Financing forefront technology entrepreneurship. 
Issues concerning biotechnology

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Abstract: This paper surveys financial issues that characterise the US biotechnology scenario. They regard public institutions and companies. The financing approaches available to New Biotechnology Firms (NBFs) force them to operate in a weak competitive position vis-à-vis large companies. Allowing NBFs to somewhat uncouple their investment decisions from the impact on company balance sheet, could give a fundamental contribution to enhance their competitive capacity and fully exploit their potential. The scheme of an off-balance-sheet financing is proposed. It is of the type that regulated the Research and Development Project Limited Partnership (RDLP) in the USA till 1986 when its tax benefits were cancelled by the Tax Reform Act. After 1986, NBFs have proposed to financial markets substitutes for RDLPs, which have proved to be much less interesting to investors. Restoring the rules originally governing RDLPs could be a strategically winning move at the present stage of the biotechogenetic revolution in the USA.

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1 The biotechnogenetic revolution

The biotechnogenetic revolution has emerged through a series of progressive discoveries, which are unravelling the complexities of living organisms at the molecular level, and through multi-directional entrepreneurial endeavours to industrially exploit such findings. There is convergence of opinions that the biotechnogenetic revolution will produce changes as sweeping as those of the electronic revolution that started in the 1940s of the last century and, in successive waves, has quickly changed the operational behaviour of mankind and its economic standing.

In the case of biotechnology, though, changes are coming along much more slowly, because of the inherent hurdles in constructing bridges between a knowledge whose complexities are only progressively, and often contradictorily, understood and the capacity of elaborating the instruments (technological and financial) capable of exploiting it economically.

2 The leading position of the USA

The biotechnogenetic revolution, which started in the 1970s and is progressively, though slowly, gaining momentum, has been and still remains the science-pushed offspring of basic and generic applied research carried out mainly in the USA.

In this country, the constant, consistent and efficiently addressed public financial support to basic research has caused an impressive accumulation of knowledge advancements in life sciences. This has been possible because of a network of scientific research centres (universities, public and private institutions of different types including health care) that possess a qualified structural and cultural backbone.

The free framework of action, in which such centres have been operating institutionally, stimulated both constructive interactions among them and competition to obtain funds based on the results of their research achievements. The significant degree of freedom to economically exploit the results of research favoured the support of private capital to such centres and their self-financing as adjuncts to public financing. The defence of the priority rights to research discoveries and findings, by a well designed patent legislation, also helped to position the US research at the forefront of entrepreneurship in life sciences. The commercial potential of such a research has found a natural channel in small dedicated NBFs, which, supported by risk capital, were in many cases formed by university professors and, in general, by scientists involved in the research achievements.

It is worth mentioning a few features of the contribution of other relevant areas of the world to the research that is fuelling the biotechnogenetic revolution.
Though of minor dimension, a highly qualified structure of centres devoted to research in life sciences has been present in the UK, adequately supported by public finance. Probably, a certain limitation of freedom of action and a more bureaucratic system to channel research results into commercialisation caused hiatuses in the pathways of knowledge transmission and utilisation.

This was particularly unfortunate in a country like the UK, where the quality of research is particularly high and the capability of exploiting it industrially is, at least potentially, more adequate than in other European countries.

A typical case has been that of patenting the hybridoma cell fusion technique for producing monoclonal antibodies. These are the facts.

In the UK one of the responsibilities of the National Research Development Corporation (NRDC), a state investment agency, was rights to the fruits of UK university and Research Council research funded by the UK tax payer. UK university and national laboratory inventions were normally patented by the NRDC.

The hybridoma cell fusion technique for producing monoclonal antibodies was invented by Milstein and Kholer at the Medical Research Council’s (MRC) Laboratory of Molecular Biology, Cambridge. In 1975 Milstein sent a copy of his paper to an MRC (not to an NRDC) official but went ahead, nonetheless, with publication in the scientific press in August 1975, so establishing the claim to a scientific discovery. The MRC official eventually passed a message on to the NRDC, 13 months later, in September 1976, with a note apologising for the delay.

Parallel work at the Wistar Institute in Philadelphia, Pennsylvania, enabled Hilary Koprowski and Carlo Croce to obtain US patents for a “Method of producing viral antibodies” and a “Method of producing tumour antibodies”, describing the procedures leading to the production of monoclonal antibodies against viral and tumour antigens. According to the Wistar Institute, the Milstein publications were reviewed by the US Patent and Trademark Office before any patents were granted.

The failure of the MRC to obtain patent protection, for the discovery of the hybridoma cell fusion technique for producing monoclonal antibodies, was an important factor in the decision of the National Enterprise Board (NEB), in 1980, to give a recently founded company, Celltech, the right of first refusal for biotechnology discoveries from the MRC and the university research it funded. By such an arrangement the NEB group had usurped long-standing rights of the NRDC.

Celltech was a joint industry–government venture formed in the UK after the 1980 Spinks report urged the government to support biotechnology and that the support should take several forms (Fishlock, 1982). The first positive response from the Thatcher Government was support for Celltech, a company conceived by the NEB which asked for government money only after it had raised from private sources more than 50% of the finance that it estimated was needed. Because of the private capital presence and its priority option of utilising the findings of the MRC research, Celltech had the characteristics of an all-UK rival to the pioneering US biotechnology companies that were more spontaneously born to commercially exploit the results of the US research. So, the same, though partly guided, process was started in the UK on the mishap of a patent flop and on the basis of a more entrepreneurially oriented reorganisation of research institutions.

The failure of the MRC to take care of obtaining patent protection of its breakthrough discovery was blamed on the NRDC and led an irritated Prime Minister, Mrs. Thatcher, to merge the NRDC with the NEB to form the British Technology Group (BTG),
an agency of the Department of Industry. The Financial Times commented this “marriage of convenience”: “Eventually, a powerful and possibly profit-making organisation may emerge able to encourage industrial innovation and development across a wide spectrum from university laboratories, Government research establishments and individual investors to small businessmen and large companies” (Elliot, 1981).

France, in contrast, adopted a rather rigidly-controlled approach to bio-research with a tendency to create government funded bio-start-ups, in some cases jointly funded by the Government and large private companies interested in biotechnology. This strategy means, in practice, public aid to large companies to set up their own biotechnology research laboratory in the form of a controlled company. The public ‘mobilising’ plan, produced in 1982 by the Government (Ministry of Research and Industry), did not reach its objective to recover the French delay in the biotechnology arena.

The German government, at the beginning of the biotechnogenetic revolution, had no particular plans for substantially supporting biotechnology and practically disregarded any type of incentive to the creation of small firms fully dedicated to biotechnology, because “they are not in line with the German mentality” (Bio/Technology, 1983).

Hoechst, one of the main German chemical companies, took unilateral action in a situation in which it recognised that the indigenous scientific base was weak and transferred its biotechnology research to the Harvard Medical School. West German scientists were furious that Hoechst, one of Germany’s biggest industrial patrons of science, would not sponsor biotechnology research in their universities or the Max Planck institutes. The initiative of Hoechst prompted the Ministry for Research and Technology (BMFT) to promote similar initiatives between German chemical groups and German universities. This strategy proved highly insufficient.

Only much later, the strategy of the French and German Governments changed in a way that more effectively supported entrepreneurship in forefront biotechnology, but of course that implied quite a delayed start in the biotechnology arena.

In any case, the strategies of the European Governments were such as not to give, initially, an important contribution to enhance Europe’s standing in biotechnology.

There is no other way for Europe but to behave strategically in an inter-nation coordinated way leading to a common legislative and operational scheme. Europe has started on this route, though very slowly. Indeed, a positive point was the creation of the so called ‘Industrial Platforms’, technology driven industrial groupings established on the initiative of industry around Biotechnology Research and Technological Development Areas. They were started in 1990 when the BRIDGE programme was approved and are intended to increase European competitive advancements in biotechnology (Aguilar et al., 1998).

In another important economic area of the world, which has its own characteristics, Japan, the strategy has been to support bio-research in large manufacturing companies belonging to the three industrial sectors with primary interest in biotechnology, drugs, chemicals and food. A Biotechnology Development Research Association has been formed by the companies eligible for funds. So, government support has been mostly directed to applied research effected by large companies interested in diversifying into biotechnology (Biofutur, 1988). Japan has also relied on significant acquisition of know-how and licenses from abroad and in particular from the USA (Klausner, 1987). This model has somewhat evolved, but, in the author’s opinion, remains of minor relevance and interest as a reference to design strategies for an economically successful development of biotechnology in Europe.
In a scenario where the gap of performance between Europe and the USA remains significant, the US models, in research/development and financing of the biotechnology sector, should be attentively considered. Much can be learnt and further elaborated from them to devise better strategies for the ‘United States of Europe’.

The presentation, in this paper, of a number of issues in financing biotechnology refers, therefore, to the scenario in the USA.

3 The US public research in biotechnology

Twelve Federal agencies and one cross-agency programme, the Small Business Innovation Research Program (SBIR), have made investments in biotechnology research, mainly basic and, for a limited amount, generic applied research (US Congress O.T.A., 1988).

The National Institute of Health (NIH) covers about 85% of the investments. It supports research and training conducted either within its own laboratories or through a system of grants and contracts with academic institutes, research institutes and industrial ventures. Support is given to both research directly related to biotechnology and to broad research underlying biotechnology.

The National Science Foundation (NSF) is essentially devoted to support research in universities.

Other agencies support bioresearch as a limited part of their budget. The Department of Defence (DOD), a distant second to the NIH in federal funding, mainly focuses on diagnostic methodology and vaccine development for military relevant diseases. The Department of Energy supports bioresearch on medical problems connected with atomic energy radiation and the utilisation of biomass as a source of energy. The Department of Agriculture, through its Cooperative State Research Service, supports the State university system for the conduct of agricultural research; its Agriculture Research Service supports intramural research programmes. The Department of Commerce, through the National Bureau of Standards, performs research related to measurement methods and standards in order to advance the commercialisation of biotechnology in the USA. The Agency for International Development (AID) is the foreign assistance arm of the US Government and is not, per se, a research agency, but works with developing countries in their efforts to meet basic human needs. Its support to bioresearch is directed to obtain products or systems that will be useful in improving human health conditions, agricultural production and rural development in the developing world. Research of the Environmental Protection Agency (EPA) is focused on the risk that might result from the release of genetically manipulated organisms into the environment. Bioresearch of the Veteran Administration is in support of clinical medicine. The National Aeronautics and Space Administration (NASA) is interested in research on how microgravity can improve processes of purification of biological materials for therapeutic and diagnostic applications, on how it can enhance crystallisation of proteins and on how biological processes in cells can be affected by microgravity. Bioresearch at the Food and Drug Administration (FDA) is focused on gathering information that the agency needs to make regulatory decisions.

The SBIR programme was established to encourage innovation by requiring Federal Agencies to set aside a small (1.25%) portion of their extramural research funds to finance applied research programmes in small firms. Small businesses, among which
are bio-start-ups, submit proposals in response to research topics contained in agencies’ solicitation agreements, published at least annually by each participating agency and take part in sharing such funds (US Congress, General Accounting Office, 1987).

Reverting to the main supplier of funds for research, the NIH awards grants to institutions in support of investigators who have meritorious proposals and also if the research involves the support of another Federal agency. Inventions made by government investigators in the course of intra-mural research are patented and licensed to companies under provision of patent law. When Federal laboratories and private companies conduct research jointly, the collaborative company acquires patent rights at the outset of the collaboration and the law also provides for sharing, with government inventors, the gains from product development. Occasions for partnership have increasingly emerged between biotechnology companies and universities, the institutional sites for most of the NIH-funded extramural research relevant to biotechnology. NIH supports the interactions of universities with industry as long as safeguards against conflict of interest are maintained and government-supported research results are disseminated unrestrictedly.

A number of States are also engaged in some form of promotion of biotechnology research.

All evidence indicates that this system works well.

An important consequence of this research structure is that the component of bio-research done by each agency is well motivated and supported by its institutional goals. This leads to efficient allocation and utilisation of research funds. In fact, in each agency, financial resources are concentrated on enhancing the knowledge which is the specific area of responsibility of the agency, thereby strengthening its operational context. Possible inter-agency project overlaps are coped with by joint work on certain projects. In 1993, the Clinton administration created the National Science and Technology Council responsible for the coordination of the whole array of federally funded research activities.

It was observed by a number of parties that the clear split, between basic research sponsored by Federal funds and applied research, does not cater sufficiently to generic applied research such as, especially in the early phase of the biotechnogenetic revolution, bio-processing engineering and applied microbiology. Comparisons were made with Japan which concentrated resources on such areas through, partly government supported, large manufacturing companies. The fear was that, because of this strategy, Japan could surpass the USA in the commercial results obtained from biotechnology, an issue which, probably, was posed with incomplete consideration of other factors.

The evaluation of the performance of the Federal funding system in biotechnology research could be attempted by examining the following factors. The value of the proceeds from the licensing of patented scientific findings could be estimated, by the agencies themselves and by those institutions which act as sites for their extramural research, on the basis of their accomplished licensing deals, of those under discussion and of a tentative extrapolation to the patented knowledge still waiting for a licensing partner. Such an estimate should be compared with the Federal funds invested. In addition, one should check whether the Federal system requires an increase of funds to maintain certain average levels of performance in terms of value (as defined above) of the scientific findings produced or if this value can be maintained in spite of a decrease in the allocated government funds. A non-irrelevant problem is also to measure the amount of funds actually devoted to biotechnology research by each agency, because of their often different definition of biotechnology.
The evaluation of the impact of Federal funding of bioresearch on the economic performance of the US biotechnology sector is particularly difficult. Two points should be analysed. One is the amount of Federal funding in percentage of the total funding from all sources. The other is the economic performance of the biotechnology sector whose estimate is certainly a complex issue. As stated by the Office of Technology Assessment of the US Congress: “Tracing outputs through the long and nebulous path from basic research to commercial products is especially difficult ...” (US Congress O.T.A., 1986).

However, analyses of the type mentioned above should be attempted in order to monitor the decision-making process of fund allocation by public strategists.

4 Other types of US public financial support to biotechnology

Tax relief is a very common method that governments use to support R&D-intensive industries. It is usually devised to enhance the development of industrial sectors that, in perspective, are deemed to have a high potential of contributing to the national economy and to the objectives of the country’s government.

The types of tax provisions resorted to are the result of an economic and political balance of costs and benefits, often difficult to quantify.

In the USA, the Office of Technology Assessment (OTA) of the Congress and other Offices, after OTA was closed in 1995, have been the source of important studies and recommendations on tax provisions.

Tax provisions are often given to sustain the starting phases of innovation or to accelerate their development. In the USA, this was the case with the starting phase of the electronics industry, where small start-ups could almost immediately benefit from such provisions because they became quickly profitable. This profitability was the joint result both of the strategic fallout of the consent decree (1956) which ended an antitrust suit against American Telephone and Telegraph (ATT) and of the Federal funding made available from the US Government and its DOD and NASA agencies, all craving for the miniaturisation and reliability that the electronic revolution could make available (Dellepiane, 1988).

Matters are much more difficult in biotechnology. A large part of the emerging biotechnology sector is formed by small firms that have progressively entered the scene in a number that has been increasing with the accumulation of research results and the parallel increase of attempts to exploit them commercially. The times required to receive product approval from the regulatory bodies are long even in the most successful cases. They are getting longer as research attempts to exploit increasingly complex molecular and cellular bio-pathways. So, small biotechnology firms are typically in long-lasting red.

While established companies operating (often partly) in biotechnology can almost invariably take advantage of carry-forward tax provisions, such provisions can have a significant impact on the small biotechnology company’s financial position only if acting over a long period of time. Indeed, carry-forward rules of seven years in the USA have proved to be insignificant for NBFs which have to wait very long to have approved products capable of generating revenues.

Tax credits for incremental research and development and investment tax credits are typical provisions to stimulate research and development and to encourage capital formation.
Tax credits for incremental R&D imply an additional deduction of a percentage of the difference between the current year’s R&D expenditures and the moving average of an n-year period’s R&D expenditures.

Investment tax credits are tax allowances usually calculated as a percentage of purchase price and not to exceed a percent of the tax liability for the year when the equipment is placed in service; the excess may be carried over.

These tax credits have a limited effect because many NBFs operate in the red for long times and carry-forward rules are insufficient for them. Forms of refund of tax credits when earned have been proposed that would help significantly NBFs, especially in the initial phase of their development.

Other types of tax provisions that allow, though less directly, to take fiscal advantages from losses, in the time when they are generated, are those implemented through individual shareholders’ taxation. These can only be applied to closely held companies with few shareholders. It may be the case of bio-start-ups. In the USA, any company, satisfying the requirements described in the Subcharter S Corporation Act and subsequent revisions (usually very small businesses), can ‘pass through’ to individual shareholders company operating losses. Shareholders can use these losses to offset other taxable incomes with a consequent increase in their net personal income and the possibility of devoting it to sustain company capital structure.

Guaranteed loans for production scale-up were proposed by the OTA to finance cash starved biotechnology firms and give some oxygen to company balance sheets. The guarantees would not be tied to a particular loan but to a particular level of debt and they would serve as a system of revolving credit. As periodic payments reduce the outstanding debt, additional loans could be taken out as long as repayment kept the debt within the face amount of the authorisation. The funds could be authorised for a specific amount and aimed at a well limited level of debt. The Federal agency guaranteeing a loan would be obliged to purchase a stated percentage of the loan if the borrower defaulted. Experience with this type of approach in the early phase of the semiconductor industry was positive (Dellepiane, 1988).

Cutting the tax rate on corporate capital gains obtained from the sale of capital assets (tangible and intangible) can be important for bio-start-ups, which, while waiting to become profitable, in order to survive independently may resort to sales of tangible and intangible assets. If capital gains and the company’s ordinary losses in the same fiscal year could be offset against each other and any remaining net gain after offsetting were treated at the reduced rate of capital gain, this form of incentive could help bio-start-ups to partly avoid accumulating losses to a level that jeopardises company survival.

All the forms of public financial support mentioned above contribute to curb the deterioration of the income statement and balance sheet of bio-start-ups due to the long times such companies need to generate positive cash flows.

A particular mechanism present in the US legislation contributed to sustain the economic and financial structure of biotechnology companies by means of a flexible form of commitment of financial resources to company investment projects. This mechanism was present in the original rules governing the Research and Development Project Limited Partnerships (RDLPs). These rules grant particularly important fiscal advantages to investors who are not stockholders of the company, but also require that they shift into their private financial sphere the risk of the project they finance. Such rules allow the company to commit financial resources to become the owner of the results of the projects, financed by the RDLP, at times when more knowledge is available about the
economic and financial consequences of the projects. The original rules governing RDLPs offered powerful strategic pathways in the management of high tech companies with long product development times and parallel high cash burn, of which bio-start-ups are the most typical example. This type of financing, which is only mentioned here, will be discussed at the end of this paper after the presentation of the financing issues relative to the other component of the biotechnology scenario, that is private investors. This presentation will give the opportunity to think about how important RDLPs, operating under the original rules governing them, could have been to support biotechnology financially and the opportunity to ponder over the consequences of having made them unusable for bio-start-ups because of the Tax Reform Act of 1986. After this Act, tax strategies that address their key issues have become increasingly crucial for biotechnology firms (Burril and Hamm, 1987).

5 Issues confronting private investors in biotechnology

In the USA, two distinct sets of firms are pursuing the commercial applications of biotechnology: Established Companies (ECs) and NBFs. This distinction is progressively becoming present also in the European scenario.

The ECs pursuing applications of biotechnology are generally process-oriented, multi-product companies in traditional industrial sectors, such as pharmaceuticals, agriculture, chemicals, food processing, environmental control and energy. Decisions about how, where and when to enter the biotech arena are a component of the overall strategy of such companies.

NBFs, a typical US characteristic, are entrepreneurial ventures started specifically to commercialise innovative biotechnology.

Financing issues confronting the two sets of firms are quite different.

ECs have always been in a position to finance the biotechnology component of their activity using both proprietary and third party funds. Proprietary funds are generated from a variety of sources: sale of products, interest income on capital and other sources. Third party funds come from issues of bonds and other forms of borrowing for which ECs can obtain favourable rates because of their economic and financial standing. Even if the potential returns from investments in biotechnology, financed from the pool of company financial resources, are substantially postponed in time, such investments can be safely decided with an appropriate allocation of company financial resources between the existing lines of business (to make them grow and increase their capacity to generate financial resources) and the biotechnology R&D and new experimental products whose contribution to company earnings is destined to be quite differed in time.

Financing NBFs is more complex and challenging. It is provided through two channels: operations (to be intended in broad meaning) and financial markets.

5.1 Financing NBFs from operations

Operationally, generating as early as possible consistent financial resources from sales of products would be highly desirable for NBFs, but has proven very difficult to implement, especially in the case of products destined for final users. Enzo Biochem is a successful example of a company that, since its early days, could finance advanced new product research by profitably selling internally-manufactured diagnostic products based on
proprietary knowledge. A little more frequently successful cases are those in which the start-up, while waiting to have its products ready for the market, sells common commercial products, for example pharmaceutical or other products. This approach has sometimes been implemented through a merger of the NBF with a small, economically sound, commercial company. Forest Laboratory, now a full fledgling pharmaceutical company, acted that way when it was a start-up. It joined with a candy company and also sold vitamins.

Somewhat different is the case of companies that can be defined service bio-companies, because they support the work of the final producers of bio-products (the so called ‘omic’ companies are the most relevant example). They provide technology packages conceived to help carry out advanced products design. These companies are earlier cash producers. On the other hand, they are subject to the limits of the intermediate market where they operate, consisting of the bio-companies that utilise such technology packages. The requirements of the utilising companies are quantitatively and qualitatively very variable and, most important, rapidly evolving. This is often a serious hurdle, for service bio-companies, to steadily generate cash inflows.

Because of the long time usually necessary for bio-start-ups to generate cash from sales of their own products, the prevailing form of financing from operations is research and development contracts with ECs.

By means of such contracts ECs outsource the riskiest part of their research, use such contracts as feasibility studies and, in general, to monitor and somewhat pilot the development of the biotechnology sector. One can often read statements that ECs make such contracts mainly because their pipelines are getting dry due to insufficient capability of their internal R&D efforts to conceive and bring to approval new products to substitute those facing patent expiration. Since, in most cases, new product approval is the result of contributions of both a NBF and an EC, because of the types of R&D deals involving the two partners, more in depth analyses should be effected before making such statements.

The relevance, for NBFs, of research and development contracts with ECs to generate revenues is almost without parallel, except perhaps for the small firms that do defence contracts. The small firm obtains financial resources to carry out the agreed project and also receives fees as intermediate targets in the project are reached. On the other hand, the examination of such contracts between ECs and NBFs often shows very tight clauses that make it difficult for many NBFs to pursue other findings which might occur in the course of the contracted work (Dellepiane, 1988).

NBFs usually retain rights to any patents resulting from the research performed and give license to the ECs in exchange for royalties. If the sale of products, obtained using the licensed R&D results, is entirely left to the EC, the small firm receives royalties if and when the EC decides to bring or succeeds in bringing to the market the products based on the findings of the research contract. The ifs and whens of this process are regulated by the strategy of the EC.

Established companies suffer no disadvantages from such R&D contracts with small firms except the loss of the funds invested should the research be unsuccessful. ECs often protect themselves by imposing clauses of discontinuing the contract if results are lagging behind.

The R&D contracts with ECs have often proven to give insufficient contributions to make available the financial resources that NBFs need to carry out proprietary R&D projects. This is well documented in many bio-companies’ annual reports that present company business plans and their evolution over time. The main reason for such an
imbalance is that NBFs are more and more forced to ride advanced learning curves in their proprietary R&D because of the prevailing presence of ECs in the areas most close to fruitful exploitation. This compulsory shift to advanced learning curves increases NBFs’ financing needs for their proprietary R&D.

The R&D contracts between NBFs and established foreign large companies (among which Japanese firms seem to prevail) are, in general, more favourable to the US based biotechnology firms than the contracts they make with US established companies. In fact, US NBFs, in their R&D deals with large US based ECs, seldom manage to retain any direct marketing rights of the products that can be obtained from the utilisation of their research. On the contrary, large non-US companies, eagerly needing the advanced knowledge and technology that can be obtained from their R&D contracts with small US based NBFs, often allow them to retain US marketing rights, besides paying royalties on sales made in the rest of the world. These more interesting conditions seem to have remarkably stimulated such deals. Though they can help somewhat the financial position of weak US NBFs, the resulting transfer of technology out of the USA does not work in favour of the USA’s competitive position in biotechnology (Klausner, 1987).

NBFs can also obtain financial resources from operations by selling part of their know-how and of the results of their proprietary research (patents, process and product designs). This is a decision that certainly reduces the future potential and competitive position of the small company that resorts to such a sale, but it can provide the company with the financial resources to continue its own research and development, though in a more limited area. Deciding which know-how or technology to sell to a potentially strong competitor, such as a large company operating in biotechnology, is a thorny issue. It involves the evaluation of the eventual long-term negative impact, because competitors utilise the NBF’s proprietary know-how, vs. the advantage that the NBF has to obtain financial resources without resorting to financial markets.

It may happen that the EC’s objective in such deals is only to prevent the NBF from using the technology directly, or licensing it to others, if it estimates that the technology may lend itself to the creation of competing products. Of course, such cases negatively affect the progress of the biotechnogenetic revolution.

Similar issues are raised by licensing deals whereby an EC gets license to use a NBF’s know-how and technology in exchange for a one-off payment or payments by installments linked to use, and also pays royalties on the sale of products manufactured using the licensed technology. The amount of financing that the small firm obtains from such deals is often lower, and certainly more diluted in time, than from a comparable operation of technology sale, because royalties are spread over time and may not be paid if the licensed technology does not significantly contribute to the creation of commercial products.

Service start-ups, constituted with the objective of proposing to biotechnology companies innovative instruments for conceiving, designing and implementing new products (a typical example are ‘omic’ companies), are obliged sellers or licensors of their supportive technologies. These companies may have problems of survival in the medium to long term unless they significantly update and re-qualify the products they offer, which is not easy to do in a scenario of rapidly evolving technologies aimed at unravelling and interpreting biological systems. Because of this difficult strategic position, these companies may attempt to transform themselves into users of
their own instruments, becoming designers and producers of biotech products, a risky extension of scope difficult to implement.

In conclusion, in many circumstances financing through licensing can weaken the long-term strategic position of start-ups. It may also lend itself to legal controversies on how to implement the deal, thereby increasing the amount of financial resources burnt in the biotechnology arena, all the more so as more advanced and complex technologies enter the scene.

Another way which a NBF can resort to operationally, in order to obtain financial resources, is to have ECs invest in its equity. ECs often operate through corporate venture capital funds.

Although only individual corporate strategies can specifically explain why established US companies have taken positions in NBFs, some of the investments may have been viewed by the ECs as a defensive strategy against loss of market share to unknown technologies or an avenue for diversification and greater return on investment or as a means of gaining a window on new technologies. When a NBF resorts to this form of financing, the company risks being eventually acquired by the established firm, which can take advantage of particularly low points in terms of valuation.

NBFs can reduce the financial resources necessary for a well defined project by means of an equity joint-venture with an EC wherein equity capital is provided by both partners. It is a deal that somewhat shelters the small company from the risk relative to a particular project which is shared with the EC. This company usually sets rather strict conditions about the progress results to be attained for continuing the common endeavour. It is usually the EC that takes the initiative of proposing this type of venture as a substitute, for example, of an R&D contract with the small firm.

In all the above discussed operational approaches to financing NBFs through various types of deals with ECs, defined by OTA “collaborative ventures or strategic alliances” (US Congress O.T.A., 1988), NBFs are often at a disadvantage and often obtain financial resources in exchange for weakening their strategic position more than such resources can contribute to enhance company economic potential and independent profitable growth. There may also be forms of synergies deriving from such deals, though ECs are often in the position to get the lion’s share.

Operationally, NBFs can try to find better synergies by means of deals with other small bio-companies. The approach may not be so easy to practice because of the difficulty to find a significantly positive interaction of their core activities. Such deals between NBFs may go as far as a merger. On the other hand, mergers between ECs can disproportionately increase their contractual strength and augment the weak position of NBFs in their deals with such giants. Antitrust legislation could curb such a power. Looking at what happened at the start of the electronic revolution, one can say that the very catalyst, that caused it to develop so quickly and be so successful economically, was the antitrust 1956 consent decree that imposed ATT to license its existing patents to small US firms without royalty and established moderate rates for licenses under future patents. ATT was also restricted to its existing markets of telecommunication, government defence and aerospace, and prohibited from entering into highly lucrative markets such as commercial electronic computers (Dellepiane, 1988). Though the technological scenario of the biotechnogenetic revolution presents different characteristics from those of the electronic revolution, antitrust rules can have favourable effects on the standing of small biotechnology companies. An example is that of the start-up OSI Pharmaceutical. This company was developing an anti-cancer drug, OSI-744, jointly with Pfizer, and was
in an advanced stage of development of this new product that would have ended mainly under Pfizer’s control. When Pfizer, in 2000, wanted to acquire Warner Lambert, thereby further increasing its gigantic standing, the Federal Trade Commission judged the possibility of Pfizer’s control also of OSI-744 to be an excessive concentration of power and ordered Pfizer to divest itself of the drug at favourable conditions for OSI. OSI’s stock increased significantly and this helped the company to more conveniently collect other financial resources from the capital markets.

Antitrust rules could also reduce the concentration of market power in the hands of ECs by preventing, for example, full licensing to ECs and imposing at least a minimum of market rights for the small firm licensor.

The possible ways of financing NBFs through various types of deals with ECs suggest that such approaches may compel the small biotechnology companies into pathways where compulsory one-way symbioses prevail and allow the small companies only to get oxygen for survival as long as the large companies think that this suits their strategy (Dellepiane, 2003a).

Financial markets are the other main channel for financing NBFs.

Both types of channels, operational and financial, are to be resorted to, in order to design the financing mix capable of dealing with the complexities and risks of the targets to be reached. Deciding the financing mix is strictly connected with technology and market decisions.

5.2 Financing NBFs from financial markets

Venture capital gave, and still gives, a fundamental contribution to finance NBFs in the USA. The birth of venture-capital backed NBFs in the USA began in the 1970s.

Had research on biotechnology been entirely left to large US companies operating in the areas where it has potential applications, the rate of progress of the biotechnogenetic revolution would have been slower. In fact, the techno-scientific achievements of NBFs, sometimes only provisional and prospective, stimulated the attention of potential large users of such technologies, typically ECs interested in defending their dominant product and market position, and caused them to devote financial resources to the biotechnology area.

On the other hand, a point progressively emerging in the US scenario is the impressive number of venture-capital backed start-ups created either for producing biotechnology products for the final consumers or for supplying instruments to support the process of product development. This proliferation has been triggered by the great variety of advanced findings of a richly financed basic and generic applied research which suggest an ample spectrum of potential tentative industrial applications. The risk is to attract too many financial resources into the early phases of such highly diversified tentative applications and to enlarge the speculative scenario fed by a mass of venture capital, which, because of its typical strategy, is not interested in what will happen after it has retreated, with good profits, from the initiative to which it has given an initial contribution. This point is discussed in another study by the author (Dellepiane, 2005b).

The almost non-existent venture-capital sustained NBFs in Europe, in the 1970s and 1980s, were a basic cause of the slow start of the biotechnogenetic revolution in that area. This situation has pushed a number of European ECs with interest in biotechnology to search for acquisitions of US NBFs. There have also been cases of ECs that have transferred their internal research activity to the USA and, as in the case of Hoechst,
have joined it with that of an important US research centre such as the Harvard Medical School.

More recently, there have been efforts in the European countries to stimulate, from the fiscal point of view, venture capital to form NBFs. This way of attracting venture capital to biotechnology has been inadequate. The presence of a scientific and entrepreneurial cultural tissue, capable of formulating proposals (at least interesting from the speculative point of view) that can significantly attract venture capital, is necessary. This tissue in the USA has been built by the entrepreneurial endeavours of many scientists, researchers and academics who have been, and still are, the starters and main propellers of many NBFs. And this is more complex than stimulating fiscally venture capital initiatives.

Certain European Governmental Authorities have often claimed that the only weak point in their country’s strategy is the insufficient incentive to venture capital formation and channelling into biotechnology. This means missing one main point that causes a certain sluggishness in the development of the biotechnogenetic revolution in Europe. In fact, measures should be devised in Europe to help scientists, researchers and academics to play a real double role of scholars and of not-too-much constrained starters of entrepreneurial initiatives. This double role is now hindered by bureaucratic rules limiting the behaviour of such potential entrepreneurs. Even in the case of improvements in legislation, one weak point remains, due to a certain insufficiency, as an average, of European research to formulate proposals capable of attracting robust venture capital support.

All in all, the US scenario remains the one which should be attentively pondered by a more unified scientific and financial Europe that must overcome the limitations of specific nationalistic approaches to biotechnology.

There has been a lot of writing about US venture capital and entrepreneurship in the high technology field.

The amount of venture capital invested in biotechnology has been quite abundant in certain times, in others much more limited, depending on factors such as the general economic conditions and availability of risk-oriented money, changes in fiscal laws relative to capital gains and regulations of pension funds regarding the types of investment they are allowed to make.

The variable distribution of venture capital investments, between the electronic or telecommunications and the biotechnology area, mainly depends on the speculative opportunities that the two areas are believed to present at different times. The switches of venture capital from one area to the other have sometimes taken place after suffering bad blows in one of them, in the hope that switching would lead to more successful speculations. In other cases, such switches have been decided because the speculative objectives in one area are deemed to have been reached and hopes are that higher potential exists in the other area.

The legislation regarding the minimum time that must elapse from the foundation of a company before the founders can liquidate their ‘restricted’ stock holdings (for example Rule 144 of the Security and Exchange Commission) has influenced the flow of biotechnology venture capital. This flow also depends on the time necessary to have sufficient market appreciation of the company’s stock value that makes exit speculatively attractive. This is a more volatile parameter in biotechnology than in the electronics or telecommunications area. In fact, such an appreciation in biotechnology is based on the attainment of partial targets along the way to product approvals,
on possible remunerative licensing of technology to third parties and, more often, on the expectation, very variable according to available news or circulating rumours, that favourable events will materialise soon.

The coefficients of multiplication of venture capital invested have been usually high even in cases of initiatives that have subsequently failed after the exit of venture capital. This shows, as an average, a good speculative capacity of venture capitalists to take the maximum advantage from their investment at the right moment for them, which is often not the right one for the future of the company.

Venture capital’s fundamental presence in NBFs’ equity usually decreases remarkably after it has had an opportunity to cash in because of contingent favourable events, though it may continue for less important amounts, a strategy more typical of large venture capital funds diversified among industries. Sometimes venture capital comes back when it can take advantage of new possibilities of speculation. For example, it can re-enter after negative results of an already publicly traded company have caused collapse of the company’s stock value.

In the far past, venture capitalists were accustomed to waiting five to seven years before seeing their investments achieve liquidity in the public markets. With the advent of the microprocessor, a number of electronic companies developed applications that became profitable quickly. In some cases, these companies were able to achieve profitability within 18 months and a subsequent public offering within two or three years from founding. As a result, venture capitalists have shortened their investment horizon and decreased the time to bring NBFs to the market. In fact, venture capitalists rarely wait for the biotechnology company to become profitable. Rather, they have learnt how to ride the ups and downs of market value that the company inevitably experiences in its long-lasting development process and to take advantage of upswings that allow a quick and attractive return on capital invested.

When venture capital, acting as the main financing source for a start-up, decides to relinquish equity, this liquidation often takes place through an Initial Public Offering (IPO) which is effected at a time that is often not the right one for the future of the company. Indeed, the IPO should be effected when strategically sound, in the medium to long term perspective, for the company. Private placements are sometimes an alternative that delays going public.

After the IPO, if cash generation from operations lags behind expectations, as it often happens, the small company, attempting to progress in its development plan, remains exposed to the vagaries and constraints of public financial markets. Debt financing remains quite limited or often non-existent for cash hungry companies with income statements in the deep red. Hence, resorting to successive rounds of public offerings or to private placements remains, for NBFs, the main source of the financing needed in order to continue their long-lasting development process. If this situation persists, such offerings or placements are made at progressively lower prices with considerable dilution of stockholders’ investments. Repeated operations of this type can quickly lead small biotechnology firms to collapse.

When writing these notes I reminisce about the lapidary statement “Avoid venture capital if you can” (Forbes, 2000), made by Alexander Zaffaroni, named the Jim Clark in biotech, who created and nurtured important pharmaceutical companies such as Syntex, and bio-companies such as Alza, Affymax, Maxygen and others. One year earlier the Economist wrote: “If small biotech start-ups are not protected from impatient venture capitalists they will be battered by unforgiving stock markets” (The Economist, 1999).
A legislation that allows venture capital ample freedom of speculation, that provides unwarranted fiscal incentives and has antitrust rules too lenient to bridle the hegemonic behaviour of ECs, puts small biotechnology firms in a weak strategic position where they have to cope with the difficulties of operating at the forefront of the biotechnogenetic arena and with the effects of the behaviour of powerful ECs.

In line with the above remarks are the statements, often informally private, of those CEOs or Presidents of biotech start-ups who are running companies with entrepreneurial objectives of medium to long term development and not with the increasingly frequent objective, always undisclosed and even publicly denied, of making much quick money on the first occasion that lends itself to that purpose.

Designing, implementing and continuously adjusting the balance between the financial resources that the company asks the financial markets and those obtained from operations is, and will be, the top challenge for bio-start-ups. Managing such a balance would be much more rewarding if legislation could make available forms of off-balance-sheet financing capable of attracting investors without including them in the company’s decision-making process. This would add an important component to the mix of financing sources that bio-start-ups can utilise.

The off-balance-sheet mechanism sketched in the following paragraph could offer a significant contribution to help small biotechnology firms to express their full entrepreneurial potential, leveraging a more peer-competitive position in the biotechnology arena.

5.3 An off-balance-sheet financing mechanism for small biotechnology companies

It is centred on the following key points.

The small company is the executor of the investment project but not the supplier of the necessary financial resources, which are provided specifically for the project by investors who do not become shareholders of the company and cannot take part in the company’s decision-making process. They commission the project to the company, which is, therefore, entitled to be paid for this work, and remain, provisionally, the owners of the results of the project. The consequent cash inflow benefits the company’s balance sheet. An additional positive effect is the increased capacity of the company to collect other financial resources, typically through stock offerings, at convenient conditions, because it is often in a position to present a profit.

The company is fully protected from the consequences of the project’s failure since it has no financial resources invested in it.

If the project is successful (for example a patent is obtained or a new product is approved), the biotechnology company is not obliged to acquire the property of the project. Someone else can, or the venture investors may have to keep it for themselves if they cannot find any purchaser and try to licence it.

Therefore, a robust buffer is created between the effects of the firm’s decision to start a project and the decision to commit financial resources to acquire the property of its results, a decision which can be made when a more accurate appraisal is available.

This financing mechanism entails a revolutionary change from the usual approach to project financing where investments bring about unfiltered impacts on the financial structure of the company.
This kind of venture investors must have great financial incentives to effect such types of investments, since they have to face high risk. If the project fails, they lose all the money invested. Investors can obtain cash during the development of the project only if other investors step in. The amount they can make from selling or licensing the result of the project is uncertain. While in equity financing investors sit on the board and can affect company decisions, in this mechanism investors provide financial resources without participating in the management of the project and in the company’s decision-making process. Hence, the company is sheltered, in its financial structure and decision-making process, from the speculative behaviour, strategically conditioning, of the capital providers.

To make this approach attractive, incentives to venture capital are to be cancelled if it is allowed to operate freely in deciding, as it usually does, the amounts of financial resources to commit, and for how long, to the firm, with full liberty of ins and outs and consequent participation in the company’s decision-making process. At the same time, very high incentives, regarding both their personal income tax and the tax treatment of the profits from the projects they have financed, are to be devised for investors accepting to operate according to such a financing mechanism.

This approach would help new ventures, especially the riskier ones verging on the frontiers of technology, to gain a much more peer competitive position in the biotechnology arena.

Another advantage could be a more rapid and fruitful progress of the biotechnogenetic revolution, because bio-start-ups would be in a position to develop long-term strategies of independent growth, rather than being compelled to become the weak puppets in the speculative ballet that is too often present in the biotechnology arena.

5.4 The Research and Development Project Limited Partnership

An operational instrument, the Research and Development Project Limited Partnership, based on the key points sketched above, was available, until 1986, in the US legislation (Springham et al., 1999). It was available before the start of the biotechnogenetic revolution (that began in the 1970s of the last century) and was widely utilised in real estate and oil and gas businesses.

Since the very first steps of the biotechnogenetic revolution, bio-start-ups perceived the relevance of the RDLP as an instrument for tackling their thorny financial problems and sustaining their shaky balance sheet structure in a scenario of high uncertainty. The unique problems and circumstances confronting biotechnology companies, including risky product development cycles and an uncertain and sometimes unreceptive public market, high cash burn rates and speculative financial markets, caused RDLPs to become more and more relevant as an instrument to protect the company against premature failure because of financial collapse and against the speculation of financing providers.

The rules originally governing the RDLPs in the USA are summarised hereafter. The RDLP allows the company to run its research and development projects and to finance them by external capital in a way that neither affects the company’s capital structure during the development of the project nor brings about the decisional presence of such external financing parties into the management of the company. Operationally, each project, that the company decides to finance by means of a RDLP, is carried out according to the agreement signed for that partnership and under the general rules that regulate RDLPs.
The limited partners are those private individuals who bring to the partnership the financial resources required to carry out the project, the results of which become the property of the partnership. Hence, the company’s financial structure remains unaffected while the project is carried out and is completely sheltered from the failure of the project since the partnership contract typically provides for the limited partners to bring to the partnership the total amount of the financial resources necessary to carry out the project. If more than the forecast amount is necessary (and this may be considered in the contractual provisions), the company may become liable for the difference.

The company carries out the project on behalf of the RDLP, which pays the company for it. Many NBFs that used limited partnerships stated that they prefer the RDLP as a method of financing because the payments that the company receives from the partnership for carrying out the project are revenues for the company, which can show a profit even if it has few or no products to sell (Borgman and Co., 1983). The company could, therefore, take advantage of this situation to get financial resources at much more favourable conditions such as issuing stocks at higher prices and could avoid searching for venture capital or procuring funds by selling or leasing technology.

The use of the company’s financial resources takes place if the company decides to buy the results of the project from the partnership instead of letting the partnership sell them to a third party or keep them for licensing. This decision can often be taken when the company is in a position to better evaluate the consequences of committing its own financial resources or letting third parties purchase the property, hence the use, of the results of the project.

It seems very appropriate the statement of the US Department of Commerce that “RDLPs are both an off-balance-sheet funding source and a management concept” (Merrifield, 1986). Indeed, they cause the mix of financing alternatives, which NBFs can resort to, to become remarkably much wider and flexible.

There are many financial incentives for the limited partners. RDLPs, unlike corporations, are treated under the US Internal Revenue Service (IRS) Code as non-taxable entities, meaning that the partnership profit and losses are ‘passed through’ to the individual partners who combine them with their other items of revenue and expense. Corporate profits, by contrast, are taxed both at the corporate and at the shareholder level and deduction for losses incurred by the corporation is not available to the individual shareholders. Since a project typically generates losses because of the expenses to carry it out, limited partners can use those losses, in the year when they are incurred, to offset other income which might be taxable at very high rates. Furthermore, limited partners can deduct as much as 85–95% of their initial investment, decreasing their after tax cost (US Congress O.T.A., 1984).

Such tax deductions are allowed if the limited partners result in risk. To prove this, the partnering agreement must not contain clauses implying forms of guarantee that the general partner will have to buy the results of the project from the limited partners, because this would imply no risk for them.

Moreover, limited partners have any income from sales or licensing of the results of the project treated at the reduced rate of long-term capital gains. The one-year period necessary for the sales of a capital asset to qualify for a capital gain treatment does not apply to patents, but it does to any other asset resulting from the project.

The Office of Technology Assessment of the US Congress indicates in one of its reports (US Congress O.T.A., 1984) that “RDLPs, next to public offerings, have so far provided the most funds for NBFs”. In this report OTA states:
“RDLPs are providing the small biotechnology firms with the financial ability to undertake their own proprietary research and early product development and in some cases trials for approval without relying on established companies and venture capital firms.”

and “Such partnerships may allow more NBFs to enter markets such as that of pharmaceuticals, where extensive regulation makes the cost of entry very high. Given the very large amount of capital which will be required to support the further development of biotechnology and the variability of the stock market as a source of funds through public offerings, RDLPs are probably critical to the survival and growth of NBFs.”

and “Licensing of technology and products market rights from small biotechnology companies to large corporations, for self-financing purposes, will tend to reduce the competitive stimulation to the industry that small bio-start-ups could otherwise provide”

and “If small firms can surmount the financial hurdles of commercial production, the pace of technological advance and market development of the biotechnology revolution will be accelerated and the competitiveness of the US firms using biotechnology will be increased.”

There is broad consensus that RDLPs, as long as they were operational under their original rules, have shown a remarkable capacity to help NBFs to reach a more competitive standing in the biotechnology arena and have also contributed to the development of the biotechnogenetic revolution in the USA.

An example of the fundamental support offered by RDLPs to sustain the competitive capacity of NBFs is that of Cetus Corporation (Dellepiane, 2005a). The Company had difficulty in obtaining approval of its Interleukin-2 in the USA and forecasts were that times would have been much longer than expected. Cetus decided to try to obtain approval to market this product in Europe. To preserve its proprietary rights it set up a subsidiary, Eurocetus in the Netherlands, with manufacturing facilities to supply the product necessary for the several sets of trials required to obtain European approval. This operation needed a rather heavy engagement of financial resources. So, the Company resorted to a RDLP to finance the process of obtaining the necessary European patents and performing the clinical trials for market approval of Interleukin-2 in Europe for certain uses. The product received approval and the Company judged it convenient to buy back the relative rights from the partnership. Without this support, the Company would not have been able to bear the whole financial burden of this international operation resorting to its internal financial resources or to other already too much utilised types of financial sources.

OTA, in its reports to the Congress, constantly supported the maintenance of the rules originally governing RDLPs as a means to enhance the progress of the biotechnogenetic revolution in the Unites States of America. It also recommended further improvements in the rules governing them, two of which are worth mentioning. The first was an amendment of the IRS Code to eliminate the distinction between patents and plant variety protection certificates. This distinction was deemed to limit the use of RDLPs for biotechnology R&D in agriculture. The second was also to amend the IRS Code so that universities are included in the definition of patent holder. Under Section 1235 of the code, a holder is defined as any individual whose efforts created the patentable property or any other individual who has acquired interest in the patentable property in exchange for money paid to the creator prior to the actual reduction to practice of the invention. Universities that have obtained patent rights through employment agreements with
their scientists are excluded from the definition of holder. Amending Section 1235 to include universities in the definition of holder would have enabled wider use of RDLPs.

All the recommendations to maintain the rules governing RDLPs for companies operating at the forefront of technology, principally NBFs, have been ignored in the Tax Reform Act 1986 (TRA), public law 99–514, which cancelled the appealing characteristics of RDLPs for any type of business (Knight and Knight, 1997). This drastic legislation change caused RDLPs to become unattractive in general and particularly for NBFs (Meeks, 1986).

The Tax Reform Act of 1986 was a major legislation change towards closing tax loopholes with the objective of restoring greater equity to the Federal Tax Code (Petska and Nelson, 1990). TRA was conceived as a general legislative compromise which blended tax rate reduction and income base-broadening. To reach this target it was felt necessary to curb drastically the fiscal haemorrhage caused by tax sheltering activities. These are usually defined as “investments in which a significant portion of the investor’s return is derived from the realisation of tax saving with respect to other income, as well as the receipt of tax favoured income from the investment itself” (Joint Committee on Taxation, 1985).

Especially in the real estate business, the utilisation of RDLPs had peaked in the 1970s and 1980s and created tax shelters defying economic reality, with inflated appraisals and tax benefits far in excess of economic benefits. The Treasury Department found an increasing number of wealthy tax payers paying only 5–10% of their positive income in taxes because of shelters. Besides the revenue loss, the Congress was concerned that extensive shelter activity contributed to the public belief that the tax system was unfair and that only the naïve and unsophisticated paid taxes.

The Tax Reform Act was appropriate for large business areas such as oil and gas and real estate where dollar volume is very high and business characteristics lend themselves more easily to abuses in tax shelters with a consequent significant portion of the investor’s return derived from the realisation of tax saving with respect to other income and to receipt of income from the investment itself.

The emerging biotechnology sector is quite different from the massive commercial business of real estate and oil and gas and far from being the right place for abuses in tax sheltering. Tax incentives to investors in RDLPs caused a part of the public financial support to the biotechnology sector to be piloted by the NBFs to strengthen their strategic position. This partial allocation of public financial support could be much more rewarding than having the whole public financial support to biotechnology R&D flow into agencies and institutions where its effect cannot be easily quantified to evaluate the soundness of the decisions about where and how funds have been allocated.

In the context of his presentations at international conferences on management of technology, the author expressed his strong agreement with OTA about the great relevance, for NBFs, of the original rules governing RDLPs (Dellepiane, 2003b, 2005b).

### 5.5 The SWORD and BDC Financing Instruments

After the 1986 Tax Reform Act, biotechnology firms have proposed to the attention of financial markets a form of off-balance-sheet financing of their projects that attempts to attract investors even though it is far from offering them the incentives to invest which were present in the original rules governing RDLPs cancelled in 1986.
This shows the strategic relevance that bio-start-ups attribute to attract investors through off-balance-sheet financing.

This form of project financing is called Stock Warrant Off-Balance-Sheet Research and Development (SWORD).

The SWORD operates as a special purpose corporation with its own organisation created with the scope of financing a project that the biotechnology company intends to undertake without committing its own financial resources, at least for some time. The SWORD commissions the company to carry out the project and uses the funds it has collected to pay the company from which it has received a worldwide, exclusive, royalty-free licence in perpetuity to use the know-how and the technologies necessary to carry out the project. It also maintains a perpetual claim on the future stream of operating income generated by the granted know-how and technologies.

A SWORD is a form of project financing that uses only equity. It is financed by means of public units offering (Vaughan, 1990). Each unit consists of one share of the venture common stock that can be called by the parent and one warrant to purchase one share of common stock of the parent, which may be acquired at a price that cannot be less than the stock market price at the time of the offering, to avoid transfer of wealth from current to new venture shareholders. The unit usually becomes unbundled after a period of 3–30 months, at which time the stock and warrant begin to trade separately. Since the units are publicly traded, investors in such ventures can divest any time from the stock.

The funds from the unit offering are invested in short-term securities and paid over time to the parent as specified in the project development contract. A SWORD has independent financial statements which have no impact on those of the parent. As in the case of the RDLP, the SWORD causes the company to account as revenues the payments it receives to carry out the project. On the other hand, the SWORD accounts such payments as expenses.

Operationally, the SWORD acts as a financial intermediary. Hence, it has minimal need for technical and operating managers. It commissions the parent company to carry out the project for which the venture has been constituted, pays the parent company for that job using the funds obtained from the units offering and gives the parent a real option to acquire worldwide license to manufacture, use and market any resulting product in exchange for royalty payments. Actually, the SWORD represents a bundle of real options since the parent can exercise its rights choosing which products to manufacture and market and which to sublicense.

The parent can reacquire the property rights to the results of the project only by calling the venture shares. The call option on the SWORD stock allows the parent to capitalise on the project development. In essence, biotechnology firms create, through SWORDS, their own research sponsors and retain the option to buy out the sponsor by calling all the stock of the venture, paying in cash or common shares at discretion.

The warrants protect the venture investors from having the parent taking excessive advantage from the results of the project by not calling the venture shares. By exercising their warrants, the venture shareholders can share in the parent’s income stream and assets while continuing to receive royalty payments. Even if their stock is called, the venture shareholders can continue to participate in the parent’s results by exercising their warrants. In case of failure of the project, the venture shareholders can attempt to offset losses of value of their shares by carefully and timely exercising their warrants.
Since the warrants and the callable stocks of the venture allow both the venture stockholders and the parent company to maintain claims on the project’s outcome, the incentives of both partners appear to be aligned in a SWORD.

When offering the units, the company should consider carefully the proportion of the shares represented by the exercise of the warrants. The warrants lead to equity dilution if exercised and may offer a sort of Horse of Troy to competitors who could purchase units and then exercise warrants to establish a position within the parent. If the company decides for a high number of warrants, that may constitute a potential threat, it should be ready to purchase units or to buy out the venture, before such a threat materialises.

All in all, complex decisional issues are raised in company planning by the use of SWORDs which have to operate within the constraining framework of the stock market, while RDLPs could operate outside it.

Only fairly well established NBFs, with a proven record of prevailing successes in their R&D projects and a sufficiently solid financial structure, can possibly attract investors in a SWORD deal, thereby enhancing their innovation capacity that might otherwise be partly foregone if attempting to use conventional forms of financing. The names of the companies that have successfully arranged such deals, Genentech, Genzyme, Alza, Centocor, Immunex, confirm this hypothesis.

Less well established companies, rather cash-hungry and with a pipeline of several potential products at different stages of development, with prevalence of earlier stages, have recently started to propose to private equity firms particular deals, sometimes called Biotechnology Development Corporations (BDCs) (Dickman, 2006), to carry out projects that typically consist in advancing a potential drug to its next significant clinical milestone. Such deals retain certain elements of SWORD, but are much less exposed to the operational complexity of the stock market. The biotechnology company grants the BDC a license to the intellectual property necessary for the project and the private equity firm provides the financing needed to carry out the project. The clinical development is carried out under the control of the two partners. The BDC retains all rights if the project is successful. The biotechnology company has an exclusive right to reacquire the intellectual property at any time by acquiring all the BDC’s equity at a predetermined price (in cash or a combination of cash and common stocks), which is agreed upon when the BDC is formed and guarantees a high yearly yield to the financing providers. In addition, the biotechnology company grants to the private equity firm an n-year warrant to purchase a number of its shares at a premium over the company’s prior n-day average trading price. The biotechnology company also agrees to compensate its partner for structuring the transaction. If the drug fails the trial, the biotechnology company owes nothing, but the private equity company keeps rights to the drug, a clause present in the few cases of BDCs that have been created till now.

There seems to be a certain interest of biotechnology companies, of the type mentioned above, to create BDCs that temporarily carve out drugs in development from their clinical portfolio and independently finance their advancement towards approval in a way that reduces dilution and offloads some risk in the process of offering to Big Pharmas drugs in an advanced stage, a stage which allows bio-companies to obtain better financial terms. On the contrary, private equity companies seem to be very selective in embarking on such deals, especially with companies in the early stages of development and a limited record of significant achievements (Dolan, 2006).
The evidence is that too many small bio-firms, which may have long-term high potential of independent, profitable growth, are not in a position to resort to BDCs and to SWORDs. They are indeed relegated to the role of research boutiques and their potential risks to remain partly unexploited and partly gobbled up by more established companies that utilise it in the way most convenient for them. If such firms could have access to forms of off-balance-sheet financing of the type governing RDLPs before 1986, they would be in a position to pilot such financing along strategic pathways capable of enhancing their economic potential, competitive capacity and independent, profitable growth.

A legislation that makes available a financing mechanism of the type presented in Subsection 5.3 seems highly desirable.

6 Conclusions

This paper surveys matters relevant to the public and private financing of biotechnology research and industrial implementation. They regard public institutions, companies, especially those entirely devoted to biotechnology and financial operators, and are relative to the USA, which was the starter of the biotechnogenetic revolution and still maintains the scientific, technological and economic leadership of it. Such a leadership, whose origins are sketched in the first two sections of the paper and in a part of Subsection 5.2, could be further enhanced if NBFs, which contain the highest economic potential of life science discoveries, were set in a position to strengthen their competitive capacity vis-à-vis ECs, often only partly involved in biotechnology.

The organisation of the Federal funding system, one main channel of public support to biotechnology R&D, and the ways of operation of its agencies offer a valid model to monitor for public funding decision-makers in a still non-homogeneous multi-country context such as Europe.

Criteria, such as those suggested to evaluate the performance of the Federal funding system, should be used, and possibly improved upon, as support to the decision-making process of fund allocation by public strategists. This evaluation is even more challenging when alternative ways for providing public funding, such as tax provisions for companies, are comparatively analysed.

The range of tax provisions made available is highly diversified and takes into account what was successfully designed and implemented in the very successful start-up phase of the electronic revolution, and also the structural differences between the electronic and the biotechnogenetic revolutions. This tax provisions system, however, remains bound to a mechanism of action centred on the balance sheet and income statement, which bear without a filter the impact of company investment decisions. It is conceived to help curb the deterioration of the financial structure of the company consequent to the long time usually necessary to generate positive cash flows.

The off-balance-sheet financing, in the form originally available through RDLPs, can constitute another important alternative way of allocating public funds to NBFs’ R&D by injecting such funds into their strategic decision-making system. An analysis of whether such a channel should be made operational, and for what amount, needs a sound estimate of its effects compared with those of Federal funding and tax provisions. Probably the favourable effects of public funding through RDLPs were not adequately appraised.
by the Government when it was decided to cancel the original rules governing them for fear that such a funding could be manipulated to create abuses in tax sheltering.

In designing and implementing their strategic plan, NBFs have available an ample range of channels to obtain financial resources from their operations and from financial markets. All such channels should be used with careful attention to the weak point(s) present in each of them. Sound planning has to balance them qualitatively and quantitatively. Designing, implementing and timely adjusting the mix, of the financial resources that NBFs typically ask the financial markets and of those obtained from operations is, and will be, the top challenge for bio-start-ups. The availability of off-balance-sheet financing, effected through RDLPs, could make decisions more complex for NBFs, but strategically much more rewarding, as wisely remarked by the OTA.

The forms of off-balance-sheet financing, trying to preserve some aspects of the RDLP, that NBFs have proposed to the market after the rules originally governing the RDLP were cancelled, present weak features that make such substitutes much less attractive for investors.

The RDLP allows limited partners to quickly recover most of the funds invested through the fiscal rules regarding their personal income. This is particularly important in case of project failure. In this case, SWORD shareholders have a more difficult way to attempt to recover their losses through the exercise of warrants. If the results of the project are positive, investors in the RDLP enjoy the reduced capital gain rates when its results are sold or licensed. Instead, the SWORD has no particular tax relief on the royalties received and when its stock is called by the parent. SWORD shareholders have no tax relief when they sell their shares.

The recently experimented BDC is designed to give financial help for parts of an investment project, mainly relative to steps towards product approval and commercialisation. It forces the NBF to agree, before the project is started, on the purchase price of its results, a hard gamble between the NBF and the BDC. It will be interesting to observe the performance and frequency of such a type of deal just recently proposed.

The scenario of biotechnology financing in the USA looks interestingly complex. Monitoring its evolution should provide important points of reference and of reflection for the actors operating in the European context. It could help them to design and implement a common strategy instead of lingering on regional approaches and would help Europe to reduce the risk of remaining behind in the biotechnology arena, while it should strive to become a co-leader of definite relevance.

References


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