VOLUME 17 | NUMBER 2 | SPRING 2005

Journal of APPLIED CORPORATE FINANCE

A MORGAN STANLEY PUBLICATION

In This Issue: Real Options and Corporate Strategy

Morgan Stanley

Value-Based Management in Biosciences Research and Development

by Gill Eapen, Decision Options, LLC

The U.S. biosciences industry—a category that includes pharmaceuticals, biotechnology, and medical equipment companies—invests over $100 billion a year on research and development programs that aim to discover and develop new therapies to prevent, diagnose, cure, or alleviate diseases affecting humans and animals. These expenses are spread over a long time, with progress from the idea-generation stage to marketed product often taking decades. And with only one out of over 100 ideas turning into a commercially viable product, the risks are enormous.

R&D programs generally have a macro objective, such as finding a cure for Alzheimer's disease using a specific mechanism and technique. To meet this objective, R&D programs generally aim to develop a number of different "candidates" that may fit a general profile. Each candidate has expectations in terms of the end products, delivery mechanisms, pricing, and other factors. Each candidate also has a project plan with various investment options and schedules, and some plans contemplate expansion of the product into other disease areas, population groups, and delivery mechanisms (dosage forms).

To reach their goals, the project plans must coordinate a number of different "specialty" areas or disciplines, including clinical, toxicology, chemistry, biostatistics, substance manufacturing, and pharmacy. Adding further to the complexity, the development plan for each candidate may also include many partners outside the company—research collaborations, universities, contract research organizations, contract manufacturers, governments, regulators, insurance companies, physicians, and patients—who may provide resources and services specific to the program. It is indeed a massive undertaking, with the overall required investments for some development plans surpassing the GDP of small countries.

The complexity of these development plans creates significant uncertainty about outcomes—but along with such uncertainty comes considerable opportunity to build managerial flexibility into the design and execution of such programs. This article discusses possible applications of real options concepts and valuation methods to both the design and the valuation of corporate R&D programs.

The Disease

Biosciences companies have long recognized that their primary assets are the R&D programs in the pipeline. Although most managers have an intuitive understanding of the *value* of R&D programs, the quantification of that value has been a challenge for a variety of reasons:

- There are conceptual misunderstandings about what is meant by *value.*
- Traditional techniques such as discounted cash flow (DCF) and decision tree analysis (DTA) do not capture the uncertainty and flexibility inherent in R&D programs.
- The availability of tools to conduct valuation based on more generalized and appropriate frameworks has, thus far, been limited.
- Existing managerial incentives within departments may prevent needed changes in decision processes.

The industry practice in external transactions such as licensing and contract manufacturing has been to use rules of thumb developed over the years. At the same time, however, "internal transactions" such as project selection, prioritization, and resource allocation are evaluated primarily using traditional techniques such as DCF and decision trees. Decision-makers understand that current practices are limited and potentially misleading, and they attempt to compensate for these limitations by making qualitative adjustments based typically on technical aspects of the program.

Symptoms

The following are fairly reliable indicators that the concept of *value* is not understood or applied in a consistent way in valuing R&D.

Reliance on rules of thumb and/or proxy-based licensing and contract deals with external partners. This is similar in many respects to the valuation practices used in the venture capital industry. Factors such as the size of the overall market, the reputation of management, and any available technical data tend to be the main drivers of transactions. Initial bid prices, which typically take the form of milestones and royalties, are based on those in previous transactions or, more likely, a single successful transaction in the past. There is often some negotiation around such rules, but almost always within limits established by sacred cows (for example, "absolutely no milestone payments at filing").

Discussions and debates focus on technical details (such as "the rat study is very promising and that is the primary basis of this deal"). How all this translates into shareholder value added is almost never mentioned. Moreover, the split of value between the licensee and licensor created by the deal structure is also generally not subjected to much analysis. The tacit assumption underlying such practices is that if the deal is structured according to the rules of thumb, it is a good deal for the company.

Prioritization of programs (and entities) using rankings and multiple evaluation criteria. R&D programs are complex and provide significant flexibility for multi-dimensional rankings (on criteria such as safety, efficacy, manufacturability, differentiation, and cost of raw materials). Traditional decision trees have been used widely in pharmaceutical companies, and they can be used to calculate the same net present values (NPVs) produced by DCF analysis. But such NPVs are generally viewed by decision-makers as only one of several criteria—one that may be too narrowly financial to capture the "spirit" of the program under consideration. Moreover, the use of traditional decision trees has led to some confusion in the marketplace, as some practitioners have mistakenly labeled it "options analysis" (to denote the branches in the tree). As most first-year business school students know, traditional decision trees are nothing more than pictorial representations of the mechanics of the DCF analysis. That is, decision tree analysis does not take account of all uncertainties nor does it account for the value of management flexibility that is inherent in the decision process.

Resourcing (budgeting) decisions are segmented by departments, products, and specializations, and are generally based on last year's budgets. Since there isn't a common currency to compare investment choices across departments, products, and specializations, resourcing decisions (budgets) are typically done in a segmented fashion. Resources are allocated into buckets, typically according to a formula based on overall sales, last year's budget, and growth rates. Once a departmental (or product) budget is set, managers further divide that amount based on local formulas. Such allocations in turn typically depend on last year's budget—and on managers' negotiating skills. It is not unusual to find strong correlations between departmental budgets and the seniority and education of their managers.

It is intuitively clear to decision-makers that every product or investment opportunity has an intrinsic value to the company. It is also clear that investment opportunities may present various paths forward and each path (or "design") may have different values. If a method could be established to systematically value every investment decision (including alternative designs), one could create a common currency for use in selecting, comparing, prioritizing, designing, and buying and selling investment opportunities. If the method were applicable across all investment choices, the common currency of *value* would be the only decision variable regardless of the nature, location, time horizon, and size of the available investment choices. This is because *value,* if calculated using an economically consistent method, would capture the information related to all parameters and the uncertainties in the estimation of those parameters. Moreover, such a valuation method should be roughly consistent with the intuition and thought process that experienced decision-makers go through when they select the best opportunities (management flexibility).

To put this in the right context, consider a pharmaceutical company with the following types of investment choices in R&D:

- A full-development candidate that is entering Phase III (large-scale clinical studies undertaken after proof of concept has been established).
- An early-development candidate that has just filed an IND (Investigational New Drug Application) and is ready to enter the clinic (first human trials to assess safety).
- An IT infrastructure improvement project that is expected to enhance productivity in record-keeping.
- An expansion of a pilot plant that requires significant capital expense.
- Hiring of new personnel with specific expertise in oncology.
- A licensing opportunity with a biotech company on a drug candidate in an area where the company has its own program.

Suppose also that the company has a hard resource constraint (a limited budget)—one that is imposed by senior management (or set by market forces) and based on the level of R&D that appears optimal at the current time. The question is, how should such a resource constraint affect investment decisions about R&D? How does the company decide which investment opportunities to select and how to prioritize them? And how and when should the company execute the projects it decides to undertake? In a traditionally managed company, investment opportunities will be selected, prioritized, and funded by different departments in a largely uncoordinated process—and, as mentioned earlier, the budgets for those departments are likely to be determined mainly by prior years' budgets. Such segmentation introduces the possibility that the best opportunities, if located within the wrong department, may be underfunded or passed over completely for "lack of budget." To make matters worse, finance departments may make tactical adjustments to the departmental budgets to improve quarterly financial statements (apparently believing that investors focus mainly on next quarter's earnings). As such tactical allocations (cutbacks or increases) flow through departments, they further affect the optimality of the investments undertaken by department managers.

In sum, existing practices and incentives are more likely to reward management for their ability to negotiate budgets than to add value for shareholders, resulting in overinvestment in some projects and underinvestment in others. One requirement for changing such practices and incentives is to devise a better measure of the value added by R&D projects. But this, of course, is far easier said than done, since the payoffs from such investments tend to be realized years after the initial decisions are made (and managerial incentives, of course, tend to be based on relatively short time periods).

Toward a Possible Cure

The fundamental issue, then, is the lack of a common currency, denominated in terms of shareholder or economic value added, that can be used by management to assess the company's entire investment opportunity set. Traditional financial techniques such as DCF and decision trees are applicable only to a small subset of such opportunities. The reason is that the constraining assumptions in DCF and decision trees—namely, that cash flows are "deterministic" and there is thus no decision flexibility in the future—do not hold for most investment opportunities in R&D. Although decision-makers may ask that such analysis be conducted on a larger number of opportunities, they generally know that the results will not be sufficiently robust to make decisions. In such situations, smart decision-makers will be more interested in the assumptions used by the analyst and less in the results of the analysis.

To remedy this situation, we need methodologies and tools that satisfy the following criteria:

1) The methodology is sufficiently generalized to be applicable across the entire investment opportunity set.

2) A tool is available that can be consistently and systematically used across all opportunities.

3) Application of the methodology and the tool is as fast and easy as the application of traditional techniques such as decision trees.

4) Senior decision-makers understand both the advantages of the method and the need for change.

5) Application of the tool is sufficiently systematic so as to be repeatable throughout the organization.

Although the third criterion—quick and easy application—is not a necessary condition to move to a higher fidelity in investment decisions, in practice it tends to be quite important. Organizations resist change and people with the power to effect change are generally reluctant to recommend (much less mandate) processes that substantially differ in appearance from status quo. Quick and easy application is also very helpful in accomplishing the fourth criterion—gaining the understanding and support of senior management, which is also likely to be a necessary condition for widespread implementation of a new valuation method.

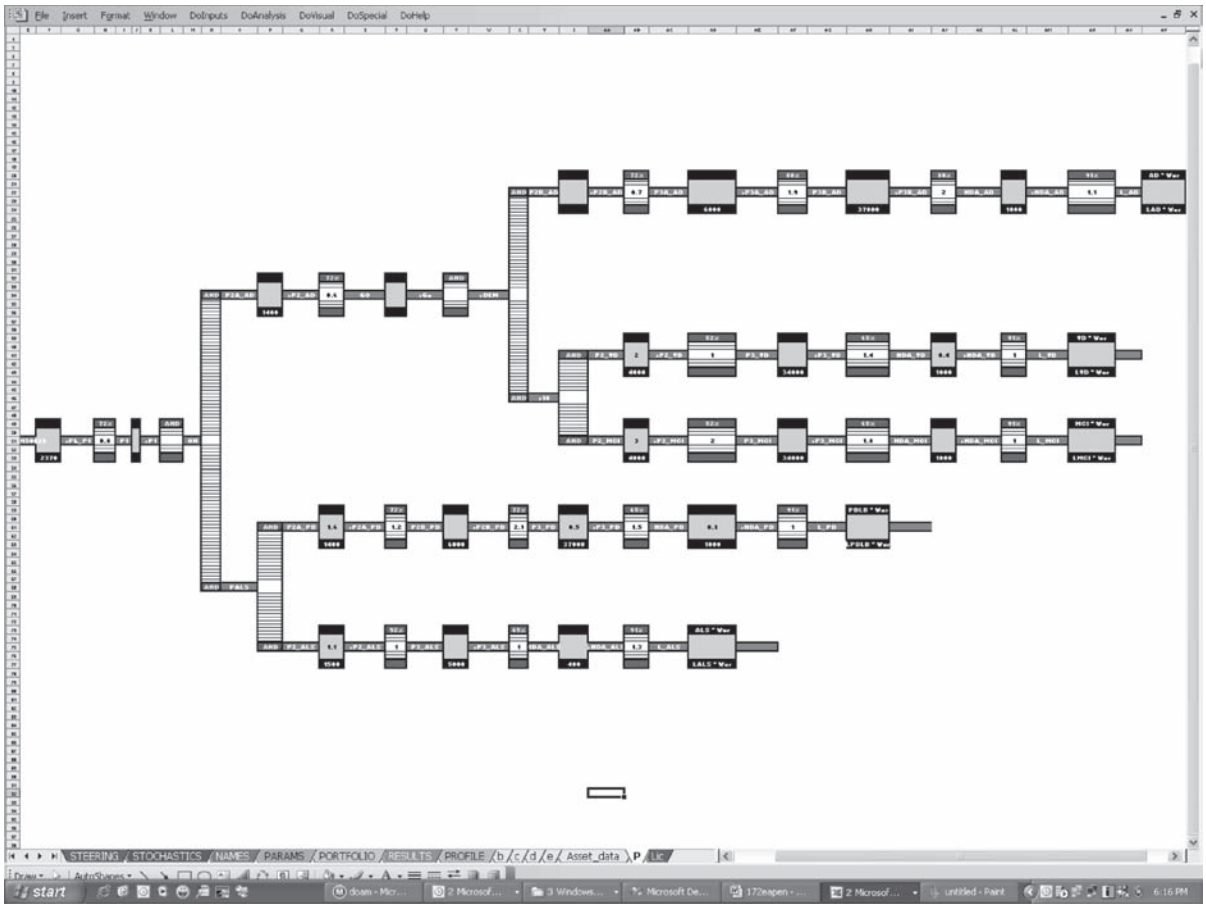
The methodology for the valuation of all investment opportunities has been available for over a decade. In the finance literature, it is typically referred to as "contingent claims" or "real options" analysis. Although research has progressed to the point of providing responses to many of the vexing theoretical questions in this area, access to these ideas and technologies in practice (especially tools that make the application easy) has been limited. This has led to skepticism among decision-makers about the practicality of the technique.

To analyze all investment opportunities in an enterprise, we need a flexible methodology that allows problems to be specified that have both technical (sometimes called "private") risks and market risks. In pharmaceutical R&D, technical risks are related to experiments testing the safety and efficacy of the candidates. There may be technical risks in R&D manufacturing as well, leading to non-scalability, lack of stability, or inability to manufacture within certain cost thresholds. Such risks should be treated separately and differently from market-related risks. Market risks have to do with the anticipated revenue streams from those products that end up passing the technical hurdles and are actually brought to market.

Another important consideration is that the follow-on capital investments required at different stages of the experiment, and the duration of the experiments, are highly uncertain at the outset. Nevertheless, there are large amounts of data from repeated and standardized experiments run in pharmaceutical R&D that enable companies to form probability-weighted expectations—and such expectations should be used in the analysis instead of the averages typically used in DCF and decision tree analyses. Because of the focus on averages in traditional analysis—average cost, average time, average revenue—significant time and effort can be devoted to getting these averages right. But as experienced managers and analysts recognize, the averages that result from such analyses generally obscure more than they reveal. Given the variability and uncertainty associated with the costs and benefits of R&D programs, the best approach when contemplating a new program is to start by providing a good description of the range of possible outcomes.

With that as a starting point, one can then use a real-options-based valuation methodology that I call "decision options." It uses decision-tree-like constructs to represent managerial choices in response to variability in expected costs and revenues; and in so doing, it enables the analyst to distinguish between flexible and committed decisions, and between the effects of technical risks and market risks. Since it is not specific to any situation or set of assumptions, it is applicable across the entire investment opportunity set in the company. Moreover, by adopting such a framework, which focuses on uncertainty rather than average outcomes, companies can actually *reduce* both the data requirements and the mechanical intensity of the valuation process (which,

Figure 1 **Decision options tree constructed using DoOptima™ software showing investment decisions, timing, and technical risks for a project plan with sequential and parallel investment paths to five distinct indications for the candidate under consideration.**



by the way, runs counter to a criticism of real options that is commonly made by advocates of traditional methods).

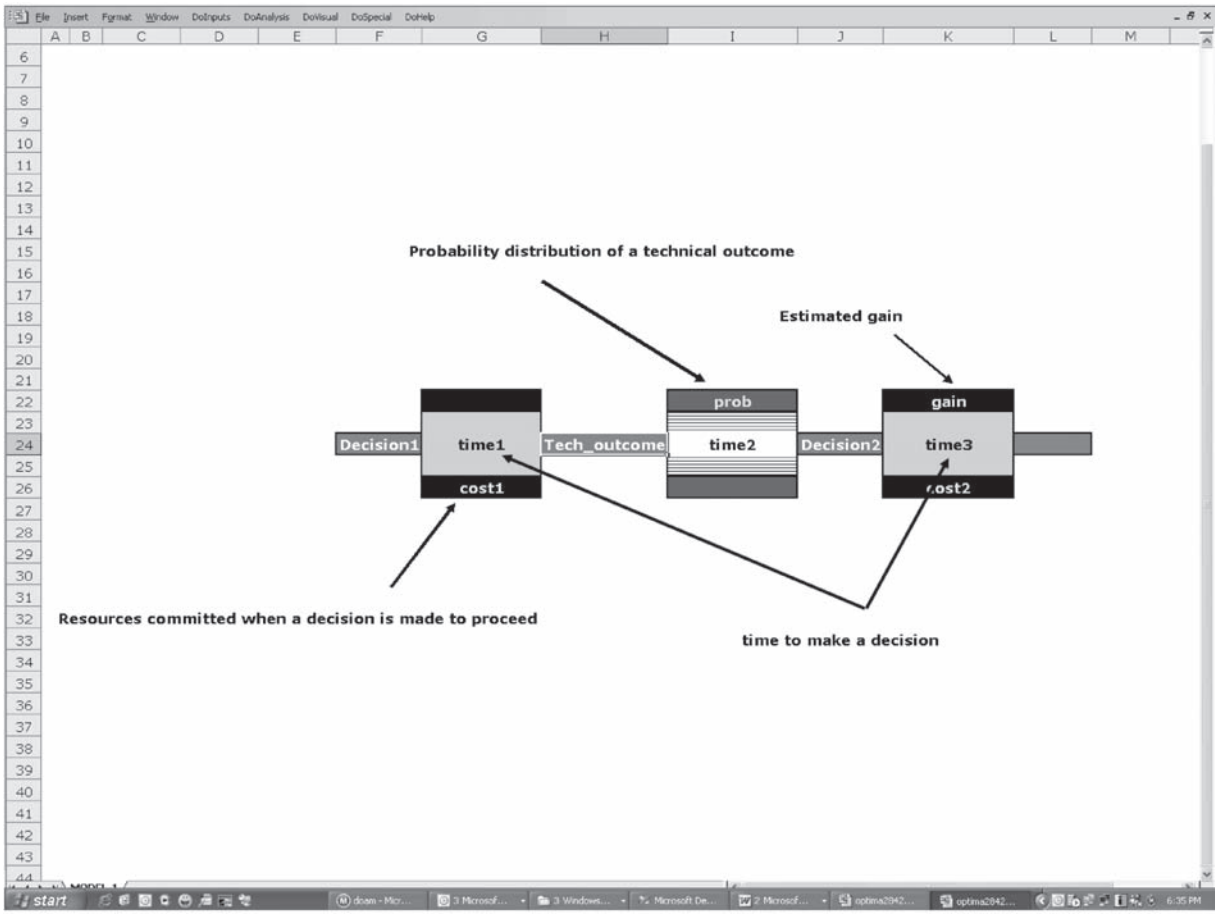
Anatomy of an External Transaction

EGEN, an innovative biotechnology company in Eastern Europe, has a few promising drug candidates in its pipeline. But rather than raise more equity and dilute the current shareholders, EGEN intends to raise money internally by licensing the European marketing rights for one of its drug candidates to a pharmaceutical company called MAXO.

The licensable drug candidate is currently undergoing Phase I studies (early human trials to assess safety). The candidate's primary indication is Alzheimer's disease, but there are four other secondary indications supported by EGEN's preclinical studies. There are also multiple possible designs that EGEN can pursue (some investments in sequence and some in parallel) so as to maximize the value of the candidate.

To maximize shareholder value from EGEN's perspective, it should enter into a deal with MAXO while retaining the highest possible percentage of the candidate's value. Of course, MAXO would like to extract the highest percentage of that value for its own shareholders. To solve this problem, we first identify the various development plans EGEN could pursue and the costs, timing, risks, and benefits associated with each plan (and each indication). Since it is impossible to produce exact numbers for any of these categories, we use possible ranges for all of them. For each design, we lay out a project plan that shows both the decision options and the resolution of technical risks (that is, the outcomes of experiments) over time. Development of each indication requires a series of staged investments, each of which is designed to reveal more information about the candidate's safety, efficacy, cost of production, and revenue potential (differentiation). In the case of this specific drug candidate, three indications were closely related to one another, which led to a project plan with a combination of sequential and parallel experiments. The probability of technical success for each experiment can

Figure 2 **Graphical representation of a portion of a decision options structure using DoOptima™ software.**



be estimated using historical data on similar experiments conducted by different companies.

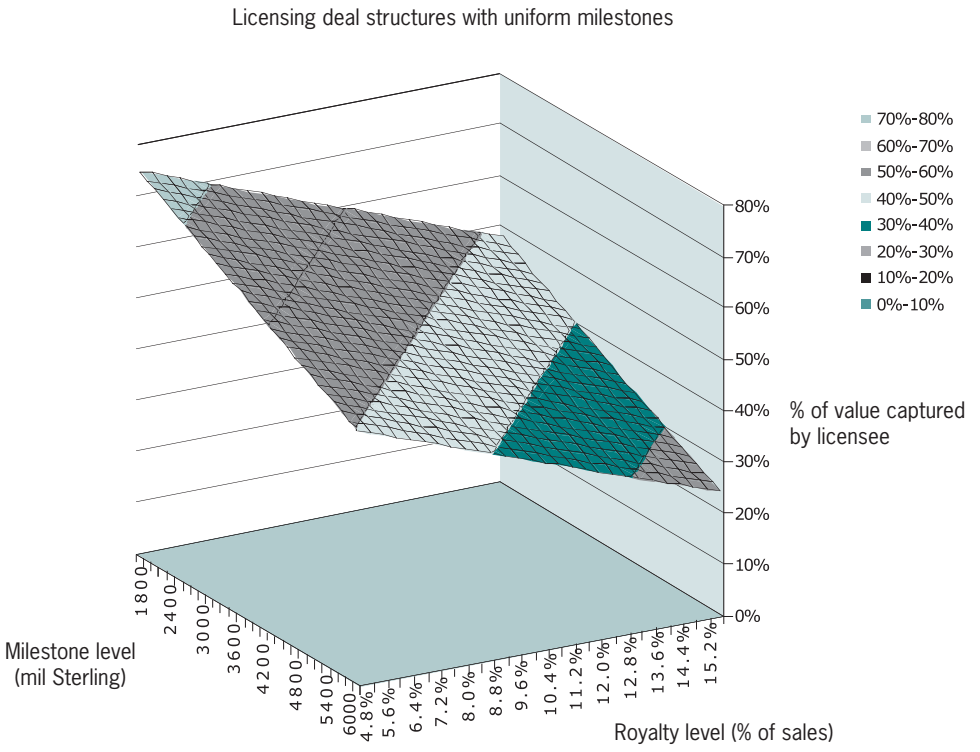
Figure 1 presents a decision options tree for a single drug candidate. It attempts to show all major expected investment decisions in response to technical outcomes with respect to all indications that are likely to arise in the future. Although it appears complex, the tree is just a description of the various development plans that the company could pursue. For each decision option—that is, each right retained by the company to invest more in the candidate in pursuing its indications—the tree projects the investments required and the timing of those investments. Since these are not known with precision, they are estimated within a range. The underlying asset, which is the expected value of the product at launch, is also unknown but it too can be estimated within a range.

Figure 2 shows a detailed view of part of a decision option tree that has two decisions and one technical outcome. The decisions may require an investment (denoted "cost 1" in the figure, for example) that needs to be made within a certain time ("time 1"). Once a decision option is exercised, a technical outcome may be revealed with an estimated probability (this can be a binary outcome or a probability distribution) after a certain amount of time (say, "time 2") has elapsed.

Since our estimate of the value of the asset (based on the expected cash flows from the launched product) will become more precise as time passes and new information arrives (about competitive actions, differentiation, pricing, cost of production, and so on), we represent them in stochastic functions. We do the same for development costs, since our estimates of the costs of future experiments will also improve as a result of information from completed experiments.

The terms and structure of the contract with MAXO can then be analyzed with the same framework using known milestone payments and royalty percentages to represent increases in costs (from MAXO's viewpoint if the candidate is licensed). Milestone payments are made by the licensee to the licensor as the candidate progresses through specific points in the R&D process. In this specific case, milestone payments were proposed for each indication and at multiple

Figure 3 **An example of decision options analysis output that shows value sharing between licensee and licensor for various license parameters.**



stages of the R&D process. Royalty payments are typically based on total revenue or net income if the product is successfully marketed. Various combinations of milestones and royalties can be analyzed and the value captured by both the licensee and licensor can be calculated. In each analysis, the uncertainties about costs, time, and revenue potential are represented. Additionally, the expected technical risks in various experiments and the alternative paths to market are also pictured. The sequencing of experiments, given the possible interactions among the different indications, is also taken into account.

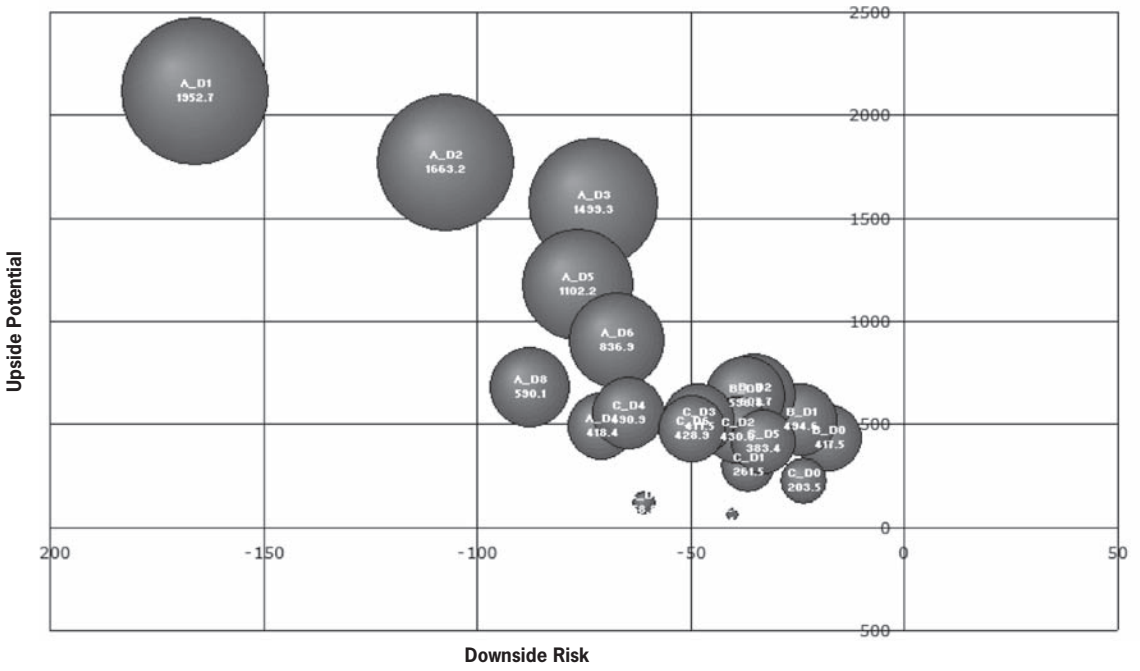
The outputs of one such analysis are shown in Figure 3. The envelope represents the percentage of the value captured by the licensor for various combinations of milestone payments and royalty levels. Multiple such analyses were conducted using graduated milestones and royalties, with the milestones increasing as the candidate progresses in the pipeline and with royalty percentages based on different levels of overall sales. In all cases, the goal was to determine the share of the overall (current) value of the candidate captured by the licensee. This information was subsequently used by the licensor in negotiations with the licensee to create an equitable deal based on value.

Holistic Medicine: Real-Time, Value-Based Analysis for Resource Allocation Decisions

As discussed before, to make a tangible impact on shareholder value, companies should use value-based analysis systematically and consistently across the entire investment opportunity set. Once again, we will focus on R&D, but the methodology and tools are applicable at the enterprise level.

The life of an R&D manager in a large pharmaceutical company is not an easy one. There may be over 100 candidates in the pipeline spread over dozens of specific programs. Each such candidate could be advanced (using internal or external means) through many different development paths or "designs." Each design could require many millions of dollars and, again, the most likely outcome is failure. To make it more interesting, new information arrives daily (if not hourly) about important aspects of the candidate—safety, efficacy, manufacturability, competitive actions, regulatory changes, and other market factors. If the R&D manager is to maximize shareholder value, each opportunity (including all possible alternative designs) should be valued considering available information, uncertainties, and constraints. Constraints can be imposed by contracts

Figure 4 **Sample output of a decision options analysis showing downside risk versus upside potential (size of bubble represents total value).**



(committed decisions), regulations, or limits on internal or external capacity. If there are constraints on resources (people, money, space, or skills), the manager will be forced to make selection and prioritization decisions among viable and valuable programs. In such cases, the decision is not whether to do it, but rather when and how.

In the past, some decision-makers have attributed this problem to lack of data, and have attempted to solve it by investing heavily in collecting large amounts of additional data. In most cases, however, the problem is the lack not of data but rather of systematic valuation methodologies and tools that can digest dynamic and uncertain data and provide decision guidance in real time. A mental shift is needed to accept the fact that uncertainty is unavoidable and that any decision based on deterministic factors is unlikely to succeed even if a large amount of past data is available for establishing average expectations.

We at Decision Options LLC have been working with a large pharmaceutical company to tackle this problem head on. Although the company has an enviable pipeline with a large and diverse number of candidates, decision-makers have increasingly been finding it difficult to make investment decisions in the face of such a large portfolio of choices. Decision options methodology is being used in this case to systematically capture the most important value drivers (costs, timing, risks, and benefits) for candidates in late-stage development. Each candidate plan is effectively disaggregated into "packages" of experiments, and the incremental value accruing to the program from each package can be quantified and used to make resourcing decisions. Additionally, the analysis provides a means of assessing downside risk and upside potential for each design, thus providing decision-makers with a good grasp of the risk in the portfolio. For example, Figure 4 provides a sample output of decision options analysis showing the downside risk and upside potential of all of a company's major investment opportunities.

There are now systems that channel new information about costs, project plans, and risk into centralized databases. With a valuation engine operating "on top" of such systems, the value implications of such information can be made available to decision-makers over accessible interfaces such as the web and mobile devices. Because the information content in newly arrived test results or competitive intelligence decays over time, such knowledge should be immediately reflected in the value of investment choices and communicated to the relevant decision-makers.

Conclusion

Shareholder value maximization should be the ultimate goal of every corporate department and activity, including R&D in a biosciences company. But valuing R&D is

not an easy exercise, and the people who manage the large portfolios of disparate investments that make up such programs face big challenges in selecting, prioritizing, and designing the investments—and in valuing them for external transactions. There are some readily observable organizational symptoms that indicate the need for value-based management, including heavy reliance on rules of thumb, qualitative multi-dimensional rankings for selection and prioritization of investment projects, and ad hoc and segmented budgeting based on pre-established formulas. A focus on building systems that collect large amounts of data to tackle uncertainty is also misguided, leading to both higher data intensity and thus higher-cost, but in fact lower-quality, decisions.

To maximize shareholder value, decision-makers should apply value-based management across the entire investment opportunity set. To accomplish this, they need to deploy generalized methodologies and tools that are applicable across all investment choices, and not just specialized subsets. These tools should be able to digest uncertainty of all kinds, while representing decision flexibility and technical and market risks in a way that is economically consistent with market valuation. Such tools should have the ability to reflect the impact of newly arrived information on the value of assets and investment decisions.

Methodologies and tools are now available to accomplish these goals and, in a number of cases, have been used with success. What is required, however, is a mental shift in the organization—a shift toward viewing uncertainty and management's ability to respond to it as primary determinants of corporate value. Because of the long decision horizons in R&D programs, systematic errors in a company's investment decision-making process can take a long time to surface. And that's why managements should move in this direction even if they believe their qualitative processes have served them well in the past.

GILL EAPEN is Founder and Principal at Decision Options, LLC, a boutique consulting firm specializing in valuation, risk, and portfolio management. Decision Options is the creator of DoOptima™ (patent pending), a general purpose valuation and portfolio management framework.

Journal of Applied Corporate Finance (ISSN 1078-1196 [print], ISSN 1745-6622 [online]) is published quarterly on behalf of Morgan Stanley by Blackwell Publishing, with offices at 350 Main Street, Malden, MA 02148, USA, and PO Box 1354, 9600 Garsington Road, Oxford OX4 2XG, UK. Call US: (800) 835-6770, UK: +44 1865 778315; fax US: (781) 388-8232, UK: +44 1865 471775.

Information for Subscribers For new orders, renewals, sample copy requests, claims, changes of address, and all other subscription correspondence, please contact the Customer Service Department at your nearest Blackwell office (see above) or e-mail subscrip@bos.blackwellpublishing.com.

Subscription Rates for Volume 17 (four issues) Institutional Premium Rate* The Americas† $330, Rest of World £201; Commercial Company Premium Rate, The Americas $440, Rest of World £268; Individual Rate, The Americas $95, Rest of World £53, €80‡; Students**, The Americas $50, Rest of World £28, €42.

*Includes print plus premium online access to the current and all available backfiles. Print and online-only rates are also available (see below).

†Customers in Canada should add 7% GST or provide evidence of entitlement to exemption.

‡Customers in the UK should add VAT at 5%; customers in the EU should also add VAT at 5%, or provide a VAT registration number or evidence of entitlement to exemption.

**Students must present a copy of their student ID card to receive this rate.

For more information about Blackwell Publishing journals, including online access information, terms and conditions, and other pricing options, please visit www.blackwellpublishing.com or contact our Customer Service Department, tel: (800) 835-6770 or +44 1865 778315 (UK office).

Back Issues Back issues are available from the publisher at the current single-issue rate.

Mailing *Journal of Applied Corporate Finance* is mailed Standard Rate. Mailing to rest of world by DHL Smart & Global Mail. Canadian mail is sent by Canadian publications mail agreement number 40573520. **Postmaster** Send all address changes to Journal of Applied Corporate Finance, Blackwell Publishing Inc., Journals Subscription Department, 350 Main St., Malden, MA 02148-5020.

Journal of Applied Corporate Finance is available online through Synergy, Blackwell's online journal service, which allows you to:

- Browse tables of contents and abstracts from over 290 professional, science, social science, and medical journals
- Create your own Personal Homepage from which you can access your personal subscriptions, set up e-mail table of contents alerts, and run saved searches
- Perform detailed searches across our database of titles and save the search criteria for future use
- Link to and from bibliographic databases such as ISI.

Sign up for free today at http://www.blackwell-synergy.com.