



## Due Diligence

In partnership deals, risks and rewards change like infinitely complex poker hands. Here's how to protect the lot you're dealt.

BY JOSEPH S. DILLON

**P**oker has become one of the most popular attractions on television and the Internet, right up there with online auctions. And if the two were ever combined—so that players could auction off their hand early in a game, with several rounds of cards remaining to be dealt—bidders might seek advice from folks in pharmaceutical business development. Because that's what we do. When we buy or sell the rights to a compound in development, we are putting a price on a gamble.

A poker player can tell you, for instance, that even with five unknown cards to come, two jacks will have a better chance of winning the pot than, say, two sevens. But they may not know how much more the better hand would be worth if, in our fanciful blend of poker and auctions, they could sell their seat at the table in the middle of the game. In the end, the hand with the two jacks may not win the pot (one or two more sevens might come along for the other player), so the new player who pays for the hand and continues to invest in it through

additional rounds of betting, may receive no payout at all.

This is the usual state of affairs in pharma, where companies buy or sell the rights to develop a compound early in the clinical-trials process, when crucial outcomes that determine the value of the drug remain unknown. They may invest tens of millions in a drug that is never approved, and thus receive nothing in the end.

Of course, pharma players do buy, sell, or even share their seats at the table. And they must always ask, like two poker players wanting to share the risks and rewards on a hand in progress, what value to put on a potential compound. The rewards are huge, but the probability of surviving to final FDA approval—and cashing in their chips—is quite low.

So, at the considerable risk of overextending our poker metaphor, the upfront payment reflects the size of the ante (research costs borne by the deal originator) and the value of the hand (how good the compound is and how large the winning “pot” might be, given the number of players at the table).

Research and development expenses and milestone payments correspond to the additional bets made as the cards continue to fall. Royalties, of course, are a percentage of the winner's pot. Throw in equity positions, special debt issues, and strategic operational alliances, and the game becomes infinitely more complicated than poker. But it is still a betting game, so it's critical to understand the wagers, odds, and payoffs of a pharma-product deal.

Another factor complicates the relationships between pharmaceutical players. Not all the bets, risks, and payoffs are evenly divided. For instance, the cost and risk of just one aspect of the deal may be borne wholly by one partner, while the payoff may be shared by both. Also, partnerships extend over long periods, making the value of money over time a significant factor. Development could go on for a decade, and royalty payments could go out for another decade or two. So it's important to compare the value of money, at the time the bets are made, to its value at the time of payoff.

Tracking investments is especially important in licensing deals for products in development. Unless the product is in Phase III, the most likely scenario is that the project fails in development and no positive cash flows ever occur. Therefore, it's critical

*For more information about value drivers for deals, go to [www.mattsonjack.com](http://www.mattsonjack.com)*

to forecast who will have what cash on the table, should the game end prematurely. Once players clearly understand these components of the game, or of the pharmaceutical deal in our case, they are in an excellent position to negotiate a deal structure that delivers the best chance of creating value within a pharma organization.

Achieving this level of understanding requires due diligence. Pharma players who sit at the poker table with the other companies need to figure the odds if they want to place smart bets. To illustrate the process, let's look at how an actual deal breaks down to its parts. This is the easiest way to understand how risks and rewards can best be shared in a quest for value.

**Risk Diligence: A Case Study**

Most people consider net present value (NPV) to be the best valuation method for assessing pharmaceutical transactions. It is defined as the value—in today's dollars—of the cumulative annual after-tax net cash flows directly stemming from the product deal. NPV is adjusted for risk by multiplying cash flows by the probability that those cash flows will actually occur. There is an easy way to do this calculation, and a hard way. In this instance, the hard way is well worth the trouble, as demonstrated through this case study.

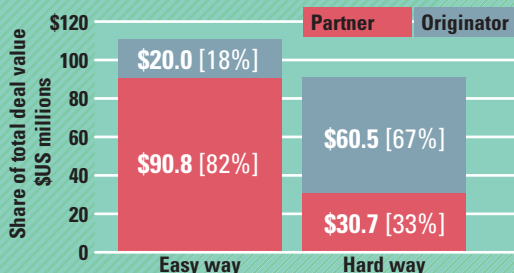
In a pharmaceutical partnership deal made in early 2004, a pre-clinical drug candidate was licensed from one party (the "originator") to another party (the "partner"). It was a relatively straightforward licensing deal, in which the partner agreed to develop and market the product, while the originator received upfront, milestone, and royalty payments. (See "Terms of the Deal," page 30.) Although there are generally accepted averages for the probability of a drug surviving to launch, we conducted a custom risk assessment for this particular deal.

We'll examine the details of that risk-sharing analysis later. First, let's return to the two ways, easy and hard, that executives can calculate risk-adjusted NPV.

The easy way to adjust NPV for the probability of success is to multiply the deal NPV by the probability of launch—in this case, 11 percent. To begin with, we calculated the NPV using an itemized cash flow forecast, which is a familiar accounting procedure. The NPV was just over \$1 billion (\$1.002 billion). Multiplying by 11 percent, we arrived at a risk-adjusted NPV of \$110 million.

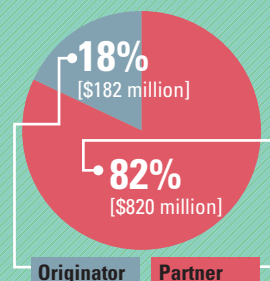
The hard way to calculate a risk-adjusted NPV is to assess the risk of each individ-

**FIGURE 1: Probability-Adjusted NPV: Two Approaches**



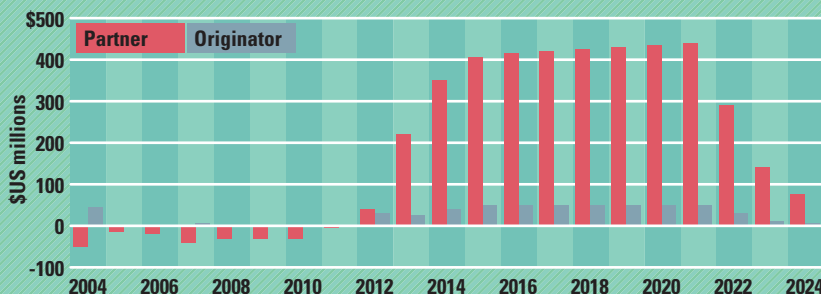
There are two ways to adjust NPV for the probability of success. The easy way—just one calculation—inaccurately depicts the partner as getting the most value out of the deal. Instead, the likelihood of the product's failure during R&D means the value of the deal is less, and the lion's share of that value goes to the originator.

**FIGURE 2: Total Net Present Value**



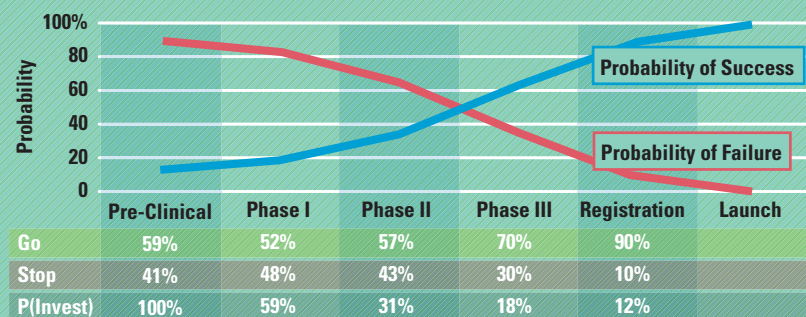
Without risk adjusting the shares, it appears the partner is gaining more value out of the biopartnership deal.

**FIGURE 3: Cash Flow Share**



There are two distinct phases of a partnership deal, as shown above. The art of the deal is to find the correct mix and timing of payments during development, and royalty distributions during the commercial phase, to equitably distribute the risks and rewards.

**FIGURE 4: Probability of Project Success and Failure by Phases in Development**



The probability that a deal will succeed increases as a compound moves from one phase of development to the next. The Go figure listed in the table below the graph shows the probability, at each stage, that the partner will reach end points that move the deal into the next phase. P(invest) shows the probability, at deal begin, of making the milestone payment associated with each phase of clinical trials.

ual year of the eight-year development program and commercial period, and then to multiply that probability by each year's respective cash flow. This calculation takes into account the probability that any year's cash flow will actually occur, which of course depends on the outcome of events in previous years. It helps to know this probability if a large milestone payment is due in a particular year. This calculation results in a risk-adjusted NPV of \$91 million. (See Figure 1, page 29.)

Many might say there's only about a 20-percent difference between the number derived using the hard-way calculation and the number derived using the easy way. However, the difference in these numbers merits close examination, for it provides insight into the value of the deal going to each partner.

Clearly, the easy way to probability-adjust NPV yields a misleading answer. It overstates the likelihood of success and the value of the deal to the partner. Whether the partner makes the upfront payment, pays R&D expense, and makes the Phase III

## Terms of the Deal

Probability of launch ..... 11%  
 Forecast development expenditures: .. \$284 million  
 Launch year ..... 2012  
 Forecast peak-year sales ..... \$808 million  
 Partner pays all development expenses. Originator to receive the following fees:

- \$50 million at signing
- \$10 million milestone payment if the product enters Phase III
- \$40 million milestone payment if the product is launched
- 10% fixed royalty on net sales

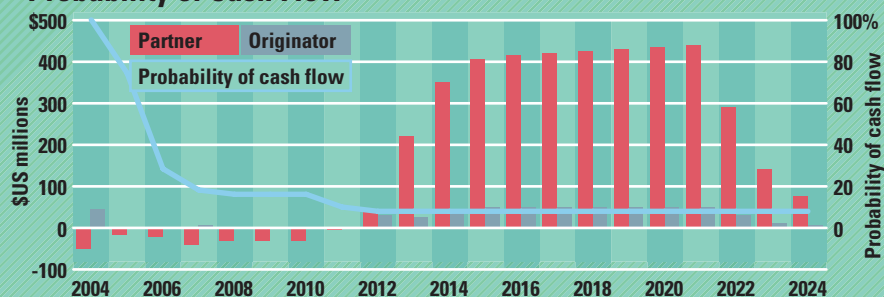
milestone payments must be considered discreet events, with different probabilities, because each depends on success in the previous stage. So they cannot be accurately reflected in a single calculation of the adjusted NPV, as in the easy way.

Now let's return to the case study. Figure 3 on page 29 shows the annual cash flows of

our deal. Two things are immediately apparent. First, the deal lifecycle has two very distinct phases. The first phase is dominated by negative cash flows—payments made by the partner during the development process—and the second phase shows the positive cash flows during the lifecycle of the commercialized product. The partner makes cash payments to the originator whenever an event, such as a trial success, reduces risk during development. After approval, the partner makes royalty payments to reward the originator for dis-

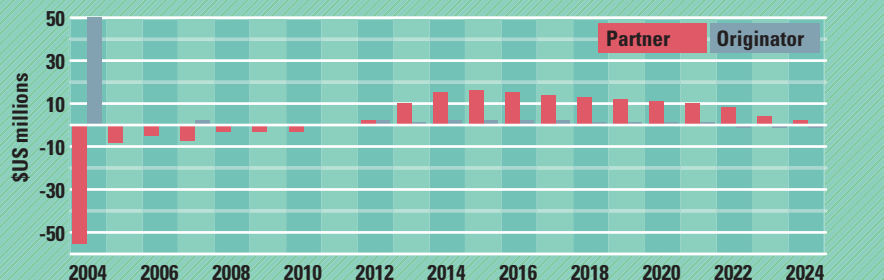
covering a drug candidate with commercial value. In Figure 3, you can see that royalty payments are small relative to the returns on the drug, which rewards the partner for the risk assumed during development. If the deal succeeds, the share of cash going to the partner seems very large. But because the risk of failure far outweighed the chance of succ-

FIGURE 5:  
Probability of Cash Flow



The probability that each year's cash flow will actually occur drops quickly during the first half of development, then begins to stabilize as the project survives Phase II, and moves into the later stages of clinical trials.

FIGURE 6:  
Probabilized and Discounted Cash-Flow Share



In addition to figuring in the annual probability of success, it's important to account for the loss of value over time due to inflation. Note how the upfront payment looms large, given that the company is paying the sum today.

FIGURE 7:  
Risk-Adjusted NPV

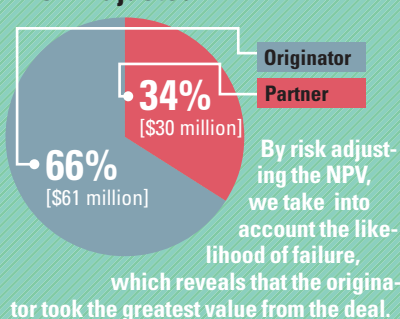
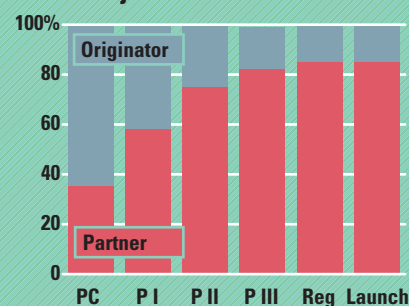


FIGURE 8:  
Risk-Adjusted Share of Value



Over the course of the deal, the partner's share picks up value, since the partner bears the greater share of development risk.

cess, this sort of payment was necessary to persuade the partner to assume the risk. The art of the deal is to find the correct mix and timing of payments during the development stage, and royalty distributions during the commercial phase, to equitably distribute the risks and rewards.

The pie chart in Figure 2 (page 29) indicates the unadjusted shares of the \$1 billion deal based on the cash flows in the previous chart, which assumes that the deal succeeds. Clearly, the partner appears to be getting the better deal. But when we performed the “hard-way” calculation, which included the probability of the project moving forward from each phase to the next, we came up with a chart that told a different story.

Figure 5 (page 30) shows the year-by-year probability of success as a line set on top of the cash flow bars from Figure 3 (page 29). Note that the probability that each year’s cash flow will actually occur drops quickly during the first half of development, then begins to stabilize as the project survives Phase II.

The graph in Figure 6 (page 30) shows the series of cash flows. But in addition to figuring in the year-by-year probability of success, we also have discounted them to

### Clinical development could continue for a decade, and royalty payments may go on for another decade or two. Therefore, it is important to compare the value of money, at the time the bets are made, to its value at the time of payoff.

account for loss of value over time due to inflation and other factors. There’s a very different outlook now—note, for example, how the upfront payment looms large.

Figure 7 (page 30) shows the risk-

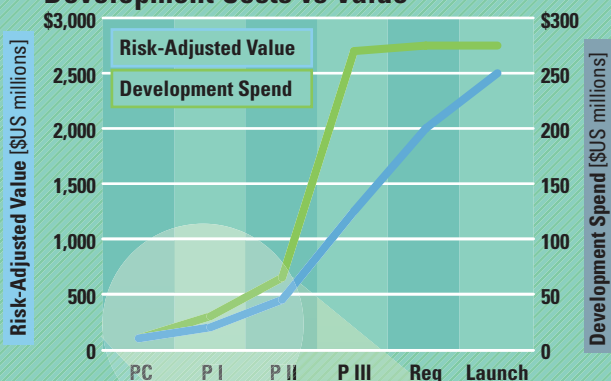
adjusted deal value split. We can clearly see that the deal structure tilts in favor of the originator. It’s interesting to note, however, that even with this skewed structure, the risk-adjusted value to the partner still provides a nominal rate of return of 13.4 percent, which clears the rate-of-return hurdle at most biopharma companies.

Two parties contemplating a deal could adjust the values for different payments within this model to arrive at a deal-value split that seems equitable. For instance, if they moved \$18 million from the upfront payment to the Phase III milestone, and reduced the launch milestone to \$20 million, they would split the value evenly. Of course, not every equitable deal results in a 50/50 split of financial value, as other factors and value drivers, such as the potential value of the molecule or the marketing niche, are likely to come into play.

### Risk and Value Shifts

Now that we have demonstrated that risk shifts over the course of a deal, let’s examine how the share of value in this deal shifts

FIGURE 9: Development Costs vs Value



Above: Note that the value scale axis on the left is set at ten times the dollar scale on the development-spend axis on the right. Deal value creation outpaces R&D

investment starting in Phase I. But after risk adjustment, the value appears to increase faster than development spend during Phase I, while R&D costs outpace value gains in Phase II.

FIGURE 10: Another Look

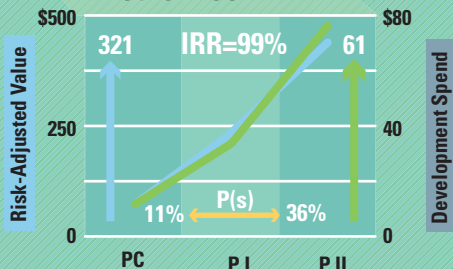
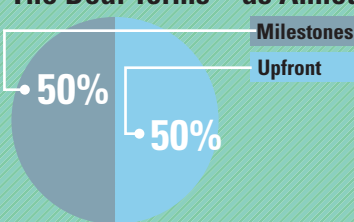
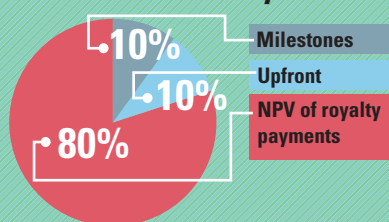


FIGURE 11: The Deal Terms—as Announced



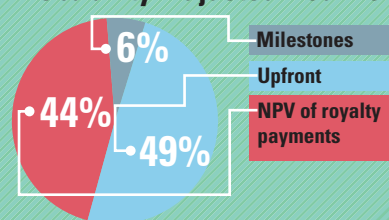
Companies typically do not publish all terms of the deal. The press usually portrays even deal-value splits, but omissions and differing R&D expense-accounting make comparing two deals difficult without more data.

FIGURE 12: Deal Terms with Royalties



In many cases, royalties are not made public. But they can represent a major percentage of the deal, as shown in this chart. Press accounts miss key terms of deals.

FIGURE 13: Probability-Adjusted Deal Term Mix



Royalties are the least likely payments to be made in a deal. Upfront payments are certain. Probability-adjusting the deal terms will put the mix in perspective.

over time. Figure 8 (page 30) depicts the split of value at each phase of development. Note that the partner picks up value over time. This is justified by the fact that the partner is carrying the risk by covering the costs of development and facilitating the development process. And ultimately, the partner's commercial expertise provides the post-launch value.

### Deal Timing

A product increases in risk-adjusted value as it moves through the trial phases, because the probability of success increases after each successful trial, in particular after Phase I. The value of the product can be thought of as the NPV of the deal times the probability of success at a given stage of development—that is, risk-adjusted NPV calculated the hard way at that stage.

During this diligence process we can see another interesting shift. A gap appears between the acceleration of value and the

large upfront payment and high royalties, if he can hold onto the drug well into Phase II, since the product would then be a more viable (and valuable) drug candidate. It is possible that a premium will be put on the deal, as there is a certain scarcity of quality Phase II compounds available for license. The difference between the IRR and the cost to fund the development can be retained by the originator's investors, should they pursue this approach—remembering, of course, the steep probability that the project will fail during this period. The decision must be based on the investor's capacity to put large sums of money at high risk.

### No Comparison

We all are interested in comparing the deals we've done or contemplated to what deals others are making—if for nothing else but a sanity check. The problem is that the publicized terms of biopartnership deals are often difficult to compare because crucial

**The publicized terms of biopartnership deals are often difficult to compare. Crucial information is left out of press accounts. For instance, royalties are usually one of the largest value components of a deal when the product is actually launched. But the value of royalties is rarely included in any payments announced as part of the deal value.**

development investment as the product survives the clinical trials. This is apparent in Figure 9 (page 31)—and don't be fooled by the scale of this chart. The value scale axis on the left is at 10 times the dollar scale of the development-spend axis on the right. The value creation is outpacing development investment starting in Phase I. This analysis is very useful in helping the originator determine the best time to do a deal. In this case, it is in the originator's best interests to wait at least until Phase II before doing this deal.

Figure 10 (page 31) shows how risk-adjusted value increases faster than development spend during Phase I, while development costs outpace value gains during Phase II. In this case, a \$61 million investment in development gets the product well into Phase II, increasing the value of the product by \$321 million. Without going into the calculation, this comes to an annual investment return ratio (IRR) of 99 percent.

An originator is more likely to negotiate a

information is left out. For instance, royalties are usually one of the largest value components of a deal in which the product is actually launched. But the value of royalties is rarely included in any amounts announced as part of the deal value—which primarily comprises upfront payments, milestone payments, equity investments, and reimbursed R&D expenses.

Determining the true value of these components can be tricky. For instance, some deal milestone-payment provisions may cause only a portion of all possible milestones to be payable even if the product is launched. The equity-investment component is often expressed as the total equity purchase, instead of premiums paid above the market value of the stock, which represent the actual transfer of value from one partner to the other. Furthermore, R&D expenses included as part of the deal value are typically part of complicated co-development arrangements, in which both parties create value.

However, R&D expense, when borne by the partner, is not usually included in deal value. This reporting inconsistency, among others, makes deal values difficult to compare. Throw in options and creative financial instruments, and it can be very difficult for an outsider to add up the true value of the deal for each side of a transaction. But even after all that, it's still interesting to check out the terms of other deals.

A couple of examples will illustrate this point. The pie chart in Figure 11 (page 31) shows the proportion of the terms in our case-study deal as they would typically be publicized. Press releases and other community communications typically make the deal look like an equal partnership.

But Figure 12 (page 31) shows the same deal with the royalty component included. We've expressed royalties as the NPV of the royalty stream discounted back to the launch year—which makes a big difference. Since the royalties are less likely to occur (compared with the upfront payment) and are therefore of less value, we probability adjust them in Figure 13 (page 31), using the same process we've just been discussing, to arrive at this view of the situation. Royalties are still a major part of the deal value, and the upfront payment again looms large (49 percent).

### The Shifting Mix

Even if it is difficult to determine the true value split of confidential deals, a definite shift occurs in the comparable deal-term mix for products early in development, compared to drugs later in development. Of course, the prices paid for products are higher as they survive development, but it is also evident that the deal-component mix shifts. Early product deals are heavier with contingent milestones, while later-stage deals merit higher upfront fees and equity investments. Deal-makers adjust the terms of the deal in order to balance risk and cash at risk.

All deals are different. Finding two identical product-license or acquisition opportunities is no more likely than finding two identical poker hands. Like each bet at the gaming table, the wagers and payoffs of pharma deals must be considered on their own merits, using careful due diligence to achieve a beneficial deal structure. ■

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