Real options valuation of a biotech project using fuzzy numbers

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Executive summary

The purpose of this thesis is to introduce the concept of real option valuation with the use of fuzzy numbers through performing different fuzzy real option valuations on a constructed biotech drug development project. The main argument among practitioners for not applying a real option approach is the difficulty of implementation. The fuzzy pay-off method to real option valuation sees to this and makes real option valuation accessible for practitioners with a non-financial background.

In the first part of the thesis the underlying assumptions for performing a fuzzy valuation in a biotech setting are reviewed, discussed and concluded on. First the current business environment as well as the valuation practices most commonly applied is examined. The most used DCF method is criticized as it does not incorporate the value of managerial flexibility stemming from the high uncertainty surrounding a biotech project. To include this value, an analysis of the classic real option valuation methods best suited for a biotech setting is then performed, the result of which is that the event tree and the binomial tree are well suited for applying a real option approach to the valuation – dependent on the practitioner’s financial level. Next the concept of fuzzy numbers is introduced. The fuzzy pay-off method to real option valuation is presented and applied to simple DCF valuations in an uncomplicated manner in order to transform it into a real option valuation. Also a fuzzy approach to a binomial tree valuation is analysed and applied.

The last part is centered on the actual valuation of the constructed biotech project. The valuation setting is outlined and analysed in order to provide reliable input variables for the valuation. Through strategic analyses and empirical findings the capital budgeting is performed to allow three different valuations aimed at different levels of financial understanding to be performed. First, the fuzzy pay-off method is applied to the traditional DCF valuation. It is shown how the fuzzy approach creates a real option valuation that captures the value of managerial flexibility neglected by the traditional. Second, the fuzzy pay-off method is adopted on the risk adjusted event tree valuation and again demonstrates its ability to value managerial flexibility compared to the original approach. Third, fuzzy numbers are applied to a binomial tree valuation, where the fuzzy version puts more weight on the managerial flexibility stemming from the amplified volatile development in the underlying asset. Compared to the fuzzy DCF valuation the fuzzy risk adjusted valuation is preferred due to its inclusion of a structured risk perspective and ease of implementation for practitioners. For more advanced practitioners the fuzzy binomial approach is preferred due to its superior alignment with the real option thinking.
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1 Introduction

The biotech industry has a good reputation due to the constant quest for inventing drugs which can cure or prevent diseases. For investors, the admiration is somewhat smaller because of the complexity, opacity and risk of these industries. Individual drug development projects are characterized by a long time horizon and consequently high uncertainty regarding the competitor and customer situation and when and if the drug is fit to be launched to the market. This uncertainty about the prospect of the projects is of course instrumental to the high volatility in the share price of biotech companies, where it is not uncommon to see companies’ share prices drop or rise significantly in one single day. Recent examples are Genmab falling 30% on 17 August 2009 and Neurosearch rising 98% on 3 February 2010 (Bloomberg).

Drug development projects also carry enormous research and development (hereafter referred to as R&D) costs which generate no cash flow until marketed, which more often than not does not happen. These characteristics make it very difficult to value a drug development project and subsequently the whole company using classic static valuation methods such as the discounted cash flow model which is widely accepted and used in the pharmaceutical and biotech companies due to its simplicity (Hartmann & Hassan, 2006, p. 348). But the method is unable to capture the constantly changing environment surrounding a drug development project.

Theorists like Copeland, Antikarov and Mun have all argued that the real option approach is the most correct when it comes to valuing a drug development project as it better captures and values the managerial flexibility of such a project. Applying real options valuation to highly uncertain projects could also explain the often very high multiples that such stocks trade at based on traditional valuation methods and as such is a strong argument for why the conventional valuation methods are insufficient (Boer, 2000, p.30). But when it comes to practice, the real option method is seldom used. Previous studies have showed that the reason why it is not used by practitioners who values such projects is the complexity of the method. The method is too difficult and sophisticated to understand and use for people with a non-financial background, which we often find in biotech companies (Block, 2007, p.261-263).

The complexity of the method is a problem for investors in their process of valuing the companies correctly, but even more for the companies themselves when they have to decide which projects to proceed with and which to discard. Wrong decisions here could mean the
difference between success and failure for especially small biotech companies. Hence it is crucial for the companies to value their own drug development projects by a method which captivates all the unique attributes of such a project.

Recent research in real option analysis has come up with a new, simpler and more intuitive method for valuing real options. It is called the fuzzy payoff method for real option valuation and according to the researchers it is suited as a bridge between real option theory and financial valuation of drug development projects for people without a solid financial background. Hence it should be easier to incorporate real option analysis in pharmaceutical and biotech companies to enhance the quality of the decision making process about which drug development projects to proceed with and which to cancel. And consequently reduce the volatility for both the companies and the investors.

Through a constructed case of a fictive biotech project we will test and evaluate whether the fuzzy payoff method for real option valuation is the “missing link” that can make real option theory applicable for practitioners valuing drug development projects. We will see if it is suited for valuing a drug development project in a theoretically correct and a practically simpler and more pragmatic way.

1.1 Problem statement
As argued in the introduction we wish to examine whether the application of fuzzy numbers on real option analysis can be a valuable tool for practitioners. Thus our primary research question is:

◊ Can fuzzy numbers be applied to perform a real option valuation of a biotech project and how applicable is this method compared to traditional valuation methods?

In order to give a satisfactory answer to our primary research question we will investigate the following secondary research questions

◊ What are the characteristics of the biotech industry, which valuation methods are used and to what degree is real option analysis applied?
Is real options analysis superior to the traditional discounted cash flow model in a biotech context and if so what real options valuation methods are the easiest applicable?

How can fuzzy numbers be applied to perform a real options valuation of a drug development project?

In order to create a reliable valuation setting for a drug development project, which factors should be discussed and estimated?

What is the effect of a fuzzy approach to the selected traditional valuation methods?

1.2 Target group

The primary target group of this master thesis is the management and practitioners valuing drug development projects in pharmaceutical and biotech companies. The thesis serves as a remedy to see if the fuzzy payoff method for real option valuation can assist in making the valuation process in the companies more theoretically correct without significantly hampering the valuation process by increasing the workload or by enhancing the financial skill level needed to perform a valuation.

Secondly it serves to clarify for equity research analysts and scholars with an interest in financial valuation theory whether this addition to the real option theory is applicable on any level.

It can also serve as an introduction to the pharmaceutical and biotech industry for people with an interest in these industries and to gain insight of the methods used in valuing drug development projects today.

In accordance with the primary target group it is assumed that the reader has basic knowledge of financial theory and strategic analysis.

1.3 Delimitations

This thesis is method-oriented and will thus focus on whether the fuzzy payoff method for real option valuation is capable of taking the rocket science out of real option theory and making it applicable for practitioners with a non-financial background who are valuing drug development
projects. Hence we are not interested in finding a “true” value of some biotech company to see whether it is overvalued or undervalued by the stock market.

In our discussion of real option theory we will look at pharmaceutical and biotech companies that undertake research in new drug candidates to prevent or cure diseases. So companies that use biotech for other purposes such as enzymes for food production or agriculture will not be considered in this thesis.

The focus will be on the valuation of single drug development projects so we will not consider issues related to having a portfolio of projects and what effects that will have on the single project. This could be the failure of the lead drug of a company which might lead to the company not surviving and consequently to a discounted sell-off or termination of the remaining projects (Angluin, Southworth & Walker, 1997, p.26). Nor will we take company specific characteristics that can alter the circumstances for the optimal decision-making regarding the development of the drug project into consideration. That could be the liquidity problems many biotech companies face today as investors are more reluctant to invest in high risk projects due to the economic slump. Hence our objective is to look at the long term value of a project without taking any discounts in the value due to company specific restraints.

Our analysis of the surrounding factors for the pharmaceutical and biotech companies are not supposed to be a complete industry analysis but merely a study to pinpoint the most important economic factors which influence the capital budgeting process.

We are convinced that real option theory is the theoretically most correct valuation method for valuing drug development projects so we will not consider other valuation methods such as economic value added or the comparables approach.

1.4 Methodology
The focus of this thesis is applicability and we will thus only investigate the relevant valuation theories in line with this main focus. It will be done by a review and discussion of relevant theories presented by academics.
To understand the current valuation process in the companies we have conducted a qualitative analysis which enables us to get thorough and in-depth answers to our questions in preference of a quantitative analysis which instead would have provided us with more data due to its more standardised structure. However we favoured a more profound knowledge of the valuation process instead of a larger but more superficial data base as the objective is not to make an overarching and statistical valid examination of the industry.

To evaluate the presented valuation methods we have created a drug development project which we will use to test them on. This is preferred instead of a real-life case which would complicate things due to the high degree of uncertainty in finding correct estimates for the different input variables. As the focus is on applicability of the valuation methods and not finding the value of a specific project we have chosen the fictive drug development project as it will present the comparison results without any noise stemming from issues regarding weak estimates of a real-life case. Also a real-life case would remove focus from the comparison of the methods to the exact valuation of the case which is not desirable.

The estimation of the input variables to our fictive drug development project will be based on previous studies conducted by various researchers. Also analyses from investment banks will be used in order to give an as accurate as possible picture of a real-life drug development project.

1.4.1 Contextual theories
The use of contextual analyses might seem obscure as this thesis more looks like a theoretic assignment instead of a normal valuation of a company. But we argue that it is essential to include these contextual analyses to better assess and adjust historic data on different input variables in a valuation setting. Normally when dealing with valuation of companies it is also important to focus on the internal value chain to see what kind of competitive advantages the company has, but as we only value a single project the need for an internal analysis disappears.

Thus a picture of the biotech context is important to understand the issues reviewed in this thesis. So in order to figure out the competitiveness in the biotech industry we will make use of Porter’s Five Forces model which analyses the competitiveness of the industry by assessing the possible substitutes, the bargaining power of suppliers and customers and the entry and exit barriers (Porter, 1980, p.6).
In order to get a better overview of the macroeconomic factors we have chosen to conduct a PEST analysis of the political, economic, sociological and technological factors of the industry, which was first introduced as “ETPS” by Francis J. Aguilar in his book *Scanning the Business Environment* from 1967 (Aguilar, 1967). Eventually it took on the more idiomatic name PEST. We use the model to describe the macroeconomic factors in a biotech context and thus provide a better understanding of issues related to this industry.

These models will enhance the understanding of the capital budgeting progress that we will work on in section 5.2 and 6.2.

### 1.4.2 Financial theories

In this thesis we utilize many different financial theories and models. First of all we will briefly introduce the discounted cash flow model (hereafter referred to as DCF). Due to its simplicity the DCF model is widely applied as it uses only few input variables such as the periodic discount rate and the periodic cash flows. The formula is presented in equation 1.1 below (Rådgivningsudvalget, 2003, p.43).

\[
NPV = \sum_{t=1}^{\infty} \frac{CF_t}{(1+r)^t}
\]  

(1.1)

As shown in equation 1.1, the DCF model discounts all future cash flows to find the net present value (hereafter referred to as NPV). By accepting the DCF model as a valid tool we accept the underlying assumption that there exists a perfectly competitive capital market that can act as intermediary to exchange future and present cash. As the capital markets are rather well-functioning this assumption is fulfilled to a satisfactory level and the DCF model can be accepted.

In order to find the NPV we need an appropriate discount rate, which embeds the risks connected to the specific case. We will use the risk free interest rate and the weighted average cost of capital (hereafter referred to as WACC) when discounting cash flows. The reason for this will be discussed in section 5.2.2.

The WACC is computed from the following formula (Penman, 2007, p.473)

\[
WACC = R_E \cdot \frac{E}{V} + \frac{D}{V} \cdot R_d \cdot (1 - t)
\]  

(1.2)
where $R_E$ replicate the return on equity, $\frac{E}{V}$ represents the share of equity owned compared to the total value of the company. On the other side $\frac{D}{V}$ determines the debt ratio compared to the total value of the firm. At last we have $R_d$, which represents the cost of debt while $t$ denotes the corporate tax rate.

The return on equity, $R_e$, is found through the standard theory of the Capital Asset Pricing Model where it accordingly can be found by equation 1.3 (Brealey, Myers & Allen, 2006 , p.189)

$$R_e = R_f + \beta \ast R_m$$  \hspace{1cm} (1.3)

The Capital Asset Pricing Model makes use of the risk free interest rate, $R_f$, the expected market premium $R_m$ and the beta of the asset, $\beta$, which all will be estimated in section 6.1.

### 1.5 Source criticism

A main part of the literature used in this thesis has been gathered at the library at Copenhagen Business School, which we consider to be a valid source of information. We have also used a broad variety of scientific articles. These articles are all published in scientific papers, hence they have been revised and accepted, and must be considered reliable. In addition the authors of these scientific articles must be considered to be scientists who are very serious about their work as a flawed paper with incorrect information can damage their reputation in the future.

Analyses from investment banks have been used to gain knowledge about the industry and as an input source to estimating different input variables. Also figures gathered from the financial provider Bloomberg have been used in the capital budgeting process. We consider both sources objective with a high degree of credibility as subjectivity would undermine their businesses.

In our investigation we have interviewed a number of companies. The information gathered from the interviews should be seen as subjective to a certain point as employees of a company have an interest in creating a positive image and hence might paint a brighter picture of how things are. But these circumstances are taken under consideration when interpreted.
1.6 Structure

The purpose of this section is to clear the path of this thesis. The thesis is divided into five central parts containing different sections, which all contribute to the analysis of the classic and fuzzy valuation methods.

In part 1, we present the special characteristics of the pharmaceutical industry with a focus on biotech companies and the conditions in Denmark. After this industry overview we have conducted an investigation of the valuation practice in Danish companies. The purpose has been to get a picture of how the industry acts towards issues regarding the capital budgeting process and which valuation methods are currently used. We conclude part 1 with a review of an external analysis regarding valuation methods used in the pharmaceutical industry.

In part 2, we review the classical valuation methods existing today, starting with the traditional and widely used DCF model. After this we introduce the real option framework followed by a presentation of different real option types relevant for the industry. We conclude part 2 with an analysis of the real option valuation methods that are attractive to the industry.

The concept of fuzzy numbers is introduced in part 3. We start off with a short introduction to the general understanding of fuzzy numbers and continue by showing how different fuzzy numbers can be used in different valuation settings. Finally we will conduct an analysis of the fuzzy binomial valuation method.

In part 4, we look at the settings for a valuation. We begin with two contextual analyses, the PEST model and Porter’s Five Forces to enhance the understanding of the context of the industry as well as its competitiveness to be able to make more precise estimates for the input variables used in a valuation. We continue with presenting the framework for a valuation in the biotech industry discussing issues such as uncertainty, cost of capital and agency problems. We finish off discussing the various key input variables used in our valuation.

Part 5 contains our case valuation. We start out by estimating the cost of capital and the input variables needed to create a cash flow forecast for our project. With a complete cash flow forecast we can now value our project with different perspectives. First we use the traditional DCF method and subsequently apply a fuzzy approach to the DCF method. Next we apply some real option thinking to the valuation by conducting a risk adjusted valuation with both a
traditional DCF and a fuzzy DCF. Last we perform a clean real option valuation using a binomial tree, both normal and fuzzified. A sensitivity analysis on our results is then conducted to test the robustness. Finally we discuss the results obtained and the possibilities of an implementation of fuzzy real options valuations in the industry.
Part 1 – Industry study

This part outlines the context in which our valuation analysis will be conducted. It is important to know the characteristics and practices of the industry in order to be able to make recommendations about the possibility of implementing alternative valuation methods.

2 The biotech industry in a Danish context

The biotech industry in Denmark started in the 1970s when the first companies were founded as a result of the newly acknowledged genetic engineering opportunities. These genetic engineering opportunities made it possible to manufacture proteins that are used for R&D in new products such as vaccines, drugs and diagnostic tests.¹

Today there are about 160 biotech companies in Denmark, testifying the development of the industry since the 1980s (Dansk Biotek, 2010, p.1). This development is illustrated in figure 2.1 below, which shows the annual number of new companies along with the total number of companies.

As seen on the figure there is a clear connection between the trends in the industry and the business cycle. It appears that especially the period after the burst of the dot.com-bubble in 2001 along with the start of the recent financial crisis resulted in a decline in the number of new companies. The reason for this decline lies in the risky conditions of the industry where there is never any guarantee that when a drug or vaccine is being developed it will actually end up as a

¹ www.danskbiotek.dk/biotekindustrien
product with a positive effect and safety profile and hence make it to the market. These uncertainties will be reviewed in section 5.1.1.

Recent years have seen a number of smaller companies trying to make it in this highly competitive industry. These companies often only operate with one single project or a few projects and they do not have the facilities to manufacture and market the drugs due to the heavy capital costs.

Given these conditions, there will always be a basic need for financing. As seen in figure 2.1, the investment level declines during periods of recession as investors become more risk averse, which leads to fewer company start-ups. The national governments try to increase the incentive of starting new biotech companies by giving direct subsidies to the companies. The reasoning is to retain and attract companies in the local business environment to maintain and create new jobs. The companies can also get tax savings during the first years but this incentive is often insignificant as the smaller biotech does not have a positive income the first many years (Ernst & Young, 2010, p. 52).

Another thing which can be determined from figure 2.1 is that the numbers of newly started companies and the total do not add up. This is the result of the relatively large number of defaults encountered in the industry due to the issues mentioned above.

But all in all, the figure illustrates a generally good development of this industry in Denmark through the last 25 years. This is based on the industry’s ability to adapt to the Danish labour market, for instance the high level of know-how that exists in Denmark along with the outstanding research environment present (Jensen & Klyver, 2008, p.638). Appendix 1 contains a map over the phenomenon “the Medicon Valley of Denmark” showing the area around greater Copenhagen and how intensely the pharmaceutical and biotech industries are represented there (Jensen & Klyver, 2008, p.637). This location is not random as it is a highly favourable business environment with several hospitals, three very large educational institutions and six science parks as the most important elements. Hence the potential for further growth is certainly there.
2.1 The drug developing process

2.1.1 The regulatory platform

A very important issue for drug developing companies is to get the drugs approved by the authorities. Such regulatory approval is necessary in order to ensure that the drug complies with national legislation and restrictions, and in that sense it provides a safety measure to the community. It would be impossible for the industry to exist without this tight and thorough control to ensure that end-users get drugs that actually have an effect as well as not being malicious.

In order to get a drug or a vaccine approved, Danish companies have to seek permission from the European Medicines Agency (EMEA), who controls the legislation in EU countries. If the companies wish to get a product on the market in the USA they have to seek permission from the American authorities’ US Food and Drug Administration (FDA) and so on with the rest of the world. EMEA and FDA publish guidelines for “Good Manufacturing Practice” which the companies are to follow\(^2\). Actually it is just a plan of the test studies that the companies have to make and complete step by step in order to get the drug approved.

The role of the authorities is to analyse the information regarding the development of the drugs in question and more specific the test results for the research studies completed in each phase. The different phases a normal drug development process has to complete will be reviewed below. The authorities must decide to either approve or discard the drug on the basis of the test results received from the companies. If the test results raise any doubt about the safety or the efficacy of the drugs, the authorities can demand more test results, which of course will prolong the period of a phase. This is done in order to ensure that the drugs that eventually will end up on market do not have any fatal complications. Hence the regulatory area is a very important and costly parameter for the biotech companies.

The approval of the different phases and test results often takes time, which places the companies in a ‘limbo’ standby period. Of course the companies often have a good feeling about obtaining approval, but it may take up to three months where they do not know if the drug has been cleared for the next phase.

\(^2\) http://www.gmppublications.com/iGMPs.htm
The authorities also have the role of speeding medical innovations to the market (Berndt, Gottschalk & Strobeck, 2006, p.91). They try to raise the incentives of doing research into rare/new diseases by designating an orphan status to drug developments\(^3\) with small patient groups. Drugs with an orphan designation gets shortened approval period in order to get the product on the market faster. In that case, the test studies from phase I do not need to be approved in order to start phase II, which is normally restricted. Also the application fees for seeking drug approvals are reduced and thereby making the application process cheaper.

### 2.1.2 The phases of a drug development

The drug development phase is a long and demanding process that requires several different tests and phases cleared in order to obtain a final approval. Each phase can be seen as an option as you at the end of the phase have to take a decision on whether to discard the project or continue developing it (exercise the option). The decision is based on the prospects of the drug (the underlying asset) which test results reveals at the end of each phase.

The drug development process is very risky because it is difficult to know how long and how much it will take to get a phase approved as the research requirements are very different for different disease areas.

Below we have illustrated the process of a drug development process.

![Figure 1.2: Own Construction](image)

**2.1.2.1 The discovery/lead optimisation phase**

The first phase is the discovery phase or lead optimisation phase. A drug development often starts by either identifying a new biochemical compound to find out if it has a positive effect on a known disease or trying to find a cure or vaccine for a disease by testing different biochemical compounds on it.

On a more technical level, the biochemical compound is tested on human tissue in order to get an indication of an effect. If this indication is positive, the work for a chemical structure will

\(^3\)[http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000029.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac95800240ce]
continue so as to end up with a useable drug that has a therapeutic effect. These primary tests are purely in vitro tests, which mean that they are not performed on living organisms.

2.1.2.2 The preclinical stage
The next step in the process is the preclinical stage where the lead compound has been identified. In the preclinical stage the scientists still do not have a lot of information of how it affects the targeted disease. The main goal at this stage is to get more information about the drug and its effects, e.g. how toxic the drug is, how long time the drug stays effective in the body, the level of doses needed and the most effective way to adopt the drug (injections, pills etc.). At the same time it is also important to obtain information about the negative things, most importantly, if any serious side effects exist. If all of these studies look good, the company will file an “Investigational New Drug” (IND) to the authorities to get approved for phase I. The IND contains all the information obtained at this stage along with a future plan for the clinical phases, which is the next step in the development process. At this stage the research studies are still not performed on humans, but on animals.

2.1.2.3 Phase I
In phase I, the testing is performed on a small (20-80) group of persons, who at this point are healthy people.\(^4\) The aim of the research studies in phase I is to evaluate the effects the drug has on human beings and compare them to those found in the preclinical phase. They seek to find answers about the pharmacokinetics\(^5\), which describe the processes of absorption, metabolism and excretion of the drug in question on a living organism. Another aspect of phase I is to secure the drugs’ safety profile by assessing how the toxic substances act on a human beings.

But the most important thing is how well the drug handles the transition from being applied on animals to now getting applied on real human beings. Therefore it would be ideal that the picture of the test results obtained in the preclinical phase resemble the picture obtained when the drug is applied on human beings. The test results obtained in this phase are the foundation for the work that continues in phase II.

\(^4\) [http://www.clinicaltrials.gov/ct2/info/understand#Q01](http://www.clinicaltrials.gov/ct2/info/understand#Q01)

\(^5\) [http://www.clinicaltrials.gov/ct2/info/glossary#phase1v](http://www.clinicaltrials.gov/ct2/info/glossary#phase1v)
2.1.2.4  Phase II

Phase II continues the work begun in phase I, but the tests in phase II include a larger group of test persons (100-300)\textsuperscript{6}. Furthermore, a part of these people suffer from the disease in question. This is necessary in order to track the effects that the drug has on both sick people and healthy people, and to find out how the drug acts in different settings. So the questions raised earlier still need to be answered, again and again.

In phase II the effects of the drug are studied more carefully. It is important at this stage to make sure that the new drug has a positive effect on the sick people and is more efficient than drugs already on the market, if that is the case. This is also called finding the “proof of concept”, why the use of placebo drugs is applied in order to co-determining this.

Phase II is often the phase where most applications are dropped (if the drug enters the preclinical phase), which is documented in table 5.3. This is often because the drug does not have the efficacy as expected as can be seen in figure 5.3. The rejection of the drug development project is often done by the company’s management at this stage, and not by the authorities.

2.1.2.5  Phase III

The objective of phase III is to look at the long term effects as well as the effects on a much larger scale. The group of test persons is increased severely now (1,000-3,000)\textsuperscript{7}. This is done to increase the documentation of the effects found in the previous phases and to confirm the effectiveness of the drug, while still monitoring side effects, toxic level and so on. This increase in the test group size also results in much higher research costs.

In fact phase III is primarily done in order to verify that the drug can be used by “everybody” without any serious complications. As phase III is the last phase it is time to complete the development and hopefully end up with the conclusion that the drug is strong enough to enter the market. Due to the heavy R&D costs it is obvious that a rejection of a drug in phase III has serious consequences and will create considerable problems for the company. In Denmark this was the situation when Genmab’s phase III project “Arzerra” showed poor test results and a consequently the need for another phase III study, which was punished immediately by the

\textsuperscript{6} http://www.clinicaltrials.gov/ct2/info/understand#Q01
\textsuperscript{7} http://www.clinicaltrials.gov/ct2/info/understand#Q01
investors with a decline in Genmab’s market capitalization of more than 35% in just one day. This is among the reasons for why the industry uses this divided phase process so it is possible to discard a project at an early stage due to bad test results.

2.1.2.6 Approval
When a company has completed all the phases it is time to file the entire information as a “New Drug Application”, NDA, to the EMEA. Then it is up to the authorities to decide whether the test results and the documentation are enough to approve the drug. Sometimes the documentation is not thorough enough, and the authorities will demand extra studies completed before a final decision can be made. In some cases the authorities will accept the drug but still demand more test results. Therefore we can sometimes experience the use of a phase IV that covers this exact situation.

2.1.3 Patent
Patent is filed for at the beginning the development process to protect the drug. The patent period is normally 20 years, but with an R&D period of normally 12 years as found in table 5.2, it only leaves 8 years with market exclusivity.

Normally patent protection is sought in those countries where the company in question wants to market the drug. So for a larger company with consumers all over the world the patent seeking process could end up as a rather expensive cost.

Patent protection is basically a method for companies to devote many resources to the R&D process without the risk of generic competition when completed. The 20-year period is estimated to be long enough for the companies to cover all the R&D costs experienced during the development phases and still make a profit. After the 20-year period the patent expires and the chemical structure is released on the market. With the chemical structure in hand it is possible for other companies to make a generic copy of the product and sell it at a far lower price because they only need to be concerned about the manufacturing costs and not any R&D expenditures.

The number of patents that companies seek varies a great deal and is of course dependent on the size of the company. Also there is a big difference between companies that are listed or not. In 2008 and 2009 Lundbeck filed 54 applications, Neurosearch 99 while the smaller unlisted Leo

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8 http://borsen.dk/nyheder/investor/artikel/1/163730/genmab_taber_en_tredjedel_af_vaerdien_paa_faa_minutter.html
Pharma only filed 8\textsuperscript{9}. The number of filed applications is not just a testimony of how innovative the company is. Unlisted companies have the benefit of undemanding owners when it comes to public available information about the company which allow the company to conduct research in certain areas without revealing it to competitors. First when a significant effect is observed a patent is filed for compared to the listed companies who file for patent as soon as a possible effect has been discovered. These repetitive patent applications are both time consuming and costly.

2.1.4 Product life cycle

The typical product life cycle for a normal drug development (assumed that it is approved and enters the market) is illustrated in figure 2.3 based on annual net incomes. The figure recaptures the different stages in a full life cycle of a drug, not only the development phase. The product life cycle shows how biotech companies experience a long period at the beginning of the process where the company has a negative net income due to huge R&D costs. When the product enters the market, the net income rises very much due to the patent protected price, which generates a huge net income during the patent protected period. When the patent expires, the income of the product will drop instantly as a result of other players entering the market with an identical product offering, but at a fraction of the price.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{product-life-cycle.png}
\caption{Product life cycle for a marketed drug. Source: Dimasi & Grabowski, 2007; Bogdan & Villiger, 2008; Grabowski, 2002}
\end{figure}

\textsuperscript{9} www.business.dk/industri leo-pharma-forfoelger-alternativ-patentstrategi
The figure clearly illustrates that a company would make a lot of money getting a product through to the market. But it is very important to remember that the risk of failure is high as only one out of 10,000 explored compounds enters the market and only 30% of drugs succeed in recovering their costs (Banerjee, 2003, p.61). Looking at the graph it is intriguing to believe that a product development is always good due to the huge upside, but it should be remembered that a typical company often has several projects in the clinical phases which end up being a sunk cost.

### 2.1.5 Funding

Another special aspect of the biotech industry is the way in which the companies raise funds. As described above the industry is subject to different uncertainties which together affect the funding conditions of the industry. The biotech industry is characterized by companies that have difficulties in generating a “normal” income compared to regular manufacturing companies. These circumstances force the companies to raise funds in different ways than normally seen. Thus we split the funding up in an early stage funding and a later stage funding.

The early stage of funding is often characterised by being equity funding. This implies that the companies raise funds in return of giving ownership of the company.

A commonly form of equity funding is venture capital which account for roughly one-third of start-ups capital (Day & Shoemaker, 2004, p.313). Venture companies often know the risky conditions of the industry and at the same time recognise the possibilities of such investments. Venture capital is often an expensive form of funding usually available at a rate of 15-18% with a time horizon of 18-24 months (Avance, 2008, p.2). The biotech companies also receive business consulting services in order to optimise the firm and make it more competitive. These joint venture agreements often imply that the company will keep receiving additional funds as they go through the development phases. Hence the venture companies get security for their investment as they know the company will not spend all the funds recklessly when received as they have to reach certain milestones in order to get additional funds.

Another popular method of raising funds for young companies is through licensing. When licensing the biotech company license the project to an industry partner who makes an upfront payment. As the development of the drug progresses, the biotech company will receive additional funds when each phase is successfully finalized or when other contract agreements are
met, which is known as milestone payments. But when settling such an agreement the biotech company loose the right to commercialise the product if it should reach the market, hence accepting a large reduction of the potential upside (Avance, 2008, p.1).

Equity financing can also be obtained through an initial public offering, but this way of funding is more risky for the investors as they do not have full information about the company and their plans. Of course a prospectus is made but it will surely be more positive than negative in order to make the investors invest in the company. An important issue with raising funds through initial public offerings is that it is very normal that biotech companies have to seek funds multiple times, hence additional share issues would dilute the stock’s value, putting the initial investors in a bad position forcing them into investing again to maintain their ownership share of the company.

It is a method that is widely used in Denmark as it enables the biotech companies to obtain the liquidity needed10. However, the economic crisis the world has experienced the last years affects this way of raising funds in a negative way, as many investors have become more risk averse11.

When companies become larger the funding strategy changes as well the possibilities changes. If the company now generate an income the possibility of debt financing increases. The good thing about debt financing is that it has no dilutive effect on the equity, but instead it requires payments at certain times at certain rates. Even though that dept financing does not have a dilutive effect on the equity, one has to remember that the creditors of the dept have seniority over the existing shareholders in case of default.

A final method of late stage financing is royalty financing (Avance, 2008, p.3). It implies that the smaller biotech company outsource the heavy capital expenses that are needed for marketing and producing the drug to a larger pharmaceutical company. By doing so the biotech company does not need to raise a large amount of capital in order to initiate a complete production facility but instead having the pharmaceutical company to produce and market the drugs. For outsourcing the project the biotech company gets a royalty payment for each item sold in return. This implies that this way of financing is often first seen in the later stages where a drug shows promising prospects.

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10 http://www.business.dk/biotek/dansk-biotekvirksomhed-faar-750-mio
11 http://www.business.dk/biotek/investerer-stadig-skeptiske-overfor-biotek
These different forms of funding all have the same outcome, which is that the biotech industry is clearly being equity financed. This fact will be used in section 6.1 when discussing and estimating the cost of capital.

2.2 Valuation processes in practice

The purpose of the following section is to get an overview of how companies in the biotech and pharmaceutical industry perform their valuation processes. It is essential to know how real-life practice works when presenting new methods for valuing projects in order to assess whether such new methods are applicable.

Secondly, the aim of this survey is to see how the different companies deal with issues such as estimating solid forecasts, capital budgeting and organizational structure influence.

2.2.1 The companies in our survey

Initially the intention was to include many different companies, large as small and listed as non-listed because that set-up would provide the best possible picture of the whole industry. Unfortunately a number of companies did not have the time or interest to participate in our survey, but the participation rate is still at an adequate level to determine the standard practice in the industry as the participating companies are among the largest and thus expected to have above average valuation practice.

We also chose to seek information from companies who act as stakeholders in the industry (such as consultant houses, investments banks and venture capital companies), to get a picture of the industry from a more objective perspective. Exactly this more objective and external view of the processes was found to be of special interest as it gives a better possibility to critically assess the information from the companies.

Below are listed the companies that have participated as well as a short introduction to each of them.

Novo Nordisk A/S

Novo Nordisk A/S is the biggest pharmaceutical in Denmark which develops, produces and markets drugs. Their position means that they are involved in very much in Denmark, both
supporting small companies and having strategic alliances with other major actors. Their main area of concern is within the diabetes area, where they are world leaders and secondary the haemophilia area.

**Lundbeck A/S**
Lundbeck A/S is the second biggest pharmaceutical in Denmark and develops, produces and markets drugs. Beside their proprietary drugs they also form different kind of partnerships with biotech companies. Their expertise lies within the area of the central nervous system.

**Zealand Pharma A/S**
Zealand Pharma is a minor player in the industry when compared to Novo and Lundbeck. Zealand Pharma primarily develops new drugs, based on the use of peptides. They research within three different areas: diabetes, gastrointestinal and cardiovascular diseases. Zealand Pharma runs their operations differently than Novo and Lundbeck as they form development partnerships with leading global pharmaceuticals, e.g. Pfizer and others and thereby does not produce or market their drugs.

**Sunstone Capital:**
Sunstone Capital is a venture capital company acting in the biotech industry as well as the IT industry. Sunstone is the acquirer of former “Vækstfonden”, which makes them accountable for more than DKK 3.5 billion. In general Sunstone Capital invests in companies that they believe to be a good investment, preferably in the early stages. They offer financial and managerial aid to make the project development better through their expertise.

As Sunstone Capital encounters many different unlisted biotech companies they have a thorough understanding of how project valuation is performed in the biotech industry.

### 2.2.2 Survey procedure
The procedure of this survey was initiated by an introductory email sent out to the companies. Many companies answered they did not have time to participate or did not reply at all. We called the participating companies to establish a personal contact. This led to a couple of telephone interviews as well as one personal meeting, which called for the same interview approach where we could get thorough answers to our questions. In one instance we were asked to send a
questionnaire, which we did. The downside of this method was that we could not ask additional questions if the answers received were not 100% satisfactory, hence making it harder to conclude a final answer as a small doubt might exist. For the venture capital company we formulated the questions differently as our original questions were aimed at the companies internally.

The questionnaire and the list of questions used in the survey are constructed in order to get the most relevant information from the companies with regard to this thesis and can be seen in appendix 2, 3 and 4.

2.2.3 Survey results

2.2.3.1 Which kind of valuation models is used in the industry?
Our findings showed that the companies used the DCF method in order to end up with a NPV. In all cases they made use of excel models based on the principles of the DCF method. These excel models were often risk adjusted in regard to the success rate of approval in the sense that they would end up with a risk adjusted NPV, creating a better, more correct value to conclude on.

Sometimes the use of financial valuation models was initiated before and during the discovery phase while other companies initiated the use at phase I/II. The reason for this was the big uncertainty that exists within the discovery phase, where qualitative judgments based on earlier research history were used. In the earlier phases of a drug development they argue that the uncertainty of the potential of a new drug is too big to throw into a model as the picture would not be of any value, or only little value.

None of the companies used any form of real options analysis as the application of it was considered to be too complicated and thus not in line with the goal of creating a simple valuation process that is understandable for all parties involved.

2.2.3.2 What are the key inputs in the valuation models?
The general picture showed that many of the models were constructed on the basic of two parts, the R&D part and the commercial part. In the R&D part the most essential parameter was the success rates of finishing the different phases. The estimation of these rates was in general based on earlier experience. The estimates were from time to time revised to ensure that updates from the authorities such as new, stricter demands were included in the estimates. The estimate differs
greatly depending on the kind of project. Another important input in the R&D part is the estimation of the R&D costs. In many cases the estimates were based on earlier projects, but again the costs differed depending on the type of project.

Finally, another important input was the estimation of the length of the different phases. As we saw above with the R&D costs, the time estimates are also based on earlier studies as well as industry benchmarks. If the point of interest was within a new area of expertise, results and estimates could be considered purchased from consults or experts externally.

In the commercial part, the key inputs were price, volume, post-approval costs among many others. All the companies used different prices when looking at different geographic segments and different target groups. Price and volume was mostly based on historical figures but the use of consumer surveys was also applied.

The commercial part of the input variables was in general seen as the most difficult to estimate due to the complexity of predicting future influences. Thus the estimation of the commercial part is more time-consuming than the technological part as it demands more discussion and analysis from the project group.

2.2.3.3 What kind of discount rate is used?
Throughout the survey we experienced that WACC was used as the discount rate and here the type of project was irrelevant. The simplicity of only one WACC was preferred within the companies as it was easier to work with for all employees. The goal of keeping it as simple as possible was mentioned by several. The WACC was in most cases obtained in collaboration with the finance or/and economic department. Our survey showed that WACC was typically estimated to be in the range of 8%-13%.

The WACC was typically revised once a year or in connection with large, important projects.

2.2.3.4 Are the inputs updated/evaluated from time to time?
Generally, our findings revealed that around once a year the financial valuations were revised and updated if necessary with special importance on discussion of the different input variables. Especially in phase II or III the key inputs would be examined and discussed again to ensure that the project is still on track before entering these more expensive stages.
Some of the companies reported that sometimes they continued projects that at first were expected to have a negative NPV. The reason for this is first of all that the structured financial models do not capture all the value or at least not the full potential of a project, which may well become a positive project later on. Other reasons were of a more strategic nature, e.g. that more knowledge about the compound could become of greater value in the future in connection with other in-house developments or in collaboration with other actors in some kind of strategic alliance.

2.2.3.5 Are sensitivity analyses conducted?
All the companies conducted sensitivity analysis on some of the key inputs. The key inputs are specific for each project as in some cases the commercial side was more important to focus on than the R&D part.

2.2.3.6 Is the value of flexibility included in the valuation?
Several companies were able to see the advantages of flexibility and the value of this information. Yet with this information at hand it was not found important enough to add as an additional value to the static NPV. They mentioned the issue of adding managerial flexibility in their static excel models as the value of this flexibility would become too arbitrary.

2.2.3.7 How is the valuation process?
The key inputs of the project were thoroughly discussed. This means that the project manager receives estimates from the scientists as well as the marketing division for instance. The project manager will here question and review the estimates received and determine if the forecasts are valid and usable in the valuation model.

It is our impression that it is considered very important to keep the valuation process as simple as possible so that everyone involved in the forecasting process understands what is going on.

2.2.3.8 Are there any goal conflicts between scientists and the people conducting the valuation?
The forecasts received from the scientists were most often accepted but in many cases the project manager had the final word. In the case of any doubts arising about the forecast, external resources were often consulted. Industry benchmarks are then applied to ensure that the estimates are correct and not too optimistic. But problems regarding scientists and their forecasting were
familiar to the project managers and the senior management. In the larger companies, the project
groups were a mixture of employees with different backgrounds, such as economists, chemists
and biologists. This made it possible for the project division to assess the forecast from the
scientists on a much better scale as the discussion was conducted by people with expertise within
those areas, thus ensuring the best possible inputs to obtain the most precise results.

2.2.4 Results from external survey
We have also chosen to look at external analyses of valuation practices, which will be discussed
in this section. The primary aim is to get industry-specific information about the valuation
methods used across the world. Secondly, to confirm that the test results of our own survey are
not special to our sample companies, but more or less follow the industry trend, and hence to
ensure that our survey can be used as a proxy for the industry.

This area of research holds many different surveys and investigations. We will make use of a
survey by Hartmann and Hassan from 2006 that covers the largest pharmaceutical and biotech
companies in the world, as well as surveys external stakeholders such as consulting houses and
investment banks.

This very wide survey reveals a substantial use of the discounted cash flow model. The results
are presented in appendix 5.

It appears that only 59% make use of the DCF method at the discovery phase, while at the
clinical phases the rate is 85% to 100%. Around 26% of the participants make use of the real
options analysis at the clinical phases which testifies that the method gradually is getting
accepted by the practitioners. The survey also reveals that some participants use other economic
models, such as the IRR and EVA.

The survey also presents the risk analyses that the companies conduct where especially there is a
massive use of risk analyses at the clinical phases. The most used analysis is decision trees with a
74% rate of use, while the use of sensitivity analyses is right behind with 67%. Scenario analyses
were also used by 67% of the participating companies.

The results for the stakeholders showed a somewhat similar picture. The DCF method was
widely used and again most often in the later stages where approximately 87% used it while it
was only applied by around 70% in the earlier phases. Interestingly, the use of real option analysis was less applied than at the companies with only 13-16% of the participants performed this sort of analysis.

Apparently the stakeholders were not interested in risk analysis as the overall percentage of these studies was substantially lower. Here the most used method was the scenario analysis in 53% of the times in the clinical phases while the use of decision trees and sensitivity analysis only was performed 37% of the times.

Another good thing about this survey is the breakdown of the actors in sizes and maturity. This allows us to see how the companies and the stakeholders differ in conduct relating to their size. Risk analysis was conducted at a higher rate for the more mature companies compared to the newly established ones which indicate that the reason for the mature companies keeps being competitive is a stronger focus on risk analysis. Also regarding size there are differences in the type of risk analysis conducted. 80% of the large companies used scenario analysis, while only 9% of the small companies made use of scenario analysis. Instead the smaller companies found break-even analysis more interesting, which indicates a stronger focus on near-term revenue which is important to attract investors.

2.2.5 Conclusion

Our investigation presents a picture of a very uniform industry practice. The main conclusion we can draw from the survey is that the involved parties all used the DCF model to value their R&D projects. The reason for this use of the DCF model was primarily because of its simplicity as well as its wide acceptance throughout the industry. The use of real option was not an alternative due to the high complexity and lack of understanding. The external survey revealed the same picture, and we argue that the results of our survey are representative for the entire industry. The external survey also showed indications of the use of real option analysis, and we argue that real option analysis is more used outside Denmark.

The fact that the DCF model is very simple increases the importance of the input estimation. The inputs used in the model were all discussed immensely before deciding the final value. Among the companies the key inputs were a bit different, but it transpired that the inputs from the commercial part were discussed more than the inputs from the technological part often based on
historical figures. Due to the changes in the context of the biotech industry the inputs are revised frequently to stay updated with the guidelines from the authorities. Regarding the estimation of the commercial side we saw a great deal of internal estimation rather than the use of experts with a wide understanding of the market. This can lead to acceptance of loss-making projects due to the rapid changes in the market conditions.

We noted that project managers collected data from the scientists, assessed this information and submitted a project recommendation to the senior management. Issues with tentative estimates handed in from the scientists occurred from time to time. Yet in most cases due to the long-term and large economic perspectives of such a project the credibility was found good, which would be expected in a working relationship like that.

Our survey revealed that the discount rate of choice was WACC. Generally, WACC was used throughout the entire company to keep it simple.

Finally the survey concluded that all the sample companies conducted some sort of risk analysis. The most used method was scenario analyses along with sensitivity analyses, which primarily were done by making changes to the key inputs.
Part 2 – Classic valuation methods

Part 2 introduces the concept of real option analysis as an alternative to the DCF model. It is applied to the industry characteristics discussed in part 1 to make it practically applicable. Also it makes us able to step further into the real options universe in the next part as the basic understanding of real options will be in place.

3 Discounted cash flow method

The traditional valuation method which is also the most commonly used method among practitioners is the discounted cash flow method. Studies such as the one performed by Hartmann & Hassan as well as our own found in section 2.2 have proved that the discounted cash flow method by far is the most preferred method when it comes to putting a number on the value of a biotech research project. Before analysing the drawbacks of the DCF method we will briefly consider why the discounted cash flow analysis is so widely used.

The discounted cash flow method has clear and consistent decision criteria for all projects it values, which makes it easy to communicate to the management. The simplicity of the method makes it easy to understand for people with a non-financial background and is the main reason for its widespread acceptance. The method is quantitative and economically rational as it factors in the time value of money.

But the simplicity of the method is also why it is not suitable for more complex investments with a high uncertainty regarding the future cash flows. In this section we will look into the potential disadvantages of using the discounted cash flow method on strategic optionalities, as the drug development projects can be considered. The disadvantages of the method will be briefly discussed to point out the need for a more sophisticated method, which can better identify and cease the uncertainty that so heavily surrounds these research projects with decade-long time horizons.

When valuing a drug development project with a long time horizon, all the decisions regarding the future cash flow streams are made at the time of the valuation. In the model, the future cash flows are fixed and seen as highly predictable and thus do not take the uncertainty of the future
into account. But cash flows are not very predictable as variability on the future cash flows occurs, and particularly in the world of biotech research projects. In reality, many decisions regarding the individual project are deferred to a later point in time where more information about the project and the market opportunities is available. This is something the model does not account for.

The discounted cash flow model assumes that projects are passively managed when in fact many research projects are actively managed through the many different options of expanding or contracting the research project as uncertainty unfolds.

This managerial flexibility is a key asset in all research projects as it makes it possible to incorporate all the new information into your decision making as the project goes along. So the lack of valuing that flexibility in the discounted cash flow model is the biggest drawback and is what makes it inadequate when it comes to valuing projects in a high-uncertainty environment. Externalities or immeasurable factors that cannot be modelled into the discounted cash flow analysis are neglected in the model even though they can represent a huge upside potential if they represent themselves as value-adding options. Or new information can alter the profitability prospects of the projects and give the management the opportunity to shut the project down.

To sum up, the traditional discounted cash flow analysis underestimates the value of flexibility as it assumes that cash flows are determined and irreversible. In reality the cash flows are highly uncertain and the management can exploit this uncertainty to make the most of the opportunities that present themselves as time reveals new information.

### 3.1 Real options analysis

#### 3.1.1 Application of real options valuation

As discussed in section 3 there are many shortcomings of the DCF model when it comes to valuing highly uncertain projects. Adjusting the DCF model with a risk-adjustment factor tries to take the uncertainty into account but it cannot give a complete picture of the management’s flexibility throughout the entire project. This flexibility of the management can be described as options. They have the option, but not the obligation, to proceed in any direction with the project as more information changes from unknown to known. The management can choose to expand
the project if the drug shows promising qualities or the market changes in a favourable direction. They can also choose to shut the project down or scale it down if negative information about the drug or the market is revealed. These options add value to the project. The more uncertainty embedded in a project, the higher the values of the options are as they take advantage of the uncertain conditions. So in order to calculate the full value of the project both the DCF value and the real option value are needed to express the expanded net present value (Trigeorgis, 1993, p.4). Trigeorgis argued that the traditional NPV approach is built on assumptions which are hard to value when working in an environment embedded with uncertainty. As mentioned earlier, the DCF approach does not include the value of managerial flexibility so when looking at investment projects he argues that the valuations should include this managerial flexibility and presents the formula for the expanded NPV as

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\text{Expanded NPV} = \text{Static NPV} + \text{value of option from active management}
\]

The expanded NPV is also called the strategic NPV as it includes the value of the strategic possibilities.

Real options valuation can be used to value any project where it is possible to find the net present value of the underlying asset. But the usability of real options increases with the uncertainty of the project. Thus a real options valuation of a project with very stable and certain cash flows like a sugar plantation will not add any value besides the value you get from the DCF model. But with the very high uncertainty surrounding the biotech industry real options valuation will be ideal for these projects. Supporting the application of real options valuation is the well-defined setup of a drug development project. The differentiated stages make the use of real options more accessible as the end of each phase marks a real option for the management with the disclosure of new information.

A general check list for the relevance of real options valuations could look like the following.

- The value of the project should come from a number of cash flows in the future which are not known today.
- The management should have the possibility to alter the strategy as new information is revealed.
• New information should reveal itself to uncover the uncertainty during the maturity of the project.

3.1.2 Financial options
The real option philosophy originates from financial options. Consequently they share a lot of characteristics. However, there are important areas where this is not the case and neglecting this can lead to a valuation based on incorrect assumptions. These areas will be discussed in the following together with a review of the development of options theory.

The first ones to introduce financial options theory were Fisher Black and Myron Scholes in 1973 (Black & Scholes, 1973). A financial option can be defined as a right but not an obligation to buy an underlying financial asset at a predetermined price (Brealey, Myers & Allen, 2006, p.542). Whether the owner can exercise the option on a predetermined date or anytime before that date depends on whether it is a European or an American option. When the option gives the right to buy the underlying asset at the concluded price, it is called a call option. And when it gives the right to sell the underlying asset, it is called a put option.

The defining difference between financial options and real options is the nature and liquidity of the underlying asset. Financial assets such as equities, bonds or foreign exchange are traded in a transparent market with a close-to-perfect pricing (depending on the fundamental view on how perfect the market is). These attributes of the underlying assets make it possible to trade the matching options at market prices on exchanges in a similar way. Real options are on the contrary written on very illiquid assets which are often unique and consequently very difficult to price at a market price. It can be real options on underlying assets such as different mineral mines, oil fields or life science development projects. For clarity, the main differences between financial options and real options can be seen in figure 3.1
These differences in the characteristics of the underlying assets have implications for the valuation of real options compared to financial options, which will be discussed later in this part. Before that the most common types of real options will be described and analysed.

### 3.1.3 Types of real options

The different types of options model the different ways a company can react to new information. The management’s flexibility is thus embedded in several different real options. The different real options where it is possible to either exercise it or let it pass are described as simple options (Copeland & Antikarov, 2003, p.121). The multifaceted real options are described as advanced options (Kodukula & Papudesu, 2006, p.145).

First we will discuss the simple real options we perceive as most important for the biotech industry and then the advanced options which are most often encountered.
3.1.3.1 Simple real options

3.1.3.1.1 Option to abandon
If a project develops worse than estimated and fails to live up to the expectations, the project management can consider abandoning the project and thus saving future costs related to the project (Kodukula & Papudesu, 2006, p.102). For projects where the NPV is very marginal the abandon option is particularly important as even minor changes to the estimates can change the outlook from profitable to loss-making.

3.1.3.1.2 Option to license
Often biotech companies do not have the capital, organization and distribution power to maintain several late-stage drug development projects and/or market them. The option to license gives the companies the right to sell some degree of the project often to a larger pharmaceutical company, who has the capacity and funds to market the drug worldwide if that is needed. In exchange for these rights the biotech company receives capital on an ongoing basis in the form of milestone payments and royalties. This allows the company to maintain a constant focus on research without having to wait for a drug to be launched and in this manner new capital is injected.

For biotech companies this is a very important option as it allows them to focus on several different drug development projects and thus maintain a diversified product portfolio (Copeland & Antikarov, 2003, p.126).

3.1.3.1.3 Option to defer
The option to defer can be viewed as a trade-off between risk and return (Bogdan & Villiger, 2008, p.54). In a high-uncertainty environment the option to wait can be used to get more information about the market potential or the abilities of the drug and thus defer the decision on continuing or discontinuing the research program until a more certain outlook for the sales potential has been obtained. By waiting to further invest in the drug development the cash flows will occur later in the future and consequently be discounted with a higher factor. Also the protected period for patented sales will be shortened and it will compete with generic productions earlier.

The value of the option to defer will diminish with the degree of competition in the industry. By waiting, the competitors will get the opportunity to obtain a first mover advantage if they choose
to invest. Thus the higher the barriers to entry in the industry are, the more valuable an option to defer is (Kodukula & Papudesu, 2006, p.126).

3.1.3.1.4 Option to expand
In industries with a high growth rate the option to expand can be very useful and value-adding (Kodukula & Papudesu, 2006, p.110). Projects with a low or even negative NPV may in the long run provide added possibilities if the market develops in the desired direction. But these possibilities only occur if the initial investment has been made. So in order to make a profitable investment at a later point in time it is essential that the foundation has been laid. It can be the expansion of a manufacturing plant if demand rises (Copeland & Antikarov, 2003, p.12) or the testing of a drug in one market before the decision is made on whether to launch in all markets (Bogdan & Villiger, 2008, p.55).

3.1.3.1.5 Option to contract
This real option incorporates the possibility to scale down the project if the market does not develop quite as anticipated. It can be production facilities that need to be scaled down if demand suddenly fluctuates. Accordingly it is important that the management is aware of that future option when the facility is being designed and built. Also the option to outsource parts of the value chain is considered an option to contract (Kodukula & Papudesu, 2006, p.116). Thus this option has had growing importance for nearly all industries in the last decades due to wage increases in the Western World.

3.1.3.1.6 Option to switch
In markets with high uncertainty and long time horizons the option to switch can be of high value. Due to the low visibility in the markets sudden changes in consumer demand can be very difficult to predict 5-10 years ahead. The project can be designed in such a manner that it is possible to alter the final output if consumer sentiment differs from what was expected. It could be the possibility of an automobile producer to change the motor from gasoline-driven to a gas-electric hybrid if the environmentally-friendly wave kicks in sooner than expected (Mun, 2002, p.241). Or the possibility for a detergent producer to switch from a powder solution to a liquid solution if that is what consumers dictate.
3.1.3.2 Advanced real options

3.1.3.2.1 Compound option
A compound option can be described as an option on options (Copeland & Antikarov, 2003, p.12). In multiphase projects this option is very common as the initiation of one phase is dependent on the completion of the earlier phases or in other words the exercise of the earlier options (Kodukula & Papudesu, 2006, p.61-62). Therefore the value of compound options is contingent of the value of other options (Copeland & Antikarov, 2003, p.163). Due to this cohesion between several real options a compound option is described as an advanced option.

3.1.3.2.2 Rainbow option
When there is more than one type of uncertainty embedded in the option, it is called a rainbow option (Copeland & Antikarov, 2003, p.221). This is often attached to development projects as there is a technological risk regarding the efficacy and safety of the product and then a market related risk which determines the sales potential.

3.1.3.2.3 Learning option
If some kind of resolution of the uncertainty either related to the technological risk or the market risk occurs during the span of a real option it can be called a learning option (Kodukula & Papudesu, 2006, p.62). The example of making a pilot test of a drug in one market before making a full scale launch, as described in the part about the option to expand, would be considered a learning option.

A combination of simple options constitutes advanced options

Figure 3.1: Own construction
3.1.3.3 Compound, learning and rainbow options

In a bigger perspective all the different simple real options of a drug development project can be seen as parts of a compound, learning and rainbow option as illustrated in figure 3.1. At the end of each phase in the development process any of the options available can be chosen or things can continue as planned based on the findings of the most recently completed phase. The options in the earlier phases can especially be viewed as rainbow options as both the technological risk and the market risk are very much present. As the project approaches market launch the technological risk will diminish and at the end the options will almost solely be based on market risks and thus can no longer be considered rainbow options.

For drug development projects the single most important option is the option to abandon a project when it is not profitable anymore. The other mentioned option also creates value but not on an everyday basis as the option to abandon does (Bogdan & Villiger, 2008, p.56).

3.1.4 Valuation methods

There are several different methods for valuing options. They can be divided into three categories based on the principles and framework behind the calculation method. That is partial differential equations, simulations and lattices (Kodukula & Papudesu, 2006, p.66).

<table>
<thead>
<tr>
<th>Option Valuation Technique</th>
<th>Specific Method</th>
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<tr>
<td>Partial differential equations</td>
<td>• Closed form solutions using Black-Scholes and other similar equations</td>
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Table 3.2: Own Construction. Source: Kodukula & Papudesu, 2006
3.1.4.1  Partial differential equations
By valuing an option with a closed end formula all the attributes of the option are encapsulated into an equation. This is well suited for the valuation of simple options with predetermined input parameters. Such is the famous Black-Scholes equation which uses the value of the underlying asset, the strike price, the time to maturity, the interest rate and the volatility (Black & Scholes, 1973). However it is almost impossible to capture the complexity of real options in a closed form formula due to the distinctive features of the many different embedded real options that must be included in the valuation (Bogdan & Villiger, 2008, p.58). In order to model such a complexity into a formula a very high mathematical understanding is required which is very seldom found among the practitioners who are valuing development projects in the industry as discussed in section 2.2. Furthermore the closed end solutions lack the possibility of visualising possible scenarios. The real option framework should not only be considered a tool for the calculation of a project’s value but also as a tool that helps people involved with the valuation of a project, especially the decision-makers, to grasp the entirety of the project and understand the different real options that appear during the span of the project (Shockley, Curtis, Jafari & Tibbs, 2002, p.55). Consequently, a black box solution where approximated information calculated on the back of mathematically complex numerical methods such as the finite difference method is entered into a formula that calculates a number is not the way to apply the real option framework for practitioners in the industry.

3.1.4.2  Simulations
A simulation of the future is obviously a valuable tool for deciding the prospects of a development project. It is often done by simulating the sales number many times with an algorithm that randomly chooses the outcome. The future is forecast with an estimate for the volatility which determines the probability distribution of the cash flows. A higher volatility produces more extreme scenarios in the tails of the distribution which implies a higher real option value due to the managerial flexibility. The estimation of the volatility is the tricky part as it is naturally difficult to predict the probability of the different possible future outcomes. There are several advanced methods\textsuperscript{12} which can be used to estimate the volatility, but such methods are not aligned with the goal of simplicity for applying the real option framework to industry practitioners. These methods require statistical and programming skills which again violate the

\textsuperscript{12} Methods such as Monte Carlo Simulation or the logarithmic cash flow returns method.
goal of simple application for the real option analysis. Beside the severity of using these methods, they also have trouble dealing with two different kinds of uncertainties such as the technological and market risk (rainbow options) we see in drug development projects (Kodukula & Papudesu, 2006, p.87). Additionally, simulations struggle with handling path-dependent options (sequential compound options) where each stage option is dependent on the outcome of the previous stage option (Bogdan & Villiger, 2008, p.60). This is exactly the kind of options that are embedded in a biotech project.

Based on this it can be concluded that simulations are not entirely ideal for valuing a drug development project, which can be seen as a sequential compound rainbow option.

3.1.4.3 Lattices
Lattices can also be called trees due to the way they model future scenarios. They range from simple event trees to the advanced multinomial trees. The simple event trees can be categorized as an extension to the DCF approach. It adds extra value by incorporating contingent decisions at various decision nodes in the future (Kodukula & Papudesu, 2006, p.33). We will analyze how they can be used as a simple tool for implementing some of the real option thinking into a DCF valuation. A more theoretically correct implementation of the real option framework will be analysed by the use of binomial trees. Binomial trees subdivide the time to maturity in small steps and assume that in each node the peak sales can go either up or down with a certain probability. Market states are modelled all the way to maturity and then combined in a recombinant tree. From here you can calculate the value by going back one step at a time until you reach the root of the tree. Binomial trees are the most widespread tool for real options valuation in the industry as the method can be easily explained to the management due to its intuitive simplicity in the modelling (Mun, 2002, p.100). The more advanced trinomial, quadrinomial and multinomial trees should in theory yield more precise results as they incorporate more events at each node (Copeland & Antikarov, 2003, p.279), but it is doubtful if it gives better results in practice (Lander & Pinches, 1998, p.545). As they are also computationally more complex to model (Kodukula & Papudesu, 2006, p.72) we will disregard them due to our overall objective of an undemanding implementation of the real options framework.
3.1.4.3.1 Simple event tree

To build a simple event tree, the cash flows estimated in the DCF model are separated into the phase where they occur or are expected to occur. Then the success rate for each phase is projected which can be seen as the chance of the cash flow to happen. All the cash flows are then probability-adjusted by the chance of them occurring. This sums to the risk adjusted NPV which in theory are superior to the traditional NPV (Stewart, Allison & Johnson, 2001, p.816). The event tree is modelled in figure 3.2.

As the success rates are contingent on each other, cash flows longer into the future will have a smaller chance of occurring and thus a smaller value. Consequently the forecast sales will be reduced by the highest percentage (Myers & Howe, 1997, App C.).

This method ensures that a project is not overvalued by looking at the risk of failure in each phase as well as it incorporates the risk of spending capital in the initial phases without the product ever reaching the market. But it will have a tendency to be overly negative as future costs are not omitted in the situation of an early abandon.

3.1.4.3.2 Binomial tree

Valuing real options with binomial trees can be executed in two ways. It can be done by the use of market-replicating portfolios or by the use of risk-neutral probabilities which in theory should yield the same result. The predominant assumption of the former model is that there exist a
number of traded assets in the market which can be obtained to replicate the existing asset’s payout profile (Mun, 2002, p.143). As it is not possible to obtain a matching drug development project, we will ignore this method and instead use risk-neutral probabilities to the real option valuation.

The risk-neutral probability approach was introduced by Cox, Ross and Rubinstein (Cox, Ross & Rubinstein, 1979, p.234) with the assumption that the option value is independent of the investor’s attitude towards risk. This allows a risk-adjustment of the probabilities of the cash flows. These adjusted cash flows can then be discounted at the risk-free rate. Hence it is unnecessary to discount a risky set of cash flows with a risk-adjusted discount rate as classic discounted cash flow models demand (Mun, 2002, p.143-144).

The first step is to calculate the current value of the asset without any flexibility which can be done by using the classic discounted cash flow model (Copeland & Antikarov, 2003, p. 84). A binomial tree is then constructed by using up and down factors calculated from the asset’s standard deviation. This is shown in equation 3.1 (Kodukula & Papudesu, 2006, p.72) and 3.2 (Kodukula & Papudesu, 2006, p.74)

\[ u = e^{(\sigma \times \sqrt{\Delta t})} \]  \hspace{1cm} (3.1)
\[ d = e^{(-\sigma \times \sqrt{\Delta t})} \]  \hspace{1cm} (3.2)

The up and down factors are multiplied with the asset’s value at each node defined as a step in time. This will materialize into a recombinant binomial tree showing the future possible values of the asset.

Next the risk-adjusted probability must be determined which is shown in equation 3.3 (Mun, 2002, p.144). As previously mentioned it facilitates discounting the cash flows with the risk-free rate.

\[ p^{up} = \frac{e^{(r_{f} \times \delta t) - d}}{u - d} \quad \text{and} \quad p^{down} = 1 - p^{up} \]  \hspace{1cm} (3.3)
It is important to remember that the risk-neutral probability is a mathematical intermediate and thus of no economic and financial meaning but just a step in a series of calculations (Mun, 2002, p.144-145).

To calculate the value of the option at each specific node backward induction is used (Kodukula & Papudesu, 2006, p.78). This implies that the option value at each node is dependent on the value at the node one step later in time. How to calculate the option value at each time is shown in equation 3.4 (Bogdan & Villiger, 2008, p.71-74).

\[
V_t = \frac{p_{up}V_{t+\delta t}^{up} + (1-p_{up})V_{t+\delta t}^{down}}{e^{(r \times \delta t)}} - X_t^* \quad (3.4)
\]

* Only at decision nodes

If the value at any node turns out to be negative it would be better to abandon the option if possible as a payoff of zero is preferable. For drug development projects this opportunity will present itself at the end of each phase. The payoff calculation is showed in equation 3.5 (Copeland & Antikarov, 2003, p.128).

\[
payoff = MAX[V_t, X_t] \quad (3.5)
\]

The backward induction is performed until the first node is reached which equals the value of the option.

It is the up and down certainties that generate the value in the option. A higher volatility measure leads to more extreme up-scenarios and thus a higher option value (Mun, 2002, p.146).
Part 3 – Fuzzy real options valuation

Part 3 introduces the concept of fuzzy numbers in real option valuation. We will go through the theory to fully understand the mechanics behind this new valuation method. Subsequently we will look at how the theories can be applied in practical valuation. This section begins with a short introduction of the concept of fuzzy numbers, fuzzy sets and the entire fuzzy logic. Next we present the two most applicable fuzzy numbers to show how these can be used for valuing projects that are embedded with uncertainty. The section ends with a presentation of the fuzzy binomial valuation method.

4 Fuzzy sets and numbers

The basic concept of fuzzy sets and numbers originates in the classical set theory developed by Zadeh in 1965 (Zadeh, 1965). The difference from the classical set theory is the value assigning of the membership grade, which previously was assigned using the grade of either one (for complete membership) or zero (for zero membership). Zadeh introduced the concept of not determining the value from a bivalent point of view but instead creating a continuum of grades to describe the grade of membership, hence making it possible to have e.g. a 0.6 grade of membership, defined by

\[ A(x) = X \rightarrow [0,1] \]

, where \( A(x) \) represents a fuzzy subset \( A \) of a non-empty set \( X \) in the interval \([0, 1]\).

In other words the notation of \( A(x) \) simply represents a function, the membership function of \( A \), while the \( X \) represents the universe for the fuzzy subset. The degree to which the statement “\( x \) is in \( A \)”\(^{13}\) is true, is determined by finding the ordered pair \((x, A(x))\). This degree of truth is the second element of the ordered pair. All these ordered pairs completely define \( A \), which can be written as

\[ A = \{(x, A(x))|x \in X\} \]

\(^{13}\) Where \( x \) denotes a fuzzy quantity and \( A \) is the membership function
The purpose of introducing this algebra, “fuzzy sets”, was to handle imprecise elements in a decision making situation, e.g. regarding uncertain future cash flows. Normally, when dealing with uncertainty, the outcome is depicted by using the classical probability theory but instead fuzzy numbers use the theory of possibility. This means that fuzzy numbers can be seen as possibility distributions (Mezei, Fullér & Collan, 2009 (1), p. 5).

A \( \gamma \)-level set (or \( \gamma \)-cut off) of a fuzzy set \( A \) of \( X \) is the non-fuzzy (crisp) set denoted by \([A]^{\gamma}\) which separates the possibility distribution in positive outcomes and negative outcomes. As negative outcomes in the real option world are considered having a value of zero due to the managerial flexibility that makes it possible to terminate projects with a projected negative NPV, only the positive area of the possibility distribution is needed to calculate the value of the real option.

So if \( A \) is a fuzzy number the following notation is introduced

\[
a_1(\gamma) = \min[A]^\gamma, a_2(\gamma) = \max[A]^\gamma
\]

where \( a_1(\gamma) \) denotes the left-hand side while \( a_2(\gamma) \) denotes the right-hand side of the \( \gamma \)-cut off, \( \gamma \in [0,1] \).

The article “The mean value of a fuzzy number” (Dubois & Prade, 1987) argued how to calculate the mean value of a fuzzy number in a closed interval by using the upper and lower distribution functions. This was the precursor for the work of Carlsson and Fullér who have further developed the application of the theory. In 2000, they defined the crisp (single number) possibilistic variance\(^{14}\) and the crisp possibilistic mean value which are shown below (Carlsson & Fullér, 2001, p. 316).

\[
E(A) = \int_0^1 \gamma (a_1(\gamma) + a_2(\gamma)) d\gamma = \frac{\int_0^1 \gamma \frac{a_1(\gamma) + a_2(\gamma)}{2} d\gamma}{\int_0^1 \gamma d\gamma} \quad (4.1)
\]

These findings will be used to calculate the fuzzy real options value.

\(^{14}\) \( \sigma^2(A) = \int_0^1 \gamma \left( \frac{(a_1(\gamma) + a_2(\gamma))}{2} - a_1(\gamma) \right)^2 + \left( \frac{(a_1(\gamma) + a_2(\gamma))}{2} - a_2(\gamma) \right)^2 \right) d\gamma = \frac{1}{2} \int_0^1 \gamma (a_2(\gamma) - a_1(\gamma))^2 d\gamma \quad (4.2) \)
4.1 Triangular fuzzy number

The use of triangular fuzzy numbers is applicable for a standard valuation as the concept of a triangular fuzzy number harmonizes with a standard cash flow set-up with three different scenarios.

A fuzzy set $A$ is called a triangular fuzzy number if it is noted by a peak (centre) $a$, a left width $\alpha > 0$ and a right width defined by $\beta > 0$ and its membership function has the following form

$$A(t) = \begin{cases} 
1 - \frac{a-t}{\alpha} & \text{if } a - \alpha \leq t \leq a \\
1 - \frac{t-a}{\beta} & \text{if } a \leq t \leq a + \beta \\
0, & \text{otherwise}
\end{cases}$$

(4.3), with the use of the notation $A = (a, \alpha, \beta)$ and the support of $A$ as $(a-\alpha, a+\beta)$.

The triangular fuzzy number is visualized in figure 4.1 below. The peak, or centre of the triangle is represented by $a$, which can be seen as a fuzzy quantity “$x$ is equal to $a$”. The left width is represented by alpha, $\alpha$, and represents the distance from $a$ to the lower extreme, hence $a - \alpha$.

The right width is represented by beta, $\beta$, and represents the distance from $a$ to the higher extreme, $a + \beta$. It is important to remember that it is the distance that is represented by $\alpha$ and $\beta$ as “real positive numbers”, hence $\alpha > 0$ and $\beta > 0$.

We now end up with a fuzzy distribution where $(a - \alpha)$ and $(a + \beta)$ represent the smallest and the largest possible value respectively. The shape of the fuzzy distribution is defined from its membership function which was defined above. This means that the centre, $a$, has a membership degree of one, while the extremes have a membership degree of zero.
The support of A (membership function) is a crisp subset of real numbers ranging from \((a - \alpha)\) to \((a + \beta)\). In figure 4.1 above the triangular fuzzy number has negative values \((a - \alpha)\) to zero and positive values from zero to \((a + \beta)\) which means that the negative numbers represent the negative NPV of payoffs from a given project (which is valued at 0) and vice versa for the positive side.

4.1.1 The fuzzy payoff method for real option valuation

The fuzzy payoff method was introduced by Mezei, Collan and Fullér in 2009. They presented a new method to calculate the real option value (referred to as ROV) with the use of triangular fuzzy numbers (Mezei, Collan & Fullér (1), 2009, p.6). Their method is inspired by a real option valuation approach applied to a project in the Boeing Corporation (Datar & Mathews, 2007).

In order to calculate the ROV a process is needed to create an expected payoff distribution. To achieve this models like Black-Scholes (Black & Scholes, 1973) utilise stochastic processes while the binomial approach (Cox, Ross & Rubinstein, 1979) uses binomial processes. However, some experts argue that it is not in line with the reality of real investments to use stochastic processes, because managerial actions can affect the value, hence the value is not just random (Kinnunen, 2010, p.12).

The Datar-Mathews method uses a three-way cash flow scenario forecast, i.e. with a bad case, a base case and a good case, as the basis for the real option valuation. The method uses an expected probability distribution found by a Monte Carlo simulation. Mezei, Collan and Fullér
instead use the fuzzy pay-off method to create a *possibility* distribution by rearranging the forecasted cash flows. The cash flows are rearranged to depict every possible outcome of the project and hence become a fuzzy cash flow. To portrait the most extreme positive outcome (the good case for the fuzzy cash flow) the lowest possible costs are deducted from the highest possible revenue. And vice versa for the most extreme negative outcome (the bad case for the fuzzy cash flow). The base case from the original cash flow forecast represents the base case of the fuzzy cash flow. By performing this rearrangement of the cash flows the possibility distribution is created and becomes a triangular fuzzy number (also referred to as the fuzzy NPV), which the real option value can be calculated from.

In the calculation of the ROV the value can be found by weighing the positive values (NPV > 0) by their expected probability. For the negative outcomes (NPV < 0) NPV is set to zero (NPV < 0 → NPV = 0), as the managerial flexibility allows the management to terminate projects with a projected negative NPV and thus avoid further investment in a non-profitable project.

Mezei, Collan and Fullér present the following formula to calculate the ROV,

\[
ROV = \frac{\int_{0}^{\infty} A(x)dx}{\int_{-\infty}^{\infty} A(x)dx} \times E(A_+) \quad (4.4)
\]

The ROV is found by calculating the area of the positive side divided by the entire area of the triangle and then multiplied by the possibilistic (fuzzy) mean value of the positive side of the fuzzy distribution.

The relationship between the areas can easily be calculated by simple integral calculus but the calculation of the fuzzy mean value of the positive side needs further derivation which is presented next.

Carlsson and Fullér derived the general formula for calculation of the possibilistic mean value (4.1). Collan, Mezei and Fullér were able to derive four additional formulas for the calculation of the E(A_+) from (4.1), due to different cut-off points (Collan, Mezei and Fullér (1), 2009, p. 7). The cut-off levels determine if a, α, β is above or below zero, respectively. The four different cases are presented below (Collan, Mezei and Fullér (2), 2009, p. 7).
First case is where the whole fuzzy distribution is above zero, when $0 < (a - \alpha)$. The mean value of the positive area can then be calculated as shown in equation 4.5.

$$E(A_+) = a + \frac{\beta - \alpha}{6} \quad (4.5)$$

Second case is where the fuzzy distribution is partly above zero, which means that $a$ is above zero but $(a - \alpha)$ is below zero; $(a - \alpha < 0 < a)$, which resembles the situation that is shown in figure 4.1. The mean value of the positive area can then be calculated as shown in equation 4.6.

$$E(A_+) = a + \frac{\beta - \alpha}{6} + \frac{(\alpha - a)^3}{6\alpha^2} \quad (4.6)$$

Third case is where fuzzy distribution is partly above zero, but with the centre, $a$, below zero but $a + \beta$ still above zero; $(a < 0 < a + \beta)$. The mean value of the positive area can then be calculated as shown in equation 4.7.

$$E(A_+) = \frac{(a + \beta)^3}{6\beta^2} \quad (4.7)$$

Fourth case is when the whole fuzzy distribution is below zero. The mean value of the positive area can then be calculated as shown in equation 4.8.

$$E(A_+) = 0 \quad (4.8)$$

In order to ensure a better understanding of triangular fuzzy numbers a small illustrative example with the fuzzy pay-off method have been created in order to aid the understanding of how we create the triangular fuzzy number and how we calculate the ROV which is shown in appendix 6.

The shape of the triangular fuzzy number made it ideal dealing with the standard three-way cash flow scenario analysis but in other cases a different cash flow scenario set-up could be experienced. For instance we could image a situation where it would be difficult to estimate the base case expressed as a single value. Instead we could consider expressing the estimates in an interval. Such a situation is just what the use of fuzzy trapezoidal numbers in valuations purposes can help with (Carlsson & Fullér, 2000, p. 70) as demonstrated by Ucal and Kahraman (Ucal &
Kahraman, 2009). Although based on many of the same assumptions as the triangular fuzzy number it lacks in aiding to the mental understanding of the possible future strategic and operational decision-making. Also it is based on a cash flow forecast type which none of the participants in our survey used, why we will focus on the application of triangular fuzzy numbers. Hence a thorough examination of fuzzy trapezoidal number’s applicability to perform a real options valuation is presented along with a numerical example in appendix 7.

4.2 Fuzzy binomial valuation approach

The fuzzy approach to binomial real option valuation was presented by Liao and Ho (Liao & Ho, 2010). Fuzzy theory makes it possible to capture the right-skewed possibility distribution that characterizes the value of a real option as it retains the larger upside potential of profit but limit the downside risk. The fuzzy binomial valuation approach adopts the concept of the expanded NPV discussed in section 3.1. The NPVs are estimated by the use of fuzzy numbers, thus the expanded NPV will be called the fuzzy expanded NPV (hereafter referred to as FENPV).

As presented in section 3.1.4.3.2 the value of an option is calculated on the basis of the development in the underlying asset as presented by Liao and Ho below (Liao & Ho, 2010, p.2127)

\[
C_0 = \frac{1}{(1 + r)} \times [P_u C_{1u} + P_d C_{1d}] \tag{4.9}
\]

, where \( r \) is the risk-free interest rate and the value of the option is determined by the value in the preceding time periods and the risk-neutral probabilities presented below (Liao & Ho, 2010, p.2127)

\[
P_u = \frac{(1 + r) - d}{(u - d)} \quad \text{and} \quad P_d = \frac{u - (1 + r)}{(u - d)}, \text{or just } 1 - P_u \tag{4.10}
\]

From the equations above we see that the main factors which affect the option value are the jumping factors \( u \) and \( d \). However these two factors are very hard to estimate precisely due to the complexity of their nature. As discussed in part 1 estimates in an uncertain environment are often based on the knowledge of experts. While not being random the estimates are based on often vague information and will thus present a vague result in the end. The use of fuzzy numbers is
precisely aimed at situations like this where the information is vague and imprecise as fuzzy numbers are superior in handling uncertain estimates. Hence the theory behind possibilistic distributions is preferred over the traditional probabilistic distributions and thus the application of triangular fuzzy numbers discussed in section 4.1.

A fuzzy approach implies that the jumping factors must be fuzzified to represent triangular fuzzy numbers, denoted respectively \( u' = [u_1, u_2, u_3] \) and \( d' = [d_1, d_2, d_3] \), hence creating a three-point possibility distribution at the end of each node in the fuzzy binomial tree depicting the development of the value of the underlying asset. In the traditional binomial tree method the jumping factors are calculated based on the volatility as presented in equation 3.1 and equation 3.2. Hence in order to fuzzify the jumping factors the volatility must be fuzzified to emerge as a triangular fuzzy number. This is done by estimating a coefficient of variation (hereafter referred to as CV) on the volatility estimate to represent the possibility distribution of the volatility (Liao & Ho, 2010, p.2129). Based on the fuzzy volatility the fuzzy jumping factors can be determined as shown below in equation 4.11 and equation 4.12

\[
\begin{align*}
u' &= [u_1, u_2, u_3] = \left[ e((1-CV)*\sigma)\sqrt{T}, e(\sigma*\sqrt{T}), e((1+CV)*\sigma)\sqrt{T} \right] \quad (4.11) \\
d' &= [d_1, d_2, d_3] = \left[ \frac{1}{u_1'}, \frac{1}{u_2'}, \frac{1}{u_3'} \right] \quad (4.12)
\end{align*}
\]

In practice the fuzzy binomial valuation is done by creating three binomial trees, where the best case tree is created by the use of the highest up-factor \( u_3 \) and the corresponding down-factor \( d_3 \). Vice versa the worst case tree is created by the use of the lowest up-factor \( u_1 \) and the corresponding down-factor \( d_1 \). Due to the right-skewed distribution it is the up-factor that creates most value as the down-factor revert the value towards zero. The base case is the same as the classic binomial tree presented in section 3.1.4.3.2. The combination of these trees creates the possibility distribution and hence a fuzzy number at each node.

To calculate the option value of the fuzzy binomial trees, the risk-neutral probabilities equation from (4.10) can be rewritten as (Liao & Ho, 2010, p.2128)

\[
\begin{align*}
P_{ui} &= \frac{(1 + r) - d_i}{(u_i - d_i)} \quad \text{and} \quad P_{di} = \frac{u_i - (1 + r)}{(u_i - d_i)}, \text{or just } 1 - P_{ui}, \text{for } i = 1, 2, 3 \quad (4.13)
\end{align*}
\]
We now end up with a new, hence very similar, expression for the pricing formula for the option (Liao & Ho, 2010, p.2128).

\[ C_0' = \frac{1}{1 + r} \times [P_d' C_{1d}' + P_u' C_{1u}'] \]  

(4.14)

It is important to notice that the option values \( C_{1d}' \) and \( C_{1u}' \) now are fuzzy numbers as a result of the jumping factors being fuzzified. As discussed in section 3.1.4.3.2 the fuzzy binomial option tree is solved by backward induction of the fuzzy numbers at each node.

The value of managerial flexibility is also discussed by Yeo and Qiu (Yeo & Qui, 2003). Their work introduces the use of an asymmetric distribution as they argue that the pay-off distribution is often skewed to the right to integrate the enhanced upside possibilities that normally exist when valuing uncertain projects. The right-skewness of a project outcome as a triangular fuzzy number is illustrated below in figure 4.3.

![Figure 4.3: Source: Liao & Ho, 2010](image_url)

The assumption that the pay-off distribution is always skewed to the right alters the way to compute the mean value of a fuzzy number. Accepting this assumption makes the work presented earlier on possibilistic mean values (Carlsson & Fullér, 2003) inadequate in this case, why a new method for computing the mean value of a fuzzy number that is characterized by a right-skewness is presented (Liao and Ho, 2010, p. 2129).

Let \( C' = [c_1(\alpha), c_3(\alpha)] \) be a fuzzy number and \( \lambda \in [0,1] \), then the crisp mean value of \( C' \) is defined as
\[ E(C^\prime) = \int_0^1 [(1 - \lambda)c_1(\alpha) + \lambda c_3(\alpha)]d\alpha \quad (4.15) \]

where \( \lambda \) denotes the pessimistic-optimistic weighted index original introduced by Yoshida, Yasuda, Nakagami and Kurano (Yoshida, Yasuda, Nakagami & Kurano, 2006) and further developed by Liao and Ho to be defined by the following formula (Liao and Ho, 2010, p. 2129)

\[ \lambda = \frac{AR}{AL + AR} \quad (4.16) \]

where \( AR \) and \( AL \) are the areas shown in figure 4.3.

Thus, when \( \lambda \) is determined, we substitute the expression into (4.15) and end up with the final formula for the FENPV.

\[ E(FENPV) = \frac{(1-\lambda)c_1 + c_2 + \lambda c_3}{2} \quad (4.17) \]
Part 4 – Settings for a valuation

In part 4 we discuss the context and the different input variables that enable us to conduct our valuations with real life data. It is important to recognise that it does not matter how good and sophisticated a financial model is if the quality of the input variables is vague. Consequently inputs of low quality will result in an output of low quality.

5 Case presentation

In order to test the fuzzy payoff method for real options valuation on a business case, we have created a simulated drug development project which resembles reality as much as possible. Instead of taking a real life business case from a real company we have chosen this solution to maintain focus on the fuzzy approach to real options valuation. An investigation of a real life drug development project would result in very imprecise estimates of the different input variables unless we had a high degree of insider knowledge in the given company.

We will conduct a valuation of a central nerve system (referred to as CNS) R&D project. The CNS is the largest part of the nervous system and consists of the brain and the spinal cord. It coordinates movement and processes the input of the senses. As it plays such a vital role in the health and behaviour of a person, diseases in CNS are often critical why CNS is one of the most heavily researched areas in the biotech industry. In Denmark large companies like Lundbeck and Neurosearch have huge research programmes in this therapeutic area.

5.1 Contextual analysis

The contextual analysis focuses on the settings for drug developing companies in the pharmaceutical industry and especially the biotech companies. The macro environment will be analysed by a PEST-analysis to identify the impact of the surroundings on the industry and, next, the competitive environment will be analysed through Porter’s Five Forces model.

With no particular company to focus on we will investigate the main trends and factors that have an impact on the capital budgeting process.
5.1.1 PEST

5.1.1.1 Political factors

The well-being of the health care industry is a vital area for politicians as it is of great importance for the voters. To sustain a well functioning health care system they need to provide good business conditions for companies operating in the health care industry. The political and legislative environment that the industry is facing varies with the specific therapeutic market (Danzon, 1997, p.302-303).

The European market is highly regulated due to the comprehensive health care programs that governments provide for their citizens in most European countries. Consequently regulations and thereby the competitive environment are individual to each country depending on how involved the public health care system is in the pricing of drugs. Appendix 8 shows the significant variation in costs paid by patients across Europe (EFPIA, 2011, p.25). It is a good proxy for the degree of pricing power of the companies as a small patient payment ratio equals low pricing power because the government being the main buyer of drugs is able to negotiate a lower price.

Due to the highly varying costs between the European countries located in a small geographic area there are increasing problems with parallel trade. Products bought in low-wage countries at a low price are being imported to high-wage countries where the same product is sold at a higher price. This undermines the companies’ inclination to sell their products cheaper in low-wage countries as they as a consequence of the parallel import will earn less in the high-wage countries (Grabowski, 2002, p.857). The parallel trade does not only hurt the companies’ profits but also diminishes the R&D expenditures which in the end will lead to fewer new products and thus a lower social welfare level (EFPIA, 2011, p.4). The threat of parallel trade must be taken into consideration when choosing the price level across countries.

A more independent administration of the business environment is being worked on to which the creation of the EMEA and the EFPIA (The European Federation of Pharmaceutical Industries and Associations) testifies. One of the major goals is to introduce uniform pricing across borders in Europe due to the growing problems with parallel trade (EFPIA, 2011, p.4). As an add-on effect to getting rid of the illegal parallel trade it will lead to a much more transparent capital budgeting process for the companies in the industry as sales will be easier to forecast.
In the USA, the FDA works as the regulatory agency approving or disapproving aspiring drugs. Once a product has been proved eligible for the public there is much less regulation about the pricing as the health care facilities are largely owned and operated by the private sector. Without a central health insurance plan the market is much more deregulated, which means that the companies who compete in an area protected by patents and with few competitors are able to set a higher unit price than it is possible in Europe. This makes the American market very attractive as a low competitive intensity can lead to abnormal earnings. An evidence of the American market’s attractiveness is the amount of drugs under development in the USA. In appendix 9 it can be seen that many more drugs are being developed in the USA than in the rest of the world (PhRMA, 2011, p.14). Patient organizations such as the Public Citizen Health Research Group fight for more regulation and thereby lower prices to secure access to the medicine for a larger group of people. On the other hand, the industry association PhRMA (Pharmaceutical Research and Manufacturers of America) works for maintaining the high degree of pricing power with the companies and keeping a transparent business environment.

With the many health care reforms being introduced around the world as well as the growing market share of generics further discussed in section 5.1.2.1, it seems that the patient organisation are prevailing at the moment.

Patents can be seen as the foundation of the industry. Without the possibility of obtaining patents a lot of R&D into medicaments would never have occurred as it would not be economically feasible to develop them. Generic products will enter the market as soon as newly developed products are launched, but at a lower cost as there are no R&D costs to sustain. This will make it impossible to cover the costs related to the lengthy development process for the developing companies. So patents protect and provide the basis for ongoing R&D, which is beneficiary for both the developing companies and social welfare in general.

A patent is normally valid for twenty years after grant. This gives a product around eight years on the market as seen in section 2.1.3 before generic versions enter the market and create a close to perfect competition scenario (Berndt, 2002, p.63). If the authorities delay the approval process, it is possible to get up to five years’ extension on the patent (Bhat, 2005, p.114).

16 http://www.phrma.org/about/phrma
To secure the economic attraction of developing drugs against rare diseases with a small end market, an orphan designation can be granted in both Europe and the USA. To obtain orphan drug status there must be less than 200,000 potential patients. Obtaining this status gives economic benefits such as a guaranteed seven years of exclusivity on the market after approval and a 50 percent tax discount on certain development costs (Bergeron & Chan, 2004, p.62). This enhances social welfare as it brings more diverse medicine to the market. Also working in this direction is the US Modernization Act of 1997, which secures a shortened approval time for drugs against life threatening diseases and has the potential to fulfil the unmet need for this medicine (Food and Drug Administration Modernization Act of 1997, 1997, p.14).

Whilst these initiatives have been to the advantage of the developing companies and thus PhRMA, there have also been initiatives to the benefit of the patients. The Hatch-Waxman Act of 1984 gives generic producers the right to investigate and copy drugs still under patent in order to get approval by FDA as soon as the patent expires and thus market their generic product as fast as possible (Grabowski and Vernon, 1986, p.195). This ensures lower prices for the patients at the exact time of patent expiry.

The regulatory setting must be taken into account in the capital budgeting process as it can have a huge impact on potential sales in the different markets. The opposing forces of industry associations and patient organizations will have an influence on the future market potential.

5.1.1.2 Economic factors
The state of the economy matters less for the pharmaceutical industry than for many other industries due to its defensive characteristics. People need their medicine or need new medicine no matter if the economy is booming or in recession. So there is no need to forecast business cycles as they are not only very difficult to predict but also have a neglected influence on sales of essential medicine. But an economic downturn does affect the pharmaceutical industry for non-essential medicine. Market growth will decline in most industrialized countries which will lead to cost-cutting in the companies and maybe dismissal of future development projects (EFPIA, 2011, p.3). This jeopardises the stability and predictability needed by the companies to conduct thorough research.

17 http://www.fda.gov/forindustry/developingproductsforrarediseasesconditions/default.htm
For biotech companies it may have a larger effect as they can be very dependent on venture capital which can be difficult to raise in an economic slump.

The economic development and welfare of a country has a severe impact on how much it spends on medicine. As shown in appendix 10 a higher percentage of GDP is spent on health care as the countries get more developed (EFPIA, 2011, p.22). Accordingly the fast economic development in many large countries in Asia and Latin America provides new opportunities as they will need medicine on a much larger scale than what we see today, where Asia (excluding Japan) and Latin America represent less than 15% of world sales (EFPIA, 2011, p.17). But also the already developed countries will experience an increasing share of GDP devoted to health care which of course is beneficiary for the biotech industry (Scherer, 2007, p.268).

For drug developing companies the growing future size and number of markets will make the sales potential of drug development projects initiated today larger than what historical data would predict.

### 5.1.1.3 Sociological

The demography of the developed world is changing. Table 5.1 and appendix 11 show that in the developed world an increasing part of the population in the coming decades will be above 65. Today the largest part of the sales lies in such countries, which is documented in appendix 12 that shows that Europe, USA and Japan represent more than 80% of sales. These markets will increase substantially as the need for medicine is somewhat proportional with the age of the population. Especially the large markets in Japan and Germany with around 30% of the population above 65 in 2030 will see a boom in the need for medicine.

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*Table 5.1: Own Construction. Source: EFPIA, 2011, p.28*

The change towards an unhealthier lifestyle which has taken place during the last 20-30 years will have a big impact on the need for medicine. It has led to more people being overweight and obese. In the wake of this follows a series of lifestyle diseases such as diabetes and cardio-
vascular diseases. This can be seen in appendix 13 which shows an alarmingly accelerating trend in obesity and diabetes diagnosed adults in the USA. Also in the less developed but fast developing China this trend is evident. The aging population combined with a high degree of urbanization and a more westernized lifestyle will increase the number of people with lifestyle diseases, which can be seen in appendix 14, appendix 15 and appendix 16.

The increasing market size is obviously favourable for the companies in the industry as they can look forward to increased sales potential.

5.1.1.4 Technological

R&D is at the heart of the pharmaceutical and biotech industry, and it is no surprise that it by far has the largest R&D to sales ratio, which can be seen in figure 5.1.

![Figure 5.1: Source: EFPIA, 2010, p.1](image)

To be a part of the future winners in the industry it is essential to invest profoundly in the technological side of the business. Especially when taking into account the rapid growth in the markets and research environments in emerging markets. This has already led to a large migration of economic and research activities to these fast-growing markets (EFPIA, 2011, p.3).

The cost of R&D has gone up lately as the scientific complexity has increased and the clinical trials are getting bigger due to the stricter requirements of the regulative authorities (EFPIA, 2011, p.1). These trends will probably increase the cost of developing drugs in the future.
5.1.2 Porter’s Five Forces

5.1.2.1 Substitutes

During the patented period there are no substitutes with the exact same traits because that is legally prohibited. However it is possible for competitors to develop a slightly different drug aiming at the same therapeutic area, called a me-too drug (Kumar, 2008). This will obviously have a big impact on sales if the drug is competitive. But it is difficult to forecast the competitiveness in a specific therapeutic area as the competition will only materialize upon approval. Thus a large number of compounds under development targeting a specific therapeutic area do not necessarily imply that there will be intense competition and thus reduced profit margins as the competitors can fail before they reach the market.

When the patented period expires, the generic products enter the market. They are highly substitutable as they are legal copies of existing products. Anyone with the right facilities can produce and launch generic products on the day the original patent expires, due to the consequences of the Hatch-Waxman Act as examined in the PEST-analysis above (Grabowski, 2002, p.852). The stream of new competitors will quickly lower prices and intensifies the competition which will lead to a perfect-competition scenario with little or no excess profit for the companies.

The competition from generic products has the biggest impact in the USA where pricing is less regulated. Sales of generic products went up from 49% of prescriptions in 2000 to 74% in 2009 (PhRMA, 2011, p.18). In the more regulated Europe it has proved harder for generic products to penetrate the markets with the same magnitude as in the USA. Appendix 17 shows that particularly in Western Europe generic products have a low percentage of total sales.

Generic competition is less decisive when it comes to drugs against life threatening diseases. The switching costs are often too high as the patient has built a loyalty-band with the brand that keeps the patient alive. They trust the product and are very reluctant to switch despite lower-priced products being available. For less dangerous diseases the switching costs are much lower and more people will seek toward the generic products.

To avoid generic competition the holder of the patent can further develop and enhance the patented product to a degree where a new patent can be granted. This will ensure that generic
competitors can only compete with the existing product which probably will be inferior to a new and improved product. An example of this is Novo Nordisk’s development of their insulin products from an injection product to an oral tablet-based product. This underlines the need for constant development on both new and existing products in the industry.

5.1.2.2  Supplier bargaining power
Biotech companies are in general not facing a lot of supplier bargaining power. Most input materials such as research facilities and raw materials to manufacture drugs are uniformly priced as there are many suppliers. However, in some cases where a highly sophisticated and rare material is essential for the drug, the supplier holds a considerable bargaining power.

5.1.2.3  Customer bargaining power
The end-users of the drugs are often not the same as the ones who choose and pay for the drugs upfront. This is often large organizations such as governments or health insurance plans but it can also be associations of private hospitals who can achieve better prices by joining together. Being a large buyer gives significant bargaining power which is particularly visible in the large European economies with comprehensive public health care systems. But this is only the case if supplementary products targeting the same disease area exist. Hence unique products can be priced much higher no matter who the buyer is.

Smaller private hospitals and practices are forced to take the prices offered by the companies.

5.1.2.4  Entry/exit barriers
Patent protection is a very large entry barrier. Although it does not grant exclusivity on a market as other products can target the same therapeutic area, it guarantees that a product is not copied and sold at lower price. This entry barrier disappears at patent expiry.

The economies of scale also function as an effective entry barrier. A lot of capital is needed for conducting extensive research and subsequently to support sales where the lack of distribution channels can be very expensive for a biotech company. This can be illustrated by the latest restructuring by biotech company Neurosearch, which has put more focus on optimizing the commercialization process, which implies cost-cutting elsewhere in the organization including
R&D\textsuperscript{18}. They do this to support the expected launch of their lead product Huntextil, which has meant scaling down all other activities. Bigger pharmaceuticals can utilize the existing sales force and production facilities when launching new products, as Novo Nordisk intend to do with their obesity treatment, Victoza (Novod (2), 2011, p.60).

The many partnerships and licensing deals being made in the late stages between pharmaceutical and biotech companies such as the newly agreed research collaboration between Lundbeck and Genmab are further evidence of the great significance of economies of scale\textsuperscript{19}.

5.1.2.5 Industry competitiveness

The intensity of competition is highly dependent on the specific therapeutic area. The number of drugs under development targeting that area can be used as a proxy for the future competitiveness.

But for all therapeutic areas the important thing is the timing of the product launch. Reaching a market with an unmet need first creates substantial profit potential. There is a very significant first-mover advantage because patients quickly establish brand loyalty as it increases their life quality considerably.

In times of economic crisis it is very difficult for biotech companies to raise new capital as the competition for the very limited venture capital resources is extreme as discussed in section 2.1.5. With a great many resources being allocated towards raising the essential capital, some of the resources spent on R&D have to be sacrificed. However as there for some time have been a drought in new drugs launched from big pharmaceuticals they will to a higher degree need partnerships with biotech companies which could improve the funding possibilities in the future (Czerepak & Ryser, 2008, p.198).

The competitiveness is largest in the USA which can be seen by their dominating share of compounds under development in appendix 9. The more liberal market creates possibilities for larger earnings than does a more regulated market.

In the CNS area the level of competitiveness is decreasing as many large pharmaceutical companies such as GlaxoSmithKline and AstraZeneca have left the scene recently due to the


\textsuperscript{19} http://www.lundbeck.com/investor/releases/ReleaseDetails/Release_1451485_EN.asp
high risk involved. This increases the market potential for the remaining dedicated players (Novod (3), 2011, p.2).

Porter’s Five Forces

5.2 Framework

5.2.1 Uncertainty

Throughout the thesis we have emphasized that the biotech industry is very risky business and its context very uncertain. The factors that make this industry so uncertain are traditionally divided in two different areas, technology and market.

The technological uncertainty concerns all the issues relating to the development of the drug. In other words it is the uncertainty of getting the drug through the different phases to final approval. This uncertainty relates to the work done by the scientists as well as to the limitations of the current level of technology development.

The fact that it is the scientists who “define” the technology uncertainty also increases the complexity for the project manager, who might experience problems with post-controlling these estimates and opinions provided by the scientists. Also the fact that it is the scientists who have
in-depth knowledge about the drug development adds to the uncertainty. Issues relating to this will be discussed in section 5.2.3.

The other uncertainty concerns the market, also known as the commercial uncertainty, which relates to the estimation of market values such as sales prognoses, price levels and so on. Several issues arise when dealing with a product’s prospects before it is fully developed. An important issue is the estimation of the size of the patient group and hence the sales potential. Normally it is possible to get a pretty good estimate of this from just knowing how many people are affected by the disease in question. But this is only the case in the developed markets where these data are collected and made available, whereas in the emerging markets where this is not the case, it is very difficult to estimate the sales potential. Other issues include difficulties relating to estimating the price under national regulations, which distribution channels to use and uncertainty about patients’ willingness to substitute their present medication with a new one as discussed in section 5.1.2.1.

It could be argued that there is no reason to concentrate so much on the market risk as it will never be of any importance if the product is not approved. But it is always necessary to have a financial overview of the project to avoid proceeding with a project that is not a good investment even if marketed as one third of projects are cancelled due to economic reasons as seen in figure 5.3.

Our survey in section 2.2.3 showed that in some cases the financial valuation was initialized in phase I or II instead of the beginning of the project. This is due to the very high uncertainty relating to the market potential, which may change very quickly. An example of this is the recently passed health care reform in the USA which greatly influences the market potential as a subsequent 5% decline in the stock prices for the health care sector companies’ on the day it was released witnesses (Kelly & Teufel, 2011, p.115).

Consequently, projects showing a negative NPV in the initial phases could still be further developed as the project department might assess that the product has a very good chance of getting approved and can evolve in a positive direction. Additionally, the area of research could be of special importance for later reference, and therefore an initially negative NPV of a project is not that important. This means that the most important uncertainty is the technology, which most often is the reason for termination of a project as seen in figure 5.3.
The uncertainty in a real option framework is estimated as the volatility of the underlying asset. This can be measured in several ways, which all have flaws and cannot be characterized as industry standard methods. As it is not within the scope of this thesis to estimate an exact value of a project we will not discuss the benefits and drawbacks of different volatility estimation methods further.

As mentioned in section 3.1.1 a higher uncertainty yields a higher value from real option analysis. However this is not entirely true as the uncertainty works as a double-edged sword. The higher uncertainty should lead to a higher cost of capital which would diminish the value of the underlying asset on which the real option analysis is performed. So a higher uncertainty decreases the starting value from the DCF but increases the value creation henceforth by the real options (Arnold & Crack, 2004, p.81).

### 5.2.2 Cost of capital

A common misperception is that drug development companies should be viewed as risky investments due to the high risk rooted in each single project’s ability to get successfully through the development phases. And from looking at the often high failure rates discussed in section 2.1.4 it is easy to believe this and discount projects with a higher discount rate. However, the risk associated with a specific project or company is diversifiable and according to financial theory should not be accounted for in the cost of capital (Ross, Westerfield & Jordan, 2006, p.408). The reason is that an investor can hold a number of different projects or companies in his portfolio and the asset-specific risks should in theory cancel each other out. Hence an investor should not be paid for taking unsystematic risk.

In this thesis we use the opportunity cost of capital as the discount factor when discounting the cash flows. We use two different costs of capital, one relating to the R&D costs and another relating to the expected revenue of the project to obtain results that are more theoretically correct. With the use of two different costs of capital it becomes possible to deal more accurately with the specific risks when discounting different kind of cash flows.

In terms of the R&D costs of a specific project continual investments have to be made throughout its entire development process. The cash flows of these costs have a relatively low risk as they will only occur if there are good prospects of a successful market launch. They are
actively managed by the management and therefore have a relatively low risk. With the cash flows relating to the R&D costs being known and secure they should be discounted with a rate reflecting such cash flows. We argue for the use of the risk free interest rate, which we will determine in section 6.1.1.

When discounting the expected revenue we use another cost of capital. For practical reasons the company’s WACC is chosen (Brandão & Dyer, 2005, p.23). The WACC resembles the rate of return that the company needs in order to give the owners their required return subject to the embedded risk. The operating cash flows are subject to market risk and these cash flows should therefore be adjusted by an appropriate discount rate that incorporates the same risks as the WACC does.

Using the WACC implies the use of the CAPM-model as mentioned in section 1.4.2. Hence a number of assumptions are accepted that are fundamental to the model such as government bonds being risk-free and lending and borrowing at the same interest rate. These assumptions are not completely fulfilled as no government bonds are 100% risk-free and borrowing rates are typically higher than lending rates (Brealey, Myers & Allen, 2006, p.197). Many assumptions of this model are questionable but as there are few alternatives, we intend to use the model bearing in mind the above-mentioned.

As discussed in section 2.1.5 biotech companies generally have the same capital structure, which is close to being 100% equity financed. It is clear that with such a capital structure the cost of equity has a significant influence on the value of the final WACC. This distinct capital structure makes the job of computing the WACC easier as a 100% equity ratio, which is used by most industry analyst20, implies that there is no need to estimate the return on debt as the debt ratio is 0.

The components used in the CAPM-model and consequently to estimate the WACC will be discussed and estimated in section 6.1.

As the WACC is a company-specific discount rate one could argue whether it is suitable to evaluate individual projects that might have another risk profile than that of the entire company.

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20 For instance Michael Novod on page 3 in his analysis of Bavarian Nordic A golden bird is getting ready to fly.
(Brandão & Dyer, 2005, p.23). Especially the estimation of the beta to compute the return on equity requires some discussion about the theoretical correctness of this application.

The classic approach to finding a beta is to do a peer analysis where peers with the same systematic risk characteristics are used to estimate the beta. However, it is practically impossible to find beta values for a single project as no or very few listed companies only have one project in their pipeline portfolio. So to be able to find a beta value we must relax our assumptions a bit and look at companies which resemble the characteristics (the systematic risk) of our project but are not exact matches. This restriction on the benchmarking material leads to the use of biotech companies with no or only little sales as the peer group. Including pharmaceuticals in the peer group would be incorrect as the production and sales activities would lower the beta of the company compared to higher beta R&D activities just as the more mature state of a pharmaceutical would imply a more debt-heavy capital structure.

To obtain an even more precise estimate of the beta we could choose to only look at biotech companies that research in the same therapeutic area as our project. Also the use of an equity index benchmark including the relevant sales regions could enhance the exactness of our beta estimate. However as the main focus is on the valuation methods and not on the value of the project, we will conduct a simpler estimation process of the beta which will be discussed in section 6.1.2.

From the discussion above it is clear that the WACC is not optimal for finding a discount rate as it will only be an approximation. But with hardly any alternatives we accept the error margin involved in using the company WACC for a single project. For internal decision makers in a biotech company the estimation of the cost of capital might be more accurate as they have access to more information than an external analyst.

The use of two different costs of capital is recommended by several authors dealing with the valuation of development projects. For instance this practice is applied by Datar and Mathews in their article *A Practical Method for Valuing Real Options: The Boeing Approach* (Datar & Mathews, 2007). They argue strongly for the use of two costs of capital. The somewhat same argumentation is seen in the work of Collan, Fullér and Mezei (Collan, Fullér & Mezei (1), 2009) who also make use of two different costs of capital.
5.2.3 Principal-agent problems

Before continuing with the estimation of the input variables the principal-agent problems that can arise in the capital budgeting process will be discussed. This is important, especially when this thesis is internally aimed, so as to make the persons involved understand the pitfalls associated with the principal-agent roles.

The agency theory originally concerned two different problems that can arise in principal-agent relations. The first problem arises when the agent and the principal have different goals with the work they are doing. It can be very difficult for the principal to make sure that the agent’s work is aligned with the interests of the principal, which creates the problem that the principal cannot verify that the agent has behaved appropriately. The second problem is risk sharing, which means that the principal and the agent have different attitudes towards the risks they take hence creating problems where they wish to make different choices (Eisenhardt, 1989, p.58).

One way of minimizing these problems is by making a contract between the principal and the agent. But the use of such a contract may give rise to additional issues as it is not always easy to monitor such contracts due to the basic assumptions about people, organizations and information (Eisenhardt, 1989, p.58). Eisenhardt argues that the issues of self-interest, goal conflict, bound rationality, asymmetric information and risk aversion may create problems in the principal-agent relationship. The consequences arising from these issues are also known as moral hazard and adverse selection (Eisenhardt, 1989, p.61).

The most obvious situation to create problems is when scientists estimate values for the capital budgeting of a project. When dealing with a drug development project it is likely that the scientists give estimates that are more optimistic than conservative, hence giving the project a more positive outcome. The reason for this lies in personal affiliation. Considering the perspectives of a scientist’s career, it is quite clear that the main goal for a scientist is to complete the project to have something to be remembered by (personal success) or have contributed something to society. With a project usually taking more than 10 years as shown in section 5.2.1, it only allows scientists to participate in a few projects during their entire career. This act of self interest from scientists creates an uncomfortable situation for the project manager (the principal who acts on behalf of the company and thus the investors) as he cannot be completely sure that the estimates given by the scientists are not too optimistic.
This situation is very likely to happen in the later development phases, when it is harder to get the project approved. For the reasons mentioned above the scientist will go very far in order to hold off a termination of the project, especially if the project is in phase II or III. On the other hand, the project manager has to consider terminating the project due to the issues arising in the process of getting the project approved and the corresponding increasing costs.

It is safe to assume that the scientist possesses expert knowledge about the development and thus the estimates compared to the project manager. This implies that the project manager will use the scientist’s estimates as he does not have the specific knowledge to question the estimates coming from the scientist. The scientist is aware of that and can use it for own good if the risk of termination increases. This could lead to moral hazard on the part of the scientist who might be giving overly optimistic estimates despite knowing otherwise. This is also described as asymmetric information, where the involved parts do not share the same level of information.

Our survey showed that more and more people in the project departments have a scientific background. This makes it possible for the project department to assess the estimates given by the scientists more thoroughly, which could limit the problems outlined above.

The principal–agent theory also exists externally at company level. The biotech companies are all stock corporations with investors behind them. It is safe to assume that the investors work from a profit maximization point of view, creating a pressure to receive a return in the future. Their goal might not be the same as the goal of the company, which could be more focused on developing drugs to enhance social welfare and less on developing profitable drugs.

In section 2.1.5 we discussed how the smaller biotech companies sometimes seek financial aid from the larger pharmaceuticals. Such interaction raises the same issues as analyzed above as there is a high degree of asymmetric information between the companies. It is very likely that the biotech company wants to release as little information as possible thereby causing a principal-agent problem. One has to remember that once a contract between two companies is terminated, the companies are again rivals in a very competitive industry.
5.3 Input variables

5.3.1 Phase lengths

The length of the different clinical phases depends on the therapeutic research area. With high uncertainties surrounding each specific project and its progression, it can be very difficult to estimate the precise time span for each phase in an explicit therapeutic research project. Two projects in the same therapeutic area can differ vastly in the time spent in the different phases due to the large amount of externalities that can affect the outcome of the project. That is also reflected in the many studies conducted on the length of the phases in biotech research projects. The majority of the studies have not grouped the different therapeutic areas together when summarizing the average phase lengths.

We will use the two recent studies to find an estimate of the time spent in each phase. Both studies are produced by people with a thorough understanding of the biotech industry and whose works are much cited.

The first study is from 2008 by Ralph Villiger and Boris Bogdan (Bogdan & Villiger, 2008), both partners in the Swiss consultancy Avance which is specialized in valuing biotech research projects. The second study is from 2007 by Joseph A. DiMasi and Henry G. Grabowski (DiMasi & Grabowski, 2007) who have both made several publications about various subjects related to valuing a drug development project. Their statistics are based on their article from 2003 together with Ronald W. Hansen (DiMasi, Grabowski & Hansen, 2003) where they looked at data for pharmaceutical drug developments projects from the 1980s and up until the article was published. The new article (DiMasi & Grabowski, 2007) includes data from Tufts Center for the Study of Drug Development and is focused specifically on biotech drug development, which makes it highly applicable for our case.

As both studies are heavily cited we feel comfortable using their estimates to forecast the lengths of the different phases for our CNS research project.

To estimate the time spent in each phase in our CNS research project, we have taken the average phase length from Bogdan & Villiger’s interval and compared it with DiMasi & Grabowski’s estimate to get the average time horizon for both studies.
As seen in table 5.2 the combined time for developing a drug is estimated to 142.5 months which is close to 12 years. This is in line with the consensus of the European Federation of Pharmaceutical Industries and Associations who estimates that it takes an average of 10-13 years to bring a drug from the initial research to the market\textsuperscript{21}.

### 5.3.2 Success rates

The chance of getting a product from the early lead optimisation stage all the way to a market launch is subject to high uncertainty due to the many factors affecting the development in each specific case. The reasons for abandoning a drug development project are shown in figure 5.3 (DiMasi, 2001, p.304).

![Reasons for abandoning R&D projects](image)

One third of the failures are for economic reasons which would be projects which suddenly turned out to have a negative NPV in the valuation model due to changed circumstances and

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therefore were cancelled. As mentioned in section 3.1.1 this number would have been smaller if more companies used a real options framework for valuing their drug development projects. In this framework more projects would go on to market launch as the massive upside potential would have a bigger impact in a real options valuation model than in the classic static DCF model.

The efficacy and safety failures are both technical reasons which are difficult to overcome as the drug and available technology is what it is. Unless the scientists can enhance the drug or develop new scientific research methods the technological failures are enduring.

Previous studies have shown that the success rates for the earliest phases in the drug development project are independent of the disease group. For the lead optimization, where medicinal chemists make a more thorough analysis of the primary leads and try to improve them, the success rate is 70%. For the preclinical testing, where the lead compound is tested on animals to investigate its safety profile, the success rate is 65% (Bogdan & Villiger 2008). We have combined these two phases and assigned a success rate of 67.5% for completing the lead optimization and preclinical phases.

For the rest of the duration of the drug development project, different success rates are assigned to each particular therapeutic group in accordance with the specific circumstances and characteristics surrounding each group. The following table compares a study of success rates in the industry by Kola and Landis (Kola & Landis, 2004) and DiMasi (DiMasi, 2001). Together with the industry-specific knowledge of Avance, gained by their long involvement in the biotech industry, Bogdan and Villiger have estimated the success rates for each phase in each therapeutic group which can be seen in table 5.3 (Bogdan & Villiger, 2008).
For CNS drug development projects the cumulative success rate, which is the chance of launching the product, is 9.8% before you enter the lead optimization phase. The cumulative success rate increases the later in the development process you assess it. A complete illustration of the cumulative success rates depending on which phase you are in can be seen in table 5.4.

Table 5.3: Own construction. Source: DiMasi & Grabowski, 2007, Kola & Landis, 2004 and Bogdan & Villiger, 2008

<table>
<thead>
<tr>
<th>Therapeutic Group</th>
<th>Lead Optimisation/Preclinical</th>
<th>Clinical Phase I</th>
<th>Clinical Phase II</th>
<th>Clinical Phase III</th>
<th>Approval</th>
<th>Cumulative Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthritis/Pain</td>
<td>67.5%</td>
<td>76.9%</td>
<td>38.1%</td>
<td>78.1%</td>
<td>89.1%</td>
<td>13.8%</td>
</tr>
<tr>
<td>CNS</td>
<td>67.5%</td>
<td>66.2%</td>
<td>45.6%</td>
<td>61.8%</td>
<td>77.9%</td>
<td>9.8%</td>
</tr>
<tr>
<td>CV</td>
<td>67.5%</td>
<td>62.7%</td>
<td>43.3%</td>
<td>76.3%</td>
<td>84.4%</td>
<td>11.8%</td>
</tr>
<tr>
<td>GIT</td>
<td>67.5%</td>
<td>66.8%</td>
<td>49.1%</td>
<td>71.0%</td>
<td>85.9%</td>
<td>13.5%</td>
</tr>
<tr>
<td>Immunology</td>
<td>67.5%</td>
<td>64.8%</td>
<td>44.6%</td>
<td>65.2%</td>
<td>81.6%</td>
<td>10.4%</td>
</tr>
<tr>
<td>Infections</td>
<td>67.5%</td>
<td>70.8%</td>
<td>51.2%</td>
<td>79.9%</td>
<td>96.9%</td>
<td>18.9%</td>
</tr>
<tr>
<td>Metabolism</td>
<td>67.5%</td>
<td>47.8%</td>
<td>52.0%</td>
<td>78.9%</td>
<td>92.8%</td>
<td>12.3%</td>
</tr>
<tr>
<td>Oncology</td>
<td>67.5%</td>
<td>64.4%</td>
<td>41.8%</td>
<td>65.4%</td>
<td>89.7%</td>
<td>10.7%</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>67.5%</td>
<td>66.0%</td>
<td>39.0%</td>
<td>64.0%</td>
<td>92.0%</td>
<td>10.2%</td>
</tr>
<tr>
<td>Respiratory</td>
<td>67.5%</td>
<td>63.4%</td>
<td>41.4%</td>
<td>59.9%</td>
<td>76.9%</td>
<td>8.2%</td>
</tr>
<tr>
<td>Urology</td>
<td>67.5%</td>
<td>50.0%</td>
<td>38.0%</td>
<td>67.0%</td>
<td>79.0%</td>
<td>6.8%</td>
</tr>
<tr>
<td>Women’s Health</td>
<td>67.5%</td>
<td>39.0%</td>
<td>42.0%</td>
<td>48.0%</td>
<td>59.0%</td>
<td>3.1%</td>
</tr>
</tbody>
</table>

Table 5.4: Own construction. Source: DiMasi & Grabowski, 2007, Kola & Landis, 2004 and Bogdan & Villiger, 2008

5.3.3 Costs

All development costs are very dependent on the size of the company as large pharmaceuticals spend much more in each phase than a small biotech company. So studies made on large pharmaceuticals as DiMasi et al. (2001, 2003, 2007) are not relevant for estimating the costs for smaller biotech companies. As a rule of thumb the drug development costs of a pharmaceutical is five times higher than that of a biotech (Bogdan & Villiger, 2008, p.15). We will use the costs estimated by Bogdan and Villiger as they are focused solely on the costs related to biotech companies and not on the costs related to the much bigger pharmaceuticals.

The development costs appreciate with the size and length of the clinical phase. Typical expenses in a phase are drug supplies, study design, project management and toxicology, which is the study of the adverse effects of chemicals on living organisms\(^{22}\).

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\(^{22}\) [http://www.toxicologysource.com/whatistoxicology.html](http://www.toxicologysource.com/whatistoxicology.html)
In table 5.5 the costs for each phase are summarized (Bogdan & Villiger, 2008, p.14-15). The early phases are characterized by highly variable costs as it depends highly on how fast you find promising compounds and how well they respond in the initial testing. When moving beyond the first two of the clinical phases, the development of the drug follows a more rigorous model with rather standardized procedures. The small sample groups needed for conducting the required trials facilitate keeping the costs in a narrow range. Phase III is the most expensive phase as it requires the largest sample group. How many subjects are needed for an individual project in phase III is highly dependent on the disease category. It can also be necessary to conduct more phase III studies if the first study does not live up to the regulatory requirements. This will of course escalate the costs, so the cost estimate for phase III is subject to some uncertainty.

<table>
<thead>
<tr>
<th>Phase</th>
<th>Estimated Cost (USD)</th>
<th>Average Cost (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead optimisation</td>
<td>0.5-6 million</td>
<td>2.5 million</td>
</tr>
<tr>
<td>Preclinical Phase</td>
<td>1-9 million</td>
<td>3 million</td>
</tr>
<tr>
<td>Clinical Phase I</td>
<td>4-5 million</td>
<td>4.5 million</td>
</tr>
<tr>
<td>Clinical Phase II</td>
<td>10-11 million</td>
<td>10.5 million</td>
</tr>
<tr>
<td>Clinical Phase III</td>
<td>30-60 million</td>
<td>45 million</td>
</tr>
<tr>
<td>Approval</td>
<td>2-4 million</td>
<td>3 million</td>
</tr>
</tbody>
</table>

Table 5.5: Own construction. Source: Bogdan & Villiger, 2008, p.14-15

It appears that the costs in the later phases are significantly higher than in the initial phases. This confirms what we saw in section 5.2.1 where we discussed how large companies were not fixed on a negative outcome early in the development phases but more on the realistic chance of getting the drug approved. So the larger companies are more willing to take calculated chances and accept minor financial losses in the earlier phases. This is not something we will find in small biotech companies as they do not have the possibility to take this kind of chances.

Our estimate for the production costs are based on the reported cost of sales for the pure-play CNS pharmaceutical company Lundbeck. As Lundbeck has activities throughout the value chain, including production and sales, it is suitable to use as a proxy for the production costs of our CNS project. The last 3 years (2010,2009 and 2008) Lundbeck reported production costs as a percentage of sales to be respectively 20%, 19.3% and 18.4% and thus approximately 20% on average (Lundbeck, 2011, p.63).
Due to the uncertainty regarding the costs there are several possible costs scenarios. A positive cost scenario could be if the drug went quickly through the phases thereby diminishing the cost spent on the trials. A more negative scenario could be if the clinical trials showed safety or efficacy problems and thus required additional testing in order to get approval. This would increase the costs substantially. Also higher input prices due to the growing demand for raw materials could result in higher costs than anticipated. To summarize we find it more likely that a negative cost scenario will occur as more factors suggest a negative development in costs.

After the drug is approved by the authorities a new cost-phase begins. The costs of this phase are predominantly marketing related and centred on the first couple of years following market launch. There are also costs related to an ongoing investigation and testing of the safety profile of the new drug. Post-approval out-of-pocket\(^\text{23}\) costs are estimated to 34.8% of pre-approval (R&D) out-of-pocket costs (DiMasi, Hansen & Grabowski, 2003, p.173).

**5.3.4 Sales**

It is very difficult to come up with a reliable estimate of the future sale in the early phases of the drug development process as it have to be estimated more than ten years ahead. With the uncertainty resolving with the progression of the project it becomes easier to predict future sales as information about competitors, market size, market evolvement and so becomes available. Due to this uncertainty we will base our sales forecast on historical sales numbers instead of making a detailed calculation with a bottom-up approach. The bottom-up method is more useful in the valuation occurring in the later stages when a lot of the information about the market has been revealed.

Potential sales differ vastly between disease categories. Drugs for diseases in the CNS lie in the upper sales tier with median sales of USD 422 million and average sales of USD 746 million (Bogdan & Villiger, 2008, p. 18-19). The reason for the average sales being much higher than the median sales is that they include the unlikely scenario of reaching a blockbuster. As this is so improbable we will not include the chance of creating a blockbuster in our base sales forecast. Instead we will use median sales as an estimate of what sales the drug can expect to reach during its life cycle in our base case forecast. Supportive of this conservative valuation forecast is the time of the valuation. In the earliest stages we have no indications whether the drug will show

\(^{23}\) Not discounted
any signs of blockbuster potential, so it will be too naïve to include it in the base sales forecast. Later on if the drug seems promising we can include the chance of hitting a blockbuster in our base sales forecast.

For the good case we use average sales numbers as we include the chance of reaching a blockbuster. Due to our findings in the contextual analysis we will add 50% to the average sales number in the good scenario. This is among other things due to the substantial market potential in many emerging economies and the higher share of elderly people in many markets with a higher need for medicine.

In the bad case scenario we will reduce the median sales by 33% to reflect the negative trends found in the contextual analysis such as the increased competition from generics, the possibility of reaching the market later than the competitors or a superior product outperforming and capturing the majority of the market. Also public health care reforms would lower sales as it would lower prices due to the increased customer bargaining power.

The probability of entering into a positive or negative sales scenario is very difficult to predict in the initial development phases. The future competitive scene is impossible to forecast as potential competitors will only reveal themselves in the later stages, which makes it impossible to know if there will be few or many competitors. Also the traits of the drug and thus the potential of being a blockbuster are not fully known in the initial phases. With so little information about the future being present at this time we will be conservative and allocate low possibilities to both a negative and positive sales scenario.

5.3.5 Volatility

The volatility can be understood as an indicator of the underlying asset’s uncertainty. For a drug this uncertainty is primarily influenced by the characteristics of the drugs and its position in the market.

We will use a volatility based on historical data rather than estimating it via advanced methods such as Monte Carlo simulations or logarithmic cash flow returns methods. Doing this would compromise the goal of simplicity for non-financial practitioners.
The uncertainty of the peak sales associated with the safety and efficacy of the drug is the most important component of the overall uncertainty (Bogdan & Villiger, 2008, p.89). As earlier discussed this is due to the potential inferiority or superiority of the drug compared to competitors which hugely impact the peak sales. The post-commercialization uncertainty is somewhat lower as the uncertainty relating to the clinical development is well explored (Bogdan & Villiger, 2008, p.89). After market launch the uncertainty relates to things such as national health care reforms or newly discovered side effects of competitors’ drugs.

Bogdan and Villiger argue for a volatility of 25-35% based on their studies. But when accounting for special factors such as first-in-line products, new market developments or extreme competition they finally arrive at a volatility in the range of 20-50% when assessing it in the initial phases. Banerjee argues that the volatility of R&D projects should be estimated to 35% based on several previous studies by reputable authors (Banerjee, 2003, p.69). Thus the volatility of the CNS project is set to 35%.
Part 5 – Case valuation

In this final part we capitalize on the findings in all the earlier parts. We conduct the final capital budgeting and test the fuzzy valuation approach on three different classic valuation methods ranging from simple to advanced thus making the theory applicable for practitioners with different levels of financial understanding.

6 Excel model

All the results obtained in the case valuation in part 5 can be found in the enclosed excel model. Here the cash flow forecast and the different calculations are showed to clarify any issues and if necessary to aid to the understanding of the different valuations.

6.1 Estimation of cost of capital

6.1.1 Risk-free rate

The risk-free rate is set to the rate of return on a government default-free bond. As discussed in section 5.2.2 government bonds are not completely risk-free but in a developed country it is the closest we get why we will use it in our estimation. As a project typically lasts for ten years or more it would seem reasonable to use a bond with a mid-to-long-term maturity to match the cash flows of the project. The use of longer time horizons is recommended by Damodaran (Damodaran, 2001, p.63) why we for simplicity will use the 10-year Danish Treasury bullet bond. According to the Danish Central Bank the effective rate of return for the 10-year Treasury bullet bond with a coupon rate of 4% is 2.98% as per 30 December 201024. However, this change constantly as factors such as supply and demand and credit risks play a role in determining the effective rate of return. As the expected development length is estimated to 12 years the risk-free rate should be somewhat higher as the interest rate theoretically appreciates when moving further out on the yield curve. Along with our expectation of a strengthening turnaround in the economy in the coming years, which will lead to higher interest rates, we will round up the risk-free rate to 3.5%.

24 http://nationalbanken.statistikbank.dk/nbf/139413
6.1.2 Beta
For estimating the beta we use the industry standard by comparing the beta of Nordic biotech companies. To get a wider and more representative sample group we will not only use Danish publicly traded companies but also their Nordic counterparts. As the fundamental conditions for operating a biotech company across the Nordic region are much the same, we see no problems in including them in our sample. The method of using the industry standard is also recommended by Damodaran (Damodaran, 2001, p.69-70).

To find the betas of the companies we have conducted a survey via Bloomberg which can be found in appendix 18. We have used weekly observations to avoid the volatility of day-to-day fluctuations in stock prices. Data have been collected for a five-year period to diminish the impact of the recent year’s extremely high volatility on the stock prices. The stocks are benchmarked against their relative indices which are the all-share indices of Copenhagen and Stockholm. The all-share indices are chosen over the more popular large cap indices (OMX C20 and OMX S30) as most biotech companies are in the mid-cap or small-cap segment. The average beta was found to be 0.91 which is in line with the findings of Kerins, Smith and Smith (Kerins, Smith & Smith, 2002, p.24), who found the average beta of the biotech industry to be 0.78.

As the beta measures the correlation with the market it is expected that the beta should be below 1 as a biotech company is typically less affected by the development of the economy as a whole. Being part of the health care sector a biotech company is often referred to as a defensive company because people will always need their medicine no matter the general health of the economy. Also, the beta does not include the risk of failure, which will be considered in the actual valuation.

6.1.3 Risk premium
The calculation of the CAPM uses the risk premium, which is a premium for the additional yield an investor can require when agreeing on an additional risk in connection with the investment. Historically several empirical studies have been conducted about the equity premium and this is the empiricism we will use in estimating our risk premium.

A survey from 2001, conducted by Claus Parum, CBS, includes risk premiums from 1925-1997(Parum, 1998). His conclusion was a risk premium for that period of 3%, which agrees with
the 3-4 % Elling and Sørensen argue for (Elling & Sørensen, 2005, p.52). Risager conducted a
survey of the Danish stock market from 1950-2004 and his findings suggest a risk premium of
4.2 % (Risager, 2005). Finally we have the study by Fama and French where they argue through
their thorough study of the S&P index from 1872-2000 that the risk premium should be equal to
4.32% (Fama & French, 2002).

Besides these historical studies we also use a more recent publication from an investment bank
that estimates the risk premium on equity markets (Granholm-Leth, 2011, p.33). An overview of
the estimated risk premiums for different countries can be seen in appendix 19, which shows that
the current risk premium is somewhat higher than the historical ones. As we are recovering from
a financial crisis and many investors are still risk averse25, we argue for a higher risk premium
than historically seen. With this in mind we estimate the risk premium at 5%, which allows us
able to calculate the return on equity as shown below.

\[ R_m = 3.5\% + 5\% = 8.5\% \]

6.1.4 WACC

In section 1.4.2 we listed the formula for calculation of the WACC. The input needed for the
calculation has been determined in the previous sections. As discussed in section 5.2.2 drug
development companies have a very high equity-to-debt-ratio, and the industry standard is to use
a capital structure of 100% equity in the WACC calculation when assessing biotech companies.

This unique capital structure makes the computation of the WACC simple, as the only value
needed is the estimation of the return on equity. The return on equity, \( R_E \), is found from the
CAPM showed in equation 1.3 and discussed in section 5.2.2. The calculation of \( R_E \) is shown
below

\[ R_e = 0.035 + 0.9(0.085 - 0.035) = 0.08 = 8\% \]

With the return on equity calculated the WACC can be computed.

\[ WACC = 8\% \times \frac{1}{1} + 0 = 8\% \]

6.2 **Cash flow forecast**

The following section outlines the different input variables we use in our cash flow forecast and our valuations. The complete forecast is pictured at the end of section 6.2.

All the development costs are discounted with the risk-free interest rate, while the revenue and the revenue-related costs are discounted with the WACC due to our findings in section 5.2.2. We have estimated the risk-free interest rate to be 3.5% as seen in section 6.1.1, while the WACC is 8% as found in section 6.1.4.

In contrast to the standard cash flow forecast procedure we will not give any value to the terminal period. As discussed in section 5.1.2 the competition from primarily generic products but also new improved products that enter the same therapeutic area will turn the competitive scene into more or less perfect competition after the patent has expired, so we estimate no cash flows after year twenty. It is a bit conservative as there will be some revenue due to the switching costs discussed in section 5.1.2.1. However the little cash flows that do occur are not in line with the generally large contribution of the terminal period to the NPV. Hence we will ignore the terminal period.

For each cash flow variable we have estimated three different scenarios in line with common practice in the industry. These different scenarios should reflect the uncertainty of the future. A bad case scenario is estimated to include the possibility that the cash flows turn out worse than estimated in the base case. If the cash flows on the other hand turn out to be better than anticipated a good case scenario is included for each cash flow variable.

All the numbers are denominated in US dollars.

6.2.1 **Time**

The cash flows of our CNS project are limited to the twenty-year period where the patent is valid. The patent is sought as soon as a compound shows promising attributes. This implies that the valuation should start in the lead optimisation phase. The length of the different phases is in accordance with our findings in section 5.3.1. As they do not match precisely with our subdivision of the time period in years, we have approximated the phase lengths to a best possible yearly basis. The length of each period can be seen in table 6.1. The lead optimisation
phase and the preclinical phase are merged into one phase due to the similarities regarding time span, success rates and on the cost side of the two phases as discussed in section 5.3.

### Table 6.1: Own construction

<table>
<thead>
<tr>
<th>Phase</th>
<th>Lead Optimisation/Preclinical phase</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Appr.</th>
<th>Market</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011e</td>
<td>2012e</td>
<td>2013e</td>
<td>2014e</td>
<td>2015e</td>
<td>2016e</td>
<td>2017e</td>
</tr>
<tr>
<td>2015e</td>
<td>2016e</td>
<td>2017e</td>
<td>2018e</td>
<td>2019e</td>
<td>2020e</td>
<td>2021e</td>
</tr>
<tr>
<td>2019e</td>
<td>2020e</td>
<td>2021e</td>
<td>2022e</td>
<td>2023e</td>
<td>2024e</td>
<td>2025e</td>
</tr>
<tr>
<td>2023e</td>
<td>2024e</td>
<td>2025e</td>
<td>2026e</td>
<td>2027e</td>
<td>2028e</td>
<td>2029e</td>
</tr>
<tr>
<td>2027e</td>
<td>2028e</td>
<td>2029e</td>
<td>2030e</td>
<td>2031e</td>
<td>2032e</td>
<td>2033e</td>
</tr>
</tbody>
</table>

#### 6.2.2 R&D costs

The R&D costs are estimated in line with our findings in section 5.3.3. For the bad case the costs are set to be the maximum possible in the range estimated. Vice versa the R&D costs for the good case are set to the lowest possible in the estimated range. For the base case we use the average cost from our analysis. The costs are outlined in table 6.2.

<table>
<thead>
<tr>
<th>Phase</th>
<th>USD million</th>
<th>Bad</th>
<th>Base</th>
<th>Good</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead Optimisation/Preclinical phase</td>
<td>15</td>
<td>5.5</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Clinical phase I</td>
<td>5</td>
<td>4.5</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Clinical phase II</td>
<td>11</td>
<td>10.5</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Clinical phase III</td>
<td>60</td>
<td>45</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Approval</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>95</td>
<td>68.5</td>
<td>47.5</td>
<td></td>
</tr>
</tbody>
</table>

Table 6.2: Own construction

There is a significant difference between the costs in the good case and the bad case, which implies that the cost scenario is an important value driver.

The costs are pro rata distributed to each year according to the duration of the specific phase (Kellogg & Charnes, 2000, p.78). This subdivision into years is shown in table 6.3

<table>
<thead>
<tr>
<th>Phase</th>
<th>USD million</th>
<th>Bad</th>
<th>Base</th>
<th>Good</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead Optimisation/Preclinical phase</td>
<td>3.8</td>
<td>3.8</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>Clinical phase I</td>
<td>2.5</td>
<td>2.5</td>
<td>5.5</td>
<td></td>
</tr>
<tr>
<td>Clinical phase II</td>
<td>2.3</td>
<td>2.3</td>
<td>5.3</td>
<td></td>
</tr>
<tr>
<td>Clinical phase III</td>
<td>3.3</td>
<td>3.3</td>
<td>5.3</td>
<td></td>
</tr>
<tr>
<td>Approval</td>
<td>3.3</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

Table 6.3: Own construction

Regarding the probabilities for the different scenarios we have assigned a higher probability for the bad case than the good case as there are more sources that can make the development process more expensive than anticipated. It could be higher input prices on the more sophisticated input materials due to scarcity and/or a rising demand. Trouble reaching satisfactory results in the clinical trials could also lead to prolonged phase lengths as the authorities would demand new trials. This will obviously lead to higher costs.
A more optimistic cost scenario would imply lower input prices and clinical trials with smaller sample groups and a swift execution of the trials.

As there is a substantially larger risk for ending up in a bad case scenario than a good case scenario due to the many things that can easily turn out more negative than anticipated we have assigned a probability of 30% for the bad case, 10% for the good case and 60% for the base case.

### 6.2.3 Sales

The peak sales capture the complete amount of sales throughout the drug’s life cycle. In section 5.3.4 we found that the base case peak sales for our CNS project are estimated to 422 million which is similar to the median sales found in previous studies. For the good case we use the average sales found in previous studies as a base number as it better includes the potential of blockbuster or near-blockbuster sales. On top of the average sales number of 746 million we add 50% to express the increasing market potential in the future as discussed in our contextual analyses in section 5.1. The peak sales in the good case can then be calculated to 1,119 million. The bad case sales are the median sales adjusted down by 33% to reflect the possible negative effects we discussed mainly in the Porter’s Five Forces analysis in section 5.1.2.

The distribution of the peak sales throughout the product life cycle has been made in accordance with the standard development in the industry as found in section 2.1.4, which can be seen in figure 6.1.

![Sales distribution in percentage](image)

**Figure 6.1: Own construction**

Sales reach the top during the patented period following the launch and penetration of the market in the initial three to four years. After a few years with maximum sales they begin to decline as the competition from new product launches increases. At the end of the patented period the generic products enter the marketplace and in line with our discussion in section 6.2, sales will come to an end. The complete peak sales forecast for the three scenarios can be seen in table 6.4.
Sales only start to materialize 12 years into the future and are thus subject to severe uncertainty. In light of that we have, conservatively, assigned only a 10% possibility for either ending up in the positive case or the negative case. Consequently we assign an 80% probability of reaching base case sales.

### 6.2.4 Production costs

Production costs are linked to sales and vary accordingly. In our project we estimate the production costs to be 20% of sales as found in section 5.3.3. As the production costs vary with the sales the scenario probabilities will be aligned with those of the sales. Due to required capital expenditures in the initial production phase to set up drug-specific production capacity we have set the percentage-of-sales to 25% in the first year of production.

In table 6.5 below the production costs are outlined according to the estimated peak sales.

### 6.2.5 Post-approval costs

The costs associated with the time period after the drug is launched cover primarily marketing-related costs and to a smaller extent a persistent safety profile testing. In section 5.3.3 we found that the post-approval costs are estimated to be approximately 35% of the pre-approval costs. The total pre-approval costs are calculated to be 74.4 million (not discounted) and thus the post-approval costs are 25.9\(^{26}\) million (not discounted).

The distribution of the post-approval costs throughout the sales period can be seen in figure 6.2.

---

\(^{26}\) 0.348 * 74.35 = 25.87
The highest part of the post-approval costs is spent in the first years of the sales period. In this period it is very important to create brand awareness among the potential patients/customers and penetrate the market as fast as possible. This is done by allocating many resources to marketing in the launch period. Eventually the marketing scales down in line with the drug establishing a large and recurrent customer base. In table 6.6 the actual out-of-pocket post-approval costs for our CNS project are outlined.

The post-approval costs for the good case and the bad case are both adjusted by 20% to reflect scenarios with decreased or increased competition and thus less or more marketing-related costs. Both scenarios are assigned a 20% possibility due to the high uncertainty regarding the competitive scene as discussed in section 5.1.2.

The complete forecast from the findings above is shown in table 6.7.
6.3 Simple valuation

6.3.1 DCF valuation

The forecast for our CNS project was presented in the previous section, and it is now possible to find its NPV.

We start by finding the NPV of the aggregated costs. As can be seen from the forecast the costs are divided in three different subcategories and are scenario weighted. This means that the final NPV for each category is multiplied by its individual probability rate.

When estimating the total NPV of the R&D costs we get the following computations.

\[
\text{NPV R&D costs scenario-weighted} = 74.1 \times 30\% + 52.6 \times 60\% + 36.2 \times 10\% = 57.4 \text{ million USD}
\]

We do the same for the post-approval costs, the production costs and the sales, so we end up with the following values.

\[
\text{NPV post-approval costs scenario-weighted} = 16.29 \text{ million USD }^{27}
\]

\[
\text{NPV production costs scenario-weighted} = 13.65 \text{ million USD }^{28}
\]

---

27 19.6 \times 20\% + 16.3 \times 60\% + 13.0 \times 20\% = 16.29 \text{ million USD}

28 4.1 \times 10\% + 12.4 \times 80\% + 32.9 \times 10\% = 13.65 \text{ million USD}
Thus the total NPV of costs is

\[ 57.4 + 16.29 + 13.65 = 87.3 \text{ million USD} \]

The NPV for the scenario-weighted revenue is

\[ 10\% \ast 40.2 + 80\% \ast 121.7 + 10\% \ast 322.28 = 133.7 \text{ million USD} \]

As a result the final NPV is \(133.7 - 87.3 = 46.4 \text{ million USD}\)

### 6.3.2 Fuzzy DCF valuation

As we are working with a cash flow forecast that is scenario weighted and divided into three categories, it is obvious that we should use triangular fuzzy numbers to our fuzzy valuation approach, which we presented in section 4.1.

To calculate the fuzzy NPV we need to rearrange the forecasted cash flow differently than in the standard scenario-weighted cash flow forecast by the use of the fuzzy pay-off method presented in section 4.1.1. The fuzzy cash flow (hereafter referred to as FCF) is constructed in order to model the most extreme cash flows possibly. For the bad case FCF we use the bad case total costs and the bad case total revenue to depict the worst possible cash flow scenario and vice versa for the good case, while the base case remains the same.

Total revenue for the good case is calculated as the highest estimated sales minus lowest estimated production costs. Appendix 20 shows the FCF for the three cases. The summarized FCF forecast is outlined in table 6.8.

| FCF          | 2011e | 2012e | 2013e | 2014e | 2015e | 2016e | 2017e | 2018e | 2019e | 2020e | 2021e | 2022e | 2023e | 2024e | 2025e | 2026e | 2027e | 2028e | 2029e | 2030e | 2031e |
|--------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Lead Opt./Preclinical phase |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| FCF - Bad    | -3.8  | -3.8  | -3.8  | -3.8  | -2.5  | -2.5  | -5.5  | -5.5  | -10.0 | -10.0 | -10.0 | -4.0  | -7.3  | 7.7   | 8.8   | 14.4  | 17.2  | 18.5  | 17.2  | 14.7  | 8.2   |
| FCF - Base   | -1.4  | -1.4  | -1.4  | -1.4  | -2.3  | -2.3  | -5.3  | -5.3  | -15.0 | -15.0 | -15.0 | -3.0  | 1.7   | 23.9  | 40.4  | 50.6  | 55.7  | 56.7  | 52.9  | 45.3  | 26.1  |
| FCF - Good   | -0.4  | -0.4  | -0.4  | -0.4  | -2.0  | -2.0  | -5.0  | -5.0  | -10.0 | -10.0 | -10.0 | -2.0  | 21.1  | 75.4  | 116.7 | 138.9 | 150.0 | 150.9 | 140.8 | 120.6 | 70.1  |

**Table 6.8: Own construction**

The NPV of the FCF for each case is shown below, which are used to generate the fuzzy NPV (hereafter referred to as FNPV).

\[
NPV_{\text{Bad case}} = -57.6 \text{ million USD}
\]

\[
NPV_{\text{Base case}} = 40.5 \text{ million USD}
\]
\[ \text{NPV}_{\text{Good case}} = 240.6 \text{ million USD} \]

The resulting FNPV (-57.6, 50.5, 240.6) is the pay-off distribution for the project.

In section 4.1.1 the fuzzy pay-off method to calculate the fuzzy real option value (hereafter referred to as FROV) was presented. Hence we will lead out with identifying our ‘a’, \((a - \alpha)\) and \((a + \beta)\):

\[
\begin{align*}
\text{NPV}_{\text{Bad case}} &= -57.6 \text{ million USD} = (a - \alpha) \\
\text{NPV}_{\text{Base case}} &= 40.5 \text{ million USD} = 'a' \\
\text{NPV}_{\text{Good case}} &= 240.6 \text{ million USD} = (a + \beta)
\end{align*}
\]

Thus the value of \(\alpha\) is \(40.5 - (-57.6) = 98.1\) and the value of \(\beta\) is \(240.6 - 40.5 = 200.1\)

As the method stipulates we have to find the mean value of the positive side of the triangle, denoted \(E(A_+)\). Also we have to compute the relationship between the positive area and the negative area of the triangle.

The mean value of the positive area \(E(A_+)\) is found by equation (4.6).

\[
E(A_+) = 40.5 + \frac{(200.1 - 98.1)}{6} + \frac{(98.1 - 40.5)^3}{6 \cdot 98.1^2} = 60.79
\]

The relation between the positive area and the negative area is found by simple mathematics as it is actually two right-angled triangles. The fact that we are working with two triangles with a limit of 0 and 1 as shown in figure 4.1 makes the calculation simpler. Appendix 21 shows the calculations as well as a figure to help the understanding. In order to compute the area relationship we have to determine the intercept of the y-axis so we can compute the area of the negative side.

We already have the known points of (40.5; 1) along with (0; -57.6) and (0; 240.6). The next step is to compute the slope of the lines, going from peak ‘a’ to the two extreme points, so we end up with the formulas of the lines. This presents a situation where we in order to calculate the area relationship have to solve two equations with two unknowns.
Given the points mentioned we can form two equations that follow the traditional guidelines of simple equations $y_1 = ax_1 + b$ and $y_2 = ax_2 + b$ and thus we end up with

$$y_1 = 0 = a \times (-57.6) + b \quad \text{and} \quad y_2 = 1 = a \times (40.5) + b.$$ 

This gives us the possibility to eliminate one of the factors and replace it in the other equation in order to find $a$. So if we rearrange the first equation we will get $y_1 = 0 = a \times (-57.6) + b \leftrightarrow 0 = -57.6a + b \leftrightarrow b = 57.6a$. With our $b$-value expressed as a function of $a$, we substitute the equation into the remaining equation to find $a$

$$y_2 = 1 = 40.5a + b \rightarrow 1 = 40.5a + 57.6a \leftrightarrow a = 0.0102$$

With the finding of $a$, we can easily calculate the value of $b$

$$y_1 = 0 = a \times (-57.6) + b \rightarrow 0 = 0.0102 \times (-57.6) + b \leftrightarrow b = 0.587$$

Now we have all the values to calculate the positive and negative area, respectively. To calculate the area relationship we have to split the area in three different pieces, the positive areas from ‘a’ to $\beta$ and from 0 to ‘a’ as well as the negative area from $\alpha$ to 0. The areas are calculated from the area formula for right-angled triangles given as $A = \frac{1}{2} \times \text{height} \times \text{baseline}$

The area of the negative side is then $A(\alpha \text{ to } 0) = \frac{1}{2} \times 0.587 \times 57.6 = 16.915$. Next we find the positive areas in the same way, and thus get $A(\alpha' \text{ to } \beta') = 100.07$ and $A(0 \text{ to } \alpha') = 32.11$

Hence the relation between the positive and entire area is $\frac{(100.07+32.11)}{(16.915+100.07+32.11)} = 0.8866$

This means that we can compute the final FROV from equation 4.4.

$$FROV = 60.79 \times 0.8866 = 53.89 \text{ million USD}$$

6.3.3 Review of the DCF valuation versus the fuzzy DCF valuation

Both methods produced a positive value for the CNS project, which was expected as none of the methods take the risk of failure into account but assumes that the project will be completed. The classic DCF method yields a value of USD 46.4 million while the fuzzy DCF method gives a value of 53.9 million USD. As advocated in section 4.1.1 the fuzzy DCF approach yields a
higher value than the traditional DCF approach as it puts more emphasis on the potential upside than the potential downside. Thus the results obtained are in line with the theoretical arguments.

According to the results of both the classic DCF model and the fuzzy DCF model the project should be initiated as the results provide significantly positive values.

However as none of the approaches include the risk of failure as mentioned above we will next evaluate the project with a simple DCF model that now incorporates the success rates for completing each phase.

### 6.4 Valuation with a real option perspective

#### 6.4.1 Risk adjusted DCF valuation

As mentioned in section 3.1.4.3.1 it is easy to expand the traditional DCF method to include the conditions of the probabilities of success rates in each phase to have an effect on the final NPV in the form of a simple event tree. From the template in figure 3.2 we have modelled the CNS project in figure 6.3 with the estimated success rates.

![Figure 6.3: Own construction](image-url)
This requires a minor adjustment of our original forecast. In our original forecast the costs and revenues are arranged based on the year in which they occur. In this case we need to allocate the discounted costs and revenues in the different phases where they occur while still being scenario weighted. The result of the transformation is shown below in table 6.9.

<table>
<thead>
<tr>
<th>R&amp;D costs summarized</th>
<th>Optim.</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
<th>Market</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bad</td>
<td>14.3</td>
<td>4.3</td>
<td>8.8</td>
<td>44.0</td>
<td>2.7</td>
<td>0.0</td>
</tr>
<tr>
<td>Base</td>
<td>5.2</td>
<td>3.9</td>
<td>8.4</td>
<td>33.0</td>
<td>2.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Good</td>
<td>1.4</td>
<td>3.4</td>
<td>8.0</td>
<td>22.0</td>
<td>1.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Scenario-weighted R&amp;D costs</td>
<td>7.6</td>
<td>3.9</td>
<td>8.5</td>
<td>35.2</td>
<td>2.2</td>
<td>0.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Post-approval costs summarized</th>
<th>Optim.</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
<th>Market</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bad</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>19.6</td>
</tr>
<tr>
<td>Base</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>16.3</td>
</tr>
<tr>
<td>Good</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>13.0</td>
</tr>
<tr>
<td>Scenario-weighted post-approval costs</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>16.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Revenue net of production costs summarized</th>
<th>Optim.</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
<th>Market</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bad</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>36.1</td>
</tr>
<tr>
<td>Base</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>109.3</td>
</tr>
<tr>
<td>Good</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>289.9</td>
</tr>
<tr>
<td>Scenario-weighted Revenue net of production costs</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>120.1</td>
</tr>
</tbody>
</table>

Table 6.9: Own construction

The next step in our risk adjusted DCF method is to find the sum of the different phases as well as add the probabilities of success to each phase. The result is recapped in table 6.10.

<table>
<thead>
<tr>
<th>Lead optimisation/preclinical</th>
<th>Period (months)</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
<th>Market launch</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-46.5</td>
<td>46.5-66.3</td>
<td>66.3-94</td>
<td>94-125.5</td>
<td>125.5-142.5</td>
<td>142.5-125.5</td>
</tr>
<tr>
<td>Revenue</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>120.1</td>
</tr>
<tr>
<td>Costs</td>
<td>7.6</td>
<td>3.9</td>
<td>8.5</td>
<td>35.2</td>
<td>2.2</td>
<td>16.3</td>
</tr>
<tr>
<td>Earnings</td>
<td>-7.6</td>
<td>-3.9</td>
<td>-8.5</td>
<td>-35.2</td>
<td>-2.2</td>
<td>103.8</td>
</tr>
<tr>
<td>Risk adjustment factor</td>
<td>100%</td>
<td>67.50%</td>
<td>44.70%</td>
<td>20.40%</td>
<td>12.60%</td>
<td>9.80%</td>
</tr>
<tr>
<td>Risk adjusted earnings</td>
<td>-7.56</td>
<td>-2.66</td>
<td>-3.79</td>
<td>-7.19</td>
<td>-0.28</td>
<td>10.17</td>
</tr>
</tbody>
</table>

Table 6.10: Own construction

All revenue and costs are now allocated in the different phases, including the different success rates for each of the phases denoted as the risk adjustment factor.
In order to compute the final risk adjusted NPV we simply sum the risk adjusted earnings.

\[ rNPV = (-7.56) + (-2.66) + (-3.79) + (-7.19) + (-0.28) + 10.17 \]

\[ rNPV = -11.30 \text{ million USD} \]

### 6.4.2 Risk adjusted fuzzy DCF valuation

As done in the risk adjusted DCF method presented above the costs and revenues are allocated to the different phases. But as the costs and revenues from the former section were scenario-weighted we have to allocate them again but this time in line with the fuzzy payoff method as shown in the fuzzy DCF calculation in section 6.3.2. The results are listed in table 6.11.

<table>
<thead>
<tr>
<th>Total costs</th>
<th>Opt.</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
<th>Market</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bad</td>
<td>14.3</td>
<td>4.3</td>
<td>8.8</td>
<td>44.0</td>
<td>2.7</td>
<td>19.6</td>
</tr>
<tr>
<td>Base</td>
<td>5.2</td>
<td>3.9</td>
<td>8.4</td>
<td>33.0</td>
<td>2.1</td>
<td>16.3</td>
</tr>
<tr>
<td>Good</td>
<td>1.4</td>
<td>3.4</td>
<td>8.0</td>
<td>22.0</td>
<td>1.4</td>
<td>13.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total revenue net of production costs</th>
<th>Opt.</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
<th>Market</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bad</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>36.1</td>
</tr>
<tr>
<td>Base</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>109.3</td>
</tr>
<tr>
<td>Good</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>289.9</td>
</tr>
</tbody>
</table>

**Table 6.11: Own construction**

With this transformation of the cash flows we can make three cases that represent respectively the extreme cases and the base case. We use the same analogy as in the previous section, thus getting the results presented below in table 6.12, 6.13 and 6.14.

<table>
<thead>
<tr>
<th>Bad case</th>
<th>Lead optimisation/preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
<th>Market launch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Period (months)</td>
<td>0-46.5</td>
<td>46.5-66.3</td>
<td>66.3-94</td>
<td>94-125.5</td>
<td>125.5-142.5</td>
<td>142.5-361</td>
</tr>
<tr>
<td>Revenue</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Costs</td>
<td>14.3</td>
<td>4.3</td>
<td>8.8</td>
<td>44.0</td>
<td>2.7</td>
<td>19.6</td>
</tr>
<tr>
<td>Earnings</td>
<td>-14.3</td>
<td>-4.3</td>
<td>-8.8</td>
<td>-44.0</td>
<td>-2.7</td>
<td>16.5</td>
</tr>
<tr>
<td>Risk adjustment factor</td>
<td>100%</td>
<td>67.5%</td>
<td>44.7%</td>
<td>20.4%</td>
<td>12.6%</td>
<td>9.8%</td>
</tr>
<tr>
<td>Risk adjusted earnings</td>
<td>-14.3</td>
<td>-2.9</td>
<td>-3.9</td>
<td>-9.0</td>
<td>-0.3</td>
<td>1.6</td>
</tr>
</tbody>
</table>

**Table 6.12: Own construction**
The resulting risk adjusted NPV (hereafter referred to as the rFNPV) (-28.8, -9.5, 15.2) is the pay-off distribution for the project.

With our three points found we can now compute the risk adjusted fuzzy real options value (hereafter referred to as rFROV) as we did in section 6.3.2. We use the identical procedure but instead we now have a situation where ‘a’ (centre) along with the low point is negative values while the summit is positive. According to section 4.1.1 we have to make a minor change to the procedure for the computation of $E(A_+)$, but in general we follow the same procedure as in section 6.3.2. Our calculations are shown in appendix 22.

It results in a rFROV of

$$rFROV = 0.9569 \times 0.1970 = 0.1886 \text{ million USD}$$

### 6.4.3 Review of risk adjusted DCF valuation versus fuzzy risk adjusted DCF valuation

The risk adjusted DCF method results in a value of –11.3 million USD for the project in contrast to the significantly positive value of 46.4 million USD of the traditional DCF method. This is
due to the high risk of failure in the development of a new drug given the high degree of uncertainty. Thus it gives a more reasonable, although conservative, estimate of the value of the project, and with this method the project should not be initiated.

As with the traditional DCF method, the risk adjusted DCF method values the possible negative outcomes equal to the possible positive outcomes and assumes thus that the cash flows are normally distributed around the base. But in a real options framework the positive outcomes are given a higher value than negative outcomes as they can be avoided by the use of the embedded abandonment option in a drug development project. Thus the downside exposure is contained while the upside exposure is emphasized (McGrath & Nerkar, 2004, p.3). The use of a fuzzy approach incorporates this line of thought and yields a rFROV of 0.19 million USD. This is a distinctive difference to the -11.3 million USD which the traditional risk adjusted DCF method yielded. Yet this does not mean that the project is suddenly more worth when using a fuzzy approach. It simply means that the negative outcomes are equalled to the value of zero and accordingly the positive outcomes are given a higher weight. As a consequence of this methodology the FROV will always be positive and thus very small values should be assessed with caution as they do not explicitly offer a basis for decisions. In practice it is impossible to avoid losses when abandoning a project as some costs must be expected in connection with the termination of the project. To account for these costs the introduction of a minimum project value that must be reached in order for the project to be considered profitable is a possibility. An exact value of such a minimum requirement should be set individually from case to case. The application of this will be discussed further in section 6.7.

Hence a more thorough assessment of the project will be needed to evaluate whether or not to initiate the project.

6.5 Valuation with real options

6.5.1 Binomial tree valuation

In section 3.1.4.3.2 we discussed how to calculate the real option value of a drug development project with a binomial tree. We identified that the current value of the underlying asset, the volatility of the underlying asset and the time step between each node are needed input variables.
We use a time period of six months to increase the accuracy of the modelling and a volatility of 35% as estimated in section 5.3.5. The underlying asset is the value of the peak sales deducted the sales dependent costs which are the production costs and the marketing costs. We can then calculate the value of the underlying asset to 103.8 million USD\textsuperscript{29} which is the root of the tree. This is then multiplied by the up and down factor at each node until reaching the end node’s 24 time periods (12 years) later. The up and down factors are calculated below as shown in equation 3.1 and equation 3.2.

\[ u = e^{(0.35\times\sqrt{0.5})} = 1.28 \quad \text{d} = e^{(-0.35\times\sqrt{0.5})} = 0.78 \]

The binomial tree of the development of the underlying asset is shown in appendix 23.

With the peak sales calculated at each node the real option value of the CNS project can be calculated. As mentioned in section 3.1.3.1.1 the most important option is an abandonment option, where the future R&D costs can be avoided if a termination of the project is chosen.

First the value at the end nodes is calculated where no options are present as there is no gain in abandoning the market launch. So the value is simply the probability of getting an approval (77.9%) multiplied with the maximum of the value of the underlying asset at that node or zero, as equation 3.5 prescribes.

When all the end nodes are solved, backward induction is used to solve the value at the remaining nodes as showed in equation 3.4 (As we have already discounted the cash flows in our DCF-model we will not discount them again as equation 3.4 prescribes).

The up and down risk-neutral probabilities used to calculate the value at t from the up and down state in t+1 is calculated below from equation 3.3

\[ p_{up} = \frac{e^{(0.35\times0.5)} - 0.78}{1.28 - 0.78} = 0.474, \quad p_{down} = 1 - p_{up} = 0.526 \]

At the end of each phase the option of abandoning the project presents itself. In a negative market state with only small expected peak sales expressed by the value of the underlying asset in that node, it could be more valuable to close down the project and avoid future development.

\textsuperscript{29} NPV Revenue scenario-weighted – NPV Production Costs scenario-weighted – NPV Post-approval Costs scenario weighted (133.7 – 13.65 – 16.29 = 103.76)
costs than continuing with the project and only reaching very modest peak sales. So the value at the decision nodes is the probability of successfully completing the current phase times the value at the node \( V_t \) minus the future development costs or zero if the mentioned calculus turns out to have a negative value. This is shown in equation 6.1 based on equation 3.4 and equation 3.5.

\[
Value_{\text{decision node } t} = p_{\text{phase } t} \times \text{Max}[V_t - X_{t+1}, 0], \quad (6.1)
\]

In appendix 24 the binomial tree of the real option value can be seen where it materializes into a final value of 4.75 million USD\(^3\).

### 6.5.2 Fuzzy binomial tree valuation

In section 4.2 we discussed how the binomial tree can be fuzzified by creating triangular fuzzy numbers at each node in the binomial tree. This implies the use of fuzzy jumping factors \( u' = [u_1, u_2, u_3] \) and \( d' = [d_1, d_2, d_3] \) which creates a three-point possibility distribution at the end of each node. To calculate the fuzzy jumping factors the volatility must be fuzzified. This is done by estimating a CV on our volatility estimate of 35%. As discussed in section 5.3.5 the volatility is estimated to be in the range of 20-50%, hence we estimate the variance on our volatility estimate to be 15%. It allows us to calculate the triangular fuzzy number known as the fuzzy volatility.

\[
\text{Fuzzy volatility} = [ (1 - 0.15 \times 0.35, 0.35, (1 + 0.15) \times 0.35] = [0.2975, 0.35, 0.4025]
\]

The fuzzy jumping factors can now be calculated for the bad case scenario, the base case scenario and the good case scenario by equation 4.11 and 4.12.

\[
u_1 = e^{(0.2975 \times \sqrt{0.5})} = 1.234 \quad \quad d_1 = \frac{1}{u_1} = \frac{1}{1.234} = 0.8103
\]

\[
u_2 = e^{(0.35 \times \sqrt{0.5})} = 1.281 \quad \quad d_2 = \frac{1}{d_1} = \frac{1}{1.281} = 0.781
\]

\[
u_3 = e^{(0.4025 \times \sqrt{0.5})} = 1.329 \quad \quad d_3 = \frac{1}{d_3} = \frac{1}{1.329} = 0.752
\]

With the fuzzy jumping factors calculated the value of the underlying asset can be modelled for the three scenarios, which can be found in appendix 25.

---

\[^{30} V_t = p_{\text{up} \times V_{t+1}^{\text{up}}} + p_{\text{down} \times V_{t+1}^{\text{down}}} = 0.474 \times 7.45 + 0.526 \times 2.31 = 4.75\]
Similar to the traditional binomial tree approach we calculate the real option value by first solving the end nodes and then using backward induction to unveil the fuzzy binomial option tree. However we use fuzzy risk-neutral probabilities in line with equation 4.13. As discussed in section 4.2 the fuzzy approach creates a possibility distribution at each node that respectively maximizes and minimizes the possible pay-off. To secure this, the minimum fuzzy risk-neutral up and down possibilities are assigned to the bad case whilst the maximum fuzzy risk-neutral up and down possibilities are assigned to the good case. The base case is solved similar to the traditional binomial tree above.

\[
p_{up1} = \frac{e^{(0.035-0.5)-0.81}}{1.234-0.81} = 0.4893, \quad p_{down1} = 1 - p_{up1} = 1 - 0.4893 = 0.5107
\]

\[
p_{up2} = \frac{e^{(0.035-0.5)-0.781}}{1.281-0.781} = 0.4737, \quad p_{down2} = 1 - p_{up2} = 1 - 0.4737 = 0.5263
\]

\[
p_{up3} = \frac{e^{(0.035-0.5)-0.752}}{1.329-0.752} = 0.4599, \quad p_{down3} = 1 - p_{up3} = 1 - 0.4599 = 0.5401
\]

In line with the thinking behind fuzzy logic and as presented by Liao and Ho the fuzzy risk-neutral probabilities are created in order to portray the extreme possibility distributions (Liao & Ho, 2010, p.2131).

\[
p_{up}^{fuzzy} = [0.4599, 0.4737, 0.4893] \quad \text{and} \quad p_{down}^{fuzzy} = [0.5107, 0.5263, 0.5401].
\]

We are now able to solve the three different fuzzy binomial trees with equation 6.1 similarly to the traditional binomial approach described above. This is shown in appendix 26.

The final fuzzy value of the project is calculated in the fuzzy binomial trees to be [0.70, 4.75, 19.37], which are the three points of the final possibility distribution, denoted respectively \( c_1 \), \( c_2 \) and \( c_3 \) as showed in figure 4.4.

To obtain the FENPV we first need to calculate the pessimistic-optimistic weighted index as discussed in section 4.2. This is done by equation 4.16 and shown in appendix 27. In order to compute this index we have to find the different areas first. As we discussed in section 6.3.2, we are dealing with two right triangles why the calculations of the areas are fairly simple. First we calculate the baseline and then the area can be calculated.
\[ c_3 - c_2 = 19.37 - 4.75 = 14.62, \text{ why} \]

\[ AR = 0.5 \times 1 \times 14.62 = 7.31 \]

We do the same for the left area and get \( AL = 2.02 \), why the pessimistic-optimistic weighted index is

\[ \lambda = \frac{7.31}{7.31 + 2.02} = 0.78 \]

From equation 4.17 we can now calculate the FENPV of the CNS project.

\[ E(FENPV) = \frac{(1 - 0.78) \times 0.7 + 4.75 + 0.78 \times 19.37}{2} = 10.04 \]

### 6.5.3 Review of binomial tree valuation versus fuzzy binomial tree valuation

In the real options approach we can see the impact of the right-skewness of the fuzzy binomial valuation. The traditional binomial approach values the drug development project at 4.75 million USD, while the fuzzy approach values the project at 10.04 million USD. This higher value is a result of the fuzzy upside extreme value being 19.37 million USD, while the fuzzy downside extreme is 0.7 million USD. These results verify the thorough real option thinking in the fuzzy binomial approach as the downside risk can be reduced significantly, whilst the upside can be magnified.

As with the risk-adjusted method above, this does not mean that the project is suddenly worth more if valued with the fuzzy binomial approach. It just emphasizes that the fuzzy binomial approach puts more weight on the possible positive outcomes and assumes that the negative outcomes can be prevented by the use of the implied abandonment option. And this way of thinking is highly in line with the real option framework as a whole.

### 6.6 Sensitivity analysis

In this section we will make three different sensitivity analyses based on the valuation results we obtained earlier in this part. The input variables chosen to alter are the inputs we perceive as the key drivers of the final value. The reason for making these risk analyses is to ensure that the
conclusions we have drawn in the valuation analyses are robust and will not change if the inputs fail to meet the estimated values. Additionally, we want to see if the effect of changing input variables has the expected impact on the result of the different valuation methods. In other words these tests will provide us with a picture of the consequences if the factors change.

6.6.1 DCF valuation versus fuzzy DCF valuation

The first case is the traditional DCF versus the fuzzy DCF. We argue that the two factors that have the most significance influence on the outcome are the WACC and the total value of the sales. Sales are chosen as representing all the positive cash flows. To portray different sales scenarios we use a sales adjustment factor with which sales in all cases are multiplied. The WACC is chosen due to its significant impact on today’s value of cash flows occurring in the future. In drug development projects revenues are expected to occur many years from the starting point, which is why WACC is of great importance.

Initially the intention was to compare the two tables in relative terms, but traditional NPV is significantly smaller, implying that this NPV would appear to have a much larger relative increase due to changes in the input variables. Consequently we will instead look at it from an absolute point of view. Here we see that an increase in sales as well as a drop in the WACC will lead to a higher absolute increase for the fuzzy NPV than the traditional NPV. With the assumptions behind the two models we expected the fuzzy NPV to be better at capturing the upside potential of a project due to the construction of the fuzzy NPV. With a higher WACC or lower sales the fuzzy NPV still yields higher values than the traditional NPV. Especially at the negative extremes there is a significant difference between the two methods. As discussed in section 6.4.3 this is partly due to the omission of the negative values in the calculation of the fuzzy NPV. However, the results obtained are robust as the fuzzy NPV yields a higher value than the traditional NPV in all situations.
### 6.6.2 Risk adjusted DCF valuation versus fuzzy risk adjusted DCF valuation

The second case is the risk adjusted DCF versus the fuzzy risk adjusted DCF. The factors utilised here are again sales and maybe more importantly the phase probability rates of success. These probability rates of success have an immense influence on the outcome of the project. We change the phase probability rate by adding or deducting 0.05 percentage point from our initial probability rates in all development phases.

The comparison of the two tables and their results is complicated as the traditional risk adjusted NPV initially is of negative value while the fuzzy risk adjusted NPV has an extremely low positive value. A relative comparison analysis is not applicable, so instead we use differences in absolute figures to see the different shifts the methods present as input variables change.

The traditional risk adjusted DCF shows a negative outcome for success rates around the initially estimated success rate. As revenues occur in the latest stage the size of sales has little influence compared to the probability of getting the product to the market. A sales factor of 1.5 yields a negative outcome of -5.2 compared to the initial result of -11.3, which shows that even a 50% increase in sales has an insignificant effect. On the other hand an increase in the phase probabilities presents a much more positive outcome. A percentage point increase of 0.1 in the success rate yields -5.9 compared to the initial -11.3 and thus has practically the same effect as a 50% sales increase. This shows that a minor shift in phase probabilities is of the same value as a major shift in the sales factor. Hence, a reduction in the technological uncertainty is of more value than a higher commercial sales upside.

The fuzzy risk adjusted DCF shows a more positive outcome of the project but as previously discussed we never end up with negative values with the fuzzy method. Instead there are many values of zero or close to zero. Again the most important key input seems to be the phase probability where an upward shift of 0.1 percentage point yields an outcome of 1.6 compared to...
0.2, whilst a 50% sales increase yields 1.2 and thus has a smaller effect than the 0.1 percentage point increase in the success rate.

As mentioned a comparison of the results of the two methods is difficult to make. In order to interpret the results of the fuzzy risk adjusted DCF we argue that the figures have to be adjusted by a minimum value as discussed in section 6.4.3. The size of the minimum value seems to be of smaller significance to the overall difference between the two methods. For instance, with an estimated minimum value between 1 and 5 the fuzzy risk adjusted DCF will in general still present a more positive result than the traditional risk adjusted DCF. However the absolute value added by a change in the key inputs is in general higher for the traditional risk adjusted DCF than the fuzzy risk adjusted DCF. This is of course due to the negative starting point of the traditional risk adjusted NPV, which allows a much higher value increase.

The results obtained in our valuation seem robust as we would have reached the same conclusion with different key inputs. The fuzzy risk adjusted DCF yields a higher value under all circumstances than the traditional risk adjusted DCF and is thus in line with the theory.

6.6.3 Binomial tree valuation versus fuzzy binomial tree valuation

The last case is the binomial method versus the fuzzy binomial method. The factors that we change are again the sales but this time pitted against the volatility. The high influence of the volatility on the final value makes a sensitivity analysis of the volatility of great importance when using it in real option analysis (Arnold & Crack, 2004, p.81). We will look at the impact of the volatility in the interval of 20-50% as it is the expected range as discussed in section 5.3.5. In section 5.2.1 we discussed how a higher volatility results in a higher value in real option analysis but at the same time increases the discount rate and thus decreases the starting value of the real option analysis. In this sensitivity analysis we will only look at the effect on the real option analysis where a higher risk translates into a higher volatility and thus a higher final value would be expected.
Comparing the results of the two methods we find that both methods yield positive values for the projects as expected. However, with the introduction of a minimum threshold value as discussed in section 6.4.3 the negative scenarios with low sales and a low volatility do not look so promising. This is especially the case for the traditional binomial method where many of the values are below 5.

From table 6.19 and 6.20 we see that the traditional binomial method yields a more conservative estimate than the fuzzy binomial method which generally yields the highest value. In the outlying low volatility scenario, we see that the traditional binomial method yields a higher value. This is in line with the theory discussed in section 4.2 where we pointed out that fuzzy numbers are better at capturing the value of possible extreme positive scenarios. For instance table 6.19 shows that a drop in the volatility of 15 percentage points yields a value of 3 for the traditional binomial method while the fuzzy binomial method only yields a value of 2.5 as seen in table 6.20. When increasing the volatility the positive difference in favour of the fuzzy binomial method only gets larger. As the underlying asset develops more rapidly up and down at each node, the final real option value will of course increase more for the fuzzy binomial method as the good case has a significant upside potential compared to the base case of the traditional binomial method. The size of sales appears to have an increasing significance with an increasing volatility. Again this is due to the mechanism of the fuzzy binomial method that includes the extreme upside scenarios to a higher degree than the traditional binomial method.

From the discussion above we conclude that the results from our valuation are robust. The fuzzy binomial method yields a higher value than the traditional binomial method. Only at very low volatilities, which are very unlikely with a biotech project, would the conclusion have been different.
6.7 Applicability

Real option valuation, which differs greatly from traditional valuation methods such as the DCF method, gives more exact assessments since it incorporates the effect of future uncertainties. By using real option valuation methods to analyse risky investments such as drug development projects it is possible to avoid wrong decisions based on a too conservative estimate for the project value.

As estimations made by people are many-sided compositions that do not have sharp certainties, the use of fuzzy numbers are more expressive than classical mathematics used by the traditional valuation methods. Instead of limiting the assessment to the most possible outcomes and thus leaving out the tails of the distribution we argue that the tails should be included, as even remote possibilities should be taken into consideration. Thus using a fuzzy approach will lead to more rational results that concern the inadequacy of human reasoning which implies that the obtained results are more trustworthy.

Comparing the traditional approaches with the fuzzy approaches to valuing a drug development project gives an unequivocal picture. The fuzzy approach assigns significantly higher value to the project, no matter what valuation method is chosen. In table 6.21 the valuation results are summarized.

<table>
<thead>
<tr>
<th>USD m</th>
<th>DCF</th>
<th>Risk Adjusted DCF</th>
<th>Binomial Tree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional Approach</td>
<td>46.4</td>
<td>-11.3</td>
<td>4.8</td>
</tr>
<tr>
<td>Fuzzy Approach</td>
<td>53.9</td>
<td>0.19</td>
<td>10</td>
</tr>
</tbody>
</table>

Table 6.21: Own construction

This is in line with the theoretic findings and thus our expectations for the outcome. The down weighting of the potential negative outcomes and the exaggerated emphasis on the potential upside are clearly shown in the results from our three different valuations. On a general note the fuzzy approach assigns more value to the learning about the technological risk and the market potential and hence the value of flexibility.

The findings from our DCF valuation show that the fuzzy pay-off method is easily applicable to a standard DCF forecast. Only an uncomplicated rearrangement of the already forecasted cash flows is necessary. Once this is done it is possible to capture some of the value that high
uncertainty can generate without having to use complicated models. Despite adding value to the
traditional DCF method the fuzzy pay-off method is not optimal for valuing drug development
projects. It lacks the quality of modelling different scenarios and the management’s actions in
response to these scenarios. Also the absence of a risk perspective makes the DCF method as a
standalone model inadequate for valuing drug development projects. This could however be
handled by applying the estimated cumulative success rate to the final value. It would be an
imprecise estimate of the projects value but a much more realistic estimate than without any risk-
adjustment. Also would it be theoretically wrong as the different cash flows are subject to
different risks.

From the above discussion we conclude that the fuzzy pay-off method is superior to a traditional
DCF method when valuing high uncertainty projects such as a drug development project. It is
easily applicable to already completed scenario-based cash flow forecasts, which are present in
most companies.

A theoretically more correct way of adjusting for the risk of failure in a DCF valuation model is
by the use of event trees to model the risk of failure in each phase. This ensures that future cash
flows are weighted by the chance of them actually occurring, which implies that the negative
R&D cash flows will have a bigger impact on the project value than the potential sales cash
flows. This is overly conservative as it takes a very static perspective on future cash flows.
Improved market potential as a consequence of better drug traits or fewer competitors in the
market space than anticipated is not accounted for in the model just as depressing project
information that could lead to a premature termination of the project is unaccounted for.
Therefore the managerial flexibility that creates value in uncertain projects is missing and only
the negative side of the uncertainty, which is the high risk of failure, is present. So while being
theoretically more correct than the traditional DCF valuation it lacks the power of
acknowledging the value stemming from managerial flexibility. The application of the fuzzy
pay-off method enables the event tree valuation to take account of this value of flexibility. Fuzzy
event tree valuation assigns no negative project value to the possible negative outcomes of the
project as it regards them as avoidable by the use of abandon options. This is an exaggeration as
it is not possible to avoid all costs as they are not all variable, which implies that fixed costs such
as rent are contractually tied for a longer time horizon and are thus not avoidable in the short
term. Also, there will be costs related to the actual termination of a project. However while overstating what is possible the fuzzy event tree does incorporate the real option perspective of the value of flexibility through the opportunity to close down non-profitable projects. To cope with the unrealistic assumption of a cost-neutral abandonment of a drug development project, a minimum threshold level for the project value must be set. The size of the threshold level should be project-specific and thereby dependent on the characteristics of each specific project allowing projects with more fixed costs to set a higher threshold level than projects with more variable costs. Already incurred costs should not be included in the threshold level as they should be viewed as sunk costs according to economic theory. The threshold level should be revised as the project develops as it should reflect the actual level of future fixed and abandonment costs. Due to the structure of drug development projects with low R&D costs in the early phases the argument of a cost-light termination of projects is valid as a great deal of information about the prospects of a project can be revealed in these early phases.

The actual application of an event tree is straightforward for practitioners as they just have to rearrange the cash flows from their forecast into the different phases. The application of the fuzzy pay-off method to the event tree and in consequence the phase allocated cash flows is equally uncomplicated as with the application to the traditional DCF model.

To conclude, the application of the fuzzy pay-off method to the event tree valuation has the attractive feature of including the potential huge upsides of a project as well as the possibility of abandoning projects with depressing outlooks. Thus the fuzzy event tree valuation emphasizes both the high risk of failure for drug development projects as well as the value of flexibility. As the fuzzy event tree valuation is also easily applicable for practitioners it is preferred over both the fuzzy DCF valuation and the very conservative traditional event tree valuation.

To fully capture and model the consequences of high uncertainty it is not sufficient to use the fuzzy pay-off method on top of an event tree valuation. To obtain this an actual real option model is needed to portray and value the many possible outcomes of a volatile drug development project. With the goal of simplicity for the valuation process in mind we argue that a binomial tree valuation is the best way of doing this due to its intuitive nature and ease of implementation compared to other more advanced real option models as discussed in section 3.1.4.3. Binomial trees are also well suited at identifying the key drivers of the value of flexibility which is an
important part of the real option analysis. Focusing on estimating the key parameters will lead to
a more efficient valuation process as less time is spent on estimating insignificant parameters.

Both the classic binomial tree and the fuzzy binomial tree assign significant value to the
management’s ability to take action down the road in response to changed input variables. This is
especially true for the fuzzy binomial tree which particularly rates the huge upside potential of a
drug development project high. As was the case with fuzzy the risk-adjusted method discussed
above there must also be a minimum threshold level for the binomial tree valuation as the
arguments presented are also valid for the clean real options approach.

In theory the real options approach is preferable for uncertain projects such as a drug
development project as it captures a large share of the possibilities that high uncertainty presents
for the management of the project. In practice however the more difficult implementation for
practitioners makes the pure real option approach less applicable for those without a sound
financial understanding. This is especially the case in smaller companies where the complex real
option approach will be too time-consuming and faulty to be of any significant value.

Dealing with the valuation of projects with a high degree of uncertainty makes it relevant to
discuss whether it is meaningful to develop and use sophisticated valuation models when the
input variables are vitiated with such uncertainty. It is a valid critique, assuming the input
variables are close to impossible to estimate, as a models output is only as good as the quality of
the inputs. However, it is certain that the use of real option analysis clearly provides a better
understanding of the uncertainties and options of a project and therefore provides valuable
managerial insights.

As is the case with all valuation methods it is important to bear in mind that a project is not
suddenly worth more because another valuation method is used to assess the project. A real
option approach or a fuzzy approach does not make a drug development project more
prosperous. Different valuation methods are only weighing and valuing different parts of the
project differently. We argue that the classical valuation methods do not value risky projects
correctly as they assign no or little value to flexibility of the management. A real option or a
fuzzy approach does exactly that and the results obtained from these methods are therefore closer
to the true value of a risky project.
For small or medium sized companies with only modest valuation skills the fuzzy risk-adjusted DCF method in the form of an event tree is recommended as it captures a large part of the value of flexibility and is simple and easy to use. Companies which are more ambitious with their valuation process and large companies with more advanced in-house financial capabilities are recommended to use fuzzy binomial trees when valuing risky drug development projects.

In the last stages of a drug development project when most of the uncertainty has been resolved and the projected cash flows are most likely to occur it can be sufficient to use the fuzzy DCF method when performing a sanity check on the valuation.

The implementation of a fuzzy approach to the existing valuation methods is very simple. The fuzzy pay-off method and thus triangular (and trapezoidal) fuzzy numbers are easily implemented in the most commonly used spreadsheet software and thus in the valuations. Thus the fuzzy approach can serve as the bridge that makes real option valuations find their way to the practitioners. However the fuzzy valuation approach faces the same challenges as all other novel approaches to an area with a very standardized way of conduct do. Users of the standard approach which in this case is the DCF method are very reluctant to switch to other unfamiliar methods as our survey in section 2.2 showed. Consequently the fuzzy approach will not be embraced by the practitioners immediately as they will need a habituation period to get accustomed to the dynamics of the method. Practitioners will need experience in conducting the different parts of the analysis such as setting the threshold level and outlining the fuzzy cash flow distribution before they are willing to adopt it. Therefore we recommend that the fuzzy real options valuation initially is performed simultaneously with their standard valuation method. Obviously this will be a more time-consuming and demanding process in the beginning but eventually as they get used to the fuzzy approach the superior applicability of it will prove it worth the effort.
7 Conclusion

The main objective of this thesis is to investigate whether fuzzy numbers can be applied to real option valuation of a biotech project and how applicable this method is compared with the traditional valuation methods. This primary research question will be answered after a review of the five secondary research questions.

The biotech industry

The primary activity in the biotech industry is R&D projects targeting the development of new drugs. Drug development is a lengthy, expensive process and is characterised by a structured breakdown into different phases where the regulatory approval requirements for efficacy and safety increase from phase to phase. The high uncertainty of obtaining approval of a phase implies a substantial amount of risk for the company and its investors. Due to this high risk most biotech companies are primarily equity funded as this kind of funding best cope with the high uncertainty involved.

Each phase is structured as an option in the sense that a decision has to be taken at the end of each phase regarding whether to continue or discard the project based on the progress of the drug development (the underlying asset). As the development of new drugs is for the greater good of society patents are granted to new drugs in order to give the companies a reasonable opportunity to cover the very expensive development costs in a limited period of market exclusivity.

Our survey of the valuation process for drug developing companies in Denmark presented in section 2.2 shows that they primarily use the DCF model to value their internal drug development projects. This is supported by our findings from external analyses which also showed a predominant use of the DCF model among international biotech and pharmaceutical companies. Our survey also showed that the real option framework was not used by any of the participating companies, which again matches the results from the external analyses that showed a very limited use of real options.

Real options analysis

The characteristics of the biotech industry with heavy R&D costs, high uncertainties (both technological and commercial uncertainty) and a long time horizon all point to the use of a flexible valuation model that can accommodate these distinctive traits. The commonly used DCF
model is not such a model as it performs a very static valuation and does not incorporate the effects of changing input variables in the future. As changing input variables occur widely during the time span of a drug development project, the DCF model is far from optimal for valuing the project. The structural resemblance of a drug development with options suggests that real option analysis would be ideal for valuing drug development projects because the characteristics of the biotech industry as referred to above are all essential value drivers in a real option valuation.

The real option framework should not only be considered a tool for the calculation of the value of a drug development project but also as a tool that aids the understanding of the different real options that appear during the span of the project. This is exactly what lattices do as they visibly model future scenarios. On the contrary partial differential equations, such as the Black-Scholes model, are more a closed-end solution and are also mathematically more complex than lattices. As the focal point for practitioners is applicability, a simpler model is preferred. Statistically based models such as simulations also violate this point of preference.

A lattice model which easily expands the DCF valuation to include a partial real option framework is a simple event tree that incorporates the risk of failure in each phase. The real option framework can be fully included in a valuation by the use of binomial trees, which are relatively easily applicable for a person with a sound financial understanding, and the most widely used real option valuation method.

**Fuzzy real options analysis**

Fuzzy numbers can be applied to perform a real options valuation by using the fuzzy pay-off method. It uses a fuzzy number, most often in the form of a triangular fuzzy number, to represent the expected future distribution of the cash flows also known as the FNPV, which is the pay-off possibility distribution of the project. To obtain this the forecasted cash flows are rearranged to portray the extreme possible scenarios. The real option value can be calculated from the FNPV as the fuzzy mean value of the positive area of the fuzzy net present value multiplied with the ratio of the positive area to the total area of the fuzzy net present value. Only the positive outcomes of the fuzzy net present value are included as the negative outcomes are valued at zero in the real option framework.
The fuzzy pay-off distribution from where the real option value is derived can be constructed directly from the cash flow scenario of a given project. So the fuzzy pay-off method is not dependent on a given process to model the future, which makes it applicable in most valuations of uncertain R&D projects.

The fuzzy approach can also be applied to binomial tree valuation where each single node is portrayed as a triangular fuzzy number by applying a fuzzy volatility. The jumping factors are being fuzzified by the fuzzy volatility hence creating two extreme binomial trees to depict the diverse development of the underlying asset. The value of option can then be calculated from the fuzzified risk-neutral possibilities.

**Valuation settings**
Valuing a drug development project requires an extensive amount of research on the different input variables. A lot of comprehensive studies have been conducted on phase lengths, success rates, costs and sales for the different therapeutic areas and they should be used as a guideline for estimating the cash flow forecast. Contextual analyses should be used to clarify whether the historical findings are valid as a proxy for the future values or if they should be adjusted. As the drug will not be marketed the first many years the contextual analyses also aid to understand the future market conditions. For the actual valuation it is important to discuss the cost of capital that is used to discount the cash flows as it has a significant impact on the final value as found in the sensitivity analyses in section 6.6. Also the uncertainty related to the project is important to discuss in order to ensure a reliable estimation of the volatility.

**Fuzzy valuations**
From our analysis in part 5 we found that a fuzzy approach to traditional valuation methods in general yields a more positive outcome than without the use of fuzzy numbers, as it puts more emphasis on the potential upside of an uncertain project than the potential downside. In section 6.3 our case study showed that the application of the fuzzy pay-off method to a DCF valuation yielded a higher real option value than the stand-alone DCF valuation did. Due to the construction of the fuzzy number the possible upside of a project is enlarged and the possible negative outcomes are valued at zero. When adjusting the DCF valuation for the risk of failure by the use of an event tree, our risk-adjusted valuation in section 6.4 showed that the fuzzy version of it turned the negative net present value of a traditional event tree calculation into a
slightly positive number. Again this is due to the possible use of abandon options which can terminate projected loss-making projects. As a fuzzy valuation per definition cannot estimate projects to have a negative value as analyzed in part 4 it is necessary to settle on a minimum threshold value which the valuation should exceed in order to offset the unavoidable costs related to the termination of a project as discussed in section 6.7. In the clean real option valuation performed in section 6.5 the fuzzy approach again demonstrates its ability to value the value of managerial flexibility. The binomial tree setting shows how the diverse development of the potential sales can be better captured and valued with a fuzzy approach. The results obtained for all three valuation perspectives are considered to be robust as the sensitivity analysis in section 6.6 showed an unequivocal result when changing the key input variables.

To answer our primary research question our findings in part 5 confirm that the use of fuzzy numbers to perform a real option valuation of a biotech project is well applicable compared with the traditional valuation methods because it captures the real option thinking without the normal difficulties of implementing it for practitioners. It can be relatively easily applied to different levels of valuations and is therefore applicable for practitioners both in companies with advanced valuation approaches and companies with more simple valuation practices. For practitioners with a simple valuation approach the fuzzy event tree is recommended as it combines the inclusion of a risk perspective as well as the value of managerial flexibility with an uncomplicated implementation. For more advanced practitioners the fuzzy binomial tree valuation could be interesting to apply as it stresses the managerial value stemming from the possible excessive development in the underlying asset.

8 Perspectives
The use of fuzzy real option valuation is not only suited to value CNS drug development projects as showed in the thesis. Other drug development projects - and in general all projects surrounded by uncertainty and with an illiquid underlying asset that is not traded on a regular basis - could benefit from a fuzzy valuation approach to catch the uniqueness that stems from the unpredictable prospects. So for assessing the value of projects such as oil fields, infrastructure systems and wind power farms it would be interesting to apply a fuzzy valuation approach.
Reflections on the value of real option analysis

A key assumption behind option analysis is that the economic agent, i.e. the project manager, acts rationally. This is most definitely true in the case of financial options where the agent exercises the option if it is in the money and otherwise does not. However, with real options it could be considered doubtful whether the agent acts rationally at all times. An example could be the selection between two projects that have the same expected return but different volatilities. To optimize the profits of the company the manager should choose the high risk project as in theory it will have a higher NPV. But the manager could be biased to choose the low risk project as it will have a higher likelihood of success and thus secure his own job. Or choose a project that requires his particular skills over a project where another project manager would be needed even though that project would be of higher value to the company. Such irrational entrenchment behavior is a classic principal-agent problem where the main hypothesis is that the manager makes the investment that makes him valuable (Shleifer & Vishny, 1989, p.125). Also, on an ongoing project assessment level the question of the rational agent can be raised. A project manager has often worked several years on a project and is therefore very attached to it which could imply a reluctance to let go of the project if for instance negative market information occurs.

As discussed in our analysis a part of the value that real option analysis brings to the valuation is the assessment of which future scenarios and possibilities that may arise. When outlining the project the management gains important strategic insights in how to act under different circumstances which is highly valuable with an ever-changing project. It could be interesting if companies operating in uncertain environments focused on creating an organisation that is prepared for change and strives at catching the opportunities that present themselves in the constantly changing surroundings. Being best at capturing and taking advantage of such possibilities could be a competitive edge that would be hard to imitate because – to ensure its success - it would be embedded throughout the organisation.

The application of real option analysis implies that companies in general will take on riskier projects as they have a higher expected value. As companies have to maximize profit on behalf of the shareholders they should not worry about diversifying and reducing the unsystematic risk by taking up lower risk projects as this is a job for the investors. However, being the optimal
strategy for the companies does not imply that it is also the optimal strategy for the society. Higher risk will lead to more failures and consequently defaults thereby causing uncertainty for stakeholders such as the employees. It would result in a more insecure job market which puts a bigger burden on society as they have to pay for the consequences. Especially in the wake of the financial crisis where excessive risk-taking was a major source to the turmoil would it be unfortunate to signal higher risk aversion to the public.

Further Research

It would be interesting to present the fuzzy valuation approach to the companies in our survey (and others too) to find out how many of the practitioners would be interested in applying this method and how many would be capable of actually applying it to their valuations. This knowledge would be very helpful in determining the necessary requirements such as software programs or education that would facilitate a wider implementation. Applying the method from an investor’s point of view would be interesting to determine how well it works in putting a price on a company’s different projects and thereby the company as a whole compared to the standard methods applied. This could be achieved by valuing a number of companies by the different valuation methods and 12 months later determine which method had been most accurate when comparing the forecasted stock prices with the actual stock prices.

For advanced users of fuzzy valuations it could be interesting to consider the application of fuzzy numbers on other elements of the valuation. Applying fuzzy numbers to input variables in the cash flow forecast could be valuable as many of these cannot be considered crisp numbers which they are defined as in standard valuations. An example of such an input variable is the success rates for each phase used in the risk-adjusted DCF valuation which could be portrayed more accurate with a fuzzy number. Thus the entire valuation could be fuzzified to represent a pure possibilistic approach and possibly an improved result. But it would also complicate the valuation process further and as such is not in the scope of this thesis due to the goal of applicability. Also the possible mathematical constraints for substituting probabilistic numbers with possibilistic numbers could be interesting to investigate.
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10 Appendices

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Appendix 2 – List of questions for our interview with the companies
Appendix 3 – Our used questionnaire
Appendix 4 – List of question for our interview with the consultant
Appendix 5 – Table of results from Hartmann and Hassan’s investigation
Appendix 6 – Illustrative example of fuzzy triangular numbers
Appendix 7 – Real options valuation with fuzzy trapezoidal numbers
Appendix 8 - The fragmented European pricing structure
Appendix 9 – Number of compounds under development in USA versus the rest of the World
Appendix 10 – Spending in percentage of GDP on health care
Appendix 11 – Distribution of elderly people
Appendix 12 – Distribution of World sales
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Appendix 15 – Escalating Chinese diabetes rates
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Appendix 19 – Risk premium – a recent assessment from SEB
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Appendix 22 – An overview of the calculation of the FROV
Appendix 23 – Binomial tree – value of the underlying asset (the sales)
Appendix 24 – Binomial tree – real option value
Appendix 25 – The combined fuzzy binomial tree – value of the underlying asset
Appendix 26 – The combined fuzzy binomial tree – real option value
Appendix 27 – Calculation of the fuzzy binomial value
Appendix 1 – Map over the Medicon Valley

Source: Biotech Focus – Denmark: going from strength to strength, 2008, p. 637
Appendix 2 - List of questions for our interview with the companies

1. Benytter I strukturerede modeller til at værdiansætte jeres projekter?
   Hvis ja – hvilken slags model benytter i? Bruger i forskellige modeller til forskellige projekter?

2. Hvordan estimeres værdien i jeres benyttede model? Hvilke nøgleinputs bruger i?
   Hvordan estimeres de forventede fremtidige cash flows? Hvor langt frem estimeres de?
   1. Hvordan er R&D omkostningerne estimeret?
   2. Hvordan er tiden i de enkelte faser estimeret?
   3. Hvordan er sandsynlighederne for succes i enkelte faser estimeret?
   4. Hvordan er investeringerne estimeret?
   5. Hvordan er produktionsomkostningerne estimeret?
   6. Hvordan er marketing- og salgsomkostningerne estimeret?
   7. Hvordan er markedsstørrelsen og salget estimeret for de relevante regioner?
   8. Hvordan er salgsprisen estimeret?

9. Hvilken diskonteringsrente er benyttet til at tilbagediskontere cash flowsne?
   a. Er den samme diskonteringsrente benyttet til alle projekter?
      i. Hvis ja; har det været overvejet at benytte forskellige diskonteringsrenter til udviklingsomkostninger og kommercielle cash flows?

10. På hvilke faktorer er der foretaget sensitivitetsanalyse?
11. Bruger i forskellige scenarier i modellen? Hvis ja, hvilke scenarier er benyttet i modellen?

1. Værdiansættes de mulige ledelsesmæssige beslutninger?
   a. Hvilke beslutninger er de vigtigste at modellere?
2. Er fleksibilitet inkluderet i modellen ved brug af finansielle reale optioner?
   a. Hvis ikke, hvad er grunden til at finansielle optioner ikke er benyttet?

4. Hvilke procedurer indgår i værdiansættelsen af interne R&D projekter?
   Hvordan ændres procedurerne fra projekt til projekt?
5. Hvem beslutter konsekvenserne for et specifikt projekt?
   Hvem er brugerne af modellen?
   Hvor vigtig er modellen ved strategiske beslutninger angående fremtiden for projekterne? Hvilket krav har lederne til at resultatet er let at kommunikere videre?

6. Hvilke former for målkonflikt kunne der være mellem forskere og finansgruppen eller de andre administrative grupper?

7. Hvilke tiltag er der implementeret for at minimere de potentielle målkonflikter?
Appendix 3 – Our used questionnaire

8. Benytter I strukturerede modeller til at værdiansætte jeres projekter?
   a. Hvis ja – hvilken slags model benytter i? Bruger i forskellige modeller til forskellige projekter?

9. Hvordan estimeres værdien i jeres benyttede model? Hvilke nøgleinputs bruger i?
   a. Hvordan er R&D omkostningerne estmeret?
   b. Hvordan er tiden i de enkelte faser estimeret?
   c. Hvordan er sandsynlighederne for succes i enkelte faser estimeret?
   d. Hvordan er markedsstørrelsen og salget estimeret for de relevante regioner?
   e. Hvordan er salgsprisen estimeret?

10. Hvilken diskonteringsrente er benyttet til at tilbagediskontere cash flowsne?
    a. Er den samme diskonteringsrente benyttet til alle projekter?
       i. Hvis ja; har det været overvejet at benytteforskellige diskonteringsrenter til udviklingsomkostninger og kommercielle cash flows?

11. På hvilke faktorer er der foretaget sensitivitetsanalyse?

12. Bruger i forskellige scenarier i modellen? Hvis ja, hvilke scenarier er benyttet i modellen?

13. Værdiansættes de mulige ledelsesmæssige beslutninger?
    a. Hvilke beslutninger er de vigtigste at modellere?

14. Er fleksibilitet inkluderet i modellen ved brug af finansielle reale optioner?
    a. Hvis ikke, hvad er grunden til at finansielle optioner ikke er benyttet?

15. Hvor ofte evalueres eller genovervejes de benyttede inputs i modellen?

16. Hvem tager de endelige beslutninger omkring et specifikt projekt?
    a. Hvem er brugerne af modellen?
    b. Hvor meget værdi tillægges modellen ved strategiske beslutninger angående fremtiden for projekterne?

17. Hvilket krav har lederne til at resultatet er let at kommunikere videre?

18. Hvilke former for målkonflikt kunne der være mellem forskere og finansgruppen eller de andre administrative grupper?
    a. Hvilke tiltag er der implementeret for at minimere de potentielle målkonflikter?
Appendix 4 – List of question for our interview with the consultant

1. Er strukturerede modeller noget I ser anvendt i selskaberne?
   Hvis ja, hvilke modeller mener I er mest anvendt/udbredt?
2. Hvilke input til modellerne betragter I som de vigtigste?
3. Hvordan ser I at nogle inputs bliver estimeret?
5. Er der aspekter ved R&D omkostninger som er specifik anvendt?
6. Denne brug af historiske tal, hvordan betragter I denne strategi?
7. Hvilken diskonteringsfactor ser I mest anvendt?
8. Ved I endvidere om der er brug af forskellige diskonteringsfaktorer ved forskellige projekter?
9. Arbejder I med scenario analyser i modellerne? Er det af interesse for jer?
10. Hvordan foregår et samarbejde med Jer? På hvilke måder har I indflydelse hos virksomhederne?
11. Hvem blandt andet har I valgt at investere i? og hvorfor?
12. Er I med til at træffe beslutninger om de enkelte projekter?
13. I forbindelse med ”capital budgetting process” er der så ting som I går ind og påpeger hvis I føler de kan optimeres?
14. Hvor ofte evaluerer I de valgte estimat inputs i projektet?
15. Oplever I konflikter af signifikant betydning mellem forskerne og projektafdelingen?
16. Hvorfor oplever I ikke at virksomhederne benytter real option analyser til at værdiansætte deres projekter?
17. Hvordan betragter I de muligheder som ligger ved brug af andre modeller end den traditionelle DCF metode?
18. Følsomhedsanalyser er det noget I finder værdifuldt? Benytter I dem selv? Eller anvender I bare virksomhedernes for at få den bedre forståelse for mulige risici der er i forbindelse med projektet?
Appendix 5 – Tables of results from Hartmann and Hassan’s investigation

<table>
<thead>
<tr>
<th>Valuation methods</th>
<th>Risk analysis and further criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPV / ENPV / DCF</td>
<td>Decision trees</td>
</tr>
<tr>
<td>RoE / Ro / EVA®</td>
<td>Scenario analysis</td>
</tr>
<tr>
<td>Internal rate of return</td>
<td>Sensitivity analysis</td>
</tr>
<tr>
<td>Scoring model</td>
<td>Payback period</td>
</tr>
<tr>
<td>Real options analysis</td>
<td>Regression analysis</td>
</tr>
<tr>
<td>Net asset value</td>
<td>Other</td>
</tr>
<tr>
<td>Capitalized earnings value</td>
<td>Number of answers</td>
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<tr>
<td>Multiples</td>
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<tr>
<td>Other</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>R&amp;D stages</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Research</td>
<td>50% 6% 18% 47% 6% 6% 8% 6% 20% 20% 13% 18% 17</td>
</tr>
<tr>
<td>Pre-clinic</td>
<td>76% 12% 24% 24% 12% 4% 4%</td>
</tr>
<tr>
<td>Clinical phase I</td>
<td>85% 15% 27% 19% 23% 4% 4% 19% 56% 69% 63% 23% 26</td>
</tr>
<tr>
<td>Clinical phase II</td>
<td>100% 19% 22% 11% 26% 7% 7% 26% 74% 67% 74% 26% 27</td>
</tr>
<tr>
<td>Clinical phase III</td>
<td>100% 22% 30% 11% 26% 7% 4% 11% 33% 74% 67% 78% 30% 27</td>
</tr>
<tr>
<td>Registration</td>
<td>96% 21% 99% 8% 21% 8% 4% 13% 38% 71% 67% 75% 29% 24</td>
</tr>
</tbody>
</table>

| Company valuation | |
|-------------------||
| Early biotech | 82% 18% 9% 9% 9% 27% 9% 18% 9% 45% 36% 11 |
| pYoung biotech | 89% 11% 11% 11% 11% 22% 11% 22% 22% 55% 56% 9 |
| Old biotech | 80% 40% 20% 20% 40% 80% 60% 40% 5 |

Table A5.1
Evaluation methods in the pharmaceutical section (E)NPV: (Expected) Net Present Value, DCF: Discounted Cash Flow, RoE: Return on Equity, RoI: Return on Investment, EVA®: Economic Value Added

<table>
<thead>
<tr>
<th>Valuation methods</th>
<th>Risk analysis and further criteria</th>
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| Company valuation | |
|-------------------||
| Early biotech | 71% 8% 6% 18% 16% 6% 6% 53% 8% 24% 17% 47% 53% 6% 12% 6% 17 |
| Young biotech | 74% 11% 5% 16% 16% 5% 5% 47% 11% 22% 25% 47% 11% 5% 10% 5% 19 |
| Old biotech | 85% 30% 15% 15% 10% 20% 76% 3% 15% 15% 50% 50% 5% 15% 5% 20 |
| Small/Medium Pharma | 70% 33% 4% 15% 11% 15% 15% 85% 7% 11% 7% 48% 52% 4% 11% 4% 27 |
| Big Pharma | 81% 38% 8% 15% 8% 12% 12% 58% 4% 12% 12% 50% 51% 4% 12% 4% 26 |

Table A5.2
Evaluation methods in the capital market service section (E)NPV: (Expected) Net Present Value, DCF: Discounted Cash Flow, RoE: Return on Equity, RoI: Return on Investment, EVA®: Economic Value Added

Source: Hartmann & Hassan, 2006, p.348
Appendix 6 – Illustrative example of fuzzy triangular numbers

A cumulative NPV scenario

[Diagram showing cumulative NPV scenario with Base, Optimistic, and Pessimistic scenarios]

Figure A6.1 and figure A6.2: Own construction. Fictive values – just for illustration purpose only.

Triangular fuzzy number & ROV

[Diagram showing triangular fuzzy number with ROV = 1713]

ROV = 1713

a-α = -180  a = 1500  a+β = 4500
Appendix 7 – Real options valuation with fuzzy trapezoidal numbers

A fuzzy number is called a trapezoidal fuzzy number, with a core value of \([a, b]\), the left and right width expressed as \(\alpha\) and \(\beta\) respectively and has a membership function of the following form,

\[
A(t) = \begin{cases} 
1 - \frac{a - t}{\alpha}, & a - \alpha \leq t \leq a \\
1, & a \leq t \leq b \\
1 - \frac{t - b}{\beta}, & a \leq t \leq b + \beta \\
0, & otherwise
\end{cases} \tag{4.9}
\]

which can be expressed as \(A = (a, b, \alpha, \beta)\) and is visualised in figure 4.2.

![Figure 4.2: Possibility distribution of the present value of the expected cash flow. Own construction. Source: Carlsson and Fullér, 2000](image)

If we have the notation of the fuzzy trapezoidal numbers defined as \(A = (a, b, \alpha, \beta)\) and the fuzzy mean value derived from (4.1) we can calculate the fuzzy mean value with the formula presented below (Carlsson & Fullér, 2000, p. 71)

\[
E(A) = \int_0^1 \gamma [a - (1 - \gamma)\alpha + b + (1 - \gamma)\beta]d\gamma = \frac{a + b}{2} + \frac{\beta - \alpha}{6} \tag{4.10}
\]

And likewise for the variance

\[
\sigma^2 = \frac{(b - a)^2}{4} + \frac{(b - a)(\alpha + \beta)}{6} + \frac{(\alpha + \beta)^2}{24} \tag{4.11}
\]
A hybrid approach to real option valuation

The trapezoidal fuzzy number valuation approach by Fullér & Carlson is adapted from the classical real option theory, and especially from the Black-Scholes model. They developed the pricing formula\(^ {31}\) for a call option (Black and Scholes, 1973).

By using the mindset behind calculating financial options Leslie and Michaels showed how to value strategic options with a Black-Scholes approach (Leslie and Michaels, 1997). The most important difference is the transformation of key parameters in the pricing formula to make it applicable to a real option, such as \(S_0\) denotes the present value of expected cash flows instead of the price of the underlying asset, and \(X\) is no longer the exercise price but the value of fixed costs.

Carlsson and Fullér adopted the work of Leslie and Michaels and applied the use of fuzzy numbers to create a hybrid valuation method. They presented the opportunity to express the present value of the expected cash flow \(S_0\) by using a trapezoidal possibility distribution in the form of \(S_0 = (a, b, \alpha, \beta)\). The most possible outcomes of the expected cash flow is in the interval \([a, b]\) with \((b + \beta)\) being the potential upside and \((a - \alpha)\) being the potential downside. Likewise we have the same for the present value of the expected costs, but they are instead denoted by \(X = (x_1, x_2, \alpha', \beta')\) (Carlsson and Fullér, 2003, p. 6).

According to this notation they presented the following formula on how to calculate the fuzzy real option value (referred to as FROV):

\[
FROV = S_0 \times e^{-\delta T} \times N(d_1) - X_0 \times N(d_2) \quad (4.12)
\]

\[d_1 = \frac{\ln \left( \frac{E(S_0)}{E(X_0)} \right) + \left( r - \delta + \frac{\sigma^2}{2} \right) T}{\sigma \sqrt{T}}, d_2 = d_1 - \sigma \sqrt{T}\]

From 4.12 the final FROV can be computed as a single crisp value. Alternatively there could also be situations where getting FROV shown as a possibility distribution (of the same form as

\(^{31}\) \(C_0 = S_0 \times N(d_1) - X \times e^{-rT} \times N(d_2)\)
figure 4.2) is of more interest. In order to get to this result FROV can be computed from the following formula.

\[
FROV = (s_1, s_2, \alpha, \beta)e^{-\delta T} N(d_1) - (x_1, x_2, \alpha', \beta') N(d_2) =
\]

\[
(s_1 e^{-\delta T} N(d_1) - x_2 N(d_2), s_2 e^{-\delta T} N(d_1) - x_1 N(d_2),
\]

\[
\alpha e^{-\delta T} N(d_1) + \beta' N(d_2), \beta e^{-\delta T} N(d_1) + \alpha' N(d_2))
\]

(4.13)

As mentioned before the computing is much like the approach used in Black-Scholes. This means that many of the same parameters exist as when dealing with the Black-Scholes model such as the time horizon (time to maturity), \(t\), the uncertainty of the expected cash flows (standard deviation)\(^{32}\), \(\sigma\), the risk-free interest rate, \(r_f\), and finally the extra variable \(\delta\), which covers the value lost over the duration of the option.

When all information is gathered the FROV can then be computed.

Below we will give an example on how to compute the FROV using fuzzy trapezoidal numbers.

Let us say that the present value of the expected cash flow is set to

\[
S_0 = (€300 \text{ million}, €500 \text{ million}, €100 \text{ million}, €100 \text{ million})
\]

and our present value of the expected costs is set to

\[
X_0 = (€200 \text{ million}, €300 \text{ million}, €50 \text{ million}, €50 \text{ million})
\]

Additional we have the following parameters

\[
R_f = 5\% \text{ per year}, T = 5 \text{ years and } \delta = 0.03 \text{ per year}
\]

This means that our only unknown variable at this time is \(\sigma\) (uncertainty of expected cash flows), which we will find next. The way to find \(\sigma\) is described in footnote\(^{33}\) 4, but first we need to calculate the mean value and the variance of the expected cash flows.

\(^{32}\) The uncertainty, sigma, is computed from the \(\sigma(S_0)/E(S_0)\)

\(^{33}\) The uncertainty, sigma, is computed from the \(\sigma(S_0)/E(S_0)\)
\[
E(S_0) = \frac{s_1 + s_2}{2} + \frac{\beta - \alpha}{6} = \frac{300 + 500}{2} + \frac{100 - 100}{6} = €400 \text{ million}
\]

\[
\sigma(S_0) = \sqrt{\frac{(s_2 - s_1)^2}{4} + \frac{(s_2 - s_1)(\alpha + \beta)}{6} + \frac{(\alpha + \beta)^2}{24}} = \sqrt{\frac{(500 - 300)^2}{4} + \frac{(500 - 300)(100 + 100)}{6} + \frac{(100 + 100)^2}{24}} = €135,04 \text{ million}
\]

Which means that \( \sigma(S_0) \) in percentages terms is

\[
\frac{\sigma}{S_0} = \frac{€135,04 \text{ million}}{€400 \text{ million}} = 33,85\%
\]

After we have computed \( \sigma \), we now need to calculate the values for \( N(d_1) \) and \( N(d_2) \) in order to calculate the FROV from (4.12). First we find the values of \( d_1 \) and \( d_2 \). \( X_0 \) is computed like we did with \( S_0 \)

\[
d_1 = \frac{\ln \left( \frac{E(S_0)}{E(X_0)} \right) + \left( r - \delta + \frac{\sigma^2}{2} \right) T}{\sigma \sqrt{T}} = \frac{\ln \left( \frac{400}{250} \right) + \left( 0,05 - 0,03 + \frac{0,3385^2}{2} \right) * 5}{0,3385 * \sqrt{5}} = 1,1315
\]

\[
d_2 = d_1 - \sigma * \sqrt{T} = 1,1315 - 0,3385 * \sqrt{5} = 0,3746
\]

We now have to find the normal distribution of these two values, which is

\[N(d_1) = 0,8711 \text{ and } N(d_2) = 0,6460\]

Now we have all the variables for the computation of the FROV.

\[
FROV = S_0 * e^{-\delta T} * N(d_1) - X_0 * N(d_2) = 400 * e^{-0,03*5} * 0,8711 - 250 * 0,6460 = €138,39 \text{ millions}
\]

The fuzzy real option value is then €138,39 millions.
As discussed you might want to express the fuzzy real option value as an interval. It is simply done by using the formula, presented in (4.13).

\[
FROV = (s_1, s_2, \alpha, \beta)e^{-\delta T}N(d_1) - (x_1, x_2, \alpha', \beta')N(d_2) =
\]

\[
(300 \cdot e^{-0.03 \times 5} \cdot 0.8711 - 300 \cdot 0.6460, 500 \cdot e^{-0.03 \times 5} \cdot 0.8711 - 200 \cdot 0.6460,
100 \cdot e^{-0.03 \times 5} \cdot 0.8711 + 50 \cdot 0.6460, 100 \cdot e^{-0.03 \times 5} \cdot 0.8711 + 50 \cdot 0.6460) =
\]

\[
FROV = (\text{€31,13 million, €245,68 million, €107,28 million, €107,28 million})
\]

Below you can see the possibility distribution of the fuzzy real option values illustrated.
Appendix 8 - The fragmented European pricing structure

Appendix 9 - Number of compounds under development in USA versus the rest of the World

Appendix 10 - Spending in percentage of GDP on health care

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* estimate

Note: Japan, Luxembourg, Portugal; 2006 data; Turkey: 2005 data
Europe: non-weighted average (22 countries) – EFPIA calculations
Source: OECD Health Data 2009, Statistics and Indicators for 30 Countries, November 2009

## Appendix 11 - Distribution of elderly people

### Percentage of Elderly People (65 and over) in Total Population

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</tbody>
</table>

*Note: Figures for the years 2010, 2020 and 2030 are United Nations projections. Source: World Population Prospects (United Nations), OHE*
Appendix 12 - Distribution of World sales

Appendix 13 - Obese people in the United States

Source: Novod, 2011, p. 52
Appendix 14 - Age profile trend of the population in China

Appendix 15 - Escalating Chinese diabetes rates

Chinese diabetes prevalence rates 2007-25, by age group

Source: Diabetes, the hidden pandemic and the impact on China; Chinese Diabetes Society and Diabetes Leadership Forum 2009

Source: Novod, 2011, p. 31
Appendix 16 - Diabetes in China

Source: NEJM March 25, 2010; Yang et al

Source: Novod, 2011, p. 32
Appendix 17 - Generic share of sales in Europe

Appendix 18 – An overview of β-values from Bloomberg
Appendix 19 – Risk premium – a recent assessment from SEB

Source: Granholm-Leth, 2011, p. 33
## Appendix 20 – The fuzzy cash flow forecast

<table>
<thead>
<tr>
<th>Costs</th>
<th>Lead Opt./Preclinical phase</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>App.</th>
<th>Market</th>
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<tr>
<td></td>
<td>2011e</td>
<td>2012e</td>
<td>2013e</td>
<td>2014e</td>
<td>2015e</td>
<td>2016e</td>
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<td>R&amp;D - Bad</td>
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<td>3.8</td>
<td>3.8</td>
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<tr>
<td>R&amp;D - Base</td>
<td>1.4</td>
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<td>R&amp;D - Good</td>
<td>0.4</td>
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<td>Post-app. - Bad</td>
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<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
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<tr>
<td>Total costs - Bad</td>
<td>3.8</td>
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<td>3.8</td>
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<td>2.5</td>
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<tr>
<td>Total costs - Base</td>
<td>1.4</td>
<td>1.4</td>
<td>1.4</td>
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<tr>
<td>Total costs - Good</td>
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<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
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<tr>
<td>Total revenue - Bad</td>
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<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
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<tr>
<td>Total revenue - Base</td>
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<tr>
<td>FCF - Bad</td>
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<td>-3.8</td>
<td>-3.8</td>
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<td>FCF - Base</td>
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<td>-1.4</td>
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<td>-0.4</td>
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<td>-2.0</td>
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</table>
Appendix 21 – An overview of the calculation of the FROV

Given a positive 'a' and a positive summit but a negative low point

The three points

<table>
<thead>
<tr>
<th></th>
<th>a</th>
<th>a-α</th>
<th>a+β</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>40,5</td>
<td>-57,6</td>
<td>240,6</td>
</tr>
</tbody>
</table>

\[ E(A^+) = 60,788 \]

\[ FROV = 53,892 \]

alpha = 98,1  
beta = 200,1

Calculation of the proportionality  
2 equations with 2 unknowns

Equation 1:  
\[ y_1 = ax_1 + b \]
\[ y_1 = 0 \]
\[ y_2 = 1 \]
\[ A(pos(a \text{ til } pos)) = 100,07 \]

Equation 2:  
\[ y_2 = ax_2 + b \]
\[ x_1 = -57,6 \]
\[ x_2 = 40,5 \]
\[ A(neg \text{ til } a) = 49,03 \]

\[ a = \frac{(y_2 - y_1)}{(x_2 - x_1)} \]

\[ a = 0,0102 \]

\[ b = 0,587 \]

\[ A(pos) = 132,19 \]

\[ A(neg) = 16,915 \]

Forhold \( \frac{A(pos)}{A(pos) + A(neg)} = 0,8866 \)
Appendix 22 – An overview of the calculation of the rFROV

For a negative 'a' along with negative low point and a positive summit

The three points

<p>| | |</p>
<table>
<thead>
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<th></th>
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<tbody>
<tr>
<td>a</td>
<td>-9,5</td>
</tr>
<tr>
<td>a-α</td>
<td>-28,8</td>
</tr>
<tr>
<td>a+β</td>
<td>15,2</td>
</tr>
</tbody>
</table>

\[ E(A+) = 0,9569 \]
\[ rFROV = 0,1886 \]

\[ \alpha = 19,3 \]
\[ \beta = 24,6 \]

The calculation of the relation

\[ \frac{A(\text{pos})}{A(\text{pos})+A(\text{neg})} = 0,1970 \]

Computation of the area

Equation 1:
\[ y_1 = ax_1+b \]
\[ y_1 = 0 \]
\[ x_1 = 0,8 \]
\[ a = 4,3293 \]
\[ b = 0,5714 \]
\[ A(\text{neg til a}) = 9,6633 \]

Equation 2:
\[ y_2 = ax_2+b \]
\[ x_2 = -8,1 \]
\[ x_2 = 10,8 \]
\[ A(\text{a til pos}) = 12,3082 \]
\[ A(\text{pos}) = 4,3293 \]
\[ A(\text{neg}) = 17,6421 \]

\[ a = \frac{(y_2-y_1)}{(x_2-x_1)} \]
\[ a = -0,0529 \]
### Appendix 23 – Binomial tree - value of the underlying asset (the sales)

#### Input data

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<td>132.89</td>
<td>170.21</td>
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<td>279.22</td>
<td>357.63</td>
<td>458.06</td>
<td>586.68</td>
<td>751.42</td>
<td>962.42</td>
<td>1232.67</td>
<td>1578.81</td>
<td>2022.15</td>
<td>2589.97</td>
<td>3317.24</td>
<td>4248.74</td>
<td>5441.80</td>
<td>6969.87</td>
<td>8927.03</td>
<td>11433.77</td>
<td>14644.41</td>
<td>18756.61</td>
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<td>81.01</td>
<td>103.76</td>
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<td>170.21</td>
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Appendix 24 – Binomial tree – real option value
Appendix 25 – The combined fuzzy binomial tree – value of the underlying asset
Appendix 26 – The combined fuzzy binomial tree – real option value
Appendix 27 – Calculation of the fuzzy binomial tree – Real option value

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<th>The 5 points</th>
<th>Area calculation</th>
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<td>c2</td>
<td>Area left: 2,0214</td>
</tr>
<tr>
<td>c3</td>
<td>Area total: 9,3314</td>
</tr>
<tr>
<td>c2 - c1</td>
<td>( \lambda = 0.76 )</td>
</tr>
<tr>
<td>c3 - c2</td>
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</table>

\[ B(FENPV) = 10.94 \]