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Technological Transfer Office's Organization and Efficiency: The Case of the French System.

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GRENOBLE ECOLE DE MANAGEMENT

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1. Introduction

1.1. Context

The French knowledge production ecosystem was really built after the Second World War. It is based on a Colbertist model characterized by a big involvement of the state.
The international scientific performance in France is quite average, the transfer of the production and the return on investment stayed weak (OECD 2014).
Since the 1980's this ecosystem has changed a lot. New laws were implemented in order that France stayed competitive regarding innovation and industrial application. One important question during this period was how we can transfer new knowledge from public research to the industry.
According to different studies and reports, France stayed weak in this domain comparing to other countries as USA and UK (Curi et al. 2012; Curi et al. 2014; Conti & Gaule 2011; Kiskiene 2014; Jackson et al. 2012). We will try to understand how this sector was built and designed. To this end, we will study the history of the organization of the French knowledge production. Then, we will focus on other countries in order to understand why we are not as competitive in transferring technology as these countries.
Based on that study, we will suggest a solution to enhance this sector and to allow the office in charge of the knowledge transfer (Technological transfer office) to be more independent and more attractive for private investment. The final goal will be to develop new drugs at late stage.

1.2. Interest of the subject

French Technological Transfer Offices (TTO's) are mostly support by public institutions. A few ones are outside of Public Research Organizations (PRO's). Most of them are only departments of PRO's without financial resources and the right knowledge that would make them profitable. Even if some structures are more independent and have built business around the Technological Transfer, they are still dependent of the institution behind them.
The only TTO's that are "independent" are the SATT (*Société d'Accélération du Transfert de Technologies*). They were developed after the "grand emprunt" made by french government. They were created to develop the technological transfer and at the end of the "grand emprunt" they will have to be sustainable.

In order to answer the first question: how the French TTO's are organized? We will review the historical set-up of the knowledge production in order to understand the particular French ecosystem. After, we will review the TTO's organization and we will try to explain why we need them.
Based on this first part, we will compare the performance of the French TTO's to another European country, the United Kingdom and to the USA in order to understand what are the differences between those models. We will then answer the second question:
What is the performance of the French TTO's compare to the UK and USA models? How can we improve it?

One problem in the sustainability of TTO's is the lack of financial asset. Some experts think that a business based on the management of the IP (Intellectual Property) needs 10 years in average to be financially sustainable (Thomas 2007; Carboni & Esteve 2015). In the actual economic context, Universities have to face and deal with the lack of fund to ensure the education. They also have to find money to run the laboratories (Vavakova 2006). That is why they cannot afford to wait for royalties or milestones. They need to find other ways to develop and push their best projects in late development stages (at least phase IIa/IIb). This would ensure a better Return On Investment (ROI) and the sustainability of TTO's.
But in order to make it possible, TTO's have to find a way to attract private investors while they stay the owner of the product they want to license or to sell after its development.
To involve more private funding in the Technological Transfer you have to make it more attractive. Why a VC (Venture Capital) will invest in an early project when it will be later licensed (if it is) to a biotech company or big pharma?
The idea is to build a biotech like company with private/public equity. Investors would not put money in the company but in one or more projects the company will support.
In this part, we will demonstrate how huge can be the return on investment. And also how TTO's will became sustainable by building this kind of company. We will build a business model that can be used to benchmark select projects based on the preclinical results.

2. Research presentation

2.1. Why technological transfer is important?

We need to study and set metrics to compare the different TTO's and their respective efficiency. The questions will be: what is the efficiency of the French TTO's in an international context? Can we improve it?

The main challenge of this project is to transform an inefficient system in something that allows more financial liberties to TTO's.
The main problem in public research is the lack of fund. TTO's are here to transform knowledge into money in order to support further research. This system is not as successful as wanted by French institutions. Increasing the ability of TTO's to push new drugs candidates into late stage will have two main effects:

- More private fund involvement in public research. This will help and accelerate the development of new drugs. At the end it will enhance the performance of international scientific production in France.
- More help to public institutions and TTO's. They will then become more sustainable. Sales of product licenses in last development stage will increase the fees.

The objective is to develop a model that allows TTO's to benchmark a project in order to attract private investors.

2.2. Research questions

First objective: What is the efficiency of French TTO's compared to UK and US.

To study and compare TTO's we will try to answer those questions:

- *What is the national organization of TTO's?*

Through an historical review, we will try to understand the organization of the knowledge production in France. That will lead us to understand the need or TTO's.
Then we will review the organization in two other countries: UK and USA.

- *What kind of metrics are we using and why?*

We will use different databases:

- AUTM (Association of University Technology Managers),
- OECD (http://stats.oecd.org/),
- European community (http://ec.europa.eu/eurostat/web/science-technology-innovation/data/database)

Those databases are built to follow different indicators as:

- Number of patent,
- Number of people involved in the research,
- Financial involvement of different institutions/states,
- Age of TTO's.

We will also use some surveys (Piccaluga et al. 2011; Réseau C.U.R.I.E 2014; Conti & Gaule 2011). We will use those that already exist for different reasons:

- It is quite hard to make French people talk about money (in order to know more on the deals made with the industry). The survey used for the French part of the analysis came out in 2014. It is the first one with clear results.
- Those surveys are based on questions about metrics that are comparable between countries. With those, we had enough results.

- *How can we compare them?*

We will use two different models. The first one is based on ratios between TTO's production of the amount of money spent in it. The second one is a Data Envelopment Analysis to assess the relative efficiency of the TTO's. We will built those models regarding the literature and adapt it to the available data.

- *What are the differences?*

This last question will be the conclusion and the discussion of the first part. With the result of this analysis, we will choose at least one point that can be improved.

Second objective: How can we improve it?

At the end of this study we will try to explain what we can do to improve the efficiency of the TTO's. The idea is to modify at least one metric that is really important to explain the differences between the different organizations.

One possibility will be to build a biotech like company that can push the project in late stage. We will develop why it can be a solution regarding the market and the financial points of view.
It will be developed in 4 questions:

- What will be the business plan of this company?

Through a business canvas, a SWOT analysis and a Porter analysis, we will explain the positioning of the company. We will also explain the differences between this new company and what already exists. In the end we will show why this kind of business plan can become the add value of the company.

- What will be the financial structure?

As the business positioning will be in what is called the "valley of the death", we will build a particular financial structure to allow private and public investors to fund public research.

- How projects are chosen?

In this study we will explain how we can select a project based on a financial analysis. We will assume that the project is already selected on scientific bases. So we will evaluate what we have, what we need and what can be the market.

- What will be the NPV (Net Present Value) of the project regarding the different stages?

With the financial analysis and regarding the investment of each partners of the project we will set-up the expected return on investment (ROI). The NPV will be calculated taking into account the investment in each clinical phases and the expected market.

3. Literature review

3.1. Knowledge production in France

France is traditionally a country of science and technology. Even today, France is at a significant place in this domain. Since the 17th century, France participates actively to scientific and industrial revolution. After the Second World War, the French system of research and innovation is built to become what we know today (OECD 2014).

3.1.1. An Historical review: the Colbertist State

It is commonly accepted that the French science and technology system has been developed following a so called "Colbertist model" (Papon 1998; Papon 1973).
This model can be described by state intervention in the economy through publicly owned companies (Papon 1998).

Historically, this model was set during the 17th century with two main objectives. The first was the production of knowledge through the support of academic science and the second was the implementation of national missions or public oriented policies through "mission-oriented" institutions (Papon 1998; Ergas 1986).

This model can be described by three principal characteristics:
(1) Some institutions as the CNRS, INSERM, INRA… manage the organization and the funding of the largest part of the fundamental research and are distinct from Universities.
(2) A dual higher education sector producing at least one type senior technical person little known elsewhere, namely the "Grandes Ecoles" technical experts elite of engineers cum industrial managers, cum high level political and administrative personnel.
(3) A pervasive involvement of the State in the production of general scientific and technical knowledge, and in the production of patentable and/or immediately usable products (Mustar & Larédo 2002; Ergas 1986).

One of these characteristics began with the creation of the CNRS just before the Second World War in 1939. It is one of the only public fundamental research institutions in Europe with this size and central role. At that time, University research was weak and this creation developed the model of full time professional researcher. It was created to reinforce the

University research but does the exact opposite: accentuate its weaknesses. In the 1960's was took the decision to create units known today as Joint Units ("unites mixtes"). These Joint Units set-up in University were able to host CNRS personnel, but it took around 20 years for have, in full-time equivalent, as researcher between CNRS and Universities (Picard 1999; Mustar & Larédo 2002).

We can also point out that the clear division between the research and Universities is reinforcing by the creation of own governmental research structures after the WWII. INSERM, INRA, INRIA and other were built. Comparing to other countries this kind of structure became more autonomous; in France it stayed under the authority of the State (Mustar & Larédo 2002). More of that, each of them are place under the guardianship of different ministries: CNRS under the "Ministère de l'éducation", CEA under the "Ministère du développement et de l'industrie"… At the end the State played a great role in the national economy by investing in the research (Papon 1973). In 1983 the percentage of share of government-financed R&D carried out within the government sector was 47% (26% in the USA) (Ergas 1986).

Another major trait is the major contribution of public funding in the research. Between the end of the WWII and the 1970's, the French public authorities concerted their efforts and budgets on large program. Those kind of program existed in other countries but it was quite systematically implemented in France. It led to the creation of the General Delegation for Scientific and Technology Research (DGRST, that regrouped all civil R&D budgets from the State), to the creation of the CEA (Atomic Energy Commission), the creation of INRIA ("Plan Calcul"), *etc*… (Mustar & Larédo 2002).

And finally at the other end of knowledge production there is Industrial Research.

In this area the literature statue on three specific characteristics:

(1) The large amount of share financed and performed by the public sector relative to that of industry.

(2) The importance of State subsidies and order for firm and the fact that SMEs (Small and Medium Enterprise) are not involved in it (Mustar & Larédo 2002).

(3) "The instinctive over cautiousness of our manufacturers, their fear of risk, their ignorance of how to take advantage of university research, in sum the ignorance of the benefits and process of innovation…" (Salomon 1986). Looking at number comparing other countries, the share of French enterprises in national R&D was only at 40% as compared to 60% in

Germany and 63% in Japan. The firms in France were employing about 41% of all researcher while the in the USA it was 56% (OECD 1982, 1985, 1991).

3.1.2. The first revolution 1980-2000: changes in Innovation and Research policy

"In the course of the 1980's and 1990's, the French research system – in both public and private dimensions – has, in effect, experienced profound transformation" (Mustar & Larédo 2002).

The gap between research and Universities no longer exists. For example at the end of the 1990's, ten new positions were created in the University for only one for the CNRS. That led to a proportion of teacher researcher highly superior to the number of professional researcher. Even in the "Grandes Ecoles" this number increased and for every five thesis produced in France one came out research centers of those school (Papon 1998).

In 1982 a law for science and technology (*The Law on programming of research and technological development*) was voted giving to scientific agencies (CNRS, INRA, Inserm) both general and specialized tasks. Those agencies were entrusted new tasked and responsibilities as the transfer and application of science and technology in the economy. In each institution a service of valorization was created. The CNRS was allowed to engage in industrial ventures (Papon 1998). There was a clear trend to build interdisciplinary approach made by the CNRS to fight against the weakness established by the elitist attitude of the French scientific community.

It was nearly the end of the large program as the laboratories have now a large degree of freedom for choosing scientific issues (Papon 1998; Mustar & Larédo 2002). New entities were created to enhance the collaboration between industry and governmental laboratory (Grouping for public interest: "les GIP").

Another major change of the system was the cooperation between France and Europe and the launching in 1985 of the EUREKA program (it is still running today). It is an intergovernmental organization focused on mobilizing funds and fostering collaboration. It has been responsible for bringing together SMEs, large company, research institutes and University (Anon 2015). Similarly new kind of joint unit were created between University, CNRS and mission-oriented institutes like CEA, INSERM…

Region had a growing role following the Decentralization Act (1982). It allowed them to support SMEs R&D and built their own new projects and policies (Mustar & Larédo 2002). In addition of the right of the CNRS to build spin-off, between 1982 and 1992 more than 200 SMEs were created (Vavakova 2006; Mustar 1994).

"…Relation between public research and the enterprise sector…is one area where the change were the deepest over the last years, thus rendering the critique of academic research as unrelated to the enterprise sector, no longer pertinent today" (Mustar 1994: 352). The cooperation between research and industry was confirmed by looking at the growing number of contract and the growing number of patent application (Vavakova 2006).

Those changes led to decrease of the State sovereignty. The privatization of most state-owned industrial company, bank, Assurance Company… has deprived the state of an essential tool to influence national technological development. The support of industrial research by the State is now limited to two major interventions. The first is through the ANVAR (Agence Nationale de Valorisation de la Recherche) that allowed to SME's reimbursable form of aid. The second are taxes credit to promote the research. But the management of those intervention is largely decentralized to the regional level (Mustar & Larédo 2002).

Nevertheless, at the end of the 1990's, two reports, one from the Revenue court (Cours des Comptes 1997) and another commissioned by the government (Guillaume 1998), made a negative appraisal of the valorization practices of publicly funded institutions. The income of the collaboration only account for 5 to 11% of their total budget, it appears that neither the research laboratory nor the central administration benefit from contract with industry. An anarchic situation is pointed out; only 60% of collaborations are reported to central administration. Worst of that, the CNRS estimated that up to 2000 patent were given to industry without any fees (Vavakova 2006).

3.1.3. The second revolution 2000-2015

In 1999, a law was voted (the *July 1999 Innovation Law*) followed by a reform in 2001 (*New Public Management Oriented Reform*). The first impact was to increase the number of TTO's (Curi et al. 2014). This increase is explained by the fact that before the law, not all Universities had their own internal TTO. The Innovation law imposes to all universities to

develop an explicit policy for commercializing their result and some private accounting rules were introduced for technology transfer activities.

With this new policy, academic researchers must be more involved in the valorization of their research. It became legally possible to develop their academic result with an industrial approach. They are helped to build spin-off. In fact they can directly exploit it under some conditions (Vavakova 2006).

2001 reform was introduced to accelerate and improve the quality of technology transfer process by defining the funding scheme of technological transfer, identifying the key driver of TTO's performances and also defining the metrics aimed at monitoring the efficiency of public spending. Even if an increase in the metrics was observed after the introduction of the reform, the evidence of substantial growth in productivity of French TTO's cannot be assured (Curi et al. 2014). The French technological transfer process is a complex process characterized by different kind of TTO's. Their productivity is strongly dependent of their environment (presence of hospital, age…). Nevertheless, the two laws provided a stimulus for some TTO's to push upward the frontier.

In 2005, the National Research Agency (ANR) was launch, and with it the fund directly allocated to the CNRS and Inserm were reduce. In contrast with them, ANR doesn't have any scientist on its governed board and it grants fund to project based on a new system: call for proposal. The research proposal have to be in line with particular field of research (Dente 2009). This new organization change the way research was funded. A major role of Technological transfer offices appeared: sourcing and helping researcher to construct projects in line with the call for proposal. In the other hand, with this evolution of funding, TTO's became a major actor in finding collaborations with industrials for projects that were not in line with the policy of the ANR. The creation of the ANR was the result of the *Pacte pour la Recherche.* The Research Pact project is based on three axes (i) a balanced development of the three basic components of the research, (ii) the development of interfaces and cooperation between actors and (iii) introduction of global and long-term strategy to increase confidence between research and society (Muller et al. 2009). Some TTO's were built in this period, enjoying the policy of the government (SATT). PRO's also need to have specific affiliates that build expertise in the area of technological transfer and built strong relationship with the private sector.

3.1.4. Challenges and new Theories

One problem is the high number of patents that are not licensed and the few number of licenses that turn into significant earners. Based on the AUTM report (Figure 1), only 50% of patents were licensed and only 0.5% of it had royalties (Fraser 2009) .

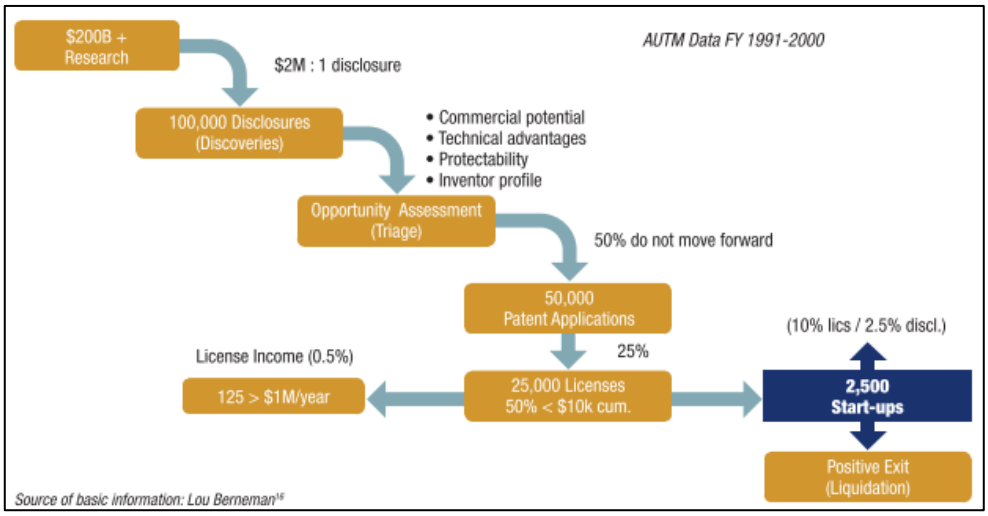

Figure 1: From Research expenditure to Value creation (Fraser 2009)

Part of the challenge of managing a technological transfer activity is the tension between the reality that economic success is largely driven through a small proportion of the inventing individuals, and the egalitarian nature of a university (Thomas 2007). For the Public Research Organizations all research is important so all inventions have to be patented. One new theory is not to play on the number of patent but on the maturation of a project (e.g a Patent and its application) before its licensing. The other shift that occurs comparing to old theories is to move more on start-up companies (Huggett 2014)

These two theories are really linked to the point of view of the investors on the technology and on the institution they have to deal with. Looking at the technology, one main complaint is that owners of new technology over-evaluate it. That is maybe an explanation on the very small number of license deals.

Looking at the institution, investors prone to work with all institutions, they just want to avoid a process that take time and delay the process of spinning out.

To enhance the technological transfer in France, Public research institutions have to enhance their abilities to analyze and to market their patents. This is the main role of TTO's and of the SATT in particular.

3.2. Technological Transfer Office's

3.2.1. Why do we need them?

Worldwide, Technological Transfer Offices (TTOs) are at the interface between academic research and industrial exploitation.

They play a critical role in the diffusion of innovation and the development of new technology (Siegel *et al* 2007).

They have a large scale of activity:

- Sourcing: they have to manage different researcher,
- Portfolio management: they manage patents, study if an invention is patentable, license it, sell it,
- Project management: they select different projects to invest in,
- Institutional relation.

In the biotechnological environment, this activity is highly important looking at the fact that industries put less money in their R&D department. More of that it help start-up to build a project and developed their business.

In fact they help to bridge the gap between research and innovation.

To build this bridge across the "Valley of death" (Landry et al. 2013) TTO's emerge as intermediation organizations. On one side of this valley we find producers of knowledge. Universities and government laboratory respond to the need to maximize measurable research unit. On the other side we find the users of this knowledge. This User, industry, acts to maximize their commercial and financial assets (Landry et al. 2013).

In 2007, Macho argues that good industry-science relations have a positive impact on the innovation performance. They conclude by explaining how TTO's can play a specific role in this relation (Macho Stadler et al. 2007). TTO's have to build a reputation for laboratories /institutions that they represent because their activities are not large enough. They point another critical role: to reduce the asymmetric information between industry and science. Industry can have some trouble to evaluate the quality of an invention when researcher have problem to estimate the commercial value.

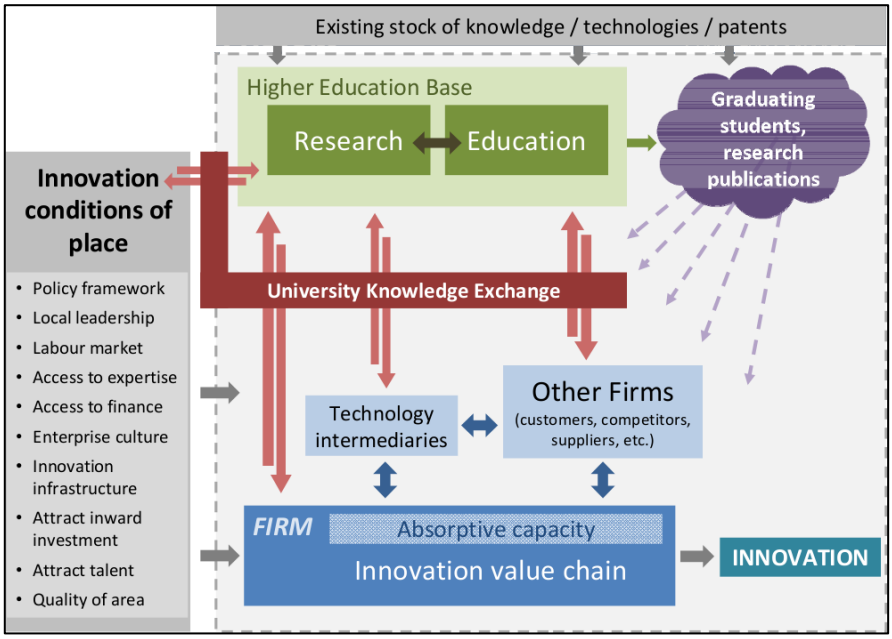

Figure 2: Intermediary role of TTO's

As summarize in the figure. 2, technological transfer offices (in red) have a translational role between Public research offices (Higher Education Base), Firm and environment (Innovation conditions of place.

TTO's have to deal with a complex development road from basic research to production and marketing (Figure 3). Nowadays the role of TTO is mainly focus on the two to three first phases of product development and this work does not involved private investors as business angel and Venture capital.

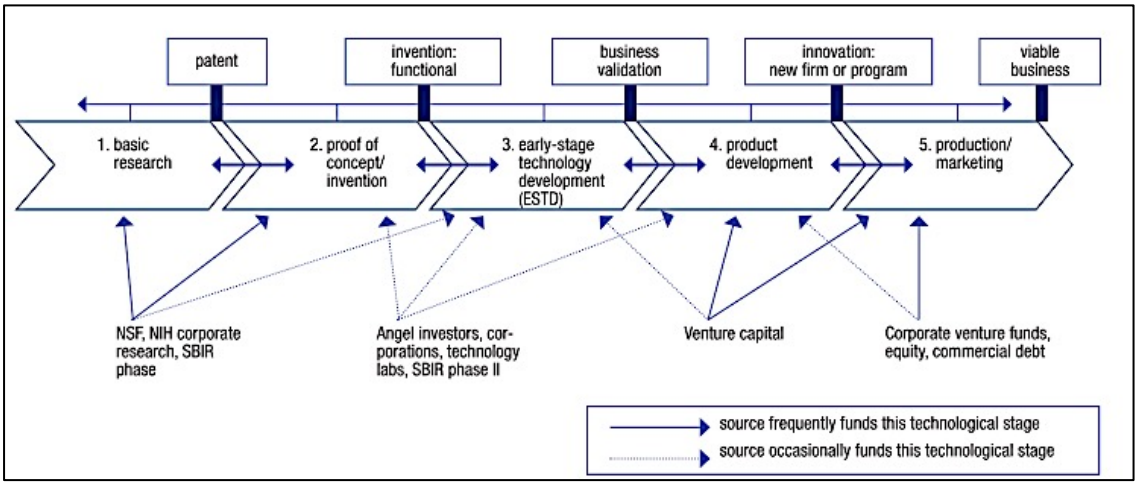

Figure 3: From basic research to marketing (Fraser 2009)

3.2.2. Role and Business Model

"Knowledge extremely important economic resource if exploited efficiently".

(Jackson et al. 2012).

According to OECD and to the ENTENTE Consortium, TTO's have different role. These two reports identified the same main role that is to establish relationships with firm and community actor through research collaborations. Theoretical and empirical work in innovation economics suggests that setting up and maintaining good industry-science relations positively affects innovation performance. The link with scientific knowledge is especially important in fast growing technologies like biotechnology (Macho Stadler et al. 2007).

Collaborations can be defined by the provision of infrastructure and research expertise to address a research need of an industrial partner (ENTENTE White Paper). Research collaborations are the first step to other kind of activities. To build this partnership, TTO's developed different activities as sourcing and identifying technology opportunities. They have to identify research that has potential commercial interests and strategies to exploit it.

One of the other activities is managing the intellectual property through patent application and licensing. And the last activity is around the formation of university-connected companies utilizing public research organization technology and/or people (Start-up/Spinoff).

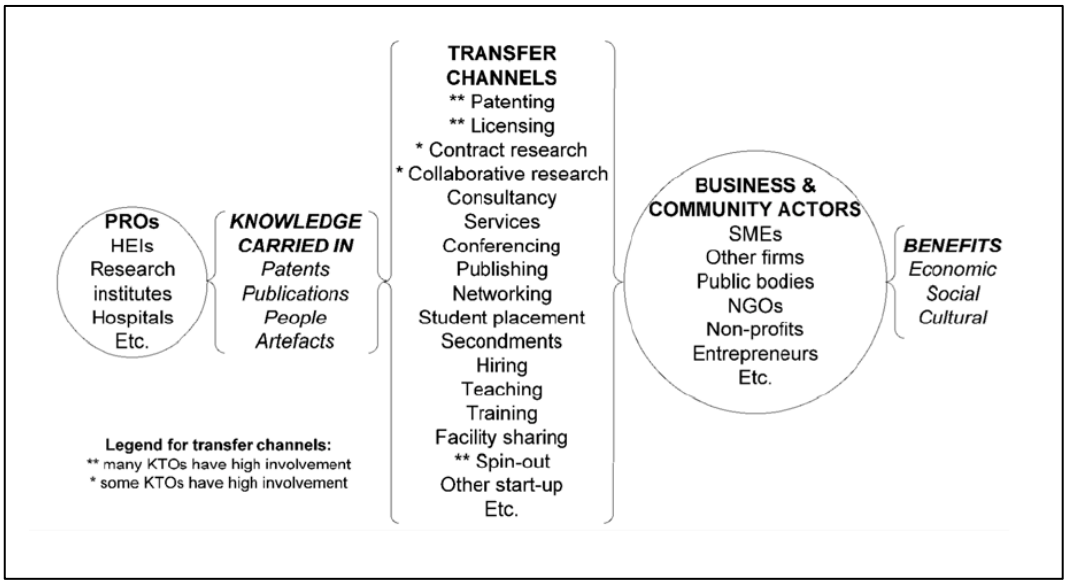

Figure 4: Knowledge transfer from PROs (European Commission 2009)

Technological transfer offices offer development and management services and are instrumental in bridging between knowledge providers and knowledge users. The focus on open innovation and the complexity of models of innovation (multiple and/or geographically spatial partners), leads on a real need for intermediation. This role is also amplified by the fact that in one hand large companies develop "knowledge gatekeepers" who search opportunities and develop knowledge transfer while smaller company doesn't have resources. The other point is that Universities are encouraged to work with SMEs that cannot fund knowledge gatekeepers (Alexander & Martin 2013). So for the public research institution, the most important role of TTO's is to build legitimacy for new technology.

Summarizing technological transfer process with only one business model is difficult, as it exist different kind of TTO's. Nevertheless, TTO's general business model is built around the following building blocks: they offer mixed and customized solutions to their clients, target very small firms, do not primarily depend on revenues from scale of services, develop strong ties with their partners and clients, formulate differentiated strategies for the different stages of the value chain and dispose of differentiated types of human resources for different stages of the value chain. We can also add that four different types of business model emerge by positioning the different types of TTO's on the different building blocks (Landry et al. 2013).

- The *validation-centered business model*: providing customized solution for single client firms with a well-defined market segment. The generation of revenue from sales of services and the implementation of a well-defined market strategy are the first goal. It is support by a strong attention to the validation of knowledge-based opportunities.
- The *exploitation-centered business model*: this business model is more involved than the previous in the provision of services at the three sub-stages of the exploitation of knowledge-based opportunities: solving legal issue, facilitating access to capital and fostering the commercialization of innovation. This business model is strongly dependent of the government innovation policies.
- The *PRO's government dependent exploration-centered business model*: more based on technical resources and human resources. Implementation of well-defined strategy regarding the promotion of their services but less involved in the provision of services at the three stages of the knowledge value chain.
- The *undifferentiated exploration-centered business model*: more involved regarding services linked to legal issues at the exploitation stages of the value chain (figure 5), and more involved in the provision of services linked to issues of access to capital at

the exploitation stage. This model can be describe as an undifferentiated knowledge and technology transfer business model.

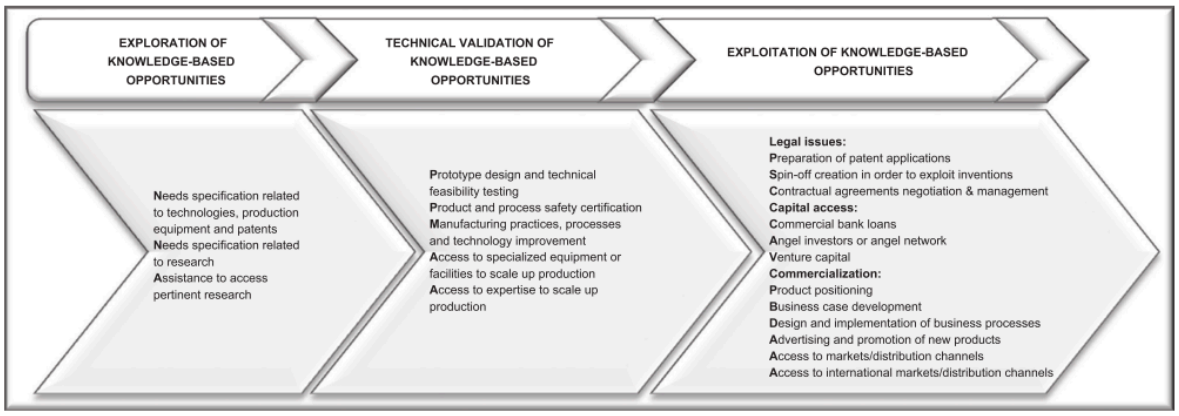

Figure 5: the three sub stages of the exploitation of knowledge (Landry et al. 2013)

3.2.3. Organization

There are different types of organizations regarding the type of Technological transfer offices. In this part, we will see that the government policy play a role in the organization of the Research and Development in the different countries we will study. This organization has a big impact on the organization of the technological transfer across the world.
Even if the TTO's play the same role their organization and implementation will change regarding the country.

3.2.3.1. In France

As we saw before, the French research environment is quite complicated. Since 2001, Universities and Schools have to transfer their knowledge. The number of TTO's increase and you can find a lot of different organizations, about 352 (Réseau C.U.R.I.E 2014). With the introduction of the SATT the environment change one more time. Now Universities and some PRO's (like the CNRS) don't valorize their result and patent, this role is played by the SATT. Nevertheless, we are in a tri-parties system. Most of the researches are still paid by the state. This funding is done through different way: ANR, Europe, region… And when a project is founded, you will find at least different PRO's (they managed the UMR). So when the project is not about fundamental research but about a future product there will be some industrial involved.
This triple helix organization (Etzkowitz 2003) is really regulated. A commercial project cannot be funded with public fund if there is no return. So one of the roles of TTO's will be to secure this collaboration. Their other role is to find and fund project (sourcing). Those two

roles are mainly done by the valorization service in universities, school and PRO's. When it comes to licensing or selling patent, SATT play a big role. Even if some PRO's still have an office that play this role (Inserm Transfert, Inra Transfert), all the Universities, school and other PRO's give right on their patent to the SATT. Those offices will evaluate patent and find industrial that will exploit it. Their business model is based on in licensing out licensing; they will keep a percentage on each transaction. They really just transfer the technology without any amelioration. No TTO's will invest directly in one project to improve it. The second role of such offices is to provide services: managing intellectual property, set-up projects and set-up international collaborations.

3.2.3.2. In the USA

In 1980, Congress enacted the Bayh-Dole Act1 and allowed U.S. universities, teaching hospitals, and research institutes to have the automatic right to take title to inventions developed with federal funding. In response, these institutions have established offices to seek patent protection on these inventions and license them to existing and new businesses for development and commercialization. Since 1991, the Association of University Technology Managers (AUTM) has published an annual survey that has quantified the magnitude of this enterprise(Abrams et al. 2009; Tseng & Raudensky 2014).

Commercial institutions pay royalties for the right to put inventions and discoveries from universities to commercial use in products such as computer-imaging technology, medical diagnostic testing, and treatment of disease. Institutions of higher education, in turn, can use the revenue to increase investments in research and development. This technology transfer also leads to sponsored research agreements between firms and universities, often to undertake additional research needed to commercialize technologies. Universities now receive approximately 7 percent of all research funding from industry, compared to about 3 percent in the 1970s. Institutions of higher education also reported spinning off nearly 350 companies and receiving 3,450 U.S. patents for new technologies and inventions. Since fiscal year 1998 when the question was first asked, 178 U.S. survey respondents have reported a total of 2,230 new products introduced to the market place (http://www.referenceforbusiness.com/management/Str-Ti/Technology-Transfer.html#ixzz3sJepTvzi).

In the U.S. Fewer than 15% of TTOs are organized as independent corporations. An independent corporation can develop a culture that is quite distinct from that of the parent

institution, whereas if the TTO is an integral part of the institution, it will inevitably share its culture (Abrams et al. 2009).

3.2.3.3. In the U.K

Each university in the UK is independent and develops its own strategic goals, emphases, brand and approach to intellectual property management and the commercial development of research outputs. UK universities are almost all charitable bodies, required to comply with charity law. Their charitable objectives are research, teaching and scholarship and the application of new knowledge arising from these activities. Everything that universities do must be directly in line with these objectives. This applies to their business transactions, including the commercial development of their research outputs (Brady et al. 2015)

3.2.4. Why comparing France, USA and UK?

When we talk about technological transfer we firstly think about the United State of America. Historically it is the first state to allow its university to manage their patents. As the right on patent are allocated automatically, PRO's constructed structures to manage this Intellectual property. That is why it can be taken as a model for the technological transfer.
We also have to take into account one major difference between USA and Europe: it is the lack of venture capitalist. That induces a gap in research productivity between Europe and the US due, in part, to a lack of financial resources made available for universities and research in Europe (Conti & Gaule 2011).

In Europe, knowledge transfer between industry and higher education underachieves when compared directly with the United States. Europe is usually considered among the best world performers in terms of research capacity, but this potential often fails to transform into innovative products and services and the potential contribution to economic growth is lost (Jackson et al. 2012; Alexander & Martin 2013). French and UK governments' have wholeheartedly subscribed to the knowledge-based view of society. The authors agree that knowledge is an extremely important economic resource, if exploited effectively (Jackson et al. 2012)

In the UK and in France, there traditionally has been a strong focus on publication of papers rather than patenting. This is encouraged strongly by the allocation of government research

funding through the Research Assessment Exercise (RAE), which rates University Departments in terms of publications, research students and studentships, and amounts and sources of external research in the UK. In France it is quietly different, PRO's rate the research unit and allocate resources to them. This appears to contrast with the USA perspective outlined above in that the UK/French focus has been on information, whilst the USA focus has been more on invention (Decter et al. 2007) .

Nevertheless, we saw by looking at the different organization of the technological transfer offices, that those three country tend to have the same model. Technological transfer offices are either internal or external to Universities. TTO's in those three countries are organized around two business models:

- The *validation-centered business model*
- *PRO's government dependent exploration-centered business model*

The other reason to compare France with UK and USA is that worldwide, technological transfer process is considered to be the best in the USA and in Europe, UK is consider to be the most advanced country (Commission 2009; OECD 2014; OECD n.d.).

4. Comparative study of the efficiency of the different TTO's organizations

The efficiency of university TTOs can be measured in numerous ways. The simplest method would be to rank universities purely based on licensing income. (Anderson et al. 2007).
Numerous study access the efficiency of TTO's around the world. In the USA, Association of University Technology Managers (AUTM) makes each year a licensing survey for more than 20 years. In Europe, this role is support by the Organization for Economic Co-operation and Development (OECD).

4.1. The Metrics

We will use the main metrics that are recommended by the European commission.
Those metrics are:

- Invention disclosure
- Patent application
- Patent grants
- Licenses executed
- Licenses income earned
- Spin-off/Start-up established.

As it is explain in this report measuring the amount of knowledge transferred is quite impossible. So we will focus on the transfer himself. Number of contract research, number of patent… can be measured.
Nevertheless, we have to remember that metrics are just number. The number of patent for example is not as important as the value it creates. Increasing the number of patent or the number of spin-off can be a bad policy. Non-viable spin-off, patent with no final value will cost more than the revenue generated for the PRO's. We will try to find out how the value is created.
The comparative study will help us to understand what TTO's have to improve to become sustainable.
The main data we will use cam from different survey and databases:

- USA's data came from association of technology managers and business (AUTM: http://www.autm.net). We also use data from Timothy R. Anderson *et al.* (Anderson et al. 2007) and data from the Proton survey (Piccaluga et al. 2011).
- UK's data came from the Proton survey, Chapple *et al.* (Chapple et al. 2005), European commission (Commission 2009).
- France's data mainly come from the CURIE survey (Curi et al. 2014).

We made an average of the number from those different sources per year for the period from 2005 to 2011.

We found the following metrics:

Location	Research spending	Number of TTO	Invention disclosure	Patent application	Licenses executed	Licenses income	Spin-off-start-up
USA	40360065600	186	21856	13271	6051	1800000000	671
UK	2658334000	163	4222	2256	5074	119000000	266
France	4314000000	163	3392	1711	724	161000000	262

Table 1: Average metrics of TTO's from 2005 to 2011

4.2. Method

To compare efficiency of TTO's in different countries, we will firstly made a simple ratio of each output compare to investment.

Location	ID/RS	PA/RS	LE/RS	LI/RS	SO/RS
USA	5,41525E-07	3,28815E-07	1,49925E-07	0,04459854	1,66253E-08
UK	1,58821E-06	8,48652E-07	1,90871E-06	0,044764879	1,00063E-07
France	7,86277E-07	3,96616E-07	1,67826E-07	0,037320352	6,07325E-08

Table 2: Ratio of metrics

When we look at those ratio, the first thing that we see is that UK TTO's have the best one in each metrics. But what is the effectiveness of TTO's and what is their relative efficiency?

This issue has been explored by using different methods.

Thursby and Thursby (Thursby & Thursby 2002) describe a three-stage process to calculate the total factor productivity. This approach is based on Data Envelopment Analysis (DAE).

This method was firstly developed by Charnes, Cooper and Rhodes in the early 1970's to assess the relative efficiency between different Decision making units (DMU). This model was built on the earlier work of Farrell in 1957.

We can represent the mathematical model by this schema.

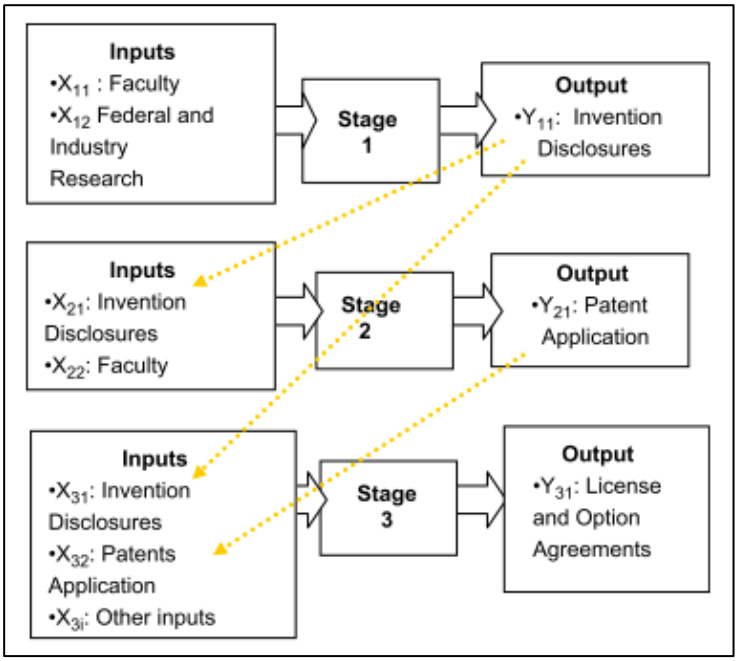

Figure 6: Thursby and Thursby three stages DEA model (Anderson et al. 2007)

The authors decided to exclude two widely exposed metrics in the measurement of technology transfer: "patent issued" and "Licensing income". This is because of the time lag involved in the process of converting key input into those two outputs in their respective stage.

In 2007, Anderson *et al.* (Anderson et al. 2007), developed another model to assess the efficiency of university technology transfer in the USA. This one stage process only take into account one input: Research Spending and by using the DEA model compare the relative efficiency of TTO's regarding their outputs.

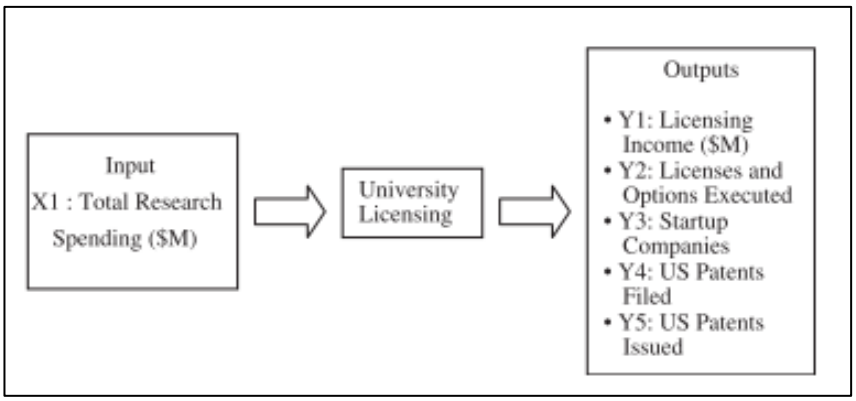

Figure 7: DEA outputs oriented model (Anderson et al. 2007)

We choose to use the same model: the mathematical explanations are in Attachment 1.

This model is an Output-oriented model. We assess that it is hard to change the research spending. The second assessment is that TTO's can work on the outputs they produce.

4.3. Comparison

When we look at the ratio we found earlier, it seems that United Kingdom's technological transfer offices are the best one, so we will run the DEA outputs-oriented model in order to know how we can improve output from USA and France.

We used the average Inputs and outputs per TTO.

Location	Research spending	Invention disclosure	Patent application	Licenses executed	Licenses income	Spin-off	Output	Input	Efficiency
USA	216989600	117,5	71,3	32,5	9677419	3,6	1	1	1,00
UK	16308797	25,9	13,8	31,1	730061	1,6	0,08	0,075	1,00
France	26466257	20,8	10,5	4,4	987730	1,6	0,10	0,122	0,84

Table 3: DEA analysis maximizing USA output

By applying the model on the USA we found that its relative efficiency is 100% as the UK. France has a relative efficiency of 84%. That means that by increasing its output, French TTO's can became relatively more efficient.

Location	Research spending	Invention disclosure	Patent application	Licenses executed	Licenses income	Spin-off	Output	Input	Efficiency
USA	216989600	117,5	71,3	32,5	9677419	3,6	8,2	8,2	1,00
UK	16308797	25,9	13,8	31,1	730061	1,6	0,6	0,6	1,00
France	26466257	20,8	10,5	4,4	987730	1,6	0,8	1,0	0,83
Weight	3,78E-08	0	0	0	8,44E-07	0			

Table 4: DEA analysis maximizing French output

By running the model to maximize the French output, we also find a relative efficiency of 83%. The model shows us that the only output that is important regarding the efficiency is licenses income.

4.4. Discussion and Conclusion

With a ratio approach, we saw that regarding all the output one by one, the UK seems to have the best efficiency and it is harder to compare France and USA. By implementing the Data envelopment analysis output-oriented model, we saw that the USA and the UK have the same relative efficiency and the efficiency of French technological transfer offices is lower.

The model also showed us that in order to improve their efficiency, French TTO's have to increase their licenses income.

Nevertheless, we have to take this result with caution. This is only a relative efficiency between TTO's in France, UK and USA. For example in 2009, Abrams *et al.* (Abrams et al. 2009) assume that only 16% of the US TTO's were self-sustaining, bringing in enough

income that, after distributions to inventors and for research, there are sufficient funds to cover the operating costs of the program. They also argue that sustainable TTO's have a blockbuster in their executed licenses.

The model show us that working on the licenses income will help French TTO's to became more efficient, but it doesn't show us if that will be enough made TTO's self-sustainable.

In the next part we will develop a model to sell at higher price a license without other fund from government or from Institution.

5. How can we improve the efficiency of the French TTO?

In this party we will propose a new type of structure adapted to the French policy and Knowledge production model.

As we seen before, reforming the French system can be hard and will take time. The important structures are already present but private investors are quite absent. The problem is that projects licensed are in their early development. With this kind of project, the return on investment is not as interesting as projects in late development stage.

The second important thing is that most of the TTO's are only a department of PRO's or are totally owned by them (Inserm transfert and Inra transfert for example). In the first case private funding or investment directly in the structure is not legally possible. For the second case, PRO's wanted to remain the only owner of their TTO. PRO's want to keep the choice of the project they want to fund and the main objective of PRO's is to promote all the research, not only projects that only have an economical interest.

With this approach, raising fund is quite hard and the main problem to push projects in late stage is the lack of fund. The idea of this structure is to select, build, raise fund and drive different project. As this structure will not be own directly by public research organization, private investors can invest in it. But as we will see in this chapter, the idea is not to involve investors in the financial structure but directly in projects.

5.1. *Financial structure and Business Model*

5.1.1. Business Model

The business model of this company will be based on evaluating and building project for the clinical phases (I and II). The goal is to push the best research projects in late stage development. Nowadays, this work is mainly done by building spin-off or start-up or by licensing the potential drug to a big pharma. In the first case researcher who wants to continue the development of its own invention make the job. The main problem for them is to find partners and fund. Secondly most of them have no business experiment. In the second case, as this is the big pharma that takes risk to develop the drug the term of the license are not as good as it would be for later stage products. Nevertheless, there is a lot of patent that are dying because researchers as big pharma don't want to exploit them.

At the end, this is a big lost for the Public Research Organizations. The return on investment is not as good as it could be.

The business positioning will be in this "valley of the death". The company will work closely with the TTO to select project in their early development. With this approach, the researcher who works on it will be guided to develop the product with the idea of making a clinical trial at the end. The company will have all the pre-clinical data to evaluate different projects and choose the best on scientific and financial bases.

This company will not be a seed fund. Conventionally, a seed fund invests in project or start-up that brings the project, they don't own it. The company will build the project and fund it.

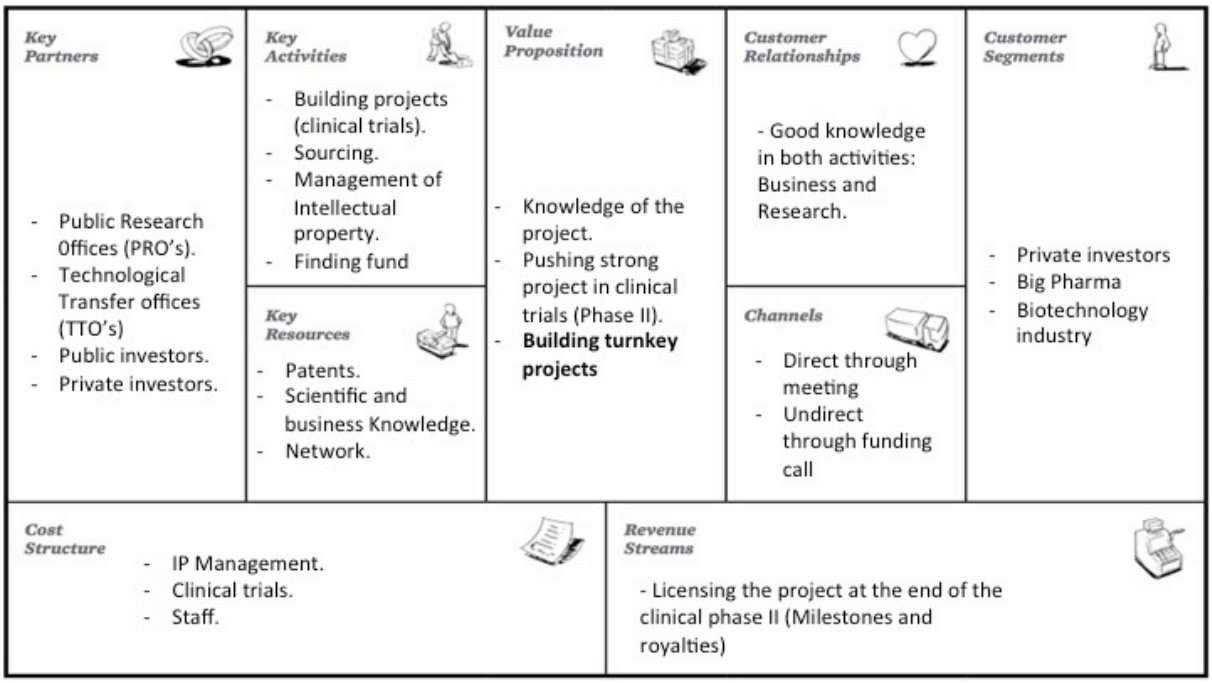

Figure 8: Business Canvas

If we take a look at the value chain, the company will have a great role in the organization of the Inbound logistic through the selection of the project and by working closely with Public research organization. In our case, we will not create one company per project supported: the best team in the domain of the project will support each project.

This team will be in charge of the "operation", in other words, the team will develop the project regarding its phase.

The next step, looking at the results and taking the decision to go into the next phase or to license the project will b the next role of the company. Once the decision is taken, the company will either choose the new team to develop the project in the next phase or market the product in order to license it.

Those activities will be support by a particular structure (Figure 9) defined in the next part.

Due to this organization, the company will be support by human resources of PRO and TTO. It will have access to Scientifics, business developers, IP manager and legal department.

As the company will mainly develop IP in collaboration with other PRO, it will not directly have to develop a specific technology to support the value creating activities. The heart of its activity will be to develop new technology, and by supporting research, creating new IP to develop.

The procurement will be made directly by the team in charge of the development of the project: the company will support it.

This value chain will focus on differentiation. By focusing on the improvement of the core competencies of the TTO (Sourcing, IP Management) and with the support of the best scientists, the company will be able to select and develop the best projects and license them to the best firm for the best price.

5.1.2. Financial structure

The Financial structure of this company will be unusual. The goal of the structure is not to become public but to stay under the control of the TTO. Investors (public as private) will not put money in the structure but project by project.

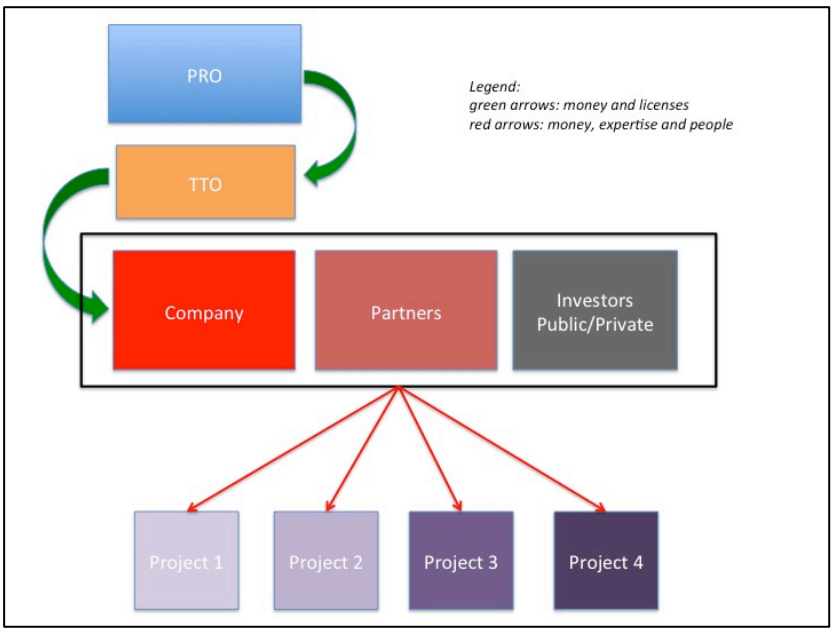

Figure 9: Financial organization of the company

In figure 2, the organization is explained; PRO's already put money and let their TTO manage their patents. The company will be owned by the TTO. This company will be specialized in building project in clinical trials. Until now, TTO's were licensing before and are not

specialized in this kind of activities. TTO's have to find an industrial to achieve this goal, especially for the phase III. The company will work closely with public structures that already made clinical trials as AP-HP in France (Partners). By working closely with researchers, clinician and business expert, the company will built strong project that can achieve clinical trials.

And as soon as each project will be built, the company will find some investors.

The company can be seen as a holding. Its vocation will be to group different partner and built projects. Each project will be comparable with a start-up. This kind of structure will enable private investors to invest directly in the project.

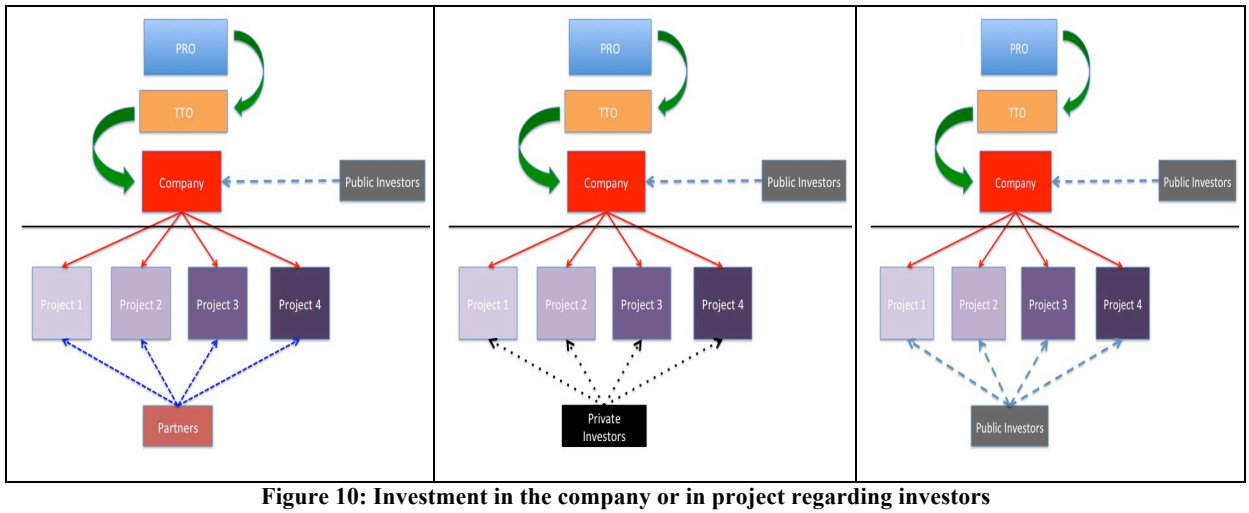

Figure 10: Investment in the company or in project regarding investors

The organization describe in the figure 3 explain how each parties involved in financing each project will invest. We will found different kind of funding. The partners will more invest with material, people and infrastructure. The private investors will invest with "smart money". They will invest money and bring their business expertise in the project they choose to fund. And the public investors (as ANR, ANRS, BPI, European commission…) will bring money. As this last kind of investors are more involved in building an ecosystem, and in developing research, they will be allowed to invest directly in the company.

We will see in how the different partner will invest and what will be the financial model.

5.2. Building one Project

The project we will choose in example will be in the area of the Immune-Oncology drug.

It will be an armed Antibody-Drug conjugates. This antibody will be specific of a particular subtype of ovarian cancer.

How it work:

Comparatively to the monoclonal antibody, Antibody-Drug conjugates (ADCs) carry a drug and provide a delivery vehicle to transport the drug inside the cell. Once inside the cell, the ADC will be degraded and will release the drug. It will lead to the cell death (fig…).

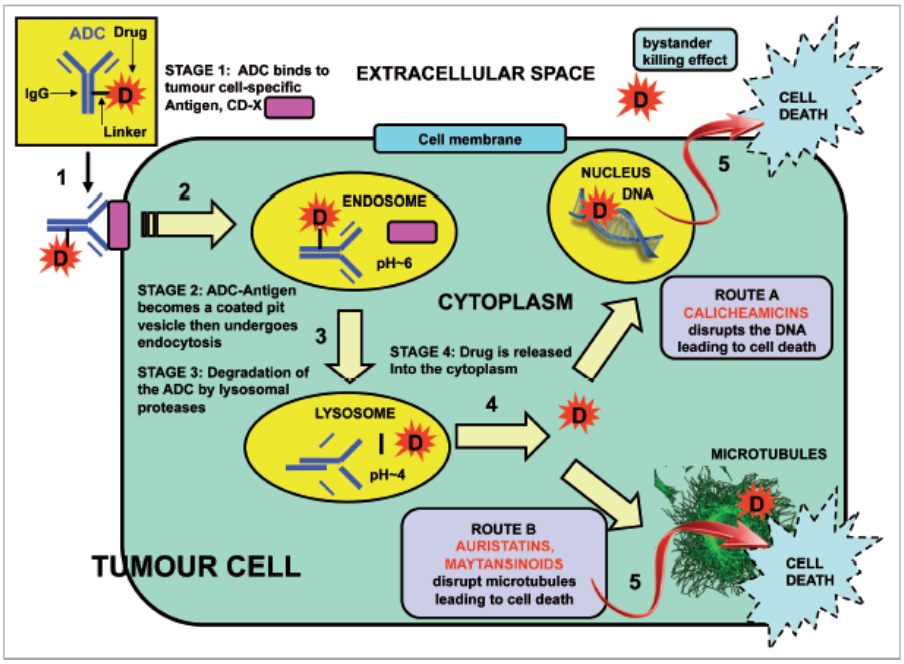

Figure 11: Action of an ADC

The main advantage of this kind of drug is that we can use molecules (drugs) that are cytotoxic for healthy cells. With a classic chemotherapy, all the cells are targeted, but by using an antibody to address the drug specifically to the tumor, we will control this cytotoxic effect. It will be healthier and have fewer side effects. The second advantage is to enhance the response of the cancer. Some of cancer are resistant against classical chemotherapy, coupling the drug with an antibody will increase the effect of the drug (by increasing the concentration of the molecule inside the cell).

There are three important aspects in the design of the ADC:

- The antibody.
- The linker.
- The drug.

The antibody has to be humanized (to prevent allergic reaction) and must target a receptor or a membrane protein that is only expressed or over expressed in the tumor. The critical factor in manufacturing ADC is the linker. The linker must undergo into hydrolysis only in the cell in order to have the best effect.

Actually they are 70 ADC's on clinical trials and 10 of them are in the area of the ovarian cancer. As the chances of success of the clinical trials of drugs in oncology is around 10%, we can assume that there is a chance that one product reach the market before us.

5.2.1. Market Analysis

Around the world, ovarian cancer has an incidence of 15 per 100.000 people. Our drug will be able to target around 50% of ovarian cancers.

Incidence	**0,000075**
Population	331000000
Selling price	10000
Production cost	1000
Length of the treatment	10
Number of patient/month	2068,75
Income/patient/month	12000
% Death/month	1%

Table 5: Parameters for the market analysis

The table 5 gives the parameters used for the market analysis. We will mad three scenarios, the variable will the market penetration and growth. According to the market in oncology, regarding the evolution of the sale of Roche (who owns the only ADC actually on the market), and the fact that there is no real treatment against the Ovarian cancer other than the surgical removal of an ovary or ovaries.

Comparing to the preclinical data and to other similar drug, the length of the treatment will be 10 months.

The selling price is also estimated regarding similar drugs already on the market as the production cost.

% Market share median	**20%**	**24%**	**28%**	**32%**	**32%**
% Market share pessimist	10%	12%	14%	16%	16%
% Market share optimist	20%	27%	34%	41%	41%

Table 6: Market penetration and market growth

The evolution of the number of patient is given by this equation:

(Number of new patients) + (Number of patients from the previous month) – (Number of patient who have reach the end of the treatment) – (Number of death).

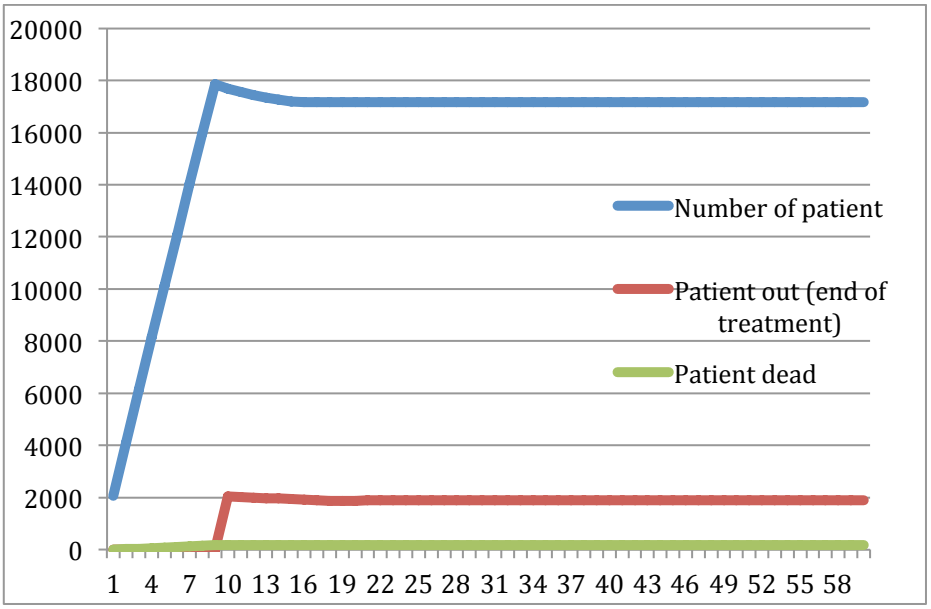

Figure 12: Evolution of the number of patient

On the graphic, you can see that if we control 100% of the market, we will be able to sell our product to 17,176 patients per month. We will reach the maximum of patient (18,000) after 9 month. After while, this number will decrease for 5 month and became stable.

But, as there is competitor on this market, we will not be able to reach this maximum. Regarding the market, we can expect an average of 4,3% growth for 4 years after the FDA approval.

We built three scenarios summarize in the table 6.

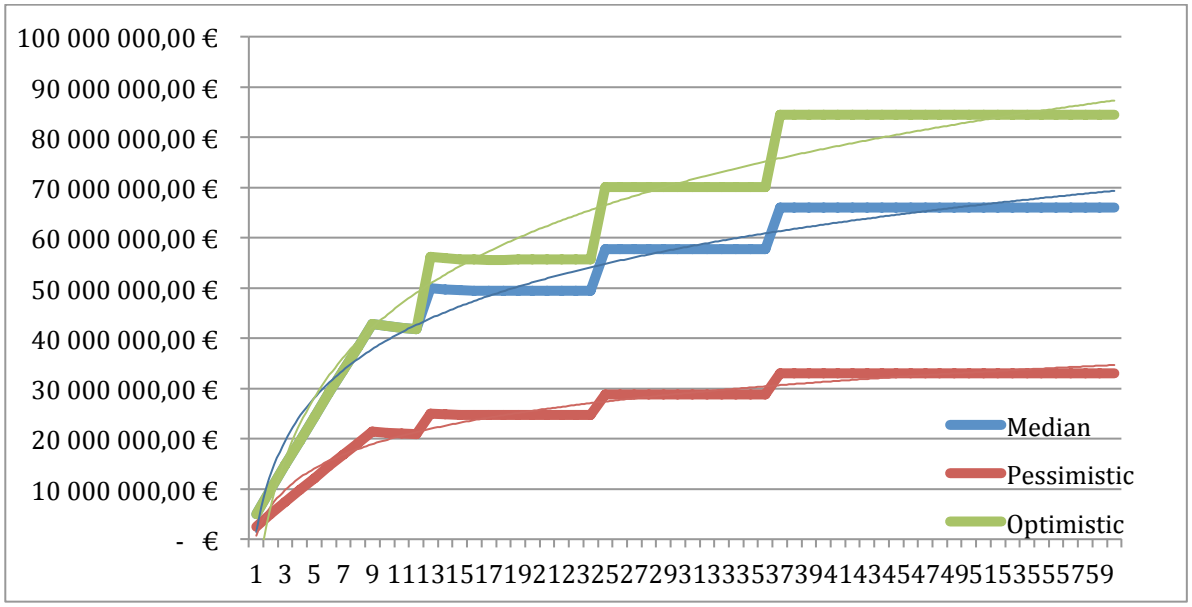

Figure 13: Income from the three different market scenarios

Those three scenarios give us the income we can expect for the five first years on the market. Based on the scenarios we can implement the average cash flow.

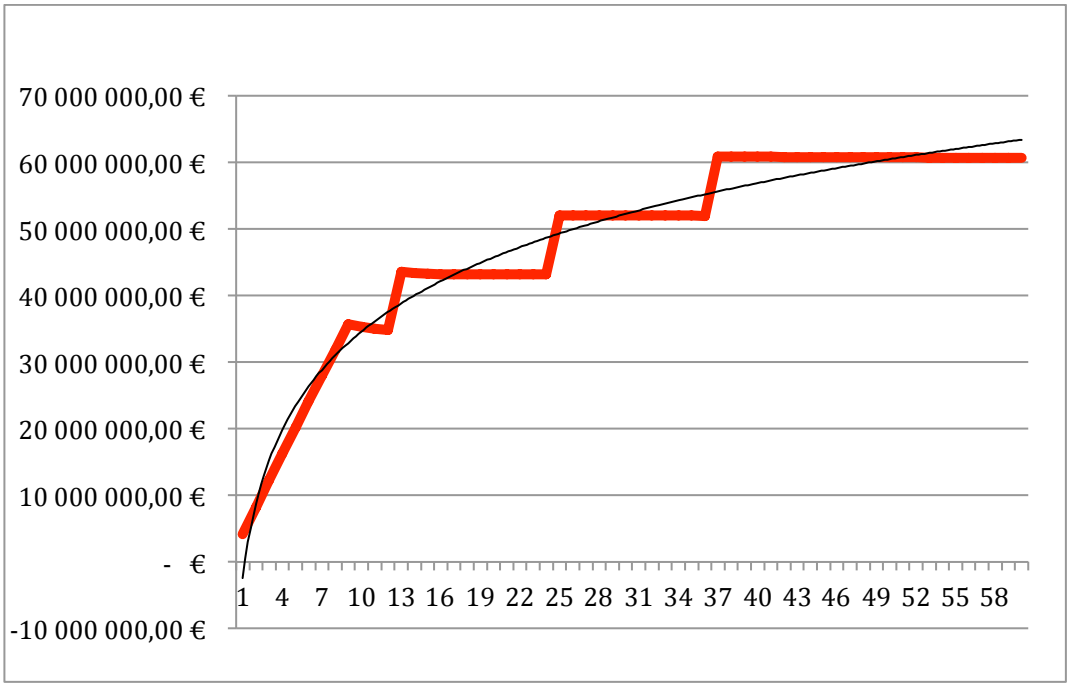

Figure 14: Average Cash Flow

We can now, based on those assumptions, calculate the expected NPV of our product after the FDA approval.

5.2.2. Financial Model

Now we have estimated the NPV of our product. We can estimate the expected NPV of it at each stage of its development. We will make a regressive approach from the FDA approval to the present point.

We will use the decision tree. To estimate the investment at each stage we will take into account:

- The production cost of our ADC (including cost of the license of the linker).
- The cost per patient of a hospitalization during the clinical trial (infrastructure, insurance, cost of the health professional, price of the international board review).
- The cost of data analysis.

The total investment estimated is 49,8 Million Euros.

FDA approval:

For this stage that take around 1 year, the only investment to take into account is the administrative price of the FDA approval. Nowadays this price is 2 Million Euros.

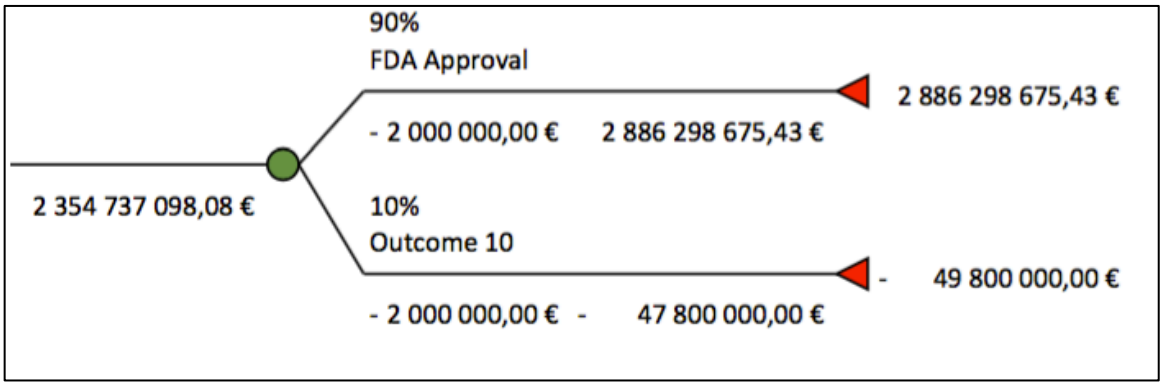

Figure 15: FDA approval of the decision tree

The estimation of success of this approval is 90%. We can estimate the expected NPV before to the approval at 2,354,737,098 Euros.
This result is given by the following equation:

$$\left(\frac{Finale\ value * 90\%}{(1{,}1)^1}\right) - Iphase + (Itotal * 10\%)$$

Phase III:

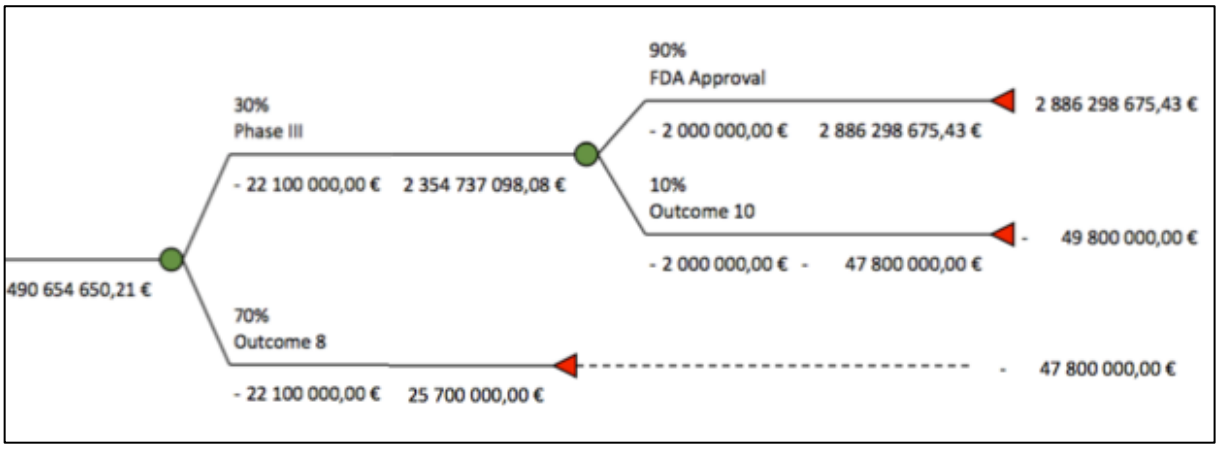

Figure 16: Phase III of the decision tree

In this phase, we have to make a multi-center, multi-parametric. The investment is estimated at 22,100,000 Euros. The number of patient we have to recruit explains this investment. The

Investment is based on the production of our drug and on the cost per patient of the hospitalization.

Similarly to the precedent step the equation that will give us the expected NPV of our product is:

$$\left(\frac{Finale\ value * 30\%}{(1{,}1)^3}\right) - Iphase + (Itotal * 70\%)$$

And the expected NPV of our product in the phase III is 490 654 650 €

Phase II:

This phase is really important for us. We will sell our product during this phase or at the end of this phase. In the phase II we have to test our product on patient that are not responsive to other treatments in 3 different conditions: placebo and two concentrations. This study will be drive on around 200 patients. This phase is to find the good concentration.

We estimate the investment around 11,200,000 Euros.

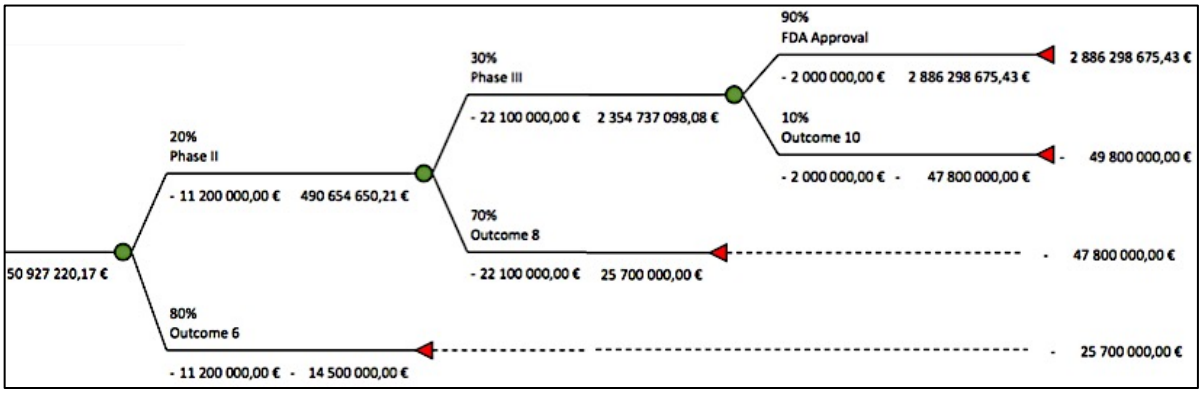

Figure 17: Phase II of the decision tree

$$\left(\frac{Finale\ value * 20\%}{(1{,}1)^3}\right) - Iphase + (Itotal * 80\%)$$

The expected NPV of our product during this phase will be 50 927 220€.

Phase I:

In this first phase, we have to test our drug on patients (in oncology we do not test the drug on healthy patients) to evaluate its toxicology, its future in the organism and the safety of usage. Usually it is done on 50 patients and the investment is based on the production of the ADC for the phase I and II and on the cost of the hospitalization of the patient.

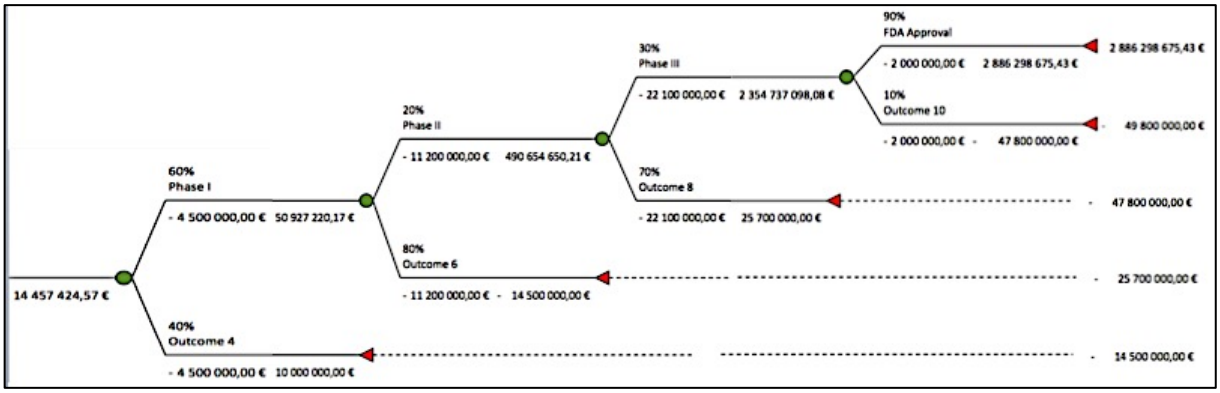

Figure 18: Phase I of the decision tree

$$\left(\frac{Finale\ value * 60\%}{(1{,}1)^3}\right) - Iphase + (Itotal * 40\%)$$

The expected NPV of our product during this phase will be 14 457 424€.

Preclinical stage:

We already own the murine antibody. This antibody shown really good result in mice model, it is able to target 50% of all ovarian cancer. We have to humanize it. Once it is done, we have to make some additional test to have more data to move to the clinical phase I. As we already have strong data on it, we estimate the success of this phase around 100%.

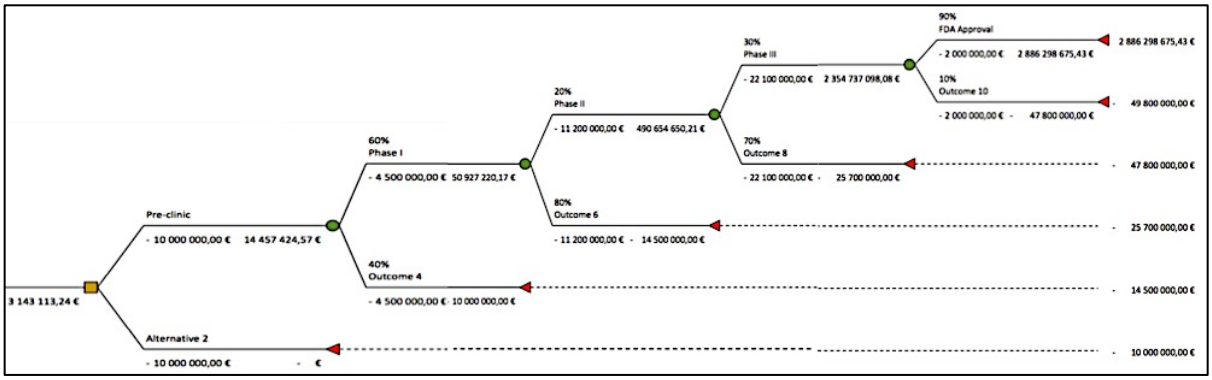

Figure 19: Preclinical stage of the decision tree

From pre clinical to the market:

Phase	Pre-clinic	I	II	III	FDA
Duration (year)	1	3	3	3	1
Go to next	100%	60%	20%	30%	90%
NPV	3 143 113 €	18 457 425 €	62 527 220 €	508 644 650€	2 359 517 098€
Investment	10 000 000 €	4 500 000 €	11 200 000 €	22 100 000€	2 000 000 €
Time	1	4	7	10	11
Cumulative investment		10 000 000 €	14 500 000 €	25 700 000€	47 800 000 €
eNPV	3 143 113 €	14 457 425 €	50 927 220 €	490 654 650€	2 354 737 098€

Table 7: Value and investment of the project from preclinical stage to FDA approval

This table summarizes the investment, NPV and expected NPV of our product from pre-clinical phase to FDA approval. In seven years, our eNPV will be 16,4 time more than the eNPV of the product in the pre-clinical phase.

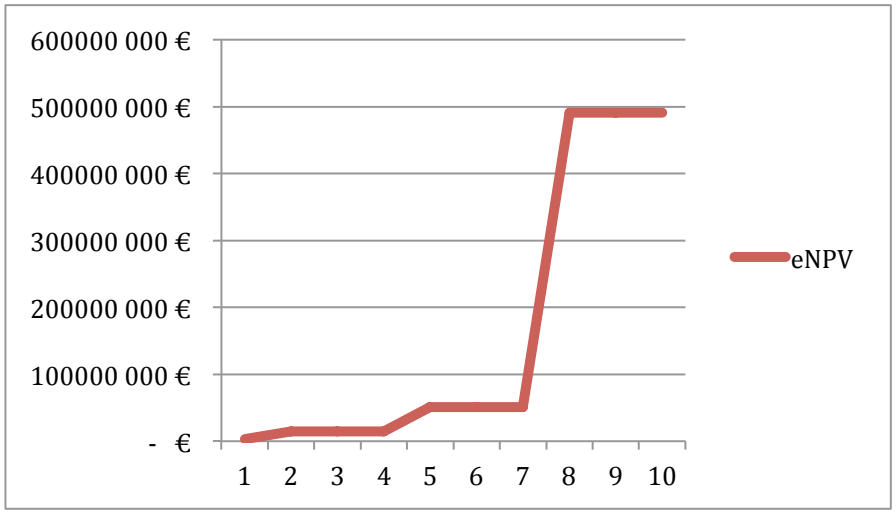

Figure 20: Evolution of the eNPV

5.3. RETURN ON INVESTMENT

We can also calculate the Return on Investment (ROI) for each phase regarding the investment of all the investors.

Each ROI is based on the percentage of ownership calculate on the Investment. In this approach we consider that the same investors are present from the beginning to the end. We also consider the investment as people/infrastructure equivalent to cash investment.

The idea to involve other PRO (as hospital) in this project is to give them ownership and not consider them as subsidiaries.

At the end of the phase I:

Investor	Investment	% of ownership	ROI Phase I
Company	8 000 000 €	55,17	7 976 510 €
Public investors	1 000 000 €	6,90	997 064 €
Private investors	5 000 000 €	34,48	4 985 319 €
PRO	500 000 €	3,45	498 532 €
Total	14 500 000 €	100,00	14 457 425 €

Table 8: ROI per Investors in the Phase I

At the end of the phase II:

Investor	Investment	% of ownership	ROI Phase II
Company	12 000 000 €	46,69	23 779 247 €
Public investors	2 000 000 €	7,78	3 963 208 €
Private investors	10 000 000 €	38,91	19 816 039 €
PRO	1 700 000 €	6,61	3 368 727 €
Total	25 700 000 €	100,00	50 927 220 €

Table 9: ROI per investors in the Phase II

At the end of the phase III:

Investor	Investment	% of ownership	ROI Phase III
Company	18 000 000 €	37,66	184 765 349 €
Public investors	4 000 000 €	8,37	41 058 967 €
Private investors	18 000 000 €	37,66	184 765 349 €
PRO	7 800 000 €	16,32	80 064 985 €
Total	47 800 000 €	100,00	490 654 650 €

Table 10: ROI per investors in the Phase III

5.4. Choosing one project regarding only its financial assets

This model is built to become an adaptive model. Using it and adapting it regarding each project that are choose on their scientific strength will give us good advice on their value once on the market.

For example if we consider a similar project that has the same scientific result, is at the same stage of development but the result of similar product in clinical trials are lower than in the ovarian cancer. But its target is the lung cancer. Firstly we will say this project is better, you target men and women, the incidence is higher, and length of the treatment is the same. But if you look inside of the project, you will discover that the production price is higher and there are more people on the market.

For this one the result will be:

Phase	pre-clinic	I	II	III	FDA
Duration (year)	1	3	3	3	1
go to next	100%	55%	17%	24%	90%
Investment	11 000 000€	5 500 000 €	13 200 000 €	25 100 000€	2 000 000€
time	1	4	7	10	11
Cumulative investment		16 500 000 €	29 700 000€	54 800 000€	56 800 000€
Lost if fail		-7 425 000 €	-24 651 000€	-41 648 000€	-5 680 000€
eNPV	-9 759 704€	1 364 324 €	34 580 165€	567 093 418€	3 515 178 867€

Table 11: Result of the financial analysis for the second project

As you can see in the table 11 the NPV before the FDA approval and the NPV in the phase III are higher than the previous but the other are lower. As the business plan of the company is to sell the product in phase II, and the success rate is lower, the best choice is to develop the first project.

Summarize of this project at the end of the phase II:

Investor	Investment	% of ownership	ROI Phase II
Company	13 500 000,00 €	45,45454545	12 725 233,64 €
Public investors	2 500 000,00 €	8,417508418	2 356 524,75 €
Private investors	12 000 000,00 €	40,4040404	11 311 318,79 €
PRO	1 700 000,00 €	5,723905724	1 602 436,83 €
Total	29 700 000,00 €	100	27 995 514,01 €

Table 12: ROI per investors in the Phase II (second project)

As the company has to select different projects in different area, you cannot select it only on scientific bases. This model will allow you to benchmark different project and present it to different investors. Nevertheless, the NPV or the ROI are not the only metrics investors will use. Some of them will prefer a project with a good % of success; others will prefer a higher ROI, etc. The last step to select projects will be to compare them between each of them.

We can use an adaptive model to rank them regarding all the metrics we used to build our financial analysis. Comparing 2 projects is not so easy. The company will have to compare a lot of them.

We made the same analysis for five different projects and the majors metrics are summarize in this table.

Phase II	Total Investment	Investment of private investor	Success rate	eNPV	% of ownership	ROI	Time
Lung	29 700 000 €	12 000 000 €	9,35	27 995 514 €	40,4	11 311 319€	8
Ovarian	14 500 000 €	10 000 000 €	12	50 927 220 €	69,0	19 816 039€	7
Leukemia	23 400 000 €	9 000 000 €	12	29 460 962 €	38,5	11 331 139€	5,5
Melanoma	27 200 000 €	10 500 000 €	10,26	9 693 410 €	38,6	3 741 941€	6,5
Breath	23 700 000 €	9 000 000 €	10,8	29 622 030 €	38,0	11 248 872€	7

Table 13: Financial analysis for five projects

With this table we can rank the different project by scoring the different metrics.

We use this scoring matrix to rank our project.

Rank/Score	Total Investment	Investment of private investor	Success rate	eNPV	% of ownership	ROI	Time
1	0,5	10	8	1	6	8	7
2	0,4	8	11	2	7	11	6
3	0,3	6	14	3	8	14	5
4	0,2	4	17	4	9	17	4
5	0,1	2	20	5	10	20	3

Table 14: Scoring each metrics

For us, the two main metrics that investors look at are the success rate and the ROI. All the metrics are rank in an increasing order. That is why, for example, less you invest better is the score and higher is the success right highest will be the score.

Phase II	Total Investment	Investment of private investor	Success rate	eNPV	% of ownership	ROI	Time	Score
Lung	0,1	2	8	2	9	14	3	38,1
Ovarian	0,5	6	17	5	10	20	5	63,5
Leukemia	0,4	10	17	3	7	17	7	61,4
Melanoma	0,2	4	11	1	8	8	6	38,2
Breath	0,3	10	14	4	6	11	5	50,3

Table 15: Score of each project

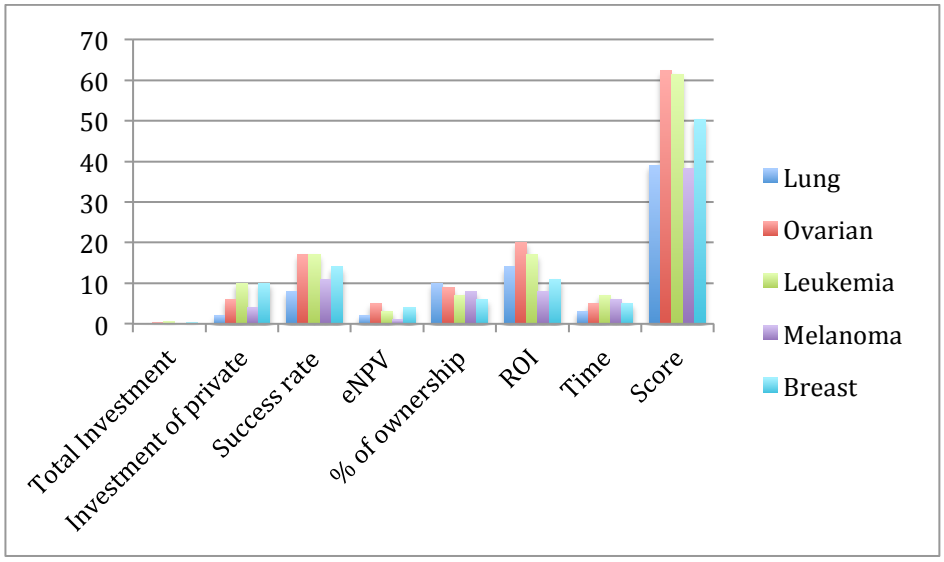

Figure 21: Score of each project

As you can see we already can exclude at least two projects: Lung and Melanoma. They have the worst grad in all metrics except in the ownership. But, we know that some investors will give a higher grade to the ROI than the success rate. Even if the success rate is low they will have the best ROI and sooner is the best. So by adapting the metrics matrix, we can rank our project regarding what the investors will hear and select the best project, maybe the 2 best to present them.

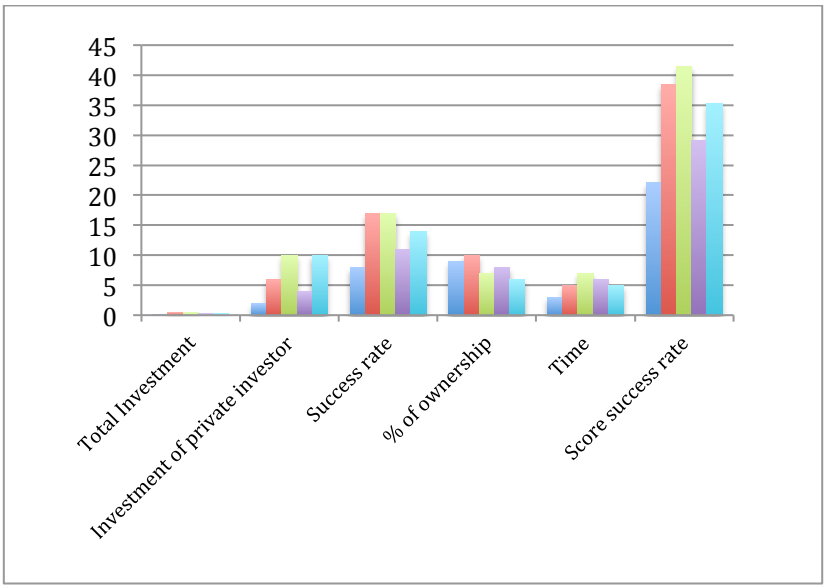

Figure 22: Score based on the success rate

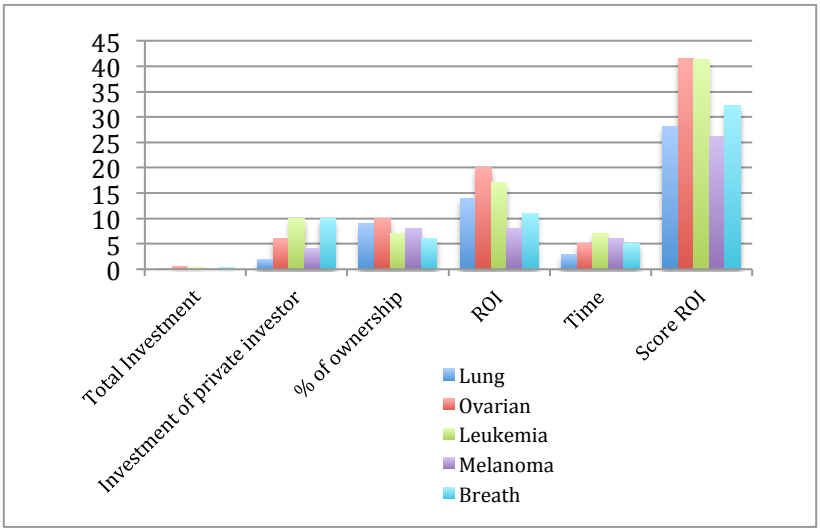

Figure 23: Score based on the ROI

With this approach the two projects we will choose to present to investors are Ovarian and Leukemia project. But one thing is to keep in mind; there are more drugs already on the market for leukemia and more research on it. That is why we choose to build the model on the Ovarian project.

5.5. Milestones and Royalties

Once you have chosen the project and investors give you money to develop it, you have to calculate the price you will sell the project and implement the milestones and the royalties.

With the eNPV you have the potential price of your product, but as it is not on the market, you will licensed and implement the milestone. The initial price and the milestone will reflect the eNPV.

With our example, if we want to license it at the end of the phase II, the eNPV will be 50 927 220€. So before it reaches the market you can expect an initial amount of 15% of the estimate value of the project and 3 milestones. Each milestone will be a percentage of the eNPV.

milestones	initial	access to phase III	access to FDA approval	access to the Market	eNPV
price	7 639 083€	10 185 444€	12 731 805€	20 370 888€	50 927 220€

Table 16: Value of each milestones

Based on this table we can calculate the ROI regarding the milestones by investors.

Investor	initial	access to phase III	access to FDA approval	access to the Market
Company	3 566 887 €	4 755 849 €	5 944 812 €	9 511 699 €
Public investors	594 481 €	792 642 €	990 802 €	1 585 283 €
Private investors	2 972 406 €	3 963 208 €	4 954 010 €	7 926 416 €
PRO	505 309 €	673 745 €	842 182 €	1 347 491 €
Total	7 639 083 €	10 185 444 €	12 731 805 €	20 370 888 €

Table 17: Milestones per investors

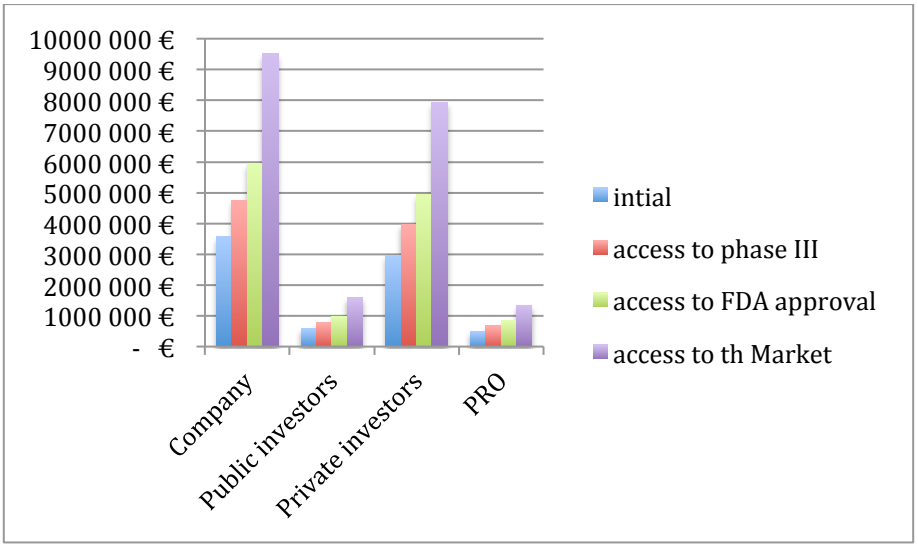

Figure 24: Evolution of milestones per investors

Once it is on the market we will earn each year the royalties. Usually in the Pharmaceutical industry it is between 5% and 10%.

Years	1	2	3	4	5
royalties 5%	14 304 020,95 €	25 928 479,27 €	31 197 233,48 €	36 472 843,24 €	36 412 356,83 €
royalties 6%	17 164 825,14 €	31 114 175,13 €	37 436 680,18 €	43 767 411,88 €	43 694 828,19 €
royalties 7%	20 025 629,33 €	36 299 870,98 €	43 676 126,87 €	51 061 980,53 €	50 977 299,56 €
royalties 8%	22 886 433,52 €	41 485 566,84 €	49 915 573,57 €	58 356 549,18 €	58 259 770,93 €
royalties 9%	25 747 237,71 €	46 671 262,69 €	56 155 020,27 €	65 651 117,83 €	65 542 242,29 €
royalties 10%	28 608 041,90 €	51 856 958,55 €	62 394 466,96 €	72 945 686,47 €	72 824 713,66 €
Average	21 456 031,43 €	38 892 718,91 €	46 795 850,22 €	54 709 264,85 €	54 618 535,24 €

Table 18: Estimation of Royalties for five years after the FDA approval

As the percentage will depend of the market, the status of the exploiting firm, we will use the average royalties to calculate what will be the return for each partner.

Investor	% of ownership	Royalties years 1	Royalties years 2	Royalties years 3	Royalties years 4	Royalties years 5
Company	0,47	10 018 380€	18 160 024€	21 850 202€	25 545 182€	25 502 818€
Public investors	0,08	1 669 730€	3 026 671€	3 641 700€	4 257 530€	4 250 470€
Private investors	0,39	8 348 650€	15 133 354€	18 208 502€	21 287 652€	21 252 348€
PRO	0,07	1 419 271€	2 572 670€	3 095 445€	3 618 901€	3 612 899€
Total	1,00	21 456 031€	38 892 719€	46 795 850€	54 709 265€	54 618 535€

Table 19: Royalties per investors

This table summarizes the potential return only based on the royalties. The table show the values of the royalties after the FDA approval, based on the average cash flow calculate in the market analysis.

We are now able to calculate a cumulative ROI for each investor regarding their percentage of ownership.

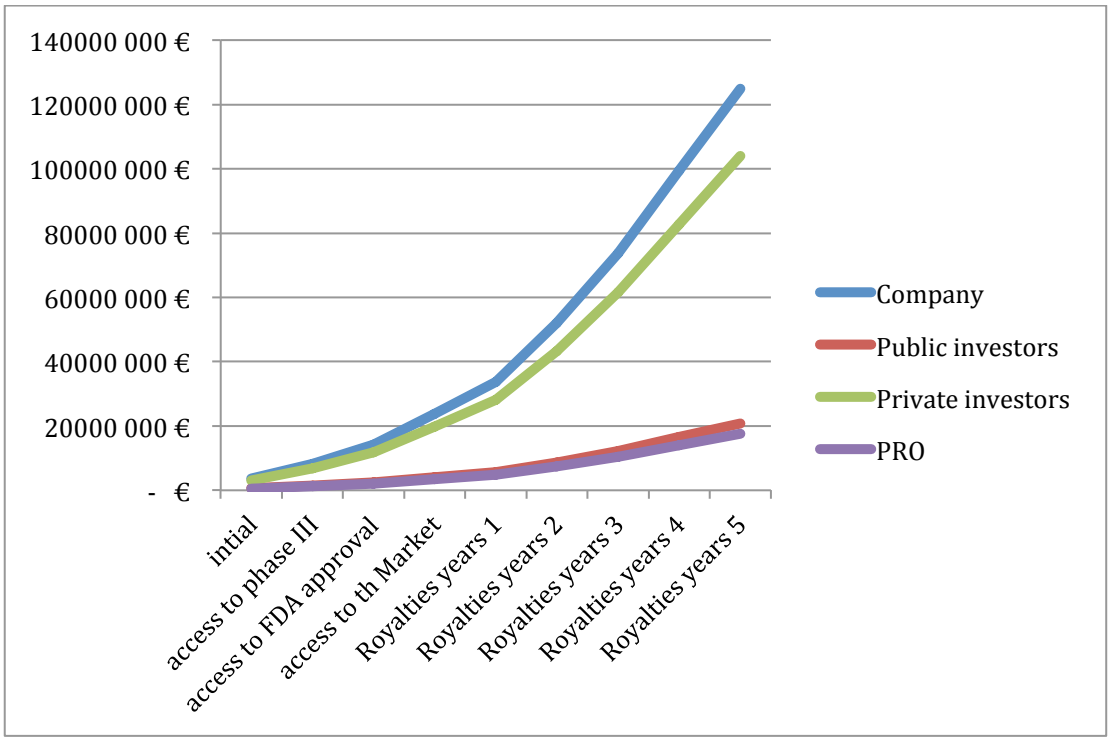

Figure 25: ROI per investors from phase II to five years on the market

After 5 years on the market, the cumulative return on investment will be 120 000 000€ for the company and 100 000 000€ for the private investors.

5.6. Impact on global Research.

The main goal of TTO's is to licensed project. It is mainly done for projects that are in pre-clinical phase. That is almost due to the cost of development in next phases. With this

approach, we will enable TTO's to fund project in late phase. That doesn't mean they will stop to fund project that have less chance of success or project with a reduced ROI. We have to take it as growth lever. The money generated by the company will be injected in research.
We have to keep in mind that the goal of PRO is to promote all the research, not only the one that can bring back money. TTO's try to license the entire patent and it will go on. The big difference is, with this organization, they will be able to develop in late stage some of them and generate more money. At the end all project will become beneficiaries of the investment of private investors in few projects.

5.6.1. Classical model vs. Company

If we take a look at the money generated by early licensed project we understand that it could be a big win to involved private investors in the development of some project.
For example we will take a look on the Ovarian project if we licensed it now.
The model will be different. In the first model, the eNPV on the pre-clinical phase was negative. Here to evaluate the deal we only look at the potential profit after one year of commercialization. Taking into account that we didn't take the risk to develop the project, we will multiply the eNPV by the success rate and that will give us an idea of the licensed price.

This licensed price will reflect what we think we can expect for the milestone. Once the product will be on the market, we can expect fewer royalties too. That is explained by the fact that we don't take any risk. The next table summarizes what we can expect for each milestone

Milestones	Price
Initial deal	150 404 €
Access to phase I	300 808 €
Access to phase II	752 021 €
Access to phase III	1 353 637 €
Access to FDA approval	2 105 658 €
Access to the Market	3 008 083 €
Royalties year 1	11 590 496 €
Royalties year 2	27 147 583 €
Royalties year 3	45 865 923 €
Royalties year 4	67 749 629 €
Royalties year 5	89 597 044 €

Table 20: Milestones and royalties for the PRO with the classical model

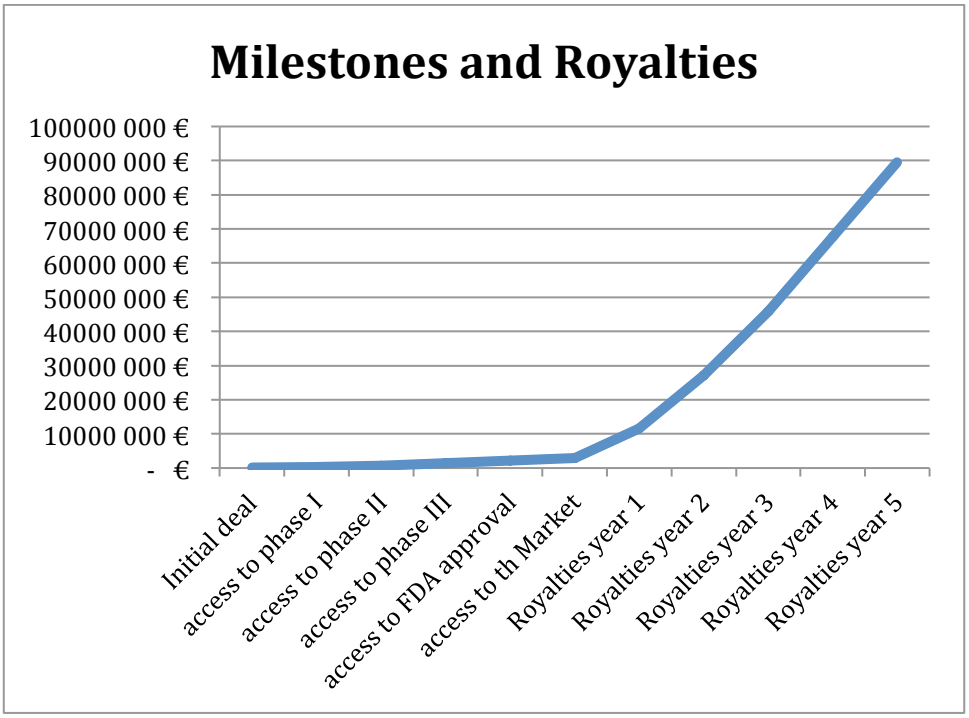

Figure 26: Evolution of the ROI with the classical model

The cumulative return for the Public Research Organization that own the patent is 90 000 000€ with the classical model.

Now if we compare with what we can expect as return with the company we will understand why this proposition of model for the valorization could be interesting.

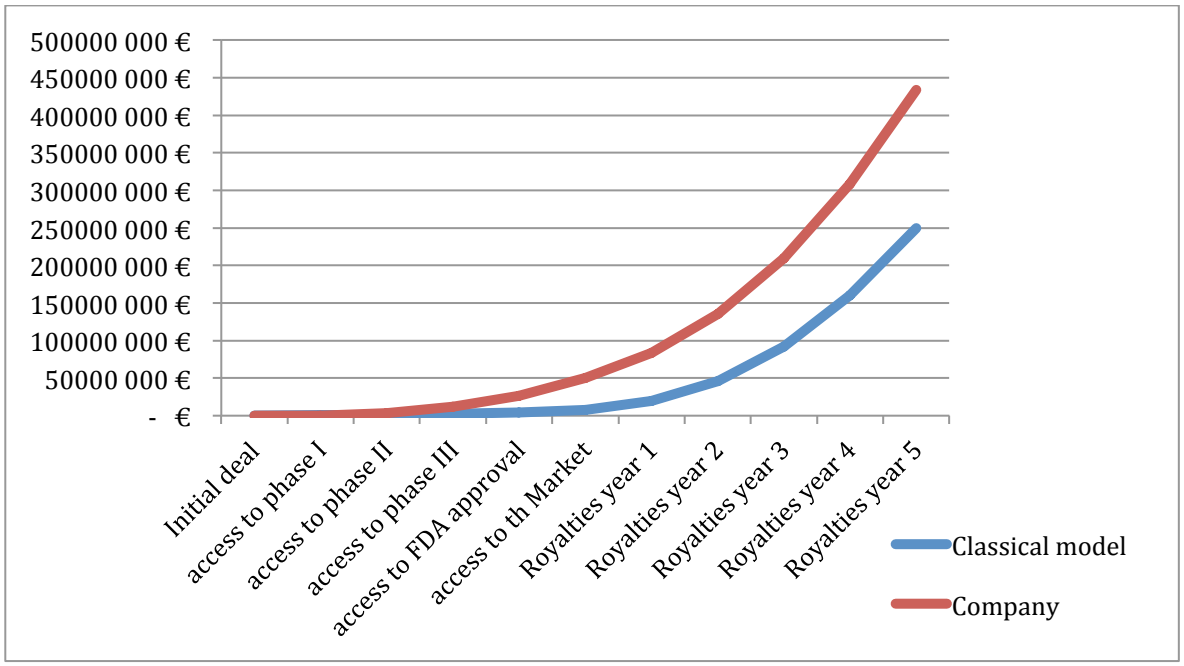

Figure 27: Comparison of ROI between Classical model and Company

As you can see on this graphic, this model has two main advantages:

- As soon as we are in the phase II the ROI is superior

- After 5 years on the market, we will earn 159% more with the company than with the classical model.

5.6.2. Return for the Public Research Organization

Technological Transfer Offices and SATT will take a percentage of the royalties. Even if this percentage increase with the model presented here, the return for the PRO will be higher at the end (here we talk about the PRO that own the patent, not the PRO that can take a part of the development of the product).

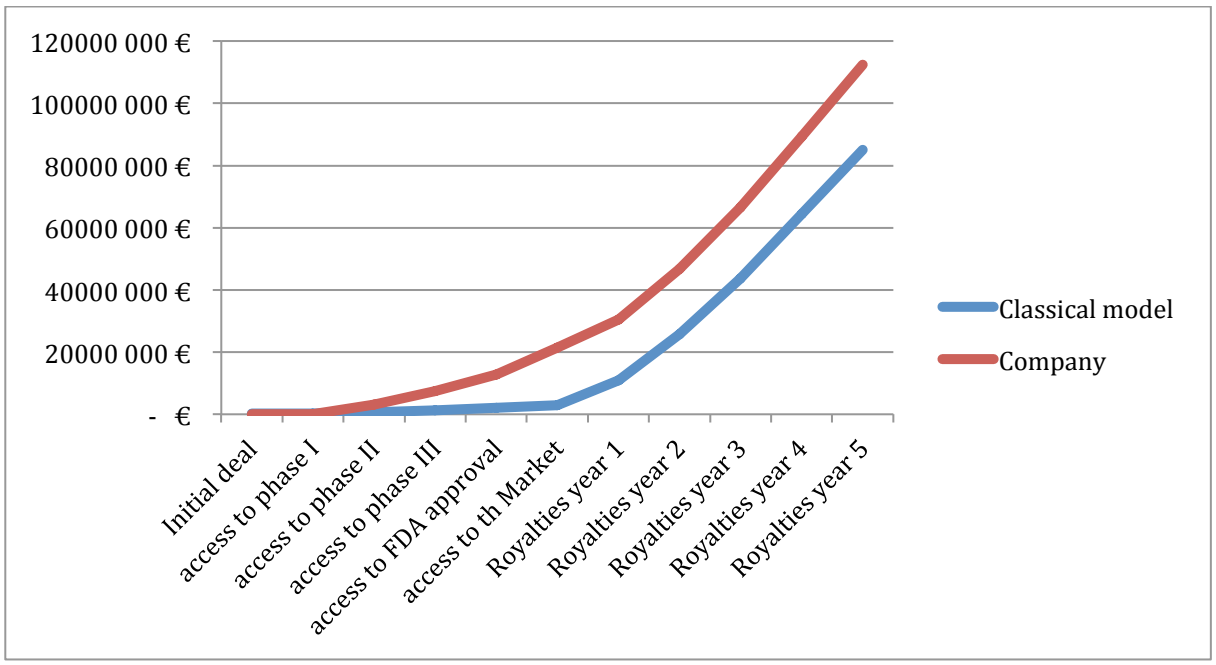

Figure 28: Evolution of the ROI taking into account the percentage perceived by the TTO

Milestone	Comparison by phase	Cumulative comparison
Initial deal	0%	0%
access to phase I	0%	0%
access to phase II	449%	281%
access to phase III	582%	441%
access to FDA approval	642%	531%
access to the Market	749%	617%
Royalties year 1	276%	412%
Royalties year 2	181%	277%
Royalties year 3	152%	215%
Royalties year 4	139%	183%
Royalties year 5	132%	165%

Table 21: Evolution of the ROI taking into account the percentage perceived by the TTO

The figure 28 and the table above represent the advantage of the model proposed. With this new model, we can generate around 150 Million Euros more than with the classical model after 5 years on the market. This money can be invested in all early development projects that PRO's have to promote.

5.6.3 Return for the company

A part of the ROI will be for the company. The main goal at the end is to be self-sufficient. The business model of the company is to build 2 projects each year. If we take a look at what the company can earn with one project, we can see that

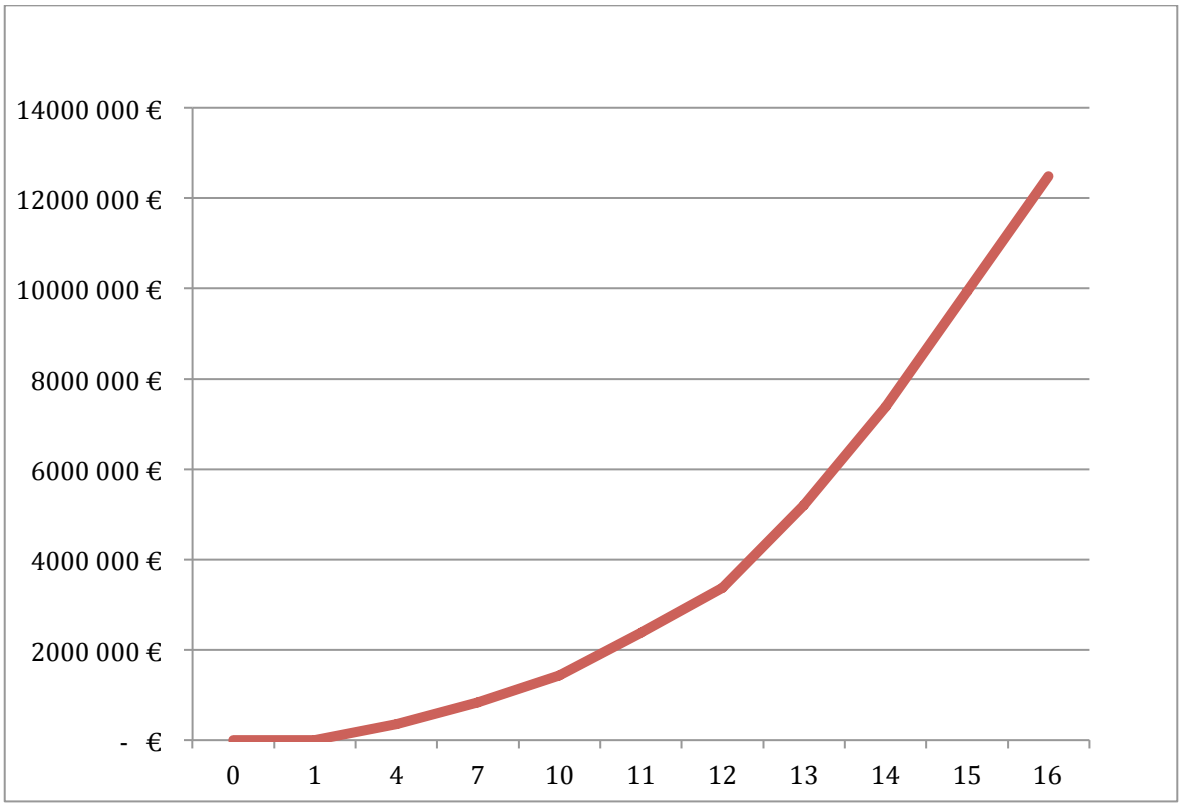

Figure 29: Company gain on one project

With this graphic, we can estimate the time before the company became sustainable. The first revenue for the company will come after 4 to 7 years. This revenue can be considered as benefice, we already take into account the investment in the project. So if this project is a success, the company will earn money for 10 years at least. But, the goal of the company is to develop several projects at the same time. And they would not all be a success.

The average investment to go through phase I and phase II is 20 million. If the ovarian project is a success, the company will be able to fund one project without private investors.

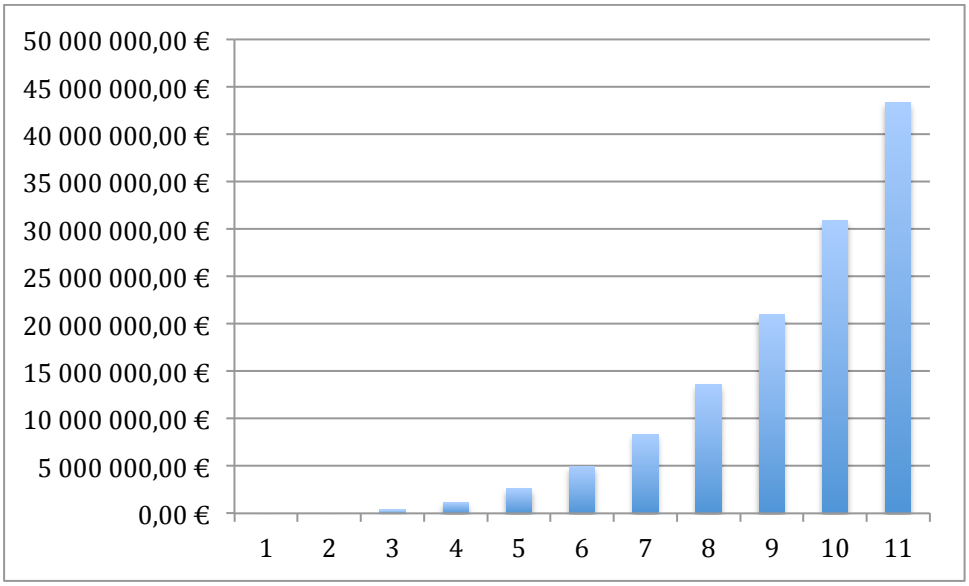

Figure 30: Cumulative gain from initial deal to five years on the market

But we have to take into account that we will support 2 new projects by year. Projects will not all be a success. The next chart will show us future benefices if one or two projects reach the market.

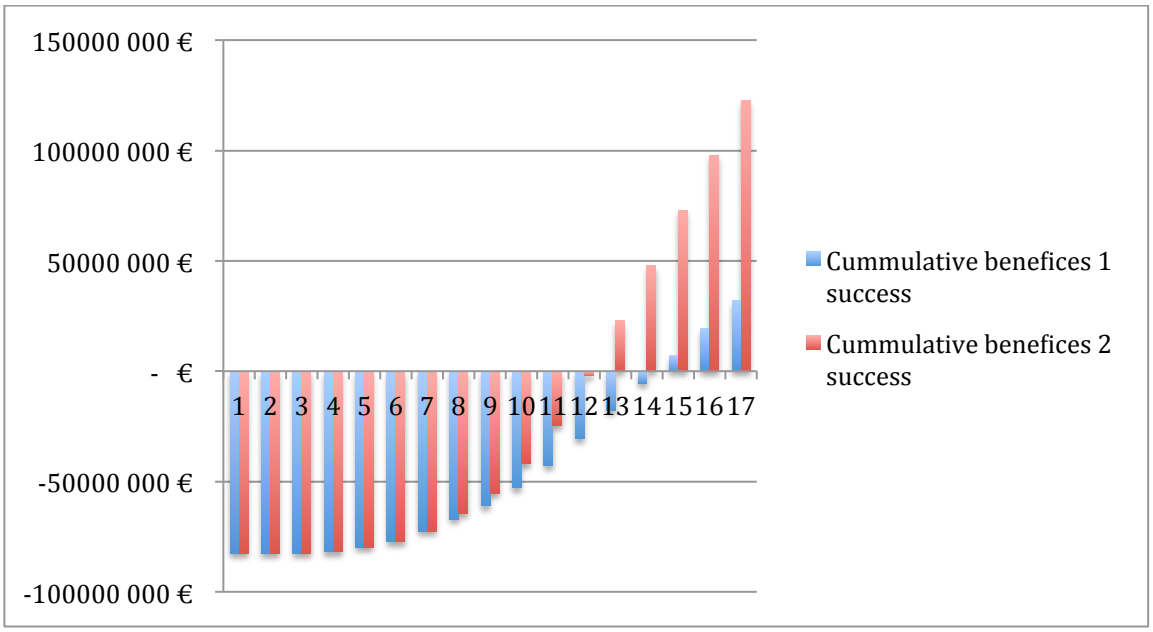

Figure 31: Cumulative benefices with one or two success

With the figure 31 we can see that if only one of the ten projects we will develop during the next 5 years, we will begin to make benefices after 15 years. If two projects reach the market, it will take 13 years.

Nevertheless, even with this approach, we cannot compress the time to become sustainable. It will take 13 to 15 years to make some benefit.

6. Conclusion

Valorization and technological transfer, as we consider it now, is a young business. In the pharmaceutical and biotechnological sector, it is a costly and risky business. Involving private investors in it can be really hard. If we take a look at the different technological transfer offices in United Kingdom, United State of America and France, only those that can sell or license project in advance phase become sustainable.

In France most of the TTO's are public organizations. This organization does not allow private investors to put money in it. A lot of licensing deals are made on early-developed project. The return for the Public Research Organizations is not as important as it can be. The second important problem that we can point is the fact that it is a young business and the investment of the PRO in it is not as important as it can be in the other country we study. One attempt to help PRO to valorize their research was made by the government through the SATT. But those new entities based their business on support services. They search the best industry to license the patent; their role is not to develop a project.

We saw by comparing TTO's from France, UK and USA that French TTO's are relatively less efficient than the other. To improve their efficiency, they can work on their licenses incomes. As the licenses income is mainly based on the development stage of the product, we propose a model to push projects in late stage development. This model also shows that it can also increase the return on investment for the public organization offices by 150% after five years on the market. The other aspect that we can discuss with this model (the company) is that it will create another kind of value. It will increase the reputation of the reputation of the Technological transfer offices and through it the reputation of the public research organization. This model will enhance the virtuous circle between TTO's, PRO's and Firm and improve the relation between private investors and public research.

With the model we propose, the role of the TTO's will be enhancing. Until now, due to the lack of money, Technological transfer offices played a role mostly in identifying the best project for the best industrial. With this model that will involve private, public investors and different Public research organizations, Technological transfer offices will be able to develop project. By developing the project, they will take more risk and have more return if the project work. We saw that with this approach, the return (e.g licenses income) will be increase by 150%. So if we take it into account and increase licenses income by 150%, the relative efficiency of French technological transfer offices will become higher.

Location	Research spending	Invention disclosure	Patent application	Licenses executed	Licenses income	Spin-of	Out put	Inp ut	Efficie ncy
USA	216989600	117,5	71,3	32,5	9677419	3,6	5,52	8,2	0,7
UK	16308797	25,9	13,8	31,1	730061	1,6	0,62	0,6	1,0
France	26466257	20,8	10,5	4,4	1481595	1,6	1,00	1,0	1,0

Table 22: DEA analysis with an increase of 150% of French licenses income

Nevertheless, even if the relative efficiency increase, we have to take into account that Licenses income does not all the value creation of the technological transfer offices. The creation of spin-off, the creation off employment also is a creation off value. But those value are harder to evaluate in a short term. Those indicators as licenses income have to be evaluate constantly in order to assess the efficiency of this new business. We also see through the literature review and through our model that a business based on the management of intellectual property can take 10 to 15 years to become sustainable and French technological transfer offices are still young so we will see in the next ten years the ones that success and what will be their business model. But to become sustainable, TTO's have to become more efficient in the way they manage the IP in order to develop the best project and to license those that they cannot develop to increase the return on investment made by public research organizations in basic research.

ATTACHMENT 1: MATHEMATICAL MODEL FOR THE DATA ENVELOPMENT ANALYSIS

In the chapter 2 of his book, Ozcan (Ozcan 2014) describe a mathematical model to calculate the DEA efficiency scores. We adapt it to our problem.

The efficiency score (Θ_0) for the group of three countries (j= 1, 2, 3) are computed for the selected outputs (y_{rj},r = 1,…,s) and inputs (x_{ij}, i = 1, …, m) using the following formula:

$$Maximize\ \Theta_0 = \frac{\sum_{r=1}^{s} u_r y_{r0}}{\sum_{i=1}^{m} v_i x_{i0}}$$

$$subject\ to\ \frac{\sum_{r=1}^{s} u_r y_{rj}}{\sum_{i=1}^{m} v_i x_{ij}} \leq 1$$

$$u_r, v_i \geq 0 \text{ for all } r \text{ and } i$$

The weight for outputs and inputs respectively are u_r and v_i "0" denotes a focal location (each location becomes a focal when its efficiency score is computed).

The weight for outputs and inputs are entirely determined from the initial data for each location. Therefore, the weights used for each location are those that maximize the focal location efficiency score.

Nevertheless, the solver we used in excel will convert this non-linear formula into a linear one.

The formulation becomes:

$$Maximize\ \Theta_0 = \sum_{r=1}^{s} u_r y_{r0}$$

$$subject\ to \sum_{r=1}^{s} u_r y_{rj} - \sum_{i=1}^{m} v_i x_{ij} \leq 0 \qquad j = 1, \dots, n$$

$$\sum_{i=1}^{m} v_i x_{i0} = 1$$

$$u_r, v_i \geq 0 \text{ for all } r \text{ and } i$$

The goal of this model is to maximize the efficiency by maximizing the weight of the outputs. With this approach we can which output is important and has to be improved.

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