The Path to Strategic Manufacturing Flexibility

Good decisions often translate into tremendous profits and market opportunities, while bad decisions can result in significant loss. Financial decision analysis techniques can pay long-term dividends.

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Making strategic decisions such as choosing between R&D projects, in and out licensing drug development efforts, and significant investments in CAPEX requires a rigorous process. Biopharmaceutical executives face significant technical and market uncertainties when developing product that is years away from commercialization. Making multi-million dollar investments in this type of environment requires an approach that not only helps quantify the risk associated with technology and market conditions, but also values the ability to be flexible in the staging and execution of investments. Advanced financial evaluation and decision analysis techniques using Real Options Analysis, Monte Carlo Simulation and Optimization Models are beginning to gain ground in a number of the more sophisticated biopharmaceutical companies and if used correctly, can add a tremendous amount of value and insights to the strategic decision making process.

This article explores how these relatively new techniques can be used to help value and structure strategic investment decisions in a pharmaceutical manufacturing context.

Deciding on Significant Investments in Manufacturing Capacity Is a Challenge

Biopharmaceutical manufacturing and operations executives are often required to make difficult decisions – decisions that may have significant impact on their company’s ability to successfully compete in a complex and highly uncertain business environment.

One of the biggest challenges facing these executives is securing manufacturing capacity for products that are under development and years away from launch. They face a choice between multiple alternatives which include building internal capabilities, outsourcing these to a CMO, or a combination of the above.

These decisions involve significant capital investments as well as the opportunity cost of allocating funds away from other important initiatives. An internal solution may take four to six years and cost up to $500 million to implement, yet there is no guarantee that an outsourced solution will be available when needed, or sufficiently cost-effective and flexible to meet the needs of the company.

Sizing capacity needs is also challenging. The technology risk associated with biopharmaceutical drug development efforts is high. The probability of a drug candidate in pre-clinical trials reaching the market is on average 20% at best! Market assumptions regarding price, demand and competition may change dramatically during the lengthy development process and require different capacity than initially anticipated. Build too much and the company will be left with an underutilized asset while trying to identify ways to recoup wasted investment dollars that could have been better utilized elsewhere. Build too little and the company may lose substantial revenue opportunities. Given the risks (and opportunities) inherent in drug development:

- How should manufacturing executives choose the best strategy such that risks are sufficiently mitigated while opportunities are taken full advantage of?
- What can management do to increase their decision-making confidence and improve their capacity planning capabilities?

Traditional Valuation Methods May Lead to Suboptimal Decisions

Planning for manufacturing capacity typically begins very early in the product development process; often towards the end of pre-clinical trials or beginning of phase I. The key driver used to base capacity decisions on is a forecast of product demand and anticipated product launch date. Based on these and other assumptions, planners develop a basic timeline that typically incorporates lead times for: design and engineering; construction of facility and installation of equipment; and validation. In addition, they develop initial cost estimates for various alternatives.

Planners must consider a wide range of issues. Typical questions arise:

- What are the available alternatives/strategies that can meet requirements?
- What types of uncertainties from a commercial and product development perspective should be considered?
- How to secure the appropriate amount of capacity while maintaining flexibility to expand or contract should business conditions change?
- What is the optimal strategic pathway when strategies have different investment levels, timing and impact on project value?

For example, suppose a biopharmaceutical company has a product in the pre-clinical phase of development. The company is initially targeting its most lucrative markets: the high price/low-volume markets. Marketing has also identified a secondary market – the low price/high-volume market – that the company may consider expanding into given the right conditions. Supplying the secondary market with product will require a significant expansion of capacity.

The company's operations planning group has conducted a feasibility study of various manufacturing capacity strategies and has narrowed the number of alternatives to the following (simplified for illustrative purposes):

> **Strategy A:** Retool an existing facility for launch capacity – commit capital to build new facility to accommodate both primary and secondary markets once drug has successfully completed pivotal phase II clinical trial studies. New facility is expected on-line three years after product receives FDA approval.
>
> **Strategy B:** Build a new modular facility – install capacity needed for launch and expand with additional capacity (additional equipment within existing facility) once drug successfully completes pivotal phase II clinical trial studies. Capacity to supply primary and secondary markets is expected on-line with product approval.

Traditional methods used to justify these types of investments are usually based on the discounted cash-flow (DCF) based net present value - NPV approach.

	PV of Cash Flow		**Investment**		**Time to Market**		**NPV**
	Primary	*Secondary*	*Initial*	*Expansion*	*Primary*	*Secondary*	*w/Secondary*
Strategy A - Retool existing facility and expand with new facility	$1,131	$186	$70	$400	Year 9	Year 12	$874
Strategy B - Build new modular facility and expand capacity with additional bioreactors	$1,131	$283	$400	$50	Year 9	Year 9	$1,022

Table 1: Manufacturing capacity strategies; Traditional valuation approach

Given the NPV approach used above [Table 1], management should pursue Strategy B as it provides the highest NPV of all the alternatives. But should it?

The problem with the traditional NPV approach is that it's static, *i.e.* it assumes that demand forecasts (and other assumptions driving cash flows) can be projected with 100% certainty into the future and that investments are pre-committed no matter what happens (i.e. product fails a clinical trial phase, secondary market turns out to be not profitable, etc.) But how certain can planners be of their assumptions when in reality:

- Market factors impacting demand such as competitor moves, pricing and reimbursement, regulatory, etc. may change dramatically when product finally launches.
- Uncertainty increases over time, i.e. the further in the future the forecast, the more uncertain the forecast.
- The probability of launching due to technology uncertainty is low.

The importance of incorporating uncertainty – identifying risks and opportunities

Top-line variables such as price, demand, market share, etc. are combined with cost assumptions to build cash flow projections. Each assumption driving these projections can be described as a probability distribution, a function that represents a range of values and the likelihood of occurrence over that range. For example, sales growth with a range of 0-20% and a mean growth rate of 10% can be described using a normal distribution (the classic bell curve). In addition, some of these variables may be correlated in some way. An increase in price may negatively impact demand while competitors entering or exiting the playing field will impact the drug's potential market share opportunity.

Once these assumptions and corresponding distributions have been identified, a Monte Carlo Simulation software package can be used to generate thousands of "what-if" scenarios. The result is a distribution of cash flows for each period [Figure 1, below].

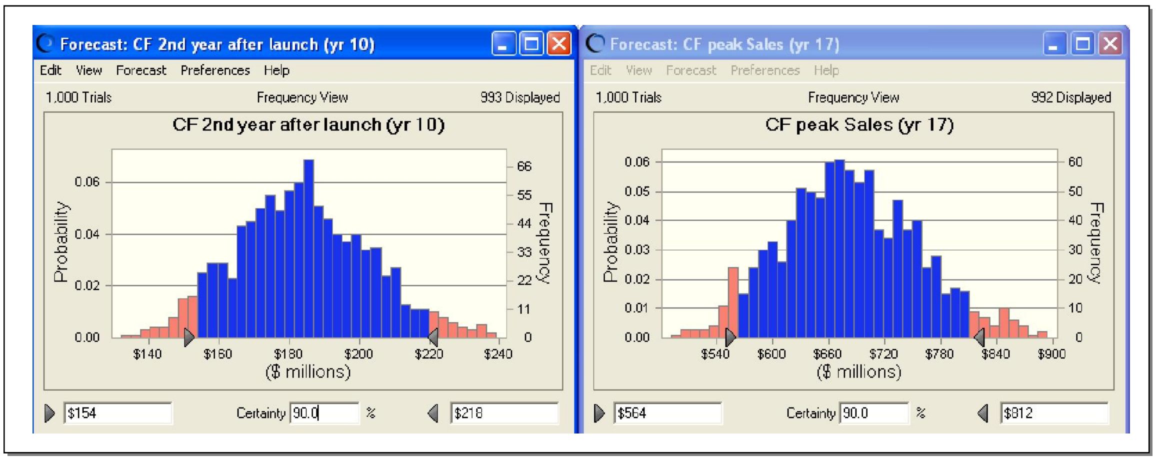

Figure 1: Distribution of cash flow values and 90% confidence intervals for different cash flow periods

These frequency charts can be used to describe how the uncertainty associated with the underlying assumptions impacts the output variable. For example, cash flows for the second year post launch will range from $154 to $218 million 90% of the time (the confidence interval), while cash flows will range from $564 to $812 90% of the time during the ninth year of sales. The wider the possible range of outcomes for each cash flow period, the greater the uncertainty.

The range or level of uncertainty of cash flow forecasts increases over time [Figure 2, below] creating a "cone of uncertainty". This width can be described as the **volatility** of cash flow projections. Volatility incorporates all measures of commercial-driven cash flow uncertainty rolled into one value.

The greater the uncertainty, the higher the volatility of cash flows and the wider the "cone of uncertainty". When volatility is 0, i.e. cash flows are 100% certain, the cone "collapses" to a single scenario – the forecast. As uncertainty increases, the cone widens and cash flow volatility increases.

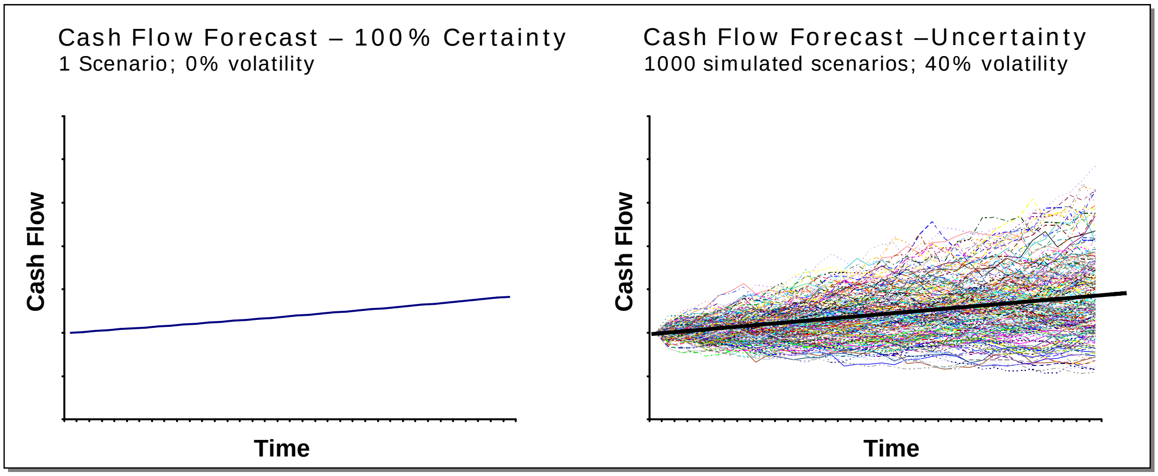

Figure 2: Cash flow forecasts – 0% and 40% volatility

Scenarios above the forecast create potential new opportunities, while scenarios below forecast represent risky scenarios. Uncertainty therefore describes the range of possible outcomes. Risk, on the other hand, is something that one bears and is an outcome of uncertainty, *i.e.* uncertainty becomes risk when a decision is made to invest.

In our example, the resulting NPV exhibits a range of possible outcomes, each with a probability of occurrence, the mean value being the "static" forecasted NPV without uncertainty. The resulting distribution [as shown in Figure 3, below] can be used to better understand the range of possible values for a desired confidence level. For example, given assumptions, how confident can management be that the investment will at least break even?

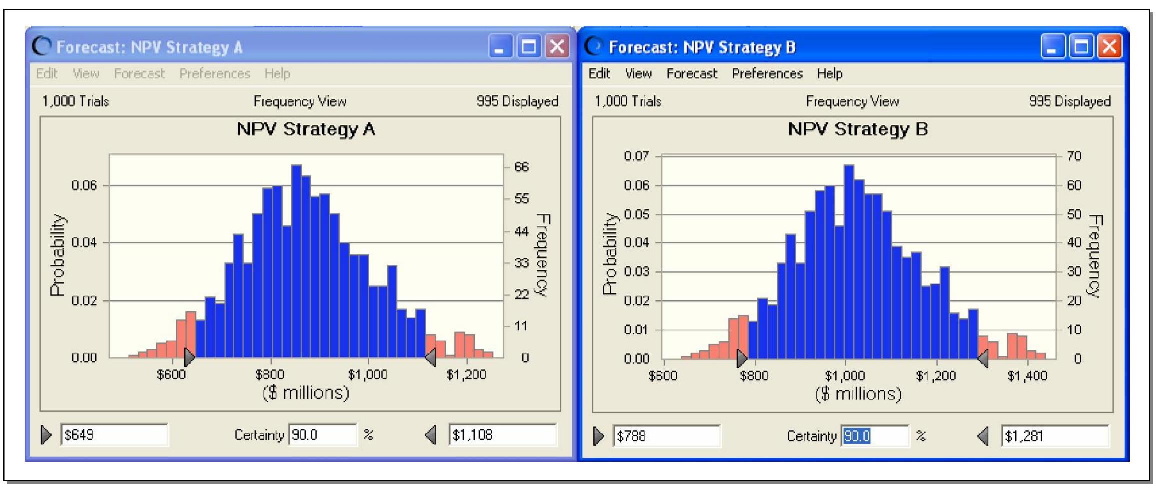

Figure 3: Cash flow forecasts – 100% certain and simulated uncertainty

Valuing Strategic Flexibility Using a Real Options Approach

Up to this point, we have described the need to incorporate uncertainty into the value equation. But given that the future is fraught with risk and opportunities, how can decision makers identify the strategies that *not only maximize returns but that also consider and manage risk*?

Traditional NPV assumes that investments are pre-committed – they will occur no matter what happens in the future. In our example, we are pre-committing today to invest in expansion into the secondary market based on information we have today. But can we be sure that the market will in fact develop as we predict? We have some time to wait and see, i.e. obtain better information on which to base our decision. In reality, managers making these types of decisions have the right but not the obligation to make investment commitments, i.e. they have the flexibility to choose if and when to invest. By not accounting for the inherent flexibility in making investment decisions, managers *may make sub-optimal decisions*.

A relatively new approach called Real Options Analysis can facilitate improved investment decision making. What are real options? A real option is the right but not the obligation to take a certain action at a predetermined cost called the exercise (or strike) price, for a predetermined time (the time to expiration). Real options are based on financial options theory developed by Nobel Prize winners Fischer Black, Myron J. Scholes and others. Real options theory applies the basic concepts developed by Black-Scholes to the analysis of real or physical assets (not traded).

Options abound when it comes to strategic investments. Manufacturing executives have numerous options at their disposal. For example:

1. Build a pilot plant as an option to develop process technology capabilities while outsourcing mfg for large scale production to a partner

2. Buy an option to expand capacity should new opportunities develop

3. Buy an option to sell off excess capacity or use unfinished facilities should business conditions change

4. Use contract manufacturing as a back up/expansion option

5. Secure the option to abandon/delay facility construction as a response to R&D failure/delay

The ability to be flexible when making significant investment decisions in order to capture opportunities and mitigate downside risk has value, value that is not captured by traditional methods.

In our example, expanding capacity in year 3 is an option contingent upon successful completion of phase II clinical trials and an NPV greater than 0, i.e. the decision to commit resources to expansion will happen in year 3 based on better information available at that point in time [Figure 3, below].

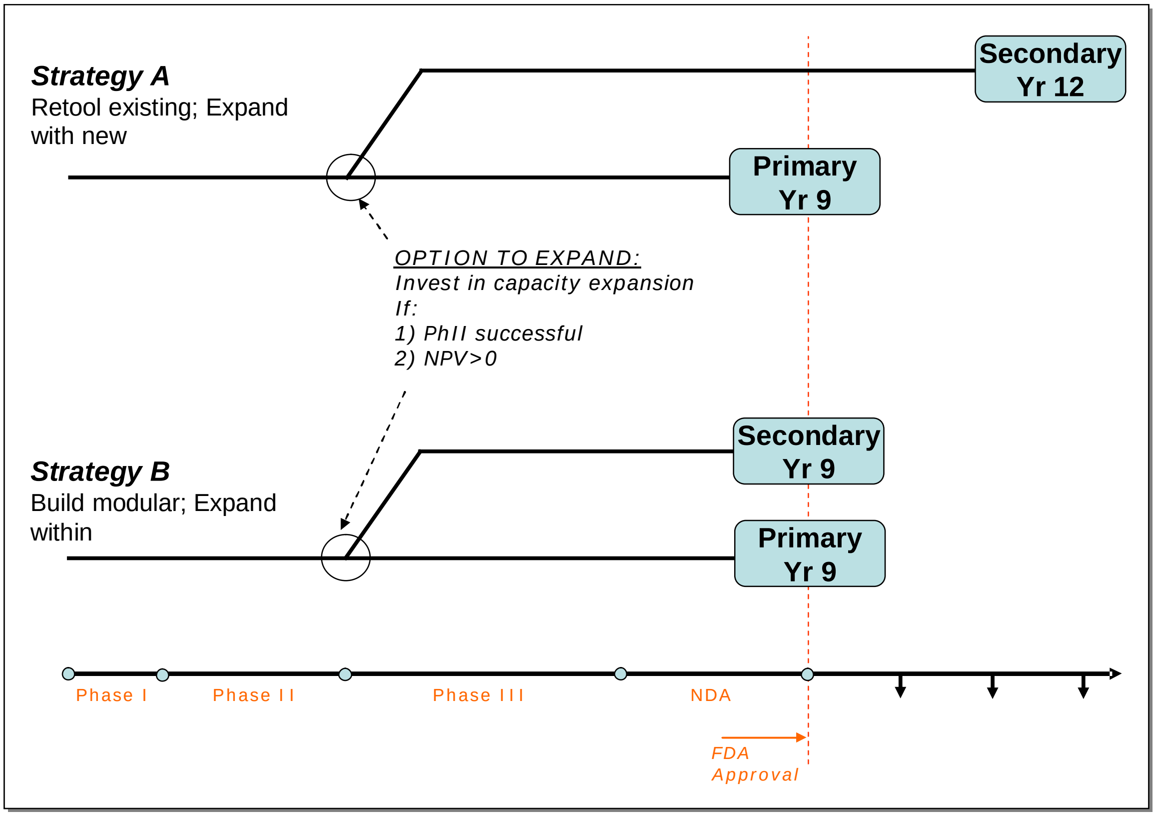

Figure 3: Decision tree for two competing strategies

Volatility as a measure of cash-flow uncertainty accounts for the range of possible scenarios given the available information. Using volatility, the cost to expand and the risk-free discount rate allows us to construct a spreadsheet-based binomial decision tree – a discrete approximation of thousands of continuous simulations generated by the Monte Carlo simulation software [Figure 4]. Each box denotes a specific cash-flow scenario.

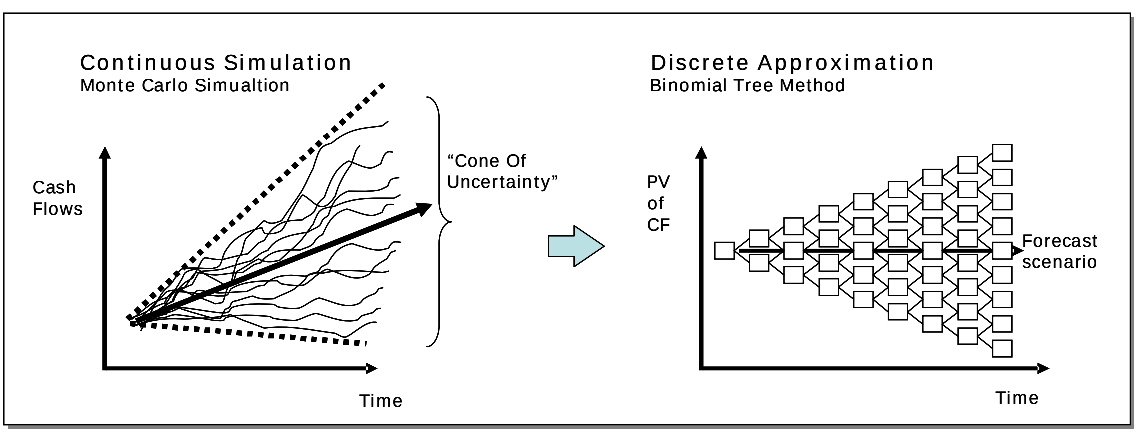

Figure 4: Continuous simulation using Monte Carlo method; discrete approximation using a binomial tree

NPV is then calculated for each of these scenarios. If NPV is equal to or less than zero, a rational decision maker will not exercise their option to expand capacity (NPV will be set at 0). If scenario NPV is greater than zero, than the option to expand will be exercised and decision makers will commit capital for capacity expansion. Each of these scenarios is then discounted back in time. The resulting NPV includes that value of expanding capacity only if the NPV in a given scenario is positive (no pre-commitment). The option value (or value of flexibility) is the difference between the calculated NPV and the "static" NPV, i.e. the NPV that does NOT account for uncertainty or flexibility.

Incorporating cash flow volatility and the option to invest in expansion capacity into our example causes our decision to change – strategy A becomes the optimal strategy. With strategy A, management will commit less capital upfront and wait to invest in expansion until better information becomes available further down the road - this despite the relatively higher cost to expand and the revenue lost due to the wait time to make additional capacity available. In fact, Strategy B is not a flexible option, i.e. it has no option value [Table 2, below]. The modular facility requires a substantial upfront investment ($400), while the cost of expansion is relatively low. For Strategy A, the cost of buying the option to later expand is only $70, while the expansion cost is considerably higher (will only invest in scenarios where NPV>0). This is despite the fact that the expansion facility will become available 3 years later than the modular facility in Strategy B (the cost of waiting).

	PV of Cash Flow		Investment		Time to Market		NPV		
	Primary	*Secondary*	*Initial*	*Expansion*	*Primary*	*Secondary*	*wo/flexibility*	*w/flexibility*	*Option Value*
Strategy A - Retool existing facility and expand with new facility	$1,131	$186	$70	$400	Year 9	Year 12	$874	$1,592	$718
Strategy B - Build new modular facility and expand capacity with additional bioreactors	$1,131	$283	$400	$50	Year 9	Year 9	$1,022	$1,022	$0

Table 2: Manufacturing capacity strategies; Real Options valuation approach

Our example illustrates in simplistic terms how a real options approach can help managers make better decision regarding significant investments in manufacturing capacity. We should mention that this approach can be utilized for significantly more complex decisions. In addition, the uncertainties described and incorporated in our example are market driven. It is important to also incorporate the probability of technical success, i.e. the probability of successfully getting a drug to market. R&D clinical trial success rate probabilities can easily incorporated into the Monte Carlo simulation.

Implementing a Real Options Approach

The Real Options approach described above incorporates a learning model, such that management makes better and more informed strategic decisions when some levels of uncertainty are resolved through the passage of time. It also forces management to focus on key decision points/milestones, *i.e.* when do we need to make key investment commitments? What are our options at a given point in time that allow us to take advantage of opportunities while reducing risk? What is the cost of waiting or deferring a decision?

This approach sets a premium on obtaining better information before making important decisions. It values flexibility (and identifies the cost of this flexibility) while improving decision-makers' risk management capabilities. As such, it can and should be linked to project management execution, since value can only be captured if the option is executed optimally.

A Real Options approach is straightforward to implement and is based on existing inputs and valuation methodologies already used in most companies. ROA adds an additional step to the existing NPV analysis by quantifying the value of the options available to management. That said, ROA should not be used in all situations. ROA is appropriate when there is a great deal of uncertainty surrounding market and technological factors, and when management really has the flexibility to take different courses of action.

A company considering implementation of this approach should start with a pilot project and assess if they have the internal resources and sophistication to really make a paradigm shift in the way they make and execute strategic investment decisions.

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