

Valuation Of Biotechnology Companies & Their Assets—Probability Effectuated Discounted Cash Flows

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What is Biotechnology?

Biototechnology is the “use of cellular and molecular processes to solve problems or make useful products.”¹

Biotechnology can be applied to basic scientific research, development of healthcare products (therapeutics, devices, and diagnostics) and services, agriculture, and nutraceuticals.

The Clinical Development Process

It is important to have an understanding of the clinical development process for human therapeutics. It is through this process that compounds identified by scientists are approved for human use (for specific purposes) by regulatory authorities. Each country has a regulatory authority such as the Food and Drug Administration (FDA) in the U.S. and the Health Protection Branch (HPB) in Canada. Clinical development risk is the largest business risk facing biotechnology companies.

We have provided an overview of the clinical development process in the Appendix.

Companies are Made up of a Group of Products

Generally a biotechnology company is a collection of one or more market opportunities or products. Therefore to value a company, each one of the products must be valued. The value of the company is then determined by adding up the value of all the products and the company’s

other assets and liabilities. Sometimes companies indicate that they have a “platform” technology with a large number of possible products or services. Management must decide where to allocate their resources and therefore which opportunities to pursue.

Two Major Stages of Product Life:

There are two major stages of a product’s life:

1. Research & Development Stage, and
2. Commercialization Stage.

The cash flow for each of these two periods can be estimated separately. It is quite usual for a valuation analysis to start with the second major time period component. By starting with the second component, the analyst can quantify the eventual market opportunity. This is how many companies begin their analysis when determining whether it makes economic sense to even contemplate starting the clinical trial process. This is the payoff! This is the opportunity sought. This is the reason to invest. The opportunity needs to be there to justify the investment to be made in clinical trials. Certain companies have minimum market opportunity sizes before they will even begin to consider whether to pursue an opportunity.

Therefore, this is how we begin our analysis.

Step One: Start with Commercialization Stage

To determine the value from market launch to the end of the product

life, estimates of the following are made:

1. The forecast cash flow from market launch until the end of the product life.
2. The discount rate to apply the cash flows.
3. The net present value at the market launch date is then determined by applying the discount rate to the forecasted cash flows.

The forecasted cash flow from market launch to product expiry (product life) requires a quantification of:

1. Expected revenue;
2. Cost of sales;
3. Operating costs; and
4. Income taxes.

For the purposes of this summary article we have made a simplifying assumption that the value of the opportunity at market launch is \$1 Billion.

Step Two: Value back through R&D Stage

The expected future cash flow during the development stages until market launch is made up substantially of the costs of pre-clinical trial research & development and conducting the clinical trials related to the specific indication. Therefore, the valuator must make an estimate of the:

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1. Source: www.bio.org, Guide to Biotechnology.

Chart 1. Decision Tree – Probabilities of Successful Clinical Trials

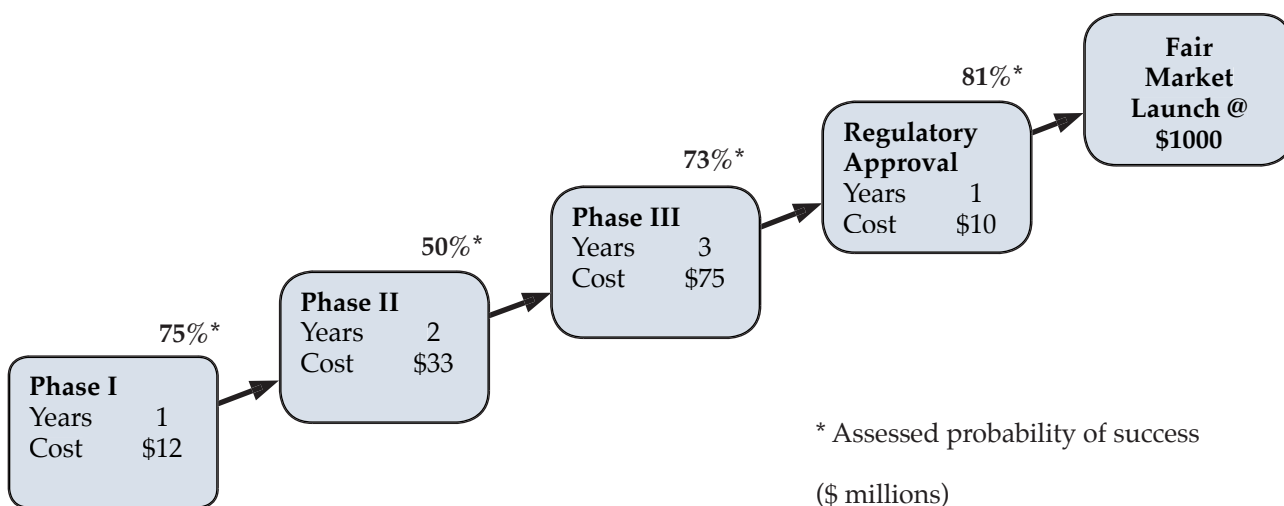


Table 1. Historical Rates of Success of Clinical Trials

	Small Molecule ⁴	Protein Therapeutic ⁵	Monoclonal Antibody ⁶	Mark Struck ⁷
Phase I	73%	75%	84%	88%
Phase II	45%	50%	72%	86%
Phase III	Not separately quantified	73%	Not separately quantified	93%
Regulatory Approval	Not separately quantified	81%	Not separately quantified	Not separately quantified

1. Cost,
2. Timing, and
3. Risks;

of each of the stages of the pre-clinical and clinical trials.

A detailed understanding of the clinical trial process is critical.² See the Appendix to this article for an outline of the clinical trial process. Understanding all the parameters and risks associated with the clinical trial process is a major task of the

2. An excellent book for understanding clinical trial design is *Fundamentals of Clinical Trials* by Friedman, Furberg and DeMets, published in 1998 by Springer.
3. If no forecast is available, one will have to be prepared using the structure outlined in this article.

valuator. Key documents that articulate a clinical trial plan include the “Investigator’s Brochure” including the “Protocol.”

Cost

Detailed build-up of the budgeted trial costs

A bottom-up estimate of the cost of clinical trial is used to determine how much cash is needed. A complete detailed budget should be prepared by management and should be reviewed by the valuator for reasonableness, as part of the assessment of the forecast.³

The costs of a clinical trial include:

1. Trial design;
2. Patient recruitment;

3. Investigator and clinician costs;
4. Pharmaceutical product;
5. Monitoring costs;
6. Data analysis;
7. Close out & reporting results;
8. Coordination with regulatory authorities; and
9. Administrative costs.

4. Reichert, J.M., “Monoclonal Antibodies in the Clinic,” *Nature Biotechnology*, September 2001.
5. Witzke, David, “Biotechnology: Biotech Platforms – Latent Value,” *Morgan Stanley Research*; October, 2002.
6. Reichert, J.M., “Monoclonal Antibodies in the Clinic,” *Nature Biotechnology*, September 2001.
7. Struck MM, “Biopharmaceutical R&D Success Rates and Development Times,” *Bio/Technology* 1994.

Chart 2. Value at the Stages of Clinical Development

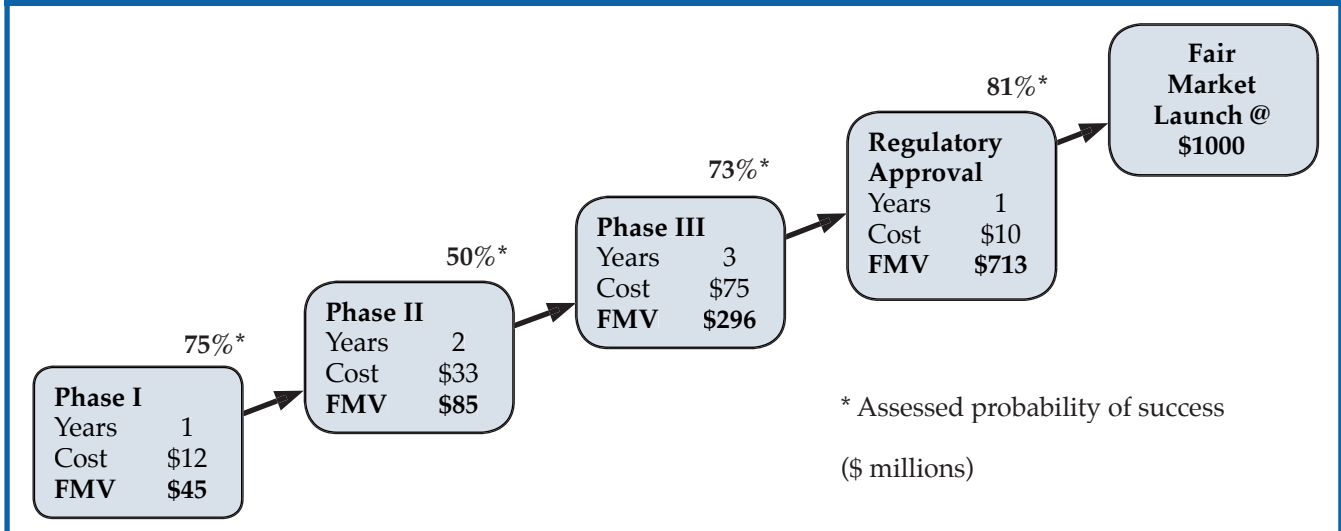
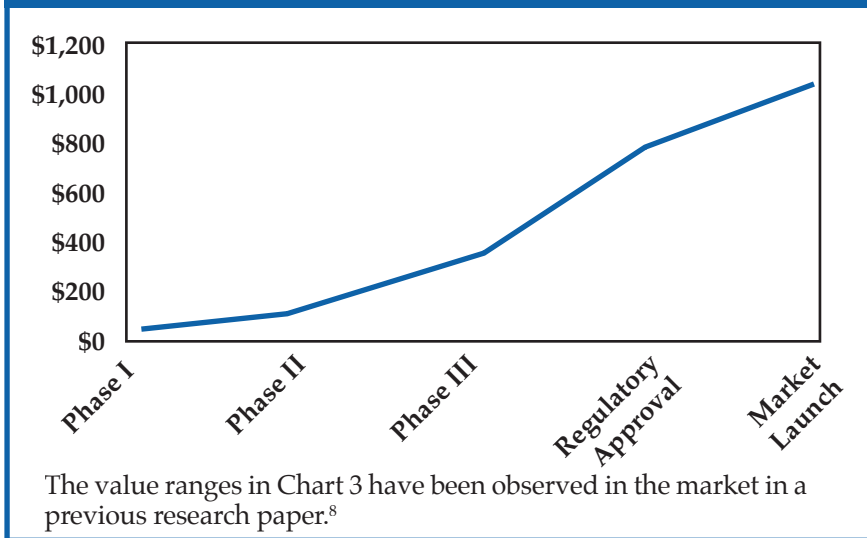


Chart 3. Value Through the Stages of Clinical Development



Estimates of trial timing can be determined through a review of the clinical trial protocol and discussions with participating clinicians. Estimates provided can be compared to trials of similar indications at similar stages of development. The Appendix to this article provides some general guidance.

Risks

Applying A Decision Tree to the Clinical Development Process

One of the major risks in the development of biotechnology is the clinical development process. Each stage of a clinical trial is a step along the journey to obtaining market approval from the regulatory authorities. By assessing the probabilities of achieving success at each stage of the clinical development of a therapeutic, the specific risk can be quantified directly in the valuation model.

A basic decision tree with the probabilities of making it through each of the clinical trials is shown in Chart 1.

For each of the stages of development there is a probability of that stage being successful and unsuccessful. For example in the above tree, we have assessed the probability of success for phase I at 75%.

Sources for Determining Probabilities of Success for Each Stage of the Clinical Trial

The primary source for analyzing

Other Costs

Other administrative costs must also be included in the budget such as the premises, equipment, management salaries, intellectual property and legal fees. These are some of the more typical other costs incurred during the development process.

Overall it is helpful to consult a number of different members of the management team in review-

ing management’s forecast. Key personnel include the director of clinical trials, the chief scientific officer, the chief financial officer and the president.

Timing

Timing of the clinical trials is a function of the length of time required to conduct the trials and the amount of time it takes to get the relevant publications and necessary regulatory approvals. The length of time that a trial takes is a function of: number of patients, speed of recruitment, natural disease progression and amount of time it takes for the therapeutic to show efficacy versus natural disease progression.

8. “Valuation of Biotechnology – Stage of Development is Most Important,” Webster, Philippon & Hotsaliuk, *Business Valuation Review*, December, 2002.

the probability of successfully moving through each of the stages of the clinical trials is discussions with the management of the company and designers of the trial.

In addition, to help put this analysis in a context, there are a number of publications that show analyses of probabilities of achieving success through each of the clinical trial stages, as shown in Table 1.

Determining Net Present Value

Once all of the above analysis is complete, the valuation is a simple matter of taking the NPV at market launch and then discounting it back through the decision tree and deducting the present value of the clinical trial costs as you go. Because the biggest risk has been directly quantified using the clinical trial probability of success, we use a more typical discount rate. In this case, we have selected 12%.

Continuing on with the example developed, the values at the beginning of each of the phases of clinical development, as shown in Chart 2.

Value of a biotechnology company through its life-cycle

Using the above data, the following chart shows the effect of the successful outcome of clinical trials on the value of a biotechnology company. These significant jumps in valuation are reflected in the stock prices of publicly traded biotechnology companies that achieve clinical milestones.

Reasonableness Check on Conclusions—Other Methodologies

As a reasonableness check on the value conclusion, it is helpful to apply one or more market approaches to value. In order for the market approach to be useful the comparable deals should be as similar as possible to the subject of the valuation. Factors to consider in determining similarity include:

1. Stage of clinical development, disease target,
2. Status of intellectual property, and
3. Other products in development.

The following is a very brief summary of four market approaches that are used by biotechnology analysts:

1. *Comparable Licensing Transactions*: the present value of the upfront payments, milestone payments and expected royalties is calculated as an estimate of value.
2. *Comparable Venture Capital Transactions*: implied pre-money valuations are calculated based on dollars invested and percentage of company received by VC Fund.
3. *Mergers & Acquisitions*: implied valuations of acquired companies.
4. *Stock Market*: implied technology values, (market cap less net assets).

Conclusion

The major risk to be quantified in the valuation of biotechnology is the risk of successfully completing clinical trials. Therefore we have found that the decision tree discounted cash flow method is often used, as it reflects how the managers and investors in biotechnology companies assess their investments and manage their business.

Appendix. Understanding the Drug Development and Clinical Trial Process							
2-3 Years	1 Year	6 Years			1-2 Years		
An Average of 10 Years							
Research	Preclinical Development	Clinical Development			Regulatory Submission for Approval	Review & Approval	Commercialisation
Idea ▼ Target ▼ Hit ▼ Lead ▼ Candidate Drug	To assess: • Safety • Biological activity	Phase I To evaluate: • Pharmacokinetics & pharmacodynamics (absorption, distribution, metabolism & excretion) • Safety	Phase II To evaluate: • Efficacy • Safety • Optimal dosage & regimen	Phase III To evaluate: • Efficacy • Safety of long term use		Review & approval by regulatory authorities	<ul style="list-style-type: none"> • The drug is made available to the public • Post marketing studies pharmacovigilance on a long term basis
Laboratory	Laboratory & animal studies	20-50 healthy subjects (patients in specific cases)	100-300 patients suffering from the disease the drug is intended to treat	500-5,000 patients suffering from the disease the drug is intended to treat			

Source: Biochem Pharma, 1998 Annual Report