

Chapter 2

Clinical Aspects of Pharmaceutical Portfolio Management

Frederic (Rick) Sax, Raymond A. Huml, and Judith Ng-Cashin

Introduction

This chapter examines the clinical aspects of pharmaceutical portfolio management from the perspective of an Executive Committee reporting on portfolio strategy to a Board of Directors.

Portfolio strategy decision-making is the single most important role of pharmaceutical executives interacting with the Board of Directors to drive shareholder value. The broad categories driving shareholder value include a thorough evaluation of manufacturing and clinical drug development costs (e.g., cost of goods [CoG]), commercial (sales) expectations, and the clinical risk–benefit assessment for each product within the portfolio.

This chapter highlights the clinical aspects of pharmaceutical portfolio management. It also discusses other important aspects of the risks associated with pharmaceutical product portfolio management, including competitive intelligence (CI), due diligence (to acquire assets and estimate the probability of technical success), patent protection and regulatory exclusivity.

For the purpose of this discussion, an “Executive Committee” is a collection of internal experts covering the disciplines of medicine and drug development sciences, regulatory science, commercialization, and finance, as they relate to portfolio development and asset prioritization. A “Board of Directors” is a body of elected or appointed members who oversee the activities of a company or organization with accountability for corporate governance, financial resources, including acquisition and allocation, and stakeholder accountability. In addition, for purposes of this

F. Sax, M.D. • R.A. Huml, M.S., D.V.M., R.A.C. (✉) • J. Ng-Cashin, M.D.
Quintiles Transnational Corp., 4820 Emperor Blvd, Durham, NC 27703, USA
e-mail: Rick.sax@quintiles.com; Raymond.huml@quintiles.com;
Judith.ng-cashin@quintiles.com

chapter, a typical pharmaceutical portfolio contains 10–15 assets, representing some mix of small molecules and biologics, as well as pre-approval assets and marketed products.

The portfolio strategy and management is examined in the context of clinical discovery and development, acquisition of external assets, life cycle management of marketed products, risk–reward tolerance, and clinical risk mitigation strategies.

While this chapter will be most applicable to portfolios of small molecules, biologics, or medical devices, it could also apply to other diversification strategies for biopharmaceuticals portfolios, including moving into other sectors such as wound healing, consumer products, generics, and agricultural or veterinary products. Smaller companies may benefit from the strategies elucidated in this chapter, but may not have the infrastructure to diversify and balance risk in a similar manner due to the more limited nature of their portfolios and available resources.

Portfolio Strategy Decision-Making

Portfolio strategy decision-making focuses on five key elements of the clinical assessment which is divided into both strategic and tactical components.

The strategic clinical components include an understanding of the overall strategy (e.g., perhaps a focus on one therapeutic area or multiple areas or types of products, the ability to assess the probability of technical success and the value of the clinical and technical assessment of the portfolio which is a combination of clinical risk and NPV risk) to obtain alignment with the overall corporate strategy (“strategic fit”) and priorities, and the value that is created from resources being appropriately deployed to maintain revenue from marketed and future products (“value creation”). Contained within this paradigm is the tension of maintaining a balance between current and future revenues through investments in the development pipeline.

The tactical components include the methods in the pharmaceutical executive’s armamentarium to assess risk. Clinical risk is assessed by known safety signals as well as unanticipated safety signals which could be seen after a product is marketed. Risk can be managed by due diligence, assessing the risk associated with in-licensed compounds as well as ongoing due diligence on the compounds in the portfolio. Other tactical components include employing methodologies to avoid bias with a careful consideration of the trade-offs for each decision in order to optimize the ever-changing portfolio.

The clinical contribution involves product development risk (but not patent risk) and estimating the probability of technical success (PoTS), which includes an evaluation of safety risk, probability of regulatory success, and market access. To avoid bias, due diligence must be conducted both for in-licensed assets and, on an ongoing basis, for the existing portfolio.

Depending on the clinical mix of the portfolio, as determined by the therapeutic areas, the value of the entire portfolio then becomes a combination of clinical risk and net present value (NPV) risk.

The strategic and tactical risks must be managed in a sustainable manner, meaning that the goals must be achievable with the available resources, and the returns appropriate to the level of investment, all in alignment with the growth objective.

Portfolio management must strike an appropriate balance between all of these factors.

Strategic Fit

The portfolio must be aligned with the overall corporate strategy and priorities. This includes both current and future strategies. For instance, if the early phase pipeline is weak and there is an aspiration to strengthen it in the near term, which strategy is more consistent with the future strategy: hiring in more expertise within a key discovery discipline or in-licensing early phase assets with the appropriate profile from external organizations? In other words, build it or buy it? The tactic taken here will certainly be determined by the infrastructure strategy, the importance of having internal expertise/capability for the future portfolio, and the cost structure associated with either course of action.

Value Creation

It is the primary goal of portfolio management to maximize value and return. Several considerations must come into play when addressing the composition of the portfolio toward this goal. The short term revenue goals of the portfolio can take priority over investment in the development pipeline. However, inattention to the future marketed product strategy enabled by assets in discovery and development can result in devaluation of long-term future revenue potential. Determining the optimal resource allocation toward sales and marketing for current revenue maximization versus investment in research and development of the less mature asset pipeline can be difficult and must be aligned with the strategic goals of the company.

Balance

The composition of the portfolio must be balanced and commensurate with the financial goals, corporate strategy, and risk tolerance of the company. The Executive Committee must carefully consider many parameters, and then make thoughtful and often difficult decisions about which product(s) to include in or exclude from the portfolio.

For pipeline assets, often the risk of a project is proportional to the projected return on investment. When thinking about pipeline opportunities, it is often the high risk-high return projects that also require the most internal resource (see Fig. 2.1).

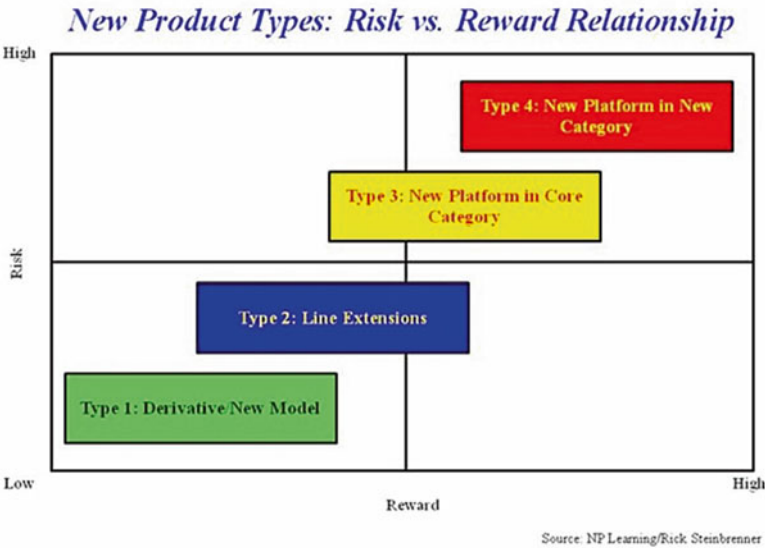


Fig. 2.1 Risk vs reward relationship for four different types of new products

Both risk tolerance and consideration of consequences of resource demand and reallocation should be considered. For example, if a high risk-high return project consumes the high performing talent, what low-medium risk but more certain revenue return projects will fall behind? A portfolio dominated by early phase assets might have a high potential value, but will also carry a high attrition rate, while a portfolio containing mostly marketed products may encounter a revenue “cliff” without revitalization from the pipeline.

Tactics for Clinical Portfolio Management

Complete analyses of tactics and strategies for continued development or termination of an asset, or inclusion, exclusion or abandonment of a product—whether in the preregistration or post registration phase of the drug cycle—is beyond the scope of this chapter. However, in terms of clinical decision-making, the product or potential product must have an acceptable risk–benefit profile for the specific indication in the appropriate patient population and must be adequately differentiated from the existing available therapies. The risk–benefit profile will be informed by severity of indication, magnitude of medical need, and local standard of care. A detailed clinical evaluation must be performed and continually reassessed at key investment milestones in order to ensure informed decision-making for portfolio inclusion.

Clinical Considerations

The best person to evaluate the practicality and clinical use of a medicinal product is a physician with clinical experience in the therapeutic area or indication for the product. The physician can provide unique insights such as:

- Ease of use.
- Potential for common drug–drug or drug–disease interactions.
- Patient population.
- Metabolic effects.
- Adverse effects common to the class of drug.
- Competitive environment.
- Clinical need for a new product.

This clinical review may also have implications from a commercialization standpoint.

The key clinical consideration is how the product addresses the unmet medical need. Another major purpose of the clinical review is to determine the safety and efficacy profile of the product—in terms of the product itself and the portfolio—as defined within the confines of a risk–benefit assessment. This assessment is easier for approved products or for a known class of products, and more difficult for new chemical entities or those entities that lack clinical data (e.g., preclinical candidates). Efficacy in animal models does not always translate to humans and thus care must be exercised—and higher risk ascribed—in the evaluation of earlier stage products. Other clinical considerations for asset/product assessment include, but are not limited to:

- Is the product unique? If not, does it complement or compete with the existing portfolio?
- How easy is the product to use?
- Can the product be sold using the existing sales force or will it require additional resources such as a specialty sales force?
- Does the product require extensive training of physicians (e.g., certain invasive cardiovascular medical devices) or patients (e.g., self-administered hemophilia product) or no training at all (e.g., OTC)?

Risk Management

Overall

Risk must be managed to protect a 10-year time horizon, which involves considerable uncertainty, in the context of current and anticipated investments within an ever-changing competitive environment.

Two key determinants for product risk management are patient risk, defined here as an evaluation of safety, and product development risk, which includes a risk assessment of clinical, regulatory and unknown product safety after approval but prior to patent expiration. Other determinants that will be discussed further include protecting existing compounds, in-licensing, mergers and acquisitions, due diligence, competitive intelligence, and patent protection and regulatory exclusivity.

Protecting Existing Compounds

There are a variety of R & D strategies to maximize or protect the value and return of a marketed product portfolio. For individual assets:

- Improving dosing schedule and patient convenience through formulation development.
 - Development of an extended release formulation from an existing immediate release formulation.
 - Improving patient palatability through improved dose presentation.
- Improvement of safety or tolerability through formulation/excipient modification.
 - Liposomal formulation to mitigate renal toxicity.
- Supplemental application for new indications for a marketed product.
 - Related indication within therapeutic area (such as a renal carcinoma application following melanoma approval).
 - New application in a dissimilar therapeutic area (e.g., an autoimmune disease application following cancer approval).
 - New application for an Orphan drug indication (this strategy also garners certain extra regulatory exclusivity that can act as patent protection).
- Approval in a new geography, region, or country.
 - Including emerging markets.
- New patent, extension of existing patent, or additional protection in a certain geography.
 - Pediatric clinical studies in response to an FDA written request (pediatric exclusivity).

In-Licensing, Mergers, and Acquisitions

If the R & D pipeline is limited, external sources of complementary (and also non-competing) products—which must meet an unmet medical need or be differentiated from the existing marketed products—should be examined to create value. Sometimes, for specific needs, it may be necessary to in-license a late-phase opportunity in a nonstrategic area, simply to maintain cash flow. If the need is considered great enough, and capital is available, an entire company can be purchased

which might include a specific compound (or compounds) or perhaps a platform technology that may either produce additional candidates or modify existing compounds in the buyer's pipeline.

One possible response may be to in-license a product similar to an existing, successful marketed product with the goal of adding (or replacing) market share from the existing product. However, the new product must be sufficiently differentiated in order to achieve regulatory approval and payer reimbursement.

Below are two case studies which highlight the success of second generation, follow-on prescription drug (Nexium®) and a patent dispute designed to ward off generic competition (Alimta®).

Case Study: AstraZeneca's Prilosec and Nexium

AstraZeneca had a dominant gastrointestinal franchise with Prilosec® (omeprazole), which was the world's best-selling drug, with global sales of \$6.2 billion. To counter the potential downside of Prilosec's patent expiry in October 2001, AZ CEO Tom McKillop considered a range of options, according to a *Harvard Business Review* Case Study titled "AstraZeneca, Prilosec®, and Nexium®: Marketing Challenges in the Launch of a Second-Generation Drug," by James G. Conley, Robert C. Wolcott, and Eric Wong (January 1, 2006). These included several "franchise-extending" strategies, such as the launch of a second generation, follow-on prescription drug (with a new patent) branded as Nexium®, and the introduction by AZ of generic omeprazole and/or an over-the-counter version of omeprazole. The *HBR* case study notes that both the generic and OTC markets were uncharted territory for AZ. "The path forward to sustain market dominance in its category, especially with respect to the OTC opportunity, would require significant channel know-how." Clearly, AZ successfully tackled this challenge, successfully launching Nexium®—with a differentiated product profile—to protect its income stream after Prilosec's patent expiry. Nexium® ranked second in sales in the US market in 2011, with sales of \$6.3 billion according to IMS Health [1]. In the second quarter of 2012, Nexium® reportedly led the US market with sales of \$1.38 billion [2].

Case Study: Lilly's Unusual Patent Dispute

In August 2013, Eli Lilly & Co. began defending a patent for its lung-cancer treatment Alimta®, which recorded global 2012 sales of \$2.6 billion, according to a *Wall Street Journal* report [3]. The patent covers the method of administering Alimta® to patients with certain vitamins designed to mitigate side effects. A different patent covers the basic chemical composition of Alimta®. The newspaper writes that the case highlights the pressure on drug makers to preserve market exclusivity for top-selling products for as long as possible in the face of generic competition,

pricing pressure and underproductive research labs. A victory for Lilly would block several generic companies from selling low-cost copies of Alimta® in the US market until at least 2,022, notes the *WSJ*. A loss could allow generics to be launched in 2017—when the patent expires for the basic compound—a development that would rapidly erode sales of the original brand.

Due Diligence [4]

For purposes of this chapter, due diligence (DD) is used to assess the probability of technical success (PoTS). Technical risk is defined as those factors that are inherent in the product and will contribute to its full sales potential, given the right sponsor.

Due diligence is simply a process for managing risk. All companies perform DD prior to making an investment. Proprietary information is first exchanged between companies after a Confidential Disclosure Agreement (CDA) has been executed. This is of critical importance to protect both parties and should be executed promptly, usually under the direction of a company's legal department/counsel.

Environments in which DD can be utilized range from simple, single-product transactions between a buyer and a seller to more sophisticated global acquisitions of multiple products. The simplest DD exercise may require only one person; more sophisticated partnering opportunities or acquisitions may require a team of experts with a range of disciplines. Due diligence proceeds with this team of experts to assess corporate strategy, research and development, intellectual property, human resources, and financial dealings, identifying the strong points and weak points of a company, a product (or products), or even a potential deal in order to better manage risk.

Competitive Intelligence [5]

Competitive Intelligence (CI), for purposes of this chapter, is used to determine market risk while identifying competitive threats so that they can be addressed as early as possible.

Pharmaceutical CI entails defining, gathering, analyzing, and distributing intelligence—both nonproprietary and proprietary—on pharmaceutical products, customers, competitors and any aspect of a particular functional area needed to support executives and managers in making strategic decisions for an organization (e.g., an expected return on investment or strategies based on the loss of patent protection).

Stakeholders are varied and include pharmaceutical companies, contract research organizations (CROs), pharmaceutical manufacturers and those associated with the supply chain, investors, patients, health payers, and government organizations. Although typically thought of as being driven by other companies, competition may also be affected by regulations (including product-based labeling), lack of regulations (e.g., lack of Guidance from FDA's Office of Prescription Drug Promotion

(OPDP) regarding social media) or long-awaited draft FDA guidance for biosimilars, finally issued in February 2012, politics (e.g., controversy around medical cannabis-derived products), accounting principles (e.g., general accepted accounting practice (GAAP), geographies (International Conference on Harmonization (ICH) vs. non-ICH), patent protection, and regulatory exclusivity). Patent protection and regulatory exclusivity is discussed separately.

Publicly available information is obtained via the World Wide Web and may be accessed for free, such as information contained on a competitor's Web site, or available for a cost (e.g., fee to print a full-text article or IMS Health data to track pharmaceutical sales). It is typically limited by the savvy of the researcher, the amount of time that the investigator has to compile the information, and by the investigator's access to company-wide databases. Large companies typically have an advantage over smaller companies in gathering CI due to their scale and resource availability.

A key caveat to this entire process is that the gathered information must be converted into intelligence and then utilized for business decision-making when assessing the market for a particular product or group of products. In essence, if the CI gathered is not usable (or actionable) then it is not intelligence. Increasingly important is the understanding of the landscape for the payer environment when assessing the overall risk of any particular product.

Patent Protection and Regulatory Exclusivity

The available patent life or regulatory exclusivity of any product must be taken into account when determining the return on investment. This is even more important for portfolios of products, such as biosimilars, where the originator company is standing ready to battle potential future competitors. Therefore, it is imperative that the pharmaceutical executive have a general understanding of the overall process for an assessment of patent protection and regulatory exclusivity.

The strength of a patent, its remaining patent life, and the potential to obtain regulatory exclusivity all form the basis of protection for a branded product from competition, including generics. Another key issue is freedom to sell a product without interference from third parties that may own relevant patents. Because pharmaceutical executives are increasingly being asked to participate on due diligence teams, they need to be familiar with the IP investigational process and the key outputs of the IP assessment. This enables their employers to better understand the risks associated with the inevitable patent challenges that arise with financially successful branded products and potential threats from third-party patent owners.

Although respected in major ICH countries (e.g., the USA, EU, and Japan), not all countries honor patent protection equally and this reality must be factored into a global marketing strategy. Moreover, the patent and regulatory exclusivity situation for a given product often varies substantially in the various countries. For sponsors of branded products, this may preclude marketing a product in a particular country.

Key considerations for understanding the value of a product relative to patent protection and regulatory exclusivity include:

- IP assessment is critical to the entire due diligence and product portfolio optimization process.
- IP protection includes both the classical IP assessment as well as the regulatory exclusivity assessment. Together they form the basis of protection for a product from competition.
- When IP vulnerability is discovered, it is often possible to diminish or even eliminate a risk through contractual language.

Avoidance of Bias

Overall

There are multiple ways to reduce or avoid the biases inherent within product portfolio management. This section provides an overview of the pitfalls associated with potential biases in decision-making and discusses several successful approaches for reducing risk.

Background

When new products come out of the discovery phase of drug development, they typically look very promising and commercial hopes are high. Most candidates, nonetheless, fail during Phase I or Phase II.

Development teams often work in “plan-to-succeed” mode, without necessarily performing war-gaming exercises to predict what might go wrong, and without adequately challenging the probability of scientific, regulatory, or commercial success as anticipated by the due diligence or product marketing teams.

War-gaming can help determine whether a portfolio plan is truly robust, using measures of the actual risk within the portfolio—clinical, regulatory and commercial—to calculate an Expected Net Present Value (ENPV, which takes into account estimated probability of success for each product under development). This metric is more useful than an NPV (which assumes 100 % probability of success) and can be risk adjusted to take into account the probability of success for compounds in the pre-registration phase of drug development. While some risks are known—for example, the probability of patent expiry is 100 %—others are less certain, such as the:

- Probability that the animal data predicts clinical outcomes.
- Probability of the occurrence of unexpected safety findings.
- Probability that a product is adequately differentiated.

- Probability and timing of competitive entries along with their level of differentiation.
- Clarity of the path to regulatory approval and market access.
- Likelihood of success for the proposed marketing and sales approach.
- Political landscape (which may favor bringing cheaper copies of products to market, such as generics or biosimilars).

These factors and the assumptions around them can be used to collectively summarize the positive and negative attributes of each product in the portfolio. This, in turn, can be used to risk-adjust the overall probabilities of success for these products, thereby giving a more meaningful assessment of individual estimated NPVs and the net value inherent in the overall portfolio.

Predictive Tools

Once the known data about the product (or the scientific class of the product) are collected—and the scientific, regulatory and commercial assumptions about the product are clearly defined and delineated—it becomes possible to model the impact of this information on the probability of successful development and commercialization of the product.

While commercial modeling is a standard process for most pharmaceutical companies, modeling of potential scientific and operational development outcomes is rarely performed. More recently, a number of companies have developed software tools to better analyze and predict these development outcomes. Estimation of enrollment, overall development time (based on critical path activities) and cost of a program are examples of how tools can be used to estimate operational outcomes. Other technology, such as Quintiles Infosario Design®, use large, patient de-identified datasets (including electronic health records), to better understand population dynamics (impact on inclusion/exclusion criteria, accessibility of patients, standard of care, clinical event rates, etc.) and their impact on the design of clinical trials and programs. Use of such data, combined with existing clinical trial data, allows for the development of combined scientific and operational scenarios—which can then inform programmatic decision-making.

Access to such data and the tools to “prototype” outcomes by developing design scenarios, empower drug developers with the knowledge locked in such data and improve decision-making. Ultimately, better design decisions by minimizing bias and unchallenged assumptions, should help to improve the probability of success at each step in a product’s life cycle.

Once drug development reaches trials in patients, these systems can be deployed as technology-assisted consulting services designed to help pharmaceutical companies optimize their clinical planning and design process. This optimization is achieved through two major steps: first, expanding the design space by generating new options and new combinations of approaches to the problem; and then optimizing time, cost, and risk parameters over the expanded space of design possibilities [6].

Adaptive Design Principles

Adaptive design principles—which address the risk embraced by both R & D and commercial factors—can be used to mitigate portfolio risk. Use of adaptive principles is an extension of the “cone of uncertainty” concept: As uncertainty is reduced when R & D milestones are achieved, or increased (e.g., due to lack of differentiation or unexplained safety events), the overall portfolio probability of success is modified as it “adapts” to the inclusion of this new information. Rather than iterative, isolated decisions are being made at a single individual product event, the overall portfolio balance is maintained, which minimizes bias, and accounts for the ever-evolving ENPV. This approach contrasts with the timing of most overall portfolio reviews performed by large biopharmaceutical companies that only may occur two or three times a year.

For a full portfolio analysis, the “cone of uncertainty” can be applied across all 10–15 molecules. Although potentially time consuming, each molecule has a risk adjusted ENPV, which changes at each R & D milestone. Adaptive statistics are applied across all “cones of uncertainty,” taking into account variability in the confidence that can be attributed to the ENPV. This process has the important benefits of being more methodical and less subject to bias than traditional, infrequent portfolio reviews.

Aspirational Drug Development

Other biases that can corrupt the portfolio include teams engaging in “aspirational” drug development. In this case, the drug development team aspires to an outcome—that may or may not be grounded in the scientific realities of the drug’s safety and efficacy performance. For example, a marketing team may have the desire to have a safer drug, but the clinical data may not demonstrate a difference in adverse events (AEs) using descriptive statistics, or the drug may not have even been studied in such a way that a superiority safety claim can be justified. Since the sales team is limited, from legal and ethical standpoints, to discussing only those claims that are justified in the approved label, this leads to a mismatch in the desired “target product profile” and the “actual product profile” (as manifested in the approved label) and with corresponding impact on the commercial forecast. On the flip side, if designs of clinical trials and programs are based solely on the desired attributes of the drug rather than the manifest scientific “actual” attributes of the drugs, there is a high probability that the trials will fail to deliver against expectations, and thus generate little to no value for the product.

Increased or Decreased Chances of Success

Some situations may warrant optimism when determining the chances of product’s success either in the clinic or the market. Well understood drugs, with a strong track record of historic sales, for example, should be expected to sell well when positive data is generated in the pediatric setting. An increase in the PoS for registration

should also be expected for products with extended release formulations or 505(b)2 applications. The converse is also true. For example, some drugs that work in some settings may not work well in adjunct but apparently similar indications (at least from a therapeutic class standpoint), for example a schizophrenia drug moving into manic depressive disease.

Sustainability

The portfolio must be able to deliver on its short term goals with appropriately allocated resources and ensure a sustainable stream of revenue to continue to fuel product development and sales and marketing support. For any asset, competitive strength versus market attractiveness should be considered. Competitive strength is reflected based on a composite of market share, size/scale, quality, technology, cost of goods, brand strength, and customer loyalty to the class. Market attractiveness is a composite of size, growth, competitive rivalry, profit levels, and ability to differentiate.

While these parameters will be data-based for marketed products, modeling with careful assessment of the underlying market assumptions will need to be employed to assess this rubric for assets in earlier phases of development. Keen focus on the optimal target product profile is critical to ensure differentiation and reimbursement. To this end, the development plan must be designed such that robust data informing clear “go/no go” decisions is available at appropriate stage gates. These decisions, especially when the data support termination of development, can be difficult for organizations. However, rigor around this process is critical to make the best use of limited resources.

Portfolio Growth

Here, the goal is not only to protect but to increase revenues. Revenues can be obtained through strategic in-licensing (utilizing due diligence teams) or through desperation in-licensing. The latter may be due in part to known confounders, such as patent expiration. It may also be a response to unknown events such as an untoward safety signal (e.g., immunogenicity) that arises in clinical development of a company’s own product or a competitor’s, or a change in the regulatory climate (lack of FDA guidance or additional restrictions in a therapeutic area [e.g., cardiac outcome investigations with new compounds used to treat diabetes mellitus]). Some franchises may prove to be a scientific dead-end, with no new mechanisms-of-action coming out of R & D to create value. In that case, a company would need to create a new franchise, most likely adjacent to an existing, successful franchise, where the target market would be similar—for example, it might make sense for a company that is strong in diabetes to move into antiobesity products. Serendipity can also play a role in portfolio growth—for example, when scientists who are looking for activity in one therapeutic area find it in another (see Viagra case study).

Case Study: Viagra Discovery Based on Serendipity

“The surprising truth is drug design owes more to serendipity than careful design, and their potential may only be discovered when we take them,” wrote *BBC.co.uk* on January 20, 2010 [7]. Quoting Viagra as an example, *BBC.co.uk* reported that this product, code named UK92480, started life as a new treatment for angina. Trials in people were disappointing, and Pfizer was “about to abandon further trials when the trial volunteers started coming back and reporting an unusual side effect—lots of erections.” Until Viagra’s 1998 launch “there was no oral treatment for erectile dysfunction... Now, thanks to a failed angina treatment, men had another option. Viagra is now one of the most prescribed drugs in the world.”

Summary

Portfolio strategy decision-making—taking into account development and manufacturing costs, commercial expectations, clinical risk–benefit assessments, competitive intelligence, due diligence, and intellectual property protection—is a key element in driving shareholder value.

Sustainable pharmaceutical portfolio management is guided by principles that maximize the value of the portfolio, balance its components, and make sure that additions and subtractions represent a strategic fit. Choices should be guided by an acceptable level of risk, as determined by the risk–benefit assessment for each product in the portfolio. The pharmaceutical physician is usually the best person to perform this review and make this assessment, although other persons with appropriate clinical and medical training can also conduct these assessments.

The key clinical decisions that must be made are based on an understanding of the pathophysiology of the compound, the safety and subject risk interpretation and the use of the product in the appropriate clinical setting (surgery suite, private practice, hospital, outpatient, etc.). Once the safety risks have been identified, they need to be managed within the bounds of regulatory affairs mandates (annual safety updates, annual reports, pharmacovigilance, etc.), ethical mandates, and best clinical judgment.

The portfolio must be balanced and driven by corporate financial goals, strategy, and risk tolerance. The portfolio must be able to deliver on its short term goals with the appropriately allocated resources to ensure a sustainable stream of revenue to continue to fuel product development and sales and marketing support. In addition to product development, a company can leap-frog this process and in-license a product or acquire a product or products via merger and acquisition.

When looking for products to acquire, it behooves the company to conduct due diligence and determine the positive, negative and unknown attributes of each product. The lynchpin of the due diligence process is the IP assessment which includes a thorough investigation of both patent protection and potential for regulatory exclusivity.

War-gaming is a useful approach in helping marketing teams determine whether the portfolio plan is truly robust, using measures of the actual risk within the portfolio—clinical, regulatory, and commercial—to calculate an Expected Net Present Value (ENPV).

Portfolio managers need to be aware of biases that can be inherent in portfolio decision-making, balancing those factors that may artificially increase or decrease the estimated probability of registration or commercial success. Complex tools, such as including adaptive design principles, and large data software tools, such as Infosario, can also be utilized to minimize and mitigate the risk and bias embraced by both the R & D and commercial factors.

References

1. Herper M (2011) The Best-Selling Drugs in America. *Forbes*, 19 Apr 2011. <http://www.forbes.com/sites/matthewherper/2011/04/19/the-best-selling-drugs-in-america/>. Accessed 24 Jul 2014
2. Staton T (2012) AZ's Nexium tops Q2 sales ranks, with BMS' Abilify on its heels. *Forbes*, 23 Aug 2012. <http://www.fiercepharma.com/story/azs-nexium-tops-q2-sales-ranks-bms-abilify-its-heels/2012-08-23>. Accessed 24 Jul 2014
3. Loftus P (2013) Eli Lilly enters unusual patent dispute. *Wall Street Journal*, 18 Aug 2013. <http://online.wsj.com/article/SB10001424127887323455104579015291810290818.html>
4. Huml RA (2010) Introduction to the due diligence process. RAPS, p 126, copyright 2010, ISBN: 0-9787006-4-3
5. Huml RA (2012) Pharmaceutical competitive intelligence for the regulatory affairs professional. Springer, p 82, Copyright 2012; ISBN: 978-1-4614-3681-2 (Paperback); ISBN 978-1-4614-3682-9 (eBook)
6. Quintiles press release (2013) Quintiles Infosario receives Computerworld Data+ Editor's Choice Award. 26 Aug 2013. <http://www.quintiles.com/library/press-releases/quintiles-infosario-receives-computerworld-data-editors-choiceaward/>. Accessed 24 Jul 2014
7. Jay E (2010) Viagra and other drugs discovered by accident. *BBC News*, 20 Jan 2010. <http://news.bbc.co.uk/2/hi/health/8466118.stm>. Accessed 24 Jul 2014

Optimization of Pharmaceutical R&D Programs and
Portfolios

Design and Investment Strategy

Antonijevic, Z. (Ed.)

2015, VIII, 202 p. 38 illus., 24 illus. in color., Hardcover

ISBN: 978-3-319-09074-0