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REAL OPTIONS IN BIOTECHNOLOGICAL FIRMS VALUATION. AN EMPIRICAL ANALYSIS OF EUROPEAN FIRMS.

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ABSTRACT

Firms' intangible assets are becoming more and more relevant in the different areas within the financial discipline. Its management, its quantification and its valuation nowadays constitute one of the main challenges which economy and business try to face. Through this paper we will evaluate some models based on the real options theory in order to estimate the intangible assets value of certain firms, specifically I+D biotechnological firms projects. With this aim, and after deep research on biotechnological industry, we will establish the parameters regarding one model which can be considered as a quantitative valuation method that we apply to a sample of biotechnological European companies. The results obtained through the empirical analysis are promising and they support the use of the real options theory to evaluate biotechnological firms.

INTRODUCTION.

One of the most complex problems in the field of firms' valuation is the value determination of high technology projects, and more specifically those dealing with biotechnological firms. Many of these firms haven't got any benefit; however, they are listed in stock exchanges and keep a wide capitalization in capital markets. It is obvious that the usage of the classical discounted cash flow method is not easy; besides that, this use would lead us to results which would be quite different from the prices established in the markets. In the case of biotechnology, how to evaluate a patent is the main focus of interest from the economic point of view; another relevant aspect is how much investors must pay for such patent through the markets, a merger, an acquisition or another type of strategic agreement. In previous research[1], we have explained some arguments which led us to the application of the so called *"Real Options Method"*. Nevertheless, the most difficult point is the insertion of necessary and

[1] Rubio Martín, G.(2004).
Lamothe, P., Rubio G. (2004).

accurate data or parameters in the models. We did so in the case of the Spanish biotechnological firm Zeltia, a case based on previous research by Kellogg and Charnes (2000) in which data from Myers and Howe (1997) were taken; moreover, this research showed some work carried out by medicine in its developing phase; we will also analyse latest research by Di Masi, Ron Hansen and Grawoski (2002) regarding this field dated at the end of the 90's; then we will contrast that research with other recent studies and we will apply it to the development of a model based on different authors such as Schwartz (2001), Pindick (1993) and Trigeorggis (1996) as we will describe in the next paragraphs. Finally, we will prove its efficacy on a broad European technological firms center.

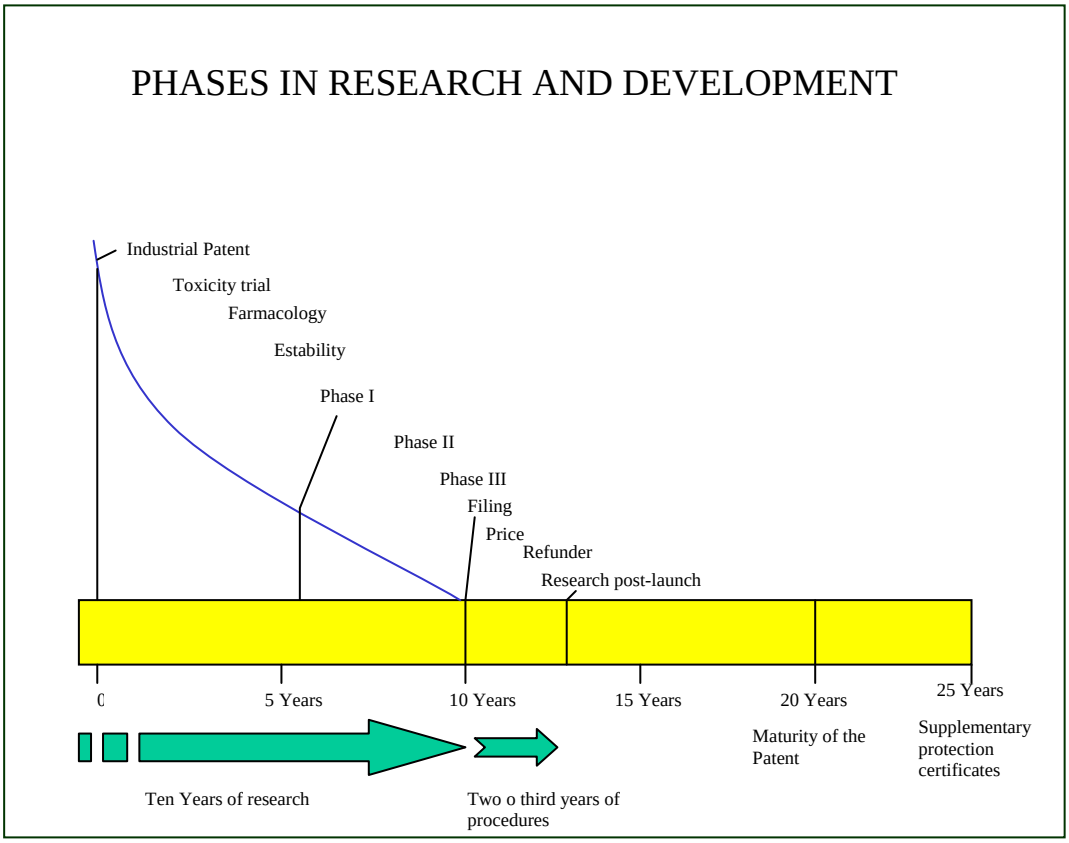
The discovery of a new substance or active component with therapeutical capacity is the first part of this scientific research process and technological development (See figure 1). Then a series of tests and trials must be carried out with the aim of guarantee the effectiveness and the reliability of the medicine to be marketed.

Grawoski and Di Masi (1994), studies regarding the industrial behaviour in the 80's.

Through this paper we will develop some *"average"* parameters which must be considered as common to every

1. - Preclinical phases: the active component is subjected to a complex battery of tests in vitro as well as to tests with animals in order to identify possible toxic effects and establish the pharmacological characteristics of the new substance.
2. - Clinical phases: once the previous tests have been overcome, the promising products are exposed to a second process in which, at the same time, we can distinguish a group of phases generically called "*clinical trials*".

Figure 1.



Source: EFPIA 2003.

According to the previous paragraphs, it is easy to determine that the innovation of a new medicine is a process whose features are uncertainty, risk and resources and time consumptions. This process complexity is shown even in the first phases for the obtaining of the chemical compound which will constitute the basis for the next drug;

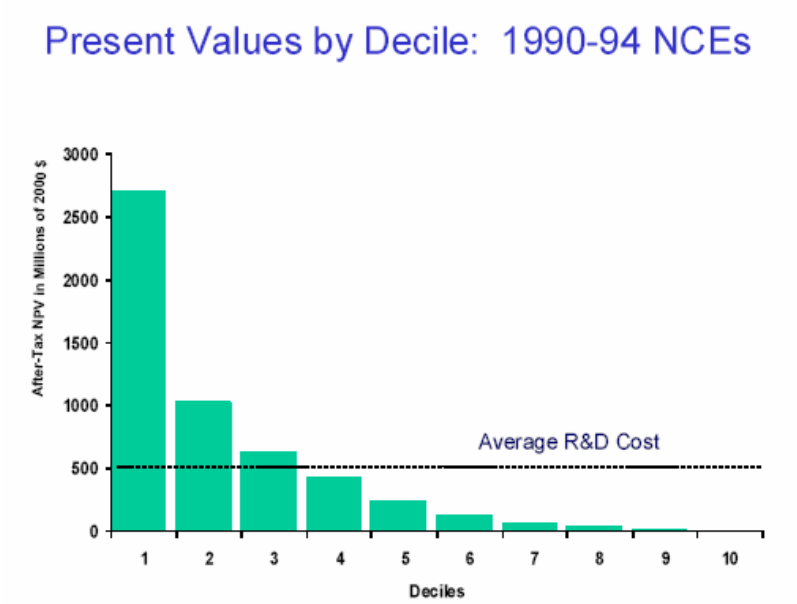
in fact, we can see how probability of a drug becoming commercialised is lower than 2% and, according to other research, even 0.02%. Once the drug has reached the clinical phases, its success probability increases in a remarkable way. This process of scientific research requires a great number of financial and human resources which have considerable increased in the last twenty years. It is not unusual to talk about 12/13 years when referring to the period of time taking place from the obtaining of a new active component up to it is launched to the market, an aspect which leads to losses and to non-obtaining benefits during long periods of time.

As a consequence of this situation, full of competitiveness, uncertainty and risk, we consider that it would be possible to set a "benchmark" which can be common to all components in their developing phase in order to be useful when evaluating biotechnological firms.

ESTIMATION AND SIMULATION OF FREE CASH FLOWS: A DRUG'S LIFE.

In the same research quoted before, its authors, Di Masi, Ron Hansen y Grawoski (2002), show a return study, specifically dealing with free cash flows which _at the drug's launching time_ are valued by deciles:

Figure 2. Cash flows present values.



Source: Grawoski, Vernon and Di Masi 2002.

The test study shows a great concentration on sales, due to the fact, that only the three first deciles would cover the cost of necessary research and development in order to launch a product as figure 2 shows. So the levels of uncertainty and risk generating this kind of projects are higher than the ones in more traditional fields.

From this data we elaborate the "overage net present value" NPV at the time the product is launched:

NPV=0,10*(2700+1000+733,33+433,33+233,33+133,33+66,66+33,33+16,65+0)=525

We divide the cost by the number of periods in which it is generated (twenty years); then we obtain the annual cash flow "Co=26, 24" (mill$).

Our model will show the flows projection according to the compound life following these premises: The patent expiration will take place twelve years after its launch. Sales, and subsequently cash flows, will have a rising progression up to the end of the 9th year. The growth rate used is the historical rate in the field, as Grawoski, Vernon and Di Masi declare (2002); their research gives a profitability percentage of 11% from the usage of the CAPM and previous studies[2].

From the 23th quarter, a mean reversion process with an annual adjustment speed of 69,3147% will occur; this fact will imply that, at the beginning of the 7th year or the 28th quarter, the growth rate has reverted to a medium rate growth estimated as 2%; this rate will remain up to the end of the 9th year[3]

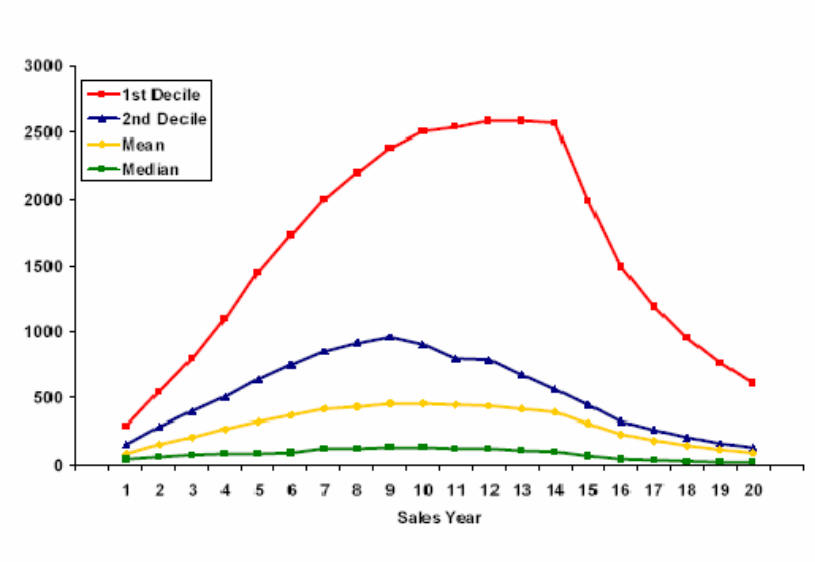
Later, a degrading process in the growth rate will take place and it will reach zero at the end of the 10th year by using an

[2]For other research, see Myers and Shyum-Sunder. (1993) and Myers and Howe. (1997).

[3]Medium growth of the Euro Zone according to foresights by the Comisión of financial matters.

adjustment speed of 100%. During the 11th year, the sales growth rate will be zero, which will turn the process into a random trip.
From the patent expiration moment, year 12th, basically due to the introduction of generics products, the decreasing percentage mean _according to some research_ will be 31%, 28%, 20% and 20% respectively. In order to simulate the process, we have applied a average decreasing annual speed over the flow of 25% until the process is totally extinguished in the 20th year.

Figure 3. Sales by decil.



Source: Grawoski, Vernen and Di Masi 2002.

From the previous data, we will analytically elaborate the cash flow generating process through Monte Carlo simulation for 30.000 paths and quarterly periods following the stochastic functions below:
1º- A Geometric Brownian motion, also means that the differences between both moments in time, t_1 y t_0 are represented by a normal distribution "dw", in which σ is volatility (uncertainty about future movements in the underlying asset) and α is the average annual rate of growth used by investors.

$$dC = \alpha C dt + \sigma C dw$$

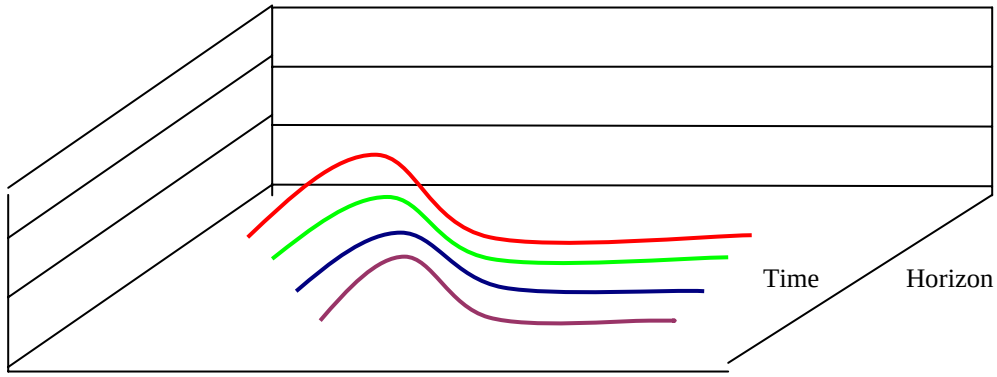
In the equation above we could use a "*Risk Premium*" associated with the dynamic generating process of the cash flow:

$$dC = (\alpha - \eta) C dt + \phi C dw$$

Assuming the proposal of a dynamic "*Capital Asset Pricing Model*" by Merton, we can determine a simple way of calculating the "*Risk Premium*" rate for the project:

$$\eta = \beta(r_m - r)$$

Figure.3. Distribution of portfolio prices for different temporary horizons.



Changes in the cash flow value.

Source: own elaboration.

Developing the previous equation in discrete time, we find that

$$C_1 = C_0 e^{(\mu t + \sigma n(0,1))} ;$$

$$LnC_1 - LnC_0 = \mu t + \sigma n(0,1) ;$$

$$Ln(\frac{C_1}{C_0}) = \mu t + \sigma n(0,1)$$

Where

$\mu = (\alpha^* - 1/2\sigma^2)$. In order to develop the stochastic process, we need to determine the derivation of the prices logarithm by applying ITO's lemma, whose verification is not included in the following research; this result leads us to the following formula:

$$d(Ln(\frac{C_1}{C_0})) = (\alpha^* - 1/2\sigma^2)dt + \sigma dw$$

Subsequently, we find the simulating equation of a Brownian geometric process in discrete time:

$$C_1 = C_0 e^{(\alpha^* - 0,5\sigma^2)t + \sigma n(0,1)\sqrt{t})} \quad (1)$$

2º- An Orstein-Ulemberck mean reversion process for the cash flow rate of growth generating process from the 7th year of commercialisation[4]

$$d\alpha = \kappa_1(\alpha - \overline{\alpha})dt + \theta dz$$

Implies that there is a reversion force over the variable α towards a medium level $\overline{\alpha}$, according to the reversion speed κ_1. Variable α has a normal distribution with the following expression for its mean and for its variance:

$$E(\alpha) = \alpha(0)\exp(-k_1 t) + \overline{\alpha}(1 - \exp(-\kappa_1 t))$$

In the expected value, the mean is just a mid-point between the initial value and the long-term value.

$$Var(\alpha) = (1 - \exp(-2\kappa_1 t)) * \sigma^2 / 2\kappa_1$$

In an average time, the movement of variable α towards its mean will remain as the addition of the expected value and its volatility with a random component which is a normal (0,1)[5]:

$$\alpha_t = \alpha_{t-1}\exp(-k_1 t) + \overline{\alpha}(1 - \exp(-\kappa_1 t)) + \sigma\sqrt{(1 - \exp(-2\kappa_1 t)) / 2\kappa_1}\, N(0,1)$$

In order to adjust the process to the firm risk premium:[6]

$$\alpha_t = \alpha_{t-1}\exp(-k_1 t) + (\overline{\alpha} - \beta / \kappa_1)(1 - \exp(-\kappa_1 t)) + \sigma\sqrt{(1 - \exp(-2\kappa_1 t)) / 2\kappa_1}\, N(0,1); (2)$$

There is a relationship between the adjustment speed κ_1 and the average life or the time which α takes to reach half of the way to get its long-term level $\overline{\alpha}$:

$$H = Ln(2) / \kappa$$

3ª- A degrading process for the growth rate until it disappears implies that the flow would move once the adjustment was finished only according to its stochastic component[7].

$$d\alpha = -\kappa_2 \alpha(t)dt$$

By integrating, we find its discrete version:

$$\alpha_t = \alpha_{t-1} * \exp(-k_2 t) \quad (3)$$

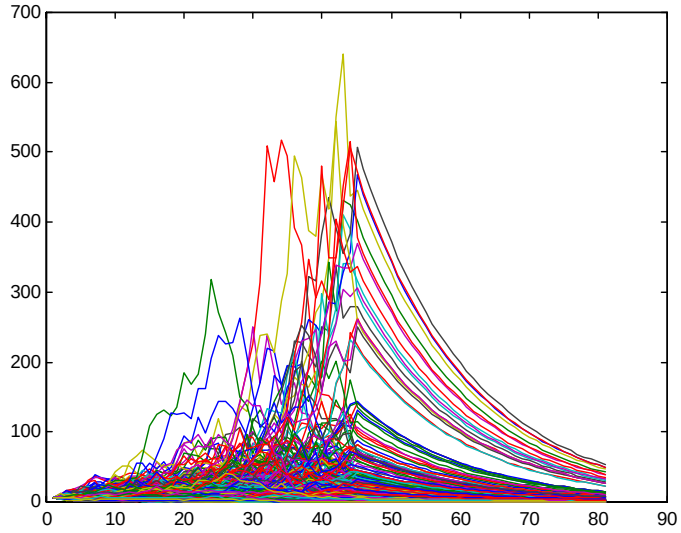
4º- Another degrading process would imply the market definite exhaustion, considering that it is perfect, through the introduction of new and best products.

$dC = -\kappa_3 C(t)dt$; Its discrete time version:

$$C_t = C_{t-1} * \exp(-k_3 t) \quad (4)$$

[4] Grabowski, Vernon and Dimaxi..(2002)
[5] Dixit and Pindyck.(1994)
[6] Schwartz. (2002).
[7] Lamothe and Aragón.(2002).

Figure 4. Cash flows simulation in Mat-Lab.



Source: own elaboration.

REST OF ESTIMATION OF THE FREE CAHS-FLOW'S PARAMETERS FOR EUROPEAN BIOTECHNOLOGICAL FIRMS' CICLE LIFE.

Volatilities and Betas in the market.

Market volatilities and betas will be used for free cash flow simulation along the new drug's commercial life. We have selected a representative group of european biotechnological firms whose volatility and beta parameters are shown in chart 1:

Chart 1. Market Volatilities and Betas of our firms' sample.

	Volatility(Q)[8]	Beta	Sources
Elan	66,11%	1,62	Yahoo Finance
Serono	32,30%	1,1	Volatility.com
ARK Therapeutic	41,03%	Nd	focus.com
Celltech	47,64%	0,71	Yahoo Finance
Vernalis	150,62%	0,22	Yahoo Finance
GPC Biotech	44,17%	0,89	Yahoo Finance
Medigene AGN	44,30%	0,86	Yahoo Finance
Nicox	72,03%	0,79	Yahoo Finance
Zeltia	19,61%	0,77	Yahoo Finance
Average	57,53%	0,87	Elab propia

Source: own elaboration. .

[8] Volatilities are provided according to annual terms. However, Yahoo Finance volatility is calculated on four-monthly data. It is calculated on monthly data within the website of financial analysis "Focus.com". Results shown by "Volatility.com" correspond toa n implicit volatility over the ordinary price of a call option.

Chart 2. Volatilities for ten of the biggest biotechnological firms. Market data.

	Volatility(Q)
Amgen	26,47%
Genentech	36,94%
Serono	32,30%
Biogen	37,27%
Genzyme	36,96%
Chiron	47,68%
Medimune	30,76%
Celltech group	47,64%
Gilead Science	36,76%
Averages	37,07%

Source: Top Biophamaceutical companies report. 2003[9]

Profits volatilities will be used to determine the costs evolution. Accounting rules dispersion in the financial information provided by the firms appearing in our sample does not let us extract volatility regarding research and development. Nevertheless, since these expenses are incorporated in the profit and loss account, variation and volatility of the account according to every firm are substitute indicators for the previous ones.

Chart 3. Profits Volatilities..

	Currency	Profit 03	Pofit 02	Profit 01	Profit 00	Volatiliity
Elan	(mill $)	-535,40	-2362,3	268,9	-294,5	
Var Lg		148,44%	-787,52%	633,40%		722%
Serono	(mill $)	389,96	320,78	316,7	301	
Var Lg		19,53%	1,28%	5,08%		10%
ARK Therapeutic	(mill L)	-8,11	-5,72	-4		
Var Lg		-34,91%	-35,77%			35%
Celltech	(mill L)	-58,50	-54,8	-45,2	-426,2	
Var Lg		-6,53%	-19,26%	224,38%		137%
Vernalis	(mill L)	-34,25	-29,99	-53,33	-40,97	
Var Lg		-13,28%	57,56%	-26,37%		45%
GPC Biotech	(mill €)	-26,83	-32,94	-26,20		
Var Lg		20,52%	-22,89%			31%
Medigene AGN	(mill $) VER	-31,06	-38,87	-110,49	-9,26	
Var Lg		22,43%	104,47%	-247,92%		184%
Nicox	(mill €)	-19,48	-15,69	-11,52	-3,008	
Var Lg		-21,64%	-30,89%	-134,28%		63%
Zeltia	(mill €)	2,85	4,68	9,13	12,71	
Var Lg		-49,60%	-66,83%	-33,08%		17%
Averages[10]						65%

Source: own elaboration from the annual account of the firms..

[9] www.contractpharma.com
www.Yahoo.Finance.com

[10] Elan firm has been eliminated in the calculation of the average variation in our sample since this firm caused a huge distorsion.

Risk-Free rate.
We will use this rate in order to discount cash flows and, later on, the I+D Cash-Cost flows differences counterfoil. We have applied a rate of 5% with the aim of determining the value of the project. Its estimation is taken from the euro denominate bond yield for ten years.

Risk Premium.
We have assumed a Risk Premium rate for the risky assets portfolio of 4,25% taking into account financial research about the European case.[11]
In the figure 4 we show the simulation evolution of the cash-flows across 30.000 paths with quaterly periods, incorporating reversion and exhaustion process.

FUNCTION COST DESCRIPTION: SUCCESS AND DEVELOPMENT COST PROBABILITIES FOR THE PRODUCT.

By the end of the 90's (94-97 period), Grawoski, Vernon and Di Masi (2002) establish a cost of 480 million dollars, after taxes, including unsuccessful drugs cost (it is necessary to discover 5.000-10.000 molecules so that one of them can be launched) and capitalised to a rate of 11% at the drug launching moment. From this data, we will present an "*out- pocket*" expense chart which will not include failure probability or phase-to-phase capitalization. To do so, we will take Parexel expense distribution (2001):

Chart 6. Discovery and development process for the component.

	Years	cost %
Basic research	2.5	4
Discovery	3	15
Preclinical Development	1	10
Phase I	1.5	15
Phase II	2	22
Phase III	2.5	31
FDA review and approval	1.5	3
Total	14.0	100

Source: Parexel. 2001.

We will distribute the cost among the different phases in order to elaborate the most realistic model:

Chart 7. Cost assignment.

PHASES	PHASES	PERCENTAGES	ASSIGNMENT
PRECLINICAL PHASE 124,41(mill $)	Discovery Preclinical	19% 10%	81,51 42,9
CLÍNICAL PHASE 304,59 (mill$) POST-LAUNCHING.	Phase I. Phase II. Phase III. FDA Filing.	15% 22% 31% 3%	64,35 94,38 132,99 12,87 51 Σ 480 (mill$)

Source: own elaboration and Parexel 2001.

[11] Vease Welch.(2001).

We determine discounted costs at the beginning of each phase using a discount rate of 11%:

Chart 8.

Total	Post-Launching	Approval	Phase III	Phase II	Phase I	Preclinical	Discovery
429	51	11,0051	87,6046	50,4594	29,4188	17,6690	18,9099

Source: own elaboration .

We know that probabilities are multiplicative[12] ; for instance, if we have the average probabilities for a component and we want to establish its probability of reaching the market, we will follow this procedure: 0,60*0,90*0,75*0,50*0,85*0,75= 0,1291; this means that it is necessary to discover 7,75 active molecules so that one of them can be commercialised: 1/0,1291=7,7459. If the cost for a compound in its discovery phase is over 76,57 million dollars, each compound will have a cost of 9,88 million dollars without taking into account unsuccessful probability. The lower the success probability we assign is, the higher the number of molecules which must enter one phase will be so that one of them can be launched (thus, the cost we will assign to an isolated compound will be lower).

[12] The same process we are describing is developed in apendix "B" by Myers &Howe (1997) from data concerning success probabilities for certain compounds carried out by Di Masi (1991) for the pharmaceutical field.

Chart 9. Success probabilities.

	Success intermediate probabilities	Success final probabilities
R&D	60%	16%
PRECLÍNICAL	90%	27%
PHASE I	75%	30%
PHASE II	50%	40%
PHASE III	85%→90%	63%→ 81%[13]
FDA. FILING	75%→90%	75%→ 90%

Source: Kellog & Charnes. 2000. Myers & Howe. 1997.

[13] Myers & Howe probabilities (1997) are subsequently modified by Kellogg & Charnes (2000). At this point of the research we will set the original probabilities by the previous authors.

In previous analysis by the biotechnological spanish firm Zeltia, we considered costs and probabilities used in Kellogg & Charnes (2000); however, these authors took into account originary research by Di Masi (1991); this autor established probabilities only from the drug clinical phase I; that is the reason why previous probabilities are assumed by the models with no difficulty. An explanation to something with a poor scientific basis is found in Myers and Howe (1997): it makes no difference if a higher probability is used for the two first phases when we are rising the cost in a proportional way. Then, we must formulate the following question: if we can change costs while keeping the same proportion in probabilities. They seem not very realistic and they should be considered as a valuation distortion.

In his latest research, Di Masi points at two relevant facts: Costs are increasing due to a higher number of open paths. Success costs and probabilities for the pharmaceutical and biotechnological fields tend to converge.

In fact, Gosse (1996) declares that success probabilities for a biotechnological component in its preclinical phase extremely decrease at the end of the 80's until they reach a percentage of only 10% compared to the 36% which Struck Marck (1994) establishes and the 27% by Myers & Howe (1997). These estimations coincide on later research about the pharmaceutical field since they establish lower probabilities:

Chart 10. Survival degree for compounds from 29 pharmaceutical firms.

Start of stage	Probability of reaching market %
Preclinical development	10.3
Phase I	18.4
Phase II	28.1
Phase III	65.8
FDA review & approval	90.6

Source: Parexel. 2001.

For this reason, under conservative criteria, we will compare both possible uses so that we can analyse whether our model can use higher probabilities (chart 11) with higher costs or it is necessary to adopt a more realistic point of view, including lower success probabilities and lower costs in a proportional way (chart 12).

Chart 11. Costs and probabilities.

	Discovery	Preclinical	Phase I	Phase II	Phase III	FDA approval
Success probability.	16%	27%	30%	40%	63%	75%
Number of drugs.	7,746	4,648	4,183	3,137	1,569	1,333
Cost per approved drug[14]	18,90	17,67	29,42	50,46	87,60	11
Cost per phase and drug.	2,44	3,81	7,04	16,12	55,80	8,27

Source: own elaboration from Kellogg and Charnes' probabilities (2000); up to date according to costs evolution by Di Masi et al. 2002.

From the chart above, we obtained a total figure of 93,48 million dollars which, adding post-launching costs, makes 144,48 million dollars.

Chart 12 . Costs and probabilities.

	Discovery	Preclinical	Phase I	Phase II	Phase III	FDA approval
Success probability[15]	0,02%	10,3%	18,4%	28,1%	65,8%	90,6%
Number of drugs.	5000[16]	9,7	5,43	3,56	1,52	1,10
Costper approved	18,90	17,67	29,42	50,46	87,60	11

[14]Di Masi .(2002) and Parexel. (2001).
[15] PHARMA Annual Survey. (2001).
[16] It implies that, from each 5000 molecules which have been discovered, only one will reach the market.

drug.						
Cost per phase and drug.	0,0038	1,82	5,42	14,17	57,63	10

Source: own elaboration from Parexel 2002 and Di Masi et al. 2002. probabilities.

However, according to data in chart 12, they reach a figure of 89,04 million dollars which, added to post-launching research costs, makes a total figure of "*out-pocket*" expenses of 140,04 million dollars.
In the next paragraphs we will show the stochastic simulation process through 30.000 paths, whose explanation is described as follows: we assumed the same widespread process which was previously developed by Pindyck[17] establishing two sources of uncertainty according to costs. The first uncertainty source will be known only after the phase is carried out, since expenses will change as a consequence of this fact; we cannot know that before and this is the reason why the expected value of the costs increases. The second uncertainty can be known before initiating the phase; this fact involves an abandonment Option; that is to say, this phase will start only if costs have been reduced or have not increased so much as for the project to be profitable; if it was not this way, it would be neglected. The first uncertainty (technical uncertainty), is related to the amount of time, effort and materials which would be necessary in order to finish the project because of previous unexpected problems in its implementation. The second uncertainty (the one regarding costs prices for the raw materials which must be used) takes place because of changes in the State regulation and also is due to general economic framework:

$$dk = -Idt + g(I,K)dz \text{ ,}$$

Where I, is the investment rate in every period, dz is a Wienner process which may or may not be related to finance and market prices. The above equation implies that the costs decrease gradually when the investment is being carried out; however, there is also a stochastic component due to technical factors or costs matters.
The author assumes that there is a maximum type of investment K; F(K)= F(K;V;k) ; the investment opportunity value fulfills:

$$F(k) = \max\ E_0\left[Ve^{-rT} - \int_u^T I(t)e^{-ut}\,dt \right],$$

He sets the costs structure as follows:

$$g(I,K) = \beta K(I/K)^{\alpha} \text{ , with } 0 \le \alpha \le \frac{1}{2}$$

Pindyck restrict the analysis to $\alpha = 0$ y $\alpha = \frac{1}{2}$, which corresponds to both types of uncertainty.

The first case corresponds to variations in the price of costs; in this case the instant variance of dK/K is constant e independent from I, K; it may fluctuate even if the investment is not carried out:

$$g(I,K) = \gamma K$$

The second case deals with technical uncertainty. K may change only if an investment is initiated; the total costs will only be known at the end of such investment; moreover, variance dk/k increases lineally according to the increment of ratio I/K:

$$g(I,K) = \beta(IK)^{1/2}$$

Subsequently, this is K evolution:

$$dk = -Idt + \beta(IK)^{1/2}dz + \gamma K dw$$

Where dz and dw are two Wienner processes; the first one is not correlated with the market, but the second one is. To sum up, the previous equation combines uncertainty about the degree of effort required to complete the project over the costs price and the time it will take.
Schwartz only includes technical uncertainty and not uncertainty derived from changes in the costs evolution:

[17] Robert. S. Pindyck. (1997).

$$dk = -Idt + \sigma(IK)^{1/2}\,dz$$

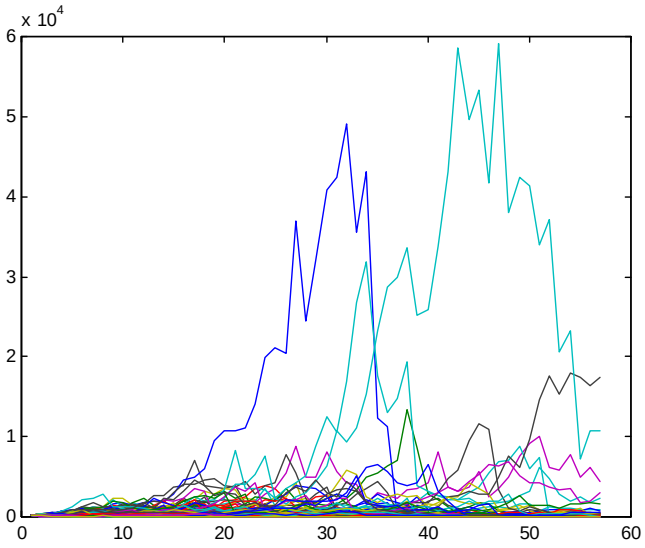
In a discrete time, this would be the development of the equation above:

$$K(t+\Delta t) = K(t) - I\Delta t + \sigma(IK)^{1/2}(\Delta t)^{1/2}\varepsilon_1 \quad (5)$$

Besides this, during the simulation process we have rejected values in the costs function which may be considered negatively.

Now we will show the result of the costs function simulation. We find a lower exhaustion slope than in the case of nutraceutical products[18]. This is due to the fact that they keep a very high I+D costs in the post-launching phase in the parameters that have been used, which implies a lower exhaustion in the costs function[19].

Figure 5. Costs function.



Source: own elaboration.

INVESTMENT OPTION AND ABANDONMENT OPTION VALUES.

The Investment Option in a moment in time before it is finished the investment is F(C,K,t); it depends on the cash flows which may be accrued, the remaining costs in order to finish the project and how long it will take until its end. This value must fulfils the following differential equation based on previously developed research Pindyck[20] with four differences: Schwartz introduces the "*risk premium*", a correlation between I+D expenses and cash flows, which the previous author did not notice; he does not take into account costs uncertainty and introduces unsuccessful possibility for the Project through the Abandonment Option and a Poisson distribution:

$$Max\left[\frac{1}{2}\phi C^2 Fcc + \frac{1}{2}\sigma^2(IK)Fkk + \phi\sigma\rho C(IK)^{1/2}Fck + \alpha * CFc - IFk + Ft - (r+\lambda)F - I\right] = 0$$ With the following limited condition:

$$F(C,0,t) = V(C,t)$$

That is to say, when the investment process is finished, the project value will be that of the outstanding cash flows, where λ is the Poisson probability, per time unit, for the project to be unsuccessful.

[18] Lamothe,P., Rubio G. (2004).
[19] See Di Masi et al (2002).
[20] Robert. S. Pindyck. (1997).

The limited condition difficult the process in the fact that we do not know the investment project length; thus, it turns into a new random variable and makes the differential equation unsolved by traditional numerical methods.
The author shows the way the equation must be solved following a simulation system with two simplifying conditions:

- The investment strategy takes two probable extremes: investing with the highest possible rate, or not investing. This policy is ideal only when cash flows and I+D expenses are not correlated with each other.
- Once the project is abandoned, it will not start again if the cash flows do not improve in the future: since there is no expiration date for the patent, all this neglecting and restarting process may be excessively expensive.

Without any uncertainty, the project value would be like this:

$$NPV = V(C, T_K)\exp(-[(r+\lambda)])T_K + \frac{I_m}{r+\lambda}(1-\exp(-(r+\lambda)T_k))$$

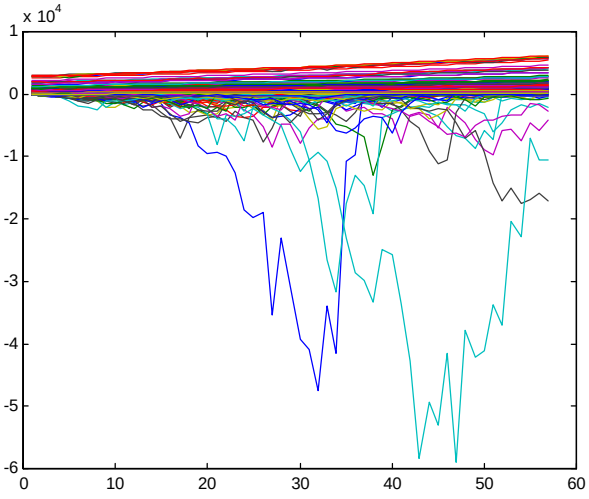
- A solution for the Process.

Since there is not an analytical solution, the author sets the way in which the process can be solved by a Monte Carlo simulation, determining the abandonment options as discreet points in the model. To do so, we define two phases:
The "*Backward*" phase (from front to back). Once the cash flows matrix has been determined according to the formulas (1), (2), (3) y (4) applying a *"Forward"* strategy from the zero moment onwards, we will carry out the simulation from the last period backwards, obtaining the accumulated and up to date cash flows at the launching moment of the product for every path; so, if the I+D phase had finished and the project had not been left, the project value would have been as follows:

$$W(i, j) = \exp(-r\Delta t)W(i, j+1) + C(i, j)\Delta t$$

Afterwards, we simulate the outstanding costs matrix for I+D according to formula (5) and we calculate the "*Project Value*" counterfoil again W(i,j) as the rest between the previous ones for each path and time. See how the path value increases when the time project goes by and the outstanding cost is lower. Although some paths take negative values, their number becomes lower when the project is closer to its ending and its launching to the market and, as a consequence, the number of paths which must be left is lower and the project value becomes higher.

Figure 6. Values function for the project.



Source: own elaboration.

From this point we will develop the "*Backward*" strategy once more, calculating the Project values according to the *"Abandonment Option"* by Schwartz (2001). We will determine the ideal abandonment strategy through a Montecarlo "*Least-Square*" process which will be described later, following the conditions below until we arrive at the zero moment with every possible path and time:
1- The Project will be left if its expected value in the next period (a value which is obtained by the Longstaff-Schwartz algorithm) is lower than the investment required in this period. In the case the project is abandoned in the I+D phase, the project value will be zero:

$$W(i, j) = \hat{W}(i, j) - I\Delta t > 0$$

As if it was a European Option, we will "*regress*" the discounted value in every period from vectors K(i,j) y C(i,j) with the value in the previous period, using nine polynomials as regressors, from the variables and their lineal and square combinations; so we will get the best lineal and non-biased estimator for the project expected value, $\hat{W}(i, j)$.

Let us suppose an stochastic process as a simple example in order to evaluate a Buying Option where Y is the Project value variable at a "t" moment from the rest between the accounting year price 1 and the cash flows in that period (0,80;1,05;1,019;1,22) and X (1,10;0,80;1,09;1,05) represents the cash flows in the previous period. The process will maximize options value within the money: Project value > Exercise price, so we optimize the Y variable according to its correlation with the X variable through the least square procedure:

$E[Y/X]=-15,2841+33,0351X-17,4123X^2$

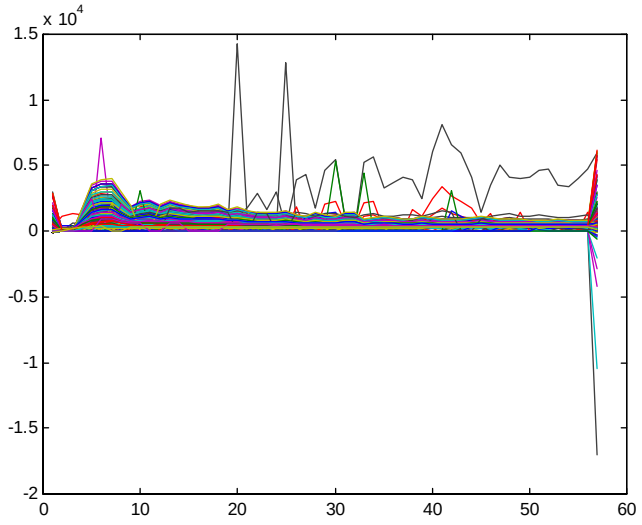
Chart 13.

Paths	X	Y	E[Y/X]	I*dt	Option
1	1,10	0	-0,0144	0,10	Neglecting
2	0	--------	--------	0,10	Neglecting
3	1,09	$0,019*e^{-0,05}$	0,0366	0,10	Neglecting
4	1,05	$0,22*e^{-0,05}$	0,2057	0,10	Continuing

Source: own elaboration.

In order to determine that the Project must not be abandoned, and as we said before, E(Y/X) must be higher than the outstanding investment I*dt in a certain period. When we neglect in certain points within the product cycle, we are introducing a "*jumping*" system similar to that one taking place in a Poisson distribution.

Figure 7.



Source: own elaboration. .

2- This is how the positive values resulting from the application of this recession, which will described later, are as follows:

$\hat{W}(i, j)$

$$W(i, j) = \exp(-r + \lambda)(\hat{W}(i, j+1) - I_j)$$

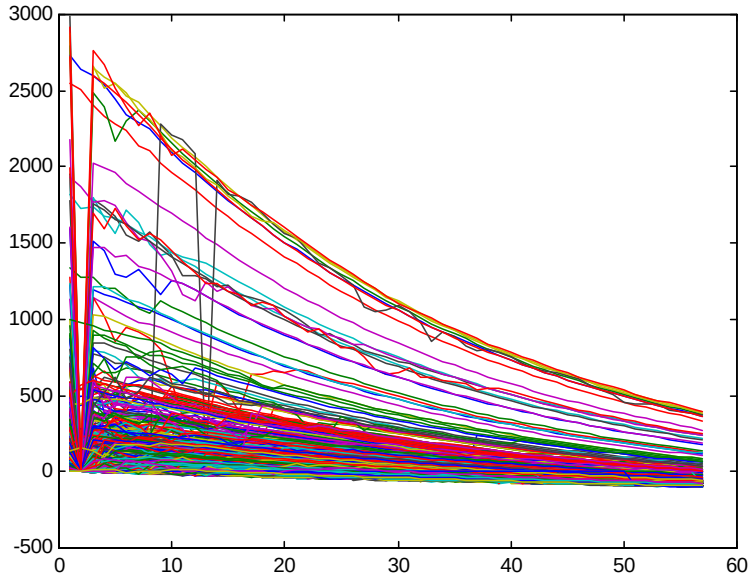
In order to finish the simulation process, we will establish the average value for every possible different path, and also its present value, by applying the success probability that the product may reach the market added to the discount rate according to data from charts 11 an 12 and following a Poisson distribution. For instance, we will apply a success probability percentage of 16%, which implies an abandonment probability of 84% (1-0.16) for a product in its discovery phase.

$$\exp(-\lambda T_K) = \exp(-8\lambda) = 0{,}16$$

$$\lambda = 0{,}23$$

We extract the up to date costs in previous periods (I_j) from every value resulting from the counterfoil difference between the outstanding cash flow and cost. These amounts represent a "*financial buffer*" that we demand of the investment since this industry nature constantly leads to the reinvestment of one part of the obtained funds. If it was not able, the firm being evaluated would not easily survive in a medium or a long term.

Figure 8. Graphic representing the project present values.



Source: own elaboration.

VARIABLES CORRELATION.

As a hypothesis for the model, we have established that the cash flows and the costs are not correlated. In the following sensitivity analysis we will see what would happen if, as Schwartz (2001) suggests[21], the correlation between both variables was very weak and had a negative sign, specifically -0,01%.

In Wienner process for the correlation of two variables which follow both stochastic processes, it would be enough if their volatilities or uncertainty sources[22], were correlated. So, this fact must be fulfilled:

$$d_{z1} * d_{z3} = \rho$$

Where Z_1 and Z_3 are two normal distributions (0,1).

[21] Regarding variables correlation also see Shimko. (1992) and Trigeorgis. (1996).

[22] Schwartz. (2000).

In order to correlate both distributions, we have provided the bivariable distribution Z_3 with some content starting from the previous ones; then:

$$\begin{pmatrix} Z_1 \\ Z_3 \end{pmatrix} \rightarrow N\left(\begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} 1\rho \\ \rho 1 \end{bmatrix}\right)$$

Which implies that: $Z_3 = \rho Z_1 + Z_2$

For an average distribution Z_2, which is a normal one $(0,(1-\rho^2))$

and a normal one Z_3 (0,1) and a correlation rate regarding Z_1, ρ.

So it is fulfilled for Z_3 that its variance is 1 :

$$\sigma^2(Z_3) = \rho^2 * \sigma^2(Z_1) + \sigma^2(Z_2) = \rho^2 * 1 + 1 - \rho^2 = 1$$

and its arithmetic mean is zero. $E(Z_3) = 0$

SIMULATION RESULTS. ANALYSIS.

In the next paragraphs we will present the analysis results for a compound in its discovery phase considering different probabilities and volatilities.

Chart 14. .Products in their discovery phases.

Different probabilities	VALUES
P*=0,16 (Kellogg &Charnes)	
$\sigma = 37\%$	12,47
$\sigma = 57\%$	82,07
P*=0,02 (Paraxel,Di Masi)	
$\sigma = 37\%$	-6,98
$\sigma = 57\%$	29,66
P*=0,0002 (Paraxel)	
$\sigma = 37\%$	-39,08
$\sigma = 57\%$	-12,93

Source: own elaboration. .

We find that, for probabilities under 2%, the project value is always negative. In order to compare the data which has been obtained applying this model and the one which has been calculated following other methods, we take the same success probability previously used (16%) for a product in its discovery phase with a volatility of 37% and we get a similar value for a product in its discovery phase (12,47 mill) as in previous research. So we are close to the "*basic"* solution established by Schwartz (2001). Nevertheless, these solutions are not completely accurate from our point of view.

Probabilities over 2%, for a compound in its discovery phase are not real. Probabilities for biotechnological products have gradually converged with probabilities for the most conventional or chemical compounds, which are under 2% or even 0,02%, according to different research. In our opinion, theories which have been applied to use higher probabilities by the quoted authors do not seem to be very convincing.

Myers & Howe start from the presupposition that probabilities and costs are directly proportional; they think that we can increase them without any problem, also increasing costs in a proportional way. However, this fact is not possible, at least in our model, since in this case the usage of lower probabilities with lower proportional costs must be the same as the usage of higher probabilities and higher costs, and this does not happen. Valuation changes automatically from positive values to negative ones starting from probabilities which are lower than 2%.

Schwartz (2002) makes a distinction between "*unsuccessful financial probability*" and "*unsuccessful technical probability*". With regards to the usage of higher probabilities than the ones in the market, he believes that the "abandonment option" (which was introduced in the model by the Longstaff-Schwartz algorithm) means the origin of financial failure; thus, there are only technical unsuccessful probabilities, which represent 50% of the total possible unsuccessful. Nevertheless, the effects deriving from the application of the neglecting option are not close to 50% of the global unsuccess/success probability effect through a Poisson distribution: we consider that this fact is not replaceable.

To sum up, we think that the usage of these probabilities (which are over the real ones) would only be recommended when a successful capacity for these products is presupposed after proving their efficiency and their new action mechanisms from the point of view of medical results, which would lead to financial results over the

average. However, we cannot forget that, when we apply probabilities over the average, we are overweighting the project value in a way.
In this case, a possible solution would be the evaluation of only one part; a percentage from the products in their discovery phase. For instance, in the case of Zeltia, which owns a really important portfolio of compounds in their discovery phase, 500 molecules, which have proved to be active in vitro against different types of cancer, we should only value 10%, so we would get final probabilities under 2%.

Now we will present a sensitivity analysis according to variables in different parameters:

Chart 15. Sensitivity analysis for a product in its discovery phase (mill$).

Correlation	VALUES
-0,10	13,27
-0,01	12,60
Without any correlation	12,47
+0,01	12,34
+0,10	11,66
Volatility	VALUES
40%	17,21
37%	12,47
45%	28,55
Risk Free rate	VALUES
5%	12,47
4%	23,06
3%	39,03
Risk Premium	VALUES
5%	5,23
4,25%	12,47
3%	22,03
Rate of growth	VALUES
10%	7,98
11%	12,47
12%	13,81

Source: own elaboration.

Finally, we present the model results for the different phases in a drug's development through the application of different probabilities and volatilities:

Chart 16.

PRODUCT IN ITS PRECLINICAL PHASE	VALOR
P=27% $\sigma = 37\%$	43,19
P=27% $\sigma = 57\%$	133,14
P=10,3% $\sigma = 37\%$	14,23
P=10,3% $\sigma = 57\%$	77,79
PRODUCT IN ITS CLÍNICAL PHASE I	VALOR
P=30% $\sigma = 37\%$	55,76
P=30% $\sigma = 57\%$	187,31
P=18,4% $\sigma = 37\%$	34,5
P=18,4% $\sigma = 57\%$	140,53
PRODUCT IN ITS CLÍNICAL PHASE II	VALOR
P=40% $\sigma = 37\%$	87,04
P=40% $\sigma = 57\%$	267,17
P=28,1% $\sigma = 37\%$	66,88
P=28,1% $\sigma = 57\%$	219,62
PRODUCT IN ITS CLÍNICAL PHASE III	VALOR
P=63% $\sigma = 37\%$	126,43 (146,03; P=81%)
P=63% $\sigma = 57\%$	360,95 (426,65; P=81%)
P=65,8% $\sigma = 37\%$	126,99
P=65,8% $\sigma = 57\%$	369,33
PRODUCT IN ITS APPROVAL PHASE	VALOR
P=75% $\sigma = 37\%$	203,09
P=75% $\sigma = 57\%$	518,44
P=90,6% $\sigma = 37\%$	220,14
P=90,6% $\sigma = 57\%$	565,47

Source: own elaboration.

APPLICATION OF THE MODEL TO A SAMPLE OF EUROPEAN BIOTECHNOLOGICAL FIRMS. A COMPARISON TO THEIR MARKET VALUES.

Compounds values in their different research phases change outstandingly according to the probabilities and volatilities that have been used; to give a more specific explanation, for a certain probability and different volatilities, we see how values multiply by 2,5 and 3 times, obtaining a wide range of values and proving the extremely high sensitivity of the model when facing cash flows volatility changes.

These firms may really work with quite wide ranges according to the diverse probabilities and volatilities used as parameters. This is the reason why we establish a confidence interval for each one and, along this interval, values will quote according to the parameters that investors weight at every moment. However, it is necessary to consider folowing points:

Regarding the analysis of the used volatilities, it is important to say that the mean referring to the ten most relevant biotechnological firms (all of them quoting in Nasdaq) is 37% (see chart 2), whereas our firms volatilities (see chart 1), firms that quote in European markets, is 57%. This data may mean the effects of a less efficient european market in the resources assignment comparing it to the american market. In Europe, the markets patchwork where these firms quote, the national disparity concerning the different rules which are applied up to this moment, referring to the accounting representation of research and development expenses, and the lack of investors and analysts specialized in these areas, are some of the many factors which have contributed to the existence of a more irrational and rougher movement of prices if we compare it to the one occurring in the american markets; this fact causes the appearance of different volatilities in both samples.

Subsequently, there is a type of volatility which can be called "*destructive*", a volatility that, in our opinion, creates a paradox concerning values. Compounds values increase and, however, this may be due to irrational movements (even with a decreasing feature), with a relevant tendency towards instability.

In order to determine a "*parameterized*" confidence interval, we will set two ranges: firstly, the lower one is calculated by using higher probabilities from Kellogg and Chames research and including average volatilities belonging to firms quoting in the American market; secondly, the higher range, including lower probabilities as in Parexel research and, simultaneously, containing higher volatilities from the firms in our sample research.

The firms we have selected fulfil two common characteristics: the first one is that all of them are biotechnological firm specialized in drugs production, firms which assure new action solutions in the healing of illnesses such as cancer, alzheimer or multiple sclerosis; the second characteristic is that every firm quotes in "*new stocks national markets*" in a european level, more specifically in the Tech Market (London), where ARK. Therapeutic, Celltech and Vernalis also quote (firms which are selected in our research); the Neuer Market in Frankfurt, for GPC Biotech and Medigene AG; the Nouveau Marché in Paris, where the french firm Nicox quotes, or the New Spanish Market, with the spanish firm Zeltia. Other european industries which are not provided with a nacional market to do so, quote in Nasdaq, as it happens to the irish firm Elan, or the swiss one, Serono

To illustrate these datas, we will show a resume of these companies' evaluations:

Chart 17. ZELTIA. (MILL €).

	Fase Desc.	Fase Preclín.	Fase I.	Fase II.	Fase III.	Fase registro.
	500 (10%)	7	1	2[23]	1	0
Rango inferior.	Vu 12,47	Vu 43,19	Vu 55,76	Vu 87,04	Vu 146,03	Vu 220,14
Total.	623,5	302,33	55,76	174,08	126,43	0
					$\sum totales$	1282,1
Rango superior.	0	Vu 77,79	Vu 140,53	Vu 219,67	Vu 369,33	Vu 565,47
Total.	0	544,53	140,53	439,34	369	0
					$\sum totales$	1493,4

Valor Opción rango bajo.	1282,1
Valor Opción rango alto.	1493,4
Gordon.	140,73[24]
Nº de acciones.	200,7
Valor min/Valor max por tit.	(3,98)[25]/7,08/8,14[26]
Cotización 08/10/2004	5,60 $\Longrightarrow$ Bien valorada.

The chart below resumes the final situation of our firms group according to the results obtained in our evaluation. The next one includes some interest indicators which analysts and investors should take into consideration when evaluating this kind of firms to invest on them: level of liquid asset, number of years up to the first drug launching to the market and strategic agreements.

Chart 18.Data resume.

[23] Según datos proporcionados por la propia compañía el compuesto Kahalalide F valorado anteriormente en fase clínica I ha pasado a fase II para determinadas aplicaciones.

[24] $V_0 = \left(\frac{6,88}{0,0885-0,0706}\right) * \left(1 - e^{-(0,0885-0,0706)*10}\right) + \frac{6,88}{0,0885} = 140,73$;

[25] Si no sumásemos el valor de la cartera de compuestos en fase de descubrimiento.

[26] Si hubiésemos conservado la valoración por fundamentales de la compañía del capítulo 5 y mantenido el número de acciones, la valoración del rango bajo sería muy parecida para ambos modelos.

Firms	Evaluation (€)	Number of shares/ Capitalization.	Price (10/08/04 €)	Result
Elan	(3,72)-3,85-5,80	390,45/ 8.472	21,7	Overvalued
Serono	374,78-505,21	22,7/ 11.372,7	501	Well valued
ARK Therapeutics	2,50-7,71	110,63/ 132,756	1,20	Undervalued
Celltech	3,86-6,70	278,46/ 2.302,86	8,27	Overvalued
Vernalis	1,58-3,82	319,23/ 392,65	1,23	Well valued
GPC Biotech	(8,12)-11,60-20,94	28,62/ 315,11	11,01	Well valued
Medigene AG	41,11-88,04	13,47/ 99,543	7,39	Undervalued
Nicox	22,70-55,82	32,15/ 123,777	3,85	Undervalued
Zeltia	(3,98)-7,08-8,14	200,7/ 1123,92	5,60	Well valued

Source: own elaboration.

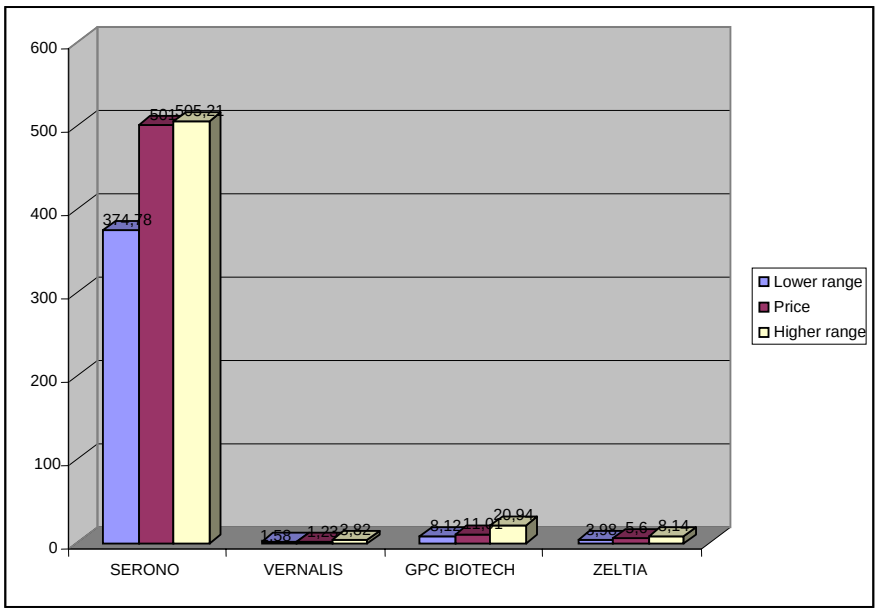
After analysing our research, we conclude by confirming that the values obtained through the parameterized model constitute "*reasonable prices*" for these firms which may let their usage for firms evaluation and biotechnological projects. Nevertheless, it is necessary to consider the following points:

Due to the uncertainty and the risk that these firms incorporate to their investment projects because of possible and unpredictable changes in their business' evolution, we can only determine a confidence interval for them. The companies' prices should move along the interval for certain compound portfolio information according to some factors weighted by investors at any moment. Out of this confidence interval which we have set for every value, the firm would be undervalued or overvalued.

According to the results that we have obtained, we can establish three ranges concerning firms:

Well valued firms: companies whose price moves along the values range shown by our model. These firms are Serono, Vernalis, GPC Biotech and Zeltia.

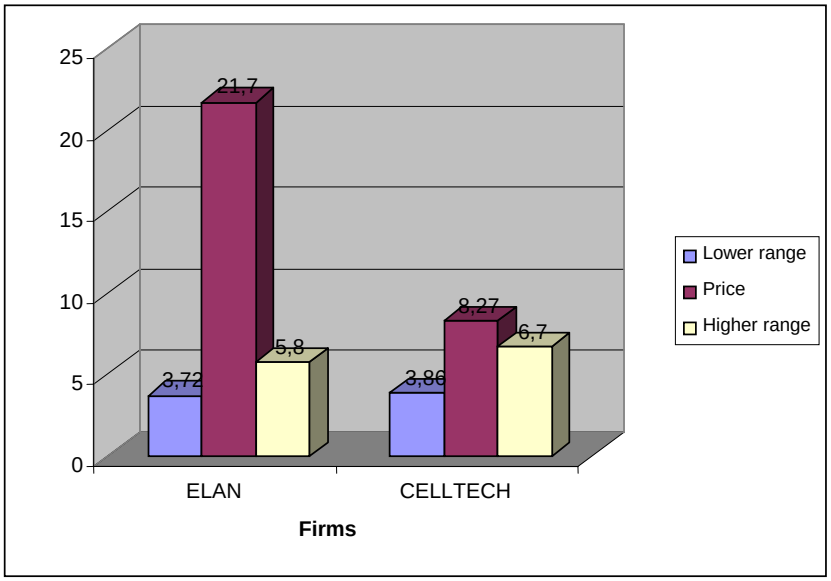
Figure 9.Comparison of theorical values and market prices for analyzed firms.



Source: own elaboration.

Overvalued firms according to the models in the dates and from data analysed by Elan and Celltech: in the case of Celltech, this overvalued result was due to a "*control premium*" which was paid by UBD in order to buy the company in 2004, more specifically, when the agreement was announced, the shares increased 26%. Without this increase, the firm prices would have been situated within the trust interval determined for our evaluation. Elan's case is different: it seems that investors are betting on their drugs to become "*block-buster*" products whose sales and cash flows generation are situated in the sales higher range, whereas our model considers a mathematic expectation or average value for every possible range.

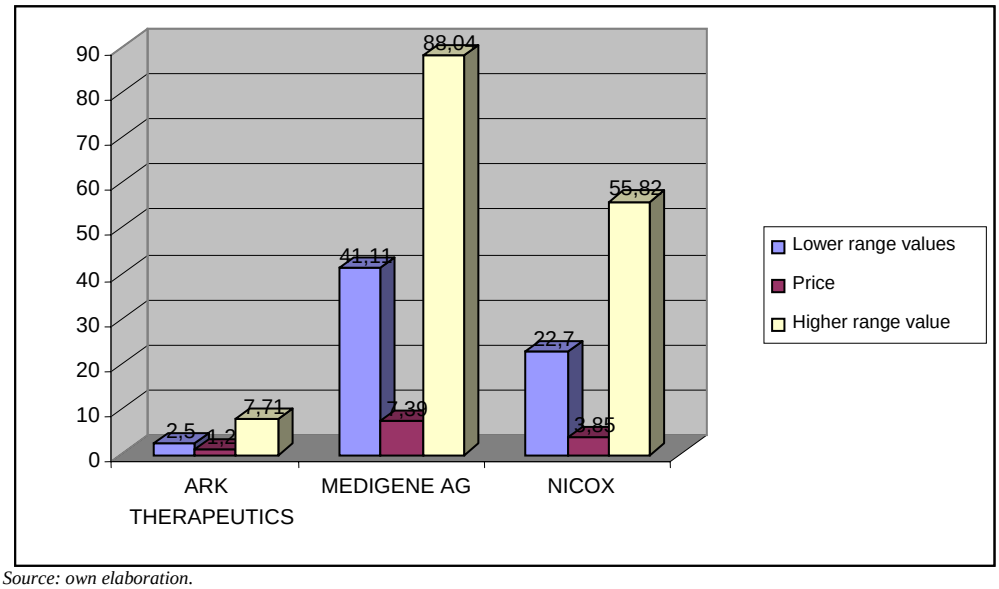
Figure 10.Comparison of theorical values and market prices for analyzed firms.



Source: own elaboration.

Undervalued firms such as ARK Therapeutics, Medigene AG and Nicox: firstly, it is relevant to say that stock market capitalization of the firms which constitute our sample is really diverse. The model presents a bias for those which have lower capitalization rates, especially Medigene AG and Nicox. It is a control or liquidity premium which can be found in these firms with a low number of issues and poor capitalizations. Subsequently, new shares issues and capital expansion in these companies (as a possible solution to defray their research costs) may produce a comparative advantage over the rest of firms and not a disadvantage, always carrying out this procedure within some logical limits according to their needs and to the compounds they may develop.

Figure 11.Comparison of theorical values and market prices for analyzed firms.



Source: own elaboration.

Besides that, it is important to state that these three companies do not keep or have broken strategic agreements dealing with their products' development, which leads us to conclude by saying that investors penalize or reward this

kind of facts which, from a quantitative point of view, are difficult to consider in our model. In fact, Nicox kept product development agreements with Axcan Farma, Bio polis and Astra Zeneca (its agreement with the later firms was broken in September and nowadays its issues quote 65% under precedent prices. Medigene AG also broke its agreement with Aventis in 2004 (an agreement dealing with an anticancerous vaccine); this fact had a negative influence on its price. Medigene AG keeps another agreement with the Japanese firm Yamanouchi, but about commercialization and not of product development.

Finally, ARK Therapeutics did not keep any collaboration agreement with any firm by the time of this research; however, it collaborates with other companies, such as "Crucell", in the development of a new compound carried out by Crucell, a new component dealing with gene therapy (PER C6 TM, in November, 2000). Nevertheless, ARK Therapeutics only keeps product commercialization agreements.

Chart 19. Strategic indicators.

Firms	Liquid assets state. 1st week 2004. (mill UM)	Drugs in the market.	Latest drug's most advanced phase.	Strategic agreements dealing with drug development.
Elan	915,8 ($)	2	Launching phase.	Biogen Idec.
Serono	2383,05 ($)	8	Launching phase.	Several
ARK therapeutics	53,73 (L)	1(year 2004)	Phase II	
Celltech	155 (L)31/12/03	67[27]	Phase III	UCP[28]
Vernalis	24,21(L)	1 (year 2003)	Phase III[29]	Biogen Idec, Roche, Serono.
GPC Biotech	74,75 (€)	None	Phase III	Altana.
Medigene AG	32,81 (€)	1 (year 2003)	Phase III	
Nicox	40,09(€) 31/12/03	None	Phase III	
Zeltia	114,44 (€)	None	Phase III	Ortho Biotech.

Source: own elaboration.

[27] In spite of counting on a great number of products, the majority of them deal with chemistry and none of them has got a high rate of sales.
[28] It has been taken over by this dutch group in august 2004.
[29] It is the same drug which was approved (Frvatriptan) for others of its applications.

All these indicators (added to other aspects such as their cash-flows state, the presupposition that they have not launched any product to the market and the years up to their first drug launching) are data which should be a part of a strategic indicator in a wider study about this field.

According to our research, we assert that the values shown by the parameterized model constitute "*reasonable prices*" for these firms which might let their usage in the management of an investment portfolio of biotechnological companies. However, due to the sensitivity in the models held to changes, it is necessary to estimate "*spreads*" or confidence intervals to the firms' valuations; these intervals will exist during a certain temporal frame in which prices should move along that interval according to the weighting of one or the other factor or parameter by the analysts or the investors. Moreover, to keep the models in good working order, it is necessary to count on the most appropriate parameters; by doing so, we give relevance to the fact of establishing generally accepted criteria, since nowadays there are important discrepancies among the quoted authors, especially concerning probabilities application and volatilities.

To end this research, it is necessary that the manager evaluates the behaviour of two factors playing an important rule in this kind of investments: diversification and time. These investments imply an extremely high level of risk; the probability for a drug to be rejected is very high; many of these companies, especially the ones searching for "*biotechnological*" products, will never get any benefit and they will disappear. However, the action mechanisms that these new drugs have are so original that success in one of these firms may fully reward the investor who has participated in a well diversified portfolio. Regarding time, the maturity cycle for a compound is very long; this is the reason why the investment dealing with biotechnology should have a temporal horizon over five years, or even ten years, since this investment yield may only be valued in a long term.

Anyway, we have verified that models based on real options seem to show "*reasonable*" values as far as its proximity to the prices of biotechnological firms in the market. In this research, as in many others, it seems that these "*theoretical*" financial models do not present very distant results to the prices of "*reality*" in the markets, including the necessary parameters which provide the evaluations with a higher level of flexibility and credibility.

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