ billions)	Name of 2	Revenue (\$ billions)	Name of 3	Revenue (\$ billions)	Top 3 drugs through 20 years		
2017	Opdivo	4,948	Cancer	4,872	Anticoagulant	2,479	Autoimmune disease	Cancer (skin, lung, renal, lymphnode, head/neck, colon, liver, utinary)	
2016	Opdivo	3,774	Cancer	3,343	Anticoagulant	2,265	Autoimmune disease	Autoimmune disease (rheumatoid arthritis)	
2015	Dracenia	1,885	Autoimmune disease	1,860	Anticoagulant	1,620	Cancer	Atypical antipsychotic (prevents clotting, increased blood flow)	
2014	Abilify	2,020	Atypical antipsychotic	1,652	Autoimmune disease	1,493	Cancer	Anticoagulant	
2013	Abilify	2,289	Atypical antipsychotic	1,614	Antiretroviral	1,551	Antiretroviral	Stains (cholesterol)	
2012	Abilify	2,827	Atypical antipsychotic	2,547	Anticoagulant	1,527	Antiretroviral	Stains (cholesterol)	
2011	Plavix	7,087	Anticoagulant	2,758	Atypical antipsychotic	1,569	Antiretroviral	Stains (cholesterol)	
2010	Plavix	6,866	Anticoagulant	2,585	Atypical antipsychotic	1,479	Antiretroviral	Antiretroviral (HIV)	
2009	Plavix	6,146	Anticoagulant	2,532	Atypical antipsychotic	1,401	Antiretroviral	Diabetes	
2008	Plavix	5,603	Anticoagulant	2,153	Atypical antipsychotic	1,292	Antiretroviral	Diabetes	
2007	Plavix	4,755	Anticoagulant	1,660	Atypical antipsychotic	1,204	Blood pressure	Cancer (ovarian, breast, lung, skin, lymph nodes, cervical, pancreatic)	
2006	Plavix	3,257	Anticoagulant	1,282	Atypical antipsychotic	1,197	Stains	Cancer (blood/leukemia)	
2005	Plavix	3,623	Anticoagulant	2,256	Stains	0,982	Blood pressure	Blood pressure	
2004	Plavix	3,327	Anticoagulant	2,635	Stains	0,991	Cancer		
2003	Pravachol	2,827	Stains	2,467	Anticoagulant	0,934	Cancer		
2002	Pravachol	2,266	Stains	1,900	Anticoagulant	0,857	Cancer		
2001	Pravachol	2,173	Stains	2,049	Diabetes	1,350	Anticoagulant		
2000	Pravachol	1,817	Stains	1,732	Diabetes	1,532	Cancer		
1999	Pravachol	1,704	Stains	1,481	Cancer	1,317	Diabetes		
1998	Pravachol	1,643	Stains	1,481	Cancer	0,862	Diabetes		
1997	Pravachol	1,437	Stains	0,941	Cancer	0,579	Diabetes		
Plavix & Avapro also Sanofi (Sanofi teamed up with BMS because BMS cardio specialist 1993 to develop 2 drugs BMS pays royalties to Sanofi)									
BMS returns rights to Plavix and Avapro to Sanofi in 2013 after exclusivity loss, but will receive royalties for sales outside US and Puerto Rico (worldwide for Avapro) until 2018									

Cancer																	
	Roche	Pfizer	Novartis	Merck&Co	AbbVie	Eli Lilly	AstraZeneca	Celgene	Sanofi	Bayer	GlaxoSmithKline	Johnson&Johnson	Gilead	Amgen	Bristol-Myers Squibb	Accumulated	
Number of drugs in category	3	1	2	1	2	2	1	1	6	2	0	0	0	0	2	3	27
Number of drugs total	9	11	10	11	7	9	9	9	8	9	11	13	11	9	6	12	145
Total revenue in the category	225,168	3,126	56,484	3,809	6,06	27,93	0,734	58,636	5,749	0	0	9,926	0	69,208	0	20,112	486,942
Total revenue total top 3	237,198	291,453	145,283	176,78	128,816	158,501	213,476	61,043	155,063	52,33	166,991	164,284	114,792	176,669	0	146,655	2,389,334
Category revenue as share of all top 3	94,93 %	1,07 %	38,88 %	2,15 %	4,70 %	17,62 %	0,34 %	96,06 %	3,71 %	0,00 %	0,00 %	6,04 %	0,00 %	39,17 %	0,00 %	13,71 %	20,38 %
Total revenue company	57,64	161,409	654,368	558,736	218,215	355,25	483,012	70,427	497,987	223,665	617,297	448,801	176,227	265,21	393,984	5652,228	
Category share of total revenue	42,67 %	1,94 %	8,63 %	0,68 %	2,78 %	7,86 %	0,15 %	83,26 %	1,15 %	0,00 %	0,00 %	2,21 %	0,00 %	26,10 %	5,10 %	8,62 %	
Blood Medication																	
	Roche	Pfizer	Novartis	Merck&Co	AbbVie	Eli Lilly	AstraZeneca	Celgene	Sanofi	Bayer	GlaxoSmithKline	Johnson&Johnson	Gilead	Amgen	Bristol-Myers Squibb	Accumulated	
Number of drugs in category	1	1	3	1	0	0	2	0	0	3	0	0	1	0	2	3	20
Number of drugs total	9	11	10	11	7	9	9	9	8	9	11	13	11	9	6	12	145
Total revenue in the category	5,858	39,944	56,406	19,379	0	35,311	0	76,768	8,074	0	30,955	0	54,596	0	61,189	388,48	
Total revenue total top 3	237,198	291,453	145,283	176,78	128,816	158,501	213,476	61,043	155,063	52,33	166,991	164,284	114,792	176,669	0	146,655	2,389,334
Category revenue as share of all top 3	2,47 %	13,71 %	38,82 %	10,96 %	0,00 %	0,00 %	16,54 %	0,00 %	49,51 %	15,43 %	0,00 %	18,84 %	0,00 %	30,90 %	0,00 %	41,72 %	16,26 %
Total revenue company	57,64	161,409	654,368	558,736	218,215	355,25	483,012	70,427	497,987	223,665	617,297	448,801	176,227	265,21	393,984	5652,228	
Category share of total revenue	1,11 %	24,75 %	8,62 %	3,47 %	0,00 %	0,00 %	7,31 %	0,00 %	15,42 %	3,61 %	0,00 %	6,90 %	0,00 %	20,59 %	15,53 %	6,87 %	
Immunosuppressants																	
	Roche	Pfizer	Novartis	Merck&Co	AbbVie	Eli Lilly	AstraZeneca	Celgene	Sanofi	Bayer	GlaxoSmithKline	Johnson&Johnson	Gilead	Amgen	Bristol-Myers Squibb	Accumulated	
Number of drugs in category	1	1	3	1	1	0	0	0	1	1	0	0	2	0	1	14,000	
Number of drugs total	9	11	10	11	7	9	9	9	8	9	11	13	11	9	6	12	145
Total revenue in the category	0,246	24,543	15,927	12,1	108,424	0	2,296	1,771	11,556	0	81,439	0	52,266	0	8,281	318,849	
Total revenue total top 3	237,198	291,453	145,283	176,78	128,816	158,501	213,476	61,043	155,063	52,33	166,991	164,284	114,792	176,669	0	146,655	2,389,334
Category revenue as share of all top 3	0,10 %	8,42 %	10,96 %	6,84 %	84,17 %	0,00 %	0,00 %	3,76 %	1,14 %	22,08 %	0,00 %	49,57 %	0,00 %	29,58 %	0,00 %	5,65 %	13,34 %
Total revenue company	57,64	161,409	654,368	558,736	218,215	355,25	483,012	70,427	497,987	223,665	617,297	448,801	176,227	265,21	393,984	5652,228	
Category share of total revenue	0,05 %	15,21 %	2,43 %	2,17 %	49,69 %	0,00 %	0,00 %	3,26 %	0,36 %	5,17 %	0,00 %	18,15 %	0,00 %	19,71 %	2,10 %	5,64 %	

	Roche	Pfizer	Novartis	Merck&Co	AbbVie	Eli Lilly	AstraZeneca	Celgene	Sanofi	Bayer	GlaxoSmithKline	Johnson&Johnson	Gilead	Amgen	Bristol-Myers Squibb	Accumulated
<b>Statins</b>																
Number of drugs in category	0	1	0	2	1	0	1	0	0	1	0	0	0	0	1	7
Number of drugs total	9	11	10	11	7	9	9	8	9	11	13	11	9	6	12	145
Total revenue in the category	0	129,18	0	40,943	3,825	0	53,406	0	0	0,587	0	0	0	0	19,955	247,896
Total revenue total top 3	237,198	291,453	145,283	176,78	128,816	158,501	213,476	61,043	155,063	52,33	166,991	164,284	114,792	176,669	146,655	2389,334
Category revenue as share of all top 3	0,00 %	44,32 %	0,00 %	23,16 %	2,97 %	0,00 %	25,02 %	0,00 %	1,12 %	0,00 %	0,00 %	0,00 %	0,00 %	0,00 %	13,61 %	10,38 %
Total revenue company	527,64	161,409	654,368	558,736	218,215	355,25	483,012	70,427	497,987	223,665	617,297	448,801	176,227	265,21	393,984	5652,228
Category share of total revenue	0,00 %	80,03 %	0,00 %	7,33 %	1,75 %	0,00 %	11,06 %	0,00 %	0,26 %	0,00 %	0,00 %	0,00 %	0,00 %	0,00 %	5,06 %	4,39 %
<b>Antidepressants</b>																
Number of drugs in category	0	1	0	0	0	3	1	0	0	0	2	2	0	0	1	10
Number of drugs total	9	11	10	11	7	9	9	8	9	11	13	11	9	6	12	145
Total revenue in the category	0	24,432	0	0	0	93,905	35,311	0	0	0	14,685	31,255	0	0	20,146	219,734
Total revenue total top 3	237,198	291,453	145,283	176,78	128,816	158,501	213,476	61,043	155,063	52,33	166,991	164,284	114,792	176,669	146,655	2389,334
Category revenue as share of all top 3	0,00 %	8,38 %	0,00 %	0,00 %	0,00 %	59,25 %	16,54 %	0,00 %	0,00 %	0,00 %	8,79 %	19,02 %	0,00 %	0,00 %	13,74 %	9,20 %
Total revenue company	527,64	161,409	654,368	558,736	218,215	355,25	483,012	70,427	497,987	223,665	617,297	448,801	176,227	265,21	393,984	5652,228
Category share of total revenue	0,00 %	15,14 %	0,00 %	0,00 %	0,00 %	26,43 %	7,31 %	0,00 %	0,00 %	0,00 %	2,38 %	6,96 %	0,00 %	0,00 %	5,11 %	3,89 %
<b>Antivirals</b>																
Number of drugs in category	1	0	0	0	2	0	0	0	0	0	4	2	8	1	2	20
Number of drugs total	9	11	10	11	7	9	9	8	9	11	13	11	9	6	12	145
Total revenue in the category	1,184	0	0	0	7,386	0	0	0	0	0	19,064	3,975	113,541	0,599	10,433	156,182
Total revenue total top 3	237,198	291,453	145,283	176,78	128,816	158,501	213,476	61,043	155,063	52,33	166,991	164,284	114,792	176,669	146,655	2389,334
Category revenue as share of all top 3	0,50 %	0,00 %	0,00 %	0,00 %	5,73 %	0,00 %	0,00 %	0,00 %	0,00 %	0,00 %	11,42 %	2,42 %	98,91 %	0,34 %	7,11 %	6,54 %
Total revenue company	527,64	161,409	654,368	558,736	218,215	355,25	483,012	70,427	497,987	223,665	617,297	448,801	176,227	265,21	393,984	5652,228
Category share of total revenue	0,22 %	0,00 %	0,00 %	0,00 %	3,38 %	0,00 %	0,00 %	0,00 %	0,00 %	0,00 %	3,09 %	0,89 %	64,43 %	0,23 %	2,65 %	2,76 %

	Roche	Pfizer	Novartis	Merck&Co	AbbVie	Eli Lilly	AstraZeneca	Celgene	Sanofi	Bayer	GlaxoSmithKline	Johnson&Johnson	Gilead	Amgen	Bristol-Myers Squibb	Accumulated
<b>Asthma</b>																
Number of drugs in category	0	0	0	1	0	0	2	0	0	0	2	0	0	0	0	5
Number of drugs total	9	11	10	11	7	9	9	8	9	11	13	11	9	6	12	145
Total revenue in the category	0	0	0	28,096	0	0	22,491	0	0	0	103,457	0	0	0	0	154,044
Total revenue total top 3	237,198	291,453	145,283	176,78	128,816	158,501	213,476	61,043	155,063	52,33	166,991	164,284	114,792	176,669	146,655	2389,334
Category revenue as share of all top 3	0.00 %	0.00 %	0.00 %	15.89 %	0.00 %	0.00 %	10.54 %	0.00 %	0.00 %	0.00 %	61.95 %	0.00 %	0.00 %	0.00 %	0.00 %	6.45 %
Total revenue company	527,64	161,409	654,368	558,736	218,215	355,25	483,012	70,427	497,987	223,665	617,297	448,801	176,227	265,21	393,984	5652,228
Category share of total revenue	0.00 %	0.00 %	0.00 %	5.03 %	0.00 %	0.00 %	5 %	0.00 %	0.00 %	0.00 %	16.76 %	0.00 %	0.00 %	0.00 %	0.00 %	2.73 %
<b>Diabetes</b>																
Number of drugs in category	0	0	0	2	0	2	0	0	1	1	1	0	0	0	1	8,000
Number of drugs total	9	11	10	11	7	9	9	8	9	11	13	11	9	6	12	145
Total revenue in the category	0	0	0	37,671	0	26,485	0	0	61,828	2,335	6,722	0	0	0	6,539	141,580
Total revenue total top 3	237,198	291,453	145,283	176,78	128,816	158,501	213,476	61,043	155,063	52,33	166,991	164,284	114,792	176,669	146,655	2389,334
Category revenue as share of all top 3	0.00 %	0.00 %	0.00 %	21.31 %	0.00 %	16.71 %	0.00 %	0.00 %	39.87 %	4.46 %	4.03 %	0.00 %	0.00 %	0.00 %	4.46 %	5.93 %
Total revenue company	527,64	161,409	654,368	558,736	218,215	355,25	483,012	70,427	497,987	223,665	617,297	448,801	176,227	265,21	393,984	5652,228
Category share of total revenue	0.00 %	0.00 %	0.00 %	6.74 %	0.00 %	7.46 %	0.00 %	0.00 %	12.42 %	1.04 %	1.09 %	0.00 %	0.00 %	0.00 %	1.66 %	2.50 %
<b>Antibiotics and anti-inflammatories</b>																
Number of drugs in category	1	2	0	1	0	0	0	0	0	1	1	1	1	0	0	7
Number of drugs total	9	11	10	11	7	9	9	8	9	11	13	11	9	6	12	145
Total revenue in the category	2,997	8,203	0	8,925	0	0	0	0	0	10,404	5,683	1,55	0	0	0	37,762
Total revenue total top 3	237,198	291,453	145,283	176,78	128,816	158,501	213,476	61,043	155,063	52,33	166,991	164,284	114,792	176,669	146,655	2389,334
Category revenue as share of all top 3	1.26 %	2.81 %	0.00 %	5.05 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	19.88 %	3.40 %	0.94 %	0.00 %	0.00 %	0.00 %	1.58 %
Total revenue company	527,64	161,409	654,368	558,736	218,215	355,25	483,012	70,427	497,987	223,665	617,297	448,801	176,227	265,21	393,984	5652,228
Category share of total revenue	0.57 %	5.08 %	0.00 %	1.60 %	0.00 %	0.00 %	0.00 %	0.00 %	0.00 %	4.65 %	0.92 %	0.35 %	0.00 %	0.00 %	0.00 %	0.67 %

Antibiotics and anti-inflammatories														
Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling drug	Year entered the market US	Original patent granted US	Main patent expiry US	Total years under exclusivity US	Years from FDA approval to top selling	Year generics launched US	Years from generics approved US to no longer top selling	Year generics launched India	Years from broad drug is launched to generics enter market	Years from generics approved India to no longer top selling
Roche	Rociprin	2,337	3	5	1984	1985	2005	20	15	2005	-2	2011	N/A	N/A
Pfizer	Zithromax	1,041	3	7	1991	1991	2005	14	7	2005	-1	1991	N/A	1996
Bayer	Ciprobay	10,404	1	7	1987	1990	2004	24	11	2005	-1	1987	1988	2003
GilletteSmith Kline	Augmentin	3,653	3	3	1984	1984	2002	8	16	2002	0	1984	N/A	2000
Johnson & Johnson	Levofloxacin	1,135	3	1	1996	1995	2011	16	13	2011	-2	1995	N/A	N/A
Pfizer	Celebrex	1,762	3	3	1998	1994	2014	20	3	2014	-5	1995	N/A	2014
Merck & Co.	Vioxx	8,325	3	3	1993	1995	2004	31	2	Banned	N/A	1995	N/A	2002
Total revenue		37,762												
Average		3,423						11,286	9,667		-0,500			11,2
Max.		10,404						24	16		1,000			16
Min.		1,041						8,000	7,000		-1,000			3,0

Statins (cholesterol medications)														
Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling drug	Year entered the market US	Original patent granted US	Main patent expiry US	Total years under exclusivity US	Years from FDA approval to top selling	Year generics launched US	Years from generics approved US to no longer top selling	Year generics launched India	Years from broad drug is launched to generics enter market	Years from generics approved India to no longer top selling
Pfizer	Lipitor	123,180	2	14	1996	1992	2011	19	3	2011	1	1996	0	2005
Merck & Co.	Zocor	27,661	1	6	1991	1986	2006	20	9	2006	-1	1983	0	2002
Merck & Co.	Zetia	19,282	2	5	2001	1996	2017	21	11	2017	-1	2003	0	2010
AbbVie	Tricor/Triplicor	3,257	3	1	1998	1995	2014	19	17	2013	-1	N/A	N/A	N/A
AstraZeneca	Crestor	53,406	Still no 2	12	2003	1994	2016	22	3	2016	0	2002	0	2003
Bristol-Myers Squibb	Pravastatin	19,955	3	10	1991	1983	2006	17	6	2006	0	1990	0	1998
Bayer	Lipobay/Evcol	10,387	3	1	1997	1993	2001	8	3	Nones	N/A	1997	N/A	N/A
Total revenue		247,896												
Average		35,414						18,000	7,400		-0,400			8,400
Max.		123,180						22,000	11,000		1,000			10,000
Min.		10,387						8,000	3,000		-1,000			6,000

Diabetics														
Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling drug	Year entered the market US	Original patent granted US	Main patent expiry US	Total years under exclusivity US	Years from FDA approval to top selling	Year generics launched US	Years from generics approved US to no longer top selling	Year generics launched India	Years from broad drug is launched to generics enter market	Years from generics approved India to no longer top selling
Merck & Co.	Januvia	35,520	Still no 1	9	2006	2003	2022	19	3	Nones	Not relevant	2007	N/A	N/A
Merck & Co.	Janmet	2,151	3	1	2007	2003	2022	19	8	Nones	Not relevant	2008	N/A	2011
Elil Lilly	Humalog	22,245	Still no 1	10	1996	1993	2014	21	8	Nones	Not relevant	1996	N/A	2004
Elil Lilly	Humulin	4,240	4	4	1983	1972	2000	28	18	N/A	Not relevant	1982	N/A	1995
Sandoz	Lantus	61,928	Still no 1	17	2000	2000	2031	31	1	Nones	Not relevant	2000	N/A	2004
GilletteSmith Kline	Avandia	5,722	2	3	1995	1999	2026	27	5	2018	-6	2000	0	2003
Bristol-Myers Squibb	Gliclazide	13,243	2	5	1995	1976	2003	27	2	2011	-16	1997	N/A	N/A
Total revenue		193,826												
Average		19,382						24,17	1,167		-11,000			5,400
Max.		61,928						31	18		5,000			10,000
Min.		2,151						13,000	1,000		-16,000			4,000

Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling drug	Year entered the market US	Original patent granted US	Main patent expiry US	Total years under exclusivity US	Years from FDA approval to top selling	Year generic launched US	Year generic approved US to no longer top selling	Years from brand drug is launched US to generic enter market	Year generic launched India	Years from generic approved India to no longer top selling
Amgen	Enbrel	4,216	2	1	1995	1997	2015	20	5	2003	-13	6	N/A	N/A
Amgen	Enbrel	3,454	2	7	1993	2000	2015	23	12	2001	14	10	2007	2007
Amgen	Enbrel	2,266	14	14	1993	2000	2015	23	6	None	Not relevant	Not relevant	2007	2007
Amgen	Enbrel	1,154	Still no 1	4	2001	2008	2023	18	4	None	Not relevant	Not relevant	N/A	N/A
Novartis	Novartis/Sandimmun	2,091	3	2000	1978	1978	1996	18	6	2000	3	18	N/A	N/A
Novartis	Cosentyx	2,071	Still no 2	1	2015	2015	2031	16	2	None	Not relevant	Not relevant	N/A	N/A
Merck & Co.	Januvia	12,100	3	15	1998	2000	2018	18	12	2016	-2	2016	2016	-9
Johnson & Johnson	Romicept	7,122	Still no 1	16	1938	2000	2018	18	4	2016	Not relevant	Not relevant	2015	2015
Johnson & Johnson	Stelira	3,717	Still no 2	3	2003	2003	2023	20	6	None	Not relevant	Not relevant	2014	2014
AbbVie	Humira	108,424	Still no 1	11	2002	2004	2023	19	5	None	Not relevant	Not relevant	2012	2012
Colgate	Dove	2,296	Still no 3	2	2014	2016	2024	8	2	None	Not relevant	Not relevant	N/A	N/A
Sanofi	Avastin	1,771	Still no 3	1	2012	N/A	2019	N/A	5	2013	4	6	2015	2015
Boehringer-Ingelheim	Verzenio	1,596	Still no 3	0	1993	1990	2001	11	13	2003	4	11	2000	2000
Boehringer-Ingelheim	Stivarga	8,261	Still no 3	0	2005	2006	2015	13	3	None	Not relevant	Not relevant	N/A	N/A
Boehringer-Ingelheim	Stivarga	6,261	Still no 3	0	2005	2006	2015	13	3	None	Not relevant	Not relevant	N/A	N/A
Boehringer-Ingelheim	Stivarga	5,714	For no longer top selling	0	2005	2006	2015	13	3	None	Not relevant	Not relevant	N/A	N/A
Average		108,424		6,714	18,533	6,750	20,000	19,000	10,000	2,000	-2,000	4,000	1,250	7,429
Max		108,424		16,000	6,000	1,000	20,000	19,000	11,000	1,000	-13,000	4,000	12,000	3,000
Min		0,246		1,000	1,000	1,000	17,000	2,000	2,000	2,000	-13,000	-8,000	3,000	-13,000

Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling drug	Year entered the market US	Original patent granted US	Main patent expiry US	Total years under exclusivity US	Years from FDA approval to top selling	Year generic launched US	Year generic approved US to no longer top selling	Years from brand drug is launched US to generic enter market	Year generic launched India	Years from generic approved India to no longer top selling
Amgen	Enbrel	4,216	2	1	1995	1997	2015	20	5	2003	-13	6	N/A	N/A
Amgen	Enbrel	3,454	2	7	1993	2000	2015	23	12	2001	14	10	2007	2007
Amgen	Enbrel	2,266	14	14	1993	2000	2015	23	6	None	Not relevant	Not relevant	2007	2007
Amgen	Enbrel	1,154	Still no 1	4	2001	2008	2023	18	4	None	Not relevant	Not relevant	N/A	N/A
Novartis	Novartis/Sandimmun	2,091	3	2000	1978	1978	1996	18	6	2000	3	18	N/A	N/A
Novartis	Cosentyx	2,071	Still no 2	1	2015	2015	2031	16	2	None	Not relevant	Not relevant	N/A	N/A
Merck & Co.	Januvia	12,100	3	15	1998	2000	2018	18	12	2016	-2	2016	2016	-9
Johnson & Johnson	Romicept	7,122	Still no 1	16	1938	2000	2018	18	4	2016	Not relevant	Not relevant	2015	2015
Johnson & Johnson	Stelira	3,717	Still no 2	3	2003	2003	2023	20	6	None	Not relevant	Not relevant	2014	2014
AbbVie	Humira	108,424	Still no 1	11	2002	2004	2023	19	5	None	Not relevant	Not relevant	2012	2012
Colgate	Dove	2,296	Still no 3	2	2014	2016	2024	8	2	None	Not relevant	Not relevant	N/A	N/A
Sanofi	Avastin	1,771	Still no 3	1	2012	N/A	2019	N/A	5	2013	4	6	2015	2015
Boehringer-Ingelheim	Verzenio	1,596	Still no 3	0	1993	1990	2001	11	13	2003	4	11	2000	2000
Boehringer-Ingelheim	Stivarga	8,261	Still no 3	0	2005	2006	2015	13	3	None	Not relevant	Not relevant	N/A	N/A
Boehringer-Ingelheim	Stivarga	6,261	Still no 3	0	2005	2006	2015	13	3	None	Not relevant	Not relevant	N/A	N/A
Boehringer-Ingelheim	Stivarga	5,714	For no longer top selling	0	2005	2006	2015	13	3	None	Not relevant	Not relevant	N/A	N/A
Average		108,424		6,714	18,533	6,750	20,000	19,000	10,000	2,000	-2,000	4,000	1,250	7,429
Max		108,424		16,000	6,000	1,000	20,000	19,000	11,000	1,000	-13,000	4,000	12,000	3,000
Min		0,246		1,000	1,000	1,000	17,000	2,000	2,000	2,000	-13,000	-8,000	3,000	-13,000

HE use cases have many years from generic enter market to launch top selling but can't prove control in only India. Also, in India, generic launch is delayed due to regulatory issues.

Company	Drug	Total global revenue	Position leaves top 3 from	Total years as top selling drug	Year entered the market US	Original patent granted US	Main patent expiry US	Total years under exclusivity US	Years from FDA approval to top selling	Year generic launched US	Year generic approved US to no longer top selling	Years from brand drug is launched US to generic enter market	Year generic launched India	Years from generic approved India to no longer top selling
Amgen	Enbrel	4,216	2	1	1995	1997	2015	20	5	2003	-13	6	N/A	N/A
Amgen	Enbrel	3,454	2	7	1993	2000	2015	23	12	2001	14	10	2007	2007
Amgen	Enbrel	2,266	14	14	1993	2000	2015	23	6	None	Not relevant	Not relevant	2007	2007
Amgen	Enbrel	1,154	Still no 1	4	2001	2008	2023	18	4	None	Not relevant	Not relevant	N/A	N/A
Novartis	Novartis/Sandimmun	2,091	3	2000	1978	1978	1996	18	6	2000	3	18	N/A	N/A
Novartis	Cosentyx	2,071	Still no 2	1	2015	2015	2031	16	2	None	Not relevant	Not relevant	N/A	N/A
Merck & Co.	Januvia	12,100	3	15	1998	2000	2018	18	12	2016	-2	2016	2016	-9
Johnson & Johnson	Romicept	7,122	Still no 1	16	1938	2000	2018	18	4	2016	Not relevant	Not relevant	2015	2015
Johnson & Johnson	Stelira	3,717	Still no 2	3	2003	2003	2023	20	6	None	Not relevant	Not relevant	2014	2014
AbbVie	Humira	108,424	Still no 1	11	2002	2004	2023	19	5	None	Not relevant	Not relevant	2012	2012
Colgate	Dove	2,296	Still no 3	2	2014	2016	2024	8	2	None	Not relevant	Not relevant	N/A	N/A
Sanofi	Avastin	1,771	Still no 3	1	2012	N/A	2019	N/A	5	2013	4	6	2015	2015
Boehringer-Ingelheim	Verzenio	1,596	Still no 3	0	1993	1990	2001	11	13	2003	4	11	2000	2000
Boehringer-Ingelheim	Stivarga	8,261	Still no 3	0	2005	2006	2015	13	3	None	Not relevant	Not relevant	N/A	N/A
Boehringer-Ingelheim	Stivarga	6,261	Still no 3	0	2005	2006	2015	13	3	None	Not relevant	Not relevant	N/A	N/A
Boehringer-Ingelheim	Stivarga	5,714	For no longer top selling	0	2005	2006	2015	13	3	None	Not relevant	Not relevant	N/A	N/A
Average		108,424		6,714	18,533	6,750	20,000	19,000	10,000	2,000	-2,000	4,000	1,250	7,429
Max		108,424		16,000	6,000	1,000	20,000	19,000	11,000	1,000	-13,000	4,000	12,000	3,000
Min		0,246		1,000	1,000	1,000	17,000	2,000	2,000	2,000	-13,000	-8,000	3,000	-13,000

HE use cases have many years from generic enter market to launch top selling but can't prove control in only India. Also, in India, generic launch is delayed due to regulatory issues.

Antibiotic (including combination)															
Company	Drug	Total global revenue	Particular revenue from	Total year sales	Year entered the market	Original patent granted US	Market entry US	Market entry US	Total year sales under	Year from FDA approval to step rolling	Year from generic launch to US	Year from generic launch to Europe	Year from generic launch to Japan	Year from generic launch to India	Year from generic launch to other markets
Roche	Penicillin G	1,954	1	2002	2002	1947	2002	2002	20	2	2004	2004	2004	2004	2004
	Penicillin V	1,954	2	2002	2002	1947	2002	2002	16	2	2004	2004	2004	2004	2004
	Gillette/Schering-Plough	3,236	3	2002	2002	1947	2002	2002	24	2	2004	2004	2004	2004	2004
Jahromi, Jahromi	Orizal/Suivit	2,302	2	2012	2012	2009	2014	2009	9	0	N/A	2015	2015	N/A	N/A
Gilead Sciences	Meropenem	2,735	3	2014	2014	2003	2014	2003	20	1	N/A	2014	2014	2015	2015
Gilead Sciences	Meropenem	19,516	3	2012	2012	2003	2014	2003	19	1	N/A	2014	2014	2015	2015
Gilead Sciences	Meropenem	3,510	3	2014	2014	2003	2014	2003	10	1	N/A	2014	2014	2015	2015
Gilead Sciences	Meropenem	8,010	4	1998	1992	1997	1997	1997	15	0	2012	2012	2012	2012	2012
Abbott	Clarithromycin	4,224	3	2004	2003	1986	2004	2003	24	10	2012	2012	2012	2012	2012
Gillette/Schering-Plough	Trimethoprim	6,152	3	2014	2009	2009	2014	2009	20	1	N/A	2014	2014	N/A	N/A
Gillette/Schering-Plough	Trimethoprim	6,152	3	1995	1997	2009	2014	2009	22	12	2009	2009	2009	2009	2009
Jahromi, Jahromi	Trimethoprim	3,894	3	2012	2012	2007	2014	2007	15	3	N/A	2014	2014	2014	2014
Gillette/Schering-Plough	Trimethoprim	1,772	3	2004	2004	2005	2014	2005	13	6	2017	2017	2017	2017	2017
Gillette/Schering-Plough	Trimethoprim	2,168	3	2004	2004	2005	2014	2005	13	6	2017	2017	2017	2017	2017
Gillette/Schering-Plough	Trimethoprim	8,237	3	2004	2004	2005	2014	2005	13	6	2017	2017	2017	2017	2017
Gillette/Schering-Plough	Trimethoprim	3,474	3	2015	2009	2009	2014	2009	24	2	N/A	2014	2014	N/A	N/A
Bristol-Myers Squibb	Roxithromycin	7,262	3	2002	2001	1997	2002	2001	16	5	2017	2017	2017	2017	2017
Tadrisone	For all	154,152	2	1992	1997	1997	1999	1997	20	14	2017	2017	2017	2017	2017
Min.	For all	3,15	1	1	1	1	1	1	16	14	1	1	1	1	1
Max.	For all	30,223	1	1	1	1	1	1	16	14	1	1	1	1	1
Min.	For all	0,05	1	1	1	1	1	1	9	3	1	1	1	1	1



## Top 3 pharmaceuticals

Roche	Drug	Type	Total years in 1	Years as 1	Years as 2	Years as 3	Total revenue	Year became top 3	Year stopped being top 3, and then
1	Rituxan	Cancer (blood, lymphnodes), Autoimmune disease (e.g. rheumatoid arthritis)	17 of 21	14	3	0	8 85 583	2001, as no 2	Still top 2017, no 1 (event 2, 1, 2, 1)
2	Avastin	Cancer (lung, kidney, ovarian, cervical cancer, glioblastoma/brain)	12 of 19	2	6	4	4 69 204	2005, as no 3	Still top 2017, no 3 (event 3, 2, 1, 2, 3, 2, 3)
3	Herceptin	Cancer (breast)	13 of 19	0	4	9	69 391	2005, as no 3	Still top 2017, no 2 (event 3, 2, 3, 2, 3, 2)
4	Rocofphin	Anesthetic	4 of 19	2	1	1	12 997	already top 1999, no 1	2002, as no 3 (event 1, 2, 3)
5	Neoflecomon/Epogr	Anemia	5 of 19	0	3	2	5 858	2000, as no 3	2005, as no 2 (event 3, not 3, 2)
6	CellCept	Immunosuppressant (Lupus)	1 of 19	0	1	0	0 246	2000, as no 2	2000, as no 2 (only no 2)
7	Pegasys/Copegus	Antiviral (Hep C)	1 of 19	0	0	1	1 184	2004, as no 3	2004, as (only no 3)
8	Accutane	Severe acne	3 of 19	1	1	1	1 279	already top 1999, no 1	2001, as no 3 (event 2, 1, 3)
9	Xenical	Dietary	1 of 19	0	0	0	1 0 666	already top 1995, no 3	1999, as no 3 (only no 3)
<b>Pfizer</b>									
1	Drug	Type	Total years in 1	Years as 1	Years as 2	Years as 3	Total revenue	Year became top 3	Year stopped being top 3
2	Prevnar 13	Vaccine (pneumococcal bacteria)	5 of 21	3	2	0	2 20 184	2013, as no 2	still top 2017, no 1 (event 2, 1)
3	Lipitor	Statin (cholesterol)	14 of 21	13	1	0	129 180	1999, as no 1	2012, as no 2 (event 1, only one year 2)
4	Norvasc	Blood pressure	11 of 21	2	9	0	39 344	already top 1997, no 1	2007, as no 2 (event 1, 2)
5	Enbrel	Immunosuppressant (e.g. rheumatoid arthritis)	7 of 21	0	1	6	24 543	2010, as no 2	last year top 2016, no 3 (event one year 2, no)
6	Brance	Cancer (breast)	1 of 21	0	0	1	3 126	2017, as no 3	still top 2017, (only 3)
7	Celebrex	Anti-inflammatory	3 of 21	0	0	3	7 162	2007, as no 3	2005, as no 3 (only 3)
8	Zolift	Anti-depressant	10 of 21	0	2	8	24 432	already top 1997, no 2	2006, as no 3 (event 2 two years, 3 next)
9	Lytice	Anticonvulsant (seizures)	10 of 21	3	6	1	140 360	2009, as no 2	still top 2017, no 2 (event 2, 3, 2, 1, 2)
10	Zithromax	Antibiotic	1 of 21	0	0	1	1 041	1996, as no 3	1996, as no 3 (only 3)
11	Diflucan	Antifungal	2 of 21	0	0	0	1 0 881	already top 1997, no 3	1997, as no 3 (only 3)
<b>Novartis</b>									
1	Drug	Type	Total years in 1	Years as 1	Years as 2	Years as 3	Total revenue	Year became top 3	Year stopped being top 3
1	Clarya	Immunosuppressant (Multiple Sclerosis)	4 of 17	1	3	0	3 547	2014, as no 1	still top 2017, no 1 (event 1, a year, 2 next)
2	Corentin	Immunosuppressant (Psoriasis)	1 of 17	0	1	0	2 071	2017, as no 2	still top 2017, only 2
3	Neoral/Sandimmun	Immunosuppressant (Psoriasis, prevent organ rejection, rheumatoid arthritis)	3 of 17	0	2	1	2 309	already top 2001, no 2	2003, as no 3 (event 2, 3)
4	Clavex	Cancer (blood, stomach/gastrointestinal)	15 of 17	5	9	1	5 112	2003, as no 2	still top 2017, no 2 (event 2, 1, 3 one year)
5	Zometax	Cancer (manage side effects)	4 of 17	0	0	4	5 372	2005, as no 3	2005, as no 3 (all 3)
6	Diovan	Blood pressure	13 of 17	11	2	0	54 575	already top 2001, no 1	2013, as no 2 (event 1, 2 last 2 years)
7	Lofel	Blood pressure	1 of 17	0	0	1	1 352	2006, as no 3	2006, as no 3 (only 3)
8	Cibacem/Lotenin	Blood pressure	1 of 17	0	0	1	0 475	already top 2001, no 3	2001, as no 3 (only 3)
9	Lucentis	Eye disease	7 of 17	0	0	7	14 700	2010, as no 3	2016, as no 3 (all 3)
10	Lamictal	Anti-fungal	2 of 17	0	0	0	2 1 766	2002, as no 2	2004, as no 2 (all 2)
<b>Merck and Co.</b>									
1	Drug	Type	Total years in 1	Years as 1	Years as 2	Years as 3	Total revenue	Year became top 3	Year stopped being top 3
1	Januvia	Diabetes	3 of 18	8	1	2	35 520	2005, as no 3	still top 2017, no 1 (event 3, 2, 1)
2	Januvia	Diabetes	1 of 18	0	0	1	2 561	2016, as no 3 (only 3)	2016, as no 3 (only 3)
3	Singulair	Asthma and allergies	8 of 18	6	0	2	28 096	2006, as no 1	2011, as no 1 (all 1)
4	Zosin	Statin (cholesterol)	6 of 18	0	0	6	27 661	already top 2000, no 1	2005, as no 1 (all 1)
5	Keytruda	Cancer (lung, skin, lymphnodes)	1 of 18	0	1	0	3 803	2017, as no 2	still top 2017, no 2 (only 2)
6	Zeta	Statin (cholesterol)	5 of 18	0	4	1	13 282	2012, as no 3	2016, as no 2 (one year 3, rest 2)
7	Remade	Immunosuppressant (e.g. rheumatoid arthritis)	14 of 18	0	2	3	10 100	2010, as no 2	2014, as no 2 (event 2, 1, 2, 3)
8	Cosenty	Blood pressure	6 of 18	0	4	2	19 379	2004, as no 3	2005, as no 2 (event 3, 2)
9	Fosamax	Osteoporosis	3 of 18	0	3	6	21 376	already top 2000, no 3	2006, as no 3 (event 3, 2, 3)
10	Yom	Anti-inflammatory	4 of 18	0	3	1	8 325	already top 2001, no 2	2003, as no 3 (event 2 last year 3 (100 trials needed longer?)
11	Garbaf	Vaccine (HPV)	2 of 18	0	0	2	4 481	2016, as no 3	still top 2017, no 3 (both 3)
<b>AbbVie</b>									
1	Drug	Type	Total years in 1	Years as 1	Years as 2	Years as 3	Total revenue	Year became top 3	Year stopped being top 3
1	Humira	Immunosuppressant (e.g. rheumatoid arthritis)	18 of 11	11	0	0	106 424	2007, as no 1	still top 2017, no 1 (all 1)
2	Inbuvise	Cancer (blood)	2 of 7	0	2	0	4 405	2016, as no 2	still top 2017, no 2 (all 2)
3	Veloxa	Antiviral (Hep C)	2 of 7	0	1	1	3 161	2016, as no 2	2016, as no 3 (event 2, 3 a year each)
4	Kalena	Antibiotic (MRSA)	4 of 7	0	0	4	4 235	2010, as no 3	2014, as no 3 (all 3)
5	ArcoGel	Androgen (hypotension)	3 of 7	0	3	0	3 121	2012, as no 2	2014, as no 2 (all 2)
6	TruCor/Talzin	Statin (cholesterol)	3 of 7	0	2	1	3 825	2010, as no 2	2012, as no 3 (event 2, last year 3)
7	Lupron	Cancer (prostate)	2 of 7	0	0	2	1 699	2016, as no 3	still top 2017, no 3 (all 3)
<b>Eli Lilly &amp; Co.</b>									
1	Drug	Type	Total years in 1	Years as 1	Years as 2	Years as 3	Total revenue	Year became top 3	Year stopped being top 3
1	Genzar	Cancer (breast, lung, ovarian, pancreatic)	7 of 21	0	3	4	1 922	1999, as no 3	2001, as no 3 (event one year 3, no year no 3, 2, 3)
2	Alimta	Cancer (lung)	8 of 21	1	4	3	20 029	2010, as no 3	still top 2017, no 3 (event 3, 2, 1, 2, 3)
3	Combalta	Anti-depressant	8 of 21	2	5	1	18 830	2006, as no 3	2015, as no 1 (event 3, 2, 1)
4	Sypria	Atypical antipsychotic (schizophrenia, bipolar disorder)	15 of 21	11	4	0	54 467	already top 1997, no 2	2011, as no 1 (event 2, 1)
5	Pozico	Anti-depressant	5 of 21	4	1	0	12 543	already top 1997, no 1	2001, as no 2 (event 1, 2 last year)
6	Caki	Eye/diabetes medication	4 of 21	0	1	3	9 236	2014, as no 3	still top 2017, no 2 (event 3, 2)
7	Humalog	Diabetes	16 of 21	3	1	6	22 249	2004, as no 3	still top 2017, no 1 (event 2 year 3, two year not, two year 1, two year not, 2 year 3, 2, 1)
8	Humulin	Diabetes	4 of 21	0	2	2	4 240	2000, as no 3	2000, as no 2 (event 3, 2)
9	Asil	H2 blocker (stomach)	2 of 21	0	0	2	0 945	already top 1997, no 3	1998, as no 3 (all 3)

AstraZeneca								
Drug	Type	Total years in 5	Years as Years as	Years as	Total revenue \$e	Year became top 3	Year stopped being top 3	
1 Symbicort	Asthma (Corticosteroid)	6 of 21	1	3	2 19 864	2012, as no 3	still top 2017, no 1 (went 3,2,1)	
2 Fulvicort	Asthma (Corticosteroid)	4 of 21	0	2	2 2 827	already top 1997, no 2	2001, as no 3 (went 2, a year 3, a year not, a year 3)	
3 Nexium	Proton pump inhibitors (antacid)	16 of 21	7	3	6 61 702	2002, as no 2	still top 2017, no 3 (went a year 2, 1, 3,2,3)	
4 Losec/Pilosec	Proton pump inhibitors (antacid)	6 of 21	6	1	1 33 736	already top 1997, no 1	2004, as no 3 (went 1,2,3)	
5 Crestor	Statins (cholesterol)	12 of 21	7	1	4 53 406	2006, as no 3	still top 2017, no 2 (went 3,1,2)	
6 Seroquel	Atypical antipsychotic (schizophrenia, bipolar disorder)	10 of 21	0	8	2 35 311	2002, as no 3	2011, as no 2 (went 3,2)	
7 Zestril	Blood pressure	3 of 21	0	3	0 3 506	1999, as no 2	2001, as no 2 (only 2)	
8 Seloken/Toprol-XL	Blood pressure	3 of 21	0	0	3 2 590	already top 1997, no 3	2005, as no 3 (all 3)	
9 Zoladex	Cancer (Breast and prostate)		0	0	1 0 734	2000, as no 3	2000, as no 3 (only 3)	
Celgene								
Drug	Type	Total years in 5	Years as Years as	Years as	Total revenue \$e	Year became top 3	Year stopped being top 3	
1 Revlimid	Cancer (bone marrow, mantle cell lymphoma-MCL)	12 of 19	11	1	0 43 731	2006, as no 2	still top 2017, no 1 (went 2,1)	
2 Thalomid	Cancer (bone marrow)	13 of 20	9	3	1 3 314	already top 1998, no 1	2010, as no 3 (went 1,2,3)	
3 Pomalyst	Cancer (bone marrow, who has already received 2 other drugs)	4 of 19	0	3	1 4 667	2014, as no 3	still top 2017, as 2 (went 3,2)	
4 Vidaza	Cancer (blood, bone marrow)	6 of 19	0	4	2 3 459	2008, as no 3	2013, as no 2 (went 3,2)	
5 Abiraterone	Cancer (Breast, pancreas, lung)	5 of 19	0	1	4 3 277	2011, as no 3	2015, as no 2 (went 3,2)	
6 Akteon	Cancer (Bone marrow, breast, ovarian, neurosarcoma,	5 of 19	0	3	2 0 209	2003, as no 2	2007, as no 3 (went 2,3)	
7 Focalin	ADHD	5 of 19	0	2	3 0 188	2001, as no 2	2005, as no 3 (went 2,3)	
8 Oestradiol	Immunosuppressant (prostate, prostatic arthritis)	2 of 19	0	0	2 2 296	2016, as no 3	still top 2017, no 3 (both 3)	
Sanofi								
Drug	Type	Total years in 5	Years as Years as	Years as	Total revenue \$e	Year became top 3	Year stopped being top 3	
1 Lantus	Diabetes	11 of 19	9	3	2 61 623	2001, as no 3	still top 2017, no 1 (went 3,1)	
2 Loxonec	Blood thinner	14 of 19	5	5	4 39 048	2004, as no 1	still top 2017, no 2 (went 1,2,3,2)	
3 Aprovel	Blood pressure	4 of 19	0	1	3 1 502	already 1999, no 2	2002, as no 3 (went 2,3)	
4 Plavix	Anti-coagulant (prevents clotting, increased blood flow)	17 of 19	0	13	4 36 219	already 1999, no 3	2016, as no 3 (went 3,2,3, one year not, 3, 2,3)	
5 Sitrova/Janbin	Insomnia	6 of 19	5	0	1 7 079	already 1999, no 1	2006, as no 3 (went 1,2 year not, 3)	
6 Aubagio	Immunosuppressant (Multiple sclerosis)	1 of 19	0	0	1 17 111	2017, as no 3	still top 2017, no 3 (only 3)	
7 Taxotere	Cancer (breast, lung, prostate, stomach, head/neck)	2 of 19	0	0	2 4 916	2005, as no 3	2010, as no 3 (both 3)	
8 Bimatoprost	Cancer (colon, rectum)	1 of 19	0	0	10 933	2003, as no 3	2003, as no 3 (only 3)	
9 Allegra	Antihistamine (allergies)	1 of 19	0	0	1 1 666	2004, as no 3	2004, as no 3 (only 3)	
Bayer								
Drug	Type	Total years in 5	Years as Years as	Years as	Total revenue \$e	Year became top 3	Year stopped being top 3	
1 Xarelto	Anti-coagulant (prevents clotting)	5 of 20	4	0	1	12 967 2013, as no 3	still top 2017, no 1 (went 3,1)	
2 Kogenate	Blood clots (acts blood clots, stop bleeding)	12 of 20	2	4	6	15 412 2005, as no 3	2006, as no 3 (went 3,2,1,3)	
3 Adalat	Blood pressure	9 of 20	0	8	1	9 074 already top 1998, no 2	2006, as no 2 (went 2,3,2 last year)	
4 Betaseron	Immunosuppressant (Multiple sclerosis)	8 of 20	3	4	1	11 558 2006, as no 3	2013, as no 2 (went 3,2,1,2 last year)	
5 Coproxon	Antibiotic	7 of 20	7	0	0	10 404 already top 1998, no 1	2004, as no 1 (all 1)	
6 Yaz/Yazmin	Contraceptive	6 of 20	3	1	2	9 316 2007, as no 1	2012, as no 3 (went 1,2,3)	
7 Mirena	Contraceptive	2 of 20	0	0	2	2 360 2014, as no 3	still top 2017, no 3 (3, 2 year not, 3)	
8 Axcemia	Diabetes	3 of 20	1	0	2	2 335 2003, as no 3	2005, as no 3 (went 3,1)	
9 Eylea	Eye disease	3 of 20	0	3	0	5 286 2015, as no 2	still top 2017, no 2 (all 2)	
10 Aspirin	Pain relief	4 of 20	0	0	4	2 412 already top 1998, no 3	2002, as no 3 (only 3)	
11 Lipobay/Baycol	Statins (cholesterol)	1 of 20	0	0	1	0 587 2000, as no 3	2000, as no 3 (only 3)	
GlaxoSmithKline								
Drug	Type	Total years in 5	Years as Years as	Years as	Total revenue \$e	Year became top 3	Year stopped being top 3	
1 Advair/Seride	Asthma (corticosteroid)	16 of 18	15	1	0	98 250 2002, as no 2	still top 2017, no 1 (went 2,1)	
2 Flovent	Asthma (corticosteroid)	4 of 18	0	1	3	5 197 already top 2000, no 3	2011, as no 2 (went 3, 8 year not, a year 3, 2)	
3 Augmentin	Antibiotic (penicillin)	3 of 18	0	2	1	5 683 already top 2000, no 2	2002, as no 3 (went 2,3)	
4 Relenza	Antiviral (flu pandemic)	2 of 18	0	1	1	3 225 2005, as no 3	2005, as no 2 (bo of flu pandemic)	
5 Truneq	Antiviral (HIV)	3 of 18	0	2	1	6 630 2015, as no 3	still top 2017, no 2 (went 3,2)	
6 Tivvy	Antiviral (HIV)	2 of 18	0	0	2	3 096 2016, as no 3	still top 2017, no 3 (both 3)	
7 Valtrex	Antiviral (genital herpes, cold sores, shingles)	3 of 18	0	2	1	6 113 2007, as no 3	2005, as no 2 (went 3,2)	
8 Sertraline/Paxil	Antidepressant	5 of 18	3	1	1	13 127 already top 2000, no 1	2004, as no 2 (went 1,2,3)	
9 Wellbutrin	Antidepressant	1 of 18	0	0	1	1 558 2003, as no 3	2003, as no 3 (only 3)	
10 Lamictal	Anticonvulsant	4 of 18	0	1	3	7 292 2005, as no 2	2008, as no 3 (went 3,2,3 last year)	
11 Avandia	Diabetes	3 of 18	0	3	0	6 722 2004, as no 2	2006, as no 2 (all 2)	
12 Infanrix/Pediaris	Vaccine (combination toddlers)	5 of 18	0	3	2	6 168 2011, as no 3	2015, as no 2 (went 3,2)	
13 Avodart	Benign prostatic hyperplasia	3 of 18	0	1	2	3 920 2012, as no 2	2014, as no 3 (went 2,3)	

Johnson & Johnson		From year of launch to present					
Drug	Type	Total years in t	Years as Years a	Years as Years a	Total revenue ye	Year became top 3	Year stopped being top 3
1	Benicade	16 of 16	11	0	5 71 722	already 2002, no 3	still top 2017, no 1 (vent 3, 1)
2	Stelara	3 of 16	0	3	0 9 717	2015, as no 2	still top 2017, no 2 (all 2)
3	Risperdal	7 of 16	2	3	2 28 686	already 2002, no 2	2011, as no 3 (vent 2, 1, 3 years not, 3)
4	Traxeta	1 of 16	0	0	1 2 563	2017, as no 3	still top 2017, no 3 (only 2017)
5	Procrit/Epren	11 of 16	3	6	2 30 955	already 2002, no 1	2012, as no 3 (vent 1, 2, 3, 2, 3)
6	Dlyso/Sostad	1 of 16	0	1	0 2 302	2014, as no 2	2014, as no 2 (only 2)
7	Prezista	1 of 16	0	0	1 1 673	2013, as no 3	2013, as no 3 (only 3)
8	Levaquin/Floxin	1 of 16	0	0	1 1 550	2009, as no 3	2009, as no 3 (only 3)
9	Zyga	4 of 16	0	1	3 8 426	2013, as no 2	2016, as no 2 (vent 2, 3)
10	Velcade	1 of 16	0	1	0 1 500	2012, as no 2	2012, as no 2 (only 2)
11	Topamax	2 of 16	0	1	1 5 184	2007, as no 3	2008, as no 2
Gilead Sciences		From year of launch to present					
Drug	Type	Total years in t	Years as Years a	Years as Years a	Total revenue ye	Year became top 3	Year stopped being top 3
1	Harvoni	3 of 21	3	0	0 27 375	2015, as no 1	still top 2017, no 1 (all 1)
2	Sovaldi	3 of 21	1	2	0 19 560	2014, as no 1	2016, as no 2 (vent 1, 2)
3	Epclusa	1 of 21	0	0	1 3 510	2017, as no 3	still top 2017, no 3 (only 3)
4	Virode	2 of 21	2	0	0 0 018	already top 1997, no 1	1998, as no 3 (both 1)
5	Amplia	9 of 21	4	4	1 21 004	first 2006, no 3	2014, as no 2 (vent 3, 2, 1, 2)
6	Truvada	13 of 21	4	5	4 30 223	2004, as no 3	2016, as no 3 (vent 3, 2, 1, 2, 3)
7	Viiad	13 of 21	4	2	7 8 237	2001, no 2 (first year with)	2013, as no 3 (vent 2, 1, 2, 3)
8	Descova	1 of 21	0	1	0 3 674	2017, as no 2	still top 2017, no 2 (only 2)
9	AmBisome	7 of 13	3	3	1 1 251	1999, as no 1	2005, as no 3 (vent 1, 2, 3)
Amgen		From year of launch to present					
Drug	Type	Total years in t	Years as Years a	Years as Years a	Total revenue ye	Year became top 3	Year stopped being top 3
1	Enbrel	12 of 21	3	7	3 52 266	2004, as no 3	still top 2017, no 1 (vent 3, 2, 1)
2	Neulasta/Neupogen	20 of 21	10	10	0 67 987	already top 1997, no 2	still top 2017, no 2 (vent 2, 1, 2, 1, 2)
3	Aranesp	15 of 21	1	3	11 33 995	2001, as no 3	still top 2017, no 3 (vent 3, 2, 1, 2, 3)
4	Epogen	10 of 21	7	1	2 20 601	already top 1997, no 1	2012, as no 3 (vent 1, 2, 1, 3)
5	Xgeva	1 of 21	0	0	1 1 221	2015, as no 3	2015, as no 3 (only 3)
6	Infergen	4 of 21	0	0	4 0 539	1998, as no 3	2001, as no 3 (all years no 3)

Bristol-Myers Squibb		From year of launch to present					
Drug	Type	Total years in t	Years as Years a	Years as Years a	Total revenue ye	Year became top 3	Year stopped being top 3
1	Opdivo	2 of 21	2	0	0 8 722	2016, as no 1	still top 2017, no 1
2	Onczia	4 of 21	1	1	2 8 291	2014, as no 2	still top 2017, no 3 (vent 2, 1, 3)
3	Abilify	3 of 21	3	6	0 20 146	2006, as no 2	2014, as no 1 (vent 2, 1)
4	Plavix	12 of 21	8	3	1 48 328	2001, as no 3	2012, as no 2 (vent 3, 2, 1, 2)
5	Eliquis	3 of 21	0	3	0 10 075	2015, as no 2	still top 2017, no 2 (all no 2)
6	Pfizerichol	10 of 21	7	2	1 19 955	Already top 1997, no 1	2006, as no 3 (vent 1, 2, 3)
7	Sustiva	2 of 21	0	1	1 3 141	2012, as no 3	2013, as no 2 (vent 3, 2)
8	Reyatac	5 of 21	0	0	5 7 232	2008, no 3	2013, as no 3 (all no 3, one year not top)
9	Glucophage	5 of 21	0	2	3 6 533	already top 1997, no 3	2001, as no 2 (vent 3, 2)
10	Taxol	7 of 21	0	3	4 8 277	already top 1997, no 3	2004, as no 3 (vent 2, 3, one year not top)
11	Sprycel	2 of 21	0	0	2 3 113	2014, as no 3	2015, as no 3 (all no 3)
12	Avapro	3 of 21	0	0	2 2 168	2005, as no 3	2007, as no 3 (not top 2006)