# Chapter 1
# The Pharmaceutical Industry: Specificity, Challenges, and What You Can Learn from this Book

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The pharmaceutical industry is an industry that is in a class of its own (Stremersch and Van Dyck 2009). It is significantly more linked to science and more regulated than any other industry. Because pharmaceutical drugs substantially impact people's quality-of-life, both regulation and the unique channel of healthcare provider (e.g., doctor or pharmacist) and payer (i.e., government or insurer) are designed to protect the patient's wellbeing at reasonable cost.

The industry consistently grows 4–7 % per year and is fast approaching the magic US$1 trillion market size. At the same time, it faces tremendous innovation and marketing challenges. These two factors drive the success of a branded drug company. A firm with subpar innovation for an extended period will see its

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M. Ding et al. (eds.), *Innovation and Marketing in the Pharmaceutical Industry*,
International Series in Quantitative Marketing 20, DOI 10.1007/978-1-4614-7801-0_1,

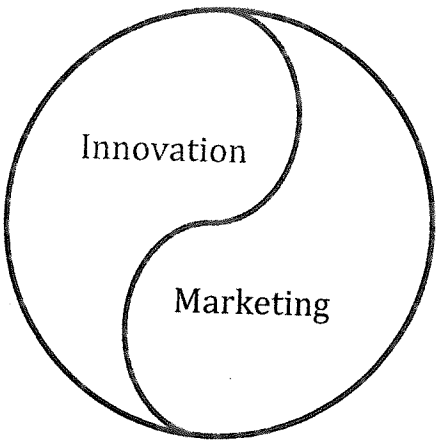


**Fig. 1.1** Innovation and marketing in pharmaceutical industry

differentiation potential decrease, with deteriorating margins as a consequence. It will succumb under price competition with generic drug firms and may, ultimately, be forced to merge with or be acquired by another company. A firm without strong marketing capabilities will not fully unlock the value of innovation and thus it stands to miss out on billions of dollars for its stakeholders and on the resources needed to sustain continued innovation. The graveyard of former pharmaceutical firms is littered with once-mighty corporate brands, such as American Home Products, Pharmacia, and Wyeth, that mismanaged either their innovation or marketing, or both. Firms that are strong in both innovation and marketing have successfully navigated the challenges and will continue to create value for their stakeholders (Fig. 1.1).

## 1.1 The Specificity of Innovation and Marketing in the Pharmaceutical Industry

Innovation and marketing in the pharmaceutical industry are not run-of-the-mill processes and challenges that an outsider to the industry can immediately grasp. To explain these complex processes, we discuss below the very specific nature and characteristics of innovation and marketing in the pharmaceutical industry.

### *1.1.1 Innovation*

Innovation in the pharmaceutical industry has three characteristics: *live or die*, *large in size*, and *finite lifespan*. A considerably large percentage of the profit of a typical branded pharmaceutical firm comes from drugs under patent protection.

The characteristic "live or die" refers to the fact that a firm cannot possibly survive if its innovation level decreases substantially and it can no longer generate new drugs with sufficiently profitable patent protection.

"Large in size" means each innovation (new drug) tends to generate a large amount of revenue for a firm. Since the late 1990s, firms have adopted the strategy of developing the so-called blockbuster drugs, which are drugs that will generate at least US$1B per year in revenue. In their search for blockbusters products, some pharmaceutical firms such as GlaxoSmithKline have already started to design medicines based on bioelectronics, which entails treating the disease through electrical signals in the brain and elsewhere rather than targeting biochemical structures (*Financial Times* 8/1/2012). While this may sound like good news, it means that a firm's loss of income from an innovation is usually accompanied by a sharp drop in its overall performance in terms of profit, which makes the challenge of delivering consistent results at the firm level every year nontrivial.

Finally, "finite lifespan," means innovations in the pharmaceutical industry, with the exception of a few biological drugs, have a finite time to create value for its shareholder. The standard lifespan is in general defined by the patent validity. Chemical drugs, which are the overwhelming majority of drugs, have no other tools (e.g., trade secret, manufacturing know-how) for extending their standard lifespan. The manufacture of chemical drugs is standardized and, in general, once the patent expires, they can be easily reproduced as generics by many competitors. The situation of biological drugs is much more complex in most cases because they are often harder to manufacture and have higher manufacturing variable costs as well, as compared to chemical drugs.

These three characteristics (i.e., live or die, large in size, and finite lifespan) set the context of pharmaceutical innovation. Within this context, a pharmaceutical firm must consider and balance four key dimensions: *cost*, *uncertainty*, *return*, and *time*. Figure 1.2 graphically illustrates the relationship and potential tradeoff in supporting various projects along these dimensions. Project 1, in this case, has large return, medium uncertainty, and will take medium time to reach the end of its development. Project 2, on the other hand, has small return, small uncertainty, and can be completed in short time. Comparing Project 1 and Project 2, we also can see the cost of supporting Project 1 is larger than that for Project 2 (represented by the size of the oval).

The *cost* of pharmaceutical innovation is gigantic. According to the most recent estimates, the average cost of developing a successful new drug has surpassed US$1B, increasing from an estimate of US$360M in the mid-1990s. While this sounds like an astronomical number, the actual cash needed to develop *one* drug is substantially smaller. The US$1B+ price tag includes two large components that people are not aware of sometimes. First, the price tag includes the cost of dry holes. If on average, 1 in 10 new drug projects succeed and 9 fail, the cost of developing one successful drug includes as well the cost of the 9 failed projects (dry holes). The second component is the opportunity cost (interest) due to the long time horizon of development. $1M in year 1 is worth much more 12 years later, which is the average time for developing a drug.

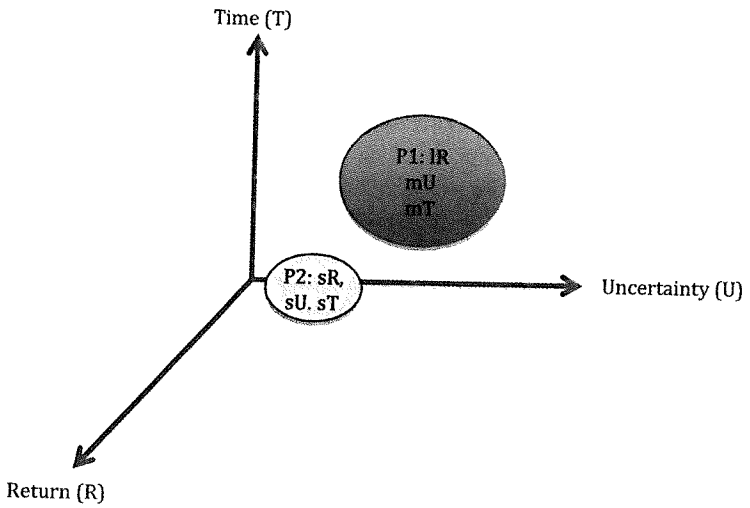


**Fig. 1.2** Four key dimensions of innovation strategy. *s* small or short, *m* medium, *l* large or long. The size of the *oval* denotes the magnitude of the cost. P1 and P2 refer to Project 1 and Project 2

Even when one leaves out these two big chunks of the cost, the money needed to develop a drug is still substantial. It can easily cost $20–$50 million to conduct 1 year of clinical phase-III testing for one drug candidate. Although drug candidates target very different diseases, in general, there is actually relatively little variation in the costs of developing these drugs. This is because most costs are associated with steps that vary little across projects. According to PhRMA (Pharmaceutical Research and Manufacturers of America 2010), on average, 53.6 % of the innovation cost is spent on clinical trials that are dependent on the number of patients needed, another 4.7 % is spent on the approval process, and 14.4 % on phase IV (postlaunch market surveillance). The general process of discovery is also similar across a variety of therapeutic categories. As a result, the cost of developing a drug plays a constraining role in the innovation decision, thus limiting the number of new drug projects that a firm can support at a given time. However the cost of developing a drug plays less of a strategic role in innovation decisions compared to the other three factors: uncertainty, time, and return.

*Uncertainty* plays a critical role in a firm's innovation strategy. The probability of success is low across therapeutic categories, and there is a need for a firm to actively manage the success rate. The challenge is that the uncertainties associated with passing each stage of the innovation process (i.e., preclinical trial, clinical phase I, clinical phase II, clinical phase III, ...) are different for different drug candidates. For example, central nervous system (CNS) drug candidates have a higher probability of failure in later stage clinical trials than other drug candidates. Furthermore, managers need to actively manage the probability of eventual success in two ways: by supporting correlated drug candidates (e.g., molecules with similar

structure or ones that target a similar signal pathway) and/or redundancy strategy where a firm funds two or more molecules treating the same disease (Ding and Jehoshua 2002); and/or by developing expertise in the same therapeutic category so learning can be more fruitful and uncertainty is reduced.

Uncertainty is closely associated with *return*: a firm needs to balance uncertainty with potential return. As mentioned above, each innovation (new drug) tends to create substantial value for the firm. A firm must select innovation projects that can potentially provide large-scale return (to at least make up for future lost income due to patent expiration of existing blockbuster drugs). Conditional upon this, the firm must also assess how much uncertainty it is willing to bear to target an even larger return. For example, many firms now settle for developing me-too drugs instead of aiming for first-in-class molecules. This is not necessarily a viable long-term strategy, and it creates a public opinion backlash. The flipside of this strategy is that the time between the launch of the first and the second drugs in a therapeutic class has shrunk from an average of 10.2 years in the 1970s to 1.2 years for drugs launched between 1990 and 2003 (Tufts CSDD). This creates additional pressure on the first-in-class innovator.

Finally, firms need to consider another moving part in their innovation strategy: *time*. The majority of the income of a pharmaceutical firm comes from drugs with patent protection, and this income will evaporate as soon as the protection ends. As a result, the revenue of a pharmaceutical firm undergoes large-scale discrete changes instead of even increase/decrease as in most other industries. To smooth out these kinks, it is critical for a firm to plan ahead so that new drugs can be launched at least in time to replace the expected loss in revenue due to patent expiration. Due to the long time horizon of development, which usually lasts 12 years, this balancing act is extremely challenging. In sum, a successful pharmaceutical firm must be able to balance return, uncertainty, and time, while constrained by a finite budget. This is not easy, especially given the constant pressure from financial analysts for firms to deliver results on a regular basis. This pressure has brought about more short-term rather than long-term optimization of innovation.

### *1.1.2 Marketing*

Society sees pharmaceutical drugs as having "double personalities": as a conventional product that addresses certain consumer needs, and as something to which human beings have a fundamental right. As a conventional product, all rules of commerce should apply to it. However, as something human beings have a basic right to, many standard marketing practices must be modified. For example, nobody will complain if his or her neighbor owns a BMW sports car while he or she cannot afford one. However, if his or her neighbor is able to receive expensive but effective medicine for a disease, he or she will most likely demand that, if the need arises, he or she too should have access to the same medicine regardless of his or her financial status.

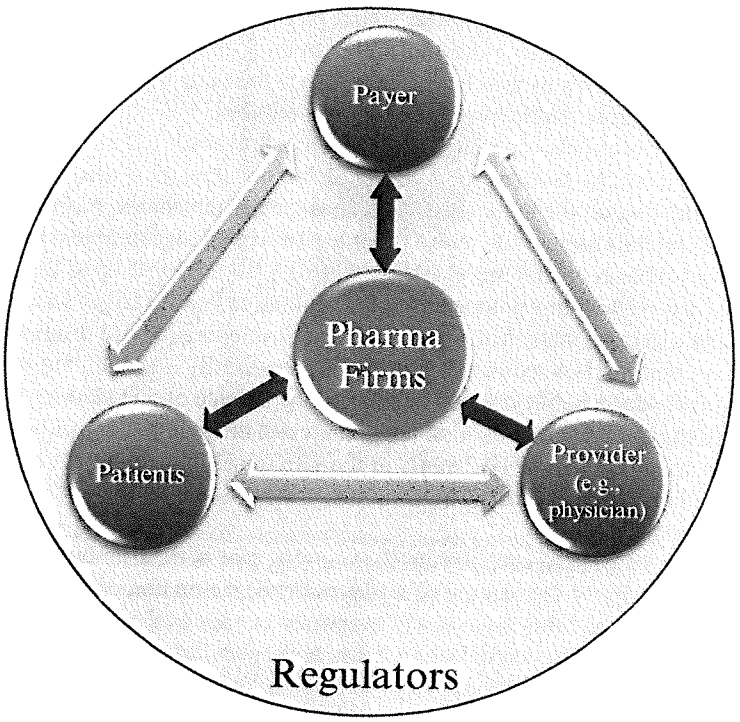


**Fig. 1.3** Players and relationships in the pharmaceutical market

Pharmaceutical companies must take into account these two conflicting characteristics/attributes of pharmaceutical drugs as they extract maximum value from their innovation. This task requires careful management of the firm's relationship with three key players—patient, provider (e.g., physician), and payer—as well as the relationship among themselves, within an environment controlled by the regulators (Fig. 1.3).

Pharmaceutical drug purchase is a joint decision made by the user (patient) and gatekeeper (physician or other healthcare provider). In this relationship, the gatekeeper has the final decision-making power on what drug a patient should use. However, on the other hand, the patient is not completely powerless, although his or her power differs across therapeutic areas (Ding and Jehoshua 2008) and countries. In most countries, a patient can easily "fire" his or her gatekeeper by switching to another physician. A patient can also passively protest by either not getting the prescription filled or not using the drug according to the recommended schedule (noncompliance). This patient–gatekeeper relationship is evolving and has changed substantially over the last 10–20 years, largely due to the availability of information about the drug itself and about other patients' experience and knowledge. Such information is now available to any individual who is willing to spend half hour on the Internet

before seeing a physician. A firm must take into consideration the delicate relationship between the two parties (i.e., patient and gatekeeper) when formulating and executing its marketing strategies. Social networks have also enabled information exchange and learning among physicians (e.g., Sermo) and patients (e.g., PatientsLikeMe) in a way that was not possible in the past. Firms have to closely monitor and understand the impact of such physician and patient social networks in medical decision making.

To complicate matters further, the majority of the drugs are paid for by a third party, which exerts tremendous influence on firms, physicians, and patients. The payers demand health economic analysis of a new drug from pharmaceutical firms and determine, among other things, whether a drug will be included in a formulary and whether it should be used as first-line or as second-line therapy. The payers also put substantial pressure on physicians, and on pharmacists in some cases, regarding what kind of drugs they should prescribe, often steering them towards low cost and older drugs. Sometimes the physicians need to get prior authorization for using a particular drug, with appropriate justification. In some cases, physicians and pharmacies receive financial incentives from payers for prescribing more generics and preferred drugs. In addition, a third-party payer may induce patients to choose lower cost drugs by imposing different levels of copayments for drugs, with only a small fixed payment (deductible) if a patient uses generics. On top of all these, the payers also use their market power to demand drug discounts.

In the background of the dynamic relationship among the firms, patients, physicians, and payers, lie the vigilant regulators. Regulation takes many forms in this industry, including new drug approval, drug monitoring, manufacturing, promotion/advertising practices to physicians, and direct-to-consumer advertising (DTCA). In the more recent phenomenon of DTCA, firms can communicate their drugs to patients, but all advertisements are subject to the oversight of the FDA and must include a balanced presentation on both efficacy and side-effects as in the corresponding label approved by the US Food and Drug Administration (FDA). Outside of the USA, DTCA is only allowed in New Zealand, and to some extent, in Canada.

Therefore, firms strongly rely on promotion to physicians to market their drugs. The relationship between firms and physicians is also regulated, for example, in the USA, a firm cannot mention off-label use to physicians, while a physician is free to use the drug for whatever purpose he or she sees fit. In other countries, the number of detailing calls the firm can make to a doctor or the number of samples it distributes, may also be capped. Many other restrictions may apply. In almost all countries, governments play the role of both regulator and largest payer.

Drug price is also heavily regulated in various ways, such as ex-manufacturer price regulation (i.e., direct capping of prices by the government), cross-country reference pricing (i.e., restricting the price based on an international comparison of the prices of the drug in reference countries), or therapeutic reference pricing (i.e., restricting the price based on a comparison of drugs with similar therapeutic potential). Several governments (e.g., the UK, as discussed in Verniers et al. (2011)) also restrict the total profits a pharmaceutical firm can make. Even in the USA, the

price of a drug is indirectly regulated through the government's role as the largest payer (Medicare). For a review of the regulation of pharmaceutical markets around the world, see Stremersch and Lemmens (2009) and Verniers et al. (2011).

In sum, a successful pharmaceutical firm must implement a marketing plan that builds upon the complex patient–physician decision-making process and the multi-faceted role of a third-party payer, while at the same time adhering to the rules set by regulators.

## 1.2 Challenges to Firms in the Pharmaceutical Industry

In the last 2 decades, the pharmaceutical industry has faced numerous changes and finds itself in an increasingly challenging environment for sustaining past profits. We discuss several of these changes and the challenges they impose on firms.

### *1.2.1 The Number of New Treatments That Are Approved for Commercial Use Continues to Decrease Substantially*

The chapter in this book by Petrova shows a consistent decline in the number of new drugs that received regulatory approval. In 2010, only 21 molecular entities were approved, a historical low (Jack 2011). Consequently, because new products typically generate a higher margin than mature products, the sales generated from relatively new drugs also substantially decreased, which resulted in a quite negative profit outlook for the industry. The following are some of the cited reasons for the decline in the approval of new drugs.

1. The industry does not invest enough in R&D. According to some, this is because of declining prices and thus declining returns on innovation. This reason is questionable, because statistics on R&D investments by firms show that those investments have consistently increased over time.
2. The regulator follows increasingly strict approval procedures that are partially triggered by an increasingly suspicious general public and heavily publicized withdrawals such as Vioxx. Events of the latter kind drive up the clinical testing costs for firms and suppress the success rate.
3. Many diseases have been satisfactorily addressed, which limits the space for big medical breakthroughs (even though the number of deaths from cardiovascular disease, cancer, or hard-to-treat diseases such as neurodegenerative or autoimmune diseases, is still large).
4. The industry has not yet developed the right competences to be successful in developing new treatments that are biological rather than chemical in nature.

The decline in the number of new molecules approved generates several main challenges for firms. How can firms optimize portfolio management to improve their risk-return ratio? How can firms use new innovation models, such as grassroots innovation programs or open innovation, to improve their innovation yield? What type of agreements with other firms (e.g., small biotech start-ups or university spin-offs) yield optimal outcomes? What can a firm do to overcome the negative consequences of a dry pipeline if R&D efforts fail? How can it move the innovation model from the blockbuster model to models with a higher likelihood of success, be it of more limited size, such as targeted therapies or orphan drugs? How can firms optimize launch success for the few approved drugs they are launching?

### *1.2.2 Competition of Generics That Branded Drugs Undergo Increases*

The drop in the number of new drug approvals has led to increasingly mature product portfolios in most firms. As drug patents expire, firms increasingly face generic competition. Generics offer the same active ingredient as the originator drug, and typically with no more than 20 % deviation in efficacy but at much lower prices. To lower the pressure on the healthcare budget, governments and insurers have increased the pressure on the healthcare system to transition to a higher generic drug use instead of branded drug use. Various countries have implemented policies such as promoting or enforcing generic prescription by physicians, prescription budgets of doctors, promoting or enforcing generic substitution by pharmacists, and public tendering for preferred molecule supply have become increasingly popular as well. Often patients are more informed about the equivalence between generic and branded drugs, potentially making patients less brand-loyal and more price-sensitive. Given the business value in generic drugs, the number of firms that supply generic drugs has increased. This is true even among the conglomerates that also supply branded drugs, several of whom have generic divisions (e.g., Pfizer). Among an increasing number of generic firms, generic competition itself has intensified, putting even more pressure on branded drugs at the end of the life cycle.

The increased competition from generics has generated several challenges for pharmaceutical firms. Should a firm have its own generic division? If yes, to what extent should it focus on generics business vs. branded business? How can the two be made compatible? If patents expire, what are the firm's optimal patent expiration strategies? Can it reengineer the molecule for improved efficacy (e.g., new administration methods)? Can the firm develop a follow-on drug (e.g., a new molecule in the same molecule class)? Should it develop combination drugs with increased convenience or efficacy? How can it sustain or strengthen its brand to retain brand-loyal physicians and patients? How should it adjust its price? Should the firm price on par with generics or higher, and if higher, how much higher?

### 1.2.3 *Price Pressure Increases Even for Drugs Under Patent Protection*

Even for new drugs that still enjoy life years under patent protection, price pressure is increasing. The main reason for this is that payers—be it insurers or governments—are increasingly under pressure from ageing. Older patients typically bear higher costs than young patients because a great number of older patients suffer from chronic diseases (e.g., diabetes), neurodegenerative diseases (e.g., Alzheimer, Parkinson), rheumatic diseases or cancer. Thus, in developed countries where much of the population is ageing (such as in the USA and Europe), the payers in these countries are increasingly pressured to attempt to lower healthcare expenses. Drug costs are an ideal target for such efforts since saving on drug prices seems to hurt only large multinational pharmaceutical firms, which typically does not concern the public at large. Attempts to lower prices for drugs that are under patent protection take many forms.

Many countries have a system in which prices are regulated, i.e., the government first needs to approve the price that a pharmaceutical firm will charge before the latter is granted market access. Often governments examine the prices of the same drug in reference countries and determine that local prices cannot rise above those reference prices. Alternatively, governments may determine a therapeutic reference, for instance drugs that bring similar benefits, and demand that prices should be comparable to that of therapeutic equivalents. Drugs that according to payers demand too high a price may be "punished" by several methods: they may be put in a lower prescription tier, thus depressing sales volumes; they may be excluded from the reimbursement system; or they may even be denied market access altogether.

Price pressure has significantly complicated the task of pharmaceutical firms. The elaborate use of cross-country reference pricing systems has led to a very complicated optimization problem for firms: they need to decide which countries to enter first and at what price, and which countries they should possibly not enter so as not to spoil global pricing levels. Pricing models have shifted, so firms need to develop competences with very new pricing models. For instance, pay-for-performance models, in which firms only receive payment if certain health outcomes are achieved in the target population, are becoming increasingly popular. Tendering has also become more popular, even for branded molecules, if multiple options exist within a category.

### 1.2.4 *The Pharmaceutical Industry Has Experienced a Serious Deterioration in its Corporate Image*

The corporate image of the pharmaceutical industry has deteriorated. Global firms, such as those from the tobacco, finance, energy and pharmaceutical industries, are increasingly under societal pressure. In the case of pharmaceutical firms, the

populist belief is that these firms try to gain financial benefit from the misery of diseased people. Several shocks to its confidence have not helped the image of the industry. Think about withdrawals of drugs such as Vioxx, which displayed the unethical behavior of firms in their sales messaging. Also the tactics of firms when threatened by generics have been scrutinized by the public, especially the ethically questionable practices, such as "evergreening" (milking a patent life cycle by extending it through dubious "innovations"), cornering the supply of the active ingredient, bribing the generic company not to supply generics, and suing generic makers over dubious patents. Much of the pharmaceutical industry was investigated by the European Commission over such practices, and class action law suits have been filed (e.g., consider AstraZeneza's marketing practices in the PPI category, in which its two drugs, (Pri)Losec and Nexium, are now being challenged by both regulators and consumers).

The weaker corporate image of the pharmaceutical industry is in desperate need of repair. Rather than focusing on the short-term, the pharmaceutical industry needs to develop long-term policies to maintain long-term trust of the population. In the words of Singh and Jayanti later in this book, the industry needs to transition from a logic of conflict (with payer, patient, or healthcare provider) to a logic of cooperation, to align itself in a win–win cooperation with the entire healthcare value chain.

### 1.2.5 *The Pharmaceutical Industry Needs to Rethink its Policies Towards Sales Representatives*

Multiple changes challenge the common way of detailing for pharmaceutical firms. First, with decreased margins, less money is available to be spent on sales representatives. This seems to finally be a trigger for rethinking the arms race in detailing that has been going on between major pharmaceutical players. Second, more and more healthcare providers are turning their backs on pharmaceutical sales representatives for behaving unethically in the past. Sales representatives' influence on prescription behavior is less and less socially tolerated. With fewer product introductions, less news is informative enough to warrant time investment by the healthcare provider to listen to a sales representative. Third, technology has entered into the detailing visit. Sales teams use iPads to present their pitches to doctors, and the virtual detailing visit (i.e., a detailing call over an electronic connection) is making its entry as well. Moreover, an increasing number of doctors network online, increasing the need for information provision by manufacturers on such online platforms.

Many firms still struggle with estimating the return on investment (ROI) of sales calls and adjusting their sales allocation to such ROI estimates. This involves questions about the efficacy of virtual sales calls, about getting into doctor's practices when such entry is increasingly discouraged, how to make sure doctors get the required information, and how to make sure that the sales representatives comply with the firms' normative and ethical guidelines and messaging, especially, say, in developing markets.

### 1.2.6 The Pharmaceutical Industry Faces a Changing Media Landscape in a Heavily Regulated Environment

Digital and social media have strongly affected many industries: publishing, entertainment, and grocery retailing. They are also starting to have an increasingly dramatic effect on the pharmaceutical industry. Pharmaceutical firms are used to communicating directly with the patient under strict regulatory conditions (in the USA, New Zealand, and Canada) or to being prohibited from doing so (in the rest of the world). Today's global social media challenge this regulatory environment. Online and in social media, patients speak freely about their experiences with pharmaceutical treatments. Some early efforts by firms to get engaged in social media (e.g., think of Sanofi's VOICES program) have shown this engagement not to be trivial for pharmaceutical firms. Sanofi's attempt to delete and then preempt, on its online platform, the entries of a cancer patient, who was being treated with a Sanofi drug and who consequently experienced permanent baldness, has shocked public opinion.

At the same time, the context is so complicated that the FDA has been notoriously slow in releasing clear guidelines on how pharmaceutical firms should behave online. Consequently, there is continuous discussion online about pharmaceutical brands, while pharmaceutical firms are struggling with such questions as whether they should get online or not; how much resources they should pour into it; which platforms to use (Facebook, Patients Like Me) or to build one themselves; how communication should be handled on such platforms: whether to do it themselves or outsource to either an independent supplier or a subcontractor; what the goals are to begin with; whether they should only listen, or only speak, or both; if they speak, what will it be about; and, if and when they agree on clear goals, how they will measure if they are getting a good ROI. It is complicated for any firm to start with calculating ROI on Facebook investments, but it is even more complicated for pharmaceutical firms.

### 1.2.7 The Patient Has Turned into an Empowered Consumer

Consumers have become more vocal in general. Call it a general trend in society. Pharmaceutical firms cannot escape this trend. The consumer takes a more dominant role in the economy. Online medical diagnosis and information has enhanced a consumer's confidence to become more involved in treatment decisions, in some cases even to take control. The cartoon where a patient tells his doctor "Doctor, I diagnosed myself online, I am just here for a second opinion" is a well-known abstraction of the reality of today's medical practice. In areas such as oncology, increased involvement of patients is welcomed. For instance, after explaining the pros and cons of different treatment options, patients are often asked if they desire to make the final choice about which treatment to pursue. This can tilt to a complete consumerism of healthcare, where consumers shop around to obtain the prescriptions

they request from their doctors, and where patients stop treatment or choose their own drug regimen out of their own initiative. While welcomed by some, this increased role of consumerist patients may be a serious worry for doctors. For instance, consumerist patients, by not completely adhering to the prescribed therapy, endanger the efficacy of the treatment. This was already anecdotally illustrated in the consumerist behavior towards Prozac, with patients going on and off Prozac at will, often with limited medical guidance. Camacho et al. (2012) quantitatively documented that more consumerist patients often do not adhere to therapy. Keeping therapy adherence on track either by introducing reminder devices or by developing customer relations management (CRM) processes gets more attention among firms.

Moreover the centrality of the patient puts pressure on the typical way in which pharmaceutical firms market their drugs. Firms are used to the physician taking a prominent role, thus much of their marketing is aligned with the physician. In today's market, pharmaceutical firms need to become substantially more consumer-centric, and this poses a formidable challenge. Together with consumer empowerment comes increased influence of the pharmacist. An increasing collection of over-the-counter (OTC) medication in pharmacies makes the pharmacy more of a retailer, with similar factors of importance as in grocery retailing. Moreover the pressure towards generic prescription gives the pharmacist more power over which manufacturer's drugs get dispensed.

## 1.3 Overview of the Chapters

The book provides state-of-the-art reviews of various relevant themes written by experts in the field. These reviews cover the topics from different perspectives: analytical/empirical models, behavioral research, case studies, and more, making the materials accessible to a wide range of audiences. Given the rapid changes the pharmaceutical industry is experiencing, all chapters conclude with suggested areas for further research. The book is organized along the following three aspects: innovation and the product life cycle of pharmaceuticals, patient and physician behavior, and marketing of pharmaceuticals.

### *1.3.1 Innovation and the Product Life Cycle*

The chapter by **Petrova** provides a comprehensive overview of the drug innovation process. The chapter reviews various mechanisms of intellectual property protection pertinent to the pharmaceutical industry. It addresses issues related to me-too and follow-on drugs, to the fundamental types of organizations that operate in the industry, as well as issues related to the modes of collaboration that have emerged in drug innovation, with a particular focus on alliances.

**Ding, Dong, Eliashberg, and Gopalakrishnan** provide definitions of portfolio management, review relevant facts and evidence about the pharmaceutical industry, and examine current portfolio management practices. They then probe deeper into specific managerial issues within portfolio management in the pharmaceutical industry.

**Betz, Camacho, Gerards, and Stremersch** provide a detailed conceptualization of grassroots, or bottom-up, innovation and show how it can be applied in the pharmaceutical industry. They anchor their conceptualization in self-determination theory. They describe principal drivers of motivation and success for employees in pharmaceutical companies to come up with and develop innovative ideas into new business lines. They share their experiences in developing *innospire*, a grassroots innovation program at Merck KGaA, Darmstadt, Germany.

**Wuyts'** chapter focuses on three important issues: competing perspectives on why firms benefit from portfolio diversity; how the differences among firms in their commitment of managerial resources to portfolio management and in their internal R&D strategies can help explain why some firms benefit more than others from portfolio diversity; and why technological developments, such as the rise of nanotechnology and institutional developments like healthcare reforms, change the very nature of collaboration and alliance portfolios in the pharmaceutical industry.

In their chapter, **Chan, Narasimhan, and Xie** address the innovation theme through an evaluation of the effectiveness and side-effects experienced by firms in the pharmaceutical industry as their innovative drug goes through clinical trials data. They argue that there are several important issues that cannot be addressed with clinical data alone and propose how researchers may benefit by supplementing such data with post-marketing prescription choice data.

Taking the perspective of the launch and diffusion decision chain, **Landsman, Verniers, and Stremersch** provide a review of both the sequence of decisions that managers must make, as well as the analytical tools pharmaceutical firms can use to improve their decision making. The rich set of decisions includes decisions regarding the specific methods for the assessment of a treatment's commercial potential, decisions aimed at optimally extracting the new treatment's potential, and decisions regarding the strategy that will be used to leverage the new treatment's potential across countries.

**Kappe** focuses on innovation strategies available for a drug that is already on the market and is approaching its patent expiration. This scenario is of interest to different parties: branded drugs/generic manufactures, physicians, patients, insurers, pharmacists, and the government. This chapter focuses on the consequences of patent expiry for branded manufacturers, and discusses the regulatory environment for prescription drugs, the determinants and impact of generic entry, and various life cycle extension strategies.

The innovation section is concluded by **Jain and Conley**'s chapter. It summarizes a broad list of patent extension and market exclusivity options and pricing of pharmaceuticals both pre- and post-expiry, analyzes how promotional activities and newer product branding actions such as advertising and product configuration impact the behavior of patients exposed to such innovations, and it closely examines two distinctly different pharmaceutical cases: the markets for gastro-esophageal reflux disease and neurological medicines.

### 1.3.2 *Patient and Physician Behavior*

How do consumers assess their own risk and that of others? Are their own risk estimates biased upwards or downwards, merely inaccurate or normative? How do biases in underestimating or overestimating risk affect consumers' behavior, and what are the implications of under- or overestimation of risk on pharmaceutical companies, medical establishments, the economy, and society in general? These represent the critical questions needed to gain understanding of patient behavior. These and more are addressed in the chapter by **Raghubir and Latimer**.

Patient adherence represents another important issue in the pharmaceutical industry. Consistent with the accepted definition of adherence as conformity to, or adoption of marketers' recommendations about medication acquisition (purchase) and correct usage, **Ilyuk, Irmak, Kramer, and Block** discuss factors that lead to poor adherence. These factors are categorized as: medication-related, patient-related, prescriber-related, pharmacy-related, and condition-related. Focusing on medication efficacy, they review different biases and heuristics that influence patients' perception of it.

**Miron-Shatz, Doniger, and Hanoch** provide a related and complementary review of factors affecting adherence to governmental warnings against the use of household products previously perceived to be safe. Their discussion starts by examining the psychological decision-making literature on such factors as trust of the source issuing the warning and safe experience with the risk-causing agent. They then go into the basic requirements of awareness and understanding of the message, review the marketing literature on message design, and discuss natural cognitive and emotional consumer biases that may reduce adherence and how these may be counteracted. They proceed with an evaluation of the specific case of the 2008 US Food and Drug Administration (FDA) warning against administration of over-the-counter cough and cold medication (OTC-CCM) to children under the age of 2 years (FDA 2008), and conclude with recommendations for optimizing the design and dissemination of similar warnings in light of the literature reviewed.

Arguing that preventive vaccines differ from therapeutic pharmaceuticals in a number of ways, **Angelmar and Morgon** suggest that consumers' and other party's behavior in this context are quite different, and hence they deserve special attention. They provide a review of the vaccine industry including its structure, entry barriers, and threats from substitutes. They then discuss the behavior of the parties involved (i.e., patients, physicians, and payers), and highlight the marketing implications.

A recent patient-related phenomenon is the emergence of the empowered patient, a topic **Camacho** addresses. He reviews key trends that precede patient empowerment such as modernization and self-expression, demographic and lifestyle changes, technological evolution, and regulatory changes. He then analyzes the consequences of the patient's new role for the patient–physician relationship and for pharmaceutical marketing. Parallel to new trends observed in patients' behavior, we also witness new trends in physicians' behavior.

An important one is the emergence of peer-to-peer networks, a theme addressed by **Bhatia**. The chapter provides an overview of the network structure and draws a distinction between physicians who prescribe high volume and those who are connected to many other physicians. It then reviews how physician social networks are built through social links, job and location links, and professional links. This leads to the emergence of opinion leaders who should be of great interest to pharmaceutical firms. The chapter concludes with the managerial implications involved in identifying and targeting the opinion leaders in the peer-to-peer network.

The chapter by **Shankar and Li** also examines recent trends that indicate how the proliferation of electronic communication through social media is reshaping the pharmaceutical industry. They note that both physicians and patients actively use online information and social networks. The emergence of social media poses several important questions for pharmaceutical firms, such as how to engage in social media within the regulatory framework; how to integrate social media into traditional marketing strategy; how and where to start a social media campaign; and what the ROIs are of social media efforts. The chapter provides a framework for analyzing the effects of social media on patients, physicians, and marketers. It offers actionable implications for pharmaceutical companies, and provides pointers to successfully develop and implement an integrated social media marketing strategy. This chapter provides an essential link to the next section.

### *1.3.3 Marketing of Pharmaceuticals*

Pharmaceutical marketing strategies and their effectiveness is the main theme of this section. Pharmaceutical marketing strategies range from sampling to detailing, to journal adverting, to DTCA, and to various promotional efforts. These and more are covered in this section.

Starting with sampling as a promotional tool, **Dong, Li, and Xie** provide an overview of common practices in pharmaceutical sampling in the USA. They discuss various data sources that can be used for drug sampling research, and present a literature review on the effects of samples on pharmaceutical sales from both academic literature and empirical studies in the industry.

**Sridhar, Mantrala, and Albers** study the following questions: How effective is personal selling or detailing to physicians? What is a generalizable quantitative estimate of detailing effectiveness? How does detailing effectiveness vary by product life cycle stage and geographic region? They provide evidence based on a meta-analysis of 373 econometric estimates of pharmaceutical detailing elasticities that appeared in 48 papers. The authors suggest that optimal detailing spending-to-sales ratios today should (1) be in the region of 6–7 % over pharmaceutical product life cycles, (2) involve judicious shifts from higher to lower detailing emphasis as products age, and (3) be larger in Europe than in the USA.

**Fischer** examines various marketing spending models: physician-oriented, patient-oriented, and ones that are oriented towards other stakeholders. This chapter

summarizes insights obtained from managerial surveys and econometric models, analyzes demand for pharmaceuticals, and then concludes with recommendations for setting optimal marketing budgets.

With a similar focus on multiple strategic marketing variables, **Wieringa, Osinga, Ruiz-Conde, Leeflang, and Stern** address the following questions: How do marketing variables affect the diffusion pattern of newly introduced pharmaceutical innovations? How do dynamics influence pharmaceutical marketing effectiveness? Focusing on aggregate demand for prescription drugs, they present an overview of papers that investigate the effectiveness of pharmaceutical promotion, and discuss the significance and relevance of pharmaceutical promotional effects, distinguishing between effects on product category level demand and effects on brand level demand. They review the applications and findings of studies that investigate how marketing efforts affect the diffusion of new pharmaceutical innovations, and provide an overview of studies that examine how dynamics impact the effectiveness of pharmaceutical promotion.

**Liu and Gupta** review the history of DTCA, claiming that expenditure on prescription drugs in the USA have been growing explosively. They survey next various methodologies designed to assess the effectiveness of such expenditures, considering patients, physicians, and governments as audience. They conclude with a summary of findings related to the short- and long-term elasticities of these marketing efforts—suggesting that these are in the lower half of the distribution of advertising elasticities.

The direct-to-consumer advertising and direct-to-physician advertising are also the main topics addressed by **Vakratsas and Kolsarici**. They provide a review of studies addressing marketing-mix efforts directed towards patients and physicians and discuss the relative effects of these marketing activities. Based on the evidence they survey, they conclude that the elasticities of DTCA are smaller than those of direct-to-physician, rendering the physician as the primary decision-making agent in the prescription process.

**Desiraju and Tran**'s chapter deals with spillovers and related externalities in the industry. A spillover may arise, for example, in the Canadian market since much of the Canadian population lives relatively close to the US border and has access to the US television broadcasts. Surveying the extant literature on spillover effects, they address in particular questions such as: Does DTCA in the USA influence sales in Canada due to spillover from a variation in government regulation? In case it does, what is the magnitude of return from such spillover?

The section concludes with **Singh and Jayanti** who adopt an institutional theory perspective and examine the dominant logic that underlies pharmaceutical marketing strategies, contrasting it with the organizing logic of the value chain partners. Two key questions are discussed in this chapter: What specific marketing strategies do pharmaceutical companies use to engage medical practitioners, and how do these strategies relate to particular tactics? And, under what conditions, and why, do pharmaceutical marketing strategies amplify (or diminish) the aversive (approving) response from its value chain partners? The analysis suggests that the pharmaceutical value chain reveals dynamics that are consistent with several aspects of

institutional theory: (1) system conflict due to coexistence of competing logics, (2) institutional failure in resolving conflict of logics that are amplified by pharmaceutical marketing practices, and (3) continued escalation of conflicted logics that invite regulatory intervention that constrains and restricts marketing efforts.

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