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A Preliminary study on Valuing Pharmaceutical R&D Projects by using Real Option Method

– A Tentative Model for Mevalotin's Case

○Luo Yongshun, Takao Fujiwara (Toyohashi University of Technology)

1) Introduction

With the intense competition in product market, the growing desire for new medicines has driven the pharmaceutical R&D into a 'high-risk-high-return' field. Companies are spending 20% of the revenue and more than ten years' of time in pursuing development of a brand-new medicine, while the uncertainty is extraordinarily high. However, the classical financial tools, such as net present value, which are inclined to underestimate the value of successful projects, are no longer suitable for evaluating risky projects. Recent years, real option theory is noticeably used in valuing R&D projects. In contrast to real property and real commodity options, it is difficult to accurately predict 'discoveries' or estimate future unit sales of developed products, and there is no established forward unit price market. Furthermore, the management has the flexibility to alter the R&D investment timing, amounts and/or ultimate project, or downsize or abandon the R&D. By doing so the optimal investment will be achieved and the opportunity cost will be minimized.

This article is a preliminary study on the real pharmaceutical R&D option. By analyzing the characteristics of pharmaceutical R&D process and reviewing the existing models, it is trying to set up an acceptable tentative model.

2) The Characteristics of Pharmaceutical R&D

. The research in screening stage is on the base of individual work. And the technological uncertainty is so high that the possibility of finding useful compounds is almost unpredictable. The management must decide, to what extent compound candidates should be included to ensure that the promising one is not omitted from the list.

. Uncertainty accompanies the whole process of pharmaceutical R&D. Almost in every stage of the process, risks come up with the form of virulence, or serious side effect, which will possibly invalidate the whole project. The flexibility of decision implies that management has the ability to alter, defer or abandon the project in reacting to the changing situation to limit the downside risk of loss.

	Screening stage	Development stage	
		Preclinical phase	Clinical phase
Probability of success	1/1000	1/2-1/3	1/2-1/3
Developing cost	100 million-200 million Yen	About 1 billion Yen	1 billion-10 billion Yen
Developing subject	individual	organization	organization

Table 1. The probability of success and developing cost of different stages of Pharmaceutical R&D of Japan's Pharmaceutical companies.

Source: Kenichi Kuwajima and Nobuo Takahashi *Organization and Decision-making.*

. The later the stages come, the higher does the R&D cost. The expenditure increases sharply with the unfolding of phase I, II, and III. The candidates should be carefully selected on considering the balance of minimal cost and minimal opportunity cost.

3) The Existing Research on Pharmaceutical Real R&D Option

. Application of the Geske Model (Perlitz, Peske and Schrank, 1999)

In this application, the pharmaceutical R&D process is split into two decision-making points. Point 1 serves for identifying active substances out of numerous possible compounds, where screening is over and the preclinical phase is to start. And point 2 is when phase III is finished and prepared for market introduction. Both opportunities form a compound option. By assuming that the value follows the usual 'gBm' process, the compound options can be valued analytically in terms of integrals of the bivariate normal distribution.

$$C = Fe^{-r\tau}M(k,h;\rho) - Ke^{-r\tau}M(k-\sigma\sqrt{\tau^*},k-\sigma\sqrt{\tau};\rho) - K^*e^{-r\tau}N(k-\sigma\sqrt{\tau^*})$$

where $h = \dfrac{\ln(F/k)+\frac{1}{2}\sigma^2\tau}{\sigma\sqrt{\tau}}$, $k = \dfrac{\ln(F/F_c)+\frac{1}{2}\sigma^2\tau^*}{\sigma\sqrt{\tau^*}}$, $\rho = (\dfrac{\tau^*}{\tau})^{\frac{1}{2}}$

$M(a,b;\rho)$ = bivariate cumulative normal distribution function with a and b as upper and lower integral limits, and correlation coefficient ρ.

F = present value of the cash inflows of the commercial venture.

F_c = critical value of the project above which the first call option will be exercised.

K = present value of the capital expenditures of the commercial venture.

K^* = present value of first year capital expenditures of the pioneer venture.

. There are other trials using Poisson process or the mixture of Poisson process and 'gBm' in order to reflect the contingence character in Pharmaceutical R&D. The famous ones are Merton(1976), Ott(1992), and Willner(1995) (reference 1). The latter I'd like to cite in the following part.

4) Mevalotin's case study and an application of real pharmaceutical R&D option

The development process of Mevalotin is reviewed by table 2.

At the preliminary stages, the effectiveness of the compound is attached more importance than economical prospect in making the go or no-go decision. The decision is made totally based on the result of screening. The comparably low cost during the preliminary stages brings down the hurdle, and drives the researchers into 'cost unconsciousness'. Finding an effective compound is viewed as an accidental event in this stage.

When the research enters preclinical phase, cost mounts up to a noticeable degree and the unpredictable failure can drag the total project into life-or-death edge. The usefulness, MOS (margin of safety), serious side effect, and in the case of Mevalotin, the species difference may act as an obstacle in carrying on the project. In this occasion, management should respond to the accidental events that

Event	Time spent(year)	Decision-making
Screening for inhibitor of cholesterol synthesis, ML-236B was found	1.5	Developed as promising compound
Preclinical with rats failed, 3 years passed until species difference was revealed	3	Go or no-go
For high MOS, pravastatin sodium was found and developed	8	Choose the best compound through trial and error method
Clinical 3 phases	4	Deal with the unfavorable data
Market introduction		License out or not

Table 2. The process-influence events in the development of Mevalotin, the time spent and the decision-making. Positive and negative events are included and the management is supposed to react accordingly. Source: Yoshio Tsujita (2001) , The development of Mavalotin.

have turned into unfavorable ones. In principle, Poisson processes can be dealt with both positive and negative occasions.

Willner's model is often cited for the real option venture. He supposed the dynamics of venture growth values are given by a jump process as:

$$\frac{dP}{P} = \mu dt + (\gamma - \delta) d\prod(Q)$$

where γ is the percentage change in P if there is a discovery, δ is the percentage reduction in P due to a concurrent entrance of competitors, and Π(Q) is a Poisson process for the occurrence of jumps with intensity Q.

Here the probability of the occurrence of jump is deemed as one constant λ, while as we know, the probability is different according to the stages, even among phase I, II, and III. It's necessary to treat it as a variance that changes with time spans. And in a deeper sense, it is functional on the accumulated experience, serendipity and R&D effort. Jump process should be split into two parts representing the different directions. Let the equation

$$\frac{dP}{P} = \mu dt + \gamma d\prod(Q,\lambda) + \gamma^* d\prod(Q,\lambda^*)$$

represents the pharmaceutical R&D project value, where λ is the positive possibility of jump event and λ^* is the negative one. γ, γ^* stand for the percentage changes in P in the two cases separately. The competition factor disappears since the competition in R&D differs from that in venture capital.

The possibility of jump is endogenized to depict the varied risk level in different R&D stage, and the classification of positive and negative jump events helps understand the different influences the events have on the valuation of the project.

5) Conclusion and future research

The high uncertainty in risky projects requires a fresh evaluation on the pharmaceutical R&D. At

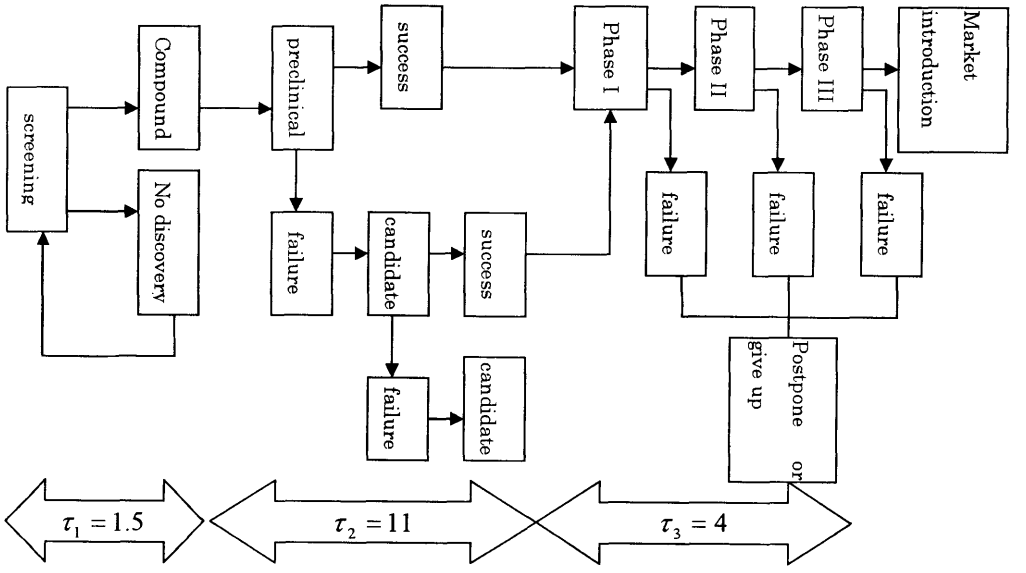

Figure 1. Pharmaceutical R&D process. The time span is in reference to Mevalotin's case.

different stages, management has the flexibility to react to the unexpected jump events. This flexibility creates the real options. In pharmaceutical R&D, the probability and the property of the jump events change as the stages move on. And this requires a new insight in modeling the process. In this article, a modified model, which includes the above idea, is raised for discussion.

By reviewing Mevalotin's case, we also find that the discovery is not totally elusive, but has theoretical connection with factors like accumulated experience, serendipity and R&D effort. This is thought to be a meaningful subject. The competition of pharmaceutical R&D also gives important impact on decision-making, which is to be analyzed by game theory in future research.

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