BIOTECHNOLOGY VALUATIONS FOR THE 21ST CENTURY

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Executive Summary

Biotechnology investment need not be made in a valuation vacuum. Biotech research and development (R&D) is risky, but applicable risks can be quantified more precisely now than in the past. One reason is that in the late 20th century, even greater than the uncertainties of clinical-trial outcomes, were the uncertainties of manufacturing organism-derived pharmaceuticals (biologics). Now, in the 21st century, the uncertainties associated with biologic manufacturing have largely been dispelled: biologics can be manufactured at scale and sold at profitable margins. Also critical, the success rates of biotech clinical trials, pivotal value drivers of biotech R&D, are reasonably estimable. Because of this, the value of biotech R&D projects may be estimated by incorporating these clinical-trial success rates into a traditional discounted cash flow analysis. In this policy brief, I present risk-adjusted net present value as a straightforward method of determining the value of biotech R&D assets. Because clinical-trial-stage projects are the most valuable assets of most biotech firms, risk-adjusted net present value may be used to assign value to biotech companies and to reassess company value in response to significant clinical-trial events.
Introduction: Clinical Projects are Biotech's Primary Assets

The biotechnology industry has matured significantly in the last 20 years. In the 1980s, a biotechnology company represented an investment that defied accurate calculation. Biotech firms argued that molecular biology and gene manipulation would provide more efficient methods of drug discovery than the traditional “brute force” screening methods favored by pharmaceutical companies. Nonetheless, biotechnology's model of rational drug discovery and at-scale protein manufacture was unproven. Would biotechnology be able to deliver organism-derived pharmaceuticals (biologics) to the market?

Now, at the beginning of the 21st century, the uncertainties that previously weakened biotech's foundations have been shored up. Biotechnology does provide a rational method of discovering new drug targets. Biotechnology can convert those drug targets into biologics. Biologics can be manufactured cost effectively at scale. In addition, biologics tend to have fewer side effects than do traditional chemical pharmaceuticals. And they are more likely to succeed in clinical trials. With these major uncertainties under control, the value of a biotechnology can be calculated with reasonable certainty so that biotech investment may be made rationally.

Moving Valuation Out of the 20th Century

Valuation has a bad name in biotechnology. Part of this bad name is justified. Some analysts have admitted estimating a biotech company’s value by tabulating lab square-footage or the number of scientists employed. When surveyed, some executives even admitted using a “best guess” to price technologies, and other executives use a cost-plus approach. Such methods are obviously inappropriate, and even well-meaning approaches have been shown to be unsatisfactory in practice.

In the 1980s and much of the 1990s, the technological, regulatory, and business risks in biotechnology development were almost impossible to calculate. When biotech companies first developed biologic therapeutics, such as antibodies to specific cancer proteins, the overriding uncertainty was the production problem. Valuations hinged on the ability to make pure proteins at scale. Given the production uncertainties, traditional valuation methodologies such as discounted cash flow (DCF) were sometimes applied in an inappropriate manner. An analyst might look at the projected market and then discount using a high discount rate (and often a discount rate that decreased over time). Inasmuch as the discount rate did reflect all the risks the company faced, then a simple DCF would have been a reasonable indicator of project value. However, picking the correct discount rate was the problem. When the key risk drivers were not reasonably estimable, then DCF suffered as a reliable indicator of value. Discount rates can now be chosen more reasonably, but they are still arbitrary, and thus traditional DCF remains an unreliable measure of biotech value.

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Some analysts began using real options analyses that calculate biotech value as a series of call options.\textsuperscript{2,3,4} While the real options methodology has a strong basis in theory, in practice many of the “options” relied upon to prop up project values are not real at all. There are several examples of options that are not exercisable in practice. In one example, a real options analysis assigns a value to the ability to pull back from a project should revised market projections be small. However, when this situation is placed in real-world terms, the option is revealed not to be exercisable in practice. For this option to be exercised, the biotech company would have to trust the revised market projection more than the original project and then pull the plug on a drug in a late-stage clinical trial. Doing so would certainly be suicidal to an executive's career. I am not the first to doubt that management will exhibit fiscal restraint when faced with a lowered market projection.\textsuperscript{5} Several other options in real options also fare poorly under scrutiny.

A final proposed method of valuing biotech involves identifying “pure play” companies that are acquired when their main assets are intellectual property (IP) rights on a biotech invention. A “pure play” company is one that has a biotech invention as its only asset. The selling price of these companies is then used to assign value to the underlying biotechnology. The main problem with this valuation method is that “pure play” biotech companies are likely to be those in poor financial shape. When a biotech company has few if any non-IP assets, then that company is in a weak selling position. Thus, a “pure play” methodology leads to an undervaluation of biotechnology IP assets. In an analogous situation, it is as if one would value real estate by surveying bankruptcy auctions and then assume that bankruptcy auctions describe the market value of real estate.

This policy brief suggests an improvement over these valuation methods. The incorporation of clinical-trial success rates into more traditional financial analyses can be used to price the current values of biotech projects as they are being developed.\textsuperscript{6,7,8} In particular, clinical-trial success rates can be combined with traditional discounted cash flow (DCF) methodology to yield a risk-adjusted net present value (rNPV) for biotechnologies.\textsuperscript{9}

\textsuperscript{5} Fink, R. Reality Check: Look Closely at Real Options, and a Basic Assumption Begins to Quiver. \textit{CFO Magazine} 2001. Sept.: 85.
\textsuperscript{8} Arojärvi, O. How to Value Biotechnology Firms: A Study of Current Approaches and Key Value Drivers. \textit{Helsinki School of Economics and Business Administration}. 2001.
\textsuperscript{9} Stewart, J. \textit{et al.} Putting a Price on Biotechnology. \textit{Nature Biotechnology} 2001. 19:813. The “Biotech Stage Funding Model” was developed by Biogenetic Ventures, Inc. and is available for download at www.biogeneticventures.com.
The rNPV method allows the investor to calculate the value of the assets that underpin biotechnology companies. Using rNPV, the investor can compare rNPV to the market capitalization of biotech companies to find relatively advantageous investments in the biotech space. The investor can also determine the effect that a significant event, such as a six-month delay in FDA approval, would have on the current value of the biotech asset. Furthermore, the rNPV method is both parameter-stingy and straightforward, and these two factors together make valuations estimated through rNPV simple to justify.

The remainder of this policy brief is devoted to describing rNPV so that, by the end of the brief, the investor should be able to apply rNPV to biotechnology investments. The method of adjusting cash flow value according to risk is explained in the next section. Then, clinical-trial risks are laid out and applied to biotech projects in the section **Incorporating Clinical Trial Success Rates as Payoff Probabilities**. Clinical-trial parameters are presented in the following section. Market projections and royalty rates are outlined in **Calculating the Income Side**. Finally, biotech input parameters are incorporated into a full rNPV model in the last section.

### Risk-Adjustment of rNPV Explained

Risk-adjusted net present value (rNPV) is a straightforward valuation method for biotechnology. In this hypothetical example, we calculate the rNPV of Neklimed, a fictitious pharmaceutical in development by the fictitious biotech company Neklim, Inc. Neklim is entering Neklimed into a phase II clinical trial for the treatment of rheumatoid arthritis. Neklim has already announced a partnership with the Acme Pharma Company (also fictitious) for the marketing and manufacturing of Neklimed. Acme Pharma will offset half of Neklimed’s remaining development costs and, for its efforts, will retain 70% of gross sales. Neklim will thus earn a 30% royalty on gross sales should Neklimed reach the market.

To calculate rNPV, four general parameters must be known: clinical success rates, projected costs, projected market (sales), and the discount rate. We will start with the clinical success rates, but first, an illustration of the risk adjustment is in order (Box 1).

#### Box 1: Risk Adjustment

What would you be willing to pay to play the following game? The game involves tossing two coins. You must spend $10 to toss the first coin. Then, if the first coin comes up heads, you can spend an additional $20 to toss a second coin. If you get heads on the second coin, you win $100. You might think this game is worth $100. But averaging the four possible outcomes yields the correct answer.

The possible outcomes are:
1. You spend $10, and the first toss is tails. The game ends. Had you tossed the second coin, it would have come up tails, also, but you never had the opportunity to toss the second coin. Total: -$10
2. You spend $10, and the first toss is tails. The game ends. Had you tossed the second coin, it would have come up heads, but you never had the opportunity to toss the second coin. Total: -$10
4. You spend $10, and the first toss is heads. The game continues. You spend another $20, and the second toss is also heads. You win $100. Total: -$10 - $20 + $100 = $70.

What is the value of this game?

\[ \times (-$10 -$10 -$30 +$70) = $5. \]

Another way to look at the same problem is to consider the likelihood of reaching each cash event and then to multiply this likelihood by the face value of each cash event.\(^\text{10}\)

- How likely are you to reach the first ante? 100% — you must pay the first ante to play. Therefore, the risk-adjusted value of the first cash event is 100% of negative $10. So far, the game costs you a risk-adjusted $10.

- How likely is the second cash event? 50% — if you get tails, the game is over, so you only pay the second ante one out of every two times you play. Therefore, the second cash event (a $20 cost) is only half as serious as its face value. The second cash event thus also has a risk-adjusted value of negative $10. So far, the game costs you, risk-adjusted, $20.

- Now, how likely is the third cash event (the payoff)? 25% — two heads. Therefore, the payoff (third cash event) is only worth a risk-adjusted $25: one quarter of the payoff’s $100 face value.

Now, by subtracting the risk-adjusted antes from the risk-adjusted payoff (-$10 - $10 + $25), the risk-adjusted value of the coin-tossing game is shown to be $5.

This type of risk-adjustment is precisely the type applied in rNPV.

**Incorporating Clinical Trial Success Rates as Payoff Probabilities**

For any new molecular entity (NME, a novel chemical pharmaceutical or biologic) to be marketed in the U.S. that NME must gain approval from the Food and Drug Administration (FDA). FDA approval, in turn, hinges on clinical trials — a series of

\(^{10}\) The risk-adjustment equation is

\[ rV = \sum_{i=0}^{k} \frac{C_i R_i}{R_0} \]

where \(rV\) is the risk-adjusted value, \(C_i\) is the cash flow at time \(i\), \(R_0\) is the current likelihood of reaching the final cash flow, \(R_i\) is the likelihood at time \(i\) of reaching the final cash flow, and \(R_0 / R_i\) is the current likelihood (i.e., at time 0) of realizing the cash flow of time \(i\).
experiments performed on humans. These clinical trials are generally conducted in three phases. In phase I, 20-80 healthy volunteers are given the NME to determine if it is toxic in humans. If the NME has a safe dose, then 100-300 patients are given the NME in a phase II trial to see if it successfully treats the condition for which it is intended. If the NME appears to be effective then it is submitted to 1,000-5,000 patients in a phase III trial in which efficacy is confirmed and patients are monitored for long-term side effects. All three clinical trials also have concurrent direct costs for animal studies that test for toxicity, the propensity to cause birth defects, and the like. These animal studies are required by the FDA to support clinical trials.

There is a reasonably large body of data on the success rates of NMEs in clinical trials. Data are published periodically in summary form by the Tufts University Center for the Study of Drug Development.\(^\text{11}\) Average success rates (the chances of reaching the market eventually) for new chemical entities are about 20% for those that successfully pass the phase I trials, 30% for those that pass phase II, and 67% for phase III.\(^\text{12}\) Note that these rates apply as drugs enter each clinical trial (e.g., about two out of three drugs in phase III trials will eventually reach the market). Biologic NMEs have been several percentage points more likely to reach the market than have been traditional chemical NMEs, and this advantage appears to be growing.\(^\text{13}\)

However, even a successful phase III trial does not guarantee the NME will reach the market. The FDA approves just over 80% of all NME requests that are submitted through either the New Drug Application (NDA, for chemical NMEs) or the Biologics Licensing Application (BLA, for biologic NMEs).\(^\text{14}\)

As an aside, the probability of success remains difficult to assess before the NME enters the clinical phase. NMEs in preclinical stages are associated with success rates that are both lower and less estimable. Obviously the likelihood of a preclinical NME reaching the market is less than that of an NME in phase I (i.e., less than about 20%), but how much less likely is highly variable. Many unsuccessful preclinical projects are quietly discontinued, so the 10% preclinical-to-market success rate cited by Pharmaceutical Research and Manufacturers of America (PhRMA) is of questionable accuracy.\(^\text{15}\) To set a value on a preclinical project, one must estimate (hopefully not in a complete vacuum) the likelihood of the preclinical project delivering an NME for a phase I trial. If the PhRMA figure were to be relied upon, about half of preclinical projects would yield an NME that is submitted to the clinical-trial process, and one in 10 eventually would deliver a product to the market.

In our hypothetical example, Neklimed is a biologic NME entering a phase II clinical trial for the treatment of rheumatoid arthritis. The likelihood of Neklimed eventually

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11 [www.tufts.edu/med/csdd/](http://www.tufts.edu/med/csdd/)
being approved by the FDA is about 35% — as a biologic Neklimed is a few percentage points more likely to reach the market than a traditional chemical pharmaceutical entering phase II. Should Neklimed pass the phase II trial, the likelihood of reaching the market from the time of entry in the phase III trial will also be a few percentage points better than the chemical pharmaceutical rate (of 67%). We estimate the phase-III-to-market likelihood of the biologic NME Neklimed at 72%. The FDA-approval rate for all NMEs under review (post-phase III) is currently 81%. Not enough biologic NMEs have been under review to analyze whether their approval rate should differ significantly from that of chemical NMEs. Therefore, if Neklimed passes phase III and is submitted to the FDA for approval, Neklim, Inc. will have about a four in five chance of seeing Neklimed approved.

**Incorporating Clinical Trial Costs**

Although there is a public debate about drug-development costs, this debate primarily centers on accounting practices rather than on direct clinical-trial costs. The costs of performing clinical trials and the animal studies required to support these clinical trials are tabulated in Box 2.

**Box 2: Clinical Trial Parameters**

**Phase I**
- Likelihood of eventual FDA approval: 20%
- Average years to completion: 0.5–1
- Supporting animal studies: ~$500,000
- Number of clinical-trial subjects: 20–80
- Per-subject cost: $8,000–$15,000

**Phase II**
- Likelihood of eventual FDA approval: 30%
- Average years to completion: 1.5
- Supporting animal studies: ~$1 million
- Number of clinical-trial subjects: 100–300
- Per-subject cost: $8,000–$15,000

**Phase III**
- Likelihood of eventual FDA approval: 67%
- Average years to completion: 3.5 years
- Supporting animal studies: ~$1.5 million
- Number of clinical-trial subjects: 1,000–5,000 (about 10× the number in phase II)
- Per-subject cost: $4,000–$7,500 (half that of earlier per-patient costs)

**FDA approval**
- FDA approval rate: 81%
- Time to completion: 0.5–2 years
- Approval costs (Prescription Drug User Fee Act II fee and the remainder for preparation of the NDA or BLA): $0.8–$1.8 million+ ($300,000 for the PDUFA II fee).

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18 Figures confirmed through an informal survey of contract research organizations.
In the case of Neklimed, Neklim still faces the costs of phase II and phase III clinical trials and then FDA approval. Neklim has already announced that 220 patients will be enrolled in phase II, and that the cost per patient will be $12,000. Based on this information, we estimate that 2,200 patients will be enrolled in the eventual phase III trial at about $6,000 per patient. The animal studies take place in the first portion of each clinical trial, so those costs are accounted for in the early portion of each clinical trial. FDA-approval costs also remain. Neklimed's costs, actual and risk-adjusted, are in Box 3. Note that Neklimed's direct costs are halved by the marketing and manufacturing arrangement with Acme Pharma (discussed earlier).

**Box 3: Neklimed's Cost Schedule in $1,000s**

<table>
<thead>
<tr>
<th>Year</th>
<th>Cost Description</th>
<th>Actual $</th>
<th>Likelihood</th>
<th>Risk-adjusted cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Phase II human year 1</td>
<td>660</td>
<td>100%</td>
<td>660</td>
</tr>
<tr>
<td>1</td>
<td>Phase II animal</td>
<td>500</td>
<td>100%</td>
<td>500</td>
</tr>
<tr>
<td>2</td>
<td>Phase II human year 2</td>
<td>660</td>
<td>100%</td>
<td>660</td>
</tr>
<tr>
<td>3</td>
<td>Phase III human year 1</td>
<td>2,200</td>
<td>49% (35%/72%)</td>
<td>1,070</td>
</tr>
<tr>
<td>3</td>
<td>Phase III animal year 1</td>
<td>375</td>
<td>49%</td>
<td>180</td>
</tr>
<tr>
<td>4</td>
<td>Phase III human year 2</td>
<td>2,200</td>
<td>49%</td>
<td>1,070</td>
</tr>
<tr>
<td>4</td>
<td>Phase III animal year 2</td>
<td>375</td>
<td>49%</td>
<td>180</td>
</tr>
<tr>
<td>5</td>
<td>Phase III human year 3</td>
<td>2,200</td>
<td>49%</td>
<td>1,070</td>
</tr>
<tr>
<td>6</td>
<td>FDA-Approval Costs</td>
<td>650</td>
<td>43% (35%/81%)</td>
<td>280</td>
</tr>
</tbody>
</table>

**Calculating the Income Side**

Once the cost schedule is in place, the returns must be estimated. Market projection is an art of its own. All valuation methods are at the mercy of these market projections, and the investor must corroborate the guidance given by the biotechnology company. A back-of-the-envelope calculation is often the best choice available to the investor. The two general ways that such a projection may be made are bottom-up (treatable population × estimated market penetration × annual cost per patient) or top-down (total current market × estimated market penetration). If, as is often the case for biologics, the target disease is currently untreatable, the market penetration and the annual cost per patient will likely be high. If, instead, the biologic is a “me-too” treatment for a disease that has other treatments, the price and market penetration will be lower, but both the total market and the annual per patient price will be easier to estimate.

In the case of Neklimed, which will be a “me-too” treatment for rheumatoid arthritis, primary competition is expected from Immunex's Enbrel™ (and any competitor drugs that reach the market in the interim). Enbrel™ currently has annual sales of $750 million. However, once Immunex's manufacturing plant retrofits are finished, Enbrel™ will probably have annual sales of about $2.5 billion. Neklim Inc. is projecting annual sales of Neklimed to be $1 Billion (a 40% share). Given that Neklimed will be a “me-too” treatment, albeit in a market with few competitors, we believe Neklim's market projection is somewhat high, and a 30% market share ($750M in annual sales) is more realistic. (To see how sensitive rNPV is to a reasonable range of market projections, the investor could

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calculate rNPV with several different projected market sizes. A spreadsheet (Microsoft Excel format) pre-programmed to do the calculations can be downloaded from http://www.milkeninstitute.org/polbriefs/biotech/biotech.xls.

The second return factor the investor has to take into account is the royalty on gross sales. Most biotech companies partner with larger pharmaceutical concerns to market and manufacture drugs. Biotech companies can use rNPV to calculate an appropriate royalty. In the absence of royalty information (i.e., before the biotech company has found a marketing and manufacturing partner), the investor may assume a 40-60% royalty that will usually be lowered significantly by co-development (milestone) payments. Pharmaceutical companies are rewarded about 40-60% of gross sales for manufacturing and marketing, and biotech companies usually also accept milestone funding in return for a further-reduced royalty.

In the case of Neklimed, Neklim Incorporated has partnered with Acme Pharma Company in a partnership where Acme is offsetting half of the remaining direct development costs. Acme also will bear the cost of manufacturing and marketing Neklimed. In return, Acme will retain 70% of gross sales and remit to Neklim a 30% royalty on gross sales. Neklimed sales should remain strong until patent protection is lost. The patent covering Neklimed's composition of matter expires in 18 years (the 17th year is the final year of significant revenue). We also assume a two-year sales ramp-up (and ramp-down). Hence, we can now craft a full projected cash-flow table for Neklimed (Box 4). We can also calculate the risk-adjusted cash flow.

### Box 4: Neklimed's Cash Flow Schedule in $1,000s

<table>
<thead>
<tr>
<th>Year</th>
<th>Cost Description</th>
<th>Actual $</th>
<th>Likelihood</th>
<th>Risk-adjusted income (loss)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Phase 2 human year 1</td>
<td>(660)</td>
<td>100%</td>
<td>(660)</td>
</tr>
<tr>
<td>2</td>
<td>Phase 2 animal</td>
<td>(500)</td>
<td>100%</td>
<td>(500)</td>
</tr>
<tr>
<td>3</td>
<td>Phase 3 human year 1</td>
<td>(2,200)</td>
<td>49% (35%/72%)</td>
<td>(1,070)</td>
</tr>
<tr>
<td>4</td>
<td>Phase 3 animal year 1</td>
<td>(375)</td>
<td>49%</td>
<td>(180)</td>
</tr>
<tr>
<td>5</td>
<td>Phase 3 human year 2</td>
<td>(2,200)</td>
<td>49%</td>
<td>(1,070)</td>
</tr>
<tr>
<td>6</td>
<td>FDA-Approval Costs</td>
<td>(650)</td>
<td>43% (35%/81%)</td>
<td>(280)</td>
</tr>
<tr>
<td>7</td>
<td>Royalty (ramp-up)</td>
<td>75,000</td>
<td>35% (35%/100%)</td>
<td>26,250</td>
</tr>
<tr>
<td>8</td>
<td>Royalty (full)</td>
<td>150,000</td>
<td>35%</td>
<td>52,500</td>
</tr>
<tr>
<td>9</td>
<td>Royalty (full)</td>
<td>225,000</td>
<td>35%</td>
<td>78,750</td>
</tr>
<tr>
<td>10</td>
<td>Royalty (full)</td>
<td>225,000</td>
<td>35%</td>
<td>78,750</td>
</tr>
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<td>11</td>
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<td>12</td>
<td>Royalty (full)</td>
<td>225,000</td>
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<td>35%</td>
<td>78,750</td>
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<tr>
<td>15</td>
<td>Royalty (full)</td>
<td>225,000</td>
<td>35%</td>
<td>78,750</td>
</tr>
<tr>
<td>16</td>
<td>Royalty (ramp-down)</td>
<td>150,000</td>
<td>35%</td>
<td>52,500</td>
</tr>
<tr>
<td>17</td>
<td>Royalty (ramp-down)</td>
<td>75,000</td>
<td>35%</td>
<td>26,250</td>
</tr>
</tbody>
</table>

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Putting It All Together

Now that we have the risk-adjusted cash flow it can be discounted normally in a DCF analysis. The DCF of the risk-adjusted cash flow is the rNPV.

\[ rNPV = \sum_{i=0}^{n} \frac{C_i R_0}{(1 + r)^i R_i} \]

In the rNPV equation shown above, \( C_i \) is the cash flow at time \( i \), \( R_0 \) is the current likelihood of reaching the final cash flow, \( R_i \) is the likelihood at time \( i \) of reaching the final cash flow, \( R_0 / R_i \) is the current likelihood (i.e., at time 0) of realizing the cash flow of time \( i \), and \( r \) is the discount rate.

An appropriate discount rate must be selected. Even though the clinical-trial risks have been accounted for elsewhere, it seems inappropriate to use the risk-free rate because there are risks that are outside of the clinical trial risks. Some have argued that the opportunity cost of capital is the appropriate discount rate and have variously calculated this rate to be between 9% and 15%. \(^{22,23,24}\)

Once the discount rate is chosen and applied according to the rNPV formula, the investor will have determined the reasonable value of the biotechnology asset. That is, the rNPV is a justifiable estimate of the reasonable selling price of the biotechnology asset.

In our hypothetical example, Neklimed's rNPV, given a discount rate of 15%, is about $160 million (Box 5).

### Box 5: Neklimed’s rNPV in $1,000s

<table>
<thead>
<tr>
<th>Year</th>
<th>Description</th>
<th>Risk-adjusted income (loss)</th>
<th>rNPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Phase 2 human year 1</td>
<td>(660)</td>
<td>(660)</td>
</tr>
<tr>
<td>1</td>
<td>Phase 2 animal</td>
<td>(500)</td>
<td>(550)</td>
</tr>
<tr>
<td>2</td>
<td>Phase 2 human year 2</td>
<td>(660)</td>
<td>(570)</td>
</tr>
<tr>
<td>3</td>
<td>Phase 3 human year 1</td>
<td>(1,070)</td>
<td>(810)</td>
</tr>
<tr>
<td>3</td>
<td>Phase 3 animal year 1</td>
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<td>(140)</td>
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<td>(700)</td>
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<td>Phase 3 animal year 2</td>
<td>(180)</td>
<td>(120)</td>
</tr>
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<td>5</td>
<td>Phase 3 human year 3</td>
<td>(1,070)</td>
<td>(610)</td>
</tr>
<tr>
<td>6</td>
<td>FDA Costs</td>
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<td>(140)</td>
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<tr>
<td>7</td>
<td>Royalty (ramp-up)</td>
<td>26,250</td>
<td>11,350</td>
</tr>
<tr>
<td>8</td>
<td>Royalty (ramp-up)</td>
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<td>19,740</td>
</tr>
<tr>
<td>9</td>
<td>Royalty (full)</td>
<td>78,750</td>
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<td>10</td>
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<tr>
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<td>16,930</td>
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<td>Royalty (full)</td>
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<tr>
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<td>12,800</td>
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<td>Royalty (full)</td>
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<td>11,130</td>
</tr>
<tr>
<td>16</td>
<td>Royalty (ramp-down)</td>
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<td>6,450</td>
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<tr>
<td>17</td>
<td>Royalty (ramp-down)</td>
<td>26,250</td>
<td>2,810</td>
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Sum rNPV = $159M

The investor may use rNPV to answer myriad questions about the value of biotech discoveries, patents and their impact on corporate market values. Are market capitalizations justified when positive clinical results are announced? Is the market overreacting when one drug in a biotech company’s portfolio fails in phase II? What effect does an “orphan drug” designation, with tax credits and shorter approval process, have on valuation?

A generic rNPV curve (Box 6) illustrates how valuation jumps instantaneously upon successful completion of each clinical trial. This is in contrast to traditional NPV, which does not take into account clinical-trial risks and thus overestimates value until the biologic is approved. Once clinical-trial risks are obviated, then rNPV and NPV are equal.
Conclusion with a Note of Caution

A note of caution is in order: new uncertainties are looming that may, in the future, draw the shades over rational biotech investment. As the century progresses, biotechnology may increasingly become a victim of its success. An rNPV analysis is at the mercy of two assumptions: 1) motivated buyers will be able to afford new drugs, and 2) investable biotechnologies are relatively scarce resources.

First, the market must be able to purchase new drugs. Obviously if new-drug discovery outpaces increases in general productivity, eventually citizens of even wealthy nations may not be able to support new-drug prices. A collapse in new-drug prices — or in patent protection, as was threatened in the federal government's aborted challenge to Bayer's Cipro™ patent — will lead inevitably to a collapse in biotech values. If projected markets were significantly reduced, for example by price controls, then biotechnology rNPV would face concurrent deflation.

Second, a regression analysis such as rNPV requires that biotechnologies in development remain scarce enough resources that they are in practice awarded the valuations indicated by rNPV. As early-stage biotech intellectual property becomes more common, other resources become relatively scarcer. The cost of capital and the cost of human resources would rise should these commodities become relatively scarcer, and in response rNPV would decrease. This collapse has already been seen in very early-stage projects such as those typically available for licensure from universities. The investment the federal government has made in basic biomedical research has yielded a moderate glut of early-stage projects that cannot be serviced efficiently by existing drug-development companies. The result is that undercapitalized preclinical projects currently fail to be accorded the full value assigned by rNPV. Inasmuch as tight capital markets are unable to service the increasing supply of biotechnologies, rNPV will erode for preclinical and eventually clinical-stage biotech projects.

As the 21st century begins, however, clinical trials still represent the main risks faced by any biotech company. Now, clinical-trial risks can be incorporated in discounted cash flow analysis as the driving factors of biotech valuation. The combination of discounted cash flow and risk-adjustment embodied in rNPV provides a clear, rational valuation methodology for biotech investment.