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R&D ALLIANCE TIMING IN THE BIOPHARMACEUTICAL INDUSTRY: A REAL OPTIONS GAME APPROACH.

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Introduction

In the actual competitive landscape companies must be responsive in making strategic decisions, notably in "high tech" industries these decisions are often taken in a context of great uncertainty regarding several factors such as changes in market conditions or the success of the firms' R&D process. In this framework, managers need to have considerable flexibility to adjust their own strategy and to refocus the company's resources since new information are progressively available.

In particular, in the pharmaceutical industry, the drug R&D process is characterised by prolonged times, high levels of investments and very low success rate. Therefore, firms' returns are characterized by high uncertainty. In this competitive landscape, pharmaceutical companies face more and more difficult to maintain the number of significant commercial drug launches each year in order to remain competitive in the market. In this context, closed innovation solutions, traditionally adopted by most of the pharmaceutical companies, are no more sustainable and firms need to look outside their boundaries and consider new open innovation solutions that allow to combine external and internal resources. Between these solutions, during last decades, strategic alliances, defined as "voluntary agreements between firms involving the exchange, sharing and co-development of products, technologies or services" (Gulati, 1998), have become increasingly common.

One fundamental element to complete this picture is related to the advent of biotechnology, which has significantly impacted the pharmaceutical industry. In fact, since the eighties, pharmaceutical companies more and more have partnered with the newcomers, i.e. the biotechnology companies, in order to pool their complementary assets along the drug R&D and commercialisation processes, and succeed in the winner-takes-all patent race. While the "raw material" is located in biotech firms, pharmaceutical companies have expertise in managing advanced phases in new drug development (i.e., clinical stages, approvals, marketing and production) and considerable amounts of financial resources, of which biotech firms are lacking. In the same vein, due to the lack of marketing capabilities and financial resources, many biotech firms are intrinsically open to collaborations to innovate.

In an open innovation business model, a wide spectrum of alternatives is at disposal of firms during the R&D process. At any stage of the process, both biotech and pharmaceutical firms can decide whether, when and how to start, continue, abandon partnership with other firms, delay or dismiss the project. In particular, whether and when firms should collaborate is currently one of the key issues debated in the industry world. As a matter of fact, in recent years, the issue of R&D alliance timing has been extensively debated in the biopharmaceutical industry. On one hand, some industry insiders have recommended that biotech firms should partner with pharmaceutical companies during exploratory phases of the development process giving up their ambition of becoming big companies, like Amgen or Genentech (Napodano, 2009). On the other hand, some industry surveys have pointed out that, in recent years, the focus of small biotech firms has shifted from simply looking for capital to fund pre-commercialization development to building clinical development and product marketing capabilities (Deloitte, 2005). As a result, biotech firms tend to postpone the alliance timing to the later stages of development and commercialization (Deloitte, 2005). These arguments help explain why a very large heterogeneity in R&D alliance timing is usually observed in the biopharmaceutical industry, for example among the top biotech licensing deals in 2012 (Carroll, 2012). Indeed, numerous authors have underscored the existence of multiple forces determining the optimal R&D alliance timing. These include the limited financial resources of the biotech firms, the high risk of project failure in early stages, the bargaining power of the parties at different stages of the project, as well as the presence of multiple biotech firms that oftentimes compete for partnering with pharmaceutical companies (Gassmann and Reepmeyer, 2005, Nicholson et al., 2005, Rogers et al., 2005, FierceBiotech, 2007).

The goal of this thesis is to study alliance timing decisions from the perspective of both pharmaceutical and biotech firms to determine which is the optimal alliance timing under different conditions. This is consistent with the fact that, in the previous literature, alliance timing has not been sufficiently investigated and the development of an analytical model is missing.

In doing so, two important characteristics of R&D alliances are considered: the uncertainty of the R&D process and the strategic interaction between firms. The evaluation of investment projects is generally done by using the Net Present Value

(NPV) methodology. However, in the field of R&D projects, this methodology is not able to correctly consider the high uncertainty, the risks, and the flexibility that characterize the projects. On the contrary, in recent years, the evaluation of pharmaceutical R&D projects through real options has been gaining growing attention, in order to choose the right project and avoid the risk of missing profitable opportunities. Specifically, on one hand, the real options approach allows to take into account the uncertainty and the flexibility embedded in the R&D process and to consider the value of future opportunities; on the other hand, the use of real options is perceived complex from the practitioners (Hartmann and Hassan, 2006). However, in case of using NPV, they should consider the risk of not properly assess the value of the project, while real options can provide a clearer and correct overview of future scenarios (Villiger and Bogdan, 2005). Therefore, in this dissertation I also investigate whether the use of the real options methodology has a different impact on the optimal alliance timing decisions as compared to the use of the traditional NPV methodology.

Nevertheless, do not consider strategic interactions between firms often creates a partial picture in competitive settings, as firms' strategies usually show interdependency. In order to consider also this aspect, the real options game approach has been adopted. Specifically, this approach is a combination of real options and game theory and it allows to examine the trade-off between managerial flexibility and commitment in dynamic competitive settings under uncertainty (Chevalier-Roignant et al., 2011). Therefore, with the use of real options games, firms "can presumably condition their decisions not only on the resolution of exogenous uncertainties but also on the (re)actions of outside parties (e.g., competitors)" (Chevalier-Roignant et al., 2011).

The choice of referring in this thesis to the biopharmaceutical industry is related to its specific characteristics. In particular, collaborations between pharmaceutical companies and biotech firms are increasing and are extremely important for the development of new drugs, furthermore the biotechnology industry is characterized by the presence of many competitors (Deloitte, 2005, FierceBiotech, 2007). In addition, the pharmaceutical R&D process has a long and dynamic life, and further investments depend on the success/failure of previous ones, which also makes the pharmaceutical R&D process an ideal field of application for real options.

Although this research context is the biopharmaceutical industry, the results and insights provided in this thesis can be also applied to other high-technology industries where collaborations are important for firms to carry out their innovation process, especially partnerships between a small innovator and an established incumbent. Particularly, environments that are characterised by a high level of competition with staged R&D projects and subject to significant uncertainty over market.

In the following I will describe the outline of this thesis.

In Chapter 1, I provide a detailed literature review of the streams of research related to this dissertation addressing their main research gaps and their synergic interaction. Specifically, in the first section I describe the main real options approaches used to evaluate R&D investments. In the second section I provide a detailed discussion on the real options games literature, which combines real options and game theory. In particular, I focus on the time characteristic, which allows to distinguish continuous time models and discrete time models. In the third section, I provide an overview on drug R&D process and research on alliance with a particular focus on research on R&D alliances with a real options perspective and the literature on alliance timing. In the end, I illustrate the goal of this thesis.

In Chapter 2, I describe the result of my collaborative work with Giovanna Lo Nigro, Azzurra Morreale and Paolo Roma. Specifically, I take the perspective of the biotech firms developing a two-stages real options game under both monopoly and duopoly case. In the chapter I analyse the effect of competition in biotechnology industry by modelling the decisions of whether and when they ally with a pharmaceutical company. Research findings provide threshold payments that determine different outcome solutions. Interestingly, depending on the level of the parameters, both players can sign the agreement and both stages can be optimal.

In Chapter 3, I extend the previous model taking the perspective of the pharmaceutical company and this is the outcome of my collaborative work with Giovanna Lo Nigro, Azzurra Morreale and Paolo Roma. In this chapter in a two-stages real options game I suppose the presence of a pharmaceutical company that has the bargaining power to offer a take-it-or-leave-it contract maximizing his payoff.

Modelling the active role of the pharmaceutical company changes the alliance timing significantly. In addition, I investigate the differences in the optimal alliance timing

when the NPV methodology, instead of the real options methodology, is utilized to evaluate the R&D project investment.

Finally, in Chapter 4 I report conclusions of this thesis. I present the main theoretical contributions and the managerial implications. I also outline the limitations of this dissertation and suggest further research developments.

Chapter 1
Literature review

1.1 The real options

The evaluation of the investments is an important issue in strategic management literature. The conventional approach is the Net Present Value (NPV) methodology, which involves the evaluation of expected cash flows deriving from the investment discounted at a discount rate that reflect the perceived riskiness of the project (Newton et al., 2004). However, especially in the field of R&D projects, where high uncertainty and risks are prominent, this method loses a large amount of its effectiveness. In fact, NPV implicitly assumes that managers will follow rigid and inflexible path. Essentially, NPV ignores managers' flexibility to respond and adjust to any changes that might occur in the future (Myers, 1984, Hartmann and Hassan, 2006, Cassimon et al., 2011).

So, in recent years, the evaluation of pharmaceutical R&D projects through Real Options Approach (ROA) has gained growing attention, in order to choose the right project and avoid the risk of missing profitable opportunities. In case of real options the underlying is a real asset and the owner has "the right, but not the obligation, to take a specific action in the future" (Amram and Kulatilaka 1999, p. 5). Real options allow to take into account uncertainty and flexibility embedded in the R&D process and consider the value of future opportunities.

Similarly to the financial options, real options can be divided in call options, giving the right to buy the underlying asset at a predetermined price, and put options giving the right to sell the underlying asset at a given price. In addition, it is possible to distinguish between European and American options. The former can be only exercised at date of maturity, whereas the latter can be exercised before this date. The real options consider the embedded flexibility of the R&D process and interpret several possible behaviours of the management. Thus it is possible to distinguish between six kinds of option (Trigeorgis, 1997):

- The option to defer an investment project
- The time-to-build option
- The option to abandon an investment project

- The option to contract, expand or temporarily shut down an investment
- The option to switch input or output
- The growth option, where an early investment allows to obtain future growth opportunities.

Real options value depends on the same variables of the financial options, such as the underlying value, the exercise price, the volatility, the time to maturity, as well as the riskless interest rate; the correspondences between financial and real options are reported in Table 1.

Table 1: Variables that characterize financial options and their correspondent in real options.

Variable	**Financial option**	**Real option**
Underlying	Current value of the stock	Present value of the expected cash flows of the project
Exercise price	Stock price	Present value of the project investment cost
Time to maturity	Expiration date of the stock	Length of time in which the investment opportunity exists
Volatility	Volatility of returns on stock	Project value volatility
Interest rate	Riskless interest rate	Riskless interest rate

Obviously these input parameters should be identified to estimate the real option value. The key parameter to evaluate is the *underlying*. Looking at practical examples and theoretical papers, in most cases the underlying is taken as the future cash flow of a project (Perlitz et al., 1999, p. 5). Different approaches have been used in literature to model the stochastic process of the underlying. Specifically, assuming continuous time contemplation of the underlying movements, several processes are conceivable: the Diffusion-Process (such as the Brownian Motion), the Jump-Process and the Mean Reverting process (Dixit and Pindyck, 1994). For discrete time movements the Lattice approach can be used. About the *volatility* of the underlying, usually past data from the

volatility of completed R&D projects are used as an approximation (Perlitz et al. 1999). The *exercise price* can be known in advance or not. In the latter case, McDonald and Siegel (1986) suggest that it has to be replicated as a stochastic variable. Lint (2004), due to the fact that the exercise price is relatively short-term oriented, proposes to obtain reasonable estimate of this cost by means of the interviews with managers involved in the R&D process. The *riskless interest* rate can be derived from government bonds that have the same time to maturity as the R&D option. Regarding the *time to maturity*, it is hard to determine since real options often have a long time to maturity (Perlitz et al., 1999) and it can be a fixed date (as in European options) or a not known date by a fixed one (as in American options).

To evaluate real options several techniques are available. In the following sub-sections, I review the main models available in the literature. In particular I will focus on the valuation of a call option, due to the fact that, in this thesis, I will consider growth options. In general, evaluation methodologies are distinguished between approaches that consider discrete stochastic process, like the binomial model (Cox et al., 1983), and approaches that assume continuous time stochastic process like the Black and Scholes model (Black and Scholes, 1973).

1.1.1 The binomial model

The binomial pricing approach was developed by Cox et al. (1983). The model assumes that the value of the underlying asset, denoted as S, follows a multiplicative binomial process over discrete periods. The option value C is computed, first building a tree of all possible discrete values that the underlying value can assume in future and then recurring to dynamic programming.

Specifically, consider only one period, the current stock price S at the end of this period can assume two possible values, as showed in Figure 1: S_u with probability q, if S has an increase, and S_d with probability $(1-q)$, if S has a decrease.

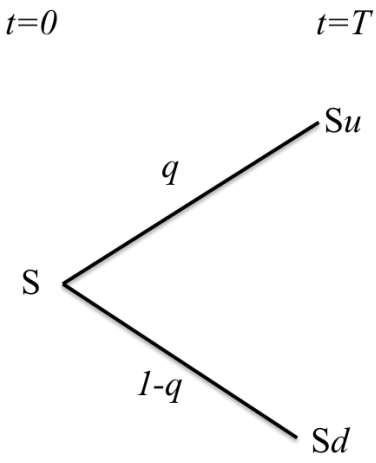


Figure 1: Binomial pricing tree for underlying value

In particular:

$$u = e^{\sigma\sqrt{\Delta t}} \tag{1}$$

$$d = e^{-\sigma\sqrt{\Delta t}} = 1/u \tag{2}$$

Where σ is the standard deviation of the underlying S and Δt is the discrete time interval and represents the length of each interval that constitutes the tree. If n is the number of time steps between 0 and T (the maturity of the option), Δt is computed as T/n. In the model, the risk neutral probability q of an up movement is given by:

$$q = \frac{e^{r\Delta t} - d}{u - d} \tag{3}$$

where r is the riskless rate. The value of the option at the maturity (T) is:

$$C_T = \max(S_i - X; 0) \tag{4}$$

where $i= u, d$ depending if S has gone up or down and X is the exercise price. Therefore, the option is exercised only if the net payoff is positive. The present value of the call option C is thus obtained by discounting back the two possible values of C, C_u and C_d, weighted by their risk-neutral probabilities, q and $(1-q)$, respectively. As appropriate discount factor is used the riskless rate r. The present value of C is equal to:

$$C = e^{r\Delta t}(qC_u + (1-q)C_d) \tag{5}$$

It is possible to extend the process of the underlying S over multiple time periods, solving the model by dynamic programming in order to obtain the call value C at $t=0$.

When a huge number of time steps n is considered, ΔT becomes so small that the discrete approximation of C will converge to the Black-Scholes continuous-time value.

1.1.2 The Black & Scholes model

Black and Scholes (1973) analyse the option pricing problem in a continuous-time framework. The main assumption of the authors is that $S(t)$, the value of the underlying S along t, follows a Geometric Brownian Motion (GBM). The Geometric Brownian Motion assumption corresponds to assuming a lognormal distribution for the underlying at the end of any finite interval time.

Considering an interval of time $(0, T)$. At the current time $t=0$ the holder of the option acquires the right, but not the obligation, to make another investment at time T, i.e. maturity. Make the investment at the maturity corresponds to exercise the option. At T new information are available, and $S(T)$ is a known realization of the lognormal distribution. As above, the option will be exercised only if $S(T)$ will exceed the exercise price, i.e. the option is "in the money". Accordingly, the payoff at maturity is equal to:

$$C_T = \max(S_T - X; 0) \tag{6}$$

It is necessary to compute the expected value of the option at $t=0$. Note that the investment at $t=0$, is a sunk cost, i.e. it does not affect the option value.

Other assumptions of the model are (Black and Scholes, 1973):

- The riskless interest rate is known and constant through the time;
- The variance rate of the return on the stock is constant;
- The stock does not pay any dividend;
- The option is "European", i.e., it can only be exercised at maturity;
- There are no transaction costs in buying or selling the stock;
- It is possible to borrow any fraction of the price of a security to buy it or to hold it, at the riskless interest rate;
- There are no penalties to short selling. A seller who does not own a security will simple accept the price of the security from a buyer, and will agree to settle with the buyer on some future date by paying him an amount equal to the price of the security on that date.

Under these assumptions, the value of the option will depend only on: the price of the stock, i.e. the underlying, the time and the variables that are assumed to be known

constants, i.e., the riskless rate, the volatility and the exercise price. In particular, the value of a call option *C* is equal to:

$$C = SN(d_1) - e^{-r(T-t)}XN(d_2) \tag{7}$$

With:

$$d_1 = \frac{\ln(S/X) + (r + \sigma^2/2)(T-t)}{\sigma\sqrt{(T-t)}} \tag{8}$$

$$d_2 = d_1 - \sigma\sqrt{(T-t)} \tag{9}$$

Where:

- S = the price of the underlying;
- X = the exercise price;
- r = the riskless interest rate;
- T = the time to maturity;
- t = the current time;
- σ = the standard deviation of the stock's returns;
- $N(.)$ = the cumulative normal density function.

According to Nielsen (1993), it is possible to split the option value of equation (7) in two components. The first component (the second in the equation 7) represents the payment of the exercise price, contingent on the option finishing in the money. The risk-adjusted probability, *P*, of the event that the option will finish in the money is $P\{S_T > X\} = N(d_2)$. Thus the present payment, discounted at the riskless rate, is $e^{-r(T-t)}XN(d_2)$.

The second component (the first in the equation 7) is the receipt of the stock, again contingent on the option finishing in the money and thus is exercised. The expected future value of this component is not simply the conditional expectation of the stock price given exercise. Rather it is the conditional expectation of the stock price given exercise times the probability of exercise. In particular:

$$E\left[S_T \middle| S_T > X\right] P\{S_T > X\} = e^{r(T-t)}SN(d_1) \tag{10}$$

and at $t=0$ is equal to $SN(d_1)$. $N(d_1)$ is the factor by which the discounted expected value of contingent receipt of the stock exceeds the current value of the stock (Nielsen,

1993, p. 5 and 6). In Figure 2 trends of the value of the call option and its components are reported.

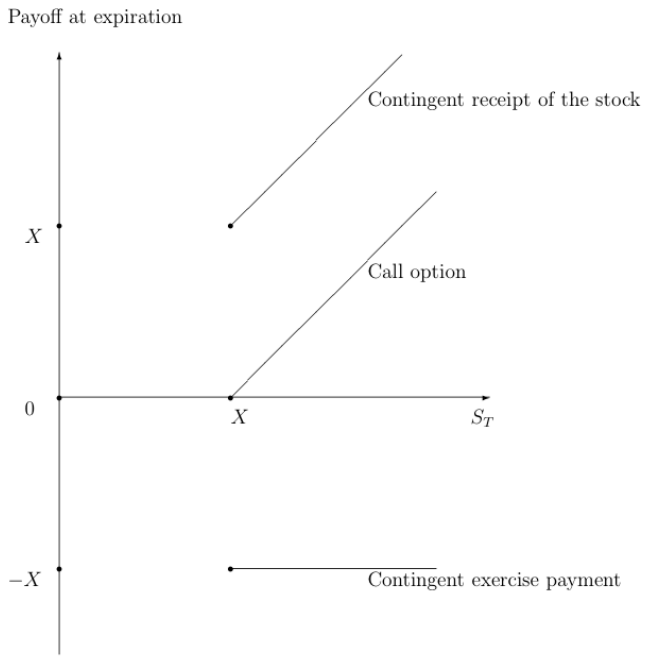


Figure 2: Trends of the value of the call option and its components

1.1.3 The Geske model

Starting from the Black and Sholes formula, Geske derived in 1979 a closed-form solution for the evaluation of an option on an option, or a 2-fold compound option. In case of compound options the holder of the option makes decisions in two separate dates. Specifically, at the expiration date of the 'inner' option, if its market price is over the correspondent exercise price the first option will be exercised. In this case, the holder will have a further option, which could be exercised at final maturity. The main assumptions of the model are (Geske, 1979 p. 68):

- The changes of the value of the stock follow a random walk in continuous time with a variance rate proportional to the square root of the value of the firm;
- Investors are unsatiated;
- The security markets are perfect and competitive;
- The riskless interest rate is known and is constant through time;
- The trading takes place continuously in time;

- The firm has no pay outs.

As above, the value of the option depends only on the the underlying, the time and constant variables. Specifically, the value of a call option *C* is:

$$C = SN_2(a_1, a_2; \rho) - e^{-r(t_2-t)} X_2 N_2(b_1, b_2; \rho) - e^{-r(t_1-t)} X_1 N(b_2) \tag{11}$$

With:

$$b_1 = \frac{\ln(S/\overline{S}) + (r - \sigma^2/2)(t_1 - t)}{\sigma\sqrt{(t_1 - t)}} \tag{12}$$

$$b_2 = \frac{\ln(S/X_2) + (r - \sigma^2/2)(t_2 - t)}{\sigma\sqrt{(t_2 - t)}} \tag{13}$$

$$a_1 = b_1 + \sigma\sqrt{(t_1 - t)} \tag{14}$$

$$a_2 = b_2 + \sigma\sqrt{(t_2 - t)} \tag{15}$$

$$\rho = \sqrt{\frac{(t_1 - t)}{(t_2 - t)}} \tag{16}$$

Where:

- S = the price of the underlying;
- $\overline{S}$ = the solution of $C_1(S, t_1) - X_1 = 0$;
- σ = the standard deviation of the stock's returns;
- r = the riskless interest rate;
- t = the current time;
- t_1 = the time to maturity of the compound option *C*;
- t_2 = the time to maturity of the underlying call option;
- X_1 = the exercise price of the compound option *C*;
- X_2 = the exercise price of the underlying call option;
- $N(.)$ = the cumulative normal density function;
- $N_2(.)$ = the bivariate cumulative normal distribution function with a_1 and a_2 as upper limits and ρ as the correlation coefficient between the two variables.

The Geske model is particularly suitable for evaluation of staged R&D projects, constituted of a series of consecutive phases, where the management moves on to the

next stage of the product development only if the expected results are satisfactory. In fact, each phase of the R&D process represents an option on executing the following phase, i.e. a compound option.

Perlitz et al. (1999) provide an application of the Geske model to a project in the pharmaceutical industry. For the sake of simplicity, the authors consider the R&D process divided into three main phases (see Figure 3). In phase 1 an active substance is identified as promising enough between numerous possible compounds. Once a substance has been identified, the testing phase, i.e., 2, starts. If this phase turns to be successfully completed, then the pharmaceutical company can make an ulterior investment in production capacity and market introduction and the drug can be commercialized. Two options are identified in this setting: the first option is the possibility to invest in testing; the second option is the investment in production capacity and market introduction. Taken together, these opportunities form a compound option, i.e., a 2-fold option, which can be evaluated by the Geske formula.

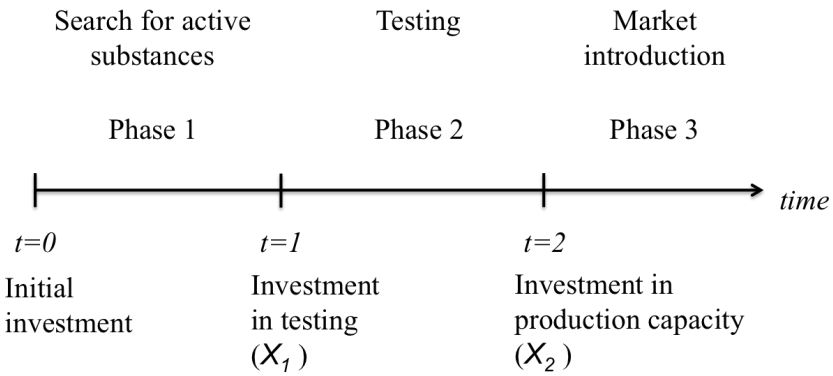


Figure 3: Simplified illustration of the drug R&D process.

At t_0, the company makes an initial investment (as above this is a sunk cost that does not affect the compound option value) to buy the compound option. If the asset value at time t_1, exceeds the investment cost X_1, i.e. phase 1 has been successfully completed, the first option is exercised and the company buys the right to exercise the second option at t_2. At that date, if the asset value exceeds the production and market cost X_2, the pharmaceutical company will exercise the second option too. Thus, the entire compound option is exercised.

The main limitation of the Geske model is that it is appropriate to evaluate only 2-fold compound options. However, it could be difficult, in the real markets, divide the R&D project in only two phases. In fact, very often R&D processes are constituted of several stages, thus they are represented by n-fold compound options and the Geske formula is not applicable. Cassimon et al. (2004) provide a generalisation of Geske's compound option model, deriving a solution for a n-fold compound option.

1.1.4 Conclusions on real options methodology

Traditional NPV methodology fails in the evaluation of the R&D projects due to the hypothesis of static cash flows. In fact, projects are assumed to proceed as planned, regardless of future events (Newton et al., 2004) and their value may be underestimated because it is not taken into account management's ability to update decisions, as new information arrive. Also, it does not take into account the dual role of risk: high risk, i.e. high volatility, can lead to a possible reduction in the value of the project, but can also be associated with the possibility of obtaining more revenues. Therefore, NPV is suitable for evaluating investments in static environments.

On the contrary, real options enable companies or managers to value projects by incorporating managerial flexibilities into the valuation model. Although, ROA is recognized by the academia as very suitable to overcome the limitations of NPV, the use of real options in new project evaluation is quite limited. This is mainly because practitioners perceive real options as a considerably complex tool (Hartmann and Hassan, 2006). However, several studies suggest how the use of different methodologies has a relevant impact on firms' decisions. For instance, Krychowski and Quèlin (2010) investigate alliance timing in a real case in the mobile telecommunication industry under NPV and ROA framework and find out that ROA produces the opposite recommendation in investment timing (delay the investment) as the NPV does (invest now). Also Cassimon et al. (2011) show that the licensing deal value is highly affected by the methodology utilized to evaluate the investment project.

Among scholars who have adopted ROA as a tool to evaluate R&D project, Cassimon et al. (2011) develop a model in the multi-phase R&D project in the pharmaceutical sector. They incorporate technical risk in a compound option models, still preserving the closed-form solution.

Rogers et al. (2002) develop a stochastic optimization model to select the optimal portfolio, always in the pharmaceutical industry. Authors use the binomial tree, in particular they adopt a quadranomial approach, i.e. a two-variable binomial tree, that allows to model both technological and market uncertainty. Each project development stage is modelled as a series of continuation/abandonment options, deciding at each phase, whether to proceed further or stop the development.

Regarding uncertainty evaluated through ROA, it can be differentiated into technical uncertainty and economic uncertainty. The former deals with the uncertainty on R&D costs and factors that can influence the R&D product success, e.g. approval probability. Economic uncertainty is related to the factors that can affect market uncertainty, like interest rates, inflation, and changes in the industry. This kind of risk is systematic, i.e. is independent from the actions of the firm.

The evaluation methodologies, as specified above, use discrete approaches, like the binomial model, or continuous approaches, like Black and Scholes. Adopting binomial model, due to the fact that it is a numerical approach, allows to manage a wide range of application. However, this method shows some limitations (Cassimon et al., 2004, 2011). In particular, the first problem arises with the choice of the up (u) and down ratios (d) and the risk of neutral probabilities (q). A second problem is due to the fact that is not known how many time steps are necessary in order to obtain an accurate option price. Black and Scholes formula provides a closed-form solution. The main limitations are that Black and Scholes can't evaluate American put and the assumption of GBM distribution for the underlying. In fact, this implies a continuous arrival of information that changes the underlying value (Pennings & Lint, 1997). However, information that affects the underlying value arrives at discrete points of time and this means that the managers, in real markets, do not continuously adjust the underlying value, but only when information with strategic impact arrives (Pennings & Lint, 1997). However, the continuous time assumption of Black and Scholes, and also Geske model, allows for closed-form solutions that makes the handling easier (Perlitz et al. 1999, p 264). In general, the choice of the model depends to the specific problem to address and no unique recipe can be provided ex ante (Munari and Oriani, 2011).

1.2 The Real Options Games

Firms not operate alone in the market, indeed, in determining their strategic investment decisions, they should consider the presence of other competitors.

For example, in a case study reported by Ferreira et al. (2009), is reported the story of MineCo. MineCo is examining the opportunity of expanding her production capacity. Her idea is to open a new mine in her regional market. This market is affected by uncertainty. In particular, if the demand exceeds the local supply, customers have the possibility to import resources from foreign sources resulting in a limitation on prices. Moreover MineCo supposes that CompCo, her largest competitor, may invest in a similar project. In this scenario there are two sources of uncertainty that MineCo should consider to establish her strategy: on one hand the uncertainty related to the demand level and, on the other hand, the strategic interactions with her competitor. Four different strategic scenarios are possible: both companies invest now, both companies wait, MineCo invests and CompCo waits and *vice-versa*. Authors analyse the four scenarios and find out that the optimal strategy for both firms is that MineCo invests now while CompCo waits (firms' profits will be $M35 and $M2 respectively). In fact, neither of them has interest to deviate from this behaviour otherwise they will get a lower profit; for example if CompCo decides to invest now as well, moving to the first scenario, she will lose $195 million. Therefore, while for MineCo the commitment value created by investing now is higher than flexibility value from delaying, the better strategy for CompCo is waiting.

MineCo's case shows the existence of a trade-off between making timely strategic investment to pre-empt the rivals and incurring in the risks related with unresolved market uncertainty. In order to take into account both the aspects a proper valuation method should be adopted. Real Options Games (ROGs) are a valuation tool that combine Real Options Approach with Game Theory and allow firms to adapt their strategies to a changing market environment, considering the importance of making an early investment commitment while maintaining managerial flexibility (Smit and Trigeorgis, 2007).

In a Real Options Game model the players of the game are usually the firms that hold the investment opportunity and they are also assumed to be rational. Usually the strategies available for the players are the choices of making the investment or defer

such a decision and their payoffs are the firms' net cash flows coming from the investment. In particular, the present value of these cash flows is a stochastic variable that follows a known process[1] and the investment cost is sunk and fixed. To fully define the game, it is necessary to specify which kind of information is available for firms (Azevedo and Paxson, 2014). In particular, there can be perfect (or imperfect information), which means all the action of the other players are (not) known, and complete (or incomplete information), which means that players' strategies and payoffs are (not) common knowledge (Azevedo and Paxson, 2010).

Once the players' payoffs are calculated, the solution of the game can be determined using Nash equilibrium. Nash equilibrium holds when game players choose a set of strategies with the property that no firm has interest to deviate from its behaviour.

Usually ROG models can be divided into two main categories, depending on the firms' investment decisions are made under the assumption of continuous time or discrete time. In the following I will report the game theoretic/RO framework foundations to explain how this kind of models work. In addition I will analyse, for both categories, their main assumptions and characteristics and describe the most interesting contributes.

1.2.1 Continuous-time ROG

Most of the literature on ROG focuses on continuous-time ROG. This stream of research starts with the study of Fudenberg and Tirole (1985), which provides the game-theoretical foundations for the adoption of new technology in a deterministic framework. Smets (1993) was the first to develop a RO model considering also competition in his PhD dissertation thesis. Starting from his work, Dixit and Pindyck (1994, chapter 6 and 9) develop a pre-emption game, which will be the standard investment model for leader-follower competition setting under uncertainty.

In the model[2] two identical firms have the possibility to invest at a cost I in the same irreversible project and they need to find the optimal timing for the investment. It is

[1] Usually a GBM.

[2] The reader can find the presentation of the standard investment model in Dixit and Pindyck (1994), Grenadier (1996), Pawlina and Kort (2006).

assumed that both firms are risk-neutral, time is continuous and infinite. Cash flows expected from the investment are uncertain and the price of a unit of output is equal to:

$$P(t) = X(t)D\left[Q(t)\right] \tag{17}$$

where D is the inverse demand function (with $D'<0$), $Q(t)$ is the industry supply process and X is a multiplicative demand shock and evolves as a geometric Brownian motion:

$$dX = \mu X dt + \sigma X dz \tag{18}$$

where dz is the increment of a standard Wiener process. The constant μ is the drift parameter and represents the instantaneous conditional expected percentage change in X per unit time and the constant σ is the instantaneous conditional standard deviation per unit time.

The authors derive firms' optimal investment thresholds and their value functions. Using the backward induction, first is determined the follower's values function, denoted as $F_F(X)$. Specifically, it must satisfy in equilibrium the following differential equation:

$$\frac{1}{2}\sigma^2 X^2 \frac{\partial^2 F_F(X)}{\partial X^2} + \mu X \frac{\partial F_F(X)}{\partial X} - rF_F(X) = 0 \tag{19}$$

Where r is the riskless interest rate. Equation (19) must be solved subject to specific boundary conditions and will exist a trigger value, X_F, such that the follower will exercise the option to invest the first time that $X(t)$ equals or exceeds X_F. The conditions are:

$$F_F(X_F) = \frac{X_F D(2)}{r - \mu} \tag{20}$$

$$F_F^{'}(X_F) = \frac{D(2)}{r - \mu} \tag{21}$$

Note that, working with backward induction, at the moment of the investment decision of the follower, the leader has already invested. Thus, in the market both firms are active and the industry output is indicated ad $D(2)$.

The first boundary condition (equation 20) is the "value-matching" condition. It reflects the fact that, at the moment of exercise, the payoff of the option is the expected present value of the duopoly cash flows in perpetuity minus the cost of the investment. The

second boundary condition (equation 21) is the "high-contact" or "smooth-pasting" condition. It ensures that X_F, is the trigger that maximizes the value of the follower's option.

Solving the equilibrium differential equation in (19), subject to the above boundary conditions, results in the following follower's values function and follower's investment threshold:

$$F_F(X) = \begin{cases} \dfrac{1}{\beta - 1}\left(\dfrac{X}{X_F}\right)^{\beta} & \text{if } X < X_F \\ \dfrac{XD(2)}{r-\mu} - I & \text{if } X \geq X_F \end{cases} \tag{22}$$

$$X_F = \left(\frac{\beta}{\beta - 1}\right)\left(\frac{r-\mu}{D(2)}\right) I \tag{23}$$

Where

$$\beta = \frac{1}{2} - \frac{r-\delta}{\sigma^2} + \sqrt{\left[\frac{r-\delta}{\sigma^2} - \frac{1}{2}\right]^2 + \frac{2r}{\sigma^2}} \tag{24}$$

Where $\delta = \mu - r$. Going back, the leader's value function is influenced by the follower's exercise strategy and is equal to:

$$F_L(X) = \begin{cases} \dfrac{XD(1)}{r-\mu} - I + \dfrac{D(2)-D(1)}{D(2)} \dfrac{\beta}{\beta - 1} I \left(\dfrac{X}{X_F}\right)^{\beta} & \text{if } X < X_F \\ \dfrac{XD(2)}{r-\mu} & \text{if } X \geq X_F \end{cases} \tag{25}$$

The leader's investment threshold, X_L, can be derived equalizing equation (22) and equation (25) for $X < X_F$, replacing X with X_L and solving for X_L.

Leader's and follower's value functions are showed in Figure 4, it is possible to individuate three regions. At any point below X_F, each player would prefer being the follower and no entry occurs. At any point between X_F and X_L each player would prefer being the leader. Specifically, firms will invest according to the principle of rent equalization explained by Fudenberg and Tirole (1985). At point X_P, the leader's value function has the maximum value, thus both firms would prefer invest at this threshold. However, due to the presence of a first mover advantage, each firm has fear of being

pre-empted by the competitor and if they invest an instant before the competitor they will get a payoff advantage. This behaviour continues until $X(t)$ reach the threshold X_L where the leader's and follower's value functions are equal. At this threshold one firm invests and enjoys temporary monopoly profit. The other player waits until X_F is reached, at any point over X_F both players are active in the market.

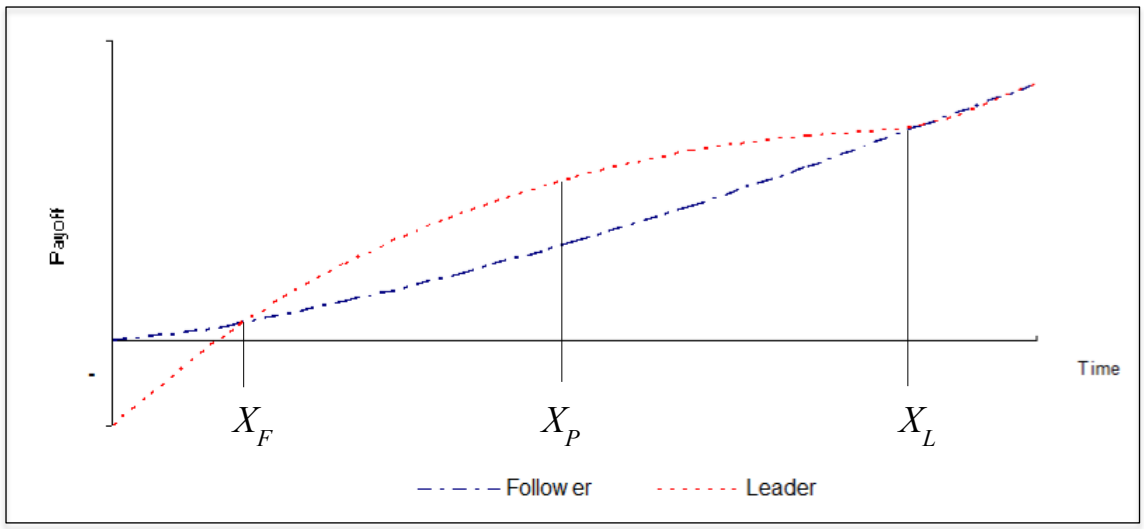


Figure 4: Leader's and follower's value functions.

The pre-emption game is the most common model treated in the literature on continuous time games. Specifically, this branch of the literature usually focuses on symmetric duopoly model, where firms act non-cooperatively and authors derive firms' optimal thresholds. The main contribution of these papers is to apply ROG setting in particular markets or consider factors that can influence the value of the option.

For example, Grenadier (1996) develops a duopoly investment game to study the behaviour of real estate markets. In the model two building owners hold the option to develop a new superior building. The exercise of the option does not yield immediate payoffs, indeed should be considered the time-to-build, i.e. the period necessary for the construction that varies across property types (e.g., residential, office or industrial buildings). The author shows that the development options could be exercised sequentially or simultaneously, depending on the initial state of demand, $X(0)$. If $X(0)$ is below X_F, leader (randomly selected) will initiate development the first moment that $X(t)$ equals or exceeds X_L, while the follower waits until $X(t)$ rises to X_F. If $X(0)>X_F$, one

firm will begin construction and the other will enter instantaneously thereafter. Grenadier suggests empirical implications for his model explaining how "development cascade" occurs more frequently when demand volatility increases and also "recession-induced construction boom" is more likely with greater time-to-build and volatility.

Huisman and Kort (2003) and Huisman and Kort (2004) analyse strategic technology adoption investment decisions. Two identical firms can initially invest in a current technology, knowing that later a new and more efficient technology becomes available for the adoption. In particular in Huisman and Kort (2003) information is complete, i.e. firms know when the new technology will be available, and if one firm has invested in the current technology she may replace it with the new one with a less cost. Depending on the investment scenario, they arrive at several different game equilibrium strategies with first mover advantage or second mover advantage. Anyway the mathematical formulation of the model is deterministic. In Huisman and Kort (2004), authors relax the assumption of complete information, indeed the time at which the new technology is available is distributed according to an exponential distribution, so that the arrival of this technology follows a Poisson process with parameter k. Different strategies are pursued according to the value of k. When the probability that the new technology becomes available soon is high, firms will wait for the adoption of this one. When this probability is not high enough, two patterns of investment behaviour may arise: usual pre-emption game, i.e. each firm tries to be the first investor, and the firm that will invest second can choose to invest for the new technology or not; attrition game, there is a second-mover advantage, i.e. both firms would like to be the follower, at the end one firm will invest and the other will wait for the new technology. It is important to notice that with no technological progress opportunity, the model exactly equals the one treated in Dixit and Pindyck (1994).

Mason and Weeds (2010) analyse irreversible investment in a project with uncertain returns in a dynamic two-player model with the aim to investigate how equilibrium outcomes are affected by the threat of pre-emption. They find out that in presence of positive externalities, greater uncertainty can accelerate rather than delay investment. This is because uncertainty can raise the leader's value more than the follower's. Pre-emptive reasoning entails that the leader must act sooner, therefore considering strategic

interactions and externalities have important effects in investment decisions in contrast to the standard real options thinking.

These authors gave important contributions to ROG literature. However, over time, scholars have relaxed some assumptions of the model above considered and have developed extensions to get closer to a more realistic scenario.

In particular, some authors focus their attention on market with several firms (Williams, 1993, Grenadier, 1999, 2002, Aguerrevere, 2009). For example, Grenadier (1999) investigates how, with imperfect information, the signal effect of the observed actions of other players influence firms' exercise decision. He considers an oligopoly with n agents that hold an identical option which can be exercised at any time. In the model there is imperfect information since every agent does not know his exact payoff at the moment of option exercise and all the agents will take their exercise decision founding not only on their own private signal but also on the signals (exercise decisions) of other agents. In particular, the author assumes that agents differ in the quality of their private information, therefore the forecast accuracy of their future payoffs (i.e. their signals) is decreasing, i.e. the forecast of Agent 1 is more precise that the forecast of Agent 2 and so on. The intuition for the equilibrium is: if Agent 1 has a positive signal, the expected value of exercising is high and he will not wait to learn from Agent 2's actions, otherwise, if the signal is low he will wait and copy Agent 2's actions. Agent 2 has observed Agent 1's actions and will proceed to exercise optimally and so on until Agent n. Anyway a suboptimal equilibrium arises when an informational cascade occurs. In case of informational cascade agents will ignore their private information and instead emulate the behaviour of previous actors, i.e. whenever two consecutive agents reveal positive signals.

Other authors relax the restrictive assumption that the duopolistic rivals are identical and consider several degree of asymmetry. In this field, Pawlina and Kort (2006) investigate options exercise decisions in case of investment cost asymmetry. Firms differ for the required sunk cost associated with the investment and the magnitude of this cost asymmetry is indicated as κ. Authors identify three different equilibrium strategies according to the level of κ and the level of the first-mover advantage, i.e. the ratio between the profit of being leader and the profit of duopoly (see Figure 5). In case the cost disadvantage is relatively small and the first-mover advantage is high, pre-

emptive equilibrium holds; when there is no significant first-mover advantage, firms invest simultaneously and, finally, when the degree of cost asymmetry is significantly high, firms invest sequentially and the leader simply maximizes the value of its investment opportunity.

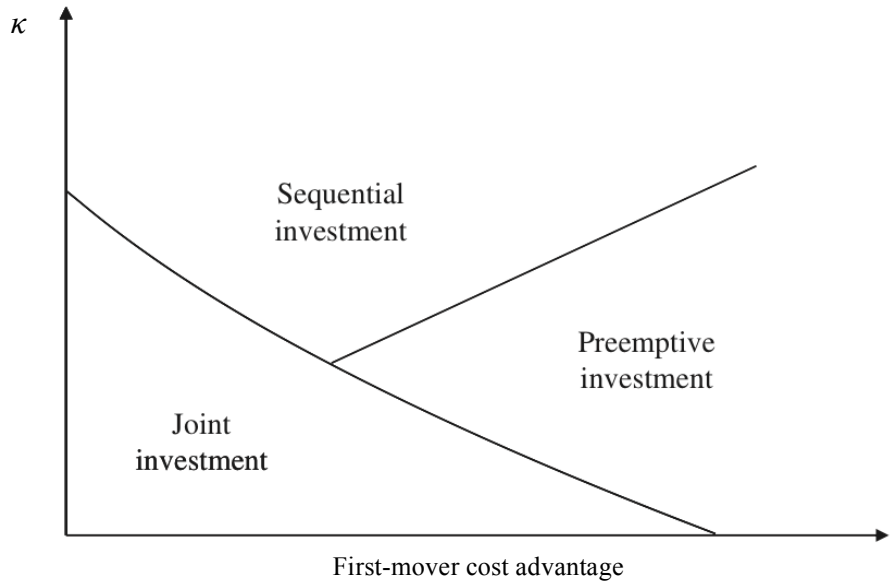


Figure 5: Equilibrium areas in Pawlina and Kort (2006).

Kong and Kwok (2007) extend firms' asymmetry in both sunk cost of investment and revenue flows. Authors provide a complete analysis of strategic equilibriums in both cases of positive externalities and negative externalities. Under positive externalities, there is not pre-emptive pressure and simultaneous or sequential entry equilibrium are possible. In case of negative externalities, when one firm dominates the other, firms enter at their respective leader's and follower's optimal thresholds, without dominance, the threat of pre-emption by the rival leads to pre-emptive or simultaneous entry equilibrium.

Weeds (2002) presents a model in which two firms have the possibility to make an irreversible investment in competing research projects to obtain the same patent. The technological success of the project is probabilistic following a Poisson process and the economic value of the patent evolves stochastically following a GBM. Even if she develops a winner-takes-all game, she also provides the investment thresholds for a cooperative scenario. In the latter scenario, the form of the equilibrium depends on the

relative magnitudes of the leader's value and both sequential leader-follower equilibrium and a joint-investment outcome are possible. In particular, for simultaneous investment the effect of non-cooperative behaviour is to increase the time to first investment as compared to the case of cooperative scenario, as each firm holds back from investing in the fear of starting a patent race.

1.2.2 Discrete-time ROG

Under the assumption of discrete time, ROG models are less common in the literature. In general, some scholars derive frameworks that provide basic principles of ROG mechanism suggesting how apply ROG logic in the real market while others papers develop models that analyse more complicated settings. In case of discrete time, games are usually settled in two stages and are represented in the extensive form. Specifically, in a two-stages discrete-time model the choice to "invest" or to "defer" is made in two possible moments by both firms.

Among these works, one of the first contributions is given by Smit and Ankum (1993). They use the binomial lattice to analyse the option to defer investment in production facilities. First, they consider, a duopoly where firms have equally market power and in this case the game takes the form of a classic prisoner's dilemma: both firms choose to invest while this is a suboptimal solution. Subsequently they suppose the presence of asymmetry between firms, in this case the dominant firm enjoys his competitive advantage. The equilibrium of the game depends on the evolution of the market: if it turns out to be favourable, and a large net present value is expected, the dominant firm will invest early, otherwise she will postpone the project. Conversely, the firm in a weak position will defer the investment until the market develops sufficiently.

Smit and Trigeorgis (2006, 2007) analyse investment opportunities, with examples and cases, that involve important competitive/strategic decisions under uncertainty and provide several insights for firms' competitive strategies. In Smit and Trigeorgis (2007), authors describe different principles for analysing competitive strategies under uncertainty, analysing both one-stage investment games and two-stage investment games adapting firms' competitive investment strategies to Fudenberg & Tirole (1984) framework. Authors suggest that in presence of competition in technological innovation, while firms usually face a winner-takes-all situation starting a race to pre-empt each other, a cooperation strategy, i.e. joint research venture, may be more

appropriate and profitable. In Smit and Trigeorgis (2006), authors discuss several examples underlining how firm's decision has an impact on competitors and in determining equilibrium outcomes and competitive strategies. The aim of their work is to show the potentiality of the use of ROG approach especially for oligopolistic and innovative industries, e.g. consumer electronics, telecommunications or pharmaceuticals.

The main limitation of these papers is that they provide only numerical approaches, but there are also present several works that develop deepened analytical treatment.

Among them, Kulatilaka and Perotti (1998) analyse a two-stage duopoly game in both the case where firms could decide simultaneously on the investment and the case of asymmetric Stackelberg game. Firms, in the first stage, have the opportunity to make an initial irreversible investment in a growth option which confers, in the second stage, a lower cost production than for competitors without growth options. In the second stage there is Cournot competition. In case of Stackelberg game, strategic investment is optimal for the leader when the level of expected demand exceeds the indifference threshold while the follower will enter in the market for a higher threshold. The entry point for the leader depends on the magnitude of the strategic advantage, i.e. the production cost for the follower. In particular, high level of strategic advantage implies that the investment has a strong entry dissuasion effect, therefore a high level of uncertainty encourages the investment; otherwise, if the strategic effect is weak, the uncertainty deters the investment. In case of log-normally distributed demand Black-Scholes-like solutions hold. In case of simultaneous investments neither player can condition its strategy on the other firm decision, so the solution will be simultaneous investment or no investment by both firms depending on the level of demand uncertainty and strategic advantage as before.

Murto et al. (2004) consider an oligopoly game several firms produce a homogeneous product, whose demand evolves stochastically, and each of them has a set of discrete investment opportunities available to adjust their production cost functions or production capacities. After the equilibrium strategies of the firms are derived, authors use simulation Monte Carlo to analyse a duopoly asymmetric case where one firm has the possibility to make smaller investments with higher cost per unit and for the other firm the reverse holds. Results offer a good picture of the trade-off between the value of

flexibility and scale economies under competition, in particular the more flexible firm is in general more able to adapt to demand changes, while the other firm takes advantage from very high demand growth. Anyway the use of Monte Carlo simulation brings some limitations due to the heavy computing capacity required, e.g. analysis is restricted to the duopoly case.

Martzoukos and Zacharias (2013) demonstrate how two competing firms can act strategically and take advantage of the positive spillovers, or take pre-emptive action against the negative spillovers. Specifically, they developed a two-stage game in presence of spillover effects. In the first stage, firms determine, between a discrete number of alternatives, their optimal level of coordination (research/technology policy choice). In the second-stage tactical decision, firms choose the optimal effort for a given level of the spillover effects and the cost of information acquisition. In this stage the Black & Scholes formula is adopted but there is no further interaction between the two firms. Authors also find that, under learning-by-doing hypothesis and in presence of switching costs for strategy revision, strategy shifts are easier to observe for dominant firms and in market environments of high growth and high volatility.

Despite their little implementation, discrete-time ROGs, as well underlined by Smit and Trigeorgis (2007), represent a flexible approach that allow to preserve many important features like the tractability of the paths in the model, the opportunity of incorporating strategic features necessary for a realistic setting, underlying stochastic processes (e.g. Brownian motion) and exogenous chance of competitive entry.

1.2.3 Conclusions on ROG literature

In Table 2 the main contributions and characteristics of the works analysed in this section are summarized. Note that time can be discrete (D) or continuous (C), information can be complete (C) or incomplete (I) and firms can be symmetric (S) or asymmetric (A).

Table 2: Main contributions of ROG literature.

Authors (Year)	**Title**	**Journal**	**Time**	**N. of firms**	**Information**	**Symmetry**	**Contribution**
Dixit & Pindyck (1994)	Investment Under Uncertainty.	*Princeton University Press.*	C	2	C	S	Develop a pre-emption game to evaluate optimal thresholds for investments under uncertainty.
Grenadier (1996)	The strategic exercise of options: Development cascades and overbuilding in real estate markets.	*Journal of Finance*	C	2	C	S	Develop a pre-emption game in the real estate markets.
Grenadier (1999)	Information Revelation through Option Exercise.	*The Review of Financial Studies*	C	*n*	I	S	Equilibrium framework for option exercise games with asymmetric private information. Analyses the occurrence of an informational cascade
Huisman & Kort (2004)	Strategic technology adoption	*European Journal of Operational*	C	2	I	S	Take into account technological

	taking into account future technological improvements : A real options approach.	*Research*					progress in making investment decisions. According to the rate of arrival of the new techno-logy, pre-emption game or war of attrition may arise.
Kong & Kwok (2007)	Real options in strategic investment games between two asymmetric firms.	*European Journal of Operational Research*	C	2	C	A	Analyse how asymmetry on both the sunk cost of investment and revenue flows of the two firms affect the optimal investment thresholds.
Kulatilaka & Perotti (1998)	Strategic growth options.	*Management Science*	D	2	C	S/A	Two-stage duopoly game. Investments in strategic growth options are encouraged when uncertainty increases.
Martzou-kos &	Real option games with	*Omega*	D	2	I	S	Two-stage duopoly game.

Zacharias (2013)	R&D and learning spillovers.						Determine the optimal level of coordination and the optimal effort in presence of the spillover effects.
Mason & Weeds (2010)	Investment, uncertainty, and pre-emption.	*International Journal of Industrial Organization*	C	2	C	S	In a pre-emption game, in presence of positive externali-ties, greater uncer-tainty can accelerate rather than delay investment.
Murto et al. (2004)	Timing of investments in oligopoly under uncertainty: A framework for numerical analysis.	*European Journal of Operational Research*	D	*n*	C	S/A	Analyse trade-off between the value of flexibility and scale economies under competition, using Monte Carlo simulation.
Pawlina & Kort (2006)	Real options in an asymmetric duopoly: Who benefits from	*Journal of Economics & Management Strategy*	C	2	C	A	Study the effects of investment costs asymmetry on

	your competitive disadvantage?						the optimal real option exercise strategies and the value of duopolistic firms.
Smets (1993)	Essays on Foreign Direct Investment.	*PhD thesis*	C	2	C	S	The first paper in real options litera-ture to consider interactions between firms.
Smit & Ankum (1993)	A real options and game-theoretic approach to corporate investment strategy under competition.	*Financial Management*	D	2	C	S/A	Using binomial lattice, develop a numerical example to analyse the option to defer investment, for both symmetric and asymmetric firms.
Smit & Trigeorgis (2006)	Real options and games: Compe-tition, alliances and other applications of valuation and strategy.	*Review of Financial Economics*	D	2	C	S	Use examples from innovation cases in consumer electronics and telecommunicat ion industries. Focus on whether it is optimal to compete independently or

							coordinate/collaborate via strategic alliances.
Smit & Trigeorgis (2007)	Strategic options and games in analyzing dynamic technology investments.	*Long Range Planning.*	D	2	C	S	Develop a framework to analyse competitive strategies under uncertainty.
Weeds (2002)	Strategic Delay in a Real Options Model of R&D Competition.	*The Review of Economic Studies*	C	2	C	S	Model competition to develop a new patent. Consider both cooperative and non-cooperative scenarios.

Nevertheless real options game literature has been developed only recently, it is emerging as a methodology for evaluating investment decisions. Indeed, ROG allows understanding firms' behaviours no longer in monopoly settings but also when several firms act in the market affecting their expected profits each other. Therefore this framework is particularly relevant as firms in the real market usually have to take their investment decisions under conditions of uncertainty and competition with rivals.

There are several directions for future researches that could allow extending ROG analysis to more complex and diversified scenarios. For instance, usually in ROG literature, investment choices available for firms are strictly defined (e.g., investment in the project or not) in a horizontal competition setting, whereas real-life investments often include a lot of different choices. Specifically, in the current competitive scenario, where cooperation outside the boundaries of the firms is one of the key factors of

success, scholars may find interesting to consider alliance setting or vertical competition setting.

Finally, the main issue to deal with is the applicability of the models. Indeed, most of the works have been focused on analytically derivation not focusing on the possibility of a real application of this methodology by practitioners. In this context, on one side, benchmarking empirical studies can help to contextualize these models in the real markets and to individuate the most promising research streams (Azevedo and Paxson, 2014); on the other side, it is possible to increase the development of discrete-time approaches and simulation tools, that are more flexible and easy to manage for practitioners (Chevalier-Roignant et al., 2011).

1.3 The pharmaceutical R&D process and the alliances

New drug development has become considerably challenging in recent years: while length and cost of R&D have been growing, chances of success have become extremely low. As a matter of fact, pharmaceutical companies have invested more than $500 billion in R&D into medical innovations since 2000, with an estimated $48.5 billion only in 2012. In contrast, only 43 new medicines were approved by the U.S. Food and Drug Administration (FDA) in 2012, being the highest number in the last 15 years (Phrma, 2013).

This setting is related with the intrinsic characteristics of the new drug R&D process. A drug may spend 10-15 years in the developmental process (Robinson and Stuart, 2007) and cost, on average, $300 million to bring to market (Rogers et al., 2002). The development starts with the discovery phase where thousands of compounds are tested in order to find one that can achieve a desirable result. The most promising compounds enter the pre-clinical testing. In this phase compounds are tested in animals, both in vitro and in vivo. If the pre-clinical phase turns out to be successful, the drug candidate starts clinical trials that are constituted of three phases. In phase I, 20–80 healthy volunteers test for safety and dosage. Phase II involves 100–300 patient volunteers used to test for efficacy and side effects. Phase III includes 1000–5000 patient volunteers in order to test the effectiveness of the drug. Using double-blind studies with placebos, it must be shown that the new drug works better than the existing treatment. If the clinical tests are successful a new drug application (NDA) is filed with the Food and Drug Administration (FDA). Once approval is obtained, the pharmaceutical company can

enter the commercialisation phase and has the right to sell the drug under a trademark protected by a patent (Cassimon et al., 2004). Of 5,000–10,000 screened chemical entities in the discovery phase, 250 enter the pre-clinical testing and only five will enter in the clinical phases (Cassimon et al., 2004). Therefore this process is characterized by technological uncertainty. Also market uncertainty is present, due to the incomplete information regarding the cost of producing the drug, the eventual pricing structure, and the captured market share (Rogers et al., 2002).

Despite these difficulties, big pharmaceutical companies cannot avoid relying on R&D activities, and keep considering them as a major source of value creation, in spite of their intrinsic risks. To achieve this goal, pharmaceutical companies more and more consider new paradigm solutions including next-generation licensing (Kleyn and Kitney, 2007) and effective pre-competitive collaboration with other companies (Dhankhar et al., 2012).

In particular, from the advent of biotechnology in the eighties, pharmaceutical companies more and more have entered into alliances with the biotechnology companies, pooling their complementary assets, with successful results. From one side, biotech firms have expertise on new drug discovery technologies, which rely on microbiology and genomics. Pharmaceutical companies are larger, can benefit from economies of scale and scope in conducting clinical trials, have more experience in the FDA approval process, manufacturing, marketing and sales. In addition, they have considerable amounts of financial resources, of which biotech firms are lacking. Therefore, large pharmaceutical companies rely increasingly on alliances to supplement their drug pipelines (Nicholson et al., 2005) and biotech firms rely on alliances with established firms for access to capital (Majewski, 1998), and for access to product markets (Hill and Rothaermel, 2003). This has determined a change from the traditional "closed innovation" business model to the "open innovation" (OI) business model (Bianchi et al., 2011).

Alliances have been widely studied in the literature analysing several key aspects involved in the alliance process. Between these aspects Bianchi et al. (2011) underline that three main decisions, on which pharmaceutical company should focus, are the organisational modes through which the firms set up their partnership, the type of partner with which enter in relationship and in which phase of R&D process signing the

agreement. Many scholars have analysed the governance of R&D alliance (Oxley & Sampson, 2004, Bosse & Alvarez, 2010, Pangarkar & Klein, 2001, Das and Teng, 2001) and partner selection (Hoang and Rothaermel, 2005, Danzon et al, 2005). The most popular theories that have been used are the Transaction Cost Economics (TCE) (Williamson 1985), and the Resources-based View (Zollo, 2002).

Another stream of research focuses on factors that could prevent or bring to stop collaborations. Among the factors potentially impeding collaborations, there are the risk of adverse selection and moral hazard. The former can arise between a new venture, i.e. biotech firm, and its potential alliance partners when there is information asymmetry regarding the value of the new venture's resources and its future prospects (Ozmel et al., 2013). According to this, Pisano (1997) suggests that small firms take advantage of asymmetric information to out-license their least promising compounds, retaining their more promising candidates to develop independently. In order to mitigate these problems new ventures can use many different types of signals to reveal their true quality to outsiders (Connelly et al, 2011). For instance, Nicholson et al. (2005) state that inexperienced biotech companies receive substantially discounted payments when forming their first alliance to signal their quality. Ozmel et al. (2013) investigate whether and how the effects of different networks are contingent upon one another. In particular, they find that both affiliations with venture capitalists (VCs) that have prominent positions in syndicate networks and new venture's prominence in alliance network signal biotech firms' quality and positively influence its likelihood of future alliance formation. Moral hazard problems in biopharmaceutical alliances may arise due to the fact that pharmaceutical companies are not sure that the funds they are providing to their biotechnology partners are not diverted to other research projects (Higgins, 2007). Contractual design helps to diminish asymmetric information, with the allocation of ownership rights firms can divide research tasks and financial resources and control the partner's behaviours. According to this several authors analysed contractual terms of alliances and the allocation of control rights. For instance, Lerner and Merges (1998) find that the allocation of control rights to the biotech firm increases with its financial resources; while Higgins (2007) underlines that the pharmaceutical companies tend, on average, to give up more rights in later stage alliances.

Regarding the alliance timing, as underlined by Katila & Mang (2003), there is a lot of variation at what stage of the drug R&D process alliance are signed. Arnold et al. (2002) suggest that the size of the deals is significantly influenced by alliance time therefore the opportunity of signing the agreement is affected by the current stage of the R&D process and Niosi (2003) reports that on one hand a too early alliance prevents biotech firm from profiting of the real value of his innovation because his new compound is underestimated and, on the other hand, if the agreement is signed too late the biotech firm could encounter financing problems in the early phases. Hermosilla & Qian (2013) underline how biotech managers have to decide the optimal stage in which license the compound considering both the R&D process risks and the higher attractiveness of licensing contracts terms in case the potential drug is closer to the market

However, scholars who have studied alliance timing don't come to the same conclusions. On one hand, Kalamas et al. (2001) carry out a Monte Carlo simulation in order to determine the optimal time of licensing, in particular they found that, with improved contract terms, early stage agreement could be more valuable for both biotech and pharmaceutical companies. Similarly Katila & Mang (2003), through an empirical analysis, investigate when companies decide to collaborate in exploiting opportunities. They show how R&D intensity, collaboration experience, increase in the intellectual property protection and increase in the number of state biotechnology centres are able to move up the alliance. On the other hand, Nicholson et al. (2005), examining the determinants of deal payments with asymmetric information, suggest that biotech forms can reach higher payments conditions in case of late stage agreement. With a different perspective, Bianchi et al. (2011), assuming the viewpoint of the pharmaceutical company, identify, through a survey, how different organisational modes of the agreements are located in the R&D process. For instance, in-licensing and partnership with biotech firm to pursue an innovative objective are mainly located in early drug stages. On the other hand, out-licensing or alliance to obtain the access to assets for commercially exploiting the new drug are more common in the second part of the R&D process. This stream of literature offers some insights regarding alliance timing but these studies use surveys or empirical approaches therefore the development of an analytical model lacks.

1.3.1 Research on R&D alliances with a real options perspective

More recently ROA has been used also to evaluate R&D alliances established between firms. Alliances are an ideal field for the application of ROA due to their characteristics of uncertainty, flexibility and irreversible costs. Some scholars studied alliance adopting a real option perspective and using an empirical approach (e.g. Tong et al., 2008, Reuer and Tong, 2010, Santoro and McGill, 2005, Vassolo et al., 2004, Bérard and Perez, 2013, McCarter et al., 2011).

However, according to Lukas (2008), there are a small number of papers adopting real options modelling approach in this context. Recently, among these works, Savva and Scholtes (2014) and Baldi et al. (2015) investigate how to structure a contractual agreement taking into account the embedded options between a small and financially constrained biotech company and a major pharmaceutical company.

Specifically, Savva and Scholtes (2014) model an environment where pharmaceutical and biotech firms collaborate in new drug R&D and consider three contractual arrangements: co-development, licensing, and co-development with opt-out options. In particular, they study a setting where the pharmaceutical company has the option to terminate the R&D project and, at the same time, is also the actor making decisions on the contractual terms (e.g., milestones and royalties). In co-development the small firm runs a risk of running out of capital as future costs rise, while licensing for milestone and royalty payments, which eliminates the latter risk, introduces inefficiency as profitable projects might be abandoned. Conversely, an option clause in a co-development contract gives the small firm the right but not the obligation to opt out of co-development and into a pre-agreed licensing arrangement avoiding the problems associated with both co-development or licensing. Baldi et al. (2015) examine how perspectives and negotiation practices between licensor and licensee of IP change under uncertainty with a real options perspective. The authors highlight the importance to use the real option logic methodology to value three licensing situations for IP managers in the context of an illustrative case study involving a French biotech firm, and compare them to conventional NPV analysis. They show how management practices change depending on who pays for the development costs, controls the continuation/development or abandonment option and thereby appropriates more of the embedded option's value.

Other papers analyse the effect of uncertainty and flexibility on joint venture duration and terminations strategies (Chi, 2000; Lukas, 2008). Specifically, Chi (2000) develops a model that is used specifically to examine the option to acquire or divest a joint venture, both in the case where the acquisition/divestiture price is specified ex ante in the initial contract and in the case where the price is to be negotiated ex post. The results derived from the model show how the value of the option and each partner's payoff from the venture vary with the structure of the option. Lukas (2008) adopts a real-option-based framework to model a joint venture-induced market entry under both economic and technology uncertainty in a continuous time setting. He determines critical thresholds for timing and termination strategy in the domain of joint ventures and finds that technology uncertainty promotes the formation of joint ventures.

Also the alliance timing has been investigated by Rogers et al. (2005) and Cvitanić et al. (2011). Starting from the above described model of Rogers et al. (2002), Rogers et al. (2005) proposed an approach by which to select the best licensing strategy for each product in a R&D portfolio. Specifically, in the OptFolio model alliance opportunities are considered as real options ad the model is based on the binomial tree method. Despite being close to reality, the implementation and use of OptFolio turns out to be very complex and difficult to manage. Authors suggest that early licensing agreements should be considered to generate the maximum value for pharmaceutical company's projects portfolio.

Cvitanić et al. (2011) analytically derive the optimal timing and the relative profits shares of a pharmaceutical company and a biotech firm involved in a co-development alliance. They develop a real options model under three different contract designs. In particular, they consider the case of risk sharing between the two firms, the case of agreeing on the time to enter, and the case of asymmetric contract decisions. In the latter case authors assume that the biotech firm decides on the initiation time, while the pharmaceutical company decides on how to share the profits. If the firms are risk-neutral the three contract designs are equivalent. However, for risk adverse firms, the three contract designs may differ significantly in the optimal contract parameters, but not much in the time of entry or in the level of expected utility.

While Rogers et al. (2005) take only the perspective of the pharmaceutical company, Cvitanić et al. (2011) consider the contract design for sharing the profits for both

alliance partners. However both studies, even if provide relevant insights on the management literature of the alliances, consider only the role of the alliance partners as if they act alone in the market. Anyway in the context of the real markets, this assumption is not realistic since firms often work in very crowded markets and the presence of strategic interactions with other actors, e.g. competition, can influence their choice of the most profitable investment strategies.

1.4 Research goal

The above sections provided a general overview of three prominent streams of research: real options methodology, real options games and R&D alliance in the biopharmaceutical industry with a real option perspective. Describing the major contributions of the scholars I have identified some aspects that have not been sufficiently addressed in previous studies.

Alliances in the pharmaceutical industry represent the new business model to respond to the significant modifications in the competitive environment (Bianchi et al., 2011). One of the main decisions that both pharmaceutical and biotech companies face is whether and when to ally. Although literature on alliance is wide, in the field of alliance timing much remains to study. Specifically, the conclusions to which arrive the scholars are not definitive. In addition, to the best of my knowledge, no studies have considered the strategic interactions with other firms in alliance timing decisions. This topic is particularly relevant as biotechnology industry is characterised by the presence of many competitors (FierceBiotech, 2007). In doing so it is necessary to take into account the multi-staged, costly and risky nature of the R&D process, the market uncertainty as well as the flexibility of managers. As suggested by Villiger and Bogdan (2005), in this field ROA should be adopted. However, the development of an analytical model to understand firms' behaviours, that take into account both aspects, is not present on previous works.

Therefore, the research goal of this thesis is to investigate the optimal timing in making an R&D alliance in a competitive environment taking both perspectives to incorporate the active role of both pharmaceutical and biotech firms. Principal aspects I would consider are competitiveness and uncertainty that characterize the market. To take into account both aspects I adopt the real options game approach. Differently from the previous literature I develop a model focusing on the choice of the alliance timing rather

than investment timing. I would also investigate the importance of adopting the real options perspective to evaluate alliance timing decisions instead of the traditional NPV methodology, showing how firms' optimal strategies are affected by the methodology utilised.

Chapter 2
Optimal timing for the biotech firms in a ROG model

2.1 Introduction

In this chapter, I develop a model to study alliance timing in presence of competition among biotech firms. Specifically, taking the perspective of biotech firms facing the decision of whether and when to collaborate with a pharmaceutical company, I investigate how the presence of competition might change firms' optimal strategies about the timing and the profitability of signing the alliance. To take into account both uncertainty of the R&D process and the presence of competition, I adopt the Real Options Games approach. In general, alliance timing decisions are the result of a trade-off. In fact, taking the viewpoint of a biotech firm, an early arrangement entails a risk sharing opportunity and the biotech firm can conduct higher quality and more successful R&D activities thanks to the considerable amount of financial resources coming from the pharmaceutical company (Gassmann and Reepmeyer, 2005). At the same time, however, an early arrangement has the negative effect of giving even higher bargaining power to the pharmaceutical company in determining the payment amount, which might financially penalise the biotech firm. On the contrary, in spite of higher risks of failure in early stages, a later agreement might help the biotech firm to better monetise from the innovation through higher payment conditions and higher royalties in the final market (Nicholson et al., 2005; Rogers et al., 2005). In general, the dominance of one of these contrasting forces over the other one determines whether a biotech should collaborate in early stages or postpone such a decision as late as possible. The existence of such conflicting forces also helps explain why is possible to observe substantial differences in the timing of real alliances. As a matter of fact, among the top biotech licensing deals in 2012, it is possible to observe a very large heterogeneity in alliance timing (Carroll, 2012). For instance, the agreements between FivePrime Therapeutics and GlaxoSmithKline and between Genmab and Novartis relate to the discovery stage in the new drug development process. On the other hand, the agreement between Enanta and Novartis relates to preclinical phase, whereas the agreement between Galapagos NV and Abbott Laboratories focuses on phase II. Some other

agreements, such as that between Thrombogenics and Merck KGaA, concern the stage of application for approval.

As reported in chapter 1, while previous studies offer important intuitions about alliance timing in the absence of competition among biotech firms, no works, to the best of my knowledge, are available when biotech firms compete in the same market. However, biotechnology industry is characterised by the presence of many competitors (FierceBiotech, 2007). Particularly, a Deloitte survey reports that a solid majority of both large and small companies in this industry believes that the alliance market will become even more competitive (Deloitte, 2005). In fact, naturally, some competitors end up working in the same therapeutic area. As an example, recent industry voices anticipate the emergence of a "horse race" in the migraine treatments among a number of biotech firms (Schatzman, 2013). Therefore, it is more realistic to incorporate the possible reaction of competitors in the decision-making process.

Specifically, I consider two competing biotech firms that have to decide whether and when to partner with a pharmaceutical company. The collaboration is in the form of in-licensing, an inbound solution, that typically, in its more general terms, involves up-front payments, milestones payments based on the successful completion of an R&D stage and royalty payments upon product commercialisation (Rogers et al., 2005; Dahlander and Gann, 2010). In the model, the alliance is mutually exclusive in the sense that the pharmaceutical company will only contract with one biotech firm. This is consistent with the observation that usually pharmaceutical companies identify and make a selection only among the most promising biotech target firms (Kalamas et al., 2001). I assume that both biotech firms can reach the market individually, which implies that they are not exactly researching on the same molecule. Therefore, if one biotech firm signs an alliance with the pharmaceutical company, the other can only continue the R&D process individually with some spillover benefits from the competitor's alliance, but with her own (limited) financial resources. This scenario is quite reasonable in reality and offers an opportunity to investigate alliance timing decisions from a wider perspective (Rogers et al., 2005).

In fact, in such case, competition might change the previous considerations about the timing and the profitability of signing the alliance. Intuitively, one could think that the introduction of competition will raise the incentive of each biotech firm to anticipate the

timing of collaboration with the pharmaceutical company in order to prevent the opponent from being faster in establishing the alliance. Therefore, the incentive to anticipate might be due to the traditional economics of pre-emption. To some extent, this might be the case of the recent alliance of Forma Therapeutics with Celgene. In fact, the small biotech firm has reached the deal right after several other biotech firms, such as Cleave Biosciences and Proteostasis Therapeutics, entered the field of protein homeostasis (McBride, 2013). However, an opposite effect might arise as well. In fact, there might be a strong competitive pressure to reach later stages or, even, the final market with products whose revenue are not shared with the pharmaceutical company in order to appropriate higher profits and win the competition against the rival. This effect seems to be consistent with several examples of successful biotech firms more and more willing to postpone potential deals in such a competitive arena (Toonkel, 2013).

By way of anticipation, my findings suggest that whether, when and who will ally with the pharmaceutical company depend on the contract terms offered by the pharmaceutical company, the market value increase due to the presence of the pharmaceutical industry, as well as the competitive advantage one biotech firm gains against the competitor due to the alliance. Identifying and understanding the conditions under which specific results arise can be particularly useful to both biotechnology and pharmaceutical companies involved in open-innovation based R&D project decisions in a competitive environment.

The remainder of the chapter is organised as follows. In the next section, I introduce the ROG model in case of only one biotech firm is active in the market. In particular, I present biotech firms' payoff expressions and the game solution. In the following section, I extend the model and relative solutions in the duopoly case. Later a discussion of results is provided. In the final section, conclusions are drawn.

2.2 The monopoly case

To better understand how the model works and how the presence of competition could affect alliance timing decisions, first of all, I present the simpler model of monopoly case. When there is only one firm in the market, it is possible to design the game as a game against nature, in which the player should optimise its payoff facing the stochastic fluctuations in project value (Smit and Trigeorgis, 2007).

I assume there is only one biotech firm in the market that has the possibility to establish a partnership with a pharmaceutical company that has the bargaining power to offer a take-it-or-leave-it contract and I maintain this assumption throughout the chapter. I consider two generic stages that model the staging of R&D investments in two phases: an investigative and confirmatory phase (first stage or stage I) and a manufacturing and commercialization one (second stage or stage II). At the beginning of the game, the pharmaceutical company offers the opportunity to the biotech firm to sign the agreement, and she has two possibilities: "Sign the alliance" or "Not sign the alliance". In case of alliance, biotech firm will receive an upfront payment (P_f) at the beginning of the stage and a certain amount of royalties upon product commercialization $(1-\alpha_f)$. If biotech firm rejects the agreement in the first stage, in the second stage the game is repeated. Also in this stage the contract offered to the biotech firm consists of an upfront payment (P_s) at the beginning of the current stage and an amount of royalties upon product commercialization $(1-\alpha_s)$.

Figure 6 depicts the extensive form of the game, biotech firm's payoffs are defined as π_j^B where $j = f$ (*first*), s (*second*) stands for the stage in which the agreement is signed. The derivation of the biotech firms' payoff expressions will be described in the following sub-section.

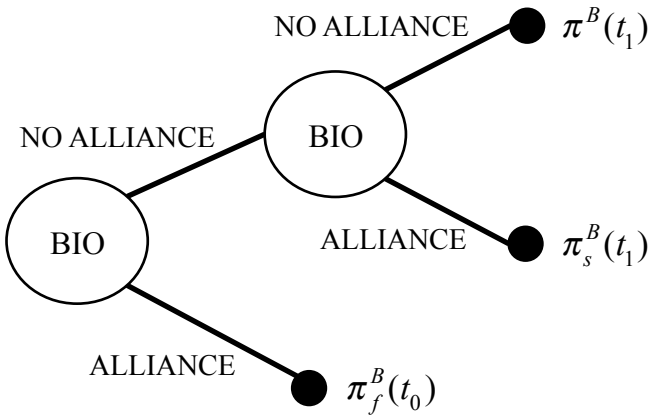


Figure 6: Game structure in monopoly case.

The collaboration between the pharmaceutical company and the biotech firm produces synergies between the two actors that increase the total size of the potential market of

the drug. Indeed, the pharmaceutical company, thanks to his advanced manufacturing and marketing capabilities, is able to amplify the value of the drug and this can be modelled by an amplification factor, denoted as δ (>1) (Rogers et al., 2005).

2.2.1 Model assumption and biotech firm's payoff expressions in monopoly case

In general, in the real world, pharmaceutical and biotechnology firms sign alliances along all the R&D process. For the sake of simplicity, I consider only two phases: the first phase (i.e., stage I) starts at t_0 and corresponds to exploratory clinical trials and confirmatory clinical trials (Girotra et al., 2007), at t_1 the second phase starts (stage II), i.e. manufacturing and commercialization phases. In the model, the expected market value of the drug, denoted as V, is based on the NPV of all expected cash flows following the end of the game.

According to the option perspective, during the interval (t_0, t_1), the expected market value of the candidate drug changes over time and it is represented by a non-negative random process $V(t)$. Specifically, at t_1 the value $V(t_1)$ is the expected market value of the fully approved drug. At any time $t < t_1$, $V(t)$ is a forecast of this market value and is updated as new information arrives. Indeed, the market value of the candidate drug changes due to several factors such as, changing disease demographics, epidemics, changes in the competitive landscape (such as entries or failures of competing drug candidates) but also as a consequence of the revealed safety and efficacy characteristics of the drug (Savva and Scholtes, 2014). In particular, the value of the project follows a Geometric Brownian Motion (GBM),[3] with drift parameter $\mu > 0$ and volatility parameter $\sigma > 0$ and its probability density function is a lognormal one. As soon as the maturity is reached at t_1, i.e. at the beginning of the second stage, the drug value is a known realization of this process, due to the fact that the biotechnology firm has more information about the value of cash flows coming from the commercialization.[4] Moreover, for the sake of modelling convenience, I make the risk-neutrality assumption for the firm. Under these assumptions, in the first stage it is possible to adopt the Black and Scholes approach to evaluate biotech firm's first stage payoff expression, which

[3] This is consistent with the previous literature on investment under uncertainty (Dixit and Pindyck, 1994) described above in Chapter 1.

[4] There is more information, but never, complete certainty about future cash flows of the project (Dixit and Pyndyck, 1994).

ensures the flexibility offered by the option to decide further investments when more information is available. Indeed, the investment in the first stage represents the price to buy the option to continue the development in the second stage. At the beginning of the second stage, uncertainty is reduced and the realization of the underlying is known, therefore I use the simple NPV methodology to evaluate biotech firm's second stage payoff expression.[5]

Before computing biotech firm's payoff expressions, I define the following parameters where subscript *f* stands for first stage and *s* stands for second stage:

- I_f = drug research and development investment cost incurred by the biotech firm in the first stage;
- I_s = drug research and development investment cost incurred by the biotech firm in the second stage;
- $V_s = V(t_1)$, i.e. expected net cash flows arising after commercialization calculated at the beginning of the second stage;
- $V_f = V(t_0)$, i.e. present value of V_s calculated at the beginning of the first stage;
- P_f = upfront payment offered, in case of alliance, by the pharmaceutical company to the biotech firm at the beginning of the first stage;
- P_s = upfront payment offered, in case of alliance, by the pharmaceutical company to the biotech firm at the beginning of the second stage;
- $(1-\alpha_f)$ = percentage of royalties that biotech firm receives in case of alliance in the first stage;
- $(1-\alpha_s)$ = percentage of royalties that biotech firm receives in case of alliance in the second stage.

Table 3 shows biotech firm's second stage payoff expressions, i.e. the payoff expressions when the alliance is signed in the second stage or no alliance is signed, calculated with the NPV methodology at t_1. Note that I restrict the analysis to a region of parameters that ensures positive payoffs.

[5] Moreover, the R&D process does not need further investments and, as a consequence, no more options are available.

Table 3: Biotech firm's second stage payoff expression.

Scenario		*Biotech firm's payoff*
Alliance at stage II	$\pi_s^B(t_1)$	$(1-\alpha_s)\delta V_s + P_s(t_1) - I_s$
No alliance	$\pi^B(t_1)$	$V_s - I_s$

Concerning first stage payoff expressions, i.e. the payoff expressions when the alliance is signed in the first stage, and the second stage payoff expressions backtracked to time t_0, as stated before, I use the Black and Scholes formula to take into account the stochastic evolution of the drug market value.[6] Payoff expressions are represented by the difference between an European call option, C_j^B (where $j = f, s$ stands for the stage in which the agreement is signed) and the investment needed in the first stage, I_f. In case of alliance in the first stage the biotech firm will also receives the upfront payment, P_f.

In Table 4 I report the first stage payoff expressions and the second stage payoff expressions backtracked to time t_0, specifying underlying values and exercise prices. Note that both I_f and P_f are sunk costs that do not affect the option value; the exercise price is equivalent to the investment required at the second stage. In case of alliance in the second stage, underlying value increases by an amount equal to the expected payment P_s of the second stage discounted at t_0.

[6] For the sake of clarity below the Black and Scholes formula (Black and Scholes, 1973) is reported:

$$C = SN(d_1) - e^{-r\tau} XN(d_2)$$

$$d_1 = \frac{\ln(S/X) + (r + \sigma^2/2)\tau}{\sigma\sqrt{\tau}}$$

$$d_2 = d_1 - \sigma\sqrt{\tau}$$

where S is the underlying value, X is the exercise price, τ is the time to maturity, r is the risk-free interest rate and σ is the volatility of $V(t)$. N represents the cumulative standard normal distribution function.

Table 4: Biotech firm's first stage payoff expression and second stage payoff expressions backtracked to time t_0.

Scenario		*Biotech firm's payoff*	*Underlying value*	*Exercise price*
Alliance at stage II	$\pi_s^B(t_0)$	$\max(C_s^B - I_f;0)$	$(1-\alpha_s)\delta V_f + P_s e^{-rt}$	I_s
Alliance at stage I	$\pi_f^B(t_0)$	$\max(C_f^B + P_f - I_f;0)$	$(1-\alpha_f)\delta V_f$	I_s
No alliance	$\pi^B(t_0)$	$\max(C^B - I_f;0)$	V_f	I_s

2.2.2 Game solution

In the game, three different scenarios of equilibrium are possible: the biotech firm allies in the first stage, the biotech firm allies in the second stage and no alliance is signed. To obtain the equilibrium the game is solved via backward induction.

Therefore, starting from the second stage I resolve the first sub-game (see Figure 7) comparing $\pi_s^B(t_1)$ (i.e., the second stage alliance payoff expression) and $\pi^B(t_1)$ (i.e., the no alliance payoff expression) to evaluate the level of P_s that makes the two profits equal.

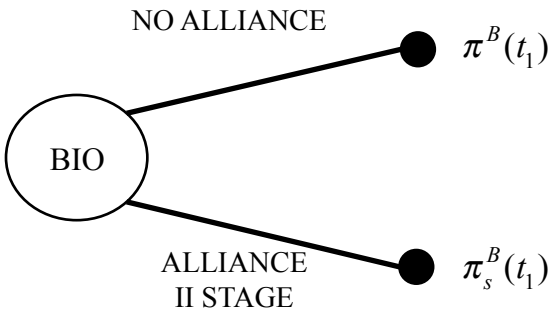


Figure 7: Second stage sub-game in monopoly case.

The minimum value of the expected P_s, which makes the biotech firm indifferent between alliance and no-alliance, is given by the following expression:

$$P_s = (1-(1-\alpha_s)\delta)V_s \quad (26)$$

Note that this payment is a linear function of the value of the project V_s. Particularly, at the beginning of the second stage the value of the project V_s, is log-normally distributed with expected value, $E[V_s]$, equal to $V_f e^{rt}$.

For values of P_s greater than this threshold (equation 26), the equilibrium of the second stage sub-game is "Alliance", and for lower values the *vice versa* holds.

Moving back to the first stage, I find the equilibrium of the game comparing $\pi_f^B(t_0)$ (i.e., first stage alliance payoff expression) with each possible scenarios of equilibrium found in the first sub-game, i.e. first with $\pi_s^B(t_0)$ and then with $\pi^B(t_0)$ (see Figure 8).

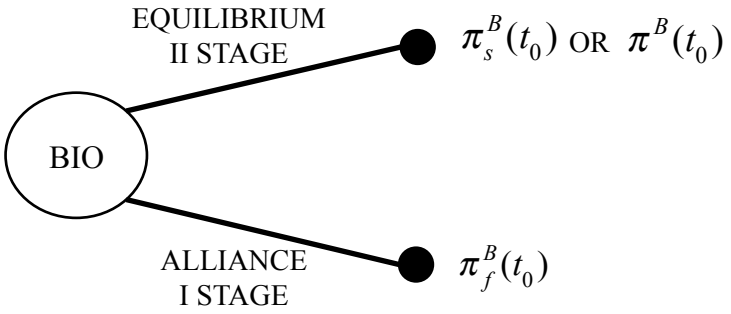


Figure 8: First stage sub-game in monopoly case.

As stated above, backtracking to t_0, as $V(t)$ is log-normally distributed, I consider the present value of V_s, i.e. V_f, and payoffs are computed as call options. Note that also the second stage payment is discounted and it is an expected value, $P_s(t_0)$, calculated at t_0. It is given by the following expression:

$$P_s(t_0) = P_s e^{-rt} = \left((1-(1-\alpha_s)\delta)V_f e^{rt}\right)e^{-rt} = (1-(1-\alpha_s)\delta)V_f \quad (27)$$

In the first stage sub-game, I find the P_f thresholds that make the biotech firm indifferent between the two alternatives. First I assume that the equilibrium of the second stage is "Alliance", therefore I compare $\pi_f^B(t_0)$ (i.e., first stage alliance payoff expression) with $\pi_s^B(t_0)$ (i.e., second stage alliance payoff expression backtracked to t_0) and the minimum value of P_f that makes the biotech firm indifferent between the two alternatives is given by the following expression:

$$P_f = C_s^B - C_f^B \tag{28}$$

If P_f is greater than this threshold the equilibrium of the game will be "Alliance in the first stage", otherwise it will be "Alliance in the second stage". Conversely, assuming that the equilibrium in the second stage is "No alliance", in the first stage I compare $\pi_f^B(t_0)$ (i.e., first stage alliance payoff expression) with $\pi^B(t_0)$ (i.e., no alliance payoff expression backtracked to t_0) and the minimum value of P_f is given by the following expression:

$$P_f = C^B - C_f^B \tag{29}$$

Indeed for values of P_f greater than this threshold the equilibrium of the game will be "Alliance in the first stage", otherwise it will be "No alliance".

In Table 5 the payments thresholds (P_f and P_s) for the monopoly game and the corresponding scenarios of equilibrium are reported.

Table 5: Threshold payments (P_f and P_s) and possible scenarios of equilibrium in the monopoly case.

			P_f	
			Low	High
P_s	$P_s < (1-(1-\alpha_s)\delta)V_s$	Low	$P_f < C^B - C_f^B$ No alliance	$P_f > C^B - C_f^B$ Alliance I Stage
	$P_s > (1-(1-\alpha_s)\delta)V_s$	High	$P_f < C_s^B - C_f^B$ Alliance II Stage	$P_f > C_s^B - C_f^B$ Alliance I Stage

Specifically, the results suggest that, if the pharmaceutical company does not offer a considerable amount of payment in the initial stage, i.e., P_s is low, the biotech firm might find more profitable waiting until the second stage to possibly obtain better payment conditions. In the second stage, in fact, the biotech firm will ally with the pharmaceutical company only under favourable payment conditions, i.e., high values of P_s. Otherwise, the biotech firm will prefer to continue the R&D process on her own. However, if in the first stage the payment conditions are sufficiently high, the biotech company will sign an early alliance independently of any value of P_s.

2.3 The duopoly case

In presence of competition in the market, firms know that their investment decisions could determine competitive reactions that would in turn impact the value of their own investment opportunity. In this case the investment decision analysis can be defined as a strategic games against competition (Smit and Trigeorgis, 2007).

Specifically, concerning my model, I suppose that exists another biotech firm that has the possibility to partner with the same pharmaceutical company. Thus, each biotech firm must be aware that she could be anticipated by the rival in case she decides to postpone the hypothetical alliance to the second stage. Therefore, my objective is to determine how competition could affect biotech firms' optimal strategy. In particular I derive the conditions under each biotech competitor should anticipate, postpone or disregard the opportunity of collaboration.

I model a Stackelberg game where there are two identical players, namely B1 and B2, that play sequentially with perfect and complete information, and two stages, that are the same as before. I suppose that B1 is the first mover, i.e. she enjoys a first mover advantage, and the alliance is mutually exclusive, i.e. the pharmaceutical company will only contract with one biotech firm. If one biotech firm signs an agreement with the pharmaceutical company, the lonely player continues the R&D process and reach the market on its own (FierceBiotech, 2015). This assumption implies that biotech firms are not exactly researching on the same molecule. The sequence of the game is as follows. At the beginning of stage 1, B1 is selected by the pharmaceutical company, which offers, as before, a contract consisting of P_f and $(1-\alpha_f)$. If B1 rejects the offer, the same contract is offered to B2 that can accept or reject the offer too. If no agreement has been reached in the first stage, in the second stage the game is repeated and the contract consists of P_s and $(1-\alpha_s)$. Note that the contract offered by the pharmaceutical company differs between the two stages but it is the same for both biotech firms due to the assumption of a symmetric environment.[7]

In case none of the biotech firms signs the agreement with the pharmaceutical company, they are able to reach the final market individually and they share the total market

[7] Also the investments required for the R&D process prosecution are the same for both biotech firms.

according to a parameter γ for B1 and $(1-\gamma)$ for B2. In case of alliance in any of the two stages, similar to the monopoly case, the partnership inflates the market according to δ (>1). Furthermore, the alliance generates spillover effects, i.e. not only the biotech firm signing the alliance, but also the "lonely" competitor receives benefit from the rival's collaboration and enjoys the larger market. The presence of R&D spillover effects is significant among different sectors as discussed in Bernstein and Mohnen (1998). Henderson and Cockburn (1996) documented the importance of spillover effects in biotechnology industry. In particular, Berndt et al. (1995) also suggested the presence of marketing spillover in the pharmaceutical industry.

However, the total market pie will be split differently between the two biotech firms. Specifically, the biotech firm signing the alliance will appropriate a higher portion, β $(\beta > \gamma)$, while the "stand-alone" competitor will appropriate of the remaining portion $(1-\beta)$.

Figure 9 shows the game structure, the first stage starts at t_0 and the second one at t_1; biotech firms' payoff expressions are denoted as $\pi_{j,Bi}^{Bk}$, where *j = f (first), s (second)* stands for the stage in which the agreement is signed, *Bi = B1, B2* represents the biotech firm that signs the agreement and *Bk = B1, B2* the biotech firm to which the payoff is referred. In case no alliance is signed the subscript (*j, Bi*) is eliminated.

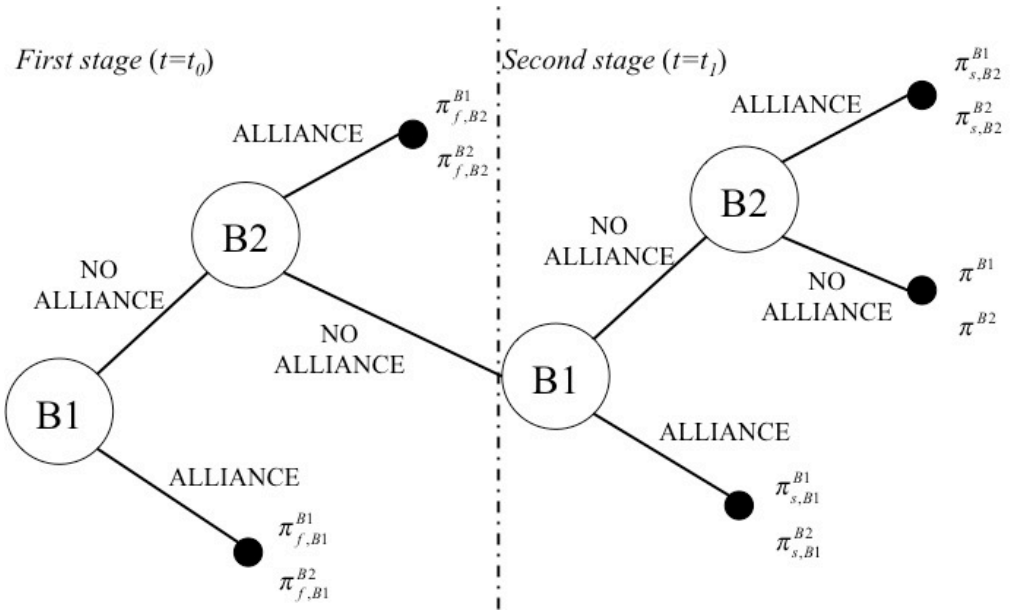


Figure 9: Game structure in duopoly case.

2.3.1 Biotech firms' payoff expressions in duopoly case

Regarding firms' payoff expressions, they are computed similarly to the monopoly case. In particular at $t=t_0$, uncertainty about the value of the project is partially resolved as a result of improved information about several factors influencing the market value of the candidate drug. The residual uncertainty is about future cash flows; their expected value, i.e. V_s, is known and, therefore, the simple NPV methodology to compute firms' payoff expressions can be adopted. Table 6 shows the biotech firms' second stage payoff expressions, $\pi^{Bk}_{s,Bi}(t_1)$, under the three possible scenarios, namely, the alliance is formed with B1, the alliance is formed with B2, and no alliance is formed.

Table 6: Biotech firms' second stage payoff expressions.

Scenario	*Payoff B1*	*Payoff B2*
	$\pi^{B1}_{s,Bi}(t_1)$	$\pi^{B2}_{s,Bi}(t_1)$
B1 signs the alliance at stage II	$(1-\alpha_s)\beta\delta V_s + P_s - I_s$	$(1-\beta)\delta V_s - I_s$
B2 signs the alliance at stage	$(1-\beta)\delta V_s - I_s$	$(1-\alpha_s)\beta\delta V_s + P_s - I_s$

II		
No alliance	$\gamma V_s - I_s$	$(1-\gamma)V_s - I_s$

In the interest of length, I provide just an example to illustrate how to obtain the present value of second stage payoff expressions (i.e., at time t_0) starting from those computed in Table 6. Specifically, I consider the case where B1 signs the alliance with the pharmaceutical company in the second stage. Backtracking to time t_0, the present values of the second stage payoff expressions for both biotech firms are respectively[8]:

$$E\left(\pi_{s,B1}^{B1}(t_1)\right) = E\left[(1-\alpha_s)\beta\delta V_s + P_s \middle| ((1-\alpha_s)\beta\delta V_s + P_s) > I_s\right]\Pr\left[((1-\alpha_s)\beta\delta V_s + P_s) > I_s\right] - \\ - I_s \Pr\left[((1-\alpha_s)\beta\delta V_s + P_s) > I_s\right] \quad (30)$$

$$E\left(\pi_{s,B1}^{B2}(t_1)\right) = E\left[(1-\beta)\delta V_s \middle| (1-\beta)\delta V_s > I_s\right]\Pr\left[(1-\beta)\delta V_s > I_s\right] - I_s \Pr\left[(1-\beta)\delta V_s > I_s\right] \quad (31)$$

As a matter of fact, B1 and B2 will only continue with the development of the drug if their expected payoffs are positive, i.e., only if $E\left[((1-\alpha_s)\beta\delta V_s + P_s) > I_s\right]$ and $E\left[(1-\beta)\delta V_s > I_s\right]$ hold, respectively. Given that the value of the project over time $V(t)$ is uncertain and follows a GBM, as before, I model the present value of second stage payoffs at t_0 using ROA by adopting the Black and Scholes formula. Therefore, it is straightforward to recognize that both equation (30) and equation (31) are two simple call options with the underlying values respectively equal to $(1-\alpha_s)\beta\delta V_f + P_s(t_0)$ and $(1-\beta)\delta V_f$ and the exercise price equal to I_s. I define them $C_{f,B1}^{B1}$ and $C_{f,B1}^{B2}$, respectively (see Table 7). In general, $C_{j,Bi}^{Bk}$ is the biotech call option where *Bk*, *j* and *Bi* have the same meaning as before. In case no alliance is signed the subscript (*j, Bi*) is eliminated. In Table 7 I report the underlying values of the biotech call options for all scenarios.[9]

Therefore, biotech firms' second stage payoff expressions at t_0 net of the first stage investment cost I_f are:

[8] Readers can refer to D. M. Chance (2014) for an exhaustive understanding of this approach.
[9] It is important to note that all the call options have the same exercise price equal to I_s.

$$\pi_{s,B1}^{B1}(t_0) = C_{s,B1}^{B1} - I_f \tag{32}$$

$$\pi_{s,B1}^{B2}(t_0) = C_{s,B1}^{B2} - I_f \tag{33}$$

Also in case the alliance is signed in the first stage, I compute biotech firms' first stage payoff expressions using the Black and Scholes formula. For instance, in case B1 allies with the pharmaceutical company, biotech firms' first stage payoff expressions are equal to:

$$\pi_{f,B1}^{B1}(t_0) = C_{f,B1}^{B1} - I_f + P_{f,B1} \tag{34}$$

$$\pi_{f,B1}^{B2}(t_0) = C_{f,B1}^{B2} - I_f \tag{35}$$

where I_f is the investment both biotech firms make in the first stage and $P_{f,B1}$ is the upfront payment B1 receives in the first stage.

Table 7: Underlying values of the call options, $C_{j,Bi}^{Bk}$.

Scenario	*Call options*	*B1's Underlying Values*	*B2's Underlying Values*
B1 signs the alliance at stage I	$C_{f,B1}^{Bi}$	$(1-\alpha_f)\beta\delta V_f$	$(1-\beta)\delta V_f$
B2 signs the alliance at stage I	$C_{f,B2}^{Bi}$	$(1-\beta)\delta V_f$	$(1-\alpha_f)\beta\delta V_f$
B1 signs the alliance at stage II	$C_{s,B1}^{Bi}$	$(1-\alpha_s)\beta\delta V_f + P_s(t_0)$	$(1-\beta)\delta V_f$
B2 signs the alliance at stage II	$C_{s,B2}^{Bi}$	$(1-\beta)\delta V_f$	$(1-\alpha_s)\beta\delta V_f + P_s(t_0)$
No alliance	C^{Bi}	γV_f	$(1-\gamma)V_f$

In Table 8 I report first stage payoff expressions and second stage payoff expressions backtracked to time t_0 for both biotech firms.

Table 8: ROA biotech firms' first stage payoff expressions and second stage payoff expressions backtracked to time t_0.

Scenario	*B1's Payoff*	*B2's Payoff*
	$\pi_{j,Bi}^{B1}(t_0)$	$\pi_{j,Bi}^{B2}(t_0)$
B1 signs the alliance at stage I	$\max(C_{f,B1}^{B1} - I_f + P_f;0)$	$\max(C_{f,B1}^{B2} - I_f;0)$
B2 signs the alliance at stage I	$\max(C_{f,B2}^{B1} - I_f;0)$	$\max(C_{f,B2}^{B2} - I_f + P_f;0)$
B1 signs the alliance at stage II	$\max(C_{s,B1}^{B1} - I_f;0)$	$\max(C_{s,B1}^{B2} - I_f;0)$
B2 signs the alliance at stage II	$\max(C_{s,B2}^{B1} - I_f;0)$	$\max(C_{s,B2}^{B2} - I_f;0)$
No alliance	$\max(C^{B1} - I_f;0)$	$\max(C^{B2} - I_f;0)$

The reader can note that in case of alliance, the biotech firm that signs the agreement have to share her market share, β, with the pharmaceutical company and receives $(1-\alpha_j)$ of royalties; whereas the "lonely" biotech takes all her market share $(1-\beta)$. In contrast, the biotech involved in the alliance receives the upfront payment, which brings to her financial support, while the other player takes on all the R&D costs. As β increases, the alliance market share increases as well.

2.3.2 Game solution

Also in the duopoly case the game is solved through the backward induction. In this case, I analyse firms' decisions starting from B2 and then I go back to B1's decision, first in the second and then in the first stage. Clearly, B1 enjoys a first mover advantage, she can observe B2's decisions and take them into account. Solving the game entirely, five scenarios of equilibrium are possible: B1 allies in the first stage, B1 allies in the second stage, B2 allies in the first stage, B2 allies in the second stage, none of the biotech firms allies. Similarly as the monopoly case, I derive upfront payment thresholds for all the possible paths of the game. I obtain different scenarios of

equilibrium solutions depending on the value of δ. Thus, I distinguish between two main cases: high synergies case with $\delta > (1-\gamma)/(1-\beta)$ and low synergies case with $\delta < (1-\gamma)/(1-\beta)$. Table 9 and Table 10 summarise the possible alliance outcomes in high synergies case and low synergies case, respectively. For the sake of simplicity, in the threshold values I reported the call options, $C_{j,Bi}^{B1}$, referred to B1. The same condition holds for BIO2: the reader can verify the correspondence with $C_{j,Bi}^{B2}$ using Table 7.

Table 9: Threshold payments (P_f and P_s) and possible scenarios of equilibrium in the duopoly case and high synergies (NA stands for not admitted).

$\delta > (1-\gamma)/(1-\beta)$			P_f		
			Low	Medium	High
P_s	$P_s < (\gamma - (1-\alpha_s)\beta\delta)V_s$	Low	$P_f < C^{B1} - C^{B1}_{f,B1}$ No alliance	$C^{B1} - C^{B1}_{f,B1} < P_f < C^{B1}_{f,B2} - C^{B1}_{f,B1}$ B2 I Stage	$P_f > C^{B1}_{f,B2} - C^{B1}_{f,B1}$ B1 I Stage
	$(\gamma - (1-\alpha_s)\beta\delta)V_s < P_s < (1-\beta)\delta V_s - (1-\alpha_s)\beta\delta V_s$	Medium	$P_f < C^{B1}_{s,B2} - C^{B1}_{f,B1}$ B2 II Stage	$C^{B1}_{s,B2} - C^{B1}_{f,B1} < P_f < C^{B1}_{f,B2} - C^{B1}_{f,B1}$ B2 I Stage	$P_f > C^{B1}_{f,B2} - C^{B1}_{f,B1}$ B1 I Stage
	$P_s > (1-\beta)\delta V_s - (1-\alpha_s)\beta\delta V$	High	$P_f < C^{B1}_{s,B1} - C^{B1}_{f,B1}$ B1 II Stage	NA	$P_f > C^{B1}_{s,B1} - C^{B1}_{f,B1}$ B1 I Stage

Table 10: Threshold payments (P_f and P_s) and possible scenarios of equilibrium in the duopoly case and low synergies.

$\delta < (1-\gamma)/(1-\beta)$			P_f	
			Low	High
P_s	$P_s < (\gamma - (1-\alpha_s)\beta\delta)V_s$	Low	$P_f < C^{B1} - C^{B1}_{f,B1}$ No alliance	$P_f > C^{B1} - C^{B1}_{f,B1}$ B1 I Stage
	$P_s > (\gamma - (1-\alpha_s)\beta\delta)V_s$	High	$P_f < C^{B1}_{s,B1} - C^{B1}_{f,B1}$ B1 II Stage	$P_f > C^{B1}_{s,B1} - C^{B1}_{f,B1}$ B1 I Stage

Starting from the high synergies case, the reader can observe that, depending on the values of P_f and P_s, all the five scenarios of equilibrium are possible. In particular, the first mover might find more profitable that the other player partners with the pharmaceutical company to enjoy generous spillover effects. Specifically, this occurs when both first and second stage payments are intermediate or when one of them is low and the other is intermediate. Interestingly, if the first stage payments are intermediate the alliance will be established in the first stage. Alternatively, in the presence of intermediate second stage payments and low first stage payments, the optimal timing is to ally in the second stage. Instead, if, in the first stage, the payment conditions are sufficiently high, there is no space for B2 to sign the agreement, as the first mover will sign an early alliance independently of any value of P_s. Moreover, the first mover will pre-empt the rival partnering with the pharmaceutical company in the second stage also when the relative payment is sufficiently high, while the first stage payment is not appealing. Finally, if the pharmaceutical company does not offer attractive payment conditions in both stages, i.e., P_f and P_s are low, no biotech firm will find optimal to sign an agreement with the pharmaceutical company.

Moving to the low synergies case, there is no possibility for the second mover to partner with the pharmaceutical company. Interestingly, in this case, the market outcomes are identical to the case of monopoly and similar considerations can be done. The intuition behind this result is that the market pie has not been enlarged enough so that B1's competitive advantage of being the first mover more than outweighs the benefits derived from the spillover effect. As a result, the alliance "window" is closed to B2.

2.4 Discussion of results

To better visualise the obtained results and provide a practical application of the relative insights, I complement the analytical derivation with a numerical analysis for both monopoly and duopoly case. The numerical analysis relies on a case study available in the literature, which considers a drug in the third clinical phase (Rogers et al., 2002). Specifically, I consider the following set of parameters: $V_f = \$400M$, $\sigma = 30\%$, $r = 5\%$, $I_f = \$75M$, $I_s = \$180M$, $\gamma = 0{,}5$. The numerical analysis allows to understand how δ combines with the payment conditions and affects firms' alliance timing decisions.

In particular, in the monopoly case, I considered different values of δ (equal to 1.1, 2.2, and 2.7 respectively) to include several scenarios of the value added by the

pharmaceutical company. For the sake of brevity, I illustrate such influence in case the alliance, if any, can only arise in the first stage, i.e., low values of P_s. In this case, Figure 10 identifies the region of alliance as a function of P_f and α_f.

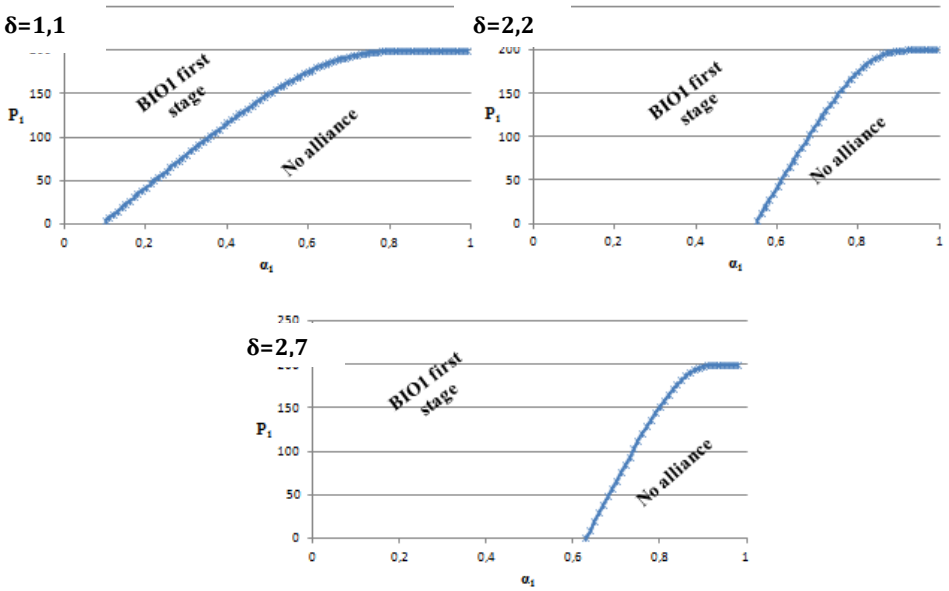


Figure 10: Monopoly thresholds $\left(P_f = C^B - C_f^B\right)$ when P_s is low and δ varies.

When the total market size increases due to the contribution of the pharmaceutical company, the biotech firm has more chances to sign an early agreement with the pharmaceutical company in order to take advantage of the high synergies. These results are consistent with Rogers et al. (2005), who find that early licensing agreements are worthy of consideration as the value added to the developed drug by the partnership increases.

Also in the duopoly case, I analyse how parameters of interest affect biotech firms' alliance timing decisions. In case of high synergies, for the sake of brevity, I report the region of alliance as a function of P_f and α_f, in the case of low values of P_s, for β equal to 0.55, 0.65 and 0.75 respectively. Specifically, Figure 11 shows payments thresholds for δ=*2.2*. When the level of competition increases, i.e. β increases, the alliance region for B2 is more and more reduced whereas the early alliance region for B1 is increased. Figure 12 shows payments thresholds for δ=*2.7*. Therefore, it is possible to note that a higher value of the amplification factor δ enlarges B2's alliance zone.

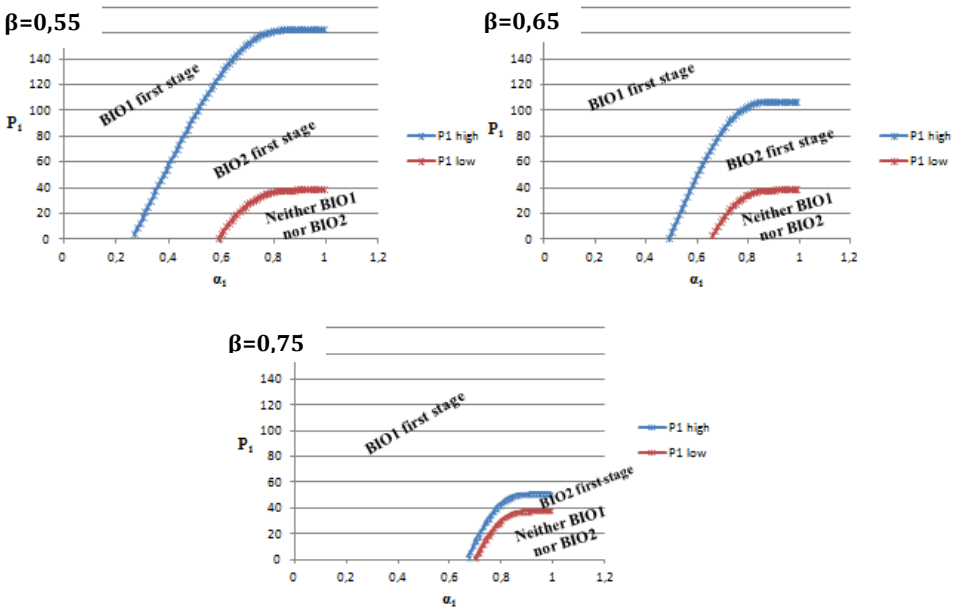


Figure 11: Duopoly thresholds $\left(P_f = C^{B1}_{f,B2} - C^{B1}_{f,B1}$ if P_f is high and $P_f < C^{B1} - C^{B1}_{f,B1}$ if P_f is low$\right)$ in case of high synergy when P_s is low, $\delta = 2.2$ and β varies.

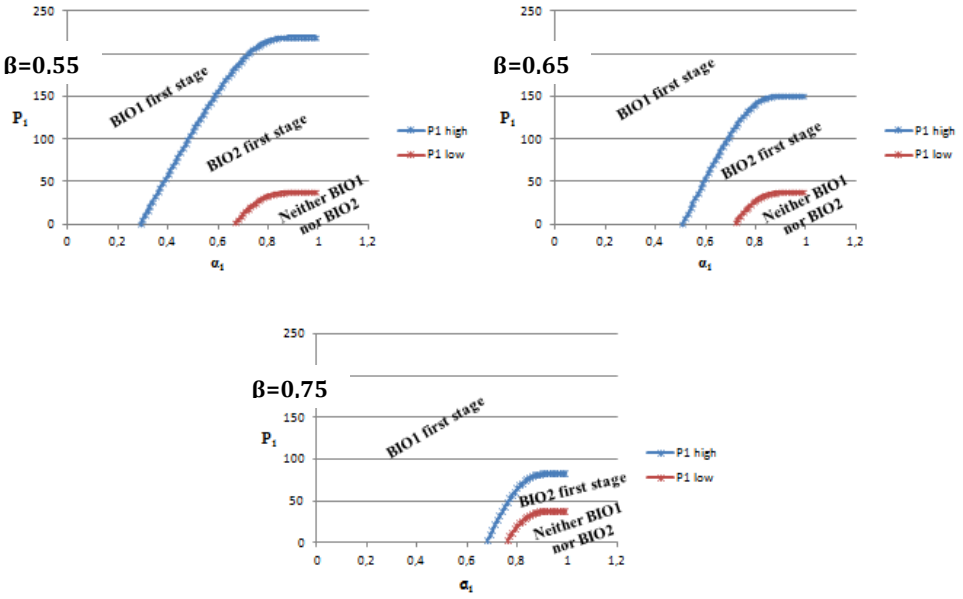


Figure 12: Duopoly thresholds $\left(P_f = C^{B1}_{f,B2} - C^{B1}_{f,B1}$ if P_f is high and $P_f < C^{B1} - C^{B1}_{f,B1}$ if P_f is low$\right)$ in case of high synergy when P_s is low, $\delta = 2.7$ and β varies.

In case of low synergies, I report the region of alliance as a function of P_f and α_f, in the case of low values of P_s, for δ=*1.1*, β equal to 0.55, 0.65 and 0.75 respectively. Figure

13 shows how a higher level of β determines an increase of the region of B1's first stage alliance.

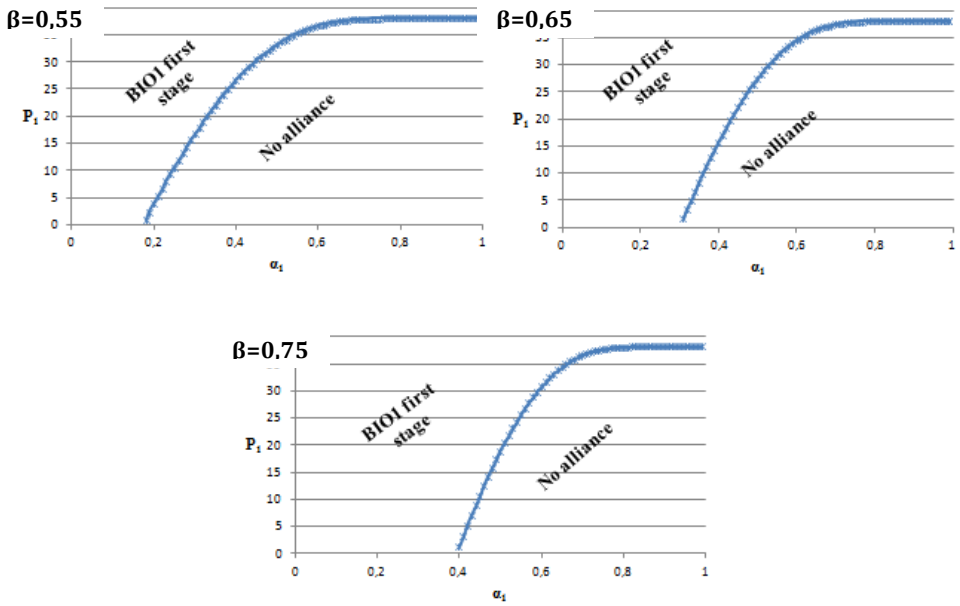


Figure 13: Duopoly thresholds $\left(P_f = C^{B1} - C^{B1}_{f,B1}\right)$ in case of low synergy when P_s is low, δ = *1.1* and β varies.

Furthermore, by comparing monopoly case (Figure 10) and low synergies case (Figure 13), it can be observed that competition leads to lower threshold payments than the monopoly structure. In fact, as the level of competition increases, lower payments are required by the first mover to ally. This result can be demonstrated by comparing the conditions $P_f(\text{in monopoly case}) > C^B - C^B_f$ and $P_f(\text{in duopoly case}) < C^{B1} - C^{B1}_{f,B1}$.

As the call options have the same exercise price, I can simply compare their underlying values, which are $V_f - (1-\alpha_f)\delta V_f$ in case of monopoly and $V_f - (1-\alpha_f)\beta\delta V_f$ in case of duopoly, respectively. Comparison yields that payments are lower in case of competition if the condition $\delta < (1-\gamma)/(1-\beta)$ holds. It is straightforward to prove that such condition is always satisfied given that the case of low synergy is considered.

A final important remark is that the ROA offers more opportunities to the biotech firms to ally if compared to the traditional use of the NPV because only positive values of future opportunities are considered. In fact, the region where alliance arises is larger when the ROA approach is utilised. Figure 14 shortly summarises this implication of

ROA flexibility. A more detailed analysis on the differences between the two methodologies will be reported in chapter 3.

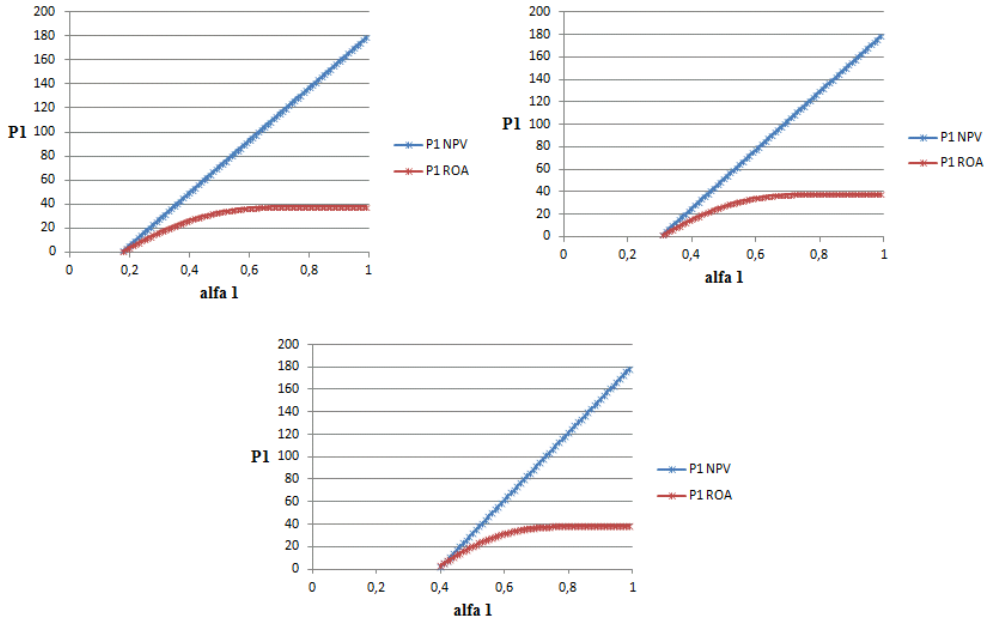


Figure 14: P_f thresholds (the same of Figure 13) evaluated with both NPV and ROA in case of low synergy when P_s is low, $\delta = 1.1$ and β varies.

2.5 Conclusion

My results suggest that under a Stackelberg game, where one biotech firm is the first mover, whereas the other is the follower, whether and when to ally with the pharmaceutical company depend on the contract terms (i.e. payments and royalties), level of competition and synergies coming from the alliance. Specifically, there are numerous interesting cases. In case the market potential, due to the contribution from the pharmaceutical company, is high it is possible to notice that all events are possible. The first mover can pre-empt or she can wait for better alliance conditions or she can leave to the follower the possibility to ally, and, in the latter case, the follower might or might not take advantage of this opportunity. The intuition behind the above findings relates to the fact that the first mover, in the presence of high market potential (or, alternatively, low competition level), allies with the pharmaceutical company when the payment conditions are satisfactory. Otherwise, the first mover prefers to continue the project individually as she can receive indirect benefits from the potential alliance between the follower and the pharmaceutical company. What is interesting, however, is

that, in the latter case, the follower will not always follow the first mover and compete against her without the support of the pharmaceutical company. Rather, the follower will sometimes prefer allying with the pharmaceutical company, thus determining an increase of the market potential and providing indirect benefits to the first mover. Essentially, under competition, the first mover will not always pre-empt the follower alliance. On the other hand, if payment conditions are acceptable, the first mover will choose to ally, instead of competing individually, due to the overall benefits that will be generated through the alliance.

A less complex picture is obtained when the level of synergies generated with the alliance with the pharmaceutical company is not high. In this case, only the first mover will partner with the pharmaceutical company. When the first-stage payment is high, the alliance will be established in the first stage, otherwise this will happen in the second stage. However, if both first stage and second stage payments are low, no alliance will be signed. Under this scenario, as the market potential is not high (or, alternatively, the competition level is very high), the first mover will never leave room to the follower to ally with the pharmaceutical company as the market potential increase is mild. In this case, the equilibrium scenarios are the same as the monopoly case.

This chapter has provided evidence of contrasting arguments from the industry world on whether and when biotech firms should partner with big pharmaceutical companies. Based on my analysis I argue that none of them is completely right or wrong, in the sense that all alliance timing outcomes are possible. In fact, biotech firms can actually anticipate, postpone or forgo on alliance with pharmaceutical companies in the presence of competitors. However, each outcome will occur under specific conditions. In this regard, my results help to provide some guidelines for practitioners with regard to the hot issue of alliance timing in the presence of competition. As a matter of fact, in a first mover-follower setting, e.g., the example of Forma Therapeutics versus new entrants in the protein homeostasis field, the market value added and payments offered by big pharma play a crucial role. Biotech firms, who enjoy first mover advantage, should always anticipate the follower in signing the licensing agreement when the market value does not increase significantly as a consequence of the alliance with the pharmaceutical company. A restricted market potential forces the first mover to adopt always a pre-emptive strategy in order to maintain the competitive advantage over the follower. As

discussed earlier, in this case, the amount of payments offered by the pharmaceutical company in different stages determines whether the deal should be signed in the first, in the second stage or never be signed. On the other hand, when the market value added by the presence of the pharmaceutical company is notably high, first mover should not always choose to partner with him. Rather, when contract terms are not appealing, first mover should let the follower ally to profit more in the final market due to the fact that she does not share the profit with the pharmaceutical company, while still benefiting from positive spillover. Even when the market potential increases due to the presence of the pharmaceutical company, the amount of payments offered by the pharmaceutical company in different stages determines whether the deal should be signed in the first, in the second stage or never be signed.

Chapter 3
Optimal timing for the pharmaceutical company in a ROG model

3.1 Introduction

In chapter 2, I have analysed alliance timing decisions, developing a model that includes the effect of the competition in determining the optimal choice taking the perspective of the biotech firms. In this chapter, I analyse R&D alliance timing decisions with a holistic perspective that incorporates the active role of both pharmaceutical and biotech firms in a stochastic and competitive environment. Indeed, the active role of the pharmaceutical company in the alliance timing decisions has been disregarded in presence of biotech firm competition. However, considering the pharmaceutical company as an active player in the alliance timing game is particularly important as well as very realistic, since the pharmaceutical companies usually have a dominant role in the strategic alliance timing decisions (Nicholson et al., 2005; Kalamas et al., 2002).

Therefore, in this chapter I intend to fill the gap present in the extant literature on R&D alliance timing in the biopharmaceutical industry by explicitly modelling the active role of both pharmaceutical and biotech firms in this important decision setting. Specifically, to model the strategic interactions among the involved parties and to reflect the flexibility of both pharmaceutical and biotech firms to react to the future uncertainties, that typically characterize the R&D process in this industry, I develop again a ROG model. In the hypothesized setting, the pharmaceutical company has the bargaining power to choose among competing biotech firms and offer different profit-maximizing contracts in two different stages of the R&D process and the biotech firms can in turn decide to accept or reject the pharmaceutical company's offer. In addition, I consider both the case where biotech firms are identical and the case where they are no longer identical. In particular, in case of non-identical biotech firms, I suppose that the market increase in case of an alliance with one biotech firm is higher as compared to the market increase originated from an alliance with the other one.

With regard to the type of alliance, I consider a licensing agreement under which only the biotech firm has control on the R&D project continuation (or abandonment) option, whereas the pharmaceutical company remits to the biotech firm an up-front payment when the agreement is signed and royalties upon product commercialization. Therefore, the biotech firms' payoffs are naturally assessed through real options analysis (ROA) because they may decide to abandon the project in later stages if the project is no longer profitable based on updated information. However, in a setting where both pharmaceutical and biotech firms strategically interact, the real options of the biotech firms indirectly affect pharmaceutical company's decisions. In this respect, I explicitly model how the pharmaceutical company evaluates and takes into account biotech firms' option exercise decisions in his profit maximization problem, through an *option-conditioned probability*. This is an important contribution of this chapter because, to the best of my knowledge, in the ROG literature, modelling how firms' project investment decisions depend on real options of other firms has never been investigated.

Finally, I also compare the alliance timing outcomes of the real options game with the case where both parties disregard the uncertainty of the underlying R&D process, thus using the NPV (Net Present Value) of the licensed drug as a tool to evaluate the project. Indeed, as stated in chapter 1, the NPV is still the dominant methodology utilized to evaluate R&D projects in the biopharmaceutical industry, in spite of the fact that, differently from ROA, it ignores managers' flexibility (Myers 1984, Hartmann and Hassan 2006, Cassimon et al. 2011). The higher popularity of the NPV methodology as compared with ROA is mainly because practitioners usually perceive real options as a complex tool, thus often leaning towards simpler methodologies such as the NPV (Hartmann and Hassan 2006). However, in doing so, managers tend to disregard the consequences of adopting the NPV or other simple methodologies instead of ROA, when evaluating the impact of important strategic decisions in the new drug development process. For such reason, a growing body of literature has started informing managers in the biopharmaceutical industry about the implications of using different methodologies to evaluate R&D projects, which may indeed drastically impact on firms' decisions and the relative outcomes. For instance, Cassimon et al. (2011) and Baldi et al. (2015) suggest that the licensing deal value in this industry is highly affected by the methodology utilized to evaluate the investment project. Indeed, I contribute to

this growing strand of literature by investigating how alliance timing decisions are influenced by the methodology utilized by managers for new drug investment project evaluation, which has never been studied before.

By way of anticipation, I show that, in presence of high synergies between pharmaceutical and identical biotech firms, the second stage is optimal from the perspective of the pharmaceutical company when ROA is utilized, whereas any stage is optimal under the NPV methodology. In this case the selected biotech firm is the second mover under both methodologies. In presence of low synergies, the optimal timing depends on the level of royalties assigned to the biotech firm, when ROA is adopted to evaluate the investment project. In this case, postponing the alliance to the second stage is optimal for the pharmaceutical company as long as the level of royalties is sufficiently high. Otherwise, the first stage is optimal. The latter outcome always occurs instead when the NPV methodology is utilized. Under both ROA and NPV methodologies, the biotech firm moving first is selected for the alliance. In case of non-identical biotech firms, if the synergies between the pharmaceutical company and the first mover are sufficiently high, the optimal timing is the second stage and the alliance is signed with the first mover under ROA. Under NPV any stage is optimal and the first mover is selected. If the synergies between the pharmaceutical company and the first mover are low, ROA leads to more ambiguous results as either firm can be selected and either stage can be optimal depending on the level of royalties offered. Differently, under the NPV methodology any stage is still optimal, but the second mover is selected.

The remainder of the chapter is organized as follows. In the next section, I present the model introducing firms' payoff expressions computed using both ROA and NPV methodologies. In the following sections, first I present and discuss my findings under identical biotech firms. Then I extend the analysis to the case of non-identical biotech firms. In the final section, conclusions are drawn.

3.2 Model development

Starting from the model presented in chapter 2, I model a two-stages Stackelberg game for B1 and B2 that have the opportunity to establish a partnership with a pharmaceutical company. In particular, B1 enjoys a first mover advantage. I assume that the pharmaceutical company has the bargaining power to make a take-it-or-leave-it contract that maximizes his profit. The pharmaceutical company selects biotech firms

sequentially and the contract offered by the pharmaceutical company in both stages consists of an upfront payment delivered at the beginning of the considered stage to the allied biotech firm and of royalties upon drug commercialization. For the sake of tractability, I assume that the pharmaceutical company maximizes his own profit by choosing the upfront payment in each stage, whereas the royalties are exogenously given and are the same for both biotech firms. If no agreement is signed the pharmaceutical company makes zero profit from the market. The stage of the game, and the correspondent R&D phases, are the same as before. Thus $V(t)$ follows a Geometric Brownian Motion (GBM) over the range (t_0, t_1) and firms are assumed risk-neutral.

In this model I consider both the case where biotech firms are identical and the case where they are no longer identical. Thus, in the former case, the level of synergies originated from the alliance is the same no matter which biotech signs the agreement. In case of non-identical biotech firms, I suppose that the market increase in case of an alliance with B1 is equal to δ_{B1} and in case of an alliance with B2 is equal to δ_{B2}. The alliance, if any, is mutually exclusive in the sense that the pharmaceutical company will only sign the alliance with one biotech firm. I also assume that both biotech firms can reach the market individually, which implies that they are not exactly researching on the same molecule. Therefore, if one biotech firm signs an alliance with the pharmaceutical company, the other can only continue the R&D process individually, with some spillover benefits from the competitor's alliance, but with her own (limited) financial resources.

Cash flows are estimated for all firms under all the possible situations that can arise in this setting. Also in this case the game is solved via backward induction by examining all the possible branches of the tree illustrated in Figure 9 in in section 2.3. Before computing firms' payoff expressions, I define:

- I_j = drug research and development investment cost incurred by both biotech firms in each stage ($j = f, s$);
- r = risk-free interest rate;
- V_s = value of the project, i.e., expected net cash flows arising after commercialization, at the beginning of the second stage (i.e., at time t_1);
- V_f = present value of V_s, i.e., expected net cash flows arising after commercialization, at the beginning of the first stage (i.e., at time t_0);

- $P_{f,Bi}$ = upfront payment offered by the pharmaceutical company to the biotech *i* at the beginning of the first stage in case of alliance (pharmaceutical company's decision variable);
- $P_{s,Bi}$ = upfront payment offered by the pharmaceutical company to the biotech *i* at the beginning of the second stage in case of alliance (pharmaceutical company's decision variable);
- α_f = percentage of royalties that the pharmaceutical company receives in case of alliance in the first stage;
- α_s = percentage of royalties that the pharmaceutical company receives in case of alliance in the second stage.
- γ = B1 market share in case no alliance is signed ($(1-\gamma)$ for B2);
- β = market share of the biotech firm signing the alliance in the first stage or in the second stage;
- $(1-\beta)$ = market share of the "stand-alone" biotech firm when the other player signs the alliance in the first stage or in the second stage;
- δ_{Bi} = amplification factor (>1) (with *Bi = B1, B2*), i.e. the value added to the drug by the synergies derived from the alliance between the pharmaceutical company and the biotech partner.

3.2.1 Computing firms' payoff expressions

Before solving the game via backward induction approach, I present biotech firms' and pharmaceutical company's payoff expressions in all possible branches of the tree in Figure 9 in section 2.3. Specifically, in computing firms' payoff expressions, I consider that all firms adopt a real option logic to evaluate the project investment and make decisions. I derive firms' second stage payoff expressions, i.e. the payoff expressions when the alliance is signed in the second stage or no alliance is signed, both computed at time t_1 and discounted at time t_0 (since they come from commercialization starting at t_1), and firms' first stage payoffs, i.e. the payoff expressions when the alliance is signed in the first stage (i.e., at time t_0). In order to comparing ROA and NPV methodologies, I also derive the same payoff expressions under the NPV methodology.

3.2.2 Biotech firms' payoff expressions

Biotech firms' payoff expressions are computed similarly as described in chapter 2. I denote the biotech firms' payoff expressions as $\pi_{j,Bi}^{Bk}$, where *j=f (first), s (second)* stands for the stage at which the agreement is signed, *Bi = B1, B2* represents the biotech firm that signs the agreement and *Bk = B1, B2* the biotech firm to which the payoff is referred. In case no alliance is signed the subscript (*j, Bi*) is eliminated.

At time t_1 uncertainty about the value of the project is partially resolved and, therefore, the simple NPV methodology can be adopted. Table 11 shows the second stage payoff expressions of biotech firms, $\pi_{s,Bi}^{Bk}(t_1)$. Note that I restrict the analysis to a region of parameters that ensures positive payoffs.

Table 11: NPV/ROA biotech firms' second stage payoff expressions.

Scenario	*B1's Payoff*	*B2's Payoff*
	$\pi_{s,Bi}^{B1}(t_1)$	$\pi_{s,Bi}^{B2}(t_1)$
B1 signs the alliance at Stage II	$(1-\alpha_s)\beta\delta_{B1}V_s + P_{s,B1} - I_s$	$(1-\beta)\delta_{B1}V_s - I_s$
B2 signs the alliance at Stage II	$(1-\beta)\delta_{B2}V_s - I_s$	$(1-\alpha_s)\beta\delta_{B2}V_s + P_{s,B2} - I_s$
No alliance	$\gamma V_s - I_s$	$(1-\gamma)V_s - I_s$

Moving to time t_0, I model the present value of second stage payoff expressions backtracked at t_0 and first stage payoff expressions using ROA by adopting the Black and Scholes formula with the same logic reported in chapter 2. In Table 12 I report the underlying values of the biotech call options for all scenarios.[10] As in chapter 2, $C_{j,Bi}^{Bk}$ is the biotech call option.

[10] It is important to note that all the call options have the same exercise price equal to I_s.

Table 12: Call Option $C_{j,Bi}^{Bk}$ underlying values.

Scenario	$C_{j,Bk}^{B1}$ *(Underlying)*	$C_{j,Bk}^{B2}$ *(Underlying)*
B1 signs the alliance at Stage I	$C_{f,B1}^{B1}\ ((1-\alpha_f)\beta\delta_{B1}V_f)$	$C_{f,B1}^{B2}\ ((1-\beta)\delta_{B1}V_f)$
B2 signs the alliance at Stage I	$C_{f,B2}^{B1}\ ((1-\beta)\delta_{B2}V_f)$	$C_{f,B2}^{B2}\ ((1-\alpha_f)\beta\delta_{B2}V_f)$
B1 signs the alliance at Stage II	$C_{s,B1}^{B1}\ ((1-\alpha_s)\beta\delta_{B1}V_f + P_{s,B1}e^{-r\tau})$	$C_{s,B1}^{B2}\ ((1-\beta)\delta_{B1}V_f)$
B2 signs the alliance at Stage II	$C_{s,B2}^{B1}\ ((1-\beta)\delta_{B2}V_f)$	$C_{s,B2}^{B2}\ ((1-\alpha_s)\beta\delta_{B2}V_f + P_{s,B2}e^{-r\tau})$
No alliance	$C^{B1}\ (\gamma V_f)$	$C^{B2}\ ((1-\gamma)V_f)$

In Table 13 I report first stage payoff expressions and second stage payoff expressions backtracked to time t_0 for the biotech firms.

Table 13: ROA biotech firms' first stage payoff expressions and second stage payoff expressions backtracked to time t_0.

Scenario	*B1's Payoff*	*B2's Payoff*
	$\pi_{j,Bi}^{B1}(t_0)$	$\pi_{j,Bi}^{B2}(t_0)$
B1 signs the alliance at Stage I	$C_{f,B1}^{B1} - I_f + P_{f,B1}$	$C_{f,B1}^{B2} - I_f$
B2 signs the alliance at Stage I	$C_{f,B2}^{B1} - I_f$	$C_{f,B2}^{B2} - I_f + P_{f,B2}$
B1 signs the alliance at Stage II	$C_{s,B1}^{B1} - I_f$	$C_{s,B1}^{B2} - I_f$

B2 signs the alliance at Stage II	$C_{s,B2}^{B1} - I_f$	$C_{s,B2}^{B2} - I_f$
No alliance	$C^{B1} - I_f$	$C^{B2} - I_f$

3.2.3 Pharmaceutical company's payoff expressions

Concerning the pharmaceutical company, his payoff expressions are indicated as $\pi_{j,Bi}^{P}$ where $j = f, s$ stands for the stage at which the agreement is signed, $Bi = B1, B2$ represents the biotech firm that signs the agreement. I derive pharmaceutical company's second stage payoff expressions adopting the simple NPV methodology. They are reported in Table 14.

Table 14: NPV/ROA pharmaceutical company's second stage payoff expressions.

Scenario	*Pharma's Payoff*
	$\pi_{s,Bi}^{P}(t_1)$
B1 signs the alliance at Stage II	$\alpha_s \beta \delta_{B1} V_s - P_{s,B1}$
B2 signs the alliance at Stage II	$\alpha_s \beta \delta_{B2} V_s - P_{s,B2}$
No alliance	0

In this setting, moving to the first stage, the pharmaceutical company does not have a proper option. However, the strategic interactions with the biotech firms imply that his decisions on the upfront payments to offer to each potential partner are naturally influenced by biotech firms' option to abandon the project development before the second stage occurs. I show in detail how the pharmaceutical company's payoff expression should be computed. In particular, I provide an example to illustrate how to obtain the present value (i.e., at time t_0) of payoff expressions coming from an alliance signed in the second stage starting from those computed in Table 14. Specifically, I consider the case where B1 signs the alliance with the pharmaceutical company in the second stage. Pharmaceutical company's second stage payoff expression backtracked to

time t_0 depends on the decision of B1: if B1 decides to continue with the project (i.e. B1 will exercise the option), the pharmaceutical company's second stage expected payoff discounted at t_0 will be given by:

$$\pi^{P}_{s,B1}(t_0) = E\left[\alpha_s\beta\delta_{B1}V_s - P_{s,B1}\middle|((1-\alpha_s)\beta\delta_{B1}V_s + P_{s,B1}) > I_s\right]\Pr\left[((1-\alpha_s)\beta\delta_{B1}V_s + P_{s,B1}) > I_s\right] \quad (36)$$

Where $E\left[\alpha_s\beta\delta_{B1}V_s - P_{s,B1}\middle|((1-\alpha_s)\beta\delta_{B1}V_s + P_{s,B1}) > I_s\right]$ represents the expectation value of $(\alpha_s\beta\delta_{B1}V_s - P_{s,B1})$ given that the option is exercised ($((1-\alpha_s)\beta\delta_{B1}V_s + P_{s,B1}) > I_s$) times the probability that the option will be exercised by B1 $\left(\Pr\left[((1-\alpha_s)\beta\delta_{B1}V_s + P_{s,B1}) > I_s\right]\right)$. Following Nielsen (1992) and Chance (2014), I express this conditional expected value as $\alpha_s\beta\delta_{B1}V_f - P_{s,B1}(t_0)$ times $N(d_1(C^{B1}_{s,B1}))$, which is the $N(d_1)$ of the call option $C^{B1}_{s,B1}$, i.e., the call option of the considered scenario, i.e. B1 allies in the second stage and I refer to it as $N\left(d_1\left(C^{B1}_{s,B1}\right)\right)$ and it represents the "*option-conditioned probability*".

In general, pharmaceutical company's second stage payoff expression backtracked to time t_0 is equal to:

$$\pi^{P}_{s,Bi}(t_0) = \left(\alpha_s\beta\delta_{Bi}V_f - P_{s,Bi}(t_0)\right)\cdot N(d_1\left(C^{Bi}_{s,Bi}\right)) \quad (37)$$

where $i = 1, 2$. Similarly, his first stage payoff expression is:[11]

$$\pi^{P}_{f,Bi}(t_0) = \left(\alpha_f\beta\delta_{Bi}V_f\right)\cdot N(d_1\left(C^{Bi}_{f,Bi}\right)) - P_{f,Bi} \quad (38)$$

In Table 15 I report payoff expressions backtracked to time t_0 for the pharmaceutical company.

Table 15: Pharmaceutical company's first stage payoff expressions and second stage payoff expressions backtracked to time t_0.

Scenario	*Pharma's Payoff*
	$\pi^{P}_{j,Bi}(t_0)$
B1 signs the alliance at Stage I	$\alpha_f\beta\delta_{B1}V_f N(d_1(C^{B1}_{f,B1})) - P_{f,B1}$

[11] It is noteworthy that when the alliance is signed in the first stage the pharmaceutical company can incur in a net loss (the upfront payment remitted in the first stage) if the partner will not exercise the option.

B2 signs the alliance at Stage I	$\alpha_f \beta \delta_{B2} V_f N(d_1(C_{f,B2}^{B2})) - P_{f,B2}$
B1 signs the alliance at Stage II	$(\alpha_s \beta \delta_{B1} V_f - P_{s,B1}(t_0)) N(d_1(C_{s,B1}^{B1}))$
B2 signs the alliance at Stage II	$(\alpha_s \beta \delta_{B2} V_f - P_{s,B2}(t_0)) N(d_1(C_{s,B2}^{B2}))$
No alliance	*0*

3.2.4 NPV firms' payoff expressions

One of the objective of this chapter is to shed light on the consequences, in terms of alliance timing decisions, of disregarding the use of ROA for new drug investment project evaluation. Therefore I present both biotech firms' and pharmaceutical company's payoff expressions as if the all involved players use the NPV methodology to evaluate their payoffs related to the new drug project investment. In this case, the second stage payoffs computed at t_1 are the same as those reported in Table 11 and Table 14 (as second stage ROA payoffs are computed as NPV because there is no further option to exercise). Differently from ROA, the second stage payoff expressions backtracked to time t_0 under NPV are just discounted by e^{-rt}. Therefore, in Table 16 I only report first stage payoff expressions of both biotech firms and the pharmaceutical company computed using the NPV methodology.

Table 16: Firms' NPV first stage payoff expressions.

Scenario	*B's 1Payoff*	*B2's Payoff*	*Pharma Payoff*
	$\pi_{f,Bi}^{B1}$	$\pi_{f,Bi}^{B2}$	$\pi_{f,Bi}^{P}$
B1 signs the alliance at Stage I	$(1-\alpha_f)\beta\delta_{B1}V_f + P_{f,B1} - -I_s - I_f$	$(1-\beta)\delta_{B1}V_f - I_s - I_f$	$\alpha_f \beta \delta_{B1} V_f - P_{f,B1}$
B2 signs the alliance at Stage I	$(1-\beta)\delta_{B2}V_f - I_s - I_f$	$(1-\alpha_f)\beta\delta_{B2}V_f + P_{f,B2} - -I_s - I_f$	$\alpha_f \beta \delta_{B2} V_f - P_{f,B2}$

3.3 Game solution with identical biotech firms (symmetric case)

First I consider the case of identical biotech firms, to which I refer as the symmetric case. Hence, the level of synergies generated from the alliance is the same for both firms $(\delta_{B1} = \delta_{B2} = \delta > 1)$. This implies that in each stage the same upfront payment P_j (where j stands for the stage) is offered by the pharmaceutical company to either biotech firms. Solving the above-described game, pharmaceutical company has to choose between different alternatives; Figure 15 shows all the sub-games and cases originated. In particular, after having solved the second stage, similarly as reported in chapter 2, I distinguish two cases depending on the value of δ. I refer to the case $\delta > (1-\gamma)/(1-\beta)$ as high synergies and to the case $\delta < (1-\gamma)/(1-\beta)$ as low synergies (please refer to Appendix A for the threshold definition). In the first stage, under ROA methodology, the case of low synergies needs to be further split in Case A and Case B for the sake of analytical tractability.

In presence of identical biotech firms under ROA yields the optimal alliance timing for the pharmaceutical company and the biotech firm chosen for the alliance, which has been summarized in Proposition 1. The detailed derivation of these results is reported in Appendix A.

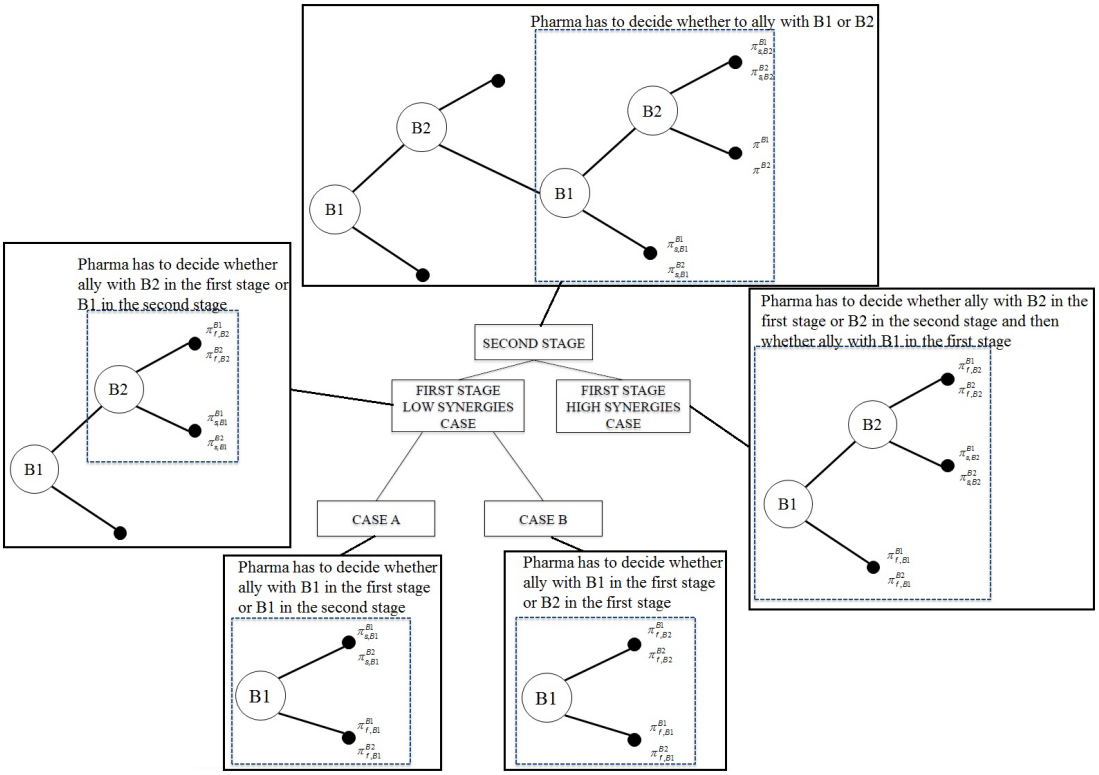


Figure 15: Cases and sub-games in case of identical biotech firms.

However, note that in presence of low synergies I not include the result of the optimal timing in this Proposition, as such result cannot be obtained analytically.

Proposition 1. (ROA Optimal alliance timing)

Using real options methodology, the pharmaceutical company allies with B2 in case of high synergies, whereas he allies with B1 in presence of low synergies. The optimal alliance time for the pharmaceutical company in presence of high synergies is the second stage.

Results from Proposition 1 suggest that both biotech firms have the opportunity to sign the agreement, and which biotech firm will be selected depends on the level of synergies. In particular in case of low synergies B1 decides to enjoy her first mover advantage and pre-empts the rival, whereas when the first mover can benefit from a high level of synergies, due to the presence of spillover effects, B1 leaves to B2 room to sign the agreement. Regarding the alliance timing, due to the fact that the pharmaceutical company has the bargaining power, he prefers to ally in the second stage. The rationale of this behaviour is related to the presence of the option-conditioned probability. That is, in my ROG model the pharmaceutical company can

take into account the risk of incurring a net loss (equal to the first stage upfront payment) in case the biotech partner does not exercise the option later. In particular, this loss becomes very relevant in presence of high synergies as the high level of δ implies a high level of upfront payment. To better understand the analytical derivation I provide a representative comparison based on a case study available in Rogers et al. (2002). Specifically, I consider a drug in the third clinical phase and the values of the required parameters are: $V_f = \$400M$, $\sigma = 30\%$, $r = 5\%$, $\tau = 2$, $I_f = \$75M$, $I_s = \$180M$, $\gamma = 0{,}5$. In addition, I suppose the following values: $\beta = 0.65$ and $\delta = 1.6$.

Figure 16 reports the trends of the pharmaceutical company's payoffs for the final comparison in the game tree, in case of high synergies, i.e. pharmaceutical company's payoff in case of an alliance with B1 in the first stage or in case of alliance with B2 in the second stage (see Appendix A). I observe that, while $\pi^{*P}_{s,B2}(t_0)$ (where * represents the optimal pharmaceutical company's payoff) is independent from the amount of royalties, $\pi^{*P}_{f,B1}(t_0)$ decreases as α_f increases due to the larger losses that the pharmaceutical company faces if the partner does not exercise the option. Consistent with Proposition 1, in high synergies case Figure 16 shows that the pharmaceutical company prefers to ally with B2 in the second stage.

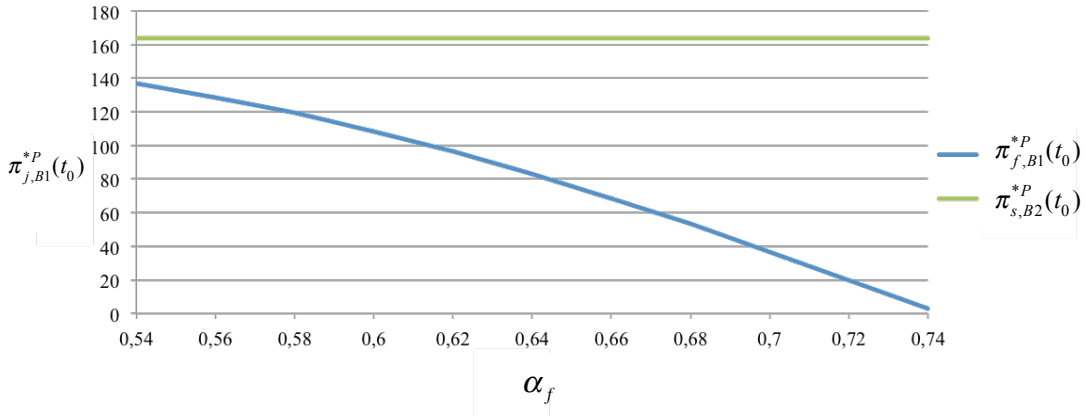


Figure 16: Trends of pharmaceutical company's payoffs in the last comparisons of the game tree in case of identical biotech firms and high synergies (i.e. alliance with B1 in the first stage or with B2 in the second stage).

In presence of low synergies, the analysis shows that two possible solutions, namely the case of alliance with B1 in the second stage and the case of alliance with B1 in the first stage, can be optimal from the perspective of the pharmaceutical company. However, I

cannot analytically determine the conditions under which one solution dominates the other solution in terms of pharmaceutical company's payoffs or *vice versa*. Thus, I conduct a numerical analysis and a sensitive analysis to derive the ranges where either solution arises as the optimum. In the range of parameters ensuring the existence of the low synergy case, I modify the level of β and also the values of δ. I rely on the same case study above. Figure 17 shows a representative comparison between pharmaceutical company's payoff in case of alliance with B1 in the second stage (in orange) and pharmaceutical company's payoff in case of alliance with B1 in the first stage (in blue) for $\beta = 0.6$. Even in presence of low synergies, the pharmaceutical company prefers to ally with B1 in the second stage for a large range of parameters. However, differently from the case of high synergies, here I notice that, for low values of α_f, the optimal solution is to ally with B1 in the first stage. The intuition behind this behaviour is again related to the role played by the option-conditioned probability. Specifically, in case of low synergies, when α_f, i.e. the percentage of royalties retained by the pharmaceutical company, is low, the upfront payment offered to the biotech firm is also low. Given the lower upfront payment, the pharmaceutical company is more willing to incur the risk of losing it in case the biotech partner decides to not exercise the option. In other words, the disadvantage for the pharmaceutical company of allying in the first stage is considerably diminished when α_f is small because the potential loss is also small. In contrast, the advantage of allying in the first stage is increased. In fact, in case of low synergies, biotech firms have even more incentive to form the alliance, as they would not be able to benefit much from spillovers if they had to reach the market individually. As a result, they are more prone to immediately accept very low payments in order to pre-empt the competitor, thus making the pharmaceutical company better off in case of alliance in the first stage.

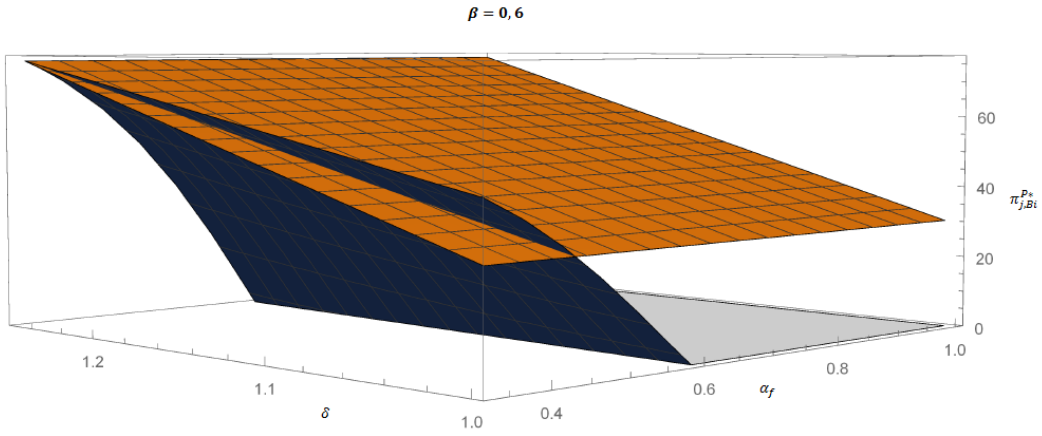


Figure 17: Trends of pharmaceutical company's payoffs in the last comparison of the game tree in case of symmetric biotech firms and low synergies (i.e., alliance with B1 in the first stage or in the second stage).

I also solved the above-described game under NPV methodology. Proposition 2 exhibits the optimal alliance timing for the pharmaceutical company and the biotech firm chosen for the alliance. The detailed derivation of this result can be found in the Appendix A.

Proposition 2. (NPV Optimal alliance timing)

Using NPV methodology, in presence of high synergies the pharmaceutical company allies with B2 and any alliance time is optimal for him. In presence of low synergies the pharmaceutical company allies with B1 and the optimal time is the first stage.

I note that, with regard to the biotech firm that is selected for the alliance, the use of the NPV methodology yields the same outcome as the ROA methodology. As a matter of fact, B2 is selected in presence of high synergies and B1 is chosen in case of low synergies also under the NPV methodology. Nevertheless, the optimal alliance timing changes radically. Indeed, when the NPV methodology is adopted to evaluate the investment project, in presence of high synergies the choice of the optimal alliance time is totally irrelevant for the pharmaceutical company as any stage yields the same payoff. This result suggests that, at least in presence of high synergies, the NPV methodology fails to capture the uncertainty characterizing the R&D process and thus fails to incorporate the risk incurred by the pharmaceutical company in case of first stage alliance to lose the upfront payment if the biotech partner decides to abandon the project in the second stage. The same intuition holds also in presence of low synergies. Indeed, while under the NPV methodology the optimal timing is to ally in the first stage due to

pre-emption reasons,[12] under ROA the second stage can be preferred in presence of low values of α_f. As I have already underscored, this suggests that using ROA rather than the NPV methodology, the pharmaceutical company is able to capture the risk related to the option at disposal of the biotech partner in case of alliance in the first stage.

3.4 Game solution with non-identical biotech firms (asymmetric case)

In this section, I extend the analysis to the case of non-identical biotech firms, to which I refer as the asymmetric case. Specifically, I assume the market increase in case of an alliance with B1 is higher as compared with the market increase originated from an alliance with B2. That is, without loss of generality, I assume $\delta_{B1} > \delta_{B2} > 1$. This implies that also the upfront payments offered by the pharmaceutical company to the biotech firms will be different. Specifically, $P_{j,B1}$ and $P_{j,B2}$ are offered to B1 and B2, respectively, in stage *j = 1, 2*.

Solving the above-described game pharmaceutical company has to choose between different alternatives, Figure 18 shows all the sub-games and cases originated. In particular, after have solved the second stage, similarly to the symmetric case, I can still distinguish two cases depending on the value of δ_{B1}. Specifically, I distinguish the case $\delta_{B1} > (\delta_{B2} - (1-\gamma))/\beta$ (to which I refer as δ_{B1} high or Case 1) and the case $\delta_{B1} < (\delta_{B2} - (1-\gamma))/\beta$ (to which I refer as δ_{B1} low or Case 2). With ROA methodology, the former case needs to be further split in Case A and Case B.

Solving the alliance timing game in presence of non-identical biotech firms under ROA yields the optimal alliance timing for the pharmaceutical company and the biotech firm chosen for the alliance. The detailed derivation of this result can be found in Appendix B.

[12] As a matter of fact, the NPV methodology is biased in favour of early market entry because it takes into account the risk of waiting (pre-emption) but not the rewards of waiting (reduced uncertainty) (Krychowski and Quelin, 2010).

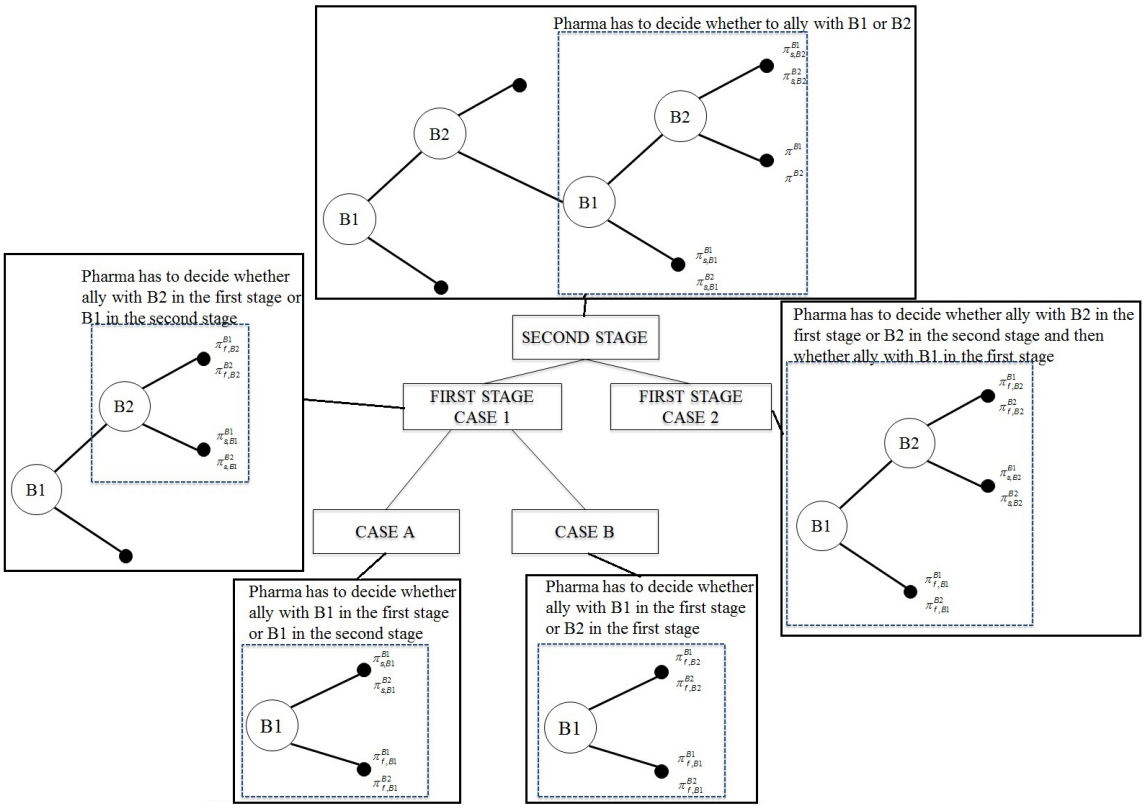


Figure 18: Cases and sub-games in case of non-identical biotech firms.

However, in Proposition 3, I can only present the case $\delta_{B1} > (\delta_{B2} - (1-\gamma))/\beta$, as the alternative case can be exclusively treated numerically.

Proposition 3. (ROA Optimal alliance timing)

Using real options methodology, if δ_{B1} is high (i.e., $\delta_{B1} > (\delta_{B2} - (1-\gamma))/\beta$) the pharmaceutical company allies with B1 and the optimal alliance time for the pharmaceutical company is the second stage.

From Proposition 3, I observe that when the synergies derived from the alliance between the pharmaceutical company and B1 are sufficiently high, i.e., $\delta_{B1} > (\delta_{B2} - (1-\gamma))/\beta$, the pharmaceutical company naturally prefers allying with the first mover, i.e., B1, given the larger benefit such partner can provide in terms of market increase. With regard to the optimal alliance timing, similarly to the symmetric case, the rationale of the result is due to the risk incurred by the pharmaceutical company of losing the upfront payment, when allying in the first stage, in case the biotech partner decides to abandon the project in the second stage. Therefore, the optimal decision for the pharmaceutical company is, to postpone the alliance to the second stage. To better

understand the analytical derivation also in this case I provide a representative comparison when δ_{B1} is high based on the case study available in Rogers et al. (2002). Furthermore I suppose that $\delta_{B1}=1.5$ and $\delta_{B2}=1.3$. Figure 19 shows the trends of the pharmaceutical company's payoffs for the final comparisons in the game tree between the possible solutions in Case A and the possible solutions in Case B. Specifically, in Case A the final comparison is between $\pi^{*P}_{f,B1}(t_0)$ (where * represents the optimal pharmaceutical company's payoff), i.e. alliance with B1 in the first stage, and $\pi^{*P}_{s,B1}(t_0)$, i.e. alliance with B1 in the second stage, whereas in Case B it is between $\pi^{*P}_{f,B1}(t_0)$, i.e. alliance with B1 in the first stage, and $\pi^{*P}_{f,B2}(t_0)$, i.e. alliance with B2 in the first stage. Similarly as the symmetric case, in case of an alliance in the first stage, pharmaceutical company's payoff decreases as α_f increases due to the larger losses in which pharmaceutical company incurs if the partner does not exercise the option. The reader can note that, as δ_{B1} is high, the profit that the pharmaceutical company obtains in case of alliance with B1, independently from the alliance timing, is higher than the profit in case of alliance with B2. Due to the lower level of uncertainty characterizing the second stage, the solution of an alliance with B1 in the second stage, i.e. Case A, dominates the other case (see Appendix B).

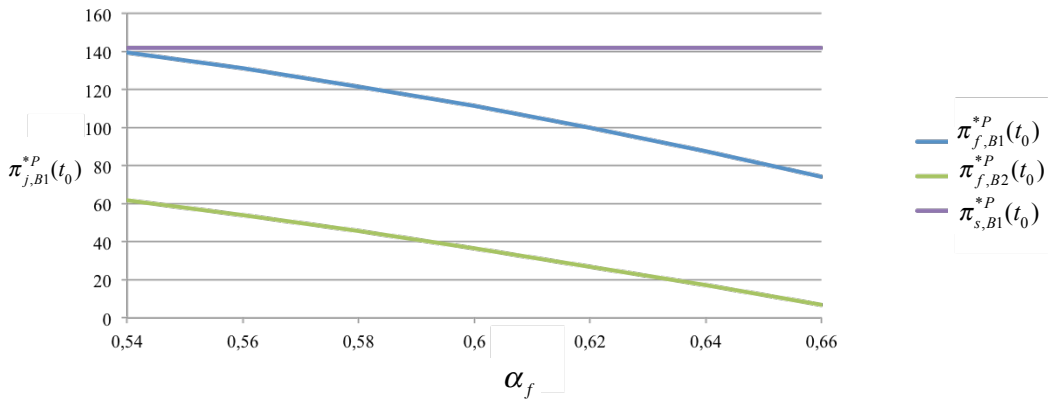
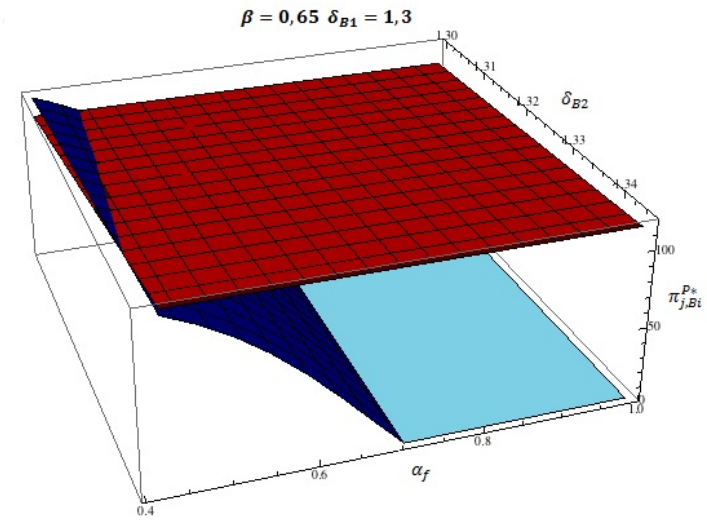


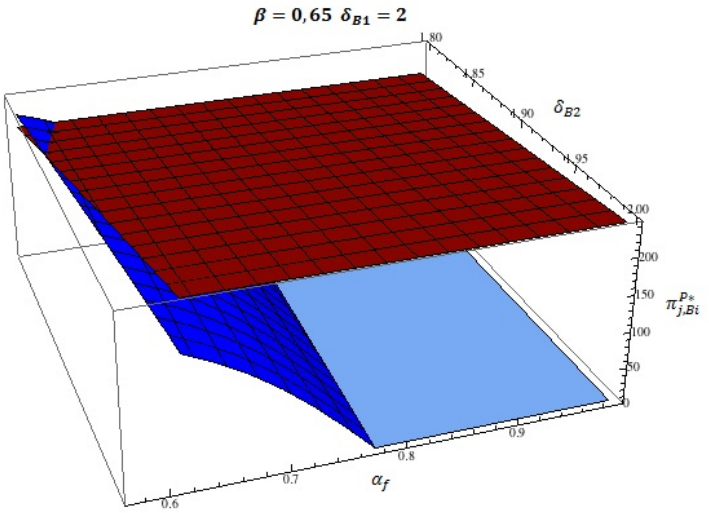
Figure 19: Trends of pharmaceutical company's payoffs in the last comparison of the game tree in case of non identical biotech firms and Case 1 (both Case A and Case B).

The case when $\delta_{B1}<(\delta_{B2}-(1-\gamma))/\beta$ cannot be solved analytically because, using the ROA methodology, it is not possible to establish whether the pharmaceutical company's

profit is higher or lower when allying with B1 in the first stage or when allying with B2 in the second stage (see Appendix B). Thus I conduct a numerical analysis also in this case. Similarly to the symmetric case, I use data provided by Rogers et al. (2002). Figure 20a and Figure 20b show a representative comparison between pharmaceutical company's payoff in case of alliance with B2 in the second stage (in red) and pharmaceutical company's payoff in case of alliance with B1 in the first stage (in blue) for $\delta_{B1} = 1.3$ and $\delta_{B1} = 2$, respectively. In the representative example, for β varying from 0.5 to 0.75 I observe that, as long as α_f is low, pharmaceutical company's payoff in case of alliance with B1 in the first stage is higher than pharmaceutical company's payoff in case of alliance with B2 in the second stage. This result suggests that, for low values of δ_{B1} and sufficiently high level of α_f, the first mover is more demanding and asks for a higher level of upfront payment. Therefore, the pharmaceutical company decides to ally with B2 in the second stage, as he would not risk of losing the upfront payment in case the biotech partner decides to not exercise the option. When α_f is low, the first mover requires a lower level of the upfront payment, therefore the pharmaceutical company prefers to ally with her in the first stage due to the higher synergies she can bring and the fact that the potential loss is sufficiently small. Finally, note that the area of the alliance in the first stage decreases as δ_{B1} increases, since the value of the upfront payment increases as well.



20a)



20b)

Figure 20a and 20b: Trends of pharmaceutical company's payoffs in the last comparisons of the game tree in case of asymmetric biotech firms and $\delta_{B1} < (\delta_{B2} - (1-\gamma))/\beta$.

I also analytically solved the asymmetric case under the NPV methodology. Proposition 4 exhibits the optimal alliance timing for the pharmaceutical company and the biotech firm chosen for the alliance. The detailed derivation of this result can be found in Appendix B.

Proposition 4. (NPV Optimal alliance timing)

Using NPV methodology, if δ_{B1} *is high, i.e.,* $\delta_{B1} > (\delta_{B2} - (1-\gamma))/\beta$, *the pharmaceutical company allies with B1, otherwise he allies with B2. In both cases alliance time is indifferent for the pharmaceutical company*.

Similarly to the symmetric case with high synergies, the alliance timing decision is irrelevant when the NPV methodology is adopted, as any stage yields the same payoff from the perspective of the pharmaceutical company. Once again, this suggests that, differently from ROA, the NPV methodology fails to capture the risk incurred by the pharmaceutical company with regard to the option at disposal of the biotech partner to abandon the project later on when they ally in the first stage. Concerning the selected alliance partner, the choice depends on the level of the synergies, δ_{B1}, between the pharmaceutical company and the first mover. When such level of synergies is sufficiently high, the first mover is selected, otherwise the alliance is formed with the follower. The result in the first case is quite intuitive, given the larger benefit B1 can

provide in terms of market increase. In case of δ_{B1} low, as stated above, pharmaceutical company prefers to ally with B2 in accordance with the fact that the first mover requires a higher level of payment than the follower.

3.5 Discussion and conclusion

In this chapter, I have examined alliance timing decisions in a setting where a pharmaceutical company can choose between two competing biotech firms to form an exclusive alliance offering different profit-maximizing contracts at different stages of the R&D process that the biotech firms can in turn decide to accept or reject. To incorporate the above-mentioned features of the typical biopharmaceutical environment, and thus better capture the trade-off facing both pharmaceutical and biotech firms, I have proposed a real options game approach. Under this approach I have determined the optimal alliance timing and the selected biotech firm to ally with. I have then shed light on whether and how alliance timing changes if firms utilize the simple NPV methodology instead of the proposed real options approach to evaluate a new drug investment project.

My findings can be summarized as follows. In a setting where biotech firms are identical, the adoption of ROA provides the pharmaceutical company with the incentive to postpone the alliance to the second stage when the market potential increases significantly as a result of the alliance, i.e., when the synergies between pharmaceutical and biotech firms are sufficiently high. In contrast, in the same scenario, if the NPV were adopted, the pharmaceutical company would be completely indifferent between the two stages. On the other hand, if the synergies are low, while only the first stage is optimal when the NPV methodology is adopted, the results in terms of alliance timing using ROA are more complex with either stage being optimal under specific conditions. Indeed, broadly speaking, the use of ROA tends to postpone the alliance timing to the second stage because, via the option-conditioned probability, it allows incorporating the risk incurred by the pharmaceutical company of losing the upfront payment when allying in the first stage in case the biotech partner does not exercise the option. This implies that the optimal alliance time is, in general, the second stage. However, I have shown that, in a low synergy scenario, when the level of upfront payment to be offered to the partner is low, which occurs in presence of low values of royalties, the pharmaceutical company does not face a relevant risk. Rather, he can benefit from the

fact that, in presence of low synergies, biotech firms are more prone to immediately accept very low payments in order to pre-empt the competitor. As a result, the pharmaceutical company can make higher profit when allying in the first stage even when ROA is utilized. With regard to which biotech firm is selected to form the alliance, I show that under either methodology the second mover is selected for the alliance in case of high synergies, whereas the first mover is selected in case of low synergies.

I have also introduced asymmetry between biotech firms by assuming that the first mover biotech firm leads to a larger market potential when allying with the pharmaceutical company than the second mover. In this case, I have found that when the value of the synergies between the pharmaceutical company and the first mover biotech firm are sufficiently large, the results in terms of alliance timing are qualitatively unchanged as compared with the symmetric case (in presence of high synergies). The only difference between symmetric and asymmetric scenarios in presence of sufficiently high synergies is related to the biotech that is selected. Indeed, in the asymmetric setting, the pharmaceutical company will form the alliance with the first mover, whereas in the symmetric case the second mover is selected. There are more significant differences in presence of low synergies between the first mover and the pharmaceutical company. In fact, under the asymmetric case, the use of real options leads to more ambiguous results as either firm can be selected and either stage can be optimal depending on the level of royalties offered, whereas using the NPV
methodology any stage is still optimal, but the second mover is selected. In contrast, in the symmetric case the pharmaceutical company selects the first mover with either methodology and signs the agreement in the first stage under NPV and in the first or in second stage (depending on the royalties value) under ROA.

Overall, in most of the cases, my findings suggest that the pharmaceutical company has more incentive to postpone the alliance to the second stage when the real options are adopted to evaluate the investment project. The intuition behind this result is that by using the real options methodology, the pharmaceutical company can take into account the risk related to the fact that the biotech firm may decide to discontinue the development process in the second stage based on updated information in case of (her own) negative profit. As a result, the pharmaceutical company naturally tends to offer a

contract to form the alliance in the second stage. There are circumstances, however, under which the alliance will be signed in the first stage when real options methodology is utilized. This can happen in presence of low synergies (under both symmetric and asymmetric cases) because in this case the first mover has less incentive to reject the offer from the pharmaceutical company, given that the benefits obtainable via spillover are much more limited. Hence, the first mover will immediately accept the offered contract leaving no room to the second mover. Moreover, my findings suggests that the NPV methodology is not effective in capturing the above risk facing the pharmaceutical company, thus leading to indifference in the preference of the optimal alliance timing in most of the circumstances.

Chapter 4
Conclusions

4.1 Contributions

The aim of this thesis is to study the evaluation of R&D alliances timing decisions under uncertainty. Pharmaceutical companies more and more partner with biotechnology companies to develop new products. The emergence of numerous alliances between these two types of actors poses several relevant questions to the innovation management community. One is certainly related to the alliance timing, which is currently discussed in the biotech industrial world. As pharmaceutical companies become more attracted to biotech products and search more collaboration opportunities, both biotech firms and pharmaceutical companies face decisions such whether and, possibly, when to ally. In this context, the objective of this work is to determine the optimal time to sign an R&D partnership by considering the important role of competition. In addition, due to the intrinsic characteristics of the drug R&D process, I have also taken into account the uncertainty of the economic environment in which timing decisions are made. In order to do so, I have adopted a real options game approach, developing a model to investigate this type of decisions in presence of competition between two biotech firms who can partner with a pharmaceutical company offering a mutually exclusive take-it-or-leave-it contract.

In the literature, papers that analyse firms' optimal alliance timing mainly adopt empirical approaches. Few works develop analytical models considering the uncertainty that characterize the market. However all these studies do not consider the role of competition. Starting from this premise, this thesis provides several contributions to these streams of research, as already anticipated in the conclusions of chapter 2 and chapter 3.

The main contribution is to shed light on the optimal timing for firms to sign an agreement when uncertainty and competition in the market are considered. I take a holistic perspective considering the active role of both biotech firms and pharmaceutical company. Specifically, I have found that who ally with and when are determined by "alliance conditions", i.e. on the contract terms offered by the pharmaceutical company,

the market value increase originated from the alliance with the pharmaceutical company, as well as the competitive advantage one biotech firm gains against the competitor due to the alliance. In particular, not only the first mover will find profitable form the alliance but also the follower. This happens when the level of synergies generated from the alliance is sufficiently high. Thus the first mover prefers to continue the project individually as she receives indirect benefits from the potential alliance between the follower and the pharmaceutical company.

Regarding the alliance timing, the presence of the option-conditioned probability determines the optimal strategy for the pharmaceutical company. Indeed, assuming that the pharmaceutical company has the bargaining power to maximize his profit, he has more incentive to postpone the alliance to the second stage due to the fact that he takes into account biotech firms' option exercise decisions in his profit maximization problem. Therefore, another important contribution is given by explicitly model how, in vertical relationships, firms' project investment decisions depend on real options of other firms.

Moreover, from a methodological point of view, my thesis contributes to the stream of research that develops real options valuation models for investments under uncertainty. Specifically, I have studied the role of the methodology utilized to evaluate the new drug investment project in the alliance timing decisions. Essentially, I found that the use of the real options methodology has a different impact on the optimal alliance timing decisions as compared to the use of the traditional NPV methodology. In particular, NPV methodology is not able to capture the uncertainty characterizing the R&D process and the decision maker flexibility, leading to indifference in the preference of the optimal alliance timing in most of the circumstances. In fact, NPV methodology fails to incorporate the risk incurred by the pharmaceutical company in case of first stage alliance to lose the upfront payment if the biotech partner decides to not continue the project in the second stage. Therefore, real options are the appropriate tool to evaluate the R&D process because can tackle with the managers' flexibility that allows making further investments only in case of positive expected payoffs. To take into account also the strategic interactions between firms the real option game approach has been adopted. Differently from the previous literature, I developed a setting where firms strategically interact not for investment timing decisions but for alliance timing

decisions. In doing so, I have overcome the traditional distinction between discrete and continuous time ROG models. Specifically, I developed a two stage game model where the underlying follows a continuous process, i.e. Geometric Brownian Motion, but the strategic decisions of ally or not are made in discrete points of time. This structure allows to model accurately the drug R&D process, which is divided into several stages, and firms' decision process, in which decisions are usually made in discrete points of time, for instance at the beginning of a new R&D stage. Moreover the model provides a closed-form solution that allows to preserve analytical tractability and provides more accurate solutions.

4.2 Managerial implications

The research provided in this thesis has also several important managerial implications. These offer some guidelines and recommendations for supporting managers, involved in the R&D alliance timing decisions in the biopharmaceutical industry, in the important decision on whether and when they should collaborate with other firms in a competitive environment, characterized by an amount of uncertainty over the future rewards from the investment.

Particularly, from the perspective of the biotech firms, managers should pay attention to the market value increase due to the alliance, the contract terms offered by the company partner as well as to the level of competition. Specifically, supposing that the firm enjoys first mover advantage and the potential market is high enough, managers should not always choose to sign the agreement. Thus, when contract terms are not appealing, first mover may find more profitable let the follower ally to reach the market alone benefiting from positive spillover and without sharing the profit with the partner company. Conversely, when contract terms are satisfactory or the potential market is not sufficiently high, or, alternatively, the competition level is very high, managers should always pre-empt the other firm. In case the first mover leads to a significantly higher potential market when ally with the pharmaceutical company as compared to the second mover, managers of the leader firm should resort to the alliance.

From the perspective of the pharmaceutical company, managers should take into account on one side benefits, in terms of synergies generated in alliance, that each biotech could bring and, on the other side, the risks of incur in high level of losses due to the fact the he cannot decide on the continuation of the R&D process. Specifically, in

case the potential partners are identical, managers should prefer to postpone the alliance to late stages to avoid losses in case of interruption of the R&D process, unless the upfront payment required by the biotech is extremely low. When the pharmaceutical company can obtain a significant higher market increase in case of alliance with the first mover, managers should partner with this company. If this advantage is not significant, managers should select the other biotech due to her request of lower contract terms. However they should always prefer the second stage unless the leader requires a sufficiently low upfront payment, in this case an alliance with her in the first stage could be possible.

In addition, through the use of real options, managers are able to capture the unique characteristics of R&D investment projects in the biopharmaceutical industry. Managers of the biotech firms can accurately evaluate the R&D project, update their information when become available and, in their considerations, consider the possibility of discontinue the development process in case of negative profit expectation. Using real options perspective, managers of the pharmaceutical companies are provided with an instrument that reflects their flexibility and thus can help them to anticipate other players' behaviours more effectively. In spite of the fact that the real options approach has often been criticized for its apparent complexity, managers should consider the consequences of choosing different methodologies to evaluate R&D investment projects, as the methodology comparison reported in chapter 3 suggest. Specifically, they should be aware that the adoption of different methodologies could yield very different outcomes in terms of alliance timing, which could ultimately influence firms' profitability. To overcome their diffidence and help them, it is necessary to develop models more adequate to their expectations. In this sense, in the models reported in this dissertation, the adoption of a closed-form solution makes the implementation of the real options models less complex, in terms of constraints and variables involved in the problem, as compared than adopting numerical approaches.

4.3 Limitations and future developments

While this research makes important contributions to alliance timing decisions, it also has some limitations. At the same time, these limitations represent potential opportunities to build upon this work for future research.

From a methodological perspective two limitations can arise related to the adoption of a closed-form solution, i.e. Black and Scholes model. First, in my models I have considered only economic risk, while it could be interesting integrating also technical uncertainty due to the high influence it has on the success of the drug R&D process. In this sense usually, numerical approaches are able to capture both technical and economic risk of the R&D process, on the contrary of the closed-form solutions that capture only the economic risk. However, Cassimon et al. (2011) developed a model to incorporate the technical risk in a n-fold compound option model, preserving the closed-form formula. Thus integrating this model could be the starting point for future researches.

Second, I have developed a two-stage real option game model in which the first stage represents the discovery and clinical phases of the R&D process and the second stage represents the manufacturing and commercialization phase. However, considering that there are several phases in the field of the R&D process, consider a multiple stages game could have an important impact in terms of alliance timing decisions. In particular, signing the alliance at the appropriate R&D stage, and so including other exploration and exploitation phases would have a key impact in contract terms and profits for both companies. In this setting, the Back and Scholes formula is no more applicable as compound options should be considered by adopting the Geske model or numerical approaches. Even if the implementation of the model could result in a more complex computational setting, it is important to provide a complete picture of alliance design and timing decisions.

From a theoretical point of view it could be possible to incorporate additional features to my framework in future studies. In this dissertation I have analysed the alliance timing decisions in a setting where the pharmaceutical company has the bargaining power to offer a take-it-or-leave-it contract to the competing biotech firms and she can terminate the project not exercising the option in case she expects a negative profit (even if the expected value of the R&D project is positive). However, in the real market biotech firms might enjoy some bargaining power (Lerner and Merges, 1998) so a fairer negotiation environment could be considered in future studies. In particular it could be possible developing a Nash bargaining game or including the possibility of re-negotiating the contract terms to encourage the biotech firm in exercising the option.

In addition, I do not consider the possibility that the biotech firm could adopt an opportunistic behaviour leading to the moral hazard problem. Specifically, once signed the agreement, the biotech firm may misuse the payment from the pharmaceutical company for purposes not related to the agreement. Including this possibility is quite interesting and could result in an even greater incentive to postpone the alliance agreement.

Also, I considered the competition between biotech firms. It would also be worthwhile to analyse a setting where also the pharmaceutical companies compete to ally with an innovative biotech firm to investigate whether my implications are robust in such new environment. These extensions could help to build a model, closer to reality, for the design of the alliance timing decisions.

Finally, it could be noteworthy to underline that the alliance timing influences other aspects of the alliances so it could be interesting to expand the approach I have adopted so far, through an empirical analysis. For instance, an interesting further development could consist on analysing the role of the alliance timing as a driver for the biotech firms to signal their own quality. In this case alliance timing could help to explain how different types of signals interact each other. As stated in chapter 2, in R&D alliances adverse selection problems may arise due to the high information asymmetry on the quality of the biotech firms' development projects. In order to mitigate these problems new ventures, i.e. biotech firms, can use many different types of signals to reveal their true quality to outsiders. Two of the main signals that can be sent from the new ventures are the involvement of venture capitalists (VCs) and alliances activity (Katila et al., 2008). I suppose that also the phase of the R&D process in which the alliance is signed could be seen as a signal of the quality of the new venture.

Indeed, on one side, new ventures seek to enter into alliances in early stages because they lack financial resources to develop a drug independently (Nicholson et al., 2005) and, in order to reduce information asymmetry they are forced to give up more control rights (Higgins, 2007, Lerner & Merges, 1998). On the contrary, in case of late stages agreements, new ventures look for manufacturing and marketing resources generally in the hands of established pharmaceutical firms. New ventures can reach higher payment conditions (Nicholson et al., 2005; Rogers et al., 2005) and more control rights (Higgins, 2007). A late agreement signals to the market that the new venture owns not only the

necessary capabilities and know-how but also a strong financial structure that has let her to carry on the research on her own until these late stages. Moreover, having one or more candidate drugs in late stage of the R&D process means that the potential revenue coming from drug commercialization are less uncertain and closer (Ozmel et al., 2013b). My intuition is that timing of the alliances can explain if these two types of signal, i.e. venture capital and alliance, act as substitutes or complements and that it influences the new venture's likelihood of future alliance formations and probability of going public or being acquired.

Appendix A
Optimal pharmaceutical company's payoffs in case of identical biotech firms

A.1 SECOND STAGE – ROA and NPV methodology

In order to sign an agreement in the second stage with B2, the profit of the pharmaceutical company must be positive. Then, his profit maximization problem is:

$$\max\left\{\pi^{P}_{s,B2}(t_1) = \alpha_s \beta\delta V_s - P_s\right\} \quad \text{Eq. (A. 1)}$$

$$\text{s.t. } P_s > (1-\gamma)V_s - (1-\alpha_s)\beta\delta V_s \quad \text{Eq. (A. 2)}$$

$$P_s > 0 \quad \text{Eq. (A. 3)}$$

Note that the minimum value of α_s to ensure positive payments is:

$$\alpha_{s\min} = 1 - \frac{1-\gamma}{\beta\delta}. \quad \text{Eq. (A.4)}$$

Since the profit expression in Eq. (A.1) is linearly decreasing in P_s, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (A.4)) and the optimal payoff, $\pi^{*P}_{s,B2}(t_1)$, is equal to $\pi^{*P}_{s,B2}(t_1) = \beta\delta V_S - (1-\gamma)V_s$. Note that * represents the optimal pharmaceutical company's payoff. This payoff is positive when $\delta > \frac{1-\gamma}{\beta}$ and this condition always holds as $\delta > 1$, $\gamma = 0.5$ and $\beta > \gamma$ by assumption. Moving backward through the tree in Figure 9 reported in section 2.3, I compare $\pi^{*P}_{s,B2}(t_1)$ with the pharmaceutical company's optimal payoff if he allies with B1 in the second stage ($\pi^{*P}_{s,B1}(t_1)$). This maximization problem is:

$$\max\left\{\pi^{P}_{s,B1}(t_1) = \alpha_s \beta\delta V_s - P_s\right\} \quad \text{Eq. (A.5)}$$

$$\text{s.t. } P_s > (1-\beta)\delta V_s - (1-\alpha_s)\beta\delta V_s \quad \text{Eq. (A.6)}$$

$$P_s > (1-\gamma)V_s - (1-\alpha_s)\beta\delta V_s \quad \text{Eq. (A.7)}$$

$$P_s > 0 \quad \text{Eq. (A.8)}$$

Depending on the value of δ, Eq. A.6 is more stringent than Eq. A.7, then two cases arise, that I call low synergies, $\delta < \frac{1-\gamma}{1-\beta}$, and high synergies, $\delta > \frac{1-\gamma}{1-\beta}$, respectively. Indeed, in case of low synergies Eq. (A.7) is more stringent and substituting it in the profit expression I obtain the optimal profit $\pi^{*P}_{s,B1}(t_1) = \beta\delta V_s - (1-\gamma)V_s$. Then, it is straightforward to see that this profit in case of alliance with B1 is identical to the profit when the pharmaceutical company allies with B2. Since B1's profit is higher in case of alliance and the pharmaceutical company is indifferent between the two biotech firms, the sub-game equilibrium for the second stage would be an alliance with B1.

In case of high synergies, the first constraint (Eq. (A.6)) is more stringent and, thus, $\pi^{*P}_{s,B1}(t_1) = \beta\delta V_s - (1-\beta)\delta V_s$. By comparing the two profits $\pi^{*P}_{s,B2}(t_1)$ and $\pi^{*P}_{s,B1}(t_1)$ I obtain $\pi^{*P}_{s,B2}(t_1) > \pi^{*P}_{s,B1}(t_1) \Leftrightarrow (1-\beta)\delta > (1-\gamma)$, which always holds in case of high synergies. Thus, in this case, the sub-game equilibrium for the second stage is an alliance between the pharmaceutical company and B2.

Next, I go back to the first stage decisions and distinguish the two cases of low and high synergies, respectively.

A.2 FIRST STAGE

A.2.1 Low synergies case $\left(\delta < \frac{1-\gamma}{1-\beta}\right)$ – ROA methodology

In the first stage, I compare $\pi^{*P}_{s,B1}(t_0)$ with the pharmaceutical company's optimal payoff if he allies with B2 in the first stage ($\pi^{*P}_{f,B2}(t_0)$), where the latter profit is obtained as a result of the following profit maximization problem:

$$\max\left\{\pi^{P}_{f,B2}(t_0) = \alpha_f \beta\delta V_f N(d_1(C^{B2}_{f,B2})) - P_f\right\} \qquad \text{Eq. (A.9)}$$

$$\text{s.t. } P_{f,B2} > C^{B2}_{s,B1} - C^{B2}_{f,B2} \qquad \text{Eq. (A.10)}$$

$$P_f > 0 \qquad \text{Eq. (A.11)}$$

The minimum value of α_f to ensure positive payments is:

$$\alpha_{f\min} = 1 - \frac{(1-\beta)}{\beta} \qquad \text{Eq. (A.12)}$$

This value is obtained imposing that $C_{s,B1}^{B2} > C_{f,B2}^{B2}$. These are two call options with the same exercise price so I just compare their underlying values (see Table 12 reported in section 3.2.2). Since the profit expression in Eq. (A.9) is linearly decreasing in P_f, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (A.12)) and $\pi_{f,B2}^{*P}(t_0)$ is equal to $\pi_{f,B2}^{*P}(t_0) = \alpha_f \beta\delta V_f N(d_1(C_{f,B2}^{B2})) - (C_{s,B1}^{B2} - C_{f,B2}^{B2})$.

Therefore I compare $\pi_{f,B2}^{*P}(t_0)$ with $\pi_{s,B1}^{*P}(t_1)$ backtracked to the first stage ($\pi_{s,B1}^{*P}(t_0)$). Specifically $\pi_{s,B1}^{*P}(t_0) = (\alpha_s \beta\delta V_f - P_s e^{-rt}) N(d_1(C_{s,B1}^{B1})) = (\beta\delta V_f - (1-\gamma)V_f) N(d_1(C_{s,B1}^{B1}))$.

This comparison is ambiguous, in fact, first I notice that while $\pi_{1,B1}^{*P}(t_0)$ is independent from α_f, $\pi_{f,B2}^{*P}(t_0)$ is decreasing with α_f (the proof is given in the Appendix C). However, even when $\pi_{f,B2}^{*P}(t_0)$ is computed at $\alpha_{f\min}$, thus yielding $\pi_{f,B2}^{*P}(t_0, \alpha_{f\min}) = (\beta\delta V_0 - (1-\beta)\delta V_0) N(d_1(C_{f,B2}^{B2}))$, I cannot unambiguously rank the two profit expressions. Therefore, I distinguish again between two cases: in Case A I suppose that $\pi_{s,B1}^{*P}(t_0) > \pi_{f,B2}^{*P}(t_0)$; in Case B I suppose that $\pi_{s,B1}^{*P}(t_0) < \pi_{f,B2}^{*P}(t_0)$.

A.2.1.1 Case A ($\pi_{s,B1}^{*P}(t_0) > \pi_{f,B2}^{*P}(t_0)$)

In Case A I compare at the same time $t=t_0$, $\pi_{s,B1}^{*P}(t_0)$ with the optimal profit that the pharmaceutical company obtains if he allies with B1 in the first stage ($\pi_{f,B1}^{*P}(t_0)$). The latter maximization problem is:

$$\max\left\{\pi_{f,B1}^{P}(t_0) = \alpha_f \beta\delta V_f N(d_1(C_{f,B1}^{B1})) - P_f\right\} \qquad \text{Eq. (A.13)}$$

$$\text{s.t. } P_f > C_{s,B1}^{B1} - C_{f,B1}^{B1} \qquad \text{Eq. (A.14)}$$

$$P_s > (1-\gamma)V_s - (1-\alpha_s)\beta\delta V_s \qquad \text{Eq. (A.15)}$$

$$P_f > C_{s,B1}^{B2} - C_{f,B2}^{B2} \qquad \text{Eq. (A.16)}$$

$$P_f > 0 \qquad \text{Eq. (A.17)}$$

In order to demonstrate which constraint is more stringent I compare $C_{s,B1}^{B1}$ with $C_{s,B1}^{B2}$ since $C_{f,B1}^{B1}$ and $C_{f,B2}^{B2}$ are identical. $C_{s,B1}^{B1}$ and $C_{s,B1}^{B2}$ are two call options with the same

exercise price, so it suffices to compare the two underlying values and, substituting $P_s e^{-rt}$ in Eq. (A.13), holds $C_{s,B1}^{B1} > C_{s,B1}^{B2} \Leftrightarrow (1-\gamma)V_f > (1-\beta)\delta V_f$, as I are in low synergies case. For $\alpha_s = \alpha_{s\min}$, the minimum value of α_f to ensure positive payments is:

$$\alpha_{f\min} = 1 - \frac{(1-\gamma)}{\beta\delta} \qquad \text{Eq. (A.18)}$$

This value is obtained imposing that $C_{s,B1}^{B1} > C_{f,B1}^{B1}$. These are two call options with the same exercise price so I just compare their underlying values (see Table 12 reported in section 3.2.2).

Since the profit expression in Eq. (A.13) is linearly decreasing in P_f, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (A.18)) and $\pi_{f,B1}^{*P}(t_0)$ is equal to:

$$\pi_{f,B1}^{*P}(t_0) = \alpha_f \beta\delta V_f N(d_1(C_{f,B1}^{B1})) - (C_{s,B1}^{B1} - C_{f,B1}^{B1}) \qquad \text{Eq. (A.19)}$$

Note that when $\pi_{f,B1}^{*P}(t_0)$ is computed at $\alpha_{f\min}$, $\pi_{f,B1}^{*P}(t_0, \alpha_{f\min}) = (\beta\delta V_f - (1-\gamma)V_f)N(d_1(C_{f,B1}^{B1}))$ and thus $\pi_{s,B1}^{*P}(t_0) = \pi_{f,B1}^{*P}(t_0, \alpha_{0\min})$. As $\pi_{s,B1}^{*P}(t_0)$ is independent from α_f while $\pi_{f,B1}^{*P}(t_0)$ is decreasing with α_f (the proof is given in Appendix C), I am sure that **in Case A** $\pi_{s,B1}^{*P}(t_0) > \pi_{f,B1}^{*P}(t_0)$ **the equilibrium for the pharmaceutical company will be an alliance with B1 in the second stage**.

A.2.1.2 Case B ($\pi_{s,B1}^{*P}(t_0) < \pi_{f,B2}^{*P}(t_0)$)

In Case B I compare $\pi_{f,B2}^{*P}(t_0)$ with the optimal profit the pharmaceutical company obtains if he allies with B1 in the first stage ($\pi_{f,B1}^{*P}(t_0)$). The latter maximization problem is:

$$\max\left\{\pi_{f,B1}^{P}(t_0) = \alpha_f \beta\delta V_f N(d_1(C_{f,B1}^{B1})) - P_f\right\} \qquad \text{Eq. (A.20)}$$

$$\text{s.t. } P_f > C_{f,B2}^{B1} - C_{f,B1}^{B1} \qquad \text{Eq. (A.21)}$$

$$P_f > C_{s,B1}^{B2} - C_{f,B2}^{B2} \qquad \text{Eq. (A.22)}$$

$$P_f > 0 \qquad \text{Eq. (A.23)}$$

Since the profit expression in Eq. (A.20) is linearly decreasing in P_f and the two constraints are identical (see Table 12 reported in section 3.2.2), the optimal payment is obtained at the boundary (i.e., satisfying Eq. (A.12)) and $\pi_{f,B1}^{*P}(t_0)$ is equal to

$\pi^{*P}_{f,B1}(t_0) = \alpha_f \beta\delta V_f N(d_1(C^{B1}_{f,B1})) - (C^{B1}_{f,B2} - C^{B1}_{f,B1})$. It is straightforward to see that $\pi^{*P}_{f,B1}(t_0)$ is identical to $\pi^{*P}_{f,B2}(t_0)$, therefore the pharmaceutical company is indifferent between the two biotech firms and B1 will pre-empt the competitor. **In Case B the equilibrium for the pharmaceutical company will be an alliance with B1 in the first stage**.

Therefore Case A and Case B do not arrive to the same solution and their comparison can be done only numerically (the reader can refer to section 3.3).

A.2.2 High synergies case $\left(\delta > \frac{1-\gamma}{1-\beta}\right)$ – ROA methodology

In the first stage, I compare $\pi^{*P}_{s,B2}(t_0)$ with the pharmaceutical company's optimal payoff if he allies with B2 in the first stage ($\pi^{*P}_{f,B2}(t_0)$), where the latter profit is obtained as a result of the following profit maximization problem:

$$\max\left\{\pi^{P}_{f,B2}(t_0) = \alpha_f \beta\delta V_f N(d_1(C^{B2}_{f,B2})) - P_f\right\} \quad \text{Eq. (A.24)}$$

$$\text{s.t. } P_f > C^{B2}_{s,B2} - C^{B2}_{f,B2} \quad \text{Eq. (A.25)}$$

$$P_s > (1-\gamma)V_s - (1-\alpha_s)\beta\delta V_s \quad \text{Eq. (A.26)}$$

$$P_f > 0 \quad \text{Eq. (A.27)}$$

The minimum value of α_f to ensure positive payments is:

$$\alpha_{f\min} = 1 - \frac{1-\gamma}{\beta\delta} \quad \text{Eq. (A.28)}$$

This value is obtained imposing that $P_f > 0$ and $C^{B2}_{s,B2} > C^{B2}_{f,B2}$. These are two call options with the same exercise price so I just compare their underlying values (see Table 12 reported in section 3.2.2). Since the profit expression in Eq. (A.24) is linearly decreasing in P_f, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (A.28)) and $\pi^{*P}_{f,B2}(t_0)$ is equal to $\pi^{*P}_{f,B2}(t_0) = \alpha_f \beta\delta V_f N(d_1(C^{B2}_{f,B2})) - (C^{B2}_{s,B2} - C^{B2}_{f,B2})$. Therefore I compare $\pi^{*P}_{f,B2}(t_0)$ with $\pi^{*P}_{s,B2}(t_1)$ backtracked to the first stage ($\pi^{*P}_{s,B2}(t_0)$).

Specifically $\pi^{*P}_{s,B2}(t_0) = (\alpha_s \beta\delta V_f - P_s e^{-rt}) N(d_1(C^{B2}_{s,B2})) = (\beta\delta V_f - (1-\gamma)V_f) N(d_1(C^{B2}_{s,B2}))$.

Note that when $\pi^{*P}_{f,B2}(t_0)$ is computed at $\alpha_{f\min}$, $\pi^{*P}_{f,B2}(t_0, \alpha_{f\min}) = (\beta\delta V_f - (1-\gamma)V_f) N(d_1(C^{B2}_{f,B2}))$ and thus $\pi^{*P}_{s,B2}(t_0) = \pi^{*P}_{f,B2}(t_0, \alpha_{0\min})$. As $\pi^{*P}_{s,B2}(t_0)$

is independent from α_f while $\pi^{*P}_{f,B2}(t_0)$ is decreasing with α_f (the proof is given in Appendix C), I am sure that $\pi^{*P}_{s,B2}(t_0) > \pi^{*P}_{f,B2}(t_0)$.

Finally I compare $\pi^{*P}_{s,B2}(t_0)$ with the optimal profit in case the pharmaceutical company signs the agreement with B1 in the first stage ($\pi^{*P}_{f,B1}(t_0)$). In particular $\pi^{*P}_{f,B1}(t_0)$ is obtained by the following profit maximization problem:

$$\max\left\{\pi^{P}_{f,B1}(t_0) = \alpha_f \beta \delta V_f N(d_1(C^{B1}_{f,B1})) - P_f\right\} \quad \text{Eq. (A.29)}$$

$$\text{s.t. } P_f > C^{B1}_{s,B2} - C^{B1}_{f,B1} \quad \text{Eq. (A.30)}$$

$$P_s > (1-\gamma)V_s - (1-\alpha_s)\beta\delta V_s \quad \text{Eq. (A.31)}$$

$$P_f > C^{B2}_{s,B2} - C^{B2}_{f,B2} \quad \text{Eq. (A.32)}$$

$$P_f > 0 \quad \text{Eq. (A.33)}$$

In order to demonstrate which constraint is more stringent I compare $C^{B1}_{s,B2}$ with $C^{B2}_{s,B2}$ since $C^{B1}_{f,B1}$ and $C^{B2}_{f,B2}$ are identical. $C^{B1}_{s,B2}$ and $C^{B2}_{s,B2}$ are two call options with the same exercise price, so it suffices to compare the two underlying values and, substituting $P_s e^{-rt}$ in the expressions, holds $C^{B1}_{s,B2} > C^{B2}_{s,B2} \Leftrightarrow (1-\beta)\delta V_f > (1-\gamma)V_f$, as I am in high synergies case.

For $\alpha_s = \alpha_{s\min}$, the minimum value of α_f to ensure positive payments is:

$$\alpha_{f\min} = 1 - \frac{(1-\beta)}{\beta} \quad \text{Eq. (A.34)}$$

This value is obtained imposing that $C^{B1}_{s,B2} > C^{B1}_{f,B1}$. These are two call options with the same exercise price so I just compare their underlying values (see Table 12 reported in section 3.2.2).

Since the profit expression in Eq. (A.29) is linearly decreasing in P_f, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (A.34)) and $\pi^{*P}_{f,B1}(t_0)$ is equal to:

$$\pi^{*P}_{f,B1}(t_0) = \alpha_f \beta \delta V_f N(d_1(C^{B1}_{f,B1})) - (C^{B1}_{s,B2} - C^{B1}_{f,B1}) \quad \text{Eq. (A.35)}$$

The comparison between $\pi^{*P}_{s,B2}(t_0)$ and $\pi^{*P}_{f,B1}(t_0)$ is ambiguous, in fact, first I notice that while $\pi^{*P}_{s,B2}(t_0)$ is independent from α_f, $\pi^{*P}_{f,B1}(t_0)$ is decreasing with α_f (the proof is given in Appendix C). However, even when $\pi^{*P}_{f,B1}(t_0)$ is computed at $\alpha_{f\min}$, thus

yielding $\pi^{*P}_{f,B1}(t_0,\alpha_{f\min}) = (\beta\delta V_0 - (1-\beta)\delta V_0)N(d_1(C^{B1}_{f,B1}))$, I cannot unambiguously rank the two profit expressions.

However, comparing $\pi^{*P}_{f,B1}(t_0)$ with $\pi^{*P}_{f,B2}(t_0)$, I notice that $N(d_1(C^{B1}_{f,B1}) = N(d_1(C^{B2}_{f,B2})$ and $C^{B1}_{f,B1} = C^{B2}_{f,B2}$ in case of identical biotech firms, therefore $\pi^{*P}_{f,B2}(t_0) > \pi^{*P}_{f,B1}(t_0) \Leftrightarrow C^{B2}_{s,B2} < C^{B1}_{f,B2}$ as I am in high synergies case. Since holds $\pi^{*P}_{s,B2}(t_0) > \pi^{*P}_{f,B2}(t_0) > \pi^{*P}_{f,B1}(t_0)$ I conclude that **the optimal solution, under ROA methodology, for the pharmaceutical company in high synergies case is an alliance with B2 in the second stage**.

A.2.3 Low synergies case $\left(\delta < \frac{1-\gamma}{1-\beta}\right)$ – NPV methodology

In the first stage, I compare $\pi^{*P}_{s,B1}(t_0)$ with the pharmaceutical company's optimal payoff if he allies with B2 in the first stage ($\pi^{*P}_{f,B2}(t_0)$), where the latter profit is obtained as a result of the following profit maximization problem:

$$\max\left\{\pi^{P}_{f,B2}(t_0) = \alpha_f\beta\delta V_f - P_f\right\} \qquad \text{Eq. (A.36)}$$

$$\text{s.t. } P_f > (1-\beta)\delta V_f - (1-\alpha_f)\beta\delta V_f \qquad \text{Eq. (A.37)}$$

$$P_f > 0 \qquad \text{Eq. (A.38)}$$

In this case the minimum value of α_f to ensure positive payments is:

$$\alpha_{f\min} = 1 - \frac{1-\beta}{\beta}. \qquad \text{Eq. (A.39)}$$

Since the profit expression in Eq. (A.36) is linearly decreasing in P_f, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (A.39)) and $\pi^{*P}_{f,B2}(t_0)$ is equal to $\pi^{*P}_{f,B2}(t_0) = \beta\delta V_f - (1-\beta)\delta V_f$. Comparing the two profits I have $\pi^{*P}_{f,B2}(t_0) > \pi^{*P}_{s,B1}(t_0) \Leftrightarrow (1-\gamma) > (1-\beta)\delta$, which always holds in case of low synergies.

Finally I compare the pharmaceutical company's profit if he chooses to establish the alliance in the first stage with B1 ($\pi^{*P}_{f,B1}(t_0)$) with $\pi^{*P}_{f,B2}(t_0)$. In particular $\pi^{*P}_{f,B1}(t_0)$ is obtained by the following profit maximization problem:

$$\max\left\{\pi^{*P}_{f,B1}(t_0) = \alpha_f\beta\delta V_f - P_f\right\} \qquad \text{Eq. (A.40)}$$

$$\text{s.t. } P_f > (1-\beta)\delta V_f - (1-\alpha_f)\beta\delta V_f \qquad \text{Eq. (A.41)}$$

$$P_f > (1-\beta)\delta V_f - (1-\alpha_f)\beta\delta V_f \quad \text{Eq. (A.42)}$$

$$P_f > 0 \quad \text{Eq. (A.43)}$$

Since the profit expression in Eq. (A.40) is linearly decreasing in P_f and the first two constraints are identical, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (A.39)) and $\pi^{*P}_{f,B1}(t_0)$ is equal to $\pi^{*P}_{f,B1}(t_0) = \beta\delta V_f - (1-\beta)\delta V_f$. In low synergies case, also in the first stage the pharmaceutical company obtains the same profit from the two biotech firms and B1 decides to do pre-emption. Therefore **the optimal solution, under the NPV methodology, for the pharmaceutical company in low synergies case is an alliance with B1 in the first stage**.

A.2.4 High synergies case $\left(\delta > \frac{1-\gamma}{1-\beta}\right)$ – NPV methodology

In the first stage, I compare $\pi^{*P}_{s,B2}(t_0)$ with the pharmaceutical company's optimal payoff if he allies with B2 in the first stage ($\pi^{*P}_{f,B2}(t_0)$), where the latter profit is obtained as a result of the following profit maximization problem:

$$\max\left\{\pi^{P}_{f,B2}(t_0) = \alpha_f\beta\delta V_f - P_f\right\} \quad \text{Eq. (A.44)}$$

$$\text{s.t. } P_f > (1-\alpha_s)\beta\delta V_f + P_s e^{-rt} - (1-\alpha_f)\beta\delta V_f \quad \text{Eq. (A.45)}$$

$$P_s > (1-\gamma)V_s - (1-\alpha_s)\beta\delta V_s \quad \text{Eq. (A.46)}$$

$$P_f > 0 \quad \text{Eq. (A.47)}$$

In this case the minimum value of α_f to ensure positive payments is:

$$\alpha_{f\min} = 1 - \frac{1-\gamma}{\beta\delta}. \quad \text{Eq. (A.48)}$$

Since the profit expression in Eq. (A.44) is linearly decreasing in P_f, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (A.48)) and $\pi^{*P}_{f,B2}(t_0)$ is equal to $\pi^{*P}_{f,B2}(t_0) = \beta\delta V_0 - (1-\gamma)V_0$. Comparing $\pi^{*P}_{s,B2}(t_0)$ and $\pi^{*P}_{f,B2}(t_0)$, the two profits are identical, so the pharmaceutical company is indifferent on which stage to choose.

Finally I compare the optimal profit obtained in case of alliance with B2 with $\pi^{*P}_{f,B1}(t_0)$ (pharmaceutical company's optimal payoff if he allies with B1 in the first stage). In particular $\pi^{*P}_{f,B1}(t_0)$ is obtained by the following profit maximization problem:

$$\max\left\{\pi^{P}_{f,B1}(t_0) = \alpha_f \beta\delta V_f - P_f\right\} \quad \text{Eq. (A.49)}$$

$$\text{s.t. } P_f > (1-\alpha_s)\beta\delta V_f + P_s(t_0) - (1-\alpha_f)\beta\delta V_f \quad \text{Eq. (A.50)}$$

$$P_s > (1-\gamma)V_s - (1-\alpha_s)\beta\delta V_s) \quad \text{Eq. (A.51)}$$

$$P_f > (1-\beta)\delta V_f - (1-\alpha_f)\beta\delta V_f \quad \text{Eq. (A.52)}$$

$$P_f > 0 \quad \text{Eq. (A.53)}$$

Since I am in high synergies case, Eq. (A.51) is more stringent than the other constraints and, thus, $\pi^{*P}_{f,B1}(t_0)$ is $\pi^{*P}_{f,B1}(t_0) = \beta\delta V_f - (1-\beta)\delta V_f$.

Comparing the two payoffs always holds $\beta\delta V_f - (1-\gamma)V_f > \beta\delta V_f - (1-\beta)\delta V_f$ as I am in high synergies case. Therefore **the optimal solution, under the NPV methodology, for the pharmaceutical company in high synergies case is an alliance with B2, but he is indifferent about the timing because he gets the same profit in each of the two stages**.

Appendix B
Optimal pharmaceutical company's profit in case of non-identical biotech firms

B.1 SECOND STAGE – ROA and NPV methodology

In order to sign an agreement in the second stage with B2, the profit of the pharmaceutical company must be positive. Then, his profit maximization problem is:

$$\max\left\{\pi^{P}_{s,B2}(t_1) = \alpha_s \beta \delta_{B2} V_s - P_{s,B2}\right\} \quad \text{Eq. (B.1)}$$

$$\text{s.t. } P_{s,B2} > (1-\gamma)V_s - (1-\alpha_s)\beta\delta_{B2}V_s \quad \text{Eq. (B.2)}$$

$$P_{s,B2} > 0 \quad \text{Eq. (B.3)}$$

Note that the minimum value of α_s to ensure positive payments is:

$$\alpha_{s\min} = 1 - \frac{(1-\gamma)}{\beta\delta_{B2}}. \quad \text{Eq. (B.4)}$$

Since the profit expression in Eq. (B.1) is linearly decreasing in $P_{s,B2}$, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (B.4)) and the optimal profit, $\pi^{*P}_{s,B2}(t_1)$, is equal to $\pi^{*P}_{s,B2}(t_1) = \beta\delta_{B2}V_s - (1-\gamma)V_s$.

This payoff is positive when $\delta_{B2} > \frac{1-\gamma}{\beta}$ and this condition always holds as $\delta_{B2} > 1$, $\gamma = 0.5$ and $\beta > \gamma$ by assumption. Moving backward through the tree in Figure 9 reported in section 2.3, I compare $\pi^{*P}_{s,B2}(t_1)$ with the pharmaceutical company's optimal payoff if he allies with B1 in the second stage ($\pi^{*P}_{s,B1}(t_1)$). This maximization problem is:

$$\max\left\{\pi^{P}_{s,B1}(t_1) = \alpha_s \beta \delta_{B1} V_s - P_{s,B1}\right\} \quad \text{Eq. (B.5)}$$

$$\text{s.t. } P_{s,B1} > (1-\beta)\delta_{B2}V_s - (1-\alpha_s)\beta\delta_{B1}V_s \quad \text{Eq. (B.6)}$$

$$P_{s,B1} > 0 \quad \text{Eq. (B.7)}$$

Therefore $\pi^{*P}_{s,B1}(t_1) = \beta\delta_{B1}V_s - (1-\beta)\delta_{B2}V_s$ as the minimum value of α_s to ensure positive payments is $\alpha_{s\min} = 1 - \frac{(1-\beta)\delta_{B2}}{\beta\delta_{B1}}$. Then, two cases arise:

In Case 1, which corresponds to δ_{B1} high in chapter 3, the second stage equilibrium yields an alliance with B1 if and only if $\pi^{*P}_{s,B1}(t_1) > \pi^{*P}_{s,B2}(t_1)$, which holds if and only if $\delta_{B1} > (\delta_{B2} - (1-\gamma))/\beta$. Otherwise, if $\delta_{B1} < (\delta_{B2} - (1-\gamma))/\beta$ the second stage equilibrium yields an alliance with B2, I refer to this case as Case 2, which corresponds to δ_{B1} low in chapter 3. Next, I go back to first stage decisions and therefore the ROA methodology and the NPV methodology require a different discussion.

B.2 FIRST STAGE

B.2.1 Case 1 (δ_{B1} high) – ROA methodology

The maximization problem for the pharmaceutical company in case of alliance with B2 in the first stage under ROA methodology is:

$$\max\left\{\pi^{P}_{f,B2}(t_0) = \alpha_f \beta \delta_{B2} V_f N(d_1(C^{B2}_{f,B2})) - P_{f,B2}\right\} \quad \text{Eq. (B.8)}$$

$$\text{s.t. } P_{f,B2} > C^{B2}_{s,B1} - C^{B2}_{f,B2} \quad \text{Eq. (B.9)}$$

$$P_{f,B2} > 0 \quad \text{Eq. (B.10)}$$

The minimum value of α_f to ensure positive payments is:

$$\alpha_{f\min} = 1 - \frac{(1-\beta)\delta_{B1}}{\beta \delta_{B2}} \quad \text{Eq. (B.11)}$$

This value is obtained imposing that $C^{B2}_{s,B1} > C^{B2}_{f,B2}$. These are two call options with the same exercise price so I just compare their underlying values (see Table 12 reported in section 3.2.2). Since the profit expression in Eq. (B.8) is linearly decreasing in $P_{f,B2}$, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (B.11)) and the optimal profit, $\pi^{*P}_{f,B2}(t_0)$, is equal to:

$$\pi^{*P}_{f,B2}(t_0) = \alpha_f \beta \delta_{B2} V_f N(d_1(C^{B2}_{f,B2})) - (C^{B2}_{s,B1} - C^{B2}_{f,B2}) \quad \text{Eq. (B.12)}$$

Therefore I compare $\pi^{*P}_{f,B2}(t_0)$ with $\pi^{*P}_{s,B1}(t_1)$ backtracked to the first stage ($\pi^{*P}_{s,B1}(t_0)$). Specifically $\pi^{*P}_{s,B1}(t_0) = (\alpha_s \beta \delta_{B1} V_f - P_{s,B1} e^{-rt}) N(d_1(C^{B1}_{s,B1})) = (\beta \delta_{B1} V_f - (1-\beta)\delta_{B2} V_f) N(d_1(C^{B1}_{s,B1}))$.

This comparison is ambiguous, in fact, first I notice that while $\pi^{*P}_{s,B1}(t_0)$ is independent from α_f, $\pi^{*P}_{f,B2}(t_0)$ decreases with α_f (the proof is given in Appendix C). However,

even when $\pi^{*P}_{f,B2}(t_0)$ is computed at $\alpha_{f\min}$, thus yielding $\pi^{*P}_{f,B2}(t_0,\alpha_{f\min}) = (\beta\delta_{B2}V_f - (1-\beta)\delta_{B1}V_f)N(d_1(C^{B2}_{f,B2}))$, I cannot unambiguously rank the two profit expressions because, depending on the values of parameters δ_{B1} and δ_{B2}, either profit can be higher.

Therefore, I distinguish between two cases: in Case A I suppose that $\pi^{*P}_{s,B1}(t_0) > \pi^{*P}_{f,B2}(t_0)$; in Case B I suppose that $\pi^{*P}_{s,B1}(t_0) < \pi^{*P}_{f,B2}(t_0)$.

B.2.1.1 Case A ($\pi^{*P}_{s,B1}(t_0) > \pi^{*P}_{f,B2}(t_0)$)

In Case A I compare $\pi^{*P}_{s,B1}(t_0)$ with the optimal profit that the pharmaceutical company obtains if he allies with B1 in the first stage ($\pi^{*P}_{f,B1}(t_0)$). The latter maximization problem is:

$$\max\left\{\pi^{P}_{f,B1}(t_0) = \alpha_f\beta\delta_{B1}V_f N(d_1(C^{B1}_{f,B1})) - P_{f,B1}\right\} \quad \text{Eq. (B.13)}$$

$$\text{s.t. } P_{f,B1} > C^{B1}_{s,B1} - C^{B1}_{f,B1} \quad \text{Eq. (B.14)}$$

$$P_{s,B1} > (1-\beta)\delta_{B2}V_s - (1-\alpha_s)\beta\delta_{B1}V_s \quad \text{Eq. (B.15)}$$

$$P_{f,B1} > 0 \quad \text{Eq. (B.16)}$$

For $\alpha_s = \alpha_{s\min}$, the minimum value of α_f to ensure positive payments is:

$$\alpha_{f\min} = 1 - \frac{(1-\beta)\delta_{B2}}{\beta\delta_{B1}} \quad \text{Eq. (B.17)}$$

This value is obtained imposing that $P_{s,B1} > 0$ and $C^{B1}_{s,B1} > C^{B1}_{f,B1}$. These are two call options with the same exercise price so I just compare their underlying values (see Table 12 reported in section 3.2.2).

Since the profit expression in Eq. (B.13) is linearly decreasing in $P_{f,B1}$, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (B.17)) and $\pi^{*P}_{f,B1}(t_0)$ is equal to:

$$\pi^{*P}_{f,B1}(t_0) = \alpha_f\beta\delta_{B1}V_f N(d_1(C^{B1}_{f,B1})) - (C^{B1}_{s,B1} - C^{B1}_{f,B1}) \quad \text{Eq. (B.18)}$$

Note that when $\pi^{*P}_{f,B1}(t_0)$ is computed at $\alpha_{f\min}$, $\pi^{*P}_{f,B1}(t_0,\alpha_{f\min}) = (\beta\delta_{B1}V_f - (1-\beta)\delta_{B2}V_f)N(d_1(C^{B1}_{f,B1}))$ and thus $\pi^{*P}_{s,B1}(t_0) = \pi^{*P}_{f,B1}(t_0,\alpha_{f\min})$. As $\pi^{*P}_{s,B1}(t_0)$ is independent from α_f while $\pi^{*P}_{f,B1}(t_0)$ is decreasing with α_f (the proof is given

in Appendix C), in Case A the optimal solution for the pharmaceutical company is an alliance with B1 in the second stage.

B.2.1.2 Case B ($\pi^{*P}_{s,B1}(t_0) < \pi^{*P}_{f,B2}(t_0)$)

In Case B I compare $\pi^{*P}_{f,B2}(t_0)$ with the optimal profit that the pharmaceutical company obtains if he allies with B1 in the first stage ($\pi^{*P}_{f,B1}(t_0)$). The latter maximization problem is:

$$\max\left\{\pi^{P}_{f,B1}(t_0) = \alpha_f \beta \delta_{B1} V_f N(d_1(C^{B1}_{f,B1})) - P_{f,B1}\right\} \quad \text{Eq. (B.19)}$$

$$\text{s.t. } P_{f,B1} > C^{B1}_{f,B2} - C^{B1}_{f,B1} \quad \text{Eq. (B.20)}$$

$$P_{f,B1} > 0 \quad \text{Eq. (B.21)}$$

The minimum value of α_f to ensure positive payments is:

$$\alpha_{f\min} = 1 - \frac{(1-\beta)\delta_{B2}}{\beta \delta_{B1}} \quad \text{Eq. (B.22)}$$

This value is obtained imposing that $C^{B1}_{f,B2} > C^{B1}_{f,B1}$. These are two call options with the same exercise price so I just compare their underlying values (see Table 12 reported in section 3.2.2). Since the profit expression in Eq. (B.19) is linearly decreasing in $P_{f,B1}$, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (B.22)) and $\pi^{*P}_{f,B1}(t_0)$ is equal to $\pi^{*P}_{f,B1}(t_0) = \alpha_f \beta \delta_{B1} V_f N(d_1(C^{B1}_{f,B1})) - (C^{B1}_{f,B2} - C^{B1}_{f,B1})$.

Comparing the two profits always holds $\pi^{*P}_{f,B1}(t_0) > \pi^{*P}_{f,B2}(t_0)$ as $\delta_{B1} > \delta_{B2}$ by assumption. Therefore in Case B the optimal solution for the pharmaceutical company will be an alliance with B1 in the first stage.

I notice that in Case A holds $\pi^{*P}_{s,B1}(t_0) > \pi^{*P}_{f,B1}(t_0)$ while in Case B holds $\pi^{*P}_{f,B1}(t_0) > \pi^{*P}_{f,B2}(t_0)$, therefore I can conclude that $\pi^{*P}_{f,B2}(t_0) < \pi^{*P}_{f,B1}(t_0) < \pi^{*P}_{s,B1}(t_0)$ and Case A dominates Case B.

The optimal solution, under ROA methodology, for the pharmaceutical company in Case 1 is an alliance with B1 in the second stage.

B.2.2 Case 2 (δ_{B1} low) – ROA methodology

The maximization problem for the pharmaceutical company in case of alliance with B2 in the first stage under ROA methodology is:

$$\max\left\{\pi^{P}_{f,B2}(t_0)=\alpha_f\beta\delta_{B2}V_f N(d_1(C^{B2}_{f,B2}))-P_{f,B2}\right\} \quad \text{Eq. (B.23)}$$

$$\text{s.t. } P_{f,B2}>C^{B2}_{f,B2}-C^{B2}_{f,B2} \quad \text{Eq. (B.24)}$$

$$P_{s,B2}>(1-\gamma)V_s-(1-\alpha_s)\beta\delta_{B2}V_s \quad \text{Eq. (B.25)}$$

$$P_{f,B2}>0 \quad \text{Eq. (B.26)}$$

For $\alpha_s=\alpha_{s\min}$, in order to get positive payments I impose that $C^{B2}_{s,B2}>C^{B2}_{f,B2}$. These two call options have the same exercise price (see Table 12 reported in section 3.2.2) so I just compare their underlying values and the minimum value of α_f to ensure positive payments is:

$$\alpha_{f\min}=1-\frac{(1-\gamma)}{\beta\delta_{B2}}. \quad \text{Eq. (B.27)}$$

Since the profit expression in Eq. (B.23) is linearly decreasing in $P_{f,B2}$, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (B.27)) and $\pi^{*P}_{f,B2}(t_0)$ is equal to $\pi^{*P}_{f,B2}(t_0)=\alpha_f\beta\delta_{B2}V_f N(d_1(C^{B2}_{f,B2}))-(C^{B2}_{s,B2}-C^{B2}_{f,B2})$.

Therefore I compare $\pi^{*P}_{f,B2}(t_0)$ with $\pi^{*P}_{s,B2}(t_1)$ backtracked to the first stage ($\pi^{*P}_{s,B2}(t_0)$). Specifically, $\pi^{*P}_{s,B2}(t_0)=(\alpha_s\beta\delta_{B2}V_f-P_{s,B2}e^{-rt})N(d_1(C^{B2}_{s,B2}))=(\beta\delta_{B2}V_f-(1-\gamma)V_f)N(d_1(C^{B2}_{s,B2}))$.

Note that when $\pi^{*P}_{f,B2}(t_0)$ is computed at $\alpha_{f\min}$, $\pi^{*P}_{f,B2}(t_0,\alpha_{f\min})=(\beta\delta_{B2}V_f-(1-\gamma)V_f)N(d_1(C^{B2}_{f,B2}))$ and thus $\pi^{*P}_{s,B2}(t_0)=\pi^{*P}_{f,B2}(\alpha_{f\min},t_0)$. As $\pi^{*P}_{s,B2}(t_0)$ is independent from α_f while $\pi^{*P}_{f,B2}(t_0)$ is decreasing with α_f (the proof is given in Appendix C), thus is always verified that $\pi^{*P}_{s,B2}(t_0)>\pi^{*P}_{f,B2}(t_0)$.

Finally I compare $\pi^{*P}_{s,B2}(t_0)$ with the optimal profit that the pharmaceutical company obtains if he allies with B1 in the first stage ($\pi^{*P}_{f,B1}(t_0)$). This maximization problem is:

$$\max\left\{\pi^{P}_{f,B1}(t_0)=\alpha_f\beta\delta_{B1}V_f N(d_1(C^{B1}_{f,B1}))-P_{f,B1}\right\} \quad \text{Eq. (B.28)}$$

$$\text{s.t. } P_{f,B1}>C^{B1}_{f,B2}-C^{B1}_{f,B1} \quad \text{Eq. (B.29)}$$

$$P_{f,B1}>0 \quad \text{Eq. (B.30)}$$

The minimum value of α_f to ensure positive payments is:

$$\alpha_{f\min} = 1 - \frac{(1-\beta)\delta_{B2}}{\beta\delta_{B1}} \qquad \text{Eq. (B.31)}$$

This value is obtained imposing that $C_{f,B2}^{B1} > C_{f,B1}^{B1}$. These are two call options with the same exercise price so I just compare their underlying values (see Table 12 reported in section 3.2.2). Since the profit expression in Eq. (B.28) is linearly decreasing in $P_{f,B1}$, the optimal payment is obtained at the boundary (i.e., satisfying Eq. (B.31)) and $\pi_{f,B1}^{*P}(t_0)$ is equal to $\pi_{f,B1}^{*P}(t_0) = \alpha_f \beta\delta_{B1} V_f N(d_1(C_{f,B1}^{B1})) - (C_{f,B2}^{B1} - C_{f,B1}^{B1})$.

The last comparison between $\pi_{s,B2}^{*P}(t_0)$ and $\pi_{f,B1}^{*P}(t_0)$ is ambiguous, in fact, first I notice that while $\pi_{s,B2}^{*P}(t_0)$ is independent from α_f, $\pi_{f,B1}^{*P}(t_0)$ decreases with α_f (the proof is is given in Appendix C). However, even when $\pi_{f,B1}^{*P}(t_0)$ is computed at $\alpha_{f\min}$, thus yielding $\pi_{f,B1}^{*P}(t_0) = (\beta\delta_{B1} V_f - (1-\beta)\delta_{B2} V_f) N(d_1(C_{f,B1}^{B1}))$, I cannot unambiguously rank the two profit expressions. Therefore, their comparison can be done only numerically (the reader can refer to section 3.4).

B.2.3 Case 1 – NPV methodology

In the first stage, I compare $\pi_{s,B1}^{*P}(t_0)$ with the pharmaceutical company's optimal payoff if he allies with B2 in the first stage ($\pi_{f,B2}^{*P}(t_0)$), where the latter profit is obtained as a result of the following profit maximization problem:

$$\max\left\{\pi_{f,B2}^{P}(t_0) = \alpha_f \beta\delta_{B2} V_f - P_{f,B2}\right\} \qquad \text{Eq. (B.32)}$$

$$\text{s.t. } P_{f,B2} > (1-\beta)\delta_{B1} V_f - (1-\alpha_f)\beta\delta_{B2} V_f \qquad \text{Eq. (B.33)}$$

$$P_{f,B2} > 0 \qquad \text{Eq. (B.34)}$$

Therefore $\pi_{f,B2}^{*P}(t_0) = \beta\delta_{B2} V_f - (1-\beta)\delta_{B1} V_f$ as the minimum value of α_f to ensure positive payments is $\alpha_{f\min} = 1 - \frac{(1-\beta)\delta_{B1}}{\beta\delta_{B2}}$. Comparing $\pi_{f,B2}^{*P}(t_0)$ with $\pi_{s,B1}^{*P}(t_0)$ holds $\pi_{s,B1}^{*P}(t_0) > \pi_{f,B2}^{*P}(t_0) \Leftrightarrow \delta_{B1} > \delta_{B2}$ and this condition always holds by assumption. Finally I compare the pharmaceutical company's profit if he chooses to establish the alliance in the first stage with B1 $\pi_{f,B1}^{*P}(t_0)$ with $\pi_{s,B1}^{*P}(t_0)$. In particular $\pi_{f,B1}^{*P}(t_0)$ is obtained by the following profit maximization problem:

$$\max\left\{\pi^{P}_{f,B1}(t_0) = \alpha_f \beta \delta_{B1} V_f - P_{f,B1}\right\} \quad \text{Eq. (B.35)}$$

$$\text{s.t. } P_{f,B1} > (1-\alpha_s)\beta\delta_{B1}V_f + P_{s,B1}e^{-rt} - (1-\alpha_f)\beta\delta_{B1}V_f \quad \text{Eq. (B.36)}$$

$$P_{s,B1} > (1-\beta)\delta_{B2}V_s - (1-\alpha_s)\beta\delta_{B1}V_s \quad \text{Eq. (B.37)}$$

$$P_{f,B1} > 0 \quad \text{Eq. (B.38)}$$

Therefore $\pi^{P}_{f,B1}(t_0) = \beta\delta_{B1}V_f - (1-\beta)\delta_{B2}V_f$ as the minimum value of α_f to ensure positive payments is $\alpha_{f\min} = 1 - \frac{(1-\beta)\delta_{B2}}{\beta\delta_{B1}}$. Then, it is straightforward to see that this profit in case of alliance with B1 in the first stage is identical to the profit when the pharmaceutical company allies with B1 in the second stage. Therefore **the optimal solution, under NPV methodology, for the pharmaceutical company in Case 1 is an alliance with B1 and he obtains the same profit in each of the two stages**.

B.2.4 Case 2 – NPV methodology

In the first stage, I compare $\pi^{*P}_{s,B2}(t_0)$ with the pharmaceutical company's optimal payoff if he allies with B2 in the first stage ($\pi^{*P}_{f,B2}(t_0)$), where the latter profit is obtained as a result of the following profit maximization problem:

$$\max\left\{\pi^{P}_{f,B2}(t_0) = \alpha_f \beta \delta_{B2} V_f - P_{f,B2}\right\} \quad \text{Eq. (B.39)}$$

$$\text{s.t. } P_{f,B2} > (1-\alpha_s)\beta\delta_{B2}V_f + P_{s,B2}e^{-rt} - (1-\alpha_f)\beta\delta_{B2}V_f \quad \text{Eq. (B.40)}$$

$$P_{s,B2} > (1-\gamma)V_s - (1-\alpha_s)\beta\delta_{B2}V_s \quad \text{Eq. (B.41)}$$

$$P_{f,B2} > 0 \quad \text{Eq. (B.42)}$$

Therefore $\pi^{*P}_{f,B2}(t_0) = \beta\delta_{B2}V_f - (1-\gamma)V_f$ as the minimum value of α_f to ensure positive payments is $\alpha_{f\min} = 1 - \frac{1-\gamma}{\beta\delta_{B2}}$. Comparing $\pi^{*P}_{f,B2}(t_0)$ with $\pi^{*P}_{s,B2}(t_0)$ it is straightforward to see that the two profits are identical, so the pharmaceutical company is indifferent on which stage to choose. Finally I compare the optimal profit obtained in case of alliance with B2 with $\pi^{*P}_{f,B1}(t_0)$ (pharmaceutical company's optimal payoff if he allies with B1 in the first stage). In particular $\pi^{*P}_{f,B1}(t_0)$ is obtained by the following profit maximization problem:

$$\max\left\{\pi^{P}_{f,B1}(t_0) = \alpha_f \beta \delta_{B1} V_f - P_{f,B1}\right\} \quad \text{Eq. (B.43)}$$

s.t. $P_{f,B1} > (1-\beta)\delta_{B2}V_f - (1-\alpha_f)\beta\delta_{B1}V_f$ Eq. (B.44)

$P_{f,B1} > 0$ Eq. (B.45)

Therefore $\pi^{*P}_{f,B1}(t_0) = \beta\delta_{B1}V_f - (1-\beta)\delta_{B2}V_f$ as the minimum value of α_f to ensure positive payments is $\alpha_{f\min} = 1 - \frac{(1-\beta)\delta_{B2}}{\beta\delta_{B1}}$. Comparing the optimal profit obtained in case of alliance with B2 with $\pi^{*P}_{f,B1}(t_0)$ holds $\pi^{*P}_{f,B1}(t_0) < \pi^{*P}_{s,B2}(t_0) = \pi^{*P}_{f,B2}(t_0) \Leftrightarrow \beta\delta_{B1} < \delta_{B2} - (1-\gamma)$ and this condition is always satisfied in Case 2. Therefore **the optimal solution, under NPV methodology, for the pharmaceutical company in Case 2 is an alliance with B2 and he obtains the same profit in each of the two stages**.

Appendix C

In this appendix I prove that, in case of high synergies and identical biotech firms (see Appendix A), $\pi^{*P}_{f,B2}(t_0)$ decreases as α_f increases, i.e. $\frac{\partial \pi^{*P}_{f,B2}(t_0)}{\partial \alpha_f} < 0$.

As stated in Appendix A, since B1 and B2 are identical (i.e. $\delta_{B1} = \delta_{B2} = \delta > 1$), this payoff is equal to: $\pi^{*P}_{f,B2}(t_0) = \alpha_f \beta \delta V_f N(d_1(C^{B2}_{f,B2})) - (C^{B2}_{s,B2} - C^{B2}_{f,B2})$. To better understand my proof I need to rewrite this $\pi^{*P}_{f,B2}(t_0)$ expression.

For the sake of tractability I express $C^{B2}_{f,B2}$ as:

$$C^{B2}_{f,B2} = S^{B2}_{f,B2} N(d_1(S^{B2}_{f,B2}; X^{B2}_{f,B2})) - e^{-r\tau} X^{B2}_{f,B2} N(d_2(S^{B2}_{f,B2}; X^{B2}_{f,B2})) = \\ = ((1-\alpha_f)\beta\delta_{B2} V_f) N(d_1((1-\alpha_f)\beta\delta_{B2} V_f; I_s)) - e^{-r\tau} I_s N(d_2((1-\alpha_f)\beta\delta_{B2} V_f; I_s)) \quad \text{Eq. (C.1)}$$

Where $S^{B2}_{f,B2}$ and $X^{B2}_{f,B2}$ represent underlying and exercise price of the related option $C^{B2}_{f,B2}$ and assume values equal to $(1-\alpha_f)\beta\delta_{B2} V_f$ and I_s, respectively (see Table 12 in section 3.2.2 for the values).

I can also express $C^{B2}_{s,B2}$ as:

$$C^{B2}_{s,B2} = S^{B2}_{s,B2} N(d_1(S^{B2}_{s,B2}; X^{B2}_{s,B2})) - e^{-r\tau} X^{B2}_{s,B2} N(d_2(S^{B2}_{s,B2}; X^{B2}_{s,B2})) = \\ = ((1-\alpha_s)\beta\delta_{B2} V_f + P_{s,B2} e^{-r\tau}) N(d_1((1-\alpha_s)\beta\delta_{B2} V_f + P_{s,B2} e^{-r\tau}; I_s) - \\ - e^{-r\tau} I_s N(d_2((1-\alpha_s)\beta\delta_{B2} V_f + P_{s,B2} e^{-r\tau}; I_s)) \quad \text{Eq. (C.2)}$$

Where $S^{B2}_{s,B2}$ and $X^{B2}_{s,B2}$ represent underlying and exercise price of the related option $C^{B2}_{s,B2}$ and assume values equal to $(1-\alpha_s)\beta\delta_{B2} V_f + P_{s,B2} e^{-r\tau}$ and I_s respectively (see Table 12 in section 3.2.2 for the values). In particular, being $P_{s,B2} e^{-r\tau} = (1-\gamma)V_f - (1-\alpha_s)\beta\delta V_f$ (as I have derived in Eq. (A.26) in Appendix A), substituting $P_{s,B2} e^{-r\tau}$ in $S^{B2}_{s,B2}$ expression I obtain $\overline{S}^{B2}_{s,B2} = (1-\gamma)V_f$.

For the sake of clarity, in the following I will indicate:

$$N(d_1(C^{B2}_{f,B2})) = N(d^{B2}_{1f,B2}) \quad \text{Eq. (C.3)}$$

$$N(d_2(C^{B2}_{f,B2})) = N(d^{B2}_{2f,B2}) \quad \text{Eq. (C.4)}$$

$$N(d_1(C^{B2}_{s,B2})) = N(\overline{d}^{B2}_{1s,B2}) \quad \text{Eq. (C.5)}$$

$$N(d_2(C_{s,B2}^{B2})) = N(\bar{d}_{2s,B2}^{B2}) \qquad \text{Eq. (C.6)}$$

Where $S_{f,B2}^{B2}$, $X_{f,B2}^{B2}$, $\bar{S}_{s,B2}^{B2}$ and $X_{s,B2}^{B2}$ have the same meaning as before (for $N(d_1)$ and $N(d_2)$ expressions the reader can refer to equation (8) and equation (9) in section 1.1.2). It is helpful to notice that Eq. (C.5) and Eq. (C.6) are independent of α_f.

Therefore, I can also write $\pi_{f,B2}^{*P}(t_0)$ as:

$$\pi_{f,B2}^{*P}(t_0) = \beta\delta V_f N(d_{1f,B2}^{B2}) - e^{-r\tau} I_s N(d_{2f,B2}^{B2}) - (1-\gamma) V_f N(\bar{d}_{1s,B2}^{B2}) + e^{-r\tau} I_s N(\bar{d}_{2s,B2}^{B2}) \qquad \text{Eq. (C.7)}$$

It follows that proving $\frac{\partial \pi_{f,B2}^{*P}(t_0)}{\partial \alpha_f} < 0$, means proving that:

$$\frac{\partial(\beta\delta V_f N(d_{1f,B2}^{B2}) - e^{-r\tau} I_s N(d_{2f,B2}^{B2}) - (1-\gamma) V_f N(\bar{d}_{1s,B2}^{B2}) + e^{-r\tau} I_s N(\bar{d}_{2s,B2}^{B2}))}{\partial \alpha_f} < 0 \qquad \text{Eq. (C.8)}$$

$$\frac{\partial \beta\delta V_f N(d_{1f,B2}^{B2})}{\partial \alpha_f} - \frac{\partial e^{-r\tau} I_s N(d_{2f,B2}^{B2})}{\partial \alpha_f} < 0 \qquad \text{Eq. (C.9)}$$

$$\beta\delta V_f \frac{\partial N(d_{1f,B2}^{B2})}{\partial \alpha_f} - e^{-r\tau} I_s \frac{\partial N(d_{2f,B2}^{B2})}{\partial \alpha_f} < 0 \qquad \text{Eq. (C.10)}$$

$$\beta\delta V_f \frac{\partial N(d_{1f,B2}^{B2})}{\partial d_{1f,B2}^{B2}} \frac{\partial d_{1f,B2}^{B2}}{\partial S_{f,B2}^{B2}} \frac{\partial S_{f,B2}^{B2}}{\partial \alpha_f} - e^{-r\tau} I_s \frac{\partial N(d_{2f,B2}^{B2})}{\partial d_{2f,B2}^{B2}} \frac{\partial d_{2f,B2}^{B2}}{\partial S_{f,B2}^{B2}} \frac{\partial S_{f,B2}^{B2}}{\partial \alpha_f} < 0 \qquad \text{Eq. (C.11)}$$

$$\beta\delta V_f \frac{\exp(-(d_{1f,B2}^{B2})^2/2)}{2\pi} \frac{1}{\beta\delta V_f (1-\alpha_f)\sigma\sqrt{\tau}} (-\beta\delta V_f) < \\ < e^{-r\tau} I_s \frac{\exp(-(d_{1f,B2}^{B2})^2/2)\beta\delta V_f (1-\alpha_f) e^{r\tau}}{2\pi I_s} \frac{1}{\beta\delta V_f (1-\alpha_f)\sigma\sqrt{\tau}} (-\beta\delta V_f) \qquad \text{Eq. (C.12)}$$

$$1 > (1-\alpha_f) \qquad \text{Eq. (C.13)}$$

Eq. (C.13) always holds for values of α_f in the range *(0,1)*. Thus $\pi_{f,B2}^{*P}(t_0)$ decreases as α_f increases.

This proof could be extended to the other pharmaceutical company's profits calculated with ROA methodology in Appendix A and Appendix B.

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