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BIOTECHNOLOGY SPIN-OFFS – A PARADIGM IN THE TRANSFORMATION OF SCIENTIFIC AND TECHNOLOGICAL INNOVATION INTO ECONOMIC VALUE

Introduction

The purpose of this paper is to briefly discuss the potential contribution of biotechnology to the achievement of economic growth. This paper is by no means an exhaustive review or recommendation but rather aimed at bringing about a discussion on possible avenues to commercially exploit scientific achievements and innovation in the biotechnology field.

It is generally accepted that biotechnology is a vital key to enabling technology for the 21st century. The biological sciences have been adding value to an array of products and services, bringing forth the "Bioeconomy" and offering the potential to make major socio-economic contributions (Konde, 2002), (ETEPS, 2007) and (OECD, 2009).

Biotechnology requires a strong academic environment and must be nurtured carefully by an often long, laborious and costly basic research. The later development and implementation is also an extensive and expensive process. There is extensive evidence that basic research does lead to considerable economic benefits (Satler & Martin, 2001). The public sector is a major player in nurturing health biotechnology and accounts for a notable share of research (Fig. 1). Experience in certain countries, such as the USA and Israel, suggests that generous public funding of high-quality academic research is a major source of new technological opportunities[1], as well as an attraction for high-quality business activities in an increasingly globalized world. The bioeconomy will therefore be influenced, among others, by public research support, regulations and intellectual property rights.

Universities and Research Institutes should seek to transfer technology to the private sector, and therefore capture the benefits of commercialization of their innovation and intellectual property rights (IPR), through a number of different mechanisms. This paper briefly

[1] A US study (F Narin, K Hamilton and D Olivastro (1997), "The increasing linkage between U.S. technology and public science", Research Policy, 26, pages 317–330) analyzed origins of the published papers that were cited in US patents. They found that nearly three quarters were to papers that resulted from publicly funded research, undertaken in academically prestigious universities and related institutions, and published in academically prestigious journals.

examines the option of using spin-off companies and discusses their potential economic value.

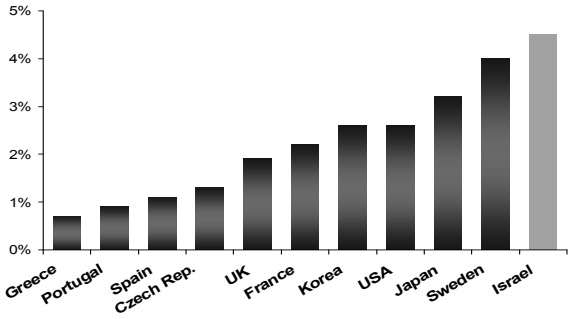

Fig. 1. Civilian R&D expenditure as % of GDP (2003)

Source: OECD Educcation at a Glance 2005 & 2006.

Commercialization of Academia Intellectual Property Rights – Role of TTO

A solid foundation of academic excellence and cutting-edge basic and applicable research are a fundamental prerequisite for commercial exploitation of universities and research institutes IPR. Moreover, strong technology transfer[2] organizations (TTO) combined with a solid IPR protection capacity is crucial for successful technology transfer transactions. TTO's are thus expected to be a valuable instrument for screening and assessing innovative applicable research projects in-campus, on one hand, and connecting researchers with the industry, on the other hand. A diligent evaluation process is essential for the selection of the most appropriate projects representing a significant commercial potential and commercialization opportunity.[3] It is advisable that TTOs recruit experienced people and retain competent consultants to proficiently carry out the assessment process. Strong IPR protection should be duly obtained for such elected inventions. Valid patent ownership and application policies should be therefore determined and applied.[4]

We reason that in order to achieve these goals, each university or research institute should establish its own TTO. TTO's should be independent legal entities and granted, by the academic institute, an exclusive right to commercialize its IPR and conclude technology

[2] Technology transfer is the process by which a developer of technological innovation and owner of IPR avails it to a business partner for commercial exploitation.

[3] Basic criteria determining the viability of an invention include, among others: (i) commercialization potential (innovation); (ii) competitive edge (uniqueness) and (iii) patentability (would it create a strong IPR position?), taking into account technological and legal risks as well as identifying the most efficient way of commercialization.

[4] It is now a common policy of universities in developed countries to own the IPR of researchers' inventions, either in accordance with pertinent laws or by way of employment agreements.

transfer transactions (e.g. licensing agreements) with the aim to generate revenue to support further research and education.[5] TTO's must seek scientists' cooperation in order to achieve successful commercialization of their applicable research results. Such cooperation will mainly depend on the trust, competence and performance of TTO officers. Scientists are likely not experts in legal and business fields and therefore their cooperation with the licensing officer may facilitate the commercialization of their inventions.

Commercialization of Biomedical Technology[6]

Biotechnology products in human healthcare may include biopharmaceuticals, biotechnology-based in vitro diagnostics, vaccines and new therapeutic approaches (e.g. gene therapy, stem cells etc.).

Biotechnology is an emerging field in which academic laboratories, large companies and SMEs are engaged. The biotechnology and pharmaceutical industries present a complex network of technology focused firms. The primary objective of the biotechnology and pharmaceutical chain relates to the discovery, development and distribution of therapeutics. The biotechnology industry may be defined as including firms that apply newly emerging innovations and technologies to life sciences.

New drug discovery and innovation in biomedical area is dependent (mainly) on basic research carried out in academia. Vital applicable research results may be therefore regarded as the "discovery stage" of a potentially new drug or medical technology. It is a common knowledge that the development of new drugs (and medical innovations in general) requires massive long term investments in R&D, expertise in pharmaceuticals development, obtaining regulatory approval, production and marketing capacities. Hence, due to the unpredictability of innovative biomedical developments, pharmaceutical companies spread R&D to divide risk across many projects. Large pharmaceutical companies find viable innovation to be much more difficult to accomplish internally (Christensen, 1997). The challenges, including, among others, lack of in house basic research set-up and activities, encourage large Pharmaceutical firms to pursue collaborative alliances. Pharmaceutical leadership seems to recognize that collaborative arrangements provide a vital mechanism enabling to expand product pipeline. Nonetheless, most of the pharmaceutical companies (and to a certain extent, medical device companies) tend to refrain from engagement in an early stage of the discovery (invention), namely in the basic research stage. Often they are willing to become involved after preclinical and toxicology studies have been satisfactory (similarly, a working laboratory prototype of a medical device can be demonstrated). Indubitably, preclinical and

[5] It is anticipated that the academic institutes provide initial finance to the TTO and later on the TTO should obtain certain management fees.

[6] Modern biotechnology applications are mainly related to the following areas: human and animal, primary production/agro-food, industrial processes and environment and energy. Our discussion will focus on pharmaceuticals, however it may be also relevant to life sciences in general, and in particular medical devices.

toxicology studies, which are costly and may require expertise unavailable on campus, are not within the scope of academic research and therefore are not presumed to be carried out at universities.

We surmise that under the said circumstances, that licensing from university IPR done directly with third parties (e.g. large pharmaceutical companies) would be impractical, and that the formation of independent new spin-off entities that would be dedicated and focused on the completion of preclinical and toxicology studies[7], would be a more adequate technology transfer avenue.

University Spin-Off Companies

In the biomedical domain, the innovation pool is continuously growing through the entry of new spin-off companies. Hence, spin-offs and entrepreneurs play a key role in innovative activities in general and in the biomedical field, in particular. Most biomedical innovation originates from academic laboratories and spin-offs which are generally based on university IPR and knowhow.

For universities, technology transfer by way of licensing out can successfully and effectively bring their innovation through to the market place. Table 1 demonstrates the volume of licensing transactions during various stages of the drug development process. Interestingly, the highest value correlates to the discovery stage, the part the typically originates from universities. However, as discussed above, in circumstances where licensing IPR to large companies is not plausible, TTO's should explore the possibility to license the IPR to a newly established spin-off company.

One of the fundamental dilemmas when considering the formation of a university spin-off company is the role of the principal inventing scientist in such a venture. We are aware of an inherent conflict between the inventor, in her/his capacity as a university professor, and her/his entrepreneurial responsibility. Entrepreneurial (spirit) and managerial skills are crucial for the creation of a startup company. Executives of such ventures are expected to obtain adequate finance, diligently manage the defined project towards achieving the determined goals, namely, successful completion of the designated work plan on time, using the budget available for its performance. The executive entrepreneur is further challenged by leading and guiding people, including the chief scientist (which may include the university professor) under uncertain and unpredictable circumstances. In addition, further capital may be required, as well as looking for potential strategic partners for completing the development of a marketable product. Needless to say, it is unlikely that a university professor would be able to cope with such responsibility without resigning from her/his university position. In our opinion, it is advisable to engage a competent executive and look for the appropriate *modus vivendi* to cooperate with the inventor-scientist. The university profes-

[7] In certain cases, even conclude phase I clinical studies, if appropriate.

sor would be extremely valuable to the new venture success. It may act as chief scientist of the company, alternatively as its scientific consultant. They should accept the executive entrepreneur authority and trust the expert – e*xperto crede*. We have witnessed numerous companies failing due to management incompetence and severe conflict between the executive and the scientist / inventor.

Table 1

Pharmaceutical Agreement value by top Phases (Q1 2010)

Phase	Value ($m)	Volume
Discovery	2,786	28
Phase II*	1,760	14
Phase III	1,000	11
Phase I	890	4
Approved	803	29

* i.e. clinical trial phases.

Source: BioPharm Insight - Licensing Activity Report, Q1 2010.

An additional issue that should be considered relates to the legal structure and ownership of the newly formed spin-off company. A likely approach is to engage an outside competent entrepreneur[8] who will undertake registering a new company, raise the adequate finance, obtain a license through the TTO for the IPR and later manage the project and act as chief executive of the company. The TTO is required to conclude an appropriate licensing agreement[9] with the newly formed company. We have also observed variations whereby the TTO obtained a minority share in the newly formed company (probably in lieu of the licensing fee) with no executive obligations. Revenues can also be in the form of running royalties and from capital gains, in the event of a merger, acquisition or initial public offering (IPO) of the spin-off company.

Evidently, the university's academic officials[10] should be concerned with the professors' incentives in cooperating with the formation of the spin-off company. In our view, and based on our experience, it is appropriate and constructive to offer to the inventor scientist an option or allocation of equity shares in the new company and receive a share of the royalties, in addition to the consulting fee.

[8] It should be properly remunerated, including by way of allocating shares and/or options to purchase shares.

[9] It is strongly recommended to seek legal advice from experts in this particular domain.

[10] e.g. vice president for R&D.

The Spin-off Life Cycle

Successful technology transfer by universities to spin-off companies depends, among others, on cutting edge innovation, a strong IPR position, entrepreneurial spirit, competent management, appropriate long term financing, significant competitive edge and market growth, a supportive board of directors and a viable business strategy.

Seeking funds is perhaps the most challenging task for any new startup company. Though the *professio* of raising equity capital, particularly by spin-offs and early stage biomedical companies is consequentially beyond the scope of this paper, and therefore will not be discussed.

Small companies should meticulously examine their business strategy and acknowledge the expectations of their shareholders. This is particularly applicable to young biomedical companies. Some fundamental questions arise in this respect. Can such biotech spin-off companies become large firms in the long run? Can they generate enough revenue to become profitable and less dependent on obtaining continuous equity capital? It is evident that bringing a new drug to market requires 10 to 15 years from its discovery to become a revenue generating product and may cost hundreds of millions of dollars. Moreover, clinical trial results are unpredictable and therefore the likelihood of the drug actually reaching the market remains low. As a consequence, biomedical young companies should consider, as soon as applicable, seeking strategic alliance with large companies, sharing endeavors in the development and marketing of a viable product. Most large pharmaceutical company strategize, on the other hand, by recruiting new technologies and new potential drugs through mergers and acquisitions[11] (M&A) or alliances with SMEs. SMEs benefit from generous upfront licensing fees as well as considerable running royalties in the long term.

Biomedical Firms and Bio-Drug Developments – Comparative Data and Indicators

The European biotechnology industry employs 96,500 people in total, mostly in SMEs. The industry is highly research-intensive with 44% of employees (42,500) involved in research and development functions. The typical European company that has existed between 6–10 years has 28 employees, and at 11–15 years it has 41 employees (Jonsson, 2006).

When looking at private biotechnology companies (i.e. not listed on the stock exchange) only, the median number of employees is 12 in Europe and 28 in the US (Hodgson, 2006). According to the HBM Pharma/Biotech M&A Report, (HBM, Pharma/, Biotech, M&A, & Report, 2010) 2009 was an exceptional year for pharmaceutical M&As that was dominated by mega transactions. In terms of total transaction volume, 2009 was a record year for Pharma/Biotech M&A, driven by three completed mega-transactions (Pfizer/Wyeth, Roche/Genentech and Merck&Co/Schering-Plough). US, Canadian and European trade sales reached

[11] Certain scholars argue that such M&A's are with some questionable results (Raghavan & Naik, 2004).

a volume of $174 billion in total. Transaction volume of private transactions also increased to $9.9 billion, driven mainly by some larger transactions of non-venture-backed companies like the acquisition of Stiefel by GSK for $3.3 billion, of Arrow Generics by Watson for $1.75 billion and of Austrian company Ebewe Pharma by Novartis for $1.2 billion.

A recent press release by Burrill & Co. (Burrill Report, 2011) reveals that the biotech industry's collective market cap was $378 billion, up 1.5% for January 2011.

The following statistical data, published in a recent OECD report (van Beuzekom & Arundel, 2009), evidently shows the contribution of biotechnology in the pharmaceutical area in the past two decades:

"…Between January 1989 and January 2009, 138 biotherapies received marketing approval in several national jurisdictions in the world. These consisted of 2 experimental therapies, 10 in vivo diagnostics, 11 bio-vaccines and 115 therapeutics. A review of the ownership and development records for all 138 approved bio-therapies identified the firm that originally developed the bio-therapy and the current owner of the bio-therapy. For 56 (40.6%) of the 138 bio-therapies, the firm that originally developed the molecule differs from the current owner. For most of these cases, the developer was a small dedicated biotechnology firm that was later purchased by a large pharmaceutical firm. In total, only 21 (15.2%) of the 138 bio-therapies were originally developed by one of the major pharmaceutical firms…".

Conclusion

The transformation of research based biomedical innovation into economic value is a complex, extensive and costly process. Spin-offs primarily depend on high risk investment to support years of research and development (R&D) and clinical trials. The availability of appropriate funding, from local venture capital funds dedicated to taking the investment risk in biomedical projects, is therefore vital for their materialization.

Governments should play a greater role in financing basic research and providing funding to support early stage biotechnology companies. Possible programs for governmental financial support[12] include, *inter alia*, seed financing, whereby the government and the investor ("business angel") will invest matching amounts in return for equity; Supporting R&D projects by providing grants (e.g. 50% of R&D budget) for royalty payment from the future product.

In summary, the interest in spin-offs is warranted because they do play a unique role in many economies, and governments can also benefit through promoting regional development.

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[12] For an example of governmental support refer to the Office of the Chief Scientist, Ministry of Industry, Trade and Labor, government of Israel: http://www.tamas.gov.il/CmsTamat/Rsrc/MadaanEnglish/MadaanEnglish.html.

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An entrepreneur and founder of two biomedical companies

Summary

Universities and Research Institutes seek to transfer technology to the private sector, and therefore capture the benefits in the commercialization of their innovation and intellectual property rights (IPR). This paper briefly examines the option of using technology based spin-off companies, particularly in the biomedical domain, and discusses their potential economic value.

A solid foundation of academic excellence and cutting-edge basic and applicable research are a fundamental prerequisite for commercial exploitation of universities IPR. Moreover, strong technology transfer organizations combined with a solid IPR protection capacity is crucial for successful technology transfer transactions.

Transformation of biomedical innovation, resulting from basic research, into economic value is a complex, extensive and costly process. Spin-offs (and startups[13] in general) primarily depend on high risk investment to support years of research and development (R&D) and clinical trials. Availability of appropriate funding, from local venture capital funds[14] and governmental grants, dedicated to take the risk of investing in biomedical projects, is therefore vital for their materialization. Governments can thus use spin-offs to promote regional development.

Spin-off should consider, as soon as applicable, to seek strategic alliances with large companies, sharing endeavors in the development and marketing of a viable product. To this end, it is worth noting that most of the large pharmaceutical companies' strategy is to recruit new technologies and new potential drugs through mergers and acquisitions or alliances with small medium enterprises (SMEs). As to the benefits, if a university holds an equity position in a spin-off or has licensed key IPR, the financial payback can be substantial and therefore, make spin-off support an attractive venture for academic institutions.

[13] In this paper "startup" refers to newly formed Hi-Tech companies.
[14] Desirably, also from international venture capital funds.