Real Option Analysis (ROA) opens Innovation: the biopharmaceutical case

Gianluca Enea[1], Giovanna Lo Nigro[2], Azzurra Morreale[2]

[1]Ernst&Young - Financial and Business Advisors
[2]Department of Chemical, Management, Mechanical Engineering and Computer Science
University of Palermo, Italy

gianlucaenea@gmail.com, giovanna.lonigro@unipa.it, azzurra.morreale@unipa.it

Abstract

Most of the Open Innovation (OI) investments can be characterized for their flexible nature that allows to the partners to abandon the project if it is no more appealing for their business model. Real Options Analysis (ROA) is acknowledged as a powerful and hard to implement tool to evaluate uncertain project that have an intrinsic flexibility. The research wants to foster the use of ROA in the OI field in order to encourage firms to undertake this innovation model; to achieve this goal the authors propose a closed form model easy to implement to evaluate OI initiative for selecting an optimal R&D portfolio. In particular authors focus their attention on the biopharmaceutical industry that shows ideal characteristics to exploit the benefits coming from OI; due to its focus on innovation, R&D process is extremely important in biopharmaceutical industry and the biotechnology advent has pushed the incumbents to sign OI agreements able to pool complementary resources. The study wants to support managers in the optimal R&D portfolio construction choosing the most promising products, the way the related project has to be undertaken (in an open or closed manner) and the auto-financing amount. The proposed model can be easily implemented in a worksheet and inputs needed to run it are usually request to evaluate project using the most used net present value based methods. Moreover, some parameters of the model allow to consider strategic aspects: for example the core/non core nature of the project, the project impending phase, the risk sharing.

Keywords: Open Innovation; Real Options Analysis; Biopharmaceutical Industry; R&D portfolio

1. Introduction and literature review

Open Innovation (OI) assumes that firms ''can and should use external ideas as well as internal ones, and internal and external paths to market'' to make the most out of their technologies (Chesbrough et al., 2006). The prevailing view is that through collaboration with others, holders of complementary expertise and resources, it is possible to access to information, tangible and intangible resources, technological knowledge extremely important in accelerating the timing of innovation, reducing the volume of investments necessary, sharing the economic and technical risk, increasing the quality of the final result (Powell et al., 1996). Many studies have focused on various aspects of the open innovation process. They offer useful insights and propose various frameworks to support managerial decision-making (Huizingh, 2010). Nevertheless, Gassman et al. (2010) recently noted that the internal process by which companies manage open innovation is still more trial and error than a professionally managed process. What is missing is a decent cookbook, an integrated framework that helps managers to decide when and how to deploy which open innovation practices.

Biopharmaceutical industry, in particular, has made extensive use of collaborative strategies due to the technology discontinuity in its core process, i.e. the way drugs are discovered since the mid 1970s. The pharmaceutical research process can be divided into two main phases: discovery and development. The first one aims at detecting new compounds; the second consists of a series of preclinical and clinical tests to check the safety and efficacy of the most promising compounds discovered in the previous step. Recently, pharmaceutical companies, to increase their efficiency, tend to develop commercial agreements with biotech companies in order to exploit the licensing of drugs and molecules discovered by them (Rogers et al., 2005). Biotechnology innovation, in fact, has been pursued largely through collaborative arrangements between new biotechnology firms (who accomplish the R&D) and established

pharma companies (who typically undertake clinical trials and marketing). This has generated an increasing number of inter-firm relationships between pharmas and biotechs where, pharmas need to understand the way they should form and manage alliances, facilitating the use of new technology platforms in a virtual manner (Gupta et al., 2007). The governance of these inter-firm relationships can vary from market like to hierarchy like solutions depending on some characteristics of the partners and of the transaction to be done (Lo Nigro et al., 2011). However, these agreements inevitably recall the paradigm of OI as a means of approach to research and development of new drugs.

The new methodologies of multidisciplinary research and development related to biotechnology favors, in fact, the development of original organizational models of the company, in which central element is the ability to pool around innovative and complex projects, a plurality of actors with different but complementary expertise, using exploration or exploitation as a paradigm of innovation (Nooteboom et Gising, 2006). Biotechnology companies rely heavily on strategic alliances with pharmaceutical companies to finance their research and development (R&D) expenditures (Nicholson et al., 2005). Furthermore the process of biopharmaceutical R&D can be modeled in steps: this allows to continue to the next step only if the expected results, estimated at that time, are satisfactory. The special characteristics of the process of pharmaceutical R&D therefore make necessary the use of assessment tools that fit them. These considerations inspired the idea of using the real options approach (ROA) for the financial evaluation of projects for pharmaceutical R&D because, unlike traditional methods, ROA allows to model the uncertainty and the flexibility inherent in the process itself (Vanhaverbeke et al., 2008). The evaluation of a single project, even if with ROA, could not be consistent with the firm's strategy that usually assumes a more comprehensive point of view; in order to encompass this limitation the whole portfolio of R&D project should be considered especially in this industry characterized by a very low percentage of success of potential new molecules that enter the R&D process and by long time to complete the entire R&D process (Rogers et al., 2002).

OI is an incentive to integrate technology management and innovation management (Licthnthaler, 2011) and this reinforces the need to evaluate the entire portfolio of R&D project rather than a stand-alone project.

Moreover OI provides an invaluable means to balance an innovation portfolio and share risk; moreover an actively managed portfolio demands judgments calls. The judgments may well be based on quantitative values and careful measurements but the shadow of false positive and false negative judgment persists (Alpheus Bingham and Dwayne Spradlin, 2011) and can be mitigated adopting evaluation method able to overcome the underrate problem inherent in the NPV based evaluation method such as the ROA.

Organizations, as pointed out by Hartmann et Hassann (2006), while recognizing the importance of the ROA, do not apply it because its perceived complexity. The models proposed in literature, Optfolio (Rogers et al., 2002) and Optfolio for alliances (Rogers et al., 2005) are very difficult to implement. Indeed, it seems hard to imagine that pharmaceutical companies can determine their own project portfolio optimization problem with hundreds of thousands of constraints and variables. The objective of this paper is therefore the development of a new model, called Open Optfolio Light (OOL), of lower computational complexity, which is useful in the selection of R&D projects in the biopharmaceutical industry, evaluated simultaneously within a portfolio, so as to consider the interdependencies in the exploitation of the same corporate resources. Project portfolio selection, in fact, is a

crucial decision in many organizations, which must make acquainted decisions on investment, where the appropriate distribution of investment is complex, due to varying levels of risk, resource requirements, and interaction among the proposed projects (Berzinsh et al., 2006). In addition, R&D activities are increasingly costly and risky and, as a consequence, measuring their performance and contribution to value becomes critical (Lazzarotti et al., 2011).

Studies on R&D portfolio management can be divided into three categories: strategic management tools, benefits measurement methods, and mathematical programming approaches (Wang J. and Hwang W. L., 2007). Moreover fuzzy set theory has been used to model imprecise and preference information in many applications. It can also be used to represent uncertain project information.(Kuchta , 2001).

In particular, the proposed model is based on the Optoflio mathematical programming method based on ROA (Rogers, 2002), but simplified to facilitate the spread among the companies (Enea and Lo Nigro, 2011a). In addition, the model considers the creation of a balanced portfolio, since it includes the possibility of self-financing products (Enea and Lo Nigro, 2011b), a tighter control of risk because it includes the option to license the R&D projects; the resulting model is named Open Optfolio Light (OOL) . The proposed model is therefore easy to implement in a spreadsheet and the input parameters required are those generally required, for the evaluation of a project, from traditional methods, such as net present value. In particular, the model is tested through a case study available in literature (Rogers , et al. 2002). The framework also is able to deal with variables that take into account the business strategy (choice of therapeutic areas in which to invest), and characteristics of possible partnership (level of synergy, profit sharing policy). The output of the model is the portfolio composition and for each selected drug it is able to suggest if it should be developed in house or through an alliance and if it will finance (and how much) other project in the pipeline when it will be commercialized.

In the next section the OOL model is presented; in section 3 it is tested through a numerical example and section 4 discusses the obtained results and suggests further developments.

2. The Proposed Open Optfolio Light (OOL)

Let us recall some assumption of the Optfolio Light model (Enea and Lo Nigro, 2011a) made to reduce the computational complexity of the original Optfolio model (Rogers et al., 2002). First of all, the R&D process is modeled through *compound options* in the case of drugs that still have to bear more than two phases, and through *development options*, in the case of drugs with only two stages to support, in order to replace, in their assessment, the complex binomial model, respectively, with the model of Geske and Black and Scholes formula (in case of project in the last phase of development, the NPV can be used to evaluate it). Furthermore it is assumed the hypothesis that a project is excluded from the portfolio if abandoned at any stage, using simply a binary variable (in the here proposed model the binary variable is double, depending on whether the drug is made by the pharmaceutical company in-house or by holding a license agreement with the biotech). Additional assumptions have to be considered if the pharmaceutical company enters into an agreement with a biotech firm. As suggested by the model Optfolio for alliances (Rogers et al., 2005), pharmaceutical companies hold a significant market power and biotech companies will grant them the license, provided that the expected NPV of the latter remains constant respect the alternative for the biotech to develop in its own the drug. The partners contribute to the alliance in a complementary way: the biotech is usually in charge of the first phases of the R&D process while the latter phases, the marketing and the production is usually a pharmaceutical concern.

The model uses the following parameters to describe the problem of portfolio optimization projects:

m=1,2,...,M products/drugs/molecules (in the following drugs)

s=1,2,...,S stage of the process of drug development

t=1,2,...,T year of the portfolio planning horizon

For each of the drug candidate, as also suggested by the Optfolio model, the impending stage at the present time t=0, is classified as $s = 1$ regardless of where the candidate drug is in its development. Subsequent development stages are numbered in ascending order until termination at product launch. Let us also defined:

V_{0i} = NPV of future incomes for drug i at $t = 0$

σ_i = estimated annual market volatility for drug i

r = risk-free interest rate

I_{is} = investment cost of developmental stage s for drug i

ϕ_{is} = probability of technical success in stage s of development for drug i

B_t = budgetary constraint for year t

C_i = Real options value of drug i if it is made in house

C_i' = Real options value of drug i if it is made in alliance

F_i =annual cash flow of drug i made in house

F'_i = annual cash flow of drug i made in alliance

r_{ph} = rate of return in the pharmaceutical industry

n = drugs commercial life

$X_i^{R\&D}$ = percentage of cash flows of drug i, made in house, invested in R&D

$X_i'^{R\&D}$ = percentage of cash flows of drug i, made in alliance, invested in R&D

As mentioned above, it is necessary to introduce the concept of indifference for biotech company (Rogers et al., 2005), in order to obtain payments that the pharmaceutical company will grant to the biotech in case of license agreement. As this company has the resources to develop the drug candidate independently, the NPV of a project at the generic time t = 0 is defined as:

$$\text{NPV}(\text{Biotech})\,no\ license = V_{0i}\gamma' \prod_s \phi_{si} - \text{NPV}(\text{development costs}) \qquad (1).$$

where the initial value of the drug is multiplied by the gain factor γ', which considers the possible added value from biotech to the simple V_{0i} that, for hypothesis, is the initial value of the drug produced by a pharmaceutical company. The term $V_{0i}\gamma'$ is then multiplied by the probability of technical success for each stage of the development process ($\prod_s \phi_{si}$). Otherwise, if the biotech company signs the agreement with the pharmaceutical company, the pharma will transfer a percentage of the revenues $(1-\alpha_i)$ an upfront payment and interim payments to the biocompany. A large pharmaceutical company, with advanced marketing resources, is able to double the value that would generate a small biotech company for a drug license. The amplification factor γ, which is greater than γ', determines the measure of value added to the project by the bio-pharmaceutical alliance, whose the NPV of future incomes

becomes $V_{0i}\,\forall$. The parameter can be considered as a measure of the convenience to form an alliance for the biotech company; actually, in this case, the NPV becomes:

$$\text{NPV}(\text{Biotech})\,license = V_{0i}\prod_s \phi_{si}\gamma\,(1-\alpha_i) - \text{NPV}(\text{development costs}) + \text{NPV (pharma payments)} \quad (2)$$

where $(1-\alpha_i)$ corresponds to the percentage of royalties paid to the biotech company. The indifference condition is:

$$NPV(BIOTECH)_{no-license} = NPV(BIOTECH)_{license}.$$

It leads to the following pharma payments:

$$\text{NPV}_i\ (\text{pharma payments}) = V_{0i}\prod_s \phi_{si}\left[\gamma^{*} - \gamma\,(1-\alpha_i)\right]\forall i \quad (3).$$

Multiplying this value by an appropriate discount factor $K_{i,s}$, the term $P_{i,s}$ is obtained that indicates the payment supported by the pharmaceutical industry in a year for the drug *i* during the stage *s*. More precisely, the factor $K_{i,s}$, considers the probability of technical success ϕ_{is} for each drug *i* and each phase *s*, the rate of return r'_{ph} and it imposes among the payments the same proportionality of the corresponding investments. The mathematical model is the following:

$$\max ROV = \sum_i \left(C'_i - P_{i,1}\right)H_i + \sum_i \left(C_i - I_{i,1}\right)L_i - \sum_{i,t}\frac{\omega_{it}RF_i}{(1+r_{ph})^t}h_i - \sum_{i,t}\frac{\omega_{it}RF'_i}{(1+r'_{ph})^t}l_i \quad (4).$$

where: C_i represents the value of the drug calculated using the Black and Scholes formula or Geske formula (depending on the type of option that is used to model the process of drug development itself), when the drug research is done in house;

C_i' represents the value of the drug calculated using the Black and Scholes formula or Geske formula, if the agreement is concluded with the biotech firm.

Moreover, the model includes four dichotomous variables, with the following meanings:

$$H_i = \begin{cases} 1 \text{ if the drug, made in house, is selected for the optimal portfolio} \\ 0 \text{ if the drug, made in house, is NOT selected for the optimal portfolio} \end{cases}$$

$$L_i = \begin{cases} 1 \text{ if the drug, made in alliance, is selected for the optimal portfolio} \\ 0 \text{ if the drug, made in alliance, is NOT selected for the optimal portfolio} \end{cases}$$

$$h_i = \begin{cases} 1 \text{ if part of cash flow of drug made in house is reinvested} \\ 0 \text{ if part of cash flow of drug made in house is NOT reinvested} \end{cases}$$

$$l_i = \begin{cases} 1 \text{ if part of cash flow of drug made in alliance is reinvested} \\ 0 \text{ if part of cash flow of drug made in alliance is NOT reinvested} \end{cases}$$

Clearly, if a drug is developed in-house, the same cannot be developed under license. Mathematically, this condition can be expressed with the following constraint, which also considers the possibility that the same drug is not developed:

$$H_i + L_i \leq 1 \qquad \forall i \tag{5}.$$

As mentioned before, further assumptions are needed to achieve a balanced R&D portfolio. The first one of them, which concerns the annual revenues distribution of a marketed product, assumes that, after its commercialization, a drug provides a company with uniform cash flows F_i for n years. The value of these annual incomes for drug i, developed in house, is:

$$F_i = V_{0i} \frac{(1+r_{ph})^n r_{ph}}{(1+r_{ph})^n - 1} \tag{6}.$$

If, however, the drug is developed within the alliance, the value of the cash flow turns out to be:

$$F'_i = V_{0i} \gamma \alpha_i \frac{(1+r'_{ph})^n r'_{ph}}{(1+r'_{ph})^n - 1} \tag{7}.$$

More precisely, we assume that r'_{ph} is less than r_{ph} because of the risk sharing coming from the agreement. So it must consider the possibility to reinvest the cash flow of a drug made in the open form (and then using the alliance), rather than in a closed form. The auto-financing by the commercialized drugs, is allowed only if drug has been selected to be part of the optimal portfolio. In mathematical terms, these concepts can be expressed with the following constraints:

$$h_i \leq H_i \qquad \forall i \tag{8}.$$

$$l_i \leq L_i \qquad \forall i \tag{9}.$$

In addition, the life of a drug after its commercialization n has been considered equal to 10 years, since after this lapse of time a drug normally loses its patent protection, causing its annual incomes to fall dramatically. However, only a share $X_i^{R\&D}$ or $X'^{R\&D}_i$ (depending on the adoption of a paradigm closed rather than open respectively) of annual cash flows is potentially reinvested to fund the development of further drugs. Thus, the actual amount of financial resources, deriving from the commercialization of drug i and planned to be yearly invested in R&D, is:

$$RF_i = X_i^{R\&D} F_i \qquad \text{if drug is made in house} \tag{10}.$$

$$RF'_i = X'^{R\&D}_i F'_i \qquad \text{if drug is made on alliance} \tag{11}.$$

$$0 \leq X_i^{R\&D} \text{ and } X'^{R\&D}_i \leq 1 \tag{12}.$$

In the objective function, the binary parameter ω_{it} allows the contribution of drug i in the period t to be considered only if the drug has been already introduced to the market in that period. Ultimately, the objective function can be decomposed into two parts: the first concerning the selection of a drug candidate to be included in the optimal portfolio (considering the possibility of developing it through alliance with a biotech firm), the second concerning the possibility of using part of the income of a drug selected to fund additional R&D projects in. Clearly the decision to include a drug in the product portfolio or leave it, is influenced by budget constraints:

$$\sum_{i,s}(P_{i,s}-\phi_{i,s-1}w_{ist})L_i+\sum_{i,s}(I_{i,s}-\phi_{i,s-1}w_{ist})H_i \le B_t+\sum_i(\omega_{it}RF'_i)l_i+\sum_i(\omega_{it}RF_i)h_i \;\forall t \qquad (13).$$

The first part of the equation is related to the expenses necessary for the development of drugs, always bearing in mind, using Boolean variables, L_i and H_i, the drug development in a open or a closed manner. The second part, on the other hand, includes the financial contributions brought to R&D by those commercialized drugs whose revenues have been partially allocated for this specific purpose. The technical success rate $\phi_{i,s-1}$ is included in order to consider the expected cost of each selected drug for the period t. The binary parameter w_{ist} appears, finally, in the OptFolio model as well and allows to include in budgetary constraints only those drugs beginning a stage of development in the period t (a phase can be longer than 1 year). The complete model formulation has equation (4) as objective function subject to constraints from (5) to (13) with: $H_i, L_i, h_i, l_i \in [0,1]$.

3. An OOL Numerical Example

The low computational burden of OOL allows its implementation in a Microsoft Excel spreadsheet. Any pharmaceutical company interested in evaluating and selecting its R&D projects could create its own optimal products portfolio simply entering drugs information and clicking a button. Particularly, the model needs inputs regarding budget limitations as well as about candidate drugs, such as their expected current values, volatilities, technical success rates and investment costs of each stage, and types, which indicates what is the impending development stage of a drug at the time of portfolio selection. Thus, the spreadsheet identifies whether Black & Scholes formula, Geske formula or none of them (because it is not an option and the NPV can be used) for each drug is needed and calculates the options parameters useful for estimating its real options value C_i (Enea and Lo Nigro 2011a) and C'_i. At last, it is sufficient to click on a macro button which launches the Excel solver, finding the balanced optimal portfolio composition. Of course, if the drug is developed jointly through an alliance with a biotech company among the input parameters the payments that the pharmaceutical company will pour to the biotech company during the agreement will substitute the investments. For the calculation of these, it is therefore necessary to introduce additional input parameters such as the values of γ, γ' and α_i , as shown in figure 1.

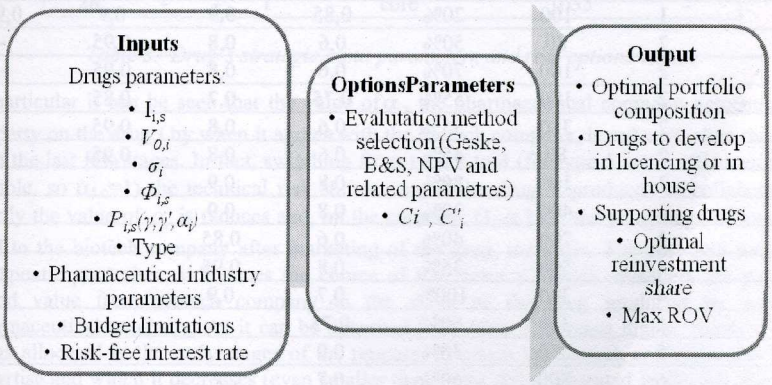

Figure 1. Optimal portfolio selection process using the new model spreadsheet.

As an illustrative example of the model OOL, we report a case study, presented by Rogers et al. (2002), concerning a balanced optimal portfolio selection by a pharmaceutical company with 20 drugs candidates (M1-M20) to be part of the R&D portfolio. Each of them is classified into six categories, depending on the stage of the development process in which it is (table 1): six drugs are at the beginning of phase I (type I, M1-M6), five drugs at the beginning of Phase II (type II, M7-M11), three drugs at the start of phase III (type III, M12-M14), two drugs in the second year of Phase III (type IV, M15 and M16), two drugs at the beginning of the process of FDA (type V, M17 and M18) and two drugs in the second year of the approval stage (type VI, M19 and M20).

Type	Beginning phase	Candidate drugs(M)
1	Phase I	1,2,3,4,5,6
2	Phase II	7,8,,9,10,11
3	Phase III	12,13,14
4	2nd year Phase III	15,16
5	1st FDA Approval	17,18
6	2nd FDA Approval	19,20

Table 1. Candidate Drugs

Bounded by a specific budget for the R&D process, the pharmaceutical company has to decide which drug candidates development finance in later years.
The parameters for the resolution (table 2) of the model such as the present value of future cash flows of drugs, probability of technical success, the estimated volatility, have been estimated based on historical and industry data (Rogers et al., 2005).

M	Type	V_0	σ	ϕ_1	ϕ_2	ϕ_3	ϕ_4
1	1	50	80%	0,6	0,7	0,8	0,95
2	1	100	70%	0,65	0,55	0,75	0,90
3	1	200	50%	0,7	0,8	0,9	0,90
4	1	200	60%	0,5	0,7	0,8	0,90
5	1	600	50%	0,6	0,6	0,7	0,90
6	1	100	20%	0,85	0,9	0,9	0,95
7	2	80	50%	0,6	0,8	0,95	-
8	2	100	70%	0,6	0,8	0,95	-
9	2	180	55%	0,75	0,7	0,85	-
10	2	380	35%	0,6	0,8	0,95	-
11	2	80	45%	0,6	0,8	0,95	-
12	3	100	80%	0,8	0,9	-	-
13	3	400	30%	0,8	0,9	-	-
14	3	700	40%	0,6	0,85	-	-
15	4	500	35%	0,8	0,95	-	-
16	4	300	100%	0,7	0,9	-	-
17	5	350	60%	0,75	-	-	-
18	5	550	30%	0,9	-	-	-
19	6	800	60%	0,7	-	-	-
20	6	1150	20%	0,9	-	-	-

Table 2. Inputs parameters.

Among the input parameters some reflect the pharmaceutical strategy and the agreement characteristics (α_i (Rogers et al.,2005) γ,γ', the therapeutic area) and they are summarized in the table 3. Moreover, in order to better understand the optimal optfolio selection, in the same table (3) are reported the real options values of each drug(C_i and C_i'). Finally, for drugs (M17-M20), it not considered a possible alliance with biotech company: it seems hard to imagine, in fact, that pharmaceutical companies can develop these drugs (which are placed in FDA phase), in alliance.

M	α_i	γ	γ'	Therapeutic Area	C_i	C'_i
1	0,85	1,5	2	Non core	4,72661563	11,75044
2	0,85	1,5	2	Non core	7,65414517	16,29557
3	0,85	1,3	1,8	core	26,7907655	48,69223
4	0,85	1,3	1,8	core	13,2645724	29,995
5	0,85	1	1,4	core	75,9343908	66,97072
6	0,85	1,5	2	Non core	13,4359365	37,844
7	0,75	1,4	1,9	Non core	14,4614674	24,51843
8	0,75	1,4	1,9	Non core	17,493214	35,4011
9	0,75	1	1,3	core	28,4593864	35,64666
10	0,75	1,2	1,7	core	98,7970845	105,8609
11	0,75	1,4	1,9	Non core	13,9801546	24,04746
12	0,65	1,3	1,7	Non core	42,5655588	53,42457
13	0,65	1	1,2	Core	159,715846	106,5761
14	0,65	1,2	1,5	Core	220,314095	175,6437
15	0,55	1,1	1,2	core	299,786776	100,4355
16	0,55	1,2	1,4	Non core	114,360311	88,41885
17	-	-	1	Non core	262,5	-
18	-	-	1	Non core	495	-
19	-	-	1	core	560	-
20	-	-	1	core	1035	-

Table 3. Drug's strategic input parameters and real options values

In particular it can be seen that the value of α_i, the pharmaceutical company percentage of property on the drug *i* by when it agrees with the biotech company, is reduced when the drug is in the last few stages. In fact, switching from type 1 to 4 (for type 5 and 6 alliances is not eligible, so $\alpha_{5,6}$=1) the technical risk shrinks, so, if the drug is produced in collaboration, clearly the value of α_i is reduces and, on the contrary, (1-α_i) i.e. the percentage of royalties paid to the biotech company after marketing of the drug, increases. The core and non core therapeutic area, then, influences the choice of the factor γ', which considers the possible added value from biotech company to the value of the drug produced by just the pharmaceutical company. As it can be observed from table 3, it takes higher values for the drugs allocated in the early stages of the process, in which the biotech enterprise has more expertise and which it decreases (even smaller than 1) for drugs allocated in the last stages of development, in which, on the contrary, it is the pharmaceutical company to have more skills. More precisely, as suggested by empirical analysis on the adoption of open innovation in the bio-pharmaceutical industry (Bianchi et al. 2011), it assumed a larger value of γ ' for a drug

placed in a non-core, whereby the biotech firm has very dissimilar competencies than the pharmaceutical industry, thus increasing the value of the project. This explains a high factor of γ, value added from collaboration to the project, which, for some drugs, also comes to double. It was also assumed a value of r_{ph} equal to 12%, as suggested by Di Masi et al. (2003), then a lower value for r'_{ph} equal to 11% is assumed. Moreover, the risk-free interest rate, r, has been set at 3.41% which corresponds to a December 2010 5-years US Treasury bond. (Source: www.bloomberg.com, January 2011).

Finally budget limitations have been considered as M$ 400 for the first year and M$ 100 for the remaining ones, with a planning horizon of 5 years. The length of phase I and II have been assumed equal to 1 year, while the length of phase III and approval equal to 2 years, with an overall 6 years length R&D process.

3.1 *Analysis of results.* In general, the drugs that reached the last stage of the development process have a higher value, as it is now very likely their market launch. However, investment and marketing costs associated with their launch on the market are significant and limit the number of products that pharmaceutical companies can bring to market. The size of the optimal portfolio balances therefore the desire to launch drugs that are most valuable and that are in the process of FDA approval, with investments in drugs that are potentially valuable in the early stages of the development process. The model results seem to satisfy this desire: 7 drugs are selected, 4 allocated in the later stages of the process and 3, placed in the early stages as shown in table 4:

Drugs selected	In alliance	In house	Supporting drugs	ROV
7	4, 7, 16	5, 14, 15, 20	16, 20	M$ 1.289,76

Table 4. The optimal portfolio composition and the overall ROV.

Moreover drugs most valuable and allocated all in core therapeutic area, are selected in house; so the pharmaceutical companies have the total ownership of them ($\alpha_i = 1$), while in alliance are selected drugs who are in different stages of the development process and in non core therapeutic area (excepted drug 4), in order to exploit complementary skills of biotech company (Bianchi et al., 2011). This result is supported by the optimal portfolio selected, ceteris paribus, in case of closed innovation (alliances are not considered): as shown in Table 5 the drugs selected are the same of table 4 (see the in house column for a comparison) and the ROV is lower as expected.

Drugs selected	Supporting drugs	ROV
5,14,15,20	20	M$ 1.199,86

Table 5. The optimal house portfolio composition and the overall ROV.

Comparing table 4 with table 5, we can observe that OI gives an important contribution to the value of the chosen portfolio: in fact the most valuable drugs continue to be chosen in house, but 3 potentially valuable drugs are selected in alliance, causing an overall increase of ROV (and an ulterior auto-financing through product 16). In particular, as suggest by Rogers et al. 2002, M20 and M15 are selected in both scenarios because they have a very largeV_0 and a high chance of being successfully launched in the market respect the other potential drugs; these two products in the Rogers et al. 2002 study show a robustness respect the budgetary constraints (they are always chosen when the budget varies).

4. Discussions and Conclusions

This paper addresses an issue related with three literature streams: Open Innovation, Real Option Analysis and R&D Portfolio Selection. R&D portfolio selection, especially in some industries, cannot help taking into consideration the OI alternative and in the meanwhile cannot deal with the intrinsic uncertain and flexible nature of the process. As a result ROA method becomes a must in this field. The managers perceive ROA adoption as a complex task, so they prefer to use a simple and easily manipulated way to evaluate investments (NPV most of all). Our main contribution to the literature is to propose a model easy to implement (but not to manipulate) to select which R&D projects finance and how to carry them on, that is developing them in house or with an alliance that represents an operative way to deploy OI. Our model, moreover, considers the auto-financing option: every portfolio should be composed by elements able to produce cash flows and others that need financial support, usually these ones will finance new-entries in the portfolio (according to the life cycle of the element). The biopharmaceutical industry is characterized by a long, uncertain, expensive and strategic R&D function then it represents an ideal benchmark for our model, even if it can be customized according to the industry considered. In the biopharmaceutical developed numerical example, each potential drug that achieves the market has an implicit option consisting in financing drugs in the pipeline and this option cannot be take into consideration without a portfolio perspective. Finally we propose to select the portfolio assuming a strategic perspective: actually, the R&D decisions have a significant impact on the firm future performances so we believe that the firm's weaknesses and strengths should impact on these decisions. The proposed model takes account for this aspect through the core/non core nature of the drugs. The results obtained for the developed numerical case suggest the selection of a multi-balanced portfolio: it is composed by drugs of different types (then in different stages of the pipeline) that are developed both in house and in alliance thus, the model gives the best mix of close-open innovation patterns in terms of risk control, and some of selected drugs are able to finance the portfolio itself.

Further developments aim at testing the model in others R&D based industries; moreover a sensitivity analysis will allow the obtained results to be generalized in order to get some more insight about the optimal selection of R&D portfolio with an inter-industry perspective.

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Seventeenth International Working Seminar on Production Economics

PRE-PRINTS VOLUME 2

Papers scheduled for
Wednesday, February 22, 2012
8.00 am to 21.15 pm

Edited by
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