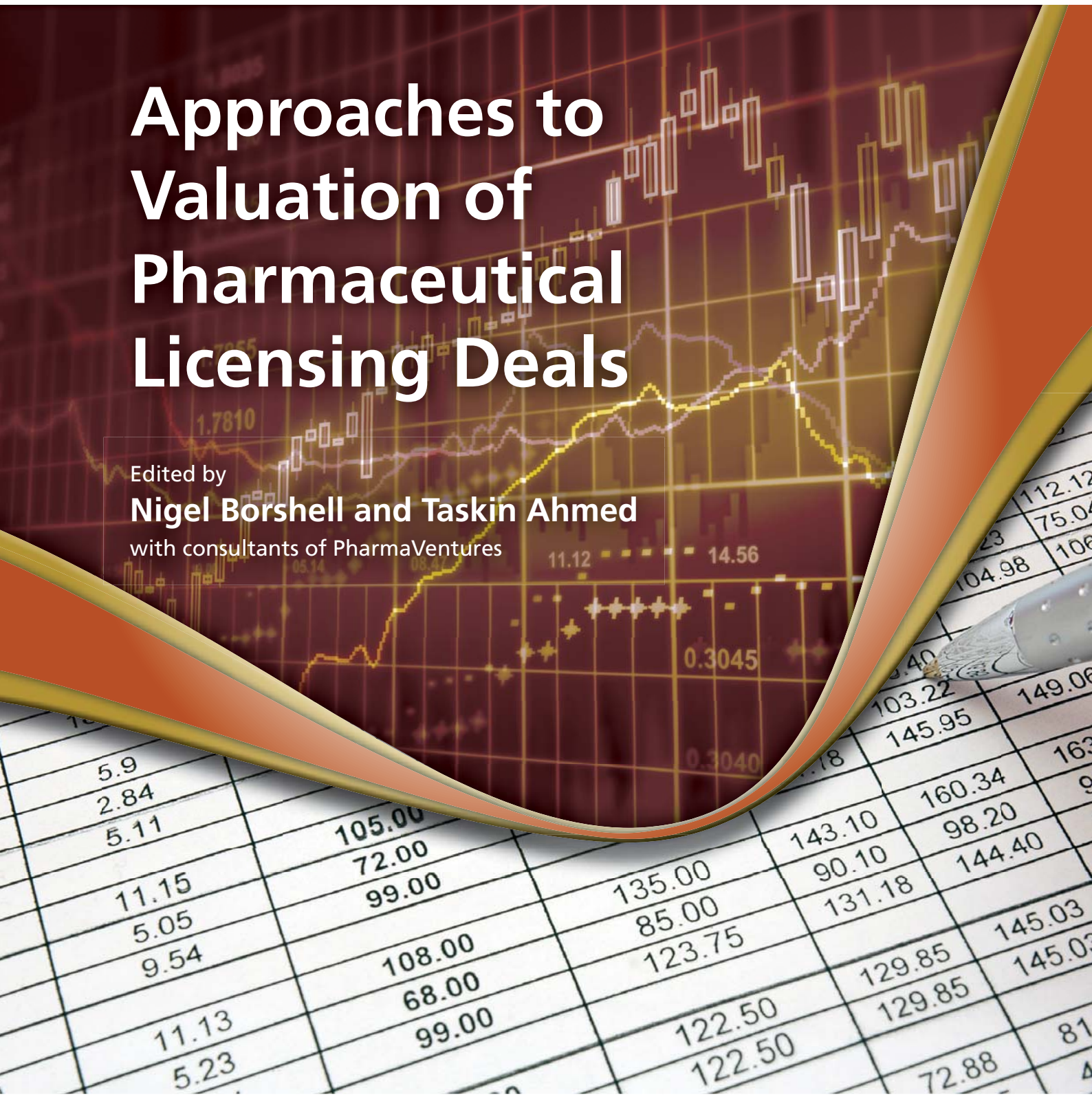
Approaches to Valuation of Pharmaceutical Licensing Deals

Edited by
Nigel Borshell and Taskin Ahmed
with consultants of PharmaVentures



PharmaVentures
Experts in deals and alliances

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Published by PharmaDeals, Imprint of PharmaVentures Ltd
Florey House, Oxford Science Park, Oxford, OX4 4GP, UK
www.pharmaventures.com

Published May 2012
Published by PharmaDeals, Imprint of PharmaVentures Ltd
Florey House, Oxford Science Park, Oxford, OX4 4GP, UK

ISBN 978-0-9568270-5-0 Electronic
ISBN 978-0-9568270-6-7 Printed

Cataloguing-in-Publication data applied for.

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1 Introduction

1.1 Dealmaking in the Pharmaceutical Industry

The discovery and development of new therapeutic agents is an expensive, lengthy and highly risky activity. Few companies have the capability of developing products all the way from the discovery of a new molecular entity to delivering the approved drug to patients. Even those that do have the capability may not have the capacity to have pipelines that are broad enough to provide a smooth flow of new drugs. The high, but unpredictable, attrition of products in development and the huge size of those programmes, mean that companies frequently encounter holes in their development portfolios. These gaps have to be filled by products from small companies that are proficient at drug discovery, but lack the capabilities to bring the new drug to the market.

Figure 1 illustrates the scale of licensing activity within the pharmaceutical industry in the last decade. More than 1,000 product deals (most of them licensing deals) were recorded each year in the PharmaDeals® v4 Agreements database since 2002. Total deals in the figure refer to a broad spectrum of transactions ranging from licensing, collaborative research and development (R&D), technology access for the discovery or improvement of therapeutic products, to manufacturing and supply agreements, and mergers and acquisitions. The proportion of product deals over total deals declined from 2006 to 2010 with a small increase in 2011.

Pharmaceutical licensing deals rarely, if ever, involve a simple one-time payment, but encompass multiple payments and royalties, and require long-term cooperation. There is a significant period of technology transfer and frequently both parties are involved together in research and/or clinical development. Deal structures must be employed that provide an appropriate allocation of the risks and the rewards.

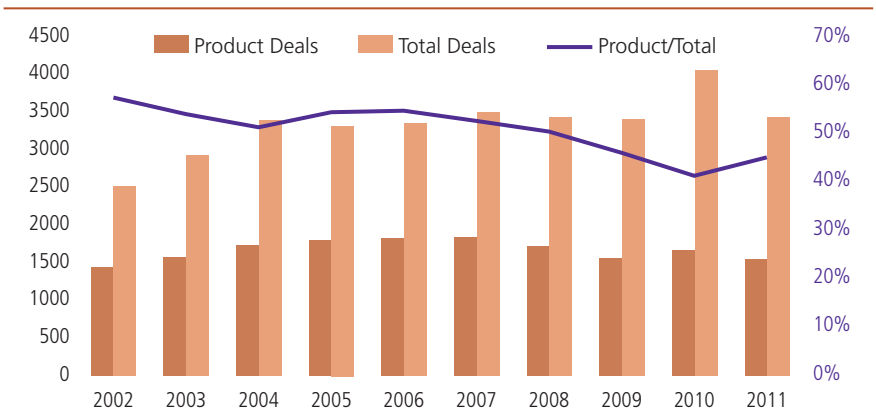

Figure 1 – Total licensing activity in the pharmaceutical industry.
(Source: PharmaDeals® v4 Agreements)

2 Valuation Methods

A variety of methods are available that purport to provide valuations of products and/or technologies. These range from arbitrary or traditional rules of thumb, through analyses with various levels of rigour, to somewhat esoteric methods that can obscure rather than illuminate the value creation process.

No single method is sufficient alone. However, two methods in combination – the Benchmarking Method and the expected Net Present Value (eNPV) Method using Discounted Cash Flow (DCF) and Decision Tree Analysis (DTA) – often suffice to provide managers, negotiators and decision makers with the information they need to value projects whether it is for portfolio management or for dealmaking purposes (*Figure 3*).

2.1 Integrated Methodologies

The benchmarking and eNPV methods should not be used alone, but employed together in an integrated manner ensuring that each is used to inform and cross-check the other.

The value of a product or technology depends on a large number of factors. These include the target market size for the final therapeutic product, the anticipated clinical qualities of the drug and the extent of competition for the drug; both current and in the future. In addition, the value depends on the need that exists in other companies for the product or technology and the number of competitors offering similar products.

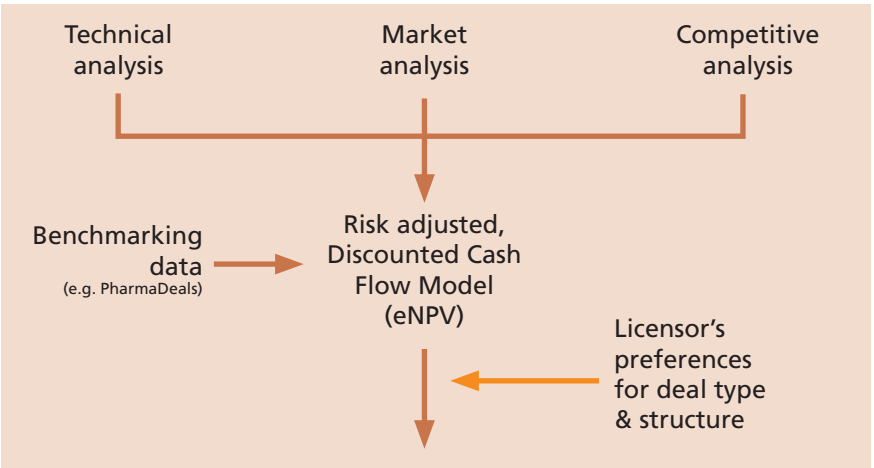

Figure 3 – Integrated valuation methods.

Substantial research is required to obtain answers to all of these questions. The figures obtained can be used to project future costs and potential revenues. In addition, part of the research will include looking at deals that have been done in the past for similar products. These will provide a guide to the value placed on similar products by the market in the past.

Reliance on either benchmarking or eNPV alone is unwise. Historical deals indicate what the market saw as the value in the past. Values agreed then may look attractive, but it is possible that the market for a particular technology has been saturated and that such valuations are no longer viable. Alternatively, any individual deal may actually have been quite poor for one or the other party and not necessarily be an adequate guide for the future. If conducted carefully, the eNPV method is much more robust and accurate. However, it has the drawback of being theoretical. Benchmarking provides concrete data on what companies have actually been willing to pay and accept. The integration of the two approaches avoids the pitfalls of either one alone.

2.2
Why use eNPV and Benchmarking?

There are a number of advantages to the use of the benchmarking and eNPV methods. Not least among these is the fact that they are both readily comprehensible to all those involved in dealmaking and portfolio analysis. Benchmarking is based on historical fact and, whilst the eNPV method involves making many assumptions, these too are based on fact or on third party verifiable estimates.

Additional benefits of the eNPV approach are derived from the necessity of building a comprehensive spreadsheet model. The spreadsheet makes all assumptions explicit, thus requiring them to be extensively researched and justified. It also permits the sensitivity of the value to each variable to be analysed by assessing different scenarios and asking 'what if'. The spreadsheets also assist cash flow planning and the prioritisation of investment decisions when portfolios of projects are assessed. Table 1 summarises the benefits and disadvantages of the two methods. Clearly, neither is ideal alone but in combination they become extremely powerful tools.

	Advantages	Drawbacks
Benchmarking	Rapid (cheap) Need less information Built on historical facts	Approximate Incomplete picture Backward-looking
DCF-based valuation	Rigorous Gives full picture Forward-looking	Slow (expensive) Need more information Conjectural

Table 1 – Pros and cons of benchmarking and DCF-based methods.

3 Benchmarking

3.1 Introduction to Benchmarking

Value is established through trade and is dependent on market supply and demand and other factors. Essentially value is the amount that both the buyer is willing to pay and the seller is willing to accept. Both sides will be interested to achieve the best deal and will want to know what other buyers might pay or sellers accept. Similar products or technologies that have been traded recently might provide an indication of the expected value.

We are all familiar with benchmarking in everyday life, for example, when buying or selling a house or used car. The principles of the benchmarking methodology are well understood in these transactions. When benchmarking pharmaceutical deals, the same principles will be applied, albeit market data may be less readily available. In addition, there are many more factors influencing the value of every pharmaceutical product and technology compared to car or house sales, and thus benchmarking is usually much more complex and difficult to apply. However, if used thoughtfully, the method is a very important part of the process of establishing value in the industry.

Benchmarking methodology consists of four steps as listed in Table 2. Firstly, it is necessary to establish whether sufficient relevant deals exist for the benchmarking to be feasible; secondly, all the data on each of the comparator deals must be collected and analysed; thirdly, an initial assessment of the value can be made; and, finally to refine the valuation taking account of the differences between the new, potential deal and the benchmark deals used in the valuation.

Step 1	Feasibility search
Step 2	Information gathering and analysis
Step 3	Approximate valuation
Step 4	Refinement of valuation

Table 2 – Benchmarking methodology overview.

It should not be forgotten that, in addition to providing some indications regarding value, benchmarking also provides important guidance to deal structures that other companies are willing to accept for such products and technologies. A study of the deals entered into by specific companies with whom you are negotiating can reveal useful information about their preferences for certain deal terms and structures. The process can also reveal trends in the industry. For example, it is important to know whether the type of product you are interested in is becoming

4 Expected Net Present Value

The benchmarking approach, which was explained in the previous chapter, is attractive because it revealed what the market is willing to pay for similar products or technologies. However, the approach has limitations because it is backward looking and the complexities of pharmaceutical product development are such that it is often difficult to find good comparator deals. Despite these factors, deal benchmarking provides an important sanity check for the numbers generated by forward looking methods.

In contrast to the apparent imprecision of benchmarking, the Expected Net Present Value (eNPV) method, with its reliance on detailed spreadsheet analysis and combined use of discounted cash flows and decision trees, provides beguiling detail. Even in the simplest eNPV model for a product in early clinical development, there will be more than a dozen variables. These will include the phase specific success probabilities, development costs and timelines, the expected market size and market share, and the costs of goods, marketing and administration. Add to these the scenarios of product life cycle and commercial performance based on predicted ethical and/or generic competition and the task of calculating the value appears almost impossible.

However, many of the valuation variables are well understood in the pharmaceutical industry and usually both sides to a negotiation can agree reasonably closely on the numbers. Average historic values for development timelines, costs and attrition rates can be found in academic research reports. Most notable among these are the publications of the Tufts Centre (see Section 4.3 for other resources). Some strategic intelligence firms provide raw or analysed data on industry R&D parameters on a service fee basis and most of the fully integrated big pharmaceutical companies keep their own historic R&D statistics. It is usually possible to distil the developmental variables down to therapy area specific figures and, in some cases, to the specific indication or pharmaceutical class. Annual revenues can be forecasted by a simple top level estimation of total expected market size and market share, or by way of a detailed bottom-up approach starting with epidemiological data. Information on market size can be found in industry publications or from service providers, and market projections in financial analyst reports. Market share can then be estimated by looking at the target product profile and the possible competitive landscape at the time of commercialization. Market share and sales of similar products and market dynamics of similar indications should always be analysed to provide a reality check for the estimated revenue figures. Commercial variables, such as COGS and sales and marketing costs, can usually be estimated directly. If direct estimation is not feasible, commercial costs can be denominated as a percentage of sales revenues,

4.6.1
Input Data and Assumptions

The assumptions used for creating the valuation model for the hypothetical drug PRI-123 are outlined below.

The total market for the hypothetical indication was estimated to be worth $1.9 B in 2012 and it is predicted to grow to $4 B by 2017 and $5 B by 2020. Growth between these points has been assumed to be linear in the model and to plateau in 2017 for four years.

PRI-123 is a new drug candidate that has successfully completed Phase I clinical trials. Experts predict that it could achieve an overall market share of 15%, five years after launch. Both this market share and the overall market value are likely to decline from 2027 due to the arrival of generic drugs. The rate of decline is estimated to be 5% per annum for the total market and 25% per annum for the PRI-123 share of that market.

The physiological target and mode of action of PRI-123 are similar to those for many cardiovascular drugs so it has been assumed that the risks of failure in clinical trials are likely to be similar to the attrition rates observed historically for cardiovascular drugs. Therefore, the chance of success in Phase II has been estimated as 57%. The historic figure of 72% success that covers both Phase III and registration has been split into 80% for success in Phase III and 90% for success at registration.

Clinical trials are anticipated to last 2 years each for Phase II and Phase III with another year being required for registration. The cost of Phase II is $10 M spread over the two years, whilst Phase III costs are $30 M and registration costs amount to $1 M.

The COGS is estimated to be 20% of sales. Sales and marketing costs are 15% of sales plus an additional $10 M in each of the two years prior to launch. Finally, an allowance of 5% of sales has been made for incremental general and administrative costs. These costs will only be incurred because of this product and hence are allowable in an NPV model. Basic overheads of the company are not included.

4.6.2
The Spreadsheet Model

Many of the assumptions described above are the best estimate for use in the model. The values are generally the average from a range of possible values that could be varied, within certain bounds, for the purpose of modelling different scenarios and assessing the sensitivity of the valuation to each variable. These issues will be discussed later. For the present model, it should be noted that cells in the spreadsheet containing values that may be modified for sensitivity analysis are highlighted in red.

In this model, the sales of PRI-123 have been predicted by using estimates of the future overall market size and the anticipated market share of the drug. It is also possible to arrive at a bottom-up estimate of the cash inflows by calculating total

5 Agreement Structure

It will be clear from the discussion of eNPV in the previous chapter that the effects of incorporating into a valuation the proper treatment of risk and discounting to allow for the time value of money have differential effects on the true value of different components in a deal. The numbers quoted in headlines for reports of deals are the simple sum of all readily identifiable payments that may occur. Royalties are usually excluded because it is not obvious what they will be in dollar terms. However, there is often a greater than 50:50 chance that most of the payments will never occur due to failure of the project in development.

Figure 15 illustrates how the combination of greater risk and longer time until their occurrence dramatically reduces the relative value of royalties compared to upfront payments. Milestones are less distant than royalties so are discounted less and, at least some of them, may be payable before all the risk has been eliminated from the project.

This chapter will look at how value and risk are shared between the parties to an agreement and will also review the different deal elements that can be used to achieve this.

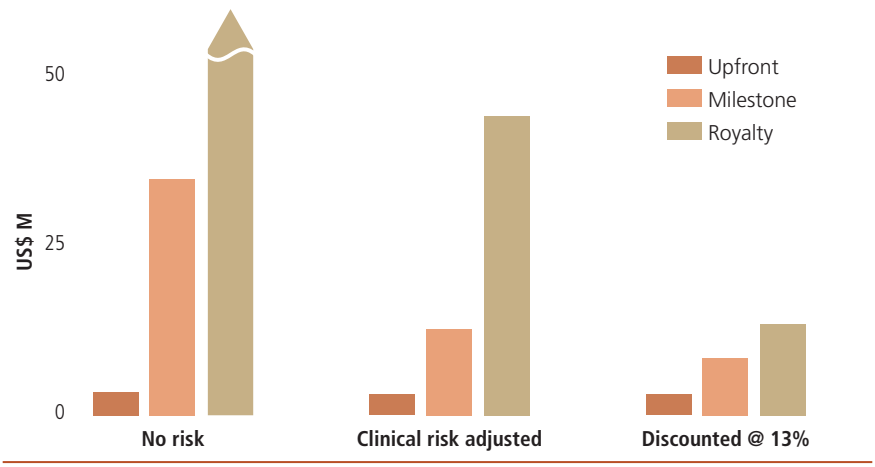

Figure 15 – The effect of time and risk on the value of deal components.

5.3
Deal Components

A variety of names for each of the components used in constructing deals may be encountered but all will fit into one or other of the categories below. Whatever the title for the payments, the value may be understood by incorporating the payment into the eNPV framework while taking care to treat it appropriately regarding discounting and risk adjustment. What hurdles, if any, must be passed to trigger the payment and when is it anticipated that the payment be paid?

5.3.1
Upfront Payments

Payments that are made immediately upon signing and that are contingent on nothing other than the signatures are often referred to as 'upfront payments'. 'Technology access fee', 'signing fee' and 'license fee' may also be used. No discounting or risk adjustment is necessary for these; unlike any of the other deal components they are worth the exact dollar amount specified!

5.3.2
R&D Funding

Generally, R&D funding does not actually add value as there is not a significant profit margin. The party paying for the work could either perform it inhouse or at a third party but would always show it as a cost in their eNPV calculations. The party performing the work can show the funding as a benefit but also has to show the costs.

Typically, R&D funding is not contingent upon success. One party may agree to support the other party's R&D for a specified number of years whatever the outcome of that research. Therefore, in the eNPV model the funding (and the costs) is discounted as appropriate for each year but not risk-adjusted.

Occasionally, later stages of the R&D may be contingent on certain levels of success having been achieved in the earlier stages. In this situation both the costs and the funding need to be risk-adjusted using the relevant risk factor.

5.3.3
License Fees

One-off license fees that are paid on closure of the deal are upfront payments as discussed above. Regular, ongoing license fees or renewal fees may also occur. The fees must be discounted and risk-adjusted according to the period in which they become due as appropriate for the risk of the technology failing and termination of the licence.

For internal reasons related to accounting practices that require matching of revenue to expense, many biotech companies now prefer to fund their own R&D, but charge higher licence fees or milestone payments instead. The biotech company must still incorporate the R&D costs that are specific to the project in their valuation model.

6 Valuation of Technologies

Technologies are a little more difficult to value than products in clinical development because the risks are less well documented and the costs and timescales are less predictable.

For this reason, it is even more important to benchmark when valuing technologies and to have a thorough understanding of the risks and rewards through eNPV modelling. Therefore, in this section the two standard methods if benchmarking and eNPV analysis are applied to the valuation of some example drug delivery and drug discovery technologies.

6.1 Drug Delivery Technology

Drug delivery technologies are making a dramatic impact on the pharmaceutical industry with more and more drugs employing these technologies either to enhance the properties of a drug or to enable the delivery of active molecules that would otherwise fail to reach the market. The approach to valuation is different for each of these two cases as discussed below (*Appendix A.2.8 – Drug Delivery Deals*).

6.1.1 Enabling Technology

The valuation of technology that is enabling is the most straightforward. There would be no product to sell without the technology so the provider of the delivery technology is entitled to a share of all the sales of the combined product – in the same way as the provider of the chemical or biological entity itself. Therefore, the first step is to calculate the eNPV for the combined product in the same way as was done for a simple product in Chapter 4. A deal structure then has to be constructed to share the risks and the rewards in a similar way to that described in Chapter 5. The key issue is the relative importance of the active ingredient and the delivery technology.

It can be useful to think of the end product that is provided to the patient as an abstract marketing concept. Pharmaceutical companies define the end product they wish to create in a Target Product Profile, which is what is described to doctors and patients in the package insert. The end product that is being marketed has essentially nothing to do with chemical structures or delivery technologies. As long as patients receive the benefits described and the side-effects are no worse than expected, the patient has no real interest in what is actually in the bottle or how it works. Therefore, if a delivery technology makes the difference between

Deal no.	**42430**
Title:	**Array BioPharma Enters into Oncology Agreement with Genentech**
Originator:	**Array BioPharma Inc.**
Partnering:	**Genentech Inc.**
Date:	**08-Aug-11**
Deal terms:	Array BioPharma has entered into an Oncology with Genentech for the development of each company's small molecule Checkpoint kinase 1 (ChK-1) programme. The programmes include Genentech's compound GDC-0425 (RG7602) and Array's compound ARRY-575. Under the terms of the agreement, Genentech is responsible for all clinical development and commercialisation activities. Array will receive an upfront payment of US$28 M and is eligible to receive clinical and commercial milestone payments up to US$685 M and of up to double-digit royalties on sales of any resulting drugs. Full financial terms were not disclosed.
Total Deal Value:	USD 713 M
Upfront payment:	USD 28 M
Royalty:	Array will receive up to double-digit royalties on sales of any resulting drugs.
Total potential milestones:	USD 685 M. Array is eligible to receive clinical and commercial milestone payments up to US$685 M.
Development milestones:	Array is eligible to receive clinical milestone payments.
Commercial milestones:	Array is eligible to receive commercial milestone payments.

Table A.1.3 – Array BioPharma and Genentech

A.2
Reference Deal Tables

Tables A.2.1 to A.2.6 present selected deals from the PharmaDeals v4 Database that disclose upfront and milestone payments for products in different phases of development from 2007 to 2012. Tables A.2.7 and A.2.8 present selected option deals and drug delivery deals.

Discovery and Preclinical Deals

Date Announced	Principal Compan(y/ies)	Partnering Compan(y/ies)	Deal Title	Primary Product Indications	Primary Deal Types	Primar Product Types	Primary Product Phases	Total Deal Value	Upfront Payment	Total Milestones	Territories Included	Territories Excluded
28/07/2009	National Institutes of Health; Leiden University	Can-Fite Biopharma Ltd	License Agreement between Can-Fite BioPharma, Leiden University and NIH	Certain disorders involving the immune mechanism; Crohn's disease [regional enteritis]	Technology access; Licensing	Drug Delivery Technology; Small molecule	Preclinical	1.25 M USD	0.04 M USD	1.21 M USD		
25/02/2011	ViroMed Co.,Ltd	Enlyton Ltd	ViroMed Enters into Licensing Agreement with Enlyton to Develop Humanised Antibody	Neoplasms	Licensing	Diagnostic; Antibodies	Preclinical	4.70 M USD	0.10 M USD	4.60 M USD	Worldwide	
04/08/2008	Labtech GmbH; APR Applied Pharma Research SA	BioAlliance Pharma SA	Licensing Agreement between APR Applied Pharma, Labtec and BioAlliance Pharma for ondansetron RapidFilm(TM)	Nausea and vomiting	Licensing	Drug Delivery Technology; Small Molecule	Preclinical	9.34 M USD	1.56 M USD	7.77 M USD	Europe	
11/03/2011	BioAlliance Pharma SA	Sosei Ltd Co.	Sosei Enters into Agreement with BioAlliance Pharma to Acquire Rights to Loramyc® in Japan	Candidiasis	Licensing	Drug Delivery Technology; Small molecule	Preclinical	21.50 M USD	3.00 M USD	18.50 M USD	Japan	
10/10/2011	Zosano Pharma Inc.	Asahi Kasei Pharma Corporation	Zosano Pharma and Asahi Kasei Pharma Enter Exclusive Licensing Agreement for Transdermal Patch Formulation of Teribone(TM)	Osteoporosis without pathological fracture; Osteoporosis with pathological fracture; Osteoporosis in diseases classified elsewhere	Technology access; Licensing	Drug Delivery Technology; Hormone	Preclinical	32.50 M USD	7.50 M USD	25.00 M USD	Taiwan; Japan; Korea; China	
08/12/2010	iCo Therapeutics Inc.	Immune Pharmaceuticals	iCo Therapeutics Enters into Option Agreement with Immune Pharmaceuticals for iCo-008	Asthma	Licensing	Antibodies	Preclinical	33.00 M USD	1.00 M USD	32.00 M USD		
30/03/2011	Takeda Pharmaceutical Co.,Ltd	Dainippon Sumitomo Pharma Co.,Ltd	Licence Agreement between Takeda and Dainippon Sumitomo Pharma for Ceftaroline Fosami in Japan	Streptococcus and staphylococcus as the cause of diseases classified to other chapters; Agent resistant to penicillin and related antibiotics	Licensing	Small molecule	Preclinical	36.59 M USD	6.10 M USD	30.50 M USD	Japan	
17/05/2010	ElexoPharm GmbH	Merck & Co. Inc.	Elexopharm Enters into License Agreement with Merck & Co. for Treatment of Cardiovascular Disease	Diseases of the circulatory system	Licensing	Therapeutic; Basic Research/Discovery	Discovery	41.78 M USD	1.85 M USD	39.92 M USD	Worldwide	
07/08/2009	Opexa Therapeutics Inc.	Novartis AG	Opexa Enters into Stem Cell Agreement with Novartis	Diabetes mellitus	Licensing	Basic Research/ Discovery; Stem cells	Preclinical	50.00 M USD	3.00 M USD	46.00 M USD		
21/07/2011	BioSante Pharmaceuticals Inc.	The John P. Hussman Foundation	BioSante Pharmaceuticals Enters into Licence Agreement with John P. Hussman Foundation for Melanoma Vaccine	Malignant melanoma of skin	Licensing	Vaccine	Preclinical	50.10 M USD	0.10 M USD	39.00 M USD	Worldwide	
27/03/2008	MethylGene Inc.	Otsuka Pharmaceutical Ltd Co.	Research Collaboration and License Agreement between MethylGene and Otsuka Pharmaceutical	Diseases of the eye and adnexa	Licensing	Small molecule	Discovery	57.38 M USD	2.00 M USD	50.50 M USD	Worldwide	
08/09/2008	Asterand plc	Allergan Inc.	Exclusive License Agreement between Asterand and Allergan for Pre-Clinical Compounds Focused on Diseases of the Eye	Glaucoma; Diseases of the eye and adnexa	Licensing	Small molecule	Preclinical	62.25 M USD	6.25 M USD	56.00 M USD		

Table A.2.1 – Discovery and Preclinical Deals.

Approaches to Valuation of Pharmaceutical Licensing Deals

Pharmaceutical licensing deals rarely, if ever, involve a simple one time payment, but encompass multiple payments and royalities, and require long-term cooperation. Value is created as the potential new drug becomes more likely to reach the market and revenue becomes a less distant hope. As each hurdle in the long research and development process is successfully overcome, the risk that the project will fail reduces. Consequently the value increases. The valuation of a deal can be the most challenging aspect in the deal negotiation and this guide equips the reader with current methodologies to calculate value.

This Guide explains:

- the principles of deal valuation
- how to use reliable methods for valuing pharmaceutical and biotech projects
- the essential framework for understanding and calculating the value of the project today and how that value can be built over time
- the potential components of deal structures as well as determining appropriate levels of risk
- how to develop deal structures and agree terms that are acceptable to both sides

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