Work Project

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The patent expiry as a major inflection point in a branded Rx drug's life and strategies to counter generic competition - exemplified at Pfizer's blockbuster drug Lipitor® in the USA

A project carried out in the area of Strategy/ Marketing under the supervision of: Luis Fructuoso Martinez
Abstract

A large number of expensive, but highly profitable branded prescription drugs will go off-patent in the USA between 2011 and 2015. Their revenues are crucial to fund the immense costs associated with the development of an innovative drug. The rising cost pressure on pharmaceutical stakeholders has increased the demand for more affordable medications, as provided by the branded drug's generic counterpart. Yet, research based incumbents are moving beyond the traditional late lifecycle strategies and deploy more aggressive tactics in order to protect their brands, as seen with *Pfizer's Lipitor®*. It is doubtful, whether these efforts will help the blockbuster business model to resist current market conditions.

Keywords: US pharmaceutical industry, counter-generic strategy, extended lifecycle, *Lipitor®*
1. Introduction

The pharmaceutical industry has reached a turning point in its history, which is commonly referred to as the "patent cliff" and marks the end of Big Pharma's blockbuster business model [1,2, p. 8]: Between 2011 and 2015, several hundred branded prescription drugs of a combined annual sales value of US$170 billion [3] – that is more than 80% of Portugal's 2012 GDP [4] – lost and are going lose patent protection. Among them are 60% of the US Top 10 selling drugs in 2011, as shown in illustration (ill.1).

Illustration 1: US Top 10 pharmaceutical prescription drugs by sales in 2011 of a combined annual sales volume of almost US$33 billion losing patent protection in the USA [5].

Many key therapeutic classes, such as high cholesterol, will be dominated by cheap generics, that address the main stakeholder's needs more effectively than the research-based industry leaders.

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1 Note that words printed in bold either indicate industry specific terms explained in the glossary (appendix) or highlight important facts in order to ease reading and comprehension.
Within six months, most branded blockbuster drugs will lose 80% market share in the respective molecule market [6]. Industry leaders are consequently left with a huge financial gap, because it is not unusual that branded blockbuster drugs account for 25% and sometimes even 50% of firm revenue (ill.1). What appears to be a nightmare for marketers, has become reality for Pfizer's ultimate cash cow, the cholesterol-lowering pill Lipitor®. In 2011, the world's best selling branded drug in history lost patent protection in the USA and was handled as the greatest generic opportunity that ever existed [1].

In contrast to generic firms, however, it is research-based pharmaceutical companies that drive medical progress through their innovations and thus benefit therapeutic advancement [7]. A steady cash flow is a necessary condition to further justify and fund R&D investments, since development of an innovative drug with associated costs of US$1 billion is very expensive [8]. With empty pipelines, however, research-based pharmaceutical firms will need to focus on extending the product lifecycle of already approved blockbuster drugs with counter generic strategies in order to recoup R&D expenditures [9, p. 225]. Each additional day of market exclusivity can earn the company as much as US$13 million [10, p. 18].

Under those circumstances, the following work project will investigate why the patent protected term is crucial to branded drugs and what strategies a firm has available to counter generic competition. The focus will hereby lie on the USA as the world's largest market for prescription drugs [11]. In order to give the reader a key understanding, a short key figure overview of the US pharmaceutical market will be provided. It follows a brief introduction to the political and regulatory market environment stressing the influence of diverse stakeholders that further increase the complexity a pharmaceutical firm is operating in. It will be shown that the pharmaceutical lifecycle follows a trichotomy consisting of a tedious, costly and risky developmental stage, a monopoly-like commercial period and a late post-patent stage, when generics will conquer the market [12]. The most popular patent extension strategies to minimize branded sales erosion will be presented and classified in terms of timely impact, nature and
popularity. The second part of the work project will deal with the patent expiry of Pfizer's Lipitor®. After a short introduction to the respective therapeutic class and a brief history on Lipitor's® commercial life, tactics deployed by Pfizer to protect its blockbuster drug sales will be presented and evaluated in terms of effectiveness. The conclusion will question the current research-based pharmaceutical business model.

2. Market overview

The pharmaceutical market can be divided into two segments: Over-the-counter (OTC) and prescription (Rx) drugs. OTC drugs are prescription-free remedies that can be obtained at any pharmacy and grocery store. Rx drugs, on the other hand, are pharmaceuticals that are available at doctor-prescription only and are solely distributed at pharmacies or hospitals as part of the patient treatment. The logic behind this classification is that some conditions can be treated without a doctor's guidance, such as a mild cold, while others require the supervision of a physician like heart disorders [10, p. 5f.]. Generics are a third group of pharmaceuticals, that can be found in either of the two market segments: Generics are chemically identical and undifferentiated copies [13] of the branded OTC or Rx product and are much more affordable, given their availability at 1/10 of the original's price [14].

Illustration 2: Key US pharmaceutical market figures with total volume [15, p. 21/30], total value [15, p. 21] and Rx value [15, p. 27] and volume in 2011 [16, p. 10] and 2015 [16, p. 13].
The first part of ill.2 displays the US pharmaceutical market share in terms of volume and value between OTC and Rx drugs. Although only every fourth pharmaceutical sold in the US is a prescription drug, Rx drugs almost conquer all market value, since branded Rx drugs are on average thirteen times more expensive than OTC remedies [17]. The second part of the graph further splits the Rx market into branded and generic drug sales and displays the increasing dominance of generics.

**Research-based** pharmaceutical companies –also referred to as Big Pharma or incumbent in this paper– such as Pfizer have earned a tremendous amount of money by developing and marketing branded Rx drugs with margins of up to 90% [18]. Some of them had lifetime revenues of over US$140 billion within 10 years thanks to the legal monopoly branded drugs hold during patent protection [19]. **Patents** are in fact the pharmaceutical industry's foundation and are issued upon application by the national government [20, p. 81]. With drugs, the most important patent protects the molecule, which is a chemical compound identified to treat a specific symptom or condition. The internationally standardized patent protection term is 20 years starting with the date the patent is filed [9, p. 230 f.] Deducting the period of drug development, a branded drugs has available a ten year market exclusivity on average, which is given in exchange for the substantial investment related to the drug discovery. This is a relatively short time in which the research-based company can extract monopoly rents from its branded remedy before patent expiry [20, p. 87]. It is the company's chance to build considerable brand equity and goodwill [9].

### 3. Regulatory and political environment

The health care system in the US can be defined by a triangular structure, which encompasses three **stakeholder** groups that can substantially impact business operations: The patients, who require medical care, the providers, who give medical care and the payers, who finance medical care (ill.3) [21].

Health care –as a public good– is either funded by government programs or private insurance
3. Regulatory and political environment

plans [12]. Government programs cover round about one third of US Americans and are only accessible by low income or disabled people and seniors. Most US citizens are privately insured through their employers. Those employers finish contracts with private insurance companies [21].

When purchasing an insurance covered prescription drug, the insured person is asked for a co-payment. This is a small fixed, non-refundable amount the consumer needs to pay, while the insurance company will pay the remaining drug retail price. The patient is charged a different level of co-payment depending on the type of drug purchased: With generics, the patient's share usually is US$10 or less. Out of pocket costs for branded products, on the other hand, are either US$25 or US$50 depending on the drug's placement on tier two or three, which is subject to the individual insurance plan [22]. In order to promote generics, their co-level payment has only increased slightly with time, while branded drugs have become more expensive to patients (ill.3) [23, p. 7].

Worldwide, the US has the highest health care expenditures, accounting for 18%\(^2\) [24] of the nation's GDP and increased by more than 1000% between 1980 and 2010 from US$217 billion to US$2.18 trillion per year [25]. The trend of escalating drug expenditures will continue given the demographic transition with elderly usually requiring more health care services than young people [26]. This development will not only put further pressure on the government's public health care programs, but also increase the financial burden of private customers and employers [27]. This is because insurance companies tend to pass on the rising health care costs by demanding higher premiums and co-payments. The arising need for a more inexpensive solution to costly branded pharmaceuticals has thus fostered the generic business boom [20, p. 39]. National laws, regulations and campaigns have been implemented to further encourage the use of generics instead of brands [9, p. 226]. Those efforts aim at controlling costs and satisfying health-care demand at a more reasonable price. In fact, thanks to the Hatch-Waxman Act enforced in 1984, an estimated US$1.2 trillion have been saved through the usage of generics between 2003

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\(^2\) In comparison, other developed countries spend 8-11% of their GDP on health care.
4. The pharmaceutical product lifecycle

and 2012 [28]. This legislation encourages generic manufacturers to challenge the branded drug's patent at any time, so that the research-based manufacturer would lose its market exclusivity and cheap generics could sooner enter the market. This process is triggered by a **180 post-patent market exclusivity** reward that is granted to the first generic manufacturer that successfully challenges a branded drug's patent and is approved by the Food and Drug Administration (FDA) [9, p. 232f., 29, p. 261]. Those are six very profitable months for the first generic, since limited competition allows for fairly high drug prices.

The **FDA** is the federal regulatory body responsible for the protection of public health. Each drug company, that wants to sell its treatments in the US – indifferent of being a branded prescription and OTC drug or a generic version of them – needs FDA approval. In order to make a decision on market authorization, the FDA will examine the drug's clinical study results [30].

**4. The pharmaceutical product lifecycle**

![Illustration 4](image)

**Illustration 4:** The product lifecycle of a branded prescription drug [20, p. 41, 10, p. 15, 31, p. 41].

The product lifecycle of branded Rx pharmaceuticals is different from the standard marketing model. In most cases, an approved drug undoubtedly passes the four different stages – intro-
duction, growth, maturity and decline— as suggested by the standard scheme. The extended pharmaceutical model however encompasses two more lifecycle periods [20]. Especially the developmental stage is crucial to understand Big Pharma's dependency on branded blockbuster revenue and their efforts to protect them in the late post-patent period. Given the number of stakeholders and market influences the lifecycle shape and duration is fairly unpredictable: Latest clinical trial results or changing regulatory requirements can essentially alter a drug's life [12]. Ill.4 displays the typical pharmaceutical lifecycle for a branded mass-market prescription drug with its three different periods. Those are presented in the following.

### Developmental life

A drug passes several phases in the R&D process that are briefly specified and characterized in terms of time, investment and risk in ill.5.

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<thead>
<tr>
<th>Phase</th>
<th>Research</th>
<th>Development</th>
<th>Review</th>
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<td>Sub-phase</td>
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<tr>
<td>Identification of a protein associated with the disease</td>
<td>Computer modeling &amp; animal testing</td>
<td>Drug tested on 20-100 healthy individuals</td>
<td>Submission of new drug application (NDA) to FDA</td>
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<td>Usage of a chemical database to identify of a chemical molecule that affects the identified protein</td>
<td>It aims at — Showing drugs safety — Asking regulatory body's permission to study the drug in the human body</td>
<td>It aims at — Observe body reactions (absorption, distribution) — Assessing possible side effects — Determining a safe dose</td>
<td>Drug approved to be sold for specific indication and formulation in respective market</td>
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<td>Chemical molecule becomes a drug candidate</td>
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<td>Drug tested on 100-500 sick individuals</td>
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<td>Drug tested on 1000-5000 sick individuals</td>
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### Illustration 5: The drug discovery process with sub-phase description [32,33,34,35], time, risk [36, p. 6] and cost characteristics [37,38].

It takes ten years on average from the discovery of a new chemical molecule to the resulting drug's market introduction. Since research-based pharmaceutical companies all use the same chemical databases for the identification of a suitable molecule to treat a specific condition, they
are advised to file a patent as soon as possible. Firms otherwise risk to have the exclusive market rights reserved by a competitor, who is equally eager to identify the chemical mechanism that could earn its company billion of dollars [10, p. 17].

In 2011, pharmaceutical companies accounted for 20% of all R&D expenditures spent by US businesses, that is US$67 billion in absolute numbers [39, p. 5]. Despite this billion dollar budget, return has been minimal [40]. Expenditures for drug development increased by 90% [41] while the approval rate of new molecular entities –a metric for R&D productivity– dropped by almost 18% compared to 15-20 years ago [42]. One reason for the development is that it becomes increasingly difficult to develop drugs that are superior to existing treatments. Likewise, approval standards for a drug's market introduction have become increasingly stringent due to safety concerns that were triggered by drug scandals as the case with Merck's blockbuster drug Vioxx® [23, p. 8]: In 2004, the very effective rheumatism treating drug was instantly taken out of the market, after press revealed that the use of Vioxx® was linked to at least 55,000 deaths in the US. Even more astonishingly: Merck knew its drug was fatal, but used statistics to hide the pill's dangerous side effects in order not to jeopardize market approval [43,44]. That some pharmaceutical companies knowingly and willingly act unethically can be explained by the fact that sunk costs for the drug development increase as time passes: A phase III failure is with almost 95% of total development cost spent considerably more expensive than a preclinical one (ill.5). Given the significant amount of drug development, it is in the company's interest to push a promising product to the market, even if data reveals negative surprises in the drug's safety profile [36].

Considering that only one out of 10,000 substances explored will receive market approval, attrition rate is high and investment risk enormous (ill 5). A Forbes article offered some perspective on how attrition drives development costs [45]: Astra-Zeneca suffered from several developmental failures, so that average costs of new drug development has been escalated to
US$12 billion, which is ten times higher than the average of US$1 billion [41,46].

Even if a branded drug masters market approval successfully, it does not mean that it will generate sufficient revenue to cover its R&D spending: Only one third of approved branded drugs is able to fully recoup their pecuniary investment [10, p. 19]. Hence, the research-based company's top performing products also need to compensate for approved drugs that have not enough financial strengths or those that have never been approved.

**Commercial life**

With the drug approval, a new molecule market is created, that is completely owned by the branded manufacturer. This market concentration will only decline when patent protection is lost and generic competitors can enter the molecule market. Meanwhile, the branded pill passes the same stages as suggested by the **standard product lifecycle** model. **Marketing mix** components will help to fully reveal the drug's potential. With the introduction of a new product, resources are often taken away from already established products in order to support newcomers [47]. Thereby, market penetration depends on a combination of already existing treatments, the new products efficacy, as well as treatment risks [10, p. 25]. Given that pharmaceuticals deal with an individual's most important assets, their health, there is unsurprisingly no other industry that is more regulated than the pharmaceutical one. Those regulations do not only affect the drug's safety profile and manufacturing processes – hence the **product** dimension – but the remaining marketing mix components accordingly [23, p. 1] and should thus not be neglected in their impact on the drug's profitability. In most countries **price** regulations are in place to counteract the patent monopoly's price setting-power and keep costs at a reasonable level [23, p. 8]. In the US however, price control mechanisms do not exist, allowing the branded manufacturer to achieve margins of up to 90% [29, p. 256, 265]. The US is one of two countries that doesn't prohibit Direct-to-

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3 Note that data on R&D costs per drug developed differ widely from US$340million to US$1,5 billion. The mean of roughly US$1 billion will be taken as reference in this paper.
Customer (DTC) advertisement for prescription drugs [23, p. 7]. This allows pharmaceutical companies to use the power of branding and position the drug according to unmet consumer needs. Prescription drug branding in non self-pay markets, such as the US, however is not as effective as it is with consumer goods or OTC products, since providers and increasingly payers dictate the buying decision [20, p. 188f.]. Providers can be convinced by scientific clinical data presented by the company’s sales force. Price sensitive payers on the other hand do not have any brand loyalty and are only interested in choosing the cheapest drug available [20, p. 40]. Distribution is the least controllable marketing mix component, as prescription drugs can only be dispensed by pharmacies, hence prohibiting firms from directly selling to the consumer [10, p. 5f.]. It will therefore not further be considered.

**Late life**

The actual turning point in a drug’s life however is the entrance of generic competition, as a consequence of patent expiry. Given that generic producers can challenge a patent at any time in the USA (Hatch Waxman Act), they might even enter the market prior to the regular patent expiry. Generic companies rely on the incumbent’s intellectual property, which is why they do not have to repeat expensive clinical studies for their products [2, p. 5]. This absence of substantial investments and liability decreases entry barriers and allows generic firms to solely compete on price [9, p. 225, 231, 29, p. 261].

As generics enter the market, branded profits erode quickly, since demand is shifted to the cheaper generic alternatives. The higher the number of competitors, the more will price levels approach marginal costs [9, p. 227]: In case no generic manufacturer is granted the 180 days market exclusivity after patent loss, several generic competitors will simultaneously enter the molecule market, causing a prompt price drop of 80% [48]. Elsewhere, prices remain fairly high and only decrease by 10-15% [49] in the first six months due to limited competition. In either case however, 90% of branded prescription volume in big therapeutic classes will be substituted by generics within 12 months after patent expiry, provoking a 65% decline in branded drug’s
Against this background, it is estimated that each additional day of market exclusivity earns the firm US$1.3 million, with blockbuster drugs it is even US$13 million [10, p. 18]. Hence, apart from maximizing sales during the drug's commercial life, a firm should apply tactics that either prolong market exclusivity or soften the impact of generic competition [9, p. 227].

5. Counter generic strategies

Research-based manufactures have a number of options available to extend the commercial life or protect the revenues of their brands. Literature provides many approaches to classify those strategies [10, p. 75ff]. The existing lack of consistency in strategy systematization gives a chance for a self-conceptualized classification model, as displayed in ill.6.

**Illustration 6:** Most popular [50] counter generic strategies deployed by research-based manufacturers in terms of impact [9, p. 227] and nature [10, p. 80].

The model above distinguishes three strategic categories – legal, marketing mix and business
model related actions—and characterizes their sub-strategies in terms of timely impact on generic competition (x-axis), nature (y-axis) and popularity of usage (size of geometrical form). Note that those options represent not all, but the most popular counter generic strategies.

**Litigation**

Drugs have multiple patents protecting it. While the most important patent covers the molecule, there are other elements that can be patented as well, like the method of manufacturing or newly approved indications. Those secondary patents are often filed in the later commercial life in order to raise barriers of entry for generic competitors. The popularity of strategic patenting has increased over time, given that a branded drug nowadays can be protected by up to 40 different patents, compared to only two patents 20 years ago [9, p. 248f., 10]. The higher the number of patents, however, the increased the likelihood of a technical defect with one of those patents, which is a promising starting point for a successful patent challenge [10, p. 80]. If a generic firm challenges one of those patents in court at any time, the incumbent is likely to defend the brand’s intellectual property. The majority of those litigations is settled out of court: In exchange for a payment or other concessions by the branded manufacturer, the generic firm will either drop the patent challenge or postpone generic market entry [20, p. 107ff]. The latter applies if one generic manufacturer was granted a six month exclusivity period. There have been settlements that delayed generic competition of up to 10 years [51], virtually doubling the branded drug’s commercial monopoly period. Those arrangements are highly controversial given the antitrust-like character [52]. **Generic settlement** is nevertheless the only tactic that effectively prevents generic competition for a certain period of time – 5 years on average [51] – and is thus the most popular one.

**Promotion**

Albeit marketing expenditures for the branded drug typically drop by two thirds as patent expiry approaches, 40% of research-based companies use promotional tactics to combat generic competition [9, p. 237]. Promotional effort in the late stage of the drug’s lifecycle is often
targeted toward stakeholder that influence the final dispensing decision, because as soon as generics enter the market, the health care system seems to rather focus on cost than value. The US is a payer-controlled market which is why promotion in the late stage focuses on both, insurance companies, that bear the major part of pharmaceutical costs, as well as patients, that are charged a higher co-payment for branded drugs (ill.2) [20, p. 188f.]. The purpose of promotional programs targeting the end-customer is to further strengthen brand loyalty by advertisement while simultaneously lowering end-user's financial exposure with co-payment coupons [53]. Payers are also addressed with financial incentives.

**Strategic Pricing**

In the US, price is the least regulated marketing variable and plays the key role with the generics' cost leadership. The more effective a branded drug, the higher the price it can charge. The argument of effectiveness however is nullified when generics enter the market and offer the same drug at a substantially lower price [20, p. 194]. Strategic pricing has become a key focus for research-based companies, since payers try to reduce health care expenditures [54]. The incumbent will either decrease or increase the drug's price – maintaining the current price level is usually no option. By charging a price premium, the branded manufacturer will accept to lose the price-elastic segment to generic competitors. Instead, it will focus on the cost-insensitive and loyal customers and retain a low, but highly profitable market share in order to offset part of the decline in sales volume [9, p. 228]. In contrast, the incumbent can also decrease the costs of therapy either by directly lowering the drugs' retail price or by giving volume rebates. Discounting has a more aggressive character, because it nullifies generics' competitive advantage, as long as the firm is able to decrease prices by the same magnitude of generic competitors [20, p. 194f.]. Given that very loyal customers are likely to stay with the brand for an extended period of time, the value extracting tactic is attributed a longer term impact than a price decrease.

**Product Line extensions**

Line extension tactics try to improve the brand's clinical profile in terms of efficacy, side effects
or patient compliance in order to differentiate it from generics [20, p. 116f./169]. Given that the incumbent knows the market very well, it can more effectively respond to unmet needs and thus provide a higher value to patients [9, p. 229]. In the past ten years, almost one third of newly approved drugs in the US have been reformulations such as easy-to-swallow pills. That tactic encompasses changes in the existing drug's form or dosage, which allows for more flexibility and better customization [20, p. 140]. Combination drugs on the other hand are fixed formulations with two molecules. They help patient convenience, as they only need to take one pill instead of two. In order for this tactic to be successful, the number of patients that receive both medications at the same dosage must be large enough, otherwise the additional costs of development will not pay off [20, p. 152ff.]. Additional clinical studies are required for all line extension tactics and often help to identify new indication areas for the branded drug [55]: Viagra®/ Pfizer, for example, was originally developed to treat angina and later approved for erectile dysfunction [9, p. 245]. Indications expansion deals with the process of identifying new areas of therapy for the approved drug apart from its current indication. Drugs approved for multiple indications need to carefully consider pricing strategies in the various markets in order to prevent the risk of arbitrage. Besides, this tactic does not prevent doctors from prescribing generic off-label for the newly approved indication [20, p. 126]. This is a major threat with all four product line extension tactics: Only the new invention will be granted an additional market exclusivity of either three years (new indication reformulation) [9, p. 245], five years (combination drug) [56] or seven years (next generation) [57, p. 2.4]. Hence, the respective tactics will contribute little to defend sales of the original after patent expiry. The ultimate purpose of a product line extension is therefore to either switch as many patients as possible to the modified original or to extend the existing market to exploit brand potential. One could even speak of a planned cannibalization, as is the case for next generation drugs that can be seen as follow-on product [10, p. 94].

**Branded generics**

The research-based manufacturer is allowed to introduce or license a generic version of its
branded drug –also referred to as **authorized generic** or fighter brand– at any time. This also applies for the 180 days exclusivity period, which is granted to the first generic manufacturer to successfully challenge a branded drug's patent [9, p. 242].

The approach enables the company to drive different pricing policies without harming brand perception: The original brand might experience a price premium in order to increase profitability. The fighter brand, on the other hand, may be simultaneously sold at a significant discount to capture part of the price conscious segment that would otherwise been completely lost to generic competitors. This allows the incumbent to expand the market and sustain an ongoing return on investment – though at a lower profitability – over a longer period of time [20, p. 198ff.]. The tactic's timely impact depends on the firm's decision on whether it wants to engage in a price war (the longer) or not (the shorter the generation of additional sales). Branded generics sales help to fully utilize existing manufacturing capacity. That way, the incumbent will not compromise economies of scale benefits, that would normally vanish with generic competition related sales erosion [20, p. 201]. Given that generic companies "have the right relationships, the right [massive] portfolios, the right selling structures and mind-sets" [20, p. 201], they are best to commercialize the copied brand manufactured by the research-based company. That may be the reason why the tactic is only applied by 28% of research-based companies (ill.6).

**Rx to OTC switch**

The OTC switch describes the process of launching an OTC version of the original Rx drug in the consumer market [10, p. 96]. Severing the prescription-free market however requires different skills and expertise –as the case with branded generics. One difference to the Rx drug segment is that pharmaceutical branding is much more effective, since the consumer takes the buying decision. The OTC switch adds an additional stream of revenue by capturing patients that typically would not go to see a doctor. Apart from an additional three-year market exclusivity period (ill.6), prescription-free drugs represent long-term opportunities [20, p. 178ff.]. *Listerine® (Johnson & Johnson)* for example, is sold over the counter since 1914 and still generates high
sales, exceeding US$1 billion in the US alone [58,9, p. 243]. An OTC switch will only be approved if the company can successfully prove patient's well-being and safety under self medication circumstances. This may not be feasible for brands of therapeutic classes with less perceptible symptoms [20, p. 185]: Patients that suffer from high cholesterol, for instance, do not instantly feel the benefits of their treatments, "nor do they feel the consequences of not taking it" [20, p. 179]. In order to further increase a drug's qualification for self-management purposes, lower dosage strengths are often introduced to the OTC market, because they cause fewer side effects [20, p. 180]. Cannibalization effects are only expected when patient's co-payment for the prescription drug exceeds the cumulated package price of OTC drugs necessary to replicate the prescription dosage [20, p. 191].

6. Context of the case – the anti-cholesterol market and Lipitor's® History

Cholesterol is a type of fat that is produced by the liver and found in animal products, such as meat, milk or eggs. High cholesterol clogs arteries and hinders the blood from flowing through the body. This can cause coronary artery disease, the most common type of cardiovascular disorder responsible for heart attacks and strokes. The probability of suffering from high cholesterol rises with unhealthy eating habits, obesity and age [59]. About one third of the US population suffers from high cholesterol [60]. Furthermore since medication cannot cure, but merely treat the disorder, market potential is huge [61].

Statins are the most effective drug class in fighting high cholesterol. The most common statin molecules are simvastatin and atorvastatin. The first statin was Mevacror®, chemically known as lovastatin, developed by Merck and introduced in 1987. It steadily lost its dominant position, as other superior statins entered the market. Ten years after its introduction, Mevacror® hardly had a 10% market share, although its patent was only going to expire in 2001. Merck meanwhile developed a drug of a second statin class, simvastatin, that was branded and commercialized as Zocor® in 1992. Zocor® was more effective than existing statins and within five years it had
become the market leader holding a 40% market share until Lipitor® was launched [62]. Apart from the second best selling statin drug that time, Pravachol® (pravastatin)/ Bristol-Myers Squibb and the less successful Locol® (fluvastatin)/ Novartis, Lipitor® entered the US market fifth in early 1997, introducing another high-potent statin class, atorvastatin [63, p. 1]. Just 18 months after its introduction, Lipitor® had taken market leadership in the statin market (ill.7) and was about to become the world's best selling drug in history, turning Pfizer into the world's largest pharmaceutical firm.

Lipitor® was developed in the early 1990's. The patent for its atorvastin molecule was filed in March 1990 in the US, granting it a 20 year protection until March 2010. Thanks to a fast track strategy, it was FDA approved in December 1996 and legally left with 13 years and three months market exclusivity [62]. Much of Lipitor's® success can be attributed to its excellent clinical studies, that confirmed its higher effectiveness, involving more than 80,000 patients⁴ [63, p. 1]. Safety is key in the pharmaceutical industry, which is why this extensive clinical program established reliability and trust among prescribers. In addition, the investigation of different dosages within those 400 clinical studies helped physicians to better determine the suitable drug strengths for a broad range of patients, facilitating their daily business [63, p. 1,64]. Lipitor® was thus positioned with a convincing value proposition of superior therapeutic performance and convenience. This combined with Pfizer's marketing skills helped to establish Lipitor's® as the dominant drug in its class. Pre-marketing efforts included a cholesterol education campaign and the identification of key opinion leaders. Pfizer pushed for a fast market penetration and targeted prescribers with the statin market's largest sales force. It additionally deployed a moderate pricing strategy for Lipitor® by pricing it slightly below the three leading competitors (ill.7). This together with the favorable clinical results, was a winning combination [62]. Lipitor's® annual sales peaked at more than US$13 billion in 2006, occupying almost half of the statin market (ill.7) [65]. When Zocor® however lost its US patent protection the same year, market dynamics

⁴ Clinical studies usually only encompass some thousand patients (ill.5).
changed dramatically. Sold at a 40% discount, generic simvastatin quickly gained market share, and –although a more effective statin –also affected Lipitor®: Its statin market share dropped by 18% from 44% in 2006 to 26% in 2009 [66]. This result exemplifies well that key pharmaceutical stakeholders value costs savings over therapeutic benefit. In less than a year lost blockbuster Zocor® almost all of its market presence. The same was going to happen to Lipitor® in early 2010, when the branded drug's US patent was going to expiry in its most important market. Until then, Lipitor's® cumulated global lifetime sales added up to US$118 billion [65]. Part of its lifecycle is summarized in ill.8.

Illustration 8: Lipitor’s® commercial life and counter generic tactics deployed [67].

7. Strategies deployed by Pfizer to protect Lipitor®

Pfizer did not leave the atorvastatin market to generics without a fight. It deployed a variety of counter generic tactics –as summarized in ill.6 and ill.8– in order to defend branded sales [68]. Pfizer's goal was to retain at least 40% of the combined prescription market share for Lipitor® and its authorized generic for at least six months after patent expiry [69].
Pay for delay

In 2003, Indian-based Ranbaxy Pharmaceuticals, was the first manufacturer to successfully challenge one of Lipitor® patent and was consequently entitled to sell its generics exclusively during the 180 days post-patent period. Since then, Pfizer has been suing Ranbaxy in court to infringe patent rights related to the manufacturing process of atorvastatin. Five years later, the two companies eventually settled the case out of court and agreed to delay the introduction of generic atorvastatin to the end of November 2011 [63, p. 2]. In return, Pfizer would stop blocking Ranbaxy's efforts in introducing its generics and additionally granted Ranbaxy the right to sell a generic version of Pfizer's less successful combination drug Caduet® seven years before its actual patent expiry [27]. This settlement earned Pfizer an extra 20 months of exclusivity associated with an additional US sales of almost US$10 billion (ill.8).

Promotion

In 2010 Pfizer launched the discount program "Lipitor® for you", that was heavily promoted through leaflets, TV ads and a website, whose subscription numbers of 750,000 US Americans [63, p. 3] exceeded Pfizer's expectations [70]. Advertisement aimed at emphasizing positive user experience and encouraging repeat purchases with messages as "If Lipitor® has been working for you, stay with it" [8].

The program was supported by a US$250 million DTC advertising budget in 2010 and US$220 million in 2011 respectively [71], maintaining Lipitor's® status as the most promoted Rx drug in the US market⁵ [2]. Given that the average annual DTC spending for Lipitor® accounted for about US$275 in previous years [2, p. 13], these are 2010/11 DTC marketing expenditures are significant and unusually high for a product only some months ahead of patent loss [54].

A co-payment offset card was the core of the "Lipitor® for you" campaign and an effective incentive to strengthen customer loyalty. The drug-maker funded coupon card reduced privately insured patient's exposure when purchasing a monthly supply of Lipitor® from US$25 or US$50

⁵ Note that the average budget of the most advertised brands in 2011 was US$100 billion [71].
to as little as US$4 [63, p. 3]. "People getting a month of lifesaving medicine for the price of a cup of Starbucks is…pretty impressive," noticed a research director [70]. In fact were those US$4 well below the usual co-payments for branded drugs or even generics.

**Price**

*Pfizer* deployed both, a retail price increase for *Lipitor®* – that was higher than the annual inflation – followed by a steep discounts for insurance companies prior patent expiry (ill.9).

**Retail prices** for a 20mg monthly supply of *Lipitor®* went up by 18% in 2011, compared to 2010’s cost of therapy. That increase was higher than the accumulated price increase between 2006 and 2009. The absolute average monthly costs of therapy in 2006 were US$108 and US$162 in 2011. That is a price increase by more than US$50 in absolute or 50% in relative numbers within five years. In 2012, retail prices for branded *Lipitor®* further increased sharply to US$178, indicating that *Pfizer* is targeting the highly profitable price-inelastic segment. The pricing policy of the final third in *Lipitor’s®* patent protected life is summarized in ill.9.

Given that the US$4 **co-pay coupon** card was available at website subscription only, *Pfizer* reached about one third⁶ [72] of those patients that have been prescribed *Lipitor®* in 2011. The remaining insured consumers though were charged up to US$50 co-pay for a monthly supply of *Lipitor®*. In order to prevent those patients from switching to the less expensive generics, *Pfizer* spent years negotiating unusual rebate agreements with insurance plans [22]: The company offered *Lipitor®* at heavily discounted retail prices to keep the drug competitive with generic alternatives. In exchange, insurance companies would effectively block the distribution of generic atorvastatin for six months after *Lipitor’s®* patent expiry until May 2012 [27]. They prevented pharmacies from dispensing unbranded copies by simply rejecting generic atorvastatin claims [73]. Some insurance companies, accepted the deal and further moved *Lipitor®* to the lowest-co payment tier, offering customers the branded drug as cheap as the generic counterpart [74].

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⁶ This percentage is based on 24 million units of Lipitor dispensed in 2011 divided by 11 (yearly supply ≈ 11 months, considering patients may forget to take the medication) with 750,000 people having subscribed to the "Lipitor® for you" website in order to obtain the US$4 co-payment coupon.
7. Strategies deployed by Pfizer to protect Lipitor®

Authorized generics
In 2011, *Pfizer* formed a partnership with *Watson Pharmaceuticals*, a generic manufacturer, to market and distribute an authorized, *Pfizer* manufactured generic atorvastatin until 2016 [75]. In return, *Watson* paid *Pfizer* a 70% royalty on generic Lipitor®-related sales [63, p. 3]. The branded generic was launched at the same time as *Ranbaxy*’s generic entered the market and was sold at a 50% discount [75]. As suggested in the theoretical presentation of counter generic strategies, *Pfizer*’s authorized generic version could capture almost half of the generic atorvastatin market in the first six months and hence mitigate financial impact of generic competition (ill.10) [76].

Rx to OTC switch
*Pfizer* is currently conducting a Phase III clinical study with a 10mg Lipitor® version in order to assess patient’s ability to autonomously lower their cholesterol levels. If clinical results are in favor of *Pfizer*, Lipitor® will be the first non-prescription statin, with a projected US$1 billion annual sales perspective. Yet, there are long-standing obstacles that dampen hopes for an extended life in the OTC drug market [77]: In 2000, 2005 and 2007 respectively, the FDA rejected to approve a non-prescription version of *Merck's Mevacor®* – the first developed statin [78, p. 2]. Although the research-based company submitted the most favorable consumer usage studies to date, concerns about the customer’s ability to manage and monitor the pill’s intake correctly and sufficiently dominated [61, p. 8].

Evaluation of Pfizer's tactical effectiveness
Ill.10 shows the US market share development of Lipitor® and its two generic equivalents in the atorvastatin market. Within six months, the branded prescription volume tumbled down from originally 100% in November 2011 to 30% in May 2012. Although *Pfizer’s* blockbuster lost plenty, data suggests that Lipitor® could preserve a higher market share than the usual off-patent blockbuster, whose prescription share six months after patent expiry accounts for roughly 20% (ill.10). Given that perspective, *Pfizer’s* counter generic strategy can be evaluated as successful.
This conclusion is further supported by a simple calculation: In the first six months after patent expiry, *Lipitor®* gained additional US sales of US$1.4 billion [72] at an average market share of 35% (ill.10). If *Pfizer* had just retained 10%, the branded drug had just generated US$0.4 billion. That is a difference of US$1 billion or the costs associated with the development of one branded drug. By the end of 2012, *Lipitor®* still owned a 18% volume market share. That is three times higher than usually the case. Apart from its successful protection in branded market share, *Pfizer* also achieved its goal of maintaining a combined market share of at least 40% at the end of the six months period: Together with *Watson's* authorized generic, *Pfizer* captured more than half of the atorvastatin market in May 2012. This share was relatively profitable given that *Watson* didn't engage into a price war with *Ranbaxy* [79].

**Illustration 10:** Prescription share (volume) of the US atorvastatin market in 2011/12 [76,80, p. 21,81].

When a branded drug's patent expiries, the original manufacturer typically shifts resources to newer products. *Pfizer* didn't because of two reasons: First, *Lipitor®* –that accounted for more than 15% of *Pfizer*’s revenue in 2010 [82, p. 20/25]– was too valuable to be casually abandoned. Second, with no new blockbuster in pipeline to fill the financial gap, *Lipitor®* was about to leave,
Pfizer could not shift resources to focus on newer products. Instead, the industry leader kept marketing expenditures nearly same level as previous years and deployed an unprecedented and aggressive mix of counter generic strategies in order to extend market exclusivity and maintain some revenue of its multi-billion dollar brand (ill.6) [47].

Pfizer's strategy worked given the following reasons. Albeit Ranbaxy challenged Lipitor's® patent successfully, Pfizer started an exhausting legal dispute, blocking Ranbaxy to introduce its own generics. Its successful defense and settlement preserved the branded incumbent multiple years of otherwise lost patent protection. It further saved the company 20 additional months of competition-free revenue, that quickly recouped litigation costs [83].

Pfizer further understood the needs and motives of consumers and did not underestimate the growing influence of payers over prescription decisions. Payers usually cannot afford to have patients staying on the more expensive branded-product, once generics are available. Thus, Pfizer offered Lipitor® at a likely 85-70% discount\(^8\), in order to nullify the projected 10-15% price advantage the first generic entrant was typically to bring [22]. When Zocor® (simvastatin) lost patent protection in 2006, the price for generic simvastain had only dropped by 19% six months after patent expiry. Only later, when more generic manufactures entered the market it declined by 60% [66]. Against these circumstances, the six-months-post-patent deal seemed feasible for insurance companies. Besides, given the preceding 50% price increase within five years, Pfizer could stay competitive and didn't lose much with those agreements [63, p. 5]. Eventually, it turned out that Ranbaxy sold its generic atorvastatin at a 60-70% discount during its 180 days exclusivity period. So insurance companies were left contracted to pay a discounted, but higher priced branded Lipitor® [79]. "The Lipitor® for you" couponing program has further been a convincing argument for patients to stay with Lipitor® –or even switch from other statin brands –since practically none branded prescription drug was available for as little as US$4. Key to

\(^8\) Given the intransparency of contracting conditions, the actual extent of the actual discount is unknown, but likely to be between 15-20%.
Pfizer’s counter generic strategy was the **six months period** following patent expiry when only a single generic competitor had entered the market. As soon as Lipitor® faced multi-source competition, this model did not make financial sense anymore [84]. The environment had become "much more hostile" [85], putting Pfizer into a position where it was to become "lead payer for branded Lipitor®" [86], if it did not stop co-pay coupons and rebates: 181 days after Lipitor® went off patent, four more generics became available offering atorvastatin for as little as 4% of the original’s costs of therapy [87]. Hence, it is only intuitive that Pfizer announced to stop its US promotional activities for Lipitor®, including further contract negotiations with payers, in early June 2012 [85].

As one can tell from ill.6, Pfizer primarily selected **short-term tactics**, which is why it could only temporarily outpace generic competition. The more longer-term product line extension tactics, were no option: Lipitor® was already available in a great number of different dosages (reformulation), a next generation Lipitor® increased, instead of decreased death rate [88] and its combination drug Caduet® was –from a Pfizer perspective– a disappointment with annual sales of just US$100 million [89]. New indications had already been investigated and patented during Lipitor's® extensive clinical study program [90, p. 7]. The intended OTC status, though is the right approach to serve a future US American health system, that will include more self-care options in order to shift more –financial– responsibility to customers [61].

### 8. Conclusion and further thoughts

Similar counter generic strategies have precedent, but Pfizer's scale and structure in manipulating the market place has been unmatched [91,3]. Although it could minimize the impact of Lipitor's® patent loss, none of the patent expiry strategies could save the firm from **devastating results**: A profit decline by 14% in 2012 [92] forced Pfizer to downsize the company with layoffs as well as spinoffs and to further cut R&D expenditures by 30% [93,94]: No company has nowadays the capacity to fund the immense R&D expenses, while aggressively marketing its fading
blockbuster. Most counter generic strategies can buy time, but they cannot stop generic competition [95]. The pharmaceutical industry undergoes a major transformation [96]. Given the increasing payer dominance and an aging population, that requires more health care service, cost pressure will continue to increase and further stimulate generic preference. The generic business model eventually better fits current market conditions by addressing stakeholder needs more effectively. The difficulties, Pfizer is facing are a lesson for the whole pharmaceutical industry. Pfizer's business model is based on giant profits from Lipitor® and few other blockbusters drugs—as most research-based companies [95]. The industry leader, created a totally profit driven corporate culture, that allowed business units such as oncology to refuse remedies developed by Pfizer scientists if management had doubts about their profitability [97]. Considering the significant imbalance between new drug introduction and the sheer number of blockbusters losing patent protection, times when Big Pharma could be arrogant enough to reject R&D projects that would may not be profitable enough have passed [98]. Most of the big chronic therapeutic classes with enormous sales potential have been harvested and are now well served by inexpensive generics [99]. Yet, the majority of the 30,000 known diseases is poorly treated exemplifying significant unexploited market potential [10, p. 82]. The remaining 80% are too complex or specific to be fully understood or targeted [100]. In order for those business opportunities to be realized, Big Pharma needs to understand that much of its success in the 1990's was due to a close and effective R&D collaboration with universities and scientists, rather than aggressive and sometimes unethical management practices, only pushing for the most profitable opportunities [95]. Research-based companies will need to manage a larger product portfolio consisting of several niche products that generate smaller, but guaranteed returns [101, p. 28,40]. This will reduce volatility, spread risk and decrease the overdependence on fading blockbusters. In late 2013, Pfizer made a step indicating that the company has learned its lesson: Pfizer introduced a highly specialized lung cancer drug –Xalkori®– that only works with a very small target group. Such a result 15 years ago would have stopped drug investigation [40].
Appendix

Illustrations

**Illustration 3:** Three main stakeholder groups in the pharmaceutical industry [102, p. 14], US insurance structure [21] and co-payment level [103].

**Illustration 7:** The US statin market the 1990's and Lipitor® pricing policy to explain market dynamics [62].
Illustration 9: $\$\$\$\$ US retail price for 20mg monthly Lipitor® supply [63, p. 4f.].
Glossary

**Big Pharma**  The world's biggest research-based pharmaceutical companies.

**Blockbuster**  A drug with annual global sales exceeding US$ 1 billion.

**Hatch Waxman Act**  A series of laws implemented in the US in 1984 to balance the conflicting interests of generic and branded drug manufactures.

**Indication**  The medical term for a disease, condition or disorder that makes a particular treatment advisable. For instance, high cholesterol is an indication for statins.

**Molecule market**  The market of a single chemical molecule intended to treat a disease, such as atorvastatin or simvastatin. Before the patent for the chemical molecule expires, the molecule market is 100% owned by the branded drug. Several chemical compounds make up a drug class, such as statins. Several drug classes can be found effective to treat a disease (e.g. high cholesterol) and are referred to as therapeutic class.

**Off-label:**  The legal usage of a drug in way unapproved by the FDA such as the case with age, dosage, formulation or indication: Sometimes, the drug works for another, but unspecified condition, which is why a physician might prescribe the drug for the unapproved indication.
References


References


