Valuation of Your Early Drug Candidate

By Linda M. Pullan, PhD

ShareVault®

www.sharevault.com

Biotech companies frequently seek to partner with large pharmaceutical companies to advance their drug candidates and to raise funds. In the process of finding a partner and negotiating an agreement, a central question arises:

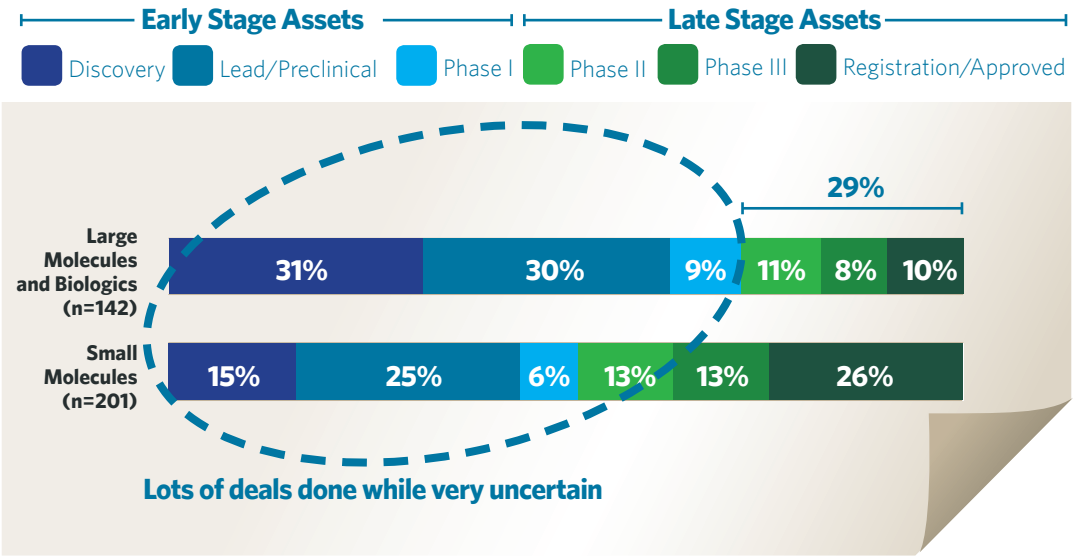
What is my drug candidate worth?

Some things are easier to value than others. A product such as an eBook, where the description of the product is a simple one that everyone understands, and where there is a standardized market, may be valued fairly similarly by different people. The values of more complex products can be harder to determine. An example might be a piece of art at an auction. The art can go unsold, or be worth a fortune, depending on what other pieces by the artist have sold for, the knowledge of collectors of that artist, whether there is a fit for it in their collection, and the number of competitors bidding.

The complexity of valuing a drug candidate for a partnering deal also varies. Drug candidates that have completed a Phase II program have more defined product profiles and can be valued using, in part, market research and physician interviews. Early drug candidates, due to numerous factors such as long development timelines before the value is realized, many questions yet unanswered, ever-changing market conditions and regulatory requirements, and the high risk of technical failure can be more difficult to value. Valuation methods exist, but are all imperfect, and at the end of the day the value of your project will ultimately be what someone is willing to pay for it. And, just like that piece of art, what a partner is willing to pay will most likely be based on how well they understand the opportunity, how well it fits in with their portfolio of drugs and strategy, and how much competition there is for it. But they, like you, will use some of these basic valuation methods to shape their thinking about the value.

In general, values for early drug candidates will be lower than values for drugs at later development stages where the uncertainty is less and the time to market is shorter. However, early stage deals can get done. Deals for early assets, still in discovery or preclinical phases, represent a significant proportion of all deals done.

2011 Licenses and Joint Ventures for Products & Platform Technologies



Source: Deloitte Recap LLC's DEAL Builder ™

Before any valuation methods are used, some fundamental questions that drive the inputs of modeling should be addressed.

The answers to these questions can form the basis for your valuation.

- What is special about this drug candidate?
- What is its potential use?
- What are the risks and when can they be addressed?
- What will need to be done or spent to deliver the value?

Valuation Inputs and Methods

As with all assets, there are several basic valuation methods.

The simplest, conceptually, are sunk costs and replacement costs, but the most commonly used methods are discounted cash flow (and risk adjusted discounted cash flow) and comparables. We will also touch on the more sophisticated, but more difficult to use decision analysis, Monte Carlo simulations, and options analysis.

Sunk Costs

The simplest method for deriving a base value for your asset is sunk costs. Sunk costs are costs that have already been incurred. It might be the sum of the NIH grants, patent costs,

or research that you've invested. Historically, sunk costs are seen as the value if you were paid with a one-time fee. Your costs (perhaps with some profit) are recovered in the deal. However, sunk costs are an imperfect valuation method because a partner may not be willing to pay for what they perceive as waste on your part. On the other hand, you may feel that your asset is a rare find and therefore much more valuable than it cost to create. Sunk costs can be a good starting point, but almost never enough to justify a deal value.

Replacement Costs

The replacement cost model is the classic "Make vs. Buy" decision that is taught in business school. What would it cost a pharmaceutical company to replicate your drug? This is a way to think about the value to the pharmaceutical company. Generally the cost to replicate is calculated using historical average costs in drug development by stage. The value can be adjusted to reflect the probability of failure. However, replacement costs fail to include the opportunity cost of diverting money from other opportunities and, most importantly, the value of the time they would lose by starting now to replicate it. That time can dramatically affect the profile needed to compete in the ever-changing marketplace. Replacement costs are an imperfect method but can help you understand the pharmaceutical company's rationale for deciding to make their own drug or buy yours.

Discounted Cash Flow Modeling or NPV

The concept behind discounted cash flow valuations is basically that money invested now is worth more than money invested later, due to the fact that money invested later does not have the benefit of compounding with an interest rate (also called a discount rate) over time. Conversely, if you borrow dollars today, you must return more to the lender in the future to pay off the debt. Thus, because of the lost interest and compounding, a dollar received tomorrow is worth less than a dollar received today. Using discounted cash flow modeling involves estimating cash flows (costs and revenues) over a period of time. A discount rate (an interest rate) is then applied to the future cash flows

(costs and revenues) to reflect the impact of time on the value of each cash flow and to calculate the sum of their value today, the Net Present Value.

Forecasting Costs

How do you know what your costs will be? Costs can be derived from your development plan, from CRO estimates, or from historical averages, and can be applied to each phase of the development process including discovery and preclinical development costs, clinical development costs, regulatory review costs, and launch, manufacturing and marketing costs.

Drug Development Costs

Forecasting Revenues

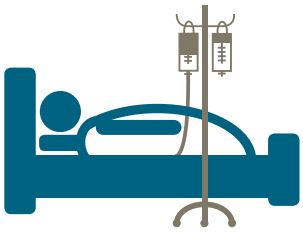
How are revenues calculated? In a more advanced drug development program, one would model the sales year by year and subtract the costs that occur year by year during those sales to net out as profits. For an early drug candidate, we can simplify and use an adjustment to revenues that is the same for every year of sales. Profits can be thought of as revenues minus a percentage of sales for the rebates, sampling and other reductions in the definition of net sales, minus a percentage for the costs of goods sold (CoGS), minus a percentage for the cost of sales and general administration, minus a percentage for taxes.

Rules of Thumb

Cost of Goods Sold	7-9% for small molecules 15-20% for biologics
Sales Costs	10%
Reduction in Net Sales	10%
Taxes	22%

How can one estimate sales? Estimating sales is less obvious than estimating costs. There are three basic methods for determining what kind of sales you might expect. One is **patient build up**, or counting the number of patients that fit a particular profile suitable for your drug and then multiplying the patient number times the price per patient treated. The second method is **sales analogies**, or using existing similar products to estimate sales (arguing your drug will have sales or patient numbers similar to that of an existing drug). The third method is to estimate a **share of a patient group or a share of a total market**. After the patient numbers are estimated, the number is multiplied by the sales per patient.

Estimating Sales



1. Patient Build-Up

2. Sales Analogies

3. Share of Epidemiology

The challenge in all three of these methodologies is that the calculations must be made in the context of the pharmaceutical marketplace.

This means factoring in the competition from available treatments and those in development, the ease of switching to your new treatment, the investment you'll have to make in sales and marketing, the impact of payer reimbursement decisions, and evidence of differentiation in efficacy, safety and convenience.

The shape of product sales lifecycles should also be considered. If your asset is a persuasive incremental improvement with the same mechanism as an existing product, the uptake in sales of your drug can be steep. If your drug is innovative and the indication is not currently treated in a similar fashion, physician education will take time and the uptake can be much slower. And, when patents expire and generic competition enters, sales will begin to decline, often quite sharply.

Discounting for Time and Risk

After estimating future revenues and costs, the valuation will need to apply the discounting for time. As stated earlier, an amount of money today is worth more than money in the future. Thus a discount rate must be used to calculate what future cash flows (revenues and costs) would be valued at today.

The discount rate varies with project risk. If the asset is early in development and risk is high, then investors will demand a greater return in the future for their dollars today, reflected in a higher discount or interest rate. A bank will loan money to an established business at a lower interest than required of a biotech start up. Because the discount rate reflects the cost of debt and equity to compensate creditors and shareholders for the time and risk of the project, the discount rate will depend on the use, not the source of funds.

Once a discount rate has been determined, your asset's Net Present Value (NPV), or value today can be calculated based on a series of cash flows with a discount rate for the time value of money for each stage of development. Traditionally, a positive NPV is considered a good investment. It's important to note that although a positive NPV is desirable, preclinical projects are often negative and yet they still get funded.

Calculating Risk or rNPV

Valuing drug development projects using NPV is widely used, however, this method is not without its limitations. Although the choice of discount rate for an NPV calculation can reflect the overall risk of the project, typically the discount rate is applied uniformly across the duration of the project, while the risk is not uniform. To make the valuation more

closely reflect the risk as it changes with the project development, a risk adjusted (also called probability adjusted or expected) NPV is calculated by multiplying cash flows by the probability that the cash flows will occur using success rates or attrition by stage of development. When using probability adjustments, the underlying discount rate before the probability adjustment should be lower than if the discount rate is used as the only means of capturing risk. A probability adjusted (or risk adjusted, also called expected) NPV lets you compare projects of unequal risk, and choose a project with a higher rNPV.

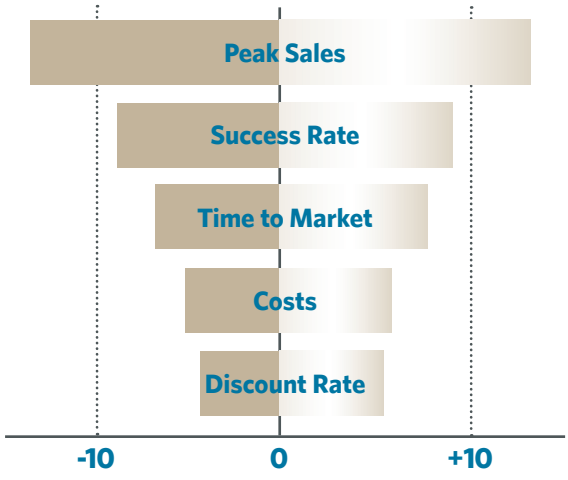
With any valuation method, it is almost inevitable that despite our best efforts, the valuation will be wrong. With an early drug candidate there is such tremendous potential for variation in inputs, that it's almost impossible not to be wrong. Instead of focusing on a single number as the valuation, it can be useful to explore the impact of variations in the assumptions, to understand what you have to believe for any valuation to be reasonable. Looking at the impact of variations in assumptions can help you plan to develop the evidence to support the most critical assumptions.

Sensitivity Analysis

A tornado plot of the sensitivity analysis visually shows the effects of different inputs (assumptions) on the calculated value.

Parameter Changes of Equal Probability:

Parameter	Pre-Clinical	Phase 3
Peak Sales	+/- 50%	+/- 50%
Success Rate	+/- 50%	+/- 50%
Time to Market	+/- 20%	+/- 10%
Costs	+/- 30%	+/- 10%
Discount Rate	+/- 5%	+/- 10%



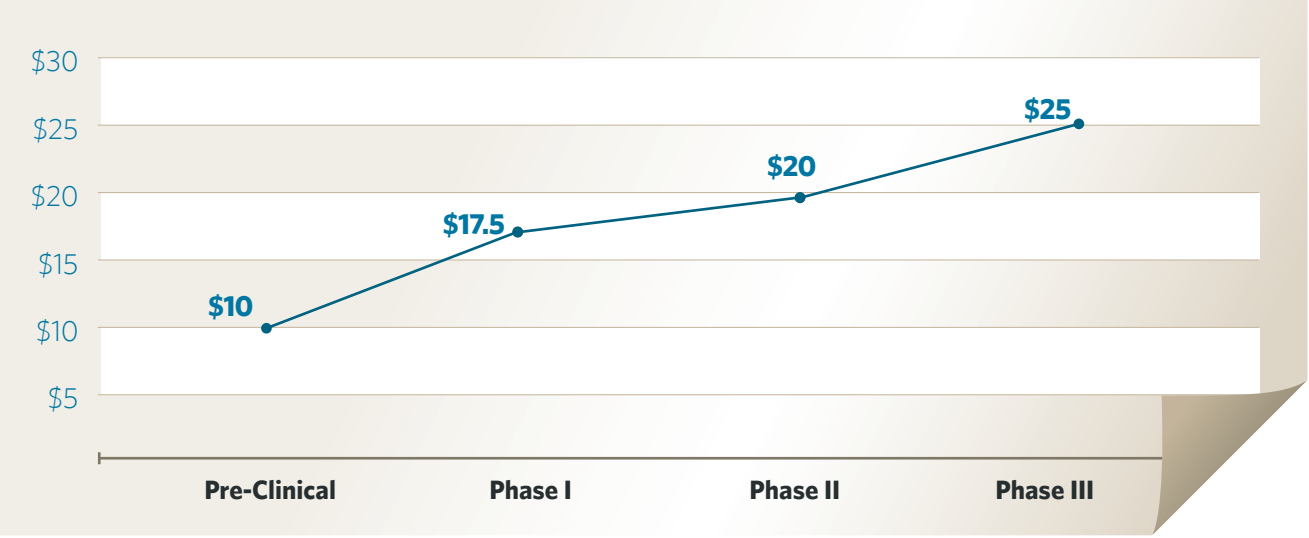
Comparables

Along with NPVs or risk adjusted NPVs, among the most commonly used valuation methods is using comparables. When appraising a home, an appraiser looks at recently sold similar homes in similar neighborhoods. The same method can be used for assigning value to your drug candidate. A comparable project is a project with similar market potential, with similar risk, and at a similar stage of

development.

Sometimes that's difficult to find; everyone else has apples, you've got oranges. If that's the case, you may have to look at deal averages for deals at a similar stage or, averages over a range of deals somewhat similar to yours. The deal value can be thought of as the NPV or risk adjusted NPV of the upfront, milestones and royalties of the deal, recognizing that much of the "total" deal value may never be paid as it is contingent upon specific outcomes that may not occur.

2013 Median Upfront Payments ($Millions) by Stage at Signing (Source: Global Data)



But even if a comparable project can be found, care must be taken. Remember that many deal terms are never disclosed publicly, and those that are disclosed usually represent the higher end of the price spectrum. Companies tend to disclose deal terms publicly if it's strategically advantageous to do so or if required by the SEC because the deal is big enough to be "material" information for stockholders.

Despite the caveats about upward bias, comparables can be very useful as a way to begin talking about the value you expect in a deal. However, in the end, pharmaceutical companies may not be persuaded that the deal is comparable or may believe others overpaid and they will rely on their own assessment, perhaps using other deals they have done as their comparables or using other methods.

More Complex Valuation Methods

Decision-Tree Modeling

Decision-tree modeling considers different scenarios and their impact on project value at key decision points along the development path, often at the completion of each stage of development or trial. This method basically takes a discounted cash flow analysis with probability adjustments and adds more branches. The valuation calculation can include the results of branches where spending stops, or where a different study outcome changes the predicted sales. Decision analysis can be a powerful tool for showing how critical decision points can have various outcomes that affect value, for identifying critical drivers that affect value, and for getting team consensus on the best path forward.

Monte Carlo Simulation

A more complex method conceptually is Monte Carlo simulation. Instead of putting in single point estimates of all the inputs to calculate a single value in a model, the Monte Carlo methodology puts in probability distributions for various inputs such as market size, costs, pricing and time to market, and then samples all those distributions to run multiple simulations, each calculating an NPV. The result provides a probability distribution of the NPV. This method provides a more nuanced result than offered by a single point estimate of value, but it is not easy to understand or communicate.

Options Analysis

Another less intuitively clear valuation method is real option analysis. NPV-based valuation methods assume that once a decision to invest is made, all investments will occur; this does not account for the value of funding flexibility in the face of economic and development path uncertainty. Real option analysis uses methods derived from the financial option markets to assign value based on the inherent volatility or uncertainty of the options available in a program. The value of a program is increased by a bigger range of outcomes. Option analysis, like decision-tree analysis, highlights the often forgotten value of flexibility. Although powerful, it is not easy to communicate the meaning of option analysis.

How a Partner Thinks About Valuation

Pharmaceutical partners will use one or more of these fundamental valuation methods, but the underlying assumptions in a partner's valuation will be driven by the fit of your project with their expertise, capabilities and sales structure, as well as with the gaps in their portfolio.

They will spend more on development than on the deal for an early project, so their first concern will be the evaluation of the potential, the risk and the costs of development, not the costs of the deal. For early drug candidates, the potential revenues and the probability of success, and hence the total valuation, increase with evidence for the relevance of the mechanism in the disease, lead time ahead of competition, the presence of backups and follow-ups, validation from a partnership or from other drugs with the same mechanism. Risk and uncertainties not only decrease the value, but also decrease the likelihood of any deal. At some level of uncertainty, no matter how low the price, there may be no deal. Thus, value discussions generally don't take place until after a technical evaluation of your opportunity has occurred. That's why for an early drug candidate, the ability to tell your "story" and help the partner understand how the project will create value is more important than any specific valuation you may come up with. And, in early negotiations, it's more advantageous to present insight into a way of thinking about the assumptions rather than proposing a specific valuation.

Roger Davies Rules of 50%

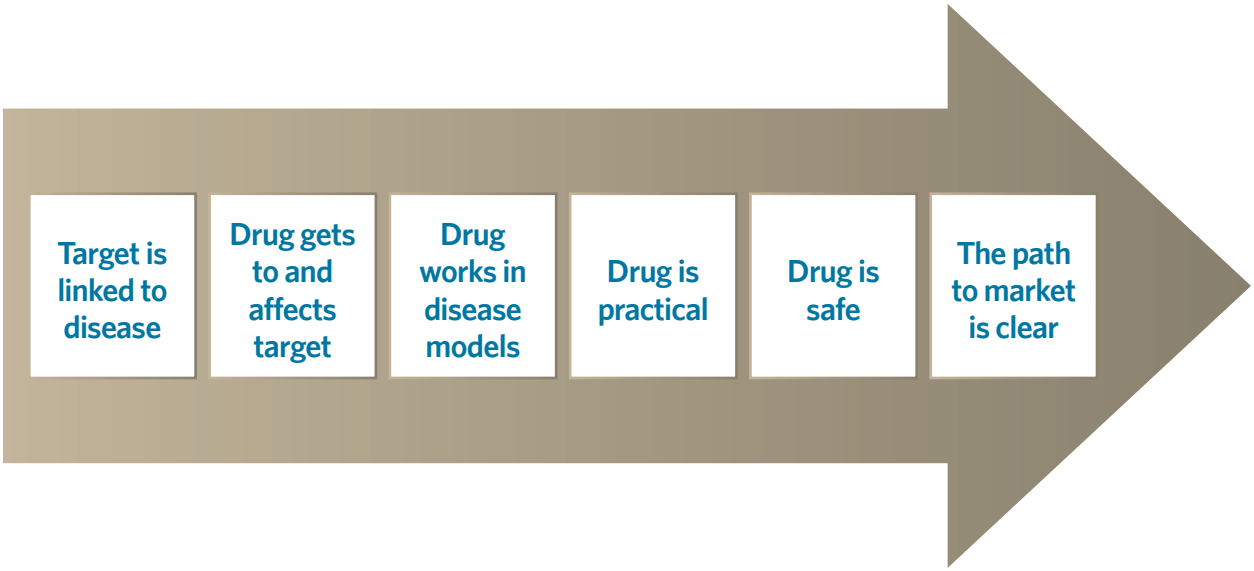
Roger Davies has a rule of 50%, which states that the partner will discount whatever value you bring them by half, because they'll believe you've overestimated sales, the stage of advancement or the impact of your differentiation, and that you've underestimated other factors such as risk, the data to persuade investors, and competition.

What Adds Value?

Mechanism	• Belief in the mechanism is a surrogate for data you don't have yet. • Novelty means you need to present your story with more solidity than if you have a mechanism that everyone understands.
Data	• Human data trumps animal data. • Removal of risk and data for evidence of potential.
Lead Time and Barriers to Entry	• The ability to get to market and prevent others from catching up and competing.
Flow of Drug Candidates	• Backups and next generations.
Validation	• Other partnerships. • Other drugs with the same mechanism.
Deal Alternatives	• Negotiating strength lies in your ability to live without the deal by virtue of having other interested parties or the ability to carry the project forward on your own.

What Does a Partner Want to Know?

When a partner looks at your opportunity what they want is to be told a story of the potential and the path to deliver that potential, in a clear and orderly fashion. In addition to your non-confidential and confidential presentations, in diligence, they will want to see the more detailed evidence behind your overviews. This data can be best presented in a virtual data room where it can be organized, secure, and accessible to the experts that need to see it when they want to see it. The following graphic illustrates the general narrative of the story a partner will want to hear. You should organize the data room information so each diligence team member can readily find the information relevant to his functional discipline, such as toxicology or regulatory, etc.



Conclusion

Even with sophisticated valuation methods, determining what a project is worth to a partner is difficult. But the exercise can help you identify what assumptions are key and help you focus attention on the evidence for those drivers. Because the drug development process is uncertain, it's very helpful to use multiple valuation models to test the reasonableness of your value estimates. No one methodology is sufficient as a decision-making tool, but multiple methods, combined with your "narrative" of the science behind the key value drivers can be paramount in giving a partner the insight to give you a good deal.

About Linda M. Pullan, PhD

Linda offers biotech and pharmaceutical companies consulting in all aspects of partnering through Pullan Consulting (**www.pullanconsulting.com**). Linda has a PhD in Biochemistry and a BS in Chemistry. She has more than 20 years of drug industry experience, beginning in drug discovery at Monsanto/Searle/now Pfizer and ICI/Zeneca/now AstraZeneca. After doing licensing at what is now AstraZeneca, Dr. Pullan continued as head of oncology and hematology licensing for Amgen. She then joined Kosan Biosciences as VP of Business Development and experienced all the tasks of out-licensing and business development in a small company. For several years, she has been providing companies help in identification, evaluation, valuation, negotiation and strategy for partnering in or out. She has an extensive deal sheet ranging from company acquisitions to Phase III compounds and from preclinical candidates to technologies, with both in- and out-licensing. She writes a free monthly newsletter *Pullan's Pieces*, with tidbits of science and business for about 3,600 readers. Interested readers may sign up by sending an email to **linda@pullanconsulting.com**.

About ShareVault

ShareVault® is the leader in supplying intuitive, innovative virtual data rooms and offers one of the few products that support both the PC and Mac platforms. ShareVault offers the highest degree of security and reliability combined with unparalleled speed, ease of use and functionality. Backed by the experience of billions of dollars in successful deal transactions, along with industry-leading customer support, ShareVault can greatly accelerate any deal or transaction.

Pandesa Corporation, dba ShareVault
Headquarters
16795 Lark Avenue, Suite 210
Los Gatos, CA 95032

ShareVault®
sharevault.com

Revision Date: 11/09/2016