Expansion Options: Strategic Opportunities Created by Research Projects at BestPharma

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Abstract

We discuss the problem of choosing among several strategic research initiatives at BestPharma, a large international pharmaceutical company. The financial value of research projects is difficult to assess because they are highly uncertain. Too often, the result is either an overly conservative approach to strategic innovation, based on financial analyses stressing the quantifiable cost side, or an overly aggressive approach based on optimistic qualitative portfolios ignoring economic realities. In the case of BestPharma, a major contributor to project value was uncovered by a quantitative evaluation of strategic expansion options, or management's ability to seize opportunities in some of the possible project outcomes.

BestPharma developed a decision tree representation of the projects, which helped to provide transparency about project value and how it was affected by the presence of strategic options. The tree representation highlighted key decision points, payoffs, and key sources of risk. It also illustrated where higher volatility of payoffs made it important to delay decisions and commitments until key uncertainties were resolved. Most importantly, carefully thinking through the tree helped to include all relevant decision branches, or expansion options, as major sources of value.

This analysis helped the team at BestPharma to recognize the presence of additional sources of value for one project. As a result, the project that initially looked inferior based on a qualitative portfolio and on an NPV analysis, came out as the most attractive.

Introduction

The financial evaluation of strategic investment opportunities has for a long time vexed managers. Strategic investments are difficult to evaluate for several reasons:

- not all possible contingencies or courses of actions are known;
- quantitative economic estimates are subject to significant uncertainty;
- continued corrective action based on new information is at the heart of strategy – how should one quantitatively represent such continued action in financial tools?

This was the question faced by the central nervous system (CNS) research group at BestPharma, a large international pharmaceutical company. The research group was relatively young and eager to prove that they could create business value for the company. Three large research projects were under discussion, and the group could not come to an agreement as to which ones to undertake.

Three CNS Research Project Candidates

Project 1: CNS-selective T-Type Calcium Channel Modulators

Various types of calcium (Ca) channels (calcium-selective cell membrane gates that can be opened or closed by the nerve cell) that can be classified according to their physiological and pharmacological properties, exist in the brain. For example, L-type and N-type Ca channels have been pharmacological targets for the treatment of neurological dysfunction after brain hemorrhaging, stroke, dementia, and psychiatric disorders. Up to now, T-type channels have not been therapeutic targets for CNS diseases, and there are hardly any chemical compounds available that are sufficiently selective to investigate their therapeutic potential.

T-type Ca channels appear to play an important role in neuronal network activity. A disturbance of T-type channels has been associated with epilepsy, and there is evidence that T-type Ca channel activation could help to normalize brain function. BestPharma's scientists suggested the research project because of its strong innovative potential. They were aware of the high uncertainty related to the project but were, at the same time, convinced of a tremendous upside potential inherent in it. Based on current knowledge, the scientists had two illnesses in mind in which T-type channel modulators might show pharmacological benefits: sleep disorders and epilepsy.

Project 2: Serotonin Receptor Modification for Stroke

Serotonin is one of the neuromodulators in the CNS. Neuromodulators regulate the excitability of neurons. The impact of serotonin on neuronal activity depends on the type

of membrane receptor which is available: an interaction with serotonin-1A receptors decreases neuronal excitability, whereas an interaction with serotonin-2 receptors increases excitability.

One of the most important events leading to neuronal degeneration after a stroke is excessive neuronal excitation. Thus, it was assumed that stimulating the serotonin-1A receptors and suppressing the serotonin-2 receptors should mitigate stroke damage, a theory supported by animal experiments, and combining both approaches might strengthen further the benefit. Indeed, such a synergistic activity had been demonstrated at BestPharma in an exploratory animal study showing that the pharmacological effect of this combination went beyond the effect of either of the two receptors alone. However, combining two chemicals with different kinetic properties is not the preferred approach because of possible interactions. Since BestPharma's chemists had extensive experience with compounds active at serotonin receptors they suggested a research program to synthesize hybrid compounds with the desired activities at both receptors and to investigate the beneficial effect of the combination in greater detail. It was argued that, despite intensive research efforts in other companies, there was as yet, no stroke therapy available. This represented an opportunity for developing innovative products.

Project 3: L-type Calcium channel suppression for dementia

There is experimental evidence that neuronal Ca overload contributes to the degeneration of the brain in dementia. This has been confirmed by reports about disease-modifying effects of Ca channel suppression in patients. Unfortunately, the observed effects have not been very robust, and there is no treatment available as yet that effectively delays deterioration in dementia patients. One reason for this may be that dementia has many causes that possibly require several therapeutic approaches in parallel.

BestPharma's scientists suggested a research program to develop L-type Ca channel antagonists (suppressants) that had also potent anti-oxidative effects, because cell membrane oxidation appeared to contribute to neuronal degeneration in dementia. Furthermore, since good anti-depressive activity had repeatedly been observed with Ca channel antagonists, a development candidate should also have effects in animal models of depression. It was assumed that a disease modifying compound with positive effects on behavior would be extremely beneficial for patients and care workers and would offer a competitive advantage.

Project Comparison

Thus, three large programs were candidates for funding, but the question was how to decide how many of them, and which ones, to choose. The company traditionally looked at three important criteria to assess the potential of a research project. One was medical need, defined as a combination of the severity of illnesses to be treated and the

existence of other drugs already used to treat them. The second was the innovative character of the product. Both these dimensions were estimated qualitatively on a scale of one to five. Finally, a rough estimate of the potential market size was made, by representing the "available patient days," or the annual number of people affected by the illnesses in question, times the average number of days a patient would remain under treatment. Available patient days is a common estimate used in the industry. In order to arrive at a monetary estimate of the market size, patient days would be weighted by the (roughly) estimated price one might be able to charge for one patient day, i.e., the price of a one-day dosage.

Stroke patients are rare, and they do not stay in the hospital for very long, so the annual number of patient days for the serotonin channel product were estimated at only 0.7 million. For the L-type and T-type calcium channel projects, in contrast, a large potential of 2 billion and 1 billion patient days, respectively, was seen. However, a stroke patient would pay much more for treatment, so the potential revenue from a patient day was estimated at $1,000 for serotonin and only $2 and $1.50 for L-type and T-type calcium channel drugs, respectively. This information is summarized in Figure 1.

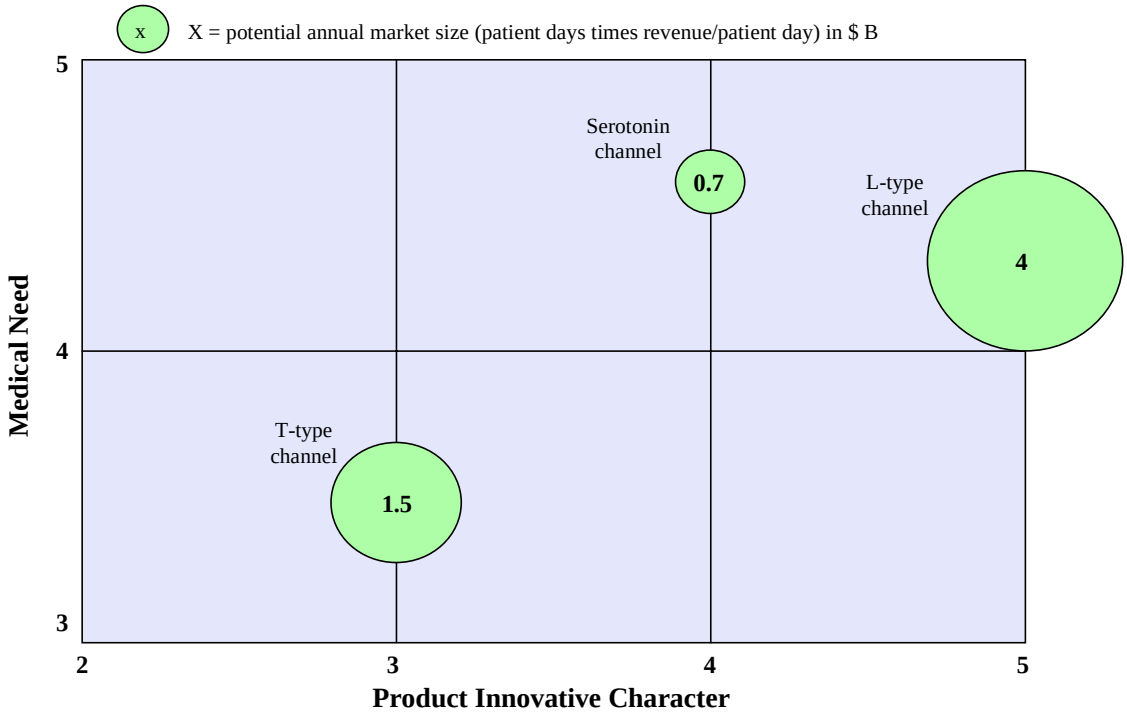

Figure 1: Qualitative portfolio assessment of the projects under discussion

Management felt that they could reasonably undertake only two of the three projects, in particular, those with the highest potential and the highest confidence in the robustness of the chemical activities. Figure 1 indicates that the T-type Ca channel project was dominated by the others, scoring lowest both on product innovation and medical need. Researchers in the group were mesmerized by the huge potential market size for the L-type channel drug and the outstanding medical need for the serotonin channel project.

The T-type channel was very innovative from a technical point of view, attempting to utilize a new neuronal mechanism to treat epilepsy and sleep disorders. However, from a market point of view, these illnesses did not look particularly new or innovative.

However, the portfolio could potentially be misleading because potential market size is very different from actual profitability – costs, market penetration, and achievable market share all intervene. A better financial analysis had the potential to change the apparently emerging prioritization. A standard net present value assessment of cash flows was not usually undertaken because financial estimates were still much more uncertain than during clinical development projects, where accurate market and risk assessments could be developed. Still, one of the researchers in the group proposed to undertake a financial analysis, which was to represent, to the best of the group's knowledge, the upsides and risks of the three projects. The researcher insisted that this was the only way to really find out whether the T-type Ca channel was less attractive than the others.

Financial Analysis for the Three Research Projects

As a first step, costs and success probabilities by phase were estimated for all three projects based on input from the technical experts. The estimates are shown in Table 1. The format of Table 1 is commonly used in the pharmaceutical industry.

The projects follow common phases: molecule screening, animal research, pre-clinical development, clinical development (phases I to III), and market launch. Each phase is shown with duration and expected costs (which can be estimated based on past experience with comparable projects). In addition, the researchers estimated success probabilities per phase, representing their best risk assessment based on the innovativeness of the molecule and the treatment pursued. The probabilities represented, for example, the likelihood that the pharmacological effect seen in the laboratory would be replicated in animals and humans, and that no severe side effects would appear. In addition, separate probabilities were estimated for cancellation of the project during research and clinical development due to external market developments (e.g., new market trends or competitor moves). Finally, the probability of "late failure" captured the risk that side effects would force the drug to be taken off the market after introduction. This had recently happened, for example, in the case of the anti-obesity drug Redux. Historical statistics for late failure existed by molecule class. Historical statistics were not ideal, but no information about the actual probabilities was available at that time, and estimating these risks from historical data seemed better than ignoring them altogether.

Project Phase	T-type Ca channel Project				L-type Ca channel Project				Serotonin Project		
	Duration (years)	Cash Flow ($ M)	Success (probabil.)	External Failure (prob.)	Duration (years)	Cash Flow ($ M)	Success (probabil.)	External Failure (prob.)	Duration (years)	Cash Flow ($ M)	Success (probabil.)
Screening											
Chemical synthesis and substance screening	1.5	-3.5	50%		0.5	1.5	0.8		0.75	-1.8	0.6
Secondary screening					0.5	1.5	0.8				
Animal Models											
Animal models first indication	1	-3	40%	10%	1.5	-5	70%	15%	0.75	-2	60%
Animal models second indication			70%	(market)*				(market)*			40%
Preclinical development (animal toxicology and pharmacokinetics, chemical development, safety pharmacology)	1.5	-6	50%		1.5	-6	50%		1.5	-6	50%
Clinical program first indication			sleep disorders								stroke
Phase I	1.5	-2.7	70%		1.5	-4	70%		1.5	-2.7	65%
Phase II	1.5	-5.4	60%	15%	2	-20	50%	15%	2	-10	55%
Phase III	2	-36	80%	(market)*	4	-70	60%	(market)*	2.5	-50	75%
Clinical program second indication (starts after phase II of 1st indication)			epilepsy								head trauma
Phase I	2	-4	70%						1	-2	70%
Phase II	2	-8	55%						2	-8	45%
Phase III	3	-40	70%						2.5	-45	70%
Annual costs in parallel to clinical development, independent of number of indications (e.g., galenical, technical, manufacturing)		-3				-3				-3	
Launch and profits first indication			sleep disorders								stroke
Pre-marketing costs first indication	1	-50			1	-70			1	-50	
Probability of approval			80%				75%				90%
Launch first indication		-60		3%		-60		4%		-70	
Expected profits over patent life (first indication)	13	1,787	+/- 60%	(late failure)**	10	2,329	+/- 70%	(late failure)**	13	2,029	+/- 70%
Launch and profits second indication			epilepsy								head trauma
Pre-marketing costs second indication	1	-50							1	-50	
Probability of approval			80%								90%
Launch second indication		-50		3%						-70	
Expected profits over patent life (second indication)	7	502	+/- 80%	(late failure)**					10	1,682	+/- 50%
Project NPV (all cash flows discounted and weighted by probability)		**12.1**				**3.6**				**18.7**	

Discount rate: 10%

* External failure "market" refers to project cancellation due to external market reasons

** External failure probability "late failure" refers to product failure in the market due to newly discovered side effects, or adverse market developments

Table 1: NPV analysis for the three projects

After screening, the T-type calcium channel and serotonin molecules were believed to possibly yield two drugs for different treatments, epilepsy and sleep disorders, and stroke and head trauma, respectively. It was customary in the company to pursue one "lead" indication first, and then start clinical development of the second indication after phase II of the lead indication was completed. This procedure is shown in Table 1.

Marketing specialists provided estimates of the lifetime profit potential of each prospective drug, based on reasonable assumptions about its efficacy and introduction timing. Their estimates are shown in the form of the expected drug life cycle (to the end of the 20-year patent protection period) along with the discounted (back to the point of market introduction) present value of the resulting profit. The discount rate used is BestPharma's cost of capital (see Insert 1 for a discussion of the right choice of discount rate). At this point, the market estimates were subject to substantial uncertainty, which is expressed by variances in the profits. For example, the profits of the epilepsy drug could vary from the expected value by as much as 80%.

The financial analysis is summarized by the "project NPV", shown at the bottom of Table 1. The NPV includes all costs and revenues from the research project, weighted by their probability of occurrence and discounted back to the present. This takes into account the fact that costs and revenues in later phases are only incurred if the earlier phases are successful.

The financial analysis did not "rescue" the T-type channel project as the researcher had hoped. The serotonin project came out best, with a project value of $18.7 M, while the L-type channel project offered the lowest value with $3.6 M, and the T-type project was in the middle with a value of $12.1 M. The T-type project was the most innovative of the three, and the researcher who had proposed the financial evaluation believed that it had value. Was this belief simply wrong, or was there something that the financial analysis did not capture?

Decision Trees: Understanding the Nature of "Options", or Managerial Flexibility

The NPV analysis in Table 1 corresponds, in fact, to a *decision tree*. Such a tree is shown in Figure 2 for the T-type Ca channel project. A decision tree explicitly represents the sequence of decisions (represented by squares, or "decision nodes") and of uncontrollable, probabilistic events (represented by circles, or "chance nodes"). The tree begins with the decision to undertake the project. If the decision is "yes," screening requires an investment of $3.5 M over 2 years, at which point there is a 50% chance of success or failure. In the case of success, a primary (sleep disorders) and, with a delay, a secondary indication (epilepsy) can be pursued.

Insert 1: How to discount cash flows from a research project

According to financial theory, efficient financial markets can provide an evaluation of an asset's riskiness. The appropriate "risk-adjusted discount rate" can be found by identifying market-traded and priced securities whose volatility is correlated with the project in question. A portfolio of cash and the traded assets can be constructed, which replicates the project's payoffs exactly. The price of this portfolio then implies the discount rate for the project. Unfortunately, the risks of a research project are typically project-specific and cannot be replicated by securities traded in financial markets.

In this case, it makes sense to represent *explicitly* all project risks in the evaluation procedure rather than treat risk via a discount rate. This implies using the risk-free discounting rate. For the evaluation of a research project, this does not mean the interest rate of government bonds (which is currently around 3-4% in Europe). A company should, at least, earn its own cost of capital in order to create economic value. Thus, the weighted average cost of capital (WACC) of the firm is a reasonable discounting rate to use.[1)] The key is that *no risk premium* is added to the discount rate; rather, the same rate is applied to all projects. BestPharma's WACC was 10%.

This holds if R&D funds are not scarce. If funds are limited, and thus, projects compete for resources, undertaking one project incurs *opportunity costs*: the value from another, displaced, project is lost. In this case, the appropriate discount rate reflects the *average return on investment* from all R&D projects. This is typically much higher than the WACC; in the pharmaceutical industry it varies between 20 and 30%.

In the case of BestPharma's CNS business unit, funds were *de facto* not scarce. One researcher remarked: "If we had a good idea and could back it up, the funds could be found. The research budget could vary substantially depending on the project proposals made." Thus, BestPharma's WACC is used in the analysis throughout.

Recommended literature:

[1)] Dixit, A. K., and R. S. Pindyck, "The Options Approach to Capital Investment," *Harvard Business Review*, May-June 1995, 105 – 115.

On top of each decision node is the expected value of going forward (future cash flow probability weighted, taking into account future decisions, and discounted). Figure 2 is somewhat aggregated in comparison to Table 1, in order to focus on the big picture of the strategic decisions corresponding to the project. For example, clinical development is shown as one phase, although there may be failure or cancellation after phases I, II or III. The success probability at the end of clinical development correctly reflects the full information: for example, the 23% shown for the sleep disorder indication are the product of the three clinical phase probabilities, combined with the probability of approval and the probability of external failure during development. Similarly, the project value incorporates all costs weighted by their probabilities of occurrence.

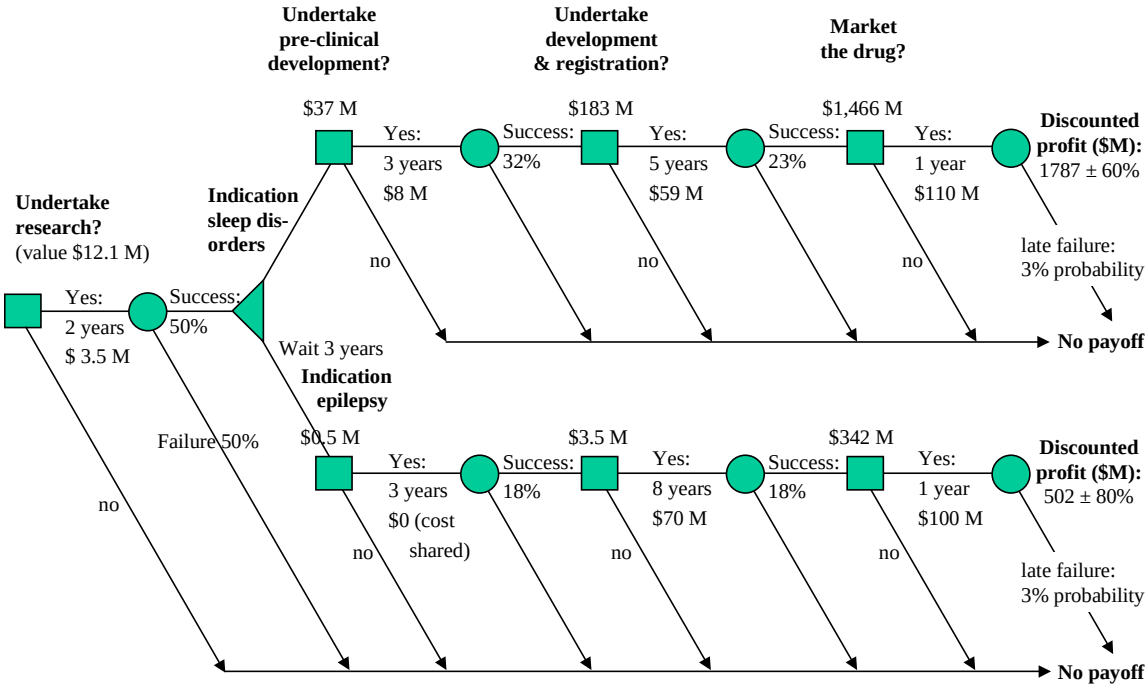

Figure 2: Decision tree corresponding to T-type Ca channel project

The tree in Figure 2 makes the project more *transparent* than the NPV Table 1 in several ways. First, the tree graphically shows the sequence of events (chance nodes) and decisions. Second, it shows clearly how the value decreases as one goes backward in time toward the beginning from the huge profits at the end. This is due to the combination of success probabilities (payoffs are only carried forward if *all* subsequent phases are successful and if continuation is chosen in the future) and discounting. Third, the decision tree demonstrates that the analysis already assumes considerable management discretion: at each decision point, a choice of go/no go will be made depending on the future payoffs (if they are negative, cancellation is preferable). In option theory terminology, these decisions are referred to as *abandonment options*. The project can be canceled if continuation is no longer worthwhile. If the project is continued regardless of the success in a given phase, costs are incurred without the chance of future revenues, and the project value decreases precipitously.

Based on the improved transparency about the analysis assumptions gained from the tree, we can now revisit the question asked by BestPharma's researcher: Are these *assumptions appropriate*? Is there additional hidden value in this research project, and if so, how have we missed it so far? Looking at the tree, we can ask several questions about hidden value: is the *timing* of decisions versus information correct? Are the *branches of the tree* correct, i.e., have we captured all possible events and actions BestPharma can take? Is the estimated *timing* for the phases correct? Are the success *probabilities* correct? By systematically examining these questions, we can find out more about the full value of the project.

Capturing the Full Value of the T-Type Ca Channel project

Timing of Decisions vs. Information

The heart of a strategic option is that it represents *managerial flexibility, or the ability to react to (at present uncertain) contingencies as they arise*. In other words, decision flexibility is only valuable if it can be executed *after* a contingency occurs or new information becomes available. Therefore, it may be valuable to *delay commitments* (such as a decision) until after information arises, or to *"pull forward"* information, for example, by performing thorough market research. This can be demonstrated in the case of the epilepsy treatment. The assumption in Figure 2 is that the decision to market the drug has to be made before the market uncertainty has been resolved. Profits may vary by up to 80% above or below the estimate. This could, for example, lead to a situation where profits are only worth $100 M (discounted to the launch year). In addition, there is a 3% chance of late failure. At the same time, pre-marketing and launch costs are $100 M. Thus, the drug may actually incur a loss. This is shown in the left part of Figure 3, where the market uncertainty is explicitly shown as a three-valued distribution (25% chance of best or worst case, respectively).[1]

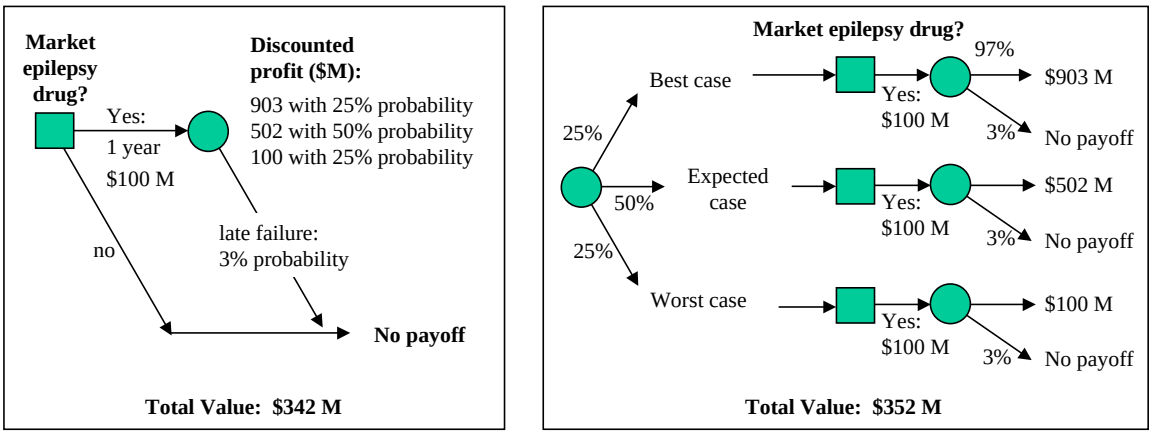

Figure 3: The value of resolving uncertainty before a decision

Now, imagine that, through market research, market uncertainty can be resolved *before* the launch decision is made, as is shown in the right part of Figure 3 (only late failure uncertainty remains after the launch decision; its sources are unforeseeable). In this case, BestPharma knows the market scenario before the launch costs are committed. Thus, they can decide not to launch the drug if they find themselves in the worst case scenario where expected profits are negative. The right decision in the worst case is to abandon the project. This avoidance of a loss results in an enhancement of the expected launch value by $10 M (to $352 M). *Resolving uncertainty before a decision* creates, in

[1] For easy exposition, this distribution is simple. The logic holds also for more complicated distributions.

this case, an additional abandonment option worth $10 M.

Note that this option is not worth anything if the project makes money even in the worst case. In this case, the left and right sides of Figure 3 are equivalent. In BestPharma's example, all treatments (except for epilepsy) are inherently so attractive at launch that indeed, resolving market uncertainty early does not create a substantial amount of value. The $10 M option in Figure 3 translates into only $0.1 M in added value for the T-type Ca channel project as a whole.

However, resolving uncertainty early may be a significant source of value in other situations. For example, imagine a situation where new information arises during the animal studies for the L-type channel project indicating that the success probability of pre-clinical development is reduced from 50 to 25%, and in addition, the external failure chance increases from 15 to 20%. In this case, one would decide to stop the project before pre-clinical development, thus avoiding an expected loss of $3 M in an early phase of the project.

This example has two important implications for R&D managers: first, *update all project information in the tree as often as possible* as the project progresses. The information in Table 1 is only the best estimate at the beginning of the project. As new information becomes available, the critical points where flexibility is relevant may change. Second, *understand where changes in the estimates may make flexibility critical*, i.e., perform sensitivity analysis on key parameters in the tree (payoffs and probabilities). The example above tells the manager to watch out for the latest estimates of the pre-clinical development success chances, and to reserve some discretion about the project (with respect to possible emergency measures or cancellation) at this point in time. In contrast, a change in the profit distribution (e.g., a change of the worst case) will not make more flexibility necessary, as the project will be so attractive at launch that some volatility will not change any decisions at all.

Creating Additional Branches in the Tree: Strategic Expansion Options

The researcher who believed in the value of the T-type channel remembered that often, new and unexpected drugs, other than the original targets, may arise from a given molecule that is screened. He asked his fellow scientists to think about additional applications related to the physiology of T-type channels. When asked, the scientists also mentioned head trauma and cognition enhancement for symptomatic treatment of dementia. Since L-type Ca channel modulators have been demonstrated to delay age-associated neuronal dysfunction in rats, the scientists assumed that T-type channel moderators might even have an additional disorder-modifying effect in dementia which would give them a competitive advantage compared to currently available cognition enhancers. As two indications already represent a promising target for a molecule, no-

body had considered these additional indications, even though they seemed as promising as the first two. Following some inquiry, the researcher was able to obtain project information of the same quality as for the two primary indications.

The researcher also analyzed files of previous research projects addressing ion-channel modulators that had been pursued at BestPharma and, as far as available, files of competitors. To his surprise, he found that in 60% of projects, additional drug indications had arisen, which had not been initially foreseen by the experts! Typically, such unforeseen applications of a molecule were further therapeutic indications and related development programs, which often had significant value. How could such a further source of value be incorporated in the evaluation, as nothing specific was known about such an unforeseen application? After some discussion, the group decided that it was reasonable to assume the *average* value of the other four drugs, but delayed for 3 years, as the additional opportunity typically arose during clinical development.

The additional applications are included in the project evaluation in Figure 4. It is assumed that head trauma and dementia clinical development would start together with that for epilepsy. The detailed project data for the two new applications are not shown here, as they look qualitatively similar to those for the two primary drugs. Figure 4 shows that acknowledging the three additional drugs almost doubles the research project value from $12.1 to $22.1 M.

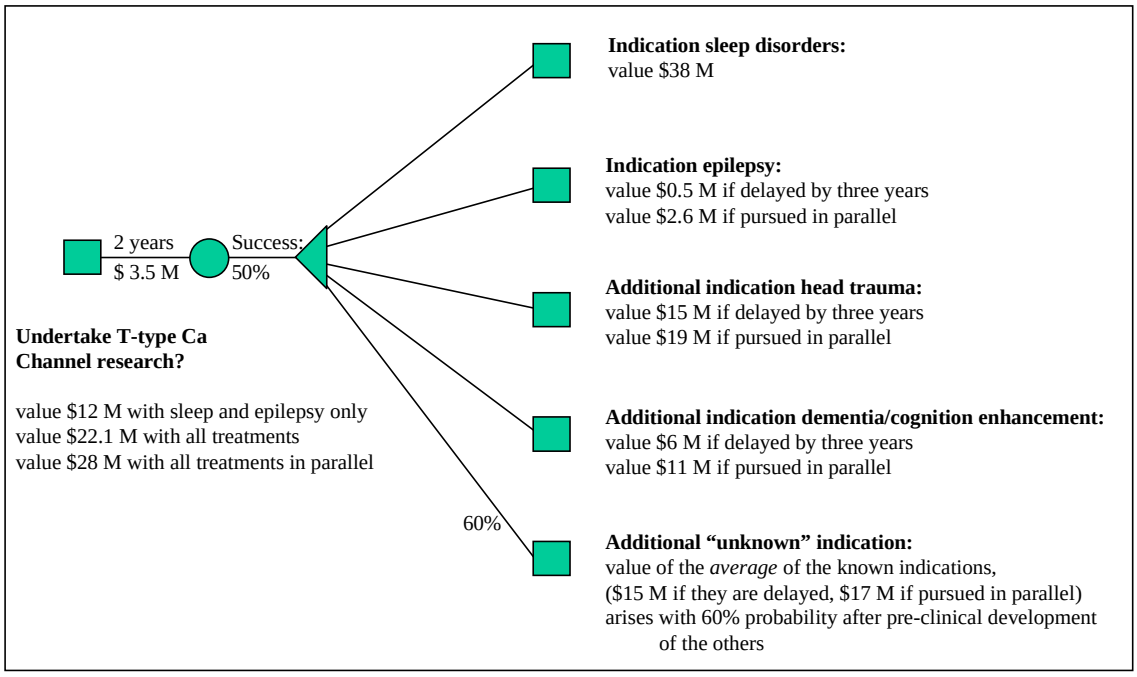

Figure 4: Value of the T-type channel project with strategic options

A further value enhancement indicated in Figure 4 is the *timing* of clinical development. Originally, it had been assumed that all other applications would go into clinical development only after the primary drug had reached phase III. This was the standard proce-

dure, traditionally adopted because sometimes additional information became available from the primary drug that could help the development of the others. It was also traditionally recommended, for capacity reasons, not to pursue more than two drugs in parallel. However, with some outsourcing and recent project management changes, BestPharma did have enough development capacity to execute four clinical developments in parallel. Moreover, the information gained from developing the sleep disorder drug first was considered negligible, as the drugs were less similar than in previous cases where cross-drug learning had occurred.

Thus, it seemed reasonable to push for pursuing all indications at once. This had a doubly positive effect: First, the drugs would have three more years before going off patent, significantly boosting their lifetime profits. Second, project payoffs would occur three years earlier, increasing their discounted value. As a result, parallel execution would increase the T-type channel project's value further from $22.1 to $28 M. It now looked two-and-a-half times as attractive as initially thought, taking into account strategic expansion options as well as more aggressive timing.

For comparison, the same exercise of identifying additional sources of value was performed for the other two research projects. On further prompting from the scientists, an additional possible application was also identified for the serotonin channel project. BestPharma's experts estimated that the chance of this occurring was (at 40%) somewhat lower than for the T-type Ca channel because the serotonin molecule was more specific, which left less potential for unexpected uses. Assuming the additional application and parallel execution of the primary and secondary indication (analogous to Figure 4) resulted in a total value of $25.5 M for the serotonin project.

No additional possible application was seen for the L-type Ca channel project. Because the proposed research program was highly specific for dementia, additional development programs aiming at other therapeutic treatments were highly unlikely. The project's value remained at $3.6 M.

In summary, the financial analysis including the identifiable strategic options assigned the highest attractiveness to the T-type channel project, followed by the Serotonin project, and the L-type as a distant third. Although the T-type Ca channel project seemed dominated on product innovation (in the eyes of the market) and medical need according to the qualitative portfolio assessment, it seemed to offer the highest financial attractiveness due to its potential for additional offshoot applications. Strategic expansion options had a major impact on project value.

Insert 2: Real Options Analysis and Volatility

Option value stems from managerial flexibility. Flexibility is valuable if *volatility* is

present or, in other words, if contingencies arise to which one needs to react. Examples of volatility in Table 1 are technical project risks (side effects or lack of chemical activity) and market risks (cancellation due to market reasons during research or development, as well as refusal by the regulatory agency to approve the product).

How can the full volatility of a project be captured? It has been proposed to use the analog of the Black-Scholes financial options pricing formula to understand the effect of volatility.[2] This approach provides a very useful qualitative metaphor for understanding the drivers of project value: first, the inherent profitability, measured by the ratio between the profits and the costs of the project (Timothy Luehrman calls this "NPV_q"), and second, the volatility, measured by the annual payoff variance σ and the time to market (combined with the factor $\sigma\sqrt{t}$ by Luehrman). Both drivers increase the project's value: the ratio of benefits and costs expresses the underlying economics, and $\sigma\sqrt{t}$ captures the opportunity to take advantage of contingencies, which increases with volatility and time.

While this approach offers a good conceptual characterization of real options value, it is too aggregate to derive quantitative estimates for R&D projects. A "variance per year" σ is a simplifying fiction – research projects suffer from discrete risks, which do not uniformly add up over time (or project phases). Moreover, the up- and downside of volatility do not build up symmetrically over time, as the Black-Scholes model assumes. Downside stems from technical or market risks, and upside from booming markets, new uses or surprising efficacy. These are generally *not* symmetric.

Finally, the value of a strategic project representation comes from a *transparent characterization of major volatility sources*, both up- and downward, in order to be able to track and manage them later. A single aggregate factor for the whole of the project results in a "black box" model that may obscure sources of risk rather than highlighting them.

An alternative approach to capturing option value, adopted in this article, is to use *decision trees*, which *explicitly* represent risks and *decision points* where flexibility is valuable. Thus, this approach is well-suited to create transparency by identifying the sources of value. It has been shown that the decision tree approach is equivalent to the Black Scholes approach if the discount rate used in the tree is risk-adjusted.[3] For project-specific R&D risks, a risk-adjusted discount rate is not available, so discounting with the firm's weighted average cost of capital (WACC) is appropriate (see Insert 1).

Recommended literature:

[2] Luehrman, T. A., Investment Opportunities as Real Options: Getting Started by the Numbers, *Harvard Business Review*, July-August 1998, 51 – 67. See also: Leslie, K. J., and M. P. Michaelis, "The Real Power of Real Options," *The McKinsey Quarterly* 3, 1997, 4 – 22.

[3] Smith, J. E., and R. F. Nau, "Valuing Risky Projects: Option Pricing Theory and Decision Analysis," *Management Science* 41, 1995, 795 – 816.

Managerial Lessons Learned

In the example of BestPharma's research project portfolio, we have seen that a qualita-

tive portfolio representation of the candidate proposals may be misleading. A traditional financial analysis, on the other hand, is too narrow for a decision basis. We have shown that a decision tree is a useful tool to represent the key project risks, and the key sources of value, in a transparent manner, that allows managers to make informed decisions. In particular, the BestPharma example highlighted the following insights into how to capture the value from research projects in an evaluation.

Explicitly represent all foreseeable major actions that management can undertake. In other words, make sure you have not left out any decision *branches* or *expansion options* in the tree, as they may be major sources of value. This requires a strategic viewpoint and creative thinking. As we saw in BestPharma's example, it is natural to think along the lines of past projects, without taking into account additional applications or actions that may be possible for the current project. In fact, expansion options turned out to be a major value contributor for the T-type Ca channel project.

Represent key uncertainties. It is most important to *recognize* them in the decision tree (*have* a chance node), rather than be overly concerned about the exact probabilities. Sources of major risks may be *technical* (e.g., technical challenges, side-effects, or manufacturing problems), *organizational* (e.g., changed management priorities), *competitive* (preemption by a competitor), or in the *market* (e.g., market trends, or meeting customer demands). In pharmaceutical development, *regulatory* risks may also be significant (changes in health care policies affecting the approval of a drug).

Represent important decision points, and understand what their timing is relative to the resolution of uncertainties. The higher the volatility of payoffs, the more important it becomes to *delay decisions* and commitments until key uncertainties are resolved. In other words, *high uncertainty makes flexibility more valuable*, and management may be willing to pay for this flexibility. A "payment" may also take the form of a willingness to suffer some operational inefficiencies in order to maintain decision flexibility, for example, by maintaining two alternative dosages throughout clinical development (causing higher costs) in order to be able later to respond to regulatory or market uncertainties. Another example is building a flexible (and thus, more expensive) manufacturing plant that can be switched over to an alternative drug if the first one is not successful.

Update all information as you "go along through the tree" (as time unfolds), and adjust the decisions as more is learned and uncertainty is resolved. *Initial information about uncertainties and payoffs is bound to change over the course of a project.* The critical points where flexibility is relevant are where an additional branch of the tree may become available (expansion option), and where a loss may occur (abandonment option). Understand where changes in the estimates may make flexibility critical, *and reserve some discretion about the project (with respect to possible emergency measures*

or cancellation) at such critical points in the project. For example, continuation of pre-clinical development for the L-type Ca channel project was sensitive to possible changes in probabilities, while the decision to launch was insensitive to such information updates, as the drug was extremely attractive at launch.

Discount at the firm's cost of capital if funds are not scarce, and at the return rate of other R&D projects (that is, the "opportunity cost") if funds are scarce and the project displaces other projects. Do not apply a "risk premium" hurdle – hurdle rates are arbitrary for R&D projects because the financial markets cannot provide pricing information. Representing the important risks explicitly in the tree provides more transparency about a research project than hiding them in a hurdle rate.

No decision support framework "decides" for a manager, relieving him or her of the responsibility of making a call. What decision frameworks can contribute is making the key features of a problem salient, and helping the manager think them through. Understanding the strategic value drivers of a research project, and where flexibility adds to the project value, is a critical problem for R&D managers. Sometimes, the source of value is not where one expects it, as BestPharma's example shows. The framework presented in this article can be a useful tool to master this challenge.