A Project carried out with the supervision of: Professor Luís Filipe Lages, Professor Luísa Agante and Professor Fernanda Llussá

Author: Ana Sofia Coutinho de Almeida Dinis Esteves

Faculdade de Ciências e Tecnologia e Faculdade de Economia

Universidade Nova de Lisboa

Technology Market Transfer Plan

Launch of DELIVES to E.U. Market©

Dissertação apresentada na Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa para obtenção do grau de Mestre em Biotecnologia

Panel:

President - Profª Doutora Ana Cecília Roque

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Thanks

First of all I would like to explain the motivation that led me to do this master thesis.

During the course of my university degree (in Applied Chemistry), I used to be fascinated by the potential that some different technologies and even certain fundamental investigations seemed to have.

At the beginning, this fascination that turned into several questions got stuck in my mind because these issues were not discussed in classrooms, or even with colleagues in the university environment. Someday I decided to release my thoughts and ask some few questions to my professors. "Wow! What great technology! So what now? And then, what happens? "

I found that these were delicate questions that brought shock to the teachers and researchers, and rarely had an aswer.

I was sure that these were not rhetorical questions, and because of that I began my journey of trying to find similar situations. And there were a lot of such situations, ie those cases where technologies nowadays known in the market, started within the white walls of a laboratory. But what remained unknown to me was the process by which they passed until reach the market.

From day by day, I increasingly realized that the laboratory would not be my home and that I needed to do something to bring these technologies to the market. At that time I thought this was a job that would be completely disruptive and innovative. Until I realized that I was wrong and that day by day were increasingly people who were dedicated to this cause.

But it was precisely when I finish my degree and moved to my first professional experience that I firstly get in contact with this area. Technology Transfer it was the name I was searching for.

It was a good feeling to know that my search finally had a name and was actually real. Was within the Science Park of Madrid that I realized the size and importance of technology transfer, and I came into contact with the real cases (many successful) in this area.

When I cameback to Portugal, I could not lose more time and therefore I proposed to do my master's thesis on a subject that came close to these areas. I understood that there was a gap between science and the marketplace and that my scientifical background could be a market opportunity in full expansion.

This was my first challenge and it is for the “actors” who made this challenge a reality to which I drive my first thanks.

So, my first thanks could not fail to be addressed to Professor Luís Lages that welcomed and supported this idea and to Professor Susana Barreiros (coordinator of the *FCT* Master in Biotechnology) who not only understood my motivation, just as supported the project and moved efforts in order to turn my proposal in reality.

At this moment, this challenge took shape and expected to be a difficult test, but of course not an impossible one.

After the permission to start this master's thesis, it was suggested that the guidance would be made by Prof. Luís Lages and Prof Luísa Agante and co-orientated made by Prof. Fernanda

Llussá. Due to my "troubled" route during completion of the thesis I want to address a very special thank to my three supervisors for the fantastic follow-up, for the teachings, for the kind words and for the directions, patience and support.

I also want to address a special thank to Pedro Vidinha, that always supports my idea and had an intensive participation in this work.

In the course of this work, made sense to approach the TTO of the FCT and it was here that I began to work daily. A large percentage of this master thesis is the fruit of the development work at the office, from my own contacts through work in the TTO, and as is obvious from the teachings of the best boss that I could ever had - Dina Chaves.

It was by the hands of Dina that I really learned the meaning of Technology Transfer and was with her that I learned almost everything I know today about this area that I intend to devote my professional life.

In addition to the technical teachings Dina gave me several lessons regarding to the professional attitude

Dina Indicate me a solution, everytime that I thought to be arriving to an intersection in my thesis work .

For all of this and much more that is not possible to put into words, I can only say: Thank you Dina!

Thanks to all who had the patience to hear me telling this story and that helped me in the development of this work, sharing their work experience in the areas of technology transfer, entrepreneurship, pharmaceutical market and legal counsel.

The biggest thanks goes to all whom not only heard me tell this story once but have heard many and many times. I would like to thank to all my friends and family who never gave up accompanying me during this walk.

Finally I would like to dedicate this work to all Portuguese innovators, who defy markets permanently, and that despite being aware of the difficulties of entrepreneurship, do not admit that a culture that do not allows them to fail, intimidates them!

Sumário Executivo

A indústria farmacêutica enfrenta uma das maiores vagas de expiração de patentes. A magnitude do potencial de perda de vendas é tal, que a Datamonitor[1], prevê que entre 2011 e 2012 as receitas do sector de medicamentos vão diminuir, pela primeira vez em quatro décadas.

Como alternativa, as tecnologias de *Drug Delivery* (DD), que consistem na ciência de entregar um ingrediente activo no local do corpo onde este é necessário, nas quantidades certas e no momento certo da forma mais efectiva e conveniente; estão a impulsionar o crescimento das empresas farmacêuticas, aumentando as suas receitas, através do prolongamento do ciclo de vida do produto e através de novas formulações e combinações.

De acordo com esta percepção, este plano de marketing foi desenvolvido para uma futura empresa, LIFE DELIVERY, que detém a patente de um novo biomaterial, e pretende lançar um novo produto – DELIVES | improving life quality –, para o mercado.
DELIVES é um novo *Targeted Drug Delivery* (TDD), que consiste num DD direccionado a libertar o fármaco localmente na zona de interesse; extremamente versátil que pode ser precisamente adaptado a fim de alcançar os objectivos específicos de cada cliente, proporcionando uma liberação controlada de fármacos e elaborado através de um processo ambientalmente amigável.

Usando três tipos de segmentação (geográfica, por tipo de indústria e por aplicação) e aplicando diferentes critérios de avaliação aos segmentos seleccionados, as conclusões finais apontam para os seguintes clientes alvo: grandes empresas farmacêuticas, da União Europeia, que actuem nos mercados das seguintes áreas terapêuticas: Inflamação e perturbações músculo-esqueléticas, desordens metabólicas e doenças cardiovasculares, sendo a última, os clientes ideiais para a estratégia de entrada no mercado.

De acordo com a percepção de valor dos clientes-alvo- traduzida em redução de custos-, a LIFE DELIEVERY adoptará um posicionamento, baseado em três pilares principais: qualidade, inovação e imagem organizacional.

[1] Datamonitor é uma empresa de pesquisa e consultoria que aconselha clientes com a tomada de decisões operacionais e estratégicas

O modelo de negócio adoptado pretende licenciar a tecnologia, recorrendo a diferentes estratégias de comunicação, sendo que 322.078.48€ é o custo para execução deste plano de marketing, no primeiro ano de vida da empresa.

Executive Summary

The pharmaceutical industry faces one of the biggest waves of patent expirations. The magnitude of the potential loss of sales is such that Datamonitor, predicts that between 2011 and 2012 the revenue from the drug will decrease for the first time in four decades.

Alternatively, the technologies for Drug Delivery (DD), which consist of the science of delivering an active ingredient in place of the body where this is necessary, in the right quantities at the right time in the most effective and convenient, are boosting the growth of pharmaceutical companies, increasing its revenue by extending the product life cycle and through new formulations and combinations.

According to this perception, this marketing plan was developed for a future company, LIFE DELIVERY, which holds the patent of a new biomaterial, and intends to launch a new product - Deliver | Improving life quality - for the market.
DELIVES is a New Targeted Drug Delivery (TDD), which consists of a DD directed to release the drug locally in the area of interest, extremely versatile and can be precisely adjusted to achieve the specific objectives of each client, providing a controlled release of drugs and elaborated through a process environmentally friendly.

Using three types of segmentation (geographic, industry type and application) and applying different evaluation criteria to selected segments, the final conclusions point to the following target customers: large pharmaceutical companies, the European Union, acting in the markets of the following therapeutic areas: inflammation and Musculosketal, metabolic disorders and cardiovascular diseases, the latter being the ideal customers for market entry strategy.

According to the perceived value, of target customers - translated in cost-saving -, LIFE DELIEVERY will adopt a position based on three main pillars: quality, innovation and organizational image.

The business model adopted aims to license the technology, using different communication strategies, and € 322.078.48, is the cost to implement this marketing plan in the first year of life of the company.

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Symbols and Notations

- Market New Molecular Entity (NME)
- Universidade Nova de Lisboa (UNL)
- Institituto Superior Técnico (IST)
- Technology Transfer Office (TTO)
- Targeted Drug Delivery (TDD)
- Drug Delivery (DD)
- Pharmaceutical (Pharma)
- Biological (Bio)
- European Union (E.U.)

1 *Introduction*

This master's thesis aims to present a marketing plan to launch a new technology into the market. This technology will be the final product of a current research project[2], and will be introduced in the market by LIFE DELIVERY – a future spin-off *of Faculdade de Ciências e Tecnologia* of *Universidade Nova de Lisboa (FCT/UNL)*, that will be created by some research team members, with the objective of developing and commercialize different products based on a technology platform, designated "Ion Jelly".

Ion Jelly is a patented new biomaterial, that arises from the combination of gelatine with ionic liquids[3] and which offers interesting properties, allowing different applications such as batteries or battery components, in chemical processes used in industry and laboratories or also in pharmaceutical applications.

Based on this platform technology, one *FCT/UNL* research team is now developing a novel gelatine-based targeted drug delivery system[4] - named DELIVES - that intends to be an interface between the patient and the drug, which will be released by a controlled process. A drug delivery system enables the introduction of a therapeutic substance in the body and improves its efficacy and safety by controlling the rate, time, and place of release of the drugs in the body (Jain, 2008). The process includes the administration of the therapeutic product, the release of the active ingredients by the product, and the subsequent transportation of the active ingredients across the biological membranes to the site of action. By using new drug delivery systems it is possible to increase potentially viable drug candidates and reformulate existing drugs extending the product lifecycle by new patent application (Figure 0.1). For now, and since this technology is at under development stage, this target drug delivery system has not yet been proved to transport any specific drug, and this implies a generalization of this thesis work. This aspect interferes in the specification of certain parts of this work, which could not be more explored due to the development phase of the product.

Being Ion Jelly, a resulting technology from *FCT/UNL and IST research teams* investigation, the Ion Jelly patent, is owned by *Universidade Nova de Lisboa (UNL) and Instituto Superior Técnico (IST)*. This

[2] The research project is funded by *Fundação para a Ciência e Tecnologia*, ongoing between September 2009 and 2012.

[3] Ionic liquids are defined as salts

[4] Targeted drug delivery is the most important goal of pharmaceutical research and development. In this context drug targeting is defined in the broadest sense, that is, to optimize a drug's therapeutic index by strictly localizing its pharmacological activity to the site or organ of action. If successful, the result of the targeting would be a significant reduction in drug toxicity, reduction of the drug dose, and increased treatment efficacy.

ownership, converts the Technology Transfer Office (TTO), of the two universities, the responsible offices for the patents management and for the first commercialization or collaborative research partnerships efforts.

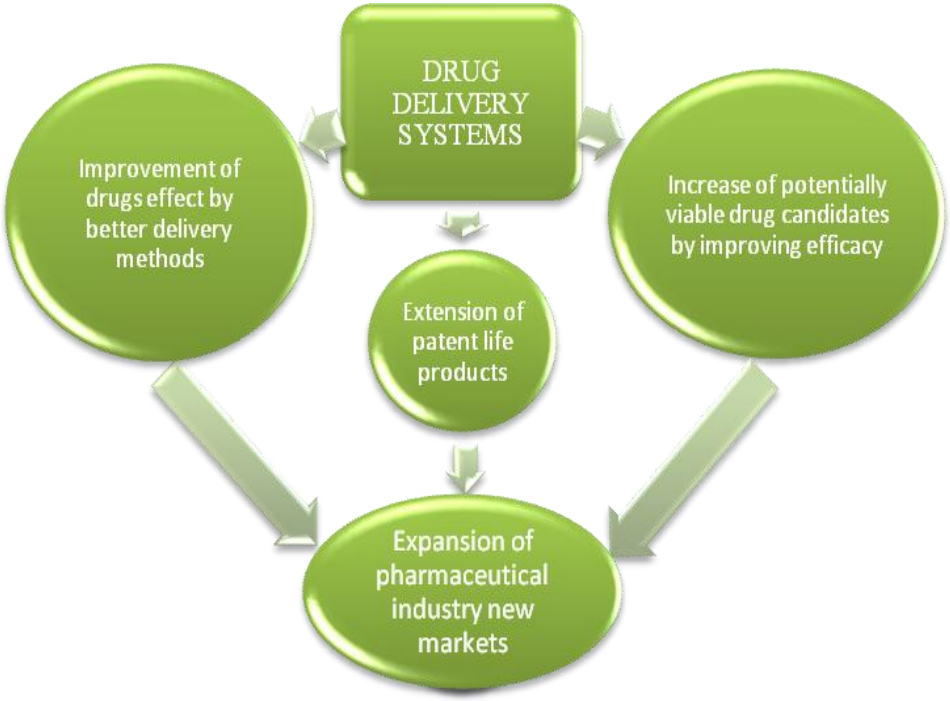

Figure 1.1 – Drug delivery systems consequences and opportunities[5]

The intention of this work is to develop a marketing plan regarding the launch of this new product (DELIVES), covering the first three years of the startup that will market the final product and also the period leading up to the company´s creation – when the platform technology is managed by *Universidade Nova de Lisboa*'s Technology Transfer Office together with the researchers[6]. During the thesis work progression, where contacted several entities in different areas, for example, related to pharmaceutical or technology transfer. These contacts are descriminated in Appendix 1.

[5] 3) Macromolecular drugs, which are largely biologics, are currently being delivered only through injections. As there are various issues related to solubility, molecular size, toxicity, ineffective absorption, off-target reaction, the use of other models of drug delivery has been a challenge (Frost & Sullivan, 2009 A).

[6] During the development of this work, I´ve been working at *UNL*'s TTO, and this is the reason why it is only refered the efforts made by UNL TTO and not the TTO of IST.

2 General Company Description

2.1 Vision

To preserve and improve people's lives using green and environmentally friendly procedures. Focus on providing value to our clients, through superior products to its customers and society in general, by improving pharmacological and therapeutic properties of existing and new drugs.

Life Delivery wants to conquer a ubiquitous status for their drug delivery systems being the most widely used system in clinical applications.

2.2 Mission Statement

Working together with pharmaceutical and biotechnology industries in order to find better and safety solutions to preserve and improve people´s lives.

2.3 Value Proposition

LIFE DELIVERY | Delivering a safety Future.

2.4 Business Model

Our strategic partnerships range from joint discovery, co-develop and licensing agreements with a wide range of organizations, for the purpose of securing exclusive access to "second generation" drugs and delivery systems.

3 *The Problem and Solution*

3.1 Current situation of DELIVE´s potential customers

For the pharmaceutical and biopharmaceutical industries, the current and next years will bring an increase in financial and regulatory pressures caused by continuing patent expirations of blockbuster drugs, dwindling product pipelines due to financial risks of drug discovery and development process, increasingly cautious government regulators in order to, for example, environmental concerns policies — not to mention company downsizings due to mergers, acquisitions and outright dissolutions caused by, the risk of this kind of business.

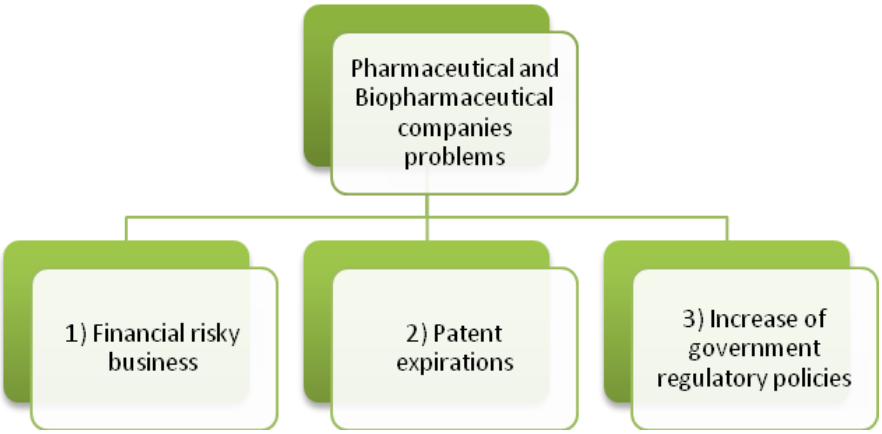

Figure 3.1 - Summary of Pharmaceutical and Biopharmaceutical companies main problems

> "The era that created the modern pharmaceutical industry is in fact over,"
>
> Richard Evans, a former Wall Street analyst and now a pharmaceutical consultant

1) Risky Financial Business

The need to reduce financial risks on new drugs development investments

Pharmaceutical and Biopharmaceutical companies and industries, which typically commercialize only 2-3 new products per year, have to face long and costly product development cycles.

According to the European Federation of Pharmaceutical Industries and Associations, the discovering[7], development[8] process and clinical trials[9] needed to market a new drug involves estimated costs of €1,059 million, and takes between 12 to 13 years to reach the market since the first synthesis of the new active substance (EFPIA, 2009). In the next years we will assist to an increasing in R&D expenditures for successful new molecular entity (NME) launch (see Appendix 2). The investment made in a new drug development process is risky, because on average, only one or two of every 10.000 promising substances demonstrates quality, safety and effectiveness in the demanding tests of research and become a marketable product (EFPIA, 2009) (see also Appendix 3). 40% of drug failures have been associated to poor pharmacokinetics properties (a process by which a drug is absorbed, distributed, metabolized and eliminated by the body) which represents on average, a loss of 4,236 trillion Euros to pharmaceutical companies, and that could be overcome, by using different and innovative drug delivery systems (Frost & Sullivan, 2010).

As was referred before, 60% of New Drug Applications submitted to the FDA during the 1990s were for drugs containing existing active ingredients. The reformulation strategy is more cost and time effective, than the development of a completely new drug (Table 3.1).

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[7] Drug discovery is the process that involves finding out the target that causes the disease. Next, chemical or biological compounds are screened and tested against these targets or assays, which are representative of these targets, to find leading drug candidates for further development (Ng, R., 2004).

[8] Tests are performed on the lead compounds in test tubers (laboratory, in vitro) and on animals (in vivo) to check how they affect the biological system. The tests, often called preclinical research activities, include toxicology, pharmacodynamics and pharmacokinetics, as well as optimization of drug delivery systems. Many interactions are carried out, and the leading compounds are modified and synthesized to improve their interactions with the targets, or to reduce the toxicity or improve pharmacokinetics performance. At the end of this process, an optimized compound is found and this becomes a potential drug ready for clinical trial in humans (Ng, R., 2004).

[9] Clinical trials are trials conducted on human subjects. The pertinent parameters for clinical trials are protocols (methods about how trials are to be conducted), safety and respect for human subjects, responsibilities of investigator, institutional review board, informed consent, trial monitoring and adverse event reporting (Ng, R., 2004). Clinical trials have to follow regulations and guidelines from the Food and Drug Administration, the European Agency for the Evaluation of Medicinal Products (EMEA) of the European Union (EU) or European Member States, Japan's Ministry of Health, Labor and Welfare (MHLW), or regulatory authorities in other prospective countries where the drug is intended to be registered and commercialized. Clinical trials are conducted in accordance with Good Clinical Practice (GCP).

This reformulation is also necessary to increase the medicines effectiveness and reduce side effects. It is urgent to enhance the existing solutions to treat diseases.

Table 3.1 – Development factors and average sales of new drugs and reformulated drugs (adapted from Pharmaceutical Lifecycle Management June 2005 cutting edge information)

	Years to develop	Cost of development (US$MM)	Average Peak sales (US$MM)
NCE / Discovery compound	9-12	900	300-500
Optimization / Reformulation	4-5	40	100-200

In the optimization / reformulation, it is obtained a final medicine with different characteristics, and therefore, according to the Division of Drug information of U.S. Food and Drug Administration (FDA), "Changing the drug delivery system to an approved drug application would likely require a supplement to the drug application", and "the types of studies required (i.e. clinical versus nonclinical data) would depend on a variety of factors" (the description of this contact is present in Appendix 1). So, using certain equivalences and reducing the number of studies required, it is possible to decrease the costs and time needed for these regulatory procedures[10].

It is possible to optimize or also put new drugs into the market using DELIVES

2) Patent Expirations

The need to overcome the drugs off-patent portfolio

According to Datamonitor Inc., a market analysis firm, about USD 140 billion in annual sales are expected to be lost by 2016 as blockbuster drugs (typically defined as one with more than $1bn in annual sales) lose their patent protection and face generic competition (see also Appendix 4).

In accordance with European Parliament, the period between the filing of a patent application for a new medicinal product and the authorisation to place it on the market constitutes one of the factors which actually reduces the effective protection afforded by the patent and can compromise the

[10] Note: These regulatory affairs must be conducted by the owner of the API or the medicine formulation patent i.e. the pharmaceutical company that will be the client of LIFE DELIVERY.

amortisation of the investment in the research. The lack of sufficient protection can also lead research centres based in the Member States to relocate to countries offering better protection[11].

In addition to cost and time consuming process of drug discovery, development and approval, the time of patent exploitation and the sales made during this period, could not be sufficient to offset the investment made and will reduce the sales revenue, being necessary new solutions to overcome this concerning scenario.

In the countries that joined to PCT (Patent Cooperation Treaty)[12] the drug patent of a new drug expires after 20 years (with a possibility of extension for more 5 years) from the date of filling[13], and taking into account the time taken for preclinical and clinical trials made after drug patent application, drugs generally lose patent protection about 12 years after they are first sold (Lichtenberg, F. 2009) (see also Appendix 3).
To cope with this massive patent expiration, manufacturers use different tactics and normally pharmaceutical companies use three main types of strategies to extend the product lifecycle: Merges & Acquisitions, enter on generic market and **Reformulation**.

Reformulation[14] is perhaps the most common. Given the high cost of creating a completely new molecular compound (NME), it should come as no surprise that 60% of New Drug Applications submitted to the FDA during the 1990s were for drugs containing existing active ingredients (Yoshitani, 2007). A relatively small investment (compared to developing a completely new drug) could buy a technology that offers a new lease on life to the drug as an "enhanced" version: longer

[11] Regulation (European Commission) No. 469/2009 of the European Parliament.
[12] The Patent Cooperation Treaty (PCT) is an international patent law treaty, dated of 1970. It provides a unified procedure for filing patent applications to protect inventions in each of its contracting states. A patent application filed under the PCT is called an international application, or PCT application. Until January 2010, were 142 the signatory states of the Patent Cooperation Treaty (online, World Intellectual Property Organization).This treaty allows a single place holder application to be filed within one year of the original filing date which reserves the right to file in most significant countries in the world, without having to actually file a patent application in each country until 30 months after the original filing date or 18 months after the PCT filing. This gives the inventor or his company more time to evaluate the invention without loss of any rights before having to file it worldwide at significant expense (Voet, 2008).
[13] The company has a period – up to 25 years after the patent application – to recover all costs in the investment phase (Marcelino, 2009).

[14] Many products have gone this way, incorporating controlled release or other drug-delivery technologies: Procardia became Procardia XL, Prozac became Prozac Weekly. Strong branding paves the way as people happily switch to a more effective version of the product.

lasting, stronger action, easier dosing (Colyer, 2003). Reformulation approaches can be classified into three categories: reformulation of the molecular entity, new deliveries and new indications.

With a reformulation made by changes in the drug delivery system it is possible to extend the patent protection or also apply for a new patent.

In order to extend the protection granted by a patent, it is possible to request a Supplementary Protection Certificate (SPC). For European Union member states, this is an Industrial Property right that extends the protection to a product, medicinal or plant protection, for a maximum period of 5 years, as long as the product is protected by the original patent.[15]

In accordance with Engª Isaura Monteiro (Patents Examiner of Portuguese Institute of Industrial Property), the reformulation of a drug (changing the system used to deliver the API), could apply for a SPC, since the API is claimed in the base patent (the API should be described in the patent claims) and the product must have obtained a Market Introduction Authorization (MIA)[16] .

Also in the United States of America, it is possible to apply for a Patent Term Extension (PTE) with a maximum duration of 5 years, as set forth in section 1.701 of Chapter 37 of the Code of Federal Regulations.

These SPC and PTE were created in order to compensate the time taken to obtain regulatory approval before drugs could be marketed. However, in some cases it is not possible to apply for these rights, and in other cases it's a better strategy to fill for a new patent application.

[15] The creation of Supplementary Protection Certificates for medicines and phytopharmaceutical products are presented at community regulations, (EEC) Nº 1768/92 of the Council of 18th June 1992 and (EC) Nº 1610/96 of the European Parliament and the Council of 23rd July 1996.

[16] Note: It isn't possible to present a single request for all the European member states. The requests need to be presented individually for each member state and it only has effect in the country for which it is granted.

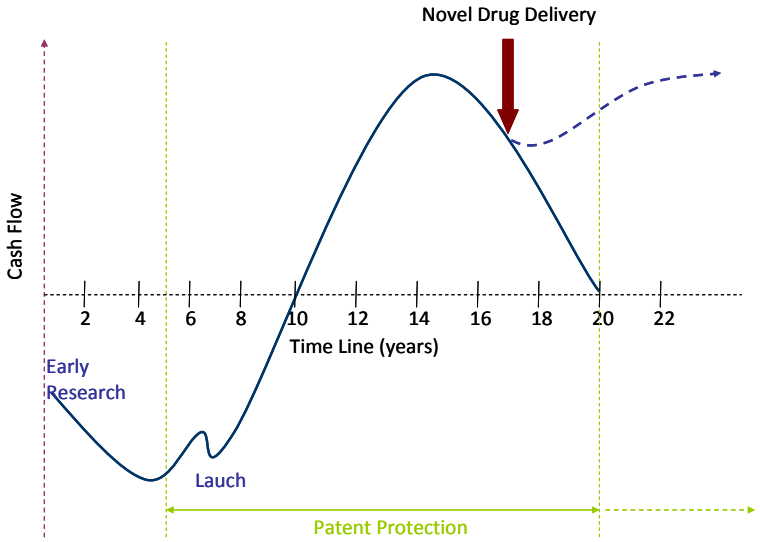


Figure 3.2 – Benefits of use Drug Delivery in drugs reformulation (Adapted from Frost & Sullivan, 2009 A)

3) Increase of Environmental Regulations and Concerns

The need of using environmentally friendly products/processes

As the world becomes focused on the environment and the potential for long-term harm from manufacturing there has been a concerted push to "go green" (Frost & Sullivan, 2009 A).

The pharmaceutical industry is finding itself under increasing pressure from patients, shareholders, and policy makers to address the growing environmental concerns associated with drug development. By making products free of dangerous chemicals, companies no longer have to deal with the cost of hazardous waste disposal or the medical bills from injured or exposed employees. This is reinforced by the last communication of commission of the European communities, where the environment issue also comes into play via the proposing of measures aimed at reducing the negative effects of pharmaceuticals on the environment and public health (Commission of the European Communities, 2008).

In addition to the advantages presented above, the production process of DELIVES, being made using environmental friendly techniques and products, enables a distinctive green character of this product, compared with TDD available solutions, which suits the needs of pharmaceutical industries with respect to the current obligations of environmental care.

Conclusion

The pharmaceutical market is very competitive and it is imperative that pharmaceutical and biopharmaceutical companies, large or small, find new solutions to remain competitive.

Novel or improved drug delivery systems (process of administering a pharmaceutical compound to achieve a therapeutic effect) can revive promising compounds which have been abandoned due to formulation problems and can be used to add something new to a marketable compound to get a market advantage, extending the life of pharmaceutical products. Drug delivery technologies can clearly differentiate a drug in today's increasingly complex, crowded and competitive markets.

Drug delivery is a fast-growing and highly dynamic segment, in the pharmaceutical and biotechnology industry. Various factors have contributed to the growth of this area. Poor drug efficacy, patent expirations and the urgent need for lifecycle management are some of the major factors facing the current drugs (Frost & Sullivan, 2009 A).

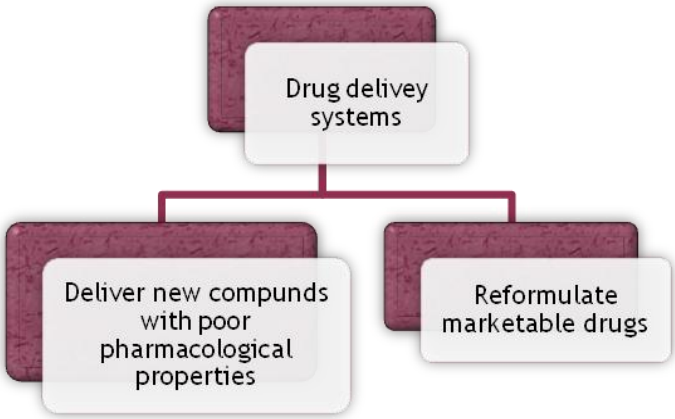


Figure 3.3 - Summary of the two main problems that could be overcome using new drug delivery system

Deliver new compounds with poor pharmacological properties:

Rescuing drug candidates

Recent advances in the field of biotechnology coupled with modern synthetic methodologies have resulted in a large number of commercially available macromolecular drugs (Singh, 2003). There are lots of new compounds in R&D companies' pipelines that could not reach the market due to a lack of an appropriate drug delivery system. DELIVES could help these molecules with potential for a wide range of therapeutic indications, to get their propouse and achieve a therapeutic effect, getting regulatory approval to enter into the market.

Reformulate marketable drugs:

Make old drugs new

Through reformulation, a drug company can change enough characteristics of a brand-name drug just to qualify for a new patent, while keeping other characteristics to use previous clinical testing results for the purpose of regulatory approval. It has been analysed that the introduction of novel delivery systems (one reformulation strategy approach), offers a definitive competitive edge, aiding in better market penetration, bringing benefits to medical community, enhancing brand image, extending lifecycle product management and thereby offering a great opportunity in increasing market share and revenues of the organization.

Improving existing pharmaceuticals using reformulation strategies, particularly drug delivery changes, means improve efficacy and specificity that can be translated in different administrated doses, administration routes; enhance convenience for patients and improvements in toxicity, stability and specific targeting.

We are moving on the direction of an ideal that consists in easy-to-use formulations with favourable side effects to increase uptake and adherence – As patients convenience gains more importance, demand for easy-to-use formulations is increasing. Due to these facts, companies are reformulating drugs more frequently (Frost & Sullivan, 2009 B).

Novel drug delivery systems can act as a strategic tool providing various advantages to patients, physicians and pharmaceutical/biotechnology companies (Frost & Sullivan, 2008 B). Given this perception, and owning a patent for a new extreme versatile biomaterial – the Ion Jelly-, **LIFE DELIVERY** is developing an innovative targeted drug delivery system called DELIVES to improve the therapeutic effects of a large number of pharmaceutical compounds and also deliver compunds that otherwise could not reach the market.

This is an urgent and needed solution with advantages to the pharmaceutical and biopharmaceutical industry, physicians, patients and the society in general.

4 *Product Description*

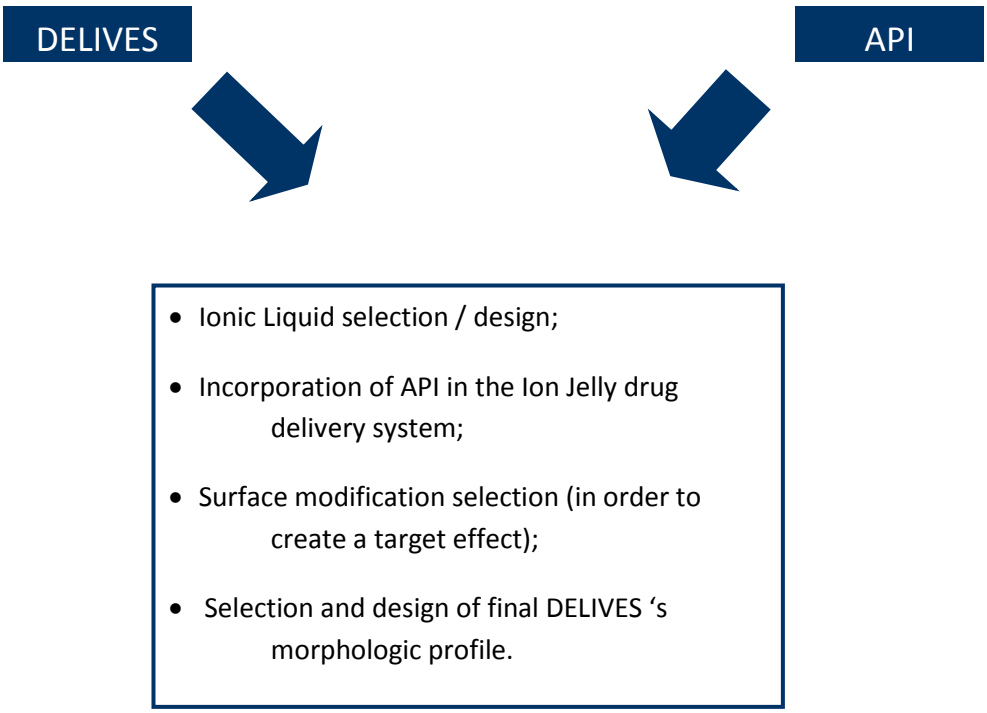
DELIVES| improving life quality; is a unique compilation of products that utilize ion-jelly based material to overcome common industry challenges and deliver cost-effective drugs and enhance the selective uptake of drugs to target tissues or cells.

Unlike other options offered in the market, DELIVES is extremely versatile and can be precisely tailored to achieve each client's specific objectives, providing the controlled release of drugs, made using an environmentally friendly process.

The composition and linker chemistry are chosen to optimize the release of the specific drug.

DELIVES helps pharmaceutical and biopharmaceutical companies achieve:

- Improved bioavailability, particularly for poorly water soluble compounds
- Different routes of administration for marketable drugs
- Improved efficacy and controlled release of marketable drugs
- Ease of scale-up and validation
- 4 to 5 years to enter in the market[17]



[17] 1 year to client´s product specifications adjustments + expected maximum of 3 to 4 years to regulatory affairs (this time was achieved using information about duration of market introduction authorization procedures made into reformulations of drug delivery forms. Consult section 2.2 – "The solution").

Due to confidentiality reasons related to Intellectual Property we are unable to give more technical details.

4.1 Intellectual Property

Ion Jelly® is an exclusive technology with protected IP. There are one Portuguese and four PCT patent applications pending for this technology, filed in 2007 (PT103765) and 2009 (EP2006231; KR10-2008-0058173; JP2008-160947; USA20080319164) respectively.

All patents are co-owned by the *Universidade Nova de Lisboa* (UNL) and *Instituto Superior Técnico* (IST); and the research team is constituted by Susana Filipe Barreiros, Pedro Miguel Vidinha, Nuno Lourenço, Joaquim Sampaio Cabral, Ines Batista Ribeiro and Carlos Alberto Afonso (inventors).

The search report and official written opinion provided so far by the Portuguese Patent Office (INPI) did not identify any relevant document regarding state-of-the-art that can hinder the novelty and inventive step of this invention. In addition, there is a high level of know-how associated with this technology which took more than 10 years to develop by the inventors. The scientific team is widely multidisciplinary, from various fields covering chemistry and bio-sciences, for example.

Also, the innovative degree of this technology has been highlighted by several prestigious sources as specified in Appendix 5.

5 *Market Selection*

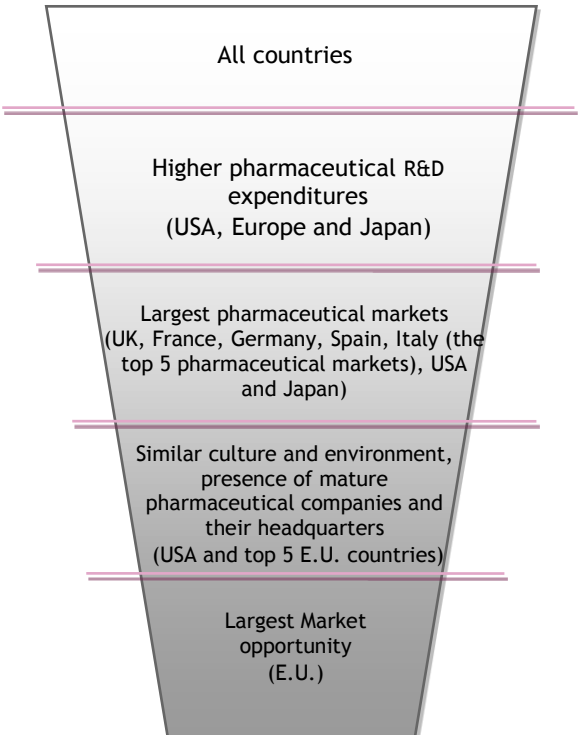


Figure 5.1 – The options to market selection

In order to select the market to enter, it was used **R&D expenditure** as a first criterion, since it provides a measure of the financial input to innovative activity that may lead to process innovation, fundamental new findings, new products or improvements of existing products.

Globally, and according to Frost & Sullivan market study about opportunities in drug delivery, USA (66,004.1 Million USD), Europe (48,673.1 Million USD) and Japan (11,081.3 Million USD), are currently the world regions with higher pharmaceutical R&D expenditures, and will continue to be until 2012 (see Appendix 7, 8,9 and 10) (Frost & Sullivan, 2009 A). According to the same source the venture capital added to the government investments in biotech R&D at 2012 will represent 120,196.9 Million USD in USA, 23,614.5 Million USD in Europe and 4,988.5 Million USD in Japan (see also Appendix 11 and 12) (Frost & Sullivan, 2009 A).

In these 3 geographical areas, the second criterion evaluated was the **dimension of the markets for pharmaceuticals**, and according to IMS Health Company, and their last figures from 2008, the largest markets for pharmaceuticals are USA, Spain, United Kingdom, France, Germany, Italy and Japan (IMS, 2008).

The following step was to evaluate the **expected growth** of each market and the last forecast estimated (IMS, 2008):

- An expected growth rate of 1 to 2 percent in 2009 for the United States which represents sales of $292 to $302 billion, and reflects the impact of continuing patent expirations, fewer new product launches and a tighter economy.
- The top five E.U. countries (France, Germany, Italy, Spain and the United Kingdom) were forecasted to grow 3 - 4 percent in 2011, reaching sales of $162 to $172 billion. In Europe, the growth is driven by the continued aging of the region's population and rising demand for preventive care and will be tempered by the increased impact of health technology

assessments, the use of contracting by payers as a means to control costs, and the decentralization of government healthcare budgets.

- Japan, the world's second-largest market, was expected to see higher growth of 4 to 5 percent, reaching $84 - $88 billion. Approvals of new anti-cancer agents, disease prevention programs, and the absence of the Japan government's biennial price cuts all contribute to stronger growth. Government efforts to promote the use of generics will have only a modest impact on the Japan market in 2009.

In addition to the similar culture and environment[18], U.S.A. and E.U. present highest mature pharmaceutical and biopharmaceutical markets. These criteria led to the disregardation of Japan.
Between the U.S.A. and the E.U. countries, our last criteria evaluated the **potential of the market opportunity**, with E.U. seeming to be the major potential market to be explored. The main reason for this is the intensive presence of Pharmaceutical companies' headquarters in E.U.[19] (where it's possible to find the decision makers[20]) and a highest number of targeted drug delivery companies in the U.S.A. market, a read ocean for drug delivery companies (consult Appendix 13).

[18] For example the uniformization of all countries in terms of clinical trials - Requirements for the conduct of clinical trials in the EU are provided for in "Directive 2001/20/EC"

[19] The choice of European Union and not all the Europe is based not only on the uniformization of laws and policies in the E.U. member states, but also on the highest revenue of E.U market ($ 90,600 Million) compared to the rest of Europe ($ 11,300 Million) (IMS, 2003).

[20] Inside the pharmaceutical and biopharmaceutical companies the decision makers are the business and product managers.

6 *Current Situation Analysis*

EXTERNAL ENVIRONMENT

According to the market selection presented above, the current situation analysis was made in European Union.

1. Economic and Political/Legal environment

According to Datamonitor, The European pharmaceutical market generated total revenues of $177.6 billion in 2008, representing a compound annual growth rate (CAGR) of 4.4% for the period spanning 2004-2008 (Datamonitor, 2010).

Intensity of R&D aid in Member States

In accordance with the Barcelona objectives, research and development (R&D) expenditure should reach 3% of the GDP of the European Union by 2010, compared with the 1.93% in E.U. 25 at 2002 (Eurostat - May 2005).

The Eurostat Report highlights three groups of countries:

- Countries with low R&D intensity (new Member States, Greece, Portugal, Spain and Ireland) showed increases in their respective R&D intensities due to a catching-up phenomenon. However, there are important disparities.
- Countries where R&D intensity is higher recorded significant progress (Austria and Denmark) or reached the 3% threshold (Sweden and Finland).
- Former Member States where R&D intensity is close to the European average (values from 1.5 to 2.5%). For this last group including in particular France, United Kingdom, Germany, the Netherlands and Italy, R&D intensity did not increase.

The European Union is responsible for policies, regulations and recommendations that affect the 27 member states. In the EU legislation, as regards to the Pharmaceutical and cosmetic products, it is possible to highlight a renewed vision for the pharmaceutical sector – a communication of 21st December 2008, that lays down objectives relating to the future of the pharmaceutical sector, like:

- The new regulatory framework should contribute to reinforcing the **safety of pharmaceuticals**, **encouraging innovation** and making medicines more accessible for European patients.

The **environment issue** also comes into play via the proposing of measures aimed at reducing the negative effects of pharmaceuticals on the environment and public health (Commission of the European Communities, Dec. 2008).

Also related with the environmental issue, E.U. made valuable contributions related with the promotion of corporate social responsibility (CSR) (Commission of the European Communities, March 2006). This communications and policies emphasize the importance of environment issues in pharmaceutical sector and encourage innovation in this industry.

2. Technological environment

Access to innovative medicines:

In a call for action to strengthen the European-based pharmaceutical industry for the benefit of the patient, the commission highlight:

The development of innovative medicines with a high added therapeutic value should be encouraged under the 6th Framework Programme for Research. In addition the Commission, through its proposal for a review of pharmaceutical legislation, has demonstrated its desire to support research into innovative medicines and provide sufficient protection for the exclusivity of the data on such medicines (Commission of the European Communities, July 2003).

According to Frost & Sullivan, in the technology area, cost-effective manufacturing of the drug delivery devices is likely to heighten profit margins. The R&D arena offers tremendous opportunity when novel drug delivery technology is expanded to various indications and therapeutic areas. In addition, huge opportunity exists for companies that develop novel drug delivery technology along with unique formulation technology. Companies focussing on drug delivery technologies must concentrate on improving the drug delivery methods, in order to expand the applications in various indications and to have a wide therapeutic reach.

The **patent expirations** are expected to stimulate a surge in novel drug delivery methods for existing products. Sophisticated reformulation, coupled with cost-effective and efficient drug delivery methods, is likely to attract commendable revenues in the European market. The future potential for drug delivery in the European market is likely to be propelled by the influx of novel drug delivery methods. Also, according with Frost & Sullivan, Drug delivery is a fast-growing and highly dynamic segment in the pharmaceutical and biotechnology industry. Various factors have contributed to the growth of this area. Poor drug efficacy, patent expirations and the urgent need for life cycle management are some of the major factors facing the current drugs (Frost & Sullivan, 2009 A).

An ideal novel drug delivery system will focus on **patient benefits**, **cost-effective** and commercially viable.

The opportunity level of drug delivery business remains to be the highest in all areas except the regulatory level, however regulatory approval and patent protection will follow suit, as the other criteria are met (Frost & Sullivan, 2009 A).

The intensity of R&D efforts made in DD systems at E.U. is very intensive, but still remains far from U.S.A.

3. Social environment

The report by the High Level Group on Innovation and Provision of Medicines (2002) recommended that the EU institutions and member states should work towards ways of **improving the penetration of generic medicines**. The communication - a call for action to strengthen the European-based pharmaceutical industry for the benefit of the patient - also points out that, as part of the reform of the Community code relating to medicinal products for human use, the Council's common position suggests the possibility of introducing a marketing authorisation application for a generic and to grant this authorisation in the last two years of the data protection period of the reference product for all products except those falling within the mandatory scope of the centralised procedure.

Another E.U. environment weakness is the increasing of competitiveness of generic manufacturing, hinder the market development. With an increasing number of generics companies based out of low-cost countries making in-roads into the European market, manufacturing is expected to get highly competitive. Companies that are strongly backward integrated into the pharmaceutical value chain and have their active pharmaceutical ingredients and excipients manufactured at very competitive prices in the Asia Pacific region are likely to significantly challenge European participants. Although the uptake of generics in Europe continues to increase, heightened competition is expected to strain margins. This fact incurs on the decreasing of attractiveness of product's life cycle management.

Is very important to clarify that this product not intends to be a competitor of generics, but a solution to already existing medicines, that effectively needs improvements or also to introduce new and needed medicines into the market.

4. Customers / Competitors analysis

Costumores´ analysis

This section is developed in part 8.1 – “Market segmentation”.

Competitors´ analysis

According to ESPICON market report about Targeted drug delivery analysis, by 2018, over 30 new products will be launched resulting in a global market for advanced targeted delivery products worth over US$8.5 billion (Epsicom, 2009).

DELIVES, is for now a technology with a huge potential to serve as vehicle to deliver a great diversity of existing and potential drugs. However, it is necessary to analyse each drug case in order to evaluate the truth potential of DELIVES application. Derived from its character, for now, more generalist of this technology, it is necessary to assume all the targeted drug delivery companies as competitors (even though most of them exploit technologies targeted only to one specific therapeutic area).

From the Epsicom report, results the number of targeted drug delivery companies (29 companies). A detailed document of the companies and respective products, based on each company´s official website information, is present in Appendix 13.

Summarizing: The pharmaceutical market growth connected with the patent expirations and dry pipelines, and still with the E.U. policies about drugs safety, R&D support and environmental issues; form great opportunities to LIFE DELIVERY. Notwithstanding, this company will face a solid and strong competition, in a untapped market, that will assist to the coming of more entrants.

INTERNAL ENVIRONMENT

1. LIFE DELIVERY:

Human resources of LIFE DELIVERY have a strong and recognized **scientific know-how**, with outstanding **commitment**, initiative; prove of **entrepreneurial spirit** and privileged relationships with another research groups, universities, and R&D institutions. The team commitment such as the entrepreneurial spirit and business knowledge are well demonstrated by LIFE DELIVERY's CRO - Pedro Vidinha - and his business plan competition and entrepreneurship prizes[21]. These competitions prizes may be important to company initial **funding.** However there is a **lack** of strong market / industry knowledge and management know-how inside LIFE DELIVERY staff that needs to be fulfilled.

Despite the **youth and non commercial experience** of this technology company (no previous performance or current offerings), LIFE DELIVERY (an University spin-off), has the advantage of using the privileged relations with *Universidade Nova de Lisboa* (*UNL*) and consequently privileged relationships with the market. Using the network of UNL's Technology Transfer Office it's easier to build interesting business relationships and access to information to successfully implement the marketing plan.

Beyond the market access advantages, the strategic alliances with referred educational institutions could allow the access to juridical services (including patent protection and management), and financial services.

2. DELIVES technology:

The combination of the chemical versatility of an ionic liquid (IL) with the morphological flexibility of gelatine (G) generated a new gelatine-based biomaterial (IL-G) (Vidinha, 2008). The excellent tuneable solvent power of ILs mixed with the biocompatibility and bioavailability of a natural biopolymer like G, makes this innovative material an excellent candidate for developing new drug delivery systems.

[21] Business plans competitions prizes and participations, wined by the research team, using the Ion Jelly Technology:

- E-DAY -2007 (2nd place) – Elevator-pitch Competition
- Idea to Product (I2P) Global Competition – 2008 (1st place) - early-stage technology commercialization plan competition
- BES – 2008 (1st place) – National Innovation Competition
- Prémio Start – 2009 (Finalist) – National Entrepreneurship Prize

According to this, DELIVES is a new targeted drug delivery system that is **extremely versatile** and could encapsulate and deliver a very large spectrum of drugs in the body. This technology also uses a **clean and environmentally friendly** production process, which is an important issue for pharmaceutical industry.

Nevertheless, is important to highlight the controversial "green" designation of Ionic Liquids. This contorversia appears due to toxicity of raw materials used in the production process. Nevertheless, this question doesnt apply to Ion Jelly because the ionic liquids are biocompatibles and do not use toxic compuonds, the preconceived image of Ionic Liquids could affect DELIVES's image.

A comparative analysis between DELIVES and its main technology competitors is made in Table 6.1 (for further information about the competitors technologies, consult Appendix 13).

Main Technology Competitors[22]:

Table 6.1 – Main technology competitors' comparative analysis

	DELIVES (LIFE DELIVERY)	Advanced Polymer Conjugate Technology (NEKTAR)	DIFFUCAPS (EURAND)	SMARTICLES® (NOVOSOM AG)
Versatility of applications	√	√	😐	x
Environmental friendly process/product	√	x	-	x
Ease of Synthesis process	√	x	x	😐
Tests made using different API's = Time to market	x	√	√	√
Different administrative routes possibilities	√	x	√	x

Summarizing: Although the worries about being a new entrant with initial funding needs, this company has an excellent and qualified team that comes from a prestige institution – and this image is extremely important to the clients.

The potential of the product that LIFE DELIVERY intends to commercialize is also increased by the versatility of applications and the environmental friendly process used. Nevertheless it will be necessary to transmit a credible image, to surpass the preconceived concept of toxicity associated with Ionic liquids.

Since the research is currently ongoing, at this moment the early-stage status of the technology is the reason for the non-existence of a current offer, being this the major constraint of the technology.

[22] This analysis was made using technologies available information and also according to previous discussions with Pedro Vidinha. According to the versatility of DELIVES, the main competitors of DELIVES technology is the Nektar's proprietary Advanced Polymer Conjugate Technology platform, where both large and small molecules, can be enabled or made more efficacious to dial in desired therapeutic properties and create an optimized and potentially superior therapeutic.

7 SWOT and TWOS Analysis

7.1 SWOT Analysis

Strengths

Organization:

- Strong scientific know-how, team commitment and entrepreneurial spirit
- University Spin-off

Technology:

- Versatility of applications
- Environmental friendly product and process

How can *Life Delivery* use the strengths?

Organization:

- Shorten the collaborative research time and speed the time to market
- Build up market relations and use the institution prestige

Technology:

- Build a medium-long term strategy to enter in new markets
- Appeal to the client´s corporate social responsibility

Weaknesses

Organization:

- Unknown company
- No funding
- Lack of human resources with market/industry knowledge and management

Technology:

- No current offer
- Poor reputation of ionic liquids (toxicity related)

How can *Life Delivery* stop the weaknesses?

Organization:

- Strength relations with client´s partners working in the distribution chain
- Outsourcing and strategic alliances to bridge the human resources gap

Technology:

- Get a first partner with privileged relations with LIFE DELIVERY´s target market

Opportunities

Organization:

- E.U. R&D support
- Pharmaceutical and biopharmaceutical market growth

Technology:

- Dry pipelines, Patent expirations and Generic competition
- Policies in order to reinforce the pharmaceuticals safety
- Companies environmental issues

How can *Life Deliver use the opportunities*?

Organization:

- Search for collaborative researh funding
- Apply for R&D funding available

Technology:

- Justify the market need for this solution
- Use the recent and growing importance of final customer opinion and concerns as a business strategy
- Link environmental issues to E.U. promotion and stimulus of corporate social responsibility

Threats

Organization:

- Merge and acquisition of companies
- Entrant of new competitors
- Possibility of a wrong perceived concept related withintention of substitution of generic medicines by DELIVES

Technology:

- High cost of advanced drug delivery solutions
- Entrant of new technologies

How can *Life Delivery* stop the threats?

Organization:

- Reinforce the product life cycle management strategy

Technology:

- Reinforce the improvements made on the products. Brand loyalty
- Practice competitive license fees

7.2 TOWS Analysis

	Strengths	**Weaknesses**
	Organization: • Strong scientific know-how, team commitment and entrepreneurial spirit • University Spin-off Technology: • Versatility of applications • Environmental friendly product and process	Organization: • Unknown company • No funding • Lack of human resources with market/industry knowledge and management Technology: • No current offer • Poor reputation of ionic liquids (toxicity related)
Opportunities Organization: • E.U. R&D support • Pharmaceutical and biopharmaceutical market growth Technology: • Dry pipelines, Patent expirations and Generic competition • Policies in order to reinforce the pharmaceuticals safety • Companies environmental issues	**SO (Identification of strategies for advancement)** Organization: • Use R&D funding available Technology: • Build a medium-long term strategy to enter in new markets • Use the technology to reformulate already marketable products in order to extend their profitable lifecycle • Appeal to the client's corporate social responsibility	**WO (Identification of strategies for overcome weakness)** Organization: • Build up market relations and use the institution prestige • Outsourcing and strategic alliances to bridge the human resources gap Technology: • Get a first partner with privileged relations with LIFE DELIVERY´s target market (collaborative R&D agreement)
Threats Organization: • Large companies due to increasing merges and acquisitions • Entrant of new competitors • The power of current competition Technology: • High cost of advanced drug delivery platforms • Entrant of new technologies	**ST (Identification of strategies for avoid threats)** Organization: • Get recognition to expand the product to new therapeutic areas Technology: • Practice competitive prices • Link environmental issues to E.U. promotion and stimulus of corporate social responsability	**WT (Identification of strategies for avoid and overcome)** Organization: ▪ Establish a close relationship with clients during all the license process ▪ Ion Jelly brand loyalty promotion Technology: ▪ Reinforce the improvements made on the products. Brand loyalty

8 *Strategic Triangle*

Once it is not possible to reach all of the market potential customers, companies have to select a specific target market, in order to avoid waste of time and resources. Considering this, the first step is market segmentation, followed by the definition of the most attractive segments (target market) and finally, the design of strategies to reach the target market, attending to the product and company positioning relatively to the competition and the consumer relevant needs.

As mentioned in Part 3 – "The Problem and the Solution", the market soluctions offered by this technology are the reformulation of existing drugs and the new solutions for the delivery of macromolecules, and as will be showed after, this two solutions are translated in two different markets, that could also be sub-divided due to the different therapeutical area of application.

8.1 Market segmentation

Besides the geographic segmentation was also used a segmentation by industry and a segmentation by specific therapeutic area.

1. Segmentation by industry

There are three main types of pharmaceutical and biopharmaceutical companies being this an U.S.A. fact, but also encountered worldwide (United States Department of Labour, 2010):

a) Large or mainline, pharmaceutical and biopharmaceutical companies (from now on, referred as companies with Development / Production and Marketing – **DPM companies**). These are established firms that have many approved drugs already on the market. These companies often have significant numbers of R&D laboratories and manufacturing plants. In contrast;

b) smaller pharmaceutical and biopharmaceutical (from now on, referred as **R&D companies**): they are usually newer firms that often do not have any approved drugs on the market and as a result, almost exclusively perform R&D. In addition to developing their own drugs, some small pharmaceutical companies perform contract research for other pharmaceutical companies; and

c) **Generic pharmaceutical companies**: these companies manufacture drugs that are no longer protected by patents. Because their products are all established drugs, they devote fewer resources to R&D and more to manufacturing. Given all that, this market segment is of no interest for this study.

According to Frost & Sullivan, it is possible to distinguish between **Pharmaceutical** and **Biopharmaceutical** companies, being the Biopharmaceutical – also called Biotech companies - the ones that have macromolecules as core while the Pharmaceutical companies have concentrated on small molecules (Frost & Sullivan, 2009 A). However, the line between pharmaceutical companies and biopharmaceutical companies is blurred, taking into account that pharmaceutical companies have been unable to ignore the benefits of investing in biotechnology and have focused on a pipeline in this direction through strategic acquisitions and partnerships with biotech companies and/or through their own in-house research efforts.

Using these definitions and profiles, we decided to segment the market in four groups of direct customers:

a) Pharmaceutical DPM;

b) Pharmaceutical R&D;

c) Biopharmaceutical DPM; and

d) Biopharmaceutical R&D companies.

1. Segmentation by application (therapeutic area)

As a result of the current credit crisis and in order to preserve liquid assets, companies in the healthcare sector are restructuring and focusing only on their most advanced, high growth therapeutic programs.

Companies are shifting focus from a fragmented approach that focuses on multiple diseases towards specialized business models such as niche therapeutic areas and generics. By focusing on specific areas companies are able to develop expertise, which promotes brand recognition and saves money by allowing the company to consolidate sales teams and R&D (Frost & Sullivan, 2009 B).

Moreover, each type of customer **should be subdivided by research areas** (therapeutic areas). The relevant therapeutic areas that should be attended are defined using two different aspects related with the **Deals between drug delivery companies and pharmaceutical and Biotechnology companies trends** (that indicate the tendency of drug delivery systems licensing) and the **Biologics pipeline** (where is possible to understand the trends of biologics drugs discovery and development).

According to Frost & Sullivan market study about European drug delivery markets, the deals between drug delivery companies and pharma / biopharmaceutical companies have been

increasing in Europe (Appendix 14) (Frost & Sullivan, 2008 A). Looking at Figure 8.1 that lists the drug delivery deals broken by therapy area and by deal type in European drug delivery market in 2007, it's possible to observe four attractive therapeutic areas to license a drug delivery product (licensing procedure is incorporated in the "others" – blue area of the chart). **Inflammation and Musculosketal**, **Genitourinary**, Neurological (from now, represented as Central Nervous System – **CNS**) and **Respiratory**.

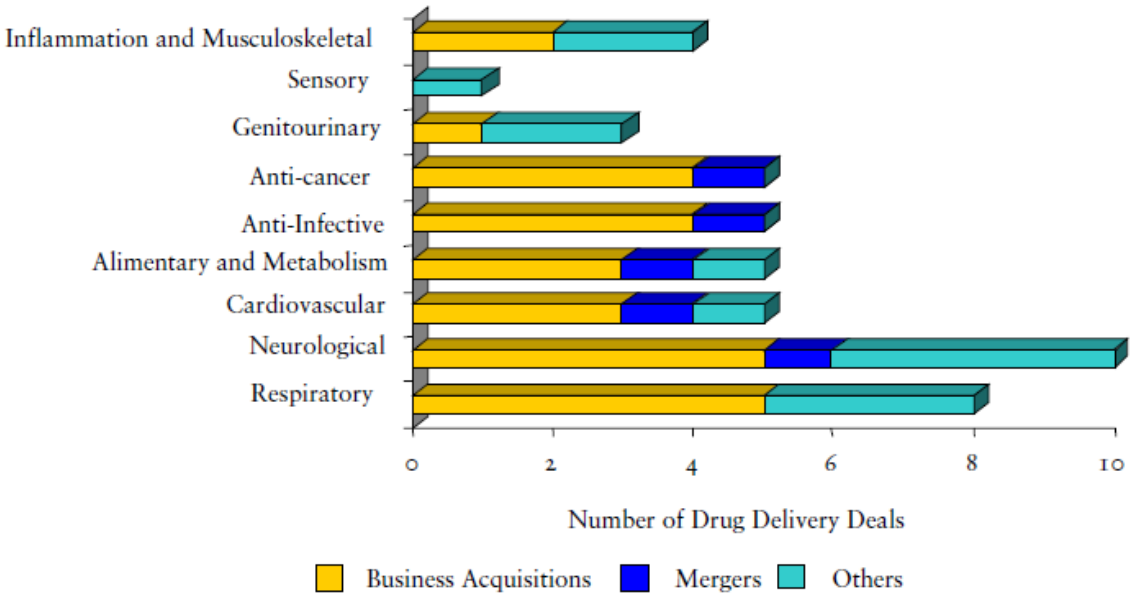


Figure 0.1 - Drug delivery deals broken by therapy area by deal type in European drug delivery market in 2007 Note: Others include licensing, co-development, collaborative R&D, rights, marketing and Manufacture. Source: Frost & Sullivan, 2008 A

On the other hand, the industry is showing a huge and growing interest in macromolecule[23] based drugs (Frost & Sullivan, 2009 A). The number of biologic drugs in the pipeline has increased significantly over the last year and it must be noted that biologics in **Cancer** therapy have been given significant attention, followed by the **Endocrine and Metabolic disorders**, Vaccines, **Cardiovascular** and Autoimmune disorders (that will be represent by **Immunologic** therapeutic area), as showed in Figure 8.2[24].

[23] Macromolecule - any very large complex molecule; found only in plants and animals ([online] Princeton word definition).

[24] Despite the vaccines represents 9% of biologics pipeline, this therapeutic area was discarded , according with Pedro Vidinha, because the product (DELIVES) does not constitute an important asset to this area. The vaccines are used to prevent illness and in all pharmaceutical descriptions they are in separated areas from prescription and OTC medicines.

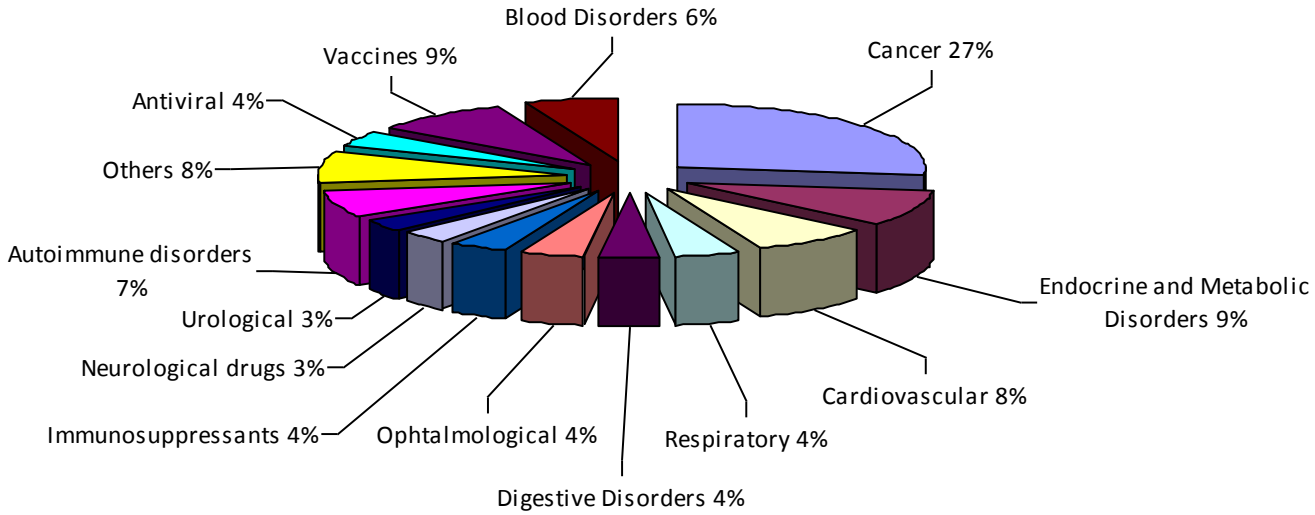


Figure 0.2 – Drug Delivery Market: Biologics Pipeline by Therapeutic Area (World), 2009. Source: Frost & Sullivan, 2009 A

On one hand license agreements tendencies are fairly representative of current trends in this business (in relation to therapeutic areas).

On the other hand it is important to know the trends regarding the emergence of macromolecules that require DD systems.

For the reasons outlined above it is important to use these two data to obtain the relevant therapeutic areas.

Segmentation summary

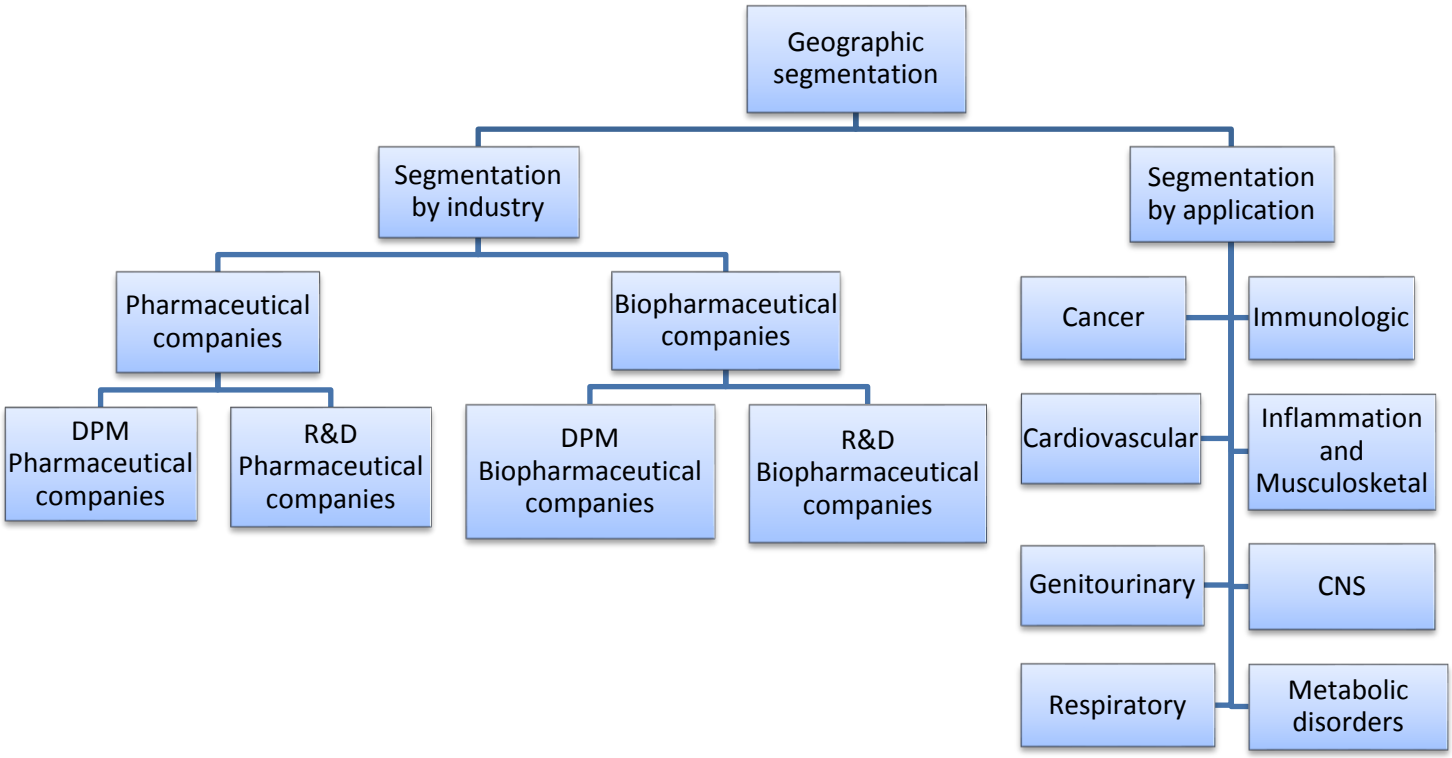


Figure 0.3 – Segmentation summary

Potential market[25]

The **total potential market** comprises **62 companies** divided by **type of customers** and **therapeutic areas of focus** as shown in Figure 8.4. To consult the list of E.U. pharmaceutical and biopharmaceutical companies that belongs to each segmented area, see Appendix 15.

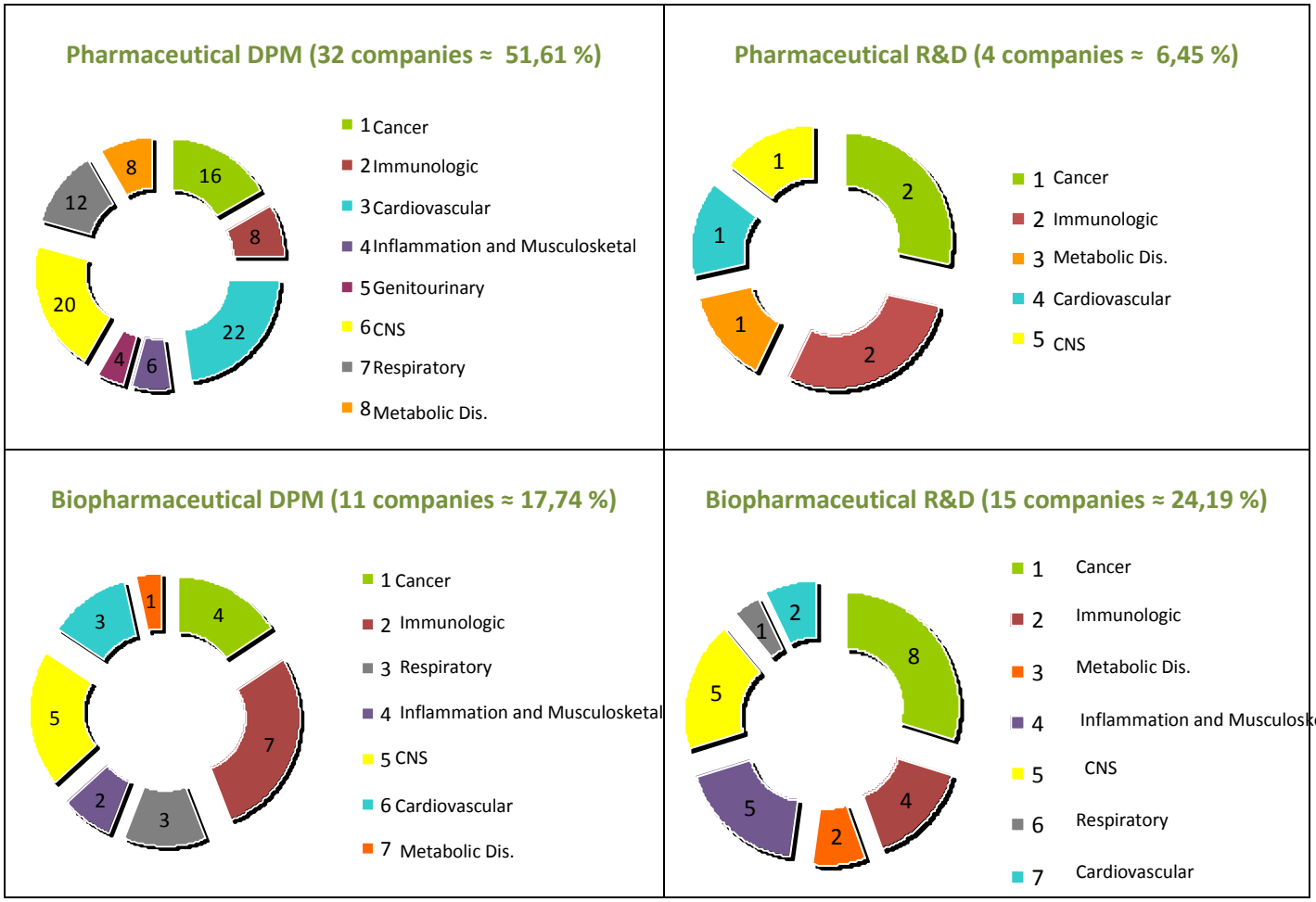


Figure 0.4 – Summary of Total Potential Market analysis

[25] The potential market represents the maximum number of E.U. customers who might be interested in the product. The list of Pharmaceutical and Biopharmaceutical companies, was achieved using the website http://pharmalicensing.com/public/, where was applied the criteria - Geographic Location: Europe to their profiled companies' database. Then it was been analysed all the companies and selected the Pharmaceutical and Biopharmaceutical companies that make R&D and/or Production, Manufacture and Marketing of products, located at European Union. Innovaro Pharmalicensing is a global resource for partnering, licensing, and business development within the life science and biopharmaceutical industries. This information was cross with the database of the Pharmaceutical Business Review (http://www.pharmaceutical-business-review.com/about-us). In order to obtain a more precise database of Pharmaceutical and Biopharmaceutical companies, all the E. U. national pharmaceutical industry associations, members of European Federation of Pharmaceutical (EFPIA) manufacturers and EuropaBio, was contacted by e-mail in order to get a list of each country companies list (see also appendix25). EFPIA represents the pharmaceutical industry operating in Europe. Through its direct membership of 31 national associations and 40 leading pharmaceutical companies, EFPIA is the voice on the EU scene of 2,200 companies committed to researching, developing and bringing to patients new medicines that improve health and the quality of life around the world.

8.2 Market Targeting

The evaluation and selection of segments to target was made attending to the attractiveness of each segment in terms of opportunity, environment, reach and response (external variables), and fitting each with internal considerations such as mission, image, core competencies, resources and performance (Wood, 2008). Each target criteria will be classified in a scale between 0 (unattractive) to 10 (extremely attractive).

Market segments differ on four major attractiveness factors: **Receptivity**, and **Capital to invest** that are the main external variables and on the other hand, LIFE DELIVERY objectives, resources and competences, that are defined by **Power against competitors** and **Match with DELIVES competencies (internal variables).**

All the criterias used to target the market were weighted, with the following percentages: 20% to Receptivity, 35 % to Capital to invest, 20 % to Power against competitors and 25 % to Match with DELIVES competencies. Although the subjectivity of these percentages, this choice takes into account several experts views, such as CEO´s of medical devices companies and Technology Transfer Officers (see Appendix 1).

Receptivity

It is possible to assume that companies more focused on R&D procedures, working in the first lines of drug discovery and development are more risky-friendly with regard to the bet made in new technologies of drug delivery. However, and taking into account the costly process of this business and the low capital available to invest, it is very difficult to this type of companies, to invest in systems to deliver their discovered drugs.

Nuno Arantes - Oliveira (Alfama CEO), believes that for a small biopharmaceutical company (more focused on R&D) the license acquisition of a drug delivery system is very risky. However if the company has a specific problem on delivering an API (active pharmaceutical ingredient), then perhaps it could occur the merging of the drug delivery and pharma / biopharmaceutical companies. According with Sérgio Simões (vice-president of Bluepharma), “smaller and bigger companies could have interest on drug delivery system acquisition”. Capital to invest is based on financial resources of the companies. The importance of this variable entails a great importance attending to the high costs of lisenses and collaborative research (needed in the previous phase of

the agreement). Despite the blurred line between pharmaceutical and biopharmaceutical companies, it is still possible to say that the companies most focused only on the segment "bio" of pharma are much more capital injection dependent contrarily to the pharmaceutical companies that are more powerful in economic terms.

According with expert's testimonials it was assigned a value to the receptivity of each type of client, as can be seen in Table 8.1.

Table 0.1 – Summary of Receptivity Assigning Values

Type of client	Receptivity
Pharmaceutical DPM	8,00
Pharmaceutical R&D	4,00
Biopharmaceutical DPM	5,00
Biopharmaceutical R&D	4,00

Capital to invest

This criteria is based on financial resources of the companies. This variable entails a great importance attending to the high costs of license agreements (for further information about these costs, please consult the section 9.2– "Pricing").

Indeed, and despite the adverse financial climate, the biotech sector seems to be holding up relatively well. Up with the support to innovation made by programmes to stimulate research in drug development such as European Innovative Medicines Initiative, the competition for investment among biopharmaceutical companies is intense. Venture Capitalists have become more selective, putting their money into later-stage companies or moving to other sectors (Schofield, 2010).

The companies' capital to invest was achieved using their 2009 turnover[26] which was converted into a 0 to 10 scale (Table 8.2). The turnover ranges and respective assigned classification were defined based on the maximum and minimum value of all the analysed companies' turnovers (for further information about each company turnover value, please consult Appendix 16).

Table 0.2 - Capital to Invest Assigning Values

Turnover range (USD $ Million)	Capital to invest (0 to 10 scale)
0-100	0
100-500	1
500-1000	2
1000-5000	3
5000-15000	4
15000-25000	5
25000-30000	6
30000-35000	7
35000-40000	8
40000-45000	9
45000-50000	10

[26] Turnover represents the Annual sales volume net of all discounts and sales taxes.

Table 8.3 summarizes the value of capital to invest by therapeutic area. To obtain this value it was made an average of capital to invest (in a 0 to 10 scale) of all companies present in the sub-segment (therapeutic area).

Table 0.3 – Summary of Capital to Invest Value (in 0-10 scale)

Type of client	Therapeutic area	Capital to invest
Pharmaceutical DPM	Cancer	4.69
	Immunologic	4.80
	Cardiovascular	5.05
	Inflammation and Musculosketal	4,20
	Genitourinary	3.50
	CNS	4.06
	Respiratory	4.11
	Metabolic dis.	7.00
Pharmaceutical R&D	Cancer	4.00
	Immunologic	0.50
	Cardiovascular	0.00
	CNS	?
	Metabolic dis.	0.00
Biopharmaceutical DPM	Cancer	0.75
	Immunologic	2.00
	Cardiovascular	1.67
	Inflammation and Musculosketal	2,50
	CNS	2.60
	Respiratory	2.33
	Metabolic dis.	0.00
Biopharmaceutical R&D	Cancer	0.25
	Immunologic	0.00
	Cardiovascular	0.00
	Inflammation and Musculosketal	0,50
	CNS	0.00
	Respiratory	0.00
	Metabolic dis.	0.00

Power against competitors

The power against competitors refers to the evaluation of therapeutic segments with more or less "actors" (**intensity of competition** based on presented therapeutic areas solutions) and to the **power** (dimension and reputation) **of competitors**

Intensity of competition

Between the main competitors it exists a clearly division at therapeutic areas of focus, representing cancer (with 54%), the therapeutic area with more market available solutions to API delivering problems / improvements. This data converts cancer in a red ocean in terms of competition). Based on the percentage of competition intensity it was made a scale in order to convert this value into a 0 to 10 scale (see Appendix 17).

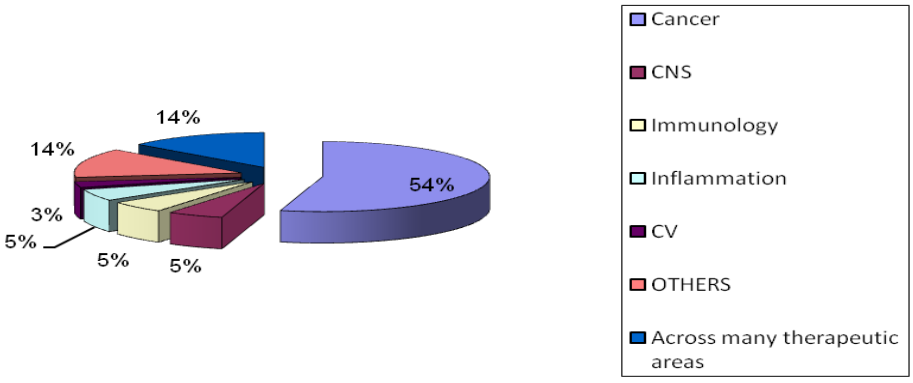


Figure 0.5 - Intensity of competition by therapeutic areas

Power of competition

According to Business Insights (an up-to-date incisive market and company analysis), Alkermes and Nektar are, with large distance comparative to others, the leading companies of targeted drug delivery, which act mainly in the segments of CNS and Immunology. Using this information it was considered that these two segments are the most powerful ones in terms of power of competition. On the other hand, and according to the versatility of LIFE DELIVERY product possible applications, was also considered that competitors that act across many therapeutic areas are the most powerful ones.

Table 0.4 - Power against competitors[27]

	Intensity of competition	Power of competition	TOTAL
Cancer	3	8	5,5
CNS	9	3	6
Immunology	9	3	6
Inflammation	9	8	8.5
Cardiovascular	10	8	9
Others	8	8	8
Across many therapeutic areas	8	1	4.5

Match with LIFE DELIVERY competencies

This criteria refers to the **competences** and **strategic interest** of the company. According with Pedro Vidinha (one of the technology inventors) and company's CRO, although DELIVES could be applied in a great range of therapeutic areas, for now, this drug delivery is more indicated to **Inflammation** and **Metabolic disorders**. Quoting Pedro Vidinha "We believe that an Ion Jelly could be extremely useful to apply to drug delivery systems where gelatin is already used as an encapsulation polymer since the presence of ionic liquids enhance gelatin encapsulation and delivery properties. This fact is particularly clear on anti-inflammatory delivery systems where gelatin is currently be used to design different anti-inflammatory delivery systems. The introduction of ionic liquids through ion jelly technology could scope the number of anti-inflammatory compounds that can be used on those systems. More recently different gelatin based delivery systems were also developed for metabolic disorders treatment. Thus we believe inflammation and metabolic disorders could very promising field to introduce Ion Jelly as drug delivery matrix".

Table 0.5 – Match with LIFE DELIVERY competencies

Therapeutic area	Match with LIFE DELIVERY competencies
Cancer	5
Immunologic	5
Cardiovascular	5
Inflammation and Musculosketal	8
Genitourinary	5
CNS	5
Respiratory	5

[27] The valuation of this criterias gave a highest value to the segmented areas where there is less intensity of competition and also less power of competitors.

Table 0.6 - Targeting variables weight summary

Type of industry	Therapeutic area	External variables		Internal variables		Total
		Receptivity (20%)	Capital to invest (35%)	Power against competitors (20%)	Match with DELIVES competencies (25%)	
Pharmaceutical DPM	Cancer	1,60	1,56	1,10	1,25	5,51
	Immunologic	1,60	1,66	1,20	1,25	5,71
	Cardiovascular	1,60	1,65	1,80	1,25	6,30
	Inflammation and Musculosketal	1,60	1,47	1,70	2,00	6,77
	Genitourinary	1,60	2,33	0,90	1,25	6,08
	CNS	1,60	1,42	1,20	1,25	5,47
	Respiratory	1,60	1,44	0,90	1,25	5,19
	Metabolic dis.	1,60	2,39	0,90	1,50	6,39
Pharmaceutical R&D	Cancer	0,80	1,40	1,10	1,25	4,55
	Immunologic	0,80	0,18	1,20	1,25	3,43
	Cardiovascular	0,80	0,00	1,80	1,25	3,85
	Inflammation and Musculosketal	0,80	-	1,70	2,00	4,50
	Genitourinary	0,80	-	0,90	1,25	2,95
	CNS	0,80	-	1,20	1,25	3,25
	Respiratory	0,80	-	0,90	1,25	2,95
	Metabolic dis.	0,80	0,00	0,90	1,50	3,20
Biopharmaceutical DPM	Cancer	1,60	0,26	1,10	1,25	4,21
	Immunologic	1,60	0,70	1,20	1,25	4,75
	Cardiovascular	1,60	0,58	1,80	1,25	5,23
	Inflammation and Musculosketal	1,60	0,88	1,70	2,00	6,18
	Genitourinary	1,60	-	0,90	1,25	3,75
	CNS	1,60	0,91	1,20	1,25	4,96
	Respiratory	1,60	0,82	0,90	1,25	4,57
	Metabolic dis.	1,60	0,00	0,90	1,50	4,00
Biopharmaceutical R&D	Cancer	0,80	0,09	1,10	1,25	3,24
	Immunologic	0,80	0,00	1,20	1,25	3,25
	Cardiovascular	0,80	0,00	1,80	1,25	3,85
	Inflammation and Musculosketal	0,80	0,18	1,70	2,00	4,68
	Genitourinary	0,80	-	0,90	1,25	2,95
	CNS	0,80	0,00	1,20	1,25	3,25
	Respiratory	0,80	0,00	0,90	1,25	2,95
	Metabolic dis.	0,80	0,00	0,90	1,50	3,20

Conclusion

Table 8.6 demonstrates that the fittest target of LIFE DELIVERY in E.U., in a first approach to the market, is the large **Pharmaceutical Companies** which have **Inflammation and Musculosketal, Cardiovascular** and **Metabolic disorders** as a business core therapeutic area.

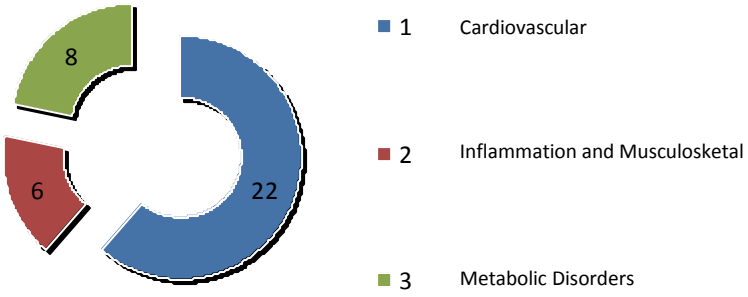


Figure 0.6 - Number of Pharmaceutical DPM companies by therapeutic area.

There are **27 European large Pharmaceutical companies** that operate in the therapeutic areas selected, as referred in the tables bellow.

Cardiovascular	Ark Therapeutics Group plc
	AstraZeneca PLC
	Bayer AG
	EGIS Pharmaceuticals Plc
	F. Hoffmann-La Roche Ltd.
	Gedeon Richter Plc.
	GlaxoSmithKline plc
	Ipsen S.A
	Krka d.d. Novo Mesto
	Les Laboratoires Servier
	Meda AB
	Merck
	Novartis AG
	Nycomed International Manag. GmbH
	Orion Corporation
	Sanofi-Aventis
	Boehring Ingelheim
	Chiesi Farmaceutici
	Grupo Ferrer
	Italfarmaco
	Rafarm
	Schwable Pharmaceuticals

Inflammation and Musculosketal	GlaxoSmithKline plc
	Chiesi Farmaceutici
	Rafarm
	Abiogen Pharma
	Dr. Kade Pharmazeutische GmbH
	Novartis AG

Metabolic disorders	F. Hoffmann-La Roche Ltd.
	GlaxoSmithKline plc
	Krka d.d. Novo Mesto
	Les Laboratoires Servier
	Novartis AG
	Grupo Ferrer
	Biomedica Foscama
	Sanofi-Aventis

8.2.1 Ideal Customers

According to targeting process made before, LIFE DELIVERY´s ideal customers it will be, at first sight to enter-to-market, the larger pharmaceutical companies (**DPM Pharmaceutical companies**), that are increasingly under pressure in order to bring forward innovative future products.

According to this perception, the use of DELIVES to reformulate already approved drugs take away the element of risk involved in the approval of main ingredients, and could also improve their efficacy and reduce the amount of drug used, giving competitive advantages to pharmaceutical market place. This means that this initial strategy presents higher potential, compared to the DELIVES use in countless number of new compounds with poor pharmacological proprieties that are not yet approved.

Looking only to DPM Pharmaceutical companies is obvious to say that their sub-segments differ only on the therapeutical focus area, and because of this, they present similar patterns of purchase, such as value-added to customers and to organization. Nonetheless the variable **size**, that measures each sub-segment dimension combined with the **historic of drug delivery systems licensing acquired to extent products lifecycle,** are important factors in order to determine the ideal customers.

According to this, the ideal customer is a company which acts in a great variety of therapeutic areas (**therapeutic area presence**); with a significant number of **pipeline products** (that will allow the reformulation of a greater number of drugs using LIFE DELIVERY product - DELIVES); and with a **past of license deals** with drug delivery companies.

The size of each sub-segment is also evaluated by the **number of companies**, using the correspondent weight.

1) *Number of companies:*

Using the number of companies present in each sub-segment (therapeutic area), it was calculated the respective weight in a 0 to 10 scale (Weight of companies' number). The **weight of companies' number** was calculated multiplying the number of companies in the therapeutic area by 10 (the maximum value of this classification), and dividing by the total number of Pharmaceutical DPM companies that exists in the 8 therapeutic studied areas (32 companies).

Table 0.7 – Assigning values for Number of companies by therapeutic area

	Number of companies	Weight of companies number (0 to 10 scale)
Cardiovascular	22	6,88
Inflammation and Musculoketal	6	1,88
Genitourinary	4	1,25
Metabolic dis.	8	2,50

2) *Therapeutic area presence:*

Considering the versatility of DELIVES applications, the value of a client that acts only in one therapeutic area with a less number of products is completely different comparing with the value of a pharmaceutical company that has different products in different therapeutic areas.

To measure the **Weight of companies therapeutic area presence**, the number of each company therapeutic areas presence was multiplied by 10 (the maximum value of this classification), and divided by the total number of therapeutic areas studied - 8.

Table 0.8 – Assigning values to therapeutic area presence for companies acting in cardiovascular therapies

	Company Name	Number of sub-segments presence	Weight of sub-segments presence	Total Size of Segment
Cardiovascular	Ark Therapeutics Group plc	2	2,5	**4,60**
	AstraZeneca PLC	5	6,25	
	Bayer AG	3	3,75	
	EGIS Pharmaceuticals Plc	4	5	
	F. Hoffmann-La Roche Ltd.	5	6,25	
	Gedeon Richter Plc.	2	2,5	
	GlaxoSmithKline plc	7	8,75	
	Ipsen S.A	3	3,75	
	Krka d.d. Novo Mesto	4	5	
	Les Laboratoires Servier	5	6,25	
	Meda AB	2	2,5	
	Merck	2	2,5	
	Novartis AG	8	10	
	Nycomed Int. Manag.	2	2,5	
	Orion Corporation	2	2,5	
	Sanofi-Aventis	4	5	
	Boehring Ingelheim	1	1,25	
	Chiesi Farmaceutici	3	3,75	
	Grupo Ferrer	5	6,25	
	Italfarmaco	4	5	
	Rafarm	5	6,25	
	Schwable Pharmaceuticals	3	3,75	

Table 0.9 - Assigning values to therapeutic area presence for companies acting in metabolic disorders therapies

	Company Name	Number of sub-segments presence	Weight of sub-segments presence	Total Size of Segment
Metabolic dis.	F. Hoffmann-La	5	6,25	**6,25**
	GlaxoSmithKline plc	7	8,75	
	Krka d.d. Novo	4	5	
	Les Laboratoires	5	6,25	
	Novartis AG	8	10	
	Grupo Ferrer	5	6,25	
	Biomedica Foscama	2	2,5	
	Sanofi-Aventis	4	5	

Table 0.10 - Assigning values to therapeutic area presence for companies acting in inflammation and musculosketal therapies

	Company Name	Number of sub-segments presence	Weight of sub-segments presence	Total Size of Segment
Inflammation and Musculoketal	GlaxoSmithKline plc	7	8,75	**5,83**
	Chiesi Farmaceutici	3	3,75	
	Rafarm	5	6,25	
	Abiogen Pharma	4	5	
	Dr. Kade Pharmazeutische F.	1	1,25	
	Novartis AG	8	10	

3) Pipeline products[28]:

Through public information of each company (as the company official website), it was determined the number of products of each company actually commercialise by therapeutic area targeted.

The weight of pipeline dimension was determined using the total number of products as the maximum of the scale.

Table 0.11 – Number of pipeline drugs for Inflammation and Musculosketal

	Company Name	Number of products	Total
Inflammation and Musculosketal	GlaxoSmithKline plc	19	38
	Chiesi Farmaceutici	2	
	Rafarm	10	
	Abiogen Pharma	5	
	Novartis AG	3	
	Dr. Kade Pharmazeutische Fabrik GmbH	2	

[28] Calculation explanation:

- Total number of products (all therapeutic areas) = 108 + 13 + 52 + 38 = 211
- 211 products correspond to the maximum value of the scale - 10
    - Cardiovascular - 108 = 5,12
    - Genitourinary - 13 = 0,62
    - Metabolic disorders - 52 = 2,46
    - Inflammation and musculosketal - 38 = 1,8

Table 0.12 - Number of pipeline drugs for Metabolic disorders

	Company Name	Number of products	Total
Metabolic disorders	F. Hoffmann-La Roche Ltd.	2	52
	GlaxoSmithKline plc	8	
	Krka d.d. Novo Mesto	19	
	Les Laboratoires Servier	1	
	Novartis AG	12	
	Grupo Ferrer	3	
	Biomedica Foscama	2	
	Sanofi-Aventis	5	

Table 0.13 - Number of pipeline drugs for Cardiovascular

	Company Name	Number of products	Total
Cardiovascular	Ark Therapeutics Group plc	No own brand products	108
	AstraZeneca PLC	10	
	Bayer AG	2	
	EGIS Pharmaceuticals	No own brand products	
	F. Hoffmann-La Roche Ltd.	19	
	Gedeon Richter Plc.	4	
	GlaxoSmithKline plc 7	7	
	Ipsen S.A	2	
	Krka d.d. Novo Mesto	12	
	Les Laboratoires Servier	6	
	Meda AB	2	
	Merck	9	
	Novartis AG	10	
	Nycomed International	No own brand products	
	Orion Corporation	2	
	Sanofi-Aventis	8	
	Boehring Ingelheim	1	
	Chiesi Farmaceutici	1	
	Grupo Ferrer	No own brand products	
	Italfarmaco	No own brand products	
	Rafarm	12	
	Schwable Pharmaceuticals	1	

The variables referred above are summarizing in Table 8.14, where the total number represents the simple average of the three variables, due to the difficulty in attribute specific weights to each variable.

Table 0.14- Size of sub-segments targeted

	Weight of number of companies	Weight of Companies therapeutic area presence	Pipeline dimension Weight	TOTAL
Cardiovascular	6,88	4,60	5,12	5,53
Inflammation and Musculoketal	1,88	5,83	1,8	3,17
Metabolic disorders	2,50	6,25	2,46	3,74

Summarizing, the ideal customers will be **DPM Pharamaceutical Companies** with a business core focused on development, production and marketing of **cardiovascular** drugs, that shows an historic interest in developing partnerships with small companies in order to reformulate already marketable drugs, improving their efficacy using a different drug delivery system.

For that, companies like Novartis AG or Bayer that already had sign licensing agreements in order to exploit new drug delivery systems, are the ideal customers of LIFE DELIVERY product – DELIVES.

8.2.2 Market Strategy

Despite the similarity between the ideal customers referred above (similar pattern of purchase - who is the buyer, why they buy and how they buy), and given LIFE DELIVERY characteristics and current situation analysis, the company will adopte a strategy of market entry, divided in two phases:

1st phase – *FCT-UNL* and the research team of DELIVES, is already developing contacts with healthcare companies that have privileged relationships with pharmaceutical companies, being their suppliers of different healthcare solutions. Using this strategy is expected to develop drug delivery systems tailored to specific objectives of healthcare companies partners (pharmaceutical companies), allowing our client to license the final product to their partner. This way, it is possible for LIFE DELIVERY to get recognition of their products in the market and use the credibility of healthcare companies to reach the pharmaceutical giants.

2nd phase - In a later stage, LIFE DELIVERY will establish contact with the rest of the European pharmaceutical companies targeted, in order to license DELIVES improved version to a specific pharmaceutical company that could apply this product to all of their pipeline medicines (after a first collaborative research necessary to fit the product to the specifications of each medicine).

8.3 Positioning

Positioning the product refers to the process by which the firm decides how it should best depict the product in the market / market segment vis-à-vis competition and hopefully in the mind of the customer (O'Shaugnessy, 1995).

Positioning factors

In the targeted drug delivery systems business, and according to the contacts made with some of the large pharmaceutical companies targeted; the most important factors are the **Product Quality and safety** as well the **Innovation** that such technology, introduces to the final product - the medicine (to see the templates used to interview several companies to know more about the positioning factors, please consult Appendix 18).

In the health business, especially when it comes to products or services that may directly affect the peoples' lives, the most important and decisive factors are the **quality** and **performance**, with the price occupying a less important position.

When it comes to drugs changes, and taking into account the inherently high investment cost and also according to the interviews it becomes obvious, that **innovation**, and **improvements introduced on the final product** (output), must be raised to their maximum, in order to make the business a good investment bet. These two factors are not optional factors, but required ones for the companys' success in the market.

Also classified as very important, is the possibility of use the same drug delivery system to different API's (**versatility**). The potential clients look for this factor, as a very important competitive advantage for the company.

In a second plan, appears the **organization's image** in the market as well as the **image of** its **research and development staff**, since these are key actors in the process of collaborative research carried out for each drug reformulation. The organization's image and reputation refers to credibility.

Then, with less weight than the above factors, is the price of the technology, which in this case, will be the licensing price (see also section 9.2 – "Pricing").

Despite the costs involved in this operation being much lower than in the case of betting on a completely new drug, this must be always evaluated at this level.

In the same level of price, appears the **environmental issue** that seems not to be already a decisive factor, comparatively with the others.

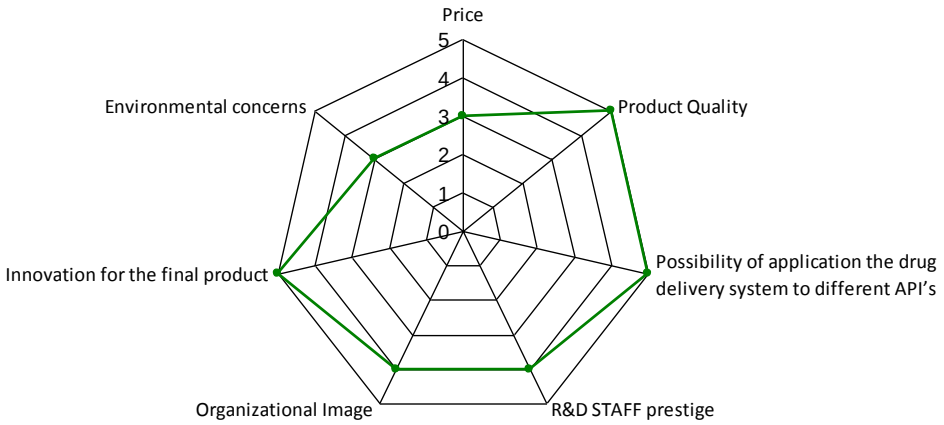


Figure 0.7 - Positioning factors classified by the clients (large pharmaceutical companies)

Competitors' positioning

LIFE DELIVERY has two main competitors in the E.U. market, **Eurand** and **Novosom AG**. This statement is based on the power of these two competitors and because they have solutions to fit the therapeutic areas targeted above.

Eurand is a speciality pharmaceutical company that develops, manufactures and commercializes enhanced pharmaceutical and biopharmaceutical products using their proprietary drug formulation technologies. One of Eurand's drug delivery technologies is directed to cardiovascular, sleep aid, gastroenterology, nutrition, pain and respiratory therapeutic areas that intends to be incorporated in products in order to create new formulations with proven patient benefits. Eurand has a broad and validated portfolio of drug formulation technologies, including platforms focused on bioavailability enhancement of poorly soluble drugs, custom release profiles, and taste-masking/orally disintegrating tablet (ODT) formulations. Within its portfolio of

drug delivery products, the product that competes, more directly, with DELIVES is Diffucaps Technology - ideal for drugs exhibiting poor solubility.

Eurand business strategy is focused on the co-development of partnered products and the out-licensing of Eurand's products worldwide, and they already established partnerships and collaborations with pharmaceutical companies such as Novartis, Bayer, Roche, among others (Eurand, 2010).

Through official documents of the company, and also according with the opinion of their partners / clientsn it is clear that the bet of this company, in order to position their drug delivery products, is made using the **innovation** introduced on the final and **improved quality** characteristics.

However, Eurand product portfolio is focused primarily on the therapeutic category of gastrointestinal disorders (GI) and cystic fibrosis (therapeutic areas that are not included in LIFE DELIVERY first target market).

Novosom AG, recently (July 27th, 2010) sold its SMARTICLES® technology (drug delivery) to Marina Biotech, Inc.

Marina Biotech is a biotechnology company focused on the development and commercialization of therapeutic products based on RNA interference (RNAi). Marina Biotech is building multiple cutting-edge drug discovery and development platforms based on the premise that no single RNAi technology or delivery approach can be broadly applied to the treatment of all human diseases.

Since the acquisition of this drug delivery is very recent, Marina Biotech has not yet made an effective entry to the market with SMARTICLES. However, two of their six collaborations have been disclosed (with AstraZeneca and Pfizer), and three effective license agreements with Hoffmann-La Roche Ltd, Novartis Institutes for BioMedical Research, Inc and ViThera Laboratories, LLC, in order to, respectively, develop and market, their RNAi based technologies.

Due to the recent enter in the drug delivery market; this company doesn't have for now a defined image to their collaborators. However, and according to the available public information about this company and according to the testimony of one of his partner / client (Appendix 1), the main positioning factors of this company are the innovation of the final product and the quality of the drug delivery system. However, the image that clients have relatively to factors such as

Organizational image, R&D staff prestige, or drug delivery solutions that serves to different applications are lower comparatively to Eurand.

The positioning of these two competitors is shown in Figure 8.8.

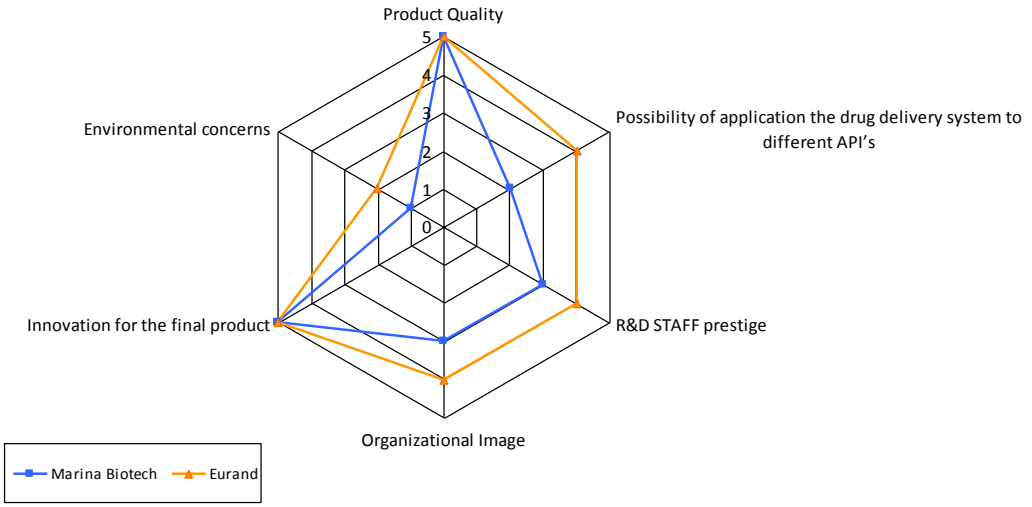


Figure 0.8 - Positioning factors of Main competitors

Note: since the product sales are in the form of licensing agreements and the details of this deal are not public, it was not possible to determine the placement criteria for the price.

LIFE DELIVERY positioning

Taking into account the relevance of each positioning factor and the competitor's positioning, as well as, the company features, LIFE DELIVERY should be perceived by customers as an **innovative biotechnology company with unique and high quality products.**

Since the **product quality** is one required factor, the company must first of all, guarantee the perception of higher **innovation** introduced to the final product.

Second, is very important to build an **organizational image** of trust, credibility and professionalism, transmit one image associated to a quality scientific staff and management board.

Finally, the **price** is the less important positioning factor that must be considered and transmitted to create the clients perception. This assumption is also reinforced by the licenses specificity profile and process, explained in detail at section 9.2.

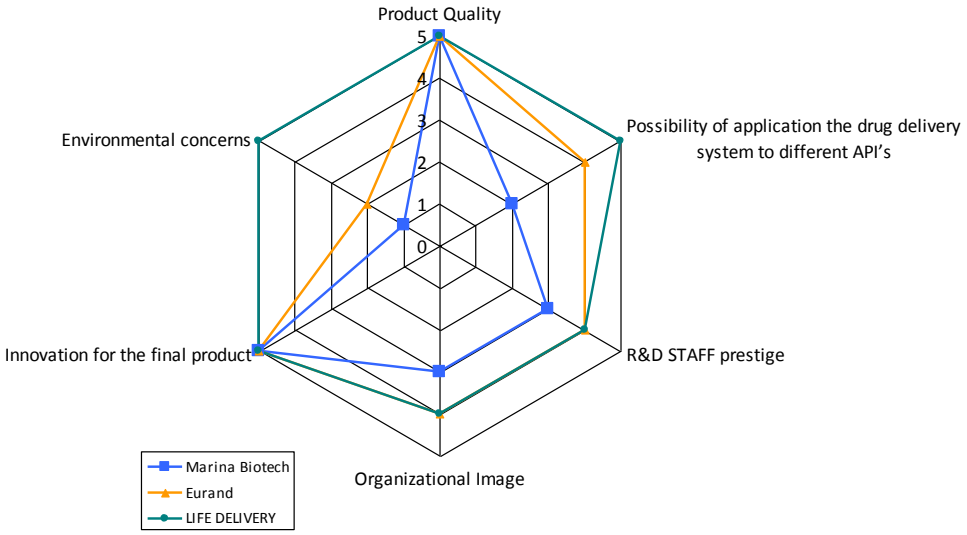


Figure 0.9 - Comparison of LIFE DELIVERY's positioning factors and their competitors

9 *Marketing Mix*

Marketing mix usually refers to the determination of four important characteristic of the business - Product, Price, Distribution and Marketing Communications. For commercialization of DELIVES, and according to the business model, that only covers one first collaborative research and a final license, the distribution was not covered in this specific marketing plan, since DELIVES is not a final product.

9.1 Product

Quality

DELIVES fits the change in adopted Pharmaceutical and Biopharmaceutical industry business models, creating a target drug delivery system appropriate for each kind of need and therapeutic area.

In order to attend the final customers aspirations, the R&D partnership between LIFE DELIVERY and their client, pretends to achieve an easy-to-use with favourable side effects drug.

DELIVES is made using one very popular vehicle material (gelatine), and all the materials used are already approved by regulatory entities in other products for medical use. These facts give a quality stamp to DELIVES.

Features and benefits

DELIVES is made using a new biomaterial (Ion Jelly) that allows the administration and the target of medicines. Gelatine - one of the main components of this new biomaterial - is already widely used and approved as component of medicines. The other main component – the ionic liquid – will stabilise the API, allowing its transport through the body. Finally, the surface modifications will direct the medicine to the specific target in the body.

Customers buy a product not only for the features - specific attributes that contribute to functionality - but also for the benefits - the need-satisfaction outcomes they want or expect.

The **core benefits** are the reduced development time reflected in a quick market entry and the lower risk compared to other available strategies. However the main benefits of this product relatively to competitor products is the large possibility of applications that this product allows (versatility), being possible to reformulate different company's drugs, through the accomplishment of only one partnership with LIFE DELIVERY. Otherwise this product is the only one in the market that addresses the environmental concerns that are increasing inside the pharmaceutical and biotechnology industry.

Brand

Company brand

The name LIFE DELIVERY transmits the essential message to reach a company in the healthcare industry and could be recognized and associated to the concept of drug delivery systems (association of company's image with the product).

Product brand

To build research, development, marketing and sales partnerships in order to fit DELIVES with clients product specifications or put the product into the market, it's essential to build a recognized and trusted R&D image related to the scientific staff and organizational image. Therefore, it is important that LIFE DELIVERY will be created as a *Universidade Nova de Lisboa* spin-off. This choice will enhance the credibility and trust of a new company and a new product, like these.

9.2 Pricing

As already mentioned, LIFE DELIVERY will be the owner, or in a first stage the licensee of "Ion Jelly" technology, that servers different applications. Currently, there is a research ongoing, in order to develop one of these possible applications. For now it is not possible to determine if the results of these new developments will have enough matter to be subject of a new patent application.

When the intellectual property is the central asset, a company can profitably exploit these rights in several ways (Megantz, 2002), presented below and ordered by degree of risk and potential of reward.

- Selling the intellectual property rights to a third party;
- Forming a strategic alliance;
- Licensing;
- Establishing a joint venture;
- Buying an existing company with the required assets;
- Initiating a new venture to develop, manufacture, and sell products.

Attending to the characteristics of DELIVES and the market in which operates, the best option to commercialization through licensing the technology, making the Industrial Property the central asset of this company. In the case of there is not sufficient material to submit a new patent to DELIVES, LIFE DELIVERY will license exclusively, the patent of Ion Jelly for application to drug delivery systems. In the case of a new patent submission, LIFE DELIVERY will license directly the patent that refers to the product DELIVES and not the base technology.

This strategy follows the trend of the healthcare companies, both large and small, where the patents are the most important intellectual property for creating competitive advantages, and even the perception of these companies about the most significant goals associated with licensing intellectual property into their organizations are compensating for lack of research and development and options for future development (Parr, 2006). Using this strategy much of the risk is transferred to the licensee, who is responsible for developing, manufacturing and marketing the licensed products (Megantz R., 2002).

Before the license agreement, it will precede a collaborative research agreement supported by the client in order to fit the product – DELIVES, to the specifications of the client medicines pipeline.

There are many considerations and options that should me made in the process of drawing and defining the strategy and process of licensing. First of all, it is very useful, valuate the technology. Beyond reasons such as mergers & acquisitions or strategic planning, this valuation is also important to define the strategy of licensing and to define the parameters of license negotiations.

After that, it is important to define some licensee variables, such as the **Scope of Exclusivity** (exclusivity versus non-exclusivity), **Duration of the Protection**, value of **Licensee Fee**, the rate of **Royalties**[29] and the **Monitoring of License Agreement.**

Technology Valuation

The valuation of DELIVES technology should be made to different field of therapeutic applications and using the **Relief from Royalty Valuation Method**. To implement this method, there are eight important inputs to be determined (the first five are related to all sorts of technologies, while the last three are required additional factors used to value cases of early-stage technologies):

_ *Remaining life of the patent protection* – This variable will change depending on the date of licensee agreement.

_ *Forecast revenues* – This variable will be estimate according to the Licensee's specific product and respective market.

_ *Royalty Rate* – It is estimated as the rate at which the owner would have had to pay to license the patent rights had it not owned them (Parr, 2006). In this case, the royalty is not available because the patent has not been licensed yet. As a result a proxy royalty rate must be developed. A proxy is often obtained from market data reporting the royalty rate at which similar patent rights have been licensed between independent third parties or using the Profit split rule of Thumbs or Profit Differential Calculation (Parr, 2006).

The highest rates of royalties are associated with pharmaceuticals, due to the high profit margins that many medical therapies can command and vary between 2 to 10%.

_ *Tax Rate* – This input converts the royalty savings into an after tax cash flow, which is converted into a patent value (Parr, 2006).

_ *Discount Rate* – represent the risk associated with obtaining the forecasted income.

The Discount Rate referred before, should impact more that the general business risk and must also reflect the time and money and time spent on development efforts, represented as

[29] Royalty definition is a fee paid for use of Licensed IP, usually a specified sum or percentage for each licensed unit sold. Some approaches used to determine (or aid to determining) royalties are discounted cash flows analysis, regular and established royaty, return on investment analysis and twenty-five percent of profits. The royalty rate is a percentage that is multiplied by a royalty base (the unit sales of wich a percentage of royalty is applied) to determine a royalty, or some other (e.g, fixed) rate (Megantz, R., 2002).

development costs and revenue timing respectively. This rate should finally account the non-acceptance of the technology by the market.

_ *Development costs* – Until this moment the research project was funded with 175 thousand euros in order to develop a first drug delivery system till 2013. The previsions estimate further additional costs of 225 thousand euros in order to develop different delivery routes and different modifications to target specific "problems".

_ *Revenue timing* – According to the CRO Pedro Vidinha the predicted time to ensure the collaborative research and put the product in the market is three years. This means that during the first three years of ownership cash flows are negative. During this time funds are expended to prove and develop the technology for commercialization.

_ *Development risk* – even if the technology is successfully developed the market may not accept the technology. Once the pharmaceutical product, where this technology will be implemented, is already accepted and successful on the market, this risk represents only the value perceived by the final clients (the patients), related to the quality and safety improvements made on the final product.

When it comes time to consider the price to pay for a license, comparable licenses are important factor to consider. In order to check the DD technology's commercialization deals made during 2009, please consult Appendix 20.

Scope of Exclusivity

In terms of scope of exclusivity, there are two types of licensing strategy, including the exclusive and non-exclusive approach. The exclusive approach over valuates the technology and is extremely important to licensees that could take competitive market advantages from this.

License Fee

The up-front license fee is meant to cover the licensor costs for transferring the patent and technical kow-how to the licensee and will be paid immediately on signing a license agreement. This license fee will be estimated by the costs of the development collaboration made between LIFE DELIEVRY and the Pharmaceutical Company, in order to fit the product to specifications of a specific client product.

Royalties

The other part of revenues obtained from license a technology is obtained in form of running royalties. The royalty arrangement will be based on a percentage of sales.

To define the royalty rates of DELIVES to a specific therapeutic area, the following impacting factors should be addressed:

- Scope of exclusivity, Comparable License Rates and Duration of protection, already mentioned above.
- Licensee anticipated profits – this could be estimated using the anterior sales of the product that will be enhanced using DELIVES technology.
- Utility over old modes, which means that licensing executives will pay more for significant enhancements over other technologies of minor enhancements.
- Commercial Success – this variable will have greater weight as the number of agreements to license increase.

Attending to all the factors explaining above and according with some technology transfer experts, in this specific case, the better approach to future royalty calculations, will be the Twenty-five percent rule. This rule is by definition an approach used in determining an appropriate royalty rate, by estimating a royalty rate that would be twenty-five percent of the Licensee's profits for the Licensed Product (Megantz R., 2002).

Monitoring of License Agreement

Is very important to not ignore the monitoring of license agreement that should be included in the license agreement, as well the future expenses made with Royalty audits that refer to an analysis of information to determine whether a licensee is performing in accordance with a license agreement.

Conclusion

According to ABG Patents Madrid - a Spanish consulting firm of Intellectual Property - a small company that intends to license a drug delivery (DD) system should apply a strategy comprising finding different licensees willing to develop the DD system for different non-competing products, benefit from the opportunity for several royalty steams licensing the DD system to drug products already on the market to avoid double risk and keep improving IP position.

According to the valuation at a specific moment in time, the terms of the license agreement should include an initial license fee and the payment of royalties based on product sales and a certain minimum commitments by licensee for commercialization expenditures during the first four years of the product launch. The agreement should also include three staged clinical and regulatory progress milestones payments, subject to LIFE DELIVERY's achievement of contractually specified conditions.

"We believe current market environment is favorable for small biotech companies in terms of out-licensing to and partnering with big pharma/biotech companies. This strategy will greatly reduce the risks associated with drug development and help to build shareholder value rapidly."

Grant Zeng, CFA, **Bio-Path Holdings, Inc**[30]

[30] Bio-Path Holdings, Inc**.** is a development stage biotech company. The Company was founded with technology from The University of Texas, MD Anderson Cancer Center dedicated to developing novel cancer drugs under an exclusive license arrangement. Since its inception, the Company has acquired three exclusive licenses from MD Anderson Cancer Center for three lead products and related nucleic acid drug delivery technology, including tumor targeting technology.

9.3 Marketing Communications

In order to better introduce DELIVES in the market, LIFE DELIVERY will adopt an Integrated Market Communications (IMC) approach, designed specifically to attend the characteristics of the product, the market, the target audience and the company communication objectives (Wood, 2008). To further details about marketing communications timeline, please consult the section "10.2 - Minute".

Communication objectives

First of all LIFE DELIVERY intends to create awareness of the product and its capacity to meet the customer's needs. In second place, the company wishes to instigate brand building by enhancing LIFE DELIVERY technologies and use the Ion Jelly brand as a new material with a considerable perceived value to the customers.

Considering the product characteristics and the market where LIFE DELIVERY will operate, is crucial to build an image of credibility.

Following this, the company proposes to achieve the following goals:

. Create DELIVES awareness, which means, sign a collaborative research (with pa preferable option for acquisition through license, at the final of the research) with a pharmaceutical company in the final of the first year;

. Create LIFE DELIVERY awareness, using the image of scientific staff and the Platform Technology;

. Build DELIVES brand, enforcing the factors of quality and safety and using their major benefits and competitive advantages offered to the clients.

. Reach 45% of the initial targeted clients in the first year which means the scheduling of 10 meetings.

Target audience

The target audience will comprise all the targeted companies referred in the conclusion of section 8.2, prioritizing segment of E.U large pharmaceutical companies focused on Cardiovascular and Inflammation therapeutic areas.

Efforts should be focused on the purchasing decision makers, who have the ultimate authority to choose between the different options to deal with a patent expiration, different suppliers and deal with the formalities of the trade.

IMC Tools:

LIFE DELIVERY will invest greatly in **Advertising** and **Personal selling** (two of the five major IMC tools). In a later stage, the company, will use **Direct marketing** tools, as well as **internet communications** and **public relations** in order to create a greater proximity with licensee's and potential clients.

- **Advertising** (see also Appendix 21)

Used in the first stage of product life cycle, in order to inform, the advertising tool will address the specific communication goals of creating product and company awareness. The advertising it will be made in the following media:

→ *European Journal of Pharmaceutical Sciences* - is the official journal of the European Federation for Pharmaceutical Sciences (EUFEPS). The journal publishes research reports, review articles and scientific commentaries on all aspects of the pharmaceutical sciences with strong emphasis on originality and scientific quality. The Editors welcome articles in this multidisciplinary field, ranging from drug discovery, over drug delivery to drug development.

The European Journal of Pharmaceutical Sciences is a free channel to publicity the product and a relevant one, according to their impact factor of 2.608[31].

[31] The impact factor is a measure of the frequency with which the average article in a journal has been cited in a particular year or period. It is one of the evaluation tools provided by Thomson Reuters *Journal Citation Reports*® (*JCR*®).

The annual *Journal Citation Reports* impact factor is a ratio between citations and recent citable items published: a journal's impact factor is calculated by dividing the number of current year citations to the source items published in that journal during the previous two years ([online] Thomson Reuters).

Beyond this, the importance of this journal is related to the impact of scientist in the build of thrust and promotion of license agreements with pharmaceutical companies. According to a study made by National Institutes of Health (NIH) Office of Technology Transfer (OTT) that analyse the origins of 281 licence agreements completed by NIH between 2001 and 2004, where the results shows that inventor contact constituted approximately 38 per cent of the leads, followed by marketing (technology transfer employees efforts and the OTT website) 34 per cent and public information 28 per cent. When analysing licensing leads that were acquired because of access to public information, it was found that "inventor publications (58 per cent) was the most important factor that led to license inquiries" and also that the role of the inventor is more effective to larger business because of their greater ability to deploy more resources to technology scouting and therefore may rely more on other sources of information such as publications, inventor presentations and personal contact between scientists and inventors (Ramakrishnan, V., 2005).

In this specific case, the strategy is the publication of a paper in this journal.

→ *Drug Delivery Technology* - is a print and digital publication exclusively committed to advancing the applied science, technology, and related business practices of pharmaceutical and biological drug development, including for example Drug delivery technologies, Business development, Life-cycle management, Pipeline/portfolio management. This publication provides pharmaceutical professionals with practical solutions to the unique issues, opportunities, and challenges in this ever-evolving industry. This website has 10,998 monthly visits from 110 countries including US, Europe, United Kingdom, Canada, India, Japan, China, Israel, Indonesia, Australia, South Korea, and Singapore ([online] Drug Delivery Tech).

The last data of 2009, indicate that 61.4% of the subscribers are Pharmaceutical / Biotechnology / Drug Delivery Companies and their job function are predominantly Pharmaceutical R&D - Drug Delivery Scientists - Pre-formulation, Formulation Development, Stability Testing (43.4%) and Business Development - Licensing, Technology Assessment, Product Life-cycle Management (16.2%).

The advertisement on this channel it will be made by the News Letter - Drug Delivery Weekly, reaching 12,000 subscribers with the banner surrounded by the latest news of business deals, alliances, and technology breakthroughs.
Beyond the recognized reputation of this channel by pharmaceutical industry, this advertisement option carries another free added value services.

Doing this advertise, LIFE DELIVERY will earn:

- **FREE Technology Showcase:** All advertisers earn a free 1/4 page, 4-color Technology Showcase (120-word write-up & photo) in the same or subsequent issue(s).
- **FREE Electronic Edition:** Advertisements & Technology Showcases appear for FREE in the electronic edition with links to your website.
- **FREE Company Profile:** All full-page advertisers in the Annual Resource Directory and Company Profile issue in November receive a FREE – 1-Page, 4-color Company Profile.
- **FREE Listings in Annual Resource Directory:** Listings in the Annual Resource Directory are free and available to all companies providing technologies, products, and services for: Drug Delivery, Specialty Pharma, Contract Services, Manufacturing and Laboratory Equipment.

→ *European Pharmaceutical Review magazine* - Covering new technologies and developments within the pharmaceutical industry, European Pharmaceutical Review is the leading bi-monthly publication and essential reading for anyone involved in the pharmaceutical business.

Typical readers of the magazine include Managing Directors, Procurement Directors, Heads of R&D, Senior Scientists, Laboratory Managers, Process Engineers, Chief Engineers, Production Directors, Plant Managers, Product Managers, Quality Assurance Managers and Quality Control Managers.

According to ABC (an independent audit watchdog service for printed publications www.abc.org.uk), the European Pharmaceutical Review magazine has a geographical breakdown that impacts mostly on United Kingdom (25%), Germany (12%), France (9%) and Italy (8%). The Job function breakdown indicates that 24% of readers are related with Production / Manufacturing, 21% are CEO /Management Directors and 20% to R&D /Product Development.

The importance of this communication channel is the distribution of this magazine per 11,494 senior managers and key decision-makers in the pharmaceutical, life sciences and drug discovery industries predominantly across Europe. The strategy designed is to make an Online & digital advertising that will target 8,800 dedicated readers through email newsletter bi-weekly and the magazine offer the possibility to target a specific segment of their subscriber list.

Due to the widespread utilization of this Magazine's website by the pharmaceutical decision makers and other players in this area (such as potential partners), in this case the advertising

strategy it will be based on a website banner advertising during three months (in different periods of one month each).

→ Finally, being a member of Europabio[32] (the European Association for Bioindustries) and GIRP[33].

- **Personal selling**

In a second stage of the product life cycle and in order to efectivate the proximity between the company and potential clients, LIFE DELIVERY will use the personal selling tool. Each therapeutic area of interest to license DELIVES, has limited potential customers and this fact enables the direct contact of companies by a sales representative. This customized tool and the sales reps are essential to explain the product features and benefits, recommend solutions, answer questions, but also to receive feedback of selected audience allowing to understanding the customer's needs and build a trust and strengthening relationship.

The process to be adopted will focus on scheduling meetings with the potential clients to present the technology and give some examples of improvements made in other already tested medicines. The conduction of approach to potential interested in licensing will be made using an information package (consult Appendix 23).

The activities of promotion and technological marketing need to be appropriately accomplished by legal issues, in order to secure the safety publicized and exchange of information. Thereby, was prepared a Non disclosure agreement (NDA) template, aimed to regulate the exchange of information (see Appendix 24).

[32] EuropaBio is the European Association for Bioindustries and was created in 1996 to provide a voice for the biotech industry at the EU level. EuropaBio's mission is to promote an innovative and dynamic biotechnology-based industry in Europe.

[33] **GIRP** is the umbrella organisation of pharmaceutical full-line wholesalers in Europe. It represents the national associations of over 600 pharmaceutical full-line wholesalers serving 31 European countries, including major pan - European pharmaceutical full-line wholesaling companies. Trough their network of operational facilities they distribute over 100 billion euros worth of medicines every year. In the performance of their public service role they absolutely guarantee the highest levels of quality, integrity and excellence. **GIRP** members are the trusted supply chain partners of manufacturers, pharmacists, healthcare professionals and above all patients for medicines safety.

- **Direct Marketing**

In a maturity stage it will be important to use the tool of Direct marketing, in order to strengthen the relationship with licensees and potential licensees and remind them the latest discoveries, products or product enhancements derived from the technology platform (Ion Jelly). This communications will be made using direct mail to the customers and potential customers database builded by the company.

- **Internet Communications**

The corporate website will reinforce the credibility of the company, creating a section in which each partner access the last information and results about the development research made on the first part of license agreement. This tool will give useful clients feedback in order to target their specific needs and share value informations about the market and final consumer's needs.

- **Public Relations**

In order to publicize the product and company inside the circuit of customers, it is important to make public relations in some important events and conferences. To consult the list of conferences and events, see Appendix 24. The presence in the conferences it will be made using a stand to publicize the company and the main products developed.

From the conferences list presented in Appendix 24 will be chosen three of four per year, based on the presence of potential customers and / or partners.

10 *Implementation and Control Plan*

10.1 Man

Nowadays, and as referred above, during the period that preceedes LIFE DELIVERY creation, the first commercialization efforts will be managed by the Technology Transfer office of FCT/UNL, with the intervention of Pedro Vidinha, the principal investigator and future Chief Research and Strategy Officer (CRO) of LIFE DELIVERY.

After the conclusion of the first part of DELIVES research, LIFE DELIVERY´s implementation and control will be managed by LIFE DELIVERY´s leader (Pedro Vidinha) and the commercial director (that will be hired). To further details about research activities and company implementation timeline, please consult the section “10.2 - Minute”.

A report will be held every four months (in a startup it is necessary to frequently updating, reporting more regularly, and this time could be expanded as the business grows to consider the most important achievements, as well as, the failures (Kawasaky, G.; 2004). This analysis will keep up-to-date information on new needs and, therefore, new actions to take further.

This part of the implementation plan is divided in Organization and Talent & Staff Required.

Organization

Preceding the launch of DELIVES, LIFE DELIVERY needs to **build a** certain amount of **legitimacy** to secure the necessary resources. This is based on **legal** terms, **localization** and **industry interaction** (Dorf, 2008).

First, LIFE DELIVERY must start by its **incorporation and legalization** as *Universidade Nova de Lisboa* spin-off, and the assurance of its patents, signing with *UNL* and *Instituto Superior Técnico (IST)* – the patent owners; an exclusive License agreement to the Ion Jelly Patent (see Appendix 19). In the License Agreement the Licensors give rights to the use and exploitation of Ion Jelly technology, in return of the Industrial Property costs supported by the two owner institutions till the moment of the agreement and also an accorded percentage of royalties. The payments will only be made when LIFE DELIVERY starts the effective commercialization.

Regarding to **location,** should be taking into account three major factors: customers and employees' location, advantages of being located in a cluster (knowledge-based business) and its costs (Dorf, 2008).

The core company's work lies on the development and optimization of the Drug delivery in accordance with the instructions and customer needs and product. Thus, the location of Researchers and technical staff in the different areas involved in the development of DELIVES (that are located at Portugal) are a key point to make this decision. Furthermore it is also important to have mobility of sales people across the EU Countries (mainly from countries where the largest number of potential customers is, such as: United Kingdom, Switzerland, Germany, Italy and France; and finally the establishment of a close relationship with European Medicines Agency (EMEA), located at United Kingdom (see also Appendix 25).

Following this, LIFE DELIVERY will be located at "*Parque Científico de Madrid (PCM)"* – the Science Park of Madrid, a Spanish incubator. This choice is based on the prestige of the incubator, its proximity and established contacts with LIFE DELIVERY's potential clients and also with the proximity origin of LIFE DELIVERY research team.

This location offers to the company great advantages like the credibility of the incubator name, relative low prices, legal and technology transfer advice and financial services (consult a list of all advantages in Appendix 26).

Finally, the industry interaction is based on **partnerships and memberships** with **associations** and **foundations** like Europabio.

Talent and Staff required

For the first three years of implementation, LIFE DELIVERY will have **three technical people** (divided by three expertise fields - biocompatible ionic liquids and encapsulation of API´s, Surface modifications to target the drug delivery and cellular release and interactions) in Spain, one Chief Research and Strategy Officer (CRO), one commercial director, one salespeople and one administrative assistant. This team will be managed by a LIFE DELIVERY leader based in Madrid, that will be the CRO that initially also accumulate the function of company CEO.

The **CRO** will be based in Madrid and will be the LIFE DELIVERY leader in Spain it will be one of the technology inventors with expertise in biocompatible ionic liquids and the encapsulation of API's.

The **Commercial director** will be based in Madrid and will be LIFE DELIVERY's leader in Spain and attending to the profile of one initial company, will also accumulate the role of LIFE DELIVERY's **CEO**.

There will be **1 salespeople** based in Germany. The number of salespeople is defined through objective-task approach, that is, number and geographic concentration of potential clients, and number of potential meetings by week (Assael, 1990). Both will report directly to the commercial director. The **administrative assistant** will also be based in Madrid and she / he will report directly to the commercial director too.

The technical staff will be selected and managed by the CRO, being mandatory to fulfill specific requisites such as scientific background in the relevant areas mentioned above.

Attending to the already established contacts and experience with the industry and also according with the inventor status of Pedro Vidinha the commercial director recruitment and selection will be led by the CRO.

The sales people **recruitment and selection** will be led by "*EUPI Consultores*"; a Human Resources company specialized in commercial departments. For the selected candidates it is mandatory to have experience on similar functions in the Pharmaceutical Industry and have good knowledge of English. Moreover, a pharmaceutical / biotechnology / chemistry background is also mandatory to salespeople (Lidstone and MacLennan, 1999).

The administrative assistant recruitment and selection will be made directly by the commercial director.

In the near future, the company will need to outsource the services of an Intellectual Property strategist.

It is extremely important not to forget the Advisory Board constitution, which should focus on three main areas: contract management, patents and research, and should be constituted by an international profile, with pharmaceutical industry connections. Among other contributions, this advisory board will be essential in order to anticipate trends.

10.2 Minute

As was referred before, this marketing plan refers to an early-stage under-development technology and the expected time to the conclusion of the research is two years (final of 2012). Therefore, we presented here, the activities timeline before and after LIFE DELIVERY formation. The forecasted time duration of each activity was discussed with the principal investigator and future CRO (Pedro Vidinha) and with the Technology Transfer Advisor of *Universidade Nova de Lisboa* (Dina Chaves).

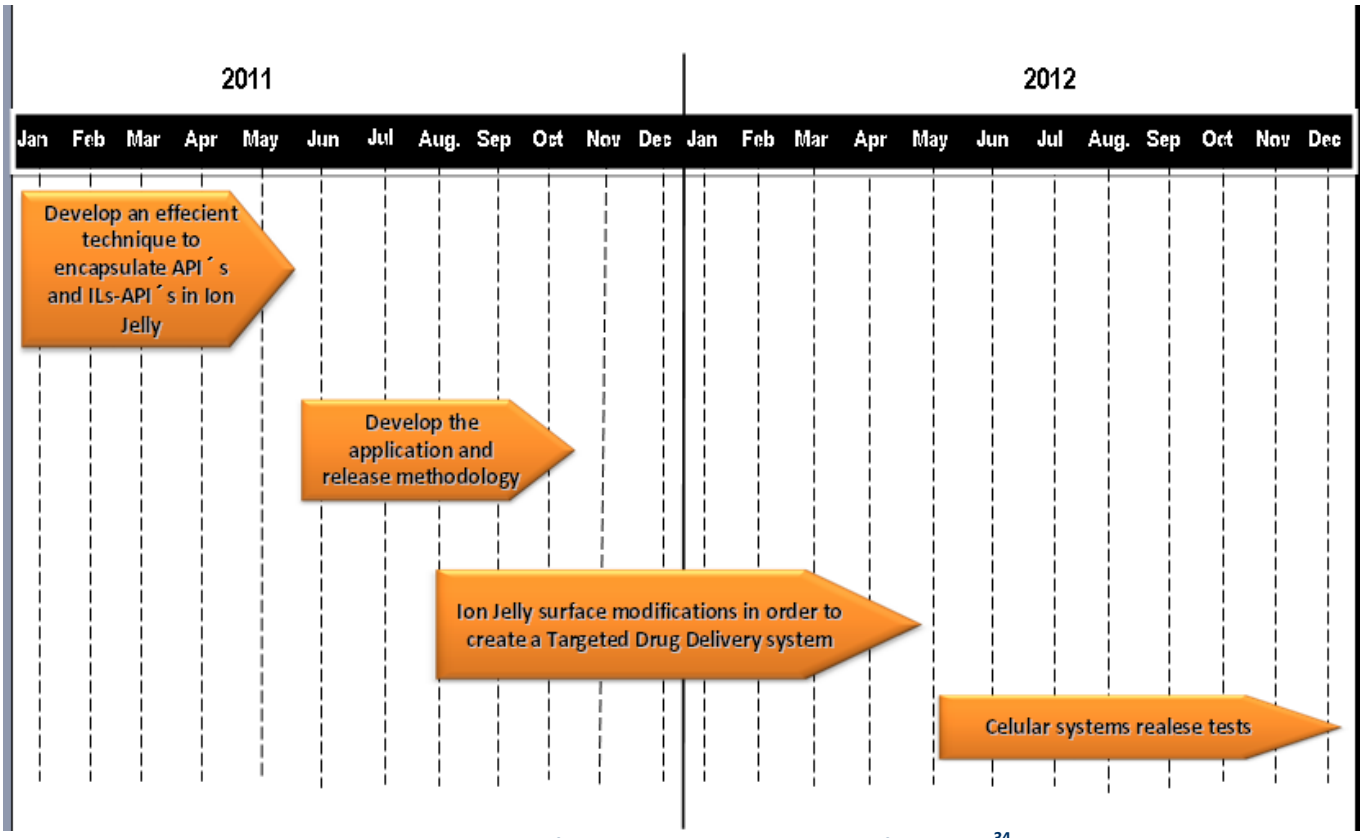


Figure 10.1 - Schedule of activities previous company formation[34]

Note: During these two years TTO will also promote efforts in order to contact the industry.

[34] To the date, the research team, designed biocompatible ionic liquids and Ionic Liquids-API (that are at this moment, generating one provisional patent application).

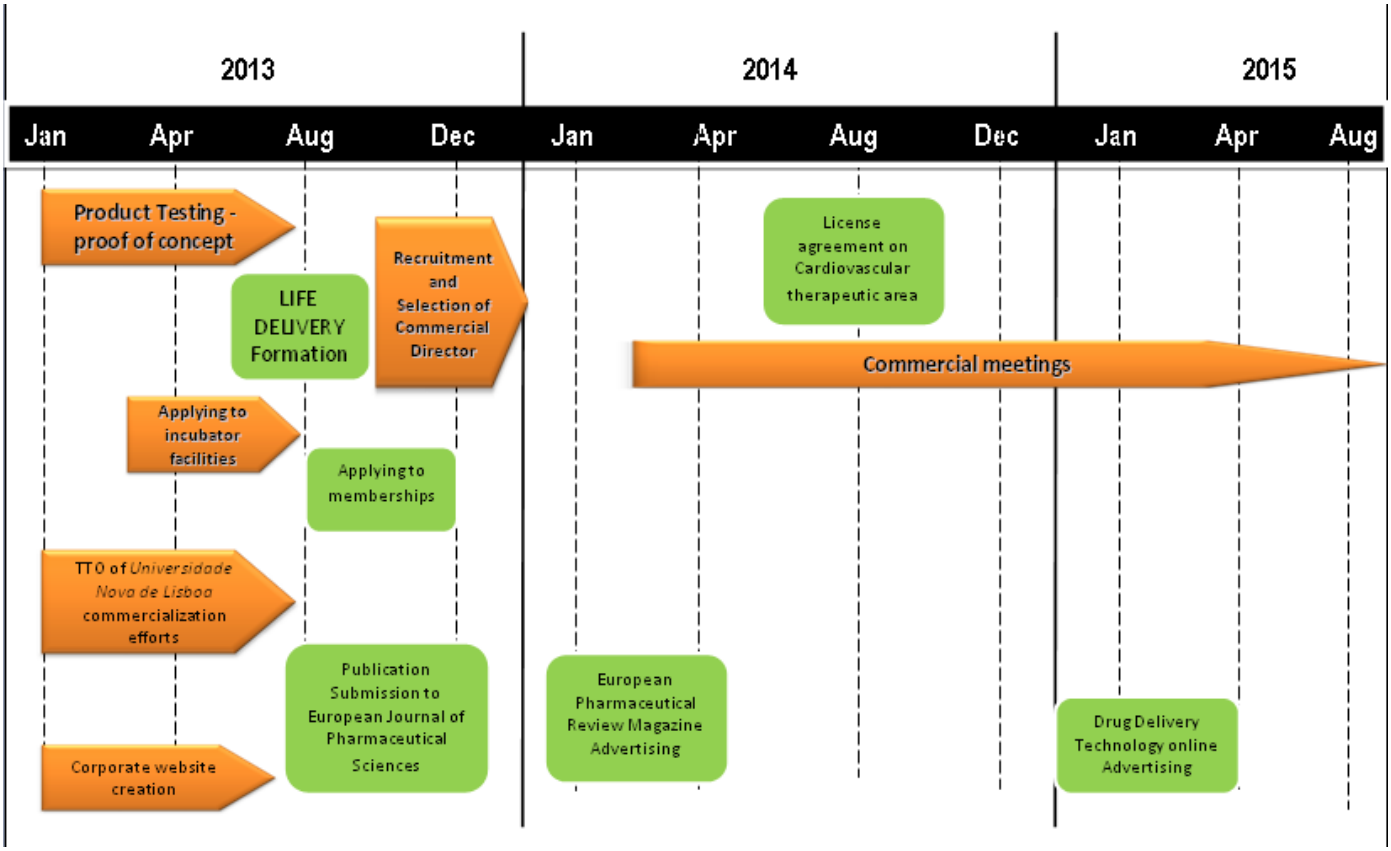


Figure 10.2 - Schedule of activities during and after company formation

10.3 Money

The presented marketing plan was made to five years. However, it is important to notice that the constitution of the company is planned to be made only in 2013, i.e. in the beginning of the third year. Until this moment, the research will continue to take place in the University, and funded by the Portuguese Science and Technology Foundation (fund already assigned). This means that the majority of the marketing actions planed in this document and the company costs are forecasting for three years, starting from 2013.

This kind of financial projections are only projections and shouldn't be assumed as "universal truths" / facts, during the implementation of this plan. Mainly the sales but even the costs could not be, at this moment, precisely estimated. This section of the marketing plan should be flexible and revised semi-annually.

In order to implement and control the marketing plan, LIFE DELIVERY will use an **objective and task budgeting method**, a floor-up option (budgets originate in the marketing department and move upward for review), that allocates marketing funding according to the cost of the tasks to be accomplished in achieving marketing plan objectives (Wood, 2008).

Regarding this, several costs were taken into account, such as: promotional costs (advertising, conferences and events travels and promotional material, associations' membership fees, corporate website construction and management); the facilities costs, human resources cost, commercial costs (business travels, communications, among others) as well as raw materials and technical equipment and analysis costs.

Promotional costs

- Advertising

Table 10.1 - Advertising estimated costs. Cost sources: [online] Drug delivery tech and [online] Pharmaceutical Business Review

Advertising channel	*Type of advertise*	*Price (month) (€)*	*Time (months)*	*Total cost(€)*
European Pharmaceutical Review magazine	Button 120x120 pixels 15 KB Flash SWF	*235,85*	*3*	*707,55*
Drug Delivery Technology	Website banner advertising (home page banner in the center with 100 x 300 pixels)	*751,17*	*1*	*751,17*

Note: 1€ = 0,848 £ and 1€ = 1,3246 $ exchange rates of 3 December of 2010. Source: [online] Banco de Portugal.

- Website creation and management

The company´s website it will be an important tool, once it will serve as connection and monitoring platform during the collaborative research agreement. In order to have a proposal for the website creation and management was contacted an Information Technology *UNL* spin-off (Javali), that presented the tender attached in Appendix 27 with a cost of 3.400,00 €.

- Travels

The importance of the travels are related with the conferences presence and meeting with the potential clients. These costs forecast were made based on the medium prices of flight travels to the main localizations of potential clients and also the conferences location.

The main locations to the travels are Paris, Berlin and London and the average travel costs are presented in the table bellow.

Table 10.2 - Annual travels estimated costs. Average prices source: [online] Momondo

Departure	*Destination*	*Average price (€)*	*Annual Estimated frequency*	*Total cost (€)*
Madrid	Paris	97	2	194
Madrid	Berlin	134	2	268
Madrid	London	100	2	200
Annual estimated total cost				662

According to the expected commercialization of the technology at the end of the first year of company life (2013), the travels costs during the second and third year it will be lower than those described above.

- Communications

In order to estimate the communications costs was made a research of Spanish teclecomunications companys and their services and respective tariffs.

The better option found was form Vodafone España and their companys plan with a monthly fee of 39,90 €, that includes daytime nacional calls and with international calls costs of 0,49 € (connection stablishment) + 0,45 € /min.

Table 10.3 - Monthly estimated communications costs

Monthly fee (€)	Monthly International calls	Average minutes per call	Total cost / month (€)
39,90	6	5	56,34

According to the expected commercialization of the technology at the end of the first year of company life (2013), the communication costs during the second and third year it will be lower than those described above.

Facilities costs

Laboratory and office rent at *Parque Científico de Madrid* (Bioincubator I)

Table 10.4 - Facilities costs

Price (€ / m^2 / month)	*Area*[35]	*Tax*	**Rent / month (€)**
36 without tax	40 m^2	18%	1.699,20

Source: Cátia Rabaça (PCM Business Development Unit)

This rent price, include:

- Electricity - 8 A;
- Water - 1 m^3 / month;
- Distilled water – 20 L /day
- Special gases:
  - N2 (99%) – 9,41 m^3/ month
  - CO2 (99,98%) – 5 m^3/ month
  - He (99,99%) – 9,10 m^3/ month
- Waste management – 428,57 Kg / month
- In addition to general services mentioned in appendix 23, the rent of bioincubator I, also includes:
  - Free access to electronic scientific magazines and specialized press
  - Access to shared infrastructures and equipment
  - Cleaning and sterilization of glass material
  - Maintenance of the Culture room
  - Share use of glass material
  - Cryoprotection sample service
  - Supply and delivery of carbonic snow

[35] This area was estimated based on the actual area of the research laboratory and respective offices.

Human Resources costs

Table 10.5 - Estimated human resources costs. These data were based on Michael Page Helthcare salary studies (Michael Page Healthcare, 2010).

Job	*Cost (€) / year*	*Number of positions*	*Total (€) / year*
CRO	45.000	1	45.000
Technical staff	20.800	3	62.400
Commercial Director	40.000	1	40.000
Sales Person	35.000	1	35.000
Administrative Assistant	15.600	1	15.600

Materials and Analytic analysis costs

According with Pedro Vidinha and costs of investigation which is ongoing, the next table present the estimated cost to materials and analytic analysis.

Table 10.6 - Estimated Materials and Analytic costs

Analyis /Raw materials	*Cost (€) / year*	*Obs.*
Analytical analysis	1.800	
200L of Ionic liquids	60.000	1L = 300€ (average price)
1 ton of Gelatine	1.000	
Functionalization materials	5.000	

Ion Jelly License costs[36]

These costs will be paid at the beginning of commercialization.

- Ion Jelly patent costs

Description	Legal Office	Value (€)
European Patent request	J. Pereira da Cruz, S.A.	6189,77
National phase of Patent in South Korea	J. Pereira da Cruz, S.A.	3282
National phase of Patent in South Korea	J. Pereira da Cruz, S.A.	3282
National phase of Patent in U.S.A.	J. Pereira da Cruz, S.A.	1500
Related to annual taxes of national , European and national phases of the patents, and preparation of answers to notifications	Garrigues	25.000
TOTAL		39253,77

- A percentage of royalties to be defined should be paid to the patent owners at the time of commercialization.

[36] - This costs were supported by the owners of the patents (UNL and IST), divided in different percentages of 40% for *Instituto Superior Técnico* and 60% for *Universidade Nova de Lisboa*. This division of joint actions and exploration of the patent was made using an agreement between the institutions celebrated at August of 2007.

Summary

Table 10.7 - Total estimated costs

	2013	*2014*	*2015*
Intellectual Property			
Ion Jelly patent costs	-	-	39.253,77[37]
Facilities costs			
Office rent	20.390,40	20.390,40	20.390,40
Office supplies	550,00	550,00	550,00
SUB -TOTAL	20.940,40	20.940,40	20.940,40
Promotion costs			
Advertising	-	707,55	751,17
Website creation	3.400,00	-	-
SUB -TOTAL	3.400,00	707,55	751,17
Commercial costs			
Business travels	662	331	331
Communications	676,08	338,04	338,04
SUB -TOTAL	1.338,08	669,04	669,04
Human resources			
CRO	45.000	45.000	45.000
Commercial Director	40.000	40.000	40.000
Sales Person	35.000	35.000	35.000
Administrative	15.600	15.600	15.600
Technical staff	62.400	62.400	62.400
SUB -TOTAL	198.000,00	198.000,00	198.000,00
Raw Materials and			
Analytic analysis	1.800	1.800	1.800
Ionic liquids + gelatine +	66.000	66.000	66.000
SUB -TOTAL	67.800,00	67.800,00	67.800,00
TOTAL	322.078,48	288.116,99	327.414,38

[37] The Ion Jelly patent costs it will be paid in the final of third year of the company, assuming that the collaborative research with the client it will be finished at this date and the final product(s) will be commercialized by the company at this date.

11 *Conclusions*

As has been discussed several times in the course of this work, the stage of technology development represents an enormous obstacle, to the realization of this marketing plan. However, like other marketing plans which envisaged the launch of technologies in a higher stage of development, this work must be periodically reviewed and updated.

Either way, this work is an important and required tool as first approximation of the technology to the market and one essential procedure of technology transfer process.

The usefulness of the issues raised during the market plan development, are very important not only for the initial work of the TTO, as also to the first steps of the startup (eg in obtaining financing), and even to direct the research activities.

Through the marketing plan presented, is possible to conclude, that this technology, though still being too early stage, responds to a real need and has innovative features that can bring major benefits to competitive markets in which will enter.

According with the competition analysis (wich has no obvious lider) and also with the disruptive and innovative profile of the technology, it is possible to conclude that this specific product has marketlace and this business represents a market opportunity.

The conclusion of market segmentation and targeting, points to Large Pharmaceutical companies with Development, Production and Marketing process, as the initial target market of DELIVES. However, it is important to highlight, that at long-term, and according with the ownership of the technology platform, it will be possible to enter in different markets (such as the biotechnology companies more focused to medicines with large compounds and consequently with higher complexity deliver process).

In order to reach this target market it will be necessary to assume a positioning that differentiate LIFE DELIVERY and DELIVES from de competition, that will be based on the versatility of the product. Nevertheless, in this market field, more than create differentiative meaning to the customers, is mandatory to fulfill required features as the product quality and the benefits to the final customers. So, LIFE DELIVERY must incorporate these mandatory criterias in the positioning values, although it is necessary to trasmite them as obvious to the product life.

If we take a deep look to the landscape of maket where DELIVES will be introduced and also to the future start-up conditionings, it is possible to assume licensing as the best commercialization option (versus patent sell and also own commercialization). The main reasons are the highest size and experience of clients compared wuth LIFE DELIVERY, the inability to produce and market the final product and also the commercial explotation possibility of different applications using the patented technology platform.

As a start-up company, the risk is very high and is a challenge to attract experienced staff and financing to an unknown business with small initial capital. The University support in the previous phase of company creation it will be, with no doubts, very important to the establishment of proximity between LIFE DELIVERY and the industry.

The biggest weakness of this work is connected to the impossibility of defining the expected return for this business. Despite being an important point, the financial provisions of a start-up company, are always plenty of unknowns, both to the company and even to the potential financiers.

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APPENDIXES

13 *Appendixes*

Appendix **1** – List of Contacts

Date	Name	Company	Theme	Type of contact	Obs.
05/02/09	Íris Batalha	MIT PhD student	Drug delivery systems	Conversation	
08/02/2010	Drª Fabiana Simões (Clinical Trial coordinator)	CEDOES – Centro de Densitometria Ossea do Espirito Santo	Clinical Trials	Skype	
19/02/10	Drº Oliveira Costa	_____ (oncology physician)	Oncology drugs and treatments	Conversation	
09/07/2010	Drª Ana Gaspar	PHARMaffais – pharmaceutical consulting	Marketing segmentations and market size	Conversation	
04/04/2005	Drº Francisco Bernardo Noriega	European Patent Attorney – ABG Patents Madrid	Managing Patent License agreements	Conference	
02/04/2009	Drª Cátia Rabaça	Scientific Park of Madrid	Scientific Park of Madrid incubation advantages	Conversation	
09/12/2010	Engª Isaura Monteiro	Portuguese Institute of Industrial Property	Supplementary Protection Certificate (SPC)	Telephone	
08/12/2010	Division of Drug information Food and Drug Administration	Food and Drug Administration	Regulatory affairs	E-mail	
13/12/2010	Thomas Johnson	Delcath Systems, Inc	Positioning factors	E-mail	
09/12/2010	Vedin Monika	Meda AB	Positioning factors	E-mail	
15/06/2010	Curt Stone	Director of Quality of Life Technology Center, Carnegie Mellon University	Targeting criteria weights	Conversation	

Appendix 2 – R&D cost increase for successful NME launch

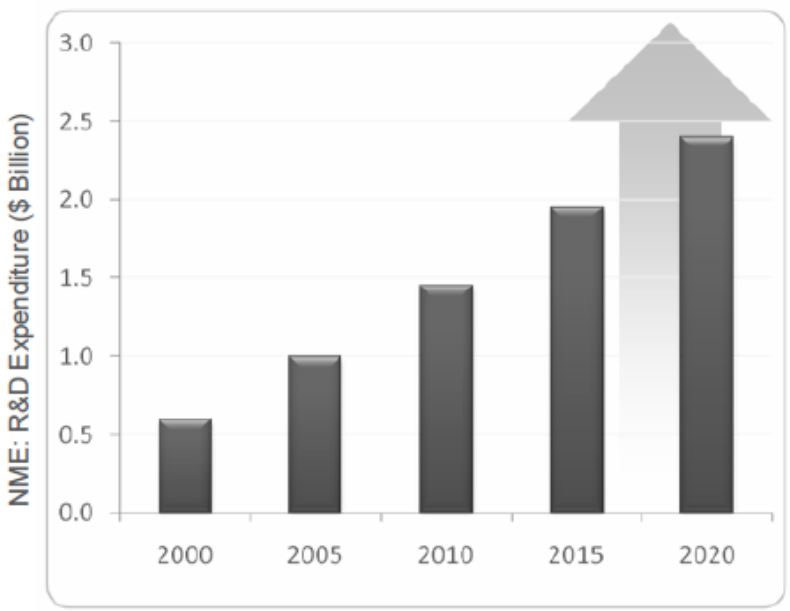

Figure 13.1 – R&D Cost Increse. Source: Frost & Sullivan, 2010

Appendix 3 – The Drug discovery process

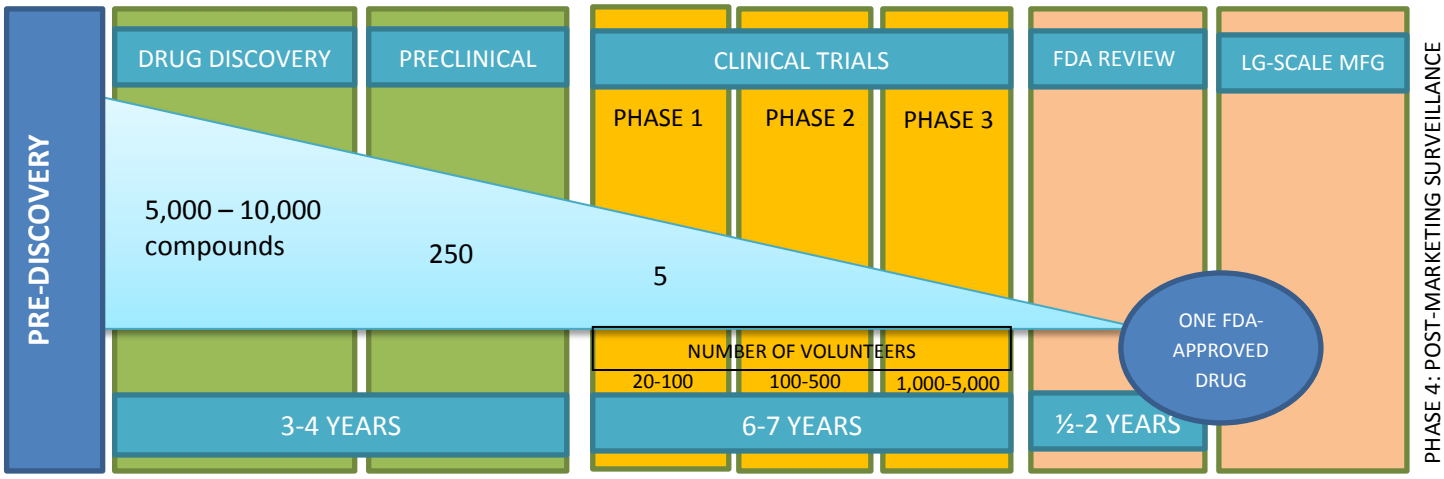

Figure 13.2 – The R&D Process: Long, Complex, and costly. Source: PhRMA, 2009

Appendix 4 – Patent Loss ($ Billion) 2008-2012

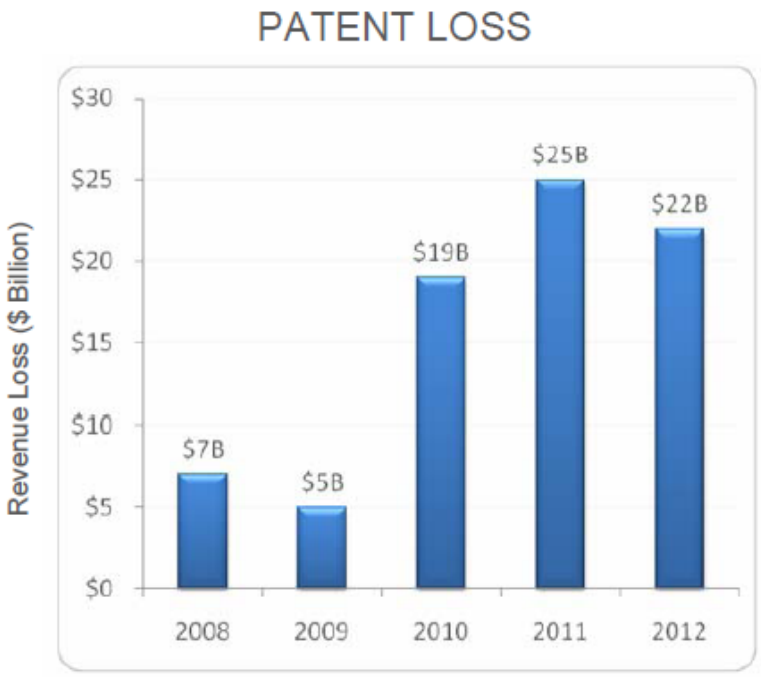

Figure 13.3 – Patent Loss ($ Billion). Source: Frost & Sullivan, 2010.

Appendix 5 – Ion Jelly publications

Papers

- Date: 30/11/2008
  Title: Ion Jelly: a tailor-made conducting material for smart electrochemical devices
  Source: Pub Med. 2008 Nov 30; (44):5842-4.

- Source: *Chem. Commun.*, 2008, Issue 44 5842-5844
  Site: http://www.rsc.org/suppdata/cc/b8/b811647d/b811647d.pdf
  Title: Ion Jelly: a tailor-made conducting material for smart electrochemical device

International

- Date: 18/10/2008
  Source: Thaindian News
  Title: Ion Jelly could be used for making eco-friendly batteries
  Site: http://www.thaindian.com/newsportal/india-news/ion-jelly-could-be-used-for-making-eco-friendly-batteries_100108716.html

- Date:18/10/2008
  Source: Nanotechnology now
  Title: Ion jelly could satisfy appetite for greender batteries
  Site: http://www.nanotech-now.com/news.cgi?story_id=31054

- Date: 17/10/2008
  Source: New scientist
  Title: Ion jelly could satisfy appetite for greender batteries
  Site: http://www.newscientist.com/article/dn14975-ion-jelly-could-satisfy-appetite-for-greener-batteries.html

- Date: 16/07/2009
  Source: printed electronics world
  Title: New Ion jelly material for use in electrolytic devices
  Site:
  http://www.printedelectronicsworld.com/articles/new_ion_jelly_material_for_use_in_electrolytic_devices_00001558.asp?sessionid=1

- Date:17/10/2008
  Source: Cleantech
  Title: 'Ion jelly' for better, cheaper batteries
  Site: http://cleantech.com/news/3724/%E2%80%98ion-jelly%E2%80%99-better-cheaper-batteries

National

- Date: 11/11/2008
  Source: Expresso
  Title: Projecto portugues premiado nos E.U.A.
  Site: http://aeiou.expresso.pt/projecto-portugues-premiado-nos-eua=f450311

- Date : 22/10/2008
  Source: Correio da manhã
  Title: Ciência: Portugueses descobrem novo material condutor Criada a receita da gelatina iónica
  Site: http://www.cmjornal.xl.pt/noticia.aspx?channelid=00000219-0000-0000-0000-000000000219&contentid=10C75722-4B7A-40CA-B61F-9F665B9FD269

Websites, newspapers and blogues

- Date : 21/11/2008
  Site: http://diario.iol.pt/tecnologia/tecnologia-electronica-gelatina/1004508-4069.html
  Title: Portugueses descobrem gelatina que pode revolucionar a electrónica

- Date: 22/11/2008
  Source: http://ciberia.aeiou.pt/?st=10399
  Title: Gelatina iónica: Portugueses descobrem novo material condutor mais barato e ecológico

- Date: 24/10/2008
  Title: Criado o "ION JELLY" receita da gelatina iónica
  Site: http://entranaciencia.blogspot.com/2008/10/criada-receita-da-gelatina-inica.html

- Date: 22/10/2008
  Site: http://cienciahoje.pt/index.php?oid=28168&op=all
  Title: Portugueses patenteiam gelatina iónica

- Date: 22/10/2008
  Title: Gelatina iónica
  Site: http://pplware.sapo.pt/high-tech/gelatina-ionica/

Drug delivery companies profile[38]

[38] All this information was based on the companies' oficial websites, according with the reference.

Access Pharmaceuticals, Inc[39]

About Access Pharmaceuticals, Inc.

Access Pharmaceuticals is an emerging biopharmaceutical company specializing in products for cancer and supportive care. Access currently has one FDA-approved product, two products in Phase II clinical development, and three products in preclinical development.

Several of the company's products are based on Access' proprietary nanopolymer technologies which provide enhanced drug delivery options for both new and approved pharmaceutical active ingredients.

While its primary focus is in oncology, Access' drug delivery technologies also yield candidates that enable and enhance the absorption of drugs by exploiting the body's own vitamin B-12 absorption system.

Mucositis is a frequent side-effect of cancer therapy for which there is no established treatment. MuGard™ is Access' approved proprietary nanopolymer formulation for the management of mucositis. This ready–to–use rinse provides a soothing oral coating. A clinical study has shown that when MuGard is used by patients at the start of cancer therapy, the incidence and severity of mucositis are reduced. MuGard is available in Europe by prescription through Access' marketing partner, SpePharm. Access will be marketing MuGard in the United States in 2010, and marketing partners in Asia are advancing Regulatory approval of MuGard in South Korea and China.

Access is focusing its development effort on three products/technologies: ProLindac™, Thiarabine™, and Cobalamin™. The company's lead development candidate for the treatment of cancer is ProLindac™, a nanopolymer DACH platinum prodrug. ProLindac has successfully completed a European Phase II trial in patients with ovarian cancer, and Access and its Asian partners are planning to start Phase II combination studies shortly. Oxaliplatin (Eloxatin, Sanofi-Aventis) is the only DACH platinum currently approved; it has sales in excess of $2 billion. Aventis) is the only DACH platinum currently approved; it has sales in excess of $2 billion.

Thiarabine™ is a Phase II nucleoside analog with considerable potential for treatment of lymphoma and leukemia. Extensive preclinical data shows that Thiarabine has good efficacy in a variety of tumor models.

Cobalamin&trade; is Access' proprietary nanopolymer oral drug delivery technology. Using a 'Trojan Horse' approach, the technology uses the body's natural vitamin B12 uptake mechanism in the gut to transport drugs that otherwise would have little or no oral bioavailability. The company is currently developing products for the oral delivery of insulin and human growth hormone (HGH), and is collaborating with a number of companies to develop additional formulations of various other pharmaceutically-active compounds.

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[39] www.**access**pharma.com

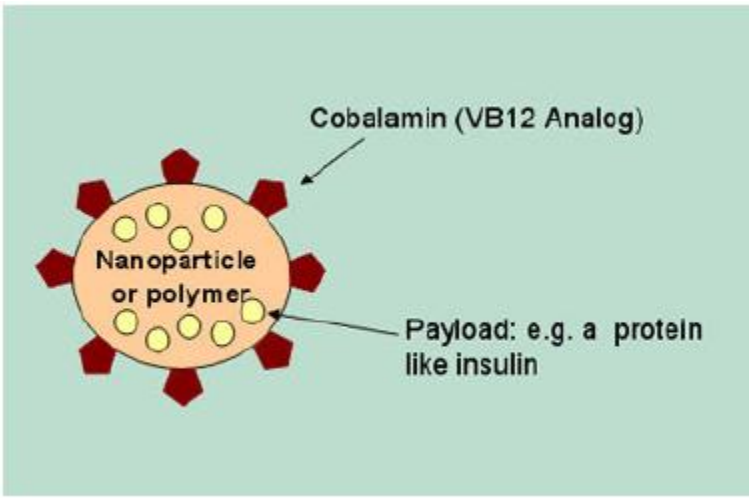
Technology

Cobalamin™ -Mediated Disease Targeting

Introduction

In many diseases which involve cell proliferation, there is increased demand for certain vitamins or vitamin analogs compared with normal tissue. Access Pharmaceuticals has developed technology which takes advantage of this increase in demand. By coupling drugs to Cobalamin™ (an analog of vitamin B12 or VB12), more drug is taken up by diseased cells. This effect can be amplified by attaching Cobalamin™ and several molecules of the drug to a polymer, or encapsulating the drug in a nanoparticle coated with Cobalamin.

Access owns several patents and patent applications which provide the company with a proprietary position in amplified Cobalamin™-mediated targeted delivery of drugs to diseased cells.



There are several diseases for which this targeting approach holds promise; for example, cancer, rheumatoid arthritis, psoriasis, acute leukemia, lymphomas, Crohn's disease, ulcerative colitis, and multiple sclerosis. Access Pharmaceuticals is developing applications of this technology in the area of oncology, while seeking collaborations and partnerships for development of this technology for other diseases.

• Access has conducted studies which have provided proof-of-principle of vitamin mediated targeting of cancer cells as well as sites of some other diseases.
• Efficacy of vitamin-targeted polymer conjugates was demonstrated in rodent tumor and rheumatoid arthritis models.

• Access has patents and patent applications which provide intellectual property protection for disease targeting of polymers and nanoparticles using Cobalamin™, folates, and biotin.

Opportunities

Access Pharmaceutical's proprietary Cobalamin™ - mediated disease targeting technology provides a **drug delivery and targeting option for a wide variety of diseases in which increased demand for vitamins or vitamin analogs in diseased cells is known to occur**. In addition to the oncology program described here, Access has conducted initial studies demonstrating proof-of-concept that Cobalamin™-mediated targeting could be very effective in treating rheumatoid arthritis and colitis. Access' approach involves the coupling of the drug to a polymer or the encapsulation of the drug in a nanoparticle and targeting these constructs to the sites of disease through the attachment of Cobalamin™.

Access has considerable expertise in drug-particle encapsulation, drug-polymer conjugation, and the chemistry of Cobalamin™ attachment, and has developed in vitro, in vivo, and ex-vivo models for the biological evaluation of Cobalamin™- targeted drug delivery systems.

Access Pharmaceuticals is currently seeking development partnerships with biotech and pharmaceutical companies requiring a targeted approach to increase drug efficacy and/or decrease side-effects of novel active pharmaceutical compounds and/or improve the efficacy/safety profile of an established active pharmaceutical agent to gain a competitive advantage over other formulations.

Business Development

The Business Development team at Access Pharmaceuticals **is interested in identifying outlicensing candidates, as well as alliance and merger opportunities** for Access oncology and dermatology products, as well as for our nanopolymer technologies, including Cobalamin™ for oral drug delivery, Cobalamin™ for disease targeting, and SEPA, Access' nail and transdermal drug delivery technology.

ALKERMES [40]

About Alkermes

At Alkermes, developing medicines with the potential to change people's lives for the better doesn't start with science. It starts with patients.

We look at the everyday needs and challenges of people living with disease. Then we apply our proprietary technologies and scientific expertise to overcome common barriers to treatment success. Our goal is to bring forward safe and effective medicines that can make it easier for patients to consistently get the medication they need, day after day.

Products

Alkermes focuses on therapies for widespread, chronic diseases, such as central nervous system disorders, addiction, diabetes and autoimmune disorders, where we feel we havethe opportunity to make the greatest impact.

Pipeline

We are building a robust pipeline of product candidates based on our proprietary technologies, scientific knowledge and clinical expertise.

Corporate Profile

Alkermes, Inc. is a fully integrated biotechnology company committed to developing innovative medicines to improve patients' lives. Alkermes developed, manufactures and commercializes VIVITROL® for alcohol dependence and manufactures RISPERDAL® CONSTA® for schizophrenia and bipolar I disorder. Alkermes' robust pipeline includes extended-release injectable, pulmonary and oral products for the treatment of prevalent, chronic diseases, and such as central nervous system disorders.

Headquartered in Waltham, Massachusetts Alkermes has a commercial manufacturing facility in Ohio.

Products Summary

"Our products use sophisticated drug technologies or novel molecules to help patients consistently and easily get the medicine they need, when they need it. It's an approach designed to offer more than just compliance or convenience. Our goal is to provide safe and effective medications that can offer improved outcomes for patients. Below, learn more about our commercial products and pipeline candidates in development."

[40] www.**alkermes**.com

Addiction

VIVITROL
VIVITROL® (naltrexone for extended-release injectable suspension) is the first and only once-monthly injectable medication for alcohol dependence.
Vivitrol is currently in development for the treatment of opioid dependence and is not currently approved for this indication.

ALSK 29
Is an oral compound in development for the treatment of alcohol dependence.

ALSK 33
Is an oral molecule in development for the treatment of addiction and other CNS disorders.

Mental Health

RISPERDAL® CONSTA® (risperidone) long-acting injection is the first and only long-acting atypical antipsychotic approved in the U.S. for the treatment of both schizophrenia and bipolar disorders.

ALSK 8070
Is an extended–release injectable product candidate in development for the treatment of schizophrenia.

Pain

ALSK 36
Is an oral compound in development for the treatment of pain.

ALSK 37
Is an oral molecule in development for the treatment of opioid-induced constipation.

Rheumatoid Arthritis

ALSK 6931
Is an extended-release formulation in development for the treatment of rheumatoid arthritis and related autoimmune diseases.

Diabetes

Exenatide once weekly
Is an extended-release injectable formulation in development for the treatment of type 2 diabetes.

Pulmonary Disease

ALSK 27
Is an inhaled candidate in delopment for the treatment of chronic obstructive pulmonary disease.

Proprietary Technology Platforms

Alkermes has four proprietary technologies that enable delivery of both small molecules and complex macromolecules.

Medisorb® Technology

Alkermes' proprietary, injectable extended-release technology, called the Medisorb® technology, enables us to develop treatments that sustain effective levels of medication in the body over a prolonged time period. We have two commercial products based on this technology, RISPERDAL® CONSTA® and VIVITROL®.

Our extended-release technology allows us to encapsulate small molecules, peptides and proteins in microspheres made of biodegradable polymers. With extended-release profiles lasting from days to months, these microspheres are designed to eliminate the need for frequent dosing.

Alkermes' extended-release technology is distinguished by:

• Clinically-proven extended-release of medication from microspheres in humans

• **Demonstrated safety and tolerability in human clinical trials**

• Potential to improve patient adherence to therapy, especially where extended-release dosage administration is an important factor for the selection of a medication for treatment

• **Broad applicability to small molecules, peptides and proteins**

• Demonstrated manufacturing capability at laboratory scale, pilot scale and commercial manufacturing scale, in compliance with cGMPs

AIR® Technology

Alkermes' pulmonary drug delivery technology, called the AIR® technology, offers a unique, proprietary delivery system for optimized drug delivery to the lungs. First published in the journal, Science, our technology represents a major innovation among pulmonary delivery systems. We are currently developing ALKS 27 based on this technology.

The pulmonary delivery system can provide efficient dry-powder delivery of small molecule, peptide, protein and other macromolecule drug particles to the deep lung, with significant advantages over other delivery methods.

Benefits include:

• Systemic delivery of small molecules, peptides, proteins, and other macromolecules

• Local or targeted delivery of wide dosage range

• A small, easy-to-use delivery device

• Proven scalability and commercial-scale production of drug

• Demonstrated safety and tolerability in large-scale human clinical trials

Medifusion ™ Technology

Alkermes' proprietary long-acting Fc fusion technology platform, called the Medifusion™ technology, is designed to extend the circulating half-life of proteins and peptides in order to create an effective, long-acting injectable medication. The Medifusion technology is able to extend the half-life of proteins and peptides through the combined action of Fc fusion and hyperglycosylation. The resulting extended systemic half-life of the therapeutic compound allows for reduced dosing frequency. We are currently developing ALKS 6931 based on this technology. We are currently developing ALKS 6931 based on this technology.

Alkermes' Medifusion technology is distinguished by:

• Systemic delivery of Fc fusion peptides and proteins

• Potential to achieve a customized extended-release profile lasting from days to months

• Potential to improve patient adherence to therapy, especially where extended-release dosage administration is an important factor for the selection of a medication for treatment

LinkeRx ™ Technology

Alkermes' long-acting proprietary LinkeRx™ technology platform enables the creation of extended-release injectable versions of antipsychotic therapies and may also be useful in other disease areas in which long action may provide therapeutic benefits. The technology uses proprietary linker-tail chemistry to create New Molecular Entities (NMEs) derived from known agents. These NMEs are designed to have improved clinical utility, manufacturing and ease-of-use compared to other long-acting medications. We are currently developing ALKS 9070 using this technology.

Alkermes' LinkeRx technology is distinguished by:

• Potential to achieve an extended-release profile lasting from days to months

• Potential to improve patient adherence to therapy, especially where extended-release dosage administration is an important factor for the selection of a medication for treatment

ArmaGen[41]

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About ArmaGen

ArmaGen® **provides platform technology solutions to the 'blood-brain barrier' problem**, and can non-invasively target recombinant proteins, therapeutic monoclonal antibodies, and siRNA to the brain.

About the blood-brain barrier (BBB)

Effective drugs have not been developed for most brain disorders

Table 1. Brain disorders responsive to small molecule drugs
depression
schizophrenia
chronic pain
epilepsy

Big Pharma only develops a certain class of drug called small molecules. Although it is widely believed that any small molecule crosses the blood-brain barrier (BBB), just the opposite is true. In order to cross the BBB, the small molecule must have a molecular weight (MW) < 400 Daltons, and must also be lipid soluble. The number of small molecules that have these chemical properties is <2% of all drugs. All other drugs do not cross the BBB. Since Big Pharma does not develop BBB solutions, >98% of all drugs that could potentially treat the brain are not developed. The only drugs currently developed for the brain are lipid soluble drugs with a MW < 400 Daltons, and only a few brain disorders respond to such drugs (see Table 1). The majority of brain disorders do not respond to lipid soluble drugs with a MW < 400 Daltons, and consequently, no treatments are available (see Table 2 below).

The global CNS drug market is greatly under-penetrated

The global market for drugs for the central nervous system (CNS) is greatly underpenetrated, and would have to grow by >500% just to equal the cardiovascular drug market.

The problem of under-penetration of the brain drug market will become even more severein the next 20 years as the population ages and the number of people afflicted with Alzheimer's disease,

[41] http://www.armagen.com

Parkinson's disease, or stroke increases by 50%. Without new drug treatments and new methods for early diagnosis, the annual cost of health care for patients with Alzheimer's disease alone could approximate $0.5 trillion in 2020 in the U.S.

Using this model, it is increasingly difficult to build a successful CNS drug development program for brain diseases other than affective disorders, pain, or epilepsy. This approach leaves un-developed very large markets of unmet needs that could be addressed if the BBB problem were not rate-limiting. The inability to treat most CNS disorders is not due to the lack of effective CNS drug discovery. Rather, it is due to the ineffective CNS drug delivery.

ArmaGen Products

• AGT-3
An avidin antibody fusion protein for intravenous RNAi and the in vivo delivery of short interfering RNA (siRNA)
AGT-3 is a genetically engineered fusion protein of avidin and a monoclonal antibody to a human cell membrane receptor, which binds mono-biotinylated siRNA with high affinity to enable intravenous RNA interference. The avidin-biotin bond is highly stable in vivo, and the siRNA knocks down target mRNAs while still bound to avidin. Avidin is fused to a genetically engineered receptor specific monoclonal antibody (MAb), which is endocytosed by virtually all human cells, including the cells comprising the blood-brain barrier (BBB). ArmaGen's siRNA delivery system is encompassed within the broad claims of issued U.S. patent 6,287,792, which covers the use of avidin-biotin technology in drug delivery.

• AGT-110
An IgG-TNFR fusion protein for acute and chronic brain disease

• AGT-120
A neuroprotection drug for stroke that crosses the blood-brain barrier and is active in brain following delayed intravenous administration

• AGT-160
An anti-amyloid drug that crosses the blood-brain barrier for reducing the brain amyloid burden of Alzheimer's disease

• AGT-181
A lysosomal enzyme replacement therapy for the brain

• AGT-185
A CNS-acting chemical nerve gas antidote

• AGT-190
A neuroprotection drug for stroke or Parkinson's disease

• AGT-2000

A non-viral, intravenous gene therapy for either primary or metastatic brain cancer

Protein drug delivery technology

ArmaGen Technologies' molecular Trojan horses deliver protein neurotherapeutics to the brain.

POTENTIAL OF PROTEIN-BASED THERAPEUTICS IN THE TREATMENT OF BRAIN DISEASES

Many disorders of the brain have proven refractory to small molecule therapeutics, and could be treated with protein therapeutics. Indeed, many protein lead drug candidates have been identified for brain diseases, but these proteins do not enter CNS drug development, because the proteins do not cross the blood-brain barrier (BBB). Instead, attempts are made to isolate small molecule peptidomimetics. However, it is very difficult to produce small molecule peptidomimetics. Moreover, in the rare case that a small molecule agonist is identified, this lead drug candidate most likely will not cross the BBB. Those small molecules that have a molecular weight > 400 Daltons, or form even a few hydrogen bonds, will not cross the BBB in pharmacologically significant amounts. An alternative strategy is to re-formulate the protein drug candidate to enable transport across the BBB in vivo. This is done by genetically engineering a novel fusion protein, wherein the protein drug is fused to ArmaGen Technologies' molecular Trojan horse (MTH). The MTH part of the fusion protein triggers transport across the BBB via an endogenous receptor-mediated transport system.

RE-FORMULATION OF PEPTIDES, RECOMBINANT PROTEINS, ENZYMES, OR MONOCLONAL ANTIBODIES AS FUSION PROTEINS TO ENABLE TRANSPORT ACROSS THE BBB

Scientists at ArmaGen Technologies have developed proprietary MTHs that cross the primate and human BBB faster than neuroactive small molecules such as morphine. The lead MTHs, AGT-1 and AGT-2, have been genetically engineered to enable chronic use in humans without immune reactions. With the genes encoding AGT-1 or AGT-2, ArmaGen scientists can create novel fusion genes that encode for fusion proteins that have dual functions: (a) cross the BBB on one of the endogenous BBB RMT systems, and (b) bind the neuronal or glial receptor in brain to trigger the desired pharmacological effect. This bi-functionality is illustrated in the adjacent figure: the "head" of the fusion protein binds a BBB receptor to trigger uptake of the fusion protein into the brain, and the "tail" of the fusion protein then activates an endogenous receptor on brain cell membranes. In the case of enzyme drugs, where the enzyme must also distribute into the intra-cellular space of brain cells, the MTH also causes the receptormediated endocytosis of the enzyme into brain cells.

Drug developers may own the intellectual property of novel recombinant proteins, enzymes or monoclonal antibodies, that by themselves do not cross the BBB, and have little chance of being successful as a brain drug in clinical trials. ArmaGen can partner with CNS drug developers to re-formulate their protein-based neurotherapeutic and create a novel fusion protein that both crosses the human BBB and acts at specific drug receptors once inside the brain. ArmaGen Technologies has genetically engineered and expressed several fusion proteins, and these recombinant proteins retain the bi-functionality of both the BBB delivery part and the protein drug part.

Small molecule BBB drug delivery technology

What restricts the free diffusion of small molecules across the BBB?

Small molecules cross the BBB in pharmacologically significant amounts only if the molecule has the following characteristics:

- Molecular weight under a 400 Dalton threshold
- Lipid solubility
- Absence of restrictive plasma protein binding
- Absence of affinity for one of several BBB active efflux transporters (AETs), such as p-glycoprotein

Gene delivery technology

- non-viral
- non-invasive
- intravenous administration in small volumes
- non-toxic, non-immunogenic
- delivers plasmid DNA to all cells in brain following an intravenous administration
- ectopic gene expression eliminated with specific gene promoters
- enables intravenous RNA interference (RNAi)
- reduced to practise in mice, rats, and Rhesus monkeys
- enables adult transgenics in 24 hours

Avidimer Therapeutics, Inc. [42]

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About Avidimer

Avidimer Therapeutics, Inc. develops and commercializes pharmaceuticals. The company focuses on cancer detection and treatment. It offers avidimers, cancer product candidates that are designed to maximize damage to disease targets and minimizes collateral damage to healthy tissue, as well as for the treatment of ovarian, breast, lung, and colon cancers.

Avidimer Therapeutics, Inc. was founded as NanoCure Corporation in 2003 and changed its name to Avidimer Therapeutics, Inc. in May 2005. The company is based in Ann Arbor, Michigan.

Technologies

Avidimer Therapeutics is producing nanosized polymer dendrimers, or “avidimers,” that act as inert scaffolding for imaging and/or therapeutic agents, which are attached via chemical linkers. The avidimer complex also includes multiple targeting vectors, which increase drug payload, tightly attached to the dendrimers to guide the desired molecules to target tissue. The vectors employ cell surface markers expressed on diseased cells to guide the avidimers to diseased, not healthy cells. A dendrimer is generally about 5 nm in diameter, which is about the same size and shape as a molecule of hemoglobin. A fully loaded avidimer is smaller than 15 nm in diameter and flexible, enabling it to move without recognition throughout the body, according to the company. Avidimers are delivered via injection and are excreted within 72 hours via the urinary tract.

Avidimer is focusing on cancer. Its lead candidate, ATI-001, is formed by the covalent attachment of 4–5 folic acid molecules and 5–6 methotrexate molecules to a dendrimer backbone.

The linker mechanism employed to attach drugs to avidimers are chosen either to retain the drug on the dendrimer throughout its lifetime or allow the drug to disassociate (i.e., cleave) after delivery to its target. Maintaining the drug attached to the dendrimer in transit to the disease target is important in sparing healthy tissue, i.e., minimizing toxicity, but in some cases, the drug must be released from the dendrimer at its intended destination to express biological activity, while in other cases, the drug retains its activity when attached to the dendrimer, the company reports.

ATI-001 targets cancers that overexpress the high affinity folate receptor on ovarian, breast, lung, and colon cancer, among others. A study published in 2005 demonstrated that thisdrug was significantly more efficacious in vitro and in vivo with much less toxicity compared to free methotrexate administered at comparable doses.

[42] www.**avidimer**.com

Calando Pharmaceuticals [43]

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About Calando

Combined with a safe and effective delivery method, RNAi-based treatments for life threatening and fatal diseases like cancer, AIDS, hepatitis C, Huntington's disease and others become possible.

Company Overview

Calando **is a clinical stage nanobiotechnology company at the forefront of RNAi therapeutics**. We develop nanoparticle therapeutics that use our patented sugar (cyclodextrin)-based polymer technologies as a drug delivery system for siRNA.

Our products are based on pioneering technology invented in the Chemical Engineering Department of the California Institute of Technology. Engineered to reduce the debilitating effects of cancer treatment, our proprietary molecules are designed to improve the safety and efficacy of cancer therapeutics using siRNA as the active ingredient. The target-agnostic platform technology has the potential to be applied to a wide range of diseases beyond cancer as well as to therapeutic classes beyond siRNA therapeutics.

In 2009, we successfully completed a Phase 1 clinical study with our first anti-cancer drug and therapeutic candidate, IT-101. IT-101, along with Calando's drug delivery platform, Cyclosert™, now is partnered for further development to Cerulean Pharma Inc.

In the Clinic

We are focused on the clinical development of RONDEL™, our siRNA delivery technology, and CALAA-01, the associated drug candidate.

RONDEL, which overcomes the significant hurdles to efficient, systemic delivery of siRNA, features many benefits: Repeat dosing with no indication of significant, dose-limiting immune reactions.

Proven to overcome the extra-and intra-cellular barriers to siRNA delivery. Scaled and manufactured for clinical use.

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[43] www.**calandopharma**.com/

CALAA-01 entered the clinic in April 2008. To our knowledge, this was the first entry into a Phase I clinical study of fully formulated and targeted of asiRNA drug candidate targeting cancer.

In addition to our therapeutic pipeline, our patented and proprietary delivery systems have utility in multiple application areas. As a result, we are exploring opportunities to combine our innovative technologies with companies that require delivery solutions.

Technologies

RONDEL™ for siRNA Delivery

Years of research leading to clinical breakthroughs.

We are creating and developing new targeted, siRNA-containing therapeutics using our proprietary three part RNAi/Oligonucleotide Nanoparticle Delivery (RONDEL) technology, the foundation of which is our cyclodextrin-containing polymer.

One of the key challenges to using RNAi therapy has been the inability to systemically deliver siRNA in humans. "Naked" siRNA is degraded and destroyed by nucleases in the bloodstream and is not taken up by cells. It also causes harmful immune reactions.

With our RONDEL system, siRNA is protected by our cyclodextrin-containing polymers and thus can reach its destination and perform its intended job, for example, to stop the runaway growth of tumor cells. By encapsulating the siRNA, RONDEL also protects the body from the immune reactions caused by naked siRNA.

Pending successful clinical testing, RONDEL provides an enabling technology for siRNAbased therapeutics to become effective disease treatments.

RONDEL™ Benefits

Benefits of Calando's RONDEL Technology

• More Effective Delivery

o RONDEL binds to and self-assembles with siRNA to form uniform colloidalsized particles. Analysis has shown that these particles are spherical and less than 100 nm in diameter, which allows for accumulation at the tumor site.

o Calando and its partners have demonstrated successful delivery of functional siRNA therapeutics to tumor cells and to hepatocytes by systemic administration and confirmed sequence-specific gene inhibition.

• Modularity

o RONDEL is a two vial system with the active siRNA included in one vial and the delivery excipients in the other, allowing easy exchange of the active siRNA ingredient.

• Fewer Immune Reactions

o The delivery vector allows for repeat dosing with no indication of significant, dose-limiting immune reactions. Unlike lipid delivery vehicles, the cyclodextrin-based

RONDEL delivery system does not cause an interferon response.

o The fully formulated polymer/siRNA particles exhibit a significant therapeutic window of safety in animals, even when repeated doses are used.

• Increased Stability

o The particles have been shown to be stable under physiological conditions.

• Designed to Work With Human Physiology and Cell Biology

o Overcomes the extra-and intra-cellular barriers to siRNA delivery.

In the Clinic

CALAA-01, Calando's leading drug candidate, is a combination of RONDEL™ and a patented siRNA targeting the M2 subunit of ribonucleotide reductase, a clinically-validated cancer target. Ribonucleotide reductase catalyzes the conversion of ribonucleosides to deoxyribonucleosides and is necessary for DNA synthesis and replication; it is a critical component in the proliferation of cancer cells. Calando's siRNA and CALAA-01 have demonstrated potent anti-proliferative activity across multiple types of cancer cells. 01 have demonstrated potent anti-proliferative activity across multiple types of cancer cells.

CALAA-01 Phase I Clinical Trial

This is an open-label, dose-escalating study of the safety of intravenous CALAA-01 in adults with solid tumors refractory to standard-of-care therapies. Patients who satisfy the inclusion and exclusion criteria will receive two, 21-day cycles of CALAA-01. A cycle will consist of four infusions administered on days 1, 3, 8, and 10 followed by 11 days of rest. If safe, a second 21-day cycle will be administered consisting of infusions on days 22, 24, 29, and 31 followed by 11 days of rest.

IT-101

Originally developed by Insert Therapeutics, a Calando predecessor company, IT-101 is an experimental, nanoparticle therapeutic that consists of the drug camptothecin (CPT) conjugated to a cyclodextrin polymer. IT-101 is based on the Cyclosert™ delivery platform developed by Insert scientists for small molecule drugs. Cyclosert™ is based on a linear cyclodextrin polymer similar to the one used in the RONDEL system. Both IT-101 and Cyclosert have been partnered with Cerulean Pharma, Inc., a Cambridge, MA based biotech company.

Partnering to extend the reach of our technology.

Cyclosert™ was designed by Calando's scientists for the delivery of small molecule drugs and provides many of the same benefits as the RONDEL™ system. Calando completed a Phase 1 trial with IT-101, the associated drug candidate that is comprised of Calando's proprietary drug delivery polymer and Camptothecin, a potent anti-cancer drug, with a positive safety profile and indications of efficacy. In June 2009, Calando entered into agreements to partner Cyclosert and IT-101 to Cerulean Pharma, Inc. ("Cerulean"), a Boston-based biotech company.

Under the terms of the agreements, Calando granted Cerulean an exclusive royalty-bearing worldwide license to certain patent rights to Cerulean related to the linear-cyclodextrin drug delivery platform and IT-101. Calando retains the rights to its RONDEL platform, as well as the CALAA-01 lead drug.

Calando's RONDEL™ delivery system extends the reach of RNAi therapy by answering the new field's most pressing need — an effective and safe systemic delivery method.

Cell Therapeutics, Inc. [44]

Cell Therapeutics, Inc. & Subsidiaries

Cell Therapeutics, Inc. Corporate Headquarters
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About CTI

"Where Cancer Treatment Gets Personal"

Within every cell of every person is a genetic blueprint. Known as the genome, this blueprint instructs the cell how to respond to its environment, when to reproduce, and when to die. These genetic blueprints help to explain why each one of us is unique. They also explain why different cells and different patients respond to cancer treatment in different ways—and why one person may respond favorably to a drug, while another may experience debilitating side effects with little or no therapeutic benefit.

At Cell Therapeutics, Inc. (CTI), we use genomic information to develop a personalized approach to cancer therapy with the goal of making standard-of-care treatment less toxic and more effective for individual patients. Our approach is based on matching a drug candidate to a person's genetic profile along with other clinical and diagnostic information to achieve the highest anti-tumor activity, at the lowest dose, and with the fewest side effects. This personalized information can also be used to identify patients for clinical trials who are most likely to respond to the drug candidate.

Significant progress has already been made. Using a personalized approach to guide our drug development and commercialization programs may potentially lower our drug development costs, shorten approval time, and help improve the lives of patients by treating cancer according to each individual's genetic blueprint.

Mission

CTI is committed to developing, acquiring, and commercializing innovative treatments for cancer. In our pursuit of making cancer more treatable, we are developing a diversified portfolio of oncology products focused on identifying and developing new, less toxic, and more effective ways to treat cancer.

Values

Our priority and sense of purpose is our customer—the PATIENT. We are reminded daily that there is not a life or a moment to lose. CTI's patient focus shapes our culture, organization, and values. Company success is dependent on our EMPLOYEES' creativity and dedication. Without this talent, commitment, and focus, we would not reach the ambitious goals we set for ourselves.

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[44] www.**celltherapeutics**.com/

Our employees are dedicated to TEAMWORK. We have a true sense of ownership for our work and how it is tied directly to products that may significantly improve the outcome of patients' lives.

We feel a responsibility to give back to our COMMUNITY. We contribute to numerous local organizations and support employee initiatives beyond the workplace.

The "patient first" focus gives us a greater understanding of our market—it is the key to serving our customers well and creating true SHAREHOLDER value. When we are successful in achieving these values, our shareholders will benefit.

Technologies

"Developing Drugs that Patients Can Live With"

Personalizing cancer therapy is a multidisciplinary pursuit based on a variety of interdependent product development programs. Our scientists are advancing these programs through close collaboration and the integration of powerful technologies that will help us achieve our goal of hurting the cancer more than the patient. These technologies include:

• Our polyglutamate delivery technology may open the way to the selective delivery of cancer therapies to tumor tissue, potentially reducing the toxic side effects of widely used and well-characterized therapies.

• Our Genetic Polymer ™ technology supports the need for new rDNA-derived protein-based drugs by potentially extending plasma half-life. This could reduce the time and cost of developing new drugs, so patients can benefit sooner from breakthrough scientific discoveries.

• Our advanced systems biology platform addresses context of vulnerability. Every tumor and every patient has a specific set of genomic and clinical characteristics. Potentially, these characteristics can be used in synchrony to accelerate drug development and identify patients who will respond to treatment.

POLYGLUTAMATE TECHNOLOGY

Special Delivery

Using polyglutamate drug delivery technology, we are developing a new way to deliver paclitaxel preferentially to tumor tissue. This approach could potentially reduce the toxic side effects of paclitaxel to normal organs and tissues and improve its anti-tumor activity.

One of the unique characteristics of our product candidate OPAXIO™ (paclitaxel poliglumex, CT-2103; formerly known as XYOTAX) is that it links, or conjugates, paclitaxel to the biodegradable polymer polyglutamate.

Potential Benefits

Based on preclinical animal studies and clinical trial data, we believe that OPAXIO may be able to achieve a number of benefits over existing taxanes, including:

- Eliminates the need for toxic solubilizing agents such as cremaphor/ethanol
- Eliminates the need for routine premedication
- Allows more drug to reach the tumor
- Decreases toxicity as a result of less active drug reaching normal tissues
- Has potential to overcome resistance to the underlying chemotherapy drug
- Similar or potentially better efficacy compared with standard taxanes

Mechanism of Action

Unlike vessels in healthy tissue, vessels in tumor tissue have openings, or pores, that make them porous to large molecules. OPAXIO molecules, which are larger than those of standard paclitaxel, leak through these pores and are preferentially trapped and distributed in the tumor tissue.

Once in the tumor tissue, OPAXIO is taken up by tumor cells through a cellular process called endocytosis. Because the biopolymer OPAXIO is made of biodigestible amino acids, it is slowly metabolized by lysosomal enzymes (principally cathepsin B) inside the lysosome in the tumor cell. This metabolism releases the active chemotherapy agent, paclitaxel into the tumor.

OPAXIO is taken up by tumor cells through a cellular process called endocytosis. Because the biopolymer OPAXIO is made of biodigestible amino acids, it is slowly metabolized by lysosomal enzymes (principally cathepsin B) inside the lysosome in the tumor cell. This metabolism releases the active chemotherapy agent, paclitaxel into the tumor.

In addition to the potential metabolic advantages, polymer-linked cancer drugs are inactive while circulating in the bloodstream, which may also lower toxicity compared to the active cancer drug substance alone.

Origin of the Technology

We licensed the worldwide exclusive rights to polyglutamate and related polymers and their applications from PG-TXL Company in 1998. The technology was originally developed at The University of Texas M.D. Anderson Cancer Center. The initial patent, issued in

November 1999, covers polyglutamate and related polymers coupled with commonly used cancer drugs such as paclitaxel, docetaxel, etoposide, teniposide, or camptothecins. The patented technology covers formulations of polyglutamate-conjugated paclitaxel that also include the use of human serum albumin and conjugation to epothilones.

Strategic Significance

Through this novel polymer technology we have the opportunity to build a portfolio of potentially safer and more effective versions of well-known anti-cancer agents such as taxanes. Taxanes such as paclitaxel are widely used for the treatment of various solid tumors, including non-small cell lung, ovarian, breast, and prostate cancers. We believe that our polymer technology may lower the risks inherent in developing new drugs because we are linking polymers to well-defined and widely used classes of chemotherapy drugs, including taxanes.

Genetic Polymer ™ Technology

Streamlining Protein Pharmaceutical Development

In the first half of 2007, we formed a spin-off company, Aequus BioPharma, Inc., to further develop a technology created by CTI scientists that extends the plasma half-life of recombinant DNA (rDNA) derived protein pharmaceuticals. This technology, called Genetic Polymer ™ technology, may simplify the development and manufacture of biologics reducing time to market and lowering costs.

Biologics, especially pharmaceuticals derived from recombinant DNA (rDNA), represent the fastest growing segment of pharmaceutical sales. Current sales reach $51 billion worldwide and expected to hit $87 billion by 2010. Industrial-scale protein production technologies are currently being applied to the development of a wide variety of these drugs, including hormones, growth factors, antibodies, and cytokine modulators, to treat a vast range of human diseases.

Extending Plasma Half-life

Frequently, rDNA-derived protein pharmaceuticals have a relatively short plasma half-life. To rectify this problem, several physical, genetic, and chemical approaches have been developed to extend plasma half-life—without compromising efficacy or introducing safety issues such as immunogenicity and other off-mechanism toxicities.

The most successful of these approaches include site-specific amino acid substitution, conjugation to carrier domains, and post-expression chemical conjugation. Genetic Polymer technology may simplify the use of chemical conjugation technology to extend plasma halflife by genetically attaching an amino acid polymer domain to a biologically active protein sequence to create a novel, unique, and patentable gene.

Mechanism of Action

To construct a Genetic Polymer, the DNA sequence encoding a specific amino acid polymer is ligated, or attached, to the DNA sequence encoding a biologically active peptide-or protein-based drug moiety in an expression vector designed for use in a bacterial, yeast, mammalian, or other recombinant protein expression system. The amino acid polymer can be attached to either the N-terminus, C-terminus or both termini of a protein. Typically, DNA encoding a secretion-leader sequence is included in the expression vector to drive secretion of the expressed protein to the extracellular space to facilitate recovery and purification.

A prototypical Genetic Polymer protein is depicted in the schematic shown below. It should be noted that potential post-translational modifications (PTM) present on more than one amino acid repeat are omitted for clarity.

Strategic Significance

In addition to its potential for producing lower cost follow-on biologics, we believe this recombinant DNA technology might be used to develop novel biologics, in a wide array of malignant, inflammatory, or infectious diseases. The Genetic Polymer technology platform should be applicable to many different protein pharmaceuticals. This, in turn, may eliminate the need to develop individualized technology for extending the plasma half-life of each protein pharmaceutical, allowing for more convenient dosing.

Our data also suggest that biosynthesis in traditional mammalian cell protein expression systems will allow for the production of a protein pharmaceutical with prolonged plasma half-life, but without the requirement for further chemical modifications subsequent to protein expression.

It is our opinion that this proprietary Genetic Polymer technology creates novel compositions of matter, allowing for the commercialization of protein pharmaceuticals without infringing on the patents of other companies with competing technologies. The first protein pharmaceutical the company plans to move into preclinical and chemical development studies is a novel, long-acting G-CSF biosimilar.

Collaborations & Partnerships

Mutually Beneficial Relationships

We enter into partnerships and collaborations with companies to maximize commercial opportunities for all parties involved. We believe in leveraging the intellectual, financial, and commercial strengths of strategic corporate partnerships to bring the full potential of our product candidates to market. We also believe in the value of strategic timing.

Before seeking development or commercialization partners, we develop our products through mid-to late-stage clinical development. As a result, we are best positioned to assess and realize their full value. Ultimately, this strategy will allow us to choose the best partner on more favorable terms than might be available if we entered into collaborative relationships during earlier stages of product development.

Some of our current collaborations are described below.

Novartis

In September 2006, we entered into an exclusive worldwide licensing agreement with Novartis for the development and commercialization of OPAXIO ™ (paclitaxel poliglumex, CT-2103, formerly known as XYOTAX). The agreement also provides Novartis with an option to develop and commercialize pixantrone based on agreed terms. As part of the agreement, Novartis made a $15 million equity investment in CTI.

PG-TXL Company, L.P.

In June 1998, we entered into an agreement with PG-TXL Company, L.P. granting us an exclusive worldwide license for the rights to PG-TXL, now known as OPAXIO ™, and to all potential uses of PG-TXL's polymer technology.

Under the terms of the agreement, we will fund the research, development, manufacture, marketing, and sale of anti-cancer drugs developed using PG-TXL's polymer technology. We are obligated to make payments upon the attainment of significant development milestones, as defined in the agreement.

Additional Collaborations

Additional collaborations came to CTI with our acquisition of Systems Medicine in July 2007, including:

Nerviano Medical Sciences (NMS), Milan, Italy

The largest pharmaceutical research and development facility in Italy and one of the largest oncology-focused, integrated discovery and development companies in Europe. NerPharMa, a pharmaceutical manufacturing company belonging to NMS in Nerviano, Italy manufactures pixantrone.

The Translational Genomics Research Institute (TGen)

A biomedical research institute that makes and translates genomic discoveries into advances in health.

The Cancer Drug Development Laboratory

A robotics-intensive division of TGen applying advanced genomic technologies (e.g., RNA interference) to translational drug development.

TGen Drug Development Services

An oncology-focused clinical research organization providing preclinical evaluation of the safety and efficacy of a drug using the most relevant animal models and genomic analyses.

The Molecular Profiling Institute

A specialty reference laboratory that helps cancer patients worldwide by applying the discoveries of the Human Genome Project to personalized medicine.

Critical Path Institute

An Arizona-based non-profit organization focused on enabling the accelerated development of new medications founded by FDA, the University of Arizona, and SRI International.

CERULEAN [45]

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About Ceruleran

Focused on novel, nanotechnology-based therapeutics

Cerulean is a private biopharmaceutical company focused on the development of novel, nanotechnology-based therapeutics in the areas of oncology, inflammation, and cardiovascular diseases.

Cerulean is pursuing three key strategies:

• Achieving rapid and clinically significant human proof of concept with its technology.
• Building a deep and diversified product pipeline and leveraging its proprietary nanotechnology platform.
• Using a multi-faceted business model, with plans to retain some products for development and commercialization to achieve full company value creation, while at the same time collaborating on other products to leverage the resources and capabilities of partners.
Cerulean has assembled a world-class management team, board of directors, and scientific advisory board that collectively have a significant track record of business building, product development, and scientific breakthroughs.

Cerulean was founded in October of 2006 and is located in Cambridge, Massachusetts.

Mission:

Cerulean's mission is to dramatically enhance patient outcomes in diseases of high unmet need through the application of nanotechnology and, in this way, enhance efficacy, lower toxicity and broaden the ability of combination therapy.

Nanotechnology will provide an avenue through which the traditional drug development pharmacokinetics and drug metabolism obstacles can be overcome by localizing drugs to their target sites at therapeutic concentrations for prolonged periods of time while at the same time reducing their systemic exposure.

[45] www.**ceruleanrx**.com

Technologies

Nanopharmaceuticals: A New Approach to Designing Drugs with Enhanced Therapeutic Utility

Cerulean is uniquely positioned to advance nanopharmaceuticals as the next generation therapeutics. Nanopharmaceuticals are particles of defined nanometer diameter size, which are designed to target and penetrate diseased tissue with “leaky vasculature” and then gradually release their drug payload at the target location. The unique characteristics of these nanoparticles allow for cellular uptake into cells as intact nanoparticles.

This fundamentally different approach overcomes the shortcomings of short exposure at target site and high systemic toxicity of conventional drugs. The technology underlying Cerulean’s nanopharmaceuticals is particularly suited for oncology, inflammation, and cardiovascular disease.

These drug-containing nanoparticles are designed to enhance the therapeutic utility of drugs and allow for: containing nanoparticles are designed to enhance the therapeutic utility of drugs and allow for:

- Low systemic exposure
- Preferential delivery of drugs to target tissue
- Intracellular uptake in target cells; and
- Controlled release of therapeutic concentrations of drugs over a prolonged period of time.

The highly differentiated product attributes of Cerulean nanopharmaceuticals result in a profound increase of therapeutic utility. Efficacy is increased by maximizing the targeting, uptake, and retention in target tissue and releasing the active drug gradually from within the target tissue. The sustained release at the target site also offers the potential to treat resistant cell lines and may reduce the emergence of drug resistance. Maintaining the integrity of the nanopharmaceutical in circulation for a prolonged period of time minimizes non-specific systemic drug exposure, resulting in enhanced drug safety and improved side effects profile. Cerulean’s present focus is in the field of oncology, but the company plans to expand the utility of its technologies in other indications such as inflammation and infectious disease.

CERULEAN NANOPHARMACEUTICALS

Cerulean Nanopharmaceuticals Improve Clinical Outcome

Nanoparticle Design and Development

The ability to optimize drug loading, particle size, particle components, conjugation linker chemistry and formulation process leads to tailored nanoparticles that have superior biological properties compared to the free drug they contain. The physical-chemical properties of the nanoparticle, such as surface charge and surface composition, affect the distribution of the particle in the body and are used to passively target the nanoparticle into target tissues. The composition and linker chemistry are chosen to optimize the release of the free drug, achieving a much improved pharmacokinetic profile and reducing systemic exposure. During the design of the nanoparticle, scale-up and manufacturing are considered, ensuring the production of nanoparticle populations of consistent physical characteristics at scale.

Cerulean has access to two complementary technologies within its nanoparticle platform. Both of these technologies provide for the formation of stable and consistent nanoparticles comprised of biocompatible components, which have high drug loading capacity, and are able to release active drug in a controlled fashion.

The Polymeric Nanoparticle Technology (PNP) allows for nanoparticle customization through conjugation chemistry, particle composition, formulation, and fine-tuning of nanoparticle size. This technology has produced product candidates with compelling preclinical validation.

The Cyclodextrin Nanoparticle Technology (CDP) produces self-assembled nanoparticles of a defined size range. The most advanced product (IT-101) from this technology is presently in Phase 1b/2a clinical development. This technology has been applied to several classes of molecules.

Biological Impact

When the Cerulean nanoparticles are administered in the bloodstream, they maintain their integrity in circulation, minimizing non-specific systemic drug dissemination and clearance.

The size and surface properties of the nanoparticles favor extravasation through leaky vasculature, followed by deep penetration and retention at the tumor site. The physical properties of the nanoparticles facilitate endocytic intracellular uptake and help to avoid multi-drug resistance as the nanoparticles are not substrates of multi-drug transporters. The polymer-drug conjugation chemistry provides for controlled and sustained drug release, maximizing drug exposure to tumor target cells. The nanoparticles are made of biocompatible building blocks that allow for safe administration and excretion.

Our nanoparticles produce significant and prolonged tumor growth delay and improved tolerability compared to free drug in multiple mouse cancer models. Favorable drug distribution supports enhanced nanoparticle localization to the tumor and the improved pharmacokinetic profile demonstrate the advantages provided by the nanoparticles such as sustained release and shielding of the active drug.

Below is an example of nanoparticles produced with Cerulean's PNP technology penetrating into tumor tissue far from blood vessels co-localizing with endosomes and demonstrating that these nanoparticles enter tumor cells as intact nanoparticles.

CRLX228, Cerulean's preclinical lead candidate from the PNP technology contains a widely used oncology drug and is presently progressing into IND enabling studies. CRLX288 shows substantial efficacy and safety improvement over parent drug in validated pre-clinical models and offers the potential to dramatically improve the therapeutic index of the parent drug.

Profound Clinical Outcome

These highly optimized Cerulean nanoparticles produce a profound clinical outcome by allowing for high and sustained therapeutic drug levels at the target tissue and, in this way, maximizing

therapeutic effects. The nanoparticles are active in drug-resistant diseases, are well tolerated, and enable full-course therapy with minimal toxicities. Because of these attributes, Cerulean's nanoparticles are highly compatible agents for combination therapies and provide for more effective disease management.

IT-101, Cerulean's lead product from the CDP technology (a nanoparticle containing a highly potent topoisomerase 1 inhibitor, camptothecin) is advancing in Phase 1 and is expected to begin testing in Phase 2 studies in 2010. This nanoparticle has shown enhanced localization of drug in tumor and superior activity in 10 xengraft mouse models spanning 7 cancer types. To date, it has also demonstrated promising safety and pharmacokinetic datain humans. IT-101 has the opportunity to address large unmet medical needs in difficult-totreat tumor types.

CERULEAN'S COMPETITIVE ADVANTAGE

Intellectual Property

PNP Technology - Cerulean has created an extensive patent estate around its internally developed PNP technology with patent applications directed to multiple inventions in this area including, for example, inventions related to the composition and use of the PNPs and specialized apparatuses and methods for producing the PNPS.

CDP Technology -Cerulean's exclusive license to the patent estates of California Institute of Technology and Calando Pharmaceutical provides broad worldwide coverage of its CDP technology platform and various uses thereof. Additional Cerulean patent applications provide coverage related to improvements to and new applications of the CDP technology with a particular focus on IT-101, Cerulean's lead product candidate and related inventions.

Cerulean's exclusive license to the patent estates of California Institute of Technology and Calando Pharmaceutical provides broad worldwide coverage of its CDP technology platform and various uses thereof. Additional Cerulean patent applications provide coverage related to improvements to and new applications of the CDP technology with a particular focus on IT-101, Cerulean's lead product candidate and related inventions.

Nanopharmaceutical Development Capabilities

Cerulean has built a unique set of capabilities critical for nanopharmaceutical development.

In its short history, the company has been able to generate a suite of homegrown technologies as well as in-licensed complementary technologies. These technologies have the capacity to incorporate different drug classes and have been validated in various preclinical cancer models. Cerulean has also generated a sophisticated set of analytical and bioanalytical tools critical for lead development and optimization of its nanoparticles.

Copernicus Therapeutics Inc. [46]

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About Copernicus Therapeutics Inc.

Copernicus Therapeutics, Inc., a biotechnology company, develops a non-viral delivery system for the non-toxic delivery of nucleic acid drugs in the United States. Its non-viral delivery system is suitable for the delivery of nucleic acid drugs that permits various therapies for human diseases. The company focuses on the development of therapies to treat diseases that have therapeutic options, including diseases causing blindness, airborne viral diseases, and diseases of the brain. Copernicus Therapeutics, Inc. was formerly known as Copernicus Gene Systems, Inc. and changed its name to Copernicus Therapeutics, Inc. in 1997. The company was founded in 1995 and is based in Cleveland, Ohio

Business Strategy

Copernicus intends to become a leading biopharmaceutical company by utilizing breakthrough DNA nanoparticle technologies to produce safe and effective DNA drugs maximize shareholder value, Copernicus is exploiting its expertise in lung gene transfer by fi developing products for the $2 billion plus cystic fibrosis market. Copernicus' recent Phase I CF clinical trial results demonstrate that DNA nanoparticles efficiently transfer their DN payload into the nucleus of differentiated airway cells, and do so without causing a significant toxicities. With additional funding, the Company also will be able to devel products to treat diseases involving the central nervous system including various causes blindness. Copernicus has developed proof of concept data using an animal model Parkinson's disease; it also has proof of concept data in treating a mouse model of gene blindness (retinitis pigmentosa -RP). With demonstrated effectiveness of its technology treating three different organs of the body (lung, brain, eye), the company will focus its intern efforts to develop these three specific treatments while partnering with others to treat the diseases impacting these organs. The core competencies demonstrated by the Copernic platform technology will position the Company to become the preferred partner of company holding rights to genomic information and therapeutic genes, and/or who wish to expand product development in our field indications. The outcome of this strategy is to provide the Company with early revenue streams obtained from research, development, and manufactory agreements from corporate partners while the Company also develops its own intern programs. Copernicus intends to be the GMP-manufacturer of all gene transfer products bas on DNA nanoparticles, thereby leveraging our core competency to provide

[46] www.cgsys.com/

additional sources revenue. Copernicus can provide assistance from preclinical proof-of concept to DNA drug production. Each product developed utilizes similar modular Copernicus platform technology. This modular nature reduces the risk of product development and permits Copernicus perform the needed tasks faster, smarter, and for less cost.

Copernicus' lead product is for cystic fibrosis. A planned second therapeutic will be for treating blindness (RP) with a third product being a treatment for Parkinson's disease. Copernicus believes it has opportunities available to it and potential corporate collaborators in the following fields:

Application	Estimated Total Market ($Million)
Cystic Fibrosis	>2000
Retinitis Pigmentosa	>1000
Macular Degeneration	>4000
Diabetic retinopathy	>6000
Parkinson's Disease	>2000
Other CNS diseases	>10000
Cancer	>8000

Technologies

Copernicus: Delivering the Promise of Nucleic Acids as Therapeutics Nucleic acid-based therapies are a natural progression from development of genetic engineering in the 70's and the Human Genome Project of the late 90's. These emerging therapies introduce nucleic acids into cells to correct or modify genetic information to restore normal functionality. This technology can also silence aberrant or disease-causing genetic sequences. In each of these cases, nucleic acids intervene at the primary control point for cellular activity, gene expression. Nucleic acid therapeutics potentially offer novel therapies that cannot be addressed using conventional small molecule drugs or proteins. Additionally, these therapies provide a high level of cellular targeting with improved specificity of action, which can lower toxicity risks. A whole new way of treating disease is possible.

As stated by Nobel Prize winner Inder Verma, the major hurdle impeding nucleic acid-based therapies is "delivery, delivery, delivery." Dr. Verma is talking about the ability to safely and efficiently deliver nucleic acids to the cells of interest.

Most of the initial attempts at delivery have involved the use of engineered viruses. This was a logical path to follow as Nature had already designed viruses to deliver their own nucleic acid into cells. However, many shortcomings have been associated with the use of engineered viruses, both minor and major (including death and causing cancer).

Alternatively, non-viral Most of the initial attempts at delivery have involved the use of engineered viruses. This was a logical path to follow as Nature had already designed viruses to deliver their own nucleic acid into cells. However, many shortcomings have been associated with the use of engineered viruses, both minor and major (including death and causing cancer).

Alternatively, non-viral approaches have been attempted and were often found to be inefficient, especially in nondividing cells, which include essentially most of the cells of the body. Non-viral systems were also transient in their effects and often included toxicity issues. Copernicus Therapeutics, Inc. ("CTI") has developed an innovative nonviral approach based on condensing nucleic acids into nanoparticles, which has been found to avoid the many pitfalls associated with both viral and previous non-viral approaches. This CTI technology provides a very attractive alternative to prior delivery systems. The Company's nucleic acid nanotechnology platform is validated in humans with the development of a first-in-class therapeutic product for the treatment of Cystic Fibrosis. Additionally, CTI's collaborative research supports the development of first-in-class therapies to treat other serious diseases that have few therapeutic options, including diseases causing blindness (macular degeneration, diabetic retinopathy, and retinitis pigmentosa), airborne viral diseases (influenza A, SARS, and avian flu), and diseases of the brain (Parkinson's disease, stroke and Alzheimer's). The Copernicus technology addresses the delivery issue and is poised to deliver the promise of nucleic acids as therapeutics.

CytImmune Sciences Inc. [47]

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About CytImmune Sciences Inc.

CytImmune Sciences is a clinical stage nanomedicine company with a core focus on the discovery, development and commercialization of multifunctional, tumor-targeted therapies. Based on an R&D strategy which harnesses the unique properties of gold nanoparticles, cytotoxic agents, and biology of tumors, the Company is developing a pipeline of proprietary drug candidates binding potent anti-cancer agents --whose toxicity profiles currently prevent or severely limit clinical use --to its patented colloidal gold tumortargeting nanotechnology.

Leveraging its expertise in colloidal gold-based nanomedicines, CytImmune has also developed a patented, semi-synthetic in vitro immune system capable of producing fullyhuman monoclonal antibody (mAb) therapeutics. The Company's ability to produce fully human mAbs provides an additional pathway to develop proprietary anti-cancer therapeutics using its platform technology to create a separate class of nanomedicines.

The goal is to mitigate the risks of drug development and build from these core technologies families of first-in-class therapeutics with accelerated clinical timelines, new commercialization value, and – ultimately – greater patient benefits.

Founded in 1988, CytImmune has emerged as a global leader in the field of nanomedicine with the successful completion of its first-in-man targeted nanotherapeutic clinical trial. The

Company has more than 60 issued and pending patents for its colloidal gold nanotechnology and 11 issued and pending patents for its mAb technology in the US, EU, Japan and Canada.

Technologies

CytImmune's **tumor-targeting technology is highly versatile** and may be used for the safe and systemic administration of drugs that traffic directly to the site of disease - avoiding uptake by or accumulation in healthy organs and surrounding tissues.

The Company's nano-scale development strategy is to engineer new colloidal gold-based drug compounds which harness the therapeutic potential of potent anti-cancer agents, limit their biodistribution primarily to tumor sites, and add to TNF's biological actions. This core platform is the key to realizing improved patient outcomes.

CytImmune's approach offers the potential to enable and/or expand the clinical benefit of a variety of toxic agents (such as tumor necrosis factor alpha (TNF), interleukins/interferons, monoclonal antibodies, chemotherapeutic agents, etc.) which may be used to treat multiple types of solid tumors

[47] www.**cytimmune**.com/

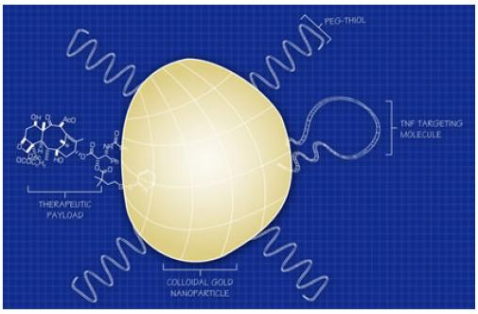
- either as monotherapies or in combination with existing standards of care. The Company[1]s nanomedicines function independent of tumor specific biochemistry and, therefore, do not depend on the type of cancer treated.

Having completed dosing of its Phase 1 trial, the early clinical data indicate that: (1) CytImmune safely and systemically delivered TNF in humans far beyond concentrations attained in previous human studies and (2) based on tissue biopsies from treated patients, Aurimune accumulates in and around tumor sites, avoids uptake by the liver and spleen, and is essentially absent from surrounding healthy tissues.

What is Colloidal Gold?

The use of colloidal gold as a human therapeutic dates back to the 1930's when it was shown to temporarily relieve joint inflammation associated with rheumatoid arthritis.Yet the lack of understanding of its mechanism of action has limited its therapeutic potential. The Company believes that the potential for colloidal gold in medicine is very broad, and, through an aggressive patent strategy the Company will seek to capture both its therapeutic and commercial potential. The Company made a rather surprising observation: animals injected with native cytokine exhibited strong toxicological responses, whereas animals receiving injections of cytokines bound to colloidal gold did not. This singular observation lead us to conclude that colloidal gold may be a universal, clinically safe, commercially sound drug/gene delivery system aggressive patent strategy the Company will seek to capture both its therapeutic and commercial potential. The Company made a rather surprising observation: animals injected with native cytokine exhibited strong toxicological responses, whereas animals receiving injections of cytokines bound to colloidal gold did not. This singular observation lead us to conclude that colloidal gold may be a universal, clinically safe, commercially sound drug/gene delivery system

How Does It Work?



• Polyethylene glycol (PEG) masks particles from immune recognition preventing uptake by liver and spleen
• Nanoparticles exit circulatory system only at the tumor neovasculature due to leakiness of blood vessels
• Particles too large to exit circulation elsewhere

• TNF targeting molecule on particle's surface binds to receptors causing vascular disruption in and around tumor sites.

Tumor Targeted Therapies

One of the most promising areas in the treatment of cancer has been the development of targeted anti-cancer therapeutics. However, past attempts to systemically deliver cytotoxic agents directly to the site of disease have been met with limited success. With the completion of its Phase 1 trial for Aurimune, a first-in-class tumor-targeted nanomedicine,

CytImmune believes that such site-specific drug delivery is now possible. areas in the treatment of cancer has been the development of targeted anti-cancer therapeutics. However, past attempts to systemically deliver cytotoxic agents directly to the site of disease have been met with limited success. With the completion of its Phase 1 trial for Aurimune, afirst-in-class tumor-targeted nanomedicine.

CytImmune believes that such site-specific drug delivery is now possible.

The mechanism underlying CytImmune's tumor-targeted delivery can be ascribed to the size and composition of the nanoparticles --regardless of tumor type. By simultaneously binding

TNF and PEG-Thiol to the surface of colloidal gold nanoparticles, the therapeutic payload travels safely through the blood stream avoiding immune detection and is preferentially delivered to the site of disease. At 27 nanometers in size, Aurimune primarily and preferentially exits the circulation through leaky, newly formed vasculature at tumor sites, selectively passing through gaps in blood vessel walls (fenestrations).

Preliminary data from our Phase 1 clinical trial indicate that Aurimuneis preferentially delivered to the site of disease with minimal accumulation in healthy tissue, as the electron microscopic analysis (below) of tissue biopsies from a cancer patient treated with Aurimune suggests.

Human Monoclonal Antibodies

Leveraging its expertise in colloidal gold-based nanomedicines, CytImmune has also developed a patented, semi-synthetic in vitro immune system capable of producing fully human monoclonal antibody (mAb) therapeutics. The Company's ability to produce fully human mAbs provides an additional pathway to develop proprietary anti-cancer therapeutics using its platform technology to create a separate class of nanomedicines.

CytImmune has developed a method to generate fully human monoclonal antibodies (mAbs) using lymphocytes from normal donors. The technology uses the properties of gold nanoparticles to create an "antigen presentation" system, which loosely mimics the natural presentation of antigens by cells. The Company has begun proof of principle studies with antibodies against multiple components of the interleukin-2 receptor to block the production of T-cells for the treatment of leukemia and lymphoma.

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ABOUT DELCATH

Delcath Systems (Nasdaq: DCTH) is at the forefront of the regional treatment of cancer with a promising therapy to shrink tumors in the liver. Delcath's Percutaneous Hepatic Perfusion (PHP™) technology allows physicians to deliver significantly higher doses of anti-cancer drugs to the liver without exposing the patient's entire body to those same potent levels of drug. PHP™ is an investigational treatment currently undergoing testing in Phase III and Phase II clinical trials.

Technologies

The Delcath System™, or Percutaneous Hepatic Perfusion (PHP)™, offers a new regionalized approach for the treatment of unresectable hepatic malignancies in which the drug Melphalan is administered via the hepatic artery and the venous effluent of the liver is collected and filtered using a percutaneously placed catheter and filtration system. The treatment is investigational, but observed benefits of the procedure include:

Minimally invasive – PHP™ utilizes a series of catheters and extracorporeal filters to infuse high doses of chemotherapeutic agents to tumors in the liver with minimal systemic exposure.

Higher Dosing – PHP™ allows infusion doses exceeding those of systemic or intra-arteriaal administration. Treatment Flexibility -PHP™ can be performed in an operating room or in a radiology suite under local or general anesthesia.

Repeatable Procedure - Unlike surgical isolated hepatic perfusion (IHP), which can be performed only once, PHP™ can be repeated several times. Patients within the trial usually receive the treatment at four-week intervals and up to ten treatments have been administered to a patient.

Decreased Toxicity - Filtration of the hepatic venous effluent can reduce systemic exposure of chemotherapy by 80% to 90% compared to hepatic artery infusion alone.

[48] www.delcath.com

DIATOS[49]

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About Diatos

Diatos S.A., a biopharmaceutical company, focuses on the research, development, and commercialization of targeted anti-cancer drugs. The company is developing a portfolio of drug candidates with new compounds that utilize its Vectocell delivery technology or its Tumor-Selective Prodrug technology, as well as with in-licensed candidate and marketed cancer therapies. Its drugs and drug candidates are designed to target various solid tumors, including breast cancer, prostate cancer, esophagus cancer, lung cancer, colorectal cancer, pancreas cancer, brain cancer, head and neck cancer, melanoma and Kaposi's sarcoma, and AML. The company's product portfolio includes DaunoXome, a drug marketed for the treatment of Kaposi's sarcoma; and DTS-301 and DTS-201, which are in clinical development for the treatment of various solid tumors. It also has a preclinical development drug, DTS-108, which aims to increase the efficacy of SN-38 while reducing the toxic effects of irinotecan. Diatos has a research and development collaboration agreement with Servier SA in order to develop the biodistribution of one of Servier's anti-cancer oncology candidate drugs by means of the Vectocell technology platform. The company was founded in 1999. Diatos is headquartered in Paris, France, and operates subsidiaries in Belgium and the United States

Diatos is a product-driven biopharmaceutical company dedicated to the development and commercialization of novel anti-cancer therapies. The company's therapeutic candidates DTS-201 and DTS-301, respectively a doxorubicin prodrug and a novel paclitaxel formulation, are planned to enter Phase I and Phase II clinical trials in 2005. Diatos is also expanding its product pipeline with new compounds that utilize the Diatos Peptide Vector (DPV) intra-cellular/intra-nuclear VectoCell® delivery technology or its Tumor-Selective Prodrug (TSP) technology as well as with in-licensed clinical-stage cancer therapies. Diatos has entered into research collaboration agreements with several European and US biotechnology and pharmaceutical companies for the use of Vectocell® technology.

Founded in 1999 as a spin-off from Institut Pasteur, Diatos has raised 33 million Euros to date from Sofinnova Partners (France), GIMV (Belgium), InterWest Partners (USA), Credit Agricole Private Equity (France), AGF Private Equity (France), Innoven Partenaires (France),

[49] www.linkedin.com/company/**diatos**

Société Générale Asset Management (France), NIF Ventures (Japan), Biotech Fund Flanders (Belgium), Sopartec (Belgium) and Institut Pasteur (France). Diatos has 43 employees, is headquartered in Paris and has operations in Belgium and the US.

Technologies

The Diatos Peptide Vector (DPV) intra-cellular/intra-nuclear Vectocell® delivery technology allows direct intra-cellular delivery using cell-penetrating peptides and provides access to previously inaccessible intra-cytoplasmic or intra-nuclear targets. Vectocell alters the biodistribution of small molecules, which may result in lower toxicity of therapeutic compounds. Servier and Diatos have been working together on applications of the Vectocell technology to Servier's development portfolio prior to entering this agreement.

"Our proprietary Vectocell® delivery technology is already being used to develop new therapies to treat cancer; and this key collaboration with a pharmaceutical partner is another example of the aptness of our technology in the efficient delivery of small-molecule therapeutics," said Dr. John Tchelingerian, President and Chief Executive Officer of Diatos.

ENZON Inc.[50]

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About Enzon

Enzon Pharmaceuticals, Inc. is a biopharmaceutical company dedicated to developing important medicines for patients with cancer. Enzon's drug development programs utilize several cutting-edge approaches, including its industry-leading PEGylation technology platform and the Locked Nucleic Acid (LNA) technology. Enzon's receives a royalty revenue stream from licensing partnerships for other products developed using the proprietary PEGylation technology.

Technologies

We continue to apply our PEGylation technology to a broad range of therapies, such as the PEGylated version of SN38, which has shown very encouraging results in preclinical studies." — Hong Zhao Ph.D., Director, Organic and Medicinal Chemistry. Enzon is dedicated to developing innovative therapies through a variety of advanced technologies. Enzon's proprietary PEGylation technology is a proven means of enabling or enhancing the performance of pharmaceuticals with delivery limitations, through the chemical attachment of polyethylene glycol or PEG via a linker. Advantages of PEGylation include increased efficacy, reduced toxicity, increased stability, and enhanced solubility. Click here to learn more about Enzon's PEGylation technologies. Enzon has also developed Customized Linker Technology™, which utilizes linkers designed to release the native molecule at a controlled rate.

PEGylation

We continue to apply this technology to a broad range of therapies, such as the PEGylated version of SN38, which has shown very encouraging results in preclinical studies." — Hong Zhao Ph.D., Director, Organic and Medicinal Chemistry. Enzon is dedicated to developing innovative therapies through a variety of advanced technologies. Enzon's proprietary PEGylation technology is a proven means of enabling or enhancing the performance of pharmaceuticals with delivery limitations, through the chemical attachment of polyethylene glycol or PEG via a linker. Advantages of PEGylation include increased efficacy, reduced toxicity, increased stability, and enhanced solubility. Click here to learn more about Enzon's PEGylation technologies. Enzon has also developed Customized Linker TechnologyTM, which utilizes linkers designed to release the native molecule at a controlled rate.

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Customized Linker Technology

Enzon's PEGylation expertise includes linker chemistries designed to incorporate a stable chemical bond between the native molecule and the PEG. Enzon's Customized Linker

Technology utilizes linkers designed to release the native molecule at a controlled rate. The customized linkers expand the utility of the Enzon's existing PEGylation technology, and offer a choice of releasable or permanent linkages to match each native drugs requirements.

Using this technology Enzon can potentially overcome the pharmacologic limitations for a broad universe of molecules and generate compounds with substantially enhanced therapeutic value over their unmodified forms.

Locked Nucleic Acid (LNA)

Enzon currently has a HIF-1 alpha antagonist in development and a Survivin Antagonistin clinical development and several additional targets in early preclinical research.

Royalty Products

We receive royalties on three marketed products that successfully utilize our proprietary PEGylation platform, namely PEGINTRON®, Macugen®, and CIMZIA®, with PEGINTRON being the largest source of our royalty income. We also could receive royalties on Hematide, which is currently in Phase III development, if approved.

PEGINTRON is a PEG-enhanced version of Merck's alpha interferon product, INTRON® A, which is used both as a monotherapy and in combination with REBETOL® (ribavirin) capsules for the treatment of chronic hepatitis C. The product has also been submitted for approval for adjuvant treatment of patients with Stage III melanoma. The application was recommended for approval by the FDA Oncology Drugs Advisory Committee in October 5, 2009. However, on October 30, 2009, the FDA issued a complete response letter to the Merck's supplemental Biologics License Application regarding PEGINTRON for this indication. Merck continues to work closely with the FDA to respond to outstanding concerns related to the PEGINTRON melanoma filing.

Macugen (pegaptanib sodium injection) is currently being marketed through a collaboration between OSI and Pfizer for the treatment of neovascular (wet) age-related macular degeneration, an eye disease associated with aging that destroys central vision.

CIMZIA was approved in April 2008 for the treatment of Crohn's disease and is marketed by UCB. In May 2009, CIMZIA was approved for adult patients suffering from moderate to severe rheumatoid arthritis.

Hematide is a synthetic peptide-based erythropoiesis-stimulating agent being evaluated by Affymax and Takeda Pharmaceutical in for the treatment of anemia in chronic kidney failure. At the end of Janaury 2010, Affymax announced that the Phase III trial was completed and top line results would be reported in the second quarter of 2010. If results are positive, the Company plans to submit an New Drug Application (NDA) later in 2010.

ENDOCYTE [51]

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About Endocyte

Great progress has been made in the development of new drugs to treat cancer and other serious illness. However, these therapies are often administered at suboptimal doses because of their effects on healthy tissue. The value of these therapies is further diminished because of the inability to predict in advance if a patient will respond to a particular therapy. Endocyte is addressing both of these issues using a new "drug guidance" technology.

Drug Guidance System

Endocyte's novel drug guidance system is designed to improve the specificity, safety, and efficacy of potent drugs by targeting them directly to diseased cells. Our technology can be used to deliver a variety of drug therapies, from small molecule cancer drugs to larger proteins and RNA-based therapies.

Predictive Medicine

Endocyte is also developing powerful companion diagnostic agents (such as EC20 and EC0652) that are designed to predict in advance if a patient will respond to our drug therapy. By linking our drug guidance system to a diagnostic imaging agent, we can generate a patient-specific targeting profile to help identify likely responders.

Strong Clinical Stage Pipeline

Today, Endocyte has six targeted cancer drugs in clinical trials. We believe our patented technology may also have applications in developing better drugs to treat diseases such as rheumatoid arthritis, osteoarthritis, and atherosclerosis. This proprietary technology is being used today by a number of drug companies in collaboration with Endocyte.

[51] www.endocyte.com

Technologies

A major problem in treating cancer and other serious illnesses is that highly toxic drugs are often administered at suboptimal doses because of their side effects on healthy tissues. By targeting drugs specifically to tumor cells or other diseased cells and avoiding normal healthy cells, it may be possible to treat patients with safer and more effective doses.

Endocyte's proprietary drug guidance system (DGS) is designed to deliver drugs directly to diseased cells. This DGS is composed of a targeting ligand that attaches to a drug and then binds to receptors over-expressed on the membranes of diseased cells.

Our lead program uses the vitamin folate to target cancer cells. Folate is required for cell division, and rapidly dividing cancer cells over-express a receptor for folate. By attaching drugs to folate, we are able to target drugs directly at cancer cells with less potential toxicity to surrounding healthy cells.

Our approach is unique from other targeting technologies, such as large antibodies. Our focus on small, high-affinity targeting ligands (300 times smaller than antibodies) facilitates their penetration into dense tumors and rapid clearance from the body, reducing the risk of toxicity to normal cells. This approach to targeted drug therapy opens up the potential for safer and more effective treatment approaches using:

. High-potency drugs that may not have been developed due to toxicity. Our pipeline includes drugs that are 1,000 to 10,000 times more potent than existing cancer therapies like cisplatin.

. A more effective dose-dense schedule to put constant pressure on the tumor. In early clinical studies, EC145 our a targeted super-potent vinca, was dosed daily for 3 consecutive weeks with minimal toxicity.

. A new combination of drugs that could not be dosed due to overlapping toxicity. Our drug EC0225 targets a combination of two highly potent chemotherapy drugs.

Preclinical data showed this drug could cure even very large tumors.

. Building a "Guided Drug"

. Endocyte's drug-discovery engine is capable of producing a number of improved targeted drugs for multiple diseases. Building a guided drug involves a three-step process designed to reduce development and clinical risk.

. *Step 1: Validate the Guidance System*

Our process begins by screening diseased cells for unique receptors. After identifying a receptor, we design a guidance system or targeting ligand that binds with high affinity to the target receptor. The guidance system is then attached to a diagnostic imaging agent that is tested in humans to ensure the guidance system targets the diseased cells and not normal cells. EC20, our folate-receptor guidance system, has demonstrated targeting in cancer and other diseases.

. *Step 2: Build a Pipeline of Targeted Therapies*

Once the guidance system (targeting ligand) has been validated in humans, a variety of potent therapeutic molecules are screened. We look for highly potent drugs with doselimiting toxicities. After a drug is identified, we attach it to the validated guidance system and compare it to the free drug in in-vitro and in-vivo models. If the guided drug is better than the free drug in terms of efficacy and safety, it is advanced into the clinic. By repeating this process for each drug, we are able to build a pipeline of unique drugs with potentially superior safety and efficacy.

. *Step 3 -Identify Patients Likely to Respond*

The final step is to use companion diagnostic imaging agents to identify patients likely to respond to a targeted therapy. These companion diagnostics use the same guidance system as the therapeutic drug and are incorporated into all of our clinical studies to determine whether each patient is an appropriate candidate for the therapeutic drug.

Predictive Medicine

A major problem with many drug therapies is the inability to predict patient response. New predictive medicine tools, such as companion diagnostic imaging, are needed to identify how well a patient will respond to a particular drug therapy.

Recognizing this critical need for new predictive medicine tools, Endocyte has developed molecular imaging companion diagnostic tools for all of its therapeutic product candidates.

The companion diagnostic agent attaches a molecular imaging agent to the same drug guidance system used for the therapeutic drug. The companion diagnostic provides a fullbody, real-time image that can be used to determine whether the guidance system is targeting the diseased cells.

These powerful companion diagnostics are being used in all of our trials to identify the most appropriate patient population for clinical testing.

The diagnostic images below were obtained following administration of our folate-receptor targeted imaging agent EC20-Tc99m. The patient on the left shows no targeting to tumor (negative profile). The patient on the right shows targeting to tumors (positive profile).

Potential Applications

Cancers that over-express folate receptors, such as ovarian, NSCLC, breast, colorectal, renal cell, and gastric cancer, affect more than 400,000 people in the United States. Folate is required for cellular division, and rapidly dividing cancer cells over-express receptors for the vitamin. It may be possible to treat these patients more effectively with a drug attached to a folate ligand that can be delivered directly to the folate receptors on the cancer cells. Endocyte is developing other targeting ligands beyond folate that may benefit additional cancer patients.

Looking beyond cancer, we are also advancing research to develop products that can target an essential immune cell – the activated macrophage – that plays a role in a number of diseases. Activated macrophages release pro-inflammatory agents, such as TNF and IL-2, which are the target of immune-modulating drugs such as Humira, Enbrel, and Kineret.

Working in collaboration with the Mayo Clinic and Purdue University, Endocyte hasdesigned and validated drug guidance systems that target activated macrophages involved in inflammatory diseases, such as rheumatoid arthritis, osteoarthritis, and atherosclerosis.

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About Eurand

Eurand is a specialty pharmaceutical company that develops, manufactures and commercializes enhanced pharmaceutical and biopharmaceutical products using our proprietary drug formulation technologies. A publicly traded company (NASDAQ: EURX), Eurand has operating units in the United States and Europe.

Eurand is dedicated to the continued development and commercialization of breakthrough products intended to satisfy patients' needs. Research efforts are focused on the development of treatment options with enhanced efficacy, superior safety, and convenient dosing. Eurand has a number of products in development for the company and its co-development partners that are commercialized worldwide. Through continued investment in R&D, Eurand has a very exciting pipeline of products in various stages of development that, upon approval for the market, will continue to bring benefits to patients and their caregivers.

Eurand's business strategy is focused in the following areas:

Sales and Marketing of Specialty Healthcare Products in the U.S.

Eurand is focused on the research, development and commercialization in the United States of products for use in the treatment of Cystic Fibrosis and gastrointestinal-related diseases.

Development & Licensing of Products and Technologies

Eurand is a leading global pharmaceutical technology company and is focused on the co-development of partnered products and the out-licensing of Eurand's products worldwide.

Eurand has one of the broadest ranges of drug delivery platforms in the industry, including:

[52] www.linkedin.com/company/**eurand**

- Bioavailability Enhancement
- Customized Drug Release
- Taste Masking / Orally Disintegrating Tablets (ODT)

Eurand uses these technologies to develop and expand the company's internal pipeline and to partner with pharmaceutical and biopharmaceutical companies to develop their products

Success in Commercialization with Industry-leading Partners

Eurand established partnerships with major pharmaceutical companies, as listed below. The relationships are based on either co-development of products using our partners' drug and Eurand's pharmaceutical technologies, or the licensing and distribution of Eurand's internally developed products.

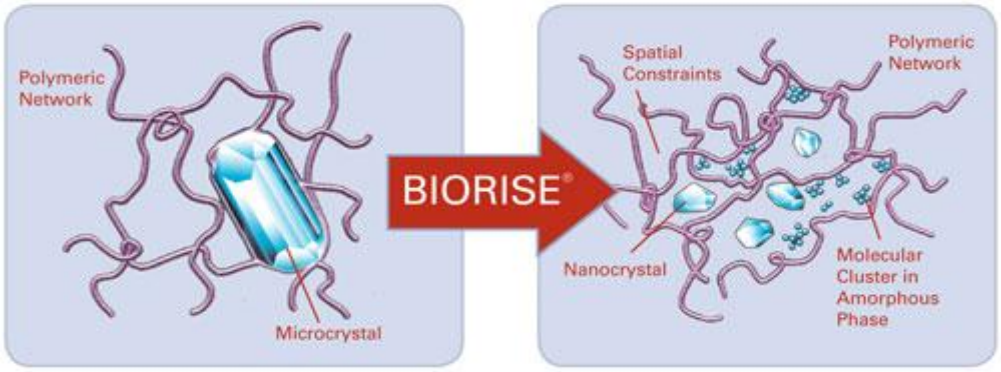
Technologies

Biorise

New Physical Entities (NPEs) are produced by breaking down the crystalline drug into nanocrystals and/or amorphous (noncrystalline) drug that is stabilized in a carrier system to maintain the drug in its activated form for the duration of its shelf life.

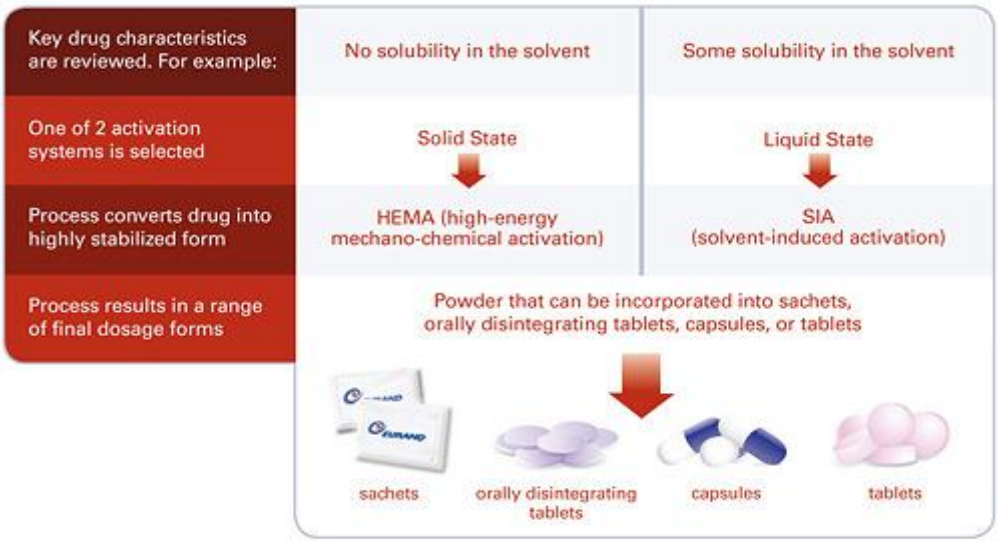
This approach creates a greater surface area to volume ratio that increases the intrinsic solubility and dissolution rate of poorly water-soluble drugs, thereby enhancing their rate and extent of absorption.

The Biorise technology can be applied to Class II compounds with solubilities in the range of **<10 to 500 µg/mL.**



Eurand has developed 2 distinct proprietary activation systems to create NPEs by converting drugs into their stabilized, thermodynamically activated state. These systems provide flexibility and allow the technology to be applied to a range of compounds with differing physicochemical characteristics.

The Biorise technology manufacturing process provides both time savings and cost efficiencies with its short cycle time, single processing step, batch consistency, and formulation stability.



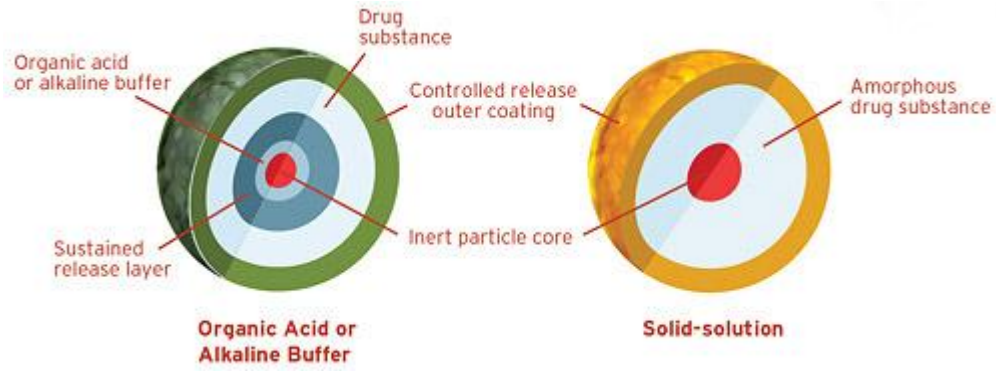
Biorise Proprietary Activation Systems

Advantages of Biorise

- Increases solubility of Class II compounds
- Provides a faster onset of action, equivalent therapy at lower doses, and/or oral dosing of poorly soluble drug candidates
- Short manufacturing cycle time and single processing step

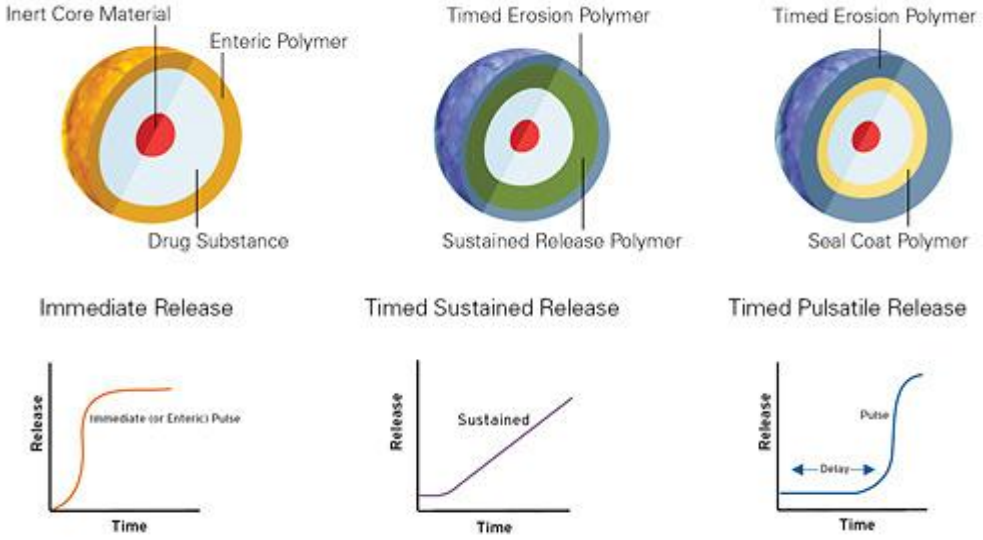
Diffucaps

Diffucaps is a multiparticulate bead system comprised of multiple layers of drug, excipients, and release-controlling polymers. The beads contain a layer of organic acid or alkaline buffer to control the solubility of a drug by creating an optimal pH microenvironment for drugs that exhibit poor solubility in intestinal pH, in environments with pH greater than 8.0, or in physiological fluids. Alternatively, the beads can contain a solid-solution of drug and crystallization inhibitor to enhance bioavailability by maintaining the drug in its amorphous state.



Diffucaps technology is especially suitable for drugs that traditionally require multiple daily doses or drugs needing customized release formulations. Each Diffucaps bead has an inert core surrounded by drug and coated with a functional polymer membrane to control the rate of drug release.

Diffucaps also can be combined with other proprietary Eurand technologies to optimize drug delivery. Diffucaps beads are <1.5 mm in diameter and can be filled into capsules or compressed into orally disintegrating tablets. In addition,as a multi-particulate system, Diffucaps products produced in capsules allow for the capsules to be opened and the contents used as a sprinkle on foods, providing a flexible dosage form for patients who experience difficulty swallowing tablets or capsules.



The flexibility of the Diffucaps system allows for easy adjustment of the release profile and dosing strength to achieve targeted *in vivo* results. For drug development partners involved in clinical testing, this flexibility simplifies dose-ranging studies because the beads can be encapsulated separately to create separate study arms.

Eurand's Diffucaps technology is used in several currently marketed products and in novel products in clinical development.

Advantages of Diffucaps

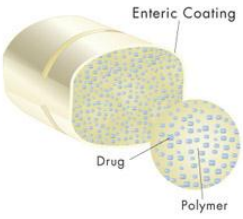
- Ideal for drugs exhibiting poor solubility in lower intestinal pH, in environments with pH above 8.0, or in physiological fluids
- Can combine multiple drugs and/or multiple release profiles in the same dosage form
- Simple formulation of dose-proportional strengths.
- Can minimize food effect

Diffutab

Diffutab technology uses a blend of hydrophilic and hydrophobic polymers to control drug release via diffusion through, and erosion of, a matrix tablet. Diffutabs are particularly useful for high-dose products and drugs that require sustained release and/or once-a-day dosing.

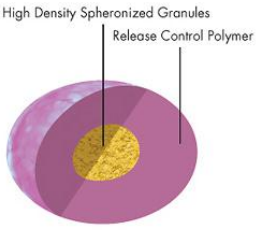
Advantages of Diffutabs

- Matrix tablet utilizes a combination of water soluble particles and active drug
- Suitable for high drug loading
- Supports sustained-release, once-a-day dosing



Orbexa

Eurand's Orbexa technology produces beads of a controlled size and density using granulation spheronization, and extrusion techniques. These beads provide high drug concentrations and can be coated with functional polymer membranes for additional release rate control.



Orbexa beads can be filled into capsules or single-dose sachets.

Advantages of Orbexa

- Aqueous or solvent-based granulation
- High-speed process is well suited for sensitive molecules like proteins
- Suitable for high drug loading

IMMUNOGEN, Inc.[53]

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About Immunogen

"ImmunoGen, Inc. develops targeted anticancer therapeutics using our expertise in cancer biology, engineered antibodies and highly potent cancer-cell killing agents.

We have established expertise in the development and humanization of tumor-targeting antibodies. As is well accepted, engineered antibodies can do an excellent job of selectively binding to cancer cells, but are typically sub-optimal in their ability to actually kill cancer cells. Thus, we have developed specialized cancer-cell killing agents to serve as payloads – to be attached to such antibodies for targeted delivery to tumor cells.

Our payload agents are 1,000-10,000 times more potent than traditional chemotherapy agents. We also have developed engineered linkers that keep the payload firmly attached to the antibody while the whole therapy is circulating through the bloodstream and then release it once the therapy has reached and entered a cancer cell.

We use our Targeted Antibody Payload (TAP) technology – together with our strong antibody expertise – to develop our own product candidates. We also selectively outlicense our technology to other companies for use with their engineered antibodies.

There are now many TAP compounds in clinical testing through our own product programs and those of our partners. The lead compound – trastuzumab-DM1 (T-DM1) – is in advanced clinical testing by Genentech* and Roche. Next are lorvotuzumab mertansine (IMGN901) for CD56+ solid tumors and multiple myeloma and SAR3419 for nonHodgkin's lymphoma.

ImmunoGen is headquartered in Waltham, Massachusetts. Our GMP manufacturing facility is in Norwood, Massachusetts. We have approximately 200 employees in R&D, clinical research, manufacturing, and administrative functions.

Our mission is to be the leader in the application of monoclonal antibodies for the treatment of cancer. We aim to achieve this by exploiting our expertise and experience in the identification of potential biological targets for cancer treatments, the development and humanization of monoclonal antibodies, and the creation of potent cell-killing agents designed for delivery by antibodies. Our Targeted Antibody Payload(TAP) technology uses tumor-targeting antibodies to deliver a highly potent cell-killing agent specifically to cancer cells to kill these cells with minimal damage to healthy tissue.

We are committed to the highest standards of scientific excellence and integrity for the benefit of patients, the medical community, our partners, shareholders and employees."

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[53] www.**immunogen**.com

Technologies

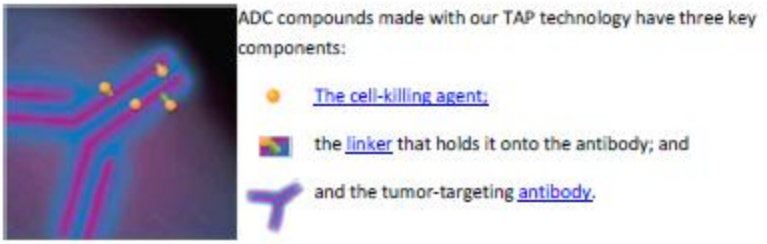
“We created our TAP technology to achieve more effective, better tolerated anticancer drugs.

A TAP compound is designed to focus its activity on cancer cells – to kill these cells while minimizing damage to healthy tissue.

A TAP compound consists of: a monoclonal antibody that binds specifically to a target – its antigen – found on cancer cells with a potent cell-killing agent attached. The antibody serves to target the compound specifically to cancer cells and the cell-killing agent serves to kill the cancer cells.

We use our TAP technology with our own antibodies to create anticancer compounds. If an antibody is proprietary to another company and not available for our own product programs, we may outlicense our TAP technology to that company. This enables us to derive a potential economic return not otherwise possible and expands the application of our technology.

ImmunoGen has established leadership in the field of antibody-drug conjugates (ADCs), with the most clinical publications on the most ADC compounds by the most companies across a range of cancers.”



“Our Cell-Killing Agents

Our cancer-cell killing agents (CKAs) are 1,000-to 10,000-fold more potent than traditional chemotherapy drugs. We developed them specifically for attachment to antibodies for targeted delivery to cancer cells.

The CKAs used in the TAP compounds in clinical testing act by interfering with tubulin and kill cancer cells when they attempt to undergo cell division. We continue to expand our portfolio of CKAs to further extend the utility of our technology, and unveiled our IGN family of DNA-acting agents at a scientific conference last year.”

“The Linker

Our linkers serve to keep our CKAs attached to the antibody until the TAP compound has entered a cancer cell. They then control the release of the CKA to kill the cancer cell.

Just as different cancers respond better to some drugs than others, we have found that different linkers work better for some cancers than others. Therefore, we have developed a portfolio of linkers to enable us, and our partners, to achieve the best product design for the cancer target. Our modular approach -separate linkers and CKAs -enables rapidly evaluation of different product designs.

We continue to expand our linker portfolio, and recently unveiled linkers that extend the utility of our TAP technology for cancers with multi-drug resistance."

"The Antibody

Each TAP compound contains an antibody that binds specifically to an antigen found on cancer cells. Each different TAP compound contains a different antibody, enabling different cancers to be targeted. For example, T-DM1, IMGN901, and SAR3419 are in development for HER2+ cancers, CD56+ cancers, and CD19+ cancers, respectively, as their antibodies target these different types of cancers.

While ImmunoGen is known for our TAP technology, we also have extensive antibody expertise.

Our manufacturing facility in Norwood, MA, helps us and our collaborators rapidly advance new TAP compounds into human trials, as it facilitates the production of drug supplies for initial clinical trials. Our Norwood facility has four production suites and all of the functions needed to manufacture TAP compounds in compliance with FDA current Good Manufacturing Practices (cGMP). ImmunoGen has gained extensive, unique experience in the production scale-up and manufacturing of conjugate compounds that a growing body of other companies have paid us to access."

NanoBioMagnetics, Inc.[54]

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About NanoBioMagnetics

NanoBioMagnetics (NBMI) is a nanobiomaterials company pioneering an emerging area of nanomedicine referred to as organ-assisting-device (OAD) technologies, in which magnetically responsive nanoparticles (MNP), under the influence of external shaped magnetic fields, are magnetically vectored to cause or drive a desired physiological event. OAD healthcare applications are being developed under two proprietary platforms (patents pending):

• Biostable Implants: MNP, implanted in tissue, nanomechanically drive tissue movement or vibration under the influence of an external oscillating magnetic field.

• Site-Specific Drug Delivery: MNP-therapeutic constructs, under the influence of external shaped magnetic fields, are vectored to a target site, followed by cell uptake.

As a nanobiomaterials company, NBMI has established collaborations with major research institutions for the validation of its OAD healthcare technologies. When successfully transferred to the clinical sector, OAD technologies will provide the physician and patient with new more effective therapeutic options for addressing the medical requirements of disease management.

The company's business model calls for the development and validation of OAD healthcare applications through collaborations with academic and pharma organizations, followed by a spin-off of a business venture in conjunction with pharma partnerships. Once established, pharma partners will move the respective OAD technologies forward through clinical evaluations and FDA clearances.

NBMI's proprietary magnetic vectoring technology also creates a pipeline of OAD technology applications, also under some stage of collaborative development, that include:

• Early stage cancer diagnostics
• Placement and positioning of stem cells
• Magnetic based biosensors
• Vectoring of down-regulating genes

A US Patent was awarded in 2008 for Hearing Amplification technology, and the company currently has 8 patents pending.

Technologies

Magnetic Vectoring

[54] www.nanobmi.com/

Nanotools for the Site-Specific Targeting of Therapeutics

The application of nanotechnology to the miniaturization of biomedical devices (Nanomedicine) is an emerging field, anticipated over the coming years to deliver a range of new therapeutic tools that will offer the patient and physician new and more effective treatment options. Biomagnetic delivery systems have been under development since the late '70's and early '80s. In general, historical magnetic delivery systems, while achieving tumor reduction via intra-arterial administration, have demonstrated little or no success through i.v. (systemic) administration.

In general, previous magnetic delivery systems have relied on accumulation of drug-carrier constructs at the tumor site, using external magnets to create gradients that encompassed the target site. The magnetic carriers, generally micro in size as opposed to nano-scaled, were to be held in place at the target site long enough for the drug to desorb from the carrier in the vicinity of the target site with anticipated tumor uptake. In theory, such systems were supposed to have significant advantages over non-targeting systemic administration; however, in actuality, as evidenced by the failure of clinical trials, little difference was observed between this procedure and the non-magnetic controls.

The solution to site-specific drug delivery is multi-factorial, combining stealthier constructs at the nanoscale, with more powerful shaped magnetic fields, the design of which present the potential for extending magnetic saturation to deeper tumor sites.

Successful magnetic vectoring of drug-loaded magnetically responsive nanoparticles requires that (1) the magnetic vectoring device produce a magnetic field of sufficient to achieve saturation of the magnetite at a distance far enough from the magnet face to reach the volume containing the tumor, and (2) the magnet must produce a field gradient strong enough to manipulate the particles as required to enhance tumor extravasation. We have established that arrays/configurations of permanent magnets can be constructed to extend and shape the magnetic field, establishing a foundation for scaling the technology to clinical levels.

We have successfully demonstrated the tumor-specific accumulation and extravasation of magnetically responsive nanoparticles on ovarian, breast and inflammatory breast cancer models in collaborations with scientists at the M D Anderson Cancer Center (Klostergaard J, Bankson J, Yuill W, and Seeney C., "Magnetic vectoring of magnetically-responsive nanoparticles within the murine peritoneum", J Magnetism Magnetic Materials, Vol 311, Issue 1, April 2007).

OAD Technology for the Site-Specific

Delivery of Chemotherapeutics

Overview: NBMI, in association with collaborators at The M D Anderson Cancer Center,

Houston, TX, have demonstrated in a live mouse model, in a scientific first, that constructs of magnetically responsive nanoparticles (MNP) can be externally vectored to a tumor site. The collaboration is now focusing research efforts on the efficacy of MNP constructs as vehicles for the site specific delivery of chemotherapeutics. Under this concept, MNP/chemotherapeutic configurations (such as MNP-Paclitaxel) are to be evaluated for effectiveness in the vectored delivery of high therapeutic doses internal to the tumor structure.

Commercialization Focus: As a vectored delivery mechanism for treating cancerous tissues, this technology offers the potential to maximize chemotherapeutic dosage forms while minimizing harmful or debilitating side effects. The effectiveness of this treatment methodology will lead to a reduction in the number of treatment per cycle with a concurrent increase in survival rates over longer time frames. The capability to vector therapeutics site specifically will lead to treatment options that do not now exist. At present, with ovarian cancer as an example, most cases present in the late stages of the disease, resulting in a survival rate of approximately 50% and a 5-year survival rate of less than 20%. There is currently no early stage detection and treatment methodology for this disease. The patient cost/benefit ratio is significantly high and breakthrough technologies are necessary for improvements in both quality of life and patient survival.

Patents are pending.

Advantages: The advantages of vectored delivery over conventional chemotherapeutic treatments are several:

- Increased effective dose forms
- Reduced treatment cycles
- Greater patient compliance
- Increased patient cost/benefit

Partnerships: NBMI is seeking joint development partnerships with major healthcare organizations with the vision and capacity for supporting the development and commercialization of new disruptive technology based on NBMI's OAD technology for the delivery of chemotherapeutics.

NanoCarrier, Inc.[55]

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About NanoCarrier

Mission:

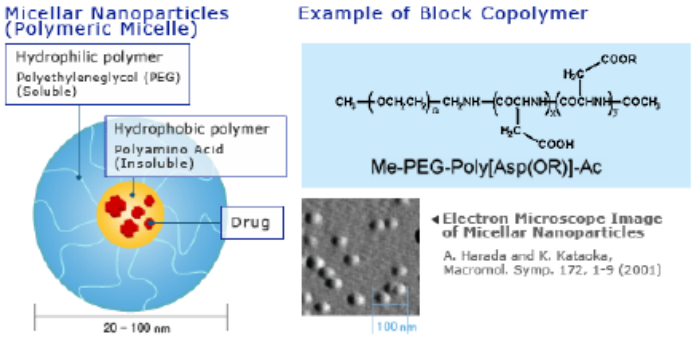
To contribute to the betterment of human health and medical progress by producing new drugs utilizing nanotechnology for improvement of patitents' Quality of Life (QOL).

Vision:

To be an innovative and leading biotech company, unrivalled in cancer field.

Technology

Micellar nanoparticles are composed of biocompatible block copolymers, comprising of hydrophilic polyethylene glycol (PEG) and hydrophobic polyamino acid. The formation of micelles, aggregates of 20-100 nanometer-size spheres, occurs when the block copolymers diffuse in water. Drugs and biologically active substances can be stably encapsulated in the hydrophobic inner core of the micelles. This technology can be applied to various types of compounds by modifying amino-acid side chains, etc. PEG coating on the surface ensures the micelles' stability in the bloodstream.



Micellar nanoparticle technology has a broad range of application in pharmaceutical development. For example, we can expect various benefits by controlling drug release from micelles: improved safety by lowering drug concentration below the level where adverse effects may occur; increased stability of drug in the bloodstream whose half-life is very short; and higher therapeutic efficacy by increasing the amount of drugs delivered to the targeted lesions etc.

[55] www.**nanocarrier**.co.jp/en/

Nano Interface Technology, Inc.[56]

Nano Interface Technology, Inc.
Lorton, VA , USA

About Nano Interface Technology

Nano Interface Technology, Inc. (NITI) was incorporated in 1998. Our mission is "Innovation in the Nano-biotechnology and Nanotechnology." We are a pioneering research organization committed to develop novel nanotechnologies in biotechnology, material sciences and the drug delivery areas. One of the major scientific challenges for the material scientists has been the development of processes that can help control the ultra-homogeneity in material properties at a molecular stage. We plan to commercialize our products by licensing technologies and developing products for the private companies. Most of our technologies are proprietary and is protected by the current patent law. We, at NITI, believe

that we have hit upon the Holy Grail of material production, where we can synthesize molecules under highly controlled conditions for specific applications. With the right reaction system and specific ambient conditions, we can control the properties and purity levels of our products. All of these processes can be easily scaled up for large-scale production, at commercial levels. Our vision is to significantly alter the processes and purity levels of materials by creating them at the molecular level.

Technologies

1. Nano-biomaterials for biomedical applications

The products and technologies developed by the NITI can be put to variety of uses. The target market has been chosen as the applications in the life sciences market. This market has been chosen in view of its relevance, ease of entry and potential size.
a. Developed superior nano-biomaterials using innovative materials processing technologies.
b. Focus on the development of the hydroxyapatite (HA) – used extensively as the latest material for the coating of the implants for the human body.c. The usage of HA synthesized by our process will decrease the failures of the implants, reduce the costs of the insurance and decrease the patient's trauma.

2. Nanorods

Alternative of the Carbon Nanotubes for the High Volume Applications: The cost of the carbon nanotubes is $100,000 -$200,000 per pound depending on the quality of the nanotubes. At that price, one can't use it for nanocomposites. In order to provide leap-frog improvement in the strength of nanocomposites and other applications, Nano Interface Technology has developed mesoporous nanorods which can provide nanorods of diameter

[56] www.**nanointerfacetech**.com/

-32 nm and of length 100-500 nm. These nanorods are synthesized by sol-gel chemistry and self-assembly of surfactants methods. Nanorods of silica, alumina or copper can easily be produced at a cost of $20 a pound.

3. Nano-encapsulated Anticancer Drugs

NITI is developing targeted controlled release of the chemotherapeutic agents which is already approved by the FDA for the human trials and was not successful due to the difficulty in maintaining high concentration of such anticancer drug around tumors. NITI's innovative targeted drug delivery system will allow to maintain high concentration of such drug around tumor to kill tumor. Hence, clinical trials and drug approval can be carried out on the fast track basis. The chemotherapeutic agents have $10 billions per year in the US alone. The world market for such drugs is $20 billions per year.

NEKTAR

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About Nektar

Corporate Overview

Nektar Therapeutics is a leading biopharmaceutical company developing a robust pipeline of novel therapeutics based on its advanced polymer conjugate chemistry technology platform. Nektar also partners with the top biopharmaceutical companies to bring new products to market. To date, Nektar's technology and drug development expertise have enabled nine approved products for partners, which include leading biopharmaceutical companies.

Technologies

Nektar's proprietary Advanced Polymer Conjugate Technology platform allows for a custom approach that capitalizes on the properties of polymer medicinal chemistry and an understanding of both a drug's characteristics and the body's mechanisms.
Our scientists identify specific drug molecules, both large and small, that with customized chemical modification using uniquely-designed polymers can be enabled or made more efficacious. With our proprietary conjugate approaches, suboptimal drugs can be designed to dial in desired therapeutic properties and create an optimized and potentially superior therapeutic
Using our novel and proprietary polymer conjugate approaches, suboptimal drugs can achieve optimal therapeutic properties. With our expertise as a leader in the field of
PEGylation, Nektar has created a set of new platform technologies. Nektar's Advanced
Polymer Conjugate Technology can be tailored in very specific and customized ways to optimize a wide range of molecule classes:

- Small Molecule Polymer Conjugates
- Pro-drug conjugates
- Large Molecule Polymer Conjugates
- Antibody fragment conjugates

Nektar has a dominant and broad patent estate with its technology platform across many therapeutic areas and modalities.

Background of PEGylation Technology

PEGylation has been a highly effective commercial strategy for the development of blockbuster therapeutics, such as Roche's PEGASYS® (interferon) and Amgen's Neulasta® (G-CSF). Nektar is the world leader in enabling therapeutics with PEGylation technology.

Every PEGylated product approved over the last fourteen years was enabled with Nektar technology. By partnering with the world's leading pharmaceutical companies, Nektar PEGylation technology has created over $6 billion in annual sales for our partners.

PEG (polyethylene glycol), a versatile technology, is a water soluble, amphiphilic, nontoxic, non-immunogenic compound that is safely cleared from the body. Its primary use to date in currently approved drugs is to favorably alter the pharmacokinetic properties of biologics. Early approaches to PEGylation were tremendously successful in creating blockbuster biologics but these did not fully leverage the flexibility and potential of the technology.

The limitations of older PEGylation approaches used with biologics are:
• Sub-optimal bioavailability and bioactivity
• Product is altered by PEG remaining attached to parent drug
• Limited ability to fine-tune properties of drug
• Did not allow for oral administration
• Not applicable to small molecules, antibody fragments, and peptides

Small Molecule Polymer Conjugates

This platform allows for the fine-tuning of the physicochemical properties of small molecule oral drugs to increase their therapeutic benefit. In addition, the approach can enable oral administration of parenterally-delivered small molecule drugs that have shown low bioavailability when delivered orally.

Benefits of this approach are: improved potency, increased oral bioavailability, modified biodistribution with enhanced pharmacodynamics, and reduced transport across specific membrane barriers in the body, such as the blood-brain barrier. A primary example of this CNS-exclusion application is represented by Oral NKTR-118, a novel peripheral opioid antagonist in Phase 2 clinical development.

Pro-Drug Conjugates

The pro-drug polymer conjugation approach can optimize the pharmacokinetics and pharmacodynamics of a drug to substantially increase both its efficacy and side effect profile. Nektar is currently using this platform with oncolytics, which typically have suboptimal half-lives which can limit their therapeutic efficacy. With Nektar's platform, these drugs can be modulated to optimize bioactivity and increase the sustained exposure of active drug to tumor cells in the body.

Nektar is using this approach with the two lead oncology candidates in our pipeline, NKTR102 and NKTR-105.

Large Molecule Polymer Conjugates

This platform builds on Nektar's expertise in enabling the successful PEGylated biologics on the market today. The approach has been designed to enable peptides, which are much smaller in size than biologics. Peptides are important in modulating many physiological processes in the body. Some of the benefits of working with peptides are: they are small, easily optimized, and can be quickly investigated for therapeutic potential. However, peptide drug discovery has been slowed by the extremely short half-life and limited bioavailability of these molecules.

Nektar scientists have designed a novel hydrolyzable linker that can be used to optimize the bioactivity of a peptide. Since the surface area of peptides is much smaller than larger biologics, the older PEGylation approaches can not be used. Through rational drug design and the use of Nektar's approach, a peptide's pharmacokinetics can be substantially improved and its half-life can be significantly extended. The approach can be used with proteins and larger molecules, as well.

Nektar is in the early stages of research with a number of peptides that utilize this proprietary approach.

Antibody Fragment Conjugates

This approach uses a large molecular weight polyethylene glycol conjugated to antibody fragments. The specially designed PEG then becomes part of the antibody fragment Fc. Since the antibody fragment is more like a biologic, this conjugation has a branched architecture with either stable or degradable linkage.

Where might this conjugation technique be beneficial?

• Parenterally administered molecules
• Need to enhance pharmacokinetics
The target of this conjugation is improved toxicity profile, extended half-life, and ease of synthesis with the antibody

Why use the Antibody Fragment Conjugates?
• Reduce antigenicity
• Reduce glomerular filtration rate
• Identify to proper linkage site to facilitate the re-production of identical conjugates from batch to batch
• Must still retain antigen-binding affinity and recognition

NeoPharm[57]

About NeoPharm

NeoPharm is a biopharmaceutical company developing and commercializing drugs for the treatment of various cancers and other diseases using enhanced and innovative drug delivery systems. NeoPharm is focused on providing life-saving and life-enhancing solutions to the drug delivery and oncology markets.

NeoPharm has multiple drug candidates in various points of clinical development, including a LEP-ETU Phase II trial for breast cancer, LE-DT Phase II trials for pancreatic and prostate cancers, an IL13-PE38 Phase I trial for idiopathic pulmonary fibrosis and an IL13-PE38 Phase I trial for untreatable brain diseases in humans.

NeoPharm's clinical trials have been structured to capitalize on broader indications of cancer and other diseases. With a reorganization strategy originally announced in April 2007, NeoPharm has achieved significant cost-savings and put into place an optimal cost structure which enables the company to focus primarily on the development of drug candidates. The company has significantly reduced its cash consumption rate and has resources available to fund current candidates in development into the third quarter of 2010.

Key initiatives completed as part of this reorganization include:

• Annualized cash consumption levels reduced to approximately $5 million
• Cost structure realigned to optimize the progress of several drug candidates to next strategic event
• Streamlined organization to include a core team of technical employees to support development activities and ensure regulatory compliance for all drug candidates.

Formed a new management team with relevant experience and expertise.

Technologies

NeoLipid® DRUG DELIVERY

NeoPharm uses novel proprietary lipids and improved procedures to entrap difficult-to deliver drugs in small, homogenous, and stable liposomes, which are microscopic membrane-like structures created from lipids (fats). Because tumor cells need to consume large amounts of fat to sustain their rapid growth, they recognize the liposomal drug as a potential source of nutrition.

NeoPharm's NeoLipid® innovative system of delivering anticancer drugs to tumors can potentially improve pharmacokinetics and reduce the toxicity of potent drugs, creating an opportunity for more comfortable-to-administer, well tolerated, and safer treatments for patients.

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[57] www.**neopharm**.com

NeoLipid® formulations are designed to produce small and homogenous drug particle sizes using simple, easy-to-use (ETU) reconstitutions of lyophilized (or freeze-dried) products with the goal of creating an extraordinarily stable liposomal product.. This is especially important during drug storage, reconstitution and administration to the patient.

NeoPharm believes NeoLipid® technology may have applications in a variety of other areas in addition to the drug product candidates in clinical development.

Potential advantages of NeoLipid® Drug Delivery Technology:

- Higher anticancer potency
- Broader range of drugs
- Toxicity may be reduced
- Fewer perceived side effects

NeoPharm intends to explore the use of its proprietary NeoLipid® liposomal drug delivery technology in terms of life cycle management, with the goal of extending patent life and/ or modifying the pharmacokinetic profile of existing cancer drugs, and by utilizing the platform to develop new drugs. NeoPharm is aware of several widely used cancer drugs that are nearing patent expiration, as well as other widely used cancer drugs with patents that have expired. When a drug is combined with another agent or delivery system in a novel way, its patent life may be extended. Additionally, while many chemotherapeutic drugs have been effective for the treatment of cancer, these drugs have been limited in their use because of adverse side effects and difficulties in administration. NeoPharm's NeoLipid® drug delivery technology may increase the usefulness of these compounds as improved anti-cancer treatments. Finally, NeoPharm believes that its liposomal drug delivery technology may provide a platform for the development of novel therapeutic agents for cancer drug development.

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LEP-ETU

LEP-ETU is NeoPharm's NeoLipid® liposomal formulation of the widely used cancer drug, paclitaxel. Paclitaxel, also known as Taxol® (Bristol-Myers Squibb Company), has been approved in the U.S. for the treatment of ovarian, breast and lung cancers. Despite paclitaxel's wide use and tumor cytotoxic characteristics, its effectiveness can be limited by its adverse side effects, which can include nausea, vomiting, hair loss and nerve and muscle pain. Because of the chemical characteristics of paclitaxel, it

cannot be introduced into the body unless it is first formulated in a mixture of castor oil (Cremophor®) and ethanol, which can lead to significant side effects such as hypersensitivity reactions and cardiac toxicities.

The Company hopes to show that its proprietary NeoLipid® technology, which eliminates the need for Cremophor and ethanol, permits delivery of paclitaxel treatment with fewer side effects.

In the first quarter of 2009, NeoPharm completed the targeted enrollment of 35 patients for the first part of its Phase II open-label, multi-center outpatient study in India designed to evaluate the anti-tumor effect and safety/ tolerability of LEP-ETU in metastatic breast cancer. All of the patients in the first part of the study have received a dose of 275 mg/m2 every three weeks without the detection of any significant infusion related problems or unexpected toxicities and showed a response rate of 46% compared to 11% with free Taxol® and 22% with Abraxane®.

NeoPharm has started another Phase II trial for recurrent breast cancer to enroll 35 more patients while rapidly working to embark on a Phase III randomized trail of LEP with free Taxol® as a comparator arm in metastatic breast cancer patients with the goal being to achieve regulatory approval of LEP as an effective modality for the treatment of cancer patients as early as possible.

LE-DT

LE-DT is NeoPharm's NeoLipid® liposomal formulation of the anti-cancer agent docetaxel, which is the active ingredient in Sanofi Aventis' Taxotere®, approved for use in certain breast cancer, non-small cell lung cancer, gastric adenocarcinoma, head and neck cancer indications, and prostate cancer.

NeoPharm has completed a multi-center Phase I clinical trial for LE-DT for the treatment of patients with metastatic solid tumors. This Phase I study was designed to define the maximum tolerated dose ("MTD") and was conducted at The Lombardi Comprehensive

Cancer Center at Georgetown University and at TGen Clinical Research Services at Scottsdale Healthcare. The data from the trial demonstrated that LE-DT has minimal toxicities compared to Taxotere®, in particular, peripheral neurotoxicity and water retention (edema).

In the first quarter of 2010, NeoPharm expects to enroll patients in a Phase II study of LEDT for locally advanced or metastatic pancreatic patients. The open-label, Phase II study is designed to determine the antitumor effect of LE-DT in locally advanced pancreatic cancer patients as evidenced radiologically with CA 19-9 as the surrogate biological marker.

In addition, NeoPharm is planning another Phase II study of LE-DT for prostate cancer patients. This open-label, Phase II study will define the clinical activity of LE-DT as an antitumor response in soft tissues as defined by the serum Prostate Specific Antigen ("PSA") level as a biological surrogate marker, disease response, progression-free survival and quality of life in patients with metastatic prostate cancer. NeoPharm anticipates a total of 63 patients to be enrolled in this Phase II trial at up to six locations in the United States and overseas.

Depending on the outcome of these clinical trials, NeoPharm may decide to undertake multicenter and multinational Phase III trials in these indications after thorough discussions with the FDA.

LE-rafAON

A new formulation of LE-rafAON, NeoPharm's NeoLipid® liposomal formulation of the antisense oligonucleotide agent, c-raf, is expected to have minimal infusion-related toxicities. All preclinical studies related to the submission of a revised IND to the FDA have been completed and the data is positive.

The antisense oligonucleotide agent, c-raf, has shown significant down regulation of the gene in Preclinical studies. Also, LE-rafAON has exhibited significant radiation sensitization and chemo sensitization with other anticancer agents such as Gemcitabine and Paclitaxel in human xenograft models in mice in Pancreatic and Prostate tumors. NeoPharm plans to perform the bridging Phase I trial with this newly formulated LE-rafAON and thereafter start

Phase II trials in pancreatic and prostate cancer models where this gene seems to be potentially over-expressed. Neopharm intends to further develop the NeoLipid® drug product candidates by using internal resources and by continuing to collaborate with other companies and leading governmental and educational institutions.

LE-SN38

LE-SN38 is NeoPharm's NeoLipid® liposomal formulation of SN-38, the active metabolite of Camptosar® (Pfizer Inc.), a chemotherapeutic pro-drug, which is used as a first-line and second-line colorectal cancer treatment. At the present time, without the NeoLipid® system, SN-38 is insoluble and can only be used to treat cancer by administering the pro-drug Camptosar®. A pro-drug is a compound that is converted into the active drug in the body. However, Camptosar® is converted into SN-38 in the liver at different rates by different patients, and this variability in conversion rates can result in suboptimal dosing and adverse side effects, such as severe diarrhea. We hope to show that our proprietary NeoLipid® technology permits delivery of SN-38 to the tumor cells without the need for conversion, therefore minimizing variability and optimizing dose with minimal side effects.

Results from our 2004 Phase I clinical trial provided evidence of the safety and tolerability of LE-SN38 and established a maximum tolerated dose (MTD) of 35 mg/m2 for all but a small subset of patients who metabolize SN-38 slowly. Pharmacokinetic analysis of blood samples from patients treated with LE-SN38 showed that blood levels and systemic drug exposure to SN-38 were comparable to or greater than that expected from the marketed Camptosar® dose based on previously published studies.

During the second quarter of 2006, in conjunction with the Cancer and Leukemia Group B, or CALGB, NeoPharm initiated enrollment in a Phase II clinical trial with LE-SN38 in metastatic colorectal cancer patients, and completed enrollment of the 21st patient in December, 2006.

In March 2007, the Company announced that the interim analysis of data following the completion of treatment of the first 21 patients demonstrated disease stabilization, but the study did not achieve the primary tumor response endpoint. The Company is reviewing the data and, in particular, examining the patients' demography, prior chemotherapy exposure, advanced stage of the disease, and other related factors. It is possible that patients whowere enrolled in this trial were exposed to other chemotherapy regimens prior to enrolling and that this prior exposure may be the reason the study did not achieve its primary endpoint. The Company is also assessing the potential next steps for this project which may include additional data analyses and the possibility of other studies related to lung cancer and breast cancer with LE-SN38.

Tumor Targeting

Cintredekin Besudotox

The drug product candidate which we have advanced the furthest is Cintredekin Besudotox, a tumor-targeting toxin being developed as a treatment for glioblastoma multiforme, or GBM, a deadly form of brain cancer.

Glioblastoma multiformes (GBM) is the most common type of malignant primary brain tumor in adults. They are very aggressive, having tentacles that spread and mix with normal brain tissue, damaging the adjacent tissue as they grow uncontrollably in the brain.

Treatment success has not significantly changed over the last 20 years, with most patients living less than one year after diagnosis despite aggressive surgery, radiation and chemotherapy.

Radiation therapy has been the most effective adjuvant therapy for these tumors, but the inherent resistance to radiation therapy and the risk of damaging the adjacent normal brain tissue limits its overall efficacy. GBM is intrinsically resistant to most chemotherapy and very few drugs cross the natural barrier present in the blood vessels of the brain (blood-brain barrier) which means that even drugs that work in the laboratory and in animals cannot reach the tumor cells within the brain. This unfortunate combination has resulted in only two FDA approved chemotherapy for this type of tumor with two forms of delivery, by vein or by local biodegradable wafers. The impact of these approved therapies increases survival in patients with this deadly tumor by only a few weeks.

Cintredekin Besudotox delivered by convection-enhanced delivery (direct micro infusion into the brain), on the other hand, is designed to molecularly target the tumor cells while sparing the healthy brain tissue. This form of regional and molecular targeting may represent one of the first scientifically sound treatment regimens, providing hope for overcoming one of the greatest hurdles in brain tumor therapy. The very problem that prevented drugs from entering the brain may now be used to keep the drug in the brain.

Cintredekin Besudotox is a recombinant protein consisting of a single molecule composed of two parts: a tumor-targeting molecule and a cytotoxic agent. The targeting component consists of interleukin 13(IL-13), an immune regulatory cytokine. Malignant glioma cells, as compared to normal

brain cells, express IL-13 receptors at a higher density. The cytotoxic agent is a potent bacterially derived toxin called PE38. Cintredekin Besudotox is designed to detect and bind IL-13 receptors on the surface of malignant glioma cells and selectively deliver PE38 to destroy tumor cells. Cintredekin Besudotox is administered by a technique known as convection-enhanced delivery, or CED, in which the drug is delivered through catheters inserted in brain tissue surrounding the tumor (peritumoral administration) or into the tumor (intratumoral administration) following surgical resection of the tumor. CED is designed to infuse Cintredekin Besudotox directly to the tumor site and adjacent brain tissue with the goal of killing resident tumor cells and preventing recurrence of tumor cell growth.

We hope to show that this method of delivery minimizes both damage to the surrounding cell and toxicity from systemic drug exposure.

We have exclusively licensed Cintredekin Besudotox from the NIH and the FDA, and have been developing this drug product candidate under a Cooperative Research and

Development Agreement, or CRADA, with the FDA Center for Biologics Evaluation and Research, or CBER. Cintredekin Besudotox has received orphan drug designation in the US and Europe and FDA has designated it for the fast track drug development program. In addition, Cintredekin Besudotox has been selected to participate in the FDA's Continuous Marketing Application, CMA, Pilot 2 program. We also hold a non-exclusive license to utilize a patented process owned by the U.S. government relating to convection enhanced delivery, or CED, for use with drugs, including Cintredekin Besudotox, in the treatment of gliomas.

Novosom AG[58]

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About Novosom AG

Novosom AG has solved the major obstacle towards DNA therapeutics delivery of the therapeutic principle towards the cell interior. Since the discovery of DNA-based therapies such as siRNA, antisense or decoy oligonucleotides, there has been a running problem of how to transmit these delicate nucleic acids undamaged to the cell interior where they can exert their therapeutic effects. Novosom has developed a pioneering fully charge reversible liposomal delivery technology for these DNA- based therapeutics (SMARTICLES) and is working with its partners to develop a range of therapeutic products addressing inflammation, oncology and liver diseases. The company is located in Halle, Germany.

Technologies

SMARTICLES®

Enabling Systemic DNA Therapeutics.
The early promise of first generation DNA-based therapeutic approaches like si RNA, antisense or decoys foundered on the difficulty of delivering these nucleic acid therapies. Chemical modification, cationic vectors, modified cationic vectors, viral vectors and other technologies have been tried with limited success so far. Novosom's solution has been develop a pioneering liposomal technology with a fully reversible surface charge: SMARTICLES.
The SMARTICLES technology allows the delivery of active substances inside the cell either for topical or systemic applications. What makes them different from standard liposomal delivery technologies is that they have a fully reversible surface charge. This unique characteristic is ideally suited to the delivery of encapsulated nucleic acids from injection, through stable and aggregate-free travel within the bloodstream, across cell boundaries to release the oligonucleotides inside the cell.
SMARTICLES are an enabler for the use of oligonucleotides in systemic and topical treatments. They have proven to be a safe and versatile technology that, as for March 2006, is available in GMP quality suitable for use in humans. Novosom has data with both singe stranded and double stranded oligonucleotide thecnologies in RA, IBD, transplant, liver diseases and xenograft oncology models. In addition, initial GLP toxicity studies have shown very high tolerability of the carrier. The company has secured SMARTICLES with a number of patent families that cover the technology, its components and manufacturing.

[58] www.**novosom**.com

Mirus[59]

About Mirus

Mirus Bio LLC is a life science company focused on discovering, developing and commercializing innovative nucleic acid based technologies and products.

Mirus R&D uniquely integrates nucleic acid delivery and chemistry, a core competency which is unmatched in the industry. This serves as the foundation for its novel research reagents

Mirus is a recognized leader in developing innovative nucleic acid research reagents, distinguished by its many accomplishments:

. First to develop an siRNA transfection reagent (2001)

. Pioneered development of high efficiency/low toxicity transfection formulations

. First to market a single step nucleic acid labeling technology

. Unique technology to label native, biologically relevant short RNA species such as microRNA

Mirus' TransIT® Reagents are unique lipid and polymer formulations that achieve superior delivery efficiency of pDNA and siRNA with minimal cytotoxic effects. They have been optimized for In Vitro delivery in a variety of mammalian cells as well as for In Vivo delivery in small animals. The Ingenio™ Electroporation Solution allows researchers to deliver nucleic acids to cells that are resistant to transfections.

The company's Label IT® Kits employ proprietary chemistry to covalently attach labeling molecules to DNA and RNA. This simple one-step process is faster and more robust than traditional multi-step enzymatic labeling, and can be used for intracellular tracking, chromosome analysis, and microarray labeling.

Technologies

TransIT® In Vivo Gene Delivery System

A nontoxic, polymer based In Vivo delivery system for the delivery of DNA or siRNA to the livers of laboratory mice using methods including hydrodynamic tail vein injection
. Polymer Mediated DNA Delivery -Achieve higher levels of gene expression compared to polylysine and PEI methods.
. Versatile Platform -Suitable for DNA delivery using methods including hydrodynamic tail vein injection to the mouse strain of your choice.
. Low Toxicity - Normal mouse activity levels are restored within minutes after the injection

[59] www.**mirus**bio.com

PCI Biotech Holding ASA[60]

About PCI Biotech

The strategy of PCI Biotech Holding ASA (PCI Biotech) is to commercialise a patented photochemical drug delivery technology for use in therapeutic treatment.

The company was established in 2000 as a subsidiary of the Norwegian pharmaceutical company Photocure ASA. PCI Biotech has been listed on Oslo Axess since June 2008 following a demerger from Photocure ASA.

PCI Biotech receives substantial public funding from the Norwegian Research Council and from the EU.

Photochemical internalisation is a drug delivery technology for targeted delivery of macromolecules and other membrane-impermeable drugs.

PCI can be used within many areas, including:

- gene therapy
- protein therapy
- oligonucleotide therapy
- chemotherapy
- nanomedicine

The PCI technology has great advantages as it may:

- enhance and target drug delivery
- make macromolecule delivery more efficient
- make possible the therapeutic use of molecules that it has hitherto been impossible to use, due to e.g. too low delivery efficiency or too high toxicity in non-target tissues.

Technologies

PCI is a technology for light-directed drug delivery and was developed to introduce therapeutic molecules in a biologically active form specifically into diseased cells.

PCI can enhance the delivery of all molecules taken into the cell by endocytosis. This includes most types of macromolecules, drugs carried by antibodies or nanoparticles, as well as some small molecule drugs.

The basis of the PCI technology is a light-induced rupture of endocytic vesicles, releasing endocytosed molecules into the cell cytosol, from where they can reach their intracellular target of action, realizing their therapeutic potential.

[60] www.**pcibiotech**.no

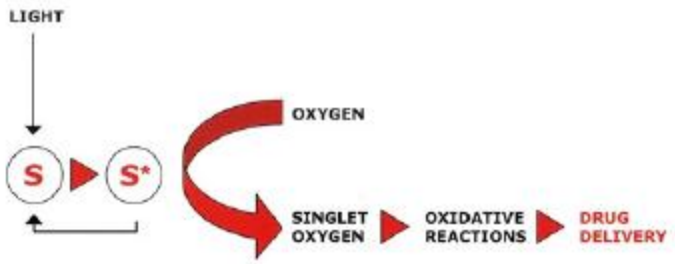
The PCI effect is achieved by the use of photosensitising compounds specifically localising in the membranes of endocytic vesicles, destroying these membranes by an oxidative process after illumination. Photosensitising compounds:

- can be administered systemically
- will in many cases localise preferentially in diseased tissues (e.g. tumours)
- generally have low toxicity in non-illuminated areas
- are in clinical use for cancer and other therapies today (photodynamic therapy)

The PCI technology has a potential to improve the effect both of existing drugs and of emerging treatments such as gene therapy and other therapies based on nanotechnology or on biotechnological principles.

In the PCI technology, photosensitising molecules (photosensitisers) are used to exploit the energy in visible light for delivering drugs.

Photosensitisers (S) are molecules that upon absorption of light become excited to an excited state (S*), initiating further photochemical reactions. The photochemical reactions of the photosensitisers used in PCI proceed mainly via a pathway where the energy from the excited photosensitiser molecule is transferred to oxygen, inducing formation of so-called singlet oxygen. Schematically: state (S*), initiating further photochemical reactions. The photochemical reactions of the photosensitisers used in PCI proceed mainly via a pathway where the energy from the excited photosensitiser molecule is transferred to oxygen, inducing formation of so-called singlet oxygen. Schematically:



* Singlet oxygen is a highly reactive form of oxygen that can oxidize various biomolecules, inducing damage in various cellular structures.

* Some photosensitisers localise in the membranes of endosomes and lysosomes, and light activation of such sensitisers destroys these membranes and releases the organelle contents into the cytosol. Thus, photochemical treatment may be used to translocate endocytosed therapeutic macromolecules from endocytic vesicles and into the cytosol, from where they have access to other intracellular compartments.

* In cells, singlet oxygen has a very short short range of action (10-20 nm). Therefore, only targets very close to the generated singlet oxygen will be affected by the photochemical reactions, and the therapeutic molecules to be delivered will as a rule be left unaffected.

* PCI Biotech is developing a proprietary photosensitiser specially designed for in vivo use with the PCI technology.

The potential of PCI

Macromolecules are widely acknowledged to have a large potential as therapeutic agents, and numerous clinical trials both with gene, protein and oligonucleotide therapy are underway.

In order to have a therapeutic effect, many of these molecules have to enter into a target cell and reach an intracellular target of action. This is also the case for several other classes of therapeutically interesting molecules, e.g. molecules carried in nanoparticles.

The therapeutic potential of such compounds is severely challenged by the obstacles of intracellular delivery, and many studies have been hampered by the lack of proper technologies for delivery of the therapeutic molecules to the target cells.

Advantages of the PCI technology

• PCI induces delivery of molecules into the cells by illumination.

• PCI makes drug delivery efficient exactly at the site where drug activity is desired, sparing non-target tissues from possible side effects of the drug.

• PCI is very efficient for delivery of classes of molecules where other efficient delivery systems are still lacking.

• PCI can unleash the therapeutic potential of a host of therapeutically very promising molecules.

The PCI technology can also have important uses in vitro as a general technology for delivery of macromolecules into cells, and can be used both in academic research and for industrial applications (e.g. in drug target validation). PCI Biotech has developed a light source, LumiSouce®, for use in in vitro research.

Quest Pharmatech Inc.[61]

About Quest Pharmatech

Profile

Quest is an Alberta-based biotechnology company developing a portfolio of product candidates for the treatment of cancer by combining immunotherapeutic antibodies with chemotherapy, photodynamic therapy, radioimmunotherapy or immunoadjuvants.

Overview

Quest is positioned as a drug development company focused on novel therapies for the treatment of cancer.

• Maximize growth by concentrating resources on drug development and extracting value to support this activity through strategic partners.

• Reduce risk by acquiring products or technologies that are close to attaining, or have already attained, clinical status.

• Participate in high-growth markets, focus on diseases with unmet treatment needs or near-to-market potential.

• Develop proprietary, unique multi-tiered approach to the treatment of cancer.

Technologies

Did not have drug delivery systems yet

[61] www.**questpharmatech**.com

Seattle Genetics[62]

About Seattle Genetics

"At Seattle Genetics, we are focused on developing innovative antibody-based therapies that improve clinical outcomes for patients with cancer and autoimmune diseases. We are dedicated to addressing unmet medical needs, and strive to achieve that goal through excellence in clinical development.

Focusing on Clinical Development Seattle Genetics is a clinical stage biotechnology company advancing a broad product pipeline of antibody-based therapies. Our lead program, brentuximab vedotin (SGN-35), is in a pivotal trial under a Special Protocol Assessment with the FDA for patients with relapsed or refractory Hodgkin lymphoma. Brentuximab vedotin is empowered by Seattle Genetics' proprietary antibody-drug conjugate (ADC) technology. In December 2009, we entered into an agreement with Millennium: The Takeda Oncology Company under which Seattle Genetics retains full commercialization rights to brentuximab vedotin in the United States and Canada, while Millennium obtained rights to commercialize the product candidate in all other countries.

In addition to brentuximab vedotin, Seattle Genetics is conducting clinical trials with four other product candidates, lintuzumab (SGN-33), dacetuzumab (SGN-40) and SGN-75, for the treatment of cancer, and SGN-70, for autoimmune diseases. We are also advancing a pipeline of promising preclinical candidates and have robust research and development capabilities that are our engine for innovation and long-term growth.

Our proprietary ADC technology empowers antibodies by stably linking them to cell-killing drug payloads. The drug payload is inactive until released from the antibody inside the targeted cancer cell, thereby sparing normal tissue the toxicity of traditional chemotherapy.

In addition to brentuximab vedotin, SGN-75 is an ADC that is in a phase I clinical trial and we are developing several preclinical ADC product candidates, including ASG-5ME, which is advancing towards planned 2010 clinical trials for prostate and pancreatic cancer."

"Expanding Our Opportunities Through Collaboration Collaborating with leading biopharmaceutical companies is a cornerstone of Seattle Genetics' business strategy.

Product-focused collaborations, such as our collaboration agreement with Millennium: The Takeda Oncology Company to globally develop and commercialize brentuximab vedotin, provide significant near-and mid-term funding while bringing in additional resources and expertise to support, advance and expand promising development programs. Collaboration and license agreements around our proprietary ADC technology also generate cash for the company - approximately $120 million to date -while providing further clinical validation of the ADC platform and, in some cases, opening the door to new product development opportunities."

Technologies

Seattle Genetics' proprietary antibody-drug conjugate (ADC) technology empowers monoclonal antibodies by attaching them to cell-killing payloads. Our ADCs employ highly stable linker systems to attach antibodies to synthetic, potent drugs. The linkers are designed to be stable in the bloodstream

[62] www.seagen.com

but to release their drug payloads under specific conditions once inside target cells, thereby sparing healthy tissues many of the toxic effects of traditional chemotherapy.

"The key components of our ADC technology are the stable, enzyme-cleavable linkers and the highly potent, synthetic cytotoxic drugs. Our novel linkers have been shown in preclinical models to be up to 10 times more stable in blood than conventional means of attaching drugs to antibodies. We have also developed a highly potent class of antitubulin drugs called auristatins, including monomethyl auristatin E (MMAE) and monomethyl auristatin F (MMAF). These auristatins are 100 to 1000 fold more potent than traditional chemotherapy drugs. Importantly, since both the linker and drug components are synthetic, our ADC technology is readily scalable, representing an improvement over natural product drug systems that are typically more challenging and expensive to produce.

Our lead ADC, brentuximab vedotin (SGN-35), comprises an anti-CD30 monoclonal antibody attached to MMAE through an enzyme-cleavable linker system. CD30 is expressed on Hodgkin lymphoma, various types of T-cell non-Hodgkin lymphomas and other hematologic malignancies. In a phase I dose-escalation clinical trial of brentuximab vedotin for CD30-positive malignancies, primarily Hodgkin lymphoma, at doses of 1.2 milligrams per kilogram and higher administered every three weeks, 54% of patients achieved an objective response (complete and partial responses), of which 39% were complete responses.

Brentuximab vedotin was generally well tolerated with the majority of adverse events being Grade 1 and 2. These promising findings are in contrast to clinical data with the unconjugated antibody, which did not induce objective responses in a similar population of Hodgkin lymphoma patients.

We have also reported substantial preclinical data with brentuximab vedotin, including data demonstrating that the targeting ability of brentuximab vedotin results in concentrations of MMAE within tumors up to 30-fold higher than non-targeted drugs. Further, MMAE tumor concentrations were 1000 fold greater than MMAE blood concentrations following dosing with brentuximab vedotin. These preclinical data demonstrate that brentuximab vedotin effectively targets and releases its cell-killing payload, MMAE, within CD30-positive tumors."

ADC Product Candidates and Collaborations

Brentuximab vedotin is in multiple clinical trials for Hodgkin lymphoma and other CD30positive hematologic malignancies, including a pivotal trial for relapsed and refractory Hodgkin lymphoma.

We are also advancing a second ADC program, SGN-75, which is comprised of an antiCD70 monoclonal antibody attached to MMAF. We have reported preclinical data on CD70 expression on a variety of solid tumors, including renal cell carcinoma, pancreatic, ovarian and lung cancer, as well as in multiple myeloma and non-Hodgkin lymphoma. SGN-75 has shown potent antitumor activity in several tumor models, underscoring its therapeutic potential in a range of cancer types. We initiated a phase I clinical trial with SGN-75 in November 2009.

Under our collaboration with Agensys, a subsidiary of Astellas Pharma, we are also advancing ASG-5ME towards planned clinical trials in 2010. This ADC has potential in several types of solid tumors.

Seattle Genetics has also licensed its ADC technology to multiple leading biotechnology and pharmaceutical companies in exchange for upfront payments, fees, milestones and royalties on net sales of products incorporating our technology.

Starpharma Holdings, Ltda[63]

About Starpharma Holdings, Ltda

Starpharma is a world leader in the development of nanotechnology-based pharmaceuticals and, through its US-based subsidiary Dendritic Nanotechnologies (DNT), a range of lifescience and industrial uses.
Starpharma is listed on the Australian Securities Exchange (ASX: SPL)and its securities also trade in the US under the American Depository Receipts (ADR) program (OTCQX: SPHRY).
Starpharma's lead development candidates are based on dendrimer nanotechnology.
Dendrimers are man made, nano-sized compounds with unique properties that make them useful to the health and pharmaceutical industry as both enhancements to existing products and as entirely new products. Dendrimers are constructed by the successive addition of layers to the branching groups. Each new layer is called a generation. The final generation incorporates the surface molecules that give the dendrimer the desired function for medical, electronic, chemical and materials applications.
Starpharma aims to create value through the commercialisation of its proprietary products based on dendrimer nanotechnology both directly and through DNT.
Much of Starpharma's value comes from its opportunities for substantial revenues from three key areas:
VivaGel® (SPL7013 Gel): The most advanced product in Starpharma's pipeline, VivaGel®, is being developed as a vaginal microbicide to prevent transmission of genital herpes and HIV. This is a mass-market application in both developed and developing countries.
VivaGel® is also under development as a condom coating and has been shown to possess potent contraceptive activity in animals.

Technologies

Starpharma has a number of products and platforms under development using dendrimer technology. Starpharma's dendrimers are precisely defined, synthetic macromolecules that are well suited to pharmaceutical applications.
Dendrimers fall under the broad heading of nanotechnology, which covers the manipulation of matter in the size range of 1-100 nanometers (one million nanometers equal one millimetre) to create compounds, structures and devices with novel, pre-determined properties.
When making dendrimers, chemists can control their physical and chemical properties. The synthesis of dendrimers involves a core molecule with branching groups to which other branching molecules are added (see figure below) in layers. Each new layer is called a generation. The final generation can incorporate additional active groups that give the particular functionality to the dendrimer.

The selection of core, branching and surface molecules determine the properties of the different dendrimers required for medical, electronic, chemical and materials applications.

[63] www.**starpharma**.com

Supratek Pharma Inc[64]

About Supratek Pharma Inc.

"Supratek Pharma Inc. is a patient and product oriented pharmaceutical company dedicated to the discovery, rapid development and commercialization of innovative anticancer therapeutics desperately needed by cancer patients with tumors that are resistant to available therapies. Many resistant cancers are at a metastatic stage. Late-stage metastatic cancers account for the majority of cancer deaths and represent one of the major unmet medical needs world-wide.
Since 1994, our scientists have steadily built on their cutting edge breakthrough research.
Their deep understanding of cancer progression and metastasis formation has resulted in the successful translation of scientific discovery into pre-clinical development and multiple novel clinical-stage drug candidates.
Thanks to its exciting science Supratek has attracted outstanding, highly productive multidisciplinary individuals to its management, clinical development and R&D functions.
The Company has also established a network of outstanding opinion leaders with recognized expertise in critical areas of cancer research and anticancer drug development. They assist the Company in designing winning drug development strategies."

Technologies

"Sustained product development is possible with our core technology platforms that include Biotransport™ and SP-MET-X™."

Biotransport™ nanomedicine technology

"Involves the proprietary use of highly flexible block co-polymer chemistry to produce nanomedicine compositions of diverse molecules. Biotransport™ compositions consist of an active pharmaceutical ingredient (API) with specific polymer combinations resulting in beneficial biological response modification and targeted drug delivery.
Biotransport™ compositions incorporate a drug molecule without chemical interactions; the resulting nano-systems, ranging from 10nm to 100nm in size, are formed spontaneously and are thermodynamically stable.
This technology is applicable to new chemical entities and generic drugs and can be an effective tool for improving pharmacokinetics, bioavailability and provide drug life extension."

[64] www.**supratek**.com

SP-MET-X™ S100 pathway inhibition

“S100A4 and some other S100 proteins are known biomarkers recently identified as unique targets in a pathway that occurs early in the signal transduction cascade leading to metastasis formation and cancer progression.

SP-MET-X™ technology includes a new library of small molecules that embodies a number of new chemical entities (NCEs) with variable pharmacological properties that inhibit the newly identified pathogenic pathway mediated by the S100 proteins.

S100 proteins play a significant role in promoting growth and the spread of cancers with poor prognosis. Tumors that overexpress these proteins include malignant melanoma, colorectal, breast, bladder, pancreatic, gastric and esophageal cancers.

A new library of S100 targeted compounds has been created, from which several NCEs have been identified to be effective against this novel cancer target. The synthesized compounds are small molecules, with low toxicities, that are orally bioavailable and show good chemical and metabolic stabilities. A set of selected compounds is undergoing pre-clinical development.”

Tekmira Pharmaceuticals

[65]

About Tekmira

As the fields of genetics, medicine and therapeutics continue to converge, the management of illness at its genetic source by silencing genes via RNA interference (RNAi) holds the very real potential to revolutionize treatment on a scale not seen in decades. Tekmira is one of a handful of biotech companies around the world working to exploit the potential of RNAi to treat disease. And it is from among these unique companies that the next wave of therapeutic breakthroughs will emerge.
Tekmira is uniquely equipped to become a leading force in the field. Guided by a cohesive vision, the company possesses leading technology capabilities and a solid intellectual property portfolio in the area of lipid-based nucleic acid delivery, known as SNALP (Stable Nucleic Acid Lipid Particles) to deliver siRNAs (small interfering RNAs) as well as other oligonucleotides in the treatment of disease.
With one RNAi drug candidate in clinical development and another in late preclinical development, plus a pipeline of up to five additional targets made possible through an agreement with RNAi leader Alnylam, Tekmira is well positioned to aggressively advance its product development strategy. In addition to Alnylam, Roche, Merck and Regulus all have access to Tekmira's technology in the delivery of siRNAs and microRNAs.
Finally, broad manufacturing capabilities and a strong capital position permit the company to move forward decisively and build a solid base for both near and longer term growth.

Technologies

Nucleic acids are relatively large molecules that are unstable in the bloodstream and unable to readily diffuse across membranes into target cells. To realize the tremendous therapeutic potential of RNAi-based drugs therefore, effective delivery is critical.

SNALP

Tekmira's siRNA delivery technology platform is termed SNALP for "stable nucleic acidlipid particles". SNALP are specialized lipid nanoparticles that fully encapsulate and systemically deliver a variety of nucleic acid molecules such as siRNA. Pre-clinical studies have shown them to be effective in delivering the drug to target organs and into cells where the nucleic acid-based drug can carry out its desired effect while minimizing systemic toxicity.

SNALP technology relies on something called the "enhanced permeability and retention effect", which occurs because these nucleic acid-containing particles have a long circulation time in the blood, resulting in increased accumulation at sites of vascular leak such as those found at sites of tumor cell growth, infection or inflammation. Once at the target site, cells take up the SNALP through endocytosis and the nucleic acid payload is delivered inside the cell resulting in unparalleled potency. hanced permeability and retention effect", which occurs because these nucleic acid-containing

[65] www.tekmirapharm.com

particles have a long circulation time in the blood, resulting in increased accumulation at sites of vascular leak such as those found at sites of tumor cell growth, infection or inflammation. Once at the target site, cells take up the SNALP through endocytosis and the nucleic acid payload is delivered inside the cell resulting in unparalleled potency.

Appendix 7 – Pharmaceutical R&D expenditure in Europe, USA and Japan (million of national currency units), 1990-2007

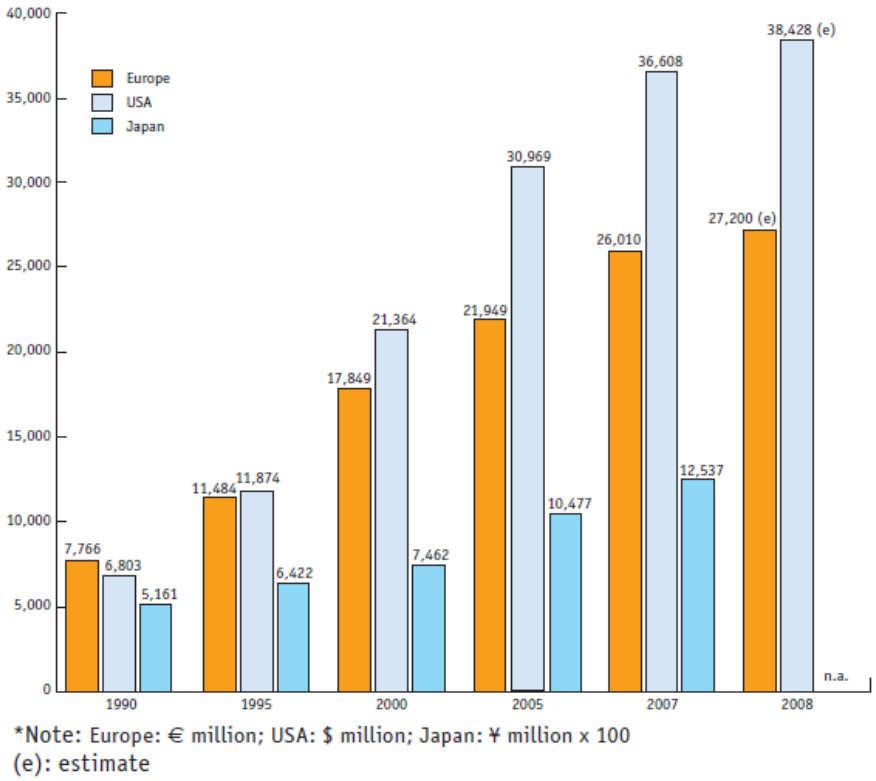


Figure 13.4 - Pharmaceutical R&D expenditure in Europe, USA and Japan (million of national currency units), 1990-2007. Source: EFPIA member associations, PhRMA, JPMA

Appendix 8 – Pharmaceutical and Biotechnology Market: Revenues by Region (Global), 2008 (source: Frost & Sullivan, 2010)

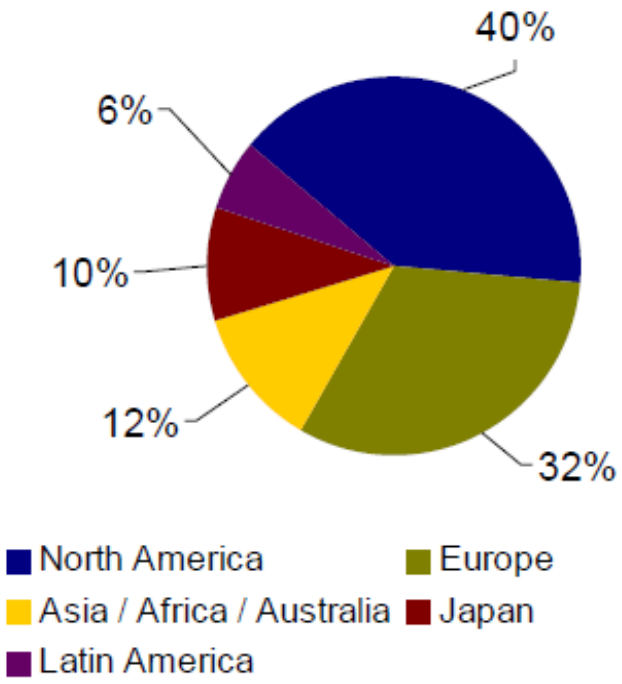


Figure 13.5 - Pharmaceutical and Biotechnology Market: Revenues by Region (Global), 2008. Source: IMS Health, Frost & Sullivan

Appendix 9 – Pharmaceutical R&D expenditures (World), 2002-2012 (million USD)

(source: Frost & Sullivan, 2009 A)

Decision Support Database

Table Pharmaceutical R&D Expenditure (Million USD)

Region / Country	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	CAGR % (2005 - 2012)
North America												
Canada	1,198.7	1,194.3	1,170.0	1,277.7	1,398.7	1,536.6	1,689.9	1,861.5	2,053.7	2,269.4	2,508.9	10.12
United States	31,012.0	34,453.0	37,000.0	39,400.0	41,894.1	44,832.7	48,222.0	51,960.9	56,196.2	60,834.6	66,004.1	7.65
TOTAL	**32,210.7**	**35,647.3**	**38,170.0**	**40,677.7**	**43,293.7**	**46,369.3**	**49,911.8**	**53,822.4**	**58,250.0**	**63,103.0**	**68,513.0**	**7.73**
Latin America												
Argentina	-	-	-	-	-	-	-	-	-	-	-	-
Brazil	-	-	-	-	-	-	-	-	-	-	-	-
Chile	-	-	-	-	-	-	-	-	-	-	-	-
Mexico	-	-	-	-	-	-	-	-	-	-	-	-
Peru	-	-	-	-	-	-	-	-	-	-	-	-
Venezuela	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
Asia - Pacific												
Australia	467.0	520.0	590.2	668.7	755.6	852.4	959.7	1,079.9	1,210.4	1,355.6	1,518.3	12.33
China	260.6	334.3	434.5	556.2	708.8	865.5	1,042.9	1,246.3	1,470.6	1,705.9	1,961.8	18.72
Hong Kong	-	-	-	-	-	-	-	-	-	-	-	-
India	154.5	217.5	295.6	340.5	415.5	502.3	602.9	718.7	852.5	1,005.5	1,181.1	19.02
Indonesia	-	-	-	-	-	-	-	-	-	-	-	-
Japan	6,177.0	6,747.0	6,949.4	7,401.1	7,880.0	8,347.3	8,848.2	9,370.2	9,913.7	10,483.7	11,081.3	5.89
Malaysia	5.4	5.9	6.4	6.9	7.5	8.1	8.8	9.5	10.2	11.1	11.9	8.03
New Zealand	64.9	61.0	67.7	76.0	93.0	91.8	101.0	111.1	122.1	134.2	147.6	10.06
Philippines	-	-	-	-	-	-	-	-	-	-	-	-
Singapore	61.7	66.0	70.8	76.0	81.7	87.9	94.7	102.2	110.3	119.3	129.2	7.94
South Korea	736.9	810.6	894.0	989.7	1,098.6	1,222.7	1,365.8	1,529.7	1,717.8	1,936.0	2,187.7	12.17
Taiwan	107.2	124.3	143.6	165.1	189.4	216.5	246.8	280.9	319.1	361.8	409.2	13.70
Thailand	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	**10,015.1**	**8,986.6**	**9,452.2**	**10,279.3**	**11,192.1**	**12,194.3**	**13,270.7**	**14,447.1**	**15,726.7**	**17,113.1**	**18,628.0**	**9.96**
Western Europe												
Austria	110.4	141.2	168.1	178.0	189.0	200.0	211.2	222.4	233.5	245.1	256.6	5.23
Belgium	1,225.3	1,534.5	1,797.9	1,907.7	2,014.6	2,116.7	2,214.8	2,312.1	2,406.9	2,497.8	2,585.6	4.25
Denmark	767.2	919.8	1,074.9	1,143.5	1,199.7	1,255.1	1,310.5	1,365.2	1,417.8	1,472.0	1,523.8	4.07
Finland	207.4	256.5	296.9	316.1	330.6	346.0	360.9	376.8	390.5	404.9	419.1	4.04
France	3,440.2	4,519.8	5,426.1	5,929.3	6,417.5	6,918.8	7,440.2	7,969.0	8,504.4	9,064.1	9,622.6	6.98
Germany	3,247.4	4,316.4	5,232.2	5,771.8	6,307.5	6,872.7	7,479.2	8,116.2	8,784.3	9,508.6	10,264.9	9.45
Greece	32.0	40.7	47.5	51.2	54.7	58.2	61.8	65.4	68.1	72.8	76.8	5.82
Iceland	-	-	-	-	-	-	-	-	-	-	-	-
Ireland	75.4	115.3	150.8	179.4	211.1	247.0	287.9	333.9	385.1	442.8	506.7	15.71
Italy	743.6	917.5	1,049.0	1,094.8	1,133.7	1,172.3	1,212.0	1,251.3	1,290.3	1,332.0	1,373.5	3.25
Luxembourg	-	-	-	-	-	-	-	-	-	-	-	-
Netherlands	386.3	514.1	633.0	707.6	780.6	856.8	936.9	1,018.4	1,102.4	1,190.2	1,278.8	8.57
Norway	101.8	141.2	169.5	183.1	197.1	211.5	226.6	241.9	257.3	273.5	290.0	6.65
Portugal	54.4	81.6	110.3	123.9	136.6	149.7	163.1	176.4	189.7	203.2	216.5	7.97
Spain	490.1	669.3	871.4	1,000.3	1,134.3	1,279.7	1,435.8	1,600.1	1,774.6	1,961.5	2,157.7	11.31
Sweden	947.2	1,153.8	1,308.6	1,360.6	1,403.6	1,442.6	1,480.9	1,516.6	1,550.1	1,584.7	1,617.1	2.39
Switzerland	2,092.4	2,595.5	3,044.6	3,254.7	3,443.5	3,632.7	3,824.9	4,015.6	4,203.9	4,397.7	4,588.1	4.90
United Kingdom	4,401.5	5,292.7	6,391.9	7,001.5	7,600.4	8,219.1	8,883.1	9,627.5	10,208.1	10,927.5	11,652.6	7.39
TOTAL	**18,322.6**	**23,239.8**	**27,759.6**	**30,202.2**	**32,554.2**	**34,977.7**	**37,509.7**	**40,106.8**	**42,767.7**	**45,576.3**	**48,429.8**	**6.94**
Eastern Europe												
Czech Republic	88.6	115.1	142.8	157.1	170.4	182.3	194.6	207.0	219.0	231.1	243.3	6.12
Hungary	-	-	-	-	-	-	-	-	-	-	-	-
Poland	-	-	-	-	-	-	-	-	-	-	-	-
Russia	-	-	-	-	-	-	-	-	-	-	-	-
Turkey	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	**88.6**	**115.1**	**142.8**	**157.1**	**170.4**	**182.3**	**194.6**	**207.0**	**219.0**	**231.1**	**243.3**	**6.12**
Middle East & Africa												
Egypt	-	-	-	-	-	-	-	-	-	-	-	-
Israel	-	-	-	-	-	-	-	-	-	-	-	-
Saudi Arabia	-	-	-	-	-	-	-	-	-	-	-	-
South Africa	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
WORLD TOTAL	**60,636.9**	**67,888.8**	**75,524.6**	**81,316.2**	**87,210.4**	**93,723.6**	**100,885.8**	**108,583.3**	**116,963.4**	**126,023.5**	**135,814.1**	**7.66**

Note: All figures are rounded; the base year is 2005. Source: Frost & Sullivan

Definition

The above figures represent Pharmaceutical R & D expenditure in million USD.

Note

1. Hyphen indicates non availability of data
2. Figures for United States represents Pharmaceutical R&D Expenditure for Companies registered with "Pharmaceutical Research and Manufacturers of America (PhRMA)"
3. Figures for Malaysia represents Medical & Health Sciences Expenditure

Appendix 10 – Percent R&D expenditures in total pharmaceutical market (World), 2002-2012 (million USD) (source: Frost & Sullivan, 2009 A)

Decision Support Database

Table: Pharmaceutical R&D Expenditure as a percentage of Pharmaceutical Market

Region / Country	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	CAGR % (2005 - 2012)
North America												
Canada	9.8	9.8	9.3	9.4	9.5	9.6	9.7	9.8	9.9	9.0	9.1	1.15
United States	18.8	18.8	20.3	20.7	20.9	21.1	21.3	21.5	21.6	21.7	21.8	0.74
TOTAL	18.2	19.0	19.4	19.8	19.9	20.1	20.3	20.4	20.6	20.6	20.7	0.64
Latin America												
Argentina	-	-	-	-	-	-	-	-	-	-	-	-
Brazil	-	-	-	-	-	-	-	-	-	-	-	-
Chile	-	-	-	-	-	-	-	-	-	-	-	-
Mexico	-	-	-	-	-	-	-	-	-	-	-	-
Peru	-	-	-	-	-	-	-	-	-	-	-	-
Venezuela	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	-	-	-	-	-	-	-	-	-	-	-	-
Asia - Pacific												
Australia	11.9	12.4	12.9	13.4	13.9	14.4	14.9	15.4	15.9	16.3	16.9	3.31
China	4.0	4.5	4.6	4.9	5.2	5.5	5.7	5.9	6.0	6.0	6.0	2.41
Hong Kong	-	-	-	-	-	-	-	-	-	-	-	-
India	3.1	4.0	5.0	5.2	5.9	6.5	7.2	7.9	8.7	9.5	10.3	9.73
Indonesia	-	-	-	-	-	-	-	-	-	-	-	-
Japan	14.8	11.9	12.0	12.0	12.4	12.8	13.0	13.3	13.5	13.7	13.8	1.80
Malaysia	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	0.00
New Zealand	12.1	12.6	12.7	13.5	14.0	14.4	14.7	15.0	15.2	15.4	15.6	1.92
Philippines	-	-	-	-	-	-	-	-	-	-	-	-
Singapore	13.4	13.7	14.0	14.2	14.4	14.6	14.7	14.9	15.0	15.2	15.3	1.02
South Korea	15.6	15.9	16.0	16.2	16.4	16.6	16.9	17.1	17.4	17.7	18.0	1.56
Taiwan	-	-	-	-	-	-	-	-	-	-	-	-
Thailand	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	10.6	10.7	10.7	10.9	11.0	11.3	11.5	11.7	11.8	12.0	12.1	1.60
Western Europe												
Austria	3.7	3.7	3.9	3.9	3.9	3.9	3.9	4.0	4.0	4.0	4.0	0.42
Belgium	37.6	36.5	37.3	37.5	37.9	38.3	38.5	38.8	39.2	39.4	39.5	0.69
Denmark	43.6	41.3	42.2	42.5	42.8	43.2	43.5	43.8	44.2	44.5	44.8	0.78
Finland	11.5	10.7	10.6	10.6	10.7	10.7	10.8	10.9	10.9	11.0	11.0	0.46
France	15.6	16.4	17.2	18.1	18.9	19.8	20.7	21.7	22.6	23.6	24.7	4.56
Germany	10.4	11.2	12.9	13.7	14.6	15.6	16.6	17.7	18.9	20.2	21.5	6.66
Greece	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.1	1.1	1.1	1.1	1.60
Iceland	-	-	-	-	-	-	-	-	-	-	-	-
Ireland	7.2	7.7	8.0	8.3	8.6	8.9	9.3	9.7	10.0	10.4	10.8	3.87
Italy	4.4	4.5	4.4	4.4	4.3	4.3	4.3	4.3	4.3	4.4	4.4	0.38
Luxembourg	-	-	-	-	-	-	-	-	-	-	-	-
Netherlands	8.9	9.3	10.3	11.1	11.8	12.6	13.4	14.1	14.9	15.7	16.5	5.75
Norway	8.4	7.6	8.0	8.2	8.5	8.7	9.0	9.3	9.5	9.8	10.1	2.92
Portugal	2.0	2.5	2.8	2.9	3.0	3.1	3.1	3.2	3.3	3.3	3.3	1.60
Spain	4.7	5.2	5.6	6.0	6.3	6.7	7.1	7.4	7.8	8.1	8.5	5.12
Sweden	34.4	35.0	35.6	36.2	36.8	37.4	37.8	38.4	39.0	39.5	40.1	1.44
Switzerland	-	-	-	-	-	-	-	-	-	-	-	-
United Kingdom	28.8	29.3	29.5	29.7	29.9	29.0	29.2	29.4	29.6	29.8	30.0	0.82
TOTAL	14.5	15.1	15.9	16.3	16.8	17.4	17.9	18.4	19.0	19.6	20.1	3.03
Eastern Europe												
Czech Republic	8.5	8.5	8.7	8.7	8.8	8.9	9.0	9.1	9.2	9.2	9.3	0.93
Hungary	-	-	-	-	-	-	-	-	-	-	-	-
Poland	-	-	-	-	-	-	-	-	-	-	-	-
Russia	-	-	-	-	-	-	-	-	-	-	-	-
Turkey	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	8.5	8.5	8.7	8.7	8.8	8.9	9.0	9.1	9.2	9.2	9.3	0.93
Middle East & Africa												
Egypt	-	-	-	-	-	-	-	-	-	-	-	-
Israel	-	-	-	-	-	-	-	-	-	-	-	-
Saudi Arabia	-	-	-	-	-	-	-	-	-	-	-	-
South Africa	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	-	-	-	-	-	-	-	-	-	-	-	-
WORLD TOTAL	15.9	16.0	16.4	16.7	17.0	17.3	17.6	17.9	18.2	18.4	18.7	1.60

Note: All figures are rounded; the base year is 2005. Source: Frost & Sullivan

Definition

The above figures represent Pharmaceutical R & D expenditure as a percentage of total pharmaceutical market.

Note

1. Hyphen indicates non availability of data
2. Regional and World total are calculated using weighted average of countries in the region and are not the simple average

Appendix 11 – Venture capital investments in Biotech R&D (World), 2002-2012 (million USD) (source: Frost & Sullivan, 2009 A)

Decision Support Database

Table Venture Capital investment in biotech R & D (Mn USD)

Region / Country	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	CAGR % (2005 - 2012)
North America												
Canada	160.0	200.0	271.0	341.5	430.5	543.1	685.5	865.8	1,094.4	1,384.2	1,752.0	26.32
United States	1,436.8	1,647.9	1,891.8	2,174.4	2,503.9	2,886.9	3,333.0	3,852.9	4,463.6	5,177.3	6,017.1	15.65
TOTAL	**1,596.8**	**1,847.9**	**2,162.8**	**2,515.9**	**2,934.3**	**3,430.0**	**4,018.5**	**4,718.8**	**5,558.0**	**6,561.6**	**7,769.1**	**17.40**
Latin America												
Argentina	-	-	-	-	-	-	-	-	-	-	-	-
Brazil	-	-	-	-	-	-	-	-	-	-	-	-
Chile	-	-	-	-	-	-	-	-	-	-	-	-
Mexico	-	-	-	-	-	-	-	-	-	-	-	-
Peru	-	-	-	-	-	-	-	-	-	-	-	-
Venezuela	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**-**
Asia - Pacific												
Australia	659.0	714.6	775.4	841.8	914.5	994.1	1,081.3	1,177.1	1,282.4	1,398.5	1,526.3	8.91
China	-	-	-	-	-	-	-	-	-	-	-	-
Hong Kong	-	-	-	-	-	-	-	-	-	-	-	-
India	-	-	-	-	-	-	-	-	-	-	-	-
Indonesia	-	-	-	-	-	-	-	-	-	-	-	-
Japan	-	-	-	-	-	-	-	-	-	-	-	-
Malaysia	-	-	-	-	-	-	-	-	-	-	-	-
New Zealand	-	-	-	-	-	-	-	-	-	-	-	-
Philippines	-	-	-	-	-	-	-	-	-	-	-	-
Singapore	141.4	169.2	232.7	290.9	363.9	455.7	571.1	716.2	899.1	1,130.1	1,422.3	25.50
South Korea	-	-	-	-	-	-	-	-	-	-	-	-
Taiwan	-	-	-	-	-	-	-	-	-	-	-	-
Thailand	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	**800.4**	**883.8**	**1,008.1**	**1,132.7**	**1,278.5**	**1,449.8**	**1,652.3**	**1,893.3**	**2,181.5**	**2,528.6**	**2,948.6**	**14.94**
Western Europe												
Austria	44.6	54.2	62.3	65.2	67.7	70.2	72.7	75.1	77.5	80.0	82.4	3.32
Belgium	368.6	482.2	533.2	561.1	585.5	609.7	634.4	658.9	683.1	708.8	733.8	3.84
Denmark	670.1	883.5	1,067.8	1,176.9	1,298.0	1,427.2	1,572.4	1,730.6	1,901.2	2,085.9	2,282.4	9.89
Finland	391.9	504.9	596.6	642.9	687.0	732.6	780.7	830.4	881.7	936.8	994.0	6.35
France	81.2	101.7	116.9	122.5	127.4	132.2	137.1	141.8	146.5	151.4	156.2	3.45
Germany	154.8	202.3	242.4	265.0	287.5	311.2	336.7	363.7	392.2	423.4	456.5	8.02
Greece	-	-	-	-	-	-	-	-	-	-	-	-
Iceland	-	-	-	-	-	-	-	-	-	-	-	-
Ireland	0.9	1.1	1.4	1.5	1.6	1.7	1.9	2.0	2.2	2.3	2.5	7.72
Italy	13.7	17.0	19.2	19.9	20.4	20.9	21.4	21.9	22.4	22.8	23.3	2.17
Luxembourg	-	-	-	-	-	-	-	-	-	-	-	-
Netherlands	12.6	15.9	18.3	19.2	20.1	20.9	21.8	22.6	23.5	24.4	25.3	3.92
Norway	1.8	2.3	2.6	2.7	2.8	2.9	3.0	3.1	3.1	3.2	3.3	2.94
Portugal	-	-	-	-	-	-	-	-	-	-	-	-
Spain	5.4	4.1	4.4	4.2	4.1	3.9	3.8	3.6	3.5	3.3	3.2	(4.06)
Sweden	4.5	5.6	6.2	6.3	6.4	6.5	6.6	6.8	7.0	7.2	7.4	2.48
Switzerland	207.6	256.5	281.8	291.6	308.7	325.7	343.1	360.2	377.1	394.5	411.8	4.92
United Kingdom	503.0	403.8	492.9	534.2	579.4	627.5	678.8	734.6	792.7	854.5	922.1	8.05
TOTAL	**2,459.8**	**2,914.6**	**3,445.6**	**3,713.4**	**3,994.5**	**4,293.2**	**4,614.2**	**4,955.2**	**5,313.5**	**5,696.4**	**6,104.4**	**7.32**
Eastern Europe												
Czech Republic	-	-	-	-	-	-	-	-	-	-	-	-
Hungary	-	-	-	-	-	-	-	-	-	-	-	-
Poland	-	-	-	-	-	-	-	-	-	-	-	-
Russia	-	-	-	-	-	-	-	-	-	-	-	-
Turkey	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**-**
Middle East & Africa												
Egypt	-	-	-	-	-	-	-	-	-	-	-	-
Israel	-	-	-	-	-	-	-	-	-	-	-	-
Saudi Arabia	-	-	-	-	-	-	-	-	-	-	-	-
South Africa	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**-**
WORLD TOTAL	**4,857.0**	**5,646.3**	**6,616.1**	**7,362.0**	**8,207.3**	**9,172.9**	**10,285.0**	**11,567.3**	**13,053.1**	**14,788.6**	**16,822.1**	**12.71**

Note: All figures are rounded; the base year is 2005. Source: Frost & Sullivan

Definition

The above figures represent venture capital investemnts made in biotech R & D.

Note

1. Hyphen indicates non availability of data
2. Figures for 2005 are Frost & Sullivan estimates
3. Figures for Denmark, Switzerland indicate Private R & D Expenditure in biotechnology

Appendix 12 – Government investments in biotech (World), 2002-2012 (million USD). (source: Frost & Sullivan, 2009 A)

Decision Support Database

Table Government R & D Expenditure in Biotechnology (Mn USD)

Region / Country	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	CAGR % (2005 - 2012)
North America												
Canada	1,385.0	1,487.0	1,814.1	2,214.5	2,705.0	3,306.9	4,046.0	4,954.7	6,073.0	7,449.8	9,148.3	22.46
United States	20,500.0	17,900.0	19,800.0	24,569.8	30,513.3	37,924.9	47,178.6	58,746.8	73,222.0	91,366.4	114,126.8	24.53
TOTAL	21,885.0	19,387.0	21,614.1	26,784.3	33,218.3	41,231.8	51,224.6	63,701.5	79,295.0	98,816.2	123,274.1	24.37
Latin America												
Argentina	-	-	-	-	-	-	-	-	-	-	-	-
Brazil	-	-	-	-	-	-	-	-	-	-	-	-
Chile	-	-	-	-	-	-	-	-	-	-	-	-
Mexico	-	-	-	-	-	-	-	-	-	-	-	-
Peru	-	-	-	-	-	-	-	-	-	-	-	-
Venezuela	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-
Asia - Pacific												
Australia	602.9	726.4	971.9	1,191	1,400	1,647	1,936	2,274	2,673	3,139	3,693	17.54
China	47.1	51.9	57.1	63.0	69.5	76.7	84.7	93.6	103.4	114.3	126.2	10.46
Hong Kong	61.3	65.0	68.9	73.1	77.5	82.3	87.4	92.9	98.8	105.1	111.9	6.31
India	48.4	61.1	76.1	94.8	114.0	136.9	164.4	197.1	236.4	283.2	339.4	19.94
Indonesia	-	-	-	-	-	-	-	-	-	-	-	-
Japan	1,968.7	2,192.1	2,564.3	2,736.4	3,010.4	3,305.4	3,593.3	3,904.0	4,239.3	4,601.8	4,988.5	8.78
Malaysia	-	-	-	-	-	-	-	-	-	-	-	-
New Zealand	51.3	79.6	112.6	148.6	189.8	241.0	297.9	367.3	453.3	559.3	686.9	23.91
Philippines	-	-	-	-	-	-	-	-	-	-	-	-
Singapore	78.5	91.8	116.7	131.9	149.1	168.7	191.1	216.7	245.9	278.3	317.5	13.43
South Korea	304.5	397.0	436.7	480.7	529.4	583.4	643.4	710.0	784.2	866.8	959.2	10.41
Taiwan	-	-	-	-	-	-	-	-	-	-	-	-
Thailand	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	3,063	3,665	4,394	4,920	5,540	6,242	6,998	7,855	8,834	9,948	11,222	12.49
Western Europe												
Austria	21.3	22.9	24.7	26.6	28.6	30.8	33.2	35.8	38.6	41.6	44.9	7.61
Belgium	211.7	218.7	226.0	233.7	242.0	250.7	260.1	270.0	280.6	291.7	303.7	3.86
Denmark	134.4	174.0	206.5	223.5	241.7	261.3	282.6	305.3	329.3	354.8	381.0	7.89
Finland	159.2	167.9	177.1	186.8	197.1	208.1	219.8	232.1	245.4	259.5	274.5	5.67
France	184.0	220.0	270.9	304.1	339.6	378.2	417.9	463.1	512.6	567.9	628.2	10.95
Germany	357.3	501.4	645.4	757.9	882.6	1,026.6	1,193.0	1,383.9	1,602.6	1,857.3	2,149.4	15.99
Greece	-	-	-	-	-	-	-	-	-	-	-	-
Iceland	1.1	1.2	1.3	1.4	1.5	1.6	1.8	1.9	2.1	2.2	2.4	8.30
Ireland	-	-	-	-	-	-	-	-	-	-	-	-
Italy	45.0	48.2	51.5	55.2	59.1	63.4	67.9	72.9	78.2	84.0	90.3	7.32
Luxembourg	-	-	-	-	-	-	-	-	-	-	-	-
Netherlands	114.9	124.3	134.5	145.5	157.5	170.6	184.8	200.3	217.1	235.5	255.6	8.40
Norway	-	-	-	-	-	-	-	-	-	-	-	-
Portugal	-	-	-	-	-	-	-	-	-	-	-	-
Spain	175.1	224.9	291.6	353.7	426.3	513.8	620.0	748.5	903.0	1,092.5	1,324.3	20.78
Sweden	36.5	38.9	44.0	44.7	45.8	46.9	48.6	50.3	52.2	54.3	56.7	3.82
Switzerland	426.1	614.9	833.5	1,046.0	1,345.5	1,727.8	2,217.5	2,842.8	3,641.7	4,666.4	5,984.0	28.24
United Kingdom	3,240.2	2,872.6	3,475.4	3,731.9	4,008.6	4,298.7	4,608.1	4,938.8	5,275.4	5,631.1	6,015.1	7.00
TOTAL	5,086.9	5,229.6	6,382.2	7,111.0	7,975.1	8,977.4	10,153.1	11,543.6	13,178.6	15,140.5	17,510.1	14.01
Eastern Europe												
Czech Republic	-	-	-	-	-	-	-	-	-	-	-	-
Hungary	-	-	-	-	-	-	-	-	-	-	-	-
Poland	-	-	-	-	-	-	-	-	-	-	-	-
Russia	-	-	-	-	-	-	-	-	-	-	-	-
Turkey	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-
Middle East & Africa												
Egypt	-	-	-	-	-	-	-	-	-	-	-	-
Israel	-	-	-	-	-	-	-	-	-	-	-	-
Saudi Arabia	-	-	-	-	-	-	-	-	-	-	-	-
South Africa	27.8	42.4	62.0	60.4	64.1	68.2	72.9	78.1	83.9	90.6	98.4	7.42
TOTAL	27.8	42.4	62.0	60.4	64.1	68.2	72.9	78.1	83.9	90.6	98.4	7.42
WORLD TOTAL	30,062.5	28,324.0	32,452.7	38,875.6	46,797.4	56,519.4	68,448.5	83,178.5	101,391.4	123,995.6	152,105.1	21.71

Note: All figures are rounded; the base year is 2005. Source: Frost & Sullivan

Definition

The above figure represents government investment in Biotechnology R & D.

Note

1. Hyphen indicates non availability of data
2. Figures for 2005 are Frost & Sullivan estimates
3. Figures for United states, Sweden and United Kingdom indicates total R & D Expenditure made in biotechnology.
4. Figures for India indicates budgetary allocations made by the department of biotechnology.
5. Figures for Spain indicates investments by Public subsidies for R&D:universities and public research centres & Public subsidies for R&D: companies

Appendix 13 – Targeted drug delivery companies and their location (Epsicom, June 2009).

Target drug delivery company	Location	Therapeutical area of focus
Access Pharmaceuticals, Inc	Dallas, TX, USA	Cancer
Alkermes	Waltham, MA, USA	CNS disorders, addiction, diabetes and autoimmune disorders
ArmaGen Technologies, Inc.	Santa Monica, CA, USA	Solutions to the 'blood-brain barrier' problem (CNS)
Avidimer Therapeutics	Ann Arbor, MI, USA	Cancer
Calando Pharmaceuticals, Inc.	Pasadena, CA, USA	Cancer, AIDS, hepatitis C, Huntington's disease
Cell Therapeutics, Inc.	Seattle, WA, USA	Cancer
Cerulean Pharma, Inc.	Cambridge, MA, USA	Cancer, inflammation, and CV diseases.
Copernicus Therapeutics, Inc.	Cleveland, Ohio, USA	Diseases causing blindness, airborne viral, and diseases of the brain
CytImmune Sciences, Inc.	College Park, Md., USA	Cancer
Delcath Systems	New York, NY, USA	Cancer
Diatos S.A.	Paris Area, France	Cancer
Enzon Pharmaceuticals, Inc.	USA	Cancer
Endocyte Inc.	West Lafayette, IN; Indianapolis, IN, USA	Cancer
Eurand N.V.	USA, France, The Netherlands and Italy	Cystic Fibrosis and gastriointestinal
ImmunoGen, Inc.	Waltham, MA, USA	Cancer
NanoBioMagnetics, Inc.	Edmond, OK, USA	Cancer
Nanobiotix	Paris, France	Cancer
NanoCarrier, Inc.	Japan	Cancer
Nano Interface Technology	Lorton, VA , USA	Cancer
Nektar Therapeutics	San Carlos, CA, USA	across many therapeutic areas and modalities
NeoPharm	USA	Cancer
Novosom AG	Germany	Inflammation, Cancer and liver diseases
Mirus Bio Corporation	USA	across many therapeutic areas and modalities
PCI Biotech Holding ASA	Oslo Area, Norway	across many therapeutic areas and modalities
Quest PharmaTech, Inc.	Canada	Cancer
Seattle Genetics	Bothell, WA, USA	Cancer, and autoimmune diseases
Starpharma Holdings, Ltd	Australia	across many therapeutic areas and modalities
Supratek Pharma Inc.	Canada	Cancer
Tekmira Pharmaceuticals Corporation	Canada	across many therapeutic areas and modalities

Appendix 14 – Drug delivery market: Deals between companies and Pharmaceutical and Biotechnology companies (Europe), 2004-2007 (source: Frost & Sullivan, June 2008 A).

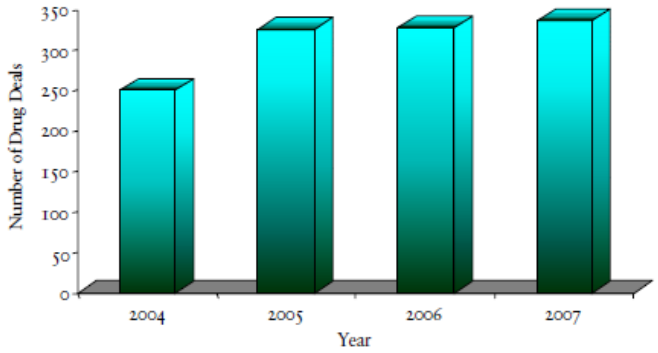


Figure 13.6 - Drug delivery market: Deals between companies and Pharmaceutical and Biotechnology companies (Europe), 2004-2007

Appendix 15 – E.U Pharmaceutical companies by therapeutic area (source: [online] Pharma Licensing and [online] Pharmaceutical Business Review).

Cancer

1. Abiogen
2. Actelion Ltd
3. Active Biotech AB
4. Alizyme plc
5. Ark Therapeutics Group plc
6. AstraZeneca PLC
7. Bayer AG
8. Biovent
9. BTG International Ltd
10. deCODE genetics, Inc.
11. Evotec Aktiengesellschaft
12. F. Hoffmann-La Roche Ltd.
13. Genmab A/S
14. GENTIUM S.p.A.
15. GPC Biotech AG
16. GlaxoSmithKline plc
17. Grupo Ferrer
18. GW Pharmaceuticals plc
19. Ipsen S.A.
20. Italfarmaco
21. Karo Bio
22. Les Laboratoires Servier
23. Medigen
24. Menarini group
25. Merck KGaA
26. Mymetics Corporation
27. Novartis AG
28. Sanofi-Aventis
29. Transgene
30. Vernalis

Immunology

1. Actelion Ltd
2. Active Biotech AB
3. ALK-Abello A/S
4. Allergy Therapeutics plc
5. AstraZeneca PLC
6. Bayer AG
7. Biotest AG
8. Elan Corporation, plc
9. Evotec Aktiengesellschaft
10. F. Hoffmann-La Roche Ltd.
11. Italfarmaco
12. GW Pharmaceuticals plc

Cardiovascular

1. Actelion Ltd
2. Ark Therapeutics Group plc
3. AstraZeneca PLC
4. Bayer AG
5. Boehring Ingelhem
6. Chiesi Farmaceutica
7. deCODE genetics, Inc.
8. EGIS Pharmaceuticals Plc
9. F. Hoffmann-La Roche Ltd.
10. Gedeon Richter Plc.
11. GENTIUM S.p.A.
12. GlaxoSmithKline plc
13. Grupo Ferrer
14. Ipsen S.A.
15. Italfarmaco
16. Karo Bio
17. Krka d.d. Novo Mesto
18. Les Laboratoires Servier
19. LifeCycle Pharma A/S
20. Meda AB
21. Merck
22. Novartis AG
23. Nycomed International Management GmbH
24. Rafarm
25. Sanofi-Aventis
26. Schwable Pharmaceuticals
27. Schwarz Pharma AG
28. Orion Corporation

Musculoskeletal and Inflammation

1. Abiogen Pharma
2. Ablynx NV
3. Chiesi Farmaceutici
4. Crucell N.V.
5. Dr. Kade Pharmazeutische Fabrik Gmbh
6. Genmab A/S
7. GlaxoSmithKline plc
8. Novartis AG
9. Noxxon Pharma AG
10. Palau Pharma
11. Rafarm
12. Revotar Pharmaceuticalsd
13. UCB Group

Genito Urinary System and Sex Hormones

1. GlaxoSmithKline plc
2. Novartis AG
3. Rafarm
4. Schwable Pharmaceuticals

Central Nervous System

1. Abiogen Pharma
2. Actelion Ltd
3. Addex Pharmaceuticals
4. Amarin Corporation plc
5. AstraZeneca PLC
6. Biomedica Foscama
7. BTG International Ltd
8. EGIS Pharmaceuticals Plc
9. Elan Corporation, plc
10. Evotec Aktiengesellschaft
11. F. Hoffmann-La Roche Ltd.
12. Gedeon Richter Plc.
13. GlaxoSmithKline plc
14. Grupo Ferrer
15. GW Pharmaceuticals plc
16. H Lundbeck A/S
17. Ipsen S.A.
18. Italfarmaco
19. Karo Bio
20. Krka d.d. Novo Mesto
21. Les Laboratoires Servier
22. Merz
23. Neurosearch
24. Newron
25. Novartis AG
26. Orion Corporation
27. Rafarm
28. Sanofi-Aventis
29. Schwarz Pharma AG
30. UCB Group
31. Vernalis

Respiratory

1. Abiogen Pharma
2. AstraZeneca PLC
3. Chiesi Farmaceutici
4. Crucell N.V.
5. Eurand N.V.
6. Evotec Aktiengesellschaft
7. GlaxoSmithKline plc
8. Grupo Ferrer
9. Krka d.d. Novo Mesto
10. Meda AB
11. Novartis AG
12. Nycomed International Management GmbH
13. Rafarm
14. Schwable Pharmaceuticals
15. Schwarz Pharma AG
16. UCB Group

Metabolic Disorders

1. Alizyme plc
2. Biomédica Foscama
3. deCODE genetics, Inc.
4. F. Hoffmann-La Roche Ltd.
5. GENTIUM S.p.A.
6. GlaxoSmithKline plc
7. Grupo Ferrer
8. Krka d.d. Novo Mesto
9. Les Laboratoires Servier
10. LifeCycle Pharma A/S
11. Novartis AG
12. Sanofi-Aventis

Appendix 16 – Potential customers 2009 turnovers

Table 0.1 – DPM pharmaceutical companies targeted turnover

Company Name	Turnover 2009 (US$m)
Abiogen Pharma	82,62
Allergy Therapeutics plc	58,53
Ark Therapeutics Group plc	1,75
AstraZeneca PLC	31.601,00
Bayer AG	48.408,82
Biomedica Foscama	NA
BTG International Ltd	160
Boehring Ingelheim	25.302,07
Chiesi Farmaceutici	1.132,64
Dr. Kade Pharmazeutische Fabrik GmbH	80,17
Eurand N.V – Resp.	144,91
EGIS Pharmaceuticals Plc	565,05
F. Hoffmann-La Roche Ltd.	42.237,96
Gedeon Richter Plc.	1.392,02
GlaxoSmithKline plc	45.947,17
Grupo Ferrer	NA
GW Pharmaceuticals plc	22,22
Lundbeck .	2.238,49
Ipsen S.A	1.427,97
Italfarmaco	389,67
Krka d.d. Novo Mesto	1.396,94
Les Laboratoires Servier	5.441,18
Meda AB	
Menarini group	3.633,02
Merck	11.114,71
Merz	5,399
Novartis AG	42.584,00
Nycomed International Management GmbH	4.923,53
Orion Corporation	NA
Rafarm	NA
Sanofi-Aventis	42.377,94
Schwable Pharmaceuticals	746,87

Table 0.2 – R&D pharmaceutical companies targeted turnover

Company Name	Turnover (US$m)
ALK-Abello A/S	353,97
Biovent	11,293
LifeCycle Pharma A/S	33,75
Vernalis	NA

Table 0.3 - DPM biopharmaceutical companies targeted turnover

Company Name	Turnover (US$m)
Actelion Ltd	1.364,36
Biotest AG	622
Crucell N.V.	392,65
Elan Corporation, plc	1.000,00
GENTIUM S.p.A.	10,94
GPC Biotech AG	18,19
Medigen	51,96
Neurosearch	240
Pharming Group N.V.	0,97
Schwarz Pharma AG	624,78
UCB Group	5.295,59

Table 0.4 – R&D biopharmaceutical companies targeted turnover

Company Name	Turnover (US$m)
Ablynx NV	25
Active Biotech AB	8,3
Addex Pharmaceuticals	24,88
Alizyme plc	3,51
deCODE genetics, Inc.	58,1
Amarin Corporation plc	2400
Evotec Aktiengesellschaft (small molecules)	58,25
Genmab A/S	147,84
Karo Bio	1,71
Mymetics Corporation	0,1
Newron	NA
Noxxon Pharma AG	NA
Palau Pharma	NA
Revotar Biopharmaceuticals	NA
Transgene	136,38

Appendix 17 – Intensity of competition by therapeutic area of focus

Table 0.5 – Therapeutic area of focus of target drug delivery companies.

Target drug delivery company	Therapeutical area of focus
Access Pharmaceuticals, Inc	Cancer
Alkermes	CNS disorders, addiction, diabetes and autoimmune disorders
ArmaGen Technologies, Inc.	Solutions to the 'blood-brain barrier' problem (CNS)
Avidimer Therapeutics	Cancer
Calando Pharmaceuticals, Inc.	Cancer, AIDS, hepatitis C, Huntington's disease
Cell Therapeutics, Inc.	Cancer
Cerulean Pharma, Inc.	Cancer, inflammation, and CV diseases.
Copernicus Therapeutics, Inc.	Diseases causing blindness, airborne viral, and diseases of the brain
CytImmune Sciences, Inc.	Cancer
Delcath Systems	Cancer
Diatos S.A.	Cancer
Enzon Pharmaceuticals, Inc.	Cancer
Endocyte Inc.	Cancer
Eurand N.V.	Cystic Fibrosis and gastriointestinal
ImmunoGen, Inc.	Cancer
NanoBioMagnetics, Inc.	Cancer
Nanobiotix	Cancer
NanoCarrier, Inc.	Cancer
Nano Interface Technology	Cancer
Nektar Therapeutics	across many therapeutic areas and modalities
NeoPharm	Cancer
Novosom AG	Inflammation, Cancer and liver diseases
Mirus Bio Corporation	across many therapeutic areas and modalities
PCI Biotech Holding ASA	across many therapeutic areas and modalities
Quest PharmaTech, Inc.	Cancer
Seattle Genetics	Cancer, and autoimmune diseases
Starpharma Holdings, Ltd	across many therapeutic areas and modalities
Supratek Pharma Inc.	Cancer
Tekmira Pharmaceuticals Corporation	across many therapeutic areas and modalities

Table 0.6 – Total number of companies per therapeutic area

Therapeutic area	Total number of companies	Total number of companies (%)
Cancer	20	54,1
CNS	2	5,4
Immunology	2	5,4
Inflammation	2	5,4
CV	1	2,7
OTHERS	5	13,5
Across many therapeutic areas	5	13,5

Table 0.7 – Intensity of competition Assigning Values

%	Intensity of competition
0-5	10
5 a 10	9
10 a 20	8
20 a 30	7
30 a 40	6
40 a 50	5
50 a 60	4
60 a 70	3
70 a 80	2
80 a 90	1
90 a 100	0

Appendix 18 – Positioning factors interviews

Questionnaire used to pharmaceutical companies targeted companies interviews

Considering the criterias that most influence your company, in the decision of be the licensee of a new and versatile drug delivery system, classify the following factors in a scale between 0 (nothing important) to 5 (extremely important).

Price

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

Product Quality

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

Possibility of application the drug delivery system to different API's

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

R&D STAFF prestige

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

Organizational Image

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

Innovation for the final product

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

Environmental concerns (related to the process and products)

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

Who is the contact person (job function) inside your company that should be contacted in case of present a new drug delivery to your marketable products?

_____
_____

Do your company has already purchase for a license of a drug delivery system?

YES	☐
NO	☐

IF you answer affirmatively, which is the licensor company?

_____
_____

Do your company; develop research in the area of drug delivery systems?

YES	☐
NO	☐

Just one question about you:

What is your job function inside the company?

_____

Thank you very much!

Note: This information it will only be used for the purpose of a master thesis in Biotechnology.

Questionnaire used to drug delivery companies interviews

Considering the positioning criterias of your company, classify the following factors in a scale between 0 (nothing important) to 5 (extremely important).

Price

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

Product Quality

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

Possibility of application the drug delivery system to different API's

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

R&D STAFF prestige

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

Organizational Image

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

Innovation for the final product

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

Environmental concerns (related to the process and products)

0	1	2	3	4	5
☐	☐	☐	☐	☐	☐

Does your company have targeted delivery systems?

YES	☐
NO	☐

If you answer affirmatively, what are the names of the products?

_____
_____

Have you already license some of your drug delivery systems?

YES	☐
NO	☐

If you answer affirmatively, what is the name of the licensee?

_____
_____

_____

Just one question about you:

What is your job function inside the company?

_____

Thank you very much!

Note: This information it will only be used for the purpose of a master thesis in Biotechnology.

Interviews positioning factors results:

Were made efforts in order to contact all the pharmaceutical targeted companies as well all the targeted drug delivery companies referred in this marketing plan as competitors. However many companies did not answer, other ones did not fill the questionnaire because of company policies, and some of the companies that completely filed the questionnaire ask for confidentiality related to their company brand.
In the Appendix 1 are present the contact persons of company's staff that answer the questionnaire without asking for confidentiality.

Average classifications of Pharmaceutical companies positioning factors valuation:

Price	Product Quality	Possibility of application the drug delivery	R&D STAFF prestige	Organizational Image	Innovation for the final	Environmental concerns
3	5	5	4	4	5	3

Average classifications of Drug delivery companies *positioning factors valuation:*

Price	Product Quality	Possibility of application the drug delivery	R&D STAFF prestige	Organizational Image	Innovation for the final	Environmental concerns
4	5	4	3	4	4	3

Appendix 19 – Template of Exclusive patent license agreement (adapted from exclusive patent license agreement template made by Portuguese Industrial Property Office)

EXCLUSIVE PATENT LICENSE AGREEMENT BETWEEN UNIVERSIDADE NOVA DE LISBOA AND INSTITUTO SUPERIOR TÉCNICO AND LIFE DELIVERY

Between

Universidade Nova de Lisboa (UNL), legal person no. xxx, with its head office at …, …-… Lisboa, represented by xxx, in his/her capacity as Rector of UNL, and **Instituto Superior Técnico (IST),** legal person no. xxx, with its head office at …, …-……, represented by xxx, in his/her capacity as Director of IST, with powers for the fact, hereinafter referred to as the R&D, Licensor or First Party;

And

LIFE DELIVERY, legal person no. …, with its registered office at …, …-… …, represented by Pedro Vidinha, in his/her capacity as CEO, with powers for the act, hereinafter referred to as the COMPANY, Licensee or Second Party;

Whereas:

a) *The R&D is the sole owner of a PENDING PATENT APPLICATION submitted in …* under number 08398007.8 dated 19/06/2008*, published in …* under number *… with the title "*SYNTHESIS AND APPLICATION OF A FAMILY OF NEW MATERIALS RESULTING FROM THE CHEMICAL CROSS-LINKING BETWEEN GELATINE AND ORGANIC SALTS*", to* European Patent Office (EPO) *(hereinafter referred to as the Office) (hereinafter referred to as PATENT* 08398007.8;

PATENT RIGHT applied for in United States under number 12/142960 dated …, with the title "", granted by … (hereinafter referred to as the Office) on … (hereinafter referred to as PATENT A); US

b) The R&D, as the sole owner of PATENT A, shall bear all the costs of its preparation and submission to the Office, those incurred with all prior art searches, the remaining procedures needed for its grant and subsequent maintenance, including all Patent Attorney fees and all other fees, charges and expenses and that said PATENT A is free of any encumbrances, third party rights and/or options and expenses;

c) R&D, acting as owner of PATENT A, wishes to license the exploitation of the invention patented through persons or entities authorised by him;

d) The COMPANY wishes to obtain from the R&D an exclusive license for exploitation of the invention claimed in PATENT A;

e) It is necessary to settle the contractual terms of the license;

The parties accept the following **EXCLUSIVE PATENT LICENSE AGREEMENT**, which is subject to the Clauses:

ONE

(Object)

Under this agreement, the parties establish the scope and conditions of the granting by R&D to the COMPANY of a license to exploit the invention claimed in PATENT A.

TWO

(License General Conditions)

2.1. The R&D, as Licensor, grants to the Company, as Licensee, an invention exploitation license, which covers the manufacture, use, sale and lease of the artefacts or products claimed in and pertaining to PATENT XXX and the use or application of the methods, means and processes claimed in said PATENT XXX, subject to Licensee full compliance with the conditions and obligations set out below.

2.2. The R&D, as the Licensor, grants to the COMPANY, as Licensee, an EXCLUSIVE EXPLOITATION LICENSE, with the following general conditions:

2.2.1. **Scope** – This license covers the patent right of PATENT XXX *"…"*, number …, all subsequent international extensions of the same patent application and all subsequent national phases validated in the meantime. Its scope or extension cannot therefore be divided or split by either party;

2.2.2. **Exclusive** – The R&D undertakes, for the entire period granted for the license, not to grant any other license to a third party, as set out in Clause Four below;

2.2.3. **Temporary** – This license shall be granted for a period of … years, possibly extendible, in accordance with Clause Five below;

2.2.4. **Under Payment** – The Licensee undertakes to pay, in return for the exclusive use of the Technology, the amounts due accordingly with Clause Six below;

2.2.6. **With the possibility of sublicensing** by the Licensee, in accordance with Clause Eight below;

2.2.7. **Performance Clause** – The Licensee undertakes to actually exploit the licensed Technology, under the sanction of agreement termination by the Licensor, as set out in Clause Twelve;

*2.2….. **Restricted to a specific field of use** – This license entitles the Licensee to exploit the aforementioned Technology with a SPECIFIC RESTRICTION TO THE FIELD OF Drug delivery systems, as set out in Clause Eight;*

2.3. This license does not cover any other patent rights or other industrial property rights owned by R&D.

2.4. No use of R&D´s commercial name, trademark or other distinctive signs owned by R&D is allowed, except on the conditions set below.

THREE

(Patent rights maintenance and registration)

3.1. The R&D undertakes to keep PATENT XXX fully valid, along with any extensions licensed under this agreement, on pain of immediate agreement termination thereof.

[*…, which will also occur should PATENT XXX, while pending, be refused or not granted for any reason*.]

3.2. The Licensee undertakes to proceed with the register of the license at the designated Patent Offices at its own expense and to inform the R&D immediately of these acts in writing, considering the provisions of Article 30.1.b) of the Portuguese Industrial Property Code.

FOUR

(Exclusivity; Improvements by the Licensee)

4.1. The R&D, as Licensor, shall refrain from granting other licenses for the Technology to any third party or from performing any other acts that may encumber, compress or limit the rights granted for the length of this agreement and in any extensions, without prejudice to the following paragraph.

4.2. The R&D shall maintain the right to use the licensed technology in its own non-commercial research activities, provided that it does not infringe the rights granted or the confidentiality provisions set out in this agreement.

4.3. Should the Licensee or any employee, in compliance with an employment agreement or as a service provider, perform modifications to the licensed technology that constitute an improvement to its performance or make an invention for which it obtains a patent depending on PATENT XXX, it undertakes to grant the R&D a free license with no territorial restrictions and extending to all applications of a non-exclusive nature for the exploitation of said patent and/or associated or dependent know-how.

4.4. In the case provided for in paragraph 4.3, the Licensee also undertakes, if granting paid licenses for the dependent patent, to give the R&D … % (… percent) of the gross profits obtained from these licenses.

FIVE

(Duration)

5.1. This license has temporary nature and is granted for a period of … years, as of the date of signing of this agreement.

5.2. The license may be extended by unanimous agreement of the parties.

5.3. This license shall always have a maximum limit of 20 (twenty) years as of the date of submission of the first application for PATENT XXX.

SIX

(Licensors Financial compensation)

6.1. The Licensee undertakes to pay to R&D as direct, necessary compensation for the use and exploitation of the Technology, in the form of an initial payment, together with a minimum quarterly royalty independent of any exploitation, plus periodic royalties indexed to gross profits from exploitation, all as set forth in the following clauses.

6.2. The R&D, as Licensor of the patent right referred to in the first part of 2.2.1, is entitled to receive from the Licensee an initial upfront payment of € 39.253,77.

6.3. The payment referred in 6.2 shall be made to the R&D by the Licensee on the date of signing of this agreement.

6.4. The payment due in 6.2 is totally independent from the remaining royalty obligations that the Licensee accepts in the following paragraphs.

6.5. Without prejudice to the previous paragraphs, the R&D is also entitled to receive from the Licensee periodic royalties indexed to the gross profits obtained by the Licensee in the exploitation of the licensed Technology, at a fixed percentage of … % (… percent), to be reported quarterly in writing in a document certified by an official auditor by the Licensee to the R&D. It shall always owe to the R&D as a minimum quarterly royalty the amount of €… (… euros).

6.6. The payments provided for in 6.5 shall be made within a maximum of 60 (sixty) days as of the end of the quarter that generated the obligation to pay.

6.7. “GROSS PROFITS” are any income received by the Licensee arising from:

- Technology incorporation in its own products and processes, in its own or subcontracted production and irrespective of its commercial efforts;
- The manufacture, use and sale of products incorporating the Technology;
- Commercial exploitation of any process belonging to the Technology.

SEVEN

(Information duties and audit clause)

7.1. The Licensee shall submit to the R&D, within a maximum of 90 days of the end of each calendar quarter, a written, hard-copy report with reasonable accounting detail, billing and gross sales reflecting the actual exploitation of the licensed Technology and subject to the calculation criteria for royalties set in Clause Six.

7.2. The quarterly report described in paragraph 7.1 shall contain gross sales data and the result of the application of the calculation criteria for royalties.

7.3. The Licensee shall keep in its possession certified accounting data in reasonable detail on the production, use, distribution, sales and other acts pertaining to the Technology.

7.4. Provided that it gives 30 days prior notice, the R&D is entitled, at its own expense, to conduct, or to commit a third party appointed by it, an audit of the records kept by the Licensee, in order to check the relevant accounting figures and thereby certify the compliance with the royalties plan that the Licensee undertook to follow.

7.5. Any audit based on the previous paragraph shall be conducted within office hours and in such a way to disrupt the Licensee's activities as little as possible. The Licensee may not refuse an audit or deny access to any accounting documents or others such as agreements, contracts, promissory or option contracts, invoices, receipts, shipping notes, letters, commercial bids, estimates and electronic communications, access to premises, vehicles, IT resources or media, be they hardware or software, contact with workers, customers, agents or suppliers, physical checks of inventory or any other form of check and audit that the Licensor and/or the appointed auditors see fit.

7.6. If the results of an audit diverge materially from the data provided by the Licensee, it shall be responsible for returning the royalty amount difference and all audit costs borne by the R&D.

EIGHT

(Agreement Assignment)

The Licensee may not assign its position in this agreement without the R&D's written consent.

NINE

(Agreement Termination)

9.1. This agreement may be revoked at any time upon Parties unanimous agreement.

9.2. The R&D has the right to terminate this agreement if the Licensee breaches or fails to properly fulfil any of the agreement accepted terms, conventions and obligations therein and in the specific case set out in the next Clause.

9.3. The Licensee has 30 (thirty) days after full acquaintance of the R&D's intention to terminate the agreement to correct or remedy any fault committed or fulfil obligations not complied with. If this is not done in a timely fashion, R&D has the right to terminate this agreement.

9.4. The R&D has also the right to terminate the agreement, if any of the following events occur:

- The Licensee fails to make any of the payments that it undertook to make in this agreement, such as those in Clause Six, in good time and fails to do so even after being so ordered within 8 (eight) days, in written form, by the R&D;
- The Licensee is declared insolvent, requests credit protection or is declared bankrupt, under current legislation. In this case, the agreement shall be terminated immediately after the R&D informs the Licensee of its intention;
- During the exercise of the R&D's right to information and auditing set forth in Clause Seven, R&D or a third party appointed by it finds a difference or discrepancy of more than 20% in the Licensee's data relevant to the calculation of royalties in each 3 (three) month period.

9.5. In the event of the stoppage of the effects of this agreement, the Licensee shall, as of the date of said cessation, be forbidden to continue the invention exploitation, including the ability to sell, exchange or transfer free of charge any item of goods or service covered by this license.

9.6. This agreement may expire in the case set out in 3.1 above. In this case, the parties expressly and unconditionally recognise and accept the non-retroactivity of the effects of the agreement expiration and the nature of continued performance of this agreement. There shall therefore be no reimbursement of any amounts paid or owed by the Licensee under this agreement in return for the use of PATENT A.

9.7. The obligation to maintain confidentiality set out in 12.4 shall survive any of the cases of cessation of the effects of this agreement and shall remain fully valid and effective.

TEN

(Performance Clause)

10.1. The Licensee undertakes to actually exploit the licensed rights in accordance with 2.2.7 above and shall initiate steps towards effective exploitation within a maximum of … days as of the date of signing of this agreement and give sufficient proof thereof.

10.2. If the Licensee fails to respect the time limit set out in the previous section, the R&D has the right to terminate this agreement unilaterally, provided that it gives 30 (thirty) days' notice.

10.3. If the Licensee begins or resumes exploitation of the licensed rights and provides sufficient proof of this exploitation before the end of the 30 (thirty) days' notice of termination of the agreement by the R&D or submits to it, within the same period, a reprogramming of the exploitation strategy that is accepted by the R&D, the right to dissolve this agreement shall be automatically suspended.

ELEVEN

(Parties Responsibilities)

11.1. The Licensee is solely responsible for the licensed Technology before end users, for any reason, and in relation to any third parties and undertakes to compensate the R&D for any amounts that it may have to disburse due to lawsuits, complaints or legal action against it on the grounds of the Technology.

11.2. The R&D, in turn, does not by any means guarantee the operability or adaptability for any use, the safety, efficacy, approval by national and other regulatory authorities, the time and any costs of the development and/or opening of the Technology licensed in this agreement.

11.3. Neither does the R&D declare or, as a result, guarantee that the Technology licensed by this agreement does not infringe other patent rights already owned by or pending for third parties or that there are no causes that may affect the validity of the right covered by this agreement.

11.4. The parties undertake to cooperate in the defence of PATENT XXX against any actions by third parties, such as violations of the right or lawsuits based thereon.

TWELVE

(Confidentiality)

12.1. The Parties expressly undertake to treat and maintain absolutely confidential all information regarding this agreement or either of the parties that may come to their knowledge within the scope of this agreement or the preliminary negotiations prior to its signing and shall also refrain from any use of said information outside its scope and irrespective of the purpose, either to their own benefit or that of a third party.

12.2. Each Party is also obliged to treat in the way mentioned above all information regarding internal and/or commercial or business matters of the other party to which it has access in any way.

12.3. Information transmitted in the following ways is exclusively excepted from this duty of confidentiality:

- To the managers, consultants and other personnel belonging to the research teams of the R&D and Licensee, provided that they are directly involved in compliance with the

agreement and the performance of the activities regulated by it. Said parties undertake to guarantee equivalent confidentiality commitments for all their employees involved in compliance with this agreement;

- Within the framework of the information to be provided by the R&D and/or Licensee to their corporate bodies for the purpose of fulfilling obligations laid down by law or their Statutes or the obtaining of the authorisations necessary for full performance of this agreement;
- All information belonging to the public domain or for which the transmitter has expressly waived the obligation set out herein.

12.4. The obligation set out in this clause shall be binding on the parties for a period of 5 (five) years as of the actual disclosure of the information, irrespective of the cessation of this agreement for any reason.

12.5. The burden of proof of the exceptions set out in 12.3 to the obligation to maintain confidentiality lies with the recipient of the information.

THIRTEEN

(Law and Dispute Resolution)

13.1. This agreement is subject to Portuguese Law.

13.2. The courts of Portugal shall be competent to settle any disputes arising from it.

13.2. In the event of a disagreement or dispute between the Parties on the interpretation, validity or application of this Agreement that they are unable to settle by consensus, either Party may submit it to an arbitration court, expressly renouncing to the intervention of any other court.

13.3. The arbitration court shall be set up and function as established by the Voluntary Arbitration Law (Law no. 31/86 of 29 August with the amendments introduced by Decree-Law no. 38/2003 of 8 March) and shall consist of three arbiters, one appointed by each Party and a third by cooption by the Parties. If they are unable to agree on the appointment of the third arbiter, s/he shall be appointed by the Presiding Judge of the Lisbon Court of Appeal at the request of either Party.

13.4. The arbitration procedure shall take place in Portuguese, in Lisbon, unless otherwise agreed by the parties in the arbitration procedure.

13.5. Whenever there is a disagreement or dispute regarding industrial property, the ARBITRARE Arbitration Centre shall be competent to settle said conflicts, to the express exclusion of any other, in which case the Arbitration Centre’s regulations shall apply.

13.6. The arbitration tribunal and/or arbitration centre shall appreciate the facts and rule in accordance with Portuguese law. Its decisions shall not be subject to appeal.

The parties declare that they are cognisant of and fully accept the terms of this agreement.

It shall now be signed by the legal representatives of the R&D and the Licensee and each of the Parties shall retain a signed copy initialled by all on each page.

Lisbon, … … …

For the R&D

For the COMPANY

Appendix 20 – Drug delivery license deals during 2009

Licensor	Licensee	Product/Technology	Therapy area(s)	Deal terms	Month signed
BioDelevery Sciences	Media	Onsolis (fentanyl buccal soluble film)	Breackthrought pain in opcid-tolerant patients with cancer	£3 million for worldwide distribution rights(except Taiwan and South Korea)	January
Pharmathen	Recordati	Undisclosed	Undisclosed	Undisclosed	January
Elan	Schein Pharmaceutical (now Watson)	Medipad minimal invasive microinfusion pump	Genetic blood disorders associated with iron overload	Undisclosed	March
Altea Therapeutics	Amylin and Lilly	Altea's proprietary PassPort transdermal delivery system	Type 2 diabetes	Up to $46 million; exclusive worldwide licence	April
Aegis Therapeutics	Phylogica	Intravail tranmucosal delivery formulations of Phylomer peptides	Undisclosed	N/A	April
Neuromed	Mallinckrodt	Exalgo (hydromorphone HCI) extended-release tablets	Pain	US rights for $15 million up front; more than $90 million in milestones	June
Calando Pharmaceuticals	Cerulean Pharma	Cyclodextrin co-polymer based drug delivery technology	Oncology	Exclusive worldwide rights	June
Penwest Pharmaceuticals	Otsuka Pharmaceutical	TIMERx oral controlled-release technology	Undisclosed	Undisclosed	June
Almac Discovery	Archimedes Pharma	ChisSys intranasal delivery technology	Chemotherapy-induced nausea and vomiying	Archmedes responsible for development to Phase II	June
Endo/Penwest	Veleant Pharmaceuticals	Oxymorphone extended-release (opana ER)	Pain	Rights in Canada, Australia and New Zealand	June
Access Pharmaceuticals	Two unnamed companies	Access's Cobalamin oral drug delivery technology	Diabetes	Companies considering entering licensing discussions	June
Flamel Technologies	Baxter	Controlled-release preparations of blod clotting factor replacement therapies	Blood clotting disorders in haemophilia	Flamel will receive technology access fees totaling €2.5 million; Baxter to pay all development costs	July
Biocompatibles International	Eisai	DC Bead and PRECISION Bead system	Vascular embolization of malignant hypervascularised tumours	Elsai paid $3 Million up front; further undisclosed regulatory and commercial milestone	July
Depomed	Merck & Co	Metformin extended-release technology	Fixed-dose combinations of	$10 million for non-exclusive licence	July

			sitagliptin and extended-release metformin		
AstraZaneca	Astellas	Symbicort (budesonide plus formoterol), inhaled	Bronchial asthma	¥3.0 billion($31.5 million) up front; up to ¥5.5 billion in milestones	August
ProStrakan	Endo Pharmaceuticals	Transdermal, once-daily, 2% gel formulation of testosterone	Hypogonadism	$210 million for US licensing and distribution rights	August
London School of Pharmacy	Encap Drug Delevery	Phloral colonic drug delivery system	Crohn's disease ulcerative colitis	Undisclosed	September
Surmodics	Genentech	Biodegradable microparticle system for sustained drug delivery formulation of Lucentis (ranibizumab injection)	Wet age-related macular degeneration	$3.5million up front; up to $200 million in fees and milestones	October
Sosei	Pharmasol	Development stage sublingual spray formulation of fentanyl	Pain	Undisclosed	October
Lupin Pharmaceuticals	Salix Pharmaceuticals	Bioadhesive drug delivery technology for use with rifaximin	Diarrhea	$5 million up front plus further payments	October

Appendix 21 – Promotional options

Advertising

Advertising channel	Proposal	Price	Contact
Drug Delivery Technology	Button 120x120 pixels 15 KB Flash SWF	£200 per JPG, GIF / month	Ralph Vitaro rvitaro@drugdeliverytech.com
European Pharmaceutical Review magazine	Website banner advertising (home page banner in the center with 100 x 300 pixels)	$995/month	Robin Johnson – rjohnson@russellpublishing.com

Membership associations:
Note: Information souce - [online] Europabio

Europabio (the European Association for Bioindustries)

"EuropaBio's mission is to promote an innovative and dynamic biotechnology-based industry in Europe. EuropaBio, (the European Association for Bioindustries), has 66 corporate and 7 associate members operating worldwide, 4 Bioregions and 22 national biotechnology associations representing some 1800 small and medium sized enterprises."

Benefits of EuropaBio membership

"Membership means a strong voice within Europe"

"At the European level we ensure you an effective representation to European Institutions by EuropaBio's board and members. Our close liaison with European regulators and opinion leaders led to successful lobbying initiatives resulting in a variety of positive legislative, regulatory and policy improvements."

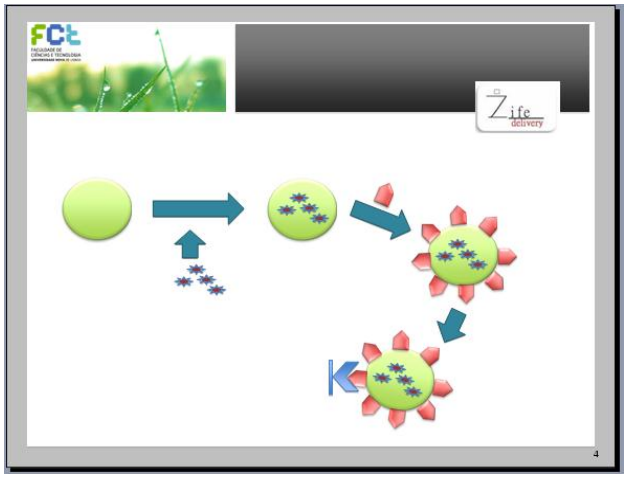
"Members also have opportunities to play a role in expert committees, lobbying, policy development alongside the promotional activities such as:

- Having a representative voice in Europe;
- Participation in European workshops and plenary discussions;
- Access to information concerning European and worldwide biotechnology developments;
- Access to information related to the current European legislation;
- Information updates, workshops and seminars relating to technology promotion;
- Access to a variety of events and network opportunities which are part of a trade association;
- Contacts with non-European associations for bioindustries (BIO, JBA, AfricaBio etc.) and life science companies."

"We lead an innovative and dynamic industry, helping our members find continuing success and opportunities."

Appendix 22 – Brief Technology Presentation

Powerpoint version




LIFE DELIVERY
CRO - Pedro Vidinha
Morada
pvidinha@lifedelivery.com
"The era that created the modern pharmaceutical industry is in fact over,"
Richard Evans, a former Wall Street analyst and now a pharmaceutical consultant

Appendix 23 – Non Disclosure Agreement (NDA) Template (adapted from bilateral NDA template made by Portuguese Industrial Property Office).

BILATERAL CONFIDENTIALITY AGREEMENT (With Comments)

Between

LIFE DELIVERY, with its registered office at …, legal person no…., represented by …, in his/her capacity as CEO, with powers of representation under the Law, as the First Party

and

…, with its registered office at …, legal person no. …, represented by …, in his/her capacity as …, with powers of representation under the Law, as the Second Party

Whereas:

- Contacts have been initiated by the parties for the purpose of develop and fit the DELIVES technology to an product or products of the Second Party;
- There is a need in this context to exchange restricted and/or non public information between the parties;
- Said information is a critical asset of the parties, with its own value, irrespective of whether or not any cooperation instrument is signed between them or between one of them and any third parties;

The parties enter into this CONFIDENTIALITY AGREEMENT, which is subject to the following clauses:

ONE

(Object)

1.1. The aim of this agreement is to guarantee the confidentiality and protection of the information classified as protected, confidential, non public or other similar description exchanged by the parties with the exclusive purpose fixed in Clause Two below.

1.2. Protected or confidential information, hereinafter referred to generally as the “Information”, is all information that, irrespective of the medium used, comprises:

- Unpublished works of any nature, such as graphic, written or sound;

- Unpublished compilations or selections of information;
- Financial documents;
- Know-how, technological data, methods, formulas, demonstrations, samples or studies;
- Computer programs, software or software programming blocks in the form of source code or object code;
- Commercial documents, such as customer lists;
- Reports, drafts and memoranda;
- Any intellectual assets, as a set of any and all research results, whether or not they are protected by any industrial property right;
- Any other information disclosed by the Disclosing Party to the Recipient in said context.

1.3. In the meaning set out in this agreement, the parties shall be called the "Disclosing Party" and "Recipient" in accordance with their capacity in the exchange of Information to be regulated.

TWO

(Purpose of disclosure and duty of confidentiality)

2.1. The Information shall be disclosed for the exclusive purpose of develop and fit the DELIVES technology to an product or products of the Second Party;

2.2. The First and Second Parties undertake not to use, disclose or transfer, for any reason or interest, in Portugal or abroad, the information disclosed by the other party for any purpose other than that set out in 2.1, unless authorised to do so in writing by the Disclosing Party.

2.3. The Recipient must protect the information disclosed by the Disclosing Party using the same degree of care that it uses to prevent the unauthorised dissemination and publication of its own information.

2.4. The Recipient shall take all necessary measures to prevent improper use of the information by any person who has access to it and guarantee the appropriate means to prevent the disappearance or loss of the information. It shall always inform the Disclosing Party of the occurrence of incidents of this nature, although said notification does not rule out its liability.

2.5. The Recipient undertakes to return any copies, excerpts or parts of the Information referred to in 1.2 above within 8 (eight) days on mere request on the part of the Disclosing Party.

THREE

(Ownership and integrity of the information)

3.1. The Information is the exclusive property of the Disclosing Party.

3.2. Disclosure of the Information to the Recipient does not grant it any intellectual property right, authority to apply for protection of any rights or any licence for any right or pending application for an industrial property right related to any information, on pain of application of Article 34.1.a) of the Industrial Property Code.

3.3. The Disclosing Party does not directly or indirectly warrant any kind of protection of the Information, namely by copyright or industrial property rights under this agreement.

3.4. The Recipient agrees and acknowledges that this agreement does not restrict the Disclosing Party's right to modify the information without prior notice.

3.5. Said modifications do not entail any responsibilities for the Disclosing Party nor do they oblige it to develop, announce, hand over, maintain or finance any products or business plans based on the Information.

FOUR

(Internal Disclosure of the Information)

The Recipient shall limit the disclosure of the Information to managers and employees to the extent that is strictly necessary for the purpose of this agreement. It shall give them appropriate instructions to this effect and enter into an equivalent written confidentiality agreement with them. The Recipient shall be fully liable to the Disclosing Party for its staff compliance with the commitments established herein and the Disclosing Party may claim proof of these agreements from the Recipient at any time.

FIVE

(Duration)

4.1. This agreement shall come into full effect on the date of signing by both parties and the recipient shall be bound by this confidentiality commitment on the exact terms stipulated above for a period of three years from the date of the last disclosure of Information pursuant to this agreement.

4.2. The parties may by agreement, at any time, revoke or amend the provisions of this agreement wholly or in part, provided that the confidentiality of the Information is not jeopardised.

4.3. Its effects may also cease on signing of any contractual commitment between the Parties that stipulates the confidentiality of the information and thereby replaces the terms of this contract, without prejudice to the following paragraph.

4.4. Nonetheless, under no circumstances are the parties bound under this agreement to enter into any legal business in the future.

SIX

(Liability)

The recipient is liable to the Disclosing Party for any losses or injuries, including material losses and lost earnings, resulting from breach of or defective compliance with its obligations to maintain confidentiality, without prejudice to any criminal liability incurred in the event of breach of this obligation, under applicable Portuguese law.

.2. Without prejudice to the previous paragraph, breach by the recipient of any of the obligations set out in this agreement shall entail payment to the Disclosing Party, as penalty clause, the sum of EUR … (…).

SEVEN

(Exceptions to Confidentiality)

6.1. An item of Information IS NOT CONSIDERED TO BE COVERED by duty to maintain confidentiality:

- If its disclosure has been expressly authorised by the Disclosing Party. Said authorisation must be requested by the recipient and granted by the Disclosing Party in writing within 8 (eight) working days, after which, in the absence of an answer, authorisation shall be deemed to have been refused;
- If it has been published, made public or in some other way clearly become part of the public domain before the time of disclosure;
- If it has been made public after disclosure or become part of the public domain for reasons not imputable to the recipient by way of intent or negligence;
- If the recipient can prove by means of written evidence that it was already in its possession before receiving from the Disclosing Party;;
- If it was received by the Recipient from third parties with no duty to maintain confidentiality, provided that they had the right to provide this information and that they did not obtain it directly or indirectly from the Disclosing Party under conditions of confidentiality;

- If the Recipient is obliged by law or judicial decision to disclose it, provided that the recipient notifies the Disclosing Party immediately and cooperates with it in all reasonable efforts to contest or limit the scope of said disclosure.
- If it is developed independently by the recipient.

6.2. The burden of proof of all exceptions to the obligation to maintain confidentiality set out in paragraph 6.1 lies exclusively with the recipient.

EIGHT

(Law and Conflict Resolution)

7.1. This agreement is subject to Portuguese Law.

7.2. The courts of the Portugal shall be competent to settle any disputes arising from it.

7.2. In the event of a disagreement or dispute between the Parties on the interpretation, validity or application of this Agreement that they are unable to settle by consensus, either Party may submit it to an arbitration court, expressly renouncing to the intervention of any other court.

7.3. The arbitration court shall be set up and function as established by the Voluntary Arbitration Law (Law no. 31/86 of 29 August with the amendments introduced by Decree-Law no. 38/2003 of 8 March) and shall consist of three arbiters, one appointed by each Party and a third by cooption by the Parties. If they are unable to agree on the appointment of the third arbiter, s/he shall be appointed by the Presiding Judge of the Lisbon Court of Appeal at the request of either Party.

7.4. The arbitration procedure shall take place in Portuguese, in Lisbon, unless otherwise agreed by the parties in the arbitration procedure.

7.5. Whenever there is a disagreement or dispute regarding industrial property, the ARBITRARE Arbitration Centre shall be competent to settle said conflicts, to the express exclusion of any other, in which case the Arbitration Centre's regulations shall apply.

7.6. The arbitration tribunal and/or arbitration centre shall appreciate the facts and rule in accordance with Portuguese law. Its decisions shall not be subject to appeal.

The parties recognise and accept the provisions of this Agreement, the content of which shall replace all previous negotiations and contacts between the parties.

DATE AND PARTIES' SIGNATURES

Appendix 24 – 2011 Drug delivery conferences. Source: [online] On drug delivery

Date (2011)	Conference Title	Location	Organiser
January 17-18	Drug Delivery & Formulation	Berlin, Germany	WTG Group
January 19-20	3rd Annual Prefilled Syringes Conference	London, UK	SMi
February 1-2	6th Annual Drug Delivery Systems	London, UK	Visiongain
February 23-24	Pharmapack	Paris, France	Canon Communications
February 23-24	BIOMEDevice	Paris, France	Canon Communications
March 8-9	Aerosol Forum	Paris, France	Oriex
March 24-25	Injectable Drug Delivery - Devices, Technology & Development	London, UK	Management Forum
March 28-29	Skin Forum, 12th Annual Meeting	Frankfurt, Germany	APV Mainz
March 30-31	8th Conference on Controlled Release	London, UK	SMi
April 4-5	Nasal & Buccal Drug Delivery	London, UK	Management Forum
May 3-4	Pharmaceutical and Medical Packaging 2011	Copenhagen, Denmark	Hexagon
May 3-6	RDD Europe 2011	Berlin, Germany	RDD Online / Aptar Pharma
October 18	Drug Delivery Devices 2011 (DDD'11)	Copenhagen, Denmark	Hexagon
October 19	Medical Plastics 2011 (MP'11)	Copenhagen, Denmark	Hexagon
October 25-27	CPhI Worldwide	Messe, Frankfurt.	UBM
October 25-27	ICSE	Messe, Frankfurt.	UBM
November 7-11	Universe of Prefilled Syringes & Iniection Devices	Basel, Switzerland	PDA

Appendix 25 – Geographical distribution of clients

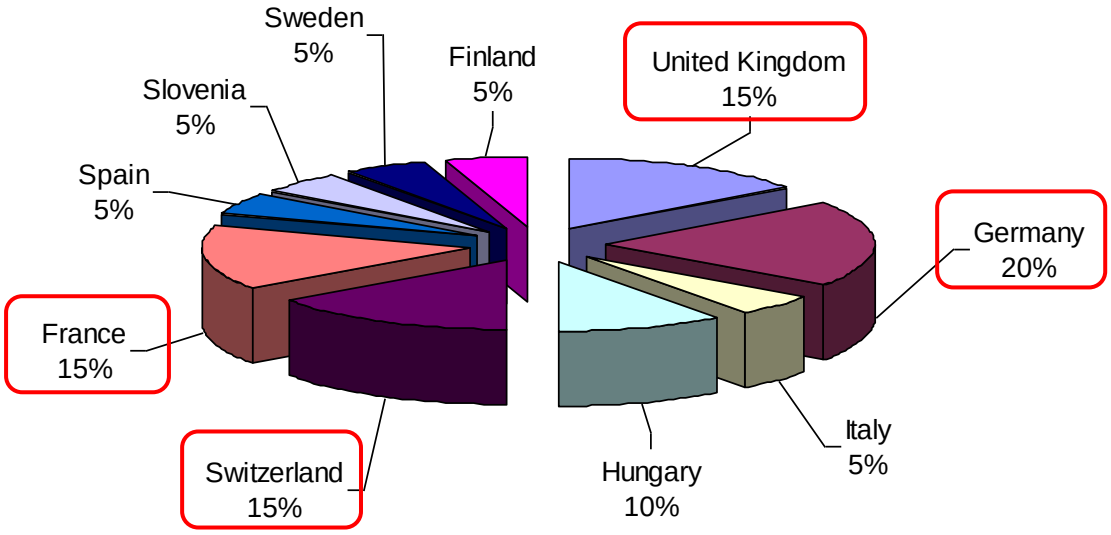


Figure 0.1- Geographical distribution of clients focused on cardiovascular therapies

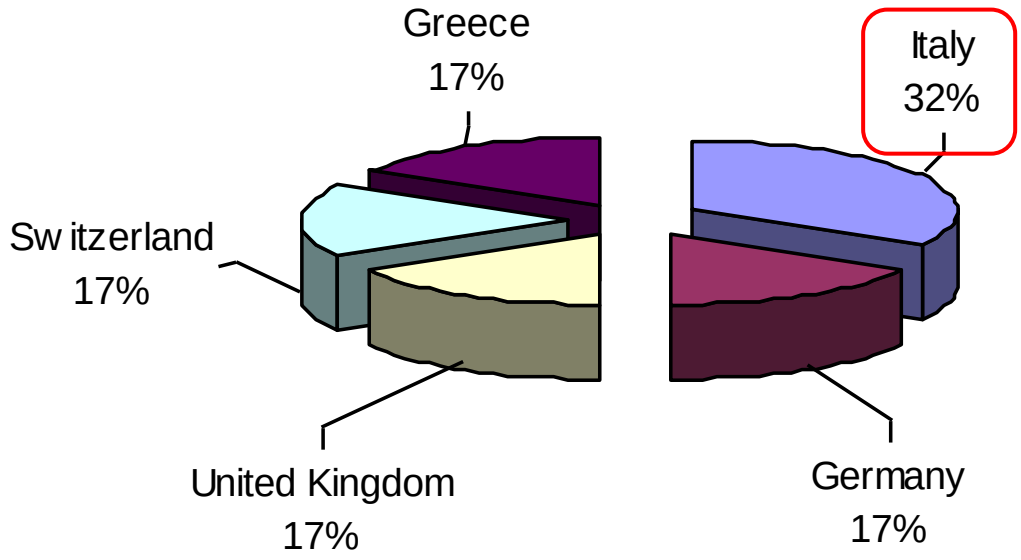


Figure 0.2 - Geographical distribution of clients focused on Inflammation and Musculosketal therapies

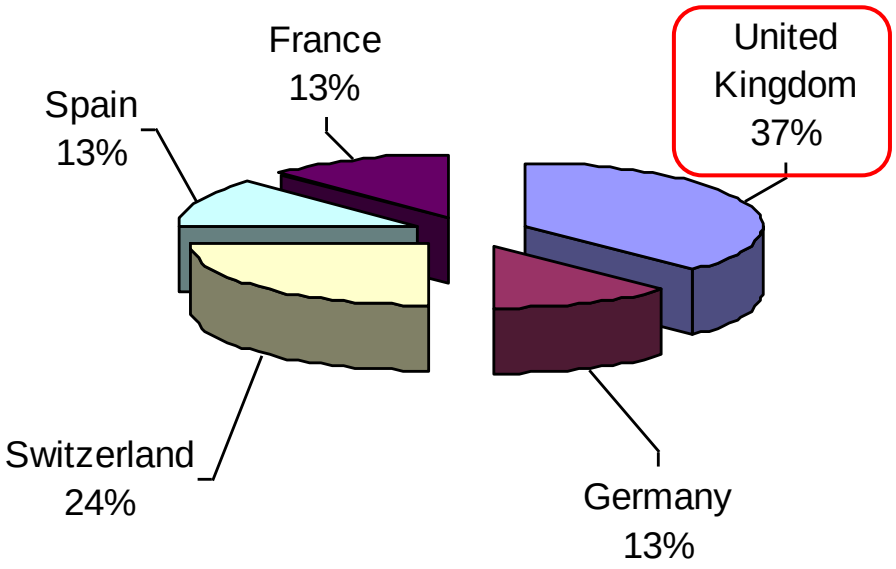


Figure 0.3 - Geographical distribution of clients focused on Immunologic therapies

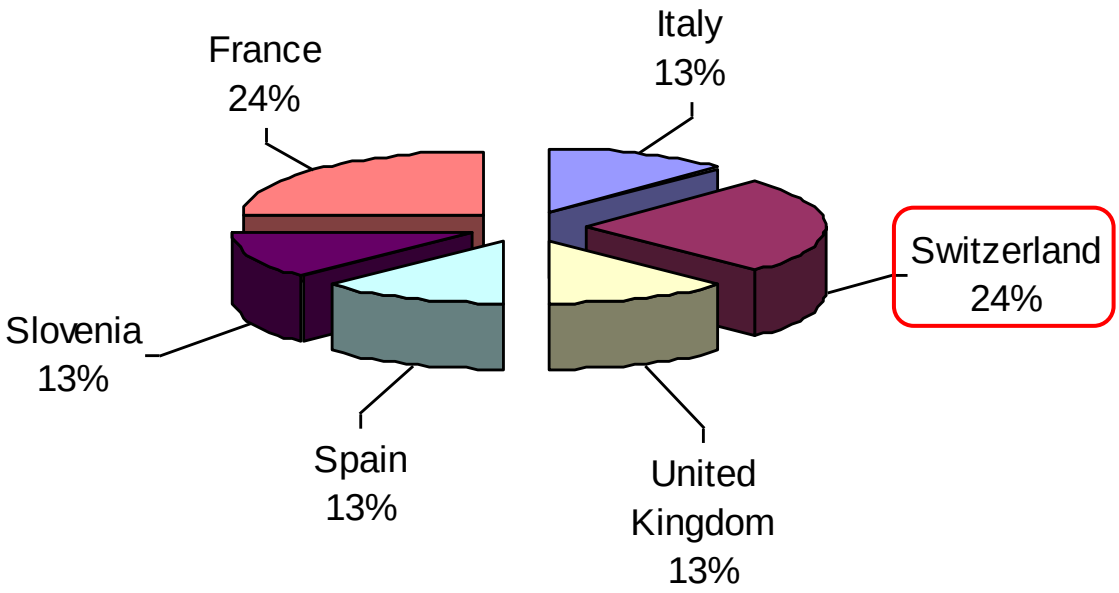


Figure 0.4 - Geographical distribution of clients focused on Metabolic Disorders therapies

Appendix 26 – Scientific Park of Madrid Advantages

General services:

- ✓ Reception
- ✓ General Secretariat
- ✓ Reception and mail delivery
- ✓ Sending and receiving fax
- ✓ Meeting rooms, classrooms, audiovisual equipment
- ✓ Photocopying and binding
- ✓ Basic office furniture
- ✓ Internet
- ✓ 24h Access
- ✓ Cleaning
- ✓ Surveillance and security
- ✓ Parking
- ✓ Canteen and vending machines
- ✓ Transportation to / from the Train station
- ✓ Social Debit

Specific services:

- ✓ Bioincubator Unit
- ✓ Economic - Financial Unit
- ✓ Projects Unit
- ✓ Business Assistance Unit
- ✓ Technological Promotion Unit
- ✓ Human Resources Unit
- ✓ Communication Unit
- ✓ Information Technology Unit
- ✓ Technology Transfer Unit

Professional services:

- ✓ Taxation R + D + i
- ✓ Aid and subsidies
- ✓ Patents and Trademarks
- ✓ Legal and accounting consulting
- ✓ Economic Intelligence
- ✓ Company Valuation
- ✓ Risk Capital

Strategic Partnerships:

Source: Cátia Rabaça (PCM Business Development Unit)

Appendix 27 – Website creation and management proposal

Implementação site e imagem LIFE DELIVERY

Documento n.º: ***Life Delivery/2011***

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Documento N.º:
Life Delivery/2011

Referente a:
01-10012011-LifeDelivery

Data:
10-01-2011

Documento n.º:	*Life Delivery/2011*
De:	*Mário Martins* *+351 91 699 32 41* *joao.martins@javali.pt*
Data de Envio:	*10-01-2011*
Versão:	*01*
Para:	*LIFE DELIVERY*
Ao Cuidado de:	*Exma. Sra. Ana Sofia Esteves*
Respeitante a:	*Proposta de criação de site*
Data de Entrada:	*Segunda-Feira, 10 de Janeiro de 2011*

Folha:
2/16

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ÍNDICE

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Life Delivery/2011

Referente a:
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Documento N.º:
Life Delivery/2011

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01-10012011-LifeDelivery

Data:
10-01-2011

1 AGRADECIMENTO

Na sequência da vossa solicitação para Proposta de criação de site a Javali - ADSI, Lda vem apresentar a sua proposta de colaboração, manifestando desde já total empenho e compromisso para assegurar o sucesso deste projecto.

Esperando que a presente proposta corresponda aos vossos objectivos, ficamos à inteira disposição para quaisquer esclarecimentos adicionais julgados convenientes.

Sem outro assunto de momento, reiteramos o nosso interesse e disponibilidade em colaborar com o Vosso projecto e subscrevemos com os melhores cumprimentos.

Atentamente,

P'la Javali - ADSI, Lda

(Mário Martins)

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2 ENQUADRAMENTO

Uma presença na Internet é hoje um primeiro local de disponibilização e obtenção de informação acerca de uma determinada instituição, sejam os *internautas* potencias patrocinadores, fornecedores, apoiantes ou meramente curiosos é necessária uma presença que dignifique e credibilize a instituição.

Devido à dependência na informação disponibilizada pelas plataformas informáticas torna-se critica a sua constante disponibilidade. O aumento de falhas de segurança informáticas devido a faltas de actualização e a sua inadequação tecnológica torna a sua evolução obrigatória.

A totalidade da colaboração proposta integra-se no âmbito das actividades desenvolvidas pela Javali - ADSI, Lda, cuja vocação se centra especialmente na área das tecnologias de informação em software livre e em particular em projectos de desenvolvimento web *based*.

Esperamos assim, que a Javali - ADSI, Lda possa vir a merecer a vossa confiança, reiterando, na oportunidade, o interesse e disponibilidade para a celebração de um acordo de prestação de serviços, cujas bases gerais se apresentam seguidamente.

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3 O PROJECTO

O projecto de Implementação site e imagem LIFE DELIVERY é compreendido pelo seguinte conjunto de grandes tarefas:

- Implementação de Design;
- Personalização da plataforma de gestão de conteúdos para suportar as funcionalidades pretendidas;
- Formação;
- Alojamento.

3.1 Design

Trabalho Web Design

A página de entrada do portal pressupõe uma apresentação moderna e contemporânea, com imagem trabalhada de forma a comunicar a identidade da instituição, com zonas de destaque visual para áreas informativas. É enviada em anexo a este documento uma proposta gráfica para o Portal.

Requisitos

Imagens de alta definição e conteúdos em formato digital

3.2 Personalização da plataforma de gestão de conteúdos para suportar as funcionalidades pretendidas

Serão implementadas e adequadas as seguintes funcionalidades e módulos

- Ferramenta de Gestão de Conteúdos do site

  Permite ao cliente administrar todos os conteúdos existentes no site, deste modo o cliente sempre que deseje poderá actualizar informação tal como

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notícias, imagens, documentos, vídeos, actualizar contactos, criar novas entradas entre muitas outras opções existentes.

- Módulo de gestão de destaques
- Módulo de notícias
- Galerias de imagens / vídeos
- Módulo de formulários para contacto
- Links
- Mapa do site
- Módulo de gestão de utilizadores
- Suporte Multilingue
- Integração com a ferramenta de estatística
- Calendário de eventos
- Newsletter
- Importação de conteúdos de fontes externas
- Ligação a redes sociais

3.3 Prazo de entrega

Após a entrega dos conteúdos em formato electrónico e aceitação do design proposto, o site ficará disponível, para avaliação, num prazo estimado de 40 dias.

3.4 Alojamento(Opcional)

A Javali disponibilizará serviço de alojamento em servidores de elevada fiabilidade, segurança e desempenho por um período de 12 meses.

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REQUISITOS

Registo e dados de domínio.

3.5 Formação

De modo a dotar os responsáveis pela gestão do site, do conhecimento necessário para a introdução de conteúdos, será dada uma breve formação que consistirá essencialmente em:

- Introdução à plataforma;
- Introdução de imagens, documentos e conteúdos;
- Outros assuntos relevantes para gestão de conteúdos.

Esta formação será ministrada nas instalações da Javali - ADSI, Lda e terá uma duração máxima de 4 horas e dois formandos.

Note-se que o motor de gestão de conteúdos ficará adequado de modo a que, qualquer utilizador com conhecimentos de navegação de Internet, facilmente seja capaz de introduzir e realizar as tarefas de introdução de conteúdos.

Se se mostrar necessária formação adicional, tal deverá ser orçamentada.

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4 APOIO

4.1 Apoio na utilização do software

Com o objectivo de apoiar continuamente os utilizadores da LIFE DELIVERY a Javali - ADSI, Lda disponibiliza um ponto de contacto, com os conhecimentos necessários a garantir que a plataforma é utilizada de acordo com o âmbito e modelo idealizados.

Seja o utilizador em questão avançado, ou iniciado, a Javali - ADSI, Lda pretende dotá-lo do conhecimento necessário à realização das mais diversas tarefas adequadas ao seu perfil.

Para o projecto em questão, consideramos 1 hora mensal, durante 12 meses para apoio e transição de plataforma.

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5 OBRIGAÇÕES DA LIFE DELIVERY

5.1 Definição de Contacto Privilegiado

A LIFE DELIVERY deverá nomear um interveniente privilegiado para interagir com a Javali - ADSI, Lda de modo a que durante a prestação do serviço proposto este:

1. Acompanhe a realização dos serviços;
2. Receba e valide a informação que seja disponibilizada pela Javali - ADSI, Lda;
3. Preste esclarecimentos sobre os diversos assuntos que se mostrem ambíguos;
4. Defina as prioridades de implementação;
5. Reúna nas datas agendadas.

NOTIFICAÇÕES E ESCLARECIMENTOS

Todas as necessidades de esclarecimento e notificações deverão ser realizadas em formato electrónico para endereço a designar.

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6 OBRIGAÇÕES DA JAVALI - ADSI, LDA

6.1 Definição de Contacto Privilegiado e Equipa de Trabalho

A Javali - ADSI, Lda deverá nomear um interveniente privilegiado para interagir com a LIFE DELIVERY de modo a que durante a prestação do serviço proposto este:

1. Informe sobre o estado realização dos serviços;
2. Reúna com a LIFE DELIVERY de modo a planear as intervenções;
3. Preste esclarecimentos sobre os diversos assuntos que se mostrem ambíguos.

A equipa assim como o número de elementos necessários à realização do serviço será determinado pela Javali - ADSI, Lda e indicado antecipadamente à LIFE DELIVERY.

Disposições Gerais

1. A Javali - ADSI, Lda procederá à implementação dos trabalhos propostos e seguirá o planeamento realizado.
2. A Javali - ADSI, Lda garantirá a confidencialidade de toda a informação, tal como senhas e dados de utilizadores.
3. A Javali - ADSI, Lda compromete-se a respeitar os procedimentos de segurança e confidencialidade conformes com as regras internas em vigor e legislação aplicável.
4. A Javali - ADSI, Lda compromete-se a zelar para que os seus colaboradores mantenham absoluto sigilo, neutralidade e descrição relativamente a informações e documentos da LIFE DELIVERY que lhe sejam confiados.
5. As partes acordam que não constituirá infracção do dever de confidencialidade, o fornecimento de informação requerida por Lei.

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7 EXCLUSÕES

1. Os serviços que dependam de intervenção humana, não serão prestados em dias de feriado oficial, tolerância total de ponto ou noutros períodos de encerramento extraordinário, como o feriado municipal.
2. Não estão incluídos no âmbito dos serviços a prestar pela Javali - ADSI, Lda, qualquer substituição ou reparação de equipamentos (hardware) ou de aplicações (software) que sejam propriedade da LIFE DELIVERY.
3. Em razão das exclusões expressas no número anterior, não poderão ser imputadas à Javali - ADSI, Lda quaisquer responsabilidades pelos prejuízos que a LIFE DELIVERY ou terceiros venham a sofrer na sua infra-estrutura própria.
4. A Javali - ADSI, Lda não poderá ser responsabilizada pelas eventuais consequências que resultem de más práticas por parte da LIFE DELIVERY, no âmbito da utilização dos serviços objecto do Protocolo.
5. A Javali - ADSI, Lda não poderá ser responsabilizada, nem lhe poderá ser exigida qualquer indemnização, decorrente de atrasos ou prejuízos resultantes de circunstâncias de força maior, acontecimentos ou incidentes alheios à sua vontade, tais como revoltas, calamidades, conflitos sociais, avarias de material, mau funcionamento ou interrupção de comunicações, incêndio, inundação, interrupção de energia eléctrica, destruição total ou parcial de informações transmitidas ou armazenadas.

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8 CONDIÇÕES COMERCIAIS, FINANCEIRAS E PREÇOS

8.1 Local de Prestação de Serviços

A prestação dos serviços será nas instalações da Javali - ADSI, Lda, excepto se acordo em contrário.

8.2 Início da prestação de serviços

O início da prestação de serviços será até 10 dias após a verificação da totalidade das seguintes condições:

1. Entrega da adjudicação, sendo esta considerada como efectivada após a recepção da nota de encomenda devidamente assinada e carimbada;

8.3 Aceitação do projecto

Após entrega do projecto cabe ao cliente num prazo de 10 dias, realizar as verificações e testes que considerar necessários e aceitáveis. Se neste prazo não se pronunciar, o projecto será considerado como aceite.

8.4 Condições de pagamento

A liquidação de todos os serviços deverá ser efectuada contra factura, até 8 dias após a data da sua emissão.

8.5 Prazo de Validade da Proposta

Todos os encargos e demais condições desta proposta são válidos pelo período de 8 dias a partir da data da sua entrega.

8.6 Valores

O pagamento pelos serviços acima descritos, será mediante o pagamento de 3400€ em duas fases, 60% na adjudicação e 40% na aceitação do projecto.

Javali - Administração e Desenvolvimento de Sistemas Informáticos, Lda

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Embora apenas tenhamos apresentado esta forma de pagamento, estamos disponíveis para encontrar outra que se possa enquadrar no desejado pela LIFE DELIVERY.

Nota: A todos os valores acresce IVA à taxa legal em vigor

Folha:
14/16

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9 CARACTERÍSTICAS TÉCNICAS

O Drupal CMS, para além de representar uma solução sem custos de licenciamento, tem a vantagem de ser evolutivo e de apresentar um vasto conjunto de módulos e componentes.

Todo o software utilizado para desenvolvimento, armazenamento e disponibilização de conteúdos será baseado em código aberto (Open Source Software), com excepção nos módulos criados de raiz para o fim em questão. Com esta abordagem pretendemos reduzir os custos com o projecto, o tempo de entrega, aumentar a estabilidade a interoperabilidade, a segurança e a robustez.

O Sistema Operativo, que albergará o projecto deverá ser preferencialmente Linux, no entanto, a plataforma proposta também funcionará em Microsoft Windows.

O Sistema de Gestão de Base de Dados (SGBD), será o MySQL server.

O Servidor de Páginas de Internet a utilizar será o Apache, servidor este que é utilizado em cerca de 70% dos servidores de páginas mundiais.

A linguagem de programação utilizada será o PHP, para base de dados será utilizada a linguagem SQL. Para disposição da informação e formatação será utilizado HTML e suas variantes, CSS e JavaScript, AJAX.

As páginas geradas serão suportadas nas plataformas mais comuns, nomeadamente Linux, MAC OS e Microsoft Windows.

Sempre que possível serão seguidas as normas definidas no seio das tecnologias da informação.

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10 A JAVALI - ADSI, LDA

A Javali é um empresa especializada na segurança, implementação e desenvolvimento de sistemas informáticos, recorrendo sempre que possível a sistemas e ferramentas de código aberto (Open Source).

Fundada no final de 2002 por uma equipa com experiência em diferentes áreas das tecnologias da informação integrou no primeiro semestre de 2003 o Parque Tecnológico de Almada e Setúbal, Madan Parque, sediando-se no Campus Universitário da Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa.

Através deste atalho para o conhecimento, a Javali garante inovação ao mais alto nível.

Há uma preocupação constante em dotar os nossos clientes de liberdade de escolha e de acção. Esforçamo-nos por apresentar alternativas viáveis que respeitem os padrões tecnológicos do mundo informático e que garantam a longevidade e interoperabilidade dos sistemas. As nossas soluções são sinónimo de robustez, fiabilidade, segurança e crescimento, apresentando-se ideais quer para o pequeno empresário quer para a grande instituição.