# 1 Introduction

The aim of this book is to help ascertain the value of biotechnology assets whether they are drugs or companies. As with any investment, it's better to be well informed ahead of making the investment decision. This requires preparation as the potential for value differences arises partly because of differing expectations among different buyers and sellers. This book should provide a background to the principles of valuation and a toolkit to establishing the value of a biotechnology company. Valuation is important to people performing different roles in the pharmaceutical, biotechnology and investment industries such as venture capitalists, investors, and business development staff. Appropriate valuation metrics put buyers and sellers together whether they are investors assessing a stock or a biotechnology company's management team assessing an out-licensing opportunity. The key aim of the industry is to transform financial resources into new drugs. In this book I try and ascribe a value to that transformation.

I started my career as an academic scientist, followed by a period in industry before moving into a commercial role at a pharmaceutical company. This gave me my first encounter with valuing drug assets, both for internal purposes and also as part of a team that assessed in-licensing and out-licensing opportunities from a commercial or valuation perspective. I was also fortunate to work on drug projects at different phases of their development and commercial life cycles, which gave me an insight into the different factors that impact valuation, as the asset moves through the drug development value chain.

The sector can be viewed as quite technical which can be off-putting for some. However in my view it is a mistake to get overzealous about the science, to the extent that it handicaps your assessment of value. Although some of the science underlying the drugs is extremely cutting edge and exciting, the basic business models employed by the majority of companies are relatively straightforward. I have included a glossary of the more frequently encountered scientific and technical terms but my advice is to use the standard metrics included in this book to assess chances of success and focus on the cash flows.

Over the past 11 years I have had a career as a sell side analyst with a number of investment banks. Sell side refers to an analyst that works for brokerage houses/investment banks where sales people sell stocks based on analysts' recommendations. In recent years this job has come in for a lot of criticism, especially post the Global Settlement on April 2003, which was an enforcement agreement reached between financial services regulators in the United States, and ten of the largest investment banks to address issues of conflicts of interest. These conflicts in essence stemmed from the investment banking divisions potentially having too much influence on the research department's publications and compensation. As trading commissions declined, the costs of the sell side research department were offset by banking fees.

Post the Global Settlement, analysts in all banks have fewer interactions with their investment banking counterparts and when those interactions occur, they are carefully monitored by management and the compliance department. One of the consequences of these events is that sell side analysts are moving their coverage universe (companies they write research on) towards larger, more liquid (heavily traded) companies. This decline in the number of analysts covering a stock can mean a dwindling exposure to investors.

Whilst I acknowledge that the sell side has been justifiably criticized in the past, I do believe that the sell side has a very important education role in more abstruse sectors such as biotechnology. Most people can understand the market for a new version of a cola drink or a novel technology widget that increases the functionality of their mobile phone but understanding how a novel cancer treatment fits into the current market is a much more difficult task. Thus I see the sell side fulfilling this broader educational role that is perhaps not required in other traditional sectors.

Typically analysts have either a scientific or a medical background plus business experience. The key priority is to provide objective, timely and value-added research to help institutional investors make profitable decisions. Analysts review financial statements of the companies, read industry news, use trading history and industry information databases, meet management and attend conferences.

Analysts form their opinions using multiple sources to understand and monitor their recommendations, including:

- macro-interest rate, business cycle
- industry newsletters
- company interaction and published information
  - management
  - press releases
  - financial statements
- clinical-trials, initiation, design and interpretation
- real time input from the markets
  - LSE, AiM, Euronext, SWX, NASDAQ, AMEX, TSX

Sell side analysts seek to develop, and communicate to investors, insights regarding the value, risk and volatility of a stock and thus assist the investor to decide whether to buy, hold or sell stocks. Valuation is an important component in this job but with a number of caveats. Analysts generally put a price target per share as part of their recommendations but valuation can never be so precise. As an analyst publishing research notes there is a danger of becoming fixated with the one year price target which is the value per share that the analyst believes the stock should rise (or fall) to. Thus the notion of valuation range must be incorporated into the analysis, coupled to where the stock may be trading now. Furthermore some of the inputs are subjective and this is where the "art" of the valuation comes into play. Each individual must make their own assessment of certain facts. I encourage readers to look beyond the confines of the valuation issue at hand and seek a variety of ways of approaching the problem. Even how the problem is addressed or the framework in which it is positioned is important and relies significantly on the individual's creativity in problem solving.

This is probably the hardest element to capture correctly in a valuation analysis. Experience does help, which is a key driver of what prompted me to write this book. However drug development has huge uncertainty involved, as one tries to predict what a biological or chemical molecule will do within the physiological system of a human. Therefore even experience can only be a guide and we, as individuals, will get analyses wrong. A key aim of this book is to impart my experience and try and help get you up the learning curves as quickly and as easily as possible.

I was fortunate to be an analyst during the recent biotechnology boom in 2000 and it was the experience of marketing to institutional investors over that time period that first triggered

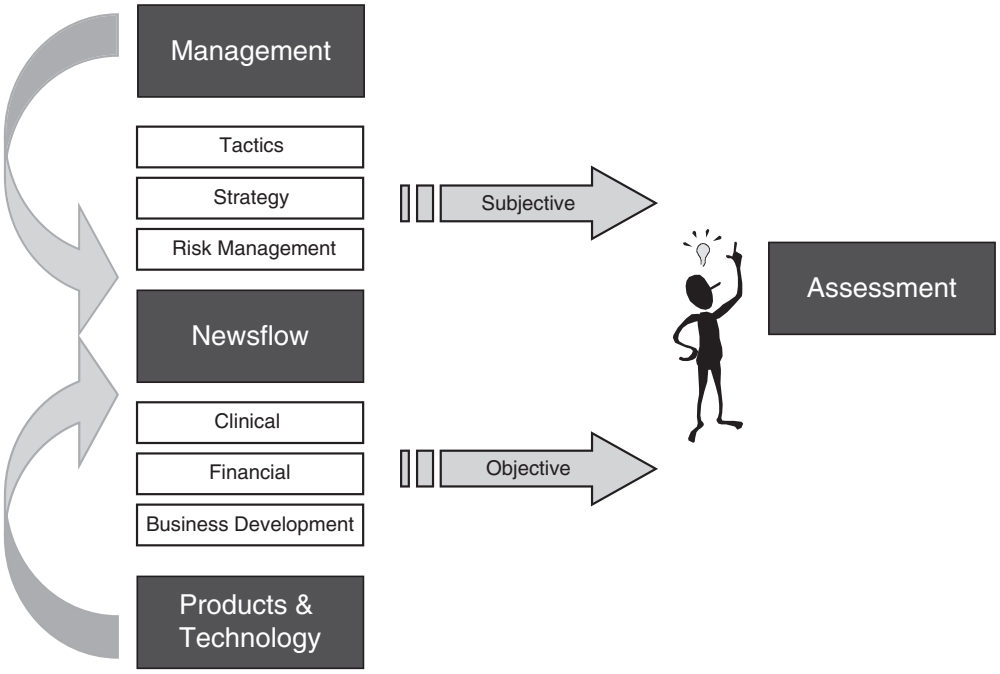


**Figure 1.1** Analysis is a combination of subjective and objective assessments

my interest in the broader aspects of biotechnology valuations. During the biotechnology boom, the valuations of biotechnology companies rocketed as companies and investors sought to capitalize on the furore surrounding the outcome of sequencing the human genome.[1,2,3] Media hype also played its part. However the lesson I learned from that exciting period was that investors looking at a stock used a variety of metrics. Furthermore when investors wanted to talk about a valuation, they really want to know the assumptions underlying the model, not the exact outputs that are derived. This prompted me to focus on applying a consistent and transparent methodology to biotechnology company and asset valuation. I believe that this is a really important point and in essence is what I am trying to do in this book. Hopefully when you have finished reading this book, you should have developed a consistent approach and have a useful toolkit to tackle the valuation of a biotechnology company or individual drug, with confidence.

As in all books of this nature, there is no standardized reader. Thus, I have included chapters addressing the regulatory and technical hurdles that define drug development. Furthermore I have tried to share some of my experiences, highlighting some of the potential pitfalls when attempting to value biotech companies. This is not comprehensive but merely consists of some of the most common errors which I have succumbed to in the past.

In this introductory chapter I focus on defining the task ahead, namely trying to value healthcare-focused biotechnology companies which are trying to develop new therapeutics. This segment of biotechnology is one of the most dynamic in terms of investment, capital raised and number of companies, both public and private. Biotechnology assets are generally composed of drugs, patents and people, all of which are difficult to value in a traditional sense.

However currently there is no consistent way to value drug assets and the methodologies that are generally used in other sectors need modification in order to apply to the technically focused and regulation bound world of drug development. This book demonstrates the areas where the practitioner will need to use skill and judgement in order to get a meaningful valuation from the analysis.

Over the subsequent chapters I briefly review traditional valuation techniques so that all readers can tackle the remainder of the book with a suitable level of financial understanding. This is not meant to be a book steeped in financial theory, more a practical guide for the interested individual who wishes to ascribe value to drug assets. I have included a bibliography which includes some general finance textbooks and a selection of other books that provide interesting perspectives on the biotechnology industry. Whilst there are many books on valuation methodology, there are not too many on biotechnology valuation. This book is my attempt to remedy this issue.

One of the features of both the pharmaceutical and biotechnology industries is that both are heavily regulated, not just in the United States but across the globe. Whilst providing a framework for analysis and a (relatively) clear pathway to take drugs to the market, the drug development process also poses many hurdles and each phase is associated with probabilities of success. In Chapter 3 I attempt to provide an overview of the process and highlight some tips and potential pitfalls for the unwary investor.

In Chapter 4, I move on to valuing biotechnology companies and again provide a framework for the valuation with an emphasis on discounted cash flow analysis, comparable company analysis and product pipeline assessments using a probability weighted net present value model. This latter approach is very important as the majority of biotechnology companies are loss-making and thus investors need to ascertain value in the absence of earnings. The key point is that no single methodology can provide all the answers and thus the use of multiple approaches to addressing the problem in hand is a far better approach.

Chapter 5 takes the analysis further by looking at individual net present values (NPV) of drug assets, a useful technique when one's estimated valuation suggests that one or two drug assets comprise the majority of the value being determined. Although the methods discussed in Chapter 4 are useful and can be successfully applied to biotechnology valuation, there are an increasing number of papers and books advocating the use of decision trees and real options analysis to capture the value inherent in management decisions through the development phase that is not captured in a straightforward discounted cash flow analysis. In this chapter I go through the mechanism and some of the theory underlying these approaches. However in my view, the use of real option analysis is more appropriate for insiders in a company. By that I mean access to management accounts and business plan, including the costs timings and expected commercial potential of the drug. The need for these "real" figures curtails the use of such analyses for those external to the company as they have to rely on publicly disclosed information on estimates.

Chapter 6 provides a guide to investing in the biotechnology industry and looks at some of the approaches that successful investors apply. This builds on the toolkit of valuation approaches discussed in the previous chapters and incorporates more of the art with an emphasis on other non-valuation driven metrics that are useful for biotechnology investing.

In Chapter 7 I review concepts applicable to the valuation of early-stage or venture backed biotechnology companies, thereby completing the valuation of all types of biotechnology companies: private venture backed, loss-making public and profitable public companies.

## BIOTECHNOLOGY BACKGROUND

Biotechnology is a general term describing the directed modification of biological processes and has been defined as "the application of biological organisms, systems and their components to industrial products and processes".[4] This may be accomplished by introducing new genes into organisms, breeding organisms to form new variants, or treating organisms with specific compounds. Thus, biotechnology in its broadest sense is about the use of living organisms with the aim of developing new products or processes to improve our health, environment or agriculture.

Biotechnology is not a separate science but rather incorporates expertise from a wide range of scientific disciplines. As the realization of the power of biotechnology has become more widespread, the biotechnology industry has in itself become global in nature. Biotechnology is being used to develop crops and breed animals with special characteristics. In addition biotechnology tools and techniques are being applied in the development of new industrial enzymes. In the business sense biotechnology could refer to the use of biological processes to make money! This also refers to the historical aspects of biotechnology when natural processes were used to improve crops and animal husbandry and to provide foodstuffs such as wine and cheese.

However the scope of the industry in this sense is way beyond the boundaries of this book. This book will restrict itself to trying to value the companies that make up the biotechnology industry involved with the discovery and development of new medicines. As such, it should be called the discovery industry because it now employs far broader technology than its original focus on recombinant DNA and monoclonal antibodies.[5] The discovery of the structure of DNA in 1953 and the identification of DNA as the genetic material in all life allowed for great leaps in our understanding of life forms from bacteria to plants to humans. However, the biotechnology industry is generally accepted to have originated in the 1970s, based largely on a new recombinant DNA technique whose details were published in 1973 by Stanley Cohen of Stanford University and Herbert Boyer of the University of California, San Francisco. These scientists had successfully extracted DNA from a toad and then inserted this DNA into a bacterium. As the bacterium multiplied, the new bacteria produced the protein encoded by the toad DNA. This technique utilizes recombinant DNA technology and today is a method of making proteins – such as human insulin and other therapies – in cultured cells under controlled manufacturing conditions. In 1974, the industry got another technological boost when Cesar Milstein and Georges Kohler discovered how to fuse an antibody-producing cell with a cancer cell, allowing the resulting combination (hybridoma) to produce large amounts of identical antibodies (termed monoclonal antibodies) essentially forever. In 1976 the healthcare-focused biotechnology industry as we know it today was born when Boyer agreed to start a company (Genentech) funded by Bob Swanson. The excitement of the new industry was attracting new capital and in 1980, Genentech went public on October 14 at US$ 35/share, raising US$ 35 million.

In my view the successful financing of independent biotechnology start-ups has been a hugely significant achievement, especially as the funds raised are raised on the basis of potential rewards rather than current cash flows or operations. This success is to be applauded but it does raise questions on how to ascribe value to the potential rewards.

I have focused on the pharmaceutical sector and the issues facing companies trying to develop new drugs, irrespective of whether these drugs are derived using biotechnology methods or not. Furthermore I have used the term biotechnology to encompass the broad

range of technologies that are used in drug discovery and development rather than the more narrow view of focusing only on biotechnologically derived drugs.

Within this restricted definition of the application of biotechnology to medicine, I have attempted to provide the layperson, or interested amateur, with a guide as to the investment potential of biotech companies, which in themselves cover a broad spectrum of technologies and business models. I do not differentiate between the technologies used to discover drugs (chemical or biotechnology) and indeed a more proper definition would be to class all of these companies as small to medium-sized emerging pharmaceutical companies.

Historically biotechnology companies could be differentiated from pharmaceutical companies by their use of biotechnology techniques (in essence a comparison between recombinant engineering and synthetic chemistry). It initially appeared that the biotechnology industry could enforce a paradigm shift in drug development that would leave traditional pharmaceutical companies obsolete. However the large pharmaceutical companies did not succumb to the introduction of the biotechnology techniques but instead learned rapidly from the new start-ups. Thus this easy categorization is no longer appropriate and companies in both biotechnology and pharmaceutical sectors utilize all of the tools available. In my view, it is more important that the term biotechnology company refers to the philosophy underlying the business model rather than the actual scientific and technical means of developing a drug.

The global biotechnology industry is an exciting investment arena because it seeks to integrate the cutting edge of science with the world of finance in order to bring us the medicines of the future. Biotechnology offers investors an exciting entry point, where the business world meets the world of scientifically driven healthcare research. Thus the investor has the opportunity to potentially add to the development of new medicines and also to capture economic value from the endeavour. Biotech companies are small to medium-sized companies operating in the pharmaceutical research and development industry (R&D) with the development of a new drug as their primary focus. A very dynamic environment and high levels of technical and commercial uncertainty are typical features of the biotechnology

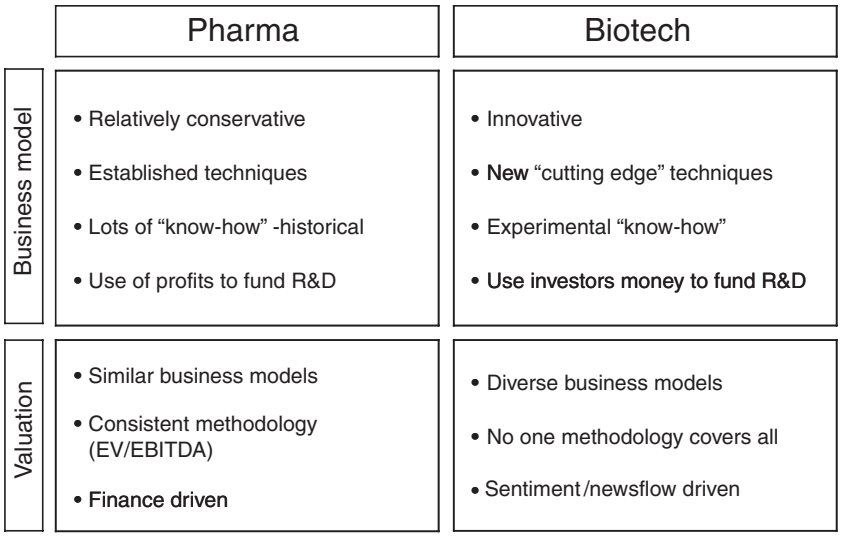


**Figure 1.2** Comparison of pharma and biotechnology valuation

**Table 1.1** Global biotechnology at a glance 2005

| | Global | US | Europe | Canada | Asia-Pacific |
|---|---|---|---|---|---|
| Revenues ($m) | 84 872 | 68 400 | 13 352 | 2 692 | 3 970 |
| R&D expenses ($m) | 31 806 | 30 000 | 6 309 | 915 | 488 |
| Net Income (loss) ($m) | −2 694 | −3 600 | −2 645 | −722 | −6 |
| Number of companies | | | | | |
| Public | 798 | 386 | 181 | 82 | 149 |
| Private | 3 616 | 1 502 | 1 563 | 322 | 615 |
| Total | 4 414 | 1 888 | 1 744 | 404 | 764 |

*Source:* Ernst & Young. Beyond Borders Global Biotechnology Report 2008, reproduced with permission

sector. Many companies have significant valuations many years before they earn any profits from selling their products.

Key difficulties in biotechnology are the long timeframes and high development costs to bring one product to the market along with the challenges of high risk and technical uncertainty. This means that a lot of money is needed for a long period of time until the investors get any compensation for their investment. Meantime, the odds against them succeeding are fairly high.

However, biotechnology-derived products have the potential to positively change our society, from improving health care and increasing agricultural products to producing a cleaner environment. The public markets recognize this potential and a lot of money has flowed into biotechnology companies. Sales, revenues and market capitalization all more than doubled during the period from 1993 to 1999. The year 2000 saw more money invested in biotechnology firms than the previous five years combined. The business models have matured and the tools of biotechnology research are refined to the extent that the industry is ready for unprecedented growth.

In this book, I have focused on product-based biotechnology investments. I believe that the structure (stages) of the product development process, the consequent predictability of news flow timing and the possibility of assigning real value to the compounds has captured investor interest in the product-based stories. In 2000, the world was focused on the hype surrounding the sequencing of the human genome (The Human Genome Project), driven for the most part by the accompanying media frenzy. However, this interest waned and with it investors' acceptance of platform technologies. In truth, it is difficult to truly differentiate among a plethora of technologies that all claim to offer drug discovery nirvana to the pharmaceutical industry. A key metric for these companies was the number of partnerships they could sign and in most cases, management was found wanting.

Unless a technology platform company is broad enough to support many deals, this model remains limited, and companies should be valued with this in mind. In addition, both management and investors often underestimate the time needed to complete a deal, and this alone limits the number of deals a company can do in any one year. Platform technology companies have been perceived as lower risk than product companies, and as the nascent European biotechnology industry emerged in the late 1990s, this model initially appealed to investors. However it is worth remembering that while platform companies are not exposed to the specific technical risks associated with drug development, commercial risk can be higher and potentially more limiting. Drug development is the driver of both opportunity and risk. Many management teams have glossy presentations providing copious detail on the minutiae of the

science but as an investor, none of this matters unless the company is either bought out or brings a drug to the market. Even then the valuation depends upon how well the management team can identify and manage development and commercial risk.

Successful investing in any product company requires a true understanding of the risks in bringing products to market. I categorize these risks as:

- Technical – Successfully taking the drug through the complete clinical trials and regulatory process and on to the market. Technical risks relate to the stage of clinical trials that a drug is in, but also the extent to which a concept and any drug based on that concept, is proven in man. Ultimately technical risks can be reduced to a binary decision; is the drug approvable or not?
- Commercial – Recognizing and realizing the true market potential of a drug and the associated commercialization hurdles, e.g. marketing, partnering. Thus the commercial risks are much broader and consist of a spectrum of possible outcomes. Is there room for five such products on the market? The later products, without the first-to-market advantage, are likely to have to show real advantages over established products (or be better marketed) to get more than a relatively small share, albeit of a potentially big market.

Commercial risks are equally as important as technical, yet are often neglected by analysts and investors alike. It is potentially possible to create enormous opportunities for drugs to treat stroke. However, the standard probabilities of success ought to be modified according to the specific hurdles associated with drug development in a particular therapy area. Most biotech companies lack a GP sales force or the resources to create one. Equally licensing a cancer drug to a company lacking any presence in this market may be less than ideal. Investors need to focus as much on commercial success as technical probabilities.

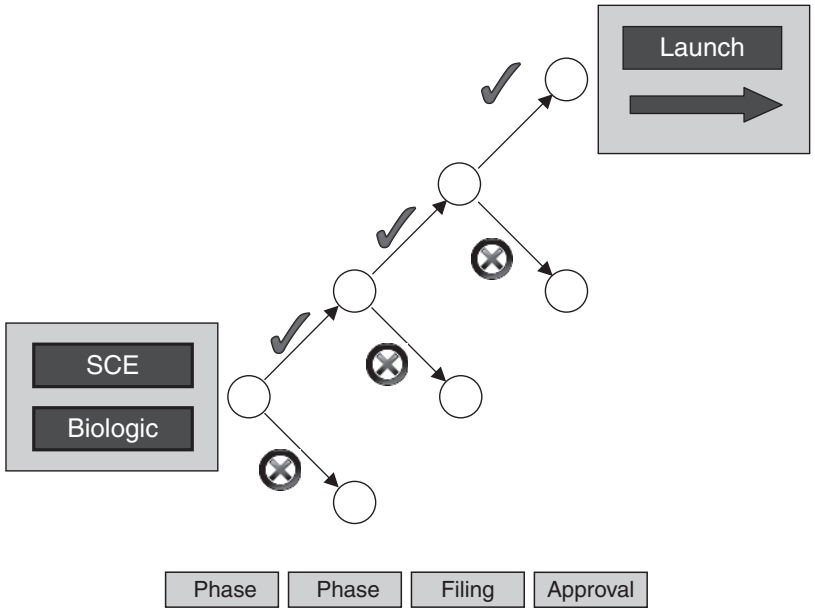


**Figure 1.3** Schematic technical risk decision tree

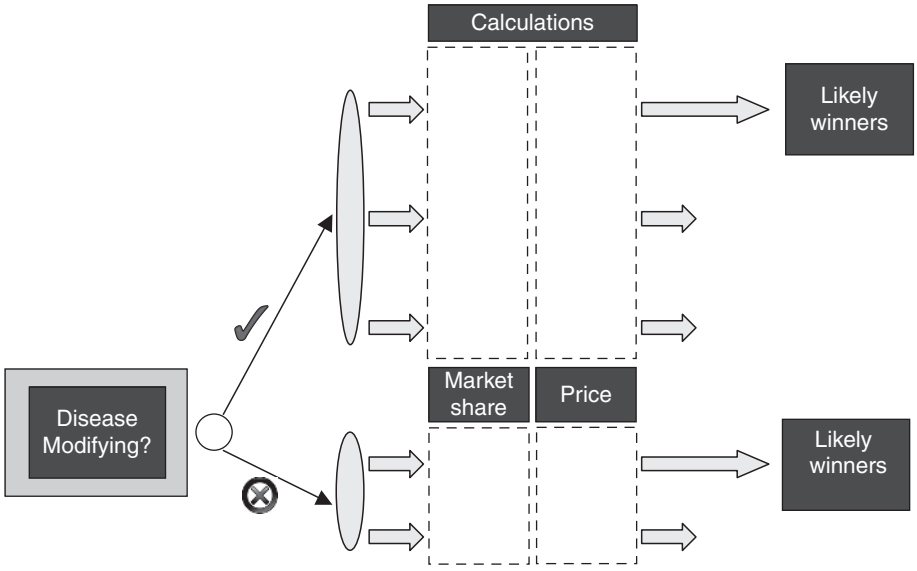


**Figure 1.4** Schematic commercial risk decision tree

Commercial risk must be considered as it impacts over the entire product life cycle, and I believe that the pressures on the pharmaceutical industry are squeezing these life cycles into narrower timeframes.

In summary innovation drives the biotechnology industry, including both the drugs and the companies formed to develop and commercialize them. Not all will succeed but there will be

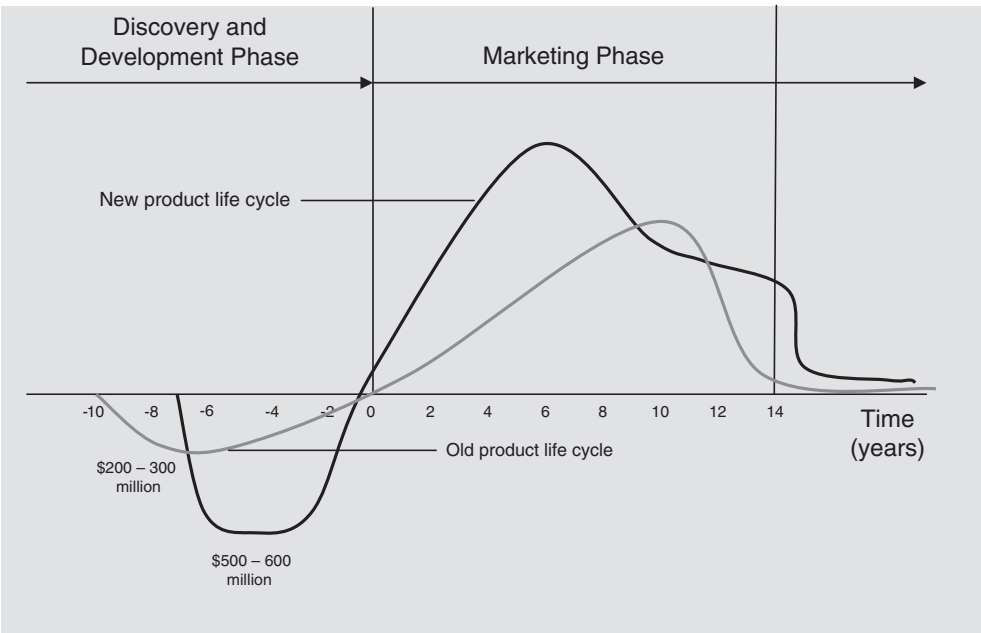


**Figure 1.5** Schematic of typical pharmaceutical product life cycle

winners, and some of these drugs, companies and investors will win on a huge scale. That is the attraction for the investor in my view. However it is not an easy path to become a successful biotechnology investor. My view is that an appropriate understanding of the potential risks and rewards can facilitate astute investment. I also believe that astute investment is driven by a knowledge and understanding of value, both relative and absolute.

I love the biotechnology industry, the wonderful fusion of science and business and the fact that I am constantly learning, unable to accept that my knowledge of the drivers of this industry have peaked. I hope I have captured some of that excitement in this book and have in some small way, better prepared you for assessing the value of biotechnology assets and companies.