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Pharma & Biotech

Drug Development
Valuing the pipeline – a UK study

March 2009

Introduction

Mayer Brown is pleased to report on the findings of a study examining the methodologies used to value drug development programmes. The study was conducted by members of our Pharmaceutical, Biotechnology & Life Sciences practice in the London office.

The year has started with major consolidation in the pharma sector and predictions that the biotech industry will see unprecedented levels of bankruptcies. There are also reports that the current market circumstances provide a “big buying opportunity” for pharma. Yet others question whether pharma is prepared for any major disruption involving biotech companies, which may result in the end of key partnerships. These are just some of the events and questions currently facing those participating in the sectors, with the overall focus remaining on increasing the chances of successful drug discovery development.

As lawyers, we remain committed to providing specialist legal expertise facilitating innovation in the pharma and biotech sectors. We believe the findings of the study contribute to the information currently available to investors to assess the value proposition offered by funding drug development programmes and by senior management seeking to identify those programmes that are most likely to maximise company value. The findings are also relevant to understanding the values assigned by parties in negotiations for the acquisition or licensing of drug development programmes and the approach of financial analysts in setting equity prices.

To all the individuals who participated in the study, we sincerely appreciate your cooperation. For those reading, we welcome any opinions you may have on the issues sought to be considered in this report.

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Please remember that this report contains general information, much of which has been provided by third parties and which we have not independently verified. We hope it will interest you but you should not rely on this report in relation to specific matters as it has not been prepared with a specific set of circumstances in mind, nor of course is this report an invitation or inducement to engage in investment activity.

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The valuation of drug development projects

Drug discovery, research and development (“**drug development**”) follows a sequence of distinct stages, each of which aims to generate “economically valuable specific knowledge”¹ about the drug candidate in question. In this way, the implementation of a drug development project generates intellectual assets capable of transfer or licensing.

Determining the monetary value of these intellectual assets is central to internal research prioritisation, investor funding decisions, business development negotiations and equity analysis in the pharmaceutical and biopharmaceutical sectors.

A range of methods, each with differing computational complexities and limitations, can be used to assign a value to a drug development programme.

This study considers:

- the methods currently used to value drug development projects;
- the different ways in which these methods are applied by different sector participants; and
- the key challenges in forecasting the revenues, costs and risks associated with drug development.

The study was conducted by interviewing individuals over a period of four months² in the UK from a representative sample of twelve leading industry participants, including small biotech business development (“**biotech**”), large pharma and large biotech business development (“**pharma**”), financial analysts (“**analysts**”) and venture capitalists (“**VCs**”).³

1 Arojärvi, O., 2001. How to Value Biotechnology Firms: A Study of Current Approaches and Key Value Drivers. *Helsinki School of Economics and Business Administration* [URL: <http://www.finbio.net/publications/pro-gradu-arojarvi-01-en.htm>].

2 September 2008 to January 2009.

3 A copy of the questionnaire is available on request.

Outline of the stages of drug development



Executive Summary

Complex science, long development times, the high risk of technical failure and changing regulatory and market conditions make it difficult to derive reliable values of a drug development project solely through the application of valuation methodology. Based on the views of the participants of this study, the current market conditions create new uncertainties and limitations around the tools used to value drug development assets.

For instance, in pricing negotiations, valuing drug development projects by comparison with prices paid in recent comparable commercial transactions for similar projects at similar stages of development is used. We now have reports of the effective disappearance of biotech IPOs and a fall in the number and value of private equity deals in the sector, together with the public bio/pharma market currently having a low value. In these conditions, even if a comparable project can be referred to, there is the additional uncertainty relating to the extent to which previous values can be drawn upon. As one participant remarked:-

“Given the current market circumstances, everything is in a bit of a muddle.”
(pharma)

Given funding constraints, some consider outright acquisitions of drug development projects as now more popular than complex licensing and partnering deals. Participants in the study reported seeing biotech rights owners using auctions on lead products to push up the value of upfront payments in a proposed licence deal as a prelude to suggesting an outright disposal. From a valuation perspective, these negotiating practices arguably further muddle the pool of comparable transactions.

The current market conditions include shifting categories of projects of interest to buyers and investors. Some point to an increase in early stage deals. Aside from comparables, risk adjusted Net Present Value (“NPV”) is the other tool predominantly used to value drug development projects, but the values yielded from it have long been considered unreliable because of the greater guess-work involved in forecasting cash flows and risk at an early stage of drug development. However, the current market uncertainties may also mean that “good quality assets” are less constrained by previous values. “Good quality assets” are seen as continuing to secure high prices. Notably, a pharma buyer is likely to place less relevance on comparables and focus more on what the individual project is worth to it:-

“Availability of deals has increased rather than prices falling. Licensees’ expectations are still as high. Good quality assets (rather than ‘bottom feeders’) will still have a high price.” (pharma)

“If one looks at the share price, things seem cheaper then once the fight begins, you cannot be sure that the price will not go up. There are no Phase III projects around.” (pharma)

Methodologies used to value drug development projects

The participants were asked to identify the methods they used to value drug development projects. Most participants only used risk adjusted NPV and comparables. Few participants (mainly the pharma participants) regularly used other methodologies such as scenario analysis, decision-tree analysis, Monte Carlo and real options.

Of course, the purpose and scenario for which a valuation exercise is undertaken, and by whom it is undertaken, ultimately explains the method used.

For example, VCs do not use NPV modelling when assessing early stage projects because of the greater guess-work involved in forecasting cash flows and risk at an early stage of drug development. VCs instead focus on “business plan” type factors and what the value will be to an acquirer. Paramount to the VC investment decision is the exit strategy.

“The starting point of the investment is: how do we get out of this?” (VC)

Some consider that even if IPOs return, these no longer offer a complete exit to VCs, who are now focused on an exit by trade sales. Consequently, VCs are having to be cleverer in how they position their portfolio companies. They do not want to position a portfolio company as a “one product” company, but nor can a company be too diverse:-

“The key challenge lies in how to position the company with products and technologies that are compatible.” (VC)

In comparison, analysts will rely on values derived from NPV modelling, but they tend to focus on late stage projects. More specifically, the focus is on when the drug candidate will be launched and when relevant sales will peak. This focus on late stage projects was criticised by the biotech participants for ignoring the fact that the value for biotech companies currently lies in being acquired. If an early stage project is of interest to an acquirer, then the acquirer will place a positive value on the project for which the analyst may have given no value.

Valuation in acquisition, licensing and partnering negotiations between biotech rights owners and pharma buyers

The theoretical value derived from valuation methods, when considered in isolation, assumes that a drug development project has an intrinsic value. Yet, most participants explained deal values simply on the basis of who wants/needs the asset more. Consequently, the key sources of value discrepancy continue to depend ultimately on *qualitative factors* and the *subjective criteria* specific to the rights owner and the buyer, and of course the *negotiating power* of the parties.

Cash flows, together with prospects of independent fund-raising, are factors relevant to determining what the project will be worth to a cash-strapped biotech rights owner. For a pharma buyer, key factors include strategic factors (e.g. whether the project fills an important strategic gap in the buyer’s product portfolio) and the synergies that a buyer can exploit (e.g. whether the buyer can leverage its existing sales force to market the new product).

Therefore, it is important to identify the subjective criteria and qualitative factors relevant to the other side and to address these issues early by having in place strategies and practices that best emphasise relevant criteria and factors.

Participants were also asked to comment on the typical value split between rights owners and buyers. Most participants were reluctant to acknowledge any typical split, preferring to treat each deal on a case-by-case basis.

Examples of the factors that would influence the value split include:

- how innovative the drug candidate is and its sales potential: The emphasis is on the sales forecast. In addition to a shift towards early stage deals, some participants observed buyers being increasingly open to considering drug candidates with smaller markets if the end product can be marketed within their sales force machinery. Buyers are also seen as now applying more rigid requirements on what a product profile must look like in order to succeed, e.g. the safety and efficacy profile that must be achieved in order for it to be worthwhile for the buyer to take the product to market. Consistent with this, participants also consider buyers more likely to terminate development projects;
- the development stage and the risk to be assumed by the buyer: A notable source of technical discrepancy arises in assessments relating to the true stage of development of a project. Buyers see rights owners as overestimating the clinical stage of development. Other participants believe that development overestimation should be less of an issue given the increased guidance from regulators (in particular, the US Food and Drug Administration) throughout clinical development;
- unsurprisingly, the scope of rights disposed of; and
- the extent to which the payment structure is frontloaded: In terms of payment structure, participants see rights owners as preferring structures that secure as much cash today as possible despite the fact that frontloaded structures are usually associated with a buyer requiring a larger percentage of the project value.

Finally, *competition* amongst the bidders is a key driver of deal value and value splits. The pharma participants acknowledged that, whilst they will work on their initial valuation and bid in detail, competition will change everything. As explained by one of the pharma participants:-

“We would of course not offer more unless we had to, e.g. if we were at risk of losing the deal. We would tend to work up the initial valuation in ‘exquisite detail’ then go in with a bid, and competition would change everything. It is a question of ‘how hungry are you?’ Passion takes over from common sense. For example, where there is an important strategic gap in the portfolio, the price would go up – but one would not start from that position.” (pharma)

Forecasting challenges

As to the current function of quantitative valuation, valuation methods remain an important tool for capturing the variables which are important to a drug development project:-

“Valuation can be seen as a tool to make a decision, a tool to persuade someone else to make a decision, or a tool for what is a piece of carpet haggling.”
(biotech)

Participants were asked about challenges in quantifying the revenues, the costs and the risks of a drug development project. They were generally comfortable with their approach to forecasting the costs of development, but significant uncertainties exist around forecasting revenue potential and risk.

- **Revenue:** The key challenge relates to an inability to control or predict shifts in the factors influencing a new product’s ability to gain market share. In particular, many struggle in assessing the impact of competition on market share, with key differences in revenue depending on whether a product is first to market or second to market. Whilst best estimates can be given based on the current understanding of the market, educated guess-work cannot, of course, account for unknown development projects. In this context, development timetables are also critical (and difficult to get right) because loss of time will have a knock-back effect on the all important competitive position.
- **Risk parameters:** Participants continue to rely on industry averages even though the limitations of applying industry averages to specific therapeutic indications are well understood.

Values derived from quantitative modelling are most sensitive to changes in revenue and risk parameters, which explains the importance in accurately estimating these parameters. The participants also highlighted new uncertainties due to the current market circumstances. For example, there was a difference in opinion on whether discount rates should be changed in line with changes in interest rates. One participant referred to the misuse of discount rates:-

“Discount rates are not used properly. For instance, discount rates do not necessarily change with changes in interest rates.” (biotech)

Others defended not changing discount rates on the basis that they are an estimate over the long term life of a drug development project.

Despite being perceived by the other groups as possessing informational advantages, pharma participants indicated that they too struggle with forecasting revenue and risk parameters.

Therefore, the key function of quantitative modelling is as a tool to gather insights into as many possible sources of value and uncertainty, requiring participants to remain proficient in their approach to valuation. In addition, the warnings against relying on a value derived from any single one approach points to considering whether there is a broader scope to apply the lesser used methodologies such as real options:-

“Any one model is just one picture. We typically use several models for one project, to capture any variables particularly important to the project and the decision making process.” (biotech)

“None of the methods alone is a single decision tool ... you combine them.”
(pharma)

An understanding and appropriate quantification of as many possible sources of value and uncertainty remains important to decreasing the risk of underselling or overvaluing drug development projects.

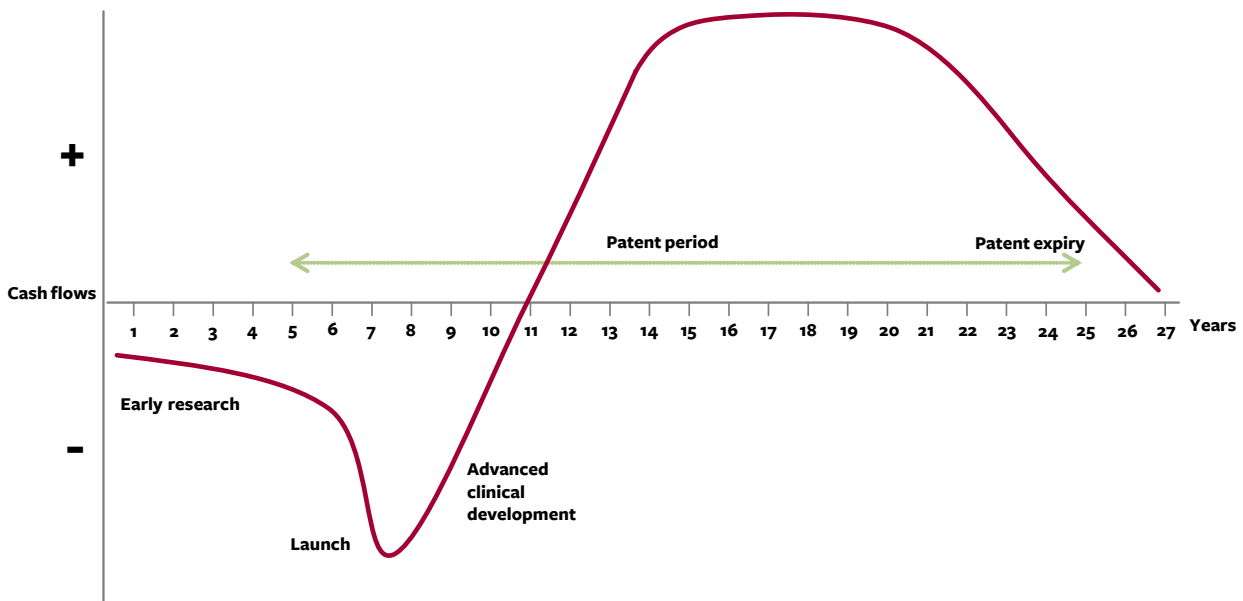
1. Introduction to valuing drug development projects

Valuation can involve a market, cost or income approach. This section seeks to provide a basic introduction to valuation theory. We start with NPV, which considers the cash flow opportunities of the asset in question and incorporates the income approach.

1.1 Summary of project lifecycle and cash flows

Figure 1 shows the typical project lifecycle from a cash flow perspective. During the early research stage, project cash flows tend to be negative. Early stage research can take several years, but is not as expensive as clinical development. The drug is launched upon marketing approval being issued, followed by relatively fast market penetration. A stable period of revenue generation follows. Finally, revenues decline following patent expiry. The project lifecycle is such that even though the basic term of patent protection lasts 20 years from issuance of the patent, the period during which revenues can enjoy patent protection is effectively reduced to the patent term remaining after regulatory approval.

Figure 1 - Example of a project lifecycle curve from a cash flow perspective



Financial models vary on how far into the project lifecycle they forecast. Patent expiry is a typical endpoint, based on revenues facing erosion after patent expiry. A famous example is Eli Lilly's anti-depressant Prozac, where patent expiry in 2001 paved the way for regulatory approval of Barr Laboratories' generic version, Fluoxetine. Prozac reportedly lost 73% of market share within two weeks of generic launch⁴.

⁴ Tuttle, E, Parece, A, & Hector, A, 2004. Your patent is about to expire: what now? *Pharmaceutical Executive*, November. [URL: http://www.analysisgroup.com/Pharma_ExecNovember_2004.pdf]

The extent and rapidity of sales and price erosion can vary. A product owner may use patent term extensions and regulatory exclusivities to extend the period of protection. The introduction of generic competition may also be delayed, for example:

- a drug may operate in a niche category that is too small, or with a brand presence too strong, to attract competition on patent expiry;
- a drug may be too complex to produce, particularly where the manufacturing processes are also protected; or
- in the case of competition from follow-on biologics, the current lack of clarity on regulatory requirements (especially in the United States) poses a key challenge to their launch.

The endpoint of a forecast period may also be the point beyond which information required to forecast is unavailable or unreliable.

1.2 Cash Flow Modelling – NPV

NPV is also known as discounted cash flow or DCF. NPV, when applied to a drug development project, involves deriving cash flows over a forecast period by projecting the costs of development and the revenues from commercialisation activities. These cash flows are then discounted in accordance with finance theory to derive a net present value of the drug development project.

Forecasting costs of drug development

The costs associated with drug development can be broadly grouped as follows:

- **Discovery and pre-clinical development costs:** These include costs relating to discovery (resulting in the synthesis of a drug candidate) and testing in assays and animal models. Assessing pre-clinical costs for a specific development project is difficult because pre-clinical costs are usually incurred as part of wider R&D programmes involving multiple projects.
- **Clinical development costs:** These include costs relating to trial design, patient recruitment, investigator and clinician costs, monitoring costs, data analysis, close-out and reporting results, and those related to the production of the clinical trial supplies and animal testing during the clinical period. Clinical development costs will vary depending on the therapeutic indication, with increased costs associated with chronic and degenerative diseases. This increase is driven by the number of patients needed in a clinical trial, the treatment costs per patient (e.g. outpatient versus intensive care treatment, cost of diagnostic procedures and co-medications, durations of treatment and requirements of follow-up) and the length of the clinical trial. Of the stages of drug development, Phase III is the most expensive and time-consuming.
- **Regulatory review costs:** The costs of marketing approval need to be considered on a territorial basis, with most drugs at least aiming for approval in the major markets (United States, Japan and certain Europe countries). The costs of preparing submissions in connection with marketing approvals can vary depending on the amount and quality of data.
- **Launch, manufacturing and marketing costs:** Marketing expenses start well before marketing approval. Launch, manufacturing and marketing costs are usually projected on the basis of conventional assumptions (e.g. the marketing expenses for year 1, 100% of the revenues, the marketing expenses for year 2, 50% of the revenues etc). The specific requirements of the target market are also important. For instance, hospital products are characterised by lower marketing costs than products promoted to specialists or primary physicians.

Forecasting revenues

Forecasting the likely eventual revenues of a drug candidate once developed, involves determining the size of the target market, the market share likely to be attained and subsequent market growth.

■ **Market size**

The bottom-up approach⁵ focuses on the number of patients and calculates market size by evaluating the following parameters:

- number of patients;
- number of patients receiving treatment; and
- price of treatment per patient.

The other approach used is a top-down approach⁶ which involves extrapolating from existing sales data of products in the same therapeutic class as the drug candidate of interest.

■ **Market share**

Commentators will typically include the following in a list of factors influencing a new product's ability to penetrate a market:

- competition from available treatments and products, as well as those in development;
- pricing;
- relative advantages compared with current treatments (i.e. cost/benefit analysis);
- dosage and formulation of the candidate;
- clinical evidence of efficacy and safety; and
- patient/physician product loyalty.

This is by no means exhaustive of the factors relevant to assessing market share. The distinction between *volume* market share (based on number of treatments) and *value* market share (based on sales value) is also relevant.

■ **Market growth**

The current market growth will only be a guide to future growth prospects. The factors behind market growth need to be identified and the distinction between *volume* and *value* growth is also relevant. Sales *volume* growth will be affected by changes in population growth, spread of an illness, frequency of occurrence, frequency of diagnosis, and treatment practice. Sales *value* growth depends on changes in pricing and product mix (older products may have significantly lower prices than newer, more efficacious ones).

Standard sales evolution curves are also used. By looking at historical peak sales of drug products, different scenarios of rates of ramp-up to peak sales and rates of market erosion can be analysed.

⁵ The bottom-up approach is also known as an epidemiological-based approach.

⁶ The top-down approach is also referred to as a market-based approach.

■ Price premium

Novel products that are more efficacious than existing products are typically priced at a premium. However, this must be balanced against the number of patients/physicians who will switch to a more expensive product. Also, during the forecast period other products may lose patent protection and become subject to competition from generics. Patient/physician switch to generics needs to be considered. Pricing regulations and policies are also relevant in pricing analysis.

Discounting to adjust for time and risk

An amount of money received today is worth more than the same nominal amount of money received in the future. Conversely, a dollar received tomorrow is worth less than a dollar received today. Applying this principle to forecasted cash flows means that not only are future revenues worth less today than in the future, but also future investments will “cost” less today. Finance theory requires that a discount rate be used to translate the future cash flows into today’s value.

Finance textbooks illustrate how discount rates account for risk. By way of example, the capital asset pricing model calculates the discount rate on the basis that investors require a project to generate at least the same return as would be expected from investing in risk-free investments and a premium for accepting the risks of investing in assets whose value is highly volatile. In the case of drug development, the key risk relates to failure of the drug candidate to meet the required safety and efficacy profile. Drug development may also be abandoned for economic reasons, e.g. change in market conditions resulting in a reduced commercial market.

Whilst not qualifying as a discount rate in the strict textbook sense, VCs tend to set discount rates representing the internal rate of return expected by their fund investors.

Once a discount rate has been identified, the present value of the net cash flow at each relevant time point (i.e. stage of development) can be calculated.

Despite being widely used, the use of NPV in valuing drug development projects is not without limitations. The remainder of this section considers the key limitations of NPV and the valuation methods seeking to overcome these.

1.3 Risk adjusted NPV

NPV does not properly account for technical risk

Technical risk (e.g. scientific or technological risk) is mitigated as a drug candidate advances through each phase of development. The use of discount rates in NPV to simultaneously adjust for time and technical risk is argued to penalise long term projects relative to short term projects⁷. Risk adjusted NPV takes technical risk outside discount rates, instead accounting for it by adjusting the cash flows at each stage of development by the probability of the drug candidate successfully reaching launch from such stage. In turn, a lower discount rate applies.

Limitations

The calculation of probability rates is problematic, particularly in relation to the pre-clinical stages. Many unsuccessful pre-clinical projects are quietly discontinued. Available probability rates tend to be presented as industry averages. The challenges of applying these rates to a specific therapeutic indication are well understood. Where the drug mechanism is understood (such as in hypertension, diabetes and asthma), the relevant probabilities of technical success are likely to be higher than industry averages. Similarly, projects dealing with lesser understood diseases (such as cancer) may be associated with lower probabilities of technical success.

1.4 Scenario analysis, decision-tree modelling and Monte Carlo simulation

NPV does not account for different outcomes

NPV valuation is based on a single projection of inputs, which are impossible to calculate with any certainty. Scenario analysis, decision-tree modelling and Monte Carlo simulation seek to deliver a range of values based on likely variations to more than one input.

Scenario analysis

Scenario analysis models the outcome of different scenarios on value. For instance, different revenue scenarios, based on the probabilities of the scenarios eventuating, can be modelled to examine the effects on value. Other examples include scenario analyses of different development options (e.g. development for indication X versus indication Y) and different commercialisation options (e.g. the stage to which the drug candidate should be developed before out-licensing or partnering).

Decision-tree modelling

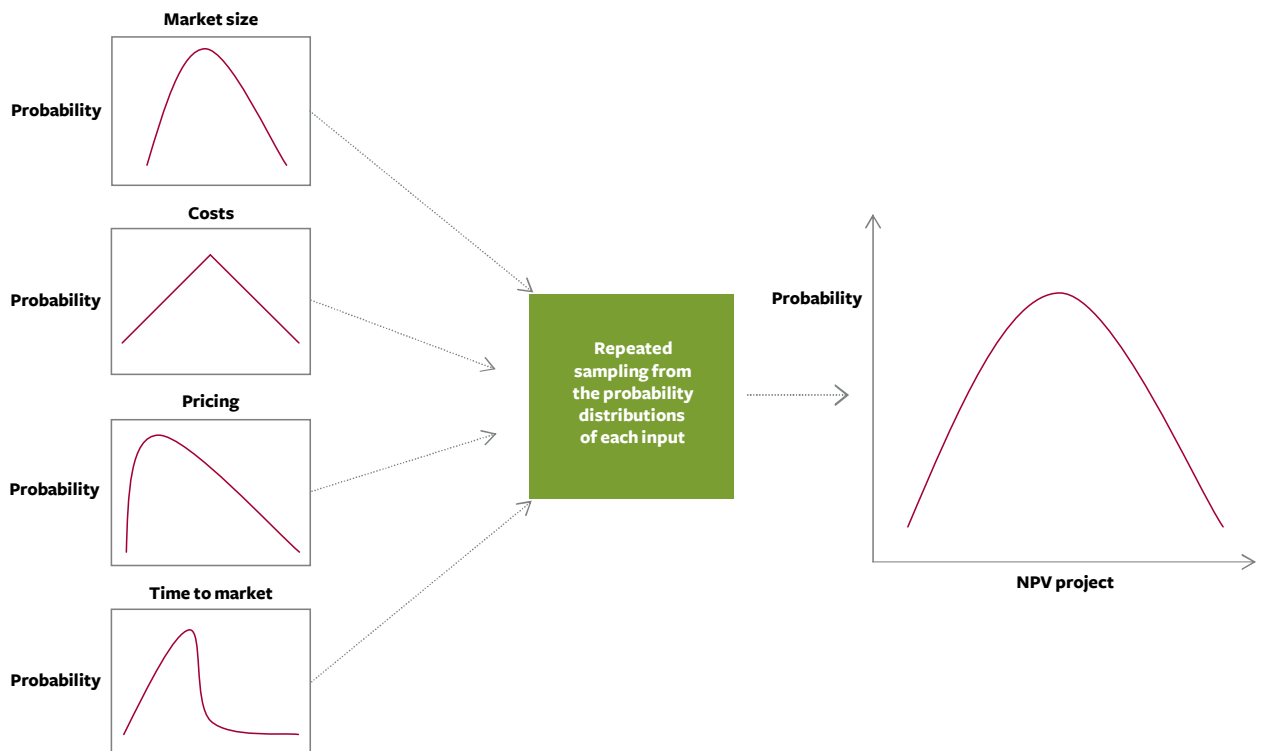
Decision-tree modelling considers the impact on project value of different scenarios (e.g. technical failure or success) at nominated decision points along the development path. Typically, decision points occur at the completion of each stage of the development path. The relevant impact on value can be pictorially represented together with relevant pay-offs if the project is abandoned at any decision point in the event of technical failure.

⁷ Randerson, D., 2001. Forensic Accounting Special Interest Group Valuing a Biotechnology Company. Acuity Technology Management Pty Ltd, Melbourne [URL: <http://www.icaa.org.au/upload/download/Valuing%20biotech%20companies.doc.pdf>]. In this regard, the high rates applied by VCs are considered to invariably render research and development programmes to a negative value.

Monte Carlo

Monte Carlo methodology simulates adjustments to multiple inputs (e.g. market size, expenditures, pricing and time to market) to produce an overall distribution of possible outcomes. This is achieved by defining the statistical probability distribution of each uncertain input of interest. Software simulation is then used to repeatedly sample values from the probability distributions of each input. Each simulation generates a single NPV estimate. The end result of the repeated simulation (as shown in Figure 2) is a range of possible NPVs and their respective probabilities of occurrence.

Figure 2 - Outline of Monte Carlo simulation



Limitations

The value derived depends on the choices of scenarios and the associated probabilities of occurrence, which are largely subjective. Although the methods are useful for assessing the spread of values for a project, they still do not assist in yielding a more reliable single value.

1.5 Real Options

NPV does not properly account for the value of managerial flexibility in the face of economic uncertainty

In addition to technical risks, drug development projects face economic (or market) uncertainty. These include uncertainties that affect all projects (e.g. loss of freedom to operate or loss of market share due to aggressive competition) and uncertainties specific to a project (e.g. lack of organisational and financial resources).

Real options methodology aims to address the impact of economic uncertainty on project value by applying financial options theory to the drug development process. This approach views the process as containing a series of options in the face of unpredictable economic developments. For example, once a project has passed Phase I, the option-holder has the option to invest in Phase II. The start of Phase II will require an investment outlay, which is the exercise price for that option. If the option-holder decides to invest, it will acquire the option to invest in Phase III, together with an option on the future commercialisation of the project⁸. It may also be that technical success in Phase III is accompanied by unfavourable market conditions. The option-holder in such circumstances may abandon the project, which limits the downside exposure to the exercise price of the option. In comparison, NPV based methods assume that once a decision to invest is made, all investments will occur. Projects can be modelled to include other options such as the options to expand, defer and license. Rational investors are assumed to place a value on those options and consequently, the value of the project is linked not only to its cash flows but also to the presence of the options.

Different methodologies exist for valuing options contained in a drug development project. In the methodology known as the binomial tree, the project returns are adjusted by a parameter referred to as volatility (δ). This represents the standard deviation of project returns due to economic uncertainty.

Limitations

Even proponents of the approach acknowledge that much work remains in developing a practical application of the real options theory. Difficulties also exist with accurately estimating the volatility parameter because the market data needed to estimate it is typically not available. Other criticisms include many of the options not necessarily being exercisable in practice.

1.6 Comparables

NPV modelling is theoretical

Cash flow based methods require forecasting inputs which are impossible to calculate with certainty. Consequently, assigning values by studying prices paid for comparable drug development projects in recent comparable transactions is considered a more accurate and reliable measure of value.

Limitations

A comparable project is a project involving a similar product with similar market potential and at a similar stage in development. In the case of a novel candidate with no obvious counterpart, finding comparable projects becomes very difficult. Even if a comparable project can be identified, care must be exercised in drawing valuation information from it because the market conditions and bargaining powers of relevant parties may have been different or the comparable project may not have been properly valued.

⁸ Borriouk, O & Peli, J., 2001. Real Option Approach to R&D Project Valuation: Case Study at Serono International S.A. *The Financier*, Vol. 8(1)-(4).

2. Findings on the methods currently used to value drug development projects

Having introduced valuation theory, the remaining sections of this report seek to consider what happens in practice.

The participants were asked to specify which of the following methods they used to value drug development projects: risk adjusted NPV, comparables, scenario analysis, decision-tree analysis, Monte Carlo or real options⁹.

Overall, most participants tended to only use the more conventional tools of risk adjusted NPV and comparables, with only a few participants (namely, pharma participants) regularly using other methodologies.

Of course, the scenario and the purpose for which and for whom the valuation exercise is undertaken, remains important to determining the method that is used. As one participant remarked:-

“Valuation is the function of what you want to achieve so consider why you are doing it, which side you are doing it for and for what scenarios ... the scenario is terribly important. The drug development industry is a science-based industry, which does a lot of analysis ...there is a feeling that valuation methods are valid and correct. At the end of the day, the correct value is what someone else is willing to pay for a project.” (biotech)

2.1 Risk adjusted NPV

Advantages of risk adjusted NPV (“rNPV”)

rNPV was considered computationally simpler and better understood relative to other methods using cash flow projections:-

“Very simple to use and explain to management.” (biotech)

“Most impactful because of the way pharma looks at its value. The board gets used to looking at NPV and value splits ...” (pharma)

“rNPV is used by all analysts, so it enables investors to make comparisons when taking advice.” (analyst)

Limitations of rNPV – Early stage research

Several participants reiterated the limitations of NPV modelling, particularly in the context of modelling the cash flows of early stage projects, where the lack of tangible results means increased guess-work and unreliability:-

“In early stage programmes ... one can do NPV on sales etc, but as you do not know what the drug profile is, and hence what the indication will be, predicting sales is a bit silly.” (biotech)

“We do not have enough information to put together NPV. If you did NPV for early stage, you would not get out of bed.” (VC)

9 Participants were also invited to specify any other method(s) they used to value drug development projects.

2.2 Comparables

Used in price negotiations

Several participants employed comparables in pricing negotiations:-

“Useful for early stage as what are the alternatives to base a valid theory/opinion on?” (analyst)

An exception arose in the case of the pharma participants, who indicated that a pharma buyer is more likely to pay what a project is worth to it. This highlights another key limitation of the comparables approach: the assumption that the comparable project has been correctly valued. One participant commented that it is common for a pharma buyer to dismiss a comparable price on the basis that it would not have paid the same price for the comparable project:-

“Comparables/comparators are used, but in the end it is what it is worth to us that matters. The other side do their own waterfall diagrams and the market price would not affect us insofar as the initial valuation was concerned, but it might be relevant when it came to bidding.” (pharma)

Limitations - Current market circumstances

Finding true comparables remains key. Several participants referred to the current market circumstances and the uncertainty relating to the extent to which historical values can be drawn on:-

“Given the current market circumstances, everything is in a bit of a muddle.” (pharma)

“Prices are being eroded. There are three key factors: the public bio/pharma market currently has a very low value; biotech companies are desperately running out of cash; and everyone is saying that values are slipping and so values are slipping...” (biotech)

“Historic rates are currently being eroded.” (pharma)

Despite a general sentiment of price erosion, participants considered that projects comprising “good quality assets”, usually offered through competitive bidding and auction processes, will continue to secure high prices:-

“Availability of deals has increased rather than prices falling. Licensees’ expectations are still as high. Good quality assets (rather than ‘bottom feeders’) will still have a high price.” (pharma)

“If one looks at the share price, things seem cheaper but then once the fight begins, you cannot be sure that the price will not go up. There are no Phase III projects around.” (pharma)

The extent of information available on comparable deals may also identify the focus of the negotiations. For example, the public information available on upfront payments was considered to explain the focus on upfront payments:-

“Upfront payments are the most heavily negotiated. These are valued on the basis of comparables. The two things that are typically publicly released are upfront fees and so called ‘biovalue deal’ value. You can also work out from company accounts, how much is paid out in milestones.” (consultant)

2.3 Multiple methodology approach

The participants as a whole did not regularly apply the other methodologies such as scenario analysis, decision-tree modelling, Monte Carlo and real options. The notable exception was the pharma participants, who tended to apply a wider range of methods.

Even though participants expressed a clear preference for particular methods, they also warned against relying on a value derived from any single methodology or valuation approach:-

“Any one model is just one picture. We typically use several models for one project, to capture any variables particularly important to the project and the decision making process.” (biotech)

“In the end a composite of the methods is used to get a blunt valuation that feels right ... This is the most important issue as discussions over assumptions and forecasts could continue ad infinitum.” (corporate finance)

“None of the methods alone is a single decision tool ... you combine them.” (pharma)

Each different valuation method seeks to evaluate certain unique sources of value and risk. The lack of use of other methods is inconsistent with the extensive literature advocating the use of such methods. In the case of real options, a study conducted in 2001 predicted that, in view of the shortcomings of NPV-based methods, real options methodologies were expected over the next five years to become the dominant valuation tool applied to drug development¹⁰. There was some recognition amongst the participants that real options is the only methodology seeking to address the value of managerial flexibility in the face of economic uncertainties:-

“For real options You look ahead one or two milestones and say ‘if X happens, what do we do’. This is a combination of business planning and valuation approach.” (biotech)

“For the investor, option-based pricing can also be useful because it allows you to look at what the cost/value increase is, i.e. it tells you the potential uplift.” (biotech)

“Real options is a good alternative approach when negotiations reach a dead end on NPV derived values, because using a different approach could provide for a more creative solution (instead of straight-out licensing).” (consultant)

On the whole, however, the present findings suggest that any efforts towards popularising real options, and persuading others of the sources of value and risk identified from using this approach, will need to first consider how best to sell the merits of the methodology:-

“We do not use real options ...life’s too short. It is a sort of luxury which might be used if you had one small company with very bright people and had a lot of time. It might have been worth it for an acquisition which was ‘life changing’. For something big, you may therefore use more complex tools.” (pharma)

¹⁰ Remer, S., & Baden-Fuller, C., 2001. Dealing with uncertainties in the biotechnology industry: the use of Real Options reasoning. *Journal of Commercial Biotechnology*, Vol. 8(2), pp. 95-105.

3. Findings on the VC approach to valuing early stage projects

The VC approach focuses on:

- qualitative “business plan” like factors:-

“What we look at is: how novel is the science, is it addressing a major market sector, what freedom do you have to operate in that sector, is it a really hot target? We really look at management. Are these people who have been there and done it before? Is management going to be able to adapt and change? Do regulatory issues raise an additional cost burden? What are the clinical issues? What is the business model?” (VC)

“We look at whether the market size is sufficient, competition, whether the proposal is sensible, whether management have done it before and whether we can we get a trade sale.” (VC)

- the costs of developing a drug candidate to the point of exit:-

“When VCs value early stage development, this tends to be a simple ‘return on capital’ methodology , i.e. how much will it cost to take it to the next stage and whether a 5 to 10-fold return is possible.” (consultant)

- the exit horizon:-

“You only know IRR when you exit. Therefore the time horizon of investment must be assumed. This is why the exit horizon is so important.” (VC)

- what the value will be at the point of exit:-

“The VC will look at what the value is to an acquirer.” (biotech)

“VCs are seen as now being very active with their portfolios. Ultimately a VC wants to get his or her money back and whatever multiple.” (VC)

“In an acquisition, the value will depend on who is doing the acquiring. VCs from day one will be grooming the company for acquisition and will have set a return on capital value - and then adjusted to what they can get in the market.” (consultant)

Not surprisingly, the exit strategy is key to the VC investment decision:-

“The starting point of the investment is: how do we get out of this?” (VC)

One of the VC participants considered that, even if IPOs return, they are no longer considered to offer a complete exit. The participant saw VCs as now more focused on trade sales and becoming cleverer at how they position the companies that they invest in. From a trade sale perspective, VCs do not want to position a portfolio company as a “one product” company, but nor can a company be too diverse:-

“The key challenge lies in how to position the company with products and technologies that are compatible.” (VC)

4. Findings on the biotech and pharma approaches in acquisition, licensing and partnering

4.1 Projects on offer

Participants noted that Phase II and Phase III projects that fit the gaps in pharma portfolios are becoming increasingly rare:-

“In the overall deal environment, it is still a tough market for good assets, and Phase III assets that could be launched in a year and fit our profile are not easy to find.” (pharma)

Some participants predicted a continuing shift towards early stage deals:-

“Note that the number of Phase II deals are going down, with pharma looking at much earlier stage projects.” (biotech)

Participants see pharma as increasingly open to considering drug candidates with smaller markets if the end product can be marketed within its sales force machinery:-

“Market share is the thing to get right ... The key issue from the pharma perspective is: can it get leverage from its existing sales force to the market under discussion? Pharma has the benefit of huge sales force machinery and is always looking to give this machinery more to sell. It also means that pharma may be open to looking at products with a smaller market share.” (VC)

Buyers are also considered to be applying more specific requirements to what a product profile needs to look like in order to succeed:-

“It is important to consider the product profile – what profile must be achieved to be worth taking to market. Many projects will be terminated.” (VC)

“When pharma is looking at things top down within the organisation, standard attrition rates would be used across all therapeutic areas. However, when looking from the bottom up, we are starting to build in very specific attrition rates for that specific drug, i.e. product-related attrition rates. These would take into account whether the drug would be best in class, or first in class, whether there were any toxicology problems etc. These rates would be very different in oncology and infection.” (pharma)

4.2 Outright acquisition

Some participants referred to outright acquisitions of biotech companies becoming more popular than complex licensing and partnering deals. Others commented that the current value for biotech companies running out of funds and with low prospects of independent fundraising lies in being acquired.

One participant referred to a trend of partnering and licensing negotiations being run in parallel with, or as a prelude to, acquisition negotiations:-

“The real game is going on with private companies where no one is actually intending to license because the licensing of lead products will be negative to a future purchaser. So they use auctions on lead product. They use this to push upfront payments and then they will often say ‘you are better off buying the company.’” (biotech)

“There used to be lots of milestones and royalties. Increasingly small companies are saying ‘give us the cash now and you can have the whole thing.’” (biotech)

“Licensing is only interesting to VCs if they are in for the long haul and the company has a platform technology or multiple products.” (VC)

4.3 Other arrangements

Pharma participants described receiving renewed requests for loans from cash-strapped biotech partners referring to the possibility of pharma directly re-financing key biotech partners in financial difficulties:-

“We have had recent requests from biotechs for loans – acting as their bank. This may be substituted for an equity stake. I think we will see loans and equity stakes again.” (pharma)

Participants considered the current market circumstances to have revived interest in the acquisition of minority equity stakes in biotech and pharma partnering arrangements:-

“Minority equity stakes are increasing but in the current market there is the insolvency risk and more concern in the financial stability of the biotech partner.” (VC)

Views expressed outside of this study also point to greater interest on other deal structures, including recent attention on the acquisition of options to acquire drug development assets (instead of the outright acquisition of the assets). The option deal structure, whilst considered disadvantageous from the biotech perspective, is reported as being considered by rights owners unable to otherwise access necessary funding.

4.4 Sources of value discrepancy

Participants also provided examples of the sources of value discrepancies between rights owners and buyers in price negotiations.

■ Differences of opinion with respect to risk, timeframe, future investment etc

The guess-work and subjective assumptions involved in predicting key inputs provide an obvious source for value discrepancies. Most participants agreed that discussions over assumptions and forecasts have the potential to continue indefinitely.

■ Differences of opinion with respect to the true stage of development

Pharma participants reported encountering overestimations of the true stage of development, meaning that a buyer would have to re-do development work, which in turn leads to a delay in development and complicates analysis of competition at launch:-

“A biotech will tell you they are risk-taking and can quickly develop the products. When you get to the biotech’s Phase III product, you discover you have to re-do the work and this is where due diligence is important to determining development overestimation and value.” (pharma)

“Biotech companies have the attitude that they knew they were going to have to partner so that they would do the least to cause harm to their products and get them through to Phase II, when they would have a value. In contrast, we would have done trials across a range of things. The biotech’s whole driver would be keeping the product clean –‘innocent until proven guilty’- whereas ours was quite the opposite i.e. ‘guilty until proved innocent.’” (pharma)

Other participants thought that development overestimation should be less of an issue in the view of regulators (including the US Food and Drug Administration) providing greater guidance throughout all phases of clinical development.

■ Different strategic considerations and negotiating power

The theoretical value derived from applying quantitative valuation models, when considered in isolation, assumes that the drug candidate/project has an intrinsic value. The participant responses indicate that, while one may argue over the assumptions and forecasts underlying the inputs of a quantitative model, the price of a drug development project ultimately depends on overriding qualitative factors and subjective criteria specific to the biotech rights owner and the pharma acquirer/partner:-

“The official version is the perception of risk and need for future investment. The unofficial version is how desperate they are for the deal, and how much they can do over the other side.” (biotech)

“There is a difference of opinion with regard to the risk, timeframe, likelihood of dilution moving forward. The overriding point is who wants/needs it more?” (analyst)

The strategic factors and synergies that the particular acquirer or partner may wish to exploit in connection with a drug development project are critical to what the project will be worth to the pharma acquirer or partner:-

“Valuing a partly developed project should be for a reason. If it is to sell the programme to a partner, it can only be a starting point. Purchasers will pay what they need to strategically (which is not the same as NPV).” (VC)

“Negotiating power is all-important when a small company is being bought. This usually boils down to financing risk – will the company shortly run out of money and what are the prospects for further independent fundraising? The other party would not be targeting if the fit was not appropriate.” (corporate finance)

Cash flows, together with the prospects of independent fundraisings, were identified as factors determining what the project will be worth to a biotech rights owner:-

“Biotech is less interested in NPV and more interested in upfronts and cash flow.” (pharma)

“A biotech is concerned with its cash flows and getting to the next point. In comparison, pharma approaches valuation by reference to the big pipeline world ...” (pharma)

One biotech participant was keen to highlight that cash flows will be less relevant to a cash-rich rights owner:-

“If a biotech has loads of cash then it may be less interested in upfronts. The pharma view stems from being margin conscious and not cash conscious. So you have this bizarre thing of sales-based milestone. Sales-based milestones do not affect the margin of the product. Also, the headline value of the deal can be increased by using sales-based milestones. Also from the perspective of a biotech, if you are in survival mode, then the NPV in 15 years is irrelevant.” (biotech)

4.5 Project value splits

Participants were asked to comment on the typical value split between rights owners and buyers. A limited number of participants acknowledged typical NPV splits:-

“In the early stages, the typical split is 80/20 in favour of licensee. If the product is in Phase III, the licensor will be looking for around 60-70% of the NPV.” (pharma)

“In relation to value split note the following: 90/10 (licensee : licensor) split for early stage; 75/25 (licensee : licensor) for phase II; above phase II, 50:50 (depending on who takes on the development costs).” (biotech)

However, most participants were reluctant to acknowledge any typical split, preferring to treat each deal on a case-by-case basis:-

“There is no definitive answer on this as it depends on the stage of the project, the size of the upfront payment (if any), who pays future development costs and whether the licensor retains exclusive marketing rights for any territories. It also depends on whether it is a competitive bidding process (which is ideal). The likely best outcome for a licensor with a product at pre-registration will be a 25% royalty on sales with some sort of upfront calculated as a percentage of estimated peak sales.” (corporate finance)

“I am not sure there is a ‘typical’ split. If you want to take a broad brush approach to it this would probably be different depending on drug/device stage of development etc.” (analyst)

“Each deal is an individual discussion.” (VC)

The participant responses also identified factors that influence the allocation of value as between rights owner and buyer.

■ **Innovation:-**

“The innovation step is critical so, even if you have not spent money on development, if you have created a huge market value potential, then there will be a royalty greater than 20%.” (pharma)

■ **Risk assumed by a party:-**

“Risk is key...if the mechanism is known, if the product is in lead, if it is close to market, you pay more.” (pharma)

“If the product is early stage, the licensor would expect a much bigger split because they are taking the risk. At the late stage, they would generally use 50/50 as a starting point. These percentages are not definitive.” (pharma)

“For a brand new product and an immature market, more risky.” (pharma)

■ **Extent to which downstream costs and responsibilities are shared:-**

“Milestone payments are calculated by reference to how much you pay for development. If the payee contributes more, then the milestone payments get bigger.” (consultant)

“The ability to fund late-stage clinical trials always limits cost sharing for a smaller company, thus balancing the NPV equation. The rest is basic economics on opportunity cost (upfront payments) and the risk of cash flows not arising or being delayed (given an uncertain regulatory environment).” (corporate finance)

“Biotechs pretty much always ask for co-promotion which would help their valuation.” (pharma)

- Whether the rights owner is seeking to retain any rights or has already out-licensed any rights (e.g. exclusive marketing rights for any major market) is clearly key. One of the participants referred to the acquisition of ImClone by Eli Lilly in 2008, where much attention focused on the fact that ImClone had already granted to BMS the rights to ImClone's blockbuster cancer drug, Erbitux.
- Where the payment structure comprises relatively larger upfront payments and smaller late-stage payments, the buyer clearly assumes more risk. Consequently, the buyer will typically require a larger percentage of the project value. The participant responses offered explanations on why this was generally advantageous from the rights owner's perspective:-

"From the perspective of the licensor, it wants everything now because it wants the cash flow." (consultant)

"Cash today is almost always preferable for a small company even if it reduces the overall retained proportion of the NPV." (analyst)

"For a small drug discovery company, it is all about how soon can you get hold of cash that is not committed to something else (i.e. Glaxo paying you £1M to hire £1M worth of biologists to work on a project is not helpful. Them paying £2M to hire £1M worth of biologists gives you £1M spare)." (biotech)

"Hedged - very sure of the value in the product and close to launching." (analyst)

Notwithstanding the obvious advantages for a rights owner of a frontloaded payment structure, participant responses also highlighted the downsides of such a payment structure that a rights owner needs to consider, including:

- Reduced share of the total deal value:-

"The obvious downside for the buyer and upside for the seller of upfronts is that the cash is handed over whether the project is a success or not. The upfront will be much smaller than the total deal value if the payment is deferred." (biotech)

"An early stage licensing deal will only attract low to mid single digits. Phase IIa complete may get high single digits. Phase IIb complete may get low to mid teens. A high upfront payment (getting rarer) will always reduce the royalty rate." (corporate finance)

"If the licensor is seeing it as a financing option to develop a subsequent pipeline, a high upfront payment will be sought, to the detriment of the royalty. If the licensor is well funded, they are more likely to retain a higher royalty rate." (corporate finance)

- Even if a buyer agrees to a frontloaded payment structure, buyers are currently less willing to agree to high upfront payments:-

"Licensees appear to be less willing to agree high upfront payments." (corporate finance)

- High early milestone payments may skew a buyer's decision against the continuation of a drug development project. This is relevant to scenarios where the payments to be made to the rights owner are contingent on the buyer progressing development and meeting future milestones:-

“One must look at the economics. Often, negotiating parties ignore that people have to make decisions. For instance, if you have a small company with a programme in early stage development and it is negotiating with a large moderately capitalised company (not as big as a pharma company) and the research is in one of those areas where you have got good Phase II data to date, the small company knows that the R&D will work and will commonly negotiate on the basis that when it gets through, they will get a really big milestone payment. This position could skew a decision against your product. Therefore, you must put yourself in the shoes of the other side and consider what the decision process will be. The product may be returned and therefore you have to also consider the value if the product/project is returned.” (biotech)

■ Competition amongst bidders:-

“The licensor share is driven by competition. We would of course not offer more unless we had to, e.g. if we were at risk of losing the deal. We would tend to work up the initial valuation in ‘exquisite detail’ then go in with a bid, and competition would change everything. It is a question of ‘how hungry are you?’ Passion takes over from common sense. For example, where there is an important strategic gap in the portfolio, the price would go up – but one would not start from that position.” (pharma)

“Competition is a key driver. A high upfront payment is more likely if a bidder perceives it must pay this to secure the licence.” (analyst)

Notably, a biotech participant pointed out that the deal structure is also relevant when evaluating value allocation between the parties:-

“From the perspective of biotechs, in the case of auctions you tend to get the position flipped with pharma saying ‘your product has huge sales potential’ but when you look at the deal structure this is not the case. So, for example, if you take a \$2 billion product and pharma says ‘we will give you huge sales milestones (\$500 million etc)’ but at the same time pharma is not agreeing to pay high royalty rates in the early stages of sales (for example, if you get a low royalty rate up to \$200 million) this indicates that pharma does not think that the data or the product is as good.” (biotech)

5. Findings on the analyst approach

Financial analysts apply valuation tools as part of setting share prices. The analyst participants confirmed that they are mainly interested in late stage projects with many analysts placing no value on pre-clinical projects, and some taking a more extreme approach:-

“We give anything prior to Phase II a value of zero.” (analyst)

The analyst approach was explained as stemming from the high risk associated with early stage projects. Once interest in a project is registered, the analyst will focus on when the drug candidate will be launched and when relevant sales will peak.

According to a biotech participant, this approach ignores the fact that the present value for biotech companies currently lies in being acquired. If an early stage project is of interest to an acquirer, then the acquirer will place a positive value on the project, whereas the analyst approach may assign no value to it at all:-

“What they should do is to actually give anything beyond Phase II a value of zero. The analyst view is based on the business model of licensing being the main route of commercialisation. Note that the number of Phase II deals is going down, with pharma looking at much earlier stage projects.

The present value for a biotech lies in being acquired and not in doing licensing deals. Therefore the value to an acquirer is completely different.

For example, consider the scenario where you have a company with the following products: Phase II diabetes product; Phase I cancer product; Pre-clinical platform for other metabolic disorders; and Pre-clinical platform for inflammation product.

The analyst will ignore the pre-clinical platforms. The analyst will do an NPV on the products. The analyst will do a licensing deal on NPV and add these all up with the cash that the company has and give you the value of the company.

If the company is bought by a company that is looking to get into metabolic disorders then the Phase II deal for diabetes (which analyst has given most of the value) is irrelevant. The acquirer will place a positive value on the metabolic pre-clinical platform and possibly put a negative value on the cancer product.

Analysts really get it wrong and the one thing they get paid to do, they don't do, that is, look at what are the chances of the product succeeding?” (biotech)

6. Forecasting challenges

Participants were asked to comment on the key challenges in forecasting the future revenues, costs and risk associated with a drug development project. They were generally comfortable with their ability to estimate the costs of drug development. In comparison, significant uncertainties existed around projecting revenue and risk parameters. The emphasis on revenue potential and risk is consistent with NPV modelling showing the highest sensitivity to changes in these parameters.

6.1 Inputs for projecting revenue

The key difficulties relating to revenue forecasting stem from the inability of participants to predict the shifts in, or to control, the factors determining a new product's ability to penetrate a market:-

“Sales inputs ... pose uncertainty. The greater the uncertainty, the earlier stage of development a candidate is in. For instance, in one project, the therapy area we looked at changed drastically over the space of one and a half years when the drug candidate moved from Phase II to Phase III trials. As a result of changes in treatment paradigms used by doctors (e.g. what drug is used in first line, second line treatment), this directly impacted potential sales for the development candidate.” (pharma consultant)

“We feel most comfortable as regards the things we can control (such as our own expenditure and development) rather than market share and competition (things which we cannot control). Sales forecast is the factor which has the biggest impact, yet over which we know the least, so it is this aspect about which we struggle the most – it is a bit of a ‘shot in the dark.’” (pharma)

“The reimbursement and pricing landscape are shifting and the value proposition may look attractive now, but turn out to be quite different. You look at the competitor landscape, how appealing it is to end users, the payer's price benchmark, and markets becoming subject to generics/forced reference pricing when one product goes generic.” (pricing consultant)

In particular, many participants emphasised struggling with assessing competition:-

“You can give best estimates of value given the current understanding of the market and anticipated product competitive profile ... but educated guesswork cannot take account of unknown development projects.” (corporate finance)

“There are real difficulties in primary care, and competition is difficult to predict ... There is a fundamental difference between being first to market and second to market.” (pharma)

“Competitive profiling at the time of launch is difficult to predict accurately as it will depend on data from pivotal trials. Should generic competition be a critical issue at the time of launch, the product will require a significant advantage to secure a price premium.” (corporate finance)

Despite being perceived by the other groups as possessing informational advantages, pharma participants indicated that they too struggle with predicting parameters underlying revenue and risk:-

“For the initial valuation, we will put in standard values to see if it is even worth going so far as to investigate whether there is a business case. Then we will work up a very specific sales forecast (taking into account the competition, the patent situation, etc, although we’ve never got it right yet. All one can ever do is a ‘best guess’ and this is where the most heated discussions are, although it is rather a waste of time because no one knows the answer. There are conversations with people saying ‘how do you know we’re going to sell this?’ Everything else can be much more precise.” (pharma)

6.2 Determining risk parameters

The key difficulty in determining appropriate risk parameters stems from an inability to derive project specific rates:-

“The probability of success is very difficult to estimate.” (biotech)

“The most difficult input metric to measure is the probability of success, as this often depends on the label sought.” (consultant)

“The greatest challenge is with respect to forecasting risk. Halving risk assumptions can effectively double value.” (consultant)

Participants tended to rely on industry averages, whilst acknowledging the limitations of using them:-

“NPVs are based on standard probability rates and these are industry-based rates which are totally unrealistic. For instance, once one gets to Phase II, some industry rates will say that there is a 30% risk ... If you take, for instance a cancer product which has a high market value, and a product aimed at a better understood disease with a lower market value, consider which one will actually make money.” (biotech)

“The DiMasi data for probabilities of success and timing is getting a bit old but is still industry standard.” (corporate finance)

In relation to discount rates, there was a difference in opinion on whether discount rates should be changed in line with changes in interest rates. One participant highlighted the misuse of discount rates:-

“Discount rates are not used properly. For instance, discount rates do not necessarily change with changes in interest rates.” (biotech)

Another participant defended not changing discount rates on the basis that discount rates are an estimate over the long term life of a drug development project.

The need to consider market risk was also raised:-

“Once launched ... the product itself can lend itself to differing take-up. Therefore, for example, a biologic which can be controversial may have a slower take-up. Equally, a company that makes the medical device to deliver a drug has other inputs which can provide additional subtleties to the valuation.” (analyst)

6.3 Forecasting costs

The findings confirm pharma's information advantages when it comes to forecasting late stage development and marketing costs. The historical division of responsibilities between biotech and pharma has the latter assuming responsibility for downstream development and commercialisation activities. Whilst pharma understand clinical investment, a pharma participant commented on how it is becoming more difficult to predict what is going to be required of a drug candidate for regulatory approval:-

"Clinical investments are well developed in big pharma but regulatory is difficult to predict." (pharma)

The non-pharma participants mainly relied on industry standards and conventional assumptions whilst acknowledging their limitations:-

"Costs/timings in clinical trials in highly competitive areas will be difficult to predict as competition for recruitment to trials becomes an issue." (analyst)

The less detailed approach by biotech investors to assessing downstream costs was also explained by the biotech business model:-

"The business model is someone buying a biotech company and you are not interested in late stage data. Pharma do not like the way biotech do that." (biotech)

6.4 Forecast period

Participants saw the key challenge in connection with forecasting the development timetable. Any delays in development have significant implications for the all important competitive positioning:-

"Development time is critical. If you lose time, then there is a knock-back effect on competition position and development costs. At one stage the development time was said to be twelve years ... now said to be nine years." (pharma)

"It is a given in the industry that everything is going to change and so one usually starts with a joint development plan (either drawn up by us alone if we were going to control it, or jointly between the parties). Within that, there would be a joint committee or our own portfolio review allowing things to shift off the initial plan. I doubt that we (or any other pharma company) have ever done a project to time and as originally specified. If things were to go badly, or warning bells were being sounded (e.g. the product was no longer going to be first in class or best in class), then we would have the right to opt out/to stop." (pharma)

6.5 Pharmaceuticals versus biopharmaceuticals versus medical devices

The participant responses also identified differences between pharmaceuticals, biopharmaceuticals and medical devices, with most responses focusing mainly on differences relating to risk:-

“Biologics have a different profile, slightly better than NCEs at the early stage but worse at the later stage.” (pharma)

“Biologics have lower risk but development takes longer (risk is lower because these are naturally occurring substances and so they already work in some capacity)” (consultant)

“Risk with medical devices is easier to predict as it is often a technical challenge rather than a clinical challenge.” (corporate finance)

“A company that makes the medical device to deliver a drug has other inputs which can provide additional subtleties to the valuation. The risk percentages used tend to be different. It is far easier to see a medical device to market than a blue sky drug, therefore your risk adjusted would differ.” (analyst)

In respect of the widely acknowledged lower risk profile of medical device development, one participant warned against assessing these lower risks in isolation in circumstances where the development of the device (and its value proposition) is tied to drug development:-

“Where the company had been manufacturing drug delivery devices, it was absolutely essential that the device timescale was not the weakest link in getting the product to market. Everyone expected that one could time the delivery of the device to the day because it was manufacturing – although in reality it is tied to the drug.” (pharma)

Differences relating to other NPV parameters include:

■ Regulatory, costs and timing:-

“Compared to NCEs, biologics and medical devices are likely to be different at the level of regulatory, product development costs and timing.” (consultant)

“There are differences between (i) medical devices and (ii) biologics and NCEs. The time lines are much shorter for medical devices. In the case of the diagnostic tools, products could be ready within five years.” (consultant)

“It is more difficult to estimate the cost of goods with biologics unless the scale-up pathway is very clear.” (corporate finance)

■ Sales:-

“Once launched ... the product itself can lend itself to differing take up. Therefore, for example, a biologic which can be controversial may have a slower take up.” (analyst)

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