In Search of the True Value of a Start-Up Firm:

Creative Destruction and Real Options Approach (CD-ROA)[*]

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Cecilia Maya [**]

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[**] Ph.D. in International Economics and Finance, Brandeis University. Assistant Professor Department of Finance, School of Business, Universidad EAFIT Address: Calle 5 Sur # 32-127 Medellín- Colombia. Phone: (574) 268 7263 E-mail: cmaya@eafit.edu.co

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ABSTRACT

In this paper I propose a Creative Destruction - Real Options Approach (CD-ROA) to valuing start-ups when only technological uncertainty is present. I claim that is the case when a company takes part of a Creative Destruction process as described by Schumpeter (1942). This approach is able to explain the high prices investors pay for growth stocks and proves that it is not a case of overpricing but recognition of the large growth potential of firms which are part of highly innovative industries. I also perform a case study on the valuation of Gilead Sciences, Inc., using the CD-ROA.

Corporate valuation is certainly a challenging subject. The challenge is greater when the firm subject to valuation is a start-up since the task must be accomplished without any information about its past performance supporting the necessary forecasts. The difficulties practically pile up when the industry is new as well. That is not all, the subject can get more complicated when the start-up is one of those firms for which innovation is the main driver of value because there is much uncertainty surrounding the success – and survival – of these firms.

Even for well established firms in mature industries, the traditional methods used in corporate valuation are not completely satisfactory nowadays. After the recent stock market bubble burst in 2000, it is clear that, although prices were inflated by this bubble, they will not come back to the previous level. Possible explanations for this fact are that traditional methods have not accounted properly for factors such as intellectual capital, market power, and real options, all of which increase the value of the firm.

The literature, mainly on Industrial Organization, have explored the importance of intellectual capital and market power for corporate strategy (Schumpeter (1934); Schumpeter (1942); Phillips (1966); Reinganum (1983); Reinganum (1985); Gilbert and Newbery (1982); Tirole (1988); Levin and Cohen (2000)). It is clear that these factors add value to the firm, however, only recent literature have tried to value them (Zucker, Darby, and Brewer (1998); Darby, Liu, and Zucker, (1999); Schwartz, E.S. and C. Zozaya-Gorostiza (2000); Schwartz, E.S. (2002)).

These drivers of value deserve special attention in the case of firms subject to a process of Creative Destruction as defined by Schumpeter. This is a process of permanent innovation described in his own words as "The fundamental impulse that sets and keeps the capitalist engine in motion comes from the new consumer's goods, the new methods of production or transportation, the new markets…[This process] incessantly revolutionizes the economic structure *from within,* incessantly destroying the old one, incessantly creating a new one. This process of Creative Destruction is the essential fact about capitalism". (Schumpeter (1942)). For these firms, both intellectual capital, as the engine of innovation, and market power, as the expectation of monopolistic power when innovating, are fundamental components of their value.

However, traditional methods up to date do not account properly for these two determinants of the value of a firm. This may explain why methods based on Discounted Cash Flows (DCF), mainly the passive NPV approach, have not been able to explain the abysm between market prices and DCF values, a fact that neither academics nor practitioners could continue ignoring.

Although it is true that part of the difference was caused by a market bubble formed around Internet stocks which pushed up prices of growth stocks mainly, it is also true that once the bubble burst in 2000, market valuations remained higher than their initial level. A study by Ernst and Young[1] estimates that only 25% of current market capitalization is based on cash flows anticipated in the next five years in a sample that includes both growth and value stocks. Certainly, new approaches to valuation need to be put in place.

During this Internet madness in the nineties, very peculiar approaches to valuation were suggested –and implemented!- in a wide range that included computing multiples of Market Price to Revenue up to multiples of the number of visitors to the Internet firm's web page. For a while, the market forgot about the essentials of firm's value such as its ability to generate future cash flows to shareholders –the basis for DCF- or to create value in general.

Simultaneously, a much more appealing approach -from a theoretical point of view- was taking a foothold into the valuation world. Building on the DCF approach yet going further in the sense of incorporating flexibility in management investment decisions, and taking advantage of the advances in option pricing theory, the real options approach (ROA) has become the alternative approach to capital budgeting and, lately, to corporate valuation. It is precisely the fact that ROA is based on a properly estimated passive NPV what explains the perception of practitioners that, more than a revolutionary solution, it is "an evolutionary process to improve the valuation of investments and the allocation of capital, thereby increasing shareholders value" (Triantis and Borison (2001, p.10)).

Some attempts have been made to use ROA for corporate valuation. Amran and Kulatilaka (1998) propose an example to value an imaginary start-up company; although it has the merit of being one of the first attempts in this direction, it is a very limited and simplified case. Copeland and Antikarov (2001) develop the subject further with the aim of guiding practitioners on the application of ROA, but their use of a discrete time model such as the quatrinomial model makes it intractable for long-term horizons as the ones required in corporate valuation.

Schwartz and Zozaya-Gorostiza (2000) apply ROA to Information Technology projects, recognizing that "traditional tools for project evaluation, like the IRR or the NPV, are inadequate for coping with the high uncertainty that characterizes most IT projects". In their paper, they develop a continuous time model which takes into account many different variables affecting the firm's value and apply the model by using Monte Carlo. Although it is a very comprehensive model, it was designed to value IT projects only.

Schwartz and Moon (2000) focus on Internet companies and shows how "the value of an Internet stock may be rational if growth rates in revenues are high enough. Even with a real chance that a company may go bankrupt, if the initial growth rates are sufficiently high and if this growth rate contains enough volatility over time, then valuation can reach a level that would otherwise appear dramatically high". Schwartz and Moon (2001) expand this model providing insights into its practical implementation.

Schwartz (2002) applies ROA to patents and patent-protected R&D projects. It takes into account uncertainty in the cost to completion of the project, uncertainty in the cash flows to be generated from the project, and the possibility of catastrophic events that could put an end to the effort before it is completed. It also allows for the possibility of abandoning the project finding that this abandonment option represents a very substantial part of the project's value when the project is marginal or/and when uncertainty is large.

Finally, Kellogg, Charnes, and Demirer (2002) apply ROA to corporate valuation but circumscribed to a specific case study on a biotechnology firm. They suggest that a

company may be considered as a portfolio of projects and, as a consequence, its value is the sum of the individual projects' value.

This paper suggests an approach to corporate valuation under the name of Creative Destruction – Real Options Approach (CD-ROA). It contributes to the literature on real options and corporate valuation by proposing a more general framework for the use of real options in valuing start-ups which may be applied to a wider range of firms than most of the studies cited above. It also has the advantage of using continuous time for modeling the value of the company, which makes the model more tractable. Although it searches for the value of a start-up company which has only one project in the beginning of its development stage, it can be applied to a company with many projects based on the fact that a firm may be considered a portfolio of projects.

The main idea underlying this model is that in the case of a company subject only to technological uncertainty, ROA may be applied to determine the value of the firm. Usually, by applying ROA, some issues arise such as which is the appropriate risk-adjusted discount rate for the expected payoff of the real option or how to build a perfectly hedged portfolio when the underlying asset is not tradable. However, those issues need not to be addressed here since this technological risk is non systematic, thus it can be diversified away.

The reason why this firm is subject only to technological risk is that it takes part of a process of Creative Destruction as described next, which gives it a monopolistic power if it successfully innovates, thereby ruling out market risk for this company. Thus, the

only risk this firm faces is the technological risk which is the probability of innovating first or being defeated in the technological race.

I. The Process of Creative Destruction

A process of Creative Destruction may be described as follows: A firm develops an innovation which makes other firms' products or processes obsolete. This firm will have a temporary monopoly until a challenger firm innovates as well. It could be the kind of innovation that Tirole (1988) calls a *drastic innovation* which allows the innovating firm to be more efficient and become a *de facto* monopolist. It could also be a legally protected monopoly i.e. by the patent system. In this last case, the monopoly lasts not until the patent expires but until another firm innovates and becomes a monopolist. In both cases, although obsolescence destroys some wealth it also breeds progress by creating wealth and stimulating innovation.

For a creative destruction process to take place, the appropriability conditions have to be guaranteed i.e. by means of a patent.[2] In what follows next, I assume that the appropriability conditions are given by a patent. When a firm earns monopolistic power by patenting an innovation, it can set the conditions in the market. The existence of such power reduces the uncertainty the firm faces by eliminating the market risk. It would remain the technological risk only, in a way that changes in the value of the firm can be linked directly to the outcome of R&D. In the next section, I model the value of a firm which takes part of a process of creative destruction.

A. *The Creative Destruction – Real Options Approach (CD-ROA)*

This approach focuses on the valuation a start-up firm which is subject to Creative Destruction, i.e. those which are part of growth industries. For this kind of firms, innovation is an essential determinant of its value which, at the same time, depends on the firm's investments in R&D and the efficiency of its research. To assess the value of a firm, the CD-ROA takes into account the expectation of producing an innovation as well as a growth option the firm may exercise in case of success.

Throughout the model, I presume a single expected innovation produced by means of a single R&D technology by a profit maximizing firm. The firm subject to valuation will be identified as the expected monopolist and the other firms participating in the technological race are the challengers. The cost function is the same for all firms involved in the race. Additionally, innovation is always "drastic" in the sense that the product developed by the current monopolist becomes obsolete, guaranteeing absolute market power to the innovating firm. This patent race is "memoryless" as named by Tirole (1988), meaning that all firms in the market start from the same point. Past R&D experience or expenses do not affect the result, only current R&D expenses determine the probability of success in innovating.

For the purpose of valuing this firm, I argue that using ROA instead of the traditional passive NPV approach provides a better estimation. This last method comprises the computation of the expected free cash flows that a project or a company will produce in

the operating period and discounting them to the present value at a constant rate, equivalent to the opportunity cost of capital.[3]

The main critique to the passive NPV approach is that it assumes a commitment to invest certain amount of money in predefined periods of time from the beginning. As a consequence, passive NPV does not account for the flexibility that exists in most cases to decide whether to invest, wait, leave the project, increase or decrease the amount to invest, among other alternatives. In reality, in most cases, the investor will have the chance to introduce changes according to the information she gathers once the project starts. This flexibility is not captured by the passive NPV approach. ROA, instead, accounts for it properly and correctly prices the project by ruling out arbitrage opportunities. According to ROA, the value of the project or company will be its value without flexibility plus the value of the real options it offers.

A1. *The Underlying Asset for the Growth Option and its Stochastic Process*

In the case of this firm subject to Creative Destruction, its value depends exclusively on the value of a single R&D project. If this value is measured by traditional methods such as passive NPV, commitment to certain investments, at determined dates, is assumed from the beginning. Clearly this approach is not satisfactory for firms in growth industries. There is a lot of uncertainty that is not captured by the passive NPV approach, mainly, the time when innovation may occur and how drastic it is. For this kind of firms I suggest the use of the CD-ROA instead. This approach accounts for this uncertainty properly since, contrary to commitment to determined investments, it

considers a real growth option according to which the firm will make the necessary additional investments to producing and marketing the product conditional on success innovating.

The underlying asset – S - for this growth option is the project's value without flexibility. In order to value this growth option, it is necessary to define which is the stochastic process its underlying asset follows. According to the CD-ROA, it follows a jump-only stochastic process as shown in equation (1):

$$dS = (J - 1)S\,dq + (Y - 1)S\,d\pi \qquad (1)$$

where:

J : size of the jump in S when the expected monopolist innovates,

q : a Poisson process which depends on λm, the probability of the expected monopolist innovating,

Y : size of the jump in S when the challenger innovates, and

π : a Poisson process which depends on λc, the probability of the challenger innovating.

This jump-only stochastic process can be used to model the value of a firm subject to creative destruction which can be explained as follows. Firstly, the firm enters into a new patent race and invests accordingly to an R&D expenditure plan. There is no uncertainty about this plan. The uncertainty comes from the probability of making a "drastic innovation", which is a technological uncertainty. If the firm succeeds in innovating, the value of the underlying asset, S, "jumps" since this firm may become the

new monopolist and exploit the corresponding exclusive market power by producing and marketing the innovation. The proportional change in the asset's value is $\xi = (J - 1)S$ meaning that when S jumps, its value changes to SJ. J is a random variable itself, independent from S, with distribution $ln\, J \sim \phi(\mu, \sigma)$.

In this process of creative destruction, another jump may occur when the challenger firm wins the race by innovating first or introduces a "drastic innovation" which puts an end to the previous firm's monopolistic power. In this case, the proportional change in the asset's value is $\gamma = S(Y-1)$, meaning it will jump to a scrap value SY, since the expected monopolist is forced to leave the market. After that, it may decide whether to participate in a new technological race which starts immediately after the challenger firm innovates. I assume Y constant but it can be a random variable as well.

As a monopolist, this firm enjoys an exclusive market power which eliminates the uncertainty coming from market competition since it can set the price in the market. At the same time, since the firm is not subject to market risk, the only risk it faces is a technological uncertainty. This type of uncertainty affects this firm only, thus it is a non-systematic risk which may be diversified away -and should not be priced by the market- by means of structuring a well-diversified portfolio which includes this project along with other assets. This technological risk can be modeled based on stochastic continuous time Poisson processes as it will be explained next.

A Poisson distribution defines the cumulative probability of n events occurring in a period of time Δt in the following manner:

$$f(n) = \frac{e^{-\lambda \Delta t} (\lambda \Delta t)^n}{n!} \tag{2}$$

For the case of small time intervals when $\Delta t \rightarrow dt$, those terms involving $(dt)^2$ and higher exponents can be ignored, therefore:

Prob [no events occur in the time interval $(t, t + dt)$] = 1 - $\lambda dt + O(dt)$

Prob [one event occurs in the time interval $(t, t + dt)$] = $\lambda dt + O(dt)$ (3)

Prob [more than one event occurs in the time interval $(t, t + dt)$] = $O(dt)$

where $O(dt)$ is the asymptotic order symbol and λ is the mean number of events (*drastic innovations*) per unit time.

Being both q and π Poisson processes, the cumulative number of "jumps" in the asset price and, based on the previous discussion, dq -and $d\pi$- can be defined, approximately, as:

$$dq = \begin{cases} 0, probability(1 - \lambda dt) \\ 1, probability(\lambda dt) \end{cases} \tag{4}$$

Thus, there is a probability $\lambda\, dt$ of a jump in S in a time-step dt. The rate λ at which an individual firm discovers and successfully markets new products is either treated as exogenously given or as a deterministic function of the firm's expenditures on R&D by most authors (Segerstrom (1990)). Later on, I will model λ as a function of the firm's R&D.

The final process for S is a jump-only stochastic process defined by Cox and Ross (1975) as follows: "A jump-only process follows a deterministic movement upon which are superimposed discrete jumps. A jump process has sample paths which are discontinuous with probability one, while those of a diffusion process are continuous with probability one". The diffusion process is the limiting case for the jump process when innovations occur continuously. In the CD-ROA the stochastic process that S follows depends exclusively on the two sources of jumps described above.

Let $f(S)$ be a function of S, the underlying asset's value. For $f(S)$, the change in function value, conditional on the occurrence of an event, is $[f(S+\xi)-f(S)]$ and the expected change in function value is equal to:

$$E[f(S+\xi)-f(S)] = \lambda\, dt\, E[f(S+\xi)-f(S)] + (1-\lambda dt)[0] = \lambda\, dt\, E[f(S+\xi)-f(S)]$$

$$E[f(S+\xi)-f(S)] = \lambda\, dt\, E[f(S+\xi)-f(S)] \qquad (5)$$

If the jump risk is non-systematic, it is possible to take expectations without pricing the risk. The expected squared change in function value is different from zero, therefore, the expectations will not be redundant. Finally, the timing of the jump is assumed to be independent from the level of S (Shimko (1992)).

The version of the Ito's lemma for the jump-diffusion stochastic process is:

$$f = f(S, t, q)$$

$$df = f_S\, dS + f_t\, dt + \tfrac{1}{2} f_{SS}\, (dS)^2 + [f(S+\xi) - f(S)]dq \qquad (6)$$

and for a jump-only stochastic process without drift, the change in the function value would be:

$$df = [f(S+\xi) - f(S)]dq \qquad (7)$$

As explained above, there are two different sources of jumps in this creative destruction process. When S jumps, it either goes from S to SJ with probability λ_m or to SY with probability λ_c. Additionally, if $f = \ln S$, then:

$$d\ln S = [\ln(SJ) - \ln(S)]dq + [\ln(SY) - \ln(S)]d\pi$$

$$d\ln S = (\ln J)dq + (\ln Y)d\pi \qquad (8)$$

If $\xi = S(J-1)$, conditional on the occurrence of a jump J, the expected capital gain as a percentage of the asset price is:

$$E(J-1) = k,$$

and the expected capital gain (loss) in a time interval dt is:

$$\lambda_m\, dt * k = k\, \lambda_m\, dt \quad \textit{(capital gain (loss) times the probability of a jump J)}$$

Also, if $\gamma = S(Y - 1)$, conditional on the occurrence of a jump Y, the expected capital gain as a percentage of the asset price is:

$$E\,(Y - 1) = h,$$

and the expected capital gain (loss) in a time interval dt is:

$$\lambda_c\, dt * h = h\, \lambda_c\, dt \quad \textit{(capital gain (loss) times the probability of a jump Y)}$$

Therefore,

$$E\,(dS) = [\, k\, \lambda_m + h\, \lambda_c\,]\, S\, dt \tag{9}$$

and

$$E\,(dS / S) = [k\, \lambda_m + h\, \lambda_c]\, dt \tag{10}$$

$$E\,(d\ln S) = \lambda_m\, dt\, E(\ln J) + \lambda_c\, dt\, E(\ln Y) \tag{11}$$

Based on the above, the stochastic process that S follows in a Creative Destruction process is as shown in equation (1):

$$dS = (J - 1)S\, dq + (Y - 1)S\, d\pi$$

and,

$$d\ln S = (\ln J)\, dq + (\ln Y)\, d\pi$$

as it was derived above in equation (8), where dq is a Poisson process which is equal to one with probability λ_m and zero with probability $(1 - \lambda_m)$. λ_m is the probability, per unit time, i.e. one year, of innovation by the expected monopolist. $d\pi$ is another Poisson process which is equal to one with probability λ_c and zero with probability $(1 - \lambda_c)$. λ_c is the probability of the challenger firm innovating.

Both, λm and λc, depend on the corresponding firm's level of investment on R&D –as a proportion of the total amount of investment required to producing, and marketing the product- in the following way:

$$\lambda_i = \lambda(R\ \&\ D_i) = (R\ \&\ D_i)^{b_i} \qquad bi < 1 \text{ and constant}$$

meaning that the expected number of "drastic innovations" that each firm can introduce in the market is a concave function of R&D, therefore, the probability of innovation increases by less as larger R&D investments are put in place. Firm *i* expends R&D*i dt* between time *t* and *t* + *dt*. *bi* is a parameter that measures the efficiency of such investment.

A2. *The Growth Option*

The value under ROA of a firm subject to Creative Destruction is the sum of the project without flexibility and a growth option, *G*. Based on this real option, the firm may defer its decision to invest until it discovers a new product, which can be considered as a "drastic innovation", instead of committing itself to large investments - such as plant and equipment - from the beginning. Innovation happens at an uncertain time *t*. If there is a drastic innovation by this firm, its value will jump. If the level of this jump is greater than the value of the investment required to producing, and marketing the product, the firm will exercise its option. By doing so, it exploits the exclusive market power guaranteed by its monopolistic position. The amount of investment necessary to exercise

the option is called the exercise price *X*. Therefore, the value of the growth option *G* at *t = 0* is equal to the present value of its expected payoff:

$$G(t=0) = \exp(-rf * t) * [\hat{E}(t=0)[Max(St(\lambda m, \lambda c) - X, 0)]] \qquad (12)$$

where $\hat{E}$ corresponds to equivalent Martingale expectations. If there is no innovation, the innovation is not drastic, or the challenger wins the technological race, the expected monopolist may abandon the project and move on to a new project, a new patent race. The value of the firm, *V(t=0)*, will be the sum of the project's value without flexibility represented by *S(t=0)* plus the value of the growth option *G(t=0)*:

$$V(t=0) = S(t=0) + G(t=0) \qquad (13)$$

A3. *The Discount Rate for The Growth Option's Expected Payoff*

The question remains of which is the adequate rate of return to discount the expected payoff offered by the real option. Merton (1976) found an analytical solution for the jump-diffusion process when the risk of a jump is non-systematic. The presence of this non-systematic risk does affect the equilibrium option price and should not be ignored. However, if this risk may be diversified away, say by conforming a well-diversified portfolio as defined by Ross (1976) on its Arbitrage Pricing Theory –APT model-, then the equilibrium option price can be computed by using the Black-Scholes formula replacing r_f by $(r_f + \lambda)$.

In a Creative Destruction process, the jump risk is non-systematic since it depends only on the technological uncertainty that surrounds the project and it affects the firm subject to this process exclusively. Being that the case, this risk may be diversified away by means of structuring a well-diversified portfolio. On the other hand, there is no market risk either since the firm has an absolute market power, as explained above. Therefore, I conclude that the appropriate rate of discount for the option expected payoff is the risk-free rate r_f.

Some final aspects of the CD-ROA need to be considered. Firstly, the time between the beginning of a patent race and an innovation is called period. The length of each period is random, because of the stochastic nature of the innovation process. Secondly, each monopolist's objective is to maximize the present value of profits over the period following the innovation, since the monopoly power will not last forever. Immediately the firm innovates, another patent race starts, and it is expected that another drastic innovation will occur putting an end to its market power. Another firm will take the previous monopolist's place. Once it occurs, the project will not produce further cash flows, thus no more value will be added to this firm's value.

B. *Monte Carlo Simulation*

In this section I apply the CD-ROA to a firm subject to Creative Destruction using the Monte Carlo method. In Maya (2003) I concluded that this is a numerical method which has the appealing characteristics of being accurate once variance reduction techniques are put in place plus being flexible to handle complex cases involving jump stochastic

processes, stochastic volatility, and stochastic exercise price. Since applying the CD-ROA involves simulating a jump-only stochastic process, Monte Carlo is an appropriate method for this purpose.

According to (8), the stochastic process *ln S* follows is:

$$d\ln S = (\ln J)dq + (\ln Y)d\pi$$

This process can be approximated by:

$$d\ln S = \ln\frac{S_t}{S_{t-1}} = (\ln J)dq + (\ln Y)d\pi \qquad (14)$$

Using Monte Carlo, *n* paths of asset prices are simulated as follows:

$$S_t = S_{t-1} * e^{[(\mu-\frac{\sigma^2}{2})+\sigma Z]*Dummym} * e^{[\ln Y]*Dummyc} \qquad (15)$$

where Z is a normal random variable. *Dummym* is one when there is a jump *J* and zero otherwise. The probability of a jump *J* in a period of time *dt* is $\lambda_m\, dt$. Then, *Dummym* will be one when the value of a simulated uniformly distributed random number is less than or equal to $\lambda_m\, dt$ and zero in the opposite case. μ and σ are the mean and standard deviation of this jump *J*, a process that is assumed to follow a lognormal distribution. On the other hand, *Dummyc* takes a value of one when there is a jump *Y* and zero otherwise.

It will be equals to one when the value of a simulated uniformly distributed random number is less than or equal to $\lambda c\, dt$.

The *n* paths of *S* are simulated up to a time period *T* which covers the average time for a "drastic innovation" to take place in the industry. Whenever a *Dummym* equals one is found on each path, the asset price jumps. At that time, depending on the size of the jump and if the corresponding value reached by *S(t)* is greater than the value of the exercise price –*X*- as defined above, the firm exercises the option, and the option payoff is discounted at the risk-free interest rate. Otherwise, the payoff from the option on that path is zero. The payoff will also be zero if the challenger innovates first preempting the expected monopolist in that case. The expected value of the growth option, *G*, will be the average of the present value of all these payoffs. Finally, the value of the firm will be the sum of the project's value without flexibility – *S (t=0)* - and the value of the growth option *G(t=0)*.

According to the CD-ROA, the main driver of firm's value is its expected innovation. In the same sense, the greater risk this firm faces is having the challenger preempting it by innovating first. In consequence, there is a clear interaction between innovation by the firms involved in this technological race. Since the probability of innovation depends on both, the amount each firm invests on R&D and the efficiency of its research, the decisions taken on this regard by the competing firms will be reflected on their value.

In this model of Creative Destruction, the probability of innovation - λ - is a concave function of R&D:

$$\lambda_i = \lambda(R\&D_i) = (R\&D_i)^{b_i} \qquad bi \text{ is constant and } bi < 1$$

In order to analyze a base case, I use parameter values from previous studies on R&D and innovation, and from the Pharmaceutical and Biotechnology industries which are supposed to reflect properly the performance of growth industries. A value of one-half for parameter *b* is suggested by Darby, Liu, and Zucker (1999) where they relate innovation to a variable called *ties*[4] which is a proxy for more efficient R&D. Since the average time for the discovery of a new drug in the Biotechnology and Pharmaceutical industries is ten years, in one year the probability of a discovery is $\lambda i\ dt = .1$. Therefore, (*R&Di*) will be equal to .01. μ and σ are assumed to be equal to the ten years mean and standard deviation of the Nasdaq Biotechnology Index, which are around 13% and 35%, respectively. The average risk-free rate for the last ten years is approximately 4.5%. (Appendix A explains these parameter values for the base case in more detail).

In the base case, both firms are assumed to invest the same amount in research with a ratio of *R&D/X* equal to .01. Also, both firms are equally efficient on research, with $bm = bc = ½$. The ratio S/X is supposed to be 1.25 in this case –close to the actual ratio from the case study that it will be discussed later-. The firm's value given by the CD-ROA in the base case is equal to 1.14. In other words, if investors properly account for the fact that this firm is subject to creative destruction –drastic innovation and temporary

monopoly- and for the growth option the firm has, they should pay 14% more for this firm over what is predicted by the passive NPV approach.

The Creative Destruction – Real Options approach gives a higher valuation than this last method because it incorporates the value of the growth option the firm has. Additionally, it properly values such option by recognizing that the value of its underlying asset follows a jump-only stochastic process instead of a diffusion one -commonly assumed process for *S*-. As Cox and Ross (1975, p.154) wrote: "the option valuation problem is really equivalent to the problem of determining the distribution of the stock variable, *S*". The CD-ROA is able to explain the high prices investors pay for a share of one of these firms. It proves that it is not a case of overpricing but recognition of the large growth potential of firms which are part of highly innovative industries as it will be shown in the following case study on the value of a biotechnology firm.

II. Case Study: Assessing the Value of a Biotechnology Start-Up Using the CD-ROA

"Deals have started trading on best-case scenarios".

Fitzsimmons (Prudential Securities) after
Gilead Sciences Initial Public Offering in 1992[5].

More than ten years after the above comment and motivated by a recent rally on Biotechnology market prices, Morgan Stanley advises its clients to invest in "high-quality, later-stage biotech names with top and/or bottom line growth" (WSJ (2003)). In general, the valuation of these companies appears to be overpriced in terms of traditional

methods such as discounted cash flows. They require large investments in R&D, depend on the success of clinical trials and on the Food and Drug Administration (FDA) decisions, and just a few of them show profits. Additionally, when these companies become public, their products are in early stages of development, consequently, there is much uncertainty around its value.

Although the Biotechnology industry is more than twenty years old, the prices of companies in this industry still present high volatility, showing investors attitude towards biotech firms fluctuates over the years, not necessarily depending on the general market behavior. For instance, in 2001 and 2002 –when the U.S. stock market was bearish- biotechnology attracted more investment than in the entire five year period from 1994 to 1998, a period characterized by a booming market[6].

How could the high valuations that are frequently encountered in this industry be explained? Generally, the value of investments in start-ups and high growth businesses is difficult to assess because payments are far in the future and its occurrence is uncertain. Traditional methods such as the Net Present Value fails to account for three drivers of value for highly innovative industries: intellectual capital as the engine of innovation, market power as the expectation of monopolistic power when innovating, and a growth option which may be exercised in the case of success innovating. These drivers of value are properly accounted for by the CD-ROA as it was discussed previously.

This Case Study applies the CD-ROA to a real biotechnology firm, Gilead Sciences Inc. For that purpose, I start discussing the characteristics of the industry, the technology, and the product, which allow me to use such approach in this case.

A. *Biotechnology and Antisense Technology for Drug Discovery*

The Biotechnology Industry Organization –BIO, henceforth- defines biotechnology as "the use of the cellular and molecular processes to solve problems or make products. Included in this definition of the industry are the firms that use cells and biological molecules for applications in medicine, agriculture, and environmental management" (BIO (2000)).

This industry has become the focus of attention of politicians as well as investors because there are many expectations about its potential to improve the quality of life, increase agricultural productivity, and generate a safer environment. Also, from an economic point of view, it gets great attention due to its fast growth –the industry has more than tripled in size since 1992, with revenues increasing from $8 billion in 1992 to $34.8 billion in 2001. In the same period, employment doubled to 191.000. It is one of the most research-intensive industries in the world; only in the U.S. it spent $15.7 billion on R&D in 2001. In U.S. there are a total of 1,457 firms from which 342 are publicly held. Market capitalization was $206 billion as of mid-April 2003. The industry has approximately one hundred fifty five biotech drugs and vaccines in the market with more than three hundred and seventy in clinical trials. Total patents granted per year increased from 1,500 to around 14,000 in the period 1985 – 2000[7].

The larger group of biotech firms is focused on therapies for human diseases. Particularly, the deciphering of the human genetic code has pushed a fast development of genetic drugs. There are two main categories of therapies based on this kind of drugs: gene therapy which involves inserting new genes into cells to produce therapeutic proteins in the body and nucleic acid-based therapy or code blocking which switches off genes so that they stop making harmful proteins. Researchers talk of total sales of genetic drugs running into tens of billions of dollars within twenty years, although such estimates are highly speculative[8].

There are three principal strategies in the development of products for nucleic acid-based therapeutics: Antisense, Triplex, and Ribozyme technologies. Exhibit B1 shows the description of each one, its major therapeutic targets, and the name of the companies competing in each technological race. From all these three technologies, this chapter focuses on the oldest one, the antisense technology, and the competition that takes place among the antisense firms to develop new drugs against HIV/AIDS[9].

In 1980 AntiVirals Inc., now AVI BioPharma Inc., became the first antisense firm, but it was not until 1986, after Dr. Zamecnik published a paper showing that the antisense strand could interfere in the life cycle of the AIDS virus, when research on this technology really took off. Mainly four companies started to compete on the development of antisense drugs against viruses, having HIV/AIDS as its natural target. Gilead Sciences Inc. in 1987, Isis Pharmaceuticals Inc. in 1989, and Hybridon Inc. in 1990, joined AVI BioPharma Inc. in a technological race to discover the first antisense compound to fight HIV/AIDS.

HIV/AIDS captured the attention of the antisense companies because at the end of the eighties it had become a major worldwide epidemic[10]. AIDS is caused by the human immunodeficiency virus (HIV). By killing or damaging cells of the body's immune system, HIV progressively destroys the body's ability to fight infections and certain cancers. Since the epidemic began, more than sixty million people have been infected with the virus. HIV/AIDS is now by far the leading cause of death in sub-Saharan Africa, and the fourth biggest global killer. In 2001, the epidemic claimed about three million lives[11].

With the aim of fighting HIV/AIDS, a group of scientists founded Gilead Sciences, Inc. in 1987. This company, located in Foster City, California, has focused its research on the development of antisense compounds against viruses, specifically HIV. Exhibit B2 shows the market price of its stock from the time of its inception up to its IPO. The last value of $214.5 millions is computed based on the offer price for the IPO, not the price actually achieved by the company of $289.6 millions, after a successful public offer which made an investment banker exclaim that "Deals have started trading on best-case scenarios". In what follows next I apply the CD-ROA to explain why investors paid 35% more than the offer price for Gilead Sciences when it became public in January 22, 1992.

B. Valuing Gilead Sciences Inc. Using the CD-ROA

Valuing Gilead Sciences on the basis of its passive NPV is inadequate. Such valuation accounts neither for the fact that this company is subject to a creative destruction process

nor for the growth option the firm may exercise if it succeeds innovating. Omitting these facts results in undervaluing this firm while the CD-ROA accounts properly for them resulting in a better estimation of this firm's value as it is discussed next.

Gilead Sciences (Gilead henceforth) is subject to a creative destruction process since it is in a patent race against Isis Pharmaceuticals Inc. (Isis), AVI BioPharma Inc. (AVI BioPharma), and Hybridon Inc. (Hybridon) to develop the first antisense drug against HIV/AIDS, in a way that the first innovating firm becomes a monopolist in the market. Immediately after that, another patent race starts where the next innovating firm takes the previous monopolist's market power away. Permanently, some value is created but, at the same time, some is destroyed.

This patent race is "memoryless" as named by Tirole (1988), meaning that all the firms in the market start from the same point. Past R&D experience or expenses do not affect the result, only the current R&D expenses determine the probability of success in innovation. The CD-ROA presumes a single expected innovation, a drug against HIV/AIDS in this case, produced by means of a single R&D technology, the antisense technology, by a profit maximizing firm. The cost function is assumed to be the same for all firms involved in the patent race.

Another assumption of the CD-ROA is that innovation is always "drastic" in the sense that the product developed by the expected monopolist guarantees absolute market power to the innovating firm. The discovery of an antisense drug for HIV/AIDS would be considered a drastic innovation since it clings to bad proteins in a much effective way

than most current drugs do with the additional advantage of not producing the unwanted side effects characteristic of current drugs.

The CD-ROA also accounts for a growth option, which also adds value to the firm. This option may be exercised in the case of innovation if the change in the firm's value is larger than the additional investments required to producing the innovation. The underlying asset to this option - *S* - is the current value of Gilead's research project without flexibility. This value follows a jump-only stochastic process since market risk is ruled out by the expectation of an exclusive market power, and the only uncertainty this firm faces is the technological risk of innovating first or being defeated in this technological race.

B1. The Case of Gilead Sciences: Assessing Parameter Values for the CD-ROA

The first input value required by the CD-ROA is *S*. I take the offer price for Gilead's IPO as an approximation to such value since it is set by the investment banker based on the valuation performed to the firm, which I assume it was done –at that time- using traditional valuation methods which do not account for flexibility. The offer price was $15, thus the value of the company at that price, including the new shares issued in the IPO, was $214.500.000[12]. However, the offer price usually includes a discount to attract investors which is typically 10%[13], thus the value of Gilead would have been $235.95 millions.

I also computed *X*, the exercise price for the growth option. It is the amount of additional investments in plant, equipment, and working capital necessary to produce the new drug. There is no information about an estimation of this amount for the industry, however, I found some evidence from the same firm under study and from Agouron Pharmaceuticals, another biotechnology firm which was studied by Kellogg, Charnes, and Demirer (2002).

In the case of Gilead Sciences, producing Viread, its successful drug against HIV/AIDS, required additional investments of 27% of the increase in revenues from 2001-2002 (See Appendix B, Exhibit B3.2: Gilead Sciences Balance Sheet and Exhibit B4.2: Consolidated Statement of Operations data). A similar percentage –22%- was required by Agouron Pharmaceuticals when it started producing Viracept, the previously successful drug for HIV/AIDS. In the period 1997-1998, Agouron's total revenue increased by $335 millions requiring $74 millions in additional investments. (See Appendix B, Exhibits B5.1 and B5.2 for Agouron Balance Sheet and Consolidated Statement of Operations data). Based on the previous evidence, an estimate for *X* of 25% of the expected additional revenues will be used in this case. Kellogg, Charnes, and Demirer (2002) cite data from Myers and Howe (1997) on expected revenues from new drugs as shown in Table I.

Table I
Expected Revenues from New Drugs

	Peak Annual Revenue	Probability
BREAKTHROUGH	1,323,920	10%
ABOVE AVGE	661,960	10%
AVGE	66,200	60%
BELOW AVGE	7,440	10%
DOG	6,620	10%
E [REVENUE]	**239,714**	

Myers and Howe (1997)

A drastic innovation corresponds to a breakthrough drug. Exhibit B6 shows the expected revenue generated by the sales of a breakthrough, and the additional investment required to produce it computed as a 25% of this revenue. The exercise price of the growth option is the present value of this investment: $189.52 millions.

In the CD-ROA mainly two factors determine the success in this technological race: the amount of R&D each firm is willing to invest and the efficiency of such investment. Average industry values for these parameters are provided by Kellogg, Charnes, and Demirer (2002)[14] where they show that, for the discovery phase, the average investment is $2.2 million, therefore, the average ratio of $R\&D / X$ equals .0116. Also, a value of b = ½ was suggested by Darby, Liu, and Zucker (1999), therefore the probability of discovery is $\lambda = (R\ \&\ D / X)^{1/2} = .1077$ per year, meaning that the average time to discover a drug is around ten years[15].

In order to compute the amount of R&D as a proportion of *X* for the firms participating in this race, I use the actual firm's expenses on R&D in 1992[16] as a proxy to the expected expenses, assuming that this was, probably, the information available to investors at the time of Gilead's IPO. Table II shows the *R&D / X* ratio for each firm[17]. See Appendix B, Exhibits B7, B8.1, and B9 for the Consolidated Statement of Operations Data of Isis Pharmaceuticals Inc., Hybridon Inc., and AVI BioPharma Inc., respectively.

Table II
R&D Expenses as a Proportion of the Exercise Price of the Growth Option

FIRM	R&D (R&D expenses / X)
Gilead Sciences Inc.	0.0720
Isis Pharmaceuticals Inc.	0.1261
Hybridon Inc.	0.0467
AVI BioPharma Inc.	0.0039
Total Challengers	0.1767

Clearly, the greater the amount of investment the expected monopolist is willing to make, relative to its challengers, the higher its probability of becoming the next monopolist. In this case, Gilead is investing more than Hybridon and AVI BioPharma combined, but less than Isis, giving this last firm an advantage in this race.

The other determinant of success in this technological race is the efficiency of the investment in research. Measuring efficiency is a difficult task in general, but even more for start-up firms which usually are on early stages of development of their products. They do not show profits, revenues are very low, and sometimes they do not have any

patents, as it is the case under analysis. However, two different ways to assess efficiency will be proposed next, recognizing that the subject calls for additional research.

The first methodology accounts for the number of patent applications filed up to the time of the IPO. It would be preferable to consider the patents approved since there is no guarantee that an application would translate into an actual patent. However, none of these firms had any patents approved at the time of this analysis. Before January 1992, Gilead and Isis had filed for ten applications each, Hybridon just for one, and AVI BioPharma had zero applications[18]. In the CD-ROA, a b = ½ represents the average efficiency, which seems to be the efficiency of Gilead and Isis, that is, ten patents filed per company. If the technological race is defined among all four companies, Gilead's efficiency is equal to the average one and the other three companies combined are 10% more efficient with eleven patent applications. This greater efficiency translates into a lower *b(challenger)* = .478, and a higher λc = .118, that is, the probability of success per period for the challenger is 10% higher than in the base case[19].

On the other hand, there are reasons to argue that the real competitors in this race were Gilead and Isis only. AVI BioPharma investments in R&D were very low until 1997[20] and Hybridon was recently founded in 1990. By January, 1992, only Gilead and Isis had expectations of filing an Investigational New Drug (IND) application[21]. According to this argument, and based on the number of patent applications filed by each company, both are equally efficient and b = ½ for both.

Another approach to measure the efficiency of R&D is computing the ratio of revenue to R&D expenses as it is shown in Table III[22]

Table III
Revenue to R&D Expenses Ratio

FIRM	***Gilead***	***Isis***	***Hybridon***	***AVI BioPharma***
Revenue/R&D	0.40	0.54	0.07	0.03

Efficiency in terms of this ratio provides another argument to support that although apparently there were four firms competing in this race, the real competition was between Gilead and Isis since the ratio for Hybridon and AVI BioPharma is close to zero. Based on the ratio shown above for Gilead and Isis, it is clear that Isis' research was more efficient. If a *Revenue / R&D* ratio of ½ is taken as the average[23], Gilead will be 20% less efficient and Isis 8% more efficient than the average case, therefore b *(Gilead)* = 0.55 with $\lambda_m = 0.086$ and b *(Isis)* = 0.482 with $\lambda_c = 0.116$.

In relation to the other parameter values, I use for the risk-free rate - r_f - the interest rate on the 10-year Federal bond which was 7.03% in January, 1992. This approach also requires data on the distribution of the size of the jump, J, where $\ln J \sim \phi(\mu, \sigma)$. As a proxy for μ and σ I take the mean and standard deviation of the NBI in the period November 1st, 1993 until June 2, 2003, and those are $\mu = 12.77\%$ and $\sigma = 35.74\%$.

Finally, for the scrap percentage, I assume 80%, meaning that when another company preempts the monopolist, this last one may still get some value by selling its assets and recovering at least 80% of their value at that time.

B2. Simulation and Results

In order to value Gilead, I use the Monte Carlo method to simulate the value of the firm *V(t=0)* following the methodology explained above. For this purpose, three different cases are analyzed. The first one considers a race of Gilead against the set of the other three competitors. This last group is 10% more efficient in terms of the number of patent applications and it also invests more on research than Gilead. If that is the case, the value of the company at its IPO should have been around $201.7 millions. Exhibit B10 shows the parameter values used to simulate each case.

The other two cases are based on the arguments given above according to which the actual race was between Gilead and Isis only. If only these two firms are considered, they are equally efficient in terms of the number of patent applications, but Isis is investing more in research. In this case, the value of Gilead should have been around $267.9 millions. Finally, a third case considers the race of Gilead versus Isis as well but measures efficiency on the basis of the ratio of *Revenue / R&D*. Isis is more efficient and it also invests more than Gilead, resulting in an estimated value for Gilead of $268 millions.

Gilead's investors actually paid $20.25 for its shares in its IPO, which is 35% higher than the offer price and translates into a market value of $289.6 millions. Comparing this value with the ones estimated by applying the CD-ROA, both the second case and the third case estimate the value in the range of $261 to $274 millions[24]. I conclude that the value of this firm is better explained when the technological race is defined against Isis only. Both methodologies used to measure efficiency give approximately the same estimation. However, I also recognize that this last subject, the measuring of efficiency on research requires further research.

Based on the findings presented above, I conclude that the CD-ROA is able to explain the apparently high price paid by investors at this IPO which made an investment banker exclaim that "deals have started trading on best-case scenarios". Although the price actually paid by investors was somewhat higher than the estimated value, still this approach shows that the success of Gilead's IPO is not due to overpricing but recognition of the value added by two facts not being considered by the traditional valuation method, the passive NPV approach. Those facts are, on one hand, that this firm is under a creative destruction process, which gives it an expectation of becoming the next monopolist, and, on the other hand, that this firm has a growth option which gives it flexibility to make additional investments only in the case of success.

This approach also accounts properly for the probability of preemption by any of the other three competitors, in addition to other determinants of the value of the firm such as the characteristics of the industry that determine the distribution of the jumps size, and

the scrap value in case of preemption. Hence, all cases, not only best-case scenarios, are considered to estimate the value of this firm.

Furthermore, history will prove Gilead's investors were right. In April, 2001, this firm applied for an FDA approval for its antisense drug Viread, after successful clinical trials proving that it is effective against HIV/AIDS. The approval came in December that year. Later, in 2002, the EU approved its sale in Europe as well. Annual revenues from this drug are estimated around $500 millions for 2003. Gilead's stock price has soared since its IPO from $20.25 to $225.56[25] in June, 2003, as it can be seen in Figure 1.

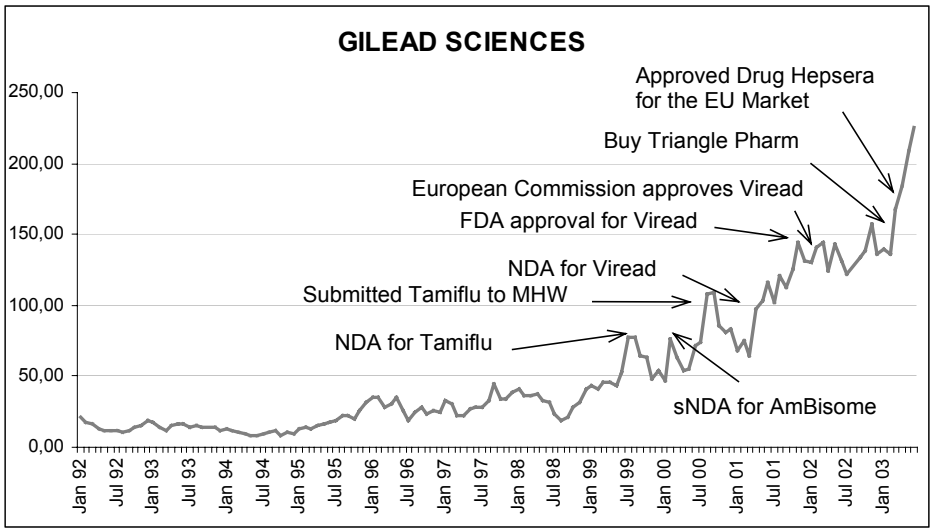

Figure 1. Gilead Sciences Stock Price
NDA: New Drug Application
sNDA: Supplemental New Drug Application
MHW: Japanesse Ministry for Health and Welfare

As for the defeated companies, they had the choice to participate in a new technological race to discover another "drastic innovation" or leave the market. In the case of the main Gilead's challenger, Isis, considered the "Microsoft of Biotechnology" in the nineties, it has concentrated all its efforts in a drug to fight cancer called Affinitak; however, recent news announced that clinical trials of this drug had failed. Isis' stock price reflects that information. Some other relevant news and its effect on the Isis' stock price are shown in Figure 2:

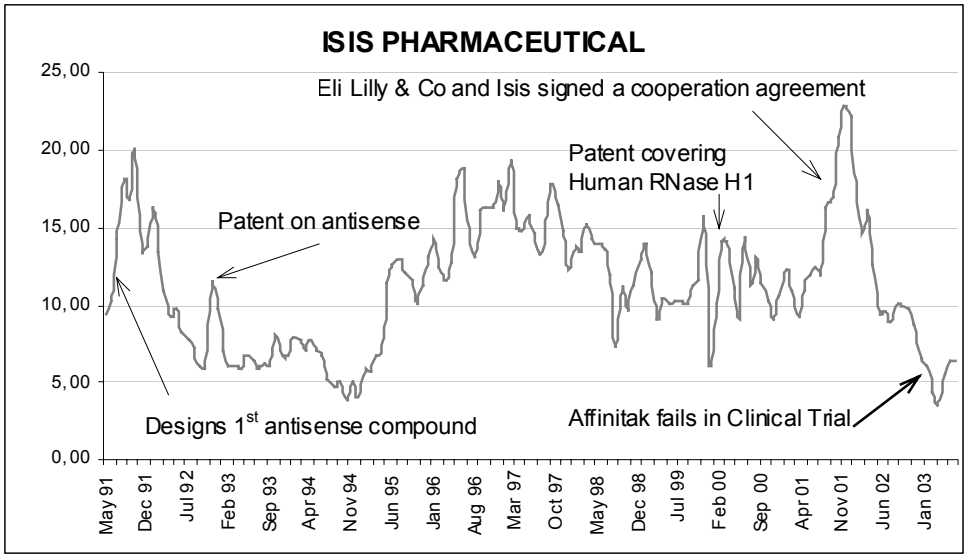

Figure 2. Isis Pharmaceuticals Stock Price

The other two firms, AVI BioPharma and Hybridon, only managed to become public by 1997 and 1998 , respectively. Although AVI BioPharma - founded as AntiVirals Inc - was the oldest of all antisense firms, after more than twenty years its research have produced poor results with only four patents by 2003, compared to 554 of Isis and 106 of Gilead. In 1997, its founder, Dr. Summerton, was forced to resign as CEO and a new management came, licensed new technologies, and now it has completed Phase II for

Resten-NG, an antisense drug against Restenosis[26] as well as for Avicine, a therapeutic cancer vaccine[27].

The fourth firm, Hybridon, is using another three technologies additional to antisense: Synthetic DNA, Cyclicon, and Immunomodulatory Oligonucleotide compounds. Its recent results are based on this last technology and is mainly focused on cancer. In conclusion, as it is predicted by the CD-ROA, all three Gilead's challengers have decided to move to new technological races, either by using new technologies different that the antisense one or aiming to discover different kinds of drugs, - mainly drugs to fight cancer.

III. Conclusions

Schumpeter considered the process of Creative Destruction as the essential fact about capitalism. In this paper, the value of firms subject to a process of this nature has been modeled using CD-ROA. According to this approach, the value of the firm will be the sum of the project's value without flexibility plus the value of the real options the project offers to the firm. Specifically, in the case of Creative Destruction, it accounts for a growth option according to which the firm may decide whether to invest conditional on the discovery of a new product which can be considered as a "drastic innovation", instead of committing itself to large investments such as plant and equipment from the beginning.

The Creative Destruction – Real Options approach gives a higher valuation than traditional methods such as passive NPV because it incorporates the value of the growth option the firm has. Additionally, it properly values such option by recognizing that the value of its underlying asset follows a jump-only stochastic process instead of a diffusion one -commonly assumed process for *S*-. The CD-ROA is able to explain the high prices investors pay for a share of one of these firms. It proves that it is not a case of overpricing but recognition of the large growth potential of firms which are part of highly innovative industries.

In this paper, a case study on the valuation of a Biotech firm is performed applying the CD-ROA. In general, the valuation of biotech companies appears to be overpriced in terms of traditional methods such as discounted cash flows considering that they require large investments in R&D, depend on the success of clinical trials and on the Food and Drug Administration (FDA) decisions, and just a few of them show profits. Additionally, when these companies become public, their products are in early stages of development, therefore, there is a lot of uncertainty around its value.

The approach proposed in this paper is applied to the valuation of Gilead Sciences Inc., and considers three different cases depending on who is the challenger and the way the efficiency of its research is measured. I conclude that the value of this firm is better explained when the technological race is defined against Isis only. Both methodologies used to measure efficiency give approximately the same estimation. However, I also recognize that this last subject, the measuring of efficiency on research requires further research.

Based on the findings presented above, I conclude that the CD-ROA is able to explain the apparently high price paid by investors at this IPO which made an investment banker exclaim that "deals have started trading on best-case scenarios". Although the price actually paid by investors was somewhat higher than the estimated value, still this approach shows that the success of Gilead's IPO is not due to overpricing but recognition of the value added by two facts not being considered by the traditional valuation method, the passive NPV approach. Those facts are, on one hand, that this firm is under a creative destruction process, which gives it an expectation of becoming the next monopolist, and, on the other hand, that this firm has a growth option which gives it flexibility to make additional investments only in the case of success.

This approach also accounts properly for the probability of preemption by any of the other three competitors, in addition to other determinants of the value of the firm such as the characteristics of the industry that determine the distribution of the jumps size, and the scrap value in case of preemption. Hence, all cases, not only best-case scenarios, are considered to estimate the value of this firm.

Furthermore, history will prove Gilead's investors were right. The price of Gilead has soared since its IPO from \$20.25 to \$225.56[28] in June, 2003. As for the defeated companies, they have decided to move to new technological races, either by using new technologies different that the antisense one or aiming to discover different kinds of drugs - mainly drugs to fight cancer - as it is predicted by the CD-ROA.

Appendix A

Parameter Values for the Monte Carlo Simulation of the Base Case

Based on information gathered from the Pharmaceutical and Biotechnology industries and studies on venture capital (Schwartz (2002), Kellogg, Charnes, Demirer (2002), Wolff (2001), Darby, Liu, Zucker (1999)) the parameter values for the basic case are the following:

- S / X =1.25
- r_f = 4.43% which is the ten year average annual rate for 3-months T-bills from 1993 to 2002.
- b = 1/2
- $\lambda i\ dt$ = .1; the average time for discovery of a new drug in the pharmaceutical industry is ten years. Therefore, the probability of a discovery in one year is .1.
- R&Di = .01
- Jump J mean = 12.77%. The mean of the returns on the Nasdaq Biotechnology Index –NBI- from November 1st, 1993 to June 2nd, 2003.
- Jump J volatility: 35.74%. The standard deviation of the NBI, same period.
- Jump Y = .8, the percentage of the firm's value that may be scrapped after being preempted by the challenger. It will vary according to the industry, but it is assumed to be 80% in the base case.
- n = 10.000 is the number of iterations used to run Monte Carlo.
- T = 15 years.

Appendix B

Exhibit B1
Strategies for the development of drugs for nucleic acid-based therapeutics

Technology	Description	Therapeutical Target	Firms
Antisense	Antisense compounds are oligonucleotides. That is, they are short strings (oligomers) of the nucleotides that constitute either DNA or RNA. Their therapeutic potential arises from the fact that these antisense oligonucleotides contain nucleotide sequences that are complementary to specific mRNA sequences, and can block the translation of the mRNA to protein.	Viral infections Inflammatory diseases Cancer therapy	Isis Pharmaceuticals Lynx Therapeutics Gilead Sciences Anti Virals, Inc Hybridon, Inc Enzo Biochem Hoffman-LaRoche Amgen Genta Incorporated
Triplex	The potential for Triplex Technology was first realized at about the same time that Watson and Crick discovered the double helix of DNA, back in the 1950s. Like antisense , triplex technology ultimately prevents the expression of an gene to its protein. But whereas antisense blocks the translation of protein from RNA, triplex technology inserts a third strand of DNA into the target gene to prevent the initial formation of the mRNA , the process known as transcription.	Cancer Viral infections Inflammatory diseases - rheumatoid arthritis	Triplex Pharmaceuticals MicroProbe Corporation
Ribozyme	Ribozymes are unique compounds that are molecules of RNA having enzymatic properties. These catalytic molecules will bind to specific sequences on mRNA and cleave it so that it is no longer functional.	Cancer Chronic viral infections Inflammatory processes autoimmune diseases Rheumatoid arthritis Organ transplant rejection	Ribozyme Pharmaceuticals Immusol, Inc Johnson & Johnson

"Antisense: A Drug Revolution in the Making", Business Week, March 5th, 1990.

Exhibit B2
GILEAD SCIENCES Inc.

Date	Amount raised	Value of Gilead at that time	Investors	Shares sold (millions)	Share value
jun-87	$ 6.100	-	Founders		
aug-87	$ 200.000	$ 810.000	Menlo Ventures	0.7	0.300
aug-88	$ 600.000	$ 3.030.000	Menlo Ventures	0.7	0.900
dec-87	$ 1.200.000	$ 10.260.000	Menlo Ventures	0.4	2.700
oct-88	$ 10.000.000	$ 24.250.000	JH Whitney	2.7	3.750
aug-90	$ 8.010.000	$ 66.600.000	Glaxo Holdings	0.9	9.000
sep-91	$ 20.150.000	$ 97.700.000	JH Whitney	1.9	10.500
jan-92	$ 75.000.000	$ 214.500.000	Public offering	5.0	15.000

Source: Recombinant Capital Inc.
Biotech IPOs Ignite Buying Frenzy
Two Bay Area firms see their stocks soar The San Francisco Chronicle
January 23, 1992

Exhibit B3.1

GILEAD SCIENCES INC 1

(Before business combination with NeXstar Pharmaceuticals)

BALANCE SHEET

(Dollars in thousands)

BALANCE SHEET	**1993**	**1994**	**1995**	**1996**	**1997**	**1998**
ASSETS						
Current assets:						
Cash and cash equivalents			27.420	131.984	31.990	32.475
Short-term	139.353	114.968	128.239	163.979	290.308	247.464
marketable securities						
Accounts receivable						
Inventories						
Other current assets			1.558	4.290	17.960	8.371
Prepaid expenses and other						
Total current assets			157.217	300.253	340.258	288.310
Property and equipment, net			**8.369**	**9.172**	**10.313**	**10.182**
Other noncurrent assets			1.073	1.248	1.498	4.368
Total	**146.809**	**126.602**	**166.659**	**310.673**	**352.069**	**302.860**
LIABILITIES AND						
STOCKHOLDERS' EQUITY						
Current liabilities:						
Accounts payable			2.412	2.501	3.303	3.422
Accrued liabilities			6.152	9.440	18.694	24.283
Deferred revenue			208	527	9.541	3.275
Current portion of capital						
Long-term obligations due within one year			2.906	3.631	1.853	770
Total current liabilities			11.678	16.099	33.391	31.750
long term liabilities:						
Long-term deferred revenue						
Long-term obligations due after one year	1.156	2.479	3.482	2.914	1.331	563
Accrued rent						
Convertible senior debt						
Convertible subordinated debt						
total long term liabilities			3.482	2.914	1.331	563
Stockholders' equity:						
Preferred stock, par value per share					1	1
Common stock, par value per share			24	29	30	31
Additional paid-in capital			265.460	426.577	479.737	489.183
Accumulated other comprehensive income(loss)			167	89	344	43
Accumulated deficit	-28.353	-54.065	-112.754	-134.486	-162.479	-218.554
Deferred compensation			-1.398	-549	-286	-157
Total stockholders' equity	139.402	115.280	151.499	291.660	317.347	270.547
Total			**166.659**	**310.673**	**352.069**	**302.860**

Exhibit B3.1

Notes

*In 1995 fiscal year changes from March 31st to December 31st. In Years 1993-1996 fiscal year ended in March 31st.

On July 29, 1999, The company entered into a business combination with NeXstar Pharmaceuticals, Inc. ("NeXstar"). The business combination has been accounted for as a pooling of interests and our historical consolidated financial statements for all years prior to the business combination have been restated in the accompanying consolidated financial statements to include the financial position, results of operations and cash flows of NeXstar.

Pooling of interests method is used in limited situations in which shares of stock in the two companies are exchanged.

Exhibit B3.2

GILEAD SCIENCES INC 2

(After business combination with NeXtar Pharmaceuticals)

BALANCE SHEET

(Dollars in thousands)

BALANCE SHEET	**1995**	**1996**	**1997**	**1998**	**1999**	**2000**	**2001**	**2002**
ASSETS								
Current assets:								
Cash and cash equivalents				101.136	47.011	197.292	123.490	616.931
Short-term								
marketable securities				247.607	247.383	315.586	459.361	325.443
Accounts receivable							74.228	125.036
Inventories				16.550	20.959	20.562	39.280	51.628
Other current assets				43.090	45.599	48.814		50.000
Prepaid expenses and other				8.506	11.029	11.544	11.400	14.722
Total current assets				416.889	371.981	593.798	707.759	1.183.760
Property and equipment, net				**51.019**	**51.398**	**55.174**	**62.828**	**67.727**
Other noncurrent assets				19.856	13.429	29.127	24.199	36.696
Total	**275.376**	**450.540**	**516.989**	**487.764**	**436.808**	**678.099**	**794.786**	**1.288.183**
LIABILITIES AND								
STOCKHOLDERS' EQUITY								
Current liabilities:								
Accounts payable				7.662	9.481	11.605	19.174	24.406
Accrued liabilities				41.555	30.372	39.244	55.455	72.600
Deferred revenue				3.275	4.833	4.355	3.996	7.692
Current portion of capital								
Long-term obligations due w/in one yr				4.842	3.191	3.034	1.492	194
Total current liabilities				57.334	47.877	58.238	80.117	104.892
long term liabilities:								
Long-term deferred revenue						10.730	7.252	16.677
Long-term obligations due after one year	13.330	18.120	9.658	8.883	5.253	2.238	389	273
Accrued rent				7.848	6.853	5.769	4.591	
Convertible senior debt								345.000
Convertible subordinated debt				80.000	79.533	250.000	250.000	250.000
total long term liabilities				96.731	91.639	268.737	262.232	611.950
Stockholders' equity:								
Preferred stock, par value per share				1				
Common stock, par value per share				42	44	189	193	198
Additional paid-in capital				716.964	749.081	857.847	898.533	950.308
Accumulated other comprehensive income(loss)				-337	-2.527	-901	7.448	2.475
Accumulated deficit				-382.746	-449.232	-506.008	-453.737	-381.640
Deferred compensation --	(3)			-225	-74	-3		
Total stockholders' equity	228.931	374.649	357.726	333.699	297.292	351.124	452.437	571.341
Total				**487.764**	**436.808**	**678.099**	**794.786**	**1.288.183**

Exhibit B3.2

Notes

*In 1995 fiscal year changes from March 31st to December 31st. In Years 1993-1996 fiscal year ended in March 31st.

On July 29, 1999, The company entered into a business combination with NeXstar Pharmaceuticals, Inc. ("NeXstar"). The business combination has been accounted for as a pooling of interests and our historical consolidated financial statements for all years prior to the business combination have been restated in the accompanying consolidated financial statements to include the financial position, results of operations and cash flows of NeXstar.

Pooling of interests method is used in limited situations in which shares of stock in the two companies are exchanged.

Exhibit B4.1

GILEAD SCIENCES INC 1

(Before business combination with NeXstar Pharmaceuticals)

CONSOLIDATED STATEMENT OF OPERATIONS DATA

(in thousands, except per share data)

	1993	1994	1995	1996	1997	1998
Revenues:						
Product sales, net	0	0	0	8477	11735	6074
Contract revenues and royalties	4177	4085	4922	24943	28302	26496
Total revenues	**4177**	**4085**	**4922**	**33420**	**40037**	**32570**
Costs and expenses:						
Cost of product sales	0	0	0	910	1167	594
Research and development	**17987**	**26046**	**30360**	**41881**	**59162**	**75298**
Selling, general and administrative	4377	7639	9669	26692	25472	31003
Total operating costs and expenses	**22364**	**33685**	**40029**	**69483**	**85801**	**106895**
Income (Loss) from operations	(18187)	(29600)	(35107)	(36063)	(457640	(74325)
Interest income, net	4105	3888	3833	15042	18260	18442
Net income (loss)	**(14082)**	**(25712)**	**(31274)**	**(21732)**	**(27993)**	**(56075)**
Basic and diluted Income (loss) per share	(0.88)	(1.37)	(1.65)	(0.78)	(0.95)	(1.85)
Common shares used in the calculation of basic and	16065	18779	18971	27786	29326	30363

Exhibit B4.2

GILEAD SCIENCES INC 2

(After business combination with NeXtar Pharmaceuticals)

CONSOLIDATED STATEMENT OF OPERATIONS DATA

(in thousands, except per share data)

	1997	1998	1999	2000	2001	2002
Revenues:						
Product sales, net	100887	114176	139890	149709	190970	423879
Contract revenues and royalties	31371	36943	29089	45846	42799	42911
Total revenues	**132258**	**151119**	**168979**	**195555**	**233769**	**466790**
Costs and expenses:						
Cost of product sales	21646	23357	29546	33512	43764	69724
Research and development	**112177**	**127773**	**112888**	**132339**	**185553**	**134758**
Selling, general and administrative	70626	78234	78347	82022	125141	181301
Total operating costs and expenses	**220480**	**230631**	**239838**	**247873**	**354458**	**385783**
Income (Loss) from operations	(88222)	(79512)	(70859)	(52318)	(120689)	81007
Interest income, net	20706	21765	16435	17634	25591	22291
Net income (loss)	**(72893)**	**(44758)**	**(66486)**	**(56776)**	**52271**	**72097**
Basic and diluted Income (loss) per share	(1,85)	(1,09)	(1,55)	(0,31)	0,28	0,37
Common shares used in the calculation of basic and	39432	41015	42826	182099	190245	195543

Exhibit B5.1

AGOURON PHARMACEUTICALS, INC.

BALANCE SHEET (000s)	**1986**	**1987**	**1988**	**1989**	**1990**	**1991**	**1992**	**1993**	**1994**	**1995**	**1996**	**1997**	**1998**
ASSETS													
Current assets:													
Cash and cash equivalents				7984	8135	11460	5966	7783	2104	4358	16451	52484	19098
Short-term					9089	1,001	33795	29617	27757	15886	74424	38833	68025
Accounts receivable				471	366	161	228	342	328	344	2966	31975	51341
Inventories												58800	103706
Other current assets				74	146	229	184	242	891	871	1800	2209	5247
Total current assets				8529	17736	12851	40173	35284	31080	21459	95641	184201	247981
Property and equipment, net				**2749**	**3128**	**2821**	**5452**	**6437**	**6098**	**5638**	**6936**	**22613**	**47212**
Total	**92**	**6529**	**8123**	**11278**	**20864**	**15672**	**45625**	**41721**	**37178**	**27097**	**102577**	**266914**	**363337**
LIABILITIES AND STOCKHOLDERS' EQUITY													
Current liabilities:													
Accounts payable				604	469	574	868	1287	1514	5426	6659	28833	44393
Accrued liabilities				140	326	364	303	380	519	683	4327	8889	35356
Deferred revenue				973	1444	2403	3005	2826	6818	5745	13788	27567	23563
Current portion of capital leases				965	584	532	882	858	1190	768	486	2526	15802
Total current liabilities				**2682**	**2823**	**3873**	**5058**	**5351**	**10041**	**12622**	**25260**	**68415**	**120253**
long term liabilities:													
Capital leases, less current portion				400	1141	1179	2126	1351	992	580	501	5940	5892
Accrued rent											1233	1277	1623
total long term liabilities											1734	7217	6915
Stockholders' equity:													
Preferred stock				6551	6551	32780	68809						
Common stock													
Accumulated deficit				9128	15352	22160	31292	(41121)	(50583)	(63522)	(83045)	(125851)	(112697)
Total stockholders' equity	*23*	*6282*	*6337*	*8196*	*16900*	*10620*	*37517*	*33757*	*24852*	*12591*	*75583*	*191282*	*236169*
Total				**11278**	**20864**	**15672**	**45625**	**41721**	**37178**	**27097**	**102577**	**266914**	**363377**

Exhibit B5.2

AGOURON PHARMACEUTICALS

CONSOLIDATED STATEMENT OF OPERATIONS DATA

(in thousands, except per share data)

	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998
Revenues:													
Product sales, net												56969	409298
Contract revenues and royalties			892	1829	2075	3781	5307	8266	16301	26722	40955	65094	38855
Interest			373	740	1274	1014	1540	1704	1350	1239			
License fees											15000	10000	18352
Total revenues	**322,3**	**536**	**1265**	**2569**	**3349**	**4795**	**6847**	**9970**	**17651**	**27961**	**55955**	**132063**	**466505**
Costs and expenses:													
Cost of product sales												24599	172644
Research and development			**3518**	**6190**	**8035**	**9353**	**13142**	**17404**	**23957**	**36317**	**71010**	**108137**	**150657**
Selling, general and administrative			657	912	1384	1880	2519	2127	2961	4358	8082	32941	58012
Interest			126	186	154	183	318	268	195	225			
Total operating costs and expenses			**4301**	**7288**	**9573**	**11416**	**15979**	**19799**	**27113**	**40900**	**79092**	**223177**	**449736**
Loss from operations													
Interest income, net													
Net loss	**(162)**	**(773,1)**	**(3036)**	**(4719)**	**(6224)**	**(6621)**	**(9132)**	**(9829)**	**(9462)**	**(12939)**	**(19523)**	**(42806)**	**13154**
Basic and diluted loss per share	0,1	0,42	1,24	1,77	1,77	1,42	1,47	1,4	1,31	1,77	1,98	3,18	(0,43)
Common shares used in the calculation of basic and	1666	1851	2456	2660	3739	4674	6199	6997	7241	7296	9844	13473	

Exhibit B6
Investments Required to Produce a Breakthrough Drug
(Investment in Plant, Equipment, and Working Capital)

YEAR	1	2	3	4	5	6	7	8	9	10	11	12	13
BREAKTHROUGH REVENUE*	275	275	275	275	775	775	775	1324	1324	1324	1324	1324	1324
INVESTMENTS (millions)	68,75	0	0	0	125	0	0	137,25	0	0	0	0	0
PV (INVESTMENTS)(millions)	**$189,52**												

* Myers and Howe (1997)

Exhibit B7

ISIS PHARMACEUTICALS

CONSOLIDATED STATEMENT OF OPERATIONS DATA

(in thousands, except per share data)

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002
Revenues:													
Research and development revenues under coliaborative agreements	1826	6261	8727	10654	10088	12966	22572	32470	34130	29357	16912	40398	67820
Research and development revenues from afiliates										4402	7967	10561	11942
Gain on sale of investment					3174								
Interest income	132	1782	2089	1486	2251	3001	4012	4067					
Licensing and royalty revenues									5041	166	12376	2316	417
Total revenues	**1958**	**8043**	**10816**	**12140**	**15513**	**15967**	**26584**	**36537**	39171	33925	37255	53275	80179
Costs and expenses:													
Cost of product sales													
Research and development	**4755**	**12381**	**23669**	**25604**	**26468**	**33175**	**45653**	**55940**	**62200**	**66413**	**57014**	**83741**	**124074**
Selling, general and administrative	1689	4399	6657	4809	5981	5402	6246	8078	9511	10571	8644	11061	8547
Interest expense				789	1245	1102	1206	3585					
Total operating costs and expenses	**6444**	**16780**	**30326**	**31202**	**33694**	**39679**	**53105**	**67603**	**76949**	**76984**	**67880**	**99375**	**130992**
Income (Loss) from operations													
Interest income, net													
Net income (loss)	**-4486**	**-8737**	**-19510**	**-19062**	**-18181**	**-23712**	**-26521**	**-31066**	**-42983**	**-59645**	**-53485**	**-46100**	**-50813**
Basic and diluted Income (loss) per share	0,70	0,84	1,51	1,22	0,93	1,10	1,04	1,17	1,6	2,08	1,48	1,7	1,35
Common shares used in the calculation of basic	6451	10355	12892	15685	19542	21514	25585	26456	26873	28703	37023	44109	54480

Exhibit B8.1

HYBRIDON 1

(Before the sale of HSP*)

CONSOLIDATED STATEMENT OF OPERATIONS DATA

(in thousands, except per share data)

	1992	1993	1994	1995	1996	1997	1998	1999
Revenues:								
Research and Development		917	1032	1186	1419	945	1100	600
Product revenue					1080	1877	3254	6186
Contract revenues and royalties					62	48		
Interest income	12	267	135	219	1447	1079	148	215
Total revenues	**12**	**1184**	**1167**	**1405**	**4008**	**3949**	**4502**	**7001**
Costs and expenses:								
Cost of product sales								
Research and development	**8762**	**16168**	**20024**	**29685**	**39390**	**46828**	**20977**	**13090**
Selling, general and administrative	5163	4372	6678	6094	11347	11027	6573	3664
Interest	782	380	69	173	124	4536	2932	750
Reestrucuturing						11020		
Total operating costs and expenses	**14707**	**20920**	**26771**	**35952**	**50861**	**73411**	**30482**	**17504**
Income (Loss) from operations	-14695	-19736	-25604	-34547	-46853	-69462	-25980	-10503
Gain on exchange of 9% convertible subordinated notes payable							8877,00	
Interest income, net								
Net income (loss)	**-14695**	**-19736**	**-25604**	**-34547**	**-46853**	**-69462**	**-17103**	**-10503**
Basic and diluted Income (loss) per share				2,13	(1,93)	(13,76)	(1,67)	(0,93)
Common shares used in the calculation				16195	24261	5050	11859	15811

*In September 21, 2000, Hybridon sold its Hybridon Specialty Products or "HSP" business and assets

Exhibit B8.2

HYBRIDON 2

(After the sale of HSP)

CONSOLIDATED STATEMENT OF OPERATIONS DATA

(in thousands, except per share data)

	1996	1997	1998	1999	2000	2001	2002
Revenues:							
Research and Development	1419	945	1100	600	179	988	29550
Service revenue			375	365	82		
Contract revenues and royalties	62			123	229	577	660
Interest income	1447	1079	148	92	83	134	46
Total revenues	**2928**	**2024**	**1623**	**1180**	**573**	**1699**	**30256**
Costs and expenses:							
Cost of product sales							
Research and development	**33150**	**35326**	**14183**	**5783**	**3620**	**4868**	**7877**
Selling, general and administrative	11347	11027	6573	3664	3184	5051	7054
Interest	34	4278	2820	683	2154	1319	150
Reestrucuturing		10345					
Total operating costs and expenses	**44531**	**60976**	**23576**	**10130**	**8958**	**13000**	**13784**
Income (Loss) from discontinued operations	-5250	-10509	-4028	-1553	5462	2663	
Gain on exchange of 9% convertible subordinated notes payable			8877				
Interest income, net							
Net income (loss)	**-46853**	**-69461**	**-17104**	**-10503**	**-2923**	**-5333**	**16972**

Exhibit B9

AVI BIOPHARMA Inc.

CONSOLIDATED STATEMENT OF OPERATIONS DATA

(in thousands, except per share data)

	1991*	1992*	1993*	1994*	1995	1996	1997	1998	1999	2000	2001	2002
Revenues:												
Product sales, net												
Contract revenues and royalties												
Total revenues					**83**	**28**	**14**	**120**	**17**	**1.297**	**706**	**837**
Costs and expenses:												
Cost of product sales												
Research and development	**725**	**725**	**725**	**725**	**2.098**	**1.730**	**2.737**	**6.307**	**6.672**	**9.268**	**12.751**	**22.414**
Selling, general and administrative					610	614	1.282	1.621	1.745	2.270	3.358	3.764
Total operating costs and expenses	**725**	**725**	**725**	**725**	**2.708**	**2.344**	**4.019**	**7.928**	**8.417**	**11.538**	**16.109**	**26.178**
Acquired in-process research and development								19.473	72			
Income (Loss) from operations												
Interest income, net										1.001	1.001	460
Net income (loss)					**-2.557**	**-2.087**	**-3.616**	**26.734**	**-8.278**	**-9.240**	**-26.925**	**-29.359**
Basic and diluted Income (loss) per share					(0,37)	(0,25)	(0,36)	(2,27)	(0,62)	(0,49)	(1,20)	(1,14)
Common shares used in the calculation of basic and												

Total expenses on R&D until 1997:
9.463.297
Source: 10-K report 1998
Total expenses on R&D until 1995: 2,898,775
*Average R&D for years 1991-1994 based on total R&D accumulated until 1995

Exhibit B10
CD-ROA: Parameter Values
(Millions of U.S. dollars)

CASE 1	
FIRM VALUE	**249,42**
error	2,52
Parameter	***Value***
path *(n trials)*	10000
n steps	40
S0	235,95
X	187,75
r	7,03%
T	10
scrap %	0,8
b (E. monopolist)	0,5
b (challenger)	0,478
RD (E. monopolist)	0,0720
RD (challenger)	0,1767
miu (J)	0,1277
sigma (J)	0,3574

CASE 2	
FIRM VALUE	**283,63**
error	3,71
Parameter	***Value***
path *(n trials)*	10000
n steps	40
S0	235,95
X	187,75
r	7,03%
T	10
scrap %	0,8
b (E. monopolist)	0,5
b (challenger)	0,5
RD (E. monopolist)	0,0720
RD (challenger)	0,1261
miu (J)	0,1277
sigma (J)	0,3574

CASE 3	
FIRM VALUE	**259,72**
error	3,46
Parameter	***Value***
path *(n trials)*	10000
n steps	40
S0	235,95
X	187,75
r	7,03%
T	10
scrap %	0,8
b (E. monopolist)	0,55
b (challenger)	0,482
RD (E. monopolist)	0,0720
RD (challenger)	0,1261
miu (J)	0,1277
sigma (J)	0,3574

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Footnotes

[1] Campbell, J. and C. Knoess. "How to Build a FutureWealth Company, Ernst and Young's Point of View on Value on the New Economy". http://www.ey.com/GLOBAL. Cited in Boer (2002).

[2] Empirical evidence shows appropriability conditions as a source of innovation. If new knowledge can be transmitted to potential competitors at a low cost, the rewards from innovation would not justify innovative effort. This is a problem that predates classical, let alone, neo-classical, economics (H.I.O. p.1090). "Still, many economists agree with Schumpeter that patents, and the concomitant static inefficiency associated with monopoly power, are required to give firms proper incentives to innovate, and that patents promote dynamic efficiency" (Tirole, 1988, p.400).

[3] This rate is usually the after tax cost of capital or WACC, although in some cases, a risk adjusted discount rate is used, without clarity about the criteria for risk adjustment.

[4] The number of prestigious scientists "tied" to the firm.

[5] Investment Dealer's Digest (1992).

[6] http://www.bio.org/investor/signs. (June 26, 2003).

[7] http://www.bio.org/er/statistics.asp and http://www.bio.org/er/BiotechGuide.pdf (Feb. 12, 2004).

[8] Robertson, Stephens & Co. say the U.S. gene therapy market for just three cancers (renal, ovarian, and melanoma) is potentially worth dollars 1.2bn a year –based on a cost of $15.000 per patient. Fresh water in the gene pool / Exploring the role which genetic drugs will play in curing diseases at their source. Financial Times. London. July 21st, 1992.

[9] The antisense drug is a "synthetic strand of genetic material which replicates the second strand of the DNA double helix, called the antisense strand. It sticks to the mRNA like Velcro, and blocks the production of proteins. It is this process, much more precise and foolproof than the tentative way in which most current drugs cling to bad proteins, that hints at so much promise for these synthetic strands, which are known as antisense oligonucleotides, or oligos for short". Antisense: A Drug Revolution in the Making, Business Week, March 5th, 1990.

[10] The first case of AIDS was reported in the U.S. in 1981.

[11] Report on the Global HIV/AIDS Epidemic 2002 http://www.unaids.org/epidemic_update/report_july02/english/contents.html (June 16, 2003)

[12] Exhibit B2 shows the number of shares issued by Gilead Sciences and the firm's value from its inception up to its IPO.

[13] Ivo Welch, a Finance Professor who has studied IPOs extensively, notes that the typical underpricing - the return from the offer price to the price when the market starts trading - is about 10%. http://www.iporesources.org/lebaron.html (Sept. 4th, 2003).

[14] They make assumptions based on previous work by Myers and Howe (1997), Office of Technology Assessment (1993), DiMasi et al. (1991), and Grabowski and Vernon (1994).

[15] Evidence showing that this is the average time required to discover a new drug is cited by Cochrane (2001), Wolff (2001), Schwartz (2002), and Kellogg, Charnes, and Demirer (2002).

[16] The information the potential investor requires is the expected expenses on R&D next period by both the expected monopolist and its challenger. I use the actual value as a proxy for this value.

[17] There is no public information for Gilead Sciences in 1992. R&D expenses on that year were computed based on 1993 data and adjusted to grow at the same average growth that this account showed in the following three years: 33.11%.

[18] U.S. Patent and Trademark Office (PTO). http://www.uspto.gov. (June 27, 2003).

[19] The base case is when these firms invest the average amount of $2.2 million in R&D in the discovery phase.

[20] See Exhibit B9.

[21] Isis filed the first IND application for an antisense drug – ISIS2105- in January 30, 1992. (PR Newswire, January 30, 1992). Gilead filed for GS504 in March, 1992 (Business Wire, March 19, 1992) and for GS393 in September, same year (Business Wire, September 23rd, 1992).

[22] This ratio is the Average revenue / Average R&D for the period 1993-1996 when public information is available for Gilead, Isis, and Hybridon. For AVI BioPharma, the ratio is computed as the average for the period 1995-1996 since public information is available only after 1995.

[23] This ratio was .51 for Isis Pharmaceuticals in the period 1990-1992 (Exhibit B7), for Agouron Pharmaceuticals was .49 in the same period (Exhibit B5.2). There is no information for Gilead in this period. The average revenue / R&D ratio for the industry is another issue that needs additional research.

[24] For a 95% confidence interval. The estimation errors are reported in Exhibit B10.

[25] This price was adjusted for splits. One share of Gilead in 1992 is equivalent to four shares today.

[26] Restenosis occurs when the arteries opened up by angioplasty become blocked again. Like cancer, restenosis involves abnormal cell division (The Register Guard, 2001).

[27] AVI BioPharma, 10k Report, 2002.

[28] This price was adjusted for splits. One share of Gilead in 1992 is equivalent to four shares today.