

Department of Business Administration

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Implementation to product D

Author: Akbar Ansari

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Thesis

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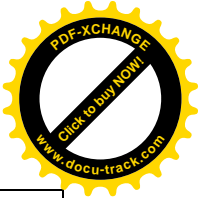
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Master of Business Administration in Marketing Management

Title	Evaluation Strategy for Candidates Drug and Implementation to product D in early Clinical Trial
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Abstract	<p>Biovitrumis is one of the larger biopharma companies in Euprope and conducts research in different niche areas. One of the interested areas for Biovitrum is Exocrine Pancreatic insufficiency. Biovitrum has a candidate drug (product D) in early development process for treatment of. Exocrine Pancreatic Insufficiency.</p> <p>The Drug development is a long, complicated and costly process. Therefore, it is very important for managers to know the commercial value of a future drug. The purpose of this report is to develop a model for evaluation of candidate drug in early development phase and analysis of market potential for product D for treatment of Chronic pancreatitis. Chronic pancreatitis is disease within sub group of Exocrine Pancreatic Insufficiency.</p> <p>The deductive reasoning approach and quantitative data is used in this report. Only secondary data is collected for this study. The sources of secondary data are research papers, Google Pub-Med database and consultant companies.</p> <p>A new model is developed for evaluation of candidate drug .This model can analyse the market potential, unmet medical need, and calculate net</p>

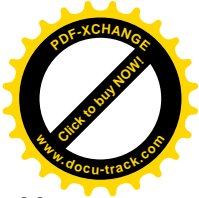


	<p>present values. This study shows that there is unmet medical need in chronic pancreatitis. The result also shows that product D has comparative advantages over present products in the market and future competitors. The product D can full fill the unmet medical need for treatment of Chronic pancreatitis.</p>
Keywords	Candidate Drug , Evaluation strategy, market analysis

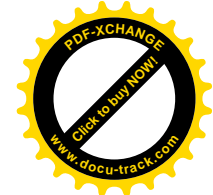
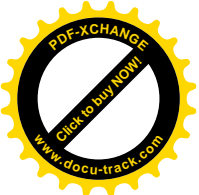


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1 INTRODUCTION

Why early evaluation of candidate drug is so important? The drug development process is very long and costly. About 75 percent of the cost of drug development is in failure of candidate drug (Boston, 2004). To reduce the cost of failure is one of the most important steps to increase the productivity. As we know the cost of development is much higher in later stages as compare to early stage of development. Therefore it is far better to fail the candidate drug in the early stage of development rather than in the later stages. Therefore managers have significant pressure to make accurate go or no-go decisions at the end of each development stage to use the resources on best projects.

Biovitrum (biovitrum.com) is pharmaceutical company with focus on specialist care medicines and listed on the Stockholm Stock Exchange since September 15, 2006. It has research and development units in Sweden and UK. Biovitrum conducts research and development for unmet medical needs for both smaller patient population (specialist care medicines) and common diseases. One of the interested areas is treatment of Exocrine Pancreatic insufficiency. Biovitrum has a new candidate drug “product D” in early clinical phase of drug development process. The Product D is potential candidate for treatment of Exocrine Pancreatic insufficiency. Pancreatic insufficiency is due to damage of pancreas resulting reduced in ability for digestion and absorption of food that contribute to the weight loss. This can happen due to hereditary disease called cystic fibrosis but also as result of chronic inflammation of pancreas or cancer.

The current treatment is oral enzyme replacement therapy. These enzymes are extracts derived from porcine and called Pancreatic enzyme products (PEPs). These enzymes help patients to digest and absorb food. These preparations are different in composition of enzymes, enzymes activities and stability in gastric acid. Many patient needs to take large number of capsules due to variation in enzymes composition and their stability in stomach.

Literature review indicates that there is room for development for more pure, effective and stable product as compare to present Pancreatic enzyme products.

Product D is a lipase. It is one of three major natural lipases responsible for digestion of fat. Product D is more stable and pure as compare to pancreatic lipase and broad specificity against different types of fats.

The main interest of this thesis is to develop a model for evaluation of candidate drug in early development process and find the market potential for Product D for treatment of Exocrine Pancreatic insufficiency other than cystic fibrosis such as chronic inflammation of pancreas.

1.1 Background

A drug, general speaking, is any substance that effect on normal bodily function. There is no single definition. In pharmacology drug is chemical substance used in the treatment or cure of a disease. There are two main groups of drug, the large molecule (biologics) such as insulin drug and small molecules such as Aspirin. Drug development process is long, complicated and costly process. The main steps of drug development process are same for large and small molecule such as preclinical testing, clinical testing, and approval of drug and marketing. But the manufacturing process and approval conditions are different for small and large



molecules. The manufacturing process is often complicated and costly for large molecules. For new drug development it is important to know the commercial value of future drug. If new drug is first in class in the unmet medical need it can be ease to get price premium. However as this is seldom the situation. There are still many unmet medical need in different disease areas such as Neurological damage, Alzheimer's, many cancers and many chronic disease have few options for treatment. For example chronic heart failure, chronic obstructive pulmonary and management of Pancreatitis diseases (Esther,2007).

The focus of this report will be on unmet medical needs within a sub group of Pancreatitis diseases called Chronic Pancreatitis (CP). Pancreas is gland and it main function is to produce digestive enzymes. These enzymes play a main role in digestion of food. If pancreas is not able to produce enough digestion enzymes it can cause insufficiency of pancreatic enzymes. Insufficiency of pancreatic enzymes leads to malabsorbtion of nuteients and resulting in weight loss. There are many diseases related to Pancreas eg, chronic pancreatitis, cystic fibrosis, acute pancreatitis and pancreatic cancer. Chronic pancreatitis is an inflammatory disorder of pancreas gland. The most common symptoms of CP disease are abdominal pain, diarrhea, and weight loss. The treatment is difficult and challenging.

1.2 Problem

Pharmaceutical and biotech companies are under greater pressure to improve the productivity of their R&D pipeline. The value of R&D pipeline is heart of company and it affects the financial value of company. The analysis of pipeline portfolio is prioritizing areas with the greatest potential in term of the market and competition. Each project should be asses with respect to rate of success and expected return on investment (ROI). Therefore it is need for rational decision making with respect to go/no-go decision. It is better to have a method / model for evaluation and analysis of projects after each main step. It is economically valuable to fail the bad project as soon as possible and use the resources for good project to reduce the time to market.

Biovitrum has product D in early development phase. The company managers are interested in an evaluation of this product to find out possibility of technical success, commercial value and competition. The Evaluation can reduce the possibility to make unprofitable / less profitable drug.

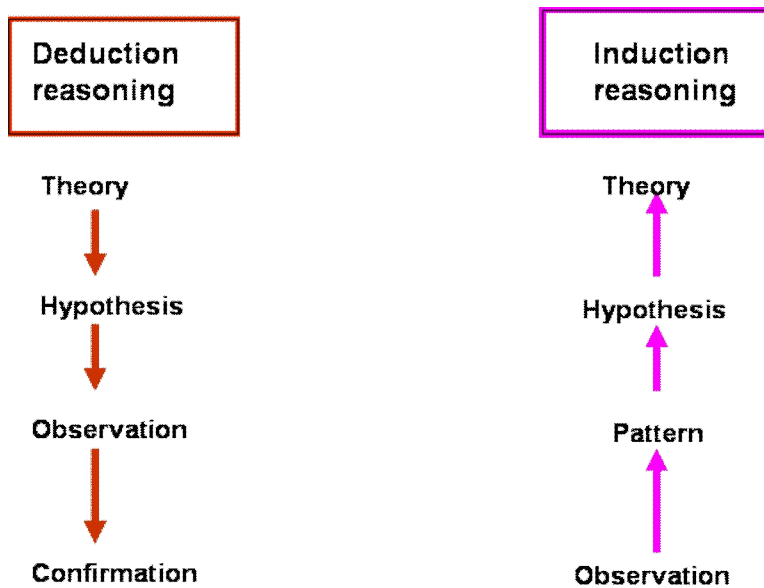
1.3 Purpose

The target of this study is to develop a strategy evaluation model for commercial evaluation of drugs in research pipeline and analyse the probability of the candidate drug "product D". The model should be capable to evaluate the candidate drug in terms of situation analysis of therapy area, Operational viability, competitor's analysis, pricing strategy, market assessment and entry of new competitors or product before/at the time of product D launch.

2 METHOD

In logic, there are two, broad methods for reasoning namely deductive and inductive approaches (socialresearchmethods.net). Deductive works from the general to the specific. This is informally called a “top-Down. This approach is narrower in nature and is concerned with testing or confirming hypotheses. An inductive reasoning works the other way around, it works from observation to generalization and theories. This is called a “bottom-up approach. Inductive reasoning is more open-ended and exploratory Main steps of both reasoning methods are mentioned in figure 1.

Figure 1: Reasoning Methods.



Source: socialresearchmethods.net

This report will follow the deductive approach and quantitative data because this method will lead to test the hypotheses with specific data. All data will be secondary because small scale (number) of primary data can be misleading the real situation, when it comes to what is happening in the real world (therapy area). Collection of large scale of primary data is not possible for me because it will take much more time to make hundreds of interview with different specialists in different countries. Therefore I will use secondary data in this report. The sources of information will be research papers, reports, Google, Pub med (databases) , IMS company, Vector values company and books such as Contemporary strategy analysis(Grandt,2002), Principles of marketing (Kolter, 2002) and Corporate Finance (Ross, 2002).

To maximize the benefit of any research, it is very important to define carefully the problem and research objectives. In this study, problem was defined by marketing manager of Biovitrum. “Analyse the market potential of product D for the treatment of chronic inflammation of pancreas”.



After problem has been defined, I did preliminary exploratory research to set the research objectives. This preliminary research has the focus on evaluation models for candidate drug and disease related to Exocrine Pancreatic Insufficiency. With the help of this research I set two different research objectives because it was not possible to find a suitable evaluation model to analyse the product D. This marketing research report contains two objectives; 1: to develop a model for evaluation of market potentials of candidate drug. 2: Implementation of the model to analyse the market potential of product D. For research plan see figure 2.

2.1 Research Design

Managers need market information in order to introduce a new products or services. Marketing research can provide the wide variety of information to managers such as market potential, market size, market share, market trend and, competition. There are three different types of research (quickmba.com).

Exploratory market research; the goal of Exploratory research is to gather preliminary information about market. This information can help to define the problem more precisely. Exploratory research can be performed using a literature search, case study and surveying people.

Descriptive market research;

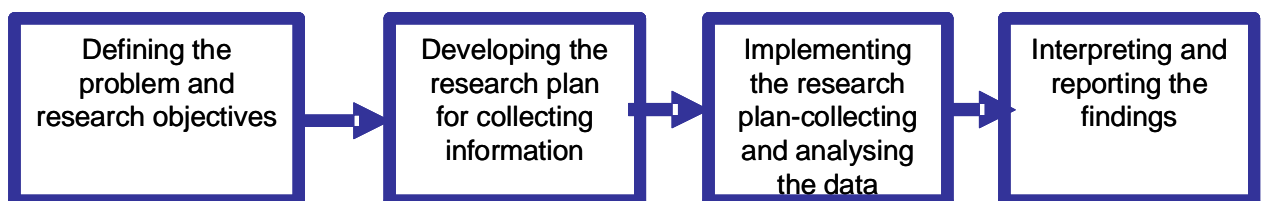
This market research is more rigid than exploratory research. This research describes users of a product, determination of proportion of the population that use a product and predict the future demand of a product.

Causal market research; This research is to test the hypotheses about cause-and-effect relationships.

2.2 Research strategy

The marketing research will follow the main steps of Marketing Research Process described (Kolter, 2002). This marketing research process contains four main steps as mentioned in figure 2.

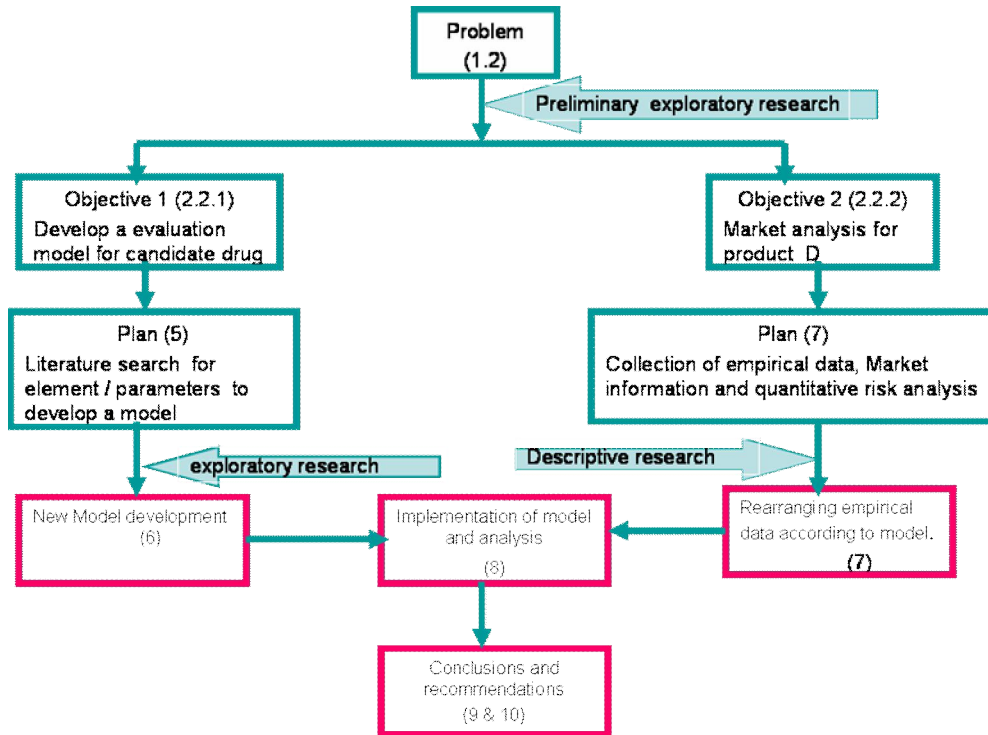
Figure 2: Marketing Research Process



Source (Kolter, 2002).

Due to two different objectives, I have modified the above mentioned marketing research process (figure no 1) to make it “fit for Purpose”. Therefore first two main steps in figure no 1 is subdivided into four different steps for this marketing research. I think these subgroups will make research process easier. It will be two different research plans for collection of relevant information, one for each objective. For more information see figure no 3.

Figure 3: Research plan for this study



Source: Own

2.2.1 Objective 1

The commercial value of a drug candidate is one of the important factors for ROI on big and risky investment. Therefore it is very important to find out the commercial value of a candidate drug with respect to the candidate characteristics, market demand and quantitative risk analysis in early phase of development process. Therefore a model should be capable to analyse these main elements/parameters.

Data collection method

The following specific information will be needed to make an evaluation model for analysis of candidate drug. What parameters are important for Market assessment and Competitors analysis? How to do situation analyse in the therapy area? What is useful method for comparison of current cost of project versus the potential benefits in the future? What is importance of operational viability and pricing strategy? The exploratory marketing research will be performed to collect related secondary data. The sources of these information will be



research papers, reports, Google, Pub med and books such as Contemporary strategy analysis (Grant, 2002), Principles of marketing (Kolter et al, 2002), and Corporate Finance (Ross et al ,2002) .

2.2.2 Objective 2

Second objective of this report is to analyse the market potential of product D in the treatment of chronic inflammation of pancreas.

Collection of empirical data method

The following empirical data / information will be required to analyse the market potential of product D. What is situation in the therapy area? What is number of epidemiology and market size in Europe, US and Japan? Who are the main competitors? What are their objective, capability, strategy, and their product characteristics? What is Operational viability and pricing strategy for product D?

The descriptive research will be performed to collect related secondary data and sources will be Google, research papers, reports, Consultant companies.

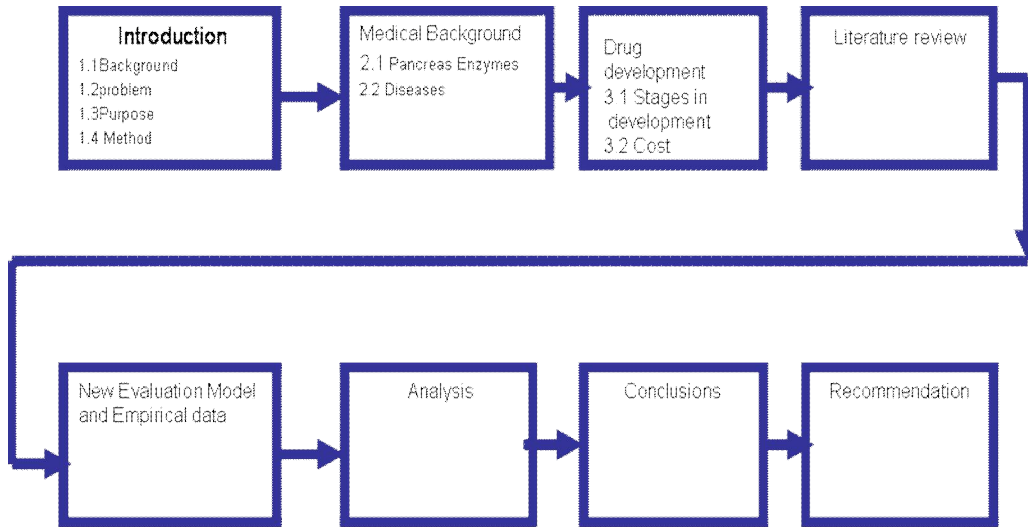
2.2.3 Model development and analyse

After collection of all necessary information, model will be developed and than analysis will be perform with help of new model.

2.3 Report Layout

This study report contains seven main parts as mentioned in figure 4. The introduction chapter is followed by the medical background and drug development process. These sections introduce the most important aspects of therapy area and drug development. Literature section explains different evaluation models. In the coming parts (New evaluation model, Empirical data)I will describe new evaluation model and its use with the help of empirical data. Finally I will move to analysis, conclusions and recommendations.

Figure 4 Report Layout



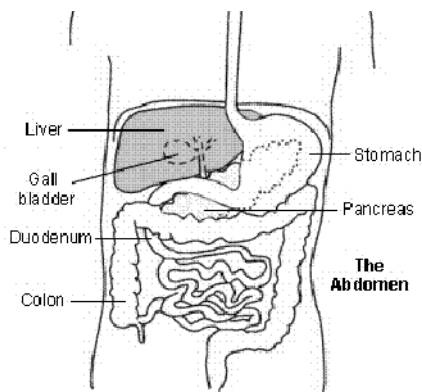
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3 MEDICAL BACKGROUND

Pancreas

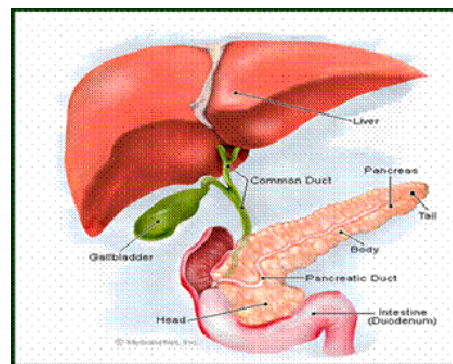
The pancreas is a large gland behind the stomach and close to the duodenum. The duodenum is upper part of the small intestine see figure 5. The small intestine is where most of the digestion and absorption of food occurs. One of the functions of the pancreas (figure 6) is to make enzymes (pancreas enzymes) that digest food. These enzymes secretes into small intestine through a tube called the pancreatic duct. The pancreas also releases the hormones such as insulin and glycagon into the blood stream. (patient.co.uk;medicinent.com).

Figure 5: Abdomen

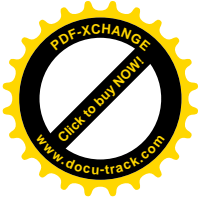


source: patient.co.uk

Figure 6: Pancreas



Source: medicinent.com



3.1 Pancreas Enzymes

Lipase

Lipase is an enzyme, whose function is to hydrolysis fats into free fatty acids and monoglycerides. In cystic fibrosis or chronic pancreatitis dietary fat absorption is lost up to 40-50 %. This leads to abdominal problems such as steatorrhea, flatulence and (dhmh.state.md.us).

Protease

In the stomach large proteins chains are cleavage to polypeptide chains by pepsin. Pancreatic proteases digest these polypeptides into small polypeptide and free amino acids. These small polypeptide and free amino acids are then absorbed in small intestine(dhmh.state.md.us).

Amylase

Amylase helps in digestion of carbohydrates. Carbohydrates digestion is very little affected by pancreatic insufficiency because most of carbohydrates digest in the mouth and stomach. Amylase breaks starch in to small glucose polymers (dhmh.state.md.us).

3.2 Diseases

Exocrine Pancreatic insufficiency

Pancreatic insufficiency is due to damage of pancreas and loss the ability to produce amylase, protease and lipase. This can lead to poor digestion and absorption of food that contribute to the weight loss. This may caused due to variety of conditions such as cystic fibrosis, Pancreatitis, and pancreatic cancer.

Cycitic fibrosis

Cystic fibrosis is hereditary disease and it mainly affects the lungs and digestive system. There is no cure for cystic fibrosis, causing progressives disability and early death. Cystic fibrosis is caused by a mutation in a gene called cystic fibrosis transmembrane. The defected gene case the body to produce unusually thick mucus that clogs the lungs and leads to life threatening lung infection and obstruct the pancreas to produce the enzymes needed for food digestion.commen symptoms are frequent lung infections, shortness of breath, greasy and bulky stools (en.wikipedia.org).

Pancreatitis

Pancreatitis is an inflammation of the pancreas. There are two types of pancreatitis. (patient.co.uk; medicinent.com).

Acute Pancreatitis

Acute pancreatitis is due to sudden inflammation of pancrease and it goes away after short period of time and usually do not do any permanent damage of pancreas. Gallstones and too much alcohol are main cause for acute pancereatitis (medicinent.com).

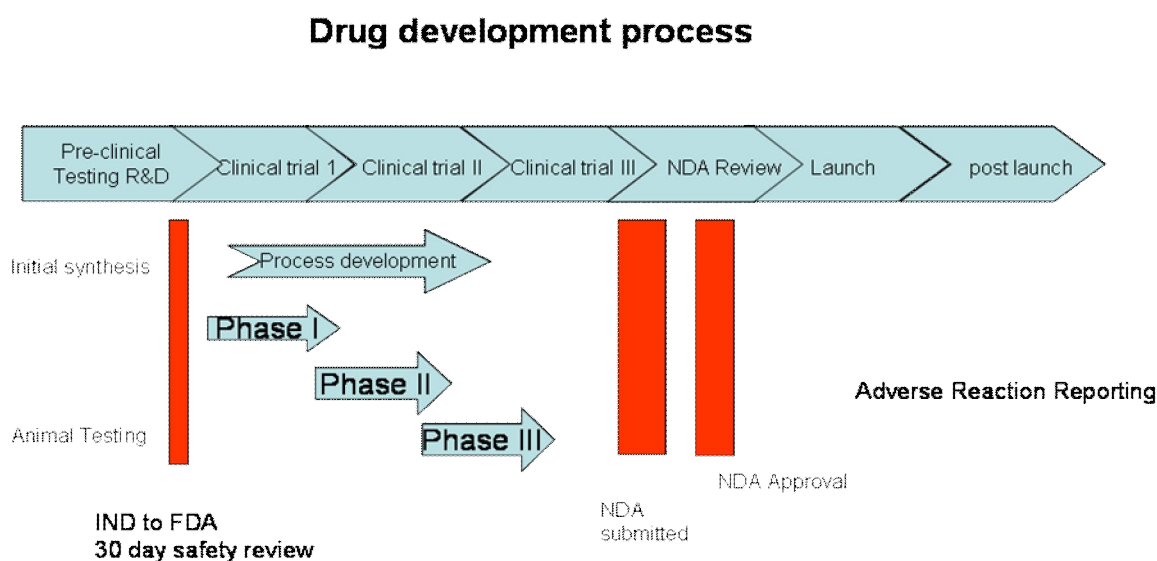
Chronic pancreatitis

Chronic pancreatitis is normally referred to long standing inflammation of the pancreas that result in irreversible deterioration of pancreatic structure, function and do not go it self. Chronic pancreatitis occurs when digestive enzyme become active inside the pancreas and start “digesting” the pancreas itself. Alcohol is the main cause about 8 in 10 cases. Other uncommon cases are hereditary, Pancrease Cancer, Ductal obstruction by scar tissue or stones. Common symptoms are steatorrhea, abdominal pain and poor digestion. (patient.co.uk; medicinent.com).

4 DRUG DEVELOPMENT PROCESS

The drug development process is complex, costly, risky and time consuming. It takes 12 years on average for a drug to reach the market. In general only one of the 10,000 compounds obtains marketing approval (Mickey, 2006). The drug development process can be divided into two main parts. First part includes discovery research, making compounds, assay, and animal testing. This is called preclinical development and second part is clinical testing (human testing). Figure 7 shows main stages of new drug development process for US market.

Figure 7: Main parts of Drug development process



Source : www.fda.gov (modified to make it sample)



4.1 Stages in New Drug Development

Preclinical testing

Drug discovery starts with making suitable compounds against the target disease. When these compounds are pure enough than biological activities tests starts. Scientists conduct vitro (out side living organism) and vivo (inside the living organism) studies to show the biological activity of compound against disease and safety / toxicity of the substance. It takes approximately 2-3 years (depends on number of research group) to find the one active and safe compound. In general 10,000 compounds can give 10 active and safe compounds for further studies (all.com).

Investigational and New Drug Application (IND)

After completing the preclinical testing the company files an IND and it takes 2-3 month to get the answer from US Food and Drug Administration (FDA). This application include all information about preparation of active substance, chemical structure, safety, toxicity, reaction mechanism in the body. FDA also needs the future study plan of the candidate drug such as how, where and by whom the new studies will be conducted. If IND is approved the drug candidate goes to next step of development “clinical phase I” study (all.com).

Clinical trials

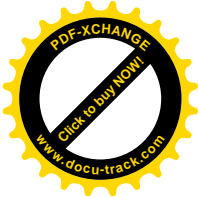
Clinical trials are research studies to find out how well new drug candidate works in people. Each study is plan to answers scientific questions such as side effects of drug, toxicity, treatment of disease. Clinical trials may also compare a new treatment to a treatment that is already available. There are three different clinical phases in clinical trial (all.com).

Clinical trials Phase I.

These clinical tests take more than one year and small number (20 -80) of normal and healthy volunteers (generally). The purpose of these studies is to find out the safety profile, safe dosage range distribution, metabolized and duration of its action.

Clinical trials Phase II

Not all substance tested in phase I make it to a phase II trial. If phase I studies are positive scientist goes to next step phase II. This study is larger than phase I. There may be 100-300 volunteer patients take part and takes about two years. The aim of this trails are to find out effectiveness of drug, more about side effects and best dose.



Clinical trials Phase III

These trails are much larger than phase I and II trails. This trail can involve 1000-3000 patients in many different hospitals and different countries. These trails take about 3 years. The phase III trail is very expensive and important stage in drug development. In these trails new medicine is compare with the standard treatment (best treatment currently available).

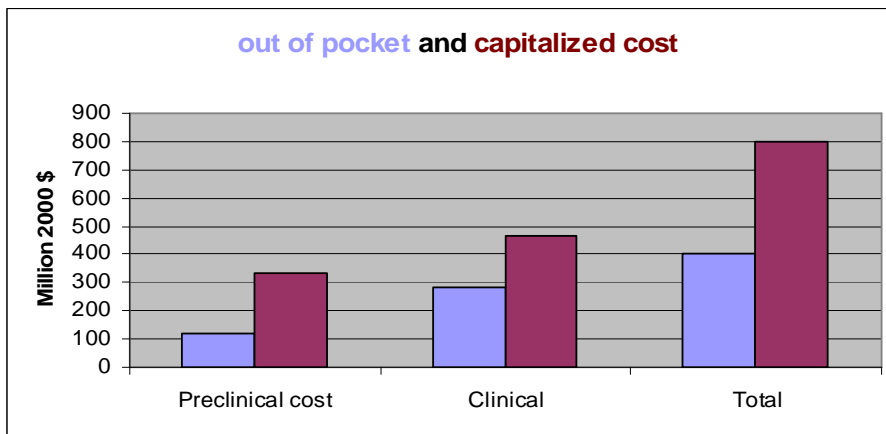
New Drug Application (NDA)

If data from phase III studies shows effectiveness and safety, the company files an NDA with FDA. It can take from few months to few years to get the approval from FDA. Once FDA approves the NDA, the new medicine is ready to launch.

4.2 Drug Development Cost

According to report (DiMasi, 2003) the average estimate out-of-pocket cost for new drug in 2003 was US\$ 403 million and capitalizing out-of-pocket cost for new drug was US\$ 802 million. It was also mentioned in the report that clinical phase is more costly as compare to preclinical phase in drug development process. See fig 8.

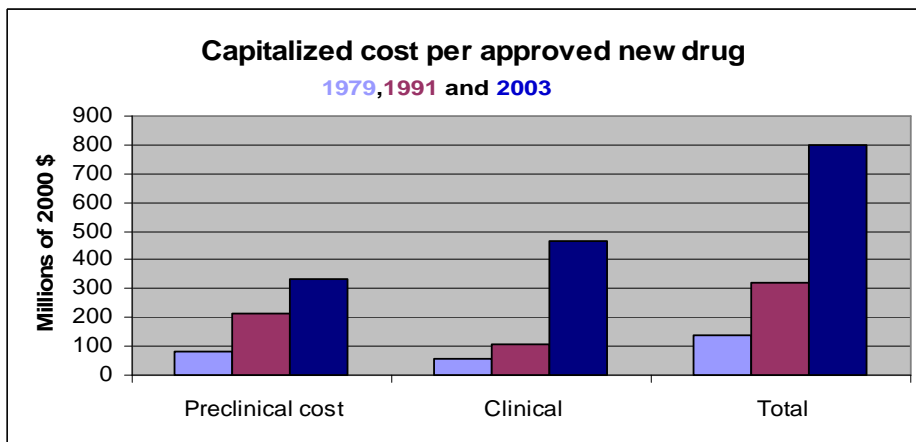
Figure 8: Cost of drug development in 2003.



Source: (DiMasi, 2003)

In Figure 9 presents the trend of capitalized cost of drug development in 1979, 1991 and 2003. The capitalized cost of clinical development was US \$ 54 million in 1979 and it increased to US \$ 467 million in 2003. This figurer also indicates that clinical development of a drug is very costly as compare to pre clinical development.

Figure 9: capitalized cost per approved new drug last 20 years



Source: (DiMasi, 2003)

5 LITERATURE REVIEW

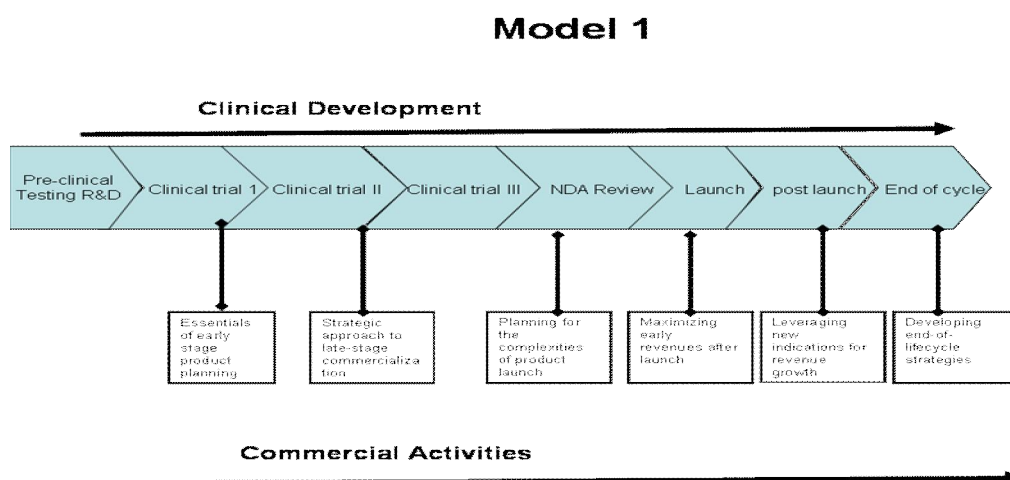
In literature it was not easy to find evaluation model for of candidate drug. There is no single model for evaluation of candidate drug. Almost all pharmaceutical companies have their own models for evaluation of candidate drug / projects. There are many different models for assessment of different parameters for candidate drug. For example Drug Life-cycle strategy (Naigamwalla, 2006), launch effectiveness(Coyleand Benner, 2005), process development strategy (Shultis, 2002), quantitative risk assessment (Tang and Taylor, 2005), Patient flow model (Porkolab, 2002) and pricing strategy (Kotler et al, 2003). These six analysis models cover at least six different important evaluation factors for candidate drug. Therefore these models can be good building blocks for a new model. In this study, I will focus on these important evaluation factors because these factors bring commercial thinking in early stage of drug development. The most successful companies recognize that by bring commercial thinking in early stage of development, they can sure that product is customer derive.

Here, I describe these models in detail to show their use and importance.

5.1 Model 1: Drug Lifecycle Strategies

A typical product life-cycle in pharmaceutical and biotech industry is 25-30 years.12-15 years before launch and 12-15 years after launch (Naigamwalla, 2006).There are many evaluation stages during the development process to drop the bad idea. According to this model pharmaceutical and biotech products have six main lifecycle stages see figure 10. These six stages are early development, Strategic Approach to late-stage Commercialization Planning, Planning for the Complexities of product launch, Maximizing Early Revenues after Launch, and Leveraging new Indications for Revenue growth, and Developing End-of-Lifecycle Strategies. All these six stages are described below in more detail.

Figure: 10 Model 1



Source: Naigamwalla, D. (2006) Reproduced

5.1.1 Essentials of Early stage product planning

In clinical trail phase II is one of the important step because in this step “prove of concept” is established. After this step managers have make decision “go” or “no-go”. According to this model manager must answers these three key questions before proof of concept is completed (Normally it phase II study).

I, What is the Potential of Market for This Compound?

New product managers must have clear understanding of target market, identify potential unmet medical needs, competitive assessment with respect to current and future products, and competitors strength and weakness.

II, What is the Value Proposition?

To be commercially successful New product must have competitive advantage as compare to current product. Therefore it is important to established / evaluate the competitive edge of new product before “go” or “no-go” decision. Key opinion leaders and preclinical and phase I trial can provide the information about product ability and competitive advantages.

III, How Big is the Commercial Opportunity?

New product planer must make a rough estimate product market potential . One can use different method to find out market potential such primary market search, under standing of



incidence and prevalence of the disease, number of diagnosed and treated patients and an average cost of therapy.

5.1.2 Strategic Approach to late-stage Commercialization Planning

The second stage of the life cycle in this model is period between phase 2 and and new drug application. This period is 12-36 months before launch. In this stage planer know the out come of the phase 2 results and they make decision to go/ no-go to phase 3. If product go to phase 3, managers must start planning for pre –launch strategy. This stage has three main elements.

I, Commercial Strategies

While product is in phase 3 brand management have to plan their primary objective, product positioning, develop a robust understanding of the current market, barriers and drivers ands commercial strategies for product.

II, Market Conditioning Campaign

During this period companies must start programs to prepare the market for new product and it benefits. It is very important to make contact to related physicians and key opinion leaders and inform them about new product advantages and benefits as compare to current product in the market.

III, Brand Team deployment

To support the above mention activities company should deploy brand team at this stage of product life-cycle. Usually brand team chose external partners for market campaigns. It is common that they select at least two external partners at this stage 1, advertising agency and medical education agency, these agencies help brand team to finalizing marketing strategy and handle the data generation.

5.1.3 Planning for the Complexities of product launch

The third stage of product life-cycle in this model is 12-18 months before product launch. At this time organization have data from phase 3 trial and planning for new product launch. It is very important phase for product success in the market. Therefore lunch team must develop a defined work plan with key objects such as identify the functional areas, determine the key deliverables, define realistic start and stop dates for each deliverable.

5.1.4 Maximizing Early Revenues After Launch

This stage of product life-cycle is very critical for brand team / marketing team. It is very important at this time to focus marketing effects to increase the sale of product. Marketing team has to talk with key opinion leaders who can communicate the product` values to other physicians and prepare a most effective sales force.

5.1.5 Leveraging New Indications for Revenue growth

The duration of a product growth stage can vary, depending on the market product indication and competitive environment. May be some new product from competitor with different or better indication is launched. That can reduce the revenue and growth period. To accelerate product sales brand team must find new indication of old product. The new indication must be supported with clinical evidences.

5.1.6 Developing End-of-Lifecycle Strategies

The last stage of product lifecycle is 12-24 month before product patent expiry.

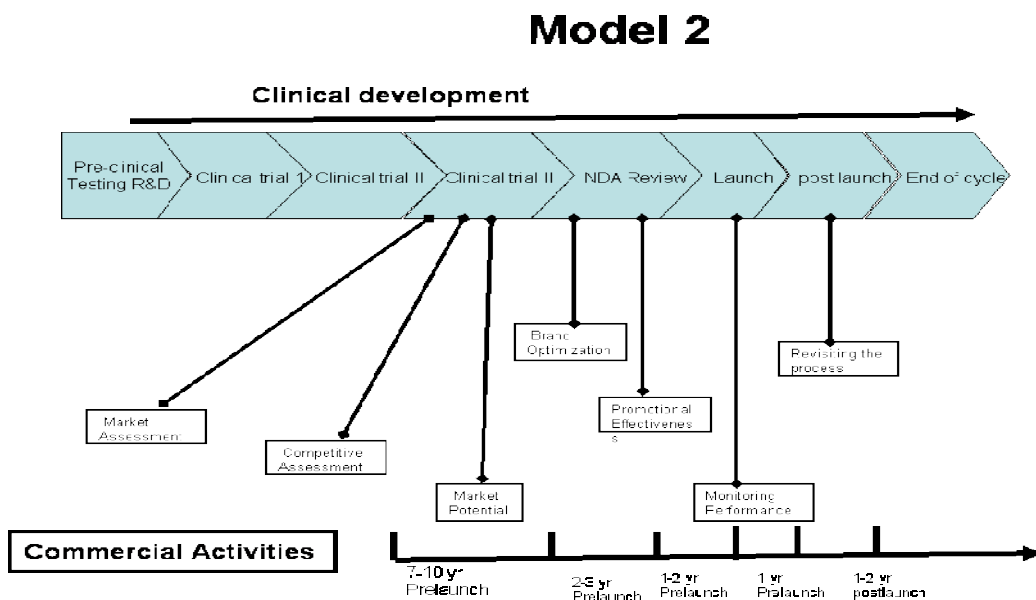
At this stage often company scaled down the brand team and other resources.

The company use recourses for new product or next generation product with better benefits as compare to present product. After patent is over generic product come to market with less price as compare to original product.

5.2 Model 2: To market, To Market: The Seven Steps of Launch Effectiveness

This model contains seven different steps in the product life cycle. In this model first stage starts 7-10 years before launch, most predominantly during the clinical trials 3. First three stages are recommended to perform repeatedly during the product life cycle because market is a moving target (Coyle L, 2005). Figure no 11 describe model cycles.

Figure: 11 Mode 2





Source: Coyle, L., (2005) reproduced

5.2.1 Market Assessment

The main aim of this assessment is to find out that product is entering into established market or new therapeutic area “unmet medical need”. The company must assess the size of market , size of untreated population and make market segmentation. Thia market evaluation will suggest entry opportunities and challenges for the product.

5.2.2 Competitive Assessment

This analysis should be 10 years before launch to understand the competitors products, their market size, product in research pipelines and SWOT analysis.

5.2.3 Market Potential

The market potential now it time for to built a brand strategy and began to make sales forecast In this model market potential was performed in the end of clinical trial 3.

5.2.4 Brand Optimization

Two to three years before launch, while company is waiting for response from FDA “ FDA reviews”, the commercial / marketing managers must consider the four Ps: product, price , promotion and place.

5.2.5 Promotional Effectiveness

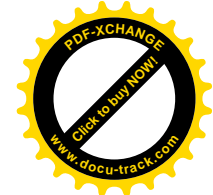
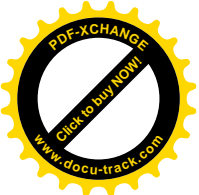
In the final year before launch marketers must decide the promotion plan and utilization of resources to get right promotional mix.

5.2.6 Monitoring Performance

It is important to measure out come of launch. The quicker a product reaches its potential, the greater product launch performance. If product launching is not meeting expectations, the company needs to find out the reasons and take correction action as soon as possible. It is also important to monitor that physicians have got clear message/information about product.

5.2.7 Revisiting the process

After a product has been in the market about one year, it is time to reanalysis of outcome of launch process. Now company has enough information, sales data and physician’s response on the product. These informations can help company to find out if they have right promotion plan. What is working and what is not?



5.3 Model 3: Process Development Strategy

Early stage of drug development required quantity of active substance is normally much less as compare to production for market. Most of the drug candidates fail in early stages drug development process and never reach to market. Therefore most of company has different process development strategy (Shultis, 2002).

5.3.1 Strategy 1

They can use R&D facilities to produce the small amount of active substance before product is in late stage of development. When product is in clinical trial 3 so failure risk is less and then they can spend resources on processes development. But this strategy can increase time to market and some time it is not easy/ even not possible to make new compound as large scale. Therefore this strategy can create problem in the late stage of development.

5.3.2 Strategy 2

The second strategy is “Develop everything”. This strategy dictates that every drug candidate has process development activities from clinical trial 1. If resources are available this strategy can reduced time to market but if product fail lot of resources wasted.

5.3.3 Strategy 3

A drug pipeline can viewed as venture capitalist portfolio. It is important that bad investments are killed fast and good investments are moved ahead as quickly as possible.

5.4 Model 4: Quantitative risk Analysis

Pharmaceutical firm’s research portfolio is very important because R&D productivity affect the firms value. Pharmaceutical R&D is a risky and long process with many stages of development. These days main question is how to do evaluation of research projects (Tang et al , 2005; Prokolab, 2002). The R&D productivity can measure in different way such as number of drugs produced per dollar invested or value of drug per dollar invested. For example two drugs with annual sales \$ 100 million each is not better than one drug annual sales \$ 200 million.

Traditional portfolio evaluation models have two main parameters such as business strength and industry attractiveness. These models are qualitative and semi quantitative and often do not correlate well with shareholders value creation. Therefore quantitative methods have been developed. These methods can calculate how much value an R&D portfolio is likely to add to a firm.

Here are some investment calculation methods

5.4.1 Net present values (NPVs).

Traditional NPV analysis is one of the popular models for investment decision. The net present value criterion is an important assessment that calculated the current value of future



cash flow. NPV is very useful tool for comparison of current cost of project versus the potentials benefits in the future. (Pandy, 2003). If NPV is positive project may be accepted. In the case of negative NPV value the project should be rejected.

5.4.2 The Real Options Analysis (ROA)

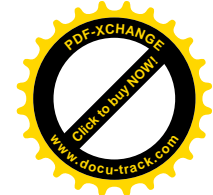
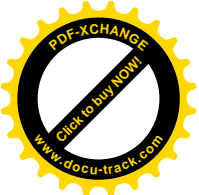
In ROA model one have right to take a decision at more than one points. ROA is a model for assessing investment decisions under uncertainty and provide possibility to change the decisions as economic condition change. In real option model, later investments are made only if results are satisfactory from the pervious stage. In ROA model discount rate is function of risk, discount rate decrease with decrease of risk. ROA takes into account uncertainty about the future.

5.4.3 Variables for Quantitative Analysis

It was not easy to find the suitable inputs variables in literature for quantitative analysis of candidate drug. In the table 1 have mentioned some important inputs variable for model and outputs generated by the model are finish date, total cost, NPV cost, NPV revenue, NPV profit, Risk assessment as compare to other projects. These outputs can help the management to make the decision about the project. I think Microsoft Excel / Monte Carlo simulation can be used for the calculation of above mention variables? Values in table are assumed.

Table 1 variables for NPV calculation with suppose values of variables

	Preclinical R&D Development	Process development	pilot-Scale up production	Formulation	Commercial production	Phase I	Phase II	Phase III	NDA Review	Special Internal and External Issues	Launch
Time to start	0	3									
Duration	3	2									
Time to complete	3	5									
Cost	10	5									
Total cost	10	15									
Discount rate(%)	0.01	0.01									
NPV Cost	10										
Probility of successful completion of a stage (%)	80	80									
Probility of success of candidate (%)	80	80									
Price	A	A									
Market size	AS	AS									
Market share	Z	Z									
Revenue	-X	-F									
NVP Revenue	-y	-W									
NVP profit	-H	-Q									
Worst case scenario	F	F									
Best case scenario	G	G									
Special Internal and External Issues (%)	0	0									
Special Risk with project (%)	0	0									
Decisions	GO	GO									



5.5 Model 5: Patient flow model

Each year, Pharmaceutical companies spend millions of dollars on marketing research such as market assessment, market planning, implementation and measurement of the market. These information can help marketers / marketing managers to identified opportunities and threats, market size and physicians and patient's behaviours. After better understanding of their market, managers can plan their marketing strategy.

Identification of unmet medical need is very important for new drug development and marketers. This will indicate, whether the product will be entering an established market or a new therapeutic area. After identification of unmet medical needs research scientists and marketers can plan better strategy and better return on investment. In drug development process it very important to define the unmet need because this can help to find market segment/ niche. Historically , primary market research has been used for identification of unmet medical need. But using only primary market research is not give the full picture of market and information about patients because it depend on physician and patients memory .

According to (Foniri, 2005) in the past marketers used three legged stool for market assessment such as Primary market research data , Traditional dispensed prescription data, and Epidemiological data . These data are very important, useful and necessary for market understanding .But he *claim* that these data sources are not good enough for comprehensive understanding of market . These sources of that do not give any information about “ how physicians are actually treating patients, which patients they are treating and what is happening during and after treatment. Market managers can get this information from Patient-level data. Therefore he proposed is Patient flow model “THE FOUR LEGGED-STOOL” for comprehensive understanding of market intelligence.

Patient flow model figure no 12 with four factors such a Primary marker research, patients level data, Epidemiological data and dispensed prescription data give better information about patient behaviours and physician ,market opportunity, as compare to model with less factors.

5.5.1 Primary market research data

Primary market research is very important tool to understand physician, what they do, how they do practice and what they recommend. Primary research data gives competitive edge such as optimization of target prospects for new product launches, improve sales efficiency, and find the niche. These information depends on the physician's and patients memory what they did and why? Therefore it is not so much correct.

5.5.2 Dispensed prescription data

Dispensed data is one of most important factor for market assessment. This data is from retail channel and suitable for to assess market category expansion and brand share growth, volume growth. Such data is extremely useful information for understanding which brand is increasing in the market. But this data can not give the information why volume is increasing, what factors that impact physician for prescription.

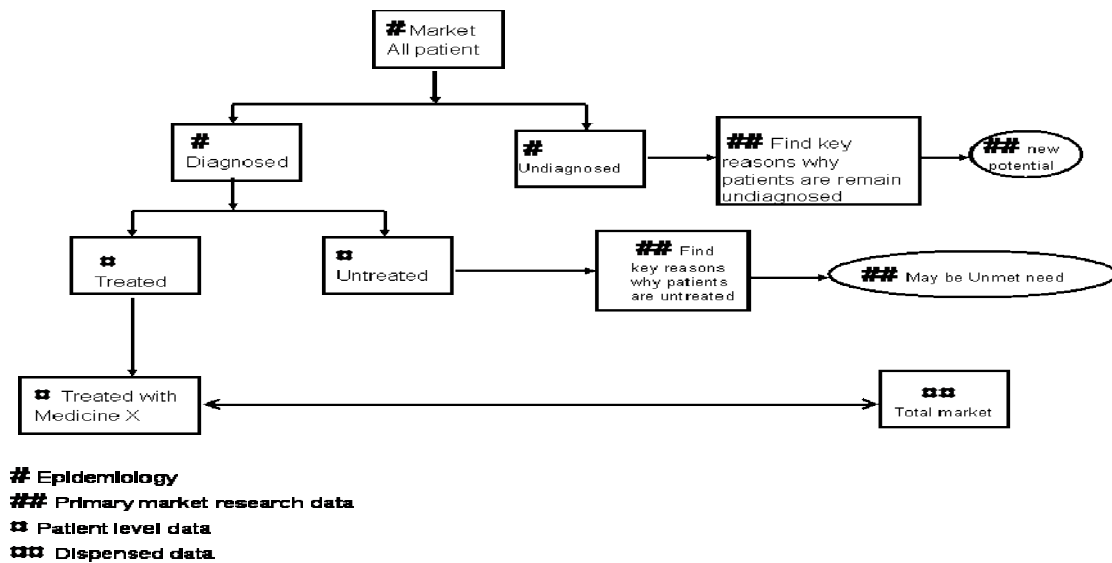
5.5.3 Epidemiological data

Epidemiological data help to find out the prevalence (Prevalence is statistical concept referring to the number of cases of a disease that present in a particular population at a given time) and incidence (number of newly diagnosed cases during a specific time period) of certain disease. This data can give to good estimate of overall market size. But epidemiological data cannot give more detail of treatment such as how patients are diagnose, reasons for treat/ no treat and what happen during and after treatment?

5.5.4 Patient-level data

The Patient data give detailed and true information about the physician treatment and patient behaviors. It is important for marketers to have an accurate and detail understanding of physician treatment and patient behaviors for better marketing strategy. This includes prescription, diagnoses, procedures, physician visits, hospitalization, lab test, length of therapy and out come of treatment. These data are very important for pharmaceutical marketing team, R&D, marketing research and segmentation of market.

Figure 12: Model 5



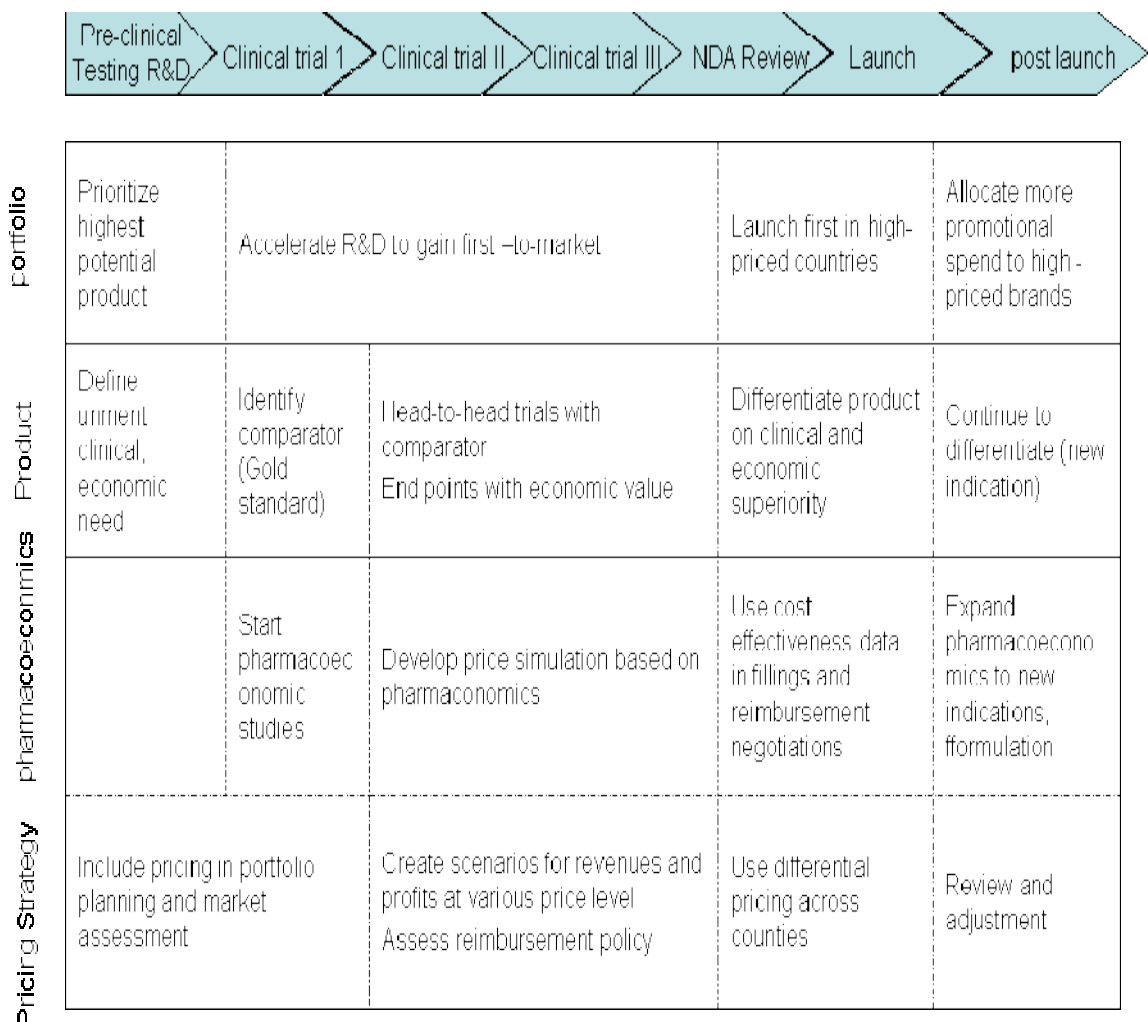
5.6 Model 6: Pricing strategy

5.6.1 Pricing

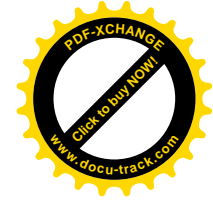
Pricing is an important factor in the marketing mix. Many internal and external factors influence the company's pricing decisions. Pricing strategy at product level will be effective only if it apply to whole life cycle of the product from idea generation, R&D, pre- and post launch. Normally R & D portfolios in pharmaceutical industries are prioritized according to

product revenue or market share potential, but pricing potential is also a key factor. There is no quick and easy way or not a single model for pricing in pharmaceutical marketing. Each pricing decision is unique depending on many factors such as cost effectiveness analysis, evidence based product differentiation (clinical trial) and alternative treatment method. A first-to-market is a key pricing advantage because no comparator product and high unmet medical need. However, as this is seldom the situation. Therefore, the competitive price environment needs to be integrated into an overall scientific, clinical and business plan as early as possible in a product life cycle. See Figure 13. Some common pricing objectives includes, gain competitive advantage, differentiate the product with respect to clinical and economical superiority, maximize return on investment, focus on customers, and enhance firm reputation (Koller et al, 2003).

Figure 13 Pricing Timeline



Source: Koller et al, 2003



5.6.2 Reimbursement

Europe

All European governments provide some level of medical reimbursement for their citizen. Reimbursement policies vary from country to country. Each country has board/ agency for reimbursement systems. For example , National Institute for Clinical Excellence (NICE) in UK, The commission of Transparence in France and Pharmaceutical Benefits Board (LFN) in Sweden.

These agencies decide which drug is “value for money”. These agencies decisions are based on clinical and economical evidence. This type of analysis called “cost effectiveness analysis”. Normally agency first do cost effectiveness analysis, total cost of drug (drug cost, doctor visit cost, health care measures and costs due to side –effect of the drug.) is compare with benefit from using the drug in question and than weighed against with the most appropriate alternative treatment. The product can be included in reimbursement system, if it has clear benefits against present treatment. Product in reimbursement system can generate 30% higher gross profit than drug out of reimbursement system. Therefore it is very important to provide clear evidence of benefits during clinical trail.

Change in economical and political, situation can affect reimbursement system. Therefore it is very important to have update knowledge about reimbursement system for large markets.

USA

US have free pricing and reimbursement system and health care cost are cover by different insurance company such as Medicare, Medicaid and other private insurance companies. Therefore it is necessary to convince and justify these insurance companies with respect to benefits of drug and its cost.

Some major reforms in Swedish reimbursement system during past years (lfn.se)

1992

Total **health care cost** paid by the patient during one year was set to 1500 SEK

1996

Total **health care cost** paid by the patient during one year was set to 2200 SEK

1997

Reimbursement system was reformed. Maximum limit was set to SEK 1300 for drug costs payable by the patient with one year.

2001

Few drugs were removed from reimbursement system.

2002

In 2002 new reimbursement system came and new board “Pharmaceutical Benefits Board (LFN) was appointed by the government. No drug will approve automatically for reimbursement. LFN will decide for reimbursement after cost-effectiveness analysis. Price of drug is part of cost-effectiveness analysis. No price negotiation.



Drug costs paid by patient during one year were set to SEK 1800 and no co-payment below SEK 900.

6 NEW EVALUATION MODEL FOR CANDIDATE DRUG

Candidate drugs pass through many different stages before reach to market. Last three stages in this process are extremely costly and might be of long duration. The decision to take a candidate drug forward is crucial because not every candidate makes it to market. Therefore, it is important to take most promising (commercially successful) candidate to next stage of development. To be commercially successful, the product must have competitive advantage as compare to present products in market. To find the market potential of product (commercially successful), managers must develop a deep understanding of target market, unmet medical need, competition and current cost versus the potentials benefits in the future. For good assessment of drug candidates, it is necessary to bring the commercial thinking in early stage of product cycle. Evaluation method with parameters such as Market understanding, operational viability, situation analysis, entry of new product, and competitors analysis can help to make optimal decision about project go or no-go and prioritization of projects within the portfolio. In literature it was not possible for me to find evaluation model with above mentioned parameters for assessment of candidate drug.

Review of analysis models from the literature

In model 1 early evaluation (before the end of clinical trial 2) was made on three main parameters, market potential, value proposition and commercial opportunity with respect to total market size. No operational viability such as process development, current Good manufacturing practices (cGMPs) and net present value of drug were included in assessment of the product.

In Model 2 they did first evaluation without process development, net present value of drug during the clinical trial 3. It is too late for evaluation because clinical trial 3 is very costly. (Of course all companies do some type of market evaluation before project start) A Good assessment of drug candidate is very important before phase 3 of development.

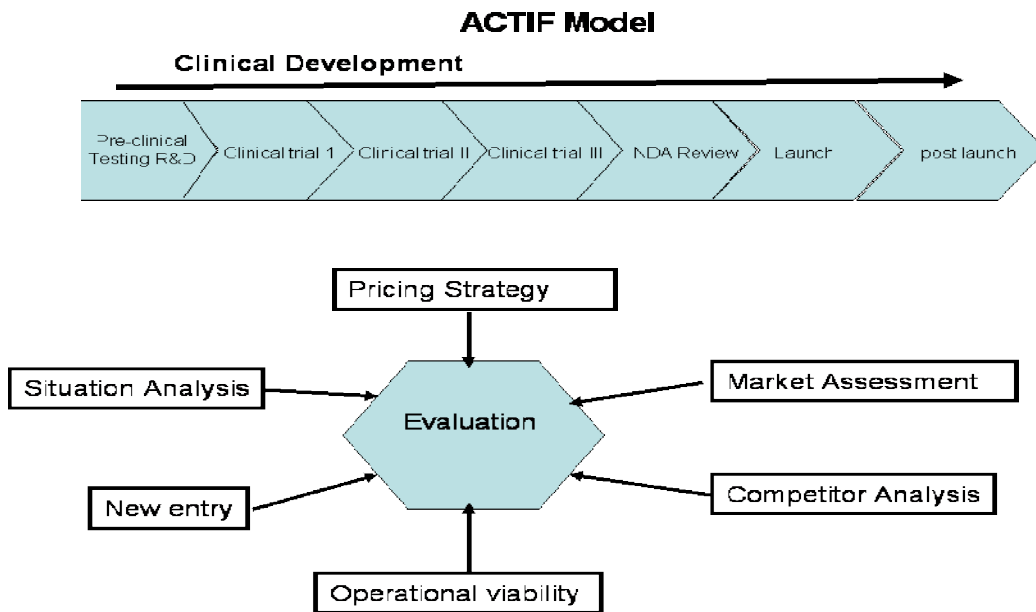
Elements such as Market understanding, situation analysis, entry new product, and Competitors analysis were not included in model 3 and 4.

Model 5 is just for market understanding and identification of unmet medical need.

None of these models have more than one important evaluation factors. I think these types of model can not give complete picture of commercial potential of a candidate. Therefore I assume none of these models (Coyle and Benner, 2005 ; Naigamwalla, 2006 ; Shultis, 2002 ; Tang et al, 2005 ; Porkolab, 2002 and Kotler et al, 2003) are good enough for analysis of candidate drug. But these models are good for different evaluation elements / parameters. These models all together cover important analytical elements such as, market understanding, large scale production, investment calculation and pricing strategy. In my opinion an evaluation model for candidate drug should contain above mentioned parameters. I can not find any model in literature with these important parameters. Therefore I have developed new model for evaluation of candidate drug with the help of above mentioned models. This model

is named as ACTIF model for evaluation of drug candidate in early stage of development. Model ACTIF (figure no 14) has six main forces / parameters such as Situation Analysis of therapy, Market Assessment, Competitors Analysis, Entry of new product, Operational viability and pricing strategy. This model can bring all teams together such as R&D, Clinical trial team, large scale production team and marketing managers and make evidence-based decision. An evidence base decision can improve product's chance in the market.

Figure 14: ACTIF Model

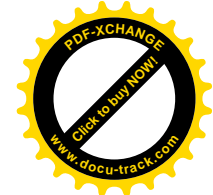
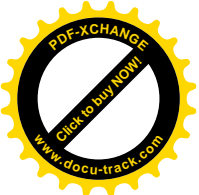


Source: Own

These six key elements (questions) are important for market evaluation of new drug. The answers of these questions are critical for go or no-go decision of a candidate drug before proof of concept (normally phase II study). This model can be used throughout the product development. These six elements are further divided into subgroups. Name of these elements and their subgroups are described here (below). In next section of the report, I will try to explain how to use these elements with help of empirical data.

6.1 Situation analysis of Chronic Pancreatitis therapy

New product managers have to developed a deep understanding of target market with the help of Therapeutic principle of disease, Standard of treatment of disease. What do specialists do today? What do they believe about present treatment? This section of model will do analysis of product D using above mentioned factors. All information are from research papers and reports.



6.2 Market Assessment

Above mentioned Model 5 will be use for market assessment, market segment and find out the unmet medical need for product D. There will be four main parameters Primary market research data, Dispensed prescription data, Epidemiological data, and Patient-level data.

6.3 Competitive Assessment

The competitive analysis will be performed according to principle of marketing (Kolter,2003), stage 2 in model 2 and modify form of competitors analyze (Grant, 2002) to make it “fit for purpose” for this research work. In pharmaceutical industries product life is 12-15 years after launch. Due to long product life, compotator’s research pipe line and their future products characteristics are very important. Therefore I have modified the competitors analyze framework (Grant, 2002) and add theone more factor “Products”. See figure 16. This assessment will include following sub elements, Competitors names, Objectives, Strategy, resources, capabilities, and Products Characteristics.

6.4 Entry of new product during the product life cycle

To be commercially successful, the product (candidate) must have competitive advantage. Therefore it is important for company to do search about today market and what it will be at the time of launch. This section will include future competitors and their products characteristic or new technology for treatment of this disease.

6.5 Operational viability

Model 3 and model 4 will be used to find out large scale process development strategy and quantitative risk analysis (Operational viability) of product D.

6.6 Pricing strategy

Product D pricing strategy will be analyzes with help of table 1. Three main factors will be assesses such as possibility to maximize the retune on investment, gain competitive advantage, and optimize Reimbursement.

7 EMPIRICAL DATA AND EVALUATION MODEL ELEMENTS

This section of report will explain all parameters of ACTIF evaluation model with help of empirical data. All empirical data are collected and arranged according to model. The collection of empirical data was not easy task in medical field. Almost no database is free for service and they have quite high charges. Therefore it took long time to find the suitable research paper or other sources with useful information.



7.1 Situation analysis of Chronic Pancreatitis therapy

7.1.1 Therapeutic principles

The small intestine is where most of the digestion and absorption of food take place. The pancreas secretes digestive enzymes into the small intestine through pancreatic duct. These enzymes help digest fats, proteins and carbohydrates in food. If pancreas does not produce digestive enzymes or enzymes can not reach to the small intestine due to ductal obstruction. This can lead to poor digestion and absorption of food as well as weight loss. (patient.co.uk; medicinent.com). Pancreatic enzyme products (PEPs) help CP patients to digest and absorb their food.

PEPs are oral enzyme extracts derived from pigs. There are two different form of PEPs formulation: Conventional (e.g Viokase) and Enteric-coated (e.g .Creon). Conventional PEPs release enzymes into duodenum and increase the level of enzymes in duodenum. This is thought to reduce secretion pressure. In some cases reduce secretion pressure is effective against pain. But lipase is almost inactivated by gastric acid when it reach to small intestine. Therefore do not help much in malabsorption.

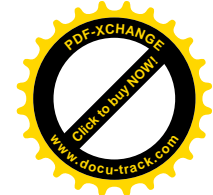
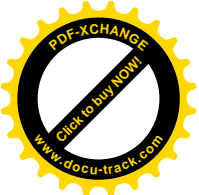
Enteric- coated PEPs do slow release of enzymes when they reach the small intestine. Therefore Enteric- coated PEPs do not relive pain but improve digestion of fat since lipase is still active. Restore digestion can reduce steatorrhea and lead to improved weight gain.

7.1.2 Standard of treatment

The major goals of treatment of chronic pancreatitis are pain relieve and reduced the level of steatorrhea /improve absorption and weight gain. Current treatment for chronic pancreatitis is oral enzyme replacement therapy PEPs. PEPs can reduced the level of steatorrhea and relieve pain in some cases of CP, depending on formulations and number of tablets (units). If PEPs do not help to reduce pain then different analgesics and surgery is needed to relieve the pain (patient.co.uk).

7.1.3 What do specialists do today?

Specialists focused on pain relive and control of steatorrhoea in chronic pancreatitis. In Some patients relieving pain is not a easy. Normally specialist starts with Pancreatic enzyme products because it reduce steatorrhoea and can relive pain. They use different preparation (Conventional/ Enteric-coated) depend on patient problem. If pain is not under control then they use different types of analgesics/nerve blocker. If pain can not be controlled with above mentioned treatment patients remain with pain surgery may be recommended to relieve pain. (Layer et al,1999; Ghaneh et al, Makoto, 2003 and medscape.com).



7.1.4 What specialists believe today?

They believe that more stable lipase as compare Pancreatic enzyme products in gastric acid can improve the digestion , food absorption and reduce steatorrhoea.

Here are some examples of research papers, which indicate that there is need for new therapy.

--Still in most patients lipid digestion cannot be completely normalized by current standard therapy and future developments are needed for optimizing treatment. (Layer et al , 2003).

In future, acid and protease stable bacterial and fungal lipases with additional pH optima in the acidic medium, or animal / bioengineered human gastric lipase preparation may offer superior therapeutic alternatives (Layer et al 1999).

“Over 30% of patients still have evidence of significant level of steatorrhoea. These results emphasise that the complete eradication of steatorrhoea is still not feasible at the present time, even using the best currently available agents, highlighting the need for further effective therapies (Ghaneh et al, 1999).

7.2 Market Assessment

7.2.1 Epidemiology

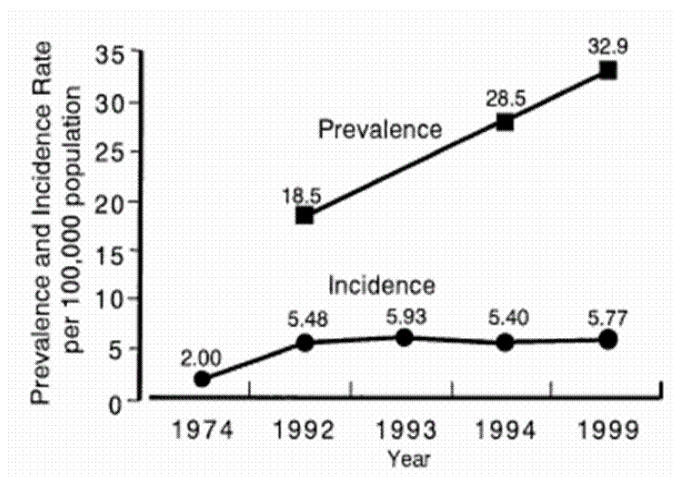
The true incidence and prevalence of chronic pancreatitis is not known, it is estimated to range between 0.04% and 5% in the normal healthy population. (medscape.com). Therefore data about incidence rate and prevalence were collected from different sources such as research papers , web search and consulting companies to estimate market size for unmet medical need.

7.2.2 Incident and prevalence rate of chronic pancreatitis in Japan

Four different research surveys have been conducted in Japan between 1977 to 1999 to find out incident and prevalence of Chronic Pancreatitis in Japan. According to research study published in (Makoto, 2003) the rate of incident and prevalence increased from 5.4 and 28.5 in 1994 to 5.77 and 32.91 in 1999. See Figure 15 for more information.

Total number patients were 42000 in 1999. *Target group 30% of 42000 is 12600*

Figure: 15



Source Makoto, 2003

Incident and prevalence of chronic Pancreatitis in US

I can not find any research report conducted about the true prevalence rate of chronic pancreatitis in United state. Therefore four different sources are used to estimate the incidence and prevalence in US.

1, In industrial report published by Eurand N.V. it is mentioned that chronic pancreatitis is often goes undiagnosed and therefore its exact prevalence is unknown. In this case study it is estimated that chronic pancreatitis results in more than 500,000 physician visits per year in the United States (eurand.com).

2, In article Diseases of pancreas from ACP Medicine the prevalence of chronic pancreatitis varies with population. There are several studies were made to estimate the incidence of chronic pancreatitis and there result indicate that incidence range is from 3 to 9 cases per 100000 population In one study it is estimated that overall prevalence is 27.4 per 100000 population (medscape.com).

In a recent paper in 2006, it is again described that Chronic pancreatitis has a large but unclear economic burden. It affects 5.6-24.2 million people in the US (DiMagno et al). Data from value vectors consultant company shows that incidence rate in US is 7.2 per 100,000 and prevalence is 23.7 per 100,000. Total number of chronic pancreatitis patients calculated from these data is 41139 in US. Target group is 12341 (30% of total).

7.2.3 Incident and prevalence of chronic pancreatitis in Europe

There have been only few reports published about incidence of chronic pancreatitis in Europe for last 80 years. A Report published (Petr et al,2001) about incident of chronic pancreatitis in Czech Republic. According to this report incident of chronic pancreatitis in Scandinavia, Switzerland, Hungary, Germany, Poland and Czech Republic varied from 1.60-23 new cases per year among 100000 inhabitant . For more detail see Table 2.



Table 2 Incidence of chronic pancreatitis per 100 000 inhabitants per year

Country Name	Incidence
Czech Republic	7.9
Denmark	8.7
Finland	23.0
Germany	7.0
Poland	4.0
Sweden	10.0
Switzerland	1.6
United Kingdom	1.0*

Source Petr et al, 2001, * prevalence is 3 per 100000, Bormman et al, 2001

Total number of chronic pancreatitis patients in France, Germany, Italy, Spain and United Kingdom are 56809. This calculation is based on information from Consultant Company.²⁵

30% Of 56809 is 17042.

7.2.4 Market size

Pancreatic enzymes

Product used today are extracts derived product from pig. Different information sources were used to estimate the global market size. According to data mentioned below global market size is increasing for these product. According to IMS Health global prescription sales of existing pancreatic enzyme replacement products were \$ 658 million in 2004 and over \$ 707 million in 2005 (altus.com). PEPs market is \$ 707 million (Morrison, 2007). Sales of pancreatic enzyme with respect to disease are mentined in table 3.

Table 3 pancreatic enzymes and prescription shares in US 2005.

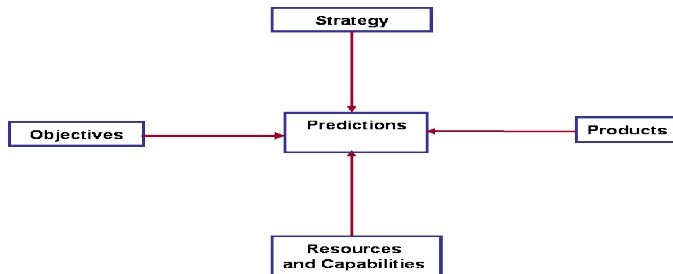
Indication	Share of prescriptions %
Cystic Fibrosis	58.90
Chronic Pancreatitis	23.60
Pancreatic Cancer	9.30
Other	8.20

Source (IMS)

7.3 Competitor Analysis

The competitor analysis is performed in terms of summary of current competitor's general company information, summary of business, Research and Development (R&D), market share, Objectives, Strategy, Capabilities, and Products Characteristics.

Figure no 16. Framework for competitor's analysis



Source: Own

7.3.1 Competitors Resources and Capabilities

1, Solvay Pharmaceuticals

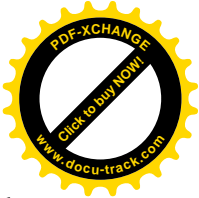
Solvay Pharmaceuticals claim that they have 100 years of experience with pancreatic enzyme products and CREON® brand is the top-prescribed pancreatic enzyme drug worldwide, and has been marketed in the U.S. for more than 15 years. (Solvaypharmaceutical .com)³¹

- Solvay Pharmaceutical is active in more than 40 countries and its products are available in more than 150 countries.
- They have own organization in Western, Central and Eastern Europe . and total number of employs are approximate 10,000.
- Solvay pharmaceutical is with in top 40 of pharmaceuticals companies . Global sales in 2006 was 2,600 MEUR. They spend 15-16 % of their annual sales on research and development.
- Creon sales is 7% of total sales.

2, Axcan Pharma

Axcan pharma is multinational company and corporate headquarters are based outside of Montreal, Quebec, Canada. The company was established in 1982. Axcan has single specialization in gastroenterology. Axcan worldwide company employs are 425. The company has several project in R&D pipeline to address the unmet medical need in the area of gastroenterology (axcan.com).

3, Altus Pharmaceuticals



Altus was created in 1993. The company focus is on developing and commercializing novel protein therapeutics for patient with chronic gastrointestinal and metabolic diseases. They develop protein therapeutics using their own proprietary and patented protein crystallization and cross-linking technology .Altus is a small company total number of employs are less than 50 (altus.com).

4, Eurand

Eurand is a global specialty pharmaceutical company with facilities in the USA and Europe. The company is specialized in drug formulation technologies. They use their own proprietary drug formulation technologies. Eurand principal operating offices are in Milan, Italy. Total number of employs are more than 500.Eurand was stated in 1969 but it was part of American home products from 1989 t0 1999. The company became independent in 1999.

Eurand's four different products has been approved by FDA since 2000 (ir.eurand.com).

7.3.2 Competitor's Objectives

1, Solvay Pharmaceuticals

Solvay Pharmaceutical intent is to be among leading global pharmaceutical companies. New pancereatic enzymes replacements in research plan and objects are increase revenues and profit in define therapeutic areas such as neuroscience, influenza vaccines, pancreatic enzymes, gastro enterology. (Solvaypharmaceutical .com)

2, Axcan Pharma

Provide value-added therapeutics for unmet need in gastroenterology and achieve leadership position in gastroenterology segment. (axcan.com).

3, Altus Pharmaceuticals

Altus will be the worldwide leader in the rapid and efficient development of valuable orally-delivered and injectable protein product to meet unmet medical needs. (altus.com).

4, Eurand N.V

Eurand objective is to use their own innovation technologies and know- how to enable the development of novel value-added products that can improve patient's lives. (ir.eurand.com).

7.3.3 Competitor's strategies

1, Solvay Pharmaceuticals

Solvay Pharmaceuticals have alliances with Wyeth, Lundback, and Bristol Myers Squabb and strategies are growth acceleration, Building promising R&D pipeline, licensing and strategic alliances and new pancereatic enzymes replacements is including in strategy plan. (Solvaypharmaceutical .com)



2, Axcán Pharma

Growth through new product launches, more in project in R&D pipeline and international expansion of the company. (axcan.com)

3, Altus Pharmaceuticals

Altus short- term strategy is revenues from technology collaboration with leading biopharmaceuticals partners and long term revenues from own products. (altus.com).

4, Eurand N.V

Eurand strategy is to be a leader in the development and commercialization of innovative specialty pharmaceuticals and biopharmaceuticals products. These products can be from their own R&D or from in-licensed from others. (ir.eurand.com).

7.3.4 Competitor's Products in Market

1, Solvay Pharmaceuticals

Creon® is capsules and contain enteric-coated microspheres . The company claim that Creon is prepared with advanced formulation. Therefore, Creon® has features of fast, homogeneous distribution in the stomach with complete protection against inactivation by gastric juices. Creon® has been in market for more than 10 years.

2, Axcán Pharma

Axcán has two products Ultrase® and Viokase® in market for a long time. These products are porcine pancreatic enzymes, predominantly lipase , amylase , and protease. Ultrase is capsules and containing enteric-coated microspheres. Due to enteric coated lipase is more stable as compared to Conventional pancreatic enzymes.Viokase is conventional porcine pancreatic enzymes in tablet and powder forms. Axcán has one product (NMK 150) in phase I clinical trail for pain relief in CP.

7.4 Entry of new product during the product life cycle

These Competitors will soon enter in to the market with new product for unmet medical need.

7.4.1 Altus Pharmaceuticals

Altus product (ALTU-135) is an orally administered enzyme replacement therapy for the treatment of pancreatic insufficiency. The company believes that ALTU 135 has many competitive advantages compared to existing products. Such as, It is microbial derived recombinant lipase, protease and amylase and manufactured in control environment, Low pills burned as compared to present products, more consistent and reliable dosing . It is more resistance in the gastrointestinal tract and potential for a liquid formulation. Data from phase 111 is expected in second quarter of 2008.



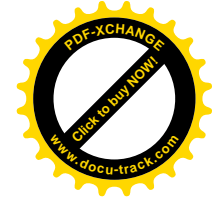
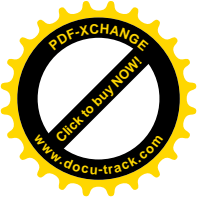
7.4.2 Eurand

Zentase® is porcine derive enzymes, it contains number of Enzymes such as lipase, protease and amylase, coenzymes and cofactors. The company thinks that the mixture of enzymes , co enzymes and cofactor are necessary for proper digestion. According to Eurand Zentase has highly stable formulation as compared to other products in the market. They claim following advantages over current pancreatic insufficiency products. Due to new formulation Zentase leads to more consistent and reliable dosing and can reduced pill burden for patients.

Multiple dosage strengths and low dose formulation for children under the age of seven expects to launch its first porcine derived pancreatic enzyme drug “Zentase” in 2008. For product characteristics and claims see table no 4.

Table 4: New products Characteristics

Company Name	Product Name	Product Characteristic	Claims	Source	Time to Market
Altis Pharmaceuticals	ALTU-135	Mixture of Lipase,protease and amylase	Treatment for CF &CP. Increase absorption of fat, proteins and carbohydrates. Stable, pure and fixed ratio of enzymes. Single pill at every meal. Resistance to degradation in the gastrointestinal tract. Potential for a liquid formulation (currently unavailable).	Microbial	Filing in first half of 2009
Eurand Pharmaceuticals	Zentase	Mixture of eight porcine derived enzymes and number of coenzymes and cofactors	Treatment for CF &CP Increase absorption of fat, proteins and nutrients. Highly stable formulation. Zero overfill. Reduced pill burden.	porcine	Launch in 2008
Axcan Pharma	NMK 150	High protease pancreatic lipase	Relief of pain in small duct chronic pancreatitis (cannot need	porcine	Phase 1 report in the beginning of 2008
Sinwitrum	Product D	Lipase	More effective More Convenience dose (one unit/ meal)	xxxxxx	Phase II



7.5 Operational viability

7.5.1 Process development strategy

The Product D is a lipase and manufacturing process has many steps. It is possible to produced Product D in large scale. But different actives are on-going to optimize formulation and develop cost efficient manufacturing.

7.5.2 Quantitative Analysis

Biovitrum`s own investment analysis model gave positive value for product D and project is on-going. Those values are company confidential values therefore I can not mention here.

7.6 Pricing Strategy

Senario 1

It can be possible to get 30-40 % price premium, if Product D is significant more effective and more convenient as compare to golden standard (Creon). Present price of Creon is 4 USD in UK and 11 \$ in US. Approximate price for Product D can be 6 USD and 14 USD respectively in UK and USA.

Senario 2

Product D is only more convenient then it will difficult to take more than few % higher price than Creon.

8 ANALYSIS OF PRODUCT D

8.1 Understanding of therapy area

Chronic pancreatitis is an inflammatory disorder of pancreas. This inflammation is irreversible and effect the pancreas function to produced the digestive enzymes. The most common symptoms of chronic pancreatitis are abdominal pain, diarrhea and weight loss. Treatment of Chronic pancreatitis is difficult and challenging. This disease has high mortality rate. First step of treatment is relived of pain with different analgesics. Pancreatic enzymes are used to improve maldigestion and malabsorption.

Specialists in the Chronic pancreatitis therapy area are not fully satisfied with present treatment method (pancreatic replacement therapy) because it can not completely normalized malabsortion and large number of patients have significant level of steatorrhoea. They believe more stable lipase in gastrointestinal tract can reduced the steatorrhoea and help to increase the patient`s weight.

Therapy area situation analyse indicates that large number of chronic pancreatitis patients do not have significant improvement /benefits with currently available treatment. Specialists are highlighting the need for further effective therapies.



8.2 Market Assessment

Strategic decision regarding to new drug development is most important question within pharmaceutical and biotech companies. A company R&D pipeline is the heart of the organisation. New drug could affect positively or negatively a company 's financial outlook. Therefore it is very important for new product planner to have deep understanding of target market and identify potential unmet medical needs. I have used patient flow model (model 5) to identify unmet medical and market size. This model has four main parts, Epidemiological data, Dispensed prescription data, patient-level data and Primary market research data.

8.2.1 Epidemiological data

It is very difficult to obtain true number of cases in chronic pancreatitis because a large number of patients often undiagnosed. Estimated prevalence in US and Japan is 27 and 32 per 100000. For more detail see section 7.2.1-7.2.3.

8.2.2 Patient-level data

In this study patients level data is calculated from the epidemiology data. In this study number of untreated (no significant effect from present therapy) patients are over 30 % of total patients. Because literature search showed that over 30% of total chronic pancreatitis have no significant effect from present therapy. This is target group for product D. Number of patients are 12341 (US), 12600 (Japan) and 17042 (west Europe).

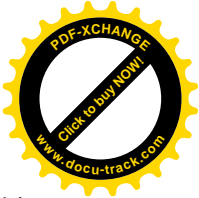
8.2.3 Dispensed prescription data

This data is very important for assessing the target market. From this data one can see the market growth, brand share. Global market of PEPs is increasing and it is up to \$750 million. Table 3 shows the prescriptions share of PEPs with respect to disease. Chronic pancreatitis has share about 23% of total market. CP has share \$ 163 million of total market, If market share ratio is similar world wide.

8.2.4 Primary market research data

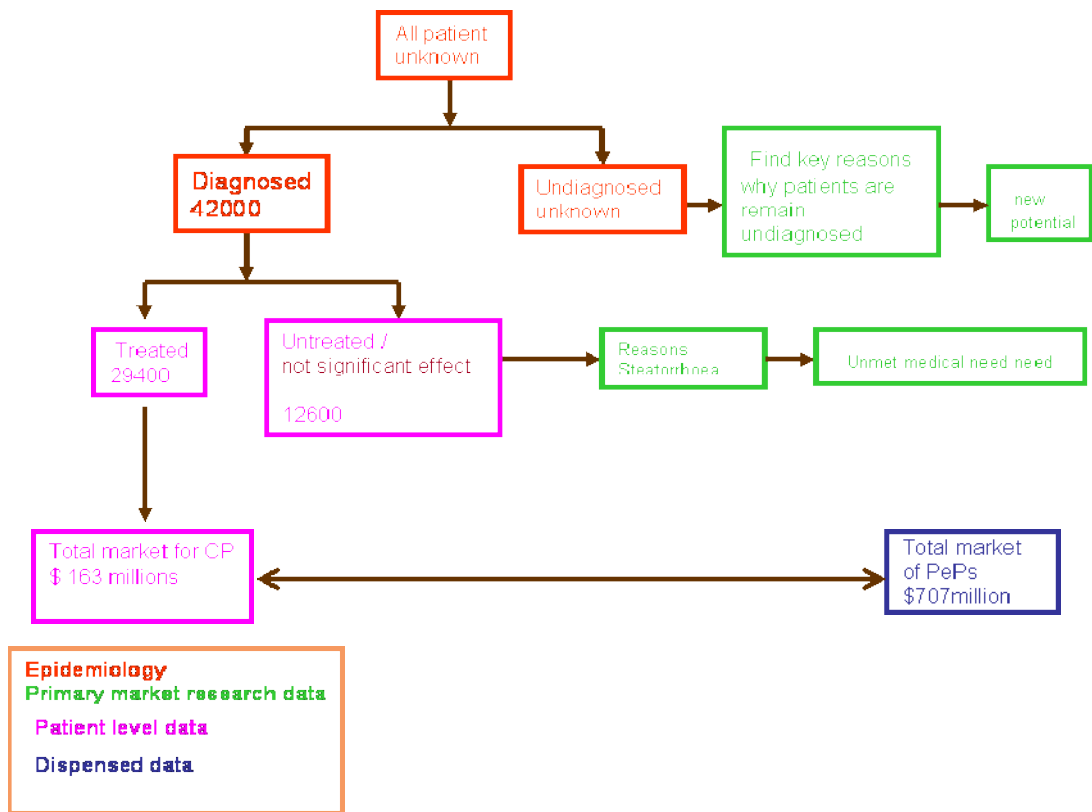
Traditionally primary market research is used to identify the unmet medical need. It helps to find out physicians and patients behaviours. With Primary research it is easy to understand about physicians thinking and their treatment. It is expensive and time consuming therefore it not included in this study. I have used secondary data in patient flow model.

In figure 17, Japanese epidemiological data is used in patients flow model to find the unmet medical need. High level of steatorrhoea (12600 patients) is one of the unmet medical needs within the chronic pancreatitis. It is a very simple example of how to use the patient flow



model for identification of unmet medical need. The untreated patient group can be divided in several subgroups. In this way one disease group can give different unmet medical need. It is very much time consuming and difficult process to collect the all data for this model. This is not main objective of this thesis.

Figure no:17 Patients flow model based on Japanese epidemiological data



Source Own

8.3 Competitors predictions

The objective of competitor’s analysis is to understand one’s rival. To understand competitors, company has to know : Who are our competitors? What are their objectives? What are their strategies? What are their strengths and weaknesses? In this study competitors analysis are performed according to framework mentioned in figure 15. This framework is based on competitors analysis described by Grant, 2002.

As we know drug development process is at least ten years long process. During this period market situation will be different as compare to present time. There is always risk that company has to compete with new competitors, new method of treatment and new technology. Therefore the evaluation model has two different factors for competitors predictions (competitor’s analysis and new entry product) to understand competitive market. The .competitor’s analysis is for present competitors with product in market and new entry include all future expected competitors/ new technology etc.



8.3.1 Present competitors

There are two main competitors Solvay Pharmaceutical and Axcan Pharma. Both companies are international and have been in market for many years. Their products (CREON, Ultra and Viokase) are world major brands. These products are derived from pig pancreas. Axcan pharmaceutical has specialization in gastroenterology and they work only in this field.

8.4 Entry of new products

Altus and Eurand have planed to laugh new product within 1-4 years. Eurand product Zental is derived from pig pancreas but Eurand claims several advantages of this product as compare to present products in the market. Altus Pharmaceutical product ALTU135 is microbial derived and Altus claims competitive advantage over present products in the market. This product is in phase III. These companies are new in pancreatic enzymes market. For more information about products see section 7.3.

Presently, it is difficult to predict competitor's behaviour after product launch because profile of product D is not fully established. The preliminary profile of product D indicates that it will be more effective and convenient as compared to PEPs. For more information about products profile see table 4.

8.5 Operational viability

The product D is in early stage of development process. Many parameters such as dose of product, commercial production cost and other risk factors are under investigation.

8.6 Pricing strategy

Price of product D depends on its characteristics. Price will be 30 to 40% higher (because it is not first to market) than Golden standard Creon, if it is more effective and convenient as compare to Creon. Only more convenient than it will few present higher than Creon.



9 CONCLUSION

The purpose of this study was to develop an evaluation model for candidate drug and analyse the market opportunity of product D. This study proposes an evaluation model with major risk factors in the drug development process. This model can help manager to analyse the market potential of candidate drug in early phase of development and can help to make go or no-go decision. The model is suitable for market assessment, finding unmet medical need, and calculation of risk benefit ratio of project. Drug development process is long with many different stages, this model can be used any stages of drug development process. If all relevant information / values are not available for early stage of development process even though model can provide other useful information such as market situation, therapy area situation, unmet medical need and competition.

The study also indicates that there is unmet medical need in pancreatic inflammation therapy area. Enzyme (lipase) which is stable in gastrointestinal tract can fill this medical need.

Competitor's analysis shows that there are two major competitors in pancreatic enzymes market and two new competitors/ products ALTU 135 and Zentase will be in market within period of 1-4 years. Manufactures of these products claim competitive advantages over PEPs.

The product D is in early stage of drug develop process (phase II). Therefore all relevant information/ values are preliminary. These values indicate that Product D has competitive advantages over present PEPs.

10 RECOMMENDATION

Presently many studies are on-going to confirm the product D profile. If product D profile will be similar to competitor products, it will be a great challenge for Boivitrum to get price premium and penetrate into the PEPs market.

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