Ralph Villiger and Boris Bogdan
are partners at Avance, Basel GmbH, a company focusing on consulting and software development within the pharmaceutical and biotechnology industry.

Papers

Pitfalls of valuation in biotech

Ralph Villiger and Boris Bogdan

Date received: 5th August, 2005

Abstract

Biotech companies face the need for valuation at various stages: fund raising, licence contracts, initial public offerings and mergers and acquisitions. The authors explain why common discounted cash flow methods are not suitable for drug development projects, sketch how real options valuation works, and address the most important misunderstandings.

Keywords: *valuation, DCF, real options, Black-Scholes*

IMPORTANCE OF VALUATION

When asked about valuation, many industry professionals say that it is factually impossible to attribute a value to a drug in development. Too many uncertainties are attached to it: issues about safety, efficacy, competition, regulation and demand have to be solved first. Typically, people want a drug to be valued to predict whether it will make money. However, valuation only calculates the odds. The value tells you whether it is worthwhile to risk the bet and how much you should bet, but it does not tell you whether you are going to win.

Knowing this, when is valuation necessary? Investors need to find out if they should participate in a venture. On the other hand, the start-ups need to know what share they are willing to cede to the investors in exchange of the additional cash. The same questions arise before initial public offerings (IPOs) and mergers and acquisitions (M&As). Internally, a company must decide where to allocate its capital, which project they should push forward, which is the most promising option. Finally, in licence negotiations the contract partners have to agree to fair deal terms.

Valuation is essential for the most crucial steps of a biotech company. The amount of money at stake justifies and requires a careful and thorough valuation. It is hard to understand that some companies enter negotiations without a sound valuation. Surprisingly, this is not a phenomenon limited to young start-ups: even some large pharmaceuticals do not value their projects properly. Some complain that the valuations always yield negative values for early stage projects and that therefore a valuation is useless. The following paper explains how valuations can be taken to the required standards.

VALUATION WITH DISCOUNTED CASH FLOWS

The standard valuation technique of the industry is discounted cash flows (DCF). Other authors call the same technique net present value (NPV), risk-adjusted net present value (rNPV) or expected net present value (eNPV). The idea underlying DCF is to compare revenues and costs. If income exceeds expenses, then the project is profitable and the company should start or continue the project. But different cash flows do not occur at the same time or have the same likelihood. So we have to adjust the cash flows for their time difference by discounting them, and for their likelihood by multiplying with their probability to occur (for a practical example see Table 1 and Figure 1).

Once the input parameters are known, DCF provides a fast and easy-to-

Ralph Villiger
Avance,
Basel GmbH,
Pfluggässlein 14,
4001 Basel,
Switzerland

Tel: +41 76 321 90 86
Fax: +41 61 273 45 49
E-mail: ralph.villiger@avance.ch

Table 1: Practical example of valuation using discounted cash flows

	Phase I	Phase 2	Phase 3	FDA
Costs (in US$m)	5	19	68	1
Success rate (%)	55	66	75	90
Length (months)	18	24	30	18
Peak sales estimate:	$190m			
Margin:	60%			
Growth rate:	1%			
Volatility:	32%			
Launch costs:	US$120m			
WACC:	18%			

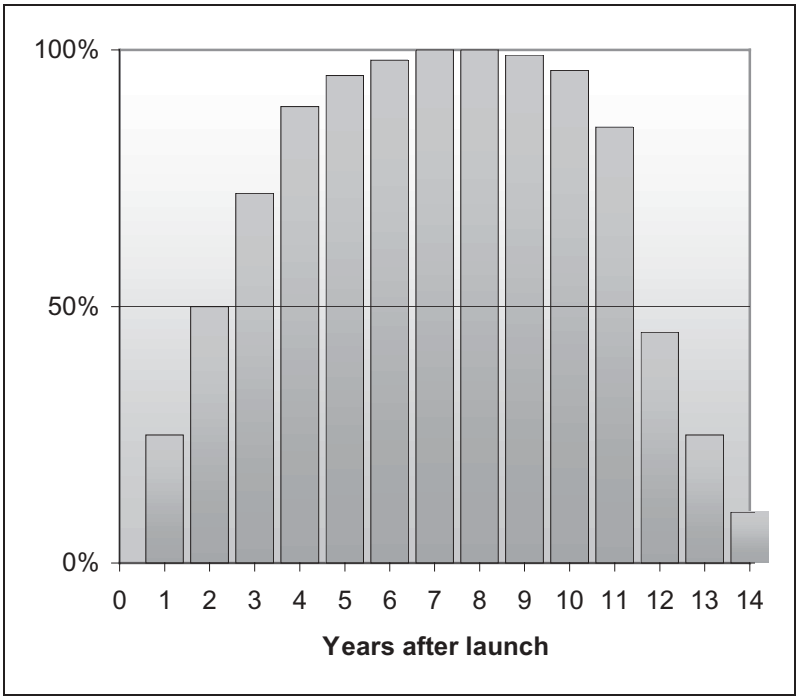

Figure 1: Development of net sales

understand method to assess the value of a project. Nevertheless, the technique has some major disadvantages. First, DCF uses the input parameters as if these were given numbers that will not change under any circumstances. This leads to an over-reliance on these parameters and does not reflect the risk of the project adequately. Second, a drug development project must pass several phases. In each phase, issues such as safety or efficacy are addressed. Bad trial results lead to abandonment of the project. The trial results reveal information not only about the feasibility, but also about the quality of the compound. Discovered side effects might lower the sales potential, or open new application areas. The companies should conduct a new valuation of the project before starting the next phase. This allows filtering out under-performing projects. Projects with negative value are abandoned. In this way the company avoids imminent losses from continuing the project. Revaluation therefore adds value to the company. DiMasi[1] estimates economic considerations to be the primary reason for abandonment in 30 per cent of all cases. Hence, it is important to consider this aspect in the valuation. DCF is not able to take account of this.

Real options

REAL OPTIONS

Real options valuation addresses the drawbacks of DCF. Its name stems from the analogy of investments and financial options. An option is the right but not the obligation to buy or sell an asset (underlying) at a prefixed price (strike) until a certain date (expiry). Some investments can be modelled as options. Suppose a company has just started a Phase III trial. The trial results are expected in 30 months. If the results are positive, the company has the option to file a new drug application (NDA) and then launch the product. However, the company will do so only if the expected sales exceed the costs necessary to bring the drug to market. The costs of clinical Phase III correspond to the purchase of this option. Equally, with the costs of clinical Phase II the company buys the option to acquire the above-mentioned option after a successful trial. The investment for clinical Phase I is then the price for an option on an option on an option. In finance these options on options are called iterated compound options, nested options or multi-stage options. The companies exercise the options only if the necessary investments (the costs of the subsequent phase or the launch costs) are less than the value the company gets in return. The launch costs are the option fee to launch the drug. In return, the company gets the sales revenues of the drug. Earlier in

development the phase costs are the option fee to acquire the subsequent options, the last being the one just described.

While in DCF calculations the estimated future peak sales are a given number, in real options valuation the sales estimate fluctuates (Figure 2). The degree of this uncertainty is called volatility. At the beginning of the project one can only guess how well the drug will sell. With every time step new information on the drug and the market allows this estimate to be adjusted. In the real options model this corresponds to the different branches of a binomial lattice (Figure 2).

We start in the root node with a sales estimate of the drug, based on present knowledge, as if it were on market today. With every time step Δt the sales estimate can go up uS or down dS with a probability p and $1 - p$. The time increment Δt, the expected average growth rate μ and the volatility σ define the size of the step. By performing these steps along the development path, we receive the binominal lattice. Every state in the lattice shows the estimated sales number. The parameters u, d and p are chosen in a way that, first, one step up and one step down leads to the same state as one step down and then up (recombining tree). Second, the peak sales estimate grows on average by the predicted growth rate μ (mean). Third, the span-width of the tree corresponds to the uncertainty of the peak sales estimate (variance). Once the lattice has been constructed we can work it back to the root node to obtain the present project value.

For each end node, corresponding to the time point just before launch or NDA, we know the peak sales. We now discount back for each end node the cash flows resulting from the sales and subtract from this value the necessary investments to commercialise the drug. Negative values lead to abandonment of the drug. The value at these nodes is consequently put to zero. Having calculated all values for one time point, in this case launch or NDA, we can deduce the values of one node earlier. The value of this node is defined by the mean values of the two subsequent nodes, taking account of discounting, technical uncertainty, investments and decisions. Again, negative values mean abandonment of the project and are set to zero. Finally, we work the tree back to the root node, ie the scenario with today's peak sales estimate. The value for this node is exactly the real options value of the

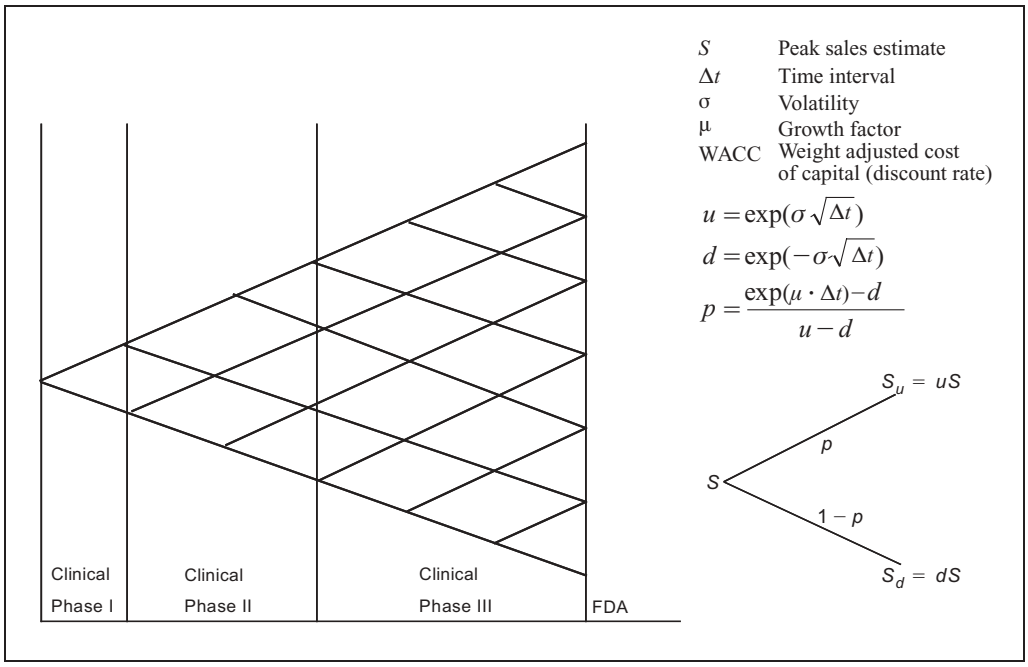

Figure 2: Binomial lattice for a project in phase 1. The lattice can go up to NDA or launch, according to the preferences of the valuator. However, the option to abandon despite FDA approval is politically hard to justify

project. For a detailed technical description of the method we refer the reader to Villiger and Bogdan.[2]

COMMON PROBLEMS WITH REAL OPTIONS

Real options are without any doubt more demanding and more complex than DCF. Nevertheless, the advantages appeal to many practitioners. Real options attributes value to good management, considers risk and the implications on the project development. A lot of literature has been written on real options; unfortunately sometimes without the necessary diligence. Many misunderstandings hinder real options from being applied in a more standard way. We address some of these misconceptions.

What about Black–Scholes?

Real options are descendants of financial options. Therefore, it would make sense to value real options just like financial options. In finance, these options can be valued with a formula, the so-called Black–Scholes formula. Unfortunately, this formula cannot be translated into a real option formula, for three main reasons. First, in finance you can hedge away all risk by building a replicating portfolio, ie a combination of underlying shares and bonds. This practice is not feasible with R&D projects, because the underlying is not tradeable. As a consequence, real option valuation uses the growth rate and the weighted average cost of capital (WACC) as discount rate. In finance these two numbers would be replaced by the risk-free interest rate. Second, and more important, R&D projects are staged and the project must achieve several milestones. This leads to nested real options, options on options. The Black–Scholes formula describes only a one-time option. Third, the Black–Scholes formula cannot capture the uncertainty inherent to clinical trials.

The Black-Scholes formula cannot be translated into a real option formula

It is possible to modify Black–Scholes by relaxing the hypothesis of the replicating portfolio. It can also be extended to nested options, like Geske[3] did for financial options, and it is possible to implement the technical uncertainty as well. However, the formula becomes huge and loses the illustrating effect of binomial trees. Furthermore, most programs do not offer the necessary mathematical functions necessary for the valuation of the formula.

Volatility

The volatility measures the degree of uncertainty of the peak sales estimate. Unfortunately this number is hardly measurable and intuition does not help much. Nevertheless, we know that in practice 30 per cent of all abandoned drugs are caused by economic reasons. Using average data we should therefore calibrate the volatility in a way that the calculations yield the same percentage for economically motivated abandonment as the practice. This leads to volatilities between 30 and 40 per cent. It is then possible to tune the volatility to the individual risk profile of the project.

Success rates

The risk of trial failures is usually taken into account by means of success rates. Usually a cash flow is multiplied with the probability that it occurs. This probability is derived from the success rates. Published success rates are statistical percentages of projects in one phase that are continued in the subsequent phase. These success rates consider abandonment for safety, efficacy and economic reasons. They are therefore lower than success rates that consider abandonment only for safety and efficacy. When using published success rates, economically motivated abandonment has a value-destroying effect, contrary to what we stated before. It is therefore necessary to clean the success rates such that they represent abandonment only for lack of safety and efficacy.[4]

Most success rates are based upon data from large pharmaceutical companies. A

small biotech has to consider the infrastructure that underlies these success rates. Large pharmaceutical companies get the best out of a promising project by providing a highly experienced science and management team along with the necessary tools and investments. Therefore, a small biotech can use the success rates by having the necessary means to achieve the same results. If the biotech has shortcomings in its experience and financing, the success rates have to be adjusted.

Peak sales

As with the success rates, predicting peak sales depends on the company's infrastructure. A small company cannot assume the same peak sales as a multinational pharmaceutical company. If the biotech considers marketing the drug itself, it has to use lower than maximum peak sales, as it will probably not trigger an investment to build a marketing department comparable to a pharma giant. On the other hand, the biotech should value its projects in a way corresponding to its outlook. Knowing that it will out-license the product, all subsequent parameters have to be chosen so they suit the licence partner and the project has to be valued as a licence contract.

PRACTICAL USE OF REAL OPTIONS

Real options consider the possibility to avoid losses when giving up an unprofitable project, ie a project where future expenses do not cover the expected revenues. The application of the method is therefore suitable to value projects that are not clearly profitable. As an example we use a project that enters clinical Phase I (Figure 3; the exact project description can be taken from Table 1). Discounted cash flows yields a net present value of US$−3.6m, while real option valuation recommends continuing the project with a value of US$1m. At states where the value of continuing the project drops below the necessary investments to start the next phase, the company stops the

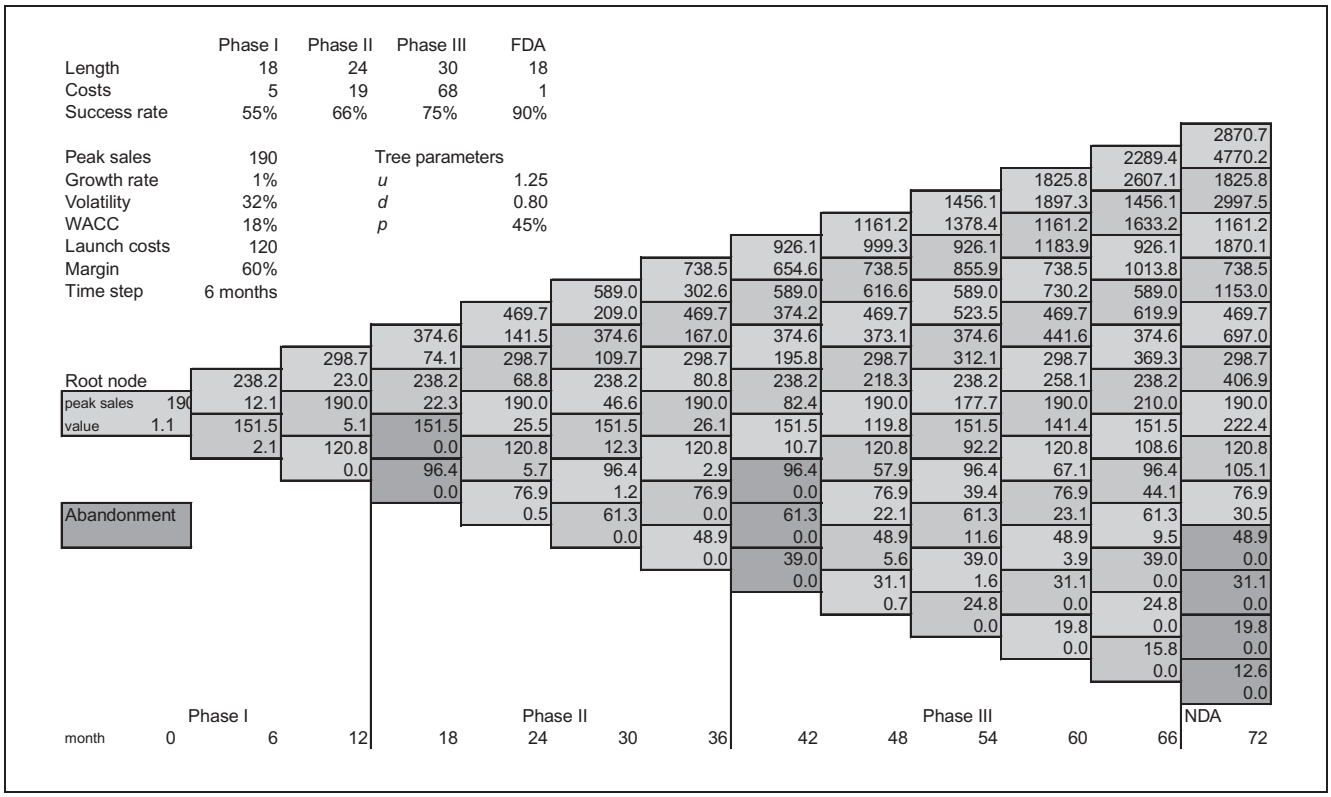

Figure 3: Example of real options valuation of a project entering Phase I clinical trials

project and avoids losses. This leads to a higher real options value compared with DCF.

A project with high peak sales is not better off with real options

On the other side, a project with high peak sales is not better off with real options. The valuation results of DCF and real options converge, as there is no necessity to stop the project because of profitability reasons. The same project as in the first example, but with peak sales of US$500m yields a project value of US$48.5m with both DCF and real options.

Valuation of licence contracts

A second application of the real options method is the valuation of licence contracts. Consider the same project as in the previous examples, but this time the company licenses to a pharmaceutical company (with a WACC of only 10%). This has the effect that costs, success rates and peak sales must be adjusted to the pharmaceutical company's proficiency. The contract partners agree on a value share of 80/20 per cent between the pharma and the biotech company. The milestone payments and royalties as displayed in Table 2 are set such that the contract achieves exactly this value share. But when valuing with real options, the outlicensing company receives only 18 per cent of the value, because it shifted the flexibility to abandon the project to the in-licensing company. The biotech company has therefore an argument to negotiate for another 1 or 2 per cent of royalties.

Table 2: Example of valuation of licence contracts with discounted cash flows

	Phase I	Phase 2	Phase 3	FDA
Costs (in US$m)	6	24	75	1
Success rate (%)	60	70	80	90
Length (months)	18	24	30	18
Milestones	1.6	3.5	5	6
Peak sales estimate:	US$195m			
Margin:	60%			
Growth rate:	1%			
Volatility:	32%			
Royalties:	4%			
Milestone at launch:	US$8m			
Launch costs:	US$140m			
WACC licensor:	18%			
WACC licensee:	10%			
Patent protection	15 years			

Real options are well suited for portfolio management

Third, real options are well suited for portfolio management. A company wants to maximise its profits, but at the same time keep them stable and robust to adverse events. This requires the modelling of the risk profile of the pipeline. Since the real option has already considered scientific and market uncertainty, it is a consequent step to model the entire pipeline, taking account of the dependencies between the projects. Two drugs using the same technology may have similar trial results. Projects aiming at fighting the same disease may have the same competitors. Making use of the quantitative background where real options originate, it is possible to quantify value, risk, diversification, exposures, liquidity needs and gaps. Real options, when combined with simulations, lend themselves to powerful risk management tools such as value at risk, cluster and sensitivity analysis. However, such a portfolio management requires a sophisticated software solution and is not feasible on a spreadsheet.

Finally, real options are a mindset. Management must be aware of their leeway and how they can react on positive and negative developments. The discussed valuation included merely options to abandon. Nevertheless, real options have a variety of applications. We can imagine options to extend a drug's application areas; to postpone development; to expand into new disciplines by building new research centres (this corresponds to the acquisition of a whole basket of options); and to profit from innovations by investing in start-ups. Many of these options are hard to quantify, but sometimes it is a big step to recognise that investments include the possibility of taking decisions at a later time, based on the then-met conditions.

CONCLUSION

Real options valuation solves the shortcomings of DCF at the cost of

increased complexity. However, once the industry has overcome the beginner's problems of this valuation method, the companies can address topics such as project and portfolio management, licence contracts and VC negotiations with firm arguments rather than intuition and vague experience.

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