VOLUME 17 | NUMBER 2 | SPRING 2005

Journal of APPLIED CORPORATE FINANCE

A MORGAN STANLEY PUBLICATION

In This Issue: Real Options and Corporate Strategy

Morgan Stanley

Valuing Pharma R&D: The Catch-22 of DCF

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There are two principal methods for valuing pharmaceutical projects—discounted cash flow (DCF) analysis and real options valuation (ROV). DCF is a straightforward method that adjusts all cash flows by the probability that they materialize. In the case of a pharma R&D project, the probabilities are typically based on expected success rates for projects of that type and in a particular stage of development.[1] For example, the expected outlays for clinical phase III of a cancer compound would be multiplied by the probability that an experimental cancer drug actually reaches phase III. Such a probability-adjusted version of DCF is sometimes referred to as expected net present value (eNPV) or risk-adjusted net present value (rNPV).

But the established success rates typically used in DCF valuations do not distinguish between projects that fail to pass safety or efficacy trials and those that are abandoned for lack of economic viability. For projects with strong market potential (and that therefore run little risk of being terminated for economic reasons), the DCF valuation will be understated because published success rates are too low for these projects. Projects with more modest sales potential (and therefore a higher risk of economic abandonment) will also be systematically undervalued by DCF because their inherent flexibility value is greater. For such products, the estimate of peak sales in a DCF valuation should be conditioned on the product not being abandoned for economic reasons, although such estimates are never used in practice. While DCF can be modified to provide more accurate valuations, the adjustments tend to rely heavily on management intuition, especially in the case of projects with modest sales potential.

Real options valuation provides a more reliable method—using more predictable inputs—for handling the complexity introduced by the possibility of economically motivated abandonment. Because ROV implicitly allows for the initial estimate of sales potential to be corrected over time in response to new clinical evidence or to changes in market factors like competition and regulation, it takes account of scenarios in which the estimate of market potential drops below the threshold of profitability and the company abandons the project for economic reasons. For this reason, ROV is better suited to project valuation both in the pharmaceutical industry and in other R&D-driven industries with staged investments that depend on periodic reevaluation of the project.

Success Rates and Abandonment

New drugs must pass through three clinical phases to establish their safety and efficacy. At the end of each phase, the company decides whether to continue development or to abandon the project. If safety and efficacy cannot be established, then abandonment is effectively mandated by the FDA. Abandonment for economic reasons, however, is a voluntary decision by the company. If the expected future cash flows from producing the drug are less than the necessary outlays to bring the drug to market, the company ends the project. According to several studies, roughly 30% of all project abandonments are for economic reasons.[2]

Published success rates generally represent the statistical average of all projects that move on to the next clinical phase. Thus, they reflect abandonment for any and all reasons—economic as well as those involving safety or efficacy. What's more, two-thirds of all commercialized drugs have peak sales of less than $100 million,[3] suggesting that most projects that go into the calculation of published success rates have fairly moderate sales potential. This in turn means that for projects with high sales potential—that is, with little risk of economically motivated abandonment—average success rates overstate the possibility of economic abandonment and are therefore too low (see Figure 1). And as discussed below, if success rates are too low, a DCF analysis based on the mechanical application of such rates will understate the value of the project.

Economic Abandonment

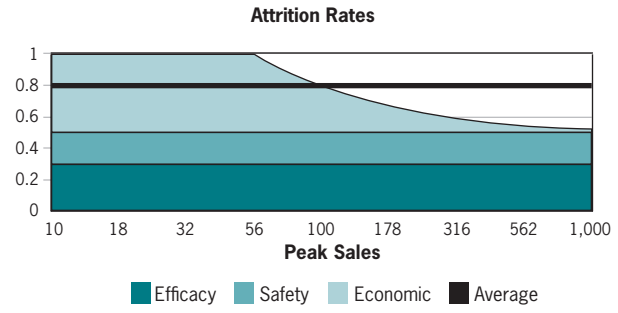
Real options techniques often yield higher values than DCF methods, with the difference generally attributed to

1. See, for example, J. Kalamas, G. Pinkus, and K. Sachs, "The New Math for Drug Licensing," *The McKinsey Quarterly*, Vol. 4 (2002), pp. 9-12; and P. Sharpe and T. Keelin, "How Smith-Kline Beecham Makes Better Resource-Allocation Decisions," *Harvard Business Review*, Vol. 76, No. 2 (1998), p. 45.

2. See J. A. Dimasi, "Risks in New Drug Development: Approval Success Rates for Investigational Drugs," *Clinical Pharmacology and Therapeutics*, Vol. 69, No. 5 (2001), pp. 297-307; and I. Kola and J. Landis, "Can the Pharmaceutical Industry Reduce Attrition Rates?," *Nature Reviews Drug Discovery*, Vol. 3, No. 8 (2004), pp. 711-715.

3. H. G. Grabowski and J. Vernon, "The Distribution of Sales Revenues from Pharmaceutical Innovation," *Pharmacoeconomics*, Vol. 18, Suppl. 1 (2000), pp. 21-32.

Figure 1 **Success Rates in New Drug Projects**



Note: For projects with low sales estimates, the rate of abandonment for economic reasons is higher. Below a certain profitability threshold, projects will not be continued in any case. The numbers are purely illustrative.

Table 1 **Input Parameters for Different Valuation Methods**

	Success Rates	Sales Potential
DCF (ideally)	Adjusted for likelihood of economically motivated abandonment	Conditioned on the product not being abandoned for economic reasons
DCF (in practice)	Reflects failures due to safety, efficacy, and profitability	Realistic estimate for the product as it is known at time of valuation
Real Options	Reflects failures only due to safety and efficacy	Realistic estimate for the product as it is known at time of valuation

the quantified value of the flexibility to pursue profitable projects or to abandon unprofitable projects and cut losses. Since ROV accounts for economically motivated abandonment in the model itself, the attrition rates used as inputs should reflect only abandonment for safety and efficacy reasons—and thus the success rates should be higher. DCF, by contrast, attempts to account for economically motivated abandonment through the use of success rates that include project terminations due to low market potential.

If the appropriate success rates are used in both cases, the two methods should yield identical project values because they assume the same scenarios. The practical reality, however, is that the two methods deal in a completely different way with the possibility of economic abandonment. For the project value using DCF to be the same as its ROV, the required inputs—that is, the success rates—must be adjusted. But because not all projects are equally likely to fall below the profitability threshold, the success rates have to be adjusted for the likelihood of economic abandonment for the *particular project being valued*. And since such an adjustment inevitably depends more on managerial intuition than historical data, it weakens the reliability of the DCF valuation.

Another problematic input in DCF is the estimate of sales revenues. Since the possibility of economic abandonment is already incorporated into the success rates, the estimates of the cash flows from product sales should be independent of the probability of abandonment for economic reasons. And this means that the sales input in DCF should reflect an estimate of not just the product's prospects in the market, but the product's prospects *given that* it has not been previously abandoned for economic reasons.

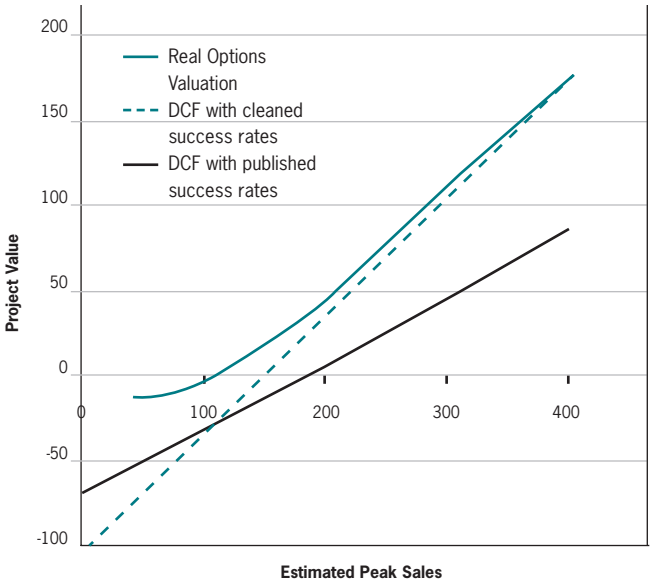
So how do we determine the sales potential of a product *conditional* on its being profitable? (After all, isn't it the fundamental task of the valuation process to determine whether a project is profitable—rather than requiring its anticipated profitability as an input?) This is not much of a problem in the case of highly profitable projects because, in such cases, the current estimate of the market potential of the product is essentially the same as its market potential given that it will not be abandoned. For such projects, there is little inherent value in flexibility because the variability in sales potential is not expected to be large enough to affect management's decision to carry out the project, and so DCF and real options will generate very similar values.

In practice, however, DCF tends to be used without any of the above adjustments (see Table 1). The estimated sales potential for a product is based on current knowledge about its efficacy, safety, applicability, and market potential. This includes the possibility of economic abandonment and is therefore inconsistent with the product's sales potential *conditional on the product being profitable*. Since the published success rates include the likelihood of economic abandonment, the most promising products, as noted earlier, tend to be undervalued. At the same time, products with more modest sales potential are also likely to be undervalued because the possibility of economic abandonment is effectively "double counted," affecting both the success rates and the estimate of sales potential. For such products, it is even more important to estimate the sales potential conditional on no economic abandonment in order to capture their flexibility value.

Figure 2 shows the value of a project at the beginning of clinical phase I depending on the peak sales estimate.[4] (The Appendix provides a more detailed description of the input data.) The top line shows the value of the project based on real options and hence using "clean" success rates. The

4. For a detailed description of DCF and real options valuation for drug development projects, see R. Villiger and B. Bogdan, "Getting Real about Valuation in Biotech," *Nature Biotechnology*, Volume 23, No. 4 (April 2005), pp. 423-428.

Figure 2 **Peak Sales Estimates and Project Values**



middle line shows a DCF valuation with the same inputs. The difference between the two is attributable to managerial flexibility and becomes negligible at higher levels of sales potential. The key line in Figure 2 is the line representing project valuation as typically practiced in the pharmaceutical industry—that is, with composite success rates and unconditioned sales estimates. The use of published success rates that include project abandonment for economic reasons leads to significantly lower project values. The vast majority of early-stage projects have negative values under the common DCF valuation practice and should presumably be abandoned.

In reality, of course, drug development companies take account of the limitations of DCF and pursue early-stage projects despite negative DCF project values, often by adjusting the discount rate until the valuation result is more favorable. But this makes the whole valuation effort a largely meaningless exercise—and decisions to continue or abandon projects become almost completely arbitrary. Sound financial management requires a solid analytical foundation for major investment decisions. Most companies fail to understand why their valuations do not reflect the current market value of projects and transactions. The main source of error is not the uncertainty associated with early-stage valuation per se, but rather the valuation method and its input parameters. In the next section we illustrate the shortcomings of DCF valuation with an example.

Valuation Example

Let's suppose we are looking at a project in clinical phase I with the same general project parameters used in Figure 2. We begin by valuing the project with ROV using success rates that reflect only abandonment for safety and efficacy reasons. We then establish the probabilities of abandonment determined by the model, which include the probability of economic abandonment. These probabilities yield new, lower success rates. Finally, we can calculate the peak sales that lead to a DCF valuation that matches the real option valuation.

For the real options valuation, we assume the following key parameters (again, the Appendix provides a detailed list of all value drivers):

- Success rate for clinical phase I: 77%
- Success rate for clinical phase II: 63%
- Success rate for clinical phase III: 84%
- Estimated peak sales: $186 million

These success rates might seem overly optimistic, but keep in mind that they reflect only the possibility of a technical halt of the project. The probability of economic abandonment is captured in the real options valuation model itself.

Using these project parameters, we estimate a value of $50.8 million using real options methods. With the same input data, a DCF calculation would yield a project value of $38.9 million. We can then revert to success rates that reflect cases in which the project is abandoned for both technical and economic reasons, as follows:

- Success rate for clinical phase I: 61%
- Success rate for clinical phase II: 52%
- Success rate for clinical phase III: 75%

Using these success rates, we can determine the peak sales that would yield a project value of $50.8 million using DCF. The result is $264 million, which is 42% larger than our initial estimate. Again, this is the estimate of peak sales *conditional on economic success*—a number that is extremely difficult to forecast. This example demonstrates the importance of the inputs in a DCF analysis and shows how valuation can easily become arbitrary.

Real options thus seems to be the more reliable method. Using success rates that reflect only abandonment for reasons of safety or efficacy, real options correctly accounts for economically motivated abandonment. And the framework of real options is completely consistent with the concept of staged investment in an uncertain world with the flexibility to react to new information as it becomes available.

Some will object that the assumptions underlying real options valuation are not applicable in the case of new drug projects.[5] In particular, the volatility of the underlying asset in standard financial options pricing is replaced in ROV

5. See, in particular, M. Amram and N. Kulatilaka, "Strategy and Shareholder Value: The Real Options Frontier," *Journal of Applied Corporate Finance*, Vol. 13, No. 2 (2000), pp. 15-28. The authors also argue that the uncertainty inherent in pharmaceutical projects is of a private nature and is uncorrelated to economic risk indicators, making such projects unsuitable for real options valuation; this concern is addressed in T. Arnold and R. Shockley, "Real Options, Corporate Finance, and the Foundations of Value Maximization," *Journal of Applied Corporate Finance*, Vol. 15, No. 2 (2003), pp. 82-88.

by uncertainty about the sales estimates, which cannot be observed directly. While the estimated values of highly profitable projects are not as affected by the sales volatility estimate because the likelihood of abandoning the project is negligible—and in such cases, as noted earlier, the real options value and the DCF value should be essentially identical—volatility is a relatively more significant value driver for projects with moderate sales potential. In our experience, however, it is possible to obtain reliable estimates of this volatility by studying consecutive clinical trial results and analyst forecasts. We find that estimates of between 30% and 40% are typical. Of course, such estimates do not capture the risk of technical abandonment, which is reflected in the success rates.

The validity of using real options valuation techniques for new drug projects has also been questioned on the grounds that such projects are seldom abandoned for economic reasons, particularly in later stages. But as we noted earlier, studies suggest that as many as 30% of all project halts are for economic reasons,[6] mainly in the late stages when it becomes easier to benchmark the product to existing drugs for establishing market potential.

Conclusion

DCF as it is typically used today generally yields lower project values than ROV. Yet the reasons for this difference lie not only, as often claimed, in DCF's failure to take account of managerial flexibility, but also in the use of conventional success rates, which are determined on the basis of an average number of products that pass from one phase to another and thus reflect project abandonment for lack of economic potential as well as for safety and efficacy reasons. To be applied effectively, both DCF and ROV require a finer breakdown of the reasons for project abandonment. The fact that 30% of all project abandonments are due to profitability considerations is a strong argument for using ROV to evaluate new drug development. Whereas DCF has difficulty incorporating the uncertainty created by the possibility of economic abandonment, the real options model is well suited to this task—indeed, that is what it is designed to do.

In sum, DCF is a simple method that can be used with some confidence to value highly profitable projects that have little risk of being abandoned for economic reasons. But in the case of less profitable projects, the apparent simplicity quickly turns to complexity—and real options valuation becomes the more useful alternative. The consistency of ROV compensates for its greater technical difficulty. And much the same is true of any kind of R&D valuation where there is a material chance that projects will be abandoned in midstream for economic reasons.

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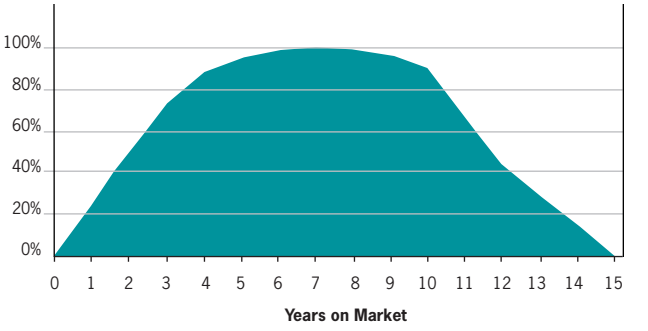
Appendix **Value Drivers in Valuation Example**

	Real Options	Discounted Cash Flows
Start of phase I	Already started	Already started
Costs of phase I	Sunk	Sunk
Success rate phase I	77%	61%
Start of phase II	In 1.9 years	In 1.9 years
Costs of phase II	$23.5 million	$23.5 million
Success rate phase II	63%	52%
Start of phase III	In 3.3 years	In 3.3 years
Costs of phase III	$86.3 million	$86.3 million
Success rate phase III	84%	75%
Start of FDA review	In 5 years	In 5 years
Costs of review	$1.3 million	$1.3 million
Success review	100%	100%
Launch	In 6 years	In 6 years
Launch costs	$200 million	$200 million
Peak sales	$186 million	$264 million
Profit margin	60%	60%
Discount rate	10%	10%
Annual volatility	40%	
Project value	$50.8 million	$50.8 million

Appendix **Realized Percentage of Peak Sales**



6. See Dimasi (2001) and Kola and Landis (2004), cited earlier.

Journal of Applied Corporate Finance (ISSN 1078-1196 [print], ISSN 1745-6622 [online]) is published quarterly on behalf of Morgan Stanley by Blackwell Publishing, with offices at 350 Main Street, Malden, MA 02148, USA, and PO Box 1354, 9600 Garsington Road, Oxford OX4 2XG, UK. Call US: (800) 835-6770, UK: +44 1865 778315; fax US: (781) 388-8232, UK: +44 1865 471775.

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